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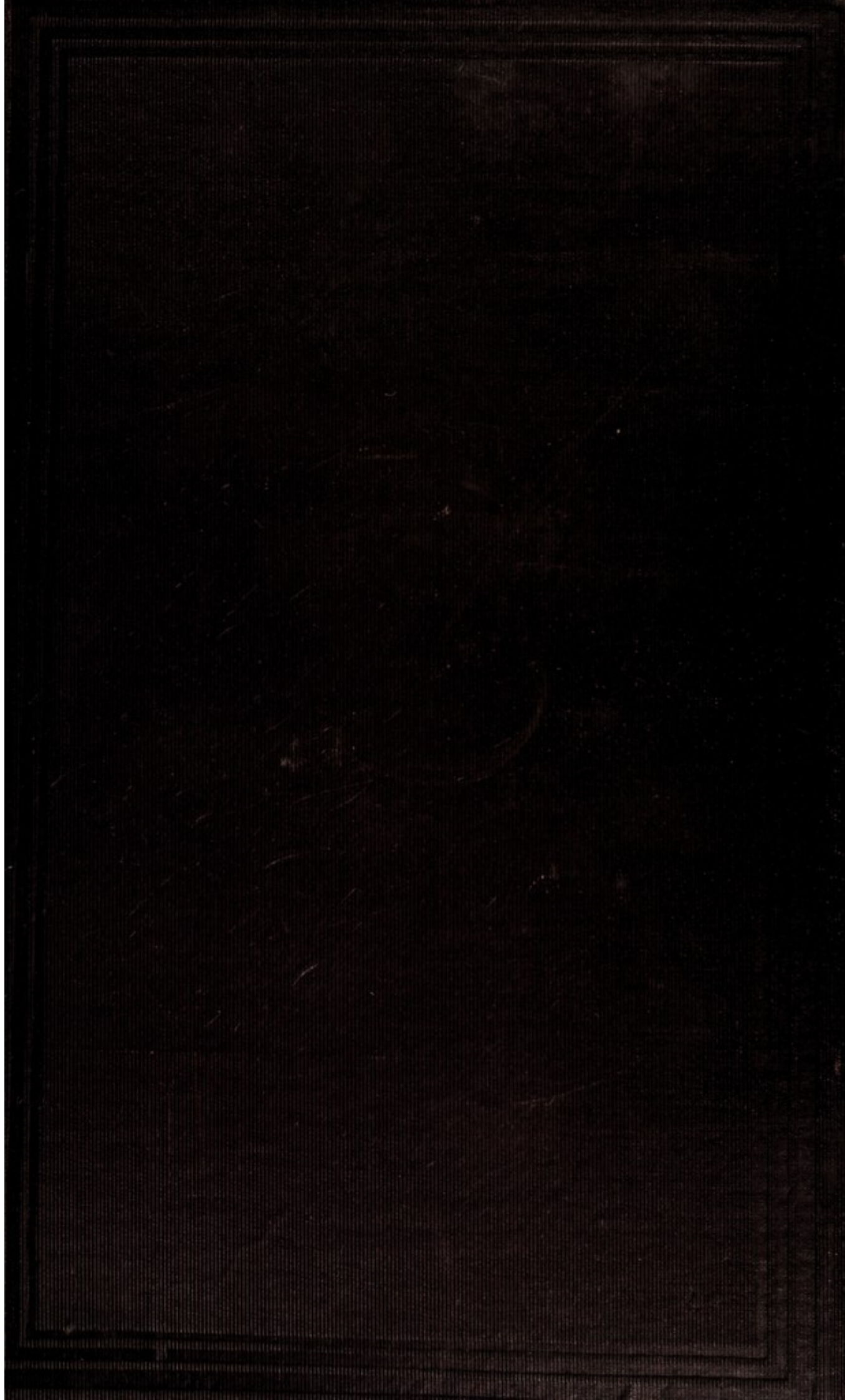
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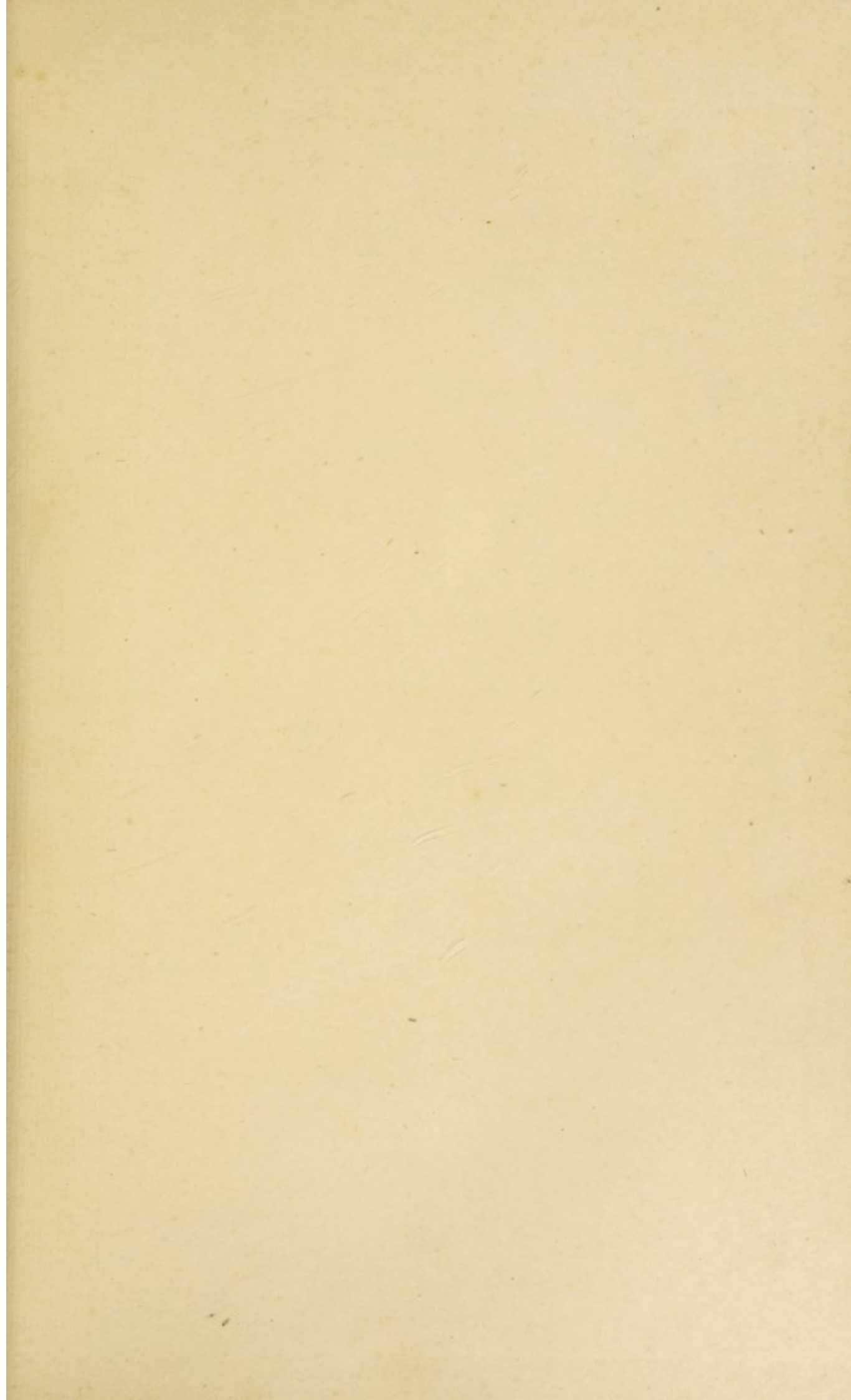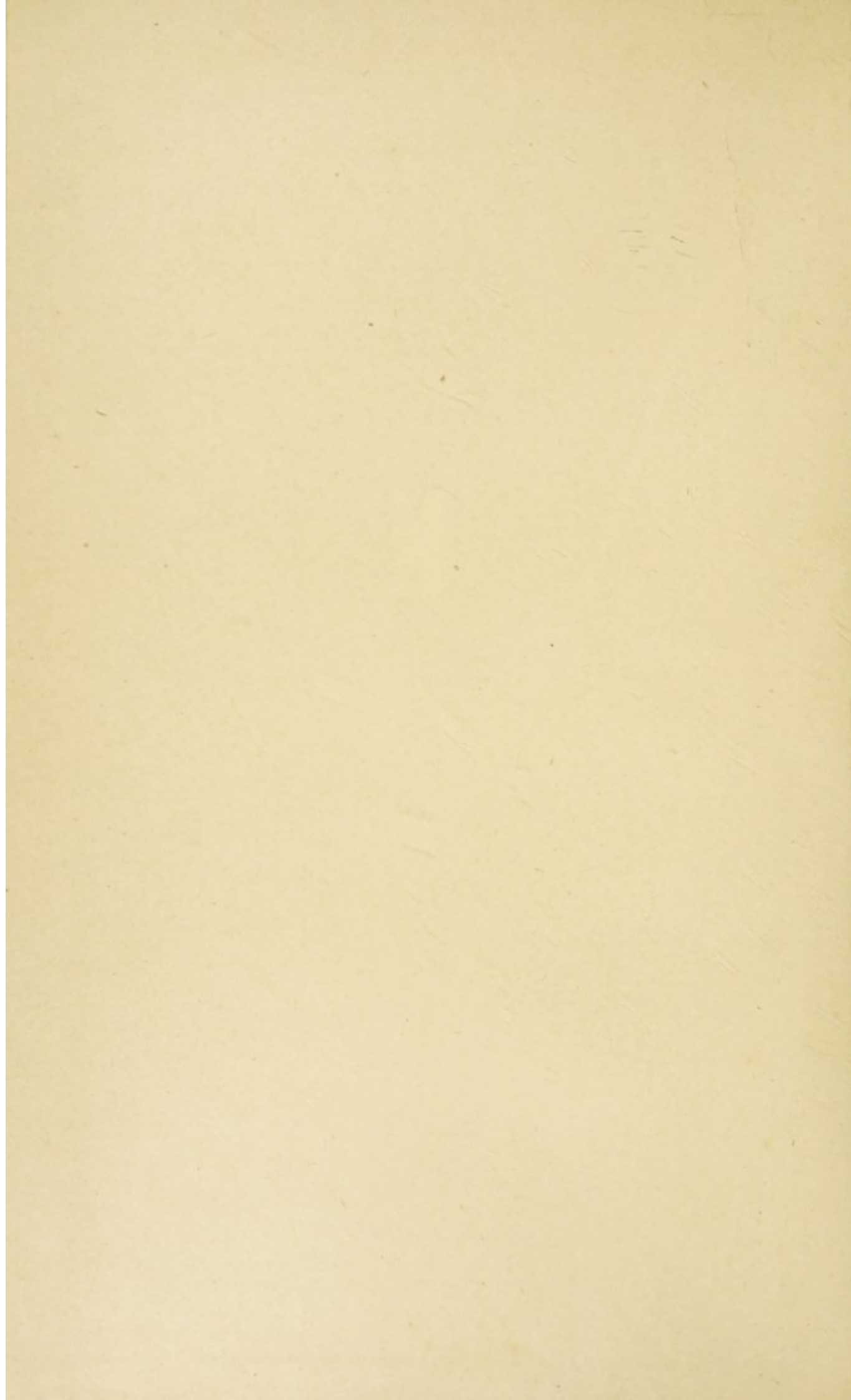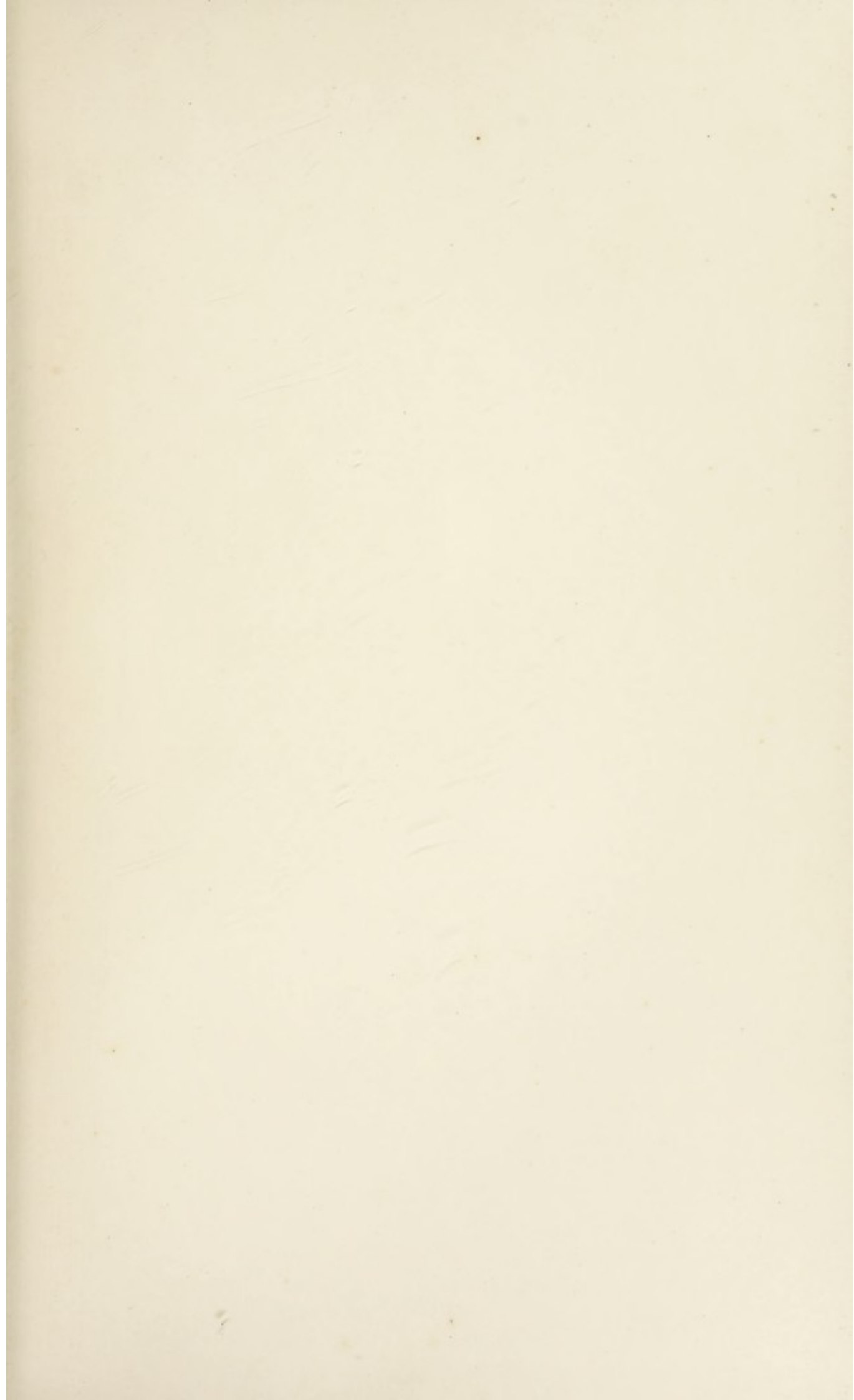
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DIPHTHERIA

BY
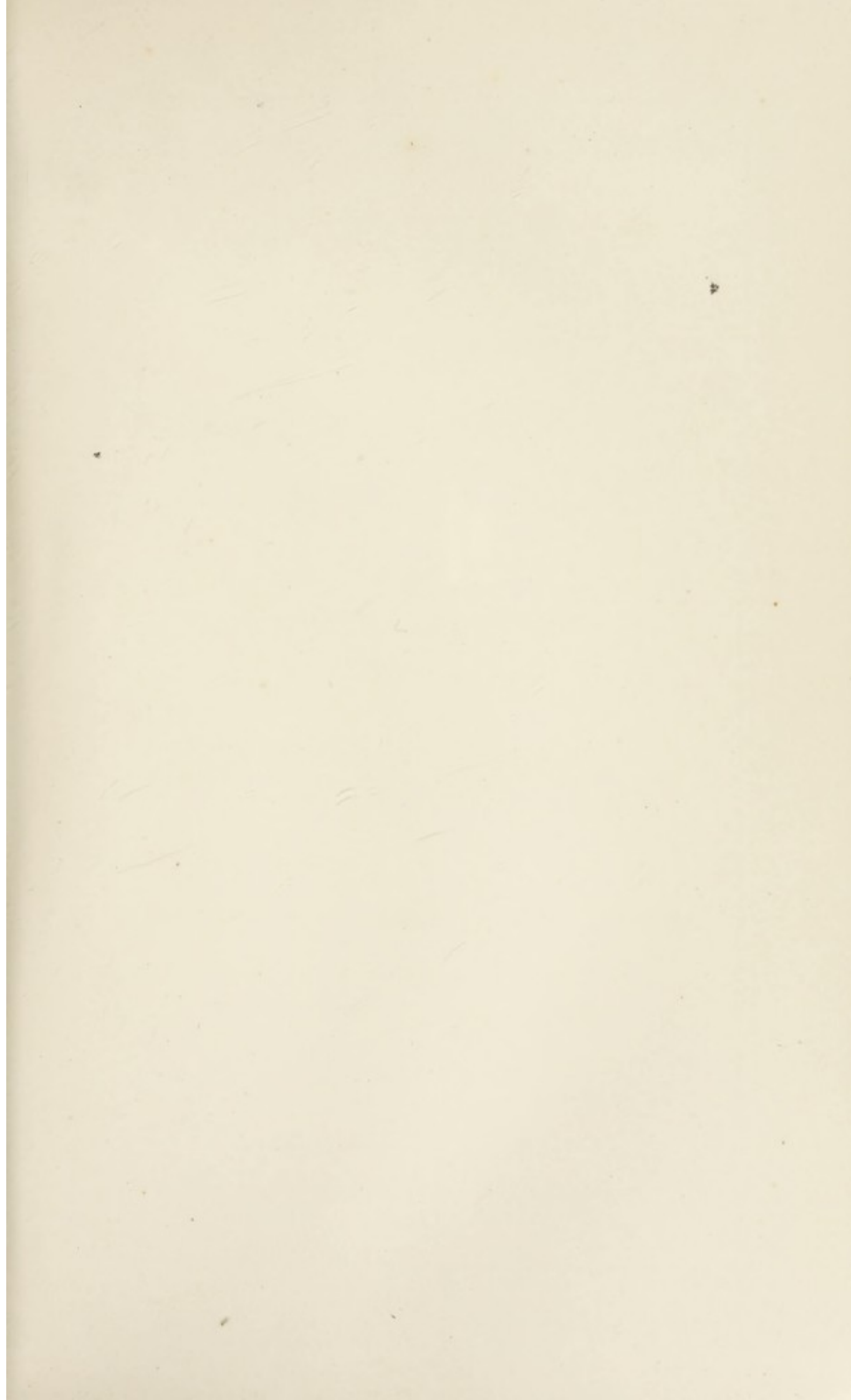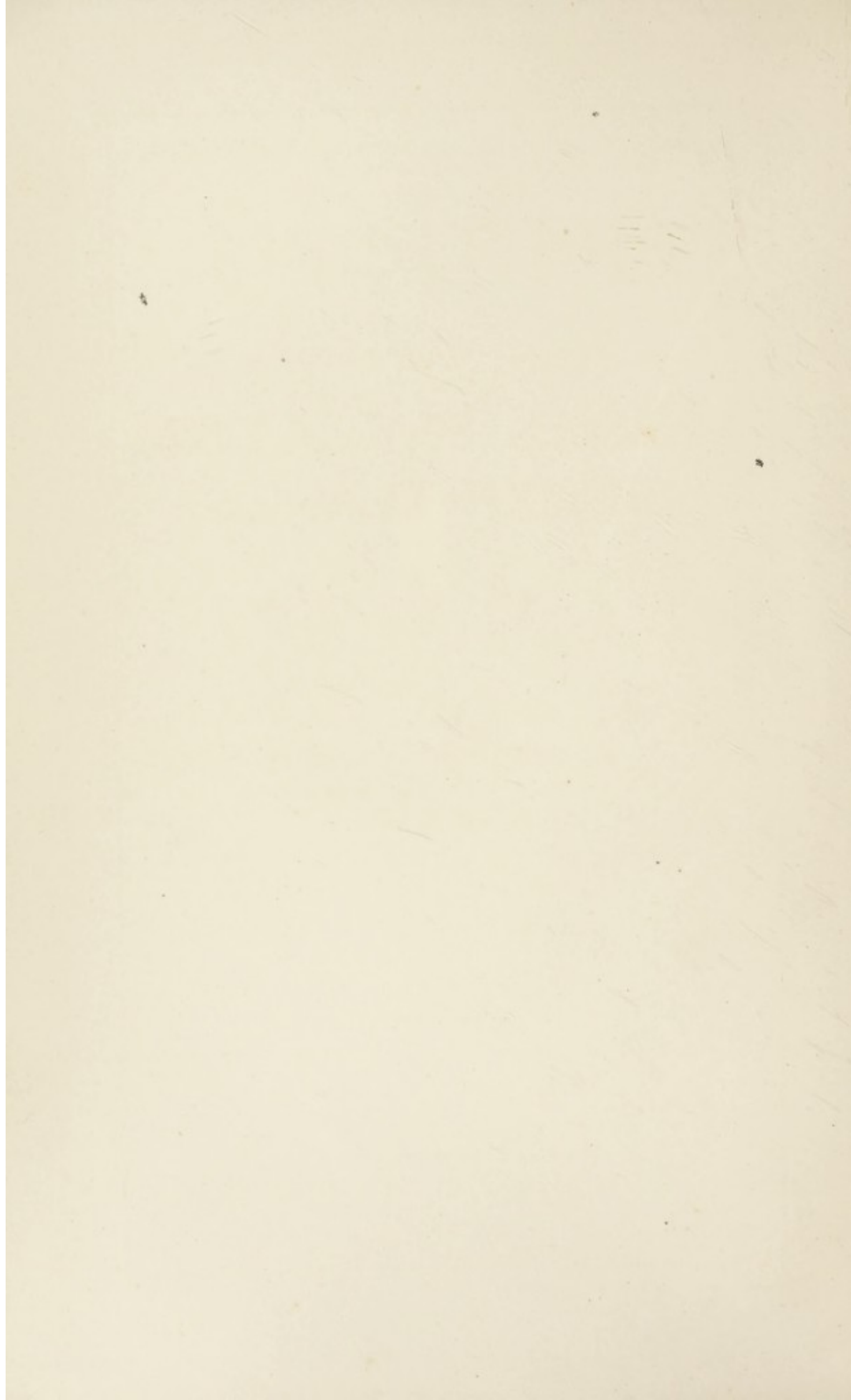
WILLIAM P. NORTHRUP, M.D.

MEASLES, SCARLATINA
GERMAN MEASLES

BY

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Professor of Medicine at the University of Tübingen

EDITED, WITH ADDITIONS

BY

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AUTHORIZED TRANSLATION FROM THE GERMAN, UNDER THE
EDITORIAL SUPERVISION OF

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PREFACE.

THE excellence of the series of monographs issued under the editorship of Professor Nothnagel has been recognized by all who are sufficiently familiar with German to read these works, and the series has found a not inconsiderable proportion of its distribution in this and other English-speaking countries. I have so often heard regret expressed by those whose lack of familiarity with German kept these works beyond their reach, that I was glad of the opportunity to assist in the bringing out of an English edition. It was especially gratifying to find that the prominent specialists who were invited to co-operate by editing separate volumes were as interested as myself in the matter of publication of an English edition. These editors have been requested to make such additions to the original articles as seem necessary to them to bring the articles fully up to date and at the same time to adapt them thoroughly to the American or English reader. The names of the editors alone suffice to assure the profession that in the additions there will be preserved the same high standard of excellence that has been so conspicuous a feature in the original German articles.

In the present volume it has been necessary to substitute for one of the German articles (that on " Diphtheria ") an article by an American writer, owing to an arrangement made by the German author to issue a translation of his article apart from this series. While I regretted the necessity of this change very much, I was gratified in securing the acceptance of the task of writing an entirely new article by Dr. William P. Northrup, and the readers of the volume will feel that the substitution has entailed no loss to them. With the exception of the article on " Diphtheria," the articles in this volume and in the remaining volumes of the series will be those of the original German edition.

ALFRED STENGEL.

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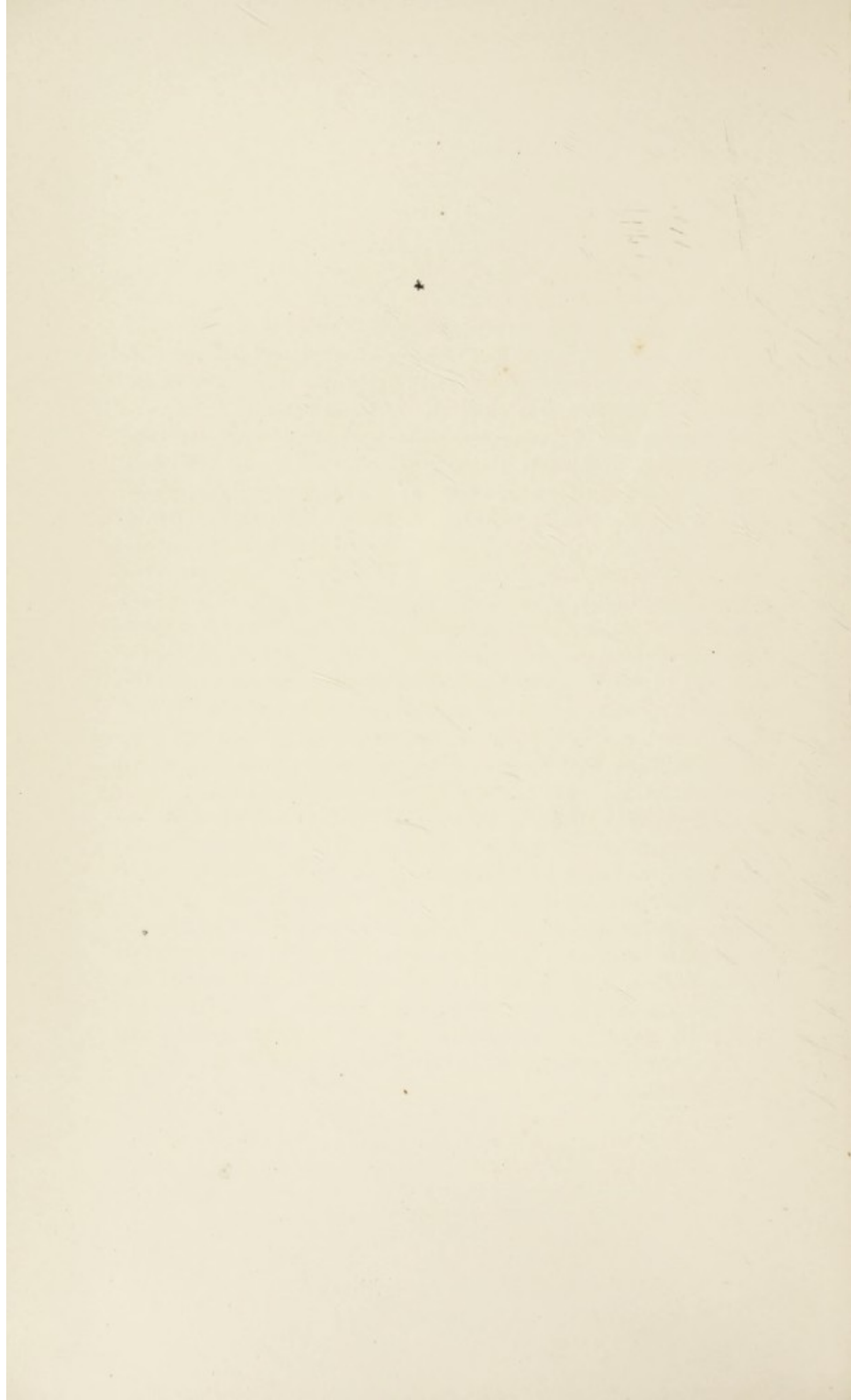
EDITOR'S PREFACE.

I⊤ has been a privilege and an honor to assist in bringing before American readers this great storehouse of modern medicine. It has been a pleasure to become intimately acquainted with Professor Jürgensen's article on measles, bringing out so fully the valuable Danish records of the Faroe Islands epidemic. Never before, to my knowledge, has so well-digested a report been put before the reader. Little has been added to the knowledge of the essential causative agents of measles, scarlet fever, and rötheln, or to the subjects of diagnosis and symptomatology of the diseases, and therefore little can be culled from recent literature to bring these valuable articles more fully up to date. What has been deemed of value has been added, and it is hoped the reader will find in this book a storehouse of all that is modern.

The article on diphtheria, emanating from New York, presents a consideration of intubation and croup rather fuller in detail than most authors would think necessary. Beginning his work as pathologist at the New York Foundling Hospital, when the first bivalve tubes were used, and having been associated with Dr. O'Dwyer at every step in the perfection of intubation tubes, the author has fulfilled a labor of love in presenting a complete description of this aspect of the treatment of diphtheria as a memorial of appreciation of his colleague and friend, Joseph O'Dwyer.

The author wishes to express his thanks to his clinical assistant, Dr. Matthias Nicoll, Jr., who aided in collecting and analyzing literature; to Dr. Henry James Prentiss, Demonstrator and Instructor in Practical Anatomy in the University and Bellevue Hospital Medical College, who aided in the preparation of illustrations; and to Mr. E. W. Caldwell, Director of the Edward N. Gibbs X-ray Laboratory.

Finally, the author wishes to join the editors of other volumes in acknowledging the courteous and liberal treatment of both the Editor-in-Chief, Dr. Alfred Stengel, and the publishers, Messrs. W. B. Saunders & Company.

WILLIAM P. NORTHRUP.

57 EAST 79TH STREET, NEW YORK.
April, 1902.

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DIPHTHERIA.

BY

WILLIAM P. NORTHRUP, M.D.

DIPHTHERIA.

DIPHTHERIA is an acute infectious and communicable disease characterized by the production of false membrane on a mucous or abraded skin surface, and due to the presence and proliferation of the Klebs-Löffler bacillus and the toxins elaborated in its growth.

The name diphtheria is derived from the Greek διφθέρα, "a skin or membrane."

The very voluminous writings on the subject of diphtheria may logically be divided into four periods:

I. From antiquity to the time of Bretonneau (1821).

II. From Bretonneau to the discovery of the diphtheria bacillus by Klebs and Löffler (1883 and 1884).

III. From 1883 to 1890, studies of the Klebs-Löffler bacillus and its relations to the disease toxins.

IV. Antitoxin period (1892 to 1901).

HISTORY.

Period I.—The first accurate description of diphtheria recorded is that of Aretæus of Cappadocia, about 50 A. D. This writer gives a faithful picture of the disease, describing the varieties of angina, benign and malignant, and calling attention to the possibility of its extension to the respiratory tract, and the occurrence of death by suffocation, of which he gives a remarkably perfect description. He notes the frequent occurrence of the disease among children, and its prevalence in certain countries, notably Egypt and Syria (whence the names Syriac and Egyptian ulcer). Aetius of Armida, in the sixth century, noted the symptoms of paralysis of the palate (regurgitation of fluids through the nose, etc.). With the exception of Galen and Cælius Aurelianus, who described the disease at about this time, little

was added to the world's knowledge of it until the end of the Middle Ages. In the latter part of the sixteenth century and the beginning of the seventeenth, diphtheria was epidemic all over Europe, and later invaded America. It was described under a great variety of names: Morbus suffocans; Morbus strangulatorius; Garotillo; Pestilential, Malignant, and Ulcerative angina; Gangrenous ulcer, etc.

By most observers the angina was regarded as a disease distinct from the laryngeal affection, and the membrane as a scar formation. Home, a Scotchman, in 1765 discarded the latter theory, and regarded the pseudomembrane as a product of thickened mucus. Though unable to recognize the relation between the throat and laryngeal lesions, he studied carefully the symptoms of the laryngeal involvement, and classified them as belonging to a separate disease, to which he gave the name of "croup," from his own language. Unfortunately, he placed under this head the various conditions now recognized as false croup and laryngismus stridulus.

In 1773, Samuel Bard described an epidemic which began in New York three years earlier, and from an extensive series of observations concluded that angina and croup were but local manifestations of the same affection. One is led to suspect, from the description of the cases included under the name of diphtheria, that other diseases, especially the exanthemata, were confounded with it. In spite of similar views set forth by other writers, and notably by Jurine, of Geneva, whose work on the nature and treatment of croup won the prize offered by Napoleon in 1807, the older views of the duality of croup and pharyngeal diphtheria continued to be generally held, and it was not until the time of Bretonneau, in 1821, that the true relations of the various manifestations were fully appreciated.

Period II (1821).—In 1821, Bretonneau gave to the public two articles on a disease which he called *phlegmasie diphtheretique*, or *inflammation pelliculaire*, presented before the Royal Academy of Medicine of Paris. In 1826 a further study was contributed on the same subject. The author's conclusions were based on observations made during local epidemics and the results of autopsies, and were, in brief, as follows: That croup was but an extension of the disease known heretofore as malignant or gangrenous angina. That the process was not a gangrenous one, the membrane not having the nature of a scar, but being made up of fibrin. The disease was regarded by the author as a distinct entity, *morbide sui generis*, and not to be confounded with other pseudomembranous affections or with what he called laryngismus stridulus. To this malady he gave the name of diphthe-

ritis, and he regarded it as contagious, although he was unable to produce it in animals.

Trousseau later elaborated the views of his master, and gave the present name, diphtheria, to the disease as better describing a general constitutional affection, and one capable of causing death not only mechanically, but by a systemic poisoning. The membrane was regarded by him not as a primary lesion, but as a result of infection. Finally, his explanation of the cause of post-diphtheritic paralysis and albuminuria accords well with modern views.

The early studies of Virchow and his pupils again tended to confuse the subject. They recognized three forms of inflammation on mucous surfaces: (1) Catarrhal; (2) croupous; (3) diphtheritic. Croupous inflammation was regarded as a superficial process with a greater or less production of young cells. Diphtheria was regarded as a true interstitial process affecting the submucous layers, the diphtheritic exudate continually necrosing, and properly described as gangrenous. The fallacy of these conclusions was only cleared up by bacteriology. From this time to the discovery of the diphtheria bacillus a great deal of work was done on the pathology of the disease by many different observers, notably by Virchow and his pupils, Wright, Cohnheim, and Peters, especially as to the nature and mode of formation of the membrane, and by Oertel, Babes, and many others on the remote pathologic lesions of the disease.

Period III. Discovery of the Diphtheria Bacillus.—This period dates from the discovery of the diphtheria bacillus by Klebs and its later confirmation by Löffler (in 1884). (See Bacteriology.)

Period IV. Antitoxin.—This period dates properly from 1892, when the plea for the treatment of diphtheria by inoculation was presented to the Congress of Budapest (Comptes rendus) by Behring, Kossel, and others (see Antitoxin). From that time to the present day great advances have been made in the production of antitoxin, in its greater concentration, in the knowledge of the proper dosage and of its value as an immunizing agent, so that to-day diphtheria may be regarded as the disease of which we have the greatest knowledge as to causation, clinical symptoms, treatment, and prevention.

ETIOLOGY.

GEOGRAPHIC DISTRIBUTION.

No country, so far as known, is free from the ravages of diphtheria. It extends from the far North to the Tropics; it occurs at high latitudes as well as in low-lying countries, on the coast and far inland.

According to many observers, the disease is found more generally distributed in the Northern Hemisphere than in the Southern. The epidemics in the latter are often characterized by sudden appearance, rapid spread, and as sudden subsidence. Statistics and reports from southern countries are, however, so often incomplete that exact deductions in regard to the occurrence of the disease there are not satisfactory.

MODES OF INFECTION.

In cities the disease is endemic. The number of cases, as well as the virulence which characterizes them, varies from year to year. In country places and villages it occurs usually in the form of distinct epidemics. Occasionally it occurs sporadically. To the best of our knowledge, one case of diphtheria is always due to infection directly or indirectly from another. The various conditions under which the diphtheria bacillus may live, often for many months, affords an ample explanation of the isolated cases which are often so puzzling. Undoubtedly the most frequent method of infection is by the inspiration of the air of rooms infected by discharges from the nose and throat of diphtheria patients. Direct infection may also occur from a diphtheria patient by coughing, sneezing, and kissing. Mild cases of diphtheria, diphtheria germs in the throat without symptoms, cases of so-called "catarrhal diphtheria," often not diagnosed as such, and the more chronic cases of diphtheria, especially rhinitis, are much more frequently responsible for the general spread of the disease than the severe cases in which proper precautions regarding isolation and disinfection are taken.

Indirect infection may occur from the use of various utensils employed by the diphtheria patient; also from towels, handkerchiefs, bedding, clothing, furniture, wall-paper, toys, and books. The hands and clothing of physicians and nurses in attendance on diphtheria

cases are undoubtedly a frequent source of infection. The massing together of children in hospitals, institutions, and schools is often the means of spreading the disease not only among these children, but among other groups with which they come in contact. In this connection the following, taken from the Bulletin of the New York Board of Health, is of interest:

"It has been the practice of the Department to plot upon a city map the location and data of every case of diphtheria in which the diagnosis has been settled by bacteriologic examination. After several months the map presented a very striking appearance. Wherever the densely settled tenements were located, there the marks were very numerous, while in the districts occupied by private residences very few cases were indicated as having occurred. It was also apparent that the cases were far less abundant, as a rule, where the tenements were in small groups, than in the regions of the city where they covered larger areas. At the end of six months there were square miles in which nearly every block occupied by tenements contained marks indicating the occurrence of one or more cases of diphtheria, and in some blocks many (15 to 25) had occurred.

"As the plotting went on, from time to time the map showed the infection of a new area of the city, and often the subsequent appearance of an epidemic. It was interesting to note two varieties of these local epidemics: in one the subsequent cases evidently were from neighborhood infection, while in the second variety the infection was as evidently derived from schools, since a whole school district would suddenly become the seat of scattered cases. At times, in a certain area of the city from which several schools drew their scholars, all the cases of diphtheria would occur (as investigation showed) in families whose children attended one school, the children of the other schools being for a time exempt."

Milk.—Reports of epidemics traceable to infected milk appear from time to time; and when we consider that milk is such a favorable medium for the growth of the bacilli, and that, too, without any observable change in its appearance, there seems to be good ground for the belief in the occasional occurrence of this method of infection. Thus, Kober,* in an analysis of 36 epidemics of diphtheria attributed to the milk-supply, states that in 13 there was evidence that the disease prevailed at the dairy. In these instances the milk was handled while the patients were ill with diphtheria. In 12 there were inflammatory conditions of the teats and udders of the cows.

* *Am. Jour. Med. Sci.*, May, 1901.

TABLE SHOWING DIPHTHERIA EPIDEMICS DUE TO MILK CONTAMINATION.

Date.	Town.	Reported by:	Reference.	Total Number of Cases.	Cases among Drinkers of Infected Milk.	Deaths.	Was the Disease Present Among the Milk Handlers?	Remarks.
Nov., Dec., 1882 to Jan., 1883	Hendon	Power	"Lancet," 1883, ii, i, 145	79	55 (?)	...	No	Seven-tenths of houses attacked had suspected milk-supply. Cans were washed in sewage-polluted water.
April, 1883	London (suburb)	Mackenzie	"Br. Md. Jr.," 1883, i, 874	9 houses	9 houses	..	No	Occurred in scattered houses.
1883	Cardiff	Paine	"Br. Md. Jr.," 1883, i, 873	......	......	..	No	Diphtheria among consumers of a certain milk. The well at the dairy contained an excessive amount of sewage. After closing the well there was no more diphtheria.
Dec., 1883	Davenport	Parsons	"Br. Md. Jr.," 1883, i, 876	31	31	5	Yes	Early in December diphtheria occurred in house next to the dairy, the privy of which was separated only by a partition from the room where the milk cans were washed.
Oct., 1886	Yorktown and Camberly	Power	"Practitioner," xxxix, 65	140	124	16	No	Ninety-three per cent. attacked between October 8th and 18th.
June and Aug., 1886	Melrose	Clark	"Br. Md. Jr.," 1887, cxvii, 100	23	23	..	Yes	Milk obtained from family in which diphtheria existed.
June and Aug., 1886	Malden	Clark	"Br. Md. Jr.," 1887, cxvii, 100	27	13	..	Yes	Source of milk same as in Melrose epidemic.
Oct. 10 to 14, 1886	Frimley	....	"Milch Zeitung," 1886, 835	......	70	15	......	Thirty families involved. Milk from a high-class dairy; no trouble found there.
May to Aug., 1890	....	Jönsberg	"Jahrsb. d. Ges. Med.," 1890, ii, 208	16	6	..	Yes	Three cases probably arose from visiting a girl sick with diphtheria at milk store.
Dec., 1890	Surbeton	Coleman	"Br. Md. Jr.," 1891, i, 44	27	27	3	No	Twenty-two houses invaded.
Oct. to Dec., 1893	Croyden	Philpot	"Br. Md. Jr.," 1894, i, 476	97 houses	65	..	No	Two-tenths per cent. of houses invaded and 12% of houses supplied by contaminated milk invaded. Three cows with eruption on teats found at farm.
June to July, 1893	Highstown.	Hunt	"N.J. Bd. of H. Rep.," 1893, 481	51	43	12	Yes	Boy employed at dairy had diphtheria.

The latter condition the author regards as probably of streptococcus origin. The difficulties surrounding the positive proof of milk infection in epidemics of this kind are necessarily very great, for during the prevalence of an epidemic of diphtheria in a rural community those who handle the milk are quite as likely to harbor diphtheria germs as those to whom it is sold; and unless the presence of the diphtheria germs is shown not only in the throats of those about the dairy or farm, but also (and this must necessarily be a difficult task) in the milk-supply, the latter cannot fairly be condemned as the source of infection.

The table on page 22, compiled by Dr. R. G. Freeman, of New York, is of interest in this connection (see "Med. Record," March 28, 1896).

Domestic animals (birds, cats, etc.) have frequently been regarded as the means of carrying diphtheria. While the susceptibility of these animals to the disease is well known, certain pseudomembranous diseases occasionally seen in them are probably not diphtheria, but of a different bacteriologic nature.

Among the more indefinite sources of infection are **defective drainage,** decomposing substances, sewer-gas, etc.; and while it cannot be denied that certain unsanitary conditions conduce to the impairment of the general health, to catarrhal conditions about the throat and nose, and thus render the system less able to withstand the assaults of any infectious disease to which it may be exposed, nevertheless the presence of the Löffler bacillus is absolutely essential to the production of diphtheria.

SEASONS.

The influence of the different seasons of the year upon the occurrence of diphtheria has been variously estimated by different observers. Thus, the London Metropolitan Asylums Board report that from 1888, when diphtheria was first admitted to the hospitals under its charge, to 1900, the maximum death-rate from this disease occurred in January, the minimum in April. Thorne reports the deaths from diphtheria in England and Wales by quarters from 1870 to 1873 (inclusive) as follows: First quarter, 1000; second quarter, 819; third quarter, 847; fourth quarter, 1192. In the old city of New York, from 1891 to 1900, cases of diphtheria and croup occurred as follows: First quarter, 23,738; second quarter, 23,904; third quarter, 15,322; fourth quarter, 20,671; which in this climate at least shows a decrease in the number of cases for the summer months.

Kirsch has made an analysis of 124 epidemics of diphtheria, and reports that 32 of these reached their height in the spring, 24 in the summer, 30 in the autumn, and 38 in the winter.

Nearly all the reports of epidemics show a diminution in the number of cases of diphtheria during the warm months. This is readily explained—first, by the diminution in the frequency of serious catarrhal conditions affecting the upper respiratory tract; second, by the more thorough airing of dwellings and the greater amount of time spent in the open air; and third, by school vacation.

CONDITIONS OF LIFE.

It has not been shown that diphtheria is more prevalent among the poorer classes than the well-to-do, except in so far as the former are crowded together in small and poorly aired dwellings.

Feer and Monti have pointed out the frequency of diphtheria in newly built houses which are occupied before they are dry. This they regard as probably due, at least in part, to the prevalence of catarrhal conditions under these circumstances.

Personal uncleanliness and filth in the dwelling-rooms contribute to the spread of diphtheria as well as other infectious diseases.

AGE.

The occurrence of diphtheria varies greatly in the different ages of life, as will be seen from the following table, taken from the statistics of the New York Board of Health:

	Under 1 Year.	1 Year.	2 Years.	3 Years.	4 Years.	Total Under 5 Years.	5	10	15
Number of deaths,..	1675	4263	3807	2900	1908	14,554	3012	248	75
Percentage of deaths at each age among 17,889	9.3	73.2	21.2	16.2	10.6	81.3	16.2	1.3	.4
Total percentage of deaths at each age among 83,635 cases reported....	1.3	5	4.5	3.4	2.2	17.3	3.4	2.9	.09

The relatively small number of cases occurring in children under one year of age is a well-established fact and goes to prove a certain immunity among nurslings.

It is very probable that the percentage of deaths here represented at this age is misleading, for the reason that the mortality is so much

higher than in the subsequent years of life. It will be seen that the greater number of deaths occurred during the second year of life and diminished somewhat to the sixth, after which there is a rapid decrease in the number of deaths.

The deductions as to the number of cases occurring at each period of life can only be approximately made from a study of these tables; for while, as has been mentioned, the number of deaths in the first year represents a large proportion of the cases occurring, in the later years, and especially after the sixth year, the number of cases occurring is larger in proportion to the death-rate.

The following table, compiled by Baginsky, of 2711 diphtheria cases gives the following results:

Age of Cases.	Number of Cases.	Percentage at Each Age.
0–6 months	15	0.55
6 months to 1 year	69	2.5
1–2 years	227	8.30
2–3 "	317	11.60
3–4 "	354	13.05
4–5 "	337	12.40
5–6 "	264	9.70
6–7 "	280	10.30
7–8 "	209	7.70
8–9 "	175	6.40
9–10 "	146	5.30
10–11 "	101	3.70
11–12 "	80	2.90
12–13 "	65	2.02
13–14 "	73	2.60

SEX.

This factor seems to have but little influence, if any, on the occurrence of diphtheria. In the New York Board of Health table it will be seen that there were 9193 deaths among the males, and 8820 among the females.

In Baginsky's table, 1311 cases occurred among males, and 1400 among females.

RACE.

If one considers the history of the occurrence of diphtheria among all races, it is difficult to believe that any people possess an immunity from the disease.

Various observations have been made to show that the Jews are especially liable to it. The districts inhabited by the poor Jews in New York undoubtedly show in many years a certain preponderance

of cases, but this would readily be accounted for by the conditions under which these people live—crowded dwellings, insufficient room, and filth.

Walsh,[*] from a study of diphtheria cases occurring in Washington, believes that the colored race shows a certain immunity to the disease.

In 1895–1896 diphtheria occurred in 4.43% of 10,000 negroes to 15.25% of 10,000 whites.

CONSTITUTION.

That certain catarrhal conditions of the upper air-passages—adenoids, enlarged tonsils, etc.—form a suitable medium for the growth of the Löffler bacillus has been shown by many observers. The frequent occurrence of diphtheria during the course of certain exanthemata which are especially characterized by catarrh of the air-passages (measles) is well known. The so-called "scrofulous habit," with tendency to enlarged lymphatics about the neck, has been shown to predispose to the disease. Finally, it is undoubtedly true that the disease shows a disposition to occur in certain families—a fact which may logically be attributed to the family disposition to the catarrhal conditions just mentioned. On the other hand, there can be no doubt that certain people, children and adults, show a greater or less immunity. This has been shown to exist especially in nursing children. Lubowski and other observers have recently shown that the blood of such persons possesses a decided antitoxic property.

BACTERIOLOGY.

Klebs, in 1883, reported the discovery of a bacillus constantly found in the pseudomembranes of the diphtheria patients. The following year, Löffler [†] isolated these bacilli in pure culture, and by inoculating them on the mucous membranes of animals reproduced pseudomembranes. He also studied the effects and postmortem lesions which followed injections of these bacilli. Löffler, however, was unable to state positively that these organisms were the specific cause of diphtheria, and chiefly for the reason that he did not at first observe the occurrence of paralysis in the inoculated animals.

Roux and Yersin [‡] were able to establish this specificity beyond a doubt, and noted, furthermore, the occurrence of paralysis. These

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[*] *N. Y. Med. Jour.*, Jan., 1898.
[†] "Mittheil. aus dem Kaiserl. Gesundheitsamte," vol. II, 1884.
[‡] "Ann. de l'Institut Pasteur," 1888–1889.

writers also made a study of the toxins produced by the germs—studies which may be regarded as the beginning of serotherapy.

The results of these early studies have been long since confirmed by observers the world over, and the bacillus described by Löffler as the true and only cause of diphtheria has been established beyond a doubt, in that it has been repeatedly shown to fulfil the conditions required for all organisms as a specific for an infectious disease: it is always found in the lesions of diphtheria; it has been isolated in pure culture; its experimental distribution is similar to that occurring in natural diphtheria; the essential lesions of the disease as seen in natural diphtheria are reproduced by animal inoculation; and, finally, diphtheria in its entirety has been produced by no other organism.

Morphology of the Bacillus diphtheriæ.—It has been said that the chief characteristic of the Löffler bacillus is polymorphism, and, indeed, the appearance of these organisms is subject to great variation, depending upon the culture-media on which they are grown, the age of the culture, the temperature, etc. Their length and breadth have been found to vary even on the same culture-medium, depending on the fluidity of the latter and the presence or absence of other organisms; and yet typical Löffler bacilli present certain appearances which it is possible to recognize in the majority of cultures examined.

Fig. 1.—Diphtheria bacilli from blood-serum culture stained according to Hunt's method; × 2000 (Wright and Brown).

If a culture taken on Löffler's blood-serum, the most favorable medium, be grown for twelve to twenty-four hours at a temperature of about 36° C. (97° F.), the bacilli stained with alkaline methylene-blue will be seen as narrow rods, either straight or slightly curved, slightly swollen at one or both ends, arranged in larger or smaller groups, singly or in pairs. In regard to their relative position to one another there is, again, much variation. As a rule, when many are found together, they have a tangled appearance, one forming an acute or obtuse angle

DIPHTHERIA.

with another. If several bacilli form a chain, it is usually a broken
one and not a straight line. Exceptionally, the bacilli lie parallel to
one another. The diameter varies from 0.3 to 0.8 μ, and the length
from 1 to 6 μ. According to Schabad, the ratio of the length to the
diameter varies from 5 : 1 to 8 : 1.

The bacilli, instead of having the form above described, may be
thickened only at one end, giving a wedge-shaped appearance; or,
again, be pointed at both ends and swollen in the middle. In addition
to the above common forms, shorter and thicker forms frequently
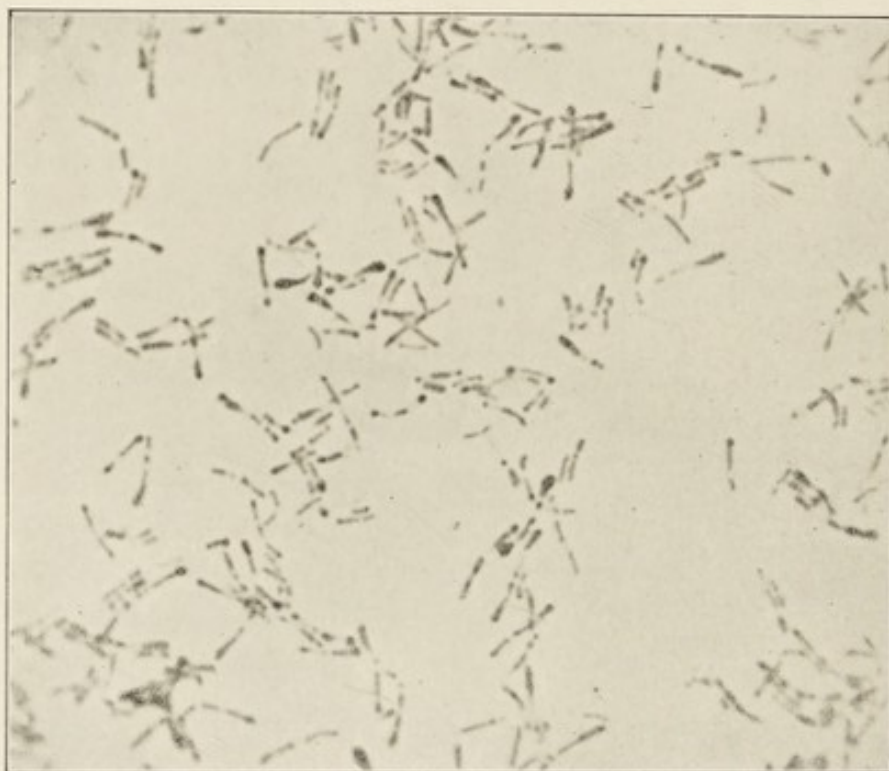
FIG. 2.—Diphtheria bacilli from a culture on blood-serum, stained by Löffler's methylene-blue solu-
tion, showing long and irregularly shaped forms of the bacillus, as well as the irregularity of staining;
× 2000 (Wright and Brown).

occur which it is often difficult to distinguish from the group of so-
called pseudodiphtheria. Club-shaped, spindle-shaped, and lance-
shaped bacilli are also seen. They are always segmented. The Klebs-
Löffler bacilli stain with many anilin dyes. They are little decolorized
by Gram's stain, and are readily stained with methylene-blue or with
Neisser's stain, the latter being made as follows:

No. 1.—1.0 methylene-blue dissolved, 20 c.c. 96% alcohol, 90 c.c.
aqua destill., 50 c.c glacial acetic acid.

No. 2.—2.0 vesuvin to 1 liter of boiling distilled water.

The culture is stained in solution No. 1 for one to three seconds, or,

better, somewhat longer; washed off in water and stained with No. 2 for three to five seconds or longer; washed off and mounted. Colored in this way, a twenty- to twenty-four-hour-old culture on blood-serum or bouillon will show the body of the bacilli stained brownish-yellow,

Fig. 3.—Diphtheria bacilli from a culture on blood-serum, stained by Löffler's methylene-blue solution, showing deeply stained points; $\times$ 2000 (Wright and Brown).

Fig. 4.—Diphtheria bacilli from blood-serum culture stained according to Neisser's method; $\times$ 2000 (Wright and Brown).

while at one or both ends may be frequently seen the so-called polar granules (Neisser-Ernst bodies) as deeply colored blue, oval-shaped areas, the diameter of which is greater than that of the bacillus in

which they are found. The outlines of these bodies are sharply defined, and, as will be noted later, they are not peculiar to true diphtheria bacilli, but are found occasionally in a slightly atypical form in certain forms of pseudo-diphtheria bacilli, especially in older cultures.

In discussing the morphology of the diphtheria bacillus, those types have been mentioned which are generally recognized as undoubtedly belonging to true diphtheria. It must be remembered, however, that between these so-called typical diphtheria bacilli and those which are generally regarded as belonging to the class of pseudodiphtheria there are a great many types which it is difficult to classify. From this fact have arisen two classes of observers:
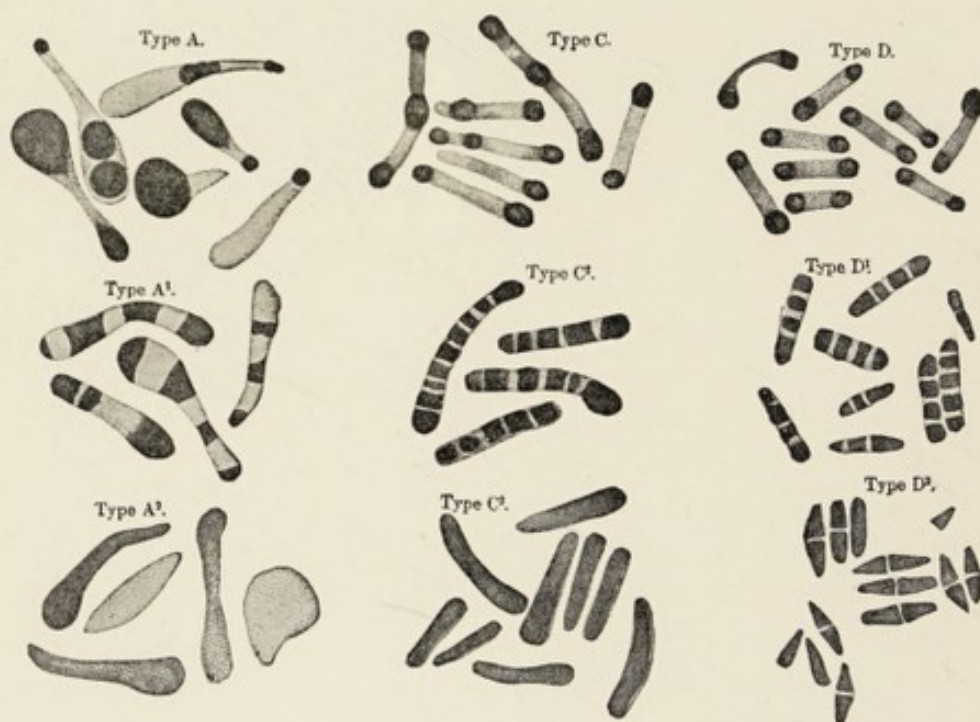
Fig. 5.—Wesbrook's types of Bacillus diphtheriæ: Granular types, A, C, D; barred types, A¹, C¹, D¹; solid types, A², C², D². × 2500.

First, principally the French school, followers of Roux and Yersin, Behring, and others, who believe that all these various types should be regarded as modifications of the true diphtheria bacillus.

Second, and by far the larger school (so-called dualists), those who believe that the pseudobacillus, of whatever variety, while it may resemble morphologically, and to a certain degree bacteriologically, the true diphtheria bacillus, is never capable of producing diphtheria and cannot be regarded as a variety of the Klebs-Löffler bacillus.

Among those who may be regarded as belonging to the first class are Wesbrook, who in 1900 presented to the Association of American

Physicians an elaborate study of the different morphologic varieties of diphtheria bacilli found. Wesbrook divided all diphtheria bacilli into three groups—the granular, barred, and solid or evenly staining. These groups were further subdivided into a number of different types. He concludes that granular types are usually the most prominent forms at the onset of the disease; that they usually give place wholly or in part to barred or solid types shortly before the disappearance of the diphtheria-like organisms; and that solid types may sometimes be replaced by granular types when convalescence is established and just before the throat becomes clear.

Gorham has lately carried on the work of Wesbrook, confirming his results and adding to them. He believes from his researches on 2375 cultures taken from persons who were healthy, whether exposed to diphtheria or not, that the change from the solid type seems to take place under the influence of the body-fluids of a person immune or becoming so.

As to the virulence of these different types or their power of producing diphtheria, little is said, as the authors do not believe that inoculation in animals is a definite test of virulence in human beings; and while this classification is undoubtedly to be recommended for its completeness, it does not seem to simplify matters for the diagnostician, whose chief aim is to determine if the germ under the microscope is capable of causing diphtheria.

Biology.—The Löffler bacillus is non-motile and non-liquefying. It is aerobic, growing most readily in the presence of oxygen, but also without it (facultative aerobic).

It does not form spores. It is killed by a temperature of 58° C. (136° F.) in ten minutes. It may live for a long time on dried membrane. Park found living bacilli after seventeen weeks; Roux and Yersin, after twenty weeks. Abel says that, dried on silk threads, the bacilli may live one hundred and twenty-two days, and on child's toys kept in a dark place for more than five months.

In culture-media kept at blood-heat the bacilli do not live, as a rule, for more than a few weeks, but under certain conditions, as when sealed in tubes and kept from heat and light, they may retain their virulence for years (Park, Klein, Löffler, and others). The persistence of virulent diphtheria on mucous membrane after all symptoms of the disease have disappeared, as well as the occurrence of virulent germs in the throat of healthy persons, are now thoroughly recognized. Freezing does not necessarily kill the bacillus. It begins to grow at a temperature of 20° C. (68° F.) or less, and reaches its maximum growth

at a temperature of 36° to 37° C. (96° to 99° F.). It may grow at a temperature of 41° C., according to Park.

Growth on Blood-serum.—This is the most favorable medium for the growth of the bacilli (for preparation of this serum see page 137, Antitoxin) and is the usual medium chosen for cultures taken for diagnostic purposes. After twelve hours' growth the colonies are seen as small, round, slightly elevated points, whitish-gray, or more rarely yellowish, in color. The borders of the colonies are somewhat uneven. After twenty-four hours they attain a diameter of $1\frac{1}{2}$ to $2\frac{1}{2}$ μ; after two days, $2\frac{1}{2}$ to 3 μ. If widely separated, they may attain a diameter at this time of $\frac{1}{8}$ of an inch. If the serum is moist, the contiguous colonies may coalesce. The colonies do not liquefy the serum.

Growth on Agar.—On 1 % slightly alkaline, plain, nutrient agar or glycerin-agar the growth is less characteristic and luxuriant than on blood-serum. It has been found that bacilli taken directly from the throat grow poorly or not at all on this medium.

Pure cultures, however, grown first on some other medium show a fairly luxuriant growth. Different preparations of agar vary as to their suitability for the growth of the bacilli. The medium, at any rate, to get the best effects, should be rendered alkaline.

The agar colonies on the surface generally show a lateral extension on one or both sides, exceeding in extent the colony itself. The deep-growing colonies, as a rule, present no such extension, but are round or oval. The surface colonies are often granular, usually showing a dark center. Their thickness is variable; the edges are irregular, and sometimes delicately fringed, or, again, rounded and smooth. The colonies are gray or grayish-white.

Agar cultures are usually employed to obtain cultures of pure diphtheria by plating. For this purpose the colonies supposed to be diphtheria bacilli are taken from a blood-serum culture and streak cultures made on the freshly prepared agar plates, which are then allowed to incubate for twelve hours.

Growth in Bouillon.—The diphtheria bacilli grow readily in alkaline bouillon, with or without a small amount of glucose; also in slightly acid and neutral bouillon. According to Madsen, in acid bouillon the acidity increases rapidly for five or six days, when it ceases to increase, evidently owing to the fact that the degree of acidity then formed is unsuitable for further development of the bacilli. In four or five days there is a diffuse cloudiness in the bouillon and a film on the surface, the latter increasing in thickness for a long time. On shaking the flask, part of the film falls to the bottom and adds to

the deposit already formed there. In two or three weeks the cloudiness begins to disappear, and in several months the bouillon has become perfectly clear. The film is usually preserved. The acid reaction may set in early or be delayed for some time. Sooner or later alkalinity begins to take place.

Madsen found that the same cultures in the same bouillon, placed under conditions as nearly identical as possible, showed different degrees of acidity at the same time, a fact which he was unable to explain satisfactorily.

In alkaline and neutral bouillon the cloudiness and the film on the surface appear early (twenty-four to forty-eight hours).

According to Schabad, the maximum acidity in the cultures occurred most often on the second day; occasionally on the third, and rarely on the fourth or later.

As to whether this acid formation is characteristic of the true diphtheria bacillus, as opposed to the class of pseudodiphtheria bacilli, there is still a question among different observers. The majority are agreed, however, that this characteristic is an important one in making a differential diagnosis between them.

Growth on Other Media.—The growth on gelatin is slow and scanty, and not characteristic.

On the potato, according to some authors, the bacillus grows well. Schabad was unable to find any true growth. Park describes the growth as a thin dry glaze near the point of inoculation.

In milk, the diphtheria bacillus grows well and at a low temperature—20° C. (68° F.) (Sternberg). The appearance of the milk is unchanged. On albumin, according to Gelpke, the diphtheria colonies show a peculiar salmon color, which he believes is seen in no other bacteria. Schabad was unable to confirm this, and found the growth scanty and not characteristic. Other media which have not shown definite results are urine-agar and alkaline serum (recommended by Cobbet).

On antitoxin serum, according to de Martini, true diphtheria bacilli do not grow. Fränkel, Spronck, Januszewska, Gelpke, and Schabad found that the true diphtheria bacilli as well as the pseudodiphtheria grew well in this medium.

In ascitic fluid, according to Januszewska and Schabad, the Löffler bacillus grows well and forms no diffuse cloudiness. There is, moreover, a marked deposit seen at the bottom of the vessel.

Agglutination.—This subject has been studied by Fränkel, Nicolle, Bruno, and others, and more recently by Lubowski. The latter, in studying several cultures of absolutely atoxic and avirulent diphtheria

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bacilli, found that the blood of patients injected with cultures of them caused agglutination of 23 cultures of typical diphtheria bacilli, as well as cultures of the original bacilli themselves.

Lesieur * has obtained similar results, and confirms the statements of other observers, that the blood of animals injected with toxin alone does not possess the power of agglutination, as does that of blood taken from cases injected with the bacilli themselves.

This subject is still in its infancy. The combined results of observers so far show that agglutination is an inconstant characteristic of not only true diphtheria bacilli, but also of several of the class of so-called pseudodiphtheria, and that, furthermore, it has no relation to the presence or absence of virulence in a given bacillus.

PATHOGENESIS.

The diphtheria bacillus is pathogenic for guinea-pigs, rabbits, chickens, pigeons, small birds, and cats; also in a lesser degree for dogs, goats, cattle, and horses, but not for rats and mice (Park). In these animals the disease is caused, as a rule, by the toxemia produced by the diphtheria bacilli, and not by the mechanical effects of the local lesion.

Under the head of Pseudodiphtheria Bacilli will be discussed that class of diphtheria-like bacilli whose proper classification is still a matter of doubt. In describing pathogenesis, reference is made only to that class of bacilli which biologically and morphologically represents the type of undoubted diphtheria bacilli. The virulence of the Löffler bacilli varies greatly. Many writers have described absolutely non-virulent and non-toxic diphtheria bacilli, notably Brieger, Fränkel, Wright, and Cobbett. Lubowski found that the blood of patients harboring this variety of bacillus had decidedly antitoxic properties against diphtheria inoculation. Roux and Yersin and others have succeeded not only in reducing to a minimum the virulence of certain bacilli, but also in restoring the virulence of certain bacilli that had lost a greater part of it. They did not succeed, however, in restoring the virulence to any bacillus which had been wholly deprived of it.

Bomstein † has succeeded in doing this by introducing in the bodies of animals cultures of a virulent bacilli in celloidin sacs and repeating the operation a number of times.

Between the virulent class of bacilli which are rapidly fatal for

* "Comptes Societe de Biologie," Aug., 1901.
† *Russ. Arch. f. Path.*, Nov., 1900.

guinea-pigs and the absolutely avirulent types there exist bacilli which, inoculated in animals, do not produce death directly, but by a slow process of deterioration of the general system, emaciation, and sometimes death from an intercurrent disease (the so-called chronic toxemia).

Diphtheria bacilli not only show a different degree of virulence in various cultures, but differ widely in the tenacity with which they retain their virulence. The bacillus used by the Board of Health for the production of toxins has, according to Park, retained its virulence almost unimpaired for four years (1898). Other cultures lose half their virulence in a few months.

Animals dying of the toxemia produced by diphtheria show the following lesions, as described by Löffler: At the seat of inoculation there is a grayish focus surrounded by an area of congestion. Edema of the surrounding subcutaneous tissues and swelling of the adjacent lymph nodes are present. The pleura and pericardium contain an excess of fluid—clear, putrid, or bloody. The lungs are congested and may show subpleural hemorrhages. Areas of necrosis are seen in various organs. The heart-muscle and voluntary muscles show degenerative changes. There is fatty degeneration of the liver and kidneys. The blood shows hyperleucocytosis.

The earliest reports on the effect of inoculations of diphtheria cultures in animals failed to recognize the occurrence of paralysis, in all probability, from the fact that the animals were killed by large doses too rapidly to allow the development of this symptom. If the animals do not succumb too soon to the disease, the paralysis is usually seen first in one or both hind legs, and from there becomes general. Rarely the muscles of the neck and larynx are first affected. As to whether a given diphtheria bacillus which is shown to be pathogenic for susceptible animals (guinea-pigs) must of necessity be so for man, there is some difference of opinion. Most writers agree that this is usually, if not always, a reliable test.

Gorham, in carrying on the work of Wesbrook, believes the test an uncertain one, especially as he doubts the possibility of isolating one type of bacillus; for, as he says, after a guinea-pig is inoculated with one type, another is frequently recovered. This opinion must for the present be considered extreme, and for all practical purposes the test of pathogenesis for man must be based upon the results obtained on the lower animals.

THE DISTRIBUTION OF THE BACILLI IN THE SYSTEM.

According to Park and others, unless an enormous quantity has been injected, diphtheria bacilli are found at the site of inoculation, and only rarely in the internal organs. That this absence of bacilli in the internal organs following injections of bacilli in moderate quantities does not correspond to the results in natural human diphtheria has been shown by many recent observers.

Frosch* found bacilli in the pneumonic areas of persons dying of diphtheria as well as in the lymphatic glands. Other bacteria were generally associated with them.

Kutscher, Strelitz, Booker, and many others have confirmed these results. Wright found the bacilli in the lungs in 13 out of 14 cases examined, and later Wright and Stokes in 30 out of 31 cases. Flexner and Anderson,† in a study of this subject made by inoculating the trachea of rabbits with virulent cultures of Klebs-Löffler bacilli, found not only that the bacilli were distributed generally throughout the body, but that the distribution took place in a remarkably short time. Thus, they were found in the lungs one hour after injection, and in three and a half to six hours in the lungs, spleen, bone-marrow, heart's blood, and liver. At the end of one hour Flexner found that the bacilli were mostly free in the tissues. In three and a half hours they were nearly all inclosed in the epithelial cells of the pulmonary alveoli.

After the pneumonia caused by the germs had developed (in twenty-four hours) it was found that the bacilli disappeared or were greatly reduced in number, or that their vitality was markedly diminished, so that they could not be cultivated. The mode of transmission of the bacilli has not been definitely determined. Flexner showed, however, that the epithelium lining the alveoli was but a poor barrier against their further progress, and believed that their movement is a mechanical one, similar to that observed in the case of dirt particles, dead bacilli, etc. Kutscher believed that they were carried from the lungs by the blood and lymph streams. As to the significance of their presence in the internal organs, Kanthack and Stephens believe that wherever found in the body, they are to be regarded as producers of toxin, and therefore adding to the general toxemia.

Councilman, Mallory, and Pearce, in cultures taken from 153 cases of uncomplicated diphtheria, and from 50 cases complicated with scarlet fever, measles, or both, found in the first group: In the

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*Zeit. f. Hygiene, XIII, 1893. † Johns Hopkins Med. Bull., 1892, p. 22.

heart's blood, diphtheria bacilli 7 times; in the liver, 30; in the spleen, 19; in the kidney, 25 times. In a majority of the cases the bacilli were found in pure culture; in others, associated with the streptococcus, staphylococcus, Diplococcus lanceolatus, pneumococcus, etc. In the second group of cases the diphtheria bacilli were found: In heart's blood, 5 times; liver, 12 times; spleen, 7 times; kidney, 12 times.

The authors do not speak positively as to the significance of this general infection, but note the fact that it occurred generally, but not always, in the cases of septic diphtheria. This would bear out the truth of the statement of Kanthack and Stephens, quoted above, and also the opinion held by Genersich, that the sepsis may be caused by the diphtheria bacillus alone, and that the association of other organisms, especially the streptococcus, is not essential to the production of various septic conditions. Councilman and his associates also found in one case of general infection complicated by scarlet fever and pneumonia, and one of ulcerative endocarditis, diphtheria bacilli in pure culture in a soft clot-like mass adherent to the mitral valve. Howard and Wright have reported cases in which the bacilli were found in valvular vegetation. In both cases, however, the bacilli were non-pathogenic for guinea-pigs. In the lungs in cases of diphtheria without complications with other exanthemata, the diphtheria bacillus was present in 52 of 98 cases examined. It occurred alone fifteen times and in the rest of the cases in combination with other organisms. In the lungs of the diphtheria cases complicated with scarlet fever, measles, or both, out of 24 cases from which cultures were made the diphtheria bacillus was present in 20. The authors agree with the opinion of the majority of observers that a combination of pathogenic organisms is generally responsible for the occurrence of pneumonia in these cases.

In abscesses of the lung the diphtheria bacillus was found 4 times in 11 cases, and always associated with other germs. In 7 cases of empyema the diphtheria bacillus occurred twice, associated with cocci.

The accessory sinuses of the nose were examined in 63 cases, and were frequently found to contain diphtheria bacilli alone or in combination with other organisms. The authors believe that this infection may in all probability account for the persistence of diphtheria bacilli in the nose.

As to the occurrence of the diphtheria bacillus in the middle ear, the report of the above writers is given under Complications of Diphtheria.

In addition to these sites, the bacilli were found in a case of thrombosis of the lateral sinus following mastoid disease, in a case of acute periostitis, and in abscesses in various situations.

VIRULENT BACILLI IN HEALTHY THROATS.

If we consider the many conditions under which the Löffler bacilli may live outside of the human body, it is not to be wondered at that many observers have been able to find them in the throats and noses of persons who gave no evidence of the disease. Persons coming into contact with diphtheria cases are very frequently found to have virulent bacilli in the throat. In hospital wards in which a few cases of diphtheria occur a good proportion of the children will be found to harbor true diphtheria bacilli. Thus Heubner, in an examination of the throats of 100 children admitted to a hospital where there were several cases of diphtheria, the examination being conducted during the three first days of admission, found true diphtheria bacilli in 24. In 20 other children the bacillus was present: in 6 on admission, and in the other 14 it was discovered at times varying from a few days to several weeks. In no cases did the children show evidences of the disease.

Inoculation was performed on immunes in 12 of these cases, and showed in 6 that the bacilli were only slightly virulent; in 6 others, entirely so.

Epidemics in public schools have given similar results.

Thus Fibiger, in a recurring epidemic in a public school, found, in an examination of the throats of 1234 pupils, 8 times cultures of true diphtheria bacilli.

Park and Beebe,* in 1894, in an examination of the throats of 330 healthy persons who, so far as known, had not come into contact with diphtheria cases, found virulent bacilli in 8, and in 24 found non-virulent or attenuated forms of diphtheria bacilli.

The occurrence of so-called bacteriologic diphtheria will be noted later. The persistence of the diphtheria bacilli in the throat long after the disappearance of the pseudomembrane is a very common occurrence. Park found that in 304 of 605 consecutive cases the bacilli disappeared within three days; in 176, within one week; in 2 cases, within nine weeks. Much longer persistence has been reported by others. Finally, cases of recurrence or relapse have been reported from time to time.

* *Med. Rec.,* Aug. 18th.

MIXED INFECTION IN DIPHTHERIA.

Instead of finding colonies of pure diphtheria in a culture, it is very common to find them associated with various cocci, principally streptococci, staphylococci, and, less frequently, pneumococci. The occurrence of these germs is especially frequent in diphtheria associated with other infectious diseases, especially measles and scarlet fever. The effect of this association upon the clinical picture of the disease will be noted later. It may be said, in brief, that mixed infection in diphtheria is always to be dreaded, as the other germs play quite as important a part in determining the final outcome as the Klebs-Löffler bacilli themselves.

PSEUDODIPHTHERIA.

A word should be said here in regard to the pseudomembranous inflammations occurring in the course of various exanthemata. The angina which so frequently occurs in scarlet fever may be taken as the type of these. While certain minor differences may usually be noted in the appearance of the pseudomembrane, or rather exudation, in these cases, only a microscopic examination of cultures will serve to exclude the presence of diphtheria bacilli. The frequency with which such diseases are complicated by diphtheria, especially in institutions, should never be forgotten, and subsequent cultures should be taken from the throat when the presence of a pseudomembrane is determined, no matter how certain the physician be in regard to the cause of it.

FIG. 6.—Streptococcus pyogenes from a culture in bouillon; × 2000 (Wright and Brown).

Such pseudomembranes are almost invariably due to the action of streptococci; less often to other varieties of cocci, alone or together with the former.

Finally, pseudomembranes occur as a part of a primary disease due to these same organisms. Here again only microscopic examination will serve to make the diagnosis. The larynx may be secondarily involved in these cases or a primary pseudodiphtheritic laryngitis may

occur. It not infrequently happens that cultures taken from a case of laryngitis in a child fail to show the presence of Löffler bacilli, and such cases are put down as pseudodiphtheria, even though presenting such severe symptoms of stenosis that operative interference is necessary. Subsequent cultures may show diphtheria bacilli. Thus, while

Fig. 7.—Staphylococcus pyogenes aureus from a culture; × 2000 (Wright and Brown).

it cannot be denied that primary cases of pseudodiphtheritic laryngitis occasionally occur, it is highly probable that they are actually more rarely met with than the reports from various hospitals would lead us to believe.

DIPHTHERIA TOXIN.

The fact that diphtheria bacilli inoculated into animals subcutaneously could only be found at or near the point of inoculation, and yet these animals showed the well-known symptoms observed in clinical diphtheria, led Roux and Yersin to make a study of the toxins of these organisms.

They took a very virulent bouillon culture of diphtheria bacilli and placed it in the incubator for a month. The culture became first alkaline, then slightly acid, and then alkaline again. When this alkalinity had become well marked, the culture was passed through a Chamberland filter. This filtered culture-medium, absolutely free from bacilli, produced all the clinical symptoms of diphtheria in guinea-pigs and rabbits, and caused the death of inoculated animals.

As has been already noted, the toxicity of true diphtheria bacilli varies greatly. It is further noted that two bacilli which will kill a guinea-pig in twenty-four hours will produce different amounts of

toxin when placed under similar conditions of growth for a definite time.

The virulence of a toxin is measured by the amount required to kill a guinea-pig of 500 gm. In general, this can be done with 0.1 c.c., but toxins are also produced of which 0.01 to 0.05 c.c. will suffice to produce a like effect.

Toxins are preserved for a long time when kept sealed and away from light and heat. As to their chemical nature, little is at present known, beyond the fact that they are related to the globulin class in many of their properties (Park).

Artificial Production of Toxin.—Park and Williams[*] have reached the following conclusion as to the best method of producing toxin artificially:

"The requisite conditions for the best development of toxin, as judged by the behavior of a number of cultures, are a temperature from about 35° to 37° C.; a slight alkalinity, which should be from 6 to 10 c.c. of normal soda solution per liter above the neutral point to litmus; suitable peptone and meat for the preparation of the neutral bouillon; and a duration of growth of the culture of from five to eight days, according to the peculiarities of the culture employed. At too early a period toxin has not sufficiently accumulated; at too late a period it has degenerated. In our experience the amount of sugar present in the meat is of minor importance; at least this is true for the varieties of beef in New York, so long as the bouillon has been made sufficiently alkaline to overcome the acid produced by the fermentation of the sugar through the products of the bacilli. In neutral bouillon, as pointed out by Smith and Spronck, the sugar does not produce sufficient acid to interfere with the growth of the bacilli and the development of toxin. This can be prevented by the previous destruction of the sugar through the fermentation caused by the growth of the Bacterium coli or other bacteria having similar action. Besides the sugar in the meat, there are other substances, whose nature is unknown, which hinder a full growth of the bacilli or production of toxin. This is true of bouillon made directly from fresh meat, old meat, fermented meats, or meat extracts. Under the best conditions we can devise, toxin begins to be produced by bacilli from some cultures when freshly sown in bouillon some time during the first twenty-four hours; from other cultures, for reasons not very well understood, not for two to four days. The greatest accumulation of toxin is on the fourth day, on the average, after the production of toxin has commenced. After

[*] *Jour. of Exp. Med.,* Jan., 1896.

that time the number of living bacilli rapidly diminishes in the culture and the conditions for those remaining alive are not suitable for the rapid production of toxin. As the toxin is not stable, the deterioration taking place in the toxin already produced is greater than the amount of new toxin still forming."

The virulence of the diphtheria bacillus as judged by clinical symptoms varies greatly. Thus, a bacillus little or not at all virulent for one person may cause grave symptoms in another. Certain epidemics are characterized by many mild cases; others, by the number of severe ones. Conditions of climate and temperature, states of civilization, and race, all influence the degree of virulence of the diphtheria bacilli. Finally, the association of other organisms with the bacilli has a decided effect on the degree of virulence noted.

PSEUDODIPHTHERIA BACILLI.

The confusion as to the proper nomenclature of certain diphtheria-like organisms increases from day to day. The two schools of opinion in regard to the relations of so-called pseudodiphtheria bacilli and true Klebs-Löffler bacilli have already been mentioned. Among those who believe in the practical identity of the two sets of organisms are, or were until recently, Roux and Yersin and their followers, Behring (see last edition of "Text-book on Diphtheria," 1901), and, in this country, Wesbrook and Gorham. Although the two latter have not expressed themselves definitely on this subject, their writings, already quoted, would lead one to place them in this category.

By far the largest number of observers, while acknowledging the difficulty which surrounds the differential diagnosis between true and pseudodiphtheria, believe that there is always a difference, and that under no known conditions of growth can the one class change into the other.

Avirulent and atoxic Löffler bacilli are in all respects identical with true diphtheria bacilli save in the absence of virulence and power of producing toxin, and, as already stated, these qualities have been artificially restored by Bomstein.

In the early days of this discussion it was customary to give names to these diphtheria-like organisms—Hoffman's bacilli, xerosis bacillus, etc. It would seem simpler for those who believe in the non-identity of the two sets of organisms to include all bacilli which do not possess the essential characteristics of the true Löffler bacilli in a separate class, that of pseudodiphtheria bacilli.

Among the recent works on this subject is that of Schabad, who has made an elaborate study of true and pseudodiphtheria bacilli in an attempt to arrive at a method of differential diagnosis.

Differentiation from Löffler Bacilli by Growth on Different Media.—On blood-serum the growth of the pseudobacillus is much slower at first. In the first twenty-four hours there is often little or no growth, while the true bacilli has formed a colony of $1\frac{1}{2}$ to $2\frac{1}{2}$ μ in diameter. From the fourth day the pseudobacillus colony overtakes that of the true diphtheria colony. Occasionally, however, pseudobacilli were found which grew quite as well as the true. In regard to the appearance of the two sets of colonies, there is often little difference. Escherich states that the colonies of the pseudobacilli may be distinguished by their milk-white color, their moist appearance, and more fluid consistence. This was confirmed by Proscheska, and denied by Hilbert and others. Kressling found that, if a culture of Löffler bacilli was mixed in a drop of water, the mixture was not a homogeneous one, but showed lumps or flakes readily detected with the naked eye. On the other hand, cultures of pseudodiphtheria made a perfect emulsion.
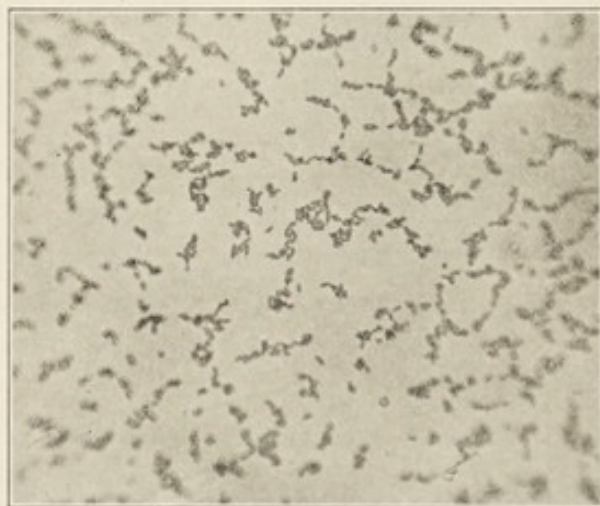
Fig. 8.—Pseudodiphtheria bacilli. $\times$ 650 (Koplik).

Schabad found that in agar, pure cultures of both true and pseudodiphtheria bacilli grew well. The colonies of pseudodiphtheria were usually of a yellow color, more luxuriant and fluid than the true diphtheria. The color of the latter colonies was usually gray. The differences between the two were more pronounced after two or three days' growth. On glycerin-agar and gelatin little difference was observed between the two.

The growth in bouillon varied. The characteristic growth of the bacilli in this media has been already described. Schabad found little difference in the character of the growth of the two bacilli. The clarification of the bouillon, if cloudiness had already taken place, was found to occur later with the pseudodiphtheria than with the true. With the former there was also observed a heavier precipitation at the bottom of the vessel. Both bacilli produced a diffuse cloudiness and

film on the surface in strong alkaline media; in fairly acid or alkaline media, a precipitate without the cloudiness.

On albumin the author was unable to confirm Gelpke's observation of a salmon-colored colony of true diphtheria, the only difference seen being a less luxuriant growth of the true diphtheria as compared with the pseudodiphtheria.

Urine-agar, potatoes, alkaline serum, and antitoxic serum gave no positive results as a means of differential diagnosis. In a limited number of observations on the growth in ascitic fluid Schabad was able to confirm the observation of Januszewska, that the pseudobacillus gave a diffuse cloudiness while the true bacillus did not.

Differentiation by Morphology.—The shape, length, and thickness of the diphtheria bacilli varies greatly with the medium, the number of colonies, temperature, age of cultures, etc. Schabad believes, therefore, that Martin's classification into short, medium, and long bacilli is purely arbitrary.

In order to give any weight to the morphology of the two organisms as a means of differential diagnosis, they must be placed as nearly as possible under the same conditions of growth. In this way the pseudobacillus may often be recognized by its shorter length, greater thickness, regular staining, and parallel disposition. The ratio of the length to the breadth of the true diphtheria bacillus varies from 5 : 1 to 8 : 1. The pseudodiphtheria bacillus varies from 2 : 1 to 4 : 1, and, furthermore, the pseudobacillus in actual thickness is usually $1\frac{1}{2}$ to $2\frac{1}{2}$ times greater. Symbiosis, temperature, and fluidity of the culture-medium were found to influence the length of the bacilli. The morphologic differentiation of the two sets of bacilli is only facultative, not obligatory, and under certain conditions of growth all the characteristics of the true diphtheria may be seen in the pseudobacillus.

According to Escherich, the true and pseudodiphtheria appear in three forms: (1) Short, wedge-shaped; (2) cylindric; (3) club-shaped. The first, with rounded ends, is the most characteristic for both true and false diphtheria. The staining in this form is usually regular. Occasionally the ends are more deeply stained than the center with alkaline methylene-blue. In the cylindric form, segmental staining is characteristic with 2, 3, or 4 joints to a bacillus. The third is not a degenerative type, as it occurs in serum cultures after twenty-four hours. It is usually found with abundant culture-media. In a fresh serum culture the diphtheria bacillus generally shows the second or third type, the pseudobacillus the first. In young serum

cultures the so-called Ernst-Neisser polar granules are regularly seen in the diphtheria bacilli, in the pseudobacilli only in old cultures.

Schabad regards the polar granules in pseudobacilli as atypical. They are round, with a diameter less than that of the bacillus, so that a protoplasmic space is to be seen about them not so deeply stained. They are often multiple in one bacillus, though but few bacilli show them at all. Occasionally the ends of the true bacillus are more deeply stained without a distinct granule. The author states that great care should be exercised in regard to the temperature at which the bacilli are grown, in order to give weight to this method of differential diagnosis, and under these circumstances he has not found an acid-forming bacillus which did not give typical granules in fresh serum cultures, and never typical granules in a pseudobacillus.

Reaction in Bouillon Cultures as a Means of Differentiation.—The value of the chemical reaction in bouillon cultures as a means of differential diagnosis is variously estimated by different observers. Zarniko first called attention to its importance. Roux and Yersin believe that both true and false diphtheria bacilli at first form acid and later alkali. The pseudobacillus, however, begins the formation of alkali earlier and more rapidly than the Löffler bacillus. Spronck, Neisser, and Kurth have seen acid-forming pseudobacilli. The latter has divided pseudobacilli into (1) B. pseudodiphtheriæ alkalifaciens, and (2) B. pseudodiphtheriæ acidumfaciens.

Schabad, in commenting on these conclusions, points out the fact that litmus-paper was used as a test of reaction, instead of the more delicate one of titration with phenolphthalein. Furthermore, he shows the importance of testing the bouillon immediately before inoculation and of using a bouillon neither too acid nor alkaline. With these precautions it was found that the pseudobacilli either forms alkali from the beginning, or a very small amount of acid, which soon is neutralized and goes over to alkali. He is strongly of the belief that the acid-forming bacilli are avirulent true diphtheria bacilli.

Pathogenicity as a Means of Differentiation.—This is by no means to be relied upon, as we now know that true diphtheria bacilli may be absolutely non-pathogenic. In regard to pseudodiphtheria there is, again, a difference of opinion. Some authors—Spronck, Fränkel, Zupnik, Gelpke, and others—believe that they are pathogenic in varying degrees. The great majority, however, have seen only local effects,—edema, loss of hair, etc.,—and occasionally a slow process of general deterioration in health, and finally death from some intercurrent disease. Schabad has seen only local effects following injec-

tion. Spronck showed that if six to sixteen hours before inoculation the guinea-pigs were given antitoxic serum equal to $\frac{1}{5000}$ to $\frac{1}{1000}$ of body-weight, the true, even if avirulent, diphtheria bacilli caused no local edema, while that caused by the pseudobacilli was not influenced. It was the result of these experiments which led Fränkel to join the dualist school. Schabad was able to confirm these experiments, but found that in some cases the guinea-pig inoculated, together with the control, died of chronic diphtheria toxemia, from injections of avirulent diphtheria bacilli. He concludes that in the case of slightly virulent diphtheria bacilli, Spronck's method of differential diagnosis gives only indefinite results.

Schabad's conclusions are as follows:

1. Diphtheria and pseudodiphtheria are two distinct organisms.

2. The difference between them lies in their growth in different culture-media (especially agar and ascitic fluid), in their morphology, reaction in bouillon culture, coloration with Neisser's stain, and pathogenesis for animals.

3. Neisser's stain and reaction in bouillon are the most important means of differential diagnosis.

4. Avirulent diphtheria bacilli should be kept distinct from pseudodiphtheria bacilli; they are in all respects identical with virulent diphtheria bacilli except in their lack of virulence.

5. To the mistaking of avirulent diphtheria bacilli for pseudobacilli is attributable the failure of many writers to attain definite results with Neisser's stain and reaction in bouillon.

6. Avirulent diphtheria bacilli can in all cases be distinguished by the above methods from pseudobacilli.

Many attempts have been made to classify the various diphtheria-like bacilli which have been found in almost every part of the body, and in association with various diseases. Thus, they have been found in cancer, stomatitis, noma, dysentery, otitis media, etc.

De Simoni has attempted a classification of the various types, according to their methods of stain, growth on different media, etc. He acknowledges, however, that this division is artificial, and not necessarily inclusive of all forms of pseudodiphtheria bacilli. He believes that the xerosis bacillus exists in several different forms and cannot be considered as more than a very frequent dweller on various mucous membranes, especially the conjunctiva, normal or inflamed.

Schanz* believed in the identity of the xerosis bacilli and pseudobacilli, and that under certain circumstances not stated the former

* Deutsch. med. Woch., 1894, S. 149.

could become virulent and cause diphtheria. Peters came to a similar conclusion.*

Among the more recent attempts at classification of pseudodiphtheria bacilli is that of Gromakowski. This observer examined 81 cultures of pseudobacilli from cases of conjunctivitis and angina; 61 cultures were taken from the conjunctiva. He divides them into three classes, according to their morphology and their growth on different culture-media. Three different kinds were found in the conjunctival sac, and on this account they may be set down as xerosis bacilli:

First, thick pseudobacilli of different lengths. In bouillon cultures these are arranged in small groups. Some are long, club-shaped; others like lengthened cocci. These do not make the bouillon cloudy. There is a precipitate at the bottom of the glass after twenty-four hours, which disappears on shaking. On blood-serum the growth is slow. There is no acid formation in bouillon. Little or no pathogenicity for guinea-pigs. Local edema is shown in a few cases, not controlled by antitoxin. These gave negative results when placed on the conjunctiva. Eight cultures gave a positive result by Neisser's stain in twelve hours; 28 cultures after eighteen hours; and 4 cultures after thirty-six hours. In some cases the stain was not to be distinguished from that shown by Löffler's bacillus. In others the bacilli were thicker and the polar granules had a less diameter than the bacilli.

Of the second variety six were found in the conjunctiva, seven in the throat. They resembled diphtheria bacilli very closely in growth and morphology, having rounded ends, two or three times longer than broad, and in old cultures showed thickening on one or both ends. Their position to one another was not characteristic. In bouillon a light cloudiness was seen after twenty-four hours, with a thick deposit and a thin film on the surface. The bouillon cleared after a week in the thermostat. Six cultures gave an alkaline reaction in bouillon and seven did not affect the reaction. No result in guinea-pigs and none in conjunctival sac of man. Neisser's stain was found negative in all cases.

The third variety was the smallest, and was found four times in the conjunctival sac and three times in the throat and nose: short rods, twice as long as thick, with rounded ends and arranged in parallel rows. They were found to stain badly with methylene-blue, the center less colored than the ends, and thus appearing segmented. The bouillon was slightly clouded after twenty-four hours with a very

* *Centralbl. f. Bact.*, 1896, Nos. 16, 17.

light precipitate. After three days only a slight clearing ensued, and there was a fairly marked precipitate of round form, not disturbed by shaking, but becoming feathery in appearance. There was no result in guinea-pigs. In bouillon four cultures gave no results in reaction; in three, alkali. In all the cases Neisser's stain was positive, but not before twenty-four to thirty-six hours.

Neisser's stain proved useless in making diagnosis of diphtheria of the conjunctiva, as the first class gave the stain after twelve to twenty hours, so that control by animal inoculation was necessary. In cases of angina the stain was of more value in making a diagnosis.

The examples given will suffice to give an idea of the confusion that exists at present as to the proper classification of the various diphtheria-like bacilli. The problem must for the present remain unsolved. The question is of great importance as a matter of scientific as well as practical interest: *i. e.*, to know if, under any circumstances not yet understood, the organisms which are generally regarded as pseudodiphtheria may develop into virulent diphtheria bacilli. As a matter of practical differential diagnosis between true and false bacilli, the results given with Neisser's stain or alkaline methylene-blue in an alkaline blood-serum culture not over twenty-four hours old, and, if necessary, the reaction in bouillon and test of virulence in guinea-pigs, will enable the clinician to reach a probably correct conclusion as to the classification of a given organism.

It may be said, in brief, that a given diphtheria-like bacillus which produces little or no acid in bouillon cultures, that shows no or only atypical polar granules in a twelve to twenty-four-hour-old blood-serum culture, and is non-pathogenic for guinea-pigs, may be safely classified as belonging to the great class of pseudodiphtheria bacilli, and rules in regard to quarantine, treatment, etc., be followed accordingly.

PATHOLOGY.*

THE PSEUDOMEMBRANE.

Distribution.—This is very wide. Holt, in a series of cases occurring at the New York Infant Asylum, gives the following:

Above the larynx (63 cases): Tonsils only, 27 cases; pharynx or pharynx and tonsils, 18 cases; pharynx and nose, or rhino-pharynx, 18 cases.

Not above the larynx (10 cases): Larynx only, 6 cases; larynx and trachea, 1 case; larynx, trachea, and large bronchi, 1 case; larynx, trachea, large and to smallest bronchi, 2 cases.

Both above and below the larynx (36 cases): Pharynx and larynx, 12 cases; pharynx, larynx, and trachea, 6 cases; pharynx, larynx, trachea, and large bronchi, 4 cases; pharynx, larynx, trachea, large to smallest bronchi, 10 cases; nose, pharynx, larynx, and trachea, 1 case; nose, larynx, and trachea, 1 case; pharynx and trachea (none in larynx), 1 case; pharynx, trachea, and bronchi (none in larynx), 1 case. Total, 109 cases.

Lennox Brown in 1000 cases reports as follows:

Above the larynx (841, or 84.1%): Fauces (including tonsils) alone, 672 cases; nose alone, 2 cases; fauces and nose, 165 cases; mouth or lips alone, 1 case; hard palate alone, 1 case.

Involving the larynx (159, or 15.9%): Larynx alone, 4 cases; larynx and fauces, 109 cases; larynx, fauces, and nose, 46 cases.

Councilman, Mallory, and Pearce, in 220 cases examined, found a definite membrane, postmortem, in 127 cases. These patients were treated with antitoxin, and in many cases the membrane had disappeared before death: Tonsils, 65 cases; epiglottis, 60 cases; larynx, 75 cases; trachea, 66 cases; pharynx, 51 cases; nose, 43 cases; bronchi, 42; left palate and uvula, 13; esophagus, 12; tongue, 9; stomach, 5; duodenum, 1; vagina, 1; vulva, 1; skin of ear, 1; conjunctiva, 1.

The membrane was found on the tonsils alone in 7 cases; trachea

*The studies of Councilman, Mallory, and Pearce have been freely consulted in the preparation of this part of the subject. "A Study of the Bacteriology and Pathology of 220 Fatal Cases of Diphtheria," by W. J. Mallory, F. B. Councilman, and R. M. Pearce, Boston, 1901.

2; larynx, 3; pharynx, 1; left palate, 1; esophagus, 1; epiglottis, 2; mucous membrane of nose, 1; and in all others several structures were involved by the membrane.

In regard to the extension of the membrane in laryngeal cases, before the use of antitoxin in 87 postmortem examinations made at the Foundling Hospital the extent of the pseudomembrane was as follows: In 9 cases it extended from the tip of the nose to the finest bronchi; in 6, from the nose to the bifurcation of the trachea; in 17, from the pharynx to the finest bronchi; in 17, from the larynx to the finest bronchi; in 17, from the pharynx to the main bronchi; in 17, in the larynx and trachea; in 3, in the pharynx and larynx; and in 1, in the larynx only (Northrup).

Autopsies made on diphtheria cases which have been treated with antitoxin seldom show this extent of membrane, and it is not unusual in laryngeal cases which have given severe symptoms of stenosis to find only a little redness and swelling of the parts at autopsy.

Histology.—The pseudomembrane may be white or yellowish or a dirty brown, or even black. It may be tough and leathery or more or less friable, firmly adherent to the underlying tissues, as when situated on the uvula or pharyngeal wall, or easily detached, as in the trachea. Councilman, Mallory, and Pearce have made minute and exhaustive studies of the pseudomembrane in the cases already referred to. The work itself must be consulted for the detailed results, a brief synopsis of which is as follows:

The tonsillar membrane shows best the variations in structure. Two varieties of it are seen, corresponding to the macroscopic appearances: First, dense, firm, elastic membrane, which can be stripped off in large flakes; and, second, the more friable variety. The first is composed of a reticular structure with considerable uniformity in the size of the beams composing it.

The tissue of the reticulum is much denser and more refractile than ordinary fibrin and is irregularly stained by Weigert's method. It is homogeneous in structure. Occasionally nodules are seen in the beams. Irregular masses of tissue resembling the membrane of the reticulum are seen adjacent to it or lying within its spaces. They are of about the same size as the epithelial cells and are occasionally continuous with the remaining epithelium. These masses are undoubtedly epithelial cells and leucocytes which have undergone hyaline degeneration and play an important part in the formation of the hyaline membrane.

A membrane of this sort may cover the whole tonsil, or, again, it

PLATE I.
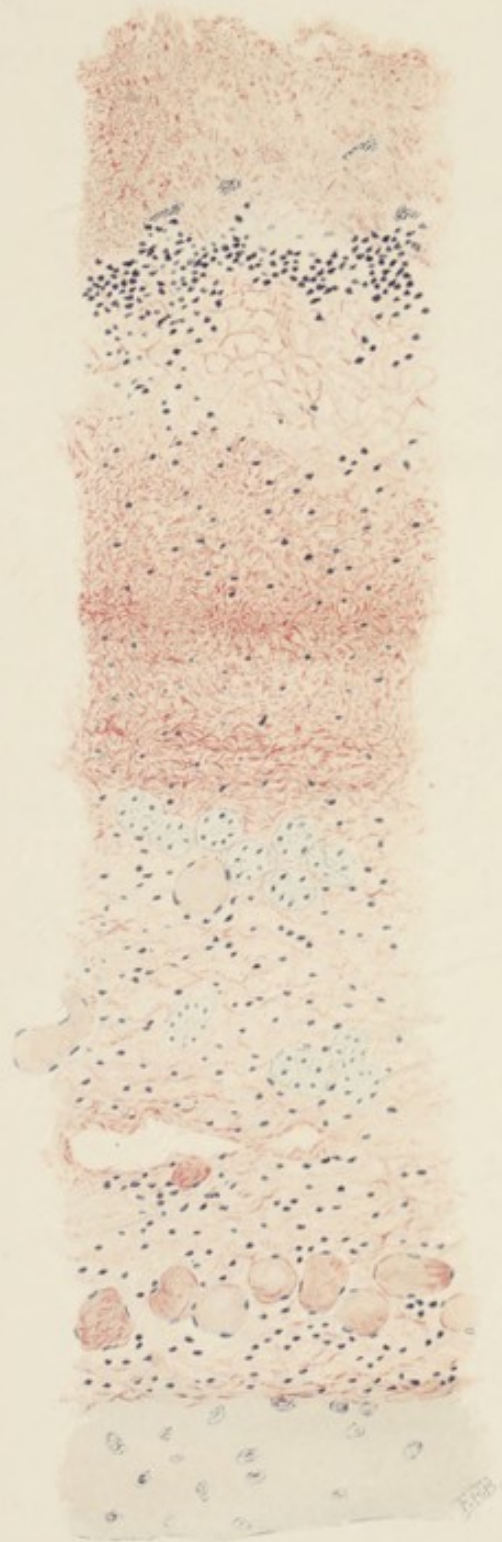
Section of trachea, showing diphtheritic membrane.
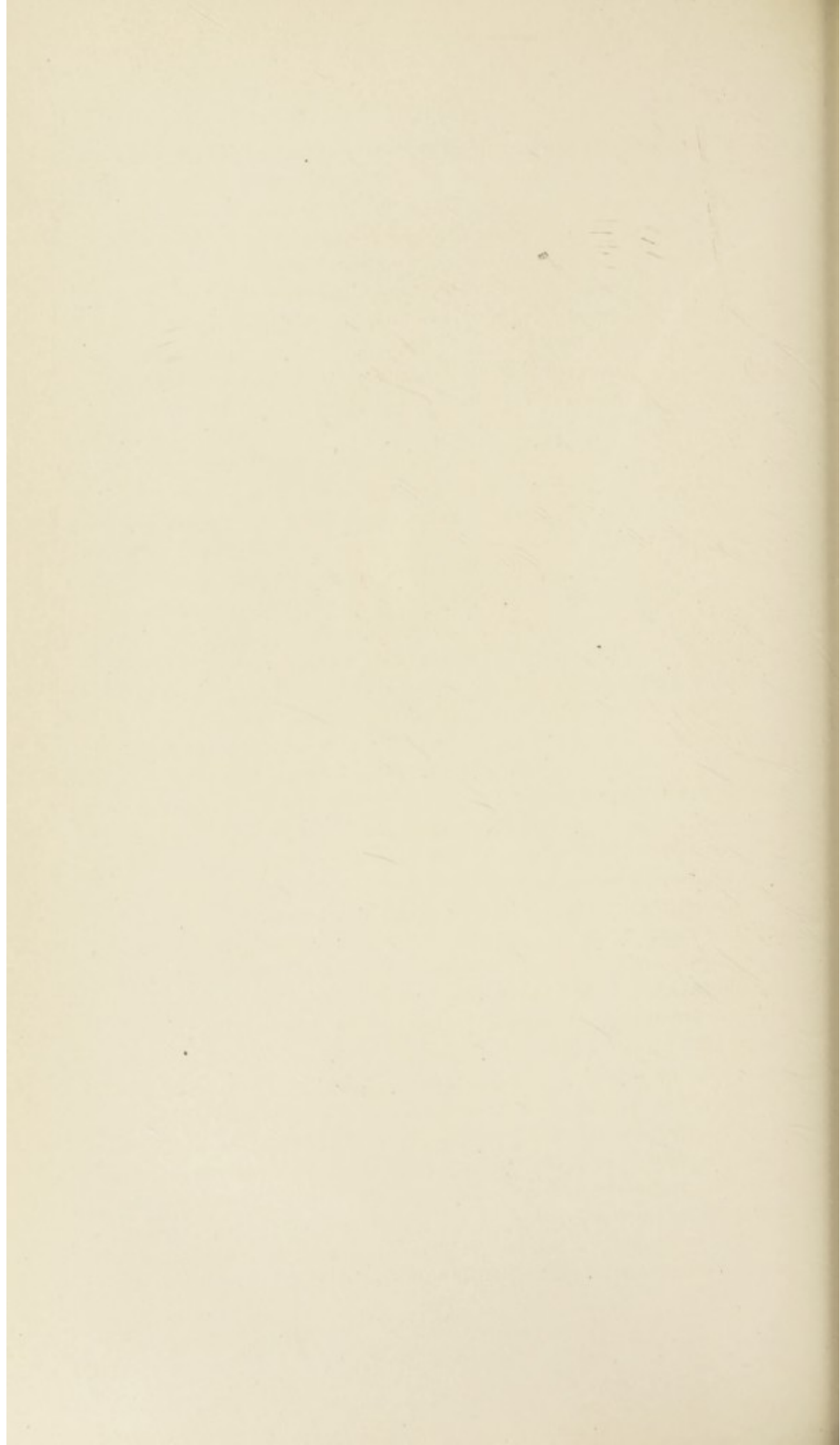
may form only the upper part of the entire pseudomembrane and be separated from the tissue beneath by fibrin. The surface of the epithelium is usually swollen and more or less disintegrated.

The second or more friable variety of membrane is composed of fibrin forming a reticulum, just as in the case of the hyaline membrane, but with more irregular spaces and fibers. The fiber is often arranged in whorls. In the fibrin spaces there are numerous leucocytes, which are well preserved or present only as a detritus. This fibrinous membrane often extends over the whole surface of the tonsil and penetrates the crypts. The hyaline membrane is never seen in the latter.

The epithelium beneath the membrane of both varieties is absent. Occasionally, however, a few cells of the lower layer remain. The meshes of the reticulum are occasionally distended and the membrane lifted up by an exudation formed beneath and in its substance. The membrane rarely is in actual contact with the mucous membrane, but is separated from it to a greater or less extent by a space containing granular material, leucocytes, and nuclear fragments. The epithelium beneath and in the vicinity of the membrane shows various alterations. It contains numbers of polynuclear leucocytes and lymphocytes situated between and in the epithelium cells. Red blood-corpuscles are also found in it, generally but not always outside of the epithelial cells. Where the epithelium comes into contact with the membrane, and in places on the surface not in contact with it, there is an enormous multiplication of the nuclei by direct division. The crypts in places denuded of the epithelium are filled with necrotic tissue and fibrin. The lining epithelium of the crypts is loose, edematous, and infiltrated with cells. The blood-vessels of the papillæ extending into the epithelium are surrounded by lymphoid and plasma cells. The tissue beneath the membrane and beneath the epithelium, when this is present, shows a necrosis with dense fibrinous exudation, often containing nuclear fragments. In some cases there is more or less extensive infiltration with red blood-cells. There may be a hyaline degeneration of the epithelium, especially in the epiglottis and trachea. A considerable amount of fibrin is found in the tissues. That coming from the fibrin factors in the exudation is simply deposited in the tissue, which is probably necrotic, and which has undergone first a hyaline metamorphosis (desmoid pseudofibrin of Baumgarten).

The changes in the trachea produced by the membrane differ in many respects from those found in other places. (See Plate 1.)

In general the membrane is distinctly fibrinous. Three or more distinct layers can be made out. On the surface is a rather granular mass composed of nuclear detritus and broken up fibrin; beneath this, the definite fibrinous reticulum with small and generally flattened spaces. In some cases it is filled almost exclusively with polynuclear leucocytes with occasional red blood-cells. The cells are either well preserved or much degenerated. Between this layer and the membrana propria, and frequently separated from the former by a dense mass of fibrin, is a layer in which the fibrinous network shows much larger meshes.

Thicker masses of fibrin pass into the membrana propria perpendicular to it. From these columns lateral communicating fibers are given off. Cells are contained in the meshes. They are arranged in a row along the membrana propria. As a rule, only the nuclei are present. Remains of the epithelium are seen in the trachea beneath the mucous membrane, but it is always profoundly affected. Among the remains of the epithelial cells are a very few red blood-cells and occasionally lymphocytes.

Beneath the membrana propria there often exists an extensive hemorrhagic exudate; also in the glands and filling up the ducts. The membrane does not usually extend into the mucous glands. The membrana propria is usually intact, and a few leucocytes may be seen passing through it. Occasionally below it are small areas of hyaline fibrinoid metamorphosis of the connective tissue. Portions of the adjacent membrana propria occasionally exhibit the same change.

In cases in which membrane was found on the tongue as an extension from the tonsils it was, as a rule, fibrinous in character. On the pharynx and palate the membrane was similar to that described on the tonsils. The fibrinous variety was more often seen than the hyaline. On the epiglottis both hyaline and fibrinous membrane were found, usually the latter.

In regard to the changes in the blood-vessels beneath the membrane the following were noted: The dark color of the membrane often found was due to the large number of blood-cells. Usually immediately beneath the membrane the blood-vessels were occluded by a mass of very much the same character as the membrane, fibrinous in some, hyaline in others. The entire wall of the vessel was swollen, hyaline, and stained with fibrin stain. The vessels were often surrounded with a membrane connected with that above and almost unrecognizable. The change affected veins, arteries, and capillaries.

The steps of the various changes could be traced in the walls of the small arteries; small masses of homogeneous material giving the fibrin stain first appeared between the muscle-cells of the media. The process bore a marked similarity to amyloid infiltration of blood-vessels; *i. e.*, a hyaline fibrinoid metamorphosis similar to that described in the connective tissue. The muscles immediately beneath the media were not altered. Thrombi were frequently found in the veins. Here, too, was found proliferation of the cells of the media. The superficial and deep lymphatics were dilated, containing a finely granular material and very few cells. Their nuclei showed no change. The changes in the mucous glands varied from congestion and slight degeneration to complete necrosis. This degeneration would account for the small amount of mucus excreted in connection with the membrane. There were found alterations in the striated muscles of the pharynx, most noted nearest the membrane. These consisted of general edema, hemorrhage, and infiltration with leucocytes. The first change consisted in the disappearance of the fibrilla, which seemed to begin in the center of the fiber. In the swollen fibers appeared a system of vacuoles, giving a reticulated appearance. In the more altered fibers this was lost, and the homogeneous material showed fine fracture lines radiating from a center or broken up into a number of masses. In the most altered fibers the nuclei had disappeared or were fragmented, and often contained leucocytes.

In the earlier cases in which there was a definite membrane the diphtheria bacilli were found almost constantly. In the later cases they were generally missed. They were found chiefly in clumps of varying sizes on the surface of the membrane, particularly in the trachea, in the necrotic areas and fibrin, and in a few instances deep down in the membrane, where they stained poorly. They were found also on the surface of the hyaline reticulum and occasionally inclosed in polynuclear leucocytes deep in the membrane. In no case were bacilli found in connection with epithelial degeneration, which should properly be regarded as the initial lesion in membrane formation. In cases where the bacilli were most numerous they were often found in pure culture. Cocci were frequently mixed with them, especially in the tonsils and in necrotic masses. The membrane and the necrosis due to it were found occasionally to be invaded by fungi.

Councilman, Mallory, and Pearce believe, from the results of their observation, that the earliest lesions in membrane-building are caused by diphtheria toxins, and that later, when necrotic

areas are formed, these form suitable media for the growth of the bacilli. The membrane is never formed on an intact epithelial surface, but may extend over it. Nothing is to be gained by making a distinction between croupous and diphtheritic membrane. They have found typical hyaline and fibrinous membranes in cysts of the ovary in the formation of which bacteria played no part.

NERVOUS SYSTEM.

No lesion of diphtheria is so characteristic of the disease as the changes which take place in the nervous system. These changes have been frequently proved by the inoculation of filtered cultures to be due to the toxins of the Löffler bacilli and not to the presence of the bacilli themselves. They are seen most frequently in the prolonged cases of diphtheria. In those running a rapidly fatal course, the lesions are frequently missed. While most authors are agreed as to the character of the lesions seen in the peripheral nerves, there is still a marked difference of opinion as to the occurrence of lesions in the brain, spinal cord, and various ganglia. Studies on this subject have been numerous, and extend over a great many years. Thus, in 1862 Charcot and Vulpian described degenerative changes in fibers of the nerves of the palate. In 1871 Oertel found capillary hemorrhages of the cerebrospinal dura mater and of the sheaths of the peripheral nerves, and also noted infiltration of the nuclei and granulations of the anterior cornua of the spinal cord. In 1878 Dejerine described not only changes in the peripheral nerves, but found that the cells of the anterior cornua were globular, deficient in processes, and that their nuclei and nucleoli were indistinct. In some cases the cells had been entirely destroyed. This author also found lesions in the anterior roots, corresponding to the distribution of the paralyzed nerves. In 1881 Paul Meyer came to the conclusion that the toxin acted on the peripheral nerves as well as on the cord.

Bikeles and Kalisko, in 1894, by using Marchi's method of staining, found a characteristic degeneration of the posterior roots where they enter the gray matter of the posterior cornua, which lesions they regard as responsible for the ataxic symptoms occurring in diphtheritic paralysis. (See Symptoms of Diphtheritic Paralysis.)

In 1896 Manicatide published a paper based on the study of 19 cases of diphtheritic paralysis, which he divides into four groups, as follows:

1. Purely muscular changes with no nerve involvement.
2. Polyneuritis.
3. Lesions of the spinal cord, which were either localized in the gray matter, leading to atrophy of muscle, or involved the white matter of the cord, in a similar way to that seen in locomotor ataxia or multiple sclerosis.
4. Cerebral paralysis chiefly due to circulatory changes.

Rainy, from a series of experiments, concludes that diphtheritic paralysis is associated not only with changes in the peripheral nerves, but also with alterations in the spinal cord itself. Such changes were invariably observed after death when symptoms of paralysis had existed. The cellular changes are the most characteristic lesion, but this may be associated with vascular ones. They consist in marked chromatolysis, increased staining capacity of the chromatic substance for acid stains, and vacuolation of the cell protoplasm. In diphtheritic paralysis these cellular changes are probably antecedent to the nerve lesions in the majority of cases, but further proof is needed of this fact.

In the gray matter of the cord many of the cells in the anterior cornual group present two types of marked alteration. Some were slightly swollen. Nissl's bodies presented the appearance of somewhat advanced disintegration; the achromatic substance stained but faintly. The nuclei and nucleoli appeared to be normal and the nuclear membrane, which, owing to the disappearance of much of the chromatic substance of the cell body, was often unusually conspicuous, was not crumpled. Some cells were markedly shrunken.

J. J. Thomas in an examination of 25 cases found, first, marked parenchymatous degeneration of the peripheral nerves, sometimes accompanied by an interstitial process, hyperemia, and hemorrhages. Second, acute diffuse parenchymatous degeneration of the nerve-fibers of the cord and brain. Third, no changes or but slight in the nerve-cells. Fourth, acute parenchymatous and interstitial changes in the muscles, especially the heart. Fifth, occasional hyperemia or infiltration or hemorrhage in the brain or cord.

Woodhaven has found certain changes in the trophic centers of the nerve-cells after twenty-four hours of intoxication, and believes that this accounts for the changes seen in the peripheral nerves as described by Sydney Martin and Dejerine. He believes with Moura-vieff * that if no great demand is made on these centers no especial *

* *Archives de Med.*, vol. ix, p. 1108.

symptoms are produced. If, on the contrary, there is such a demand, there is degeneration shown in them, perhaps of a Wallerian type.

Many writers have found no lesions of the cord, but only of the peripheral nerves. Thus Arnheim, in 1891, found no changes in the medulla or nerve-center. Hyperemia and capillary hemorrhages were seen in the peripheral nerves and spinal cord, and slight inflammatory processes in the muscles. There was marked parenchymatous and interstitial degeneration of the peripheral nerve-fibers. The ganglia cells showed no abnormality.

Vincent found lesions of the cardiac plexus in a case of diphtheria dying with symptoms of cardiac paralysis; *i. e.*, a parenchymatous and atrophic neuritis. The great degeneration or disappearance of the myelin sheath, the changes in the axis-cylinder, the clearly marked absence of multiplication of the nucleus, all seemed to indicate an actual process of degeneration and not changes due to an irritant. The pneumogastric nerve and its center were normal. This author found that these results were similar to those described by Gombault, Herrman, Huguenin, and Hochhaus. In some of the cases, however, described by these authors there were, in addition to the above lesions, a pigmentary degeneration in some cells of the sympathetic ganglia.

Councilman, Mallory, and Pearce refer to the work on this subject being done by J. J. Thomas and H. S. Steensland. The results of this work, not yet finished, show that in certain cases of diphtheria there is a slight to marked diffuse fatty degeneration of the nerve-fibers of the central nervous system and of its peripheral extensions.

HEART.

The first record of careful and systematic examination of the heart lesions produced by diphtheria is that of Hayem.* This author gives a minute description of the alterations in the cardiac muscle (granular and fatty degeneration) and of the lesions of acute interstitial myocarditis.

Rosenbach† described granular and waxy degeneration of the muscular fibers and cellular infiltration of the interstitial tissue. Waxy degeneration had been earlier described by Bouchut.‡ This lesion

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* " Etudes sur les myositis symptomatique," *Archiv de Physiologie*, 1870.
† *Virchow's Archiv*, 1877, lxx.   ‡ *Gaz. des Hôp.*, 1872.

PLATE 2.

FIG. 1.—Myocardium, showing separation and degeneration of muscular fibers.

FIG. 2.—Section of myocardium, showing acute interstitial myocarditis.
(Councilman, Mallory, and Pearce.)
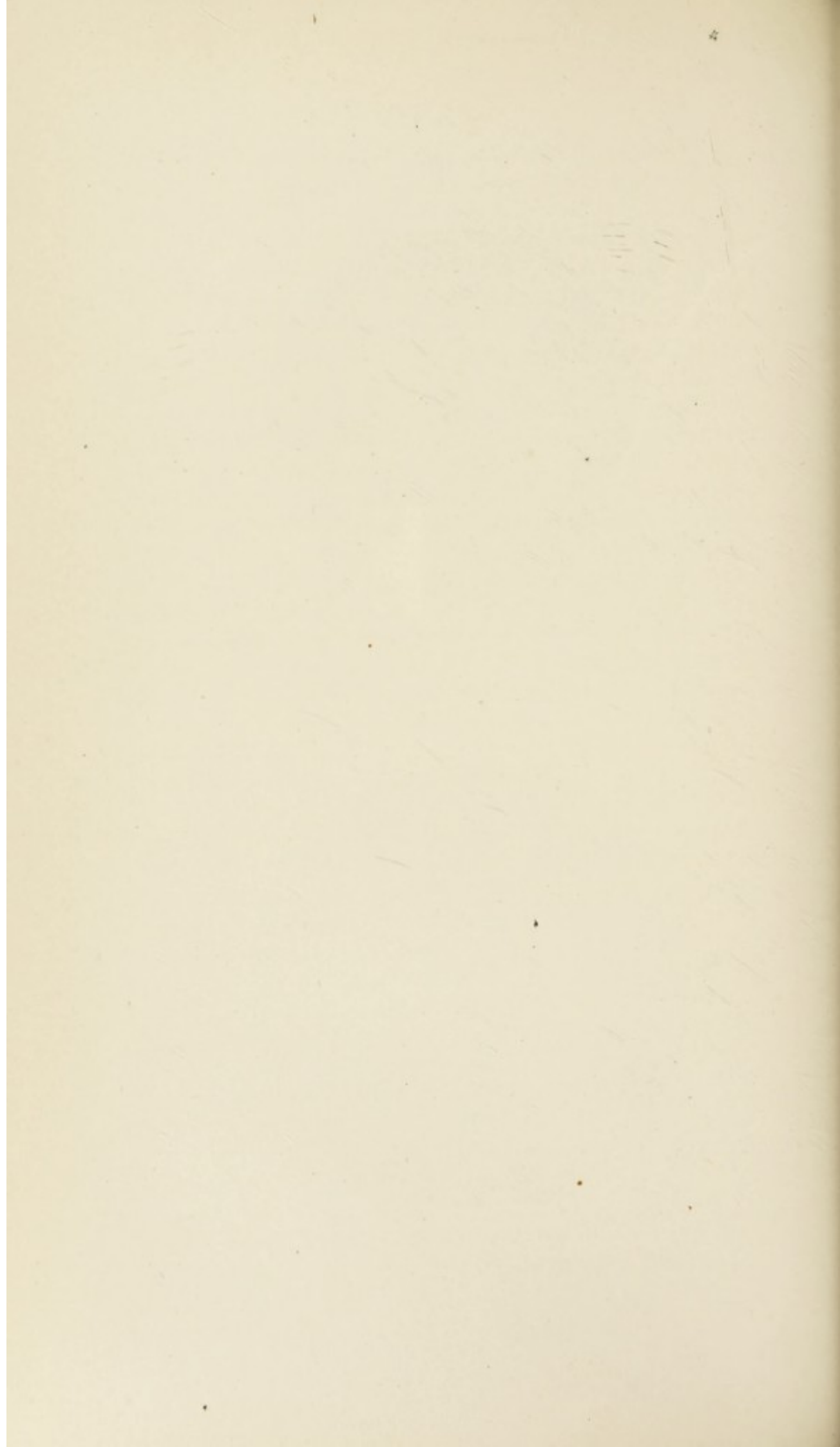
has since been noted by various investigators, notably by Ribbert. Loewenthal was unable to confirm these findings in an examination of 34 cases.

In the last decade the literature on this subject is very extensive, and the findings in most cases in experimental and natural diphtheria are fairly uniform. Huguenin* describes granular and hyaline degeneration of the muscle-fibers, increase of connective tissue and of the nuclei of the cells, and small hemorrhages. Romberg, in 1891, made a valuable contribution to this subject.† He found great difference in the extent of the lesions in sections taken from different parts of the heart. Degeneration of the muscle-fibers, with occasional vacuolation, was the most common lesion. The nuclei showed changes which were regarded by the author as a process of degeneration. Interstitial changes were found in all of 8 cases examined. They occurred in foci, and most often beneath the pericardium. These foci may heal, suppurate, or lead to fibrous myocarditis. Hesse found that the heart, as a rule, showed a well-contracted left ventricle and a flabby right. Both ventricles may be hypertrophied and dilated. The pericardium showed hemorrhages occasionally, especially in septic cases; the heart-muscle, granular degeneration affecting a great or small number of the fibers; the granules were fatty and albuminous. Hyaline degeneration was seldom noted. In the parts affected the transverse striations were poorly marked or absent. Nuclear changes were observed.

Parenchymatous degeneration was seen especially in the right heart; the base, apex, and auricles were most frequently affected. These changes were only noted to any marked extent when the disease had lasted for some days (fifth to eighth day). The blood-vessels were distended and in many cases filled with lymphocytes. They were swollen, thickened, and edematous (as though boiled). The endarteritis described by the French observers was not noted. Capillary hemorrhages occasionally occurred. As to the increase in the round cells, the author states that in many cases it is difficult to give an exact opinion, as the number of the cells is normally large in the hearts of children. In places, however, there were areas where the increase was enormous. The nerves and ganglia showed no abnormality. In only 4 of 29 cases was there very marked interstitial change, and this occurred in cases of long duration or complicated by scarlet fever.

The changes in the cardiac plexus found by Vincent have already

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* " Etudes anat. path. de la myocard.," Paris, 1890.
† *Deut. Archiv für klin. Med.*, 1891, xlviii.

been noted. This writer found in the single case examined little change in the muscular tissue, there was some loss of striation, increase in the nuclei of the sarcolemma, capillary hemorrhages, and periarteritis. The author refers to the work of Lantino, who performed unilateral section of the vagus on 16 animals and found lesions of the myocardium at autopsy, from which fact Vincent feels justified in drawing the conclusion that the degenerative changes found in the heart-muscle are secondary to those found in the cardiac nerves.

Schamschin* found the degenerative changes above noted, and also fatty degeneration of the walls of the small blood-vessels and their cells. Papkaw† believed that the fragmentation of the muscle-fibers was due to the swelling and destruction of the cement substance and to the cardiac weakness seen at an early stage of the disease. Scagliosi‡ believes that the ordinary process is an acute parenchymatous myocarditis, and that the poison produced by the diphtheria bacilli first produces changes in the blood-vessels, and thus gains access to the heart-muscle itself. Round-celled infiltration was not commonly observed.

Mollard and Regnaud§ conclude from their experiments that the muscular fiber of the heart is attacked, sometimes exclusively, in all primary cases. The lesions, starting from the muscular substance, cause changes in the striations, and later attack the nuclei and cytoplasm, causing vacuolation, exudation, etc., and may lead to complete destruction of the muscular substance. Lesions of the blood-vessels of the myocardium are seen frequently. The muscular coat of the arterioles is particularly affected. The alterations in the smooth muscle-fibers are similar to those of the cardiac muscle, and take place at the same time as the latter.

In the acute and subacute cases there is no apparent hyperplasia of the connective-tissue elements. The only important modification in the latter is a leucocytosis. The diffuse interstitial leucocytosis is apparently only a part of the general leucocytosis occurring in diphtheria. The interstitial nodular leucocytosis is seen only in connection with the areas of muscular disintegration. The primary lesion of the muscle provokes the leucocytosis, and the leucocytes absorb the muscular debris, and particularly the sarcous exudates. The areas of disintegration are areas of phagocytosis.

Councilman, Mallory, and Pearce made a complete examination of the heart in 60 cases of diphtheria, and conclude that degeneration of

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* *Ziegler's Beiträge*, 1895, xviii.   † *Wratsch*, 1895.
‡ *Virchow's Archiv*, 1896, cxlvi.   § "Annal de l'Institut Pasteur," 1897.

the myocardium is one of the most common conditions found in this disease. The simplest and most common form is that of fatty degeneration, found in the majority of all cases, and occurring in foci diffusely distributed throughout the myocardium. It may appear in the form of fine granules or in large globules involving the greater part of the muscle-cell. The fatty degeneration accompanies and seems to precede the more advanced forms of degeneration, leading to muscle destruction. In the latter there is destruction of the sarcous elements, which are converted into hyaline masses. In other cases large vacuoles are formed in the cell, differing in size and shape from the fat vacuoles. Fragmentation and fracture of the degenerated muscle-cells are often found. Simple fatty degeneration is found in the severe cases of short duration, the more extensive degenerations in the prolonged cases. The lesions are due to toxins. Acute interstitial lesions of two sorts are found. In one there are focal collections of plasma and lymphoid cells in the tissue, which may be accompanied by degeneration of the myocardium, but are not dependent upon it. In the second the interstitial change consists of a proliferation of the cells of the tissue secondary to the degeneration of the muscles. This condition may lead to fibrous myocarditis. Thrombosis due to the primary necrosis of the endocardium is not uncommon. Proliferation of the intima is the only lesion of the blood-vessels of any importance found.

LUNGS.

Comparatively few extensive studies have been made on the histologic pulmonary lesions complicating diphtheria. Most of the work has been undertaken with the object of determining the cause of these lesions. As to the frequency of occurrence of bronchopneumonia in fatal cases of diphtheria, to one who has performed many autopsies on these cases it would seem exceptional not to find at least a few areas of bronchopneumonia. Holt states that the latter occurs in at least three-fourths of the cases. Councilman, Mallory, and Pearce, in 220 cases examined, found lesions of pneumonia in 60%, divided as follows: Of 100 cases with membrane (in epiglottis, larynx, trachea, or bronchi), bronchopneumonia was present in 72%; in the remaining cases (120) examined, in only 48%; in 76 intubated cases, in 7 of which tracheotomy was also performed, 80%. This great frequency of bronchopneumonia in cases in which the lower respiratory passages are involved has been generally noted, and goes to prove the aspiration theory of the disease.

The work of Flexner has been already referred to in regard to the

rôle played by the diphtheria bacilli in causing pneumonic lesions. Flexner found by inoculating the trachea of rabbits with diphtheria bacilli that pneumonia was induced in a very short time. This he believes to take place by direct infection, and also through the blood and lymph channels. The pneumonias thus produced experimentally were of a cellular type, fibrin playing but a small part, and in their distribution were lobular or pseudolobar. The pneumonia developed from the bronchioles, atria, and air-sacs. The bronchi were only moderately involved.

While these experiments prove conclusively what is conceded by most observers, that diphtheria bacilli alone may cause broncho-pneumonia, a great majority incline to the belief that while the diphtheria bacilli or its toxins may be responsible for the beginning of this complication, its further development is carried out by other organisms—streptococci, pneumococci, etc. That the latter germs are alone found in a good proportion of the cases is no proof that the bacilli of diphtheria are not present, or were not at an earlier stage, for, as Flexner has shown, the diphtheria bacilli are difficult to find and impossible of cultivation in many cases after the actual development of the pneumonia.

Mya believes that the frequency of this complication in diphtheria is due to the mechanical and chemical disturbance caused by this disease, which, in turn, predisposes to secondary infection by other organisms.

Councilman, Mallory, and Pearce, in the cases above referred to, have endeavored by direct examination and by culture of the various bacteria found in pneumonia to determine the part played by each in causing the various lesions. They conclude that the character of the pathologic process is little, if at all, influenced by the character of the micro-organism. Thus the pneumococci, streptococci, and diphtheria bacilli were found in connection with serous, purulent, fibrinous, and hemorrhagic exudations, necrosis, and abscess formation. They believe that the pneumococcus most often produced the pulmonary lesion. The diphtheria bacillus was frequently found, and may be the cause of the various lesions described above. In 18 cases the latter were found alone, and were frequently the only bacteria found in definite foci of bronchopneumonia. In these cases they were in the air-spaces, and generally in enormous number. The infection is believed by the authors to take place mainly through the bronchi, and not to any extent by embolism. In only one case was there found evidence of the embolic action of diphtheria bacilli.

EXPLANATION OF PLATE 3.

FIG. 1.—Primary infection about atrium: *a*, Atrium; *b*, air-sac; *c*, alveolus.

FIG. 2.—Section through large area of complete consolidation. The opening in the center represents a bronchus. There is fibrinous exudation in the surrounding air-spaces, shown by the dark masses within them. In the lung elsewhere the exudation is cellular. *a*, Artery accompanying bronchus, with masses of fibrin in the lymphatics around it.

FIG. 3.—A lobule of the lung completely solidified, with very slight exudation in the adjoining lobule. The interlobular septum contains fibrin. *a*, Lymph-spaces in interlobular septum filled with fibrin.

FIG. 4.—Primary infection of terminal bronchus and atria. *d*, Bronchus; *a*, atrium; *c*, artery accompanying bronchus.

FIG. 5.—Section of lung showing several small foci of exudation affecting terminal bronchi and atria. *a, a, a,* Terminal bronchi.

(Councilman, Mallory, and Pearce.)

PLATE 3.

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.
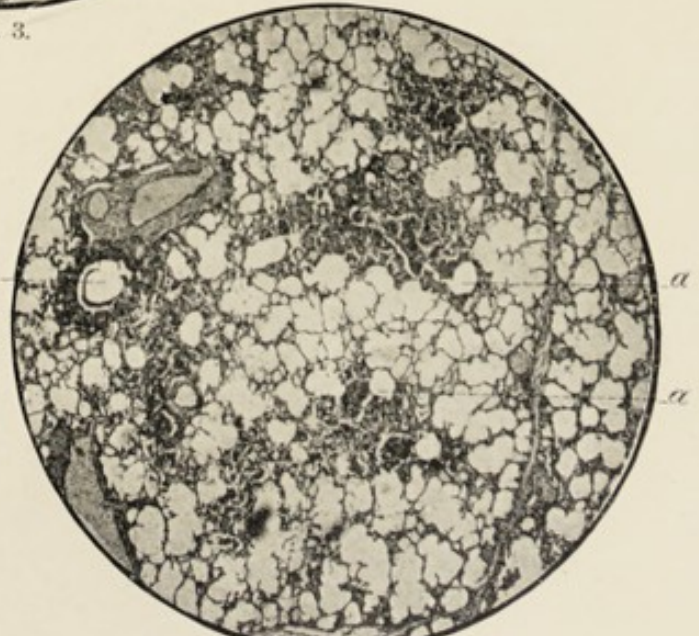
FIG. 5.
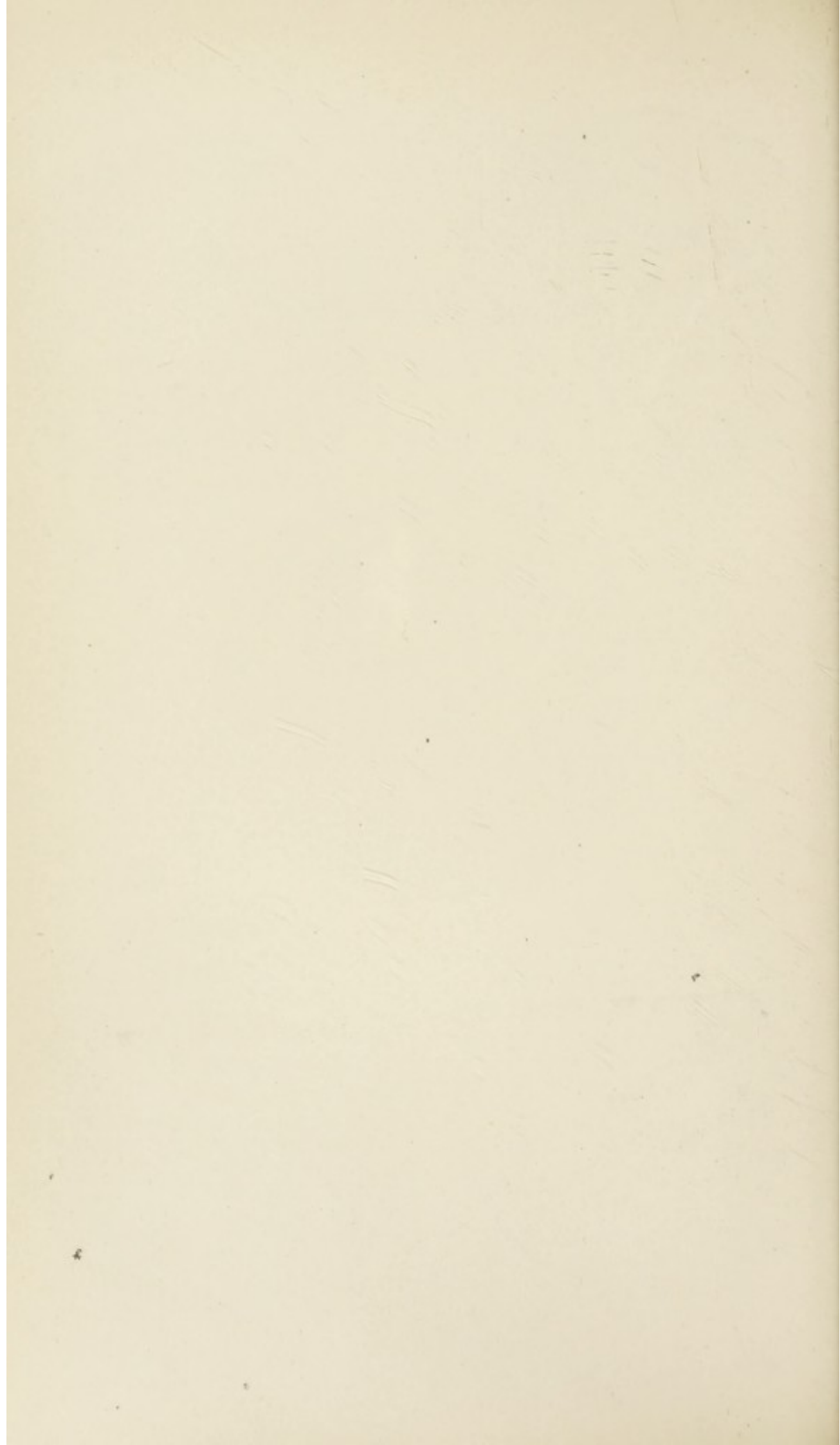
In no cases was true lobar pneumonia found. In the cases which resembled the latter, examination always showed confluence of bronchopneumonic areas. The distribution of the bronchopneumonia was as follows: In 131 cases, 27 showed involvement of only one lobe of the lung; 21 showed two or more lobes of the lung; 26 showed one or more lobes of both lungs; 57 showed involvement of all lobes of both lungs.

In regard to the histologic lesions, the authors sum up the results of a very exhaustive study briefly as follows: The bronchopneumonia begins as an infection of the atria, and from there extends. It may be limited to a single atrium, to lobules, or to groups of lobules. There is but little lateral extension of the infection through the walls of the alveoli or the bronchi into the surrounding air-spaces. Acute inflammation of the larger bronchi usually occurs, but is not constant. Atelectasis and emphysema of variable extent are very commonly seen. Inflammatory edema is of common occurrence. General edema of the lung was not met with. The exudation may be fibrinous, hemorrhagic, serous, or almost entirely cellular. In a few cases hyaline exudation was met with. The cells in the exudation were derived in part from proliferation of the lining epithelium, in part from leucocytes. Lymphoid and plasma cells were also found. Cellular infiltration of the interstitial tissue and productive changes in it were frequently met with in connection with the exudative lesions and apart from them.

In some cases organization of the exudation and connective-tissue formation within the air-spaces were found. Proliferation of the lining epithelium or the air-spaces was frequent, and always pronounced in the vicinity of the pleura and the connective-tissue septa. This may possibly be explained by the concentration in the lymphatics of substances causing proliferation.

Necrosis, in some cases leading to abscesses, is not an uncommon feature. In the capillaries were frequently found what the authors regarded as marrow-cells, frequently in a state of degeneration. Single strands of fibrin are sometimes found in the capillaries and interstitial tissues; never definite thrombi. The latter were occasionally found in the larger vessels. Dilatation of the lymphatics was common. They may contain coagulated albumin, fibrin, or cells, and are often packed with lymphoid and plasma cells and large cells resembling those in the air-spaces.

SPLEEN.

Bizzozero, according to a recent article of Waschkewitsch, first described the foci of cell infiltration in the splenic follicles. The lesions of the lymph follicles, infiltration with epithelial cells, and the presence of foci of necrosis have been since described by many writers. Babacci (1896) gives a minute description of the lesions of the spleen. He found that the follicles showed more or less marked swelling. In most cases there was also cell infiltration and cell hyperplasia, which affected the pulp about the follicle as well. In the center of the follicle were often seen masses of large epithelial cells. A local edema, either of the center or periphery of the follicles, was frequently noted. The blood-vessels of the follicle contained very little blood, very seldom showed distention, and still more seldom were hemorrhages seen. The cells sometimes showed clearly a nuclear division and ordinary karyokinesis, leading to hyperplasia. Necrotic areas were also occasionally observed, with destruction of the cellular elements. Fibrin was seldom seen. Hyaline degeneration of the follicular sheath, stroma, cells, and capillary walls were frequently observed, as well as hyaline masses in the necrotic areas; the latter probably derived from the cells. The changes in the splenic pulp consisted in cell hyperplasia, especially about the follicles and blood-vessels, and small parenchymatous hemorrhages. True necrotic areas were not observed, though occasionally cells more or less degenerated were noted. Fibrin and hyaline degeneration were rarely seen. The latter involved only the stroma. Waschkewitsch has recently made a study of the spleen in a large number of cases. Areas of large epithelioid cells were found in 21 out of 24 cases of diphtheria. That they were not characteristic of the disease is shown by the fact that in 170 other spleens examined they occurred in 11 cases. Most of the latter, however, were cases of purulent infection. Two were traumatic cases in which infection of any kind could be reasonably excluded, and one was a case of congenital syphilis. The author believes that these areas are not uncommonly found in the young dying of various diseases.

Councilman, Mallory, and Pearce have examined the spleen microscopically in 181 cases of diphtheria in which death occurred at various stages of the disease. Most of these, however, were children under four years of age, in which death occurred before the tenth day. The lymph nodules were not found to be abnormal in size. Occasionally very large ones were found, and in two cases they were unusually small. The greatest abnormality noted was the formation of small areas of

epithelioid cells, of hyaline formation, and a variable amount of nuclear detritus. The epithelioid formation usually occurred in the early cases; the hyaline changes in the later ones, rarely before the fifteenth day. These areas were found in 91 of the cases. Lymphoid cells were seen in some cases between the epithelioid cells. The cells were believed to come from proliferation of the cells of the reticulum. The center of the epithelioid areas was composed of hyalin, with remains of disintegrated nuclei. Hyalin occurred in the walls of the capillaries, and the vessels in the foci were closed by a proliferation of their cells. In most cases there was considerable nuclear detritus in these areas, chiefly found in the periphery and contained in the epithelioid cells. In some cases the cell destruction was very marked. The areas resembled closely young miliary tubercles. There was, however, no caseation or giant-cell formation. Disintegrated cells were also found in the follicle outside of these foci as well as in the spleen pulp. Fibrin was found in the nodules in 29 cases.

In 17 cases there was marked degeneration of the arteries in the lymph nodules, with or without the presence of foci of degeneration. These changes were confined to the smaller vessels of the follicles, but were not found in those of the pulp, and consisted of hyaline degeneration in the walls and narrowing of their lumen, often to a marked degree. They were found at a very early stage of the disease. The veins showed an accumulation of lymphoid and plasma cells in the intima, at times producing nodular projections into the lumen. The splenic pulp showed less change than the follicles. There was hyperemia, more or less pronounced, and in several cases hemorrhages. There was increase in lymphoid cells and a great increase in the plasma cells, which were found in masses and generally distributed. These masses were generally grouped about the small veins of the pulp. The cases showing this great increase in plasma cells had lasted, on an average, twenty-five days. In a few cases there was evidence of hyperplasia of the cells lining the blood-vessels. This was never seen in the arteries and veins of the pulp. No bacteria were found in the sections.

LYMPH NODES.

The foci of necrosis so often seen in the lymph nodes were first pointed out by Bizzozero. Later, Oertel described these foci more minutely, and noted also cell infiltration and hemorrhages, most marked in the nodes near the seat of the diphtheria lesion. Barbacci has recently made a study of the lesions found in lymph nodes, and finds swelling of the germ center and infiltration with leucocytes, espe-

cially in the periphery. Epithelioid cells were found in the interior of the nodes. Mitosis was observed in these cells. There were also areas which showed fragmentation of nuclei, and what appeared to be phagocytosis and nuclear destruction, and, finally, areas of actual necrosis, which were more frequently found in cases showing germ centers. Among the more general changes noted were: hyperemia, hemorrhages, edema of the nodes, hyperplasia, changes in the endothelium of the blood-vessels, fibrin in the glandular parenchyma, and hyaline degeneration.

Flexner has studied the lesions of the nodes produced experimentally. He describes the process of degeneration so often noted, and of cell proliferation. The phagocytic cells are believed to be derived from the germ centers.

Bezançon and Labbé have compared the results attained by injections of diphtheria bacilli with those attained by using only diphtheria toxin. In the former case no necrosis was produced, but an actual inflammation in the adjacent lymph nodes.

Councilman, Mallory, and Pearce divided the lesions found in the lymph nodes and tonsils into two classes:

1. Lesions which may follow an injury of any sort—congestion, hemorrhage, and diffuse and concentrated necrosis. Cells not ordinarily found in the tissue were noted, and appeared to be derived in part from the lymphoid cells, and also from proliferation of the cells of the sinuses and reticulum. The lymphoid cells were little, if at all, increased. The swelling of the nodes was found to be due chiefly to congestive hemorrhage and dilatation of the sinuses.

2. Lesions characteristic of diphtheria, but found in other infectious diseases. These consisted of foci very similar in appearance to miliary tubercles and formed by a process of proliferation, phagocytosis, and degeneration; thus, large epithelioid phagocytic cells, probably derived from the endothelium of the reticulum, and possibly of the blood-vessels, devour the lymphoid cells and give rise to the nuclear detritus seen in the foci. Later the epithelioid cells undergo degeneration and their nuclei are added to the detritus. Caseation and giant-cell formation were never seen. Bacteria are not regarded as the cause of these lesions, but they are the result of toxins caused by the lymphatics, and most noted in the vicinity of the afferent vessels. Certain minor differences were noted in the case of the tonsils, due to their anatomic structure and the presence of the diphtheria membrane. Lymphoid tissue of the intestinal lymphatics shows the same changes as the lymph nodes.

PLATE 4.

FIG. 1.—Section of cervical lymph-node, showing dilatation of the lymph-sinuses, which are filled with large mononuclear cells. At *a* there is a small mass of epithelioid cells.

FIG. 2.—Section of lymph-node containing circumscribed mass of epithelioid cells. The small dark points in the area represent nuclear detritus from lymphoid cells.
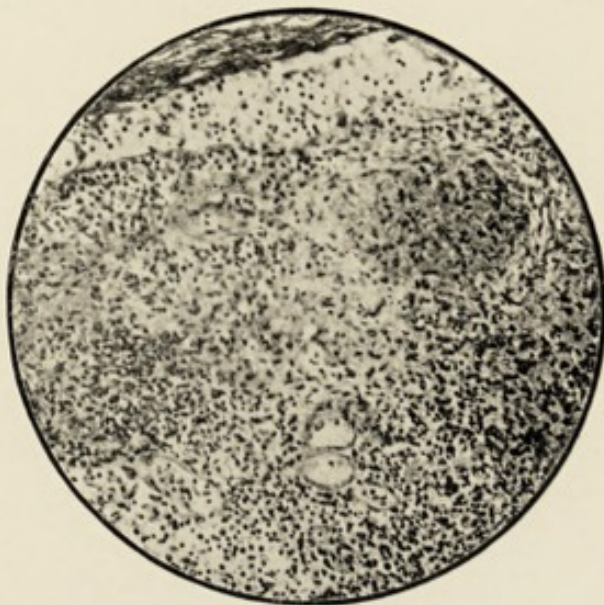
FIG. 3.—Small area of necrosis in lymph-node near the peripheral sinus. The necrotic tissue is invaded by polynuclear leucocytes, and no epithelioid cells have been formed.

(Councilman, Mallory, and Pearce.)
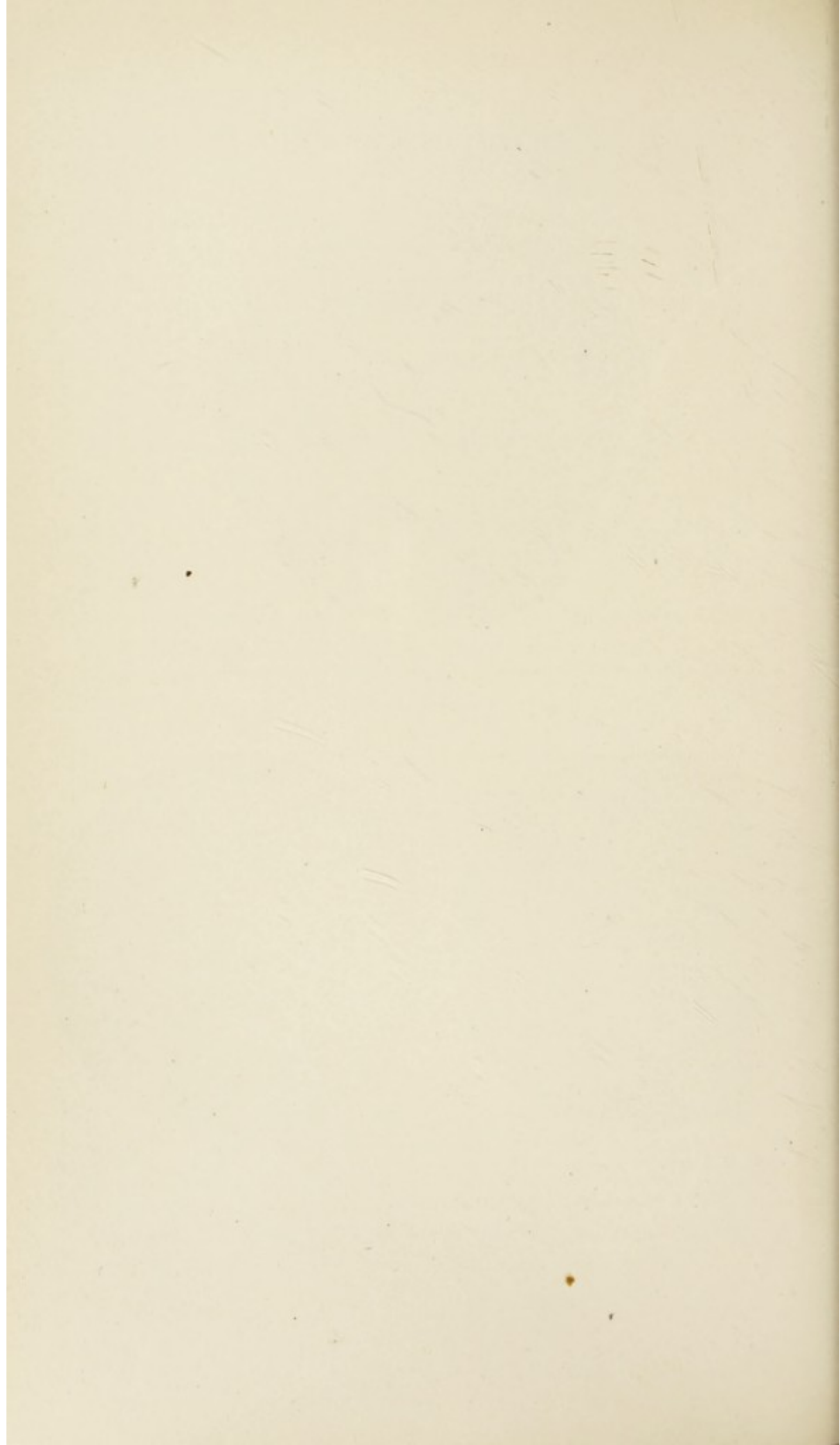
THYMUS.

Flexner found the same lesions in the thymus experimentally as in the lymphatic system elsewhere; principally cell degeneration. Councilman, Mallory, and Pearce find the same condition in 20 cases examined. This degeneration was found to be more profusely distributed than in the case of the lymph nodes, and also occurred in foci especially marked about Hassall's bodies. The lymphatics were dilated and hyaline degeneration of the blood-vessels occurred.

SKELETAL MUSCLES.

Councilman, Mallory, and Pearce find that, in cases where there is fatty degeneration of the heart and nervous system, a similar change will be found in the skeletal muscles.

BONE-MARROW.

These investigators have examined the bone-marrow in 48 cases. The changes found were not characteristic of diphtheria, but similar to that found in other infectious diseases. The marrow was found to be hyperplastic in all cases.

PANCREAS.

From the fact that the occurrence of glycosuria in diphtheria has been regarded as not uncommon, we should expect to find lesions of the pancreas. Councilman, Mallory, and Pearce find no such lesions. Girard and Guillain have examined this organ in 29 cases. They note the fact that hemorrhagic pancreatitis, simple hyperleucocytosis, and tendency to sclerosis have been found in experimental diphtheria. They, however, were unable to discover any of these lesions, but found only dilatation of the blood-vessels and some endoperiarteritis and endoperiphlebitis. The connective tissue was normal. There was perhaps in some cases a slight edema. Fatty degeneration was little marked. The authors believe that glycosuria in diphtheria is not a common occurrence, contrary to the statements of Hibbard and Morrissy, who found it in 25% of 230 patients. It is possible that too little attention has been paid to the examination for sugar in diphtheria. It is certainly not a routine practice in American institutions.

ALIMENTARY CANAL.

A number of cases of diphtheria of the stomach have been described in literature. Councilman, Mallory, and Pearce find five such

among their series of cases, and describe minutely the lesions found in connection with the presence of membrane. The membrane in all cases was found to be fibrinous in character, hemorrhagic beneath, and well developed in all cases. Very extensive degenerative changes in the glands were noted, not only in places underlying the membrane, but also where no membrane occurred. In one case the latter extended to the duodenum. Aside from the swelling and hyperplasia and the changes already noted in Peyer's patches and the solitary follicles, no lesions of any importance were noted in the intestine itself. During a recent epidemic of measles at the New York Foundling Hospital, two cases of diphtheria of the stomach were found at autopsy.

Courmont, Doyon, and Pariot, by injecting cultures of diphtheria bacilli into the circulation of dogs, found lesions of the small intestine which varied from a simple vasomotor dilatation, with or without diapedesis, to a true cellular exudation, constituting a true membranous enteritis. The lesions produced were proportionate to the amount of injection given. The authors believe that the toxins of diphtheria are eliminated by the intestines. Peyer's patches showed evidence of degeneration. Councilman, Mallory, and Pearce were unable to substantiate this theory, and believe that the slight lesions found in the intestine are the result of toxins circulating in the blood current, and are no proof of the elimination of the poisons by way of the intestines.

LIVER.

Until recently the important changes in the liver induced by diphtheria have not been noted. Among the earlier described findings are leucocyte infiltration, fatty degeneration of the liver cells, hyaline degeneration of the blood-vessels. Babes found, experimentally, changes in the liver cells, swelling, granulation, and fatty infiltration, areas of inflammatory foci in the lobules, proliferation and swelling of the endothelium of the blood-vessels, and groups of partly degenerated cells. The first exact description of the focal necrosis, which is now regarded as the most characteristic lesion of the liver in diphtheria, was given by Welch and Flexner as a result of their experiments. These lesions are regarded by Flexner as due to changes in the liver capillaries, which allow the toxins to have access to the adjacent liver cells.

Councilman, Mallory, and Pearce have studied the lesions of the liver in 180 cases. They describe two varieties of focal necrosis: First, that found about the central vein (found in 22 cases), and due,

PLATE 5.
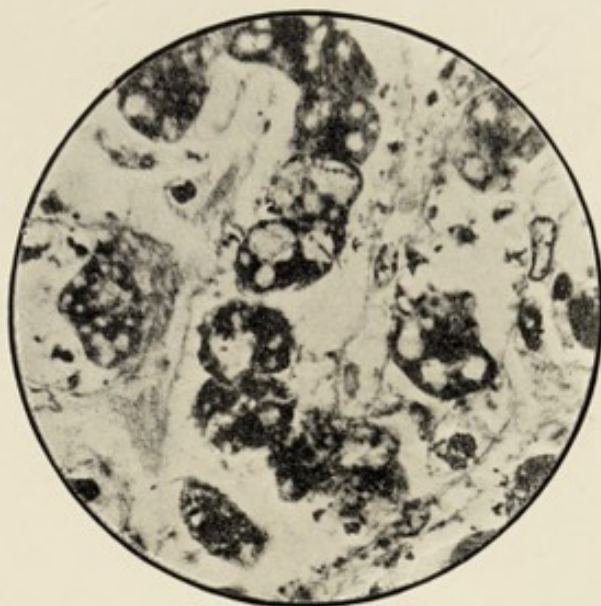
FIG. 1.—Degenerated liver cells from an area of central necrosis. There is a wide space between the degenerated liver cells and the capillary walls. The endothelial cells of the capillaries are swollen, and the vessels and spaces around the liver cells contain granular débris.
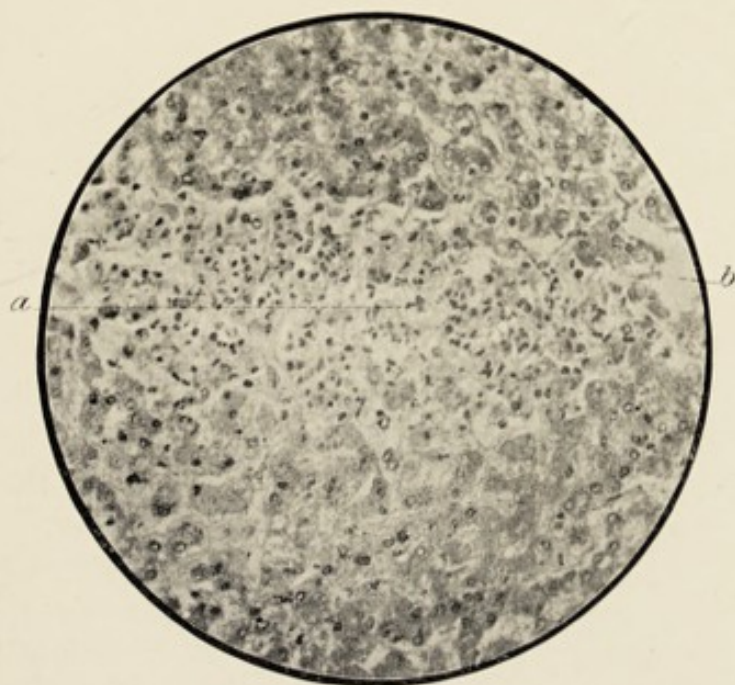
FIG. 2.—Focal necrosis of liver adjoining central vein of lobule. The small dark nuclei of the necrotic area represent polynuclear leucocytes, which have invaded the necrotic liver cells. a, Focus of necrosis; b, central vein.

(Councilman, Mallory, and Pearce.)

in their opinion, to obstruction of the capillaries by pressure exerted by the secondary exudation, and in part to occlusion by thrombi. In these foci few or no extraneous cells were found.

Second, disseminated areas of necrosis (found in 7 cases), due to capillary obstruction by fibrin, endothelial cells, and leucocytes. Many other cells apart from liver cells were mingled in these areas.

In both these varieties the necrosis is due to the action of the toxin after the changes in the blood-vessel take place. The authors point out the fact that lesions produced experimentally on animals are not exactly comparable to those found in man, as in the former case the liver cells are much more susceptible to the action of toxin, and disseminated areas of necrosis are invariably more frequent than the circumscribed. Other changes noted were a general degeneration of the liver cells (granular and fatty), slight hyaline degeneration of the capillary walls, and hyperplasia, produced by proliferation of their endothelium and by cells brought by the blood current.

It must not be supposed that these focal lesions are by any means characteristic of diphtheria. They have been found in many infectious diseases. By Councilman in yellow fever and amebic dysentery; by Reed in typhoid fever; and by Barker in malaria. They have also been noted at the Foundling Hospital in measles by Freeman.

KIDNEYS.

Lesions of the kidneys of greater or less extent are found in practically all cases of fatal diphtheria. They show no characteristics peculiar to the disease. They are classified by Councilman, Mallory, and Pearce as follows:

1. Degenerative changes. These were found in 112 of 171 cases examined. Fatty degeneration was only slightly marked. The degeneration of the epithelium of the tubes varied from a swelling and irregularity of the cells to complete destruction and desquamation. Some degree of hyaline degeneration was invariably present, even in the slight cases. Casts were always present, and were undoubtedly formed from the granular and hyaline degeneration of the cells. In the glomeruli there was often a small amount of granular coagulum between the tuft and the wall. In some cases there were swelling and hyaline degeneration of the epithelium of the capsules. In 40 of these cases the urine was examined, and showed albumin in 33. The amount of albumin, as a rule, but not always, corresponded to the degree of degeneration found. In the few microscopic examinations

made there were hyaline and granular casts.   Bacteria were found in
61 cases.   There was no apparent relation between the character of
the degeneration and general infection with various bacteria.

2. Acute interstitial changes.   These were found in 43 of the
cases.   The kidney was greatly enlarged in the most marked cases.
As a rule, but little so.   The increased size is chiefly due to the swelling
of the cortex.   The interstitial change was generally distributed
throughout the kidney, but was more intense in foci most marked at
the base of the cortex, adjoining the pyramids, just beneath the cap-
sule, and around the glomeruli.   Degeneration of the epithelium was
present to a greater or less extent.   The infiltrating cells, leucocytes,
phagocytic cells, and lymphoid cells were usually confined to the inter-
stitial tissue.   Nuclear figures were present in them.   Infiltrating
cells are also found in the blood-vessels, sometimes blocking their
lumen.   They were most abundant in the small veins in the upper
part of the pyramid.   In all of the interstitial cases the illness had
been more prolonged than in the cases of simple degeneration.   The
average duration of all cases was twenty-one and a half days.   The
severe cases occurred much more frequently in the older children
(average, nine to eleven and a half years).   The influence of the dura-
tion of the disease on the severity of the lesion was less marked.   Com-
plications played an important part in the occurrence of this lesion.
Thus, scarlet fever was present in 13; measles, in 5; tuberculosis, in
10.   In 15 cases examined albumin was present in 14.

3. Glomerular changes.   In 11 cases this was found to be the most
important lesion.   The first changes noted were an increase in the
number of cells, which in some cases projected into the lining of the
capillaries, and later the capillaries became entirely occluded and the
glomeruli converted into a confused mass.   Some of the lobules were
converted into hyaline masses and the glomeruli enlarged; the cells
of the covering epithelium were either unchanged or enlarged, increased
in number, and covered some of the lobules as a cap.   They were
found also in the capsular space.   Necrosis of the glomeruli with
hemorrhage into the capsular space was seen in two cases, one com-
plicated by cerebrospinal meningitis and the other by erysipelas.   The
average age of this class of cases was greater than that of the first two
classes.   The average duration of the disease was greater.   One case,
however, was only one and a half years of age.   The shortest duration
of the disease was four days in two.   The glomerular lesions were of
a chronic type and were probably to be referred to an acute ante-
cedent attack of endocarditis.   Four of the cases were complicated

PLATE 6.
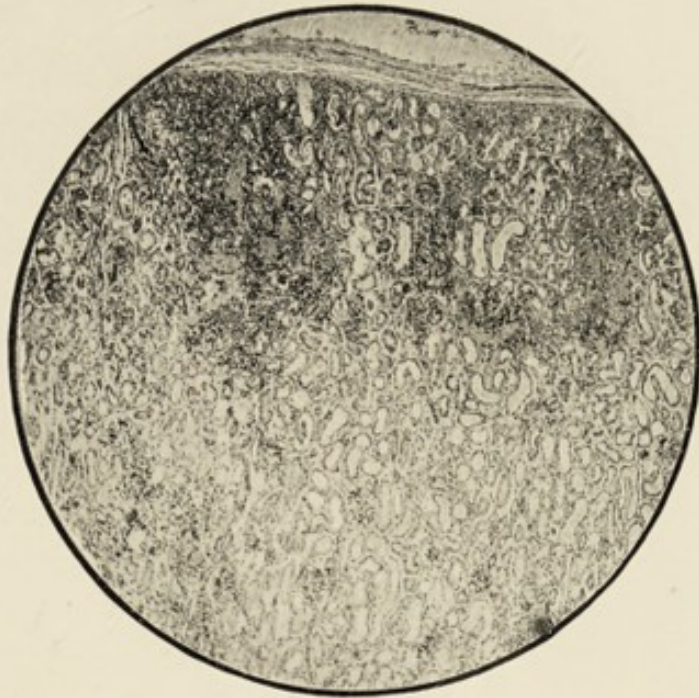
FIG. 1.—Acute interstitial nephritis, circumscribed foci of interstitial infiltration, with plasma cells chiefly beneath the capsule.

FIG. 2.—Longitudinal section of ascending loop of Henle. The ciliated border and the granules at the base of the cilia are well shown. The cells are swollen, their texture much looser than normal, and the lumen contains granules probably derived from the cells.
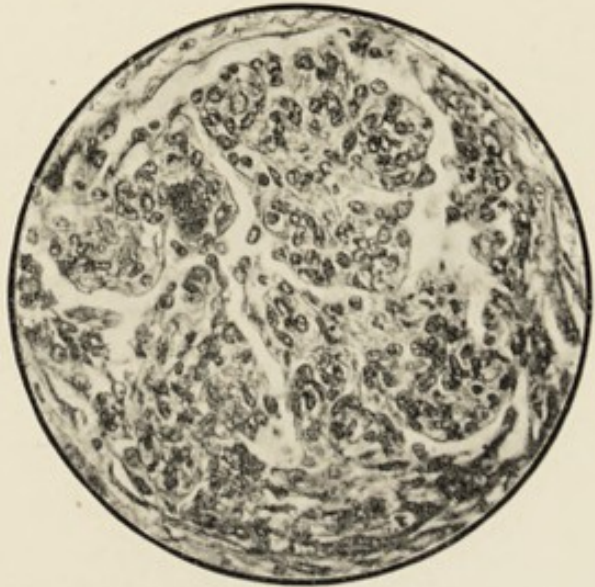
FIG. 3.—Glomerulus from an advanced case of glomerulonephritis. The glomerulus is lobulated and contains great numbers of cells. There is also a great increase of cells in the capsular space.

(Councilman, Mallory, and Pearce.)

with scarlet fever, one with measles, and one with both. In two there was general infection with the diphtheria bacilli; in four, with the streptococcus.

4. Hemorrhage. Slight hemorrhage was found in three cases and the hemorrhagic type of nephritis in one.

5. Chronic changes. Four cases showed atrophy of the tubules and increase in connective tissue. These lesions could not be referred to the disease. The authors conclude that the lesions found in the kidney are not due to the presence of bacteria in the blood, but to their toxins.

ADRENALS, THYROID, SALIVARY GLANDS, TESTICLES, AND PITUITARY BODY.

Although changes characteristic of those seen elsewhere in glandular structures have been noted in the cases of these organs by Welch, Flexner, and Wright, negative results were obtained by Councilman, Mallory, and Pearce in a large number of cases examined.

URINE AND BLOOD.

The changes in the urine and blood caused by diphtheria will be noted later (see Symptomatology).

SYMPTOMATOLOGY.

WITHIN the last few years bacteriology has enabled us to distinguish between the diseases characterized by production of false membrane. To one class belongs that caused by the presence of the Bacillus diphtheriæ of Löffler; to the other, the membranous inflammation so frequently seen as a complication of scarlet fever and measles, and occurring as a primary inflammation upon the tonsils and pharynx and elsewhere. The Streptococcus pyogenes is the germ most often responsible for the latter condition; occasionally the staphylococcus or both. The term diphtheria is here to be understood as referring to cases in which the diphtheria bacillus is present alone or combined with other organisms. The disease is so protean in its manifestations that it is necessary to divide it into several classes dependent upon its localization and clinical symptoms.

The classification followed by Monti would seem to be as satisfactory as any up to the present time: (1) Catarrhal diphtheria; diphtherie fruste; bacteriologic diphtheria. (2) Fibrinous or pure diphtheria. (3) Phlegmonous, mixed, or strepto-diphtheria. (4) Septic or gangrenous diphtheria (septicemia).

Diphtheria may be further subdivided, according to its localization, into: Angina, partial or total (angina toxique); diphtheria of the nose; diphtheria of the larynx (croup); diphtheria of the trachea and bronchi; diphtheria of the bronchi followed by infection of the larynx (so-called ascending diphtheria); occasional sites (eyes, anus, vagina, etc.).

Catarrhal Diphtheria (Bacteriologic Diphtheria; Diphtherie Fruste).—In a certain number of cases there will be found simply a redness and severe swelling of the pharynx and tonsils. If, on account of the occurrence of diphtheria in the family or neighborhood, a bacteriologic examination be made, Löffler bacilli will be found in the culture. This condition is usually transitory, clearing up in a few days; or, again, it may develop later into a membranous process. Such cases must be explained either by a low degree of virulence on the part of the organism, or a high degree of resistance on the part of the patient. As the bacilli by experimentation have been frequently found to possess great virulence, it would seem more rational to

regard the second factor as the determining one upon the course of the disease. While not of itself to be feared, this form of the disease is a constant source of real danger to those about, and should be as carefully quarantined as marked cases of diphtheria. Finally, it must not be forgotten that pseudomembrane may exist and not be noticed unless careful search be made; for instance, when it occurs on the back of the tonsil, uvula, nose, etc. Persons living in diphtheria wards—nurses and doctors—are frequently found to have virulent germs in the throat without showing symptoms of diphtheria.

Fibrinous Diphtheria.—Fibrinous diphtheria is caused by the action of the Löffler bacilli, uninfluenced by the action of any other organism. Its symptoms are local, due to the presence of the false membrane; and general, due to the toxins produced by the germs. In its benign or local form it is the least dangerous, producing few local or general symptoms, after-effects, or complications, and yielding more readily to treatment. In its toxic or general form it becomes much more dangerous, on account of the tendency of the membrane to spread to other parts, the greater amount of toxemia produced, and more frequent occurrence of complications.

Mixed, Phlegmonous, or Strepto-diphtheria.—This form of the disease is due to the associated action of the Klebs-Löffler bacilli and some other germ (in the great majority of the cases, the streptococcus) and their toxins.

Roux and Martin, by experiments on animals, have shown very clearly the effect of mixed infection. They inoculated rabbits with a virulent streptococcus taken from a diphtheritic membrane; the animals were but slightly or not at all affected. Afterward the inoculation was repeated, but the streptococcus was associated with the diphtheria bacillus and death quickly occurred. Bernheim has made similar observations. The same writers also showed by experiment that antitoxin had little or no effect in stopping the ravages of mixed infection.

Septic or Gangrenous Diphtheria (Septicemia).—This may begin as a septic condition. More often it follows a case of mixed, and more rarely fibrinous, diphtheria. As to the exact reason for a genuine case of diphtheria developing into septicemia, we are not yet in a position to determine. Most writers are agreed that it arises not from the action of the diphtheria bacillus alone, or of the streptococcus or other germs, but from their combined action, local and general.

According to Bernheim, in those cases in which the diphtheria bacillus produces the dominating influence, septicemia seldom if ever

occurs. Genersich holds the opposite view, and supports it by the results of examination of 25 cases of fatal diphtheria. In only 4 cases were streptococci found. In the other cases the staphylococci alone were found in the liver, spleen, and kidneys. Two only of the streptococcus cases had given symptoms of sepsis, and 5 of the staphylococcus. The writer concludes that the coexisting germs are not necessary to the production of septic symptoms, but that the latter may be caused by the diphtheria bacilli themselves. Few authors agree with this opinion, and it would seem probable that other germs, not necessarily the streptococci, must be associated with the diphtheria bacilli in order to produce true septicemia.

In the membrane of such a case Monti found long and short Löffler bacilli, streptococci, staphylococci, and many germs of putrefaction. The course of this disease will be described later. Suffice it here to say that it does not differ from the course of septicemia elsewhere: high fever, coming on suddenly, great glandular involvement, muscular weakness, rapid pulse, heart weakness, collapse, and generally death in a short time. The same combination of germs which produces this septic condition may cause gangrenous lesions if the patient survive. According to Girode, this occurs in a superficial form, producing small areas of loss of tissue in various parts of the mucous membrane. Severe gangrene is seen very rarely, generally about the throat, where it may cause perforations of the palate, or even invade the tissues of the neck, blood-vessels, etc.

GENERAL SYMPTOMS.

FEVER.

Fever in diphtheria is by no means characteristic, dependent, as it is, upon the localization of the membrane, its extent, the character of the germs, toxic products, and the complications—bronchitis, pneumonia, kidney involvement, etc.; and yet a knowledge of the temperature is of value in calling attention to these very conditions and in making a prognosis. Certain rules in regard to the temperature may be laid down as applicable to most cases of the disease. In pure or fibrinous diphtheria it has become almost a nursery adage that, in contrast to other conditions of the throat, there is little or no fever. In spite of this, however, if a complete record be taken it will be seen that there is an immediate rise of temperature, reaching its height as the membrane is fully formed, and then gradually declining, although the exudate persists.
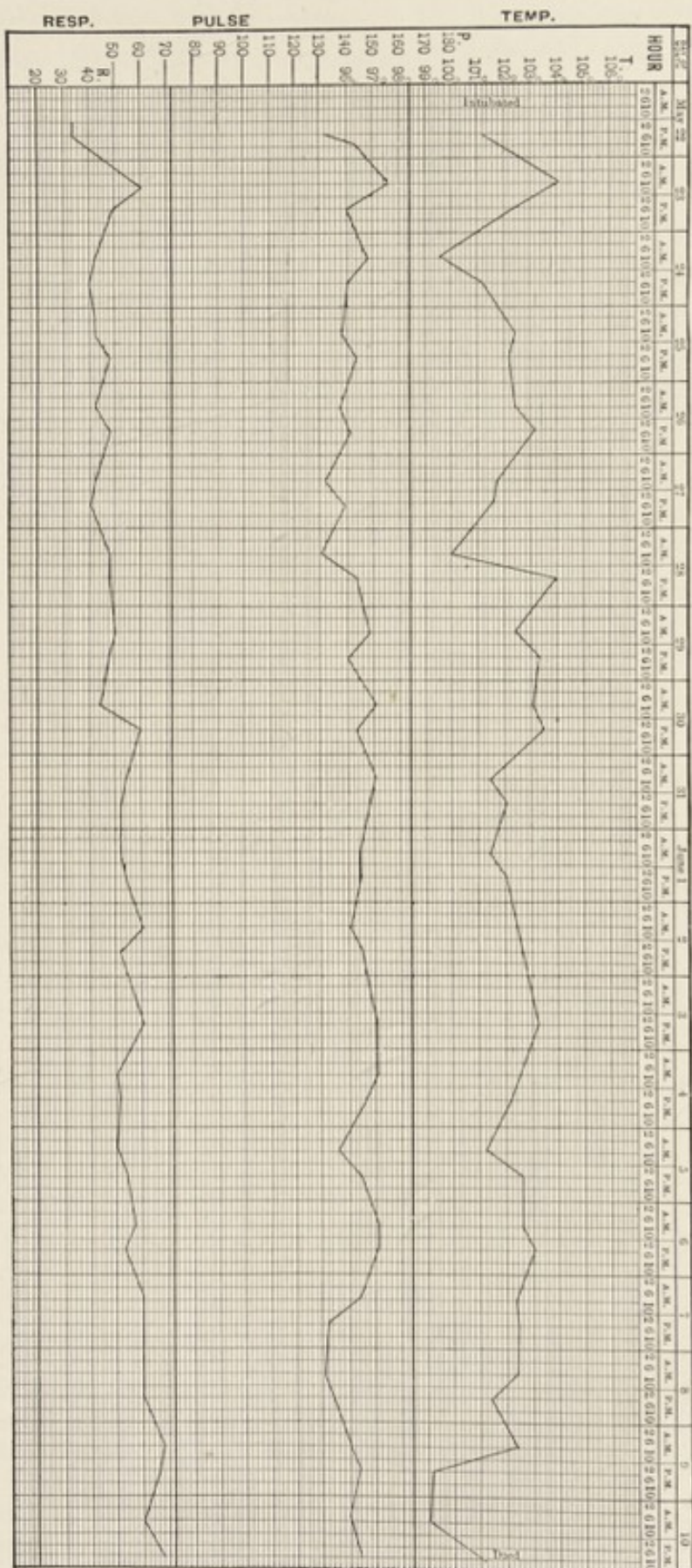
Fig. 9.—Laryngeal diphtheria; intubation; bronchopneumonia; death. M. H., aged one year and nine months; date of admission, May 22d. (Willard Parker Hospital.)

With each extension of the disease to another part there is further elevation of temperature.
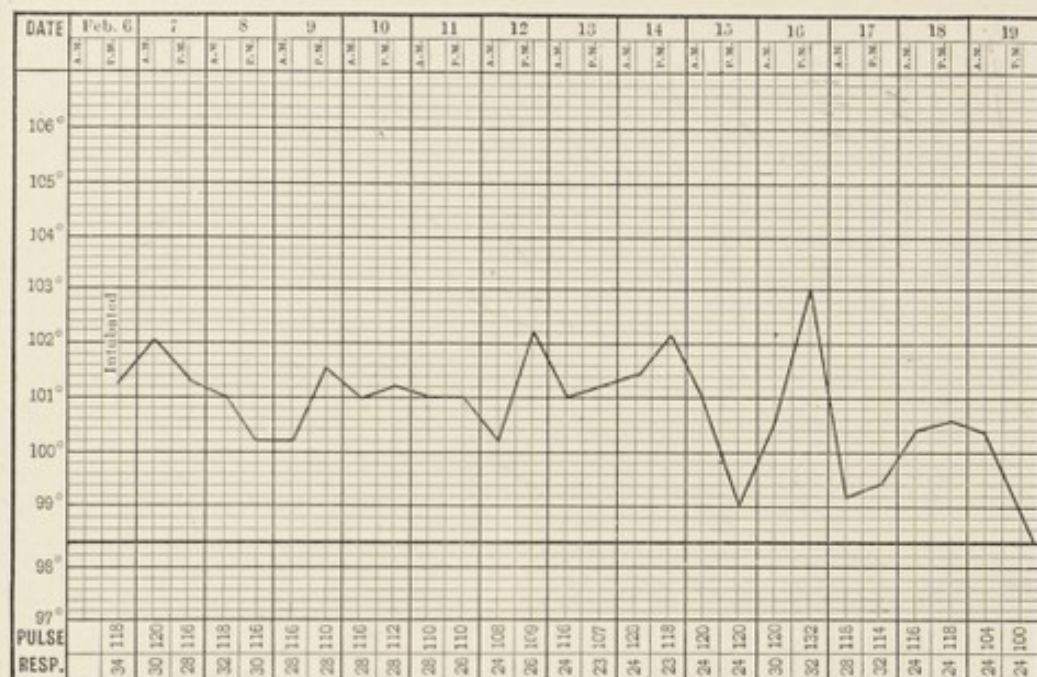
FIG. 10.—Laryngeal diphtheria; intubation; recovery. Mollie F., aged five years; admitted February 6th; discharged February 24th. (Willard Parker Hospital.)
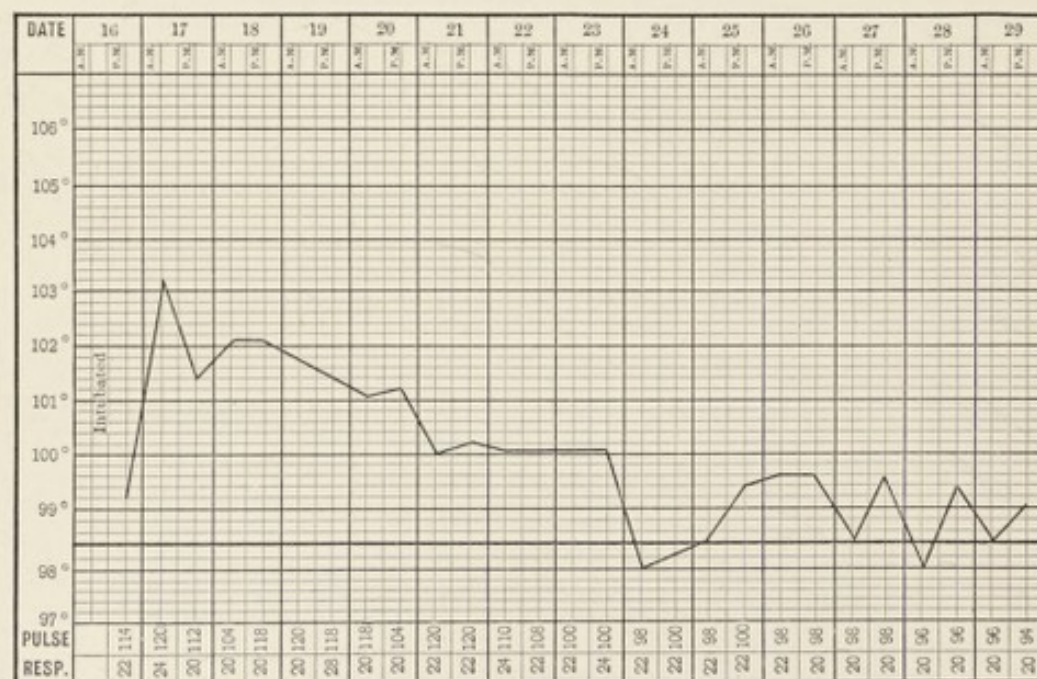
FIG. 11.—Laryngeal diphtheria; intubation; recovery. Celia G., aged four years and six months; admitted January 16th; discharged January 29th. (Willard Parker Hospital.)

In the mixed or septic form of the disease the temperature is dependent upon the amount of toxemia; the fever, however, is apt to

be higher, with frequent remissions. In any variety of the disease as each complication occurs the temperature rises. Finally, we shall note
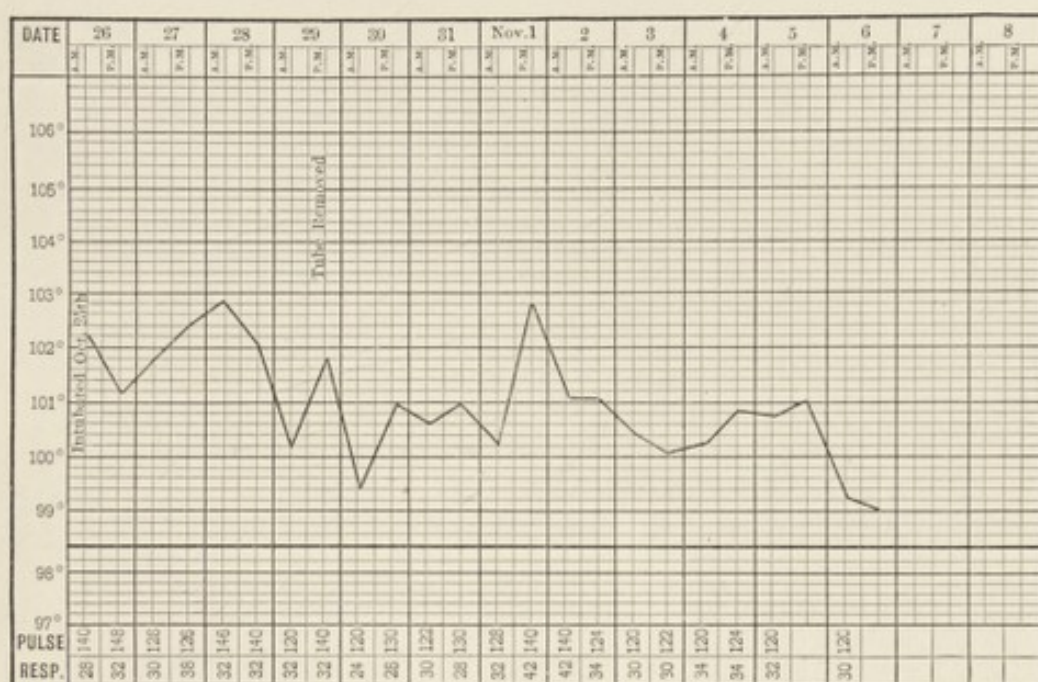
FIG. 12.—Laryngeal and pharyngeal diphtheria; intubation; recovery. Mary N., aged three years and six months; admitted October 26th; discharged November 7th. (Willard Parker Hospital.)
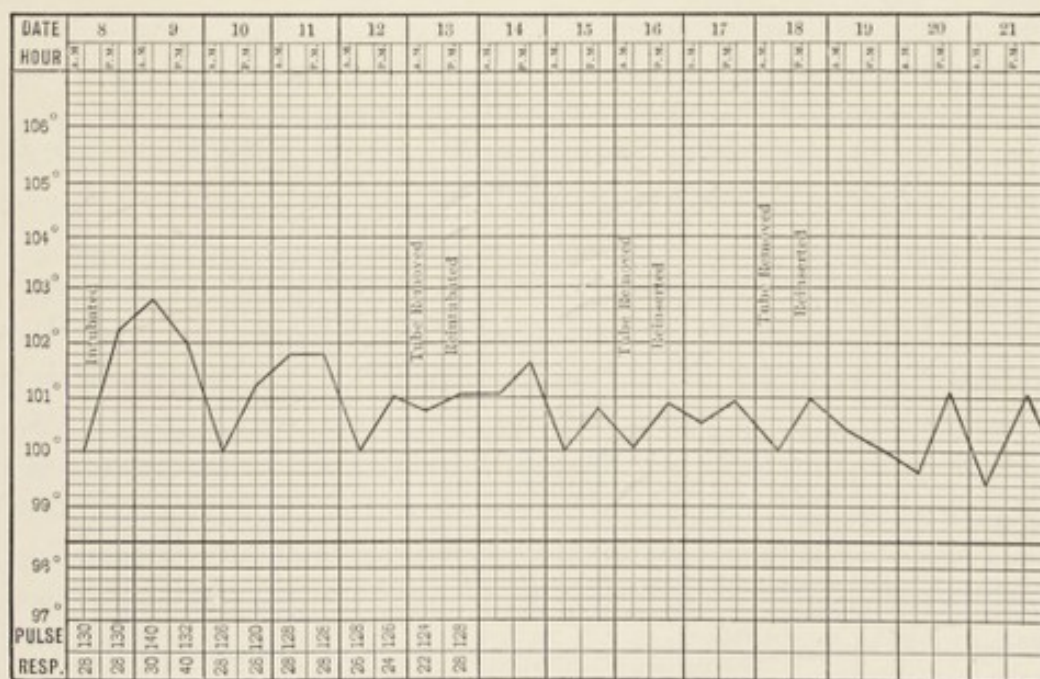
FIG. 13.—Diphtheria of tonsils, pharynx, and larynx; intubation; tube finally removed on the 24th. Nellie C., aged four years; admitted on the 8th; discharged on 28th. (Willard Parker Hospital.)

later the marked effect that serum therapy has upon the temperature. The accompanying temperature charts, from cases occurring at the

Willard Parker Hospital, give a better idea of this symptom than a further generalization.

FIG. 14.—Laryngeal diphtheria; treated with calomel fumigation and steam; recovery. C. C., aged twenty-two months; admitted March 22d; discharged April 11th. (Willard Parker Hospital.)

PULSE.

In an ordinary uncomplicated case of diphtheria the pulse is invariably increased in rapidity at the beginning of the disease. Its rate, as a rule, at this stage is directly dependent upon the amount of toxic products which is eliminated. Infants are especially liable to a high pulse-rate.

Bradycardia.—Many observations have been made on the occurrence of bradycardia in diphtheria, and all go to prove that a rapid or gradual slowing of the pulse after the acute symptoms have passed is a very grave symptom. Litchfield has given an account of a fatal case under his care in which from the fourth to the tenth day of the disease the pulse dropped from 70 to 20 per minute. Chapin has made similar observations. Hibbard, in a study of 800 cases at the Boston City Hospital, found 23 with a pulse of 60 or less on one or more occasions. He regards this symptom, if transitory and occurring in adults, as of little importance; occurring in children, and especially if carried over any considerable period, it is to be regarded as a grave symptom. In six cases of children showing the latter condition four proved fatal.

Tachycardia.—This symptom has been carefully studied, and is generally regarded as an important factor in forming a prognosis.

In the series of 800 cases above referred to, the pulse-rate and mortality were as follows:

PULSE-RATE.	RECOVERED.	DIED.	PERCENTAGE OF MORTALITY.
130	436	22	4.8
130	114	22	16.2
140	85	19	18.2
150	24	16	40.0
160	18	23	56.1
170	1	7	75.6
180	1	10	90.0

showing that less than one-half of those whose pulse-rate was 150 or over recovered.

A similar result was reached by Burrows in a series of 1962 uncomplicated cases at the Boston City Hospital during 1900:

PULSE.	RATE OF MORTALITY.
110	4.8
120	6.2
130	10.1
140	20.4
150	24.7
160	29.3
170	61.1
180	72.2

The writer states that in the majority of the cases the rapid pulse occurred as the result of nasal diphtheria, a fact which he accounts for by the greater lymphatic supply in this situation, for, as pointed out by Rotch in 1889, the toxins thus have freer access to the circulation. Burrows noted a *bruit de galop* in 22 of the cases, 8 of which died.

Irregularity of the pulse was noted by Hibbard in 10% of the cases. The author regards the gravity of this symptom as dependent upon the cause. In 70 cases in this series, 31 died with cardiac symptoms.

Reduction in Blood Pressure.—Friedman, in a series of cases in which he took careful sphygmographic tracings, concludes that a marked reduction of pressure warrants a bad prognosis. Biernacki, F. J. Brodie, Roux, and others have all shown that reduced blood pressure regularly follows absorption of diphtheria toxins to a greater or less degree. Finally in the 70 cases above referred to by Hibbard, an intermittent pulse occurred 19 times, with 9 deaths.

ANGINA (PARTIAL).

This is anatomically the most common form of the disease. If seen in the earliest stages, there will be found a general redness of the pharynx, scarcely extending beyond the anterior pillars of the fauces.

This redness, though fairly uniform, is more marked at the seat of the future membrane, and at such points the mucous membrane appears a little thickened and abraded. One of the tonsils is the most frequent seat of the primary lesion. There may be seen in the early stages, near the middle and inner surface of the tonsils, a slightly opaque exudate resembling thickened mucus, which after some hours becomes flattened out and more dense, and soon forms a whitish pellicle, which is detachable without being torn. When detached, it is soon reformed, becoming thicker and more adherent. At times the membrane is of very limited extent, and has the appearance of having eaten into the tonsil, as it were; this is produced by the swelling of the surrounding tissue. Again, the membrane may occur at the back of the tonsil, and be seen only when the latter is drawn forward. More often it spreads over a large part of the latter. On close examination one may often see at its edges a thin web-like reticulum, which is regarded by Sevestre and Martin as characteristic of diphtheria. At other times, instead of starting at a single point and spreading, the membrane starts from several parts at once, corresponding more or less closely to the tonsillar crypts. Such cases easily may be confounded with follicular tonsillitis unless a bacteriologic examination be made. In certain cases the primary lesion resembles a herpes of the pharynx or tonsil. This was first pointed out by Trousseau in the epidemic of 1858, and has recently been studied by Dieulafoy, who has shown by bacteriologic examination that such herpetic lesions frequently must be classed as diphtheritic, in spite of the simultaneous occurrence of labial herpes. It is probable that the cases of paralysis following herpetic angina as described by Gobler are of this nature.

One tonsil having been attacked by the disease, the opposite one is very apt to be later affected, probably by direct contagion. In this form of diphtheria the pseudomembrane has a velvety appearance, an opaline white color, sometimes rather gray or yellowish, more rarely a dirty gray or brown. It is rather tenacious, sometimes hard, and even horny, tearing with difficulty. After some days, either with or without treatment, it becomes more friable, detaching itself *en masse* or disappearing gradually piece by piece; the mucous membrane under it is reddened and vascular, but occasionally more or less pale.

The anterior pillars of the fauces are rarely the seat of the primary lesion; the posterior, on the contrary, are often so. Here the membrane, according to Sevestre and Martin, has a characteristic appearance; softer, or rather more moist-looking, than the tonsillar mem-

brane, greenish-white in color, and closely adherent to the underlying tissues. This these authors regard as a positive sign of diphtheria.

The back of the pharynx may also be the seat of separate patches of membrane which often fail to coalesce.

The uvula is affected secondarily to the tonsil. The membrane may be limited to one side of the former, in which case there is a deviation, or it may completely surround it. Again, the posterior surface may be alone involved. This is regarded as usually an extension from a nasal diphtheria. In some cases several of the crypts may be marked by white points, constituting a form of the disease called by Koplik "acute lacunar diphtheria of the tonsils." This form, by spreading over adjacent parts, may develop into a severe case of general diphtheria.

The cervical glands may be more or less swollen and a little tender on pressure.

The functional disturbances are very slight or absent, at least in the beginning of the disease; as a rule, there is slight pain in deglutition and some change in the voice. The fever is slight, generally one or two degrees, with frequent oscillations; the pulse corresponds to the temperature—full, of good force, and regular. The general health remains good, as a rule. There is slight anorexia and some depression. In a certain number of cases a slight and transient albuminuria may be present. Paralysis is occasionally a sequel. The disease usually lasts six to eight days. The membrane gradually detaching itself, the underlying tissues return to their normal condition. The adenitis is apt to last somewhat longer. The membrane, on the other hand, after detaching itself may be reproduced several times, a result often of too strong a local application or too violent attempts at removal. Finally, in this benign form of the disease the larynx not infrequently becomes involved; occasionally very suddenly, more often by a gradual or rapid extension of the membrane at the back of the pharynx.

ANGINA (GENERAL OR TOXIC).

This form of the disease may occasionally result from the benign form just described; more often it is characteristic from the beginning. The pseudomembrane is usually more extensive and thicker, is more gray in color, or a dirty white yellow, or occasionally brown or even blackish. In the typical cases the membrane appears to cover a greater part of the throat—tonsils, back of the pharynx, palate, and uvula. The latter may be bound down to one of the pillars, more often free; it is enveloped in membrane and frequently edematous.

The tonsils are swollen, occasionally almost occluding the opening, although the latter phenomenon is more frequent in the cases of mixed infection.

The disease usually begins with grave symptoms; as a rule, there is a marked chill, followed by fever; toxemia is marked from the onset. The patients are listless and apathetic or excited and delirious. There is often vomiting. In twenty-four to forty-eight hours the pharyngeal parts are red and swollen. There is difficulty in swallowing and an accumulation of mucus in the nasopharynx. The cervical glands become swollen and tender, and in three to six days the membrane is developed as above described. The course of the disease varies. In those cases where the toxic symptoms are less marked, the fever and glandular involvement soon disappear, and, especially in cases properly treated, the mucous membrane may return to normal in three to six days. If not treated, the membrane may reform after falling off, the toxic symptoms return, and the disease run a protracted course of three to six weeks. The longer such an angina lasts, the more grave are the toxic symptoms. The patient may die from degenerative changes, or the larynx and bronchi may become involved and cause death. Death by croup is relatively less frequent than in the benign form, as the fatal cases progress so rapidly that the larynx has not time to become involved. Albuminuria frequently occurs and is of a severe type.

PHLEGMONOUS OR STREPTO-DIPHTHERITIC ANGINA.

This form of angina is usually a total one, the whole throat being involved almost from the beginning of the disease. If a tonsil or other part shows a primary lesion, it is not long before the membrane spreads to other parts.

The mucous membrane in an early stage is dark red and much swollen, the uvula often edematous. After a few hours the membrane begins to form and spreads rapidly. It is thick and hard, and of a dirty gray or blackish color. The appearance of the membrane and its rapid formation and tendency to spread differentiate this form of the disease from that of pure diphtheria. If the membrane is removed, the mucous membrane under it is seen to be denuded of epithelium, yellowish-red in color, and studded with blood-points. It soon forms again and takes a firmer and deeper hold on the underlying tissue. The submucosa is often involved.

The symptoms of the disease, though similar to those of pure diphtheritic angina, are all greatly intensified. The cervical glands are

much more swollen and painful. The temperature varies with the extent of the process. After the exudation has reached its limit, the latter usually falls somewhat, the pulse is rapid, toxic symptoms set in early and are well marked. The patients are apathetic and weak, vomiting often takes place, and the respirations are increased in frequency. Albuminuria may be present even as early as the second day. If treated properly with antitoxin, the disease may run its course in five or six days. If, however, it has been found impossible to combat the toxic symptoms, the heart and kidneys may become involved. Paralysis of the pharyngeal organs and of accommodation are very frequent, and, if the disease is protracted, of the lower extremities. Death may occur in this form of the disease from paralysis of the heart, acute degeneration of the kidneys, or, later, nephritis, involvement of the larynx or air-passages, through functional disturbance of respiration, or general infection. Endocarditis may also cause death. The most frequent cause, however, even when antitoxin has been given in sufficient quantities, is bronchopneumonia of a very fatal variety. While this, too, may resolve, it is the exception rather than the rule.

SEPTIC ANGINA.

This disease often is an outcome of the variety just described. It is also characteristic of certain epidemics, and occurs as a septic process from the onset. From the beginning the symptoms are much more marked than in the first two forms of the disease. Vomiting is violent and frequent and may be followed by collapse. The patients may grow so rapidly worse as to be unrecognizable after a few hours. The rise of temperature is sudden; the pulse very rapid, small, and soft. Respiration is increased correspondingly. On inspection after a few hours, the tonsils usually are seen to be much swollen, livid, bluish-white, discolored, and, together with the uvula and soft palate, covered with bloody extravasations. Inclosing them is a dirty-looking, bad-smelling exudate, clotted with bloody extravasations. The cervical glands are intensely swollen on both sides and salivation may be present. Death takes place usually from the second to the fourth day, with symptoms of collapse and general sepsis. This form of diphtheria is very fatal; several deaths may occur in the same family. The disease may run a slower course than that just described, septic symptoms appearing after several days. In cases untreated, death usually occurs with symptoms of diphtheritic and septic poisoning. In cases that recover, degeneration of the nerves and kidneys is likely to follow. Finally, there are seen cases in which the symptoms of toxemia are over-

whelming, and, through the virulence of the streptococci, the affected
tissues may slough.   Recovery even here may take place, with result-
ing scars, but seldom if untreated.   The children in any case are left
in a very weak and emaciated condition.   The larynx may become
involved in the same process.   Bleeding from the mucous membrane
is common.   ✱The disease may involve the nose and the mucous mem-
brane of the lips.   The children die of sepsis, pneumonia, or endocar-
ditis.

DIPHTHERIA OF THE NOSE.

The disease, from a clinical and bacteriologic standpoint, may be
divided into three classes—viz.:

1. Pure or fibrinous diphtheria; fibrinous rhinitis.
2. Strepto- or phlegmonous diphtheria of the nose.
3. Septic diphtheria of the nose.

Nasal diphtheria may occur primarily or by extension.   To the
first class belong cases of diphtheria of the newborn and of infants.   In
these cases there is a moderate rise of temperature (one or two de-
grees), the infants are listless and apathetic, sleep a great deal, and
take their nourishment poorly.   The nasal mucous membrane is
swollen and red and there is a more or less free discharge from the
nostrils.   On account of the latter, there is apt to be an excoriation
about them and the upper lip.   The breathing is apt to be "snuffling"
in character, and often in the marked cases more or less through the
mouth.   As in a simple rhinitis, there is often a mechanical difficulty
in taking the breast and bottle.   After a day or two, the fever falls,
the local symptoms remaining.   Usually after two or three days the
fever comes on as before, or somewhat higher.   The former symptoms
are all enhanced, the children are pale and weak, and refuse the breast.
There is more or less cyanosis in crying, and sometimes, during sleep,
suffocation may take place in attempts to take the breast.   On inspec-
tion at this stage, the mucous membrane is seen to be intensely red-
dened, and there is a fibrous exudate, usually on the septum or deep
in the canal, which may be removed *en masse* with forceps, occasionally
in the form of a cast of the choanæ.   This may also be done by syringing
or douching.   The mechanical obstruction thus removed, the subject's
breathing immediately improves, and the breast is eagerly taken.   The
children either continue to improve or the symptoms all return on
account of the reformation of the pseudomembrane.   The process,
instead of remaining confined to the nose, often spreads down to the
pharynx, and may involve the entire pharyngeal ring, in which case
the symptoms are practically of the angina, above described, except,

as before mentioned, the mechanical conditions are such in patients of this age that the impediments to nourishment are very great. The respiration has a peculiar snoring, snuffling character, the mouth is held open, there is a depression about the epigastrium during inspiration. The children are unable to take the breast, and with very great difficulty are able to swallow if nourishment be introduced with a spoon. They may at this stage suffocate during sleep, attempts at feeding, or spraying the nose. Weakness increases rapidly through deficient respiration, lack of food, and the occurrence of toxemia; the patient's color is cadaverous, and the pulse soft and very rapid. Death occurs most often in from seven to nine days. This may take place through involvement of the larynx, toxemia, or functional disturbances.

Most authors regard this form of diphtheria as a phlegmonous or mixed diphtheria, and not as a purely fibrinous process. Monti holds the opposite theory, which would seem to be substantiated by the experience of other observers. Certainly it is a fact that in the city of New York, especially in institutions such as the New York Foundling Hospital, very pure cultures of diphtheria bacilli are often found in nasal discharges.

In older children the symptoms and signs are similar to those described in the cases of infants, but naturally of less severity. The membrane is apt to extend to the pharynx. When the process first involves the choanæ, there is a marked increase in temperature and difficult snoring respiration. In sleep the character of the latter is hardly distinguishable from laryngitis. The children are constantly trying to better their impeded respiration by blowing through their nostrils and snuffling. The same excoriation as above noted appears about the nostrils and lips. This may be diphtheritic in character. The glands about the neck are more or less swollen. Bleeding from the nose takes place in a few cases. When the process is confined to the choanæ, the nasal mucous membrane may be seen to be swollen and reddened; or, again, a more or less thick membrane is observed in the nasal passage. This process is usually acute, except in scrofulous children (Monti), and after a few days the mucous membrane returns to normal. Where the nose and choanæ are involved in turn, there may be complete occlusion of the nasal passage, and the children may die of an attack of suffocation or from general toxic symptoms. The latter may be very severe from the onset, and cause death very soon, an outcome which may also take place through the involvement of the larynx.

It is not an unusual occurrence at the New York Foundling Hospital to have a child brought to the physician with the history of a foreign body in the nose. Here there will be found a thick bloody discharge from one or both nostrils, swelling of the mucous membrane, and occasionally pseudomembrane to be seen in the nasal passage. In these cases a bacteriologic examination serves to render a positive diagnosis, and the diphtheria bacillus is quite often found instead of the supposed foreign body.

Nasal diphtheria may run a very protracted course; the symptoms are those of a chronic rhinitis or catarrh. The membrane may be seen generally on the septum, and usually on the anterior part. The latter may fall off and reform indefinitely, so that the disease lasts for weeks. In these cases it seems probable that the germs possess a low degree of virulence, toxic symptoms seldom appearing. Nevertheless the patients are a grave source of danger, especially in large institutions, as these cases are very apt to be overlooked. Treittel and Loppel have found very virulent bacilli in the nose fifty-five days after the disease was apparently terminated, and Wolff has seen a patient who after remaining sixty-three days in a hospital with this kind of diphtheria returned home only to infect the brother.

Phlegmonous, Mixed, or Strepto-diphtheria of the Nose.—This form of the disease is common among older children, beginning, as a rule, about the choanæ. There is often an acute onset of snoring respiration and swelling of the submaxillary glands. The nasal secretion is profuse, purulent, and rapidly causes excoriation about the nostrils and swelling and inflammation of the nasal mucous membrane. Streptococci and Klebs-Löffler bacilli are found in it. The membrane, a part of which may become detached and come away, is thick and dark colored, and reddish on its under surface from the prevalence of the blood-cells. The choanæ may be entirely closed by the exudation, in which case the children lie with mouth open, the respiration snoring in character, the tongue pressed against the hard palate, somnolent and unwilling to take other than a little fluid nourishment. The fever varies with the extent of the process. Toxic symptoms are invariably present—vomiting, apathy, and weakness. The glands about the neck are much swollen, the nose bleeds freely, the symptom-complex is one that is characteristic of the disease. The poisoning is often so intense that even in a few days the heart and kidneys may become affected. The younger the child, the worse the prognosis, and death may occur in three or four days. This form of

diphtheria especially spreads to the pharynx, when the symptoms above described, of phlegmonous angina, ensue. The disease often yields to early and radical treatment.

Septic Diphtheria of the Nose.—Either form of nasal diphtheria may terminate in general sepsis, in which case the abundant lymphatic supply about the nasopharynx readily contributes to rapid absorption of septic products, causing early and very grave symptoms and frequently death.

DIPHTHERIA OF THE LARYNX (CROUP).

This form of disease may occur primarily. In the majority of cases, however, it is secondary to diphtheria occurring elsewhere: throat, nose, or both; or, as will be later described, trachea and bronchi. The course of the disease may be properly divided into three stages: (1) Stage of invasion; (2) stage of spasm—exudation; (3) stage of asphyxia.

First Stage.—The angina or nasal diphtheria may be running its ordinary course, when, rather suddenly, the children become hoarse, and generally develop a cough characteristic of laryngeal irritation. If it is possible to make a laryngeal examination, which is by no means easy, in young children, there will be seen swelling and redness of the larynx. Cultures taken at this time will often show the specific bacilli, and yet it is to be noted that in cases of early laryngeal diphtheria where the larynx alone is involved, a negative culture is by no means proof conclusive that the disease does not exist. This experience is a common one at the New York Foundling Hospital. Repeated cultures will prove positive at a later stage. The stage of invasion lasts usually a day or two, sometimes much longer.

Second Stage.—The second stage begins with the formation of the pseudomembrane. This may proceed very rapidly, so that within twenty-four hours the patients have symptoms of laryngeal stenosis. Usually the course is somewhat slower. The first symptom noted at this stage is the characteristic voice and cough; the latter is a short and dry one and hoarse in character, and soon comes on in the form of paroxysms, lasting for several minutes and induced by attempts at swallowing, examination of the throat, or restlessness of the patient. During the attack the patient's face is cyanotic, the eyes reddened and bulging, the veins about the head and neck swollen, and the forehead covered with sweat. The cough at this stage has little effect in clearing the larynx, only a little mucus at times being brought up. Aphonia, complete or partial, soon develops; the respiration is markedly

harsh and very noisy. As the disease progresses the symptoms of stenosis become more marked. The respiration has a whistling character; inspiration is prolonged, the expiration harsh, a well-marked interval coming between the two. The accessory muscles of respiration now come into play with the progress of the stenosis. At this stage there may be seen a well-marked depression in the supraclavicular region, neck, and epigastrium. On auscultation at the bases the prolonged character of inspiration, together with diminished intensity, may be noted. The respirations, in contrast to other conditions causing dyspnea, are only moderately increased in frequency— 20 to 30 on the average. From time to time attacks of asphyxiation occur. The children sit up suddenly, cough with great violence, the face livid and anxious, the head held back, the hand grasping the throat; the respiration louder and shriller in character. After the attack has passed, the patient lies back exhausted and often covered with perspiration. The attack lasts from only a few minutes to ten or more. Occasionally it is relieved if the patient succeeds in coughing up a little membrane or mucus, or the attack recurs very soon and suffocation takes place. If at this stage it is possible to get a view of the larynx with a mirror, there will be seen redness, swelling, and membrane upon the epiglottis and vocal chords, in the sinus of Morgagni, and even in the trachea.

The vocal chords at their anterior parts are immovable, their edges lying in contact except at the posterior part, where there is a small opening between them which does not alter in size during expiration and inspiration. Rauchfuss found in the first twenty-four hours, sometimes after two or three days even, only signs of laryngeal catarrh. On the third day, as a rule, once after twelve hours from the beginning of the attack, he found the whole interior of the larynx covered with the fibrinous exudate.

In rare cases the pseudomembrane may be coughed up, either in small pieces or as a cast of the larynx and trachea. This occurs most frequently in non-treated cases at the end of this stage. The patients, although immediately relieved, are not out of danger, since the membrane may reform and all the symptoms return. The duration of this stage in non-treated cases varies from twelve hours to a week.

Third Stage.—The results of impeded respiration together with toxic symptoms are seen in this stage. Respiration is rapid and is carried on with the aid of all the accessory muscles; it soon becomes irregular. The larynx rises and falls with each breath; the depressions seen at the clavicle, jugular region, epigastrium, and

intercostal spaces are very marked. The respiration is very noisy, inspiration taking on an asthmatic character. Air hunger becomes more and more marked. The children sit up in bed, only to fall back again exhausted, or toss about restlessly, sometimes appealing for help to those about them. The head is thrown back. The abdominal muscles take part in the respiratory act. The facial expression is very anxious, the eyes dim, the face and lips cyanotic, the skin dry or covered with clammy sweat, the extremities cold. The suffocating attacks come more frequently, and death soon occurs in one of them, occasionally during convulsions.

All the cases do not progress as rapidly as above described; there are intervals in which the breathing seems to be bettered and the child rests easier. Such apparent improvement, however, should not be too much depended upon, for suddenly an attack of dyspnea may come on, with marked cyanosis about the face and extremities. Should the attack not terminate fatally, the latter conditions disappear, the child becoming of a death-like pallor and almost lifeless. As the stenosis becomes more marked, there are signs of carbonic acid poisoning, and the cyanosis disappears only with death. The skin at this stage loses its sensibility, so that with marked cyanosis of long duration there may be complete anesthesia, followed later by general muscular weakness, general paralysis, and death. As the symptoms of asphyxia recur, apathy becomes more marked and stupor finally appears. The children wake only during an attack, sitting up suddenly, gasping for breath, head thrown back, and covered with perspiration. Soon, however, the children cease to struggle, the stupor develops into coma, and death takes place.

According to Monti, death occurs in 95% to 98% of non-treated cases. A spontaneous recovery, however, is possible even in the late stage. If recovery takes place in the second stage, the process comes to a standstill and does not progress to the stage of asphyxia. The membrane may or may not be coughed up, the stenotic symptoms gradually abate, the cough is loose, and only the symptoms of a catarrhal laryngitis remain for perhaps a week or ten days. Hoarseness may last much longer. In the last stage it is barely possible to have recovery from the coughing-up of the membrane.

It is to be remembered, however, that a second membrane may form, with return of all the symptoms. Death takes place usually in the third stage, from carbonic acid poisoning or one of the common complications—edema of the glottis or the lungs, emphysema, bronchitis, extension of the process to the bronchi, or, most often, broncho-

pneumonia. In the second stage death usually occurs from asphyxia. With tracheotomy or catheterization of the larynx as practised by Bouchut, Wennlecher, and Monti, 20% to 25% of recoveries are reported by the latter. With the introduction of intubation by O'Dwyer, together with the use of antitoxin, diphtheritic croup has lost its terrors, and the percentage of deaths is very small when the disease is taken in time and properly treated.

Phlegmonous Diphtheria (Mixed Infection of the Larynx).— This form of the disease is secondary to the same condition of the nose or throat, or both. The symptoms and course are dependent upon the relative virulence of the two germs, streptococcus or diphtheria bacilli. When the latter prevails, the symptoms are not very different from those described in pure or fibrinous laryngitis; with marked streptococcus infection there is destruction of the epithelium and involvement of the whole depth of the mucous membrane by the exudative process. Occasionally before the formation of the exudate, on the first or second day, marked symptoms of stenosis may occur, due to the swelling and edema of the parts. While the stenotic symptoms of the first class of cases are similar to those described in pure diphtheria, they are apt to develop more slowly. Attacks of asphyxiation seldom occur at the beginning of the disease. The laryngoscopic examination in such cases shows the entire larynx to be intensely reddened and swollen. The epiglottis is very much thickened, the parts about the larynx, fossæ, and vocal chords are greatly swollen and more or less covered with a grayish-white membrane; or the interior of the larynx is covered with a thick, tough membrane, the glottis is narrowed, purulent exudate constantly comes up from the trachea, and may be seen between the chords. This form of stenosis usually lasts one to three days. In the second form of phlegmonous diphtheria there may be entire absence of symptoms of laryngeal involvement, no cough or change in the voice, or, if they are present, they seldom are as marked as in the previous form. Examination shows the anterior surface of the epiglottis swollen and reddened, but free from membrane. In some cases the false vocal chords are alone covered, in part or wholly, with membrane, the true vocal chords being only swollen and reddened. The duration of the laryngeal symptoms is longer than in the form just described, and is masked by the symptoms due to involvement of the nose and throat and resulting toxemia. At times suffocation takes place very suddenly and unexpectedly, or the stenotic symptoms become gradually worse and lead finally to death by asphyxia.

In the phlegmonous form of the disease, as a rule, asphyxia takes place without a high grade of stenosis of the larynx being present. The cyanosis may be seen as a livid, cadaverous coloring of the skin. Physical weakness and small pulse, anesthesia of the skin, and diminished heat production mask the symptoms of mechanical obstruction. Symptoms of carbonic acid poisoning are prominent. The duration of the asphyxia is one to two days. Death usually takes place, and is due to toxic as well as local conditions. Degenerative processes are common, together with paralysis of the vocal chords and of the muscles of the throat. Complications are frequent, and will be noticed under another heading.

Septic Diphtheria of the Larynx.—This condition follows that of septic diphtheria of the nose, throat, or both. The disease begins with apathy, much weakness, and high fever. The symptoms all develop very quickly. In some cases there is an erythema about the extremities or erysipelatous redness about the neck. On examination, the appearance of the nose and throat is as described under septic angina. The mucous membrane of the larynx, and usually that in the fossæ, is red and swollen and covered with a grayish-yellow exudate. In addition to the swelling of the cervical glands, the tissue about them is involved and the skin over them is inflamed. The tongue is heavily coated, there is marked salivation, and a muco-purulent discharge, often very offensive, from the nose. Epistaxis occasionally occurs. The lips are excoriated, vomiting is frequent, there are delirium and suppression of the urine, and a rapid small pulse develops suddenly without a high grade of stenosis; and, as a rule, the children die in collapse of general septic poisoning, preceded often by diarrhea and vomiting, great swelling of the cervical glands, with involvement of the surrounding tissue, falling temperature, and rapidly weakening pulse. In rare cases the septic symptoms develop more slowly, and recovery from the actual disease may take place. Death, however, may occur later from general weakness, anemia of a high grade, or changes in the heart and kidneys.

Cause of the Attacks of Asphyxia.—In the laryngeal form of diphtheria two symptoms deserve special attention—dyspnea and certain conditions of the radial pulse, both due to mechanical conditions. First, as to the explanation of the dyspnea in uncomplicated laryngeal diphtheria of any type: Four theories have been advanced—viz., spasm of the glottis, obstruction due to the false membrane, paralysis of the dilators of the glottis (Neimeier),

and, lastly, excitation of respiratory centers by carbonic acid poisoning and reflex action of the pneumogastric nerve (Cadet de Gassicourt). The last two theories may be dismissed as probably not tenable. It is certain that they have had few supporters.

It is a common experience, at autopsies on children dying of asphyxia due to laryngeal diphtheria, to find little or no membrane about or in the larynx. In these cases the larynx is congested and swollen to a greater or less extent. This absence of false membrane has also been noted laryngoscopically during life (Ruault, Variot). Further, the attacks of dyspnea come on so suddenly, excited as they are by the slightest cause, that it is difficult to believe otherwise than that they are of nervous origin, and caused by the contraction of the laryngeal muscles rendered hypersensitive by the disease. With one exception, as pointed out by Sevestre and Martin, the muscles of the glottis are constrictors, an additional reason for accepting the theory of spasm. Again, the fact that emetics and antispasmodics, and even attempts at quieting the patient, will often produce a temporary relief or diminish the frequency of the attacks, would go to support this hypothesis. Finally, the actual existence of this spasm may sometimes be demonstrated during intubation of these cases, where, on attempting to introduce the tube there is at first great difficulty in doing so, and in an instant, perhaps, the apparent obstruction is overcome and the tube readily enters the larynx.

While there can be little doubt as to the importance of spasm in producing this condition, it should not be forgotten that the swelling of the mucous membrane and production of false membrane upon it must of necessity be an additional factor, especially in the later stages of the disease. In the early stages spasm plays the most important rôle; as the disease progresses the effects of the swelling and exudate become more and more marked, the dyspnea does not entirely disappear between attacks as in the earlier part of the disease, and, furthermore, immediate relief follows coughing-up of the false membrane.

The spasm, however, still continues to act in producing the exacerbation of dyspnea. In the last period of the disease spasm is not a factor, the laryngeal muscles fail to respond to any stimulus, perhaps through anesthesia, which is also observed in the skin at this stage, perhaps from fatigue. Here the dyspnea must of necessity be due entirely to the presence of false membrane and the swelling of the parts.

The pale asphyxia (*asphyxie blanche* of the French), a condition

not infrequently seen in the late stages of the disease, is thus explained by Sevestre and Martin. Normally the contraction of the diaphragm is coincident with the dilatation of the glottis. In croup the latter is closed while the diaphragm contracts; the air cannot enter the lungs in sufficient quantities to inflate them, so that a vacuum is produced and the previously noted phenomena of depression in the epigastrium and supraclavicular regions, etc. (*tirage*), appear. Furthermore, the vacuum causes the blood to enter the interthoracic vessels; the peripheral vessels being thus depleted, the characteristic pallor is produced, and is always a grave symptom. When one sees a patient in this condition, there is no time to be lost. The obstruction to respiration must be immediately removed, and often with happiest results. The so-called pulsus paradoxicus, which occurs in modified form during attacks of stenosis, is due to the same physical condition as that just described; that is, on account of the partial vacuum existing in the thorax, the blood is drawn into it from the peripheral vessels, so that with each inspiration there is complete, or more often partial, obliteration of the radial pulse.

DIPHTHERIA OF THE TRACHEA AND BRONCHI.

This is usually the result of an extension of a laryngeal diphtheria, either fibrinous or phlegmonous. Sometimes the process is limited to the trachea or it invades even the terminal bronchi; or, again, it may follow a single large bronchus and its divisions. Goodall has reported several cases in which the disease appears to have been limited to the trachea and there was no sign of laryngeal involvement.

Under the name "ascending croup" is described a condition in which the disease first makes its appearance in the trachea and bronchi, the larynx being secondarily affected. This is seen most frequently in diphtheria following measles. The only positive sign of bronchial involvement is the coughing-up of a cast of the bronchus. Certain symptoms and signs, however, may often lead to a correct diagnosis, a matter of great importance in deciding as to the advisability of intubation. There is at first a more or less intense dyspnea, with rapid respiration—50 to 60 a minute. The dyspnea is continuous and is not characterized by exacerbation. The depressions (epigastric and supraclavicular) are not marked. The face is pale, the extremities and lips are blue, the physical depression is very great. Auscultation gives very meager results. A number of bruits and râles have been described, none of which seem to be characteristic or constant. One

sign, however, seems to be of great diagnostic value—namely, diminution of breathing over a certain area of the chest, if pneumonia or other causes for it can be excluded. This, if found, is almost certain proof that the bronchus and branches corresponding to this area are wholly or partly occluded. This is still more positively proved if such an area is found after the laryngeal obstruction has been removed, as by intubation, and the air is allowed to enter the lungs freely, for in such a case the diminished or absent respiration will, by contrast with the rest of the lungs, be much more clearly marked.

Diphtheria of the bronchi is a very grave disease. Death occurs from asphyxia or carbonic acid poisoning or bronchopneumonia. Still, recovery may take place by expulsion of the membrane, spontaneously or following intubation or tracheotomy, or as a result of serum treatment.

In cases of mixed diphtheria invading the bronchi, in addition to the symptoms above described, those of toxemia are soon marked. There is apathy, muscular weakness, anesthesia of the skin and stupor. The disease, as a rule, comes on with a chill, followed by high fever. It runs its course in one to three days. Serum treatment is of little or no avail in such cases when fully developed.

CONJUNCTIVAL DIPHTHERIA.

According to Jacobi, this disease occurs much less frequently than in former years. It is most frequent among children under ten years of age, and usually follows diphtheria of the nose or other parts. Occasionally, however, it occurs as a primary disease.

Sourdille has divided it into three classes—interstitial, croupal or superficial, and catarrhal.

The first is characterized by a considerable thickening of the lids, with marked infiltration, so that it becomes nearly impossible to turn them back. The conjunctiva is swollen and covered with a grayish exudate, and dotted here and there with ecchymoses. The false membrane cannot be detached. The period of infiltration lasts six to eight days, after which disintegration of the membrane begins, accompanied by a profuse and purulent discharge. The mucous surfaces are left reddened and swollen and cicatrices form, which later on may lead to permanent adhesion. Grave corneal complications may result in loss of sight. The latter is seen less often since the introduction of serotherapy.

The superficial form resembles an acute catarrhal conjunctivitis. The lids are red and swollen, but not infiltrated and stiffened, as in the

former case. There is a whitish membrane, covering only, as a rule, the inner surface of the lids to a greater or less extent, sometimes extending to the palpebral surface and culdesac. The membrane is easily detached; the mucous surface under it is found to be red and bleeding, but not infiltrated. Corneal lesions are rare and scars do not result.

In the catarrhal form the signs are less marked than in the preceding. Membrane is absent. The secretion, in contradistinction to the mucopurulent character seen in ordinary catarrhal conjunctivitis, is scanty, glairy, and thready. The swelling is more marked, the conjunctiva of the bulb less vascular, and, finally, the epithelium, instead of being dull and desquamated, is swollen, vitreous, and glancing. Sevestre and Martin suggest that this form of the disease seems like an aborted form of the second. In all three forms of the disease Sourdille has demonstrated virulent Löffler bacilli, sometimes in pure culture or associated with streptococci, staphylococci, and gonococci. The streptococcus is most often associated with the first form of the disease, and from what is known of the result of this association in diphtheria at other sites, is probably responsible for the grave results which occur. The staphylococcus is found most often associated with the Klebs-Löffler bacillus in the second and third form above described.

The disease, as already stated, begins insidiously, resembling an ordinary catarrhal conjunctivitis; there is marked congestion of the conjunctiva, especially of the lids. That of the bulb, as already stated, does not share in the process, except in rare cases. There is photophobia, epiphora, the membrane is soon formed, and the eyes are closed tightly. In the severe or interstitial form the lids cannot be turned back. When separated, a thin, straw-colored fluid exudes from them. The skin of the eyelids and cheeks is reddened, and when eroded may show a coating of membrane. The eyes are tender on pressure. The disease, as a rule, produces no other symptoms than those due to the local process, though few may occur. Often the symptoms are masked by the concurrent disease in other parts. Treatment will be considered under a separate head. (See Serotherapy, Effect on Eye Cases.)

DIPHTHERIA OF THE EAR.

Diphtheria of the External Ear.—This is caused by an extension of the disease from other parts to an eroded surface, the latter caused by scratching with the nails or an eczema, impetigo, or other lesions. These parts are covered with membrane; the external meatus may be filled with it. A serous or seropurulent discharge exudes from the latter. The

disease, as a rule, lasts ten or twelve days; the symptoms are masked by those of the disease elsewhere. The swelling and infiltration of the auricle may be very painful. The disease occasionally extends to the middle ear.

Otitis Media.—It is more than probable that this disease is frequently overlooked, especially in children too young to call attention to the pain which accompanies it. Baginsky states that, in spite of careful examination of the ears of diphtheria patients under his care, only in 5% or 6% was an otitis found. In the report of the Scarlet Fever and Diphtheria Hospital for 1901, among 78 cases of diphtheria, serous otitis media occurred in 2.6%; purulent otitis media, in 3.9%.

Many writers have reported a few cases of this disease. Lommel examined 25 cases of diphtheria and found middle-ear disease in all but one. In two there were evidences of true diphtheria. No cultures were taken. In two cases the lining membrane of the Eustachian tube was absolutely normal, from which the writer concludes that in the majority of cases middle-ear disease in diphtheria is the sign of general infection, and that the disease is not caused by an extension through the tube. Baginsky, Kossel, and Kutscher have reported cases of diphtheritic mixed infection.

That the bacilli of diphtheria occur very frequently in the middle ear, at least in severe cases of diphtheria, whether or not they caused symptoms during life, is shown by the recent report of the bacteriologic examination of 144 fatal cases by Councilman, Mallory, and Pearce. In 86 of these cases (complicated and uncomplicated) disease of the middle ear was found; in 59 cases (uncomplicated) there was an exudate in one or both ears; in 44 the exudate was purulent. The mastoid cells were involved on one or both sides in 13 cases.

In the 44 purulent cases, 35 occurred on both sides and 9 on one. In 8 of these no culture was made. In the remaining 36 the diphtheria bacillus occurred 19 times. In the non-purulent cases cultures were made in 9, and showed diphtheria 4 times. In the second group of cases (diphtheria complicated by other diseases), 23 were purulent and 4 non-purulent. Of the purulent cases 17 were double and 6 single. The mastoid cells were involved in 9 cases. Bacteriologic examination of the purulent cases gave diphtheria bacilli 14 times. Of the non-purulent cases (no cultures taken in 3 cases) diphtheria bacilli occurred twice.

The authors state that other non-pathogenic organisms were found in addition to those mentioned. The diphtheria bacilli were seldom found in pure culture, but in connection with one or more organisms.

That the diphtheria bacilli were the cause of the exudate is not proved, as no bacteriologic examination of the mucous membrane was made. The authors suggest that the otitis media may have been caused by the associated pyogenic germs, the diphtheria bacilli being accidental. In only 23 of the cases was the disease recognized during life. Six of these developed before the fifth day; 8 between the fifth and eleventh days; the remainder after two weeks of the disease, two on the thirty-fourth day. In all but three of the cases the children were under three years of age. Nasal diphtheria was present in 12 cases.

Symptoms of Otitis Media.—The disease begins usually in the course of a nasal or other diphtheria, followed by more or less deafness and considerable pain in coughing. This may be noticed only in older children. In infants the first symptoms usually noticed are due to pain, followed by a discharge from the ear. After this discharge takes place, the pain lessens. A thin, seropurulent fluid exudes from the canal, sometimes bloody, and usually fetid. Membrane may be seen deep in the canal. After some days the false membrane becomes detached, the otorrhea persisting for a long time. The complications are those of any purulent otitis.

BUCCAL DIPHTHERIA.

This is rarely seen except in cases of an extreme form or cases of severe strepto-diphtheria. In such, the pseudomembrane extends to the surfaces of the cheeks in the form of rather small patches, thick and very adherent to the underlying mucous membrane, which is red, swollen, and bleeds easily. The patches are especially marked in the interdental mucous membrane, on the tongue, dorsum, sides, or about the frenum. The membrane may occur also on the lips or in the corners of the mouth. The tongue is swollen and painful. There is an increased flow of saliva, often of a fetid odor, and occasionally streaked with blood. The submaxillary glands are swollen.

A more common form of the disease is seen in the course of measles or other infectious diseases, and occasionally as a primary infection. The lips at first become cracked, and on the bleeding surfaces a pseudo-membrane in the form of discrete patches is formed, looking somewhat like aphthous stomatitis. By the way of the commissures, which are usually fissured, the disease invades the inner surface of the cheek. Here the plaques are found as above described, except that in the present cases the membrane is more adherent. According to Sevestre and Martin, the staphylococcus is generally associated with the diphtheria bacilli in these cases. The disease has little tendency to extend,

and of itself is not dangerous. Finally, pure diphtheria occasionally occurs on the lower lip in the form of small patches found on the base of a tear, abrasion, or aphthous lesion.

ANOGENITAL DIPHTHERIA.

This is usually a mixed infection, though cases of pure diphtheria have been described. This form of the disease is rarely seen except in little girls, and is carried by direct inoculation from diphtheria in other parts of the body. It is usually situated on the vulva, sometimes in the vagina. The leison at first consists of a series of small patches which spread over the labia majora and soon develop into a complete membrane, which may extend to the labia minora and vagina, or at times to the anal region, and even to the rectum. There is swelling and redness of the affected parts, often bleeding and abundant exudation. The pain is acute; the inguinal glands are swollen. After falling off, the membrane may reform. Ulcerations occasionally result, and even a superficial gangrene. Cases where the disease has involved the uterus have been described. In boys the disease is very rare, and, as a rule, affects the glans, prepuce, and even extends into the urethra. The lesion readily heals, with or without treatment; the course may be rather long. According to Baginsky, general infection, albuminuria, and paralysis, may accompany or follow it. It would seem difficult to hold this lesion responsible for the latter sequels, as the disease invariably accompanies or follows lesions elsewhere.

DIPHTHERIA COMPLICATED WITH OTHER INFECTIOUS DISEASES.

Diphtheria may be preceded or followed by various other infectious diseases, and this is especially the case with measles; and it is not to be wondered at that the latter is especially conducive to the development of diphtheria if we consider the general catarrhal conditions which are so characteristic a symptom of measles. The combination is a most deadly one, especially in institutions. The diphtheria is not a pure infection, but the bacilli are associated with other germs, especially streptococcus. Croup is rather the rule than the exception, and death is very apt to take place from bronchopneumonia. There is marked adenopathy; the local symptoms are pronounced; the membrane is apt to be a dirty, foul-smelling one, with deep involvement of the mucous membrane. Otitis media, gangrene of the jaw, and general sepsis are not infrequent. The eruption of measles itself is apt to

be influenced by the diphtheria, and so we see hemorrhagic and septic forms of exanthemata.

Diphtheria and Scarlet Fever.—The frequent occurrence of this combination is, in general, dependent upon the care in isolation of diphtheria and scarlet fever patients; the care taken by physicians, nurses, and attendants against transmitting the diseases; and, finally, the routine examination of all throat lesions bacteriologically (cases of scarlet fever, as we shall see later, are not infrequently confounded with an antitoxin rash). The immediate separation of such patients from the other diphtheria cases is imperative. For an account of the occurrence and prevention of this condition see Gordon Pugh's report to the Metropolitan Asylums Board, 1900, London. In the 18,238 cases of diphtheria reported by the Board, the complication with scarlet fever occurred in 4.71% of the cases.

The symptoms of scarlet fever complicating diphtheria are, in brief, those of a severe streptococcus infection added to those produced by the diphtheria bacillus. There is produced a dirty looking, putrid membrane, great swelling of the cervical glands, with not infrequent suppuration, high fever, vomiting, and great prostration. The disease is less apt to invade the larynx and bronchi than in the complication with measles. The combination of diphtheria and scarlet fever is a very serious disease. It generally ends with death by sepsis.

Diphtheria and whooping-cough occurred in 2.7% of the Metropolitan Asylums Board's cases above referred to. It is a relatively rare compilcation. Its danger lies in the tendency of the disease to involve the larynx, trachea, and lungs. According to Baginsky, intubation in such cases is well borne.

Diphtheria and Typhoid Fever.—The combination of these diseases is much to be dreaded, and diphtheria is regarded by Henoch as the most fatal complication of typhoid fever. The disease is very apt to take on a septic character; croup and broncho-pneumonia are frequent. Morris Manges has reported 5 cases of typhoid fever in which the Klebs-Löffler bacilli were found in small patches of membrane on the throat. He regards these cases as examples of ulcerations occasionally occurring in typhoid, with secondary infection by diphtheria bacilli.

Varicella occasionally complicates diphtheria—in 0.93% of the cases in the above report. This condition, except in those rare cases of severe (gangrenous) varicella, does not seem to influence the progress of either disease. **German measles** occurred in 0.76% of the same series of cases.

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The association of **tuberculosis** with diphtheria is not infrequently seen. In this association diphtheria has the effect of hastening the progress of the disease, or in cases in which the tuberculosis is latent, as in the bronchial glands, of setting up a rapidly fatal miliary tuberculosis. A case of diphtheria grafted upon one of chronic tuberculosis, in which the resistance of the patient has been reduced, is apt to progress unfavorably, and the disease is very prone to take on a septic form. It is to be noted that Behring and others have observed that serum therapy in tuberculosis is not well borne.

Finally, diphtheria may be complicated by more than one of the various exanthemata; diphtheria, measles, and scarlet fever is the most common combination. Recurrences in diphtheria are not infrequent; certain people seem to be predisposed to them. Relapses occasionally occur, a fact not to be wondered at if we consider that one attack does not confer immunity for more than a few weeks, and that the bacilli may persist in the throat for a long time after the disappearance of the symptoms.

COMPLICATIONS AND SEQUELS.

ADENOPATHY.

THE lymphatic glands corresponding to the areas involved in the diphtheritic process are, as a rule, involved to a greater or less extent. According to the exhaustive researches of Councilman, Mallory, and Pearce, who examined the lymph nodes in 109 fatal cases of diphtheria, the cervical nodes and tonsils are those most frequently affected; next, the bronchial, intestinal, and mesenteric nodes. These authors failed to find bacteria in practically every case, and never the Löffler bacillus, from which it may be concluded that the lesions found are the direct result of toxic products and not due to the presence of organisms in the glandular tissues themselves.

In cases of pure diphtheria the swelling of the glands is characteristic, varying with the intensity and extent of the affection. The neighboring glands are swollen, a little tender, but always free in the surrounding tissue, which is itself never involved.

In the mixed forms of the disease the nodes are more tender on pressure. Individual nodes may in mild cases be indistinctly made out; more often, and especially in the severe cases, they form part of a mass with the surrounding tissue. In these cases the swelling about the neck may be enormous, constituting the symptom called by Saint-Gérmain "le cou proconsulaire."

Suppuration rarely, if ever, takes place in the pure form of the disease. In the mixed form it is not very common. In the septic form of diphtheria of a severe type the process may go on to a gangrenous destruction of the glandular and surrounding tissue, and even involve the underlying muscles and the skin. Even the most desperate cases of glandular involvement may be recovered from under proper treatment. The milder grades are an almost constant accompaniment of diphtheria, and are of little moment. The cases of mixed infection and septic cases add greatly to the gravity of the prognosis.

DIGESTIVE DISTURBANCES.

In the mild forms these are little, or not at all, in evidence. In the severe forms vomiting marks the onset of the disease, and there is not only loss of appetite, but often an absolute distaste for food.

According to Monti, more than half the cases of diphtheria begin with vomiting. At a later stage of the disease this symptom may be constant, and is a positive sign of severe intoxication. Diarrhea of a violent character, with frequent, profuse, fetid, and sometimes bloody stools, is also seen, which soon leads to collapse. Finally, diphtheria of the esophagus and of the stomach occasionally occurs.

URINE.

The quantity passed is variable. Often it is practically normal. Frequently it is diminished. Goodall * reports 30 cases of more or less complete anuria appearing from the third to the tenth day and terminating fatally 27 times. Albumin was abundant in the urine. The author believed that the condition was not an inflammatory one, but due to toxic action on the renal nervous system.

Burrows, in 1962 uncomplicated cases in the Boston City Hospital, found albumin in one-third of them. In 8238 cases reported by the Metropolitan Asylums Board in London in 1900, it occurred in 31.7%. In 78 cases of diphtheria reported at the Hospital for Scarlet Fever and Diphtheria in 1901, albuminuria was present in 37.2%, and signs of nephritis in 15.4%. In all but one case the condition had disappeared before the patient had left the hospital, and that case recovered after some weeks.

If we take into account the various estimates of authors as to the frequency of this symptom, it may be said to occur in from one-third to two-thirds of the cases; probably one-half would be a fair estimate. The frequency of its occurrence seems to depend on the character and extent of the diphtheria lesion. It may occur very early in the disease (first or second day) or be delayed for several weeks and long after the disappearance of the symptoms. The quantity of albumin is variable. Usually small, it may, according to Sevestre and Martin, reach the extent of 20 grams to the liter. As a rule, the albuminuria is transient, persisting from three to ten days. Sometimes it is greatly prolonged, and occasionally it is intermittent in character. It is always due, not to direct infection of the kidney substance by the micro-organisms of the disease, but is a result of their toxic products.

Chaillou and Martin have shown that it is much less common in the benign form of fibrinous diphtheria than in any other (17 cases in 30). In 11 cases of toxic angina (pure diphtheria) albuminuria was found in all as an early symptom. M. Rolland has made a study of

* *Lancet,* 1875.

this symptom, and at the Hospital for Sick Children finds in the class of cases last mentioned that albuminuria occurred 49 times in 100; in strepto-diphtheria, 59 in 100. In the latter case the albumin was much more abundant.

According to the researches of Councilman, Mallory, and Pearce, the albuminuria is generally due to an acute degeneration of the kidneys, its intensity varying with the toxicity of the germs. Interstitial and glomerular lesions occasionally occur, especially in older children and in cases of long duration. Even in cases of marked renal diseases, general anasarca is extremely rare, if it ever occurs.

The edema is generally limited to the face. Death occasionally takes place from the kidney lesion. There is nothing peculiar to the disease in the nephritis which accompanies or follows it. There may be a reduction of the urea. Hyaline, epithelial, and granular casts and blood may be present in the urine. Occasionally blood is seen alone, and was formerly attributed to the use of antitoxin. There is not now the slightest evidence that the latter causes this or any other lesions of the kidney.

ALTERATIONS IN THE BLOOD.

The most constant change which occurs in the blood in diphtheria is a more or less marked hyperleucocytosis. This, as well as the other changes to be mentioned later, is in its extent dependent upon the degree of toxemia and the presence or absence of sepsis. Often it is of a very mild type. Occasionally it may take the form of a true leukemia, as pointed out by Felsenthal and others.

Gabritschewsky first in 1894 called attention to the condition of hyperleucocytosis occurring in diphtheria, and proved that this condition was due to the toxins of diphtheria by experiments on animals. Waldstein, Billings, Nicholas, Courmont, and Besredka have done similar work. Schlesinger, by inoculating guinea-pigs, has drawn certain conclusions in regard to the condition which coincides pretty closely with the results attained by others. He showed that the hyperleucocytosis reached its height usually at the height of the disease. Occasionally the cells were increased two to four times the normal number, and the increase was most marked in the polynuclear elements. In the fatal cases the condition continued to the end, and differed in that respect from the condition caused by other infectious diseases. He found, furthermore, that experimental hyperleucocytosis corresponded exactly to that occurring in natural infec-

tion. He regards a knowledge of this symptom as an important factor in prognosis.

Schlesinger examined 24 patients, and found a normal relation between the blood elements in three of them. In the other cases the ratio between the leucocytes and red blood-cells varied from 1 : 275 to 1 : 71. He found in the cases which went on to recovery that the condition gradually disappeared in from four to seven days. In the fatal cases it continued to the end.

Lovett Morse states that hyperleucocytosis probably begins with the disease, and is most marked at the height of the latter, after which it declines. The intensity of the condition varies, as a rule, with the extent of the pseudomembrane, occasionally out of proportion to it. The amount of adneopathy seems to be without influence on this condition. According to Ewing, hyperleucocytosis may be prolonged or enhanced by the occurrence of fever from any cause or of a pneumonia. He regards the condition as a reaction of the organism against a virulent infection and as an important factor in forming a prognosis.

The red cells are diminished to a certain extent; the diminution does not seem to be directly dependent upon the extent or gravity of the disease. In septic cases, according to Monti, nucleated red cells may occur.

Billings, from a series of blood examinations, concludes that the hemoglobin decreases with the decrease of the red corpuscles. Its regeneration, however, is much slower than that of the latter.

Baginsky has laid especial stress upon the increased coagulability of the blood in diphtheria. This he regards as due to the action of toxin on the blood stream through cardiac weakness, due to reduced blood pressure, as shown by Biernacki, Brodie, and Roux and Yersin, and changes in the intima of the blood-vessels.

In severe septic cases there is a thinning or dissolution of the blood, which may result in hemorrhages in various parts of the body. Baginsky states that the increased coagulability of the blood may occasionally lead to the formation of thrombi in the blood-vessels and in the heart itself, cerebral embolism, and paralysis. Furthermore, this condition of the blood may give rise to cardiac arrhythmia, diminished impulse, symptoms of collapse, and cardiac paralysis. The author cites a fatal case of cardiac thrombus in a young girl. The heart was intact.

Grawitz, Baginsky, Monti, and others all agree that in severe cases of diphtheria the specific gravity of the blood is increased. In mild

cases there is little or no change. According to Baginsky, it ranges between 1054 and 1060 in severe cases. Monti believes that the specific gravity increases with the degree of fever in uncomplicated cases. If the latter are mild in type and of short duration, the normal specific gravity is soon restored. In septic cases and those in which the general condition of the patient has suffered, the blood becomes normal only very slowly.

HEART SYMPTOMS.

In discussing the cardiac symptoms caused by diphtheria it becomes very difficult to separate those symptoms which may be regarded as due to changes in the heart itself, and those due to the action of toxin on the nerve-centers which control its action. As a matter of fact, the exact diagnosis of the positive cause of heart failure is only made by the pathologist and by a microscopic examination of the tissues and nerves.

Under the head of cardiac paralysis we have endeavored to describe the symptoms generally referable to disease affecting the nervous control of the heart. In addition to these, there may be cardiac weakness, due, according to Jacobi, to the same conditions that determine muscular weakness in other parts of the body, and in many cases showing few or no microscopic changes to account for the condition.

Hibbard, in an exhaustive examination of 800 cases of diphtheria at the Boston City Hospital, found an irregular heart action in 70 cases. In half of these there were other heart symptoms—systolic murmurs, especially at the apex; a reduplication of the second sound in 6 cases, three of which died. The author finds that systolic murmurs at the apex with reduplication of the second sound occur in 10% of diphtheria cases. He regards these murmurs and reduplications as most often due to a relative mitral insufficiency, from insufficient contraction and dilatation, the latter due to nervous changes in the heart and alterations in the myocardium, but believes that true endocarditis caused by the diphtheria bacillus may occasionally occur.

In 11 hearts weighed, there was an increase over the average weight of 37 grams. In 4 cases cardiac thrombi were noted. The average duration of life in 22 cases of various kinds of heart failure was three weeks from the beginning of the symptoms. The vagus nerve invariably showed degenerative changes.

Hibbard believes that, if after four weeks of convalescence no

heart symptoms have occurred, the patient is safe from this complication. In regard to other symptoms, they have been described under cardiac paralysis.

As to the lesions found in these cases, they included endocarditis, myocarditis of various grades, waxy degeneration (Ribbert), heart clots and nerve changes, dilatation, etc. These have been discussed with the pathology of the disease.

EFFECTS ON THE NERVOUS SYSTEM.

In the mild forms of diphtheria little or no disturbance of the nervous system is seen. In the severe cases, however, through the action of the toxin there may be delirium and stupor. In certain cases there is seen a marked degree of somnolence and apathy. In the most severe forms of the disease convulsions may occur, and, as mentioned by Baginsky, occasionally tetanic symptoms during convalescence.

There may be apathy, dulness, irritability, and certain changes in the patient's normal disposition, probably the result of nutritive disturbances and impoverished blood following a severe attack of the disease. Paralysis of various nerves is due to the action of diphtheria toxins, as proved by the experiments of Roux and Yersin, Ransom, and others, who produced similar paralyses in animals by the injection of these toxins. Ransom showed that this condition was not only caused by the toxins, but that its severity was proportional to the amount of toxin used.

It is difficult to arrive at exact conclusions in regard to the frequency of paralysis, for in many cases it comes on long after the patients have been discharged, and have passed from observation. Cadet de Gassicourt has made an analysis which showed that in 425 cases of malign or benignant diphtheria and croup which recovered, paralysis occurred 101 times—23.76%. In 497 cases of croup which died after operation, and which had remained in the hospital only a short time, paralysis occurred in only 27 cases.

In the collective investigation of the American Pediatric Society, paralysis occurred in 3384 non-hospital cases 328 times—9.7% (antitoxin cases). Lennox Brown reports 14% in 100 cases. Sanné reports 11% in 2400 cases (antitoxin). The Metropolitan Asylums Board of London, in 1900, reports 8238 cases of diphtheria, with paralysis in 18.50%.

F. J. Woolacott has lately collected and classified 829 consecutive

cases of uncomplicated diphtheria taken from the report of the Metropolitan Asylums Board for 1898, and divided them into three classes, in order to determine whether or not paralysis was apt to follow more often in severe cases,—severe or mild referring entirely to the extent of the pseudomembrane,—with the following results:

Nature of Case.	Total.	Paralysis.	Percentage.	Severe Paralysis.	Death from Paralysis.
Severe................	223	64	28.6	19	5
Moderate	566	75	13.2	7	1
Mild	40	..	..	..	..

Figures which will go to substantiate the experimental work of Ransom above referred to.

AGE INFLUENCE ON THE OCCURRENCE OF PARALYSIS.

Bernard E. Meyers reports for 1899, 1316 cases of diphtheria at the Park Hospital: 275 cases of post-diphtheritic paralysis, or about one in five, with 80 deaths. Cases occurred as to ages as follows: Under five years, 104 cases; five to ten years, 138 cases; above ten years, 33 cases. There was a marked preponderance of paralysis among the males. In the last series of cases at the Scarlet Fever and Diphtheria Hospital in New York, paralysis occurred in 10.3%. The average day of its appearance was the twelfth; the earliest, the fourth day. The paralysis usually comes on during convalescence; occasionally, however, it occurs during the early stage of the disease, even on the second or third day, or it may go to the other extreme, and not occur until the thirtieth or thirty-fifth day (Sevestre and Martin).

A word should be said in regard to the early paralysis occurring in the course of the disease—"Diphtherische Frühlämung" of Baginsky. This occurs only in the severest forms of diphtheria and affects usually the velum palati. The speech becomes nasal, swallowing difficult, fluids come through the nose. Food may thus pass into the trachea and cause death by pneumonia—"Schluckpneumonie." The paralysis is usually total; it may, however, be unilateral. In the latter case the palate is out of line, the uvula drawn to one side, and only one side is seen to be movable. Baginsky believes that these cases are probably peripheral, and points out the fact that the paralysis occurs in that part immediately affected by the pseudomembrane, so that it is probable that the disease is really an involvement of the muscle itself—an acute myo-

sitis. At this early stage there may occur also loss of the palatal reflexes, disturbances of the sensibility, etc.

In regard to the distribution of paralysis, the American Pediatric Society report the following:

		1st.	2d.	3d.	4th.	5th.	Un-known.
					DAYS.		
Paralysis, no variety ......132 cases......	8	32	32	19	16	23
Throat ....114 " 16	21	25	11	16	24	
Extremities .... 14 " 3	5	2	3	3	1	
Ocular.................... 11 "	4	3	1	2	1	
General.................. 4 "	1	2	1			

	FATAL CASES.
Not specified	9
Cardiac	32
Throat only	6
General	4
Respiratory muscles	1

Meyers reports as follows:

	CASES.
Palate alone (40% of total paralysis)	110
Palate and ciliary muscles	5
" " external rectus	27
" " ocular muscles	3
" " right facial muscles	1
" " ciliary muscles and pupils	1
" " larynx	1
" " diaphragm	17
Total palate	166

Post-diphtheritic paralysis may be divided into: (1) Circumscribed or benign form; (2) general or severe form.

BENIGN FORM.

This is the most common variety. Its favorite site is the velum of the palate and the pharynx.

The first symptom noted is difficulty in swallowing and the return of liquids through the nose. Each attempt to swallow causes a short, sharp laryngeal cough. Often the children are only able to swallow by taking a very little at a time with the head held well back. The voice is nasal, articulation difficult. There is a snoring respiration during sleep. An examination of the throat shows the velum to be immovable, its reflexes abolished. The process may extend to the whole pharynx, where also the anesthesia is more or less complete. Death may occur suddenly from the aspiration of food or indirectly by pneumonia from the same cause. Recovery takes place in from one to three weeks.

GENERAL FORM.

This form very often begins in the same way as the discrete form just described. It is, however, more apt to involve the neighboring muscles, pharynx, and larynx.

The muscles of the eye are, next to the palate, most often affected. The patellar reflexes are apt to be diminished or lost very early. There is little or no regularity or rule in regard to the muscles affected. When the muscles of accommodation are affected, there is often hypermetropia, rarely myopia. The pupils may be unequal. If the ocular motor muscles are involved, there may be strabismus, diplopia, or ptosis, the symptoms sometimes varying from day to day. Complete recovery takes place, as a rule, even after many weeks. The involvement of the muscles of the lower extremities may be an early symptom, as already mentioned.

The patellar reflexes may be lost or diminished. According to Barlow, Monti, Bristow, and others, there is certainly an increase in the patellar reflex, and even ankle clonus, before the signs of paralysis appear. Baginsky states that the former sometimes occurs, but is by no means the rule.

The paralysis often affects the muscles of the feet and the peroneal group. If the children are old enough to describe their symptoms, they will complain of formication, numbness, or complete anesthesia. More often it is noticed that they do not lift their feet in walking, but shuffle over the floor. Atrophy of the muscles is unusual. Occasionally in the marked cases the symptoms are those of an ataxia, called by some authors "diphtheritic pseudo-tabes"; or the paralysis may become complete, the children being absolutely unable to walk or even stand, and sensation is entirely lost. Dr. C. F. Trevelyan * believes that the ataxic symptoms are entirely due to peripheral lesions, in spite of the fact that Rainey and many others have published cases where slight changes were found in the spinal motor cells. (See Pathology.)

The muscles of the upper extremities suffer less often than those of the lower. The first symptom noted, as a rule, is a certain awkwardness in the use of the arms and hands. The anesthesia, if noted, is usually more marked in or is confined to the fingers or hands. The loss of power in one or both upper extremities may be complete. Through involvement of the facial muscles and those of the neck and tongue, there is inability to support the head, which falls on the chest or

* *Lancet*, 1900.

shoulder; the facial expression is lost and idiotic in appearance; saliva flows from the flaccid lips and speech is stammering. If all the above groups of muscles have been affected in turn, the children are reduced to a helpless mass, seeing with difficulty, unable to sit up or to help themselves in any way, or even to express their wants. In addition, there may be loss of control of bladder and rectum. If the intercostal and other muscles of respiration become involved, there is complete immovability of the thorax during respiration.

DIAPHRAGMATIC PARALYSIS.

According to Bernard L. Meyers, in a series of 1316 cases previously referred to, this form of paralysis occurred 21 times (7.6% of all forms of paralysis). Of these 21, 11 died, constituting 13.7% of death from all forms of paralysis. Most of the cases occurred between two and six years. The average day of occurrence was the thirty-seventh; extremes, eleventh to fiftieth day. The average duration of fatal cases was six to seven days. Other forms of paralysis invariably preceded or accompanied that of the diaphragm.

The symptoms of diaphragmatic paralysis are depression of the abdomen during inspiration and bulging during expiration. Respiration is rapid and panting. Asphyxia may take place from the slightest cause, bronchitis, etc.

Bernhardt, Lemar, and Taub have described cases of diphtheritic paralysis of the superior laryngeal nerve.

CARDIAC OR VAGUS PARALYSIS.

While it is undoubtedly true that disturbances of the heart action are partly due, as has been shown by many authors, to changes in the myocardium, it is very difficult, often impossible, to distinguish clearly between the symptoms caused by these lesions and those caused by changes in the pneumogastric nerve. In regard to its frequency, according to the collective investigation of the American Pediatric Society, in 3384 cases from private practice which had been treated with antitoxin, paralysis of all kinds occurred 328 times (9.7%); cardiac paralysis, 32 times (all fatal cases). According to Meyers, 64 of the 80 deaths from forms of paralysis were due to involvement of the cardiac nerves. The great majority of cases occurred between the ages of two and nine years. The average day of the disease on which the symptoms of cardiac paralysis occurred was the seventh; earliest, second; latest, thirty-sixth.

The average duration of life after symptoms first developed was

four days. Subnormal temperature was the rule. The cervical glands were greatly enlarged in many of the cases.

The various symptoms noted in the circulatory system were as follows: Dilated heart; weak, irregular, intermittent, or rapid action; heart sounds approximated; first sound faint, short, with systolic murmur, or heard reduplicated over the mitral and tricuspid areas; gallop rhythm, bradycardia, and heart with systolic murmurs. Occasionally hemorrhages occurred (epistaxis). In some cases collapse and sudden death took place. The temperature was first elevated and then subnormal. The respiration may be labored and occasionally sighing. Edema of the lungs is not infrequent. Albumin is usually present in the urine. Occasionally there is suppression and hematuria. There are convulsions, drowsiness, delirium (occasionally), and restlessness (frequently).

Cardiac paralysis may occur early in the course of a progressive diphtheritic paralysis or as a final symptom. Occasionally it occurs alone. In the mild form there is merely an inequality in the pulse, slight dyspnea, and a tendency to attacks of fainting. These may soon pass away, not to be repeated, or recur with more marked symptoms and cause death very suddenly.

In the more intense form of the affection it may, according to Gulat, be ushered in by abdominal pains, nausea, and vomiting, followed shortly by sense of distress and weight about the precordia. The breathing becomes labored and embarrassed. The pulse is occasionally slow; generally, however, it is increased in frequency to a marked degree, small, feeble, and intermittent The patients are very anxious, and toss about constantly. In other cases they lie perfectly quiet, making no struggle. The patients may die suddenly during an exacerbation of the dyspnea or sudden movement, or the disease progresses rapidly, with general pallor of the body and cold and blue extremities, to a fatal termination. Cases of recovery have been reported.

In regard to the electrical reactions as a factor in making a prognosis or diagnosis in diphtheritic paralysis, it may be said that they are so irregular as to be worth but little. There may be reaction of degeneration or total loss of reaction to galvanism and faradism, or, on the contrary, the reaction may be absolutely normal. Nor does it follow that in the latter case the prognosis is always good, or in the former always bad. Muscles which have shown complete loss of reaction to both galvanism and faradism sometimes regain their functions completely after many weeks.

The course of diphtheritic paralysis varies. In the discrete form complete recovery is the rule. In the general form death may occur, as already pointed out, from inanition due to the difficulty in taking nourishment, asphyxia or pneumonia from aspiration of food, or paralysis of the pneumogastric nerve with symptoms as above described. The probable nature of the disease will be referred to under the head of Pathology. It should be noted that hemiplegia is sometimes included with diphtheritic paralysis. Its probable cause has already been pointed out as thrombosis or embolism of the brain due to changes in the blood and circulation.

LESIONS OF THE SKIN.

A variety of lesions occur on the skin in the course of diphtheria. It must be said, however, that they are by no means characteristic of this disease, and may occur equally well in other infections. Most authors agree that, while these skin lesions are occasionally seen in the course of a pure diphtheria, the mixed or septic forms are much more likely to exhibit them. The frequency of occurrence of skin lesions varies in epidemics, and is present, according to Cadet de Gassicourt and Sanné, in about 3.5% of the cases. Others state that it occurs much more frequently—from 12.63% (Mussy) to 22% (Sée). The latter examined only a small number of cases.

It is of some interest to compare with these figures the observations as to the occurrence of rash with antitoxin. At the Hospital for Scarlet Fever and Diphtheria, for 1900, in 78 cases there was a rash in 15—25.4% of those in which antitoxin was given. It was erythematous in 7 cases; urticarial in 9; scarlatiniform and morbilliform in one. The average duration of the rash was a little over two days.

Erythema is the most common form of lesion. It may occur at any stage of the disease, and is usually accompanied by a slight rise in temperature. It occurs upon any part of the body; most often on the wrists, elbows, knees, and ankles, rarely on the neck and face. It is usually distributed symmetrically. The most common form is that of an erythema multiforme. At other times the lesions have a well-defined border with a paler center. They spread by peripheral extension, and often coalesce, sometimes covering a large area of the skin. Again, the eruption may be papular in character and more discrete. The duration of these various forms is from two to four days. Brownish discolorations have been noted

after their disappearance. An eruption resembling measles occurs occasionally, without, of course, any of the other signs of the latter disease. By far the most puzzling is the scarlatiniform eruption not infrequently seen, more often in severe cases of diphtheria.

According to Sevestre and Martin, the latter form of eruption is always secondary to one of those just described. At times it is quite impossible to say whether or not we have to do with an actual case of scarlet fever complicating the disease. As has been already noted, in some septic cases there may be a hemorrhagic eruption on the skin. It must not be forgotten that measles and erysipelas not infrequently occur in the course of true diphtheria. Among the extremely rare skin lesions, Raynaud's disease has been described, with gangrene about the nose, ears, and fingers (Hyde). Finally, pyemic symptoms may occur, with abscess-formation as a part of the general sepsis.

ARTHROPATHIES.

Affection of the joints is extremely rare in true diphtheria. Bernardberg has collected 10 cases. According to this writer, they occur after the acute symptoms have passed or during convalescence. The knee and wrist are most often involved. In children the effusion may be simple (serous) or suppurative. The first is attributed by the writer to toxic action of the diphtheria bacilli; the latter, to a septic process caused generally by the streptococcus. The suppurative cases produce more local and general symptoms and usually end fatally.

BRONCHOPULMONARY LESIONS.

This complication is most to be dreaded. Its occurrence is very frequent, especially in institutions. It is most apt to follow laryngeal cases, and is the regular cause of death that follows tracheotomy and intubation. The frequency of this complication varies with the time of year, according to whether the patient is in an institution, and very probably with the plan of treatment of the diphtheria. At the New York Foundling Hospital it was found as the principal cause of death in the majority of the cases of diphtheria. In 3384 cases of diphtheria reported by physicians to the American Pediatric Society Investigation Committee, bronchopneumonia occurred in 5.9%, certainly a very small percentage. Councilman, Mallory, and Pearce, in the study of 161 fatal cases of uncomplicated diphtheria, found macroscopic evidences of bronchopneumonia in 98.

As to the bacteriologic cause of this disease, there has been much disagreement. Most authors attribute its occurrence to the action of the streptococcus, alone or associated with other organisms. As to the bacillus of diphtheria itself, we are still in doubt as to its importance in causing this condition. That it is frequently present there can be no doubt. Wright and Stokes found it in 18 out of 19 cases, 8 times in pure culture. The writers believe that the bacillus of diphtheria may cause the pneumonia. These same authors found the bacillus diphtheria in the lung in 12 cases with no bronchopneumonia.

Belfonti found it 21 times in 26 cases. Kanthack and Stephens, from their examination, believe that the disease is caused by the Klebs-Löffler bacillus. Other writers, Woodhead, Prudden, and Northrup (1889), have found the diphtheria bacillus seldom if at all. On the other hand, the streptococcus, staphylococcus, and pneumococcus are regularly found.

Councilman, Mallory, and Pearce, in the 98 cases above referred to, examined 88 cases; 6 were sterile.

The diphtheria bacillus alone was present in 49; the diphtheria bacillus with the streptococcus in 17; with the Streptococcus and Staphylococcus aureus in 5; with Staphylococcus aureus alone in 6; with the pneumococcus in 4.

The streptococcus was found alone 15 times; in combination with other organisms, not Klebs-Löffler bacilli, 13 times.

Diplococcus lanceolatus occurred twice in combination and once alone.

Staphylococcus aureus occurred alone 3 times.

In 10 cases sections were cut and stained and showed morphologically: streptococcus three times; diphtheria bacillus twice; diphtheria bacillus and pneumococcus once.

In summing up our present knowledge as to the causation of the disease, we may say, in general, that it is due to one or more organisms, alone or in combination. Those most frequently occurring are the Streptococcus pyogenes and diphtheria bacillus, generally in combination.

The disease comes on with an increase in temperature, pulse, and respiration. If it is secondary to a laryngeal case, the cyanosis, if already present, is increased, together with the dyspnea. An important symptom is the disturbance of the respiration-pulse ratio, from the normal 1 : 4 to 1 : 3. The prostration is increased; there is apathy and a rise in temperature. The physical signs at first are those of a diffuse bronchitis. As the disease progresses the signs of consolidation are present

over several different areas, a greater part of one or both bases, or even a greater part of the lung. Coarse and subcrepitant râles are heard over a good part of the chest. Bronchopneumonia may come on at any period of the disease, or after the membrane has quite disappeared. The mortality from this complication is very great, and it is doubtful if, after its occurrence, we have to-day any better means of combating it than formerly; but that serum treatment, in cutting short the diphtheria and so restoring the air-passages to their normal condition, reduces the frequency of this complication there can be little doubt.

Bronchitis is a common complication, especially in laryngeal cases. Its importance lies in the tendency to develop into a pneumonia. Fever always accompanies it. Emphysema occurs, especially in laryngeal cases. It is usually vesicular in type, but the interstitial variety may occur and the tissues about the neck be involved. (See Intubation.)

Empyema has been noted, especially in septic cases. Serofibrinous pleurisy is not infrequent. Councilman, Mallory, and Pearce find the former in 161 fatal cases 5 times; the latter, 18 times. In one case the empyema was caused by the rupture of a small abscess into the pleural cavity. Abscesses of the lung occasionally occur.

Lobar pneumonia as a direct result of diphtheria is very rare. On the other hand, bronchopneumonia with a lobar distribution is far from uncommon, and is no doubt not infrequently classified with the former in the absence of a microscopic examination.

COURSE, DURATION, AND OUTCOME.

It is obvious from the variety of symptoms presented by the disease that any attempt to give a general description of its course, as may be done in most other infectious diseases, would be useless. Suffice it to say that the latter is dependent on the localization of the membrane, the virulence of the organism itself and that of its associate organism, the degree of resistance shown by the patient, and, finally, the presence or absence of complications and sequels.

The duration of the disease varies greatly, from a few days to several weeks or even months. Again, it may cause death in twenty-four hours. In regard to the so-called recurrent diphtheria or relapses of diphtheria, from what we now know of the characteristics of the Bacillus diphtheriæ (Löffler), especially as to its ability to remain quiescent for weeks or even months upon mucous membranes, it is highly probable that these so-called relapses are due to a recurring activity of these germs, due to causes at present not clearly understood, and in other cases to a growth of newly acquired germs. In over 7000 cases reported by the Metropolitan Asylums Board of London (1900) the average stay in hospital was 52.2 days.

TERMINATION.

In spite of the apparent hopelessness of many cases and the existence of grave complications, the patients are able to make a complete recovery, especially with serotherapy. Death occurs from mechanical causes, the action of toxin on the system, or from one of the complications.

DIAGNOSIS.

THE throats of children, especially those who are too young to complain of any soreness or pain in swallowing, should be examined by the physician as a matter of routine. The child should be held, by mother or nurse, firmly against the breast, facing a good light; the right arm of the assistant confining the patient's arms close to the body, the left holding the legs, while the physician himself steadies the head with the left hand. The examination should be made very quietly, care being taken not to excite the patient. With a tongue depressor or the handle of a teaspoon the entire throat should be thoroughly and, above all, rapidly examined: tonsils, faucial pillars, and uvula. Rarely the examiner gets a quick glance at the larynx, during the reflex movement caused by the pressure of the spatula on the base of the tongue.

The nose should also be examined for evidence of discharge, membrane, swelling, etc., and, finally, the cervical and submaxillary glands for swelling and tenderness.

CLINICAL DIAGNOSIS.

The clinical diagnosis of diphtheria is beset with many difficulties. Bacteriology has taught us that the inspection of a given membrane will permit us to form but very uncertain conclusions as to whether a given case is to be classified as one of true diphtheria or as a product of the activity of other organisms—streptococci, staphylococci, etc. Especially since the introduction of serotherapy, an early diagnosis has become of much greater importance, not only on account of its influence upon the prognosis of the disease, but in order that proper means of isolation may be resorted to at once, and, if necessary, immunity be established among those who have been exposed.

Bacteriology alone can permit us to make a positive diagnosis. In large cities this is a comparatively simple matter; in small towns and country places, a much more difficult one and less frequently resorted to. A clinical diagnosis, therefore, may be of the greatest importance, and a knowledge of the local and general symptoms will often enable us to arrive at a correct one.

Among the conditions found in the throat which must be differentiated from diphtheria are, first, general redness of the pharyngeal parts. This is due in a majority of cases to an acute catarrhal process. It may, however, well be the beginning of diphtheria, and the diagnosis can only be made by culture or awaiting further development. If after twenty-four to forty-eight hours no sign of membrane appears, the latter may be excluded, always bearing in mind the rare cases of so-called catarrhal diphtheria, which cannot clinically be differentiated from an ordinary catarrh. Thrush may possibly be mistaken for diphtheria. In the former the lesions are seen less often on the pharynx, uvula, and palate than elsewhere, and if they do occur at the former site, the cheeks, hard palate, and lips and tongue are all involved. The lesions consist of small white flakes looking very much like curdled milk, but which have a tendency to adhere. They occasionally leave a bleeding surface if forcibly removed.

Broadly speaking, the differential diagnosis lies, first, between diphtheria and certain catarrhal conditions; second, the exudative or necrotic inflammation caused by various organisms—streptococci, staphylococci, Vincent bacillus, etc.

In regard to the appearance of the membrane, that of true diphtheria is very adherent to the underlying tissues, and, if removed, leaves behind it, as a rule, a more or less bleeding surface. The membrane is elastic, of varying degrees of thickness, and when pressure is brought to bear on it, does not show the tendency to crumble which the membrane of streptococcic and staphylococcic infection exhibits. The exudate, as a rule, has a greater tendency to spread than in the latter variety.

Peritonsillar Abscess; Quinsy.—As a rule, the appearance of the tonsil is quite different from that of diphtheria. The latter is much swollen, pushed forward, and the uvula often displaced. There is great pain and difficulty in swallowing, and nasal speech.

Instant relief follows the breaking of the abscess or incision. At times, however, the affected tonsil is more or less covered with an exudate which is difficult to distinguish from that of diphtheria. This disappears in a short time after incision. The incision itself is apt to leave an exudate formed about it, but shows no disposition to spread. Cultures alone will clear up the diagnosis in doubtful cases.

Aphthous and ulcerative lesions are apt to occur at other sites than the pharynx and tonsils, and, as a rule, are not easy to confound with a diphtheritic process.

Gangrenous angina occurs in the course of other infectious dis-

PLATE 7.
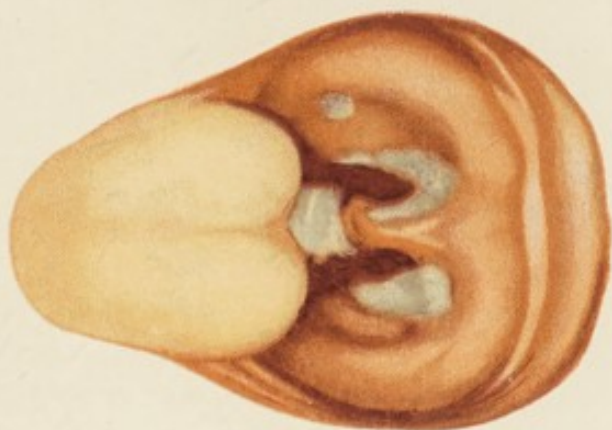
Diphtheria of the pharynx and tonsils.
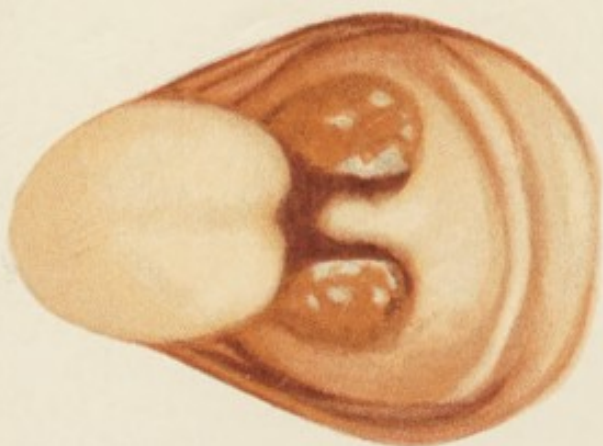
Follicular tonsilitis.
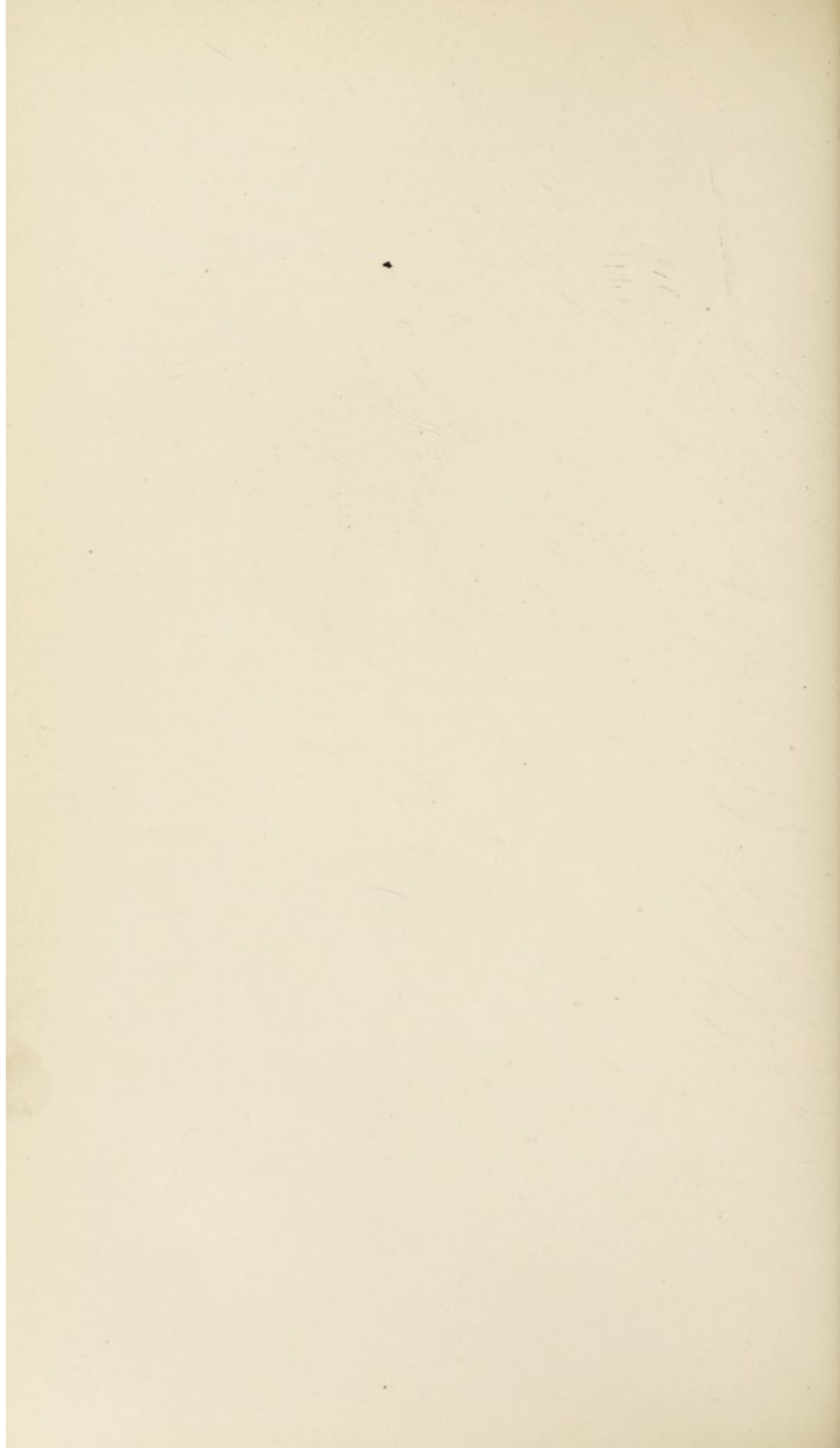
eases (measles, scarlet fever, etc.). The symptoms of gangrene are so marked that they may readily be distinguished. In this connection it will be remarked that gangrene is a not uncommon sequel of diphtheria.

Follicular Tonsillitis.—Diphtheria very rarely occurs in a form resembling this condition. That it does occasionally occur, Martin, Chaillu, and Koplik have especially pointed out. The latter has given the name of lacunar diphtheria of the tonsils to this form of the disease, which can be recognized and differentiated from follicular tonsillitis only by a bacteriologic examination.

Herpes occasionally occurs in the throat. It is usually associated with herpes labialis, and is easily recognized. Occasionally it resembles a discrete diphtheria lesion, and, as Dieulafoy and other writers have shown, the diphtheria bacillus is occasionally found in the so-called herpetic angina.

Ulcerations of the frenum due to abrasions caused by coughing, syphilitic lesions, and exudations following surgical wounds of the throat may be confused with diphtheria, and here, again, if any doubt exists, it should be removed by a bacteriologic examination.

Pseudodiphtheria.—This disease is caused by various germs other than the Bacillus diphtheriæ (Löffler); generally, however, the Streptococcus pyogenes, occasionally the staphylococcus, pneumococcus, or colon bacillus and others, alone or in combination.

It occurs as a primary disease, but more often as an accompaniment of certain exanthemata, especially scarlet fever. (In many of these cases a differential diagnosis is absolutely impossible without a bacteriologic examination.)

As a rule, the temperature is lower in diphtheria than in pseudodiphtheria. Prostration is greater in the former. The pulse is generally weaker and the patients feel and look sicker. The membrane is more apt to be limited in pseudodiphtheria and shows less tendency to involve neighboring parts. That of true diphtheria is more adherent and shows greater tendency to leave a bleeding surface. The course of true diphtheria is longer than that of pseudodiphtheria. Finally, paralysis never follows the latter, and albuminuria occurs much less often than in true diphtheria.

In the throat lesions complicating scarlet fever a positive diagnosis cannot be made until the rash appears. The possibility of the occurrence of both diseases at the same time must always be borne in mind. Koplik's spots and other symptoms should enable us to diagnose the angina occurring in measles.

Pseudocroup.—The differential diagnosis between the acute affections of the larynx, as to whether they are true diphtheria, is absolutely impossible except by a bacteriologic examination. Symptoms of croup following pseudomembranous inflammation of the throat may, in the vast majority of cases, be set down as due to diphtheria, unless there are symptoms of the presence of one of the exanthemata, especially scarlet fever and measles; the pseudomembrane seen in the latter case not infrequently extending to the larynx, trachea, and bronchi.

The most difficult cases to diagnosticate are those of primary croup or croup occurring without other lesions in the throat. Diphtheritic croup begins insidiously, with signs of laryngeal irritation, cough, hoarseness, etc. The progress of the disease is very rapid; dyspnea is soon developed, followed very soon by signs of stenosis. It may be distinguished, as a rule, from a catarrhal condition by the greater severity of the symptoms and by the rapid and steady progressive development. The catarrhal condition is usually associated with catarrh elsewhere—trachea, bronchi, etc. Dyspnea is not pronounced and the symptoms have little tendency to grow worse. Laryngismus stridulus usually occurs in the night or early morning. The symptoms come on very suddenly. There is very rapidly occurring dyspnea, harsh barking cough and voice, and a good deal of anxiety on the part of the patient. The attack, especially with prompt treatment, rapidly passes off. The children the next morning are well or perhaps a little hoarse. Occasionally these cases are more severe and the dyspnea is very marked, the symptoms in general simulating a true diphtheritic laryngitis, and, according to Sevestre and Martin, occasionally requiring intubation. A bacteriologic examination is necessary for a true diagnosis in such cases.

Retropharyngeal abscesses may occasionally be confounded with croup. A digital examination will usually serve to make the diagnosis. Other laryngeal conditions, edema, syphilis, and foreign bodies may resemble croupal laryngitis. The history of the case will usually serve to differentiate the former condition from the latter.

Catarrhal Rhinitis.—The diagnosis of nasal diphtheria may usually be made on the character of the discharge, which is thin, scanty, generally bloody, and so irritating as to cause marked excoriations about the nostrils and upper lip. This serves to distinguish it in part from a simple coryza or catarrhal rhinitis, where the discharge is profuse, viscid, and much less irritating. Moreover, the lymph nodes are invariably involved in the former and not in the

latter. Finally, pseudomembrane may be seen in some instances in the nose. A bacteriologic examination will clear up any doubt, and will also serve to distinguish diphtheria from other nasal conditions, foreign bodies, etc.

Anogenital diphtheria can hardly be mistaken for any other lesion, especially as there is, in the majority of cases, diphtheria elsewhere in the body or a history of exposure to it.

BACTERIOLOGIC DIAGNOSIS.

This may be made by direct examination of the pseudomembrane or of cultures made from it.

Direct examination of the exudate is of value when an immediate diagnosis is necessary. For the purpose, a bit of membrane is removed with forceps or cotton-covered swab and transferred to a cover-glass or glass slide on which a smear is made—which is then dried, fixed by passing it speedily through the flame, and stained with methylene-blue solution (Löffler) and examined. The bacilli, if found, are by no means typical, as are those seen in culture. They are irregular in size, shape, and staining properties, and, furthermore, are mixed with fibrin, cocci, and detritus. They are seen usually as short rods, slightly swollen at their ends, and occurring in groups of 3 or 4, often more or less parallel, sometimes end to end. The fact that no bacilli are found by this direct method is by no means proof that the case is not one of diphtheria, as subsequent cultures will often show these to be abundant. The direct method is usually unsatisfactory, and is not to be depended upon.

CULTURES.

These are taken usually on Löffler's blood-serum, made as follows: Freshly flowing calf's or sheep's blood is caught in a clean glass jar, which is covered and allowed to stand until the clot is thoroughly formed. It is then removed and placed on ice for twenty-four hours, when the clear serum is siphoned off, and one-third of the amount of nutrient beef broth is added, together with 1% of glucose.

The broth is prepared thus: One pound of finely chopped meat is put to soak in one liter of water for an hour or more. This mixture is then squeezed through a towel or cheese-cloth, and to the fluid portion thus obtained is added 1% of peptone, 1% of glucose, and $\frac{1}{2}$% of common salt. This mixture is made slightly alkaline by the addition of caustic soda or carbonate of soda. It is then boiled for half

an hour and filtered. It should then be placed in flasks and steril-
ized or used at once.

The Löffler mixture made as above is poured into test-tubes which
have been previously sterilized, about 2 c.c. to each tube. Care is
taken to avoid formation of bubbles in the process. The tubes are
then stoppered with cotton. They are placed at a proper angle in a
serum coagulator and sterilized for two hours, the temperature being
kept just below the boiling-point.

The serum thus solidified and made sterile may be kept for weeks.
The swab for making cultures consists of an iron rod wrapped closely
with absorbent cotton. This is put in a glass tube plugged with ab-
sorbent cotton and subjected to dry heat at a temperature of 150° F.
for one hour.

Method of Taking Cultures.—The patient, if a child, should be
held in the manner described for examination of the throat, the
tongue depressed with a spoon or a tongue depressor, and the swab
swept thoroughly over the membrane, if present; if not, over the
pillars of the fauces, the tonsils, and the back of the pharynx. In
laryngeal cases without visible membrane the culture is often un-
satisfactory; the swab, however, can be introduced well down the
back of the pharynx, and even occasionally to the larynx itself during
the elevation of the latter caused by the tongue depressor. The swab,
being moistened as quickly and thoroughly as possible in this man-
ner, is then rubbed gently over the entire flat surface of the culture-
medium in the tube, the cotton plug of the latter carefully re-
placed, the swab returned to its own tube, and the tube replugged.
Cultures from the nose and elsewhere are similarly made.

Cultures should not be taken shortly after an antiseptic has been
applied to the throat. It is better to wait for at least an hour after
such application.

The tubes thus inoculated are placed in the incubator and kept
at a temperature of 99° F. for at least twelve hours. The latter length
of incubation gives better results than shorter ones, although an
incubation of five or six hours, if haste is necessary, will often suffice
to render at least a probable diagnosis.

Examination of Cultures.—A drop of water is placed on a clean
cover-glass and a sterile platinum loop is passed through several of
the colonies grown on the culture-medium. The bacilli in the loop
are then washed off in the drop of water and spread over the surface
of the glass, which is allowed to dry in the air and passed through the
flame of a Bunsen burner three times in order to fix the specimen;

then covered with a Löffler's methylene-blue solution for ten minutes, after which it is washed, dried, mounted in balsam, and examined with the $\frac{1}{12}$ oil-immersion lens.

The culture thus taken will show either pure cultures of typical Klebs-Löffler bacilli, or the latter mixed with a few or many cocci, or the cocci may be in pure culture or largely in excess of the bacilli. Occasionally the bacilli, if present, are so atypical or so few compared to other organisms that no opinion can be formed as to the nature of the case. It is better either to await the result of another culture, or, if grave clinical symptoms be present, to regard the case as one of diphtheria and act accordingly.

Concetti has recently suggested a rapid method of making a bacteriologic diagnosis which has given excellent results in his hands: A sterile cotton swab is impregnated with glucose, glycerinated agar-agar, and, after the culture has been taken in the way above described, is placed in a glass tube, which is plugged and subjected to a temperature of 97° to 99° F. in the thermostat for four to six hours. The author claims that the bacilli stained with Neisser's stain can be clearly recognized, since they have grown much faster than the other organisms usually associated with them.

PROGNOSIS.

MANY factors must be taken into consideration in order to foretell the outcome of this disease. No other infection is so uncertain as to its results as that under consideration, the most hopeless cases often making a complete recovery, and those which we have reason to regard as most benign not infrequently causing death.

AGE OF THE PATIENT.

This has an important bearing upon prognosis, as may be seen by the following table, compiled by Burrows from a series of 2093 cases occurring at the Boston City Hospital during 1900 and 1901:

AGE OF PATIENT.	DEATHS.
0–1 year	4.0%
1–2 years	33.0%
2–3 years	23.0%
4–5 years	15.6%
5–6 years	14.6%
7–8 years	10.4%
8–9 years	8.6%
9–10 years	2.08%

In children under five years death occurred in 21.3%; in children of from five to ten years death occurred in 8.40%; in children of from ten to fifteen years death occurred in 3.10%.

These cases were treated with antitoxin, and if we compare them with the mortality occurring in cases not so treated, we shall see that while the death-rate for each age has decreased markedly with the use of serotherapy, the proportion remains practically the same.

The following two tables are from Biggs and Guerard:

HERTZ.	MORTALITY PERCENTAGE.	HIRSCH.	MORTALITY PERCENTAGE.
0–1 year	80	0–1 year	88.3
1–2 years	45	1–3 years	82.3
3–5 years	40	3–4 years	63.9
5 years	17	4–5 years	46.9
Above 10 years	17	6–7 years	43.2
		Above 7 years	22.2

SITE OF THE LESION.

The laryngeal or croup cases, even with serotherapy, continue to furnish the largest percentage of death-rate. The prognosis depends

also upon whether such cases come to operation, and upon the nature of the operation—intubation or tracheotomy. The following table, from Biggs and Guerard (1896), of laryngeal cases treated with anti-toxin will show the death-rate, etc.

	TOTAL CASES TREATED.			NON-OPERATIVE CASES.			OPERATIVE CASES.			
	Cases.	Deaths.	Mortality Percentage.	Cases.	Deaths.	Mortality Percentage.	Cases.	Deaths.	Mortality Percentage.	Previous Mortality.
Total in 72 reports...	15,148	2626	16.6	12,066	1491	13.5	3082	1135	36.7	70.0

METHOD OF TREATMENT.

The writers of the last-mentioned report also state that the number of cases coming to operation with antitoxin treatment has been reduced one-half. Comparing the results of tracheotomy with intubation: Of the above 3082 cases, 1355 were tracheotomized, with a mortality of 42%; 1173 were intubated, with a mortality of 30.8%. The previous mortality without antitoxin in 12,736 cases reported by Monti was 73.3%. Of 5546 intubation cases reported by McNaughton and Maddren in 1892, the previous mortality was 69.5%.

From these statistics may be seen how greatly the prognosis has been influenced in laryngeal cases by antitoxin. The death-rate has fallen from 70% to 16.6%. It will also be noted that mortality favors intubation as the operation of election. Nasal cases involving the choanæ are very fatal, especially in infants.

TIME OF BEGINNING TREATMENT.

The influence of this factor is very marked. Biggs and Guerard have made up a table of statistics which clearly demonstrates the value of early treatment:

	CASES.	DEATHS.	MORTALITY PERCENTAGE.
1st day of disease..........	1415	5	3.5
2d " " "	2640	213	8.0
3d " " "	2340	300	12.8
4th " " "	1458	346	23.6
5th day and after........	1912	671	35.0

THE INFLUENCE OF SURROUNDINGS.

Diphtheria is a much more fatal disease in institutions than else-
where.   Especially is this due to the frequent occurrence of broncho-
pneumonia in institutions with a very high mortality.

Finally, a factor of some importance is the season of the year.
Diphtheria appears to be more dangerous in the inclement and cold
months than in the mild ones, as is shown by the following report of
the Metropolitan Asylums Board of London, 1900:

In January there were admitted to the various hospitals under con-
trol of the Board 785 cases, with a mortality of 16.73%; in April, 530
cases, with a mortality of 8.17%.   The months, however, show great
irregularity.   From 1888 to the present the maximum death-rate
from diphtheria occurred in January, the minimum in April.

PROPHYLAXIS.

In preventing the spread of diphtheria, we are fighting a disease the cause of which is known to us as well as the mode of transmission. Based upon this knowledge, certain definite rules may be laid down, which if faithfully followed will go far toward reducing the ravages of the disease.

First, in regard to the patients themselves: The rules laid down by the Health Department of the city of New York appear to cover the whole ground in a clear and concise form:

"If possible, one attendant should take the entire care of the sick person, and no one else besides the physician should be allowed to enter the sick-room. The attendant should have no communication with the rest of the family. The members of the family should not receive or make visits during the illness. The discharge from the nose and mouth must be received on handkerchiefs or cloths, which should at once be immersed in a carbolic solution (made by immersing six ounces of pure carbolic acid in one gallon of hot water, which may be diluted with an equal quantity of water). All handkerchiefs, cloths, towels, napkins, bed-linen, personal clothing, night clothes, etc., that have come in contact in any way with the sick person, after use should be immediately immersed, without removal from the room, in the above solution. These should be soaked for two or three hours and then boiled in water or soapsuds for one hour.

"In diphtheria and scarlet fever great care should be taken, in making applications to the throat and nose, that the discharges from them in the act of coughing are not thrown into the face or clothing of the person making the applications, as in this way the disease is likely to be caught.

"The hands of the attendant should always be thoroughly disinfected by washing in the carbolic solution, and then in soapsuds, after making application to the throat or nose, and before eating.

"Surfaces of any kind soiled by the discharges should be immediately flooded with the carbolic solution.

"Plates, cups, glasses, knives, forks, spoons, etc., used by the sick person for eating and drinking must be kept for his especial use, and under no circumstances removed from the room or mixed with similar utensils used by others, but must be washed in the room in the carbolic

solution and then in hot soapsuds.   After use, the hot soapsuds should be thrown into the water-closet and the vessel which contained it should be washed in the carbolic solution.

"The room occupied by the sick person should be thoroughly aired two or three times daily, and swept frequently, after scattering wet newspapers, sawdust, or tea-leaves on the floor to prevent the dust from rising.   After sweeping, the dust upon the woodwork and furniture should be removed with damp cloths.   The sweepings should be burned, and the cloths soaked in the carbolic solution.   In cold weather the sick person should be protected from the drafts of air by a sheet or blanket thrown over his head while the room is being aired.

"When the contagious nature of the disease is recognized within a short time after the beginning of the illness, after the approval of the Health Department Inspector, it is advised that all articles of furniture not necessary for immediate use in the care of the sick person, especially upholstered furniture, carpets, and curtains, should be removed from the sick-room.

"When the patient has recovered, the entire body should be bathed and the hair washed with hot soapsuds, and the patient should be dressed in clean clothes (which have not been in the room during the sickness) and removed from the room."

In regard to the proper time to end the quarantine, it should depend entirely upon the result of cultures after the apparent disappearance of the disease; for as long as diphtheria bacilli are found upon the mucous membrane, the patient should be regarded as a source of danger.

Walsh, Sanitary Inspector for the District of Columbia in 1898, as a result of the examination of 2500 cultures from 800 convalescents, found the bacillus absent as early as the sixth day and present as late as the eighth week.   Antitoxin seemed to have little or no influence upon the persistence of the bacillus.

Park and Beebe, in 2566 cultures from 605 convalescents, found the bacillus absent in three days after the exudate had disappeared in 304 cases; in seven days, in 176 cases; in twelve days, in 64 cases; in fifteen days, in 35 cases; in three weeks, in 12 cases; in four weeks, in 4 cases; in nine weeks, in 2 cases.

In addition to the rules above quoted, as laid down by the Board of Health, it should be added that special rules should be made for those who are obliged to come in contact with the patient temporarily, physician and others.   The former should cover his clothes completely with a gown, which should be kept just outside the patient's room and

sterilized immediately after being used. Should the patient during the examination of the throat cough violently in the face of the examiner,—a by no means uncommon occurrence,—the latter should wash the face and hair in soap and water, and follow it with a solution of bichlorid (1 : 1000). The hands should always be treated in this way before leaving the sick-room.

Nurses should protect themselves by the same methods prescribed for physicians. The nurse's hands should be kept perfectly clean and disinfected, and, in addition, it is advisable to use some simple gargle or spray, as saturated watery solution of boric acid, Dobell's solution, or common salt.

Finally, there can be no doubt at present of the advisability of nurses and attendants receiving an immunizing dose of antitoxin, to be repeated, if necessary, in protracted cases; or at the slightest sign of throat trouble, a full dose of antitoxin. Persons in attendance upon diphtheria cases, before leaving should disinfect their person and clothing thoroughly.

In regard to disinfection of rooms occupied by diphtheria cases: The walls and ceilings are to be rubbed down carefully with bread, damp cheese-cloth, or washed in 1 : 1000 bichlorid solution. The woodwork, furniture, and floor are to be scraped and treated with the same solution. If possible, it is better to repaint and repaper. Carpets, upholstery, mattresses, etc., may be disinfected by steam. Other articles—books, toys, etc.—should be burned. It is probable that the formaldehyd vapor is effective in destroying germs upon the surface. It has proved to be valueless in penetrating upholstery, bedding, etc. It has the advantage of not being destructive to furniture or delicate fabrics. It may be conveniently used in the form of formalin candles, one or more being burned, depending upon the size of the room. The doors and windows should be plugged tightly with cotton during this process, and closets, drawers, etc., all opened and the articles to be disinfected spread out as much as possible.

PUBLIC MEANS OF PROPHYLAXIS.

The action of the Board of Health of New York in requiring reports of all cases of diphtheria, together with the system of primary and secondary culture examinations, has done much toward preventing the spread of this disease. The Board, furthermore, takes charge of such cases as are not under the care of a physician, removing them, if necessary, to one of the hospitals under its control.

The regular inspection of all public schools by a corps of physicians connected with the Health Board has given excellent results. All pupils with infectious disease are immediately excluded, and, in the case of diphtheria, not allowed to attend school until they have been notified by the Board that the cultures examined by it do not show the presence of diphtheria bacilli.

There is still much to be done along this line in the matter of greater cleanliness in public conveyances, street and railroad cars, carriages, etc., as well as stations. The recent crusade against spitting in New York marks a public interest in this matter which it is hoped will be sustained and broadened.

IMMUNIZATION BY ANTITOXIN.

Increased evidence of the value of small doses of antitoxin as a protection against diphtheria proves beyond a doubt that we have in this remedy a sure and safe means of conferring an immunity for a limited time—estimated generally as about four weeks. Lahr, Riether, and Heubner have reported excellent results in institutions, through the use of this remedy in doses varying from 100 to 500 units.

Morrill, in the Children's Hospital in Paris, reports that of 1808 children immunized at least every twenty-eight days with 150 to 500 units of serum, 7 had diphtheria, 3 from insufficient dosing, 2 within twenty-four hours of the injection, and 2 in twenty-two and twenty-three days. Of 829 who had not been given antitoxin, or in whom more than twenty-eight days elapsed after the injection, 9 had diphtheria, besides 3 immunized adults. The author states that immunity may be given in any case for at least ten days by the injection of 100 to 250 units if given twenty-four hours previous to actual infection. A larger dose—250 to 500 units, depending upon the age of the patient—will confer safety for three weeks under similar conditions.

Biggs and Guerard, from 35 reports of 17,516 cases in which small doses of antitoxin were given as an immunizing agent, state that diphtheria occurred in 131 cases; 109 mild cases and one fatal case within thirty days of the date of injection, 20 mild cases and one fatal case after thirty days. The authors believe that four weeks may be considered as an average for the continuance of immunity after injection.

At the New York Infant Asylum 107 cases of diphtheria occurred between September and January, 1865 (30 cases a month). In October bacteriologic examination showed diphtheria bacilli in almost one-half of the throats. All these were guaranteed. January 16th,

224 children were given immunizing doses of antitoxin, and up to February 15th only one case of diphtheria occurred. A second case then developed, and between February 15th and 27th, five. On the 25th 245 children received antitoxin, and no cases occurred for thirty-one days. To sum up: Before isolation and immunization 107 cases occurred in one hundred and eight days; after the latter was practised, 5 cases in one hundred and twelve days.

The occurrence of diphtheria during an epidemic of measles at the New York Foundling Hospital in past years added greatly to the mortality of the latter disease. During an epidemic of measles at that institution every child is immediately given 400 units of antitoxin. The results have been most encouraging, as is shown by a recent report from the New York Foundling Hospital:

In 149 cases of measles, 500 units of diphtheria antitoxin were given at the first appearance of measles symptoms. No cases of diphtheria secondary to measles occurred in any of those cases for a period of one month at least.

Since the appearance of the latter report, another epidemic of measles has occurred at this institution. The children were given 500 units of antitoxin each, but it was apparent in a number of instances that immunity from diphtheria did not last for more than eighteen days to three weeks, at which time several cases of diphtheria occurred, complicating or following measles, and generally proved fatal (December, 1901). This relatively shorter period of immunity from diphtheria in measles cases has been noted in France and Germany,[*] and for this reason Slawyk recommends that the immunizing dose be repeated every two weeks in measles epidemics.

W. P. Coues gives an account of an epidemic of diphtheria at St. Mary's Infant Asylum in Boston, 1898. Fifty children were given doses of antitoxin, from 50 to 500 units, the small dose in a one-day infant. Urticaria occurred in 14 as the only bad result. From February 15th to March 22d there were 18 cases of diphtheria. After the latter date, when antitoxin was begun, no cases occurred for three weeks.

Kraus (1900) gives an extensive analysis of results of immunizing doses in 122 hospital cases which were divided as follows: 44 were scarlet fever cases, 2 of which later contracted diphtheria; 31 cases of children who were sent to the diphtheria pavilion and found not to have true diphtheria; no cases contracted it; 47 measles cases, many of them complicated; one developed diphtheria.

[*] See Netter : Int. Med. Congress, Paris, 1900.

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Thus, of 122 cases, all of whom were more or less exposed to the disease, and all ill with diseases most likely to be complicated by diphtheria, only 3 became infected; on the twenty-sixth, twenty-seventh, and forty-first day after inoculation. The dose of antitoxin ranged from 200 to 400 units, the latter being given to the children with suspected diphtheria.

In addition to the results of immunization at the New York Infant Asylum, the following report of Biggs will show the result at other institutions:

Place of Observation.	Children Immunized.	Cases of Diphtheria Developing Among Those Immunized Between 1 and 30 Days.	Cases Developing Within 24 Hours.	Cases Developing After 30 Days.	Number of Cases of Diphtheria That Occurred in the Institutions Previous to Immunization.
Nursery and Child's Hospital .	136	0	0	0	46 cases in 90 days; 15 cases in 18 days.
New York Juvenile Asylum ..	81	0	0	0	12 cases; 3 cases in 2 days.
New York Catholic Protectory	114	0	1	0	5 cases in 3 days.
Bellevue Hospital .	11	0	0	0	2 cases in 10 days.
Health Department Inspectors	232	1 mild on the 19th day.	3	3 { one 30th one 31st one 55th	2 cases in 10 days. One or more cases in more than 90 families.
Total	1043	3	4	13	

Slawyk gives an account of the immunization of 500 children at the Charity Hospital, Berlin: 874 inoculations with no cases of diphtheria.

GENERAL CARE OF THE HEALTH.

Children should have plenty of fresh air, and should live, if possible, in sunny rooms; damp and poorly ventilated rooms should be avoided in that they conduce to catarrhal conditions of the air-passages so favorable to the growth of diphtheria bacilli. Adenoids

and hypertrophied tonsils should be removed or treated. Nasal catarrh, if not due to the latter, should be alleviated or prevented by regular douching of the nasal passages with salt or other mild solution, as advocated by Jacobi; and, finally, a more general knowledge of the nature of the disease should be impressed upon mothers and nurses by physicians and health officers, together with the importance of examining a child's throat when there is the slightest indication of illness.

TREATMENT.

GENERAL MEASURES.

THE patient should be put to bed as soon as possible in a well-ventilated and well-lighted room. In hospitals the pavilion system is preferable to rooms in the main building, and, if possible, a number of separate rooms are more desirable than one large one. Septic cases, and especially those complicated by bronchopneumonia, should, if possible, be kept apart from the uncomplicated cases. If one large room must be used, it is of the highest importance that the patients should have plenty of air-space. Feeding is a most important part of the treatment, and, as a rule, our main reliance is to be placed upon milk. This should be given every two hours. As a rule, there is little danger of the patient's taking too much nourishment. Semi-solids, such as bread and milk, are sometimes more easily taken by cases that have been intubated. Other preparations which may be of value are various liquid foods, beef peptonoids, etc.

In cases in which, on account of severe toxemia or local symptoms, or in intubated cases where each mouthful taken excites a violent fit of coughing, it is well to feed the children by gavage. This may be done either through the mouth or nose. Casselberry's position, with the children lying on the back with the head well down, may be useful in some intubated cases. As a rule, the latter will take the milk in a reclining position. Rectal feeding with partly digested food is to be regarded as a last resort. Its results are most unsatisfactory.

REMEDIES OTHER THAN ANTITOXIN.

There is one specific in diphtheria—namely, its antitoxin, of a standard quality, given in sufficient dosages. All of the much vaunted remedies have seen their day and are rapidly passing into disuse. The most prominent of these will be mentioned here, more as a matter of historical interest than with any idea of advocating their use.

Jacobi and others, until very recently, at least, still advocated the use of tincture of the chlorid of iron, diluted with water and glycerin, in cases of laryngeal and tonsillar diphtheria. Whatever its beneficial effects, it certainly has the undesirable result of upsetting the stomach of many children—not a qualification to recommend

it in a disease in which keeping up the strength with proper nourishment is of so much importance. Mercury internally in the form of bichlorid has been highly recommended, especially in cases of laryngeal diphtheria. The drug was given in amounts equal to $\frac{1}{6}$ to $\frac{1}{2}$ of a grain a day, with large quantities of water.

Calomel fumigation certainly gave very good results, perhaps better in laryngeal cases than any form of drug administered; 15 grains of calomel was volatilized under a canopy placed on the patient's bed every two hours for two days and nights. Then every three hours for the third day, every four hours for the fourth, and thereafter three times daily, according to the nature and progress of the case. Mercurial poisoning, stomatitis, diarrhea, and marked anemia often followed it. The attendant frequently suffered also from the effects of it.

Of many so-called specifics, may be mentioned the following:

Pilocarpin, recommended by Barsky, F. Howe,[*] Degle, and others.[†]

Guaiacol as a means of destroying the bacilli by local use and also as a preventive of diphtheria (S. Solis Cohen[‡]).

Citric acid, 10% solution given internally.

Hyposulphite of soda and glycerin as a local application (Wilkins[§]).

Tincture of myrrh—internal use (Graetzer[||]).

And, more recently, chlorin (Bracelin, Meyers, Shultz, and others[**]).

It must not be forgotten, even in the favorable reports of most of these remedies, that the diagnosis of the disease was frequently made on other than bacteriologic examination.

Of these, and many more which it is unnecessary to mention, mercury internally or by fumigation has still a further possible use—namely, in laryngeal cases and those which have been intubated in order to prevent the necessity of reintubation. Whether even with antitoxin the remedy may not be of value is still an open question. That so high an authority as Jacobi is still a believer in it justifies its trial under certain circumstances.

The modern treatment of diphtheria may be divided into local, general, and measures for relief of suffocation.

LOCAL TREATMENT.

This has for its object the cleansing of the affected mucous membrane (mouth, nose) and the removal of loose membrane, prod-

[*] *Med. Brief*, Aug., 1895.   [†] *Wiener Presse*, Dec. 9–16, 1894.
[‡] *Philadelphia Polyclinic*, No. 16, 157, 1896. [§] *Lancet*, Jan. 6, 1896.
[||] *Münch. med. Woch.*, p. 1164, 1896.   [**] *N. Y. Med. Jour.*, LXVIII, 675, 1898.

ucts of decomposition, and mucus, giving comfort to the patient and frequently improving respiration, as in nasal diphtheria; and, finally, as a help in removing the germs after the symptoms have disappeared. Forcible removal of the pseudomembrane has fortunately passed into ill repute, and probably is no longer practised among intelligent physicians. There are some who still advocate attempts at destruction by caustics, strong or weak antiseptic solutions, etc. It is doubtful if such treatment is to be recommended, except, perhaps, in cases of nasal diphtheria with total or partial obstruction to respiration, and, in infants, to feeding. In these latter cases, as well as cases of pharyngeal diphtheria in adults or older children, Jacobi recommends radical local treatment. For this purpose he advises touching the membrane thoroughly once or twice a day with 50% carbolic acid solution in glycerin, tincture of iodin, solution of 1 : 100 or 1 : 500 bichlorid of mercury, or chlorin water. He also praises the local effects on the pharynx of swallowing small and frequent doses of mild dilutions of the tincture of chlorid of iron, lime-water, boric acid, bichlorid of mercury, or benzoate of sodium.

The most common form of local treatment now in use is that given by means of the fountain syringe; that is, nasal irrigation. This is especially effective in cases of nasal diphtheria. In this operation the patients are allowed to remain in bed, or, better, placed upon a low table. They should be wrapped in a sheet or blanket over which is placed a rubber sheeting. A rubber-covered pillow and Kelly's pad are desirable adjuncts. A separate nozle should be used for nasal irrigation. The child is laid on its side, the arms and legs being confined by the sheet or blanket. The nozle of the syringe, preferably of hard rubber or glass, with a single opening in the end, is inserted into one nostril and the fluid allowed to flow freely from the opposite one. The irrigation is continued until the fluid returns clear. If more force is necessary, or if for any reason it be not convenient to use irrigation as above described, the handball syringe, with hard rubber nozle just fitting the nose, is very efficacious.

With regard to solutions, it is highly probable that antiseptics of various kinds have little or no advantage over common salt of the strength of a teaspoonful to the pint. If preferred, saturated solution of boric acid, or, better, a more diluted solution, may be used. The temperature of the solution should be about 110° F. for ordinary purposes. If, on the other hand, it is desirable to reduce pain and swelling, especially in the pharynx, it is better to increase the temperature to 130° F. or more. After the nose has been thoroughly irrigated, the

pharynx is treated in a similar way. Irrigations may be repeated three or four times in the twenty-four hours or oftener. In septic cases with a great deal of discharge, especially about the nose and pharynx, these irrigations, by reducing the products of decomposition, are all-important, and should be frequently repeated. Most children get used to this application. In some cases, however, they prove very averse to it, and great care must be observed in dealing with such cases. At times it is better to do without it if, after each attempt, the child becomes physically weaker from the resistance shown. Hemorrhage may be an occasional contraindication as well as cardiac weakness. Intubation, on the other hand, is usually not so. When properly performed, there is no evidence to prove that irrigation is a means of carrying the disease to the middle ear. Steam, either from a kettle or, better, applied as in the steam-rooms of well-equipped hospitals, may often be of decided benefit, especially in intubation cases after the removal of the tube, to prevent a recurrence, or in laryngeal cases to avoid intubation. Poultices may be of benefit for the same condition and to reduce pain. They should not be allowed to become cold on the patient, but applied for fifteen minutes at a time, and then removed to be replaced by others. After an hour's poulticing, it is a good plan to wait an hour or two before beginning another series.

STIMULANTS.

These are indicated in all cases of diphtheria where there is constitutional depression, weak heart action, irregular, intermittent, or rapid pulse, and septic conditions. Alcohol is the stimulant to be preferred, and in the form of good whisky or brandy, in doses well diluted with water, beginning from 10 to 15 drops three or four times a day for an infant, up to an ounce or more in twenty-four hours for a child of three or four years. As recommended by O'Dwyer, whisky in small doses is frequently valuable in exciting and strengthening the cough, and thus getting rid of laryngeal obstruction, especially in intubated cases. Next to alcohol, strychnin is the best stimulant, given in doses of from $\frac{1}{100}$ of a grain to a child of a year every two or three hours to $\frac{1}{50}$ or more to a child of three or four years. The deep reflexes must be watched for symptoms of poisoning. The heart stimulants of the type of digitalis may be indicated in certain cardiac conditions.

SEDATIVES.

These are often necessary to quiet a restless child, especially when the heart action is weak, and also as an anti-spasmodic in laryngeal cases. For this purpose nothing is of so great value as morphin, given in doses of $\frac{1}{20}$ to $\frac{1}{12}$ of a grain. The so-called liquid Dover's powder may be used in the same way. Emetics are not given so generally as in former years. They are of use as anti-spasmodics and in getting rid of loose membrane and mucus, especially in laryngeal cases. They must, however, be carefully watched, and should always be discontinued in the presence of cardiac disturbances. It may be desirable to eliminate the spasmodic element before resorting to intubation, or to reintubation. For this purpose Dover's powder or ipecac may be used.

ANTITOXIN.

HISTORY.

Babes and Lepp, in 1889, published the results of a number of experiments to determine " whether the fluids and cells of animals which have been rendered immune by vaccination have not become vaccines, and capable of protecting also other organisms." They showed that the blood of dogs vaccinated against rabies, when injected into susceptible animals conferred a certain degree of protection against the effect of subsequent inoculations with the virus of rabies, and appeared to prevent the occurrence of the latter when the injection of immune blood was made immediately after the inoculation.

Behring and Kitasato, in 1890, published what may be regarded as the first clear demonstration of the principles of serotherapy. The article refers especially to tetanus antitoxin, but application of the same principle was suggested in the case of diphtheria, as also in a later publication by Behring. Behring and Wernicke, in 1891, communicated to the Seventh International Congress of Hygiene and Demography, in London, the proofs that the blood of animals artificially immunized against diphtheria would protect and cure other susceptible animals inoculated with the diphtheria bacillus or its toxin. A full report of the results of these experiments was published in 1892.

Antitoxic serum was first tried in the treatment of diphtheria patients in 1891, in von Bergmann's clinic, Berlin; and later by Henoch, in 1892, in Berlin, Heubner in Leipsic, and in the Institute for Infectious Diseases in Berlin. The serum, however, was very weak, and the dosage, as we now know, entirely insufficient.

Early in 1893 Behring succeeded in obtaining a somewhat stronger serum (so-called normal serum), and reported 30 cases treated with it. Later in the same year, Ehrlich and Wasserman, by using goats instead of the smaller animals, produced a serum twenty to sixty times stronger than Behring's.

In 1894 Ehrlich, Kossel, and Wasserman reported 223 cases treated with antitoxin, with a mortality of 23%. Most of these cases were treated with approximately sufficient doses of antitoxin, and this may be regarded as the beginning of practical and successful serotherapy.

Katz, in June, 1894, presented to the Berlin Medical Society the results of treatment of 128 cases of diphtheria with serum obtained from horses by Aronson. Baginsky, in whose service the cases occurred, later increased the number of cases to 163, with a mortality of 12.9%.

Roux, in an address before the Eighth International Congress of Hygiene and Demography, held at Budapest in September, 1893, reported the result in 300 cases treated by him in the Paris hospitals, and showed by the analysis of the various statistics the great value of this method of treatment. From this time the attention of the medical world was drawn to the subject, with the result that by improvements in the method of serum production, its increased concentration, the recognition of the importance of early treatment, and sufficient dosage, another disease has been robbed of many of its terrors.

PRODUCTION OF ANTITOXIC SERUM.

As described by W. H. Park, of the New York Board of Health, the method of procuring antitoxic serum is as follows: A virulent culture of diphtheria bacilli—that known as No. 8, and used also by many other laboratories in the United States and Europe—is grown in bouillon under conditions found to be best suited to the greatest production of toxin. The culture after a week's growth is removed, and rendered sterile by the addition of a 5% solution of carbolic acid. On the following day the sterile culture is filtered through ordinary sterile filter-paper and stored in full bottles in a cold place until needed.

The horses used for inoculation should be young, vigorous, of fair size, and absolutely healthy. A number of such horses are severally injected with an amount of toxin sufficient to kill 10,000 guinea-pigs of 250 gm. weight (about 40 c. c. of strong toxin). With each injection of toxin 10,000 units of antitoxin are given. After from three to five days, as soon as the fever reaction has subsided, a second subcu-

taneous injection of a slightly larger dose is given. At intervals of from five to ten days increasing injections of pure toxin are made, until at the end of two months from ten to twenty times the original amount is given. The horses are now bled and the blood-serum is tested for antitoxin. Those having an antitoxin containing less than 200 units in each cubic centimeter are discarded. The remaining horses receive steadily increasing doses, the rapidity of the increase and the interval of time between the doses (about a week) depending somewhat on the reaction following the injection, an elevation of temperature of more than 3° F. being undesirable. At the end of three months the antitoxic serum should contain from 300 to 800 units in each cubic centimeter, according to the horses used. The best horses continue to furnish serum of a high grade for years. Each year they should be given an interval of three months' freedom from inoculations.

In order to obtain the serum, the blood is withdrawn from the jugular vein by means of a sharp-pointed cannula, which is plunged through the vein wall, a slit having been made in the skin. The blood is received in large Erlenmeyer flasks and allowed to clot, the flasks being placed at first, while clotting is taking place, in a slanting position. The serum is siphoned off by means of aseptic glass and rubber tubing, and is stored in large flasks. From this, as needed, small phials are filled. The phials and their stoppers, as, indeed, all the utensils used for holding the serum, must be absolutely sterile, and every possible precaution must be taken to avoid contamination of the serum. An antiseptic may be added to the serum as a preservative, but is not necessary, and probably inadvisable.

Of the chemical character of antitoxin little is known. It is believed to be a proteid substance, destroyed by a temperature above 55° F., resembling the globulins in some of its chemical characters. If kept in a dark cool place, it remains practically unchanged for some months. According to Park and others, it loses not more than 50% of its neutralizing power in the course of a year.

Hiss and Atkinson [*] show that diphtheria antitoxin in the blood-serum of horses is precipitated by magnesium sulphate, and that it exists to a greater or less extent in some non-immunized horses. Furthermore, these precipitates apparently contain all the antitoxic qualities and they give all the reactions characteristic of the globulins. Within the last few years much light has been thrown upon the probable mode of action of antitoxin by studies upon natural and

[*] *Jour. of Exp. Med.*, 19, IV.

acquired immunity, the action of the blood-serum of one animal on that of another, and of immune serum upon bacteria (hemolysis and bacteriolysis). While there can be no doubt that these studies are leading to important results, the conclusions so far reached are tentative and require further verification before they can be generally accepted.

Ehrlich may be said to be the originator of this new school of thought, and it is to his studies that we owe the general interest taken in the subject. Ehrlich's "lateral chain" theory is now generally accepted as at least a good working hypothesis in explaining the nature of immunity and antitoxic action. It may be stated briefly as follows: The protoplasm of the body cells is composed of a stable central group of molecules, surrounded by less stable atomic groups, constituting the so-called lateral chains. The latter are capable of forming combinations with other molecules and of thus producing various chemical changes. Furthermore, these lateral chains (receptors) may form combinations with various toxins, and under conditions which require more and more of such combinations the cell is stimulated to produce a surplus of these receptors, which are then thrown off and become free in the blood, constituting the so-called antitoxins, and conferring on the animal immunity against further assaults of the specific toxins, which must now form combinations with these free receptors; they are therefore unable to combine with the body cells, and thus do not produce serious consequences to the organism.

Certain terms are now generally employed to describe the various factors in the biologic process. Thus, in an immune serum the more stable body (specific anti-body) is known as the immune body (Ehrlich), or "substance sensibilisatrice" (Bordet); the less stable non-specific body, as the alexin or complement (Ehrlich and Morgenroth). This alexin, which is destroyed by a temperature of 56° to 60° C. (133° to 140° F.), is present in all blood, while the immune body is produced artificially.

During the solvent or destructive action of the serum on the blood-cells of another serum (hemolysis), or of an immune serum on bacteria (bacteriolysis), the anti-body links the alexin to the cell or bacterium and thus leads to their dissolution. According to Bordet, the hemolytic and bacteriolytic alexin are identical in the same serum. For a recent review and criticism of Ehrlich's theory see Gruber, "Münch. med. Woch.," Nov., 1901.

Park and Atkinson* state that the neutralizing value of a fatal dose of antitoxin is at its lowest in the culture fluid when the first considerable amounts of toxin have been produced. After a short period, during which the quantity of toxin in the fluid is increasing, the neutralizing value of the fatal dose begins to increase, at first rapidly, and then more slowly; while the culture is still in vigorous growth and new toxin is being produced, the neutralizing value of the fatal dose fluctuates somewhat, but with a generally improved tendency. After the cessation of toxin production the neutralizing value of the fatal dose increases slightly until it becomes five to ten times its original amount.

The latest definition of an antitoxin unit, as given by Park, is "that amount of antitoxin which is required to neutralize sufficient toxin to kill 100 small guinea-pigs. This amount of poison is produced by the growth for one week of a virulent bacillus in 1 c.c. of bouillon."†

RESULTS OF THE USE OF ANTITOXIN.

On the General Mortality from Diphtheria.—An analysis of a great number of statistics, in this country and Europe, will show that the general death-rate from diphtheria has decreased, roughly, about 50% under the use of antitoxin. Furthermore, it will be seen that later returns show an improvement over the death-rate of the early days of antitoxin, and this for the reason that its use has become much more general, that the preparation of the serum has been improved, and that the influence of early treatment is more generally recognized. Dr. Guilfoy, of the New York Board of Health, has kindly furnished the following statistics of the city of New York from 1891 to 1900 inclusive.

CASES OF DIPHTHERIA AND CROUP BY QUARTERS DURING YEARS 1891–1900, OLD CITY OF NEW YORK.

	1891	1892	1893	1894	1895	1896	1897	1898	1899	1900	TOTAL.
First quarter	1499	1712	1647	2699	2,788	3,235	3,171	2259	2048	2680	23,738
Second quarter	1213	1450	1628	2920	3,052	3,422	3,488	2087	2243	2401	23,904
Third quarter	974	896	1346	1827	2,048	2,045	2,081	1234	1531	1340	15,322
Fourth quarter	1678	1126	2400	2195	2,465	2,697	2,156	1593	2418	1943	20,671
Total	5364	5184	7021	9641	10,353	11,399	10,896	7173	8240	8364	83,635

* *Jour. of Exp. Med.,* vol. III, No. 4.   † *Arch. of Ped.,* vol. XVII, 1900.

DEATHS FROM DIPHTHERIA AND CROUP, BY QUARTERS.

CITY OF NEW YORK FROM 1891 TO 1897; BOROUGHS OF MANHATTAN AND BRONX, 1898 TO 1900.

FEMALES.

	QUARTER	0	1	2	3	4	TOTAL UNDER 5	5	10	15	20	25	35	45	55	65	75	85	TOTAL.
1891	First	29	58	56	46	28	217	46	3	1	2	1	..	1	..	..	..	..	271
	Second	18	47	43	28	18	154	33	..	1	2	..	..	..	..	1	..	..	191
	Third	17	37	46	37	14	151	29	2	..	3	1	..	..	..	..	..	..	186
	Fourth	21	60	58	56	35	230	64	5	1	1	1	1	..	2	..	..	..	305
	Year	85	202	203	167	95	752	172	10	3	8	3	1	1	2	1	..	..	953
1892	First	18	59	68	60	24	229	45	2	..	3	2	1	1	1	..	..	..	284
	Second	22	71	50	48	28	219	45	4	1	2	1	..	..	..	..	..	..	272
	Third	9	25	35	29	27	125	29	3	..	1	..	..	1	1	..	..	..	160
	Fourth	18	67	52	44	29	210	54	3	2	1	1	..	..	..	..	..	..	271
	Year	67	222	205	181	108	783	173	12	3	7	4	1	2	2	..	..	..	987
1893	First	31	79	65	57	35	267	57	5	3	..	1	4	3	..	1	..	..	341
	Second	28	59	72	50	29	238	61	4	4	1	..	..	..	..	..	..	..	308
	Third	24	60	47	28	27	186	41	4	1	..	2	..	1	..	..	..	..	235
	Fourth	27	75	92	64	46	304	102	9	2	1	1	..	1	..	..	..	1	421
	Year	110	273	276	199	137	995	261	22	10	2	4	4	5	..	1	..	1	1305
1894	First	44	102	97	63	44	350	64	5	..	2	1	1	1	..	..	..	..	424
	Second	30	99	101	80	60	370	76	3	2	2	4	1	..	..	..	..	..	458
	Third	14	51	42	42	22	171	65	8	..	..	1	..	1	..	..	..	..	246
	Fourth	21	49	66	43	41	220	50	4	..	..	1	1	1	..	1	..	..	278
	Year	109	301	306	228	167	1111	255	20	2	4	7	3	3	..	1	..	..	1406
1895	First	33	67	71	31	29	231	44	4	1	..	1	..	1	..	..	..	..	282
	Second	30	57	48	36	35	206	50	2	2	..	1	..	..	1	..	..	..	262
	Third	6	57	53	36	15	167	32	5	..	1	..	..	..	..	..	..	..	205
	Fourth	15	51	45	35	15	161	43	1	1	..	3	1	..	..	..	..	..	210
	Year	84	232	217	138	94	765	169	12	4	1	5	1	1	1	..	..	..	959
1896	First	23	67	71	44	28	233	36	5	2	1	3	1	1	..	..	..	..	282
	Second	19	53	50	39	34	195	46	6	..	1	2	..	..	..	..	..	..	250
	Third	16	40	35	28	26	145	28	4	1	..	..	..	..	..	..	..	..	178
	Fourth	7	37	32	30	13	119	41	1	..	3	1	..	..	..	..	..	..	165
	Year	65	197	188	141	101	692	151	16	3	5	6	1	1	..	..	..	..	875
1897	First	27	59	56	43	23	208	30	2	..	..	1	2	..	1	..	..	..	244
	Second	24	71	49	42	18	204	67	2	..	1	1	..	..	..	..	..	..	275
	Third	9	41	26	21	18	115	28	1	1	1	..	..	..	..	..	..	..	146
	Fourth	14	42	25	16	17	114	39	1	..	..	1	..	..	..	..	..	..	155
	Year	74	213	156	122	76	641	164	6	1	2	3	2	..	1	..	..	..	820
1898	First	14	34	32	19	13	112	34	6	..	..	1	1	..	..	..	..	..	154
	Second	8	25	17	21	13	84	17	2	..	..	1	..	..	..	..	..	..	104
	Third	4	14	21	12	5	56	15	1	..	..	..	..	..	..	..	..	..	72
	Fourth	4	28	24	9	17	87	26	2	1	..	1	1	..	..	..	..	..	118
	Year	35	101	94	61	48	339	92	11	1	..	3	2	..	..	..	..	..	448

Deaths from Diphtheria and Croup, by Quarters.—(Continued.)
Females.—(Continued.)

Year	Quarter	0	1	2	3	4	Total Under 5	5	10	15	20	25	35	45	55	65	75	85	Total
1899	First	11	46	30	22	14	123	18	1			3			1				146
	Second	18	39	24	23	15	119	21	3	1	1		1						146
	Third	12	27	26	14	10	89	14	1	2		2		1	1				110
	Fourth	11	37	32	27	20	127	25	3			2			1				158
	Year	52	149	112	86	59	458	78	8	3	1	7	1	1	3				560
1900	First	31	51	37	23	22	164	41	1	1	3	4	2						216
	Second	7	36	41	38	24	146	38				1	1						186
	Third	10	8	12	11	14	55	18	5			1				1			80
	Fourth	16	13	25	17	15	86	29	6		3	1							125
	Year	64	108	115	89	75	451	126	12	1	6	7	3			1			507

MALES.

Year	Quarter	0	1	2	3	4	Total Under 5	5	10	15	20	25	35	45	55	65	75	85	Total
1891	First	40	61	58	43	22	224	32	3		1		3		1				264
	Second	28	62	50	32	29	201	30	2	2		2	2						239
	Third	18	41	35	41	24	159	36	1		1			1					198
	Fourth	25	68	67	57	36	253	57	2		2	2							316
	Year	111	232	210	173	111	837	155	8	2	4	4	5	1	1				1017
1892	First	27	78	85	56	27	273	34	1	2		2	1	1					314
	Second	24	59	71	43	29	226	47	3	1	1		1	1		1			281
	Third	20	58	50	42	26	196	29	3					1					229
	Fourth	21	74	64	46	41	246	38	5	1	2		2	1					295
	Year	92	269	270	187	123	941	148	12	4	3	2	4	4		1			1119
1893	First	35	82	80	65	26	288	44	2				1	1		1			337
	Second	30	75	67	48	26	246	44	2			1	1	1					295
	Third	11	68	52	41	32	204	37	4	1	1								247
	Fourth	22	75	79	64	37	277	86	7	1	2					1			374
	Year	98	300	278	218	121	1015	211	15	2	3		2	2	1	2			1253
1894	First	42	120	102	77	54	395	61	6			2							464
	Second	37	92	94	79	49	351	70	2	1	1								425
	Third	21	61	58	49	28	217	48	1			1							267
	Fourth	25	78	57	48	36	244	54	7	1	1			1					308
	Year	125	351	311	253	167	1207	233	16	2	2	3		1					1464
1895	First	49	80	56	50	30	265	33		1	1	1	1						302
	Second	45	68	57	50	24	244	49	3	1		2			1				300
	Third	17	48	42	29	24	160	24	2	2		2	1	1					192
	Fourth	19	51	45	46	24	185	32	3			1	1		1				223
	Year	130	247	200	175	102	854	138	8	4	1	6	3	1	2				1017
1896	First	31	86	51	28	30	226	33	4		1	3	2	2					271
	Second	33	67	62	25	26	213	33	2	1		2	2						253
	Third	11	40	40	18	23	132	21	4										157
	Fourth	21	48	40	41	21	171	32	1			2		1					207
	Year	96	241	193	112	100	742	119	11	1	1	7	4	3					888

DEATHS FROM DIPHTHERIA AND CROUP, BY QUARTERS.—*(Continued.)*
MALES.—*(Continued.)*

	QUARTER	0	1	2	3	4	TOTAL UNDER 5	5	10	15	20	25	35	45	55	65	75	85	TOTAL.
1897	First	33	45	57	31	22	188	25	2	..	2	..	1	..	..	..	..	..	218
	Second	26	68	49	26	23	192	44	4	..	1	2	..	..	..	..	..	..	243
	Third	11	46	36	27	12	132	26	1	3	..	1	..	1	..	..	..	..	164
	Fourth	12	37	27	22	18	116	23	3	1	1	..	1	..	..	..	..	..	145
	Year	82	196	169	106	75	628	118	10	4	4	3	2	1	..	..	..	..	770
1898	First	21	50	26	17	11	125	19	3	1	2	3	..	2	..	1	..	..	156
	Second	12	44	26	16	15	113	15	1	..	..	1	..	..	..	..	..	..	130
	Third	7	19	16	12	7	61	13	2	..	..	..	..	..	1	..	..	..	77
	Fourth	12	36	23	12	9	92	12	..	..	1	2	..	1	..	..	..	..	108
	Year	52	149	91	57	42	391	59	6	1	3	6	..	3	1	1	..	..	471
1899	First	22	42	25	23	9	121	11	1	..	..	1	..	..	..	..	..	..	134
	Second	19	29	29	17	15	109	24	4	1	..	4	..	..	..	..	..	..	142
	Third	6	31	19	19	9	84	14	1	..	..	..	..	..	..	..	..	..	99
	Fourth	15	31	34	29	12	121	27	1	..	..	1	..	..	..	..	..	..	150
	Year	62	133	107	88	45	435	76	7	1	..	6	..	..	..	..	..	..	525
1900	First	24	55	38	38	19	174	29	2	1	1	1	..	..	1	..	..	..	209
	Second	27	42	38	34	15	156	45	3	..	..	3	2	..	..	..	..	..	209
	Third	4	23	13	20	13	73	18	4	4	..	3	..	..	..	..	..	..	102
	Fourth	17	27	27	27	15	113	22	8	3	..	2	..	..	1	..	..	..	149
	Year	72	147	116	119	62	516	114	17	8	1	9	2	..	2	..	..	..	669

The Board of Health began the treatment of diphtheria with antitoxin in January, 1895. It cannot be said to have been in general use, however, for some time later. With regard to the number of cases reported, it may be stated that the law requires a report of every case of diphtheria in the city limits, and this law is rigidly enforced by the Board. Many of the bacteriologic examinations are made by the Board itself at the request of physicians.

WITHOUT ANTITOXIN.

	CASES REPORTED.	DEATHS.	MORTALITY PERCENTAGE.
1891	5,364	1,970	36.7
1892	5,184	2,106	40.0
1893	7,021	2,558	36.4
1894	9,641	2,870	29.7
Total	27,210	9,504	Average..34.9

WITH ANTITOXIN.

1895	10,353	1,976	19.0
1896	11,399	1,763	15.5
1897	10,896	1,590	14.5 ⎫ Average for
1898	7,173	919	12.8 ⎪ last four
1899	8,240	1,085	13.1 ⎬ years,
1900	8,364	1,176	14.0 ⎭ 13.6 %
Total	56,425	8,509	Average..15%

From this report it may be seen that with the introduction of serotherapy the death-rate from diphtheria in New York city has fallen from 34.9% to 15%, a reduction of 58%. If we take the last four years, from 1897 to 1900, when antitoxin has become more generally used, and in adequate doses, we get a death-rate of 13.6, or a reduction in mortality of 64%.

Other statistics show about the same reduction in death-rate throughout the world; a few examples are as follows:

Report of the American Pediatric Society Collective Investigation (1896): 5794 cases, with 713 deaths—12.3%. Leaving out moribund cases and those that died within twenty-four hours after receiving the antitoxin, 8.8%.

In the report of the Metropolitan Asylums Board of London for 1900 the number of cases under treatment in the various hospitals was 9413, with a death-rate of 12.27%. The death-rate in 1888 was 59.35%.

Burrows reports 2093 cases in Boston City Hospital (February, 1901), of which 1962 were uncomplicated. Among the latter was a mortality of 12.23%; deducting 69 moribund cases, 9%.

In Boston the death-rate from 1880 to 1894 was 30.75%; 1895 to 1897, 12.6%.

Welch (May, 1895) collected 7166 cases from 82 reports in Europe and America, with a mortality of 17.3%, compared with a minimum of mortality of 42.1%; reduction, 55%.

Biggs and Guerard have collected, up to October, 1890, 79,075 cases from all parts of the world, with a death-rate of about 16%; compared with a previous death without antitoxin of 30% to 40%. An entire table compiled by the same writers is of great interest, showing the rate of death per 100,000 of the population of the countries of Europe from diphtheria and croup.

1894.			1895.			1896.		
Population.	Deaths.	Ratio.	Population.	Deaths.	Ratio.	Population.	Deaths.	Ratio.
29,168,860	18,732	64.2	29,667,747	11,748	39.6	29,960,743	10,700	35.7

It has been claimed by those who still persist in doubting the efficacy of this mode of treatment that since serotherapy was introduced and systematic bacteriologic examination made, a great many cases are classified as diphtheria which formerly would not have been so considered; and to a certain extent this is true. On the other hand,

no unprejudiced person can account for the steady decline in the death-rate from diphtheria under the general use of antitoxin except on the ground of the recognition of the value of early treatment and the importance of sufficient dosage.

The influence on the death-rate of the stage of the disease at which treatment is begun is very great. In the report of the American Pediatric Society's collective investigation with the use of antitoxin in private practice there was a death-rate of 12.3% in 5749 cases, including 218 moribund cases or cases dying within twenty-four hours. Of the 4120 cases injected with antitoxin during the first three days, there were 303 deaths—a mortality of 7.3%; excluding the moribund cases, 4.8%. After three days the death-rate was about the same as among cases treated without antitoxin.

Statistics from the Imperial Board of Health of Berlin, 1895–96, were furnished by 258 physicians from 204 institutions. There were 13,137 cases, occurring in a service of over eighteen months, with a mortality of 15.8%. The mortality of cases treated on the first day was 6.6%; second day, 8.3%; third day, 12.9%; fourth day, 17%; fifth day, 23.2%.

A similar table by Biggs and Guerard is as follows:

	CASES.	DEATHS.	MORTALITY PERCENTAGE.
First day of disease	1415	51	3.5
Second day of disease	2640	213	8.0
Third day of disease	2340	300	12.8
Fourth day of disease	1458	346	23.6
Fifth day and after	1912	671	35.0
Total	9765	1581	16.1

Age Influence on the Death-rate.—With or without antitoxin treatment age is a very important factor in determining the result; and while the death-rate has been reduced for all ages, it will be seen that diphtheria is still a very fatal disease in infancy. The following table is from Biggs and Guerard:

TREATED WITH ANTITOXIN.

AGES.	CASES.	DEATHS.	MORTALITY.
0– 2 years	1494	469	31.4%
2– 5 years	3678	762	20.7%
5–10 years	3184	473	14.8%
Over 10 years	1444	99	6.9%

Compare this with a table of Baginsky's:

0– 2 years	Mortality, 63.3%
2– 4 years	Mortality, 52.8%
4– 6 years	Mortality, 37.9%
6–10 years	Mortality, 24.6%
10–15 years	Mortality, 14.6%

10

These cases were treated without antitoxin.

Burrows, in a series of 2093 cases treated at the Boston City Hospital (1900), gave the following results:

Age.	Deaths.
0–1 year	40.00%
1–2 years	33.00%
2–3 years	23.00%
4–5 years	15.60%
5–6 years	14.60%
6–7 years	12.30%
7–8 years	14.00%
8–9 years	8.60%
9–10 years	2.08%

The death-rate among patients under five years of age was 21.30%; five to ten years, 8.40%; ten to fifteen years, 3.10%.

Results of Antitoxin Treatment in Laryngeal Cases.—The mortality has been reduced in two ways: First, by its effect upon operated cases—intubation and tracheotomy; and, second, by decreasing the number of cases which come to operation.

McNaughton and Maddren (1892) collected the results of 5546 cases of intubation, with a death-rate of 69.5%. The authors state that the present mortality among intubated cases treated with antitoxin (1897) is 27.24%. The mortality of laryngeal diphtheria is 21.12%. Approximately sixty per cent. have not required operation.*

Burrows reports from the Boston City Hospital (1900) 337 laryngeal cases, with a mortality of 31.4%. Of these, 213 were intubated, with 96 deaths—45%.

McCullom (1898) reports from the Berlin City Hospital, up to the year 1895, that the mortality in intubated cases was 83%; from 1895 to 1898, 457 cases—55%.

In the report of the American Pediatric Society on the antitoxin treatment of croup in private practice, there were 1704 cases, with a death-rate of 21.12%. Of these, 1036 (60.79%) did not require operation, and the mortality was 17.18%. Intubation cases, 637; 166 deaths; 26.05% mortality.

If this last report be compared with McCullom's, it will show what is well recognized—the greater mortality in those cases treated in hospitals compared with those treated outside.

In the statistics of the Imperial Board of Health of Berlin, before referred to, there were 4085 laryngeal cases, 2744 of which were operated on, with a mortality of 32.3%.

* *Medical News,* May 15, 1897.

Manges reports a mortality with antitoxin cases among intubated cases of 27.5%. His previous mortality was 66%.

Upon tracheotomy cases the effects have been similar to the above. In this country the operation is seldom used except in secondary cases, and then with very fatal results. In 20 tracheotomized cases reported in private practice by the American Pediatric Society there were 9 deaths, or 45%; intubation and tracheotomy, 11 cases, with 7 deaths, or 63.63%.

Clubbe* reports 300 laryngeal cases with 129 tracheotomies, with a death-rate of 20%; and 300 cases treated without antitoxin, with 199 tracheotomies and 158 deaths, or 52.7%.

In the report of the Metropolitan Asylums Board of London for 1900 there are reported 477 laryngeal cases treated with antitoxin, with 182 deaths. Among these, there were 377 tracheotomies, with 127 deaths, or 33.65%; Monroe gives the results of 21,853 tracheotomies in Europe and America, with a mortality of 72% without antitoxin. Sanne gives 2351 cases from 1851 to 1875, with 614 recoveries, or 21.4%.

The Investigating Committee of the Clinical Society of London (1898) report 75 cases tracheotomized with antitoxin treatment and 27 deaths, or 36%, as compared with a previous mortality of 71.6% without antitoxin. The same report gives an analysis of tracheotomy cases reported by the Metropolitan Asylums Board of London as follows: In 1894 there were over 1800 cases, with 73% of deaths; in 1896, with antitoxin, 137 cases, with a mortality of 43.7%.

The 75 cases reported by the Committee have been analyzed thus: Treated from first to third day, 31 cases, 5 deaths, 16.1%; fourth to sixth day, 27 cases, 11 deaths, 40.7%; on and after seventh day, 17 cases, 11 deaths, 64.7%.

Effect on Eye Cases.—Upon conjunctival diphtheria the results have been most happy. McCullom reports 15 cases of the latter at the Boston City Hospital, in every one of which, he states, the eye would have been lost without the use of antitoxin. The latter result occurred in but one case, where the eye was diseased before the occurrence of diphtheria. In addition to the antitoxin, red and yellow iodid of mercury was used locally, 1 grain to the ounce of vaselin, and atropin or cocain as a mydriatic.

Effect on the Occurrence of Diphtheritic Paralysis.—This is a very difficult point to determine. In looking over the various statistics relative to it, it will often appear that paralysis is more

* *Brit. Med. Jour.*, vol. xi, p. 1177, 1897.

frequent with the use of serum, and this is to be explained by the fact that in the serum cases which terminate fatally life is much prolonged, and thus the paralysis has time to develop (London Clinical Society and many other observers).

F. Ransom has made some very interesting experiments on this subject on animals, and concludes:

1. Paralysis may certainly be expected to occur after inoculation with not less than one-fourth of the minimum fatal dose. With doses between one-fourth and one-eighth paralyses are not constant. With weaker than one-eighth, no paralysis.

2. If the animal survives long enough, the larger the dose of toxin, the more severe the paralysis.

3. Neutralized mixtures of toxin and antitoxin containing only about one lethal dose or less do not appear to cause paralysis.

4. Antitoxin given fifteen to twenty-two hours after intoxication with doses of toxin not greater than the lethal dose exercises in large doses a modifying influence on the subsequent paralysis. This influence is more marked on smaller doses of toxin than on such as are but little less than the minimum fatal dose. Small doses of antitoxin have no evident effect in diminishing the paralysis.

5. In human beings we may thus expect liberal doses of antitoxin, given early, to influence favorably the subsequent paralysis, and this influence is likely to manifest itself not so much on the local paralysis (palate, etc.) as on such symptoms as heart failure. Severe cases are likely to be followed by severe paralysis, in spite of large doses of antitoxin.

Taken in connection with these experimental results, the following, by the London Clinical Society, 1898, is of interest as substantiating these views:

In 633 cases treated with antitoxin there were 145 cases of paralysis, or 22.9%—in 110 cases slight, in 35 cases severe. In another series of cases treated without antitoxin, paralysis occurred in only 10.8%. The mortality, however, among the cases treated with antitoxin was 8.9%, and 12.2% in those not so treated.

Averaged by days, the cases treated with antitoxin are as follows:

	CASES.	PARALYSIS.	SLIGHT.	SEVERE.	PERCENTAGE.
Treated on 1st day	20	1	1	0	5.0
" " 2d day	92	15	14	0	16.3
" " 3d day	133	34	29	5	25.5
" " 4th day	130	28	22	6	21.5

When treated from the fifth to the tenth day, paralysis occurred in 25.9%.

It is thus fair to assume that, in severe cases with a great deal of toxemia, paralysis will occur with or without antitoxin if the patient lives long enough; and that if treatment be begun early and in sufficient dosages, the paralysis will probably be prevented.

Except in cases treated very early it is probable that antitoxin has no effect, as the toxemia, the cause of the paralysis, has already begun to affect the nerves.

Effect on the Kidneys and on the Occurrence of Renal Complications.—A transient and slight albuminuria is no doubt a fairly frequent accompaniment of the injection of antitoxin, for it occurs without the diphtheria when immunizing doses are given.

In a series of analyses made by C. E. Michael from the returns of the Metropolitan Asylums Board of London, 1898, he found albuminuria occurring without antitoxin in 24.1% and 40% in the years 1894 and 1895 respectively, and in 60.1% in 1896 with the use of antitoxin. On the other hand, nephritis was not so frequently found with antitoxin. In 1894 nephritis occurred in 1.2% of cases; in 1895, in 2% of cases; in 1896, with antitoxin, in 0.5% of cases.

McCullom gives an interesting account of the occurrence of albuminuria in cases examined at the Boston City Hospital. The number of patients was 173: In 99 no albumin occurred before or after antitoxin; in 23 the albumin remained unchanged after injection; in 16 it was slightly increased; in 25, diminished.

With regard to the effect on the quantity of urine excreted following injections of antitoxin, writers are at variance, and this is not to be wondered at if the difficulties attending the collection of urine of young children are taken into consideration. Variot and Cochinal have noted a diminution in the amount of urine following injection, even in non-diphtheritic cases, which lasted for several days. Rolland has made similar observations. Karlinsky, on the other hand, in experimenting on himself, found no such effect.

Charrin and Roger have experimented on rabbits, and found a slight polyuria following injection of antitoxin. Poix obtained similar results with non-immunized serum.

Effect on the Heart and on Cardiac Complications of Diphtheria.—There is no evidence which goes to show that antitoxin has any effect in causing heart lesions. In the cases treated with antitoxin, other than those treated very early, Hibbard and McCullom have shown that heart complications are not infrequent. McCullom shows that the heart cases that did occur were in those cases treated on the third or fourth day.

What has been said of the effect of antitoxin on the nerves applies to the heart, both as to lesions of its nerves and changes in the myocardium; for since these are caused by the toxins of diphtheria, if the latter are overwhelming or not neutralized by early and efficient treatment we may expect to see no reduction in the frequency of these complications.

Effect upon the Occurrence of Other Complications.—Complicating diseases caused by the simultaneous action of other organisms in conjunction with the diphtheria bacilli will obviously be only indirectly influenced by antitoxin. It must not be forgotten that the serum is a specific against one disease—true diphtheria. And yet it is but reasonable to suppose that any remedy which shortens the course of diphtheria and restores the tissues rapidly to their normal condition must have an effect upon the occurrence of complicating diseases, which are dependent for their existence on the pathologic condition caused by the diphtheria bacilli. Such diseases are, especially: Bronchopneumonia, and rarely lobar pneumonia; otitis; and the adenopathies. In so far as these lesions are caused by the diphtheria bacilli themselves or their toxins, early and adequate treatment has a direct influence in preventing their occurrence or cutting short their course.

Bronchopneumonia still remains the complication most to be dreaded. With regard to the frequency of its occurrence with antitoxin: Among 8238 cases of diphtheria reported by the Metropolitan Asylums Board of London in 1900, bronchopneumonia occurred in 1.17% of the cases; lobar pneumonia in 0.34%. As these cases were treated in the various hospitals controlled by the Board, we cannot but regard this percentage as exceedingly low.

In the collective investigation of the American Pediatric Society, among 3384 cases, bronchopneumonia occurred in 5.9% of the cases. Upon the diphtheria complicating other infectious diseases the serum can have but little effect. The good to be obtained in this field is from immunizing patients with other infectious diseases against diphtheria; especially in institutions it is an imperative duty to immunize every case of measles, and possibly scarlet fever. Other infectious diseases accompanied by catarrhal conditions when occurring in hospitals should also be given an immunizing dose at the onset of the disease.

Administration and Clinical Effect of Antitoxin.—No exact rules can be laid down as to the dose of antitoxin in a given case. Theoretically, we are to give a dose sufficient to neutralize the amount of

toxin being produced. Actually, we can only judge of the proper dosage by the appearance and extent of the membrane; the amount of toxemia present, as shown by the pulse and physical depression, fever, etc.; and the site of the membrane and age of the child. It is better to give too much than too little. It is quite certain that in the early days of antitoxin much too small doses were given. It would seem that certain physicians have proceeded too far in the other direction, for in doses of 40,000 to 60,000 units antitoxin is capable of causing disagreeable symptoms, which will later be noted, and occasionally alarming ones. There is, however, not the slightest ground for believing that a good preparation of antitoxin, given under proper conditions of cleanliness, has been the means of causing a fatal result. In doubtful cases where the symptoms are at all marked, it is better not to wait for the result of a culture, knowing that each hour of delay lessens the benefit to be derived from the serum.

The following dosage may be considered adequate: From 2000 to 3000 units to a child of over a year in an ordinary case of diphtheria. From 3000 to 5000 units for severe cases and all laryngeal cases of any age. For a child under one year in an ordinary case, 1500 to 2000 units. These doses are to be repeated in twelve hours, or even less if the symptoms are increasing, and in eighteen to twenty-four hours if there is not decided improvement. A third dose or even more may be given, if necessary, in another twenty-four hours.

Experience has shown that it is preferable to use as concentrated a form of serum as possible. A special syringe is not necessary. One holding 5 c.c. is convenient, with a small needle-tip. The barrel should be boiled before using, or washed out with pure alcohol. The needle itself should always be boiled thoroughly. The skin at the site of injection should be carefully cleaned and treated with a mild antiseptic, as a weak solution of bichlorid.

The tissues of the thigh, the posterior axillary line of the chest, or the abdomen is the site usually selected. The local effects of antitoxin injection are usually slight redness and edema and moderate pain. Abscesses are due to insufficient care in the technique, and should not occur. It is better to cover the site of injection with a piece of aseptic gauze, held in place by a strip of adhesive plaster.

The local effects produced by the serum on the pseudomembrane are very marked. In cases of pure diphtheria in the pharynx or tonsils, a few hours after injection the pseudomembrane becomes blanched, the dirty color usually present is less marked, the membrane appears to swell, becoming more or less granular and seemingly

thicker. The mucous membrane around it takes on a congested appearance and a purplish color and is more or less swollen. Later the membrane becomes loosened at the edges and rolled up, and soon detaches itself, either *en masse* or in small pieces, spontaneously or following irrigation. The process takes place somewhat more rapidly on the tonsils than elsewhere in the pharynx. The time required for the complete restoration of mucous membrane, even in favorably progressing cases, varies from twenty-four hours to three or four days. Occasionally the membrane, after disappearing, will be reproduced, in which case a second dose of serum is imperative. In the mixed cases of diphtheria the phenomena are not so well marked, and the dirty appearance of the membrane persists for some time, the throat not returning to its normal condition until later.

In nasal diphtheria, after inoculation the effects are similar, the irrigation, if practised, bringing away small or large pieces of detached membrane, or sometimes a complete cast of the cavity. The nasal discharge and swelling are very soon ameliorated and mouth-breathing ceases. In laryngeal diphtheria, as we have already pointed out, the serum stays the process so that in over one-half of these cases operation has become unnecessary. If the latter has to be practised, the membrane is soon loosened in favorable cases and is coughed up. The shorter time for which the tube is required in intubation and the cannula in tracheotomy has been noted (Bokai and others). It is a notable fact that the intubation tube is more often coughed out with the use of antitoxin than in any other form of treatment.

The adenopathies are invariably influenced by this treatment, especially in cases of pure diphtheria, although a moderate swelling of the cervical glands is apt to persist for some time after the disappearance of the local symptoms. The general condition of the patient becomes noticeably bettered, the constitutional symptoms of toxemia disappear, the color and facial expression are altered, the appetite returns, and mental depression disappears. When toxemia has become well marked on account of late treatment, the above effects are much less noticeable, or take place more gradually.

If careful observations be made, it will be found that in a good proportion of cases there is a rise in temperature of one or two degrees, coming on four or five hours after injection; this phenomenon is transient, lasts a few hours, and is not generally seen on the ordinary chart when the temperature is recorded but twice daily.

The pulse is also accelerated at the same time, usually out of proportion to the temperature; this acceleration is apt to persist after the fall of the latter for a variable time. Variot has studied the effect of serum on pulse and temperature, and finds in a certain number of cases not only a markedly quickened pulse, but a weak and irregular heart action. This temporary elevation of temperature is now known to be due not to the effect of antitoxin itself, but to its vehicle, horse serum; for experiments have shown that it occurs with non-immunized serum as well as immunized; and with the greater concentration of the antitoxin, this effect on pulse and temperature is less marked.

In favorable cases, and especially in pure diphtheria, the temperature falls very rapidly, becoming practically normal in two or three days. In mixed cases, and also laryngeal cases, the fall is much less sudden, and takes place by lysis. When the temperature does not fall in the regular way, it is an indication for a second dose of antitoxin, provided the persistence of the fever cannot be accounted for by a complication (bronchopneumonia, bronchitis, intestinal symptoms, etc.).

McCullom states that a high temperature always indicates some complication. In an analysis of 800 cases, he found that 121 fatal cases had a temperature above 103° F.; the remaining 105, a temperature from normal to 103° F. Clinical symptoms on autopsy showed complication in each instance. Of 679 non-fatal cases, only 55 had a temperature of 103° F. or over.

The accompanying charts (Figs. 15 to 23) are taken mainly from the New York Foundling Hospital, and are from consecutive cases which showed no complications. Finally, chills have been noted following injection (Goodall). A delayed fever regularly accompanies certain epiphenomena now to be described.

Antitoxin Exanthemata.—The frequency of occurrence of various rashes following injections of antitoxin has been variously estimated by different writers.

In the last report (1901) of the Scarlet Fever and Diphtheria Hospital, in 78 cases of diphtheria rash occurred in 25.4% of the cases in which antitoxin was given. The average day of occurrence was the eighth; extremes, second and eighteenth days. It was urticarial in type in 9 cases; erythematous in 7. Average duration, about two days.

The Investigating Committee of the Clinical Society of London in 633 cases examined report the occurrence of a rash in 34.7% of the cases (220 cases in all). Of these, the rash was erythematous in 161,

urticarial in 37, mixed in 17, and petechial in 5. Of the latter 5 cases, 2 died. Fever accompanied the rash in 136 cases. In all but 46 of the cases the rash was first seen at the site of injection.

The day of the occurrence was as follows: First to sixth day, 33 cases; seventh to twelfth day, 147 cases; thirteenth to eighteenth
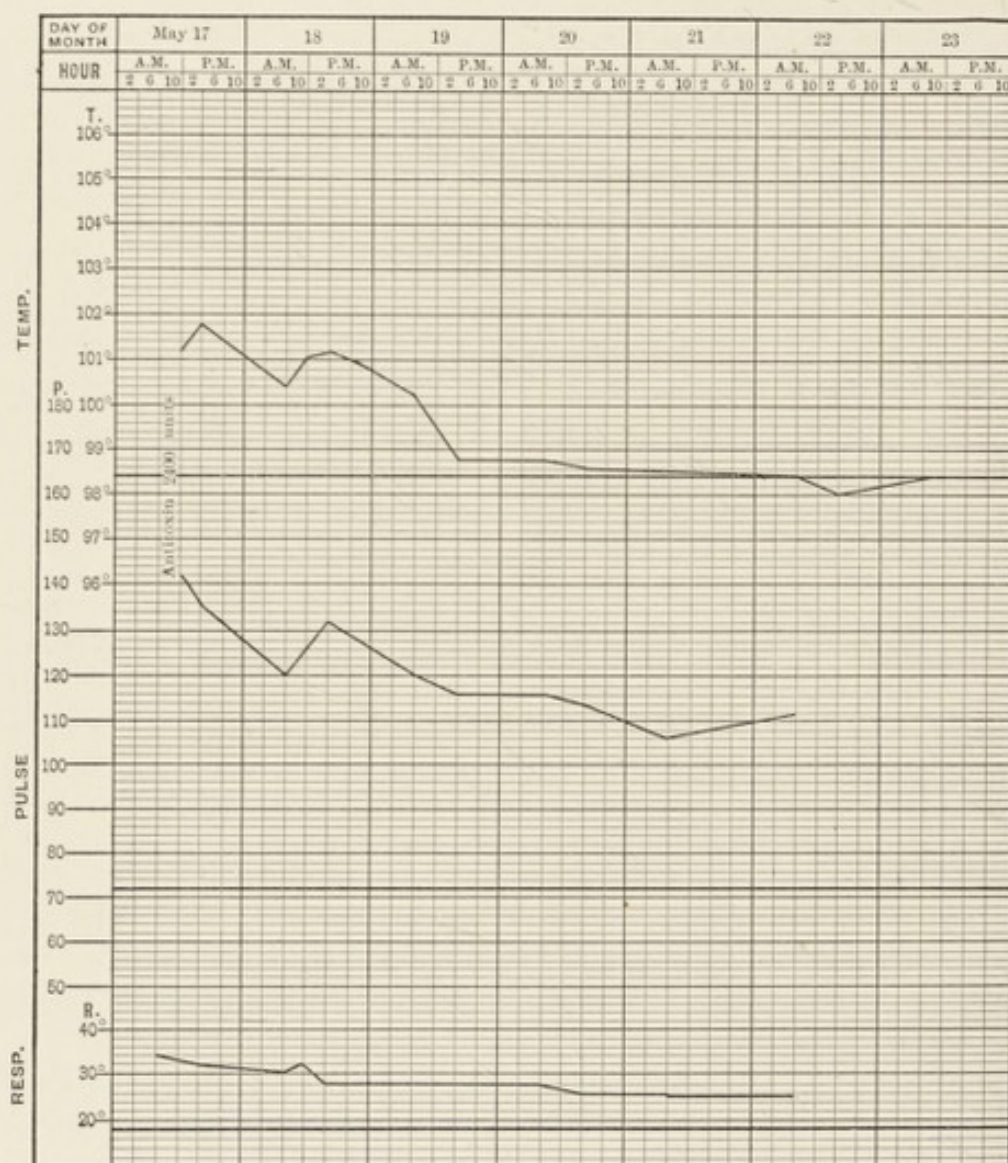
FIG. 15.—Nasopharyngeal diphtheria following operation for adenoids. Discharged cured May 31st. Stanley B., aged three years and six months. (New York Foundling Hospital.)

day, 34 cases; nineteenth to thirty-first day, 6 cases. There was a recurrence in 11 cases. The average duration was one to five days.

C. Hartung quotes a number of European observers who found antitoxin rash occurring in 11.4% of 2661 cases. Berg has made a study of this subject at the Willard Parker Hospital in New York. He found that the rash occurred 82 times in 337 cases, or 24%.

Of 33 consecutive cases of rash, 12 were simple erythema, 4 were scarlatiniform, 4 morbilliform, in 13 there was erythema multiforme or urticaria. It was noted that occasionally a rash disappears and a second one occurs later, differing in character from the first. A sharp rise of temperature preceded or occurred simultaneously with the rash,
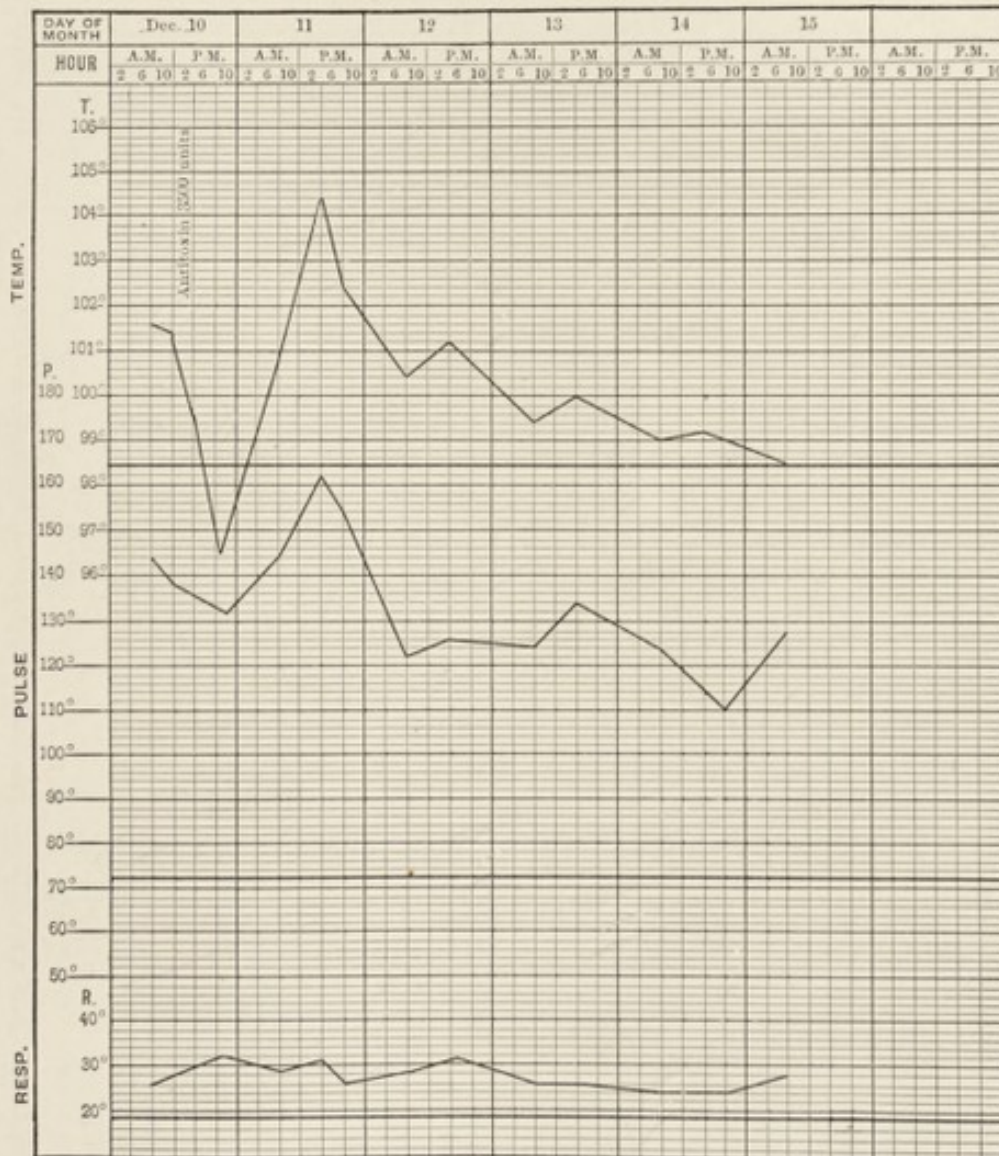
Fig. 16.—Diphtheria of tonsils and croup. Discharged cured December 15th. Intubation not necessary. Donald, aged three years and six months; day of admission December 10th. (New York Foundling Hospital.)

and reached its highest point at the time of greatest development of the latter, and then usually, though not always, rapidly declined.

The rashes are local or general. The former, as a rule, were very trifling, appearing about the site of the injection, and generally on the first and third days. The scarlatiniform and morbilliform varieties

were only seen in the severe cases. They were more persistent and accompanied by graver constitutional symptoms. Desquamation occasionally followed the more marked cases, and resembled the desquamation occurring in measles, even in the scarlatiniform variety.

The rash develops in a good proportion of the cases at the point of inoculation and spreads rapidly to other parts of the body; its
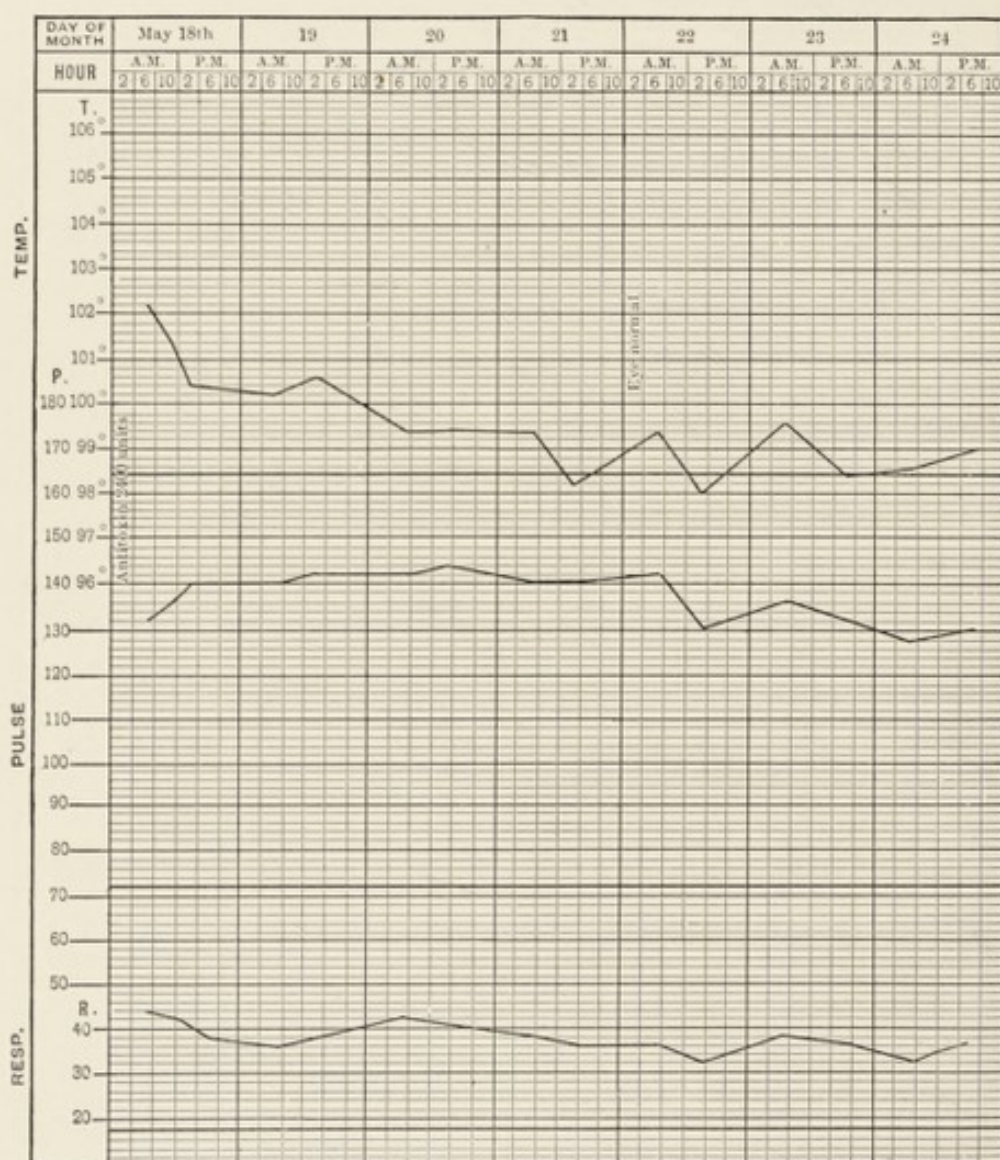
Fig. 17.—Severe conjunctival diphtheria. Discharged cured May 28th. Flora K., aged six months; day of admission May 18th. (New York Foundling Hospital.)

most frequent sites are about the buttocks, abdomen, and chest; less frequently about the wrists, elbows, and knees. Very often the spread of the rash is not continuous, but involves parts of the body widely separated. The face is less often involved. In a case of laryngeal diphtheria recently seen at the New York Foundling Hospital, the

rash affected the whole body, the eyelids were swollen, the eyes closed, the itching was intense. The patient, two years of age, had been given 8000 units of antitoxin.

The scarlatiniform eruption occurs generally on the back, upper and lower limbs, and chest; the face is usually not affected. At
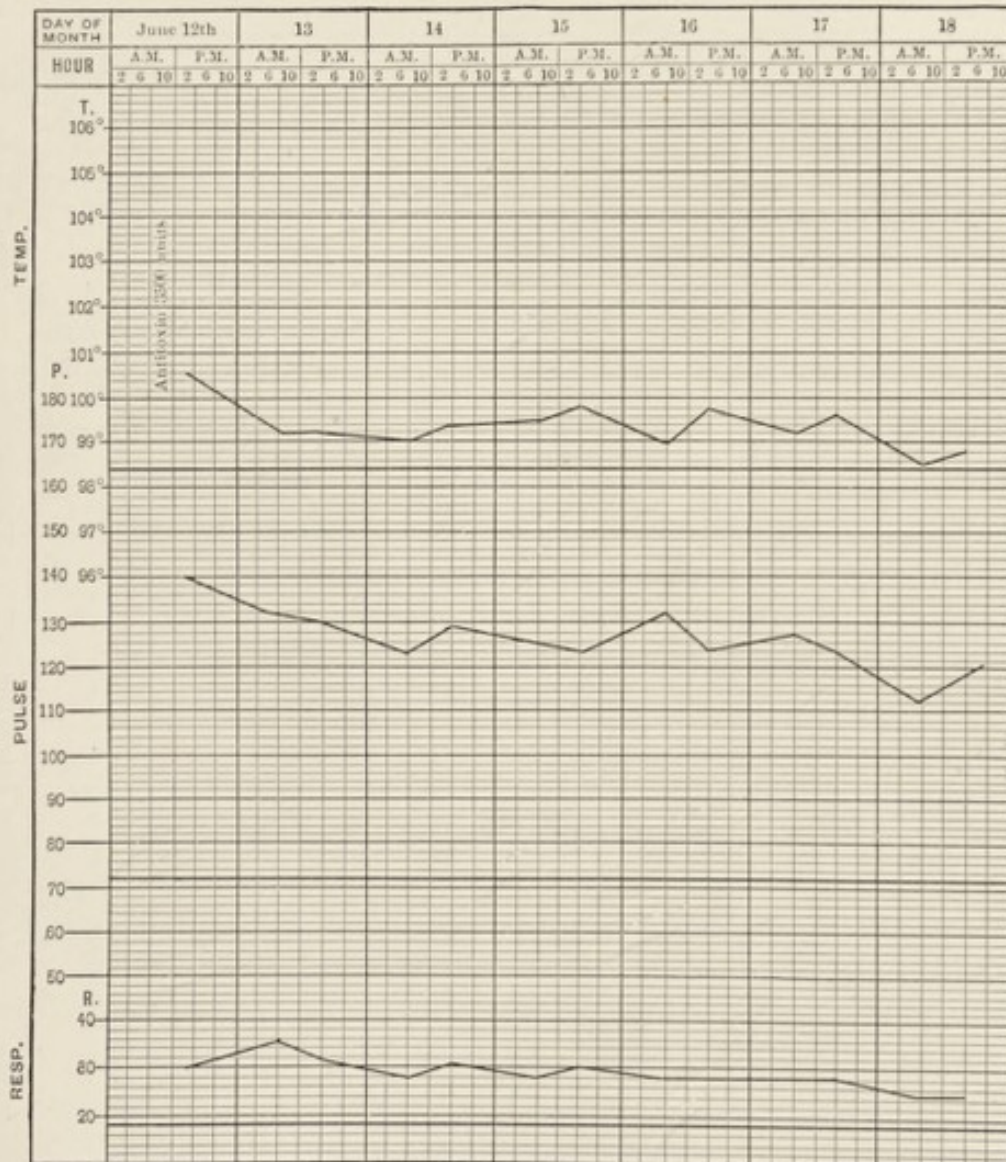
Fig. 18.—Nasal diphtheria; distinct membrane in one nostril; bloody discharge. Cured June 18th. Agatha B., aged three years and six months; day of admission June 12, 1901. (New York Foundling Hospital.)

times this form of the eruption coexists with the morbilliform; the latter is apt to occur on the buttocks, knees, and occasionally on the face. The pruritus in this form of eruption, though occasionally wanting, is usually severe.

As has already been noted, the rash is usually accompanied with

fever and restlessness, and occasionally joint pain. As a rule, the fever falls promptly and the rash and accompanying constitutional symptoms disappear. The symptoms are sometimes much more severe. There may be vomiting and diarrhea, weakness, prostration, and high temperature, or even delirium (Sevestre and Martin).
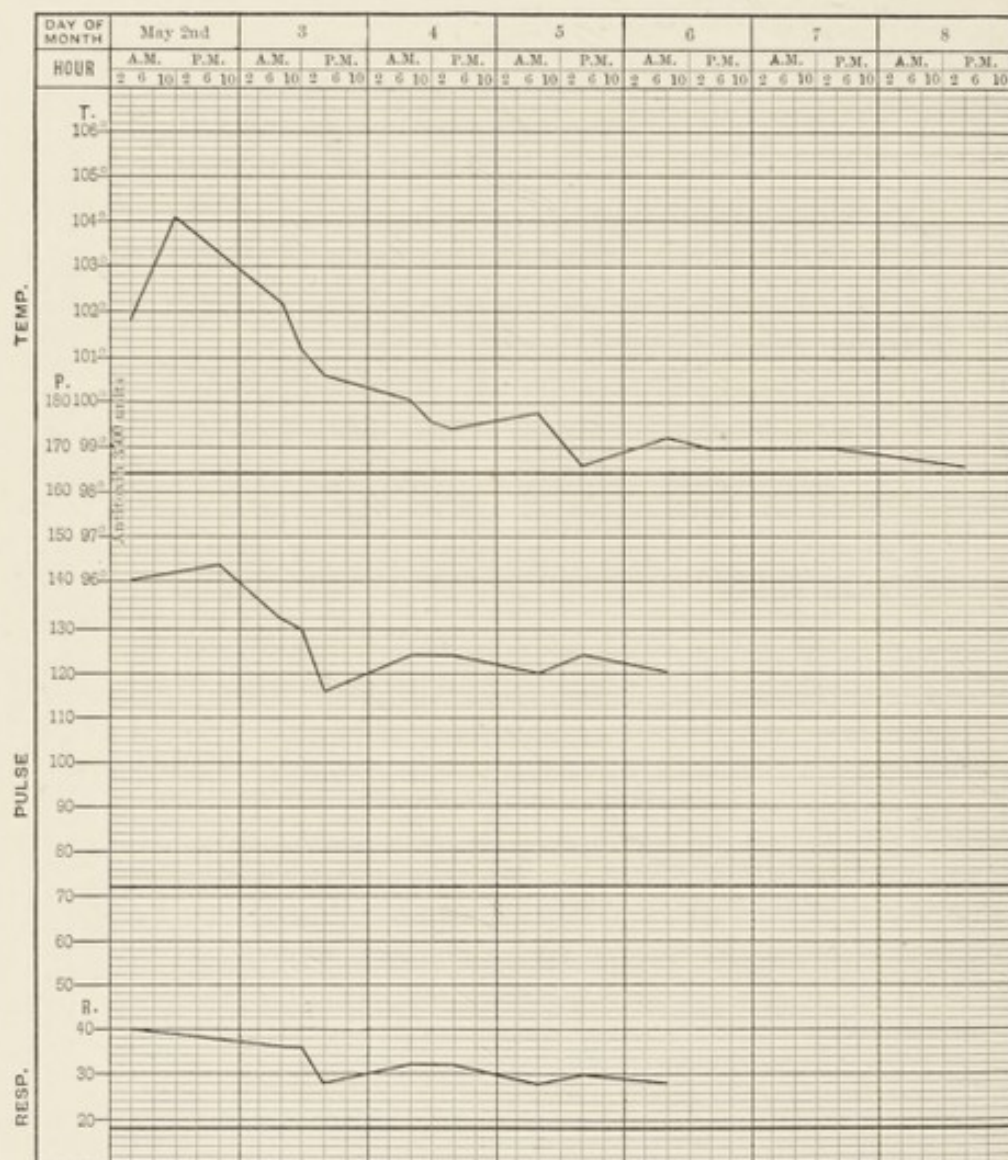
Fig. 19.—Diphtheria of pharynx and tonsils. Discharged cured May 19th. Joseph L., aged two years and six months; day of admission May 2d. (New York Foundling Hospital.)

In the great majority of cases the rash does little more than add a great deal to the discomfort of the patient. It may be of great importance from its resemblance to other exanthemata. Especially is this so of the scarlatiniform variety, which at times it is impossible to distinguish from true scarlet fever. Such a case is reported by Dr. Kellogg at the Hospital for Diphtheria and Scarlet Fever. A diphthe-

ria patient had been given antitoxin, and forty-eight hours afterward developed an erythematous rash, which soon became faintly papular, starting on the chest and spreading over the whole body. The pharynx was not characteristic of scarlet fever; the diphtheria was laryngeal. There was vomiting. The case was diagnosed as a scarlatiniform antitoxin eruption, but was isolated. Four days later typical scarlet desquamation took place. The nurse who took charge of the case four days later came down with typical scarlet fever. No Klebs-Löffler bacilli were found in her throat.

The points on which we must make the differential diagnosis are, first, the evanescent character of the antitoxin rash, the coexistence of
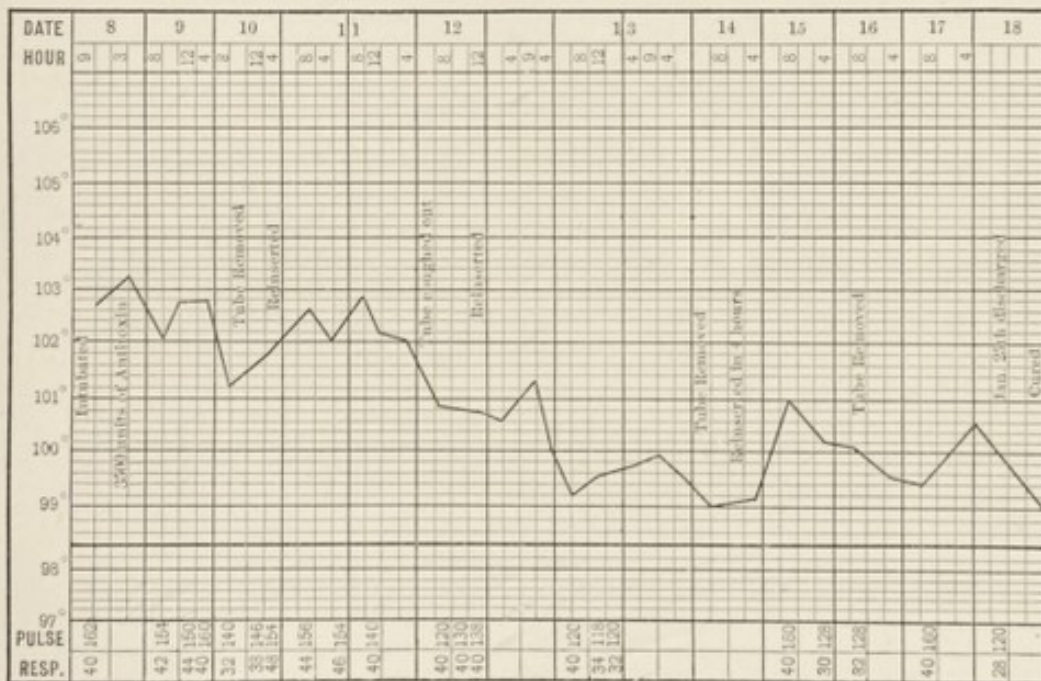
FIG. 20.—Laryngeal diphtheria; intubation; recovery. Florence C., aged one year; admitted January 8th; discharged January 25th. (New York Foundling Hospital.)

other forms of rash, its usually rapid disappearance and reappearance, the absence of vomiting, and in some cases the appearance of the throat, although with a pharyngeal diphtheria this factor must usually be excluded. Finally, as Berg has pointed out, the desquamation in the antitoxin rash, when present, has the appearance of a measles desquamation. The cases should always be isolated when there is the least doubt. The morbilliform rash should rarely be confounded with measles, as it is usually by no means typical of that disease. There is absence of the catarrhal symptoms of measles, and, finally, Koplik's spots should help us in the diagnosis of the latter.

With regard to the cause of these various exanthemata, it is now
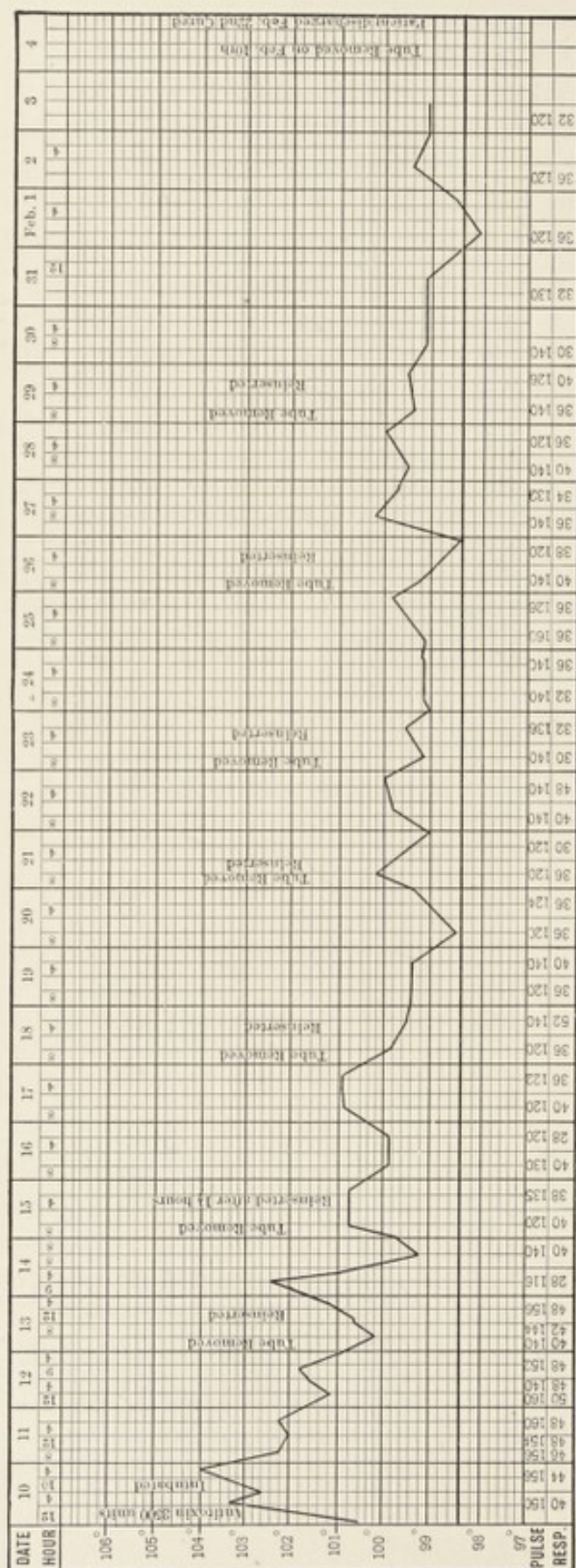
FIG. 21.—Laryngeal diphtheria; multiple intubations; recovery. Jerry R., aged fifteen months; admitted January 10th; discharged February 22d. (New York Foundling Hospital.)

regarded as beyond dispute that not antitoxin itself, but the horse serum, is responsible for their occurrence. This has been proved by experiments with non-immunized serum. The rash is more apt to follow large or frequently repeated doses than small ones. Concentrated serum has reduced the number and severity of these cases. Berg, following suggestions of Johannsen and others, believes that filtering the serum through a fine filter, and thus getting rid of certain toxalbumins, has an influence in diminishing the number of cases in which rash developed. W. H. Park does not regard this as proved, or, again, that heating the serum is of any benefit as a prophylactic measure.
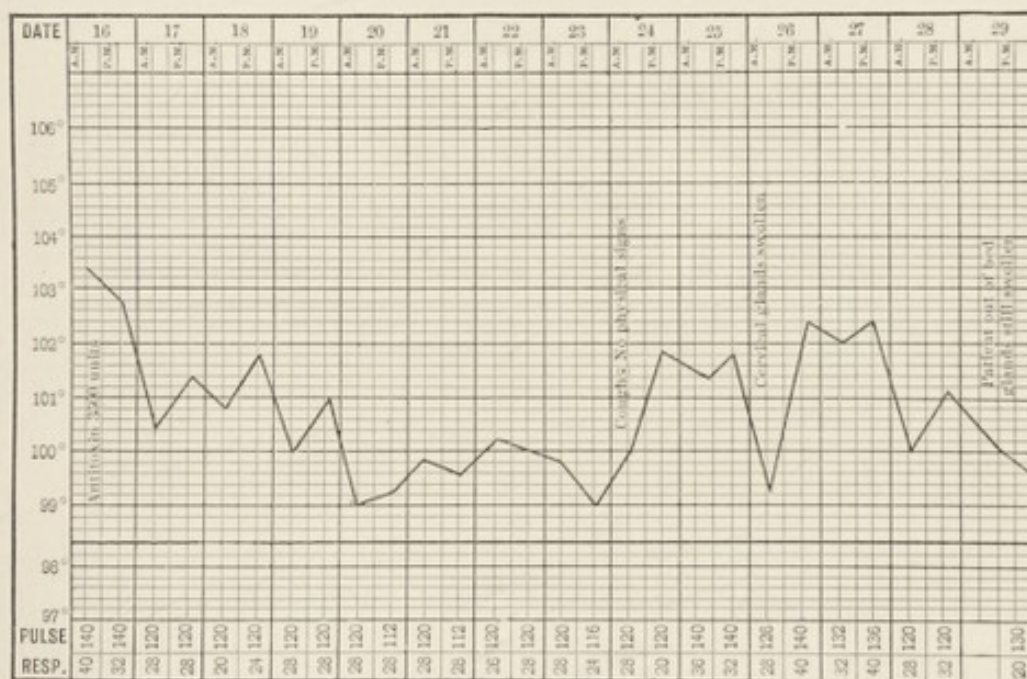
Fig. 22.—Diphtheria of the tonsils, complicated by cervical adenitis; recovery. Clifford B., aged four years; admitted January 16th. (New York Foundling Hospital.)

Sevestre and Martin have suggested an interesting theory as the cause for what they term the *exanthemata tardis*, under which head they include the rashes occurring, according to them, fairly regularly on the twelfth or thirteenth day, and accompanied by more or less constitutional disturbance. This they, together with Roux, regard as possibly due to a streptococcus infection. This hypothesis is based on the character of the symptoms, joint affections, etc., and the fact that in a certain number of observations they have found that these phenomena occur only where there is a mixed diphtheria, or a true streptococcic angina, and not in pure diphtheria. The streptococcus may alone be the cause of these phenomena. The thirteen days are re-

11

garded as the period of incubation of this infectious disease. The authors, while admitting that this is only a hypothesis, conclude: that these epiphenomena—rash, joint pains, etc.—are due, first, to a peculiar state of the organism resulting from the occurrence of a secondary infection, particularly by streptococci; and, second, the injec-
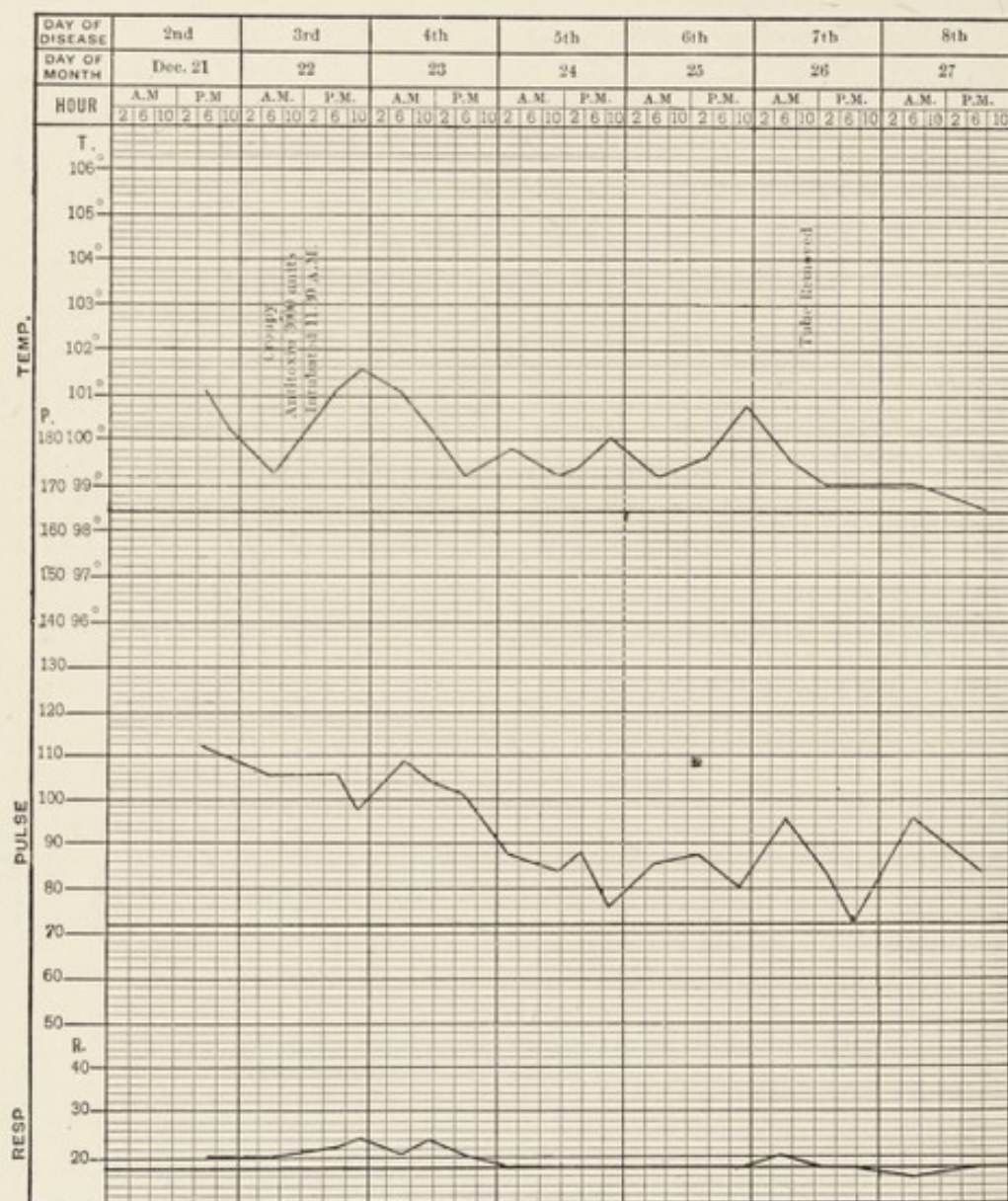
FIG. 23.—"Catarrhal" diphtheria of pharynx and tonsils followed by croup; intubation; recovery. Edward T., seven years. (Private case.)

tion of serum which acts as an occasional cause, and in a manner not yet determined.

Roger, while not accepting these conclusions, admits that the serum may have an effect in reducing the resistance of the system to certain organisms, comparable to the effect of mercury in mercurial

stomatitis, where bacteria are responsible for the secondary phenomena seen in the mouth.

Arthropathies.—Frequently accompanying the rashes just described, pains of greater or less severity occur about the large joints—hips, knee, wrist, and shoulder. One joint, as a rule, is first affected, and the pain spreads rapidly to the others.

In the report to the London Clinical Society, previously referred to, this symptom occurred 40 times in 633 cases. Thirty-five of these had a rash at the same time. In all there was fever. The writers find that it accompanies large doses more frequently than small ones.

Michael has arranged the returns of the Metropolitan Asylums Board in regard to this phenomenon: In 1895, joint pains were found in 4.7% of the cases; in 1896, 6.5%. Fever occurred in 1895 in 29.6% of the cases, and in 1896 in 19.8% of the cases. The writer states that the type of arthralgia occurring in the latter year was much less severe than in the former, which fact he attributes to greater concentration of the antitoxin and consequently smaller doses of the horse serum, which is regarded as the cause of this symptom.

With regard to the character of the pain, it is at times very severe, causing the patient to cry out. As a rule, it is increased by moving the joint, and not by pressure. On examination, there will frequently be found a slight redness and swelling about the joint, and at other times no local symptoms. Finally, muscular and true neuralgic pains are occasionally noted, in all probability due to the same cause.

Effect on the Blood.—Ewing has made some interesting observations on the effect of antitoxin on the hyperleucocytosis which has been already noted as regularly occurring in diphtheria. In 18 cases examined, there was a diminution in the number of leucocytes in 15; most marked from fifteen to forty minutes after injection, and affecting chiefly the faintly staining mononuclear and polynuclear leucocytes. He finds also that the antitoxin influenced the staining power of the leucocytes, and in 5 children in which this did not occur, death took place. Ewing believes that the hypoleucocytosis is due to the antitoxin, and when it does not occur, a fatal outcome is to be expected. Schlesinger has confirmed these results. Zagari, Calabrese, and Roger have noted a diminution in red cells and hemoglobin following antitoxin injection, which Roger believes will account for the anemia seen in children following immunizing doses of serum.

Effect on Pelvic Organs.—D'Astras has observed that antitoxin has a tendency to produce uterine hemorrhage and to increase the

menstrual flow or bring it on prematurely. Sevestre and Martin have noted a vulvitis in young girls, occurring from the tenth to the fifteenth day, which they regard as due to the serum. The same writers have occasionally seen a fatal diarrhea, sometimes with blood in the stools, following injection of antitoxin.

Apart from the epiphenomena just described, a number of other ill effects have been attributed to antitoxin. When the remedy was first used, its preparation was no doubt imperfect, the dosage too small, and conclusions were drawn from an insufficient number of cases in which it had been used. Violent attacks were made upon its use, which some writers regarded as little less than murderous. Cases of sudden death following its administration were reported, and statistics were juggled to prove the case. . Time has changed all this, and the physician who to-day does not advocate its use should be regarded as blindly prejudiced, and unfit to be trusted with the care of diphtheria cases. If an analysis is made of the accidents attributed to antitoxin, apart from those above described, and which we must accept as the price to be paid for the benefits which undoubtedly follow its use, it will be found that in not one of the fatal cases attributed to it, in which we can obtain an intelligent history or postmortem examination, may not the cause of death have been more logically ascribed to diphtheria, and not to the remedy. Sudden death occurs in diphtheria, as we well know; anuria and convulsions have been frequently seen; heart troubles, functional and organic, are very frequent; and there is no evidence that any one of these is due to antitoxin. On the contrary, it has been shown that in a large proportion of cases their occurrence can certainly be avoided if antitoxin be given in time.

The unavoidable epiphenomena are now known to be due to horse serum, and not to the antitoxin. The various methods suggested, as filtering, heating, etc., have not proved of much value in diminishing the frequency of their occurrence. It is a fact, however, that the serum of certain horses is much more prone to cause these symptoms than others, and, as suggested by W. H. Park, this should not be employed any more than is absolutely necessary. The greater concentration of the antitoxin has been of great benefit in doing away with its disagreeable effects, and it is to be hoped that in the course of time a serum will be produced which will be free from them.

Cases of tetanus following its use have been reported from Italy, and lately in this country. This, if proved, is merely an evidence of carelessness on the part of the producers of the serum, and in no way militates against the advisability of its employment.

INDICATIONS FOR ANTITOXIN.

In pharyngeal cases, if the symptoms, local and general, are mild and the children over one year of age, unless there is a distinct history of exposure, it is allowable to wait for the result of a bacteriologic examination. In nasal, buccal, conjunctival, or cutaneous cases the same rule applies.

In croup cases an injection should be given without a moment's delay under all circumstances and at every age, and a culture taken at the same time. The fact that many other germs are associated with the diphtheria bacilli is no contraindication to the use of the serum. We may at least neutralize the effect of one set of organisms.

In so-called cases of catarrhal diphtheria antitoxin is indicated. In the cases of pseudodiphtheria in which bacteriologic examination does not, after repeated examinations, show the presence of diphtheria bacilli, antitoxin cannot be expected to be of use. In cases of doubtful or atypical germs, if clinical symptoms be at all marked, antitoxin should be given; if not marked, another culture should be taken and the result awaited.

There are no contraindications to the use of antitoxin in the presence of urgent symptoms probably due to diphtheria. In wasting diseases—as in tuberculosis—the effect of antitoxin cannot be considered desirable on the general disease. In such cases, if not severe, it would be better to avoid antitoxin and depend upon local treatment.

SURGICAL TREATMENT.

TRACHEOTOMY.

This operation has a limited field in the treatment of diphtheria: (1) When, for any reason, intubation cannot be performed—through ignorance of the operation, where tubes are not available, etc. (2) With so much edema of the larynx that intubation does not give relief or cannot be performed. (3) When there is membrane low down in the trachea. (4) With extensive involvement of the nasopharynx (Somerset), where intubation has failed to give relief. (5) Secondary tracheotomy may occasionally be indicated, although the statement of O'Dwyer with regard to the latter still holds good: "If you get rid of an intubation tube by means of a tracheotomy tube, you will later, in each case, get rid of the tracheotomy tube by reintubation."

History.—The operation is said to have been first performed by

Andree, in 1782. It was later worked out by Bretonneau and proved a practical method of relieving laryngeal stenosis, and still further elaborated by Trousseau and Guersant. In this country, since the introduction of intubation by Dr. Joseph O'Dwyer, it has never been popular. In many parts of Europe and England it has remained until recently, at any rate, the operation of election. The indications for performing a primary tracheotomy are identical with those for performing intubation. (See Intubation.)

Method of Performing Tracheotomy.—The original operation, as performed by Trousseau, was what is known as low tracheotomy (*tracheotome inferieure*). The opening at the trachea began at the second ring. The external incision was carried to the sternal notch or near it. The operation was a difficult one on account of the blood-vessels and tissues overlying the trachea in this position, and has been abandoned for the high operation.

Cricotracheotomy was formerly recommended as a method of rapid operation, and was thus performed: The lower limit of the cricoid cartilage was marked with the finger-nail or a pencil. The larynx of the patient was then seized between the thumb and fingers of the left hand and pressed forward until it stood out. The cricothyroid membrane was then located and an incision made directly through the center of it. The cricoid and two first tracheal rings were cut, and, in carrying the knife outward, the overlying tissues and skin; after which the cannula was introduced. The operation as usually performed is known as superior tracheotomy. An anesthetic is usually employed, the necessity for which will depend upon the stage of asphyxiation; whenever there is time and there are no contraindications, it is better to give one, as the operation is rendered much simpler. Spasm is thus apt to be temporarily ameliorated, and the movements of the larynx are less violent and irregular. In an emergency a sharp knife, some one to hold the patient, and means of keeping open the trachea wound are all that are absolutely necessary.

For its proper performance, the operation requires an assistant to steady the child's head, and, if an anesthetic be not given, another to hold the feet and hands. The instruments required are a straight bistoury, a blunt-pointed bistoury, a dilator and a cannula of a size suited to the child's age, a pair of retractors and some artery clamps, a thumb forceps, cotton, and antiseptic solution. It is needless to say that the operation, if time be given, should be performed with every antiseptic precaution, both as to the instruments and the hands of the operator.

PLATE 8.
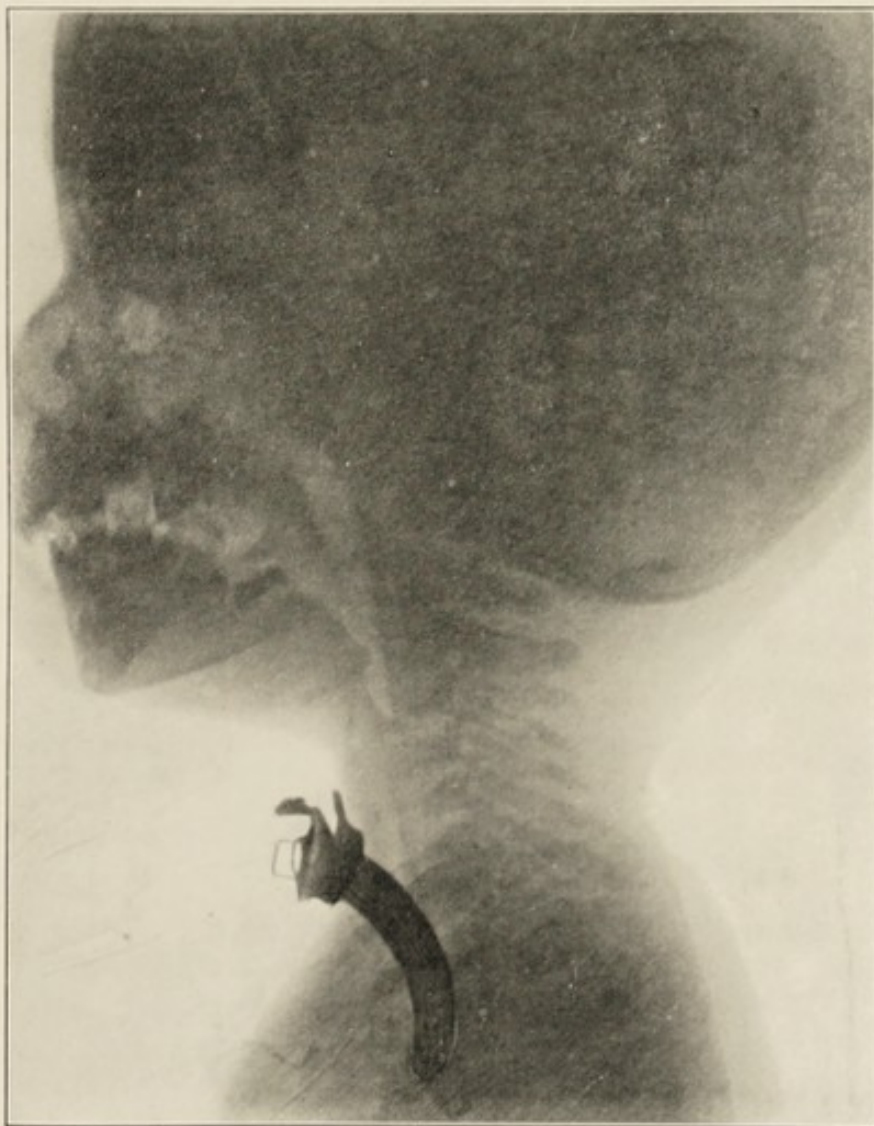
Tracheotomy tube in position.
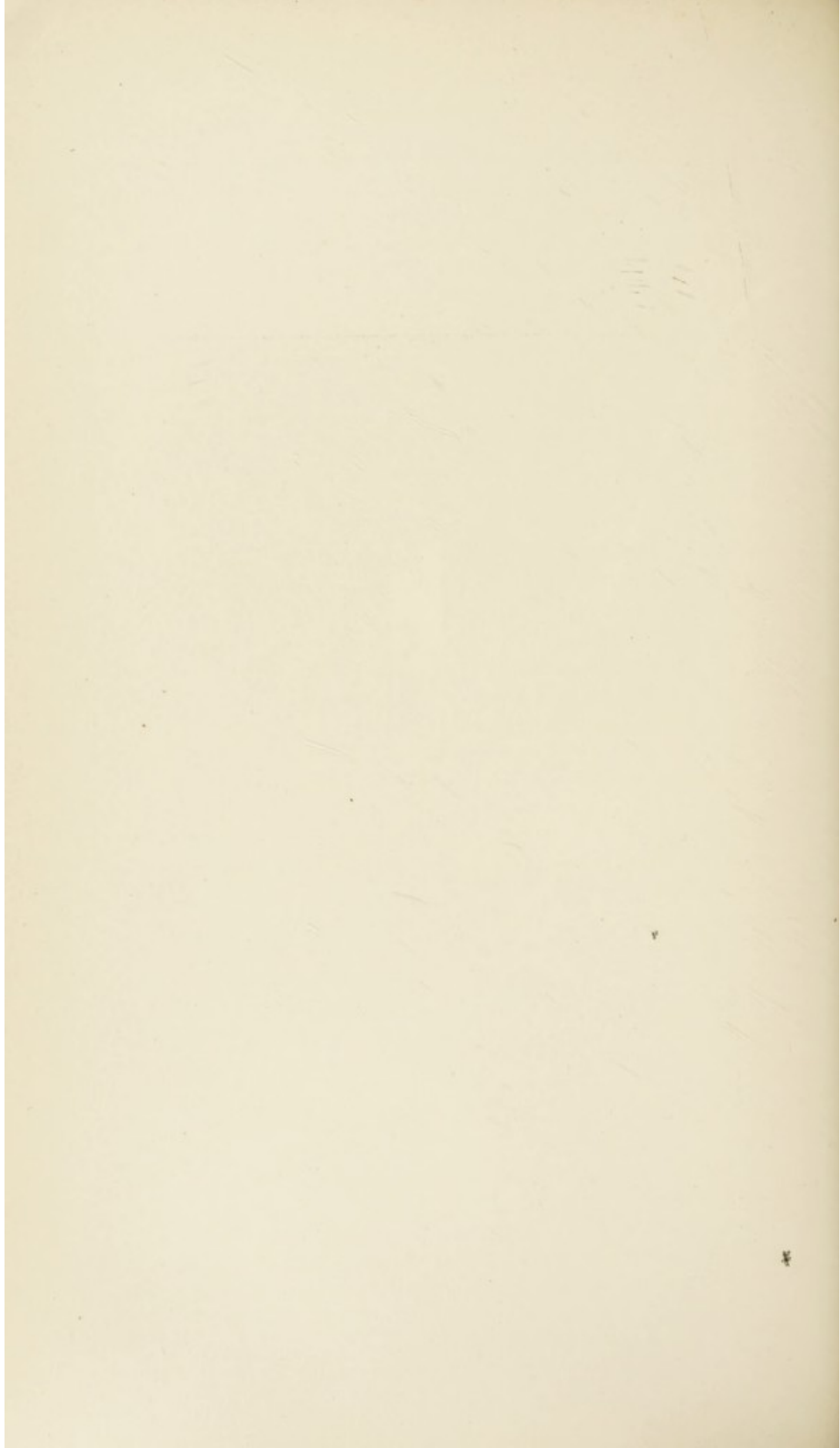
The patient should be placed on a table with a roll of some sort on which the back of the head rests, the head hanging rather far back, but not so much as to flatten the trachea and to further impede respiration. The light should be of the best, and should fall directly on the field of the operation. The child should be wrapped in a blanket, which confines the arms and hands, but not so closely that artificial rspiration, if it be necessary, cannot be immediately employed.

The most important preliminary to the actual operation is the exact location of the cricoid cartilage. The index-finger of the left hand is placed gently and firmly on this point, the larynx being firmly held in the median line by the thumb and forefinger. Care should be taken that unequal pressure on the sides of the larynx is avoided, as thus the trachea is pressed to one side. The position of the left hand is maintained until the cannula is introduced into the trachea. An incision is made exactly in the median line, from the point of the index-finger marking the cricoid, for a distance of 2.5 to 3 cm. The subcutaneous tissues over the trachea are thus divided. The guiding forefinger is then inserted into the superior angle of the wound, directly over the bared trachea. The bistoury is then passed into the trachea directly under the finger, and the incision carried sufficiently far down, directly in the median line, to admit the tip of the forefinger. This serves to keep the blood from entering the trachea and to dilate the tracheal incision. The cannula is then introduced directly into the tracheal opening, the finger being gradually withdrawn to make room.

If this does not succeed, a dilator is used and the cannula thus introduced. If the characteristic rush of air does not follow the introduction of the cannula, it may be due to a false passage or to the fact that a piece of false membrane has been pushed down by the tube. This should be removed by the thumb-forceps if possible. The cannula is then fastened in place by a tape about the neck. The inner tube should be freed from obstructions after introduction, as usually a good deal of mucus is coughed up, and a dressing of antiseptic or sterile gauze should be placed about the wound and over the opening of the cannula.

The difficulties met with in this operation are, in brief:

1. In very fat children or in those whose necks are greatly swollen from the effects of the disease (occasionally the cricoid is better mapped out in an upright position).

2. The incision in the trachea may be too small and have to be enlarged before the cannula can be introduced. It may (less often) be too large, so that the cannula does not remain in place and a secondary

emphysema takes place. A suture may be necessary in the latter case after the cannula has been introduced.

3. Hemorrhage. This is rare unless the incision has been carried to one or the other side of the median line or too low down. It may be necessary to ligate these vessels before the cannula is introduced.

4. Irregular incisions may make the introduction of the cannula very difficult.

5. False passages. The cannula may pass to one side or the other of the trachea. The diagnosis of this accident is made by the absence of the characteristic rush of air and failure to relieve the symptoms of stenosis.

Occasional Accidents.—Secondary hemorrhages occasionally occur some time after the operation, either from a partly obliterated blood-vessel, the breaking-down of ulcerations, or changes in the blood itself from diphtheria. They are often very hard to control.

Asphyxiation may take place during the operation, in which case the operation should be hurried and a dilator alone put in the trachea temporarily. This may result from the position of the patient, as a cause of increased stenosis, from false passage of the tube and pushing down of pseudomembrane by the tube. After the latter has been cleared, and properly introduced artificial respiration should be immediately performed.

After-effects of Tracheotomy.—The immediate effects are due to the relief afforded by overcoming the obstructions to respiration. Cyanosis disappears, the children, often previously exhausted, become quiet and very frequently sleep soon after the operation. There are more or less frequent fits of coughing, with mucus and sometimes pieces of membrane expelled through the tube. Fever usually follows the operation, lasting for two or three days, and probably due to absorption of toxins and secondary infection from the surface of the wound. Unless there is a complication, the temperature is only slightly elevated.

The character of the expectoration is of importance in prognosis; usually it is of a mucous character, with more or less membrane. Again, the latter may obstruct the tube, causing an attack of acute dyspnea and coughing until it comes away. When the liquid fluid coming through the cannula is of a thin, foul-smelling, and sanious character, the prognosis is bad. This is seen more often in cases of mixed diphtheria. At times the cannula remains dry, and there is little attempt at expectoration, a sign regarded by Trousseau as of grave import, and usually of a complicating pneumonia.

Complications.—These are, in brief, infection of the tracheotomy wound and of the bronchi and lungs. The first has become less frequent with the introduction of antiseptic precautions.

Infection of the wounds, however, does occur; not infrequently the wound is congested, the tissues about the neck swollen and edematous. This may resolve promptly or go on to suppuration or even gangrene. The latter may occur in a superficial form, involving only the surface of the wound; or in a severe form, affecting the tissues of the neck and even penetrating the mediastinum. The prognosis in the latter form of the disease is very bad, especially as it occurs usually only in a severe form of diphtheria.

An ulceration of the trachea at the extremity of the tube (generally superficial) is very common. Erysipelas and diphtheria of the wound also occur. Bronchopneumonia is by far the most important complication of tracheotomized cases. It occurs from the second to the seventh day after operation, and is very fatal. Secondary laryngeal complications, changes in voice, etc., frequently follow tracheotomy. They usually end in complete recovery.

After-treatment.—The internal cannula should be taken out every two or three hours, wiped dry, and cleaned. The frequency of this change depends entirely upon the amount of obstruction, as shown by the character of the breathing, respiratory sounds, etc. After twenty-four hours, the external cannula may be removed and cleaned, together with the wound. The child should be placed on the table in a similar position to that recommended for the operation; the head, however, need not be so far back. Another cannula and dilator should always be ready in cases of emergency. This changing of the external cannula should then be repeated every day, the wound being thoroughly cleaned each time. After the second or third removal the larynx should be examined to see if it is free and there is no further use for the cannula. Under serotherapy, this occurs on the second or third day, in contrast to the pre-antitoxin days, when it was necessary to use the tube for a week or more.

When the cannula has been removed, the wound should be carefully dressed and covered over. The children, however, should be watched most carefully for any sign of recurring stenosis. Cicatrization takes place very rapidly with serotherapy, generally in three or four days.

At times children are seen who choke up immediately upon removal of the cannula. This seems to be due to the established habit of cannular breathing, and may often be avoided by distracting the

child's attention, soothing and amusing it. Sedatives also may be of much service, given just before and continued after the removal of the cannula. Bromid of soda is that to be preferred, or morphin in small doses. Cold applications to the chest have been recommended, and, finally, in very obstinate cases a secondary intubation for a day or two may be necessary.

Cicatrices of the trachea leading to permanent contraction, and also granulation about the seat of incision, may necessitate prolonged retention of the cannula.

INTUBATION.

Bernard Wolff, in 1898, quotes Malgaigne as follows: "If I do real honor to the author of tracheotomy, what honor will he not deserve who shall come to deliver us from it?"

The attempts to avoid the necessity of this dreaded operation before and after the time of Bouchut, in 1858, have been numerous. The fate of the latter's really valuable suggestions and experiments is now too well known to require comment; suffice it to say that his conception of intubation was undoubtedly a step in the right direction, and fell a victim to the ridicule and abuse of his contemporaries. He lived to offer his personal congratulations to the inventor of practical intubation. Absolutely ignorant of any previous work on this subject, Dr. Joseph O'Dwyer, of New York, began a series of experiments in 1880 at the New York Foundling Hospital. The terrible results of tracheotomy at this institution may be said to be responsible for intubation as we now know it. From 1869 to 1880 no cases of tracheotomy performed for diphtheritic croup recovered. The operation was finally regarded simply as a means of preventing suffocation and permitting a less dreadful death. So great was the dread of it, on the part of mothers, the sisters in charge of the institution, and even the physicians themselves, that it was finally abandoned. The number of operations in any one year was not very great, the patients being drawn from 1800 children. Various kinds of laryngeal catheters before and after Dr. O'Dwyer's time had been employed in attempts to overcome laryngeal obstruction. They were introduced either through the nose or mouth. The absolute impossibility of keeping such a length of narrow tubing free from obstruction led to their early abandonment.

There is no more interesting illustration of the logical development of an operation than is afforded by the complete collection of O'Dwyer instruments, the property of the New York Academy of Medicine.

The first tube constructed was on the principle of a bivalve speculum introduced into the larynx with closed blades, which separated by means of a spring when the tube was released from the introducer. The regulation of the strength of the spring was found to be the insurmountable difficulty in the use of this instrument. If it was made too weak, the blades closed, with resulting apnea on the part of the patient; if too strong, laceration and destruction of the larynx resulted. Furthermore, the swollen mucous membrane gradually pressed between the blades, and thus stopped the respiration. This tube, however, was always retained, and gave prompt relief to the dyspnea, lasting sometimes for several days. Secondary tracheotomy was performed in all the most hopeful cases, and one patient recovered after wearing the cannula for six months; the voice was permanently impaired. This occurred in 1882, and was the first operated case of croup to recover since the founding of the institution (thirteen years). The shoulders of these tubes were built up with a solution of gutta-percha in chloroform, layer after layer until the desired thickness was obtained.

After three years of the bivalve, it was reluctantly given up as useless. It was at this time that Dr. O'Dwyer's friends called his attention to Bouchut's experiments, begging him to look into what had been done in that direction. Dr. O'Dwyer promptly refused, believing that if his mind was directed to a work which had been found unpractical, and therefore abandoned, it would be the end of his hopes for the discovery of practical intubation.

The next tube was of plain oval form, one inch in length, with a small slit in the posterior part of the upper extremity, into which the extractor fitted. This tube was first used in the case of an infant of about three months. The smallest size was inserted, and gave complete relief from the dyspnea until the child died, sixteen hours later.

The second case, a girl four years of age, was operated on in May, 1884. The tube was retained for sixty-seven hours and then removed. Four hours later it was reinserted, and remained for three days, when it was coughed out, and not again required. The aphonia caused by this operation was recovered from in seven weeks. This was the first and only recovery accredited to this form of tube. It was tried in seven other cases.

It was during the operation on this patient that the necessity for a mouth-gag became apparent, as she closed her teeth so tightly on the metal shield worn on the finger for protection that it was found necessary to give chloroform in order to proceed with the operation.

It was found that the mucous membrane regularly caught and was held in the extractor slit above referred to, and, as a consequence, the next form of tube had this feature omitted, necessitating a new variety of extractor. These tubes were not retained at all, showing that the previous variety were only held in place by the pouch of mucous membrane in the slit. They were used in five cases, with one recovery after ten days (December, 1884). The tube was frequently expelled, the patient on more than one occasion nearly suffocating before the tube could be reinserted.

The tubes above described were only one inch long, or even less, and they were frequently found after death to be plugged with false membrane. With a view to overcoming this fault, and also to test the retaining qualities of longer tubes, the next variety were made long enough to reach quite to the bifurcation of the trachea. The shortest of these was 1¾ inches; the longest, 3 inches. These tubes were never completely expelled from the larynx, but were projected upward by every fit of coughing, and remained in this position until pushed back into place by the doctor or nurse. The latter were instructed to replace the tube after each attack of coughing, and especially before the patients were fed.

The great length of these tubes prevented their leaving the larynx, even if the proximal end rested against the pharyngeal vault. They were used in six cases, all of which ended fatally.

A second shoulder was now made, an inch or less below the first, with the object of allowing a furrow in which the vocal chords could rest. To facilitate introduction, the lower shoulder was in the form of a wedge with the base upward. The effect of this modification was to cause the tubes to be retained so firmly that any attempts at extubation with the weak extractor then in use were absolutely unavailing. This second shoulder was consequently reduced in size, with a view to lessening the grip of the vocal chords, when it was found that such a tube was little, if at all, better retained than the long, plain, oval variety. One recovery is accredited to this tube among ten cases. After much study and experimentation on the cadaver to determine the proper size, the all-important retention swell was fairly developed, and intubation became an accomplished fact.

A careful study was now made of ulcerations due to the tube. These occurred: (1) In the cricoid division of the larynx, just below the vocal chords; (2) at the base of the epiglottis, from pressure during the act of swallowing; (3) on the anterior wall of the trachea near the distal end of the tube.

The first was found to be due to the use of too large tubes, and further measurements of the interior of the larynx showed that it was not the chink of the glottis, but the cricoid division of the larynx, which was the narrowest point, and that this part, therefore, should be used to gage the proper caliber of the tubes. Following this discovery, a process of paring down was begun, with the result that while there was still ample room for carrying on respiration, the ulceration ceased.

The second point of ulceration was avoided by giving the upper portion of the tube a backward curve and leaving the metal on its anterior part thick enough to present a blunt under-surface to the epiglottis when the latter was pressed upon it. The head was also increased in size, by which the pressure was distributed over a larger area.

The third variety of ulceration consisted of an area extending about ¼ of an inch above and below the distal end of the tube. The lower part of this ulceration was found to be due to the movement of the trachea during the act of swallowing, the mucous membrane being drawn up against the sharp tube. The upper part was produced by the return of the membrane to its position of rest. In other words, the head of the tube being fixed, its distal end was moved over a space of about ½ an inch. To surmount this difficulty the metal at the lower end of the tube was made even thicker than that above, and rounded off, so as to have a smooth blunt surface over which the tissue would slide without injury.

False Membrane and Foreign Body Tubes; Granulation Tubes.— It was occasionally found that after introduction of these tubes the lumen would be blocked by false membrane, which usually was coughed up immediately after the tube was removed. Occasionally this expulsion failed to take place, and in order to get rid of this loosened membrane many experiments were made, until a special tube was produced for this purpose. These are short hollow cylinders of large caliber, short enough not to push down the tracheal membrane, long enough to reach below the cricoid stenosis, and large enough to allow masses to pass through them. These tubes are of various sizes, seven in number. Since they have no retention swell, it is necessary to use the largest size possible, wedging it into the larynx. They require a special introducer with a long curve to carry the short tube through the cricoid constriction before withdrawing the obturator. On no account are they to be allowed to remain more than a few hours, as the pressure caused by them may lead to serious damage within the larynx.

FIG. 24.—Tubes with built-up head for granulations.
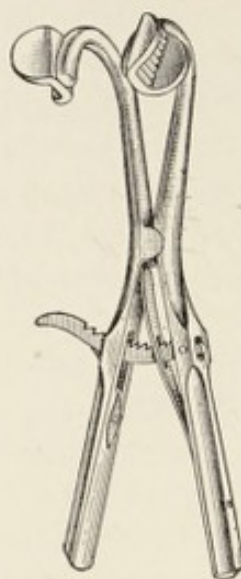
FIG. 25.—Mouth gag.
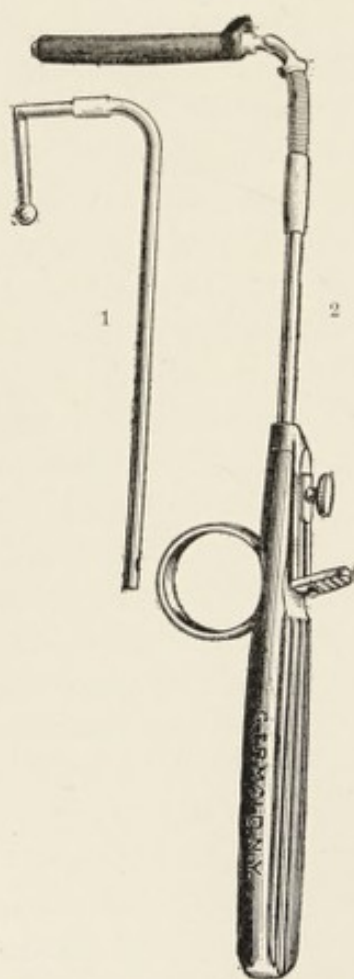
FIG. 26.—1, Obturator; 2, introducer with tube.
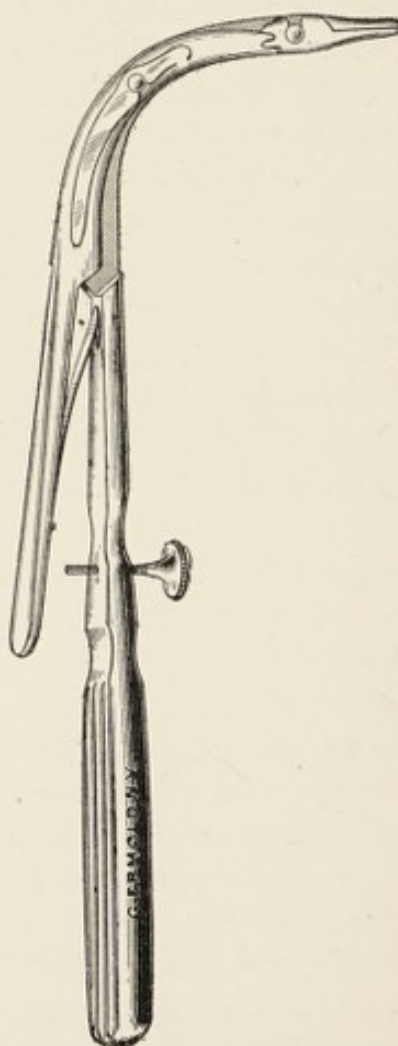
FIG. 27.—Extractor.

Another modification of the regular intubation tube is that with a built-up head, so constructed as to ride over and press upon and thus to lead to absorption of the granulations which are occasionally found within the larynx following an intubation (see Fig. 24).

The last improvement introduced by the inventor was that of a hard rubber tube, overlying metal. These are lighter, more readily coughed up when choked with membrane or thick mucus, and may be worn for a long time without injury to the larynx or trachea. The deposit of lime-salts which formed regularly upon the metal tubes, and was undoubtedly a cause of local irritation leading to exuberant granulation, in this form of tube does not take place. They are used in this country almost universally, the all metal tubes being no longer made except by special order.

The tube of Dr. O'Dwyer as it is made to-day by reliable manufacturers reaches within an inch of the bifurcation of the trachea. The lumen is elliptic. The points of interest are the retaining swell, seen from the front or behind. Viewed laterally, it will be seen that there is no anterior or posterior bulging, corresponding to this swell; the lines are perfectly straight. The sharp lateral constriction below the head will be noticed. The head is irregularly oval. Its anterior part is cut away so that it does not project beyond the anterior surface line of the tube proper. The posterior is prolonged backward and overhangs the tube. Finally, a hole is seen in the left side of the head, into which the string is inserted. The lower extremity in the modern tubes is rather more bulging and thicker than in the earlier ones. The edges are rounded off and blunt.

The perfect correlation of a properly constructed tube to the anatomic structure of the larynx can best be appreciated by placing one in position in a larynx removed at autopsy. The tubes are made in seven or more sizes, adapting them to the age of the patient. A scale is furnished so that the proper tube may be selected without difficulty. Children's tubes, even of the largest size, should on no account be used for adults, for whom special tubes have been made.

The obturator, one for each tube, is fitted to the introducer. Its lower extremity ends in a protuberance which fits accurately the lower end of the tube, and has the effect of prolonging the latter into a rounded extremity. The obturator is made in two parts, joined by a hinge, which facilitates removal from the tube after the latter is in the larynx.

The introducer, the general shape of which will be seen from the

illustration (Fig. 26, 2), has the laryngeal extremity of the central bar terminating in the obturator. About this central bar is a movable cylinder, terminating in two lateral wings, which pass one on each side of the head of the tube when the latter is in position. The cylinder is pushed forward by means of the thumb placed against the button on top of the handle. The spring seen near the end of the cylinder enables the latter to pass over the curved tip of the central bar, and by its recoil the cylinder bearing the lateral wings returns to its position.

The extractor (Fig. 27) consists of a curved handle terminating in a beak-like process which fits into the tube. By a system of levers the lower jaw is separated from the immovable upper one by pressing
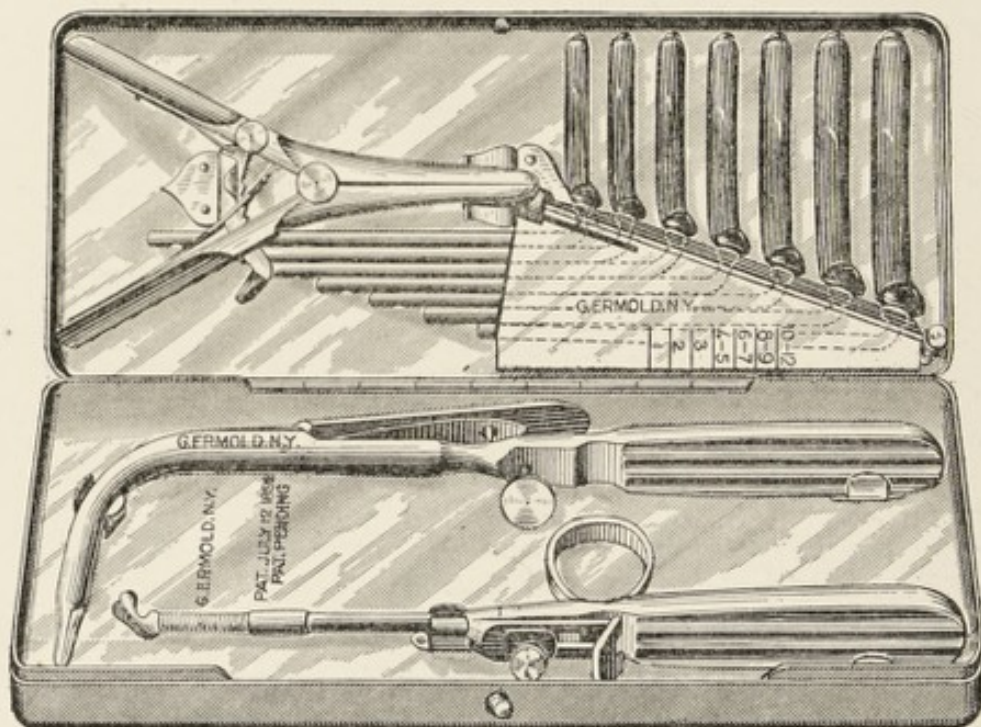
FIG. 28.—Intubation instruments (latest design).

on the long spring. The degree of separation is accurately regulated by a screw. The present extractor is a very strong instrument, and when properly used is capable of exerting a great deal of traction on the tube without causing damage.

The instruments of Dr. O'Dwyer answer every purpose for which they were intended. Yet, in spite of this fact, no set of instruments has been so constantly modified. All these modifications have been totally unnecessary. Many have been discarded as worse than useless. Putting aside the universal craze for bettering something which is absolutely good, the cause for these various modifications may be

attributed, first, to bad results obtained from improperly made tubes and instruments. Upon this fact Dr. O'Dwyer was in the habit of laying great stress. In response to a demand, makers put upon the market their own tubes. These do not fit the larynx and cause serious injury. Second, to faults of the operator—insufficient experience, or inborn and sometimes unavoidable clumsiness, apparently at times national in its extent.

The extractor perhaps has called forth more censure than the other instrument. To quote the inventor: "This cannot be improved upon except by inventing an instrument which will find the hole automatically." Perhaps, as he suggests, the electromagnet may some day be utilized for this purpose. The short tubes of Bayeux possess the single advantage that they may be enucleated—*i. e.*, pushed out of the larynx—more readily than the longer tubes of O'Dwyer.

The Indications for Intubation.—Before the days of antitoxin little was to be gained by waiting beyond the time required to make a diagnosis of probable laryngeal diphtheria. At the present time, in view of the undoubted influence of antitoxin in doing away with the necessity for operative interference in more than one-half of the cases, we are certainly justified in waiting for marked stenotic symptoms before resorting to intubation, as sometimes a second or even a third dose of serum will cause these symptoms to disappear. Furthermore, it should be remembered that the full effect of a single dose of serum is often not obtained for twenty-four hours or longer. If, however, the stenosis is fairly well marked, and it has been decided to wait, everything must be in readiness for immediate operation and the child carefully watched. As a general rule, delay is not advisable, unless the physician is within ready call, as in institutions. In general, the symptoms which call for operation are a progressive dyspnea, labored breathing, retraction of the tissues about the clavicles and epigastrium, increased exhaustion, and a failing pulse. If in a given case there is any doubt in the physician's mind as to the advisability of delay, the operation should be performed at once.

Technique of the Operation.—If the child is to be intubated in the seated position, it should be wound from chin down in a light blanket, shoulders, arms, and hands included. Care should be taken to avoid a bulky roll at the neck, which will tend to interfere with depressing the handle of the introducer. The person holding the child should sit bolt upright, and well back in a firm, straight chair, the child pressed against the left breast and shoulder and facing the operator. The arms of the nurse should be crossed in front of the

12

child's body, outside the blanket, the right hand grasping the left forearm and hand of the child, and vice versâ. The child's legs should be grasped firmly between the nurse's knees. The physician assisting stands behind the chair of the nurse and grasps the child's head between his hands, so that the position of the child is *as though it hung from the top of its head.* The operator, seated or standing directly in front of the patient, inserts the gag, opens the mouth widely, and gives the handle to the assistant, who includes it between his left hand and the cheek. The proper size tube should have been previously selected, a silk cord inserted in the eyelet. The introducer should be thoroughly tested beforehand to see that the tube slips freely from the obturator when it is released.

Everything being in readiness, the operator inserts his left index-finger, hooks up the epiglottis, crowds his finger to the left as much as possible, and passes the tube past and just under its edge until it engages in the chink of the glottis. As the tube is first introduced it should hug tightly the center of the tongue, the handle being vertical and close to the patient's chest. As the tube approaches the glottis, the handle is raised very gradually; and as it enters the glottis, rather abruptly, until the tube is pointing directly down the trachea. The tube is passed gently downward until the tip is in the box of the larynx and the introducer lies crowded upon the tongue. The trigger of the introducer is then pressed upon with the thumb, the tube released, and, while the left index-finger holds the latter in place, the obturator is withdrawn from the mouth. A gentle thrust pushes the tube's head well into the larynx. The finger and gag are then removed. The characteristic rush of air, cough, and expectoration, together with relief of the dyspnea, are indications that the tube is in place. After waiting for ten to twenty minutes to be sure that there is no obstruction in the tube by false membrane, the left forefinger is again introduced, holding the head of the tube in place; and, one end of the silk thread having been cut near the angle of the mouth, it is quickly removed and the child allowed to return to bed. On no account should the hands of the patient be released until the final step has been taken, as the first impulse of many children is to seize the offending thread and pull on it, thereby displacing the tube.

It is well to emphasize certain points in this operation. In the first place, no force is necessary. Occasionally a momentary spasm retards the immediate entry of the tube into the larynx; in which case, rather than use force, it is best to wait a second or two for this to relax, when the tube will fall into place. The introducer should be

PLATE 9.

Fig. 1.—Position for intubation as recommended by Dr. O'Dwyer and generally practised. The tip of the tube just engaging in the larynx.

Fig. 2.—Position for intubation recommended by Dr. O'Dwyer and generally practised. The tube sinking into the larynx as the handle of the introducer is elevated.
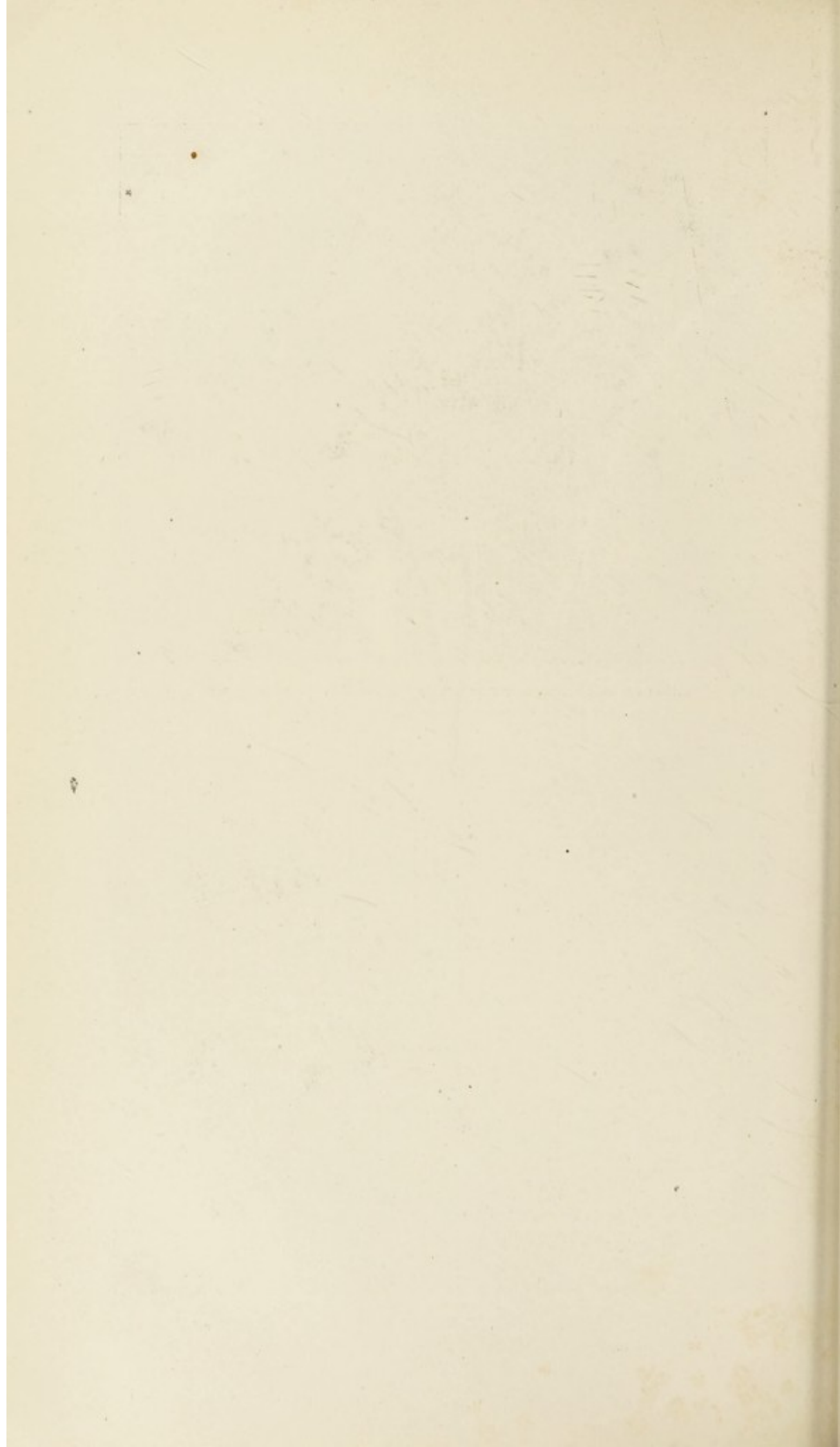
PLATE 10.
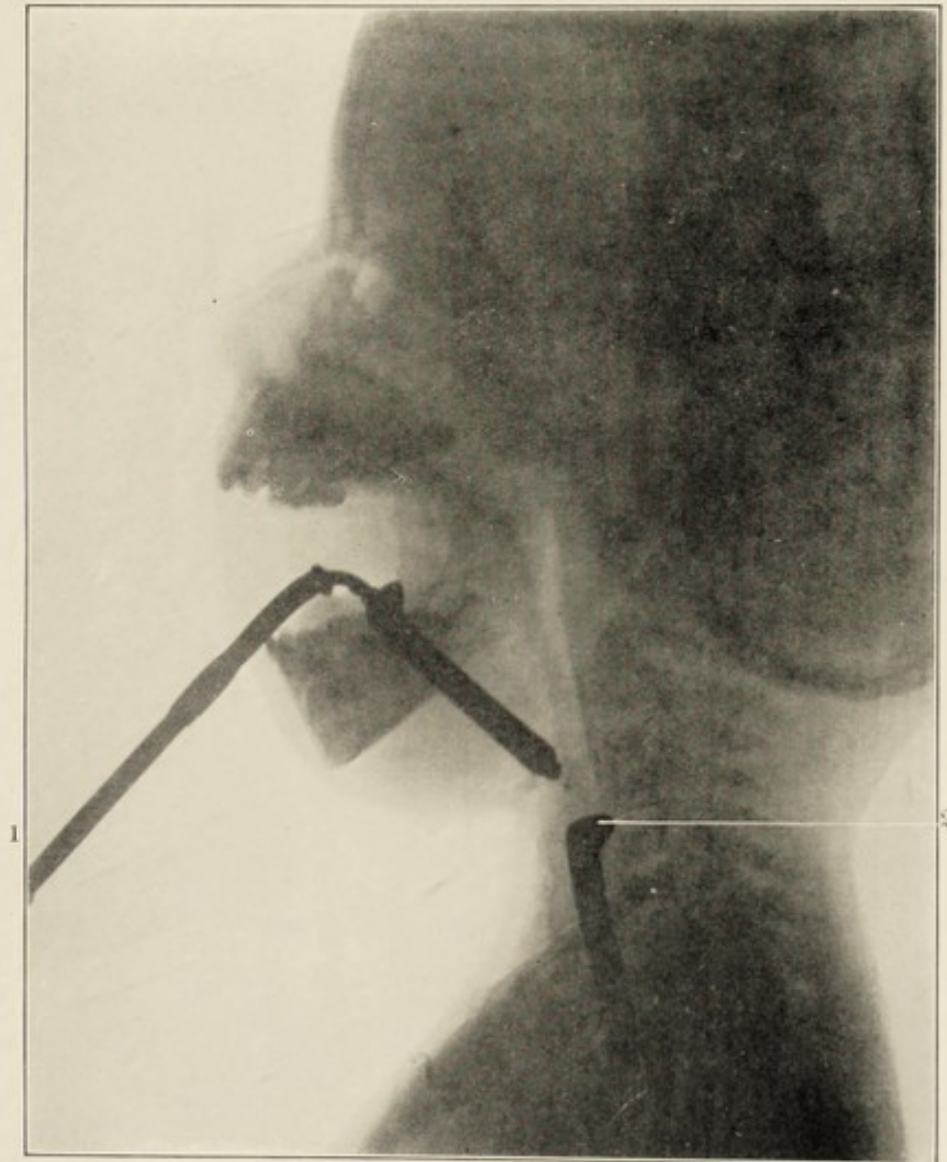
1. The tube just engaging in the larynx.   2. Tube sunk to proper position.

PLATE II.
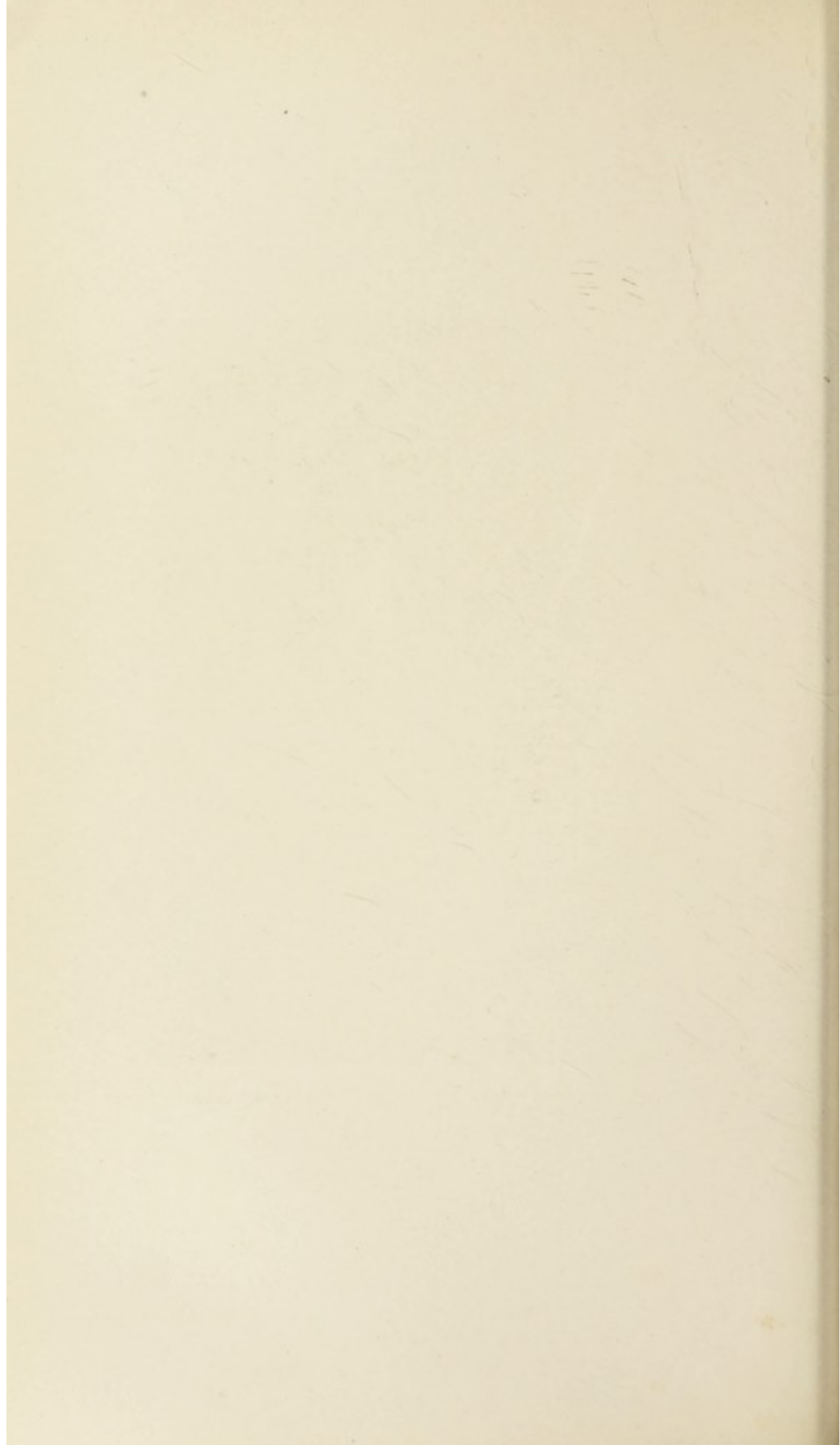
FIG. 1.—Intubation in the dorsal position. Preferred by Dr. Bryant, of the Willard Parker Hospital. First position. The handle of the introducer parallel to the body axis.

FIG. 2.—Intubation in the dorsal position. Second position. The handle of the introducer elevated ; the tube engaging in the larynx.
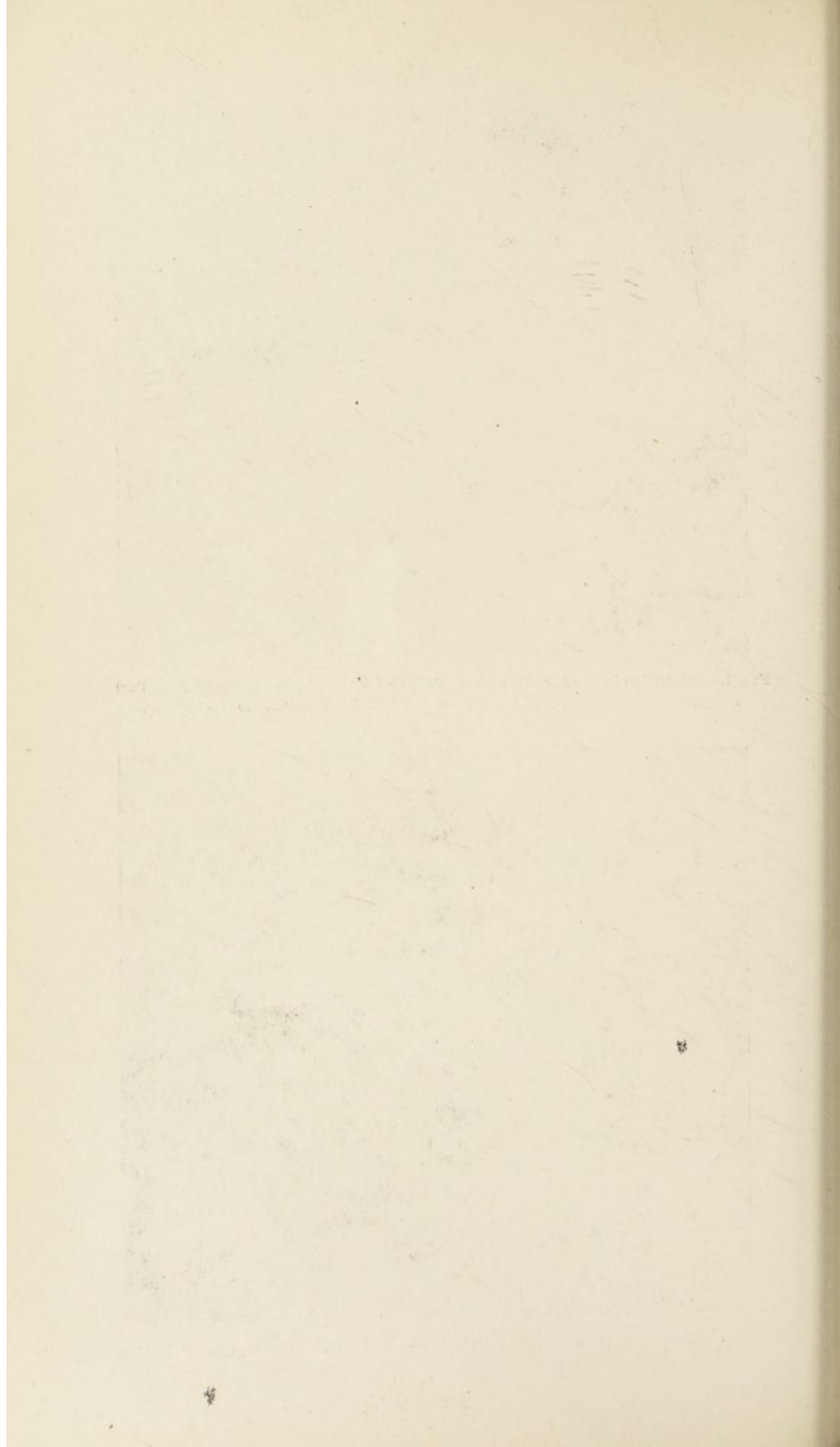
held lightly between the end of the thumb and finger, and not grasped firmly in the hand. The introducer should be kept exactly in the middle line, otherwise the obturator will pinch in the caliber of the tube and drag the latter with it as it is withdrawn. It often happens that the child manages by one effort to slip down in the nurse's lap, while the grasp that the assistant exerts tilts the head back, and the tube may impinge on the posterior wall of the larynx. The lines and angles must be maintained to insure quick intubation. The lack of observance of and carelessness in these points explain many failures of inexperienced operators. If the tube is not properly placed at the first attempt, it is better to begin all over, making repeated short attempts, if necessary, rather than a single prolonged one.

Some operators have lately made use of the dorsal position in intubation, and this method alone is now practised at the Willard Parker Hospital. The same points are to be observed as when the patient is in the seated position. This position has the advantage of making intubation possible without assistants in an emergency. Dr. Bryant, at the Willard Parker Hospital, has thus performed it on more than one occasion: The child is wrapped closely in a blanket and the knee of the operator is pressed between the thighs, the jaws pried open, and a gag introduced and left to hang in place, after which the tube is introduced as before. It need not be stated that this is not to be recommended except in the face of a great extremity, and will probably only be successful in very expert hands. To those, also, who have grown used to the older method it is well to practise intubation on the cadaver in the reclining position before operating on a living child.

Removal of the Tube.—Extubation is generally regarded as more difficult than intubation. The patient should be placed in exactly the same position as that described for intubation. Thrust the left forefinger past the epiglottis, hook it up with the tip of the finger on the two arytenoid cartilages, and carry the extractor point to the center of the pulp of the finger. The situation then is as follows: The fingertip upon the arytenoids marks the posterior boundary of the glottis in the median line. Now, if the point of the extractor be carried along the median line, to the end of the finger, and the handle elevated quickly, the point will naturally be pried forward from the end of the finger into the opening of the tube. If difficulty is experienced in holding up the epiglottis by this method, the extractor should be guided with the index-finger at the side, exactly as in intubation.

It is very important to regulate by means of the guard-screw the

distance which it is necessary to separate the jaws of the extractor in order to get a firm grip on the tube. Too great a degree of separation may cause great injury to the larynx during bungling efforts at extraction. As in intubation, no force is necessary. The extractor should be held lightly, the thumb kept off the spring until the beak of the extractor engages well in the tube.*

Some operators prefer to leave the string in the tube, thereby avoiding the difficulty of extraction with the instrument. In this case the string should be hooked up behind the left ear and fastened flat on the cheek by means of a strip of adhesive plaster.

Enucleation, or removal of the tube by pressure, has of late been somewhat extensively practised. For this purpose the short tubes of Bayeux possess a great advantage. The operation, however, is possible with O'Dwyer's tubes. The child is held with head downward and firm pressure is made on the end of the tube at the sternal notch. In this way the tube can often be pressed into the mouth and thus removed. This method requires no special skill or training, and may be of use in an emergency, especially for nurses and attendants. It is not always possible to accomplish enucleation. Again, if the tube has slipped down so that it cannot be reached readily by the finger, it is perhaps better to try enucleation and not risk pushing it still further down with the extractor.

When to Extubate.—As already noted, the length of time for which the tube is required has been materially reduced by the use of antitoxin, and, furthermore, reintubation is less often required. General rules only can be laid down as to the proper time to remove the tube. Five days for a child over two years of age may be considered a fair average. At the Willard Parker Hospital the time allowed is four days; at the New York Foundling Hospital, three days.

The longer use of the tube has the advantage of probably doing away with the necessity for a second or third operation. According to Somerset, from extensive observation at the Willard Parker Hospital, a child under two years of age may require the tube intermittently during a period of two weeks or longer. He puts the limit of time during which a tube should be worn without removal at five days, in primary intubations.

* Drawings were made by Dr. Henry J. Prentiss, Instructor in Practical Anatomy in the University and Bellevue Hospital Medical College. Exactness was obtained by the use of frozen median sections and X-ray photographs. Care was taken also to have tubes and introducers of proper size and recent pattern. X-ray photographs were made in the Edward N. Gibbs X-ray Laboratory (Carnegie Laboratory), by Mr. E. W. Caldwell, Director.

PLATE 12.

FIG. 1.—Extubation. The beak of the extractor having just grasped the tube firmly,
preparatory to removal.

(The illustrations on Plates 11 and 12 were made from instantaneous photographs of an
actual case of intubation. A few minutes after the tube was removed, reintubation was made
necessary by a return of urgent dyspnea.)
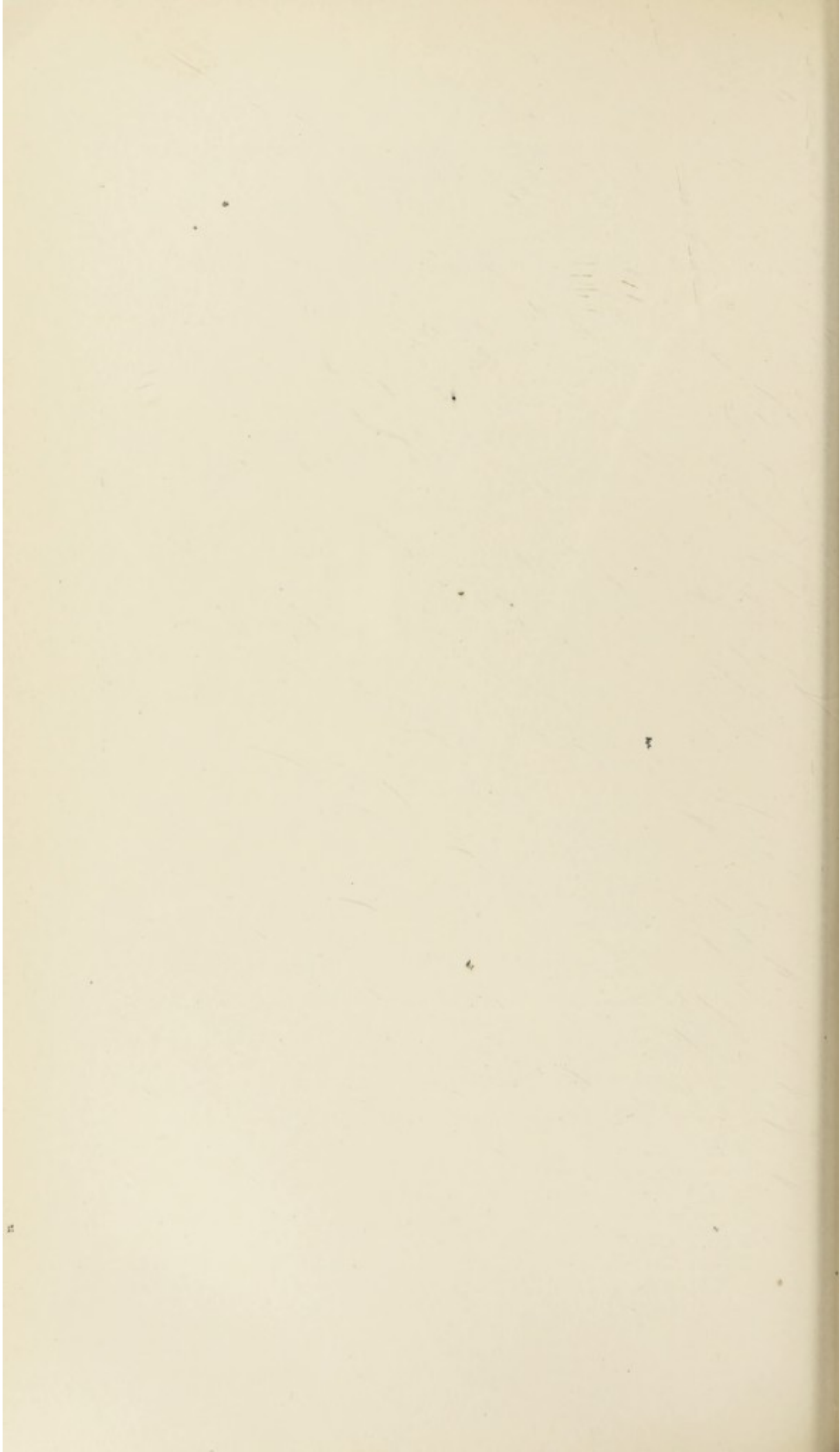
PLATE 13.
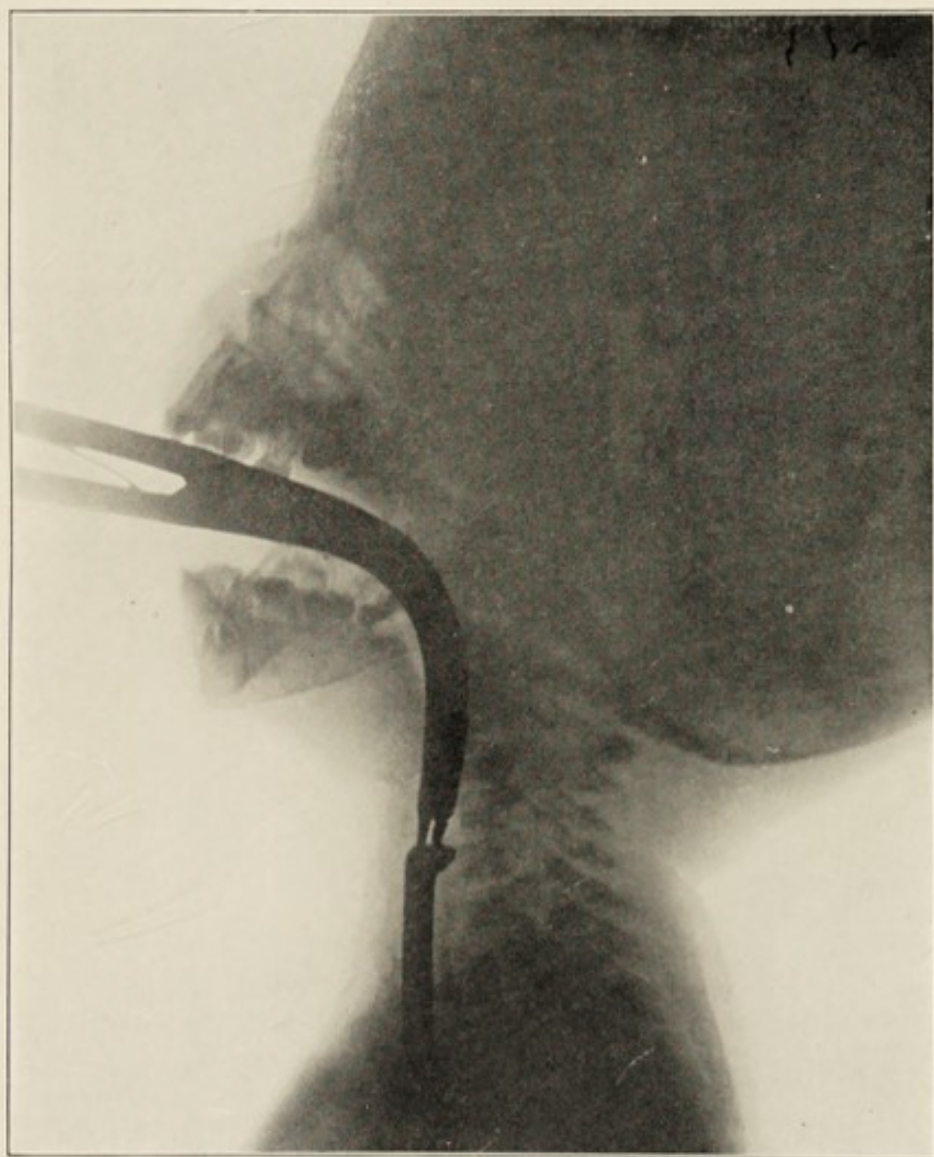
Extubation. The beak of the extractor engaging in the opening of the tube.
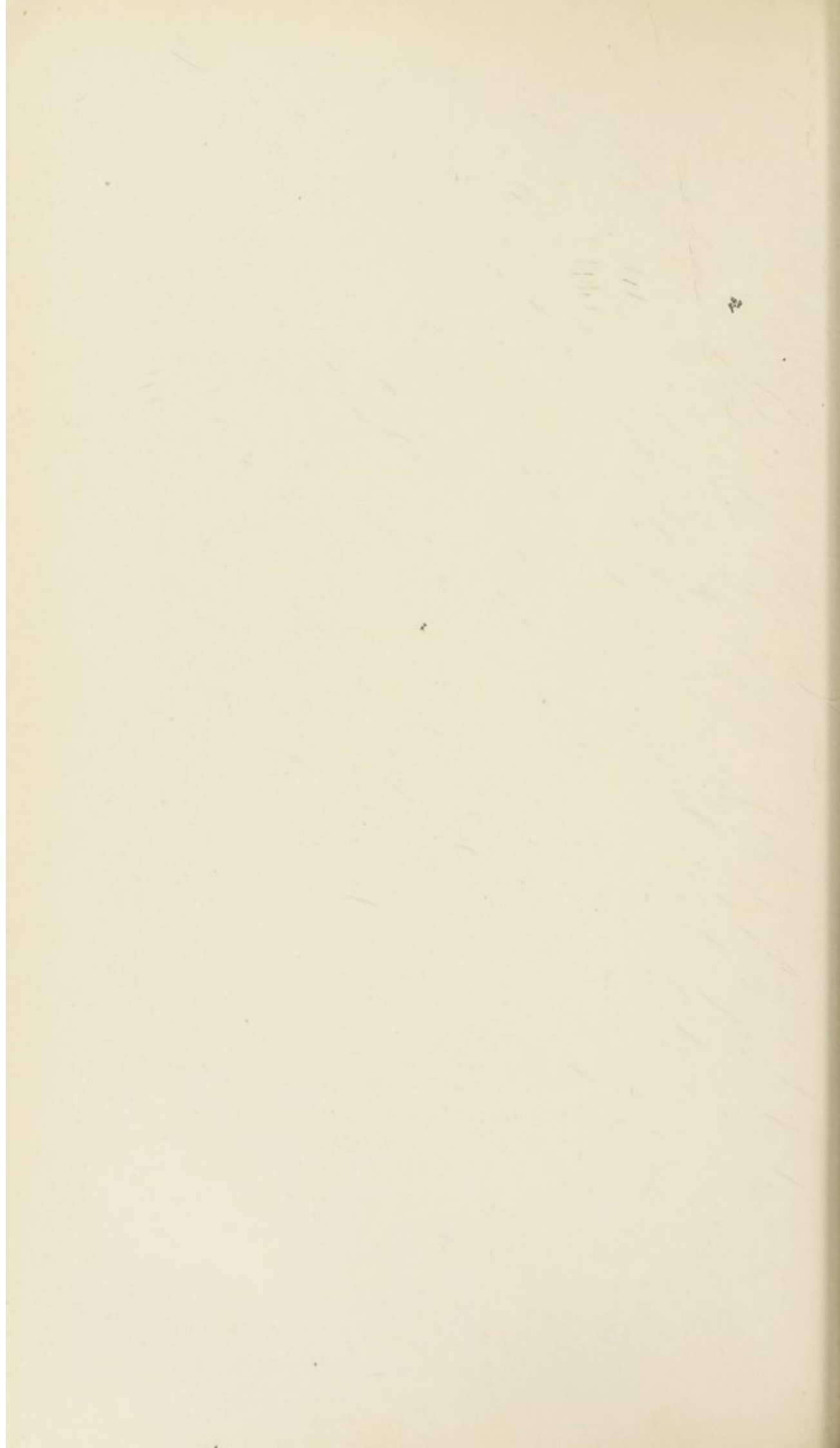
Blocking of the tube with false membrane and thick mucus is usually an indication for immediate extubation. According to Waxham, this may occasionally be avoided in an emergency if the nurses or attendants are instructed to invert the child and strike it sharply on the back and chest. Whisky and water, in equal parts, may cause violent coughing, and clearing of the tube. Usually, in these cases, however, the tube is expelled spontaneously. In any given case the retention of the tube should depend on the amount of mucus and membrane that is coughed up, the appearance of the membrane in the throat, if any existed, and the temperature, pulse, and general condition of the patient. J. C. Connell believes that it is better to extubate after thirty-six to forty-eight hours, as this is the time, with the use of antitoxin, when the false membrane, as a rule, becomes loosened. The hard rubber tubes now generally used cause little or no damage even with prolonged use. Occasionally a detached plaque of membrane may act as a valve at the end of the tube, closing on expiration and opening on inspiration, until the lungs become overdilated. This happened in 3 of O'Dwyer's 200 cases, with three deaths. The symptoms of loose membrane are: (1) Croupy cough (the tube being in); (2) flapping sound; (3) sudden obstruction to outgoing air, especially during coughing.

Dangers and Difficulties of the Operation.—In the hands of the experienced operator there are practically no dangers to life at the time of operation.

No physician should undertake to intubate a living child until he has had a thorough training in the operation through practice on the cadaver, and even then he will find a vast difference in intubating a struggling, terrified child, where every unnecessary second expended in awkward attempts at introducing the tube diminishes the chances of recovery. Dr. O'Dwyer always recommended tracheotomy in preference to intubation by uneducated fingers. The operation, however, is not a difficult one, and yet not a few men perform it very clumsily. As Caillé and others have pointed out, instances occur where the forefinger of the operator is so large and stubby that a proper intubation becomes very difficult, especially in small children.

The difficulties which may be encountered by the inexperienced operator are as follows: Asphyxia from prolonged attempts at introducing the tube; laceration of the parts; false passages, generally into the ventricles of the larynx. The explanation usually given for these common accidents is "pushing down false membrane."

In the case of an experienced operator, certain accidents occa-

sionally happen. The most important is that of pushing down the false membrane before the entering tube. This happened to Dr. O'Dwyer in 3 out of 209 of his first cases. In two of these the membrane was immediately coughed up on removal of the tube.

It is presupposed that the string is left attached to the tube when introduced, and it is rare, indeed, that immediate removal of the latter will not be followed by expulsion of false membrane. Tracheotomy may occasionally be necessary, but has not proved very successful in such cases. Bokai performed tracheotomy for this reason in 3.5% of 498 cases, in two of which no relief followed the operation and death ensued.

False membrane tubes for this purpose have already been described (short large-caliber tubes). Even in the hands of an experienced operator the point of the tube may enter one of the ventricles of the larynx. This happens more rarely with the use of the present form of very blunt rounded tubes, which readily slip over the tissues into the glottis.

We have already mentioned the occasional spasm which occurs as soon as the tube touches the vocal chords. It never causes anything more than a slight delay in introduction.

Subglottic stenosis, or so-called edema, may cause difficulty in introducing the tube. As already pointed out, the narrowest part of the passage is the cricoid ring. The constriction at this point caused by swelling of the mucous membrane may readily cause a great deal of difficulty in introducing the tube after it has passed the chink of the glottis. The tube, when it reaches this point, has been said to "creep back like an oiled cork in a bottle." If the diagnosis is positively made, the selection of a smaller tube, used with moderate pressure, will usually overcome this difficulty. This is the only condition where force is justified in intubation. It is in such cases that tracheotomy has been so frequently recommended and resorted to.

Retained Tubes.—If a tube has to be reinserted many times, it is due to one of several causes—persistence of the laryngeal membrane, edema of the tissues, ulcerations about the cricoid cartilages and their occasional destruction, cicatricial contractions, traumatism, exuberant granulations, or abductor paralysis.

In children who are small for their age, Dr. O'Dwyer always advised the choice of a tube suited to the age below rather than that above.

Many, if not all, of these complications are much less frequently seen in the hands of expert operators with the use of antitoxin and

PLATE 14.
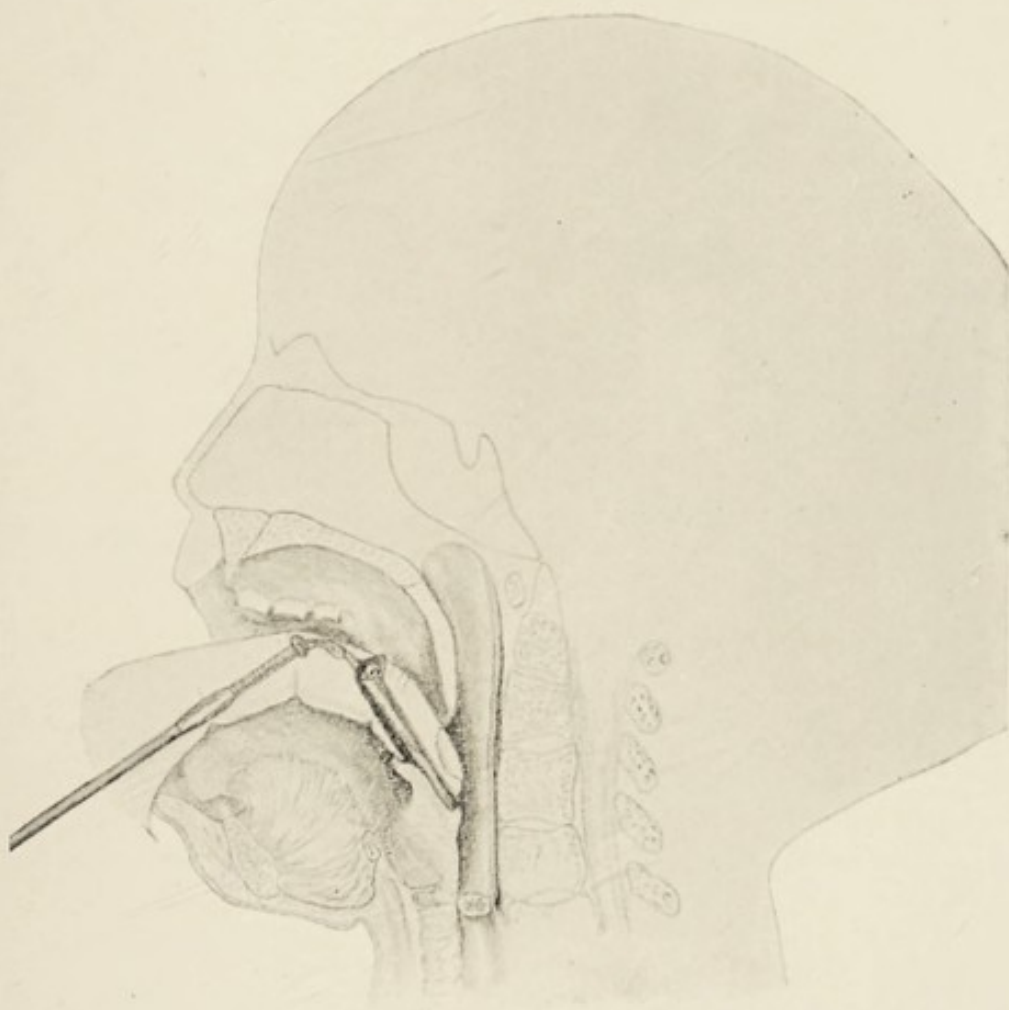
The tube engaging in the larynx. The left index-finger holding back the epiglottis and acting as guide.
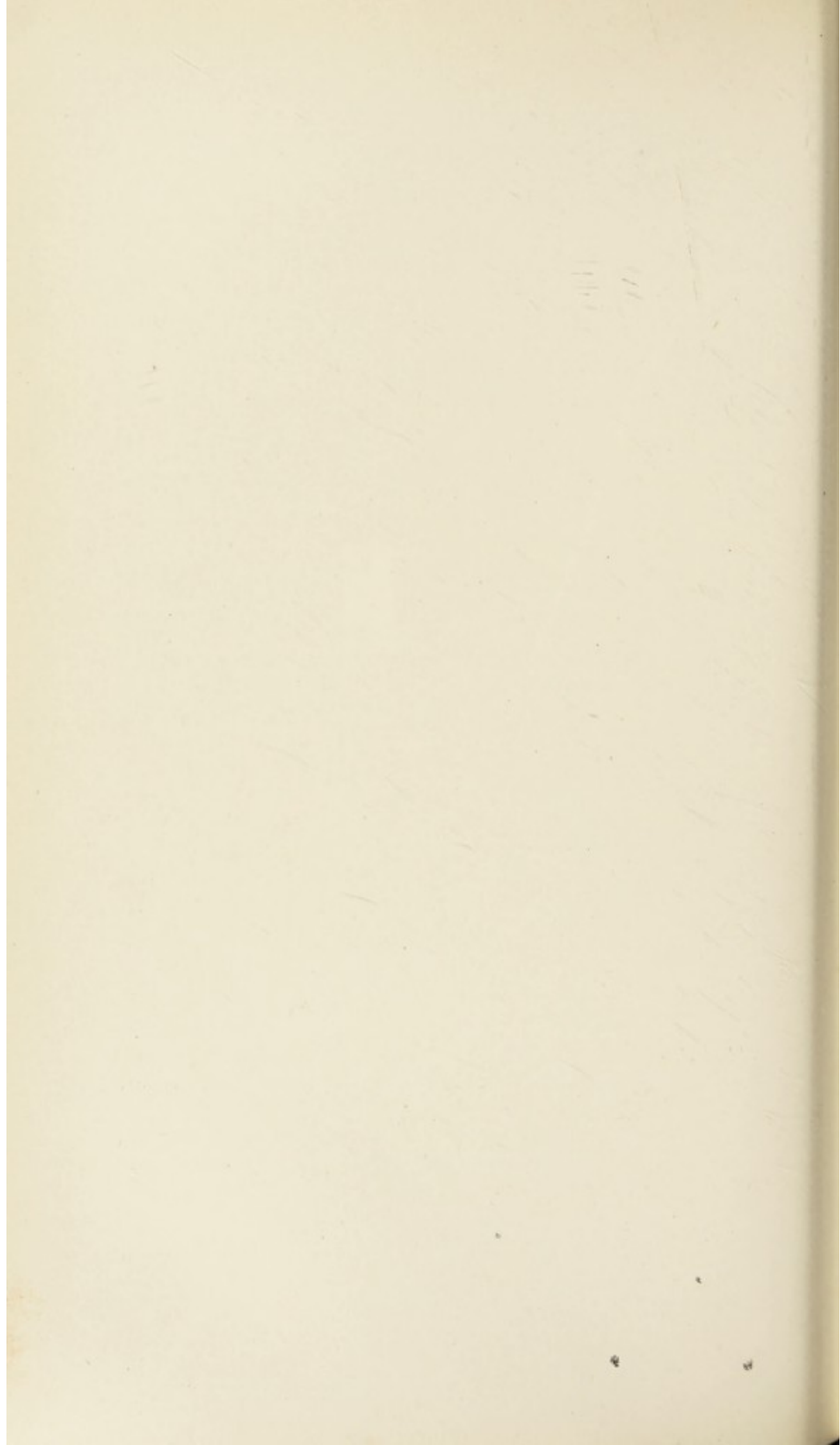
PLATE 15.
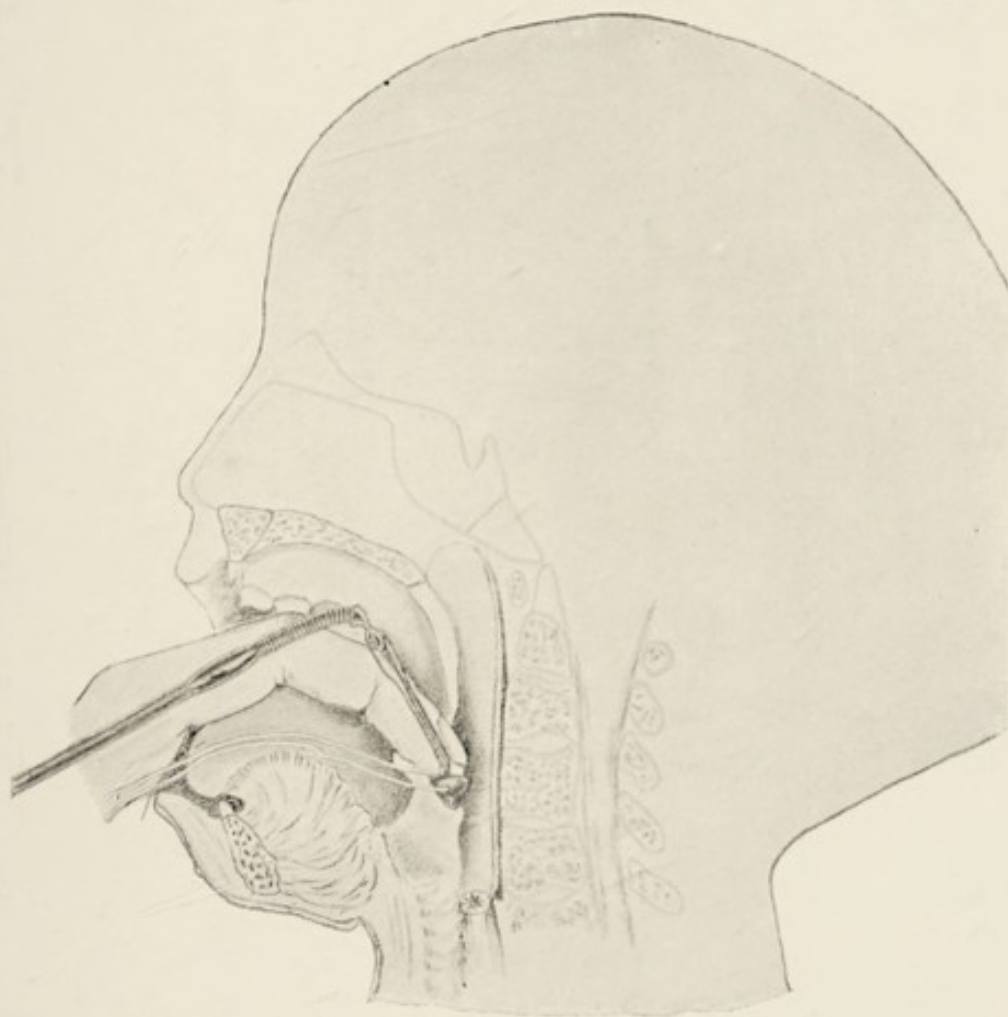
Removing the obturator from the tube. The left index-finger holding the tube
in position.

PLATE 16.
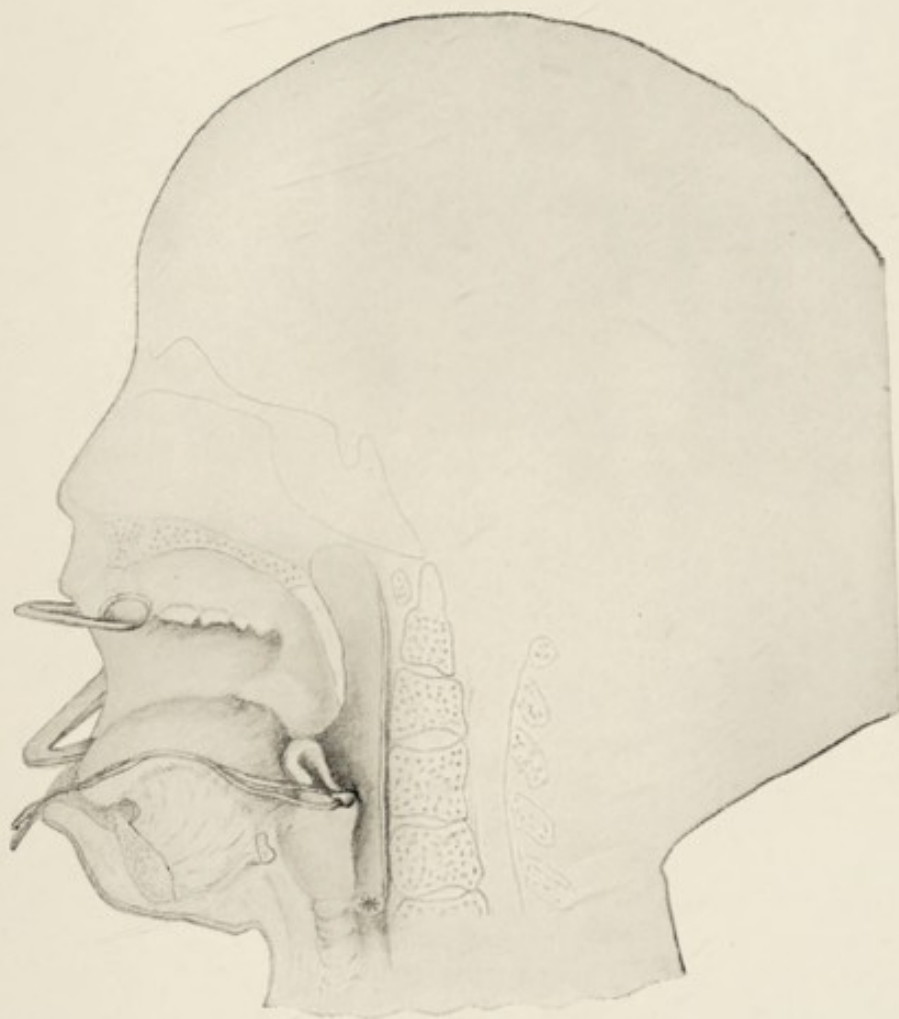
The tube sunk to its proper position. The cord still attached, and the mouth-gag in place.

(The drawings for Plates 14, 15, and 16 were made by Dr. Prentiss from frozen sections.)
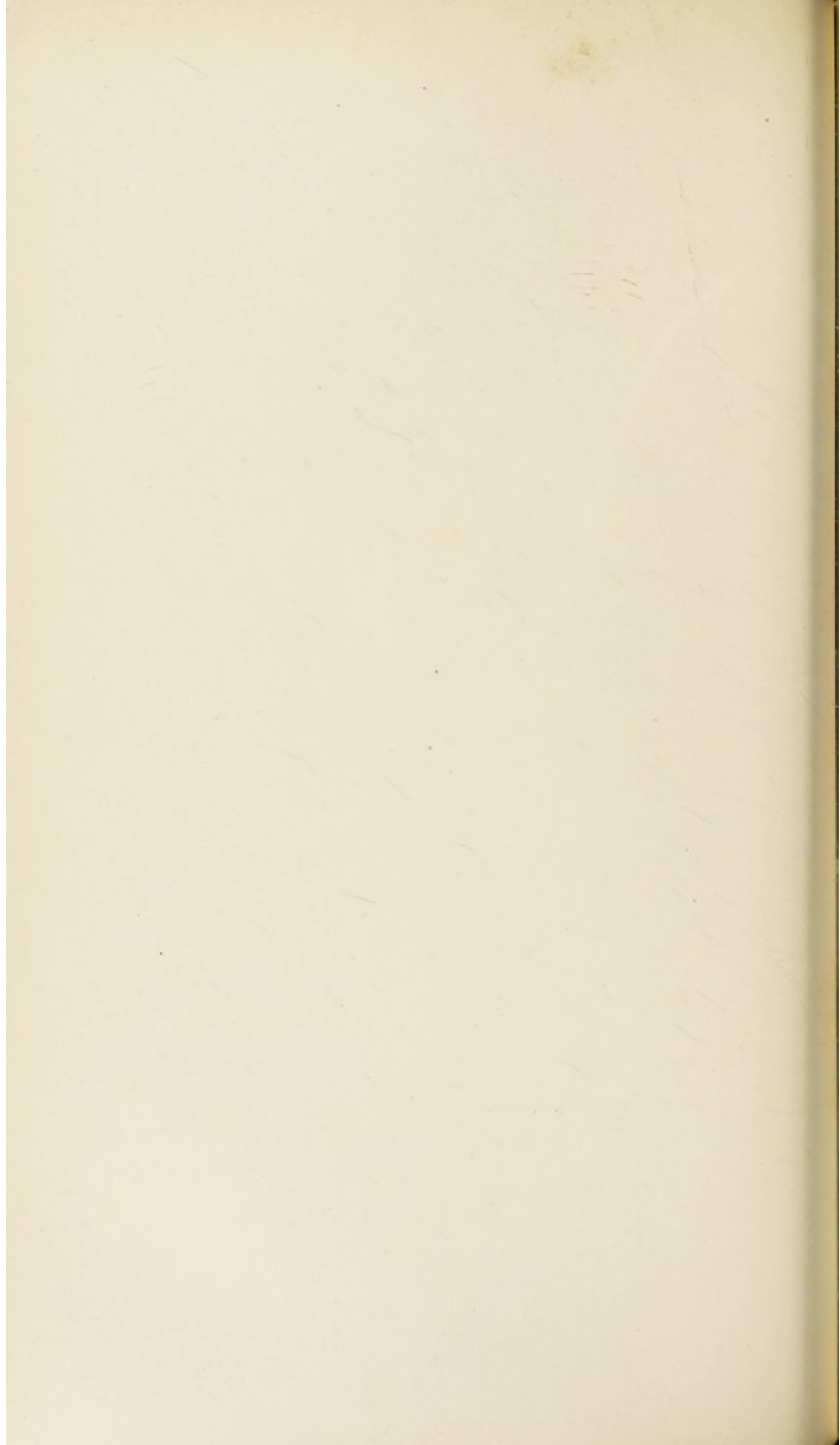
PLATE 17.
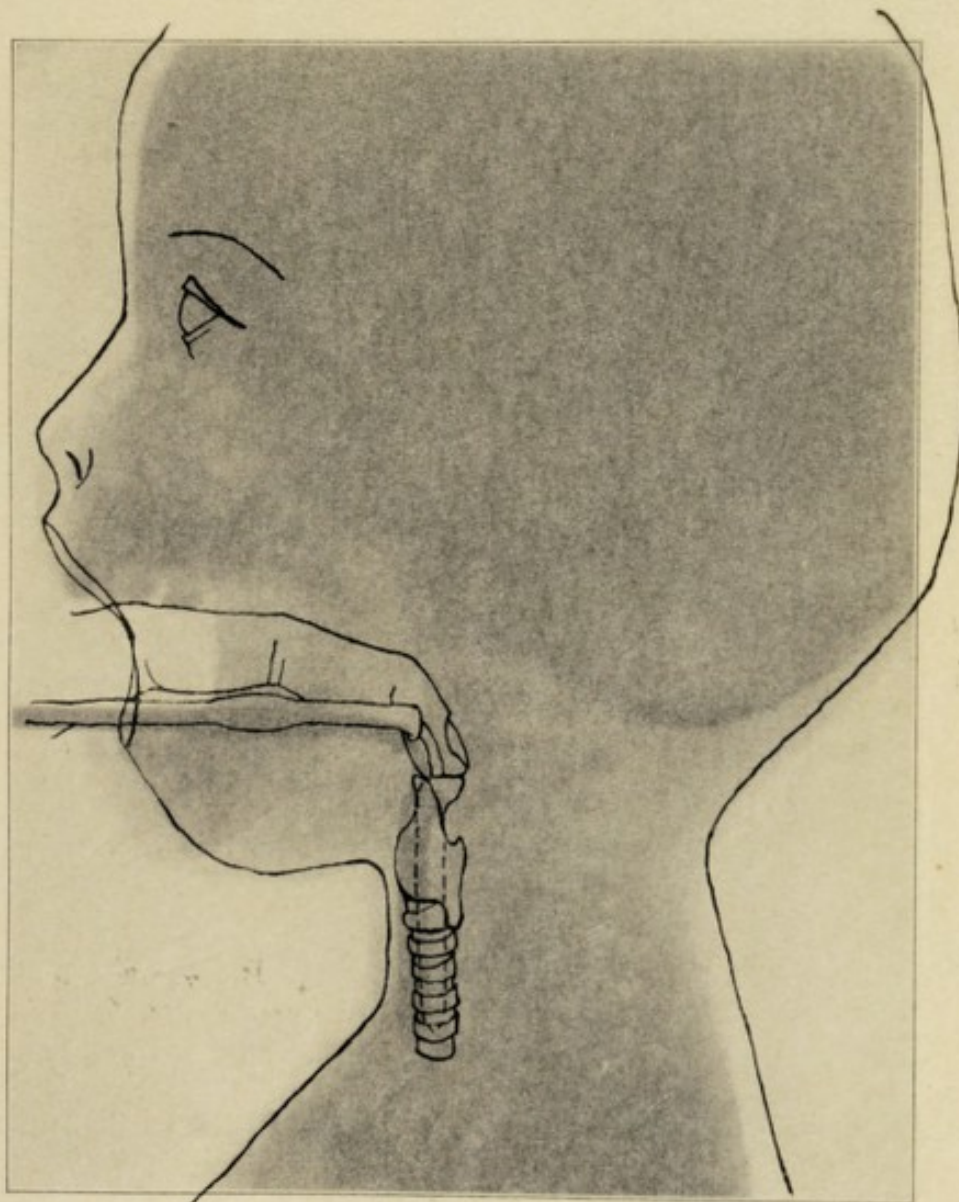
Showing relation of larynx, trachea, and tube to surface lines (made from X-ray photography). The tube thrust into position by the index-finger.
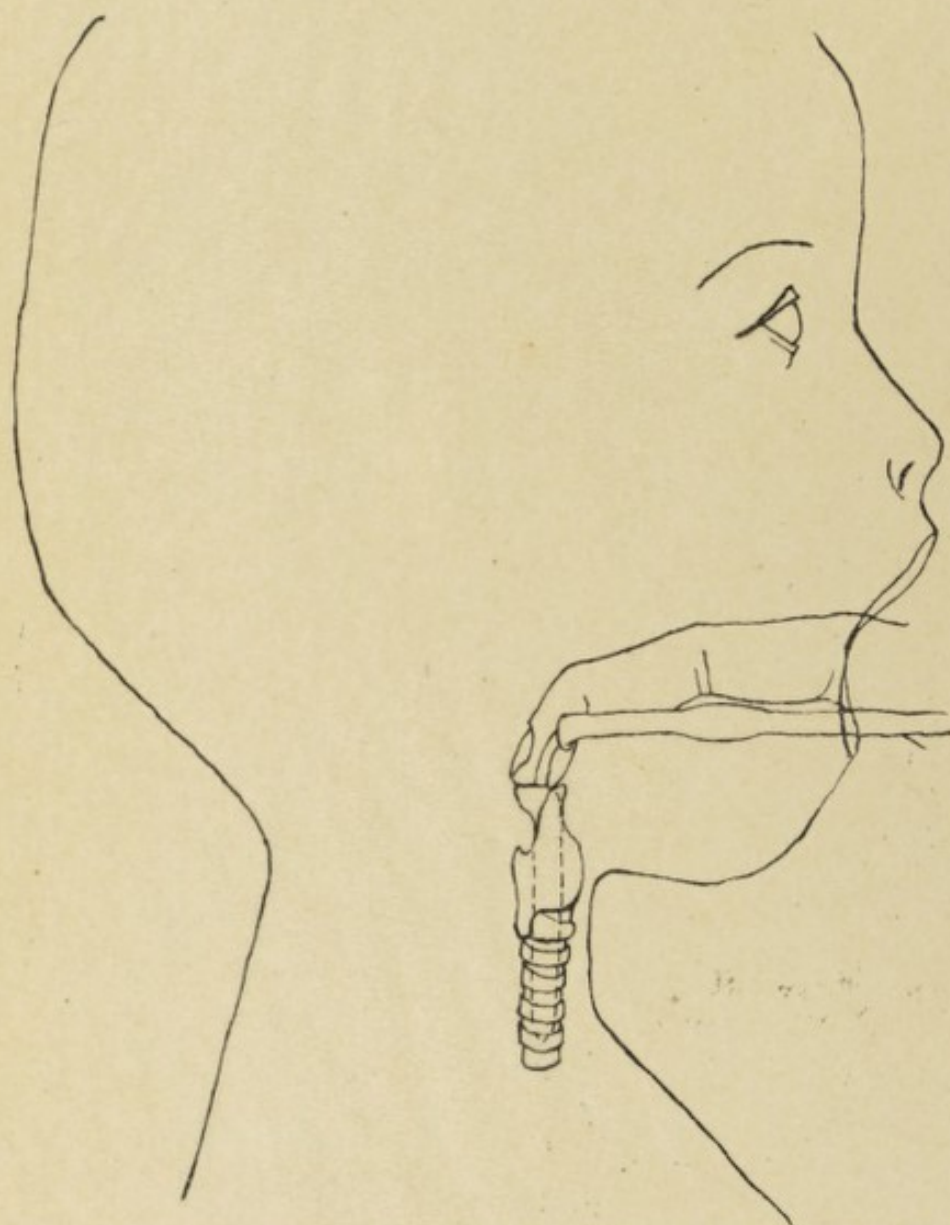
Showing relation of larynx, trachea, and tube to surface lines (made from X-ray photograph).

PLATE 17.
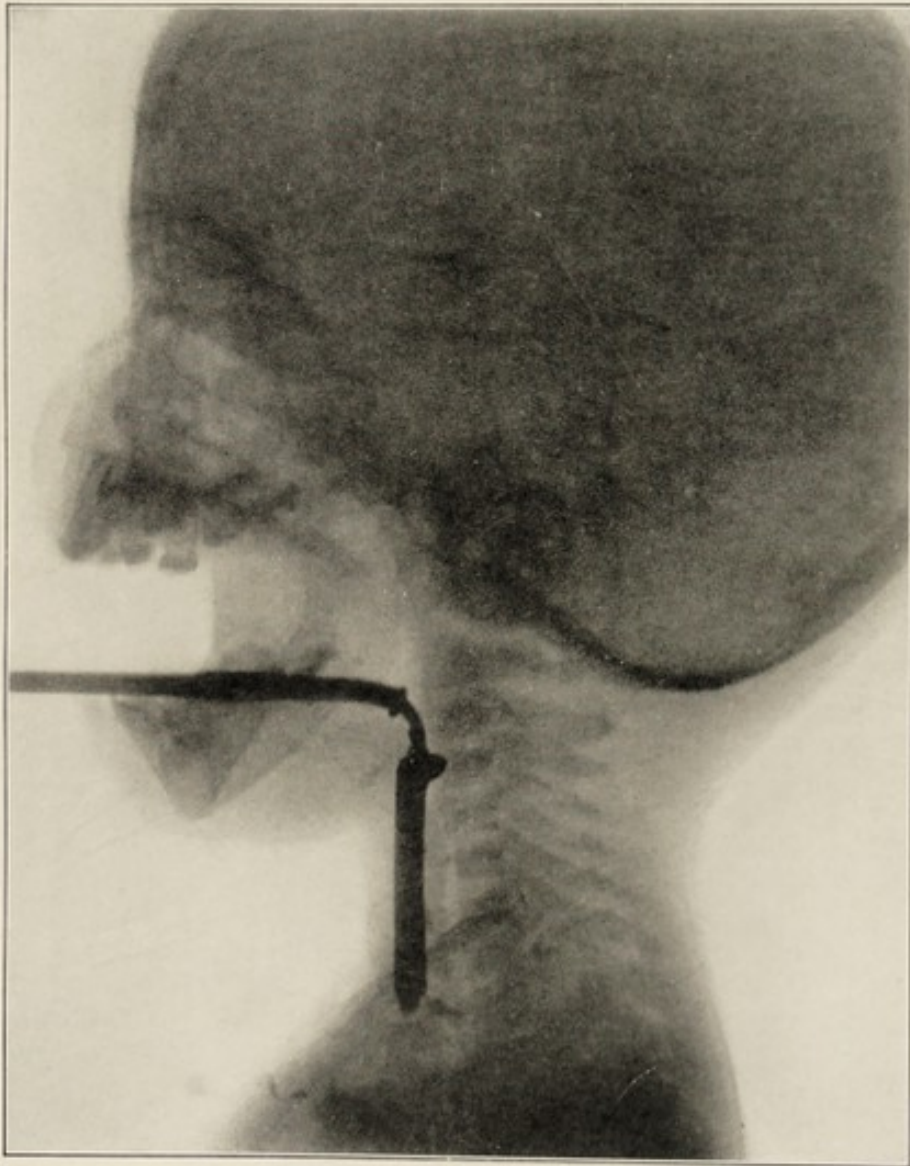
The tube thrust into position by the index-finger.
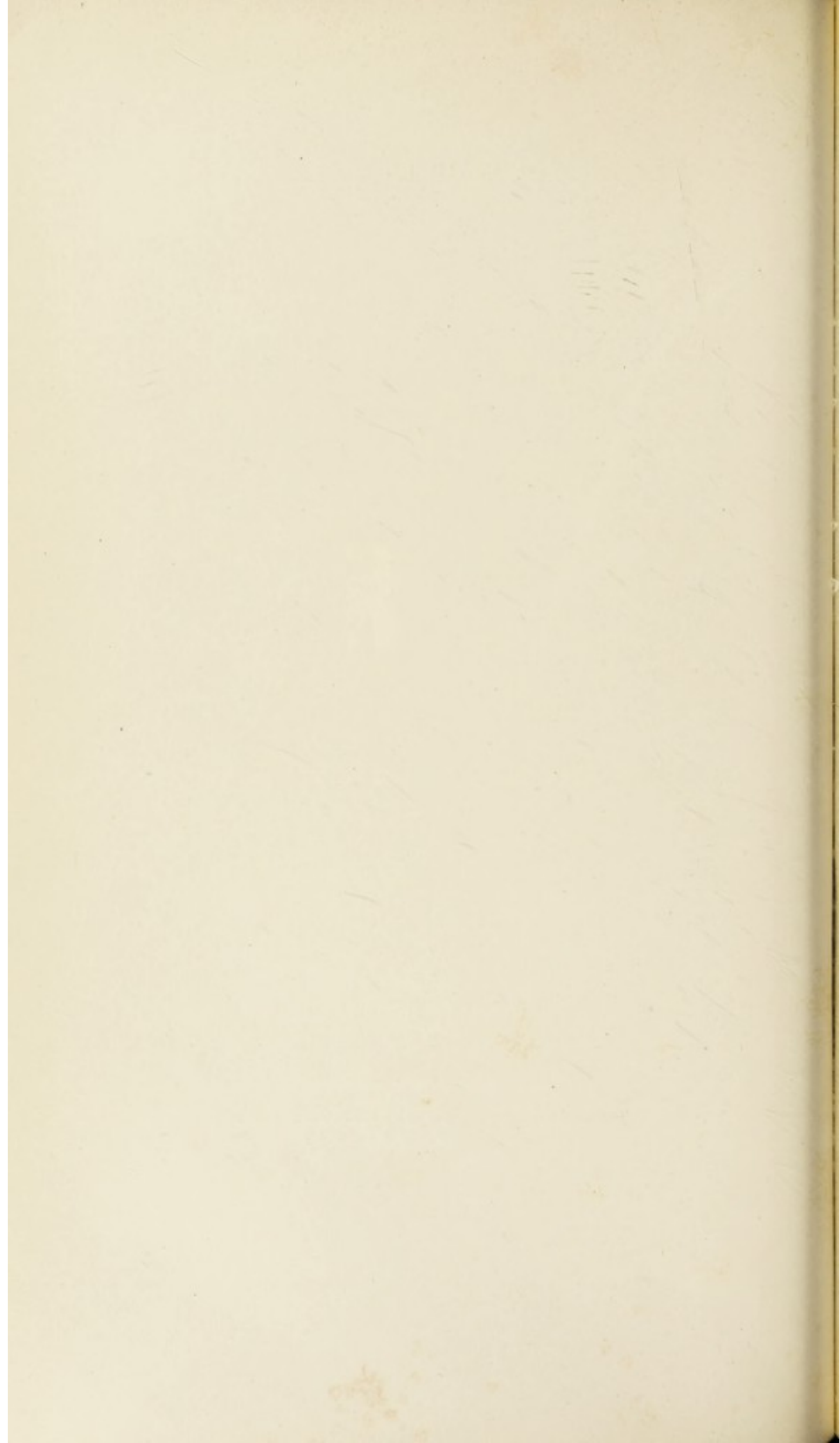
PLATE 18.
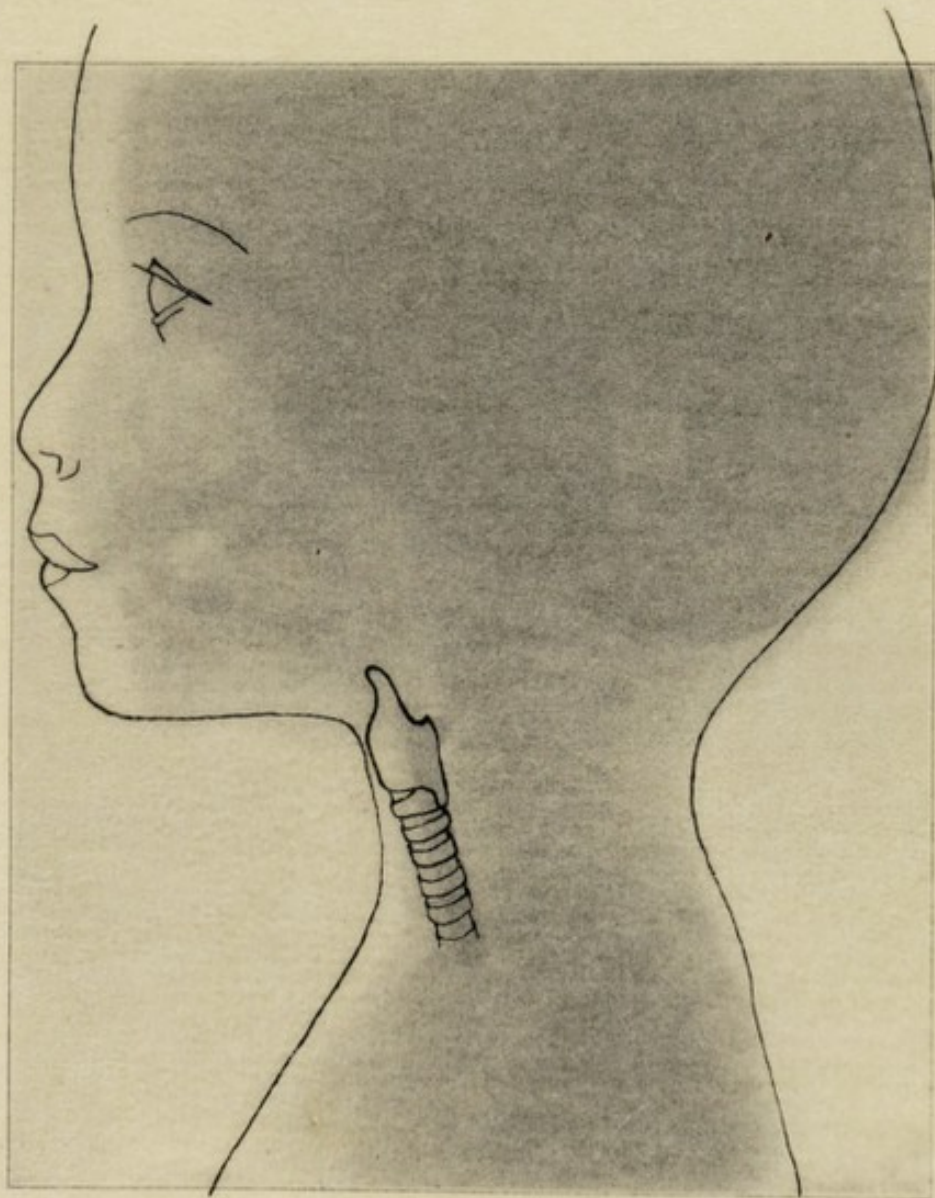
Showing the relations of the larynx, trachea, and tube to the surface lines (made from Intubation. The tube in place, showing its relation to the bony structures. X-ray photograph).
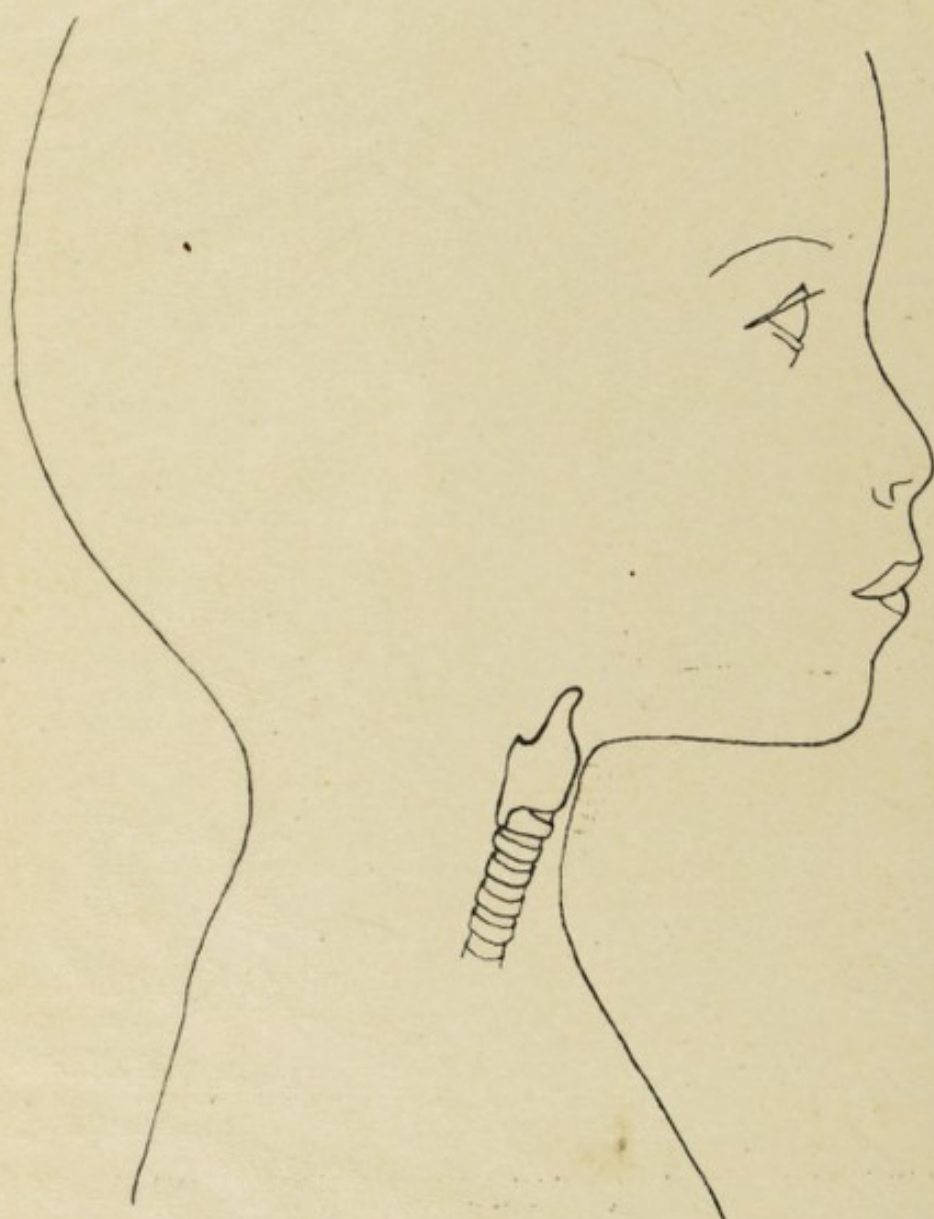
Showing the relations of the larynx, trachea, and tube to the surface lines (made from X-ray photograph).

PLATE 18.

Intubation. The tube in place, showing its relation to the bony structures.

PLATE 19.
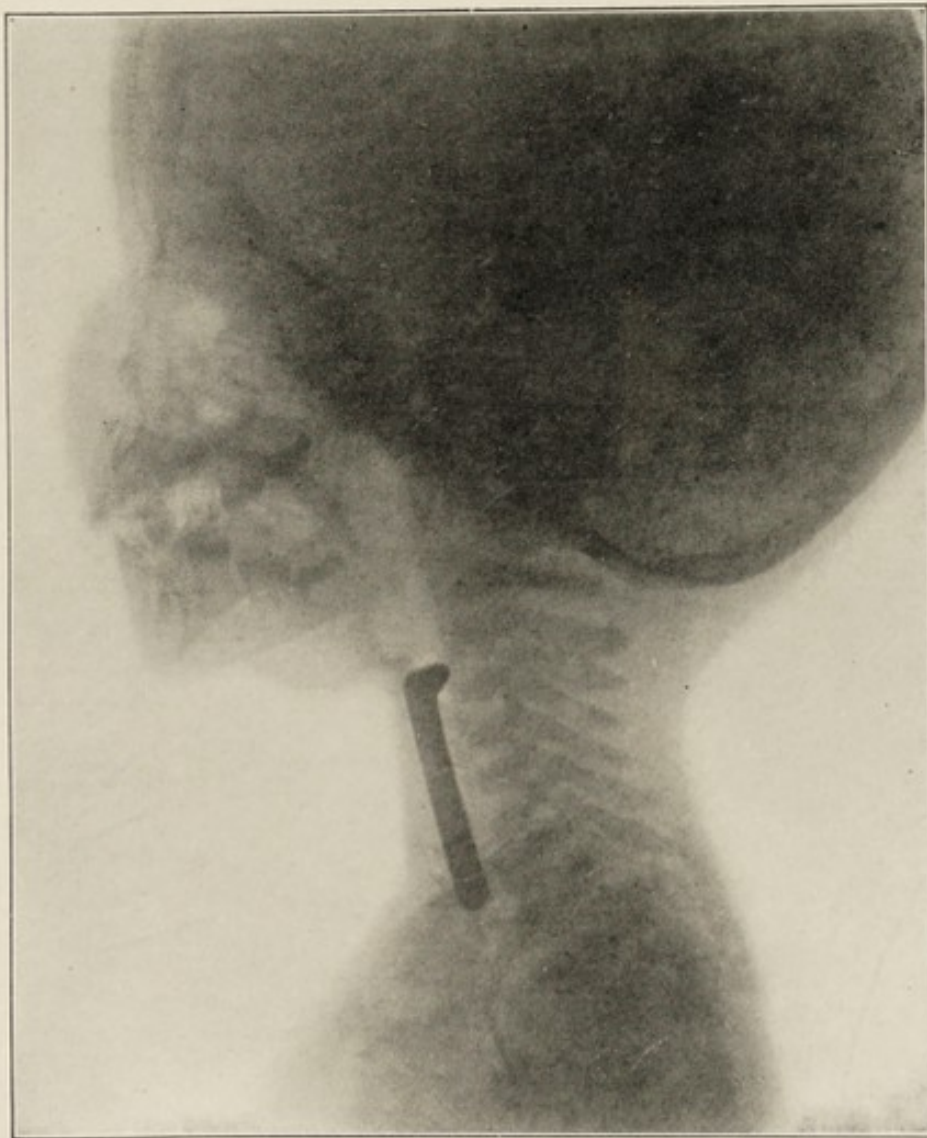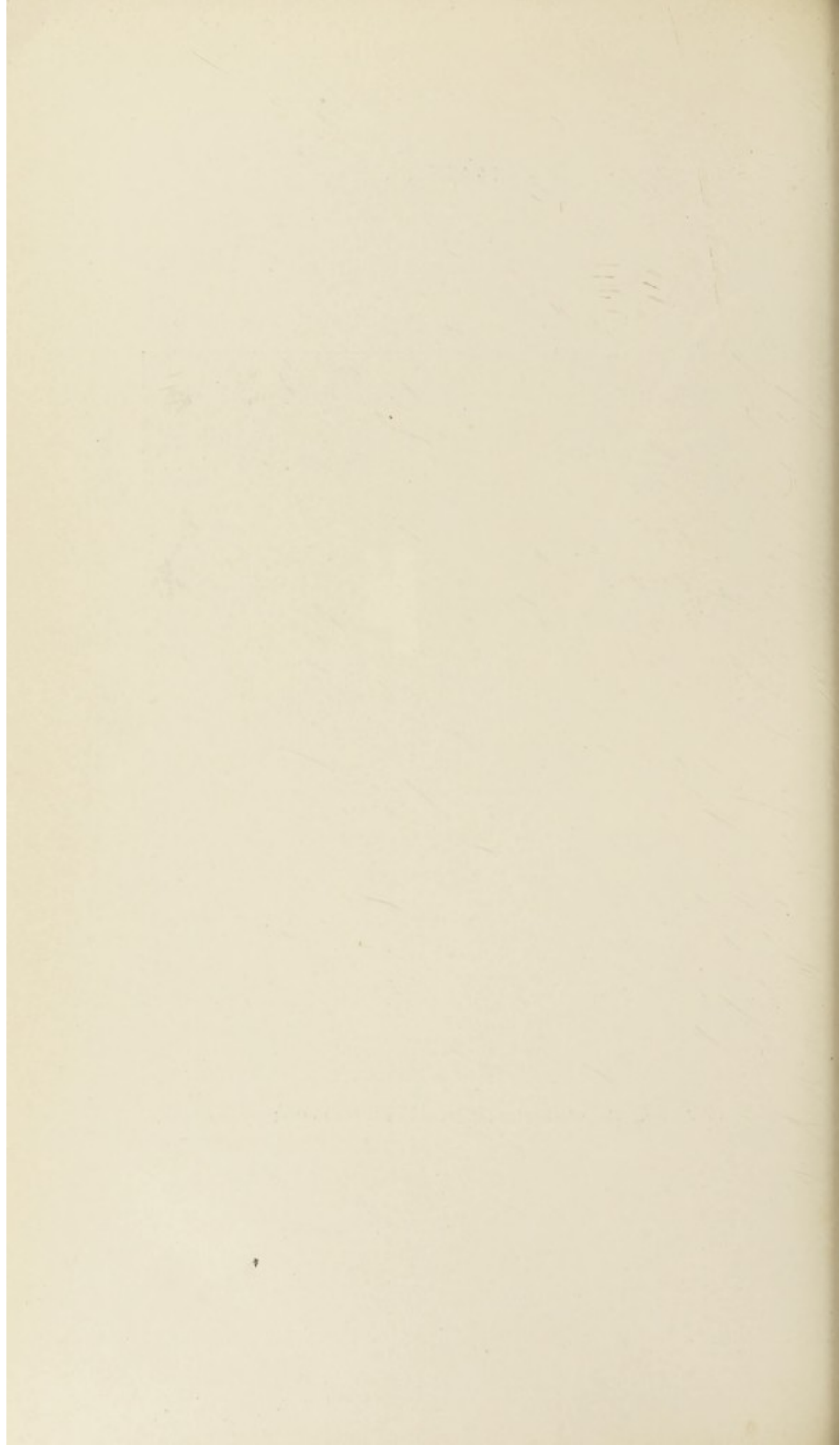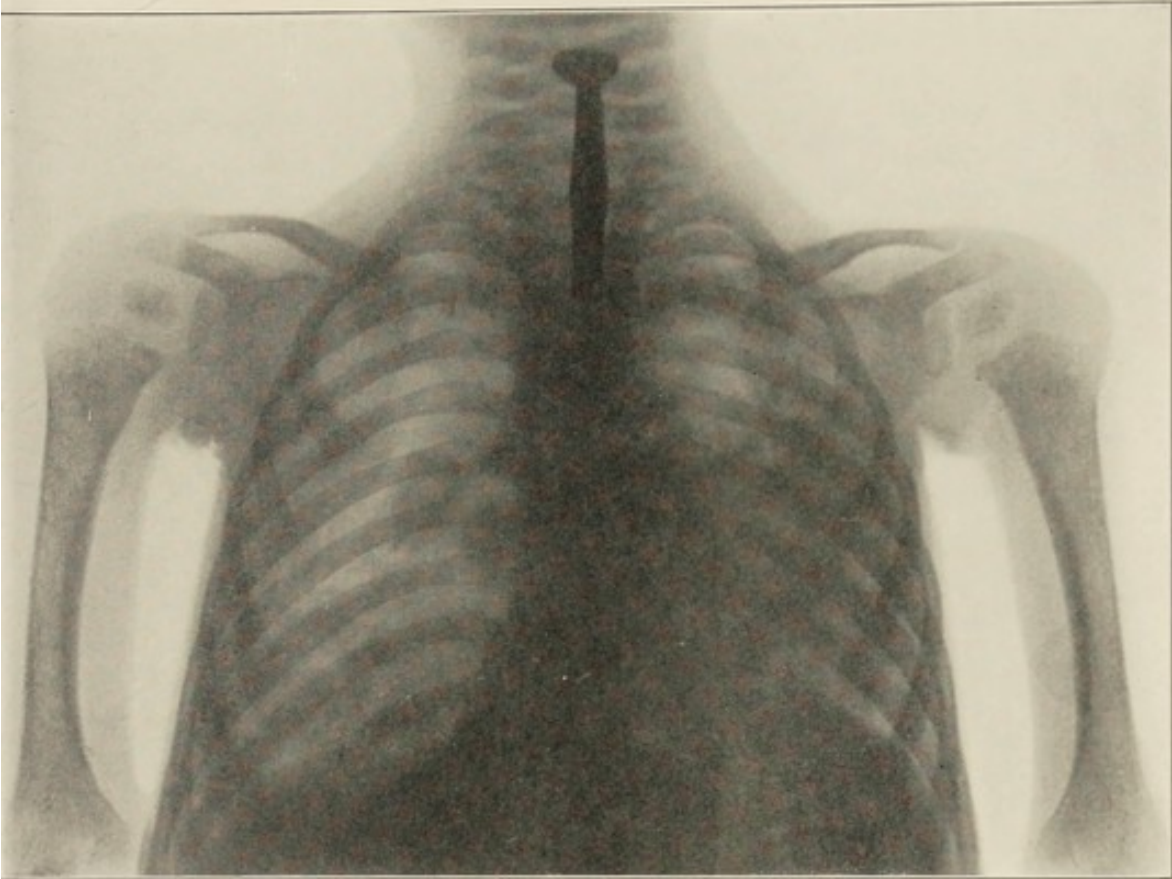
Front view.   Tube in proper relation to bony parts.
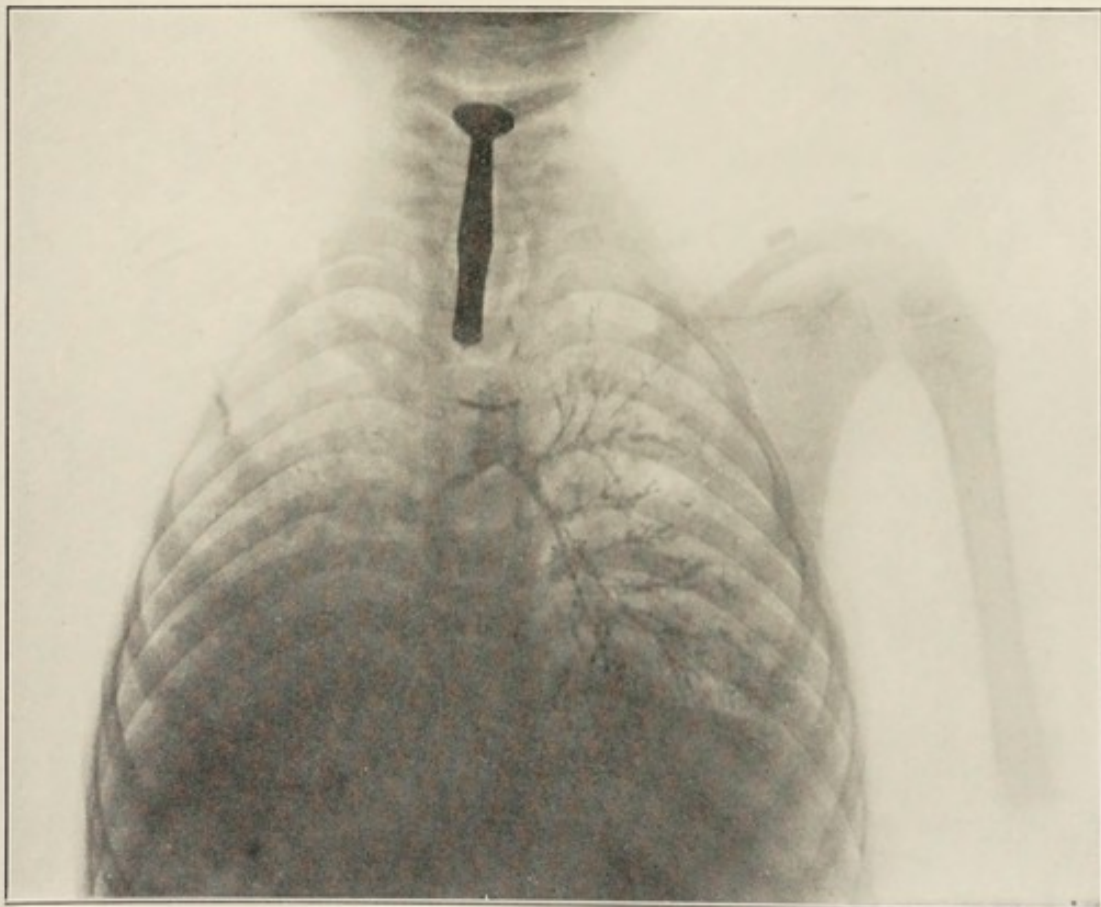
Front view.   Tube in position, showing bifurcation of the trachea and one bronchial tree.
The lower end of the tube is displaced laterally by accident of radiography.   Trachea and
bronchi, injected with bismuth and collodion, show in shadowy outline.
(Caldwell; the Edward N. Gibbs X-ray laboratory.)
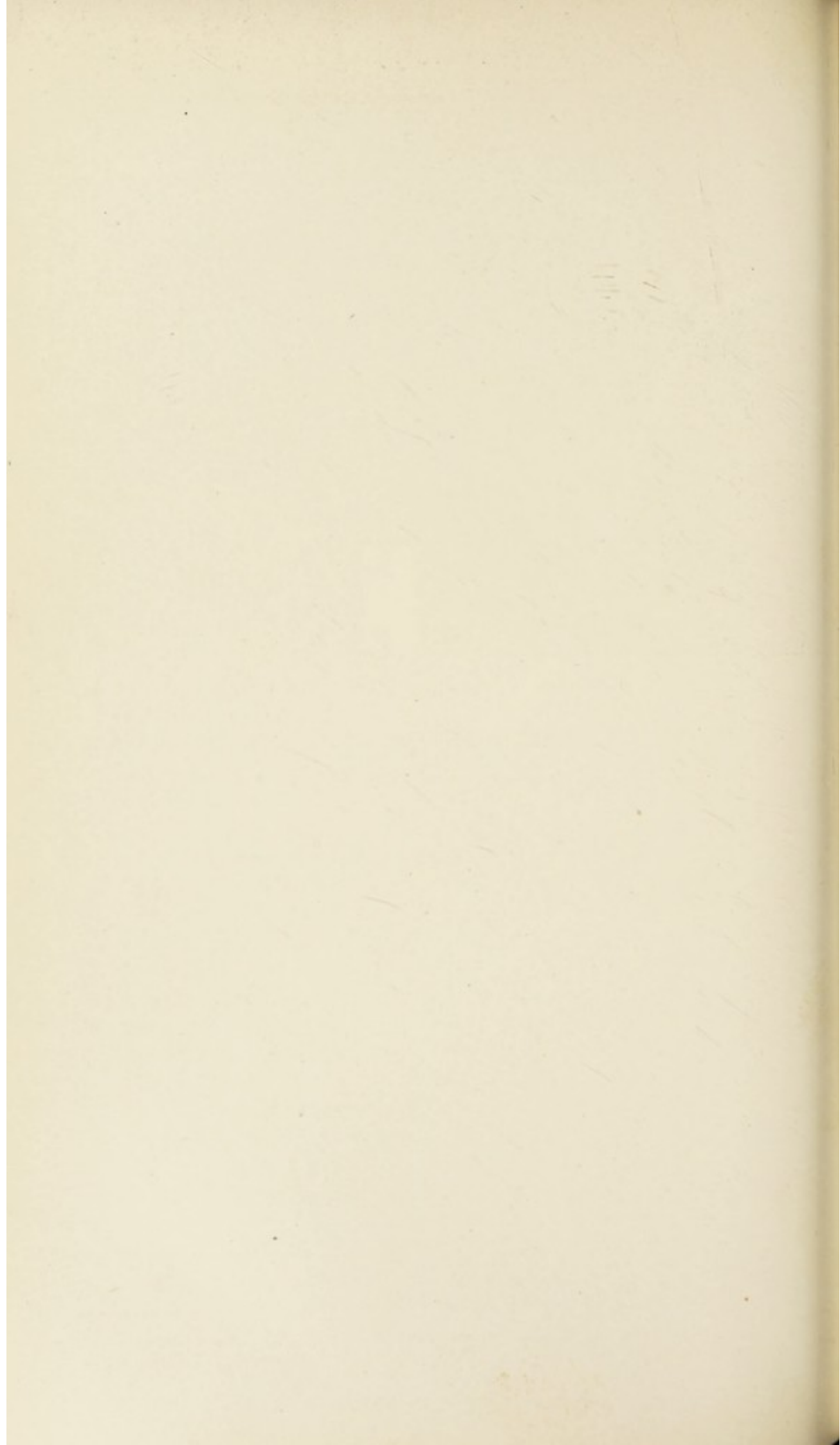
properly constructed tubes of a size suited to the larynx of the patient. For the granulations appearing about the larynx due to previous ulceration, the special tubes already described may be employed. Medicaments are occasionally placed on these tubes, in the form of ointments containing various ingredients, for the purpose of further promoting absorption of the granulation. The treatment of the various other lesions which become chronic belongs to the laryngologist.

Among the rare occurrences in intubated cases may be mentioned tube swallowing. In the cases reported no ill effects have followed, the tubes being passed through the bowel.

Asphyxia has occurred from the use of catgut in the tube, which has been aspirated and swelled under the influence of the secretions. According to O'Dwyer, silk thread may also cause obstruction.

The aspiration of food is probably of very rare occurrence. In many postmortem examinations made at the Foundling Hospital to determine the frequency of this condition, no fluids, milk, etc., were found in the bronchi.

Care of Intubated Patients; Feeding.—This is sometimes very difficult. The larynx and pharynx are often very tender; each mouthful of food excites cough and pain. It is a fact, however, that a good proportion of cases will readily take food in the ordinary way in a sitting position. If this can be done, it is by far the best method of giving food. If not possible, Casselberry's position may be necessary, and is generally very efficacious. The children should be laid across the lap of the nurse, the head back at an angle of 45 degrees or greater and hanging over the nurse's lap, the feet elevated. The food, fluid or semi-solid, should be given with a spoon or bottle, and the child allowed to swallow several times before assuming the upright position, so that the fluids in the nasopharynx may be gotten rid of.

If it be preferred, instead of lying over the nurse's lap, the child may be allowed to remain in bed, the head lowered and the foot of the bed raised. Simpson prefers to have the patient assume this position during the whole of the period of intubation. Hillis * prefers to feed these cases after placing them on their stomach, claiming that in this position the patient has greater control over constrictions of the pharynx.

Some physicians prefer to feed the patients by gavage, in those cases which cannot take food in the ordinary way. A very painful and swollen pharynx and larynx is a contraindication to the latter method

* *Medical News,* Mar. 19, 1898.

of feeding. Rectal feeding is to be used only as a desperate and last resort.

The food should be given at frequent intervals, and in such quantities as the child will take. Semi-solids are often better than fluids.

Irrigation of the throat is not, as a rule, desirable in an intubated case. Masses of mucus and membrane, if 'not rejected, had better be removed with the finger or by means of a piece of absorbent cotton. To stimulate the cough and thus clear the tube and trachea of mucus, nothing is more valuable than a few drops of whisky given at short intervals.

Intubation itself is no contraindication to nasal irrigation. In order to avoid the necessity for re-intubation, Dover's powder, gr. j, or morphin sulphate given in doses of gr. $\frac{1}{16}$ to $\frac{1}{12}$, depending upon the age of the patient, a short time before the tube is removed, is of great value in quieting the patient and doing away with the subsequent spasm. This may be repeated, if necessary, after the tube is removed. If dyspnea shows a tendency to recur, due, as a rule, to spasm of the glottis, poultices, hot baths, and steaming, especially if the latter can be performed in a steam room, may be employed. In older children attempts at quieting them—amusements, etc.—are of value.

IS TRACHEOTOMY OR INTUBATION THE OPERATION OF ELECTION?

In the pre-antitoxin days the difference in the mortality from the two operations was not very great, but was undoubtedly slightly in favor of intubation. The statistics of the latter operation in this country were more favorable, as a rule, than those collected in Europe. Some American operators were able to show far better results with intubation than have ever been achieved with the older operation.

Even if it be granted that there is little difference in the mortality of the two operations, the advantages of intubation over tracheotomy, even without antitoxin, are sufficiently obvious:

1. It is bloodless and much less terrifying, and therefore permitted by parents and relatives who would refuse to grant permission for the cutting operation.

2. No anesthetic or trained assistants are required.

3. The operation requires no preparation for its performance and is over in a few seconds.

4. The after-care of the intubated patient is far less troublesome than that of the tracheotomized. One nurse can attend to three or

PLATE 20.

Casselberry's position for feeding intubated cases.
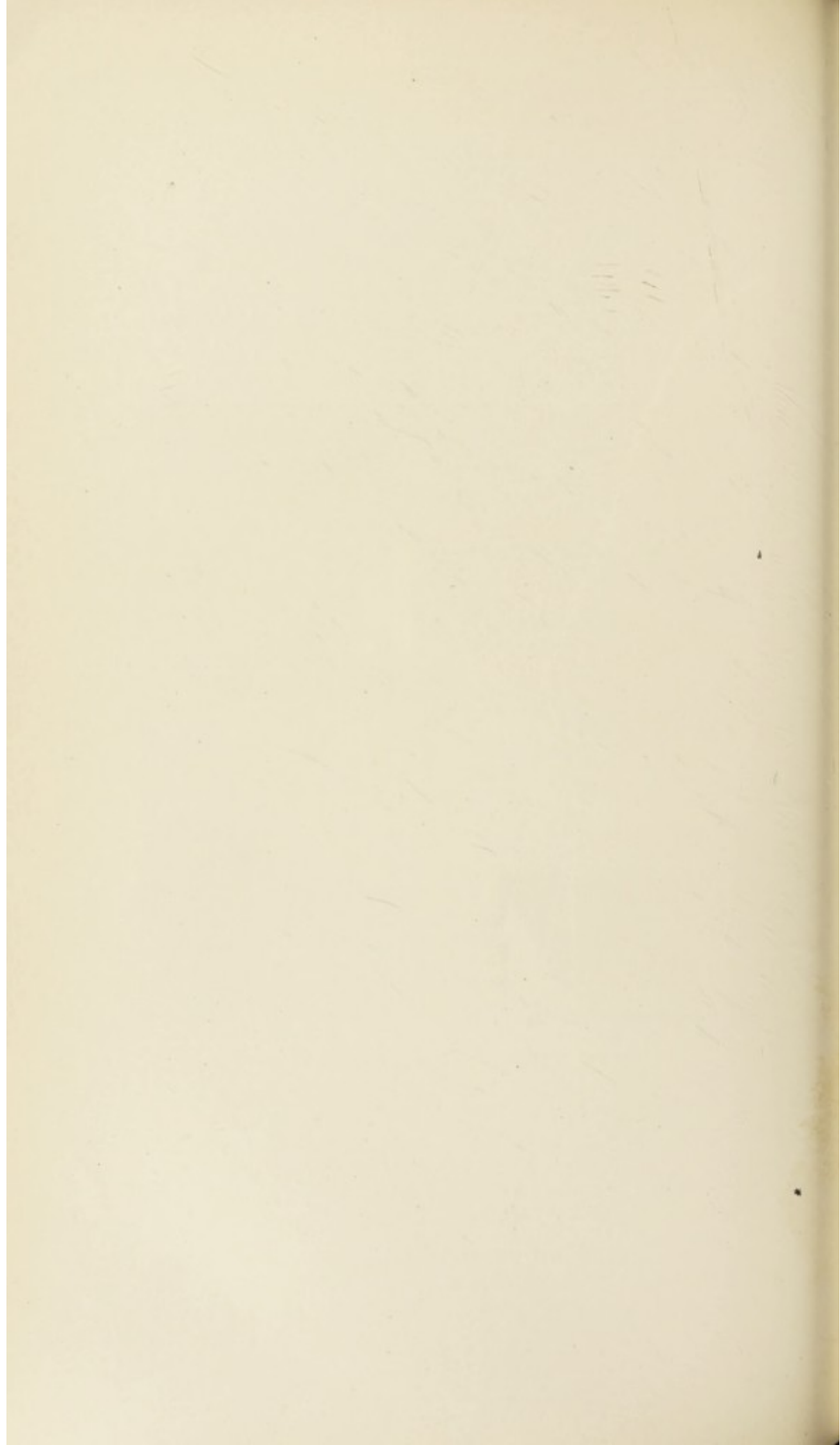
PLATE 21.
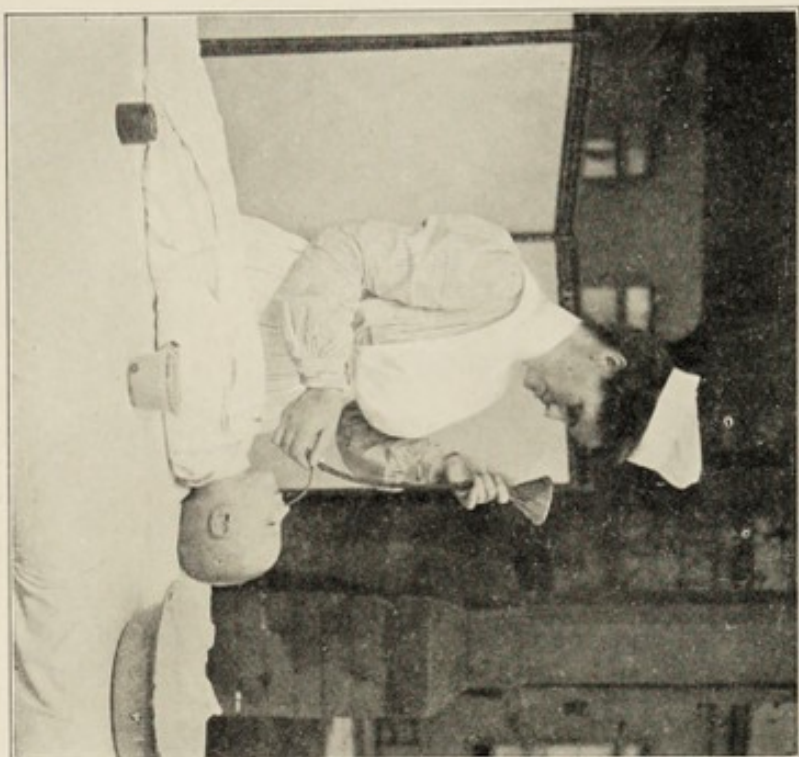
FIG. 1.—Gavage: introducing tube into the nose.

FIG. 2.—Gavage: passing tube rapidly down the esophagus.
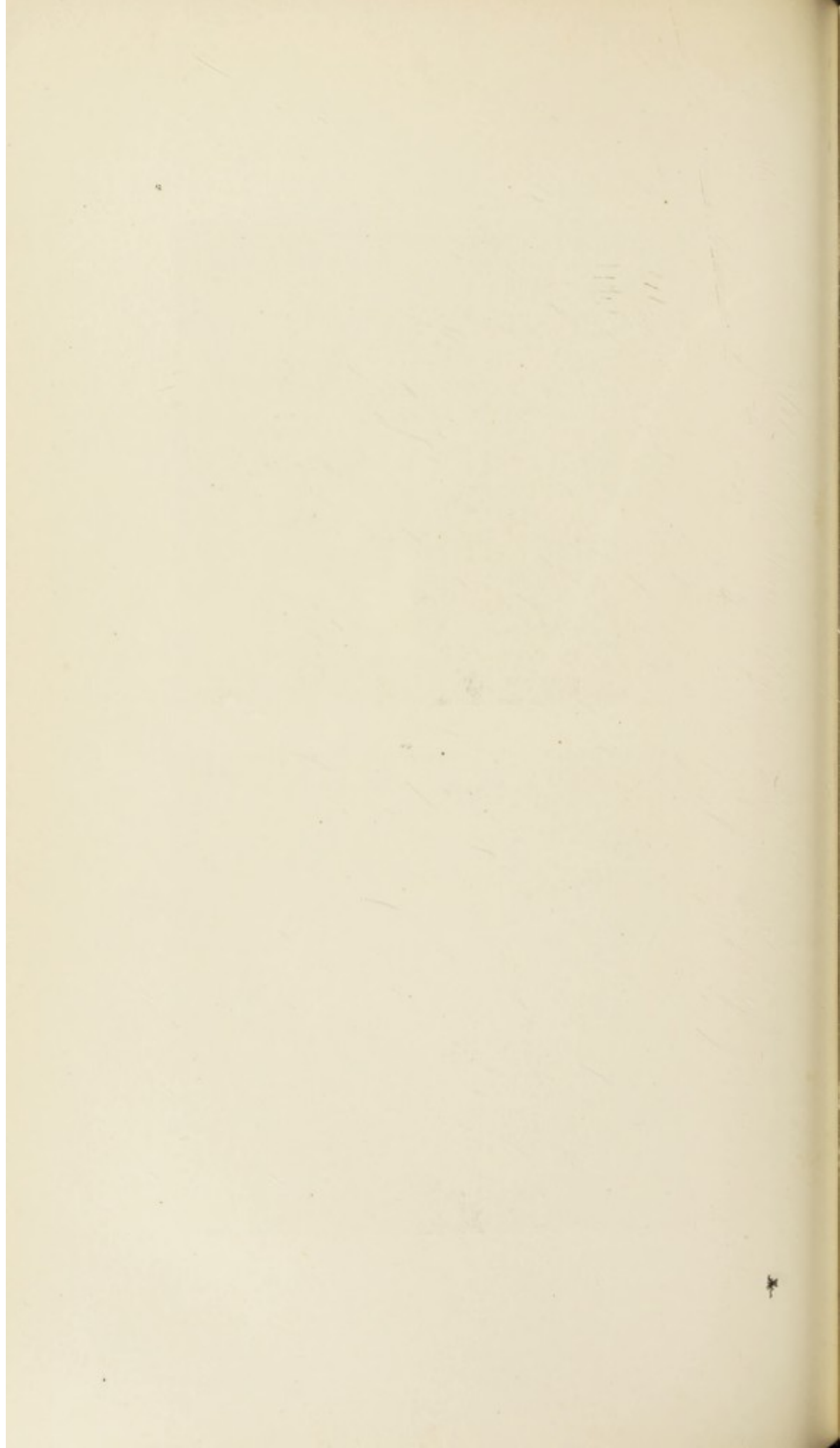
PLATE 22.
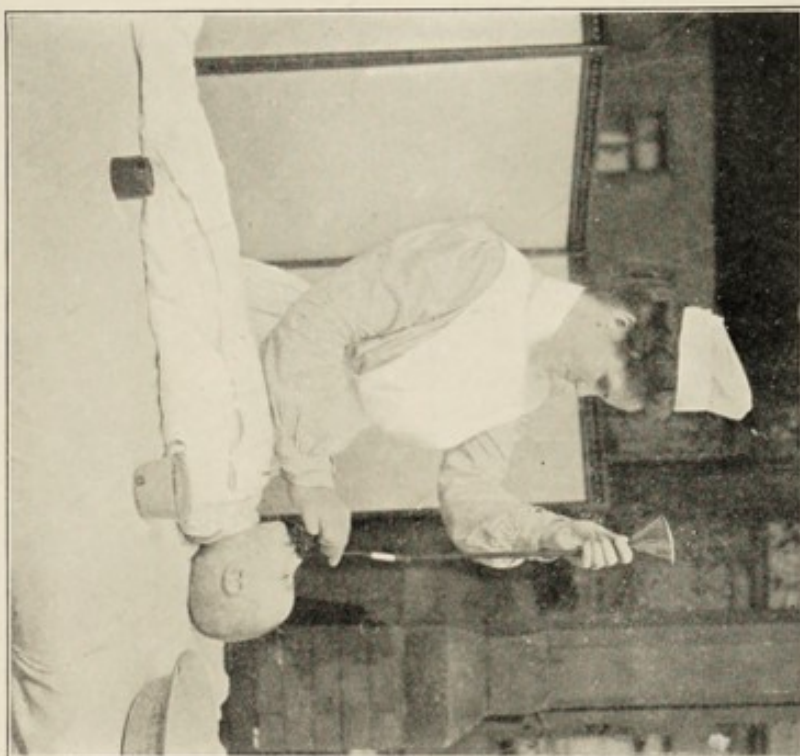
Fig. 1.—Gavage: pinching the tube preparatory to removal.
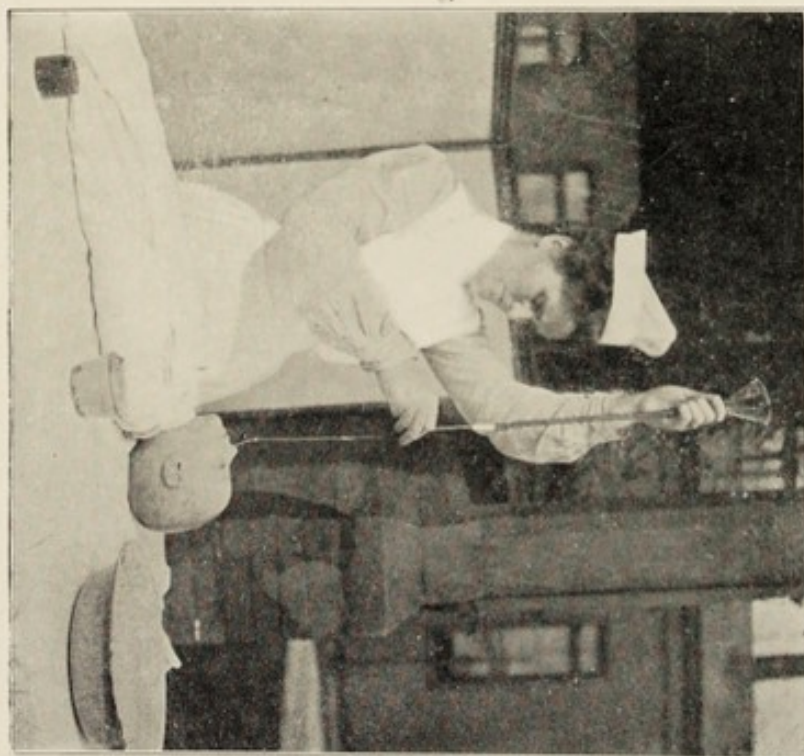
Fig. 2.—Gavage: method of quick removal in order to avoid dropping food into the larynx.
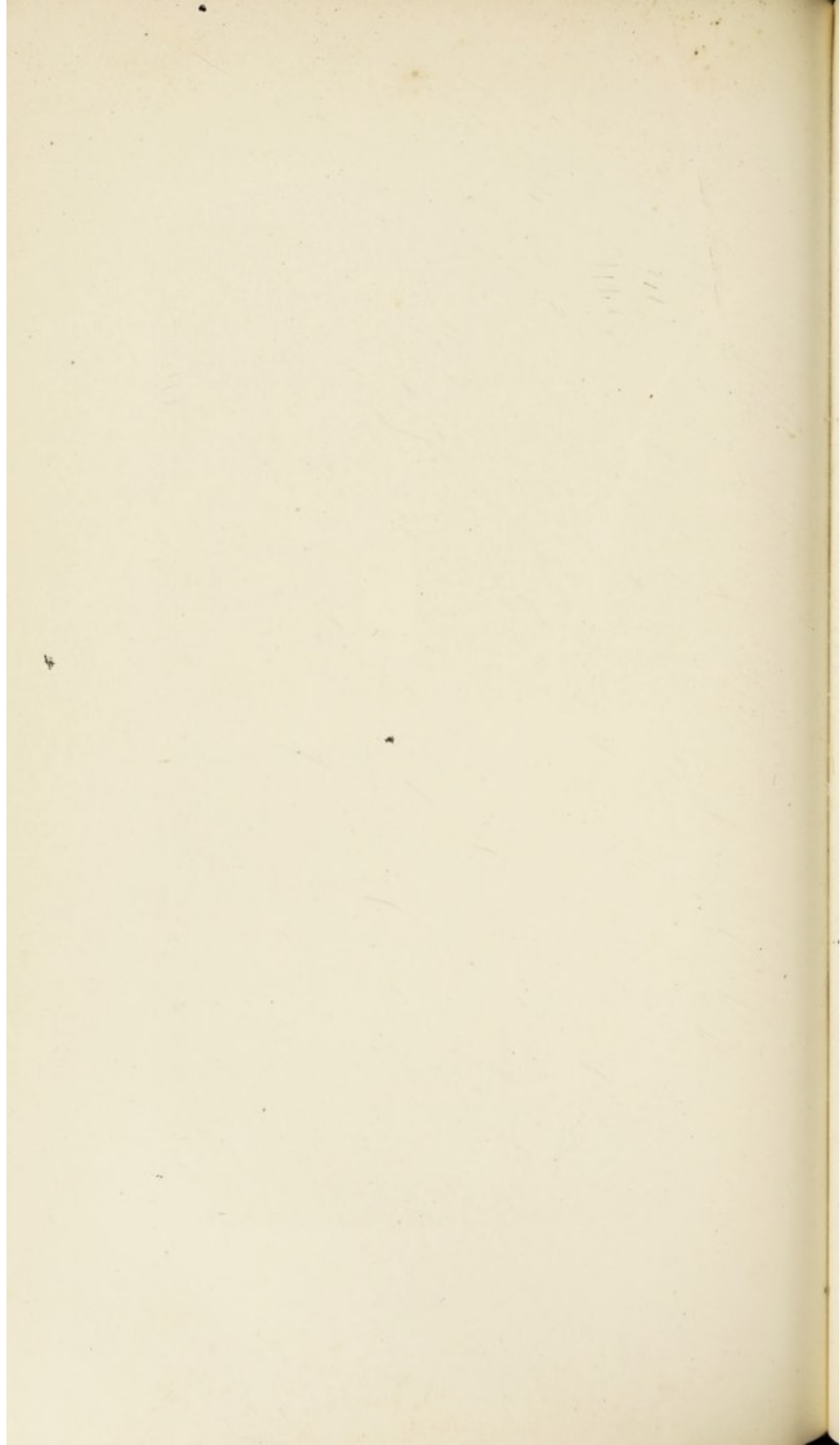
four of the former, while one of the latter will require the entire service of one nurse.

With the use of antitoxin, intubation has become so much more general that it is difficult to compare the mortality of the two operations. In brief, it may be stated that with the early use of sufficient doses of antitoxin, repeated if necessary, the latest statistics show that intubation has but little influence in increasing the very low mortality now reported in laryngeal diphtheria. For example, Waxham has lately reported 40 intubated cases with a mortality of 5%. Other operators have given a similar number with no deaths (Fischer).

These reports are much more favorable than the earlier returns of cases intubated and treated with serum (see Antitoxin), and are undoubtedly due to better serum, given in larger doses and repeated as often as necessary. Little is to be said in favor of the judgment of the physician who to-day will perform the cutting operation from choice to tide over an emergency often of a few hours' duration.

Every educated physician, be he general practitioner or children's specialist, and especially one who lives far from cities, where help may not be obtained, should be familiar with the performance of intubation.

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THE ACUTE EXANTHEMATA.

BY

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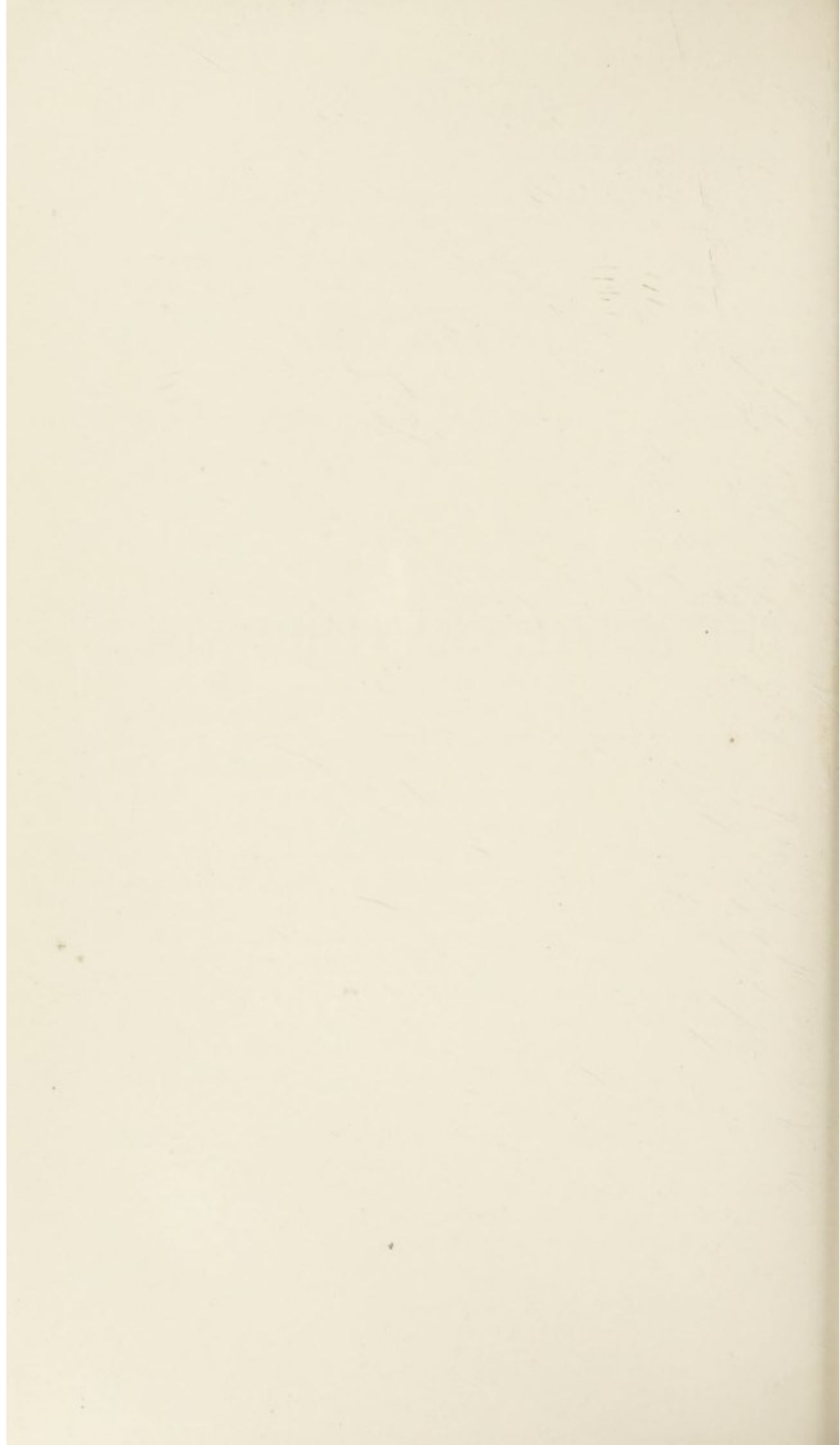
INTRODUCTION.

THE acute exanthemata belong to the acute infectious diseases, and in particular to that group in which the poison is generated within the human body. The latter is its sole breeding-place, alone furnishing the medium necessary to the development of that certain something which acts as the cause of the disease.

Of the nature of the disease agents which give rise to the acute exanthemata we have no positive knowledge. Since the methods which serve for the demonstration of pathogenic microbes fail us here, we are justified in concluding that we have to deal with something of a different nature. We have no ground, however, for assuming that this different something is not a living organism, since every argument favorable to a belief in a *contagium vivum* as the cause of infectious diseases in general applies in full force to the acute exanthemata. We may assert, therefore, with every likelihood of being correct, that the discovery of the specific micro-organisms of the infectious diseases has been delayed thus far only by the insufficiency of our methods of examination. The following points have been definitely established:

1. The disease-poisons of the acute exanthemata are transmitted from one individual to another; direct introduction into the body by means of inoculation is unnecessary, the contagium appearing, as a rule, to be conveyed through the air. This covers, in general terms, our positive knowledge, and suffices to establish the fact of contagiousness. The first part of the proposition expresses, indeed, only the conclusions naturally to be drawn from the statements made above: if the poison can develop only within the human body, it must necessarily be derived from the same source.

2. Almost every individual is susceptible to certain of the acute exanthemata (measles, smallpox), while to others (scarlatina, varicella) not every one is susceptible.

3. An individual who has recovered from one of the acute exanthemata is not, as a rule, subject to a second attack of the same dis-

ease, but is not thereby protected from the other members of the group.

4. The acute exanthemata usually make their appearance on an extensive scale, any one of them prevailing endemically or even epidemically.

Although its accuracy is less well established, there is some basis for the following proposition:

5. The study of the data placed at our disposal, covering large areas of country and long periods of time, makes it appear possible that, in respect to both the increase and the diminution of the number of cases of acute exanthemata, the group is affected as a whole. In other words, the acute exanthemata come together and go together.

In addition to this question, there are others which call for discussion, and first of all the following: Do the several forms of acute exanthemata which we now recognize really represent separate entities?

This can be considered from two different points of view:

1. Is there but one primary disease, appearing in varying form; is the disease agent really a unit which has simply undergone modification, like the plasmodium in the different forms of malaria?

2. Or, are the separate diseases, as we regard them, rather made up of several varieties, which, from an etiologic standpoint, should really be differentiated? The latter possibility should not be lightly put aside. Not many years have gone by since varicella began to be distinguished from variola.

Let us see how far these questions can be answered.

Historical Considerations.—The apparently natural division of the acute exanthemata into separate diseases was really not accomplished until late in their history. One would imagine that smallpox, at least, with its striking eruption, could hardly have been overlooked. But not so—a point which Haeser* explains as follows: Greek physicians laid most weight on general symptoms, on the character of the fever, and paid comparatively little attention to local manifestations. Least of all did it occur to them to regard the form of the eruption as the guide to the differentiation of the fevers. Haeser observes, moreover, that the larger part of Greek medical literature was lost very early, and that "the silence of those writers who have been preserved to us is therefore of comparatively small moment."

It should also be remembered that we are ignorant of the exact significance of the technical terms used in describing the external

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* "Lehrbuch der Geschichte der Medicin und der epidemischen Krankheiten," Jena, 1882, Fischer, 3d ed., p. 24.

characteristics of the disease, the skin eruptions, although it may have been perfectly clear to the contemporaries of the writers. This applies to the Arabian records even more than to the Greek. We are obliged, therefore, to depend on descriptions of symptoms written only in part by physicians, perhaps chiefly by laymen. Thus, while in the case of all plagues of which we have an account we find the general physical condition vividly pictured in the form of a severe intoxication, the technical terms which are interspersed are "*Græca, non leguntur.*"

To exemplify this in detail would take up too much space. The reader to whom the subject is of special interest is referred to Haeser for the accounts which he has compiled of the pest of Antonius and to the writings of no less an authority than Galen, who described it from personal observation. I will, however, give one quotation, which will serve to show at the same time that the researches in this direction have not always been conducted with the requisite degree of critical analysis.*

The most ancient of the records which is supposed to prove beyond a doubt the appearance of smallpox in the sixth century is found in the Koran, in the 105th Sure. As translated by Ullmann,† it reads as follows: "Hast thou, then, not seen how thy Lord hath dealt with the leaders of the elephants? Did he not lead astray their treacherous cunning and send a flock of birds against them which threw down on them stones of baked clay, making them to look like leaves destroyed by caterpillars?" This is said to refer to events in the so-called elephant war (about 570 A. D.), which was waged between the Christian ruler of Yemen, Abraha Ebn Al'Saba, and the Koreisch tribe which guarded the Kaaba. Abraha had built a magnificent church in order to deter the Arabs from making pilgrimages to Mecca, and as the effects of such rivalry grew apparent, the Koreischites caused the church to be destroyed by an emissary, an act which brought on war. But Allah helped his own; Abraha's elephants—he had set out with thirteen of these—refused to go any further, the birds appeared, and a great flood arose. Everything, it would seem, that belongs to the suitable punishment of unbelievers by the Almighty.

Learned Arabic writers who lived more than two hundred years later further embellish the tale. El Wagidi (about 800 A. D.) writes thus: "Then the birds came from the sea in flocks; each bird had three stones, two in his claws, and one in his beak; they threw the stones upon them [the enemy's soldiers]. Everything which was hit was crushed and became covered with sores (or callosities). In this manner first appeared Elgedri and Elhassba and the bitter herbs (shrubs)."

Ben Hischam, at a slightly later period, has even more to relate. He says that the birds resembled swallows and "belesan" (what these were is uncertain), and that the stones were like both "himmis" (ciceres) and "a'das" (lens). Then as to the flight: "Then they departed in all haste, dropping down on their way and dying at every drinking-place. And Abraha was struck on his body; then they took him with them,

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* See Haeser, *loc. cit.*, pp. 59 *et seq.*
† "The Koran," Bielefeld, Velhagen & Klasing, 1853, 3d ed., pp. 544, 545.

one of his members falling off after the other; and whenever one fell off, there appeared at that place an issue containing blood and corruption. Thus they came with him at last to (the capital) Ssana; he was as the young of a bird, yet he did not die until his breast had dropped from his heart. Ibn Ishay says that he has heard from Jaqob ben O'tba, to whom it was told, that the Hassba and the Gedri first showed themselves in this year in Arabia."

At the utmost, we can conclude from this only that at the time the commentators wrote the diseases called Gedri and Hassba were known to them. This is very possible, since the writings of Rhazes, who lived but a little later (born about 850), contain descriptions of the "Dschdry" which give us good reason to believe that the term denotes smallpox. What he means by "Hasbah," however, is not at all clear—certainly not alone our "morbilli," as the accepted translation of the word would imply.

I will, however, refrain from closer criticism, observing only that the identification of the disease or its sequel to which the chief sinner, Abraha, finally succumbed with smallpox is surely a very forced one. The ending of the quotation also serves to recall quite vividly the well-known song about China, in which land, it is true, the singer himself had never been.

To sum up: We find that the acute exanthemata were distinguished as separate diseases, or at least described as such, as follows:

Smallpox, certainly in the first thousand years of our chronology. Whether it was known, long before, to the Indians and Chinese is a matter of dispute.*

Varicella, in the second half of the eighteenth century; not generally recognized until our time.

Measles and scarlatina appear to be older diseases, but were not distinguished from each other. Although the characteristics of scarlatina were recognized and described as early as the middle of the seventeenth century, it was not until long afterward that this knowledge became common property among physicians.

The facts concerning rötheln are not even yet fully understood.

In view of these points, it has seemed to me wise to formulate the statement made above, under 5, with considerable reserve; the period devoted to accurate observation has as yet been too short to admit of greater positiveness.

It is, however, easy to understand how Haeser,† looking at the subject chiefly from the standpoint of historical pathology, should, in his younger years,—he did not refer to it later,—while still under

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* See Haeser, *loc. cit.;* Hirsch, "Handbuch der historisch-geographischen Pathologie," Stuttgart, Enke, 1881, 2d ed., vol. I, p. 88.

† "Historisch-pathologische Untersuchungen," Dresden and Leipsic, Gerhard Fleischer, 1839, vol. I, pp. 92 *et seq.*

the spell of the methods of thought peculiar to the school of natural philosophy, have given expression to opinions which to us seem rather strange. He speaks of a primary exanthema, nearly resembling smallpox, in which all later types were included.

The accuracy of the current belief should not be entirely taken for granted; we cannot even state, unconditionally, that it is well grounded.

For what, now, does **clinical experience** go to prove?

Here, again, we must examine the facts separately. First, in respect to the time intervening between the introduction of the cause of the disease into the body and the earliest evidences of its activity —the incubation period proper. Next, we have to consider the time dividing the appearance of the first symptoms (the invasion) from the outbreak of the eruption. It must be admitted that if these periods were of uniform length in case of each separate acute exanthema, and of different lengths in case of the different ones, there would be more definite reason for dividing them into individual diseases. We should then be able to cite the different duration of the period of fetal life in different animals as analogous facts, but as matters stand, this argument does not carry us far.

It must be taken into consideration that two factors are involved, the germ of the disease and the body on which it acts; that the virulence of the former varies in degree as does the power of resistance of the latter. Since the conditions controlling the development of the germ are never absolutely the same in any two cases, the period necessary for such development may also be subject to variations. Clinical experience does not justify us in disregarding this theory; on the contrary, it has been proved correct in respect to the transmission of certain germs.

Köbner,* for example, has shown that by thinning chancrous pus used for inoculation the regular incubation period of three days can be extended two days longer. I have had similar results.†

In such cases a change undoubtedly takes place in the infectious agent itself; the diminished number of germs inoculated furnishes the readiest explanation.

In vaccination ‡ a different phenomenon has so frequently been

* "Klinische und experimentelle Mittheilung aus der Dermatologie und Syphilidologie," Erlangen, Enke, 1864, pp. 85 *et seq.*

† "Zur Lehre von der Incubationszeit des nicht inficierenden Genitalgeschwürs," *Deutsches Archiv für klinische Medicin*, vol. I, p. 341.

‡ Compare Bohn, "Handbuch der Vaccination," Leipsic, Vogel, 1875, pp. 161 *et seq.* L. Pfeiffer, "Die Impfung"; in Gerhardt's "Handbuch der Kinderkrankheiten," Tübingen, Laupp, 1887, vol. I, p. 611.

observed—namely, an early development of the pustules in warm weather and a retarded development in cold weather—that we have to concede a certain degree of dependence on this entirely external factor.

In the instances just referred to, we are dealing with incubation periods the exact duration of which is well established. We cannot arrive at such positive conclusions when the transmission of the disease germs takes place in the ordinary manner. Nevertheless, the sum of the observations based on actual clinical experience warrants the statement that the incubation period of the acute exanthemata is subject to considerable variation. In smallpox, while it undoubtedly fluctuates between ten and thirteen days, it can probably be shortened to five or extended to fourteen days. In scarlatina the extreme limits are twenty-four hours and twenty-eight days. In measles alone is the period, as a rule, more definitely regulated.

The time elapsing between the invasion and the outbreak of the eruption is also decidedly variable. For our present purpose it is important to note that in the severe form of variola, the confluent variety, the eruption appears by the third day at the latest, while in the lighter forms it may be delayed until the sixth day. The facts are similar in respect to the other acute exanthemata. Taking everything into consideration, it is evident that, from a critical standpoint, the phenomena connected with the period of incubation fail to aid us in drawing any conclusion as to the common or individual nature of the acute exanthemata. Still less light is thrown on the subject by the length of the period between the invasion and the appearance of the eruption.

Anatomically, it is of interest to note that the skin lesion in all the acute exanthemata is an inflammatory one, although it is manifested, it is true, in very different forms.* In some instances it covers large areas of the entire body; in others, it is more circumscribed; it may be entirely superficial or penetrate deeply into the skin. Regarded from a purely anatomic standpoint, smallpox and measles show no wider difference than a furuncle and erysipelas, which, as we know, are caused by the same organism.

Careful histologic examination may possibly succeed in separating measles from scarlatina, and it can doubtless enable us to distinguish these two diseases from smallpox; no such difference can be demon-

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* Compare Unna (" Die Histopathologie der Hautkrankheiten," Berlin, Hirsch-wald, 1894, pp. 623 *et seq.*), who regards the tissue changes in the skin as essentially the same in all the acute exanthemata, differing only in degree.

strated, however, between variola and varicella. Positive conclusions are thus denied us even here.

What do we learn from **observation of the patient himself?**

In this connection we must consider the skin lesion separately from the other symptoms of infection.

The manner of invasion is in itself of importance, as shown in the sudden, violent onset with rapid rise of temperature characteristic of scarlatina and smallpox, and the more gradual onset of measles. The accompanying symptoms are each more striking—the angina in scarlatina; the pains in the back and the sweats in smallpox; the coryza, conjunctivitis, and occasional bronchitis of measles. In a "typical" case, not only the form of the eruption and its manner of spreading, but also the general course of the disease and the development of further local symptoms, give it a distinctly individual character. The same may be said of the sequels. That something peculiar to itself is really present in each variety of acute exanthema cannot be questioned. This does not necessarily prove, however, that the causative agent of the disease is a different one in each case; that is, distinctly different in its fundamental nature, as, for instance, the plasmodium of malaria and the tubercle bacillus. How little the lesion of acute osteomyelitis resembles that of erysipelas or septic endocarditis! how different are the pictures presented by lupus, caries of the vertebræ, and acute miliary tuberculosis! Yet in both instances we have to deal with a common germ of infection.

Such reflections as these should tend to make us cautious, and disinclined to base positive conclusions as to the origin of a disease on the form of its manifestations, and should, in my opinion, have greater weight with us than certain other facts which I shall cite, the significance of which, in this connection, is very questionable, or at least distinctly limited. I refer to the following: The onset of the disease does not always indicate the character of its development. Scarlatina and smallpox may set in less violently than usual, while measles may begin with great severity. Scarlatina may be ushered in by the catarrhal inflammation of the mucous membranes which we meet with in the first stage of measles, and measles may commence with angina. The form of the eruption, too, may not be well marked; that of measles sometimes simulates scarlatina, and vice versâ. Scarlatina is occasionally complicated by severe bronchitis, and measles may be followed by nephritis.

All this appears more important than it really is. Comparing the phenomena in question with those observed in connection with other

infectious diseases, as is perfectly legitimate, we find that too much weight should not be laid on the character of the invasion; one form of typhoid fever is ushered in by chills and high fever, while the sudden onset supposedly characteristic of lobar pneumonia is not infrequently absent. The local symptoms, too, compel attention. Cases of typhoid fever without diarrhea, with only slight intestinal lesions, and accompanied by a severe bronchitis may closely simulate typhus, the form of the eruption not being always a decisive factor in the diagnosis. The theory of the specific nature of these two infections, which the identification of the typhoid bacillus confirmed, was not generally accepted, on the evidence of clinical and anatomic studies, until after the middle of the nineteenth century. Even such men as Griesinger,* Murchison, and Tweedie formerly held the single origin theory to be probably the correct one. But to pursue the subject still further—I repeat that a mild catarrhal inflammation of conjunctivæ and nasal and respiratory passages is no more infrequently met with at the very onset of scarlatina than is a sore throat in measles; the local inflammation, therefore, needs only to be heightened at one point and diminished at another in order to make the local symptoms characteristic of scarlatina appear predominant in a case of measles, and those appertaining to measles a no less striking feature of scarlatina. Similar phenomena can be observed in connection with the eruption. Anatomically speaking, the lesion consists in all cases simply of a dermatitis, which, it is true, is usually characteristic of the special disease in question, both in respect to distribution and severity. The modifications met with, however, are so well marked as to have called forth descriptions of peculiar forms of the eruption observed in each separate one of the acute exanthemata, quite apart from "anomalies" in the strict sense of the word. We find, also, that the course of other infectious diseases, having nothing whatever in common with those under discussion, is sometimes marked by similar eruptions. A severe case of sepsis is reported by von Leube† to have even presented the picture of hemorrhagic smallpox. Eruptions resembling that of measles, or even of scarlatina, are not infrequently seen in septic diseases, but involve, as a rule, only limited areas of the skin. We know, too, that certain inflammatory affections of the skin, due to the action of a common poison, may differ widely in appearance, even resembling, indeed,

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* " Infectionskrankheiten"; see Virchow's " Handbuch der speciellen Pathologie und Therapie," Erlangen, Enke, 1864, vol. IV, Pt. 2, 2d ed., p. 113.

† " Zur Diagnose der spontanen Septicopyämie," *Deutsches Archiv für klinische Medicin*, vol. XXII, pp. 225 *et seq.*

the eruptions of the acute exanthemata. Still less meaning can be attached to the organic inflammations which occur during the course of the acute exanthemata or in the form of sequels, for there is always a possibility that a new disease germ is at work; that we have to deal, in other words, with a secondary infection. Neither is our knowledge as to the relation existing between the primary disease and its so-called "sequels" at all satisfactory; in what manner nephritis depends on the scarlatinal infection, for instance, is not at all clear. Some epidemics, as we know, are marked by an almost entire absence of this complication, while of others it is a nearly constant feature, a peculiarity which bears no relation to the general character of the epidemic, to its severity or mildness.

The argument against the common origin of the acute exanthemata is best supported by the fact already stated above—namely, an individual who has recovered from one of the acute exanthemata is, as a rule, not subject to another attack of the same disease, but is not thereby protected from the other members of the group.

The first part of this proposition deals with a rule which is not without its exceptions—repeated attacks do occasionally occur in connection with any one of the acute exanthemata. It is definitely known, on the other hand, that an attack of measles confers no immunity against scarlatina or smallpox, or vice versâ. It is no less a fact, however, that vaccine prevents the development of the variola poison just as efficiently as an attack of the disease itself. Here the agent is supposed to be the same in both cases, having lost, in the former, the greater part of its virulence as a result of its passage through the body of a lower animal, but retaining its original characteristics.* That such a modification may take place is shown by bacteriologic investigations as to the comparative virulence of pathogenic bacteria when cultivated on different media, some more, some less favorable to their development, the changes thus effected being very extensive. The case of vaccine and variola, however, is not quite covered by these experiments. Non-virulent pathogenic bacteria can be restored to full power by appropriate culture-media; if a cow, though, be inoculated with variola poison from a human being, it will develop vaccinia, but this can never be re-transformed to variola, even if cultivated in many successive human subjects. Nevertheless, it is hardly possible to disclaim the theory of a common origin of the two diseases,†

* Compare Bohn, *loc. cit.*, pp. 114 *et seq.;* L. Pfeiffer, *loc. cit.*, p. 606.

† If the recent researches of L. Pfeiffer (" Behandlung und Prophylaxe der Blattern," in Pentzoldt und Stintzing's " Handbuch der speciellen Therapie innerer

although we are quite in the dark as to how the change is wrought in the animal body, or how it comes that the infectious agent, thus transformed, retains its new character when re-planted in the human body, without relapsing. Aside from this uncertainty, however, the above facts can be said to point to the following conclusion: A specified disease will protect against itself. Therefore, since no single one of the acute exanthemata gives immunity against any one of the others, it is probable that each is caused by its own specific agent of infection. Even though we must admit from the facts presented above that the separate links in the chain of evidence are not all as strong as they should be, still, taking the whole sum of proof into consideration, the generally accepted belief of the present time would seem to be well-supported: viz., *Measles, scarlatina, smallpox, and varicella are distinct diseases; they cannot be traced to a common source, and do not represent merely offshoots, variously modified, from one and the same root.*

The deductions concerning rötheln will be referred to later.

It is conceivable that, in the light of new facts, these views may be disproved; we cannot speak with absolute certainty until the organisms responsible for the diseases in question become known to us. Future scientists may even have to reckon with the teachings of Darwin, since a law embracing all living matter would naturally apply also to microscopic organisms. For the present, however, we should refrain from such speculations, which are of no more practical value than a philosopher's dream.

Another important question concerns the possibility of the **simultaneous appearance of two or more of the acute exanthemata in the same individual.**

No arguments are called for as to a similar possibility in case of acute infectious diseases in general, this having been already definitely established. Since bacteriologic research can thus be drawn on in support of our position, we are justified in rejecting the following assertion of Franz Mayr*: "A simultaneous outbreak of scarlatina and measles or scarlatina and smallpox in the same individual does not coincide with our conception of a disease as originating in a specific infection of the blood." This predetermined theoretic conclusion of Mayr's seems to have taken firm root in his mind, for at the time

Krankheiten," Jena, Fischer, 1894, vol. I, pp. 218 *et seq.*) prove conclusive, the identity of the organism —a flagellate ameba—producing variola and vaccinia will have been demonstrated.

*See Hebra's "Hautkrankheiten," Virchow's "Handbuch der speciellen Pathologie und Therapie," Erlangen, Enke, 1860, vol. III, Pt. 1, p. 119.

he wrote there was evidence enough against it. Such observers as Barthez and Rilliet could hardly be discredited by statements like the following: "The medical curiosities cited by certain writers are probably to be referred to smallpox in connection with an antecedent erythema, or to a scarlatina variegata." Counter-arguments soon appeared, however, and to follow up the subject Mayr himself came on from Vienna. L. Fleischmann* showed that Mayr saw more than one patient suffering from measles and scarlatina at the same time, and that his explanation of the symptoms was untenable. There is one statement made by Mayr himself, not cited by Fleischmann, which, it seems to me, can hardly admit of more than one interpretation. It runs as follows: Inflammatory diseases and typhoid fever confer immunity only during their course, convalescents being open to attack the same as other individuals; in respect to the acute exanthemata, smallpox and scarlatina, the case is peculiar; it is possible for either to make its appearance during an attack of measles before desquamation begins.† Fleischmann adds a number of illustrative cases.

The statements of a large number of reliable physicians serve to prove beyond a doubt that at least any two of the acute exanthemata can attack the same individual simultaneously. It is, of course, possible that three of them can thus appear, but I am not aware of any reported instance of such a combination.‡ In order not to encroach too far on the territory belonging to the discussion of smallpox, I will confine myself to the other members of the group, giving in brief form the histories of a few cases.

CASE 1.—*Scarlatina complicated three days after the appearance of the eruption by the development of measles.§*
Family with three children: one of these developed scarlet fever at the beginning of May, 1876. The other two were removed at once to their grandmother's apartments in the same building. One of them was taken sick with measles while the scarlatina of the first child was at its height, the measles running a normal course. The third child, a boy, three years of age, was attacked on May 21st by high fever, accompanied

* "Ueber die Gleichzeitigkeit zweier acuten Exantheme nach neueren Beobachtungen," *Archiv für Dermatologie und Syphilis*, 4th year, pp. 223 *et seq.*

† *Zeitschrift der k. k. Gesellschaft der Aerzte in Wien*, 1852, 8th year, p. 15.

‡ A case has quite recently been published which is to a certain extent relevant: scarlatina, varicella, and measles were developed in rapid succession, not, however, simultaneously. (Th. Hase, " Ein Beitrag zur Statistik der Erkrankung an Scharlach," u. s. w., "Jahrbuch für Kinderheilkunde," New Series, vol. xxxix, p. 69.

§ Berthold Stiller (Budapest), " Zum Synchronismus zweier acuten Exantheme," *Wiener medicinische Wochenschrift*, 1877, pp. 937 *et seq.*

by angina; on the 23d a uniform, finely punctate rash broke out on his neck and trunk, rapidly spreading over his entire body, while the throat symptoms increased in severity, the tonsillitis becoming membranous in character. On the 25th the fever rose still higher—to 41° C. (106° F.) in the evening—and the condition of the patient showed an "immense change for the worse," the following symptoms being noted: redness and swelling of the eyelids, well-marked conjunctivitis, copious mucous discharges from the nose, which interfered with respiration, hoarseness, frequent cough with considerable mucous expectoration, and diffuse moist râles over both lungs. The tonsils, at the same time, were covered with grayish, dirty-looking, membranous patches and the submaxillary glands were enlarged. The rash was at its height. On the evening of the 26th the parents noticed what seemed to them a new eruption on the red hands of the little patient. Stiller saw it on the following morning, and described it thus: "The dorsal surface of both hands and forearm, reddened by the scarlatinal rash, is covered with slightly raised, irregularly rounded papules, rather large in size, the majority being somewhat larger than lentils."

By the 29th the rash had spread over the whole body; it was most marked upon the face. The skin was universally red and almost universally swollen, and was abundantly covered with the new eruption in the form of large papules, which in many cases were coalescent, and here and there considerably raised above the level of the skin. The macular form of the eruption, which was plainly that of measles, was displayed only on the arms and legs, from which the scarlatinal rash had partly faded, where it showed as more or less circular patches of a dark, reddish-brown color, standing out distinctly on the pale red background. There was an intense catarrhal inflammation of the entire respiratory tract; the child showed signs of dyspnea and continually coughed up large quantities of mucus. The temperature remained at about 40°, the spleen was enlarged, projecting from 2 to 3 cm. below the borders of the ribs, the urine showed traces of albumin, the swelling of the submaxillary glands had further increased, there was edema of the whole submaxillary region, and the membranous patches on the tonsils formed a continuous dirty-colored coating. Professor Bokai, who was called in, confirmed the diagnosis of a double exanthematous infection.

On the 3d of June there occurred a new outbreak of the measles rash, which was thickly distributed over the entire body, but lasted only one day. Desquamation was scarlatinal in character. A suppurative inflammation, which led to the development of abscesses in various parts of the body, persisted for some time, but was finally followed by complete recovery.

The genuineness of this case cannot be doubted. The opportunity for a double infection is supplied by the outbreak of scarlatina in one and measles in another of the children in the family. The symptoms of inflammation of the mucous membranes accompanying each of the two acute exanthemata developed at the usual time, and the form of the two eruptions was diagnosed by two careful and experienced observers as that characteristic of scarlatina and measles respectively. The fact that the measles rash first appeared on the

hands and forearms is the only point which seems at all unusual, and does not in the least invalidate the diagnosis.

CASE 2.—*Measles, complicated two or three days after the appearance of the eruption by the development of scarlatina.**

The patient was a boy eight years of age. On August 20, 1881, he was taken sick, with symptoms of a cold in the head. During the night of the 21st to 22d, the mother noticed that his face, neck, and chest looked exceedingly red. On the morning of the 22d the physician made the following notes: "The conjunctivæ are slightly injected, the mucous membrane of the pharynx and hard palate shows a few discrete red spots and tiny papules; the tonsils are not swollen. The face, forehead, neck and chest, and, to a less extent, the back and lower half of the trunk are thickly covered with small red papules, and spots of a yellowish-red color, which disappear on pressure. The patient coughs but little, sneezes only occasionally, and complains of thirst and itching of the skin. There is only a slight coryza." On the 23d the rash began to disappear from face, throat, and neck. In the morning the patient felt well, but in the evening he developed a sore throat and high fever.

On the morning of the 24th the condition was as follows: "In addition to the measles rash, the lower part of the abdomen, the inguinal regions, the scrotum, and Scarpa's triangles show a finely punctate redness of the skin, like the rash of scarlatina, and the skin is hot and dry to the touch. The spleen is perceptibly enlarged; the angina has increased. A few dark red spots are visible on both hard and soft palate, as well as on the rest of the pharyngeal mucous membrane. The conjunctivitis is more marked, while the bronchial catarrh has almost entirely disappeared. The patient complains of great thirst and of pain on swallowing." By the evening of the same day the scarlatinal rash had spread further on the thighs, and a finely punctate scarlet-colored eruption had also made its appearance on the upper extremities, being most noticeable on the inner surface of the elbow. The skin of the abdomen, scrotum, and thighs showed, in addition to the scarlet rash, the presence of a closely distributed vesicular eruption, the vesicles varying in size from a pinhead to a lentil, and containing a turbid, purulent fluid. A similar eruption was seen on the arch of the palate, the uvula, and the tonsils. The tip of the tongue was of a dark flesh-color, and the papillæ appeared swollen (strawberry tongue). The measles rash had faded to a yellowish-brown.

August 25th: "A fine desquamation is to be seen on the face and neck, also beginning on the chest. The scarlatinal eruption is fading from the lower half of the trunk, but on the upper extremities it extends from the wrists to beyond the shoulders and partly covers the back; small vesicles, containing a turbid fluid, are thickly scattered over the red background. There are somewhat larger vesicles of a similar character at the entrance of both nostrils, the corners of the mouth, and on the mucous membrane of the pharynx. The tongue appears somewhat less coated, is of a dark red color, and is covered, especially toward the tip, with a quantity of flat or slightly raised spots, the size of a lentil, and white or yellowish in color. Swallowing is exceedingly painful, the patient being scarcely

* Josef Herzog (Graz), "Ein Fall von Morbilli-Scarlatina," *Berliner klinische Wochenschrift*, 1882, pp. 105 *et seq.*

able to drink. Respiration is easier." By evening the scarlatinal rash had begun to fade; a small ulcer was seen on the right tonsil.

August 26th: "The fine desquamation due to the measles eruption continues; large flakes of epidermis are becoming detached on the parts where the scarlatinal rash first appeared; the latter is fading from the other parts, and the vesicles are drying up."

An ulcerative stomatitis, which was quite severe, remained troublesome for a time. Recovery was uneventful.

This case, too, is beyond dispute. The infection was in both instances a mild one, as the temperature curve, in particular, serves to show. The peculiar manifestations of both diseases, which in uncomplicated cases are looked upon as diagnostic, were well marked, as were also the affections of the mucous membranes and the skin eruptions. We are again struck by the fact that the rash, in this instance that of scarlatina, first appeared in an unusual situation.

CASE 3.—*Scarlatina, complicated three days after the eruption appeared by the development of varicella.**

The patient was an infant, a girl, fifteen months old. Its two brothers were ill with scarlatina. At midnight of January 15 to 16, 1869, the child became feverish and restless, and on the morning of the 16th its condition was as follows: "The whole body is covered by a well-marked scarlatinal rash, especially the trunk, thighs, and upper part of the arms, where it displays a punctiform character; on the legs and feet it takes more the form of blotches. The throat is moderately congested." By evening the eruption had developed considerably further, the papules appeared more raised,
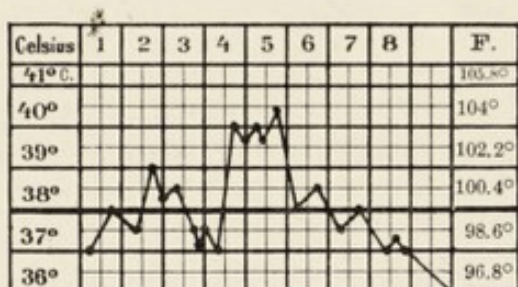
Measles. Scarlatina. Desquamation.
FIG. 29.—(*After Herzog.*)

were of a darker tint, and stood out more distinctly, especially on the forehead and temples. On the extremities the eruption was less well developed.

January 17th: "The vault of the pharynx is moderately reddened; the mucous membrane covering the hard palate appears quite pale. The tongue looks almost normal, its coating having largely disappeared. The rash is paler, all over the body, than it was yesterday evening, the change being least marked on the extremities, but its punctiform character is everywhere apparent."

In the evening: "The skin appears slightly redder than in the morning, but less so than yesterday evening."

January 18th, A. M.: "The rash is paler and the papules are indistinct.

* L. Thomas, "Neue Beobachtungen über gleichzeitiges Auftreten zweier acuter Exantheme," "Jahrbuch für Kinderheilkunde und physische Erziehung," 1870, new series, 4th year, pp. 1 *et seq.*

The face has an almost normal color. The uvula is the only part of the throat which appears at all reddened, and the lymph nodes are not perceptibly enlarged. On the scalp and over the lumbar region there are seen a few clear vesicles, surrounded by a faintly hyperemic area."— P. M.: "Only a slight scarlatinal rash remains, but it is still everywhere distinct. An eruption, consisting of numerous vesicles, very characteristic of varicella, has appeared on head and face, and is also scattered, but less thickly, over the trunk and extremities. The vesicles, the largest of which are the size of a lentil, have each a narrow, bright-red areola, and are very characteristic of varicella. The eruption is entirely unrelated to the scarlatinal rash, and develops exactly as on normal skin. In addition, there are a number of papules, much larger and of a much brighter red than those of scarlatina, some of which are changing into vesicles. There are no vesicles on the pharyngeal mucous membrane."

January 19th, A. M.: "The scarlatinal rash is everywhere less distinct, and in place of the papules which have disappeared there is a slight, yellowish pigmentation. A considerable number of fresh varicella vesicles, some of them as large as lentils, have developed in between the older ones, which appear flaccid and relaxed. They are distributed in greatest abundance over the extremities; only a few show a moderately broad areola; for the most part this is almost entirely lacking." —P. M.: "The scarlatinal rash appears still paler. There is a moderate number of new

FIG. 30.—(*After Thomas.*)—m, Height of eruption.

varicella vesicles, most of them very small, on the trunk, and a few also on the soles of the feet."

Only one other point in the further history of the case deserves mention—namely, that on the 21st a few of the vesicles on the feet became pustular and the surrounding tissue showed signs of increased infiltration.

Convalescence began on January 24th and proceeded uneventfully. In consequence of the delicacy of the child's skin, and the fact that it was bathed every day, desquamation did not occur.

The diagnosis of this case is certain; the patient suffered from a light attack of scarlatina, to which varicella was added. The accompanying chart (Fig. 30) shows the facts in regard to the temperature. Whether the rise to 40.1° C. (104° F.) noted on the second day of the varicella eruption is to be ascribed to the latter or to the scarlatina, we will leave undecided, as does Thomas himself.

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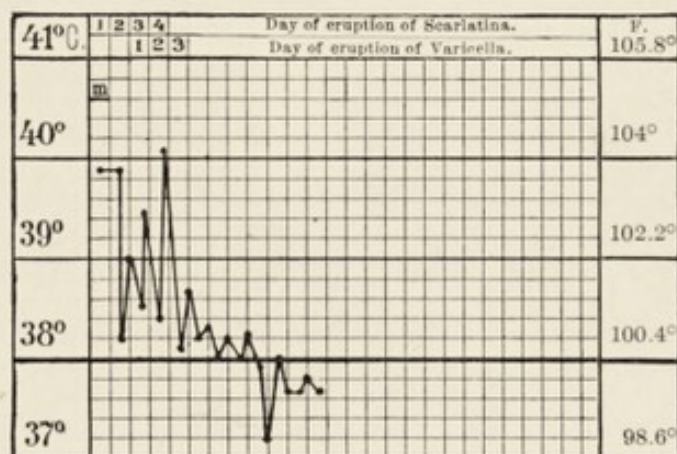
CASE 4.—*Varicella, measles developed five days later.**

The patient was a girl, one year old, who had been exposed to measles. The temperature was taken before the appearance of any symptoms of disease, in order to have a record of the same during the period of incubation.

On May 3, 1870, a few varicella vesicles were observed; on the evening of the same day, but not before, the child became restless and feverish. On the 4th it vomited and had several loose stools. It also coughed a little. By the 6th the vesicles had become quite numerous. On this day the child began to sneeze and cough, these symptoms gradually increasing in severity. On the 8th there were a few freshly developed vesicles to be seen, one of which was situated on the hard palate, and, in addition, the face and the front and back of the neck showed, though not yet distinctly, the small roseolar spots characteristic of measles. On the trunk the rash was less apparent. Photophobia and conjunctivitis were also present; the child did not sneeze or cough much.

May 9th, A. M.: "The varicella vesicles have dried to scabs, except where a few new ones, of the smallest size, and without any areola have appeared on the right thigh. The symptoms of conjunctivitis, photophobia, coughing, and sneezing remain unchanged, also those relating to the pharynx. The measles rash has grown much more distinct on face and trunk, and is somewhat raised throughout."—P.M.: "A few fresh varicella vesicles, scarcely as big as lentils, and with almost no areolæ, have appeared on the knees and fingers; otherwise they have all dried up. The whole head and trunk are covered with small moderately red papules, lying fairly close together, and showing tiny pustular points, yet unmistakably the rash of measles. The extremities are not yet involved."

May 10th, A:M.: "The extremities are now also covered, but the rash is less intense than on the trunk. In the latter situation and on the face it has already begun to pale. One fresh varicella vesicle has developed on the left leg. The child coughs a good deal, sneezes but seldom, has some diarrhea and only a slight conjunctivitis." By the evening of this day the measles rash had largely disappeared, and from the 11th on, the temperature remained normal. Recovery was uneventful.

The case does not call for special discussion. Both the measles and the varicella were of a mild character, and the temperature curve shows nothing but what was to be expected under the circumstances. The above examples should suffice to prove that more than one of the acute exanthemata can develop at the same time.†

Is it a fact that one of the two diseases appearing simultaneously so affects the other as to modify its symptoms?

This question has been answered differently by different physicians, affirmatively or negatively, according to their individual ex-

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* See Thomas, *loc. cit.*

† It is unnecessary to refer in detail to the literature on the subject here. Such references can be found in the articles above mentioned, and also in the exceedingly well-prepared extracts from the "Jahrbuch für Kinderheilkunde."

perience. In the light of all the evidence presented, we should certainly refrain from formulating any positive rule. It seems, indeed, to be clearly shown that when a disease develops under such conditions both its general course and its local symptoms are subject to wide variations. The most that we can say is that the eruption does not always follow the usual path in spreading over the body.

The assertion of some observers, to the effect that under certain conditions the virulence of the one infection may be lessened by the influence of the other, is open to question. L. Fleischmann,* for instance, makes the following statement: "If both exanthemata develop the eruptive stage at the same time, their duration is shortened, or, to put it differently, the second disease moderates the first, and the length of its own course is decreased also." Nobody, however, is in a position to speak at all positively as to the duration of an acute exanthema, nor can the dangers which may arise be determined
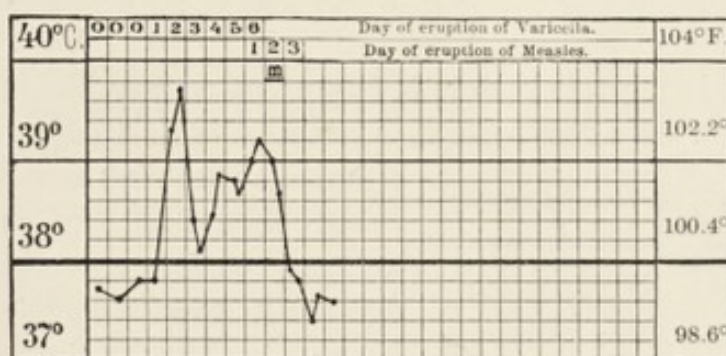
Fig. 31.—(*After Thomas.*)—m, Height of eruption.

at the onset, except in very severe cases. We get a general impression of an infection, whether it is more or less intense, but that is all. It would seem, indeed, that mild infections are, on the whole, more likely to appear in conjunction than severe ones, but this does not necessarily indicate an interaction on their part. Fleischmann, by the way, has had to admit in respect to severe cases of smallpox that a combination with scarlatina is almost certain to insure a fatal ending. Enough cases have been reported of severe double infections with other exanthemata to forbid generalization. I have myself observed several such cases, one of measles and scarlatina, both eruptions showing at the same time; one of scarlatina, in which measles developed three days later. In both instances the patient died. The descriptions contained in the histories noted down in the course of an extended epidemic are not sufficiently accurate to make

* *Loc. cit.*, p. 241.

them valuable as proofs of double exanthematous infections; it will not be out of place, however, to cite one such case, especially since it is interesting from another point of view.

CASE 5.—*Scarlatina; measles developed three days later. Aphthous inflammation, extending to the bifurcation of the trachea and the upper end of the esophagus. Death occurred on the seventh day.*
The patient was a girl one year of age. The other children of the family were ill with measles.

On February 10, 1888, the child was suddenly taken sick with coughing, vomiting, and convulsions, and was removed the same day to the hospital. An eruption like that of scarlatina appeared on the child's back on the 11th; it was not until the 14th that an unmistakable measles rash was seen on the face and covering the entire body, accompanied by diarrhea, coryza, conjunctivitis, and bronchial catarrh. The last-named affection did not extend to the small tubes until later. There was also an aphthous stomatitis. On the 16th areas of consolidation were found in the lower lobes of the lungs, being situated posteriorly. The respiration, which at first was 45, rose on the 16th to 66, while the pulse became too rapid to count, being over 200. The patient died that night.

In considering this case it is important to note the temperature curve. After an abrupt rise in connection with a poorly developed
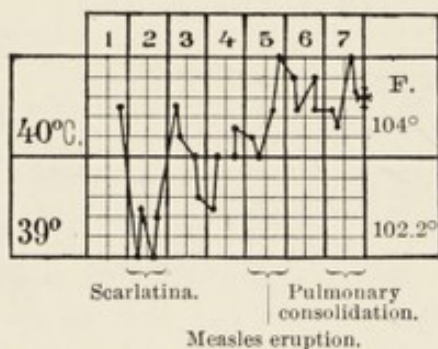
Scarlatina.   Pulmonary
                 consolidation.
       Measles eruption.
FIG. 32.—Four-hourly record from 8 A. M. to
               8 P. M.

eruption, resembling scarlatina, which lasted only a short time, the temperature sank considerably (1.5°); it then rose again for a few hours (1.5°), then fell (1°), and finally rose at the time the measles appeared to a high mark (41° C.—106° F.), continuing high until the end. As it seems to me, the first part of the curve corresponds to a light attack of scarlatina, its second part to a severe one of measles. At the last we see the influence of the bronchopneumonia, developing between areas of atelectasis. The sudden rise of temperature at the onset, and the well-marked cerebral symptoms, also point to the scarlatinal infection, quite apart from the rash.

The following data, taken from the autopsy record (of Prof. Nauwerck), are of interest: "On the right heel there is a bed-sore as large as a twenty-five-cent piece. The brain is anemic and edematous, and there is fluid in the ventricles. The lower lobes of both lungs and some parts of the upper lobes show areas of atelectasis and intense congestion of the mucous membrane, especially in the smaller bronchi. The spleen is enlarged one-third, its consistence is hard, and the trabeculæ and follicles are plainly visible. The liver, kidneys, and heart appear anemic.

The mucous membrane of the intestines is also anemic, except that a few Peyer's patches and solitary follicles in the ileum show a slight degree of congestion and swelling. The ileocecal lymph-nodes are somewhat swollen, and grayish-violet in color."

The condition of the pharynx and the upper respiratory passages is especially noteworthy:

"The mucous membrane covering the base of the tongue, the uvula, the roof of the mouth, the pharynx, and the entrance of the larynx is swollen and congested; the aryepiglottidean folds appear decidedly swollen. Scattered over all these parts we find grayish, cloudy patches, circumscribed, as a rule, but occasionally coalescent. They are moderately adherent to the mucous membrane, which, when they are scraped off, appears gray and cloudy. The deposits extend into the pyriform sinuses and the commencement of the esophagus, and are arranged [in a circle around the entrance to the larynx. The posterior surface of the thyroid cartilage and the entire lining of the larynx are beset with these grayish-yellow, cloudy masses, which extend, in diminishing quantity, as far down as the bifurcation of the trachea. The mucous membrane of the latter appears intensely congested. In the larynx, too, the deposits are not easily detached, and the underlying mucous membrane looks cloudy, and is of a reddish-gray color. Posteriorly, the uvula is almost completely covered with patches, as is also the roof of the mouth."

The appearances described above are those of an unusually widespread aphthous inflammation, or, as Ziegler * calls it, a stomatitis fibrinosa maculosa (disseminata), extending uncommonly far downward. It is certainly a rare case; according to Bohn,† "aphthæ are seldom found in the pharynx, and it is uncertain whether they ever extend further downward."

It is a generally admitted fact that other infectious processes, of widely varying nature, can develop during the course of, or immediately after recovery from, the acute exanthemata.

The pathogenic bacteria here concerned are, first of all, the various pyogenic organisms; next, the diplococcus of Fränkel and the tubercle bacillus. Löffler's diphtheria bacillus, though less frequently the one involved, is unfortunately often enough the cause of the trouble, and the ordinary bacteria of decomposition not infrequently play the part of infective agent. Such secondary infections are well known to have a very unfavorable effect on the prognosis, claiming not a few victims from among those who have successfully overcome the primary disease.

* "Lehrbuch der speciellen pathologischen Anatomie," Jena, Fischer, 1890, p. 474 of 7th ed.

† "Mundkrankheiten," in Gerhardt's "Handbuch," Tübingen, Laupp, 1880, vol. IV, Pt. 2, p. 35.

Trojanowsky * describes a **recurrent form of scarlatina and measles,** but the conditions governing its development are not yet clear. The following extracts are from the reports of his cases, which occurred in Livonia: "The majority of those affected lived in low-lying more or less swampy districts, districts in which intermittent fevers prevail, and where, in addition, cases of typhus are of yearly occurrence. Some years, indeed, are marked by typhus epidemics of varying character. Almost every year, in these districts, I had occasion to observe the recurrent form of typhus, the so-called *febris recurrens.* The cases were scattered here and there, and were, it is true, very few in number, occurring only in cold weather and among very poor and scantily fed people. The most striking sporadic cases of febris recurrens in my experience were seen by me during the winter of 1868–1869, when bad crops and high prices had combined to cause unspeakable suffering among the poorer classes of the population of Livonia, especially among the peasants in the poorest districts. It was during this season, too, that 5 of the 14 cases of scarlatina and measles which I here present occurred."

It appears, then, that the peculiar cases described by Trojanowsky did not have their origin in localities in which relapsing fever is truly endemic. Certain peculiar features of his cases of scarlatina and measles, in general, however, indicate the influence of special conditions pertaining to locality, and possibly to season as well. In another article † he reports instances of repeated attacks—giving them the name, not usually thus applied, of "recidive"—in a proportion much exceeding the ordinary. Among 300 cases of scarlatina,— he counts only those which he saw both times himself,—18 represented second attacks, occurring within a period of from six months to seven years. Among 200 cases of measles there were 14 of second attacks, within a similar length of time. These figures are very different from those usually given.

Measles and scarlatina, as described by Trojanowsky, present, on the whole, the same peculiar features. From 1865 to 1871 he met with 8 cases of recurrent scarlatina, and from 1864 to 1871, 6 similar cases of measles, and upon these he bases his statement.

Between the first and second outbreaks there was a period during which the temperature remained normal, just as it usually does after

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* " Die Recurrensform des Scharlaches und der Masern," *Dorpater med. Zeitschr.,* 1873, vol. IV, pp. 19 *et seq.*

† "Scharlach- und Masernrecidive," *Dorpater med. Zeitschr.,* 1872, vol. III, pp. 199 *et seq.*

the subsidence of an acute exanthema. Thereupon the disease was repeated, with all its local and general symptoms, In the scarlatina cases the intervening period varied in length from seven to seventeen days; in those of measles, from six to fourteen days. It is especially interesting to note that the disease was not represented in its entirety by either attack alone, but only by both taken together. This is true of the eruption as well as of the other symptoms; whatever was absent or only slightly developed in the first attack appeared well marked in the second, while it, in turn, repeated only faintly the more decided manifestations seen on the first occasion. An exception must be made in respect to the fever, which did not materially differ in the two attacks. It should be observed, however, that the temperature was no higher in the morning than in the evening. The spleen was involved to a much greater extent than is common in scarlatina and measles. It was found to be considerably enlarged as early as the first or second day of the disease, being already palpable at that time, while the patient also complained of an unpleasant sense of tension and pressure, and even of pain in the region of the spleen. During the period of normal temperature the swelling disappeared, but returned with the new attack.

The blood during the attacks showed a well-marked leucocytosis, and a diminished number of red corpuscles. Trojanowsky estimated —he made no counts—the ratio between white and red corpuscles as 1 to 6 or 1 to 10. The general symptoms were scarcely more serious than usual. Trojanowsky, to be sure, lays stress on the extreme weakness, the pains in the muscles, the tremor and loss of muscular power, and speaks of the great mental depression and the slight cerebral disturbances. If we consult the temperature chart, however, we shall not be inclined to attach any special importance to these symptoms, especially to their occurrence during the second attack, when the patient's power of resistance was already reduced. The prognosis was not at all unfavorable; only one of the 14 cases ended fatally, the patient in this instance being a woman thirty-two years of age, of weak constitution, who succumbed to measles.

Before proceeding any further, I will give the histories of two of these cases almost in full, one of scarlatina and one of measles.

CASE 6.—(Measles case No. 6 of Trojanowsky.) *First attack:* The patient was a boy nine years of age, of robust constitution, but living under unfavorable conditions. He was taken sick on October 22, 1871, showing the following symptoms: photophobia, slight blepharospasm, intense coryza, and a frequent, dry, painless cough.

Second day: The entire body is more or less covered with the eruption of measles; this is more thickly developed on the trunk than on the face and extremities, especially on its anterior surface. Examination shows enlargement of the spleen, which is sensitive to pressure. The patient's voice sounds hoarse.

Third day: The eyelids are extremely red and swollen. The patient seems very weak and complains of considerable pain in his muscles, and of painful fits of coughing in the morning. The lungs are normal. There has been some diarrhea to-day.

Fourth day: The rash is fading.

Fifth day: The coryza and eye-symptoms are becoming less marked.

Examination of the blood: The red corpuscles appear massed together in the form of islands, irregularly grouped, and varying in size. In addition to colorless granular cells and small free nuclei, there are large numbers of white blood-corpuscles, as in slight degrees of leukemia; expressed in figures, they may be said to represent about one-eighth the number of the red corpuscles.

Seventh day: All the symptoms are disappearing.

From the eighth to the twenty-second day the temperature was normal. The desquamation, of the fine-scaled variety, lasted for some time, particularly on chest and abdomen. The splenic tumor had entirely disappeared by the eighteenth day. An examination made on this day shows a normal relation between red and white corpuscles. The red corpuscles present themselves under the microscope in the ordinary form of rouleaux, but appear here and there in irregularly shaped clumps, like little islands, such as were described in the record for the fifth day.

Second attack: On the twenty-second day the patient developed fresh symptoms of coryza, photophobia, and dry cough.

Twenty-third day: The area of splenic dulness extends 1 cm. beyond the tip of the eleventh rib. The lungs are normal. Several of the cervical lymph-nodes are swollen and painful. A few measles blotches have appeared on the face.

Twenty-fourth day: There is a general eruption of measles; the rash is most intense and plentiful on the face and extremities. The patient is troubled by a very frequent, dry, hacking cough, and his voice is hoarse.

Twenty-fifth day: The area of splenic dulness extends 3 cm. beyond the tip of the eleventh rib. One of the enlarged lymph-nodes is beginning to suppurate. The patient seems very weak; he passed the morning in a kind of sopor, but toward evening complained of muscular pain. The conjunctivitis is unusually severe and is accompanied by frequent blepharospasm; there is but little coryza. The rash has faded perceptibly.

Examination of the blood: This shows a condition almost identical with that noted on the fifth day.

Twenty-ninth day: Desquamation is beginning.

There was no fever after the thirtieth day, and the spleen returned to its normal size by the thirty-second day. On the thirty-fifth day the blood was also found to be normal. Although all symptoms of the disease disappeared, the patient made only a slow recovery.

For the temperature record the reader is referred to the accompanying chart (Fig. 33).

Case 7.—(Scarlatina case No. 6 of Trojanowsky.) *First attack:* The patient was a boy sixteen years of age, of robust build. His parents were

healthy people, in fairly good circumstances. He was taken sick on September 1, 1870, his temperature rising very rapidly.

Second day: The mucous membrane of the pharynx is dark red in color, presenting a striking appearance. The patient is slightly delirious, and feels extremely weak; he suffers also from intense muscular pain, especially in the lower extremities, and amblyopia. The spleen is enlarged, extending to the tip of the eleventh rib.

Third day: A scarlatinal rash, appearing first on the face, has in the course of the day gradually spread over the whole body, in the form of a scarlatina lævigata. The rash is only a light one. The tongue presents a characteristic "strawberry" appearance. Small patches of grayish-white membrane are scattered over the tonsils; also over the soft palate, which is greatly swollen; they are firmly adherent to the underlying mucous membrane. The submaxillary gland and several of the cervical lymph-
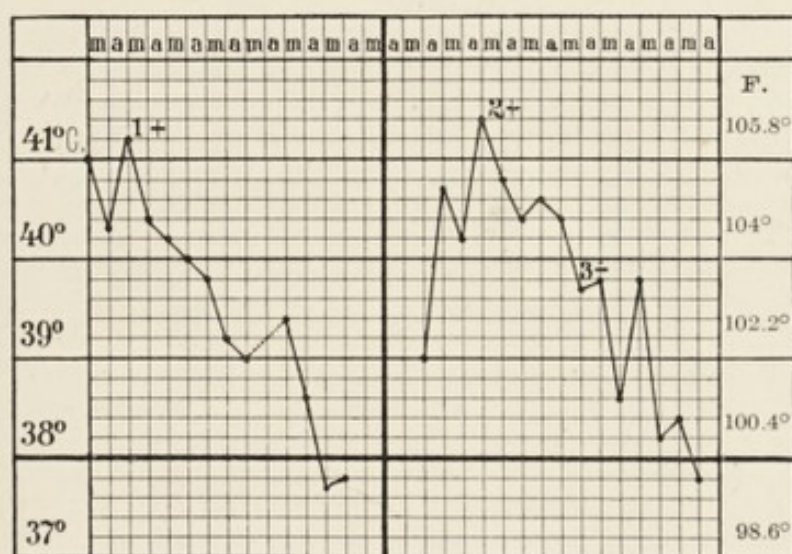
FIRST ATTACK.

1+, Measles eruption appears, chiefly on trunk.

ω, Intermediate period during which there was no fever, from eighth to twenty-second day.

SECOND ATTACK.

2+, General well-marked outbreak of measles eruption.

3+, Suppuration begins in a cervical lymph-node.

FIG. 33.

nodes appear considerably swollen. On account of intense pain on swallowing and when the throat is touched, six leeches were to-day applied to the front of the neck. A specimen of the blood taken from one of the wounds after removing the leech—this was done in the early morning, before the patient had taken any nourishment—showed on microscopic examination a striking increase in the number of white corpuscles, there being approximately one of these to every 8 or 10 red corpuscles. The latter were not arranged in the more or less orderly figures, often forming rouleaux, which are found in normal blood, but were clustered together in irregularly shaped masses or islands of different sizes. Lying between these islands and inclosed in them are seen the unmistakable large granular white cells representing the white corpuscles of the blood, and, in addition, a number of small, colorless, granular cells and small, free nuclei—a picture similar to that presented by the blood of a patient suffering from

leukæmia lymphatica. The cell outlines were rendered much more distinct by the addition of a 5% salt solution.

Percussion shows the spleen to extend 1 cm. beyond the tip of the eleventh rib; it can also be palpated on careful examination. The urine shows traces of albumin and a few casts containing fibrin; there are no blood-corpuscles present.

I will omit the daily record, which presents nothing of importance, and state only that the rash was entirely gone by the sixth day; the splenic enlargement and the patches of membrane in the throat had disappeared by the second day, while the temperature fell to normal on the ninth day.

The kidney symptoms were at no time of any consequence. The temperature remained normal from the eleventh to the eighteenth day. Desquamation was completed by the thirteenth day. The blood was found normal on the sixteenth day.

Second attack: On the eighteenth day, just as the patient was about to get up, he was again seized with fever.

Evening of the nineteenth day: The patient's whole body is covered with the rash of scarlatina, which is much more intense and brilliantly colored than it was two weeks ago. He complains of severe headache, and of occasional pains in his muscles; muscular twitchings are frequent during sleep. The pupils appear somewhat contracted. The spleen is again enlarged, the area of dulness again extending to the end of the eleventh rib. There is diminished secretion of urine; the mucous membrane of the pharynx appears slightly congested and swollen.

Twentieth day: The headache is less severe and the patient sleeps more quietly. The pupils are normal. The patient, though, seems greatly depressed, and feels very weak. The enlarged spleen is perceptible on palpation, and is sensitive to pressure; its dulness reaches 2 cm. beyond the end of the eleventh rib. The urine contains a moderate amount of albumin and a very few epithelial cells; both feet are slightly edematous.

Twenty-first day: The rash has somewhat faded from the upper half of the body. To-day the edema involves both lower extremities and the scrotum, and to a slight extent the face also. There has been some nausea. The urine shows a large amount of albumin, but no distinct casts containing fibrin are to be found. A specimen of blood obtained from a slight scratch on the arm shows, as before, an increased number of white corpuscles, but not to so marked a degree; small, granular cells and small, free nuclei are also again present, but the grouping of the red corpuscles appears much more regular and normal.

Twenty-second day: The rash has disappeared; there is almost no angina, and the area of splenic dulness has grown smaller.

Twenty-fourth day: The mucous membrane of the tongue and pharynx again look normal, and the swelling of the spleen has gone down completely. The face and scrotum are losing their edematous appearance.

Twenty-fifth day: A well-marked desquamation has begun.

Twenty-eighth day: The patient had a rather severe attack of nose-bleed to-day. The blood is again perfectly normal.

The edema disappeared entirely by the thirtieth day, the albuminuria by the thirty-fifth day. There was no fever after the thirtieth day. The patient made an uneventful recovery, getting up on the forty-second day. The temperature record is given on the chart.

Trojanowsky is unquestionably justified in emphasizing the peculiarity of these cases. Of the various special points noted in the histories, the only questionable one concerns the changes in the blood. Were these really so extreme, and so quickly overcome? In order to prove this beyond a doubt, the methods employed in examination would need to be more accurate. Any one familiar with the subject will form his own opinion from the wording of the record.

The theory of a double infection by relapsing fever, on the one hand, and measles or scarlatina on the other as an explanation of these cases, seems hardly worth considering. That malaria played any part in the matter is still more improbable. Indeed, the fact that the

FIRST ATTACK.
1+, Scarlatina rash breaks out.
ω, Intermediate period during which there was no fever, from eleventh to eighteenth day.

SECOND ATTACK.
2+, Scarlatina rash breaks out afresh.
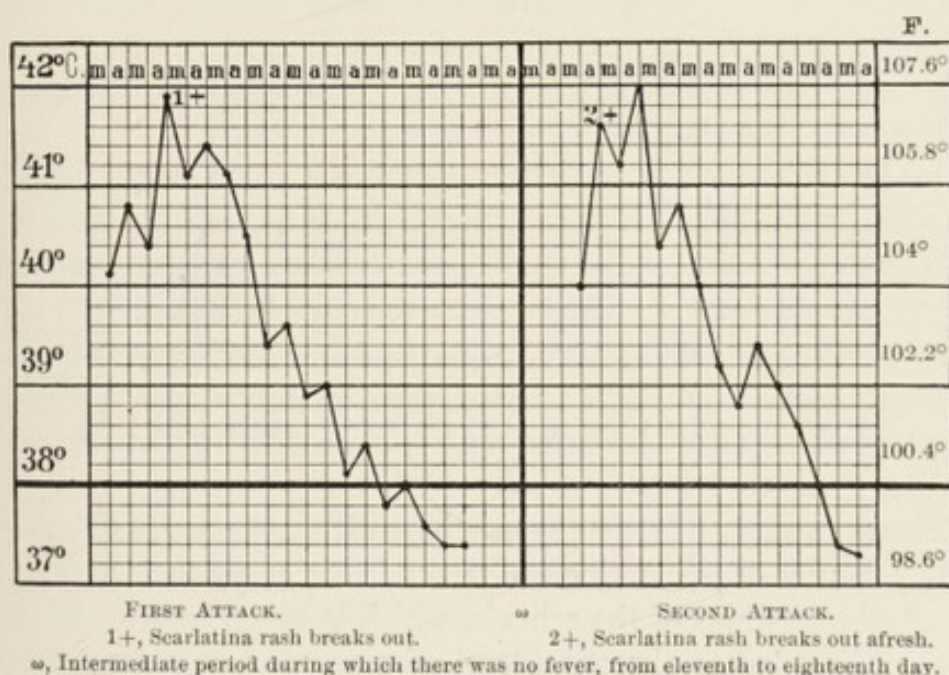
FIG. 34.

cases did not occur at one time, but at rather long intervals, and quite unconnected with epidemics of either of the diseases just referred to, is sufficient to disprove any such supposition. There must have been special influences at work which will have to remain unexplained until further records of cases and improved methods of examination shall bring enlightenment.

It is hardly possible to draw a sharp distinction between the "complications" and the "sequels" of the acute exanthemata, nor is this point, in my opinion, of any great practical importance. I would also enter a protest against the use of the terms "normal" and "anomalous" in describing their course. It seems to me best rather to discuss whichever disease is in question as a whole, following out

the various forms in which it manifests itself as exhaustively as possible, and then to consider each of the local affections separately.

The autopsy findings in cases of the acute exanthemata where death occurs at the height of the disease do not differ from those characterizing any other acute infectious disease. Later on we find the changes induced by the special features of the disease, which become the more marked the longer its duration. Cases illustrative of this point seem uncalled for at this juncture.

The next question which presents itself for consideration is that of **general prophylaxis of the acute exanthemata.** With smallpox we need not concern ourselves; the required protection is afforded by vaccination. The case is different with scarlatina and measles, in which diseases, apart from all other considerations, we have almost no practical basis for this procedure. The matter will receive full discussion in another place.

The attention of the medical world is at present chiefly directed to the schools, which are very properly held responsible, to a large degree, for the spread of the acute exanthemata. There is no doubt as to the urgent need of so arranging our school-buildings as to make them conform to the demands of public health. This general proposition is particularly applicable to the question of contagious diseases, the spread of which is highly favored by such conditions as are to be found in poorly ventilated, overcrowded school-rooms.

Let us examine the school regulations with reference to this point. The importance of preventing the transmission of contagious diseases through the medium of the schools, which is recognized by those in authority, has led to the enactment of a number of rules not fully in accord with the purpose for which they were designed. The question was discussed in detail, years ago, by von Kerschensteiner,* who can speak with the authority of long experience such as few have enjoyed, having been engaged for a great many years in official work, which for a long time he himself directed, which gave him an oversight of all the conditions prevailing throughout the broad kingdom of Bavaria. And yet it almost seems as if again could be heard the voice of the prophet crying in the wilderness—a wilderness of old dogmas.

Von Kerschensteiner bases his statements on the following proposition: "Smallpox, scarlatina, and measles are not communicable

* "Vorträge über Gesundheitspflege," u. s. w., edited by Dr. Paul Börner, No. x. —Von Kerschensteiner, "Die Verbreitung von Masern, Scharlach und Blattern," "Ein Stück der Schulgesundheitspflege," Berlin, Max Pasch, 1883.

through the medium of a third person who remains unaffected." This simple negative proposition, as he himself styles it, this "heretical opinion, immediately raised a cloud of dust." When this had settled, von Kerschensteiner proceeded to formulate the following propositions, based on data gathered from far and near, which in his opinion come close to the truth, requiring to be supplemented in exceptional cases only:

1. Smallpox, scarlatina, and measles are in the great majority of cases communicated by direct contact with an infected individual.

2. The transmission of the germ of smallpox, measles, or scarlatina through the medium of a third person is of only exceptional occurrence.

3. The communication of contagion by the brushing, beating or cleaning of garments belongs in a separate class.

4. Transmission by means of articles of common use which have been handled by or otherwise brought into contact with an infected individual must be classed as direct. The communication of a contagion which has persistently clung to a given place for an unusual length of time is also to be included in the same class.

5. The conditions most favorable to the communication of contagion are found during the eruptive stage and at the time of its development; the conditions are less favorable during the period of desquamation.

The material on which the above conclusions are based was gathered by the medical societies of Bavaria, and is made up, therefore, of facts observed by unprejudiced, practical, experienced men. Viewed in the light of other records and of personal experience,—I refer the reader to the sections on "Measles" and "Scarlatina," in which these records are subjected to a critical analysis,—there seems to be but little cause for difference with von Kerschensteiner. I will therefore follow him further in his discussion.

The rule that the brothers and sisters of a patient ill with scarlatina or measles are to be excluded from school has been observed with more or less stringency. Its practical results are thus described by von Kerschensteiner, in a manner very true to life:

"A child having several brothers and sisters who attend school is taken with scarlatina. The physician in charge, fully convinced that the disease can be communicated through a third person, yet who, by the way, finds it possible to continue his own practice without injury to his conscience, is quick to direct the·parents to remain at home with the patient, to prohibit the other children from attending school and the

family in general from making or receiving visits. So the entire family, of six or seven members, is happily isolated, and the doctor who is responsible for their imprisonment feels satisfied. But to what fate has he consigned the children? Instead of leaving the house and getting into the open air, of neutralizing, at least in part, the unfavorable effects of the hours necessarily spent in the sick-room because of limited house space by playing out-of-doors, or even by going to school, they are kept prisoners within the house, which they find very tiresome, soon becoming morose, losing their appetite, sleeping poorly, etc.

"In such a state of siege the event which is welcomed with relief and exclamations of thankfulness is that which, after a week or ten days of waiting, takes them to the sick-room to keep the original little patient company, for they, too, have begun to show symptoms of the disease, toward the conscientious acquirement of which nothing whatever has been neglected. If this solution be precluded, however, by the fact that some of the members of the family have already been through a similar time of trouble, the imprisonment begins to grow insupportable, and the prisoners try to circumvent the confining rules imposed upon them by every means in their power.

"Meanwhile one of the children of the teacher whose school they attend has also been taken with scarlatina, hence the father—that is, the teacher—should likewise remain away from school, lest he, too, should spread the contagion, as the accepted theory would have it. The teacher, however,—I am speaking from personal experience,—cheerfully keeps on with his school-work, comforting himself with the thought that a rule which is good for the pupils does not necessarily fit the case of the teacher.

"Another moving factor in this conflict of opposing duties is the importance of maintaining the regular routine of school-work, which usually outweighs the anxiety for the health of the children. Nor is this in the least unnatural, for the further we carry the consequences of transmission by third persons in imagination, the more rapidly do difficulties swell to impossibilities, soon landing us in the realm of absurdities. This is especially true of a large city, which is rarely, if ever, entirely free from acute exanthemata, even though they are seen only in sporadic cases. The above examples suffice to show how school-work in every large city would be subject to frequent and prolonged interruptions if the theory, which I am in a position to contest, were to be carried to its logical conclusion by the enforcement of appropriate regulations."

Von Kerschensteiner next proceeds to lay down certain positive rules:

"Intercourse with the family of patients suffering from scarlatina or measles is admissible; the children in such a family may therefore unhesitatingly continue their attendance at school, just as physicians in charge of the patients may visit others without misgiving.

"Since it is during the stages of invasion and eruption that communication of the acute exanthemata is chiefly to be dreaded, not during the process of desquamation, prophylactic measures should be undertaken with a view to this fact. Teachers should be carefully instructed as to the symptoms which precede the development of the

acute exanthemata, for it is on them, rather than on the medical inspector, however important his duties may be, that the chief burden of responsibility must fall. In city schools, when there is danger of an epidemic, it might be well for the inspector to see the children daily, but in the country this would be out of the question.

"The teacher sees the same children, occupying the same places, for a number of hours every day; he learns to know the appearance, habits, and ways of his pupils perfectly, and is quick to note anything at all out of the ordinary. If he has familiarized himself with the diseases to which children are liable by simple, oft-repeated observation, reinforced by instruction on important points, as it is perfectly proper to insist on his doing, without at all asking too much of him, he will seldom fail to detect the early symptoms of an acute eruptive disease.

" Whenever a teacher discovers a pupil with suspicious symptoms, pointing either to scarlatina or measles, his first duty is to send the child home, with a message explaining that the disease in question is suspected. The same precaution should be taken in all doubtful cases, for it is of practical advantage to look upon all such cases as genuine."

The matter is decided in a few days; if no further symptoms appear, the child may return to school, and resume his studies without any appreciable disadvantage from his short absence. Such pupils as actually develop the disease in question should not, as a rule, be readmitted until permission to that effect is given by a physician.

In country districts it would suffice, in my opinion, to require that a certain length of time should have elapsed, counting from the date when the disease first developed.

Von Kerschensteiner lays emphasis on the fact that his experience has shown it to be entirely practicable for teachers to be made responsible for the inspection of their pupils in respect to manifestations of the acute exanthemata. I have no doubt whatever that this is so, for, like most other practitioners, I have often known children to be sent home by their teacher on the appearance of the very first symptoms of infection.

When does it become advisable to close a school? Von Kerschensteiner takes up the case of measles, which allows of positive rules, its period of incubation being definitely established. The teacher, who, of course, must be familiar with the subject, will watch the children whose near-by seats brought them into closest contact with the sick ones with a special degree of care. If new cases should

develop about the tenth day, he should urge the authorities to close the school, as there would otherwise be great danger of a rapid spread of the disease. If the school be closed, on the other hand, the class-room epidemic will almost certainly be stamped out, though a third set of cases may possibly be looked for.

Assuredly, in this instance we are standing on firm ground. But not so, unfortunately, in respect to scarlatina, the incubation period of which is uncertain, a circumstance which greatly adds to our difficulties. These are further enhanced by the much more prolonged duration of a scarlatina epidemic, which would cause a school to remain closed for several months if strict measures of precaution were to be fully carried out. If the disease appears in severe, virulent, epidemic form, however, the danger for its victims is so great that it seems best to sacrifice every other consideration in order to prevent its spread. It is wisest, in my opinion, to judge each case on its own merits, and decide to close or not to close the school accordingly. A general rule, as applied to scarlatina, does not seem advisable.

The fundamental principles of the **treatment of acute exanthemata** still call for brief mention. They do not differ from those applicable to acute infectious diseases in general.

Negatively considered, the measures first in the order of condemnation are those belonging to an earlier day, when it was the custom to envelop the patient in thick coverings for the purpose of drawing out the rash to the skin and thereby ridding the body of the poisons circulating in it. Many a life, according to all accounts, has been sacrificed to this heating process.

The same can be said of antiphlogistic methods, which were chiefly concerned with blood-letting; and of the depleting method, in which emetics and cathartics were relied on. Nor was the excitant treatment, introduced by Brown, any less injurious.

Our object should be to avoid treatment of individual symptoms unless there is reason to fear that they may become dangerous, to keep the patient as well nourished as possible, and to guard his physical strength in every way, and, lastly, to relieve his suffering in so far as this lies in our power.

MEASLES.
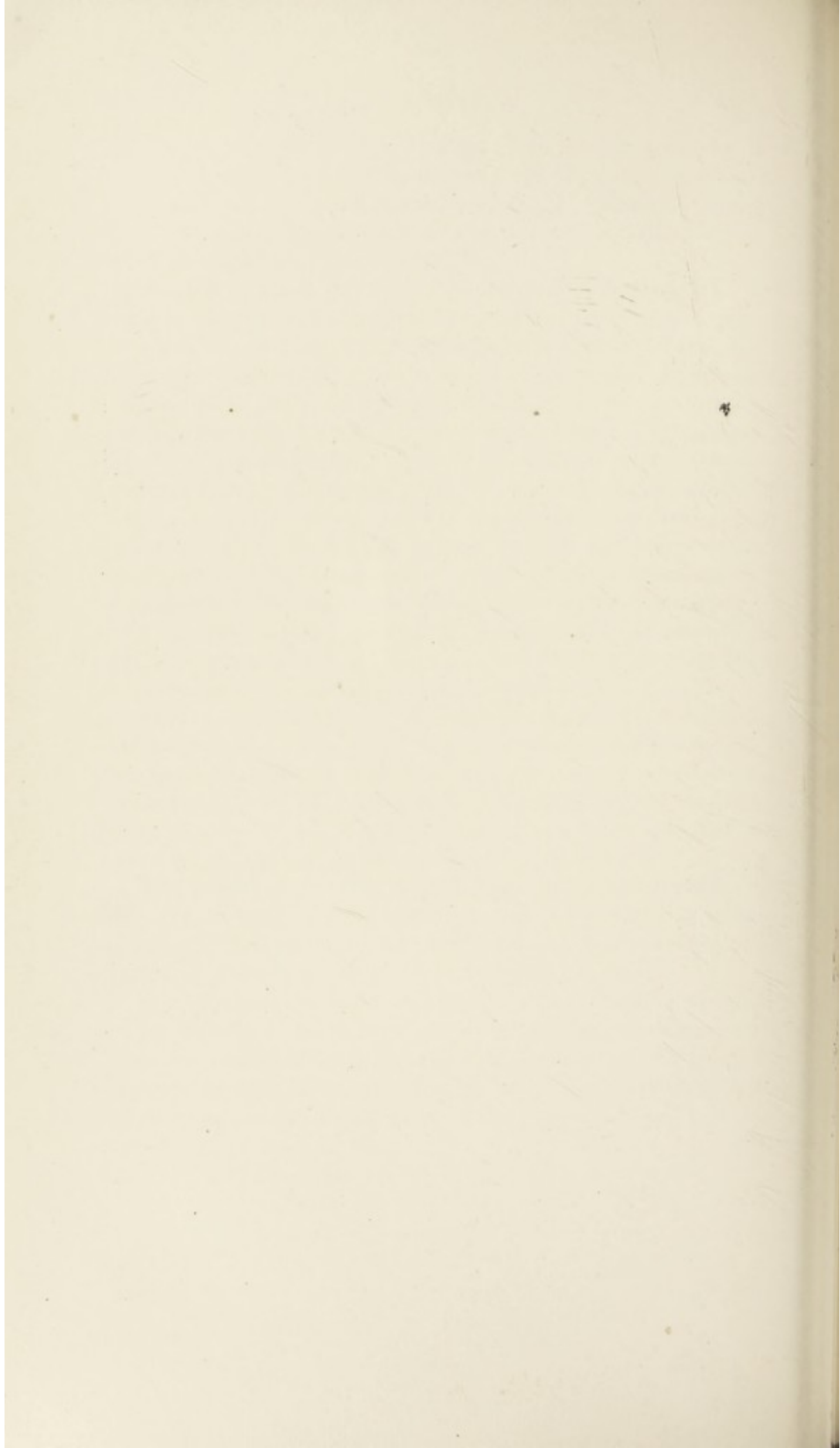
MEASLES.

ETIOLOGY.

THE fact that we have no certain knowledge as to the antiquity of measles was referred to in the introduction. Wide-spread outbreaks of the disease may possibly have occurred in early ages, but reliable data on this point are not obtainable, nor does the study of ancient records enlighten us as to its place of origin. That the disease originated somewhere is certain, for if we accept living organisms as the causative agents of infectious processes, we are forced to apply the laws governing all living matter to them also. Since we altogether exclude the possibility of spontaneous generation, it is, of course, understood that the general denial covers living germs of disease; we must still consider, however, that they may represent the product of evolution from previously existing organisms. This gives a different form to the question, but does not alter its substance.

What we do know is that measles have appeared in epidemic form ever since the eighteenth century, and have been spread by the contact of human beings with their kind.

Communication of Contagion.—The point of chief importance in the etiology of the disease lies in its transmission from man to man; everything else is comparatively unimportant and meaningless. There is one exception, however, and that is in respect to susceptibility. Almost every individual is liable to an attack of measles; thus the germs, whenever introduced into a community, are sure to find a favorable medium for their development. The only immunity, therefore, which the individual can expect is that afforded by an attack of the disease itself, which, though very effective, is still not always absolute, since repeated attacks are sometimes known to occur.

Of the many histories of epidemics which have been written, I will select for reference here the one by Panum, whose researches show him to be keenly observant and at the same time exceedingly matter-of-fact. He describes an epidemic of measles in the Faroe

Islands. The facts which he collected form the basis of our knowledge of the disease. Very valuable supplementary work has been done by E. M. Hoff, now of Copenhagen, who at one time held an official position as surgeon at the Faroe Islands, where in 1875 he had occasion to observe an epidemic of measles.* There were no cases of measles on these islands from 1781 to 1846, when the disease was carried there from Copenhagen, attacking more than 6000 of the 7782 inhabitants. The course of the epidemic was easy to trace, for the reason that the people were cut off from all contact with seafaring folk by the workings of a commercial monopoly, except with the crews of the boats in the service of the Danish government, which alone took charge of the trade with the outer world. The matter was further simplified by the comparative isolation of the different communities, which, because of the mountainous character of the islands, were confined to the valleys lying here and there along the coast. The strong currents running in the straits between the islands added a certain amount of danger to the difficulties of communication. Hence every occasion of contact with the inhabitants of other villages was generally known, and noted by everybody as an event of special interest. This was particularly the case during the measles epidemic, for the disease was greatly feared, and outside intercourse avoided. If any such took place, however, it was carefully kept in mind, so that exact details of the circumstances could be obtained a long time afterward.

Panum visited 17 of the 20 islands of the group in something over four months. "It is evident," he says, "that the opportunities for observation which I enjoyed were favorable to a rare degree." Well, he certainly made good use of his opportunities! He presents the following facts:

The disease was introduced by a cabinet-maker who had visited friends sick with measles shortly before leaving Copenhagen. He himself developed the disease after arriving at Thorshavn, the chief port of the Faroe Islands, communicating it in turn to his two most intimate friends. Then the epidemic began. In every case—Panum substantiates his statement by a number of convincing examples— contact, direct or indirect, with a measles patient could be shown to have taken place. It may as well be noted here—I shall refer to it in detail later on—that it was Panum who determined the length of the period between the date of infection and the outbreak of the eruption. He states it to be thirteen to fourteen days. Accurate

* "Sundhedskollegiets Aarsberetning," for 1876. I am indebted to the author for my acquaintance with this work.

knowledge on this point is, of course, most necessary for deciding whether, in a given case, the disease has or has not been contracted.

The following will serve as an illustration of how the contagion was transmitted by personal contact. The measles were carried to the village of Tjornvig by ten men, all of whom had been in contact with persons suffering from the disease on the occasion of a fishing expedition on the 4th of June. This was clearly proved, as was also the fact that the ten men had not met except on that one occasion, and had been in no other place where measles had broken out. The rash, in all ten cases, developed on the 18th of June.

The manner in which the contagion was introduced and spread, causing the epidemic of 1875, could also be clearly traced.

Since 1846 there had been only one epidemic, that of the year 1862, which was entirely confined to one place, and had affected only 25 persons. In 1875 it became known that measles were epidemic on the Shetland Islands, and as there was considerable trade carried on by the Shetland fishermen, whose boats were frequently seen in the Faroe harbors, sometimes, indeed, with measles patients on board, the introduction of the infection was generally feared. Nor was this long delayed. The first four Shetland fishermen who were landed sick at Thorshavn were, to be sure, so well isolated that no cases of measles were contracted from them, but the harm had already been done in another way.

On the 18th of May an English fishing smack anchored at Vestman-havn—a small port—and on the 31st the measles eruption broke out on the seven-year-old son of a customs officer whose house had been visited by some of the crew. In Thorshavn—the chief port—a clerk in a store was taken sick on May 7th. He was unable to say positively whether he had been in contact with any of the crews of the vessels which had lain there at anchor two weeks before. At any rate, the epidemic spread from him. He had been at work on the 7th and 8th of May and had served a large number of customers.

On the 9th of May his physician found the rash in full bloom. Between the 20th and 23d of May about 20 persons developed measles in the town of Thorshavn, while one person was taken sick with the disease in each of 6 separate villages. All of those affected had come in contact with the sick clerk on the 7th or 8th of May. The introduction of the epidemic into some of the more distant islands of the group was definitely traced to this source. I must content myself with these few examples, of which the article referred to contains a large number.

The epidemic continued to spread, by personal contact, until 1123 cases of the disease had occurred.

From a negative standpoint, too, the Faroe studies are of great interest. Panum states positively that " Quarantine is beyond a

doubt the most reliable measure for preventing the spread of measles."
Even in case of a house in an infected village, the family found it
possible to keep out the disease by avoiding any contact with the
other villagers, and it was still less difficult to exclude contagion from
a whole village by isolating it. About 1500 of the inhabitants, who
tried this plan on their own initiative, remained free from infection.
At the time of the epidemic of 1875, the authorities succeeded, with
the assistance of the people, in maintaining a quarantine which
entirely sufficed to protect a considerable number of the islands from
the disease.

In an exceedingly well-written report of an epidemic at Hagelloch
(a village near Tübingen) Pfeilsticker * tells, too, how a peasant
found it possible to keep his three children free from contagion
throughout by systematically isolating them at home as long as the
disease prevailed. Such a wide-spread epidemic of measles may
occur as to warrant the use of the term pandemic in describing it.
Hirsch,† for instance, speaks thus of the years 1834 to 1836, during
which period the greater part of northern and middle Europe was
affected, and 1842–1843, when the measles plague spread through
Switzerland, France, Holland, Germany, and Russia.

Epidemics, confined to small districts, break out at intervals,
which vary in length in different places. Attempts have been made
to show a regularity in the periodicity of outbreaks in a given locality,
though not necessarily according with that of any other locality.
Such calculations are entirely fallacious.

In my statistics, for instance, which are very extensive, we find the
following figures for the city of Tübingen, representing the intervals
between epidemics:

$$
\left.
\begin{array}{ll}
138 & \text{weeks} \\
144 & \text{``} \\
201 & \text{``} \\
184 & \text{``} \\
131 & \text{``} \\
63 & \text{``}
\end{array}
\right\} \ldots\ldots\ldots 6 \text{ epidemics during the years 1874 to 1893.}
$$

In the neighboring village of Lustnau these intervals were noted:

$$
\left.
\begin{array}{ll}
208 & \text{weeks} \\
175 & \text{``} \\
138 & \text{``} \\
211 & \text{``}
\end{array}
\right\} \ldots\ldots\ldots\ldots 4 \text{ epidemics in the years 1876 to 1893.}
$$

* "Beiträge zur Pathologie der Masern," u. s. w., Tübingen, L. F. Fues, 1863,
p. 10.

† *Loc. cit.,* p. 114.

When the intervals between epidemics vary all the way from sixty-three to two hundred and one weeks, it is plain that a regular time of recurrence cannot be spoken of.

Measles never entirely die out in large cities, but persist as an endemic disease, which occasionally bursts forth in epidemic form. It will not do to attempt to explain the outbreak of epidemics or pandemics in a large city by assuming the germs to have been brought from elsewhere, thus giving them an opportunity to prey upon a susceptible community. Such a theory may be justified when applied to districts which have been entirely free from cases of the disease for a long time, and may therefore suffice for country communities and small towns, but other causes must be sought for in more populous places. The presumption lies near, that the poison at such times is more effective in its action, either by reason of an increase in the number of germs present or because their individual virulence is intensified. In all probability both causes are at work together, for one of the first signs of additional vitality—and in assuming the existence of a contagium vivum its vitality naturally comes into question—is surely an increased capacity for propagation. (See p. 252.)

In studying all infectious diseases, it is necessary to consider general meteorologic and climatic conditions with a view to discovering a possible relation between fluctuations in one or more of the factors controlling them and the appearance or disappearance of a given disease. No such relation is demonstrable in the case of measles.

The contagium of measles is distributed over almost the entire face of the globe; it is known alike in the tropics and in high northern latitudes, a fact which alone speaks for its great independence of climate. Hirsch, who emphasizes this point, concedes nevertheless a certain influence to the seasons by stating that the majority of measles epidemics occur during the cold months.

Among 530 epidemics* occurring in the temperate zone of Europe and North America, 339, or 63.7%, were observed during the colder, and 191, or 36.3%, during the warmer months of the year.

Among 30,836 fatal cases of measles in England and Wales (during the years 1838 to 1840 and 1849 to 1853) the proportions reported for the different months were as follows:

January–March:	8106	26.3%	July–September:	6610	21.4%
April–June:	8907	28.9%	October–December:	7213	23.4%

*Taken from Hirsch, *loc. cit.*, p. 116.

For purposes of comparison, I will give the figures for a city of medium size, Basel, which during the period covered by the data in question increased in population from 18,933 (in 1824) to 51,700.* There occurred, in all, only 356 fatal cases of measles, distributed, as to season, as follows:

January–March:	92	25.8%	July–September:	38	10.7%
April–June:	183	51.4%	October–December:	43	12.1%

If, now, we apportion the cases with respect to the average temperature of the different months at Basel, the figures appear thus:

During the 6 colder months	188	52.8%
" " 6 warmer months	168	47.2%

All the above statistics tend to prove a slight, but only a very slight, influence on the part of the cold season. This is best seen with reference to the inception of the epidemics, eight of the eleven which fell to the share of Basel beginning during the colder, and only three during the warmer, months of the year.

The explanation which so naturally presents itself, that the spread of the contagion is favored by the shut-in life of the winter, with the close contact which this implies, is contested by Hirsch, who points out that the influence of the cooler season is perceptible even in the tropics. Whether there is not some truth in the theory as applied to our conditions of life, however, must for the present remain undecided. The nature of the soil certainly has nothing whatever to do with the dissemination of measles.

As far as individuals are concerned, the fact of prime importance is the almost absolutely universal susceptibility of mankind to the contagion of measles, which all races share in equal degree. This last-mentioned point is demonstrated by the instances of transmission of the disease to tribes which had previously remained exempt.

Many physicians are inclined **altogether to deny the possibility of immunity,** advancing arguments in support of their position, which, although very forcible, do not seem to me to be quite convincing. B. Bohn,† for instance, writes as follows:

1. It cannot be positively proved that a person declared to be immune, and who passes through an epidemic without contracting the disease, has not really suffered from measles in childhood. The attack may have been so light as to be overlooked at the time.

2. It is conceivable that what appears to be immunity is really nothing but a lack of opportunity for infection.

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*From the very carefully prepared article by E. Hagenbach, "Epidemiologisches aus Basel," "Jahrbuch für Kinderheilkunde," new series, vol. IX, pp. 46 *et seq.*

†"Ueber Morbilli adultorum," *Deutsche med. Wochenschrift,* 1888, p. 332.

These possibilities should undoubtedly be borne in mind, but the assumption, on the other hand, that a person remaining exempt must have had measles when a child, the attack having simply not been noticed at the time, is certainly no less unsupported by evidence than the one it is meant to supplant.

The second argument seems to me less easily met, if broadly interpreted. It is particularly true of the acute exanthemata that the virulence of the poison producing the disease is a varying factor, on which its ability to develop within the human body largely depends. If we admit the truth of this statement, it follows that although certain individuals may be immune to the infectious organisms in the strength which they ordinarily possess, it cannot be shown that such immunity would be maintained were their virulence to increase.*

Individual susceptibility may also be greater at one time than at another, although such variation is less frequently observed. Hoff tells of three men, who acted as nurses during an epidemic in 1846, remaining exempt, yet who took the disease in 1875.†

The questions thus raised are, to my mind, of too little importance to make it worth while to spend much time in answering them. Practically, at all events, we have to look upon almost everybody as susceptible.

To what extent such a view is sustained by statistics is strikingly illustrated in a table gotten up by Hoff. This is especially valuable for the reason that it embraces all ages and that the figures are perfectly reliable. I therefore give it complete:

	Number of Inhabitants.	Attacked by Measles.			Not Affected	Those Remaining Unaffected Lived	
		Epidemic of 1846.	In 1862 or at some other time.	Epidemic of 1875.		In the same house with measles patients.	In house where there was no measles patient.
Thorshavn	930	417	1	506	6	1	5 ‡
Vestmanhavn	315	111	22	139	43	..	..
Kollefjord	223	92	..	120	11	1	10 §
Sandwaag	166	35	2	117	12	5 in 1 house	7 ‡
Total	634	655	25	882	72	..	..

* Compare the chapter on measles by Thomas, in von Ziemssen's "Handbuch der speciellen Path. u. Ther.," Leipsic, Vogel, 1877, vol. ii, Pt. 2, p. 53 of 2d ed.

† See also a case of Pfeilsticker, *loc. cit.*, pp. 15, 16.

‡ In 3 separate houses.   § In 5 separate houses.

A partial, temporary immunity is universally conceded. This covers the first five months of infancy, the number of very young infants affected during an epidemic being a comparatively small one.

Satisfactory statistics on this point are lacking, and would probably be difficult to gather if all the conditions bearing on the question were to be taken into consideration. Of the latter, I will mention only one, on which Thomas very properly lays stress—namely, the comparatively slight opportunity for contagion afforded so young an infant if it happens to be the first child in the family.

The only statistics which will bear close inspection are those compiled by Pfeilsticker * from records of an epidemic which he himself carefully followed. The little village of Hagelloch, near Tübingen, had a population of 577 in 1861. The last epidemic of measles had occurred in the winter of 1847–48. There were 197 children under fourteen, of whom 185 contracted the disease; among the older inhabitants only 3 were affected, all of them fifteen years old, who, according to their parents, had not previously had the measles. The ages of the very young children who took the disease ran as follows:

AGE.	TOTAL NUMBER OF CHILDREN OF THIS AGE.	NUMBER WHO CONTRACTED DISEASE.	NUMBER REMAINING UNAFFECTED.
Months.			
2	2	—	2 (1 was isolated).
3	2	—	2
4	2	—	2
5	1	—	1
6	2	2	—
7	3	3	1
8	1	1	—
9	1	1	—
10	3	3	—
Years.			
1	14	14	—
2	18	16	2 (1 was isolated).

As a rule, such tables give only the number of children who contract the disease at specified ages; their value is therefore distinctly limited. As an example, I will cite statistics reported by Bartels.† There had been no epidemics of measles in Kiel since 1853, until that of 1860, which began in the month of March. The recorded cases numbered 673, being proportioned as to age as follows:

Under 1 year	31	5.4%
Between 1 and 5 years	274	47.8%
" 5 " 10 "	226	39.4%
" 10 " 15 "	32	5.6%
" 15 " 20 "	4	0.8%
" 20 " 30 "	3	0.7%
Over 30 years	3	0.7%

* *Loc. cit.*, p. 14.

† Bemerkungen über eine im Frühjahre 1860 in der Poliklinik in Kiel beobachtete Masernepidemie u. s. w., *Virchow's Archiv*, vol. XXI, pp. 26 *et seq.*

As early as the latter half of its first year the child begins to show an increasing susceptibility to measles, and by the time it enters its second year this is fully developed. It is useless, therefore, to discuss comparative susceptibility with regard to the following years, the contraction of the disease depending entirely upon the opportunities of infection. The people of the Faroe Islands had been free from it for a period, first, of sixty-five years, afterward for one of twenty-nine years, but when the epidemics broke out no one exposed to it escaped, no matter what his or her age might be. Panum[*] states that, as far as he knew, not a single one of those still living in 1846 who had been protected by quarantine in 1791 failed, when exposed to the contagion of the second epidemic, to be taken with measles. Hoff makes a similar report, except that he mentions a very few exceptions. In places where measles break out at shorter intervals, such a state of affairs cannot, of course, be observed. Cases of measles occurring after childhood are there usually to be attributed to the fact that the persons in question have never before happened to come in contact with the contagion. B. Bohn, of Königsberg, for instance, had among a total of nearly 800 measles patients, 34 who were over fifteen years of age. Forster, of Dresden, had 17 adults in 400 cases.

It is maintained by some physicians that a certain degree of immunity is afforded by chronic nervous diseases, especially those affecting the brain. I do not believe this to be so, at least I know nothing in the literature on the subject which properly substantiates such a claim. Nor do I consider it really proved, to say the least, that such nervous affections bring about irregularities in the course of the disease.[†] These are, at all events, confined to the temperature curve, in which certain variations from the normal do occasionally have to be taken into consideration.

We are next led to inquire whether the immunity conferred by one attack of measles is absolutely to be relied on.

Panum states that he has never met with an instance of second attack; Hoff, too, is inclined to doubt that such occur, and criticizes the accounts given him by two persons of what they believed to be second attacks. It has been definitely shown, nevertheless, that the disease can be contracted more than once. Maizelis[‡] has collected all the reported cases, numbering in all 106; of these, 103 concerned

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[*] "Die nosographischen Verhältnisse Dänemarks," u. s. w., *Verhandlungen der physikalisch-medicinischen Gesellschaft in Würzburg*, Erlangen, Enke, 1852, vol. II, p. 293.

[†] See Pfeilsticker, *loc. cit.*, pp. 18 and 49.

[‡] "Ueber die durch das Ueberstehen von Infectionskrankheiten erworbene Immunität," *Virchow's Archiv*, vol. CXXXVII, pp. 468 *et seq.*

second attacks, while 3 (?) purported to represent a third attack. Recurrences—that is, attacks which occur in connection with and shortly subsequent to the primary outbreak—are not included in this collection. Third attacks are exceedingly rare, at any rate; except for the very brief account of a case given by Streng[*] we have only the history reported by Hennig[†] of a patient, a woman, whom he himself attended during two attacks of measles, in her thirty-second and thirty-third years respectively, who in all probability had already had the disease in her thirteenth year.

Even one repetition is uncommon, as is apparent from the comparatively small number of instances on record. Some of these, too, may be explainable by a mistake in diagnosis, in connection with rötheln in particular. Other infectious processes may also, I think, closely simulate measles; if too much weight is laid on the appearance of the eruption, a mistake is liable to occur.

The following is a brief history of one of my own cases:

Case 8.—Anna D. was taken sick with measles in 1893 (during an epidemic). Her five-year-old brother was brought to the hospital on May 27th, with a well-developed rash; she herself followed him on June 10th, the rash showing only on her face. Her other symptoms consisted of red blotches on the soft palate, conjunctivitis, coryza, and bronchial catarrh. There was no perceptible enlargement of the spleen; the intestines were not affected, and there was no albumin in the urine. The rash developed as usual, faded gradually, and had disappeared by June 16th. The attack was, on the whole, a light one, as the temperature chart indicates.

Fig. 35.—B 1, Outbreak of eruption; B 2, no further fever.

On the 3d of March, 1894, the child was again admitted to the hospital. The mother stated that a slight cough had persisted since she recovered from the measles, which had gradually increased, also that the child's skin had frequently felt hot. On examination, we found an area of consolidation in the upper lobe of the left lung, which became more clearly marked by the end of the first week; also a general bronchitis involving the large and medium-sized tubes. On the left side the bronchitis gradually became more severe; the fever ran high (up to 40.6° C.—105° F.—per rectum), with well-marked intermissions (37° C.—99° F.). A diagnosis

[*] "Ein Fall von Masernrecidiv," *Deutsche med. Wochenschrift*, 1892, p. 1084.

[†] "Exanthematica," "Jahrbuch für Kinderheilkunde," new series, vol. VIII, pp. 417, 418.

was made of tuberculosis. The temperature continued to be taken three times a day (at 8 A. M., noon, and 6 P. M.), the record showing the temporary fluctuations commonly noted in a case of slowly healing tubercular lesions. The record for November 3d read as follows: A. M., 38.1° C. (100.5° F.); P. M., 38.3° C. (101° F.); for November 11th, A. M., 37.9° C. (100° F.). The fever had not reached 39° since the evening of July 7th.

November 13th: It is possible that the child has been exposed to measles, of which cases are being reported in the neighborhood, though not in the city proper. From the 14th on, she complained of not feeling well, had fever, and was constipated, the latter symptom being difficult to overcome.

November 22d: A rash has come out on the patient's left arm in the form of slightly raised, rose-red spots, the size of lentils, and disappearing on pressure. On the 23d it covered the chest, abdomen, and lower extremities, the blotches coalescing in places.

By November 24th the rash had also spread to the face and head. Other symptoms also began to manifest themselves—namely, coryza,
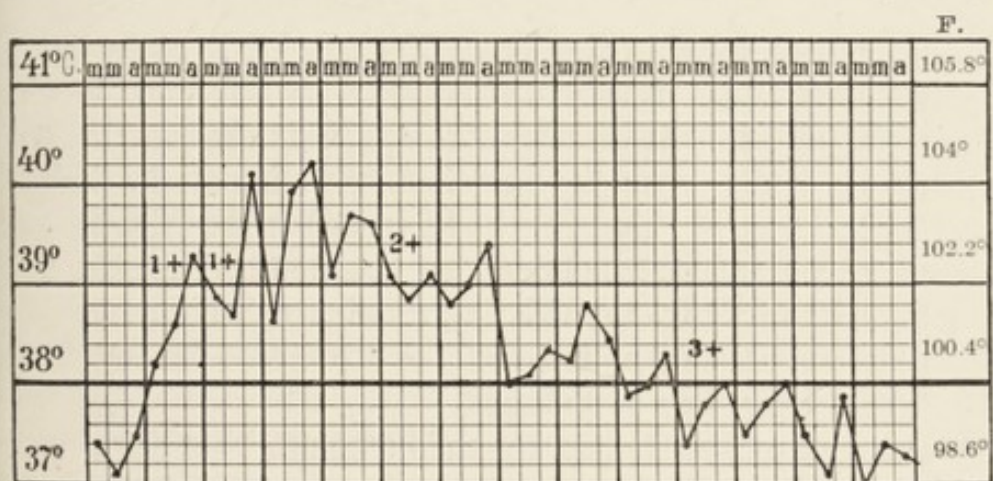
Fig. 36.—1+, Onset; 2+, outbreak of eruption; 3+, eruption almost entirely faded.

mild conjunctivitis, red blotches on the soft palate, angina, and a slight bronchial catarrh. By the 29th the rash had faded and a fine scaly desquamation supervened. Recovery proceeded uneventfully, but was followed by the old condition, with occasional unexplained rises of temperature. The temperature chart, covering the period of interest, is here appended.

I am, for my part, convinced that we really have to do with a second attack of measles in this case, but must admit the occurrence of certain irregularities the second time, to which exception may very properly be taken. I refer to the manner in which the eruption spreads and the course of the fever. Whoever is familiar with the subject will comprehend these points without further explanation; he will, however, find it difficult to draw a positive conclusion as to the case.

It is an interesting fact that a pregnant woman who contracts measles may communicate the disease to her unborn child. The poison must therefore be able to pass through the placenta. About twenty cases have been reported in all. It is presumed that the child

becomes infected very soon after the disease organisms have attacked the mother, since the disease presents the same stage of development in mother and child at the time of the latter's birth. Not only has the rash been found fully developed, but cases are also on record in which both were suffering from the so-called catarrhal stage, this being followed in due season by the outbreak of the rash.* Synchronism is not an absolute rule, however. Franz Mayr † tells of seeing measles break out in an infant one week old, though he omits, by the way, to mention the facts relative to the mother's attack. Just what this case and others like it really point to remains uncertain.

In this connection we again find Hoff's investigations very helpful. He states that "without exception, everybody born in the year 1846 whose mother, according to her own statement, and as affirmed by comparison with the church records, contracted measles during her pregnancy, was attacked by the disease, if exposed to it, at the time of the epidemic of 1875. It appeared to make no difference in what month of her pregnancy the mother had happened to be when she took the measles. While ordinarily, therefore, there is not the slightest ground for believing the contagion to be carried to the fetus through the placental circulation, it is interesting to note that one child born during the epidemic broke out with the rash when only eleven days old, —two days sooner than would normally be expected,—the rash, in the mother's case, being then at its height."

It is, of course, possible that the child contracted the disease soon after birth, but it can also be presumed, and perhaps with more reason, that it was infected by its mother during the last few days of intrauterine life.

The specific organism which causes measles is not yet known to us.

Two reports of investigations have lately been published, in which very different results are described.

Doehle ‡ examined the blood of eight measles patients, and found peculiar organisms both in the plasma and red corpuscles. These meas-

* A. Ballantyne, "Congenital Measles, with Notes of a Case," *Archives of Pediatrics*, April, 1893. This reference is taken from an abstract in the "Jahrbuch für Kinderheilkunde," vol. xxxvi, new series (1893), p. 406.

† "Beobachtungen über Masern," u. s. w., *Zeitschrift der k. k. Gesellschaft der Aerzte zu Wien*, 1852, 8th year, Pt. 2, p. 15.

‡ "Vorläufige Mittheilung über Blutbefunde bei Masern," *Centralblatt für allgemeine Pathologie und pathologische Anatomie*. Edited by Ziegler and v. Kahlden, Jena, Fischer, vol. iii, No. 4, p. 150 (February, 1892); and "Zur Aetiologie von Masern, Pocken, Scharlach, Syphilis," *Centralblatt für Bakteriologie und Parisiten-kunde*, Jena, Fischer, vol. xii, No. 25, p. 906 (December, 1892).

ured from ½ to 1 μ in diameter, showed a light margin and a dark center, were motile and provided with flagellæ. Doehle observed a number of other forms in addition, which, he thought, represented different stages of development of the same micro-organism. This he places in the class of parasitic protozoa.

Canon and Pielicke * look upon a bacillus which they have discovered in the blood as well as in the nasal and conjunctival secretions of measles patients as specific.

[In Lubarsch's serial work, "Ergebrusse der allgemeinen Pathologie," etc., fourth year, published 1899, the following review is given as to the various claims of investigators in regard to micro-organisms in measles:

Crajkowsky † obtained cultures in 19 cases out of 56 of the bacillus already described in 1892 by Canon and Pielicke. It stains with methylene-blue and eosin, and is often as long as the radius of a blood-corpuscle. Its habitat appears to be in the secretions of the nose and conjunctiva. Although this bacillus has been known since 1892, it has not yet been shown to be the cause of measles.

Other authors have demonstrated the presence of ameba-like, flagellated animal parasites in the blood and in the buccal and nasal secretions of measles patients. Behla ‡ reported such a find and also discovered the same organism in pigs which had a measles-like eruption. Barbier § failed to find micro-organisms in the blood of measles patients, although he found a germ like the Löffler bacillus in the conjunctival secretion of most of the cases studied. In the secretions from the mouth and nose, streptococci were chiefly found. Numerous observers have noted the frequent occurrence of this germ in measles, and Robet ‖ even regards it as the cause of measles. Dürck ** found the streptococcus, as a rule, in the pneumonia of measles. According to Hutinel,†† streptococcus pneumonia spreads very readily in a hospital ward from measles patients to their neighbors.

Arsamaskoff ‡‡ describes a bacillus which occurs in the blood, secretions of throat and conjunctiva, and pneumonia foci. Pure cultures were obtained on six occasions. Milk proved to be a spe-

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* "Ueber einen Bacillus im Blute von Masernkranken," *Berliner klinische Wochenschrift*, 29th year, No. 16, p. 317 (April, 1892)

† *Centralbl. f. Bakteriol.*, 1895.   ‡ *Centralbl. f. Bakteriol.*, 1896, xx, p. 561.

§ "Soc. méd. d. Hôp.," 1897, Feb. 20.   ‖ *Thèse de Paris*, 1896.

** *Deutsch. Arch. f. klin. Med.*, 1897, Bd. LVIII.

†† *Rev. mens. d. mal. d. l'enf.*, 1897.

‡‡ *Bolnitschnaja Gaseta Botkina*, 1898; *Centralbl. f. Bakteriol.*, 1899, xxv, 831.

cially good culture-medium, for the germs kept alive therein for weeks. All attempts to inoculate animals proved fruitless. The bacillus was small, in length about half the diameter of a blood-corpuscle, and three-fourths as wide as the typhoid bacillus.]

Under these circumstances it is well to determine as far as possible **how the unknown poison is spread.**

The first question to be answered is, Are we justified in assuming a definite period to intervene between the time when the measles poison enters the system and the moment when it begins to take effect? The best standard of measurement to apply to this period has been found to be the number of days from the date of infection to the outbreak of the rash.

This represents, then, the sum of the two factors—period of incubation and catarrhal stage (better termed enanthemic stage). While the duration of either of these two periods, taken separately, is liable to vary quite considerably, their sum remains constant. The longer the law formulated by Panum is subjected to the test of practical experience, the more do we become assured of its reliability for the great majority of cases. To be quite sure of our position, we must count from thirteen to fifteen days from infection to eruption. Possibly the period might be even more definitely stated; in the published records of cases I fail to find a proper distinction between calendar days and days as reckoned from the hour of exposure, and it is the latter, of course, which are to be considered.

It must not be forgotten, though, that this rule has its exceptions. By this I do not mean the apparent exceptions, where it is really only the memory of the sick ones which is at fault, as Panum points out so forcibly; but we know that living beings taking a contagion from other living beings are not governed—at least as far as we can ascertain—by inflexible rules such as can be applied to the force and frequency of the blows of a steam-hammer.

It may be that the development of some other infectious process in conjunction with measles exerts a certain influence on the period in question, as is claimed by several observers,* but our knowledge on this point does not permit of positive statements. If we will judge the so-called exceptions properly, we must bear in mind a source of error, from which we can easily draw false conclusions—namely, the fact that the rash may at first be very scanty, or may develop in successive crops. It is quite possible, therefore, to overlook it for a time, and to assume, when a little later on it becomes more apparent, that it has

* Compare Thomas in v. Ziemssen's " Handbuch," p. 47.

then just broken out. Such a mistake is all the more likely to occur if the eruption, instead of appearing first on the face, as we expect it to do, chooses a part of the body usually kept covered.

The convincing statistics placed at Panum's disposal by the exceptionally favorable circumstances attending the epidemics in the Faroe Islands cannot be matched by those obtained in any other locality. Hoff, and another physician who was also there in 1875, Petersen by name, cite a number of equally valuable cases. The latter, for instance, tells how the measles were carried to the outlying village of Gjov by a young man who had left Thorshavn, where the epidemic was in full force, on the 9th of May. The rash in his case broke out promptly on the 23d.

Data gathered under less favorable conditions can be relied on with varying degrees of certainty. Whoever is inclined to be skeptical will point out the impossibility of proving beyond a doubt that a measles patient could have contracted the disease only at the time and place named by him.

Even if the case reported by Rilliet,* which certainly seems well substantiated, should also be discredited by insistent skeptics of this ilk, the fact remains that the figures established by Panum have invariably been confirmed by every careful observer who has watched the course of one of the almost countless epidemics recorded since that time. Many a sporadic case, too, of apparently unaccountable origin, has been traced to its source by the help of this definite time-gage.

In comparison with the immense number of confirmatory reports we find but few giving different results. Among the latter is one by Dr. Tufnel,† describing the case of a young soldier, who, after forty-five days of solitary confinement, entirely cut off from communication with the outer world, developed measles, in spite of the absolute impossibility of the contagion having been brought to him during that period. The diagnosis was confirmed by another physician, but was attacked, nevertheless, by a colleague during the discussion (?) following the report of the case. Records of single cases like the above are of little value, in my opinion, because it is impossible to feel quite sure of all the points involved.

Some light may be thrown on several of the questions under discussion by the records of attempts to inoculate healthy persons with infectious material from measles patients. The facts are as follows:

Francis Home, of Edinburgh, states that in 1758 he made use of the

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* Barthez and Rilliet, "Traité clinique et pratique des maladies des enfants," Paris, 1854, G. Bailliere, 2d ed., vol. iii, p. 297.

† *Dublin Journal of Med. Science*, July, 1872. Referred to in "Jahrbuch der Kinderheilkunde," new series, v, 1873, p. 186.

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blood of persons suffering from the disease, taking it from a small incision in the epidermis between the blotches, choosing just the day when the eruption was beginning to fade, in the thought that the poison then passing into the blood would be at its strongest. He caught the blood on bits of muslin and laid one on either arm, where he allowed it to remain for three days. He inoculated twelve children with measles by this method, and in most instances with success, the disease appearing, however, only in mild form.

In addition, he took small pieces of muslin, moistened them with the nasal secretion of children sick with measles, and placed them in the noses of healthy children, but with negative result.

F. Home is quite generally looked upon as the first to perform successful inoculation experiments with the blood of measles patients, the fact that he did so at so late a stage of the infection being a special point of interest. It would seem, however, that his statements are to be taken with several grains of salt. Thomassen à Thuessink* relates that while attending Home's clinics in the Edinburgh Hospital in 1784–85 he was often doubtful of the value of his experiments, very frequently failing to see the results which were afterward reported. And further: "Many disbelieve to this day that Home really carried out his inoculation experiments in 1758, since older practitioners, living in Edinburgh at the same time, such as Profs. Black, Duncan, Cullen, and Gregory, had heard nothing of them, as they themselves have told me." This doubt in Thuessink's mind led him to persuade his friend, Dr. Themmen, to repeat the supposed experiments (in 1816). The latter did so on five different occasions, using blood taken when the eruption was at its height, "conjunctival secretion," "perspiration," and "effluvia." His results were altogether negative.

Instances of successful inoculations are still occasionally reported; the original publications are, however, inaccessible to me, and the abstracts made of them are so brief as to be quite unsatisfactory. As, for instance, one by Speranza.† It does not seem to me necessary to enter into a discussion of these cases. Almost all the reports are incomplete, including that dealing with the inoculations performed *en masse* in Hungary.

Katona‡ gives an exceedingly brief account—it does not quite

* "Abhandlung über die Masern." Translated from the Dutch by Dr. C. Doden, Göttingen.

† *Journal der praktischen Heilkunde.* Edited by C. W. Hufeland and E. Osann, 1827, vol. IV, p. 124.

‡ "Nachricht von einer im Grossen erfolgreich vergenommenen Impfung der

cover two octavo pages—of 1122 inoculations which he performed on as many people in 26 townships of the Borsoder Comitates: "When the rash was at its height, he would open one of the little vesicles, dip his needle into the fluid, which was mixed with blood, and proceed at once to inoculate, just as in vaccination. Sometimes he used the conjunctival secretions. A red areola would develop around the point of inoculation, and then gradually disappear, so that the latter could soon no longer be distinguished. The inoculation was followed on the seventh day by fever and the usual early symptoms of measles, the eruption usually breaking out two or three days later, that is, on the ninth, or at the latest on the tenth, day after inoculation, the disease running a regular course, though the symptoms were much milder than usual. The temperature fell to normal, as a rule, by the fourteenth day after inoculation; the rash was also fading and desquamation beginning at the same time. Often, too, there was a slight diarrhea. The subjects of the experiments were regarded as convalescent by the seventeenth day after inoculation, and the seventh or eighth after the outbreak of the rash. In two instances the rash did not develop until the thirteenth day."

As far as I can learn, this is the only report made by Katona.

Franz Mayr's accounts of his own experiments show some strange discrepancies. In his first report, published in 1852, he states that he inoculated from measles papules during two epidemics, on two and four occasions respectively: "A characteristic measles rash developed within a given time in all these cases."[*]

Nineteen years later we find a remark by the same author to the effect that his inoculation experiments with blood during those same epidemics had given a negative result.[†] As he unquestionably has reference to the same cases, the contradiction can only be explained on the assumption of a printer's error.

Mayr's experiments in transmitting the disease by taking nasal mucus from a patient during the eruptive stage and introducing it into the nasal cavities of two healthy children are of greater interest. The rash broke out on both children on the evening of the thirteenth day, and both remained exempt during an epidemic which occurred two months later.

His attempts to induce the disease by means of scales of epidermis

Masern während einer epidemischen Verbreitung derselben," *Oesterreichische medicinische Wochenschrift* (als "Erganzungsblatt der medicin. Jahrbücher des k. k. österr. Staates"), 1842, No. 29, pp. 697 698.

[*] *Loc. cit.*, p. 12.   [†] See Virchow's "Handbuch," *loc. cit.*, p. 106.

obtained from measles patients in the desquamative stage — the method is not given—proved unsuccessful.

We also have a report of later date, by Dr. Hugh Thomson,* concerning two experiments of his own. He applied vesicants to the skin close to patches of measles eruption, and used the serum thus obtained in inoculating two children. This he did on two occasions, both times with a negative result. Through some misunderstanding, the inoculation experiments of Home, which Thomson describes in detail, are referred to in German medical literature as having been performed by Thomson himself.

It is evident that the data at present at our disposal do not warrant positive conclusions—we must await the results of further experimentation.

When is the contagion of measles communicable?

The period of contagiousness begins, in all probability, with the first catarrhal symptoms; it lasts through the eruptive stage, and draws to an end soon after desquamation commences, only a minor degree of contagiousness being manifested during the latter process.

Generally speaking, it may be said that a susceptible individual will contract measles the first time he comes in contact with an infected person who is in a condition to communicate the disease. The length of time elapsing before the rash appears—in other words, the period of incubation plus the enanthemic stage—remains the same at whatever stage of the disease the contagion may have happened to be transmitted.

It has been positively proved that infection can occur during the pre-eruptive stage.

Panum† relates the following case: A young man developed the eruption on the 9th of June; on the 26th of May he had been in close contact with an infected person—had slept in the same bed—on whom the rash did not break out until "several days" later. The case of the clerk at Thorshavn, reported by Hoff and referred to above, appears equally conclusive. Petersen, too, who acted as district physician during the Faroe epidemic of 1875, tells of a school-teacher who continued to teach "up to the moment when the rash broke out," and so gave the disease to all his pupils.

The facts to be gathered from a study of our own epidemics all

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* "Inoculation with Suggestions for its Further Application in Medicine, Especially in Mitigating the Severity of Measles," *Glasgow Med. Journal*, vol. xxxiii, pp. 33 *et seq.*, June, 1890.

† *Virchow's Archiv*, vol. i, p. 499.

seem to point to a similar conclusion. V. Kerschensteiner* gives certain interesting figures in connection with the Munich epidemic of 1855, which he had exceptionally fine opportunities for studying. In 34 out of 37 cases, which he himself carefully investigated, from ten to twelve days lay between the outbreak of the eruption in the infecting and infected child, while in two other cases there was an intervening period of fourteen and fifteen days respectively. One case in which only eight days appeared to have elapsed, von Kerschensteiner himself did not quite credit. Pfeilsticker† also found ten days to be the usual time from eruption to eruption. To this must be added the period covering the pre-eruptive symptoms, three or four days on the average, but varying anywhere from one to thirteen days (Pfeilsticker). If we therefore take the accepted period of thirteen to fifteen days intervening between the dates of contraction of contagion and outbreak of eruption as the basis of our calculation, we are obliged to go back to the catarrhal, pre-eruptive stage as the time when the disease was communicated in the above cases.‡

There is no doubt whatever of the contagiousness of the stage of eruption. The epidemics on the Faroe Islands alone furnished ample proof of this fact, so much so, indeed, as to make the Danish physicians who were active there at the time inclined to regard this stage as the chief if not the only one to be considered from the standpoint of contagiousness. Their observations do not entirely accord with those made in our own land. Hoff states, for instance, that in the towns where the epidemic was in progress the successive crops of cases broke out from thirteen to eighteen days apart. The intervening period could be definitely determined in respect to the first and second, and second and third crops; later on the opportunities for infection were too numerous to allow of any certainty as to time and place of contracting the disease.

Since the stage of efflorescence lasts about five days, the date of infection in the cases just referred to, if we again apply the rule as to the length of the period from contraction to eruption, must fall in this stage. Hoff speaks very positively on this point, considering it to be practically demonstrated that the communication of the contagion is referable to this stage only. Panum gives a less decided opinion, say-

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* "Das Incubationsstadium der Masern," u. s. w., *Bayerisches ärztliches Intelligenzblatt*, 1857, No. 9, pp. 103 *et seq.*

† *Loc. cit.*, pp. 39 *et seq.*

‡Whoever wishes to investigate the subject more fully will find in Pfeilsticker's work a careful analysis of all the points involved.

ing that it remains uncertain whether the catarrhal and desquamative stages are also contagious. Petersen openly admits the possible contagious character of the pre-eruptive stage, at least toward its latter part, but denies the occurrence of infection during desquamation.

It is, of course, useless to attempt to explain away these differences of opinion, since we cannot understand how they arose. The fact that the contagion during the Faroe epidemics actually was communicated in the catarrhal stage is shown by the instances cited above.

It is much more difficult to arrive at a definite conclusion in regard to the contagiousness of measles during the stage of desquamation.

Before the duration of the incubation period was known, it was quite natural to believe that the disease was communicated during desquamation, since new cases were seen to develop just when earlier patients were peeling. This somewhat naïve view has now been discarded, and the opposing one, that it is impossible for infection to take place at so late a stage, has come to be pretty generally accepted. Perhaps this is carrying it too far. Conclusive evidence is wanting, and the results of inoculation have been doubtful, to say the least. If we turn to our clinical experience for guidance, we find ourselves more in the dark than ever. Take, for example, the case of a child who is supposed to have infected another when desquamating. Who can decide whether the poison was really contained in the scales of epidermis, or whether the infective organisms of an earlier stage were still harbored on or about the child?

It must be admitted that it is very unusual for the contagion to be communicated at this time, if it happens at all. But I, for my part, do not like to assert that it is impossible. As a rule, susceptible individuals contract the disease quickly, and there is hardly any one who fails to come in contact with measles patients in a stage when it is known to be contagious. Little opportunity remains, therefore, for contracting it during desquamation, all who were liable having been infected earlier.

There is still another point to be considered. Desquamation does not take place all at once, but is a gradual process, the rash, as a rule, being still at its height on one part of the body, when it has already faded on another. Positive conclusions could, of course, be reached only if there were no more fresh spots to be found, and even then the poison contained in the parts of the skin which were first to fade might meanwhile have undergone considerable modification.

All these points seem to me sufficiently weighty to deter us from

giving an uncompromisingly negative answer to the question, Is the desquamative stage ever contagious?

This brings us to the question of the transmission of measles through third persons who themselves remain exempt. Another closely related point concerns its transmission by means of articles of common use.

Panum tells of two cases, one well substantiated, the other fairly so, which, it seemed, showed the contagion to have been carried by a doctor and a midwife respectively. The one runs as follows: During the epidemic a doctor was called to a distant village, thus far exempt and having no intercourse with the infected localities. He had to make the journey of four miles in an open boat, and, as it happened, on a stormy, rainy day, and to spend the night in the village. Fourteen days later measles broke out in the house where he had slept; that is, the eruption developed. Hoff, however, gives a different version of the story. The peasant at whose house the doctor stayed overnight, who, he says, was a most trustworthy man, has assured him repeatedly that probably several and certainly one of the boatmen who brought the doctor over, and who likewise spent the night in the village, had the measles themselves at the time.

The contagion, then, would appear to have been directly introduced by the boat-crew. It is strange that the witness in the case omitted to mention whether the supposedly infected men also slept in his house. Panum distinctly states that the disease first broke out in this house.

Panum's second case is more cautiously worded: "It was said" that the measles were carried to Midtvaag by a midwife who had been spending several days in another village, in the same house with measles patients, she herself having had the disease some time before at Copenhagen. "In all the houses where the midwife called, 'they said,' measles broke out about two weeks later, and the girl who did her washing immediately after her arrival was the very first to come down with the disease."

Of this Hoff says that the midwife had never been in Copenhagen, a fact which he had no difficulty in establishing, and could not, therefore, have had measles in that city. Further, he has been told by an old and very reliable man, in whose family the measles first appeared at the time, that, to his positive knowledge, the midwife was taken sick with measles while staying at Midtvaag. He even remembered her to have been so very ill that she was hardly able to travel to her own home. Hoff himself points out that tales of what happened

thirty years earlier cannot be considered reliable evidence, however trustworthy the witnesses themselves may be.

One thing is certain—none of the official reports of the measles epidemics on the Faroe Islands contains a single instance of the contagion having been conveyed by third persons or fomites. On the contrary, the physicians in charge state this not to have occurred, a point which they had been especially careful to observe.*

Von Kerschensteiner† brought up the question for discussion by the Munich Medical Society, and, in addition, called for reports from all sections of Bavaria. The opinions expressed were almost all negative; only a few physicians thought that they had carried measles home to their children. (See p. 221.)

In order to sift out the true from the false, the mass of evidence presented must needs be subjected to searching analysis, aided by accurate knowledge of local conditions. Take, for instance, the following story,—only one of many,—which was brought forward at the time the question was under discussion by the Munich Medical Society. How convincing it sounds! A student, on a trip to Jena, fought a duel and was thereupon put in the college " Carcer," where he was isolated and entirely cut off from outside intercourse. He had already spent over three weeks in Jena, where for more than a year no case of measles had occurred. On the second day of his arrest he received a letter from a friend who was sick with measles in Erlangen; nine days later he, too, was taken with the disease.

Now, in order to decide as to the merits of this tale, it is necessary to inquire into the conditions of " Carcer life " at Jena. I happen to have heard from Jena students that at the time when this case of measles-by-letter is supposed to have occurred—it must have been before 1882, since it was reported in that year—the students confined in the " Carcer " really led a very jolly life. This was put an end to some years ago, but I am assured by one of my colleagues who was a teacher at Jena for a long time that in those days isolation was a thing unknown to the inmates of the " Carcer." Two other instances of infection, conveyed by a letter and an etching respectively, are cited by Thomas,‡ who, however, does not attach much importance to them.

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* " Jahresbericht des Sundhedscollegium für Dänemark."

† (*a*) " Ueber die Vertragbarkeit der Masern, des Scharlachs und der Blattern durch dritte Personen," *Aerztl. Intelligenzblatt.* (*Münch. med. Wochenschr.*), 29th year, 1882, p. 413 *et seq.* Also (*b*) " Die Verbreitung von Masern, Scharlach und Blattern," " Vorträge über Gesundheitspflege u. Rettungswesen während der Hygiene Ausstellung zu Berlin," 1883. Ed. by Dr. Paul Börner.

‡ See v. Ziemssen's " Handbuch," *loc. cit.*, p. 41.

In opposition to the theory which holds that the contagion of measles is carried by third persons, von Kerschensteiner very properly points out that the children of physicians whose practice brings them into frequent contact with cases of measles cannot be shown to contract the disease any earlier than other children.

The following I myself know to be a fact: The large village of Lustnau is only a ten minutes' drive away from Tübingen, and almost all its inhabitants go to the Tübingen Policlinic when they wish medical treatment, yet repeatedly, when there were many cases of measles in the city, the village would remain entirely exempt. This in spite of active traffic and intercourse between the two places, and the fact that many adults including us physicians, who, counting the student assistants, made up a goodly number, unquestionably came in contact with measles patients.

To sum up: It is certainly a rare exception for the contagion of measles to be carried by third persons who themselves are not infected, if, indeed, it is ever thus carried at all.

What are we to conclude in regard to its conveyance by articles of common utility? The rarity of this means of infection must also be emphasized. Reference has already been made to the letter fables, and as to the contagion supposed to be lurking in the doctor's clothes or hair, it is more than questionable whether it ever gave rise to a case of measles. But how about the articles which the patient has had about him for any length of time?

Conclusive instances are lacking; I can find only one, related by Förster,* which he himself considered only "fairly good proof." It was this: A tailor worked on a boy's suit of clothes in the room in which his own children lay sick with measles, and carried it to the boy's house for him to try on. The boy was taken with measles after the lapse of the usual period of incubation. If this case had occurred in an out-of-the-way place, where every possible opportunity for infection could be known, it would seem an unanswerable argument in favor of conveyance by fomites, but since the place was Dresden, and an epidemic was prevailing at the time, it does not carry much weight.

The following, taken from the report of an epidemic on the island of Samsoe by N. Flindt, is greatly to the point: In one school the children belonging to the upper class were not taken sick until more than a month later than those of the lower class, notwithstanding the fact that they sat in the same room and used the same books and desks as

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* "Einige Bemerkungen über die Verbreitungsweise der Masern und des Scharlachs," "Jahrbuch für Kinderheilkunde," new series, vol. x (1876), p. 168.

their younger school-fellows, among whom the disease was spreading, the latter attending school in the morning, while the older pupils were taught in the afternoon. The contagion was finally introduced into the class by some of its members who had contracted it at home, and then it spread as it had in the other class. This seems to me to be conclusive evidence against the probability of measles being conveyed by articles of use.

We now come to the question, closely related to all the foregoing, How long does the poison of the disease remain active outside the human body?

The general tendency nowadays is to assume such activity to be of no very long duration. It is stated in support of this view that no infectious material is left in the sick-room after recovery. There are, indeed, no authentic statistics to prove that other people who afterward inhabit such rooms are more apt to have cases of measles in their family than is ordinarily to be expected. But is this proof positive of the non-existence of the poison? There is another possibility to be considered—namely, that there is no one in the family who has not already had the disease. The almost universal susceptibility to measles here again makes itself felt. How many families, I wonder, with susceptible children move into apartments vacated by convalescents from measles? Probably very few; most children being already immune from having had the disease. And when an epidemic is in progress, it is impossible to estimate the number of cases infected in this way, since there is every chance of contracting the contagion by direct personal contact. Nevertheless, I do not wish altogether to exclude the possibility of an occasional "sporadic" case originating in the poison clinging to a room.

Why the contagion should spread in one case and not in another often has to be left unexplained, as is illustrated by the following extract from Panum's report, which I have somewhat shortened, leaving out the minor points.

1. Funding (F.). No measles cases here. A boat left this place for the trading port Klaksvig (K.) on June 2d. The members of the crew were obliged to come in contact with people who had recently recovered from measles, to enter rooms and handle articles which persons at that moment sick and in the eruptive stage had shortly before been in and touched. The crew, after returning home, washed themselves, put on clean clothes, placed those they had been wearing in water, and threw away the paper wrappings from the articles taken out of the suspicious rooms. None of them contracted the disease on this occasion, nor until much later (after July 31st).

2. On June 3d another boat left F. for K. One man felt ill and was taken into a house, and into the very room where a number of people lay sick

with measles. The others of the crew passed their time under similar conditions to those described above under 1, and came in contact with one man who came from a place where measles was raging at the time. They took the same precautions as mentioned under 1, and contracted the disease no earlier than the first set.

3. On the same day, June 3d, a boat sailed from Nordre Gjov to F. The crew fared as under 2, but took no subsequent precautions. All broke out with measles rash fourteen days later. Although Panum makes no special note of the fact, we may infer, without doubt, that the town where these men lived was free from the contagion.

4. On June 8th another boat left F. for K. The crew came into close contact with people who had just had measles, meeting them in the same rooms in which the exposure took place in the foregoing instances. In spite of the fact that the same precautions were taken as under 1 and 2, every one, except one woman, developed the rash about fourteen days later.

It was formerly held that the measles contagion was exceedingly apt to be carried in the air. This was inferred from the difficulty of protecting the other children in a family by isolating the one originally affected. Even the children of other families living in other apartments in the same building are not at all infrequently taken with the disease at the same time as the brothers and sisters of the first patient. It is, of course, very possible that infection takes place during the catarrhal stage, before the character of the affection was recognized.

We are, on the other hand, forced to conclude that the poison may really be disseminated through the air; otherwise, why should a person take the disease who has simply been in the room with measles patients, without coming into close contact with them? That such cases do occur, I must admit, in common, probably, with all other observers; how often, is quite another question—one which it would be very difficult to answer correctly by any general statement.

The following cases are related in the report of the measles epidemic on the Faroe Islands in 1882, written by the district surgeon, Effersoe.*

A small boy spent several hours in a room adjoining one in which a measles patient was lying, whose rash had broken out the day before. Although the door between the rooms stood wide open, the boy did not contract the disease on that occasion, but was infected by his brother a number of weeks later.

A family shared a house with another family, three members of which were sick with measles. Their apartments were separated only by a thin wooden partition, through which a sufficient current of air could pass to admit the contagion, but the first family remained exempt. Later on the disease was carried to them in another way, and all who had not previously had it were taken sick.

Critically speaking, these cases only prove a temporary immunity; the inference which can be drawn from them, however, that the measles poison is not carried far in the air, does not seem altogether unreasonable.

* Sundhedskollegiets Aarsberetning for 1883.

How is the contagion of measles disseminated?

As far as children are concerned, we can answer, chiefly through the schools. The poison is carried to school by children in the catarrhal stage of the disease, and given to all their classmates who are capable of taking it. These, in turn, infecting whoever is still susceptible in their own family.

This statement is amply supported by the reports of epidemics, in particular that of the epidemic in Hagelloch, written by Pfeilsticker.

The epidemic of 1878 on the island of Samsoe, an account of which was published by Dr. N. Flindt,* also furnishes important evidence. The last extensive epidemic had occurred in 1864. That of 1878 was started by a seven-year-old child, who brought the infection to the little island, and its course could be distinctly traced, as it was spread from village to village, chiefly by the school-children.

The point is illustrated in another manner in the following report by Fürbringer†: During the Jena epidemic of 1879–80, two neighboring villages, each of which had its separate school, remained exempt for almost two whole months, although physicians and near relatives of patients visited the houses of the villagers and the village children played with the city children on the street as freely as ever. But the very first case of measles in the village schools started a wide-spread epidemic in the villages. Leubuscher observed a similar sequence of events at the time of the next epidemic.

Cases very like these have occurred in my own experience.

In respect to the duration of epidemics, they can be said to last as long as there are any susceptible persons left who come in contact with the poison. In small, thickly settled communities an epidemic can run its course in a comparatively short time; in large places this takes much longer.

Another factor, too, has to be taken into consideration, one which is less easily disposed of. The virulence of the contagion appears to vary in degree at different times, this being manifested, for one thing, by the comparative rapidity or slowness with which it is disseminated among a given number of susceptible people. Without this assumption, we should be at a loss to understand why actual epidemics break out at all in a large city, where there are always cases of measles and always some susceptible people. The different duration of different epidemics in small places, where the population undergoes little change, is, in my opinion, to be similarly explained.

My patients in the Tübingen policlinic varied but slightly from year to year, both as to number and social condition; they were always drawn from the same classes of society, people who lived steadily in one place.

* Sundhedskollegiets Aarsberetning for 1879.
† Chapter on measles in Eulenburg's "Real-Encyklopädie," 2d ed.

The same may be said of Lustnau. In spite of this fact, the different epidemics varied greatly in length. As this seems to me an interesting point, I will cite some of the statistics in my possession as briefly as possible. The duration of the several epidemics was so accurately known that I simply give the date of the first and last cases as noted in the policlinic records.

For Tübingen the figures are as follows: In two epidemics, that of 1880 and that of 1891, almost the same number of cases occurred—109 and 117 respectively; the first, however, lasted ninety-two days, the second one hundred and sixty-five days, a difference of seventy-three days. In 1877, 42 cases occurred within one hundred and eleven days. In 1884, 213 cases occurred within eighty-one days.

Small epidemics in Lustnau ran as follows: In 1881, 28 cases within sixteen days. In 1888, 37 cases within ninety-eight days. In 1893, 32 cases within forty-one days. In the epidemic of 1876–77, 93 cases were reported within fifty-nine days.

Further details will be found in the table on page 254.

The occurrence of sporadic cases can be explained in several ways:

1. During the period following an extensive epidemic, there may remain so few persons who are susceptible to the poison as to preclude it from spreading on the occasions when it again happens to be brought into the community. Such opportunities for infection from importation of the disease are doubtless frequent enough, especially in places which are centers of trade or travel.

2. It may happen, intentionally or by chance, that persons suffering from the disease are so well isolated as to hinder its spread. Such a case occurred in my practice in Tübingen, when one of the children of the tower-keeper was taken sick with measles.

3. One of two other possibilities deserves consideration:

(a) The great majority of all susceptible persons may enjoy a short period of immunity. This theory takes no account of the comparative virulence of the contagion, but assumes it to have a constant strength.

(b) The virulence of the contagion may be subject to influences which cause it to vary in degree. It may be so weak as only to affect persons who are particularly susceptible, but not to be communicated by them to others. Or it may be so active as to seize on the few who have previously remained exempt among the general mass of those smitten by an epidemic.

In view of our limited knowledge it does not seem wise to set up any general theory in answer to these questions; rather let us study each case separately, and try to solve its special problems.

Among a total of 1140 cases of measles occurring in my own practice, 13 belonged to the sporadic variety; and of these, 12 were located in the city of Tübingen and 1 in Lustnau.

MEASLES CASES IN THE CARE OF THE TÜBINGEN UNIVERSITY POLICLINIC DURING THE YEARS 1873 TO 1894 (EPIDEMICS).

	1873	1874	1875	1876	1877	1878	1879	1880	1881	1882	1883	1884	1885	1886	1887	1888	1889	1890	1891	1892	1893	1894	Remarks.
Tübingen	2	133[1]	...	4	42[2]	...	...	109[3]	...	...	...	213[4]	...	...	...	152[5]	...	...	117[6]	3	90[7]	3	Number of isolated cases, 12; number of epidemic cases, 856; number of fatal cases, 53 = 6.19 %.
Lustnau	...	...	...	89[8]	6[3]	...	...	3[9]	26[9]	...	...	78[10]	...	...	...	37[11]	...	...	...	1	32[12]	...	Number of isolated cases, 1; number of epidemic cases, 271; number of fatal cases, 11 = 4.06 %.

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Duration in days of the epidemics, from the time first case was seen until the time last case was seen :

Tübingen

[1] March 11 to July 30, 1874, 142 days.
[2] Feb. 18 to June 8, 1877, 42 days.
[3] March 15 to June 14, 1880, 92 days.
[4] April 29 to July 17, 1884, 81 days.
[5] Feb. 21 to June 27, 1888, 147 days.
[6] July 6 to Dec. 7, 1891, 165 days.
[7] March 4 to July 7, 1893, 126 days.

Lustnau

[8] Nov. 15, 1876 to Jan. 12, 1877, 59 days.
[9] Dec. 29, 1880 to Jan. 13, 1881, 16 days.
[10] May 23 to July 30, 1884, 69 days.
[11] March 27 to July 2, 1888, 98 days.
[12] July 29 to Sept. 7, 1893, 41 days.

The ages of the Tübingen patients were as follows:

Years 0 to 1.......1 (8 months)   Years 1 to 2.........2
"   2 to 3.......6   "   4 to 5.........1
"   13.......1   "   21.........1

I have called such cases sporadic as broke out at least two months before or after an epidemic.

Only two of the children were of one family, the others lived in different houses, some distance apart. In respect to season they are tabulated thus:

1873:   1876:
September 25th and October 7th.   November 9th, 10th, 20th, and 23d.

1892:   1894:
March 25th, September 6th, November   September 10th and 24th.   Two in
30th.   same family on November 21st.

The statement has been made that whooping-cough is apt to precede or immediately follow measles, but this is a mistake. Out of 495 epidemics of whooping-cough, only 94 occurred in conjunction with measles. Both diseases prevailed simultaneously 58 times, 11 times measles was preceded by whooping-cough, and 25 times followed by it.*

We have an account of the epidemics of both diseases as they occurred on the island of Samsoe from 1828 to 1878, written by N. Flindt,† who fails to discover any relation between the two in his limited field of observation. The belief probably originated in an occasional coincidence which appeared to denote something more.

Measles is one of the diseases which affects the general mortality rate. I give below a table covering a wide area, showing the total death-rate from measles in the country as a whole and in the principal cities separately, during a period of thirty-three years. The higher mortality rate of the city is thus strikingly illustrated.

AVERAGE YEARLY MORTALITY FROM MEASLES DURING THE YEARS 1838 TO 1842 AND 1847 TO 1874.

The number of deaths per million inhabitants is as follows:

	ENGLAND.		LONDON.	
	Male.	Female.	Male.	Female.
Up to 1 year of age	3022	2530	3571	2987
From 1 to 2 years of age	6086	5825	8630	8050
" 2 " 3 " " "	3178	3255	4683	4757
" 3 " 4 " " "	1730	1851	2594	2620
" 4 " 5 " " "	980	1028	1358	1446
" 5 " 10 " " "	255	278	301	316
" 10 " 20 " " "	29	38	24	32
" 35 " 40 " " "	3	5	2	3

The average mortality per million for one year was:

ENGLAND.   LONDON.
Male.   Female.   Male.   Female.
457   422   620   522

* Hirsch, *loc. cit.*, vol. III, p. 30.   † Sundhedskollegiets Aarsberetning for 1880.

The mortality from measles appears to equal only half that from scarlatina or diarrheal diseases. (According to H. Courbenay, "Die Gesetze der Masernmortalität." Reference taken from "Jahrbuch für Kinderheilkunde," new series, vol. XIII, p. 384.)

The following table shows the average mortality from measles in various cities of different size. The figures represent the number of deaths from measles per 1000 inhabitants:

London (11 years) .....27.0   Geneva (13 years) 6.6
Frankfort (12 years) ...11.9   Stuttgart (15 years)....6.2
Königsberg (12 years),.. 9.2   Berlin (18 years) 3.8
Basel (50 years) 10.1

The death-rate per thousand is also graphically presented in the accompanying chart for Basel, during its growth from a small to a large city.*

The extent to which a community can be ravaged by an epidemic of measles when its susceptibility as a whole has not been lessened by
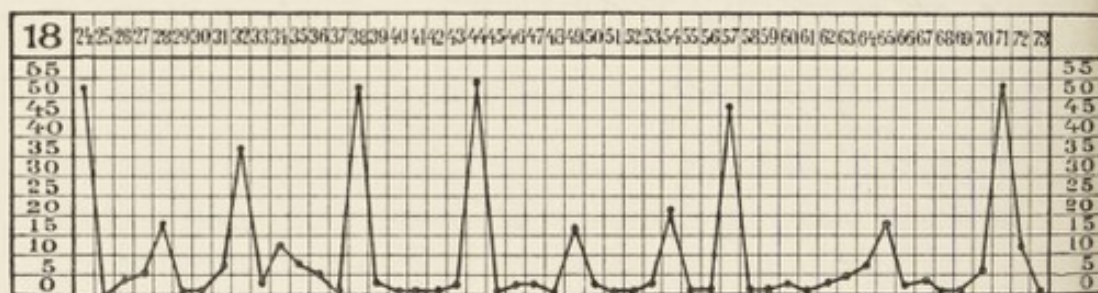
FIG. 37.

frequent outbreaks of the disease is well illustrated in the case of Iceland.† Wide-spread epidemics had occurred in 1664, 1694, and 1846; in 1868–69 the outbreak was confined to a small part of the island. On the 23d of May, 1882, the contagion was carried there from Copenhagen, and swept over the whole island, lasting until September. No measures were taken to prevent its spread,—this is expressly stated,—so we have a fairly clear picture of what it can accomplish under such conditions. The total death-rate from all causes for 1882 was 3259, whereas in the four preceding years it had varied between 1500 and 1800. The number of deaths in 1882 exceeded the births by almost 1000. Even in 1883 there was a similar excess of 21, which according to the health reports is to be regarded solely as an after-effect of the measles epidemic. From a financial standpoint the epidemic also

* From Hagenbach, "Epidemiologishes aus Basel," "Jahrbuch f. Kinderheilkunde," new series, vol. IX, p. 57.

† Sundhedskollegiets Aarsberetning for 1882.

worked havoc, since the most important industries were necessarily interfered with or brought to a complete standstill for a period of two or three weeks. The disease showed itself especially dangerous to pregnant women and those in the puerperal state, nor did it spare the, infants under six months, as it is usually observed to do.

The following figures are given for six medical districts: Population, about 5500; total mortality from all causes for entire year, 408 (about 7.5%); total mortality from measles, 250 (about 4.5%). Of the latter number, 12 were stillbirths, 47 were less that one month of age, 68 between one and twelve months, and 16 were women who had lately been confined.

It is not to be wondered at that, as the report mentions, many of the physicians in Iceland were led to discuss the advisability of making measles an endemic disease by importing it from elsewhere, or perhaps by inoculation, in order to save the country from the ravages of widespread epidemics.

The question has been raised whether the malignant nature of such an epidemic can be attributed to the influence of a northern climate; this is refuted, however, by the occurrence of an epidemic in the Fiji Islands, carried there from Sydney, which swept away between one-fifth and one-fourth of the inhabitants.*

* Compare Hirsch, *loc. cit.*, p. 120.

PATHOLOGY.

GENERAL SYMPTOMATOLOGY. SEVERE AND MILD FORMS.

THE **symptomatology of measles** is, on the whole, simple, and subject to but slight variation. The most prominent symptoms are those caused by the inflammation of the respiratory tract. The general systemic intoxication accompanying all infectious diseases, together with the fever, is next in importance, but carries with it much less danger for the affected individual, seldom acting as the cause of death. It is difficult to present a characteristic picture of the course of the disease, for the reason that it is marked by few distinctive, sharply defined features, being rather a process of gradual development. It can be briefly outlined as follows:

After infection there may be a period of entire good health, or slight disturbances of an indefinite nature may soon begin to manifest themselves, such as languor, depression, disinclination to exertion, an appearance of ill health, distaste for food, and possibly occasional chilly sensations. This condition lasts for nine or ten days, when the symptoms become more acute. The feeling of languor increases and is accompanied by headache, which is most severe in the frontal region, and by a sense of pressure over the eyes. There are also coryza and frequent sneezing, the throat feels dry and a little sore, and a cough, often of the barking, croupy type, is soon added. The local physical signs are not yet marked; the eyelids appear slightly swollen and lacrimation is somewhat exaggerated; the anterior nares are injected, as is also the mucous membrane of the pharynx. The temperature is above normal and there are a few bronchial râles. The inflammation of the mucous membranes now increases rapidly; the conjunctivitis and coryza becoming especially marked. At this stage the eruption begins to show on the hard palate and on the pillars of the fauces, which are highly congested, though not throughout their entire length. It develops in the form of circumscribed spots, somewhat indistinctly outlined, of a light red color, just barely raised above the level of the surrounding mucous membrane. The largest are the size of lentils; they are round or somewhat irregular in shape, and may be discrete or so closely packed as to run together.

Tiny, whitish, raised points are to be seen on them, which look like vesicles. The conjunctivæ, unless too red and swollen to enable the eruption to be distinguished, present a similar appearance. The skin next becomes involved; it is usually moist, and may be covered by abundant perspiration. The rash is first seen on the temples and forehead, and, perhaps rather more distinctly, on the back and sides of the chest; it is only faintly colored at first. Sometimes it develops as irregularly distributed papules, sometimes as more diffuse, crescentic patches. Vesicles are present like those on the mucous membranes. The fever and the symptoms of catarrhal inflammation now continue to increase, and the patient feels proportionately worse. As the disease progresses, the eruption on the mucous membrane takes on a darker hue, becomes slightly elevated and more or less confluent, while new spots appear on previously unaffected parts. The mucous membrane lining the cheeks, the lips, and even the gums thus gradually becomes covered with the eruption.

Externally, it usually appears on the following parts successively: face and scalp, back, wrists, forearms, anterior surface of trunk and lower extremities; finally reaching the rest of the body.

When the rash is at its height, the blotches are apt to become continuous in many places, they appear more elevated, and are of a dark red color; sometimes small petechiæ develop. *Even where the rash is thickest, islands of normal skin can be detected. The rash still disappears on direct pressure, or when the skin is tightly drawn over a spot.*

Perspiration of more or less intensity is apt to occur at this time, and the patient often complains of troublesome itching of the skin. In addition to the catarrhal affection of the respiratory tract, and the lesions in the mouth and pharynx, nosebleed is not an infrequent symptom at the height of the disease; diarrhea is observed in a still larger proportion of cases. Cerebral symptoms, such as dulness, sleepiness, and slight delirium, may be manifested, but as a rule are not of serious import. General convulsions occur only in exceptionally severe cases. The heart is not specially involved; its rate is increased, as is also the rate of respiration, but only in proportion to the fever, unless the course of the case is altered by complications. The temperature does not usually rise much above 40° C. If the bronchitis extends to the fine tubes, or, worse still, if pneumonia supervenes, the last-named symptoms take on a different aspect, as will be fully discussed later on.

In a simple, uncomplicated case the further course of the disease is as follows: The eruption disappears from the mucous membranes,

which, however, still remain inflamed. The external rash usually follows the same path in fading as in developing, beginning on the face. The dark red blotches gradually grow paler, and less raised above the surrounding skin; when this is held taut over them, it first shows a reddish-yellow discoloration, changing later to yellow, and finally to a muddy brown. The skin subsequently becomes rough, and superficially is thrown off in fine branny scales. Desquamation is soon completed, and never leaves scars. It must be borne in mind, however, that in most cases, when the rash is fading from the face, it is still at its height on other parts of the body, or even just developing. The catarrhal symptoms clear up, sometimes quite rapidly, sometimes more gradually, the cough being last to disappear. The temperature soon falls to normal, and before long recovery is complete.
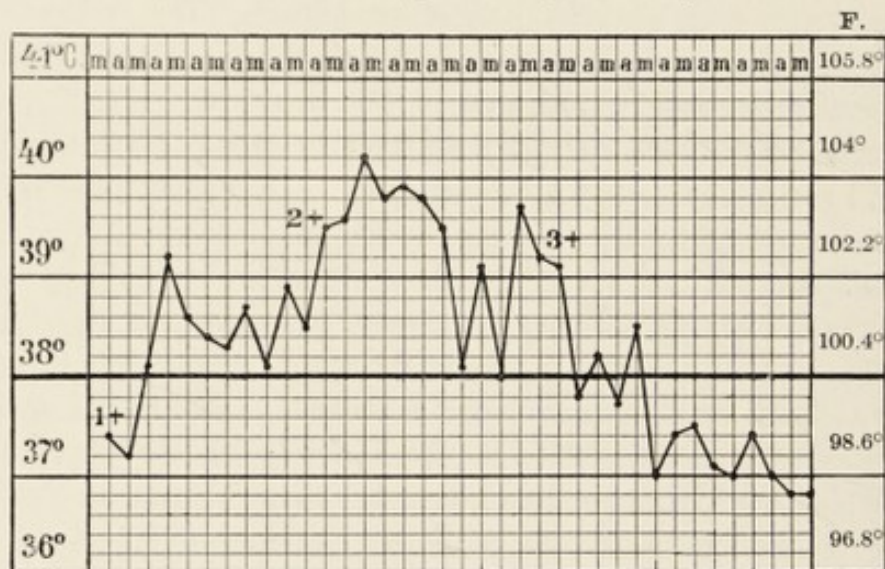
FIG. 38.—1+, Invasion ; 2+, outbreak of eruption ; 3+, beginning of desquamation.

The following will serve as an example of a well-developed case of measles, running an entirely normal course:

CASE 8.—Mathilde L., two years of age. The child was first seen on February 20, 1888. The symptoms were first a slight angina, then conjunctivitis, coryza, and bronchial catarrh, which from the 24th on also involved the fine tubes. The eruption appeared on the 26th and lasted until March 2d. The temperature record is shown in the accompanying chart (Fig. 38).

The above course is typical of many cases of measles; but we sometimes have to deal with very different conditions. Apart from the extreme virulence of the poison which occasionally distinguishes an epidemic, it is largely a question of the patient's power of resistance. It is important to remember that, except in cases of mixed infection, a fatal ending is usually the result of pulmonary involvement. This coincides with the greater mortality of children under two years of

age, the small caliber of the bronchi at this early age being particularly favorable to their occlusion, and the consequent loss of all the respiratory surface beyond, which is essential to the respiratory process.

While it is quite possible to generalize in describing the course of the disease in a fatal case of this nature, I feel that I must depend on the report of individual cases in order to convey a correct impression of the phenomena to be observed when death results from an overwhelming intoxication. The following case occurred in my own experience.

CASE 9.—Fritz D., six years of age. In his first year he suffered slightly from rachitis, which, however, left no traces of any moment; and in his second year, from cough and shortness of breath, these symptoms, too, disappearing after a time. The parents maintain that the child had measles in 1874, but so mild an attack that no physician was called. Since we did not see a single case of measles in Lustnau, the boy's home, in that year, not much faith can be placed in this statement.

The boy attended school up to the 1st of December, 1876, but began to feel rather listless on this day. On the 2d and 3d of December he continued to droop; his eyes are also said to have looked a little red and his face to have shown a few blotches. On the morning of the 4th the rash became more distinct, and the child gave further evidence of sickness, displaying a poor appetite, etc.

On the 5th the rash was observed to be spreading; by mid-day it extended to the chest. That afternoon the case was put in the charge of the policlinic, when the following symptoms were noted: Slight conjunctivitis, very slight coryza, the buccal mucous membrane and tonsils swollen and congested, the tongue coated white, a little bronchitis, and diarrhea. The eruption is in the course of development. Rectal temperature, 40.1° C. (104° F.). In the evening the patient was fully conscious, getting out of bed to open the door once when his mother was otherwise engaged. No serious symptoms developed during the night, and on the morning of the 6th the child appeared to the parents to feel no worse. When the physician called at 10 A. M. he found the following condition: skin pale and cyanotic, showing large numbers of petechiæ, which bear no relation to the patches of eruption.

12 M.: Temperature 41.4° C. (106° F.), pulse 180, respiration very labored, inspiration quick and snoring and accompanied by marked retraction of the costal arches; expiration also difficult. Tracheal râles were noted at 2 P. M.

5 P. M.: Temperature 41.2° C. (106° F.), respiration 44, pulse 170. The child has ceased to speak; he knows when he is addressed, and recognizes those about him, but is unable to call them by name. Most of the time he is unconscious. Muscular spasms involving the upper extremities have now set in. The convulsions increased up to the time of the child's death at 9.30 P. M.

Autopsy report (Schüppel): The skin is in great part covered with punctate or flat ecchymotic spots, which have no connection with the measles rash, the latter being still distinctly visible. On opening the cranium, the veins are seen to be distended with blood, the cerebral convolutions are everywhere flattened, and their surface is rather dry. The

cerebral hemispheres appear moderately edematous and there is a slight degree of capillary congestion; the ventricles are not distended and contain no effusion; there is some dark blood in the plexuses and the vessels on the floor of the ventricles are engorged. The cerebrum appears normal. The muscles are of a brownish-red color and remarkably dry. The tonsils and follicles of the tongue are slightly swollen; neither exudation nor ulcers are present. The opening of the larynx is slightly injected, and the mucous membrane at this point looks somewhat as if laid in folds. The larynx itself is normal except for a slight catarrhal inflammation. The cervical lymph-nodes are swollen, infiltrated, and contain small hemorrhages. On opening the thorax, the lungs are found to be in contact for a considerable distance, leaving only a small area of the pericardium exposed. There are a few delicate pleural adhesions at the apex of the right lung; posteriorly, the left lung presents some of greater tenacity. The pleural cavities contain no effusion. There are a few punctiform petechiæ under the right pulmonary pleura, and several areas of atelectasis are scattered over the surface of the lung, partly concealed by distended, emphysematous lung tissue. The lung is beset with small hemorrhages, located for the most part next to areas of collapse. The bronchial mucous membrane is highly congested, dark red in color, and swollen, and shows a number of small hemorrhages. The lung tissue in general is in good functional condition. The petechiæ under the left pleura are much more numerous, and there are also many more areas of atelectasis, otherwise the condition is like that of the right lung.

The heart is of normal size, and the valves are normal; the heart muscle is grayish-red in color, and resistant to pressure. The spleen is not specially enlarged; its capsule appears slightly wrinkled. The splenic substance is firm and hard, and the Malpighian follicles are not distinctly visible. The liver is of normal size; the capsule looks a little dull, the liver substance is congested and slightly fatty. The kidneys are congested, but not enlarged; the tubules in the papillæ are the seat of a severe catarrhal inflammation. The mesenteric lymph-nodes are greatly swollen, and of a purplish color. The mucous membrane of the intestine is pale, and the follicles appear considerably swollen. The stomach is distended and filled with fluid food; hemorrhagic erosions are seen in a few places.

The symptoms in this case did not seem at all serious at first, and the epidemic as a whole was of a mild character, only 2 of the 95 cases, exclusive of the above, having had a fatal termination. The severity of the intoxication did not become apparent until the rash was at its height, when all at once it manifested itself by a marked rise of temperature, wide-spread hemorrhages into the tissues, and signs of cerebral involvement—just a sudden change for the worse, rapidly leading to the end. The insignificance of the organic lesions, as shown by the autopsy, proves the cause of death to have been systemic poisoning.

The history of another case reads as follows:

CASE 10.—Bertha St., two years of age. The patient, who had always been a healthy child, probably contracted the disease from her four-year-old brother. On the 27th of March, 1893, the parents noticed that the

child seemed tired and indisposed. This continued, until on April 3d she was taken with convulsions, after which the eruption began to develop, appearing first on the face. On the 4th of April, when the case was first seen medically, the following symptoms were noted: conjunctivitis, coryza, hoarseness, wide-spread capillary bronchitis, and moderate diarrhea. Also an eruption on the hard palate. The child has high fever, seems rather dull, but has no dyspnea. On the 5th, areas of consolidation were found in both lungs. The cerebral involvement increased and the child soon became completely unconscious, with symptoms of excessive cerebral pressure. The limbs were relaxed, and when lifted fell back lifelessly to the bed. The lung symptoms also became more marked, but did not compare with the others in severity. The rash spread in the customary manner. Death occurred at 5 A. M. on April 8th, the child being completely comatose. The temperature is shown in the chart (Fig. 39).

The autopsy showed the following condition (from the records of the Pathological Institute, Dr. Roloff): The skin is covered with an abundant eruption. The brain is greatly congested, but not edematous, and there is no fluid in the ventricles. The pleural cavities are also free from effusion. On lifting up the sternum, the lungs recede only slightly, exposing an area of the pericardium no larger than a half dollar. The left lung appears strikingly bulky; there are a number of patches of fibrous exudate on the posterior surface of the lower lobe. In the parenchyma underneath these patches can be felt quantities of hard little nodules, which on section appear distinctly prominent. They are grayish-red in color and exceedingly friable. The infiltrated portions of the lung contain a number of small, yellowish foci, which have

Fig. 39.—1+, Outbreak of eruption.

not yet undergone softening. In the larger bronchi the mucous membrane is only slightly injected and is but thinly covered with mucus, while the smallest tubes contain a quantity of yellowish, purulent secretion, and the mucous membrane here and in the medium-sized bronchi is deeply congested and swollen. The findings in the right lung are similar. The heart is somewhat larger than the child's fist; the right chambers are filled with clots. The pharynx appears normal. The larynx "presents a few superficial erosions, one on the inner surface of the left vocal cord, in its posterior third; another, with a dirty-looking base, in the inter-arytenoid fold. Otherwise the mucous membrane lining the larynx and the trachea is pale and not swollen." The spleen measures 8.5 × 4.5 × 1.5 cm. Its surface is smooth; the splenic pulp is of a light brownish-red color; the trabeculæ and follicles show distinctly; the organ is moderately congested. The liver is not enlarged; its acini are not well marked. The kidneys are normal. The mucous membrane of the small intestine in general is pale, Peyer's patches also being considerably congested; those lying nearest to the ileocecal valve are particularly prominent. The mesenteric lymph nodes are enlarged, somewhat larger than beans, and appear grayish-white on section.
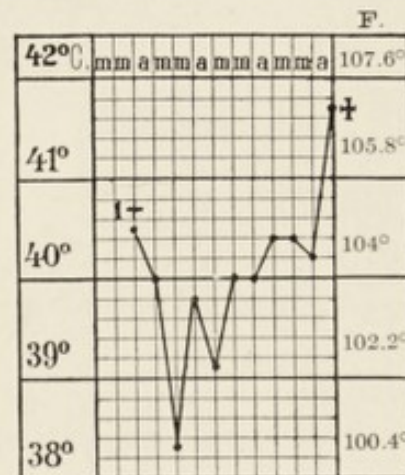
In reviewing this case, we are struck not only by the intensity of the systemic intoxication, which was foreshadowed by the occurrence of convulsions at the time the eruption appeared, and the continued mental dulness following them, but also by the early development of the inflammatory lesions in the respiratory tract. Various of the local processes characteristic of the measles poison are represented, such as intense bronchitis with bronchopneumonia and laryngeal ulceration. These local inflammations, however, did not act as the chief cause of death. This is rather to be sought in the general systemic effects of the poison, especially in the cerebral involvement, though the end may of course have been hastened by the respiratory difficulties.

It seems to me that these two cases should suffice to give a fairly clear picture of the type of infection under discussion, one containing no features specifically characteristic of measles, but simply the phenomena common to all severe intoxications, with the addition of more or less well-marked signs of respiratory inflammation.

These particular processes,—a bronchitis involving the fine tubes, and bronchopneumonia,—developing sometimes at the onset, sometimes in the course of the disease, represent the local action of the measles poison, without any relation to its general effects, and, as such, allow of generalization in describing them.

The extension of the inflammation to the finer bronchi is marked by increased rapidity of respiration, the first indication of the coming danger. Breathing then soon becomes hasty and shallow, the child begins to pant and to moan a little, the nostrils dilate, and the mouth is kept open to admit more air. Still more frequently there is a short, broken cough, accompanied by cries of pain. The pulse grows very rapid and loses in fulness; the face appears slightly cyanotic, less so if the fever is high, when the bluish coloring is chiefly noticeable in the sclera. The shape of the chest in breathing is altered, the lower ribs being drawn in with every inspiration, but not the sternum and costo-clavicular spaces. The veins of the neck stand out, not emptying fully with inspiration, and dilating during expiration.

The clavicular muscles are now brought more and more into play; the sterno-cleido-mastoids and the trapezei are distinctly outlined with every inspiration. Older children like to sit up in bed resting on their arms. The impulse of the heart against the chest-wall, previously distinct, can no longer be seen, nor is the apex-beat perceptible to the hand. Cyanosis usually increases now; the separate patches of eruption look less red, assume next a violet tinge, and

finally can hardly be distinguished from the rest of the bluish colored skin. This is the time when the layman exclaims, "The rash has struck inward!" Cyanosis next gives way to pallor, except that the lips take on a still deeper hue and the veins show dark through the skin. Respiration grows more and more rapid and shallow; the retraction of the ribs becomes less apparent except when a few deeper breaths usher in an attack of coughing.

On examination we find areas of consolidation, at first only posteriorly, at the bases, but from there spreading upward and to the side; fine mucous râles are heard all over the chest, gradually becoming louder and more distinct. Finally the breath sounds are completely obliterated over the consolidated portions, or else they become bronchial in quality. The attacks of coughing which have caused the patient such distress now decrease in frequency and severity, but are still accompanied by moans and cries of pain.

The child is excessively restless, and is constantly changing its position, throwing itself about, demanding first one thing then another, never content with what is done for it, and allowing its attendants not a moment's respite. All this changes, however, as the effects of the carbon dioxid poisoning become more manifest. Then the clamoring ceases; the child appears indifferent to its surroundings, but is still restless, throwing itself about, moaning softly, and very often scratching violently at its skin. Drowsiness next sets in, followed by severe symptoms of cerebral pressure, as in cases of meningitis, with effusion into the ventricles and cerebral edema, sometimes accompanied by convulsive seizures of short duration. Mucous râles are now heard in the large bronchi and the trachea also; these grow louder and louder, while coughing ceases entirely. In this condition the child dies.

When recovery takes place in a case of fully developed bronchopneumonia following measles, the symptoms disappear in the order of their coming. Relapses, however, may again bring on a most dangerous condition. The duration of the affection is, on the whole, a comparatively short one, its outcome, whether favorable or unfavorable, being decided within ten days or two weeks. The local changes in the lungs take longer to clear up, and while this is in process some general symptoms are very apt to persist. During the course of a severe bronchitis and subsequent bronchopneumonia the temperature usually remains high, falling, if recovery ensues, by lysis, never by crisis.

The following are cases in point:

Case 11.—Anna K., three and a half years of age. Suffered for a week

from indefinite prodromata—cough, and short temporary outbreaks of a rash on different parts of the body. The child was first seen on February 3, 1888, at which time the following symptoms were noted: conjunctivitis, coryza, bronchial catarrh, diarrhea, and enlargement of the spleen. The eruption could be seen on the mucous membranes. On February 5th a thick rash broke out, showing first on the face; the bronchitis was found to be extending to the fine tubes. On the 10th areas of consolidation developed at both bases, which did not clear up until the 20th. The rate of pulse and respiration was highest on February 12th, when it rose to 190 and 60 respectively. The temperature on the 6th and 7th reached 41° C. (106° F.). On the 18th it rose to 38.5° C. (101.3° F.), after that date remaining normal or subnormal. (The record was continued to March 2d.) The accompanying chart (Fig. 40) shows the daily changes.
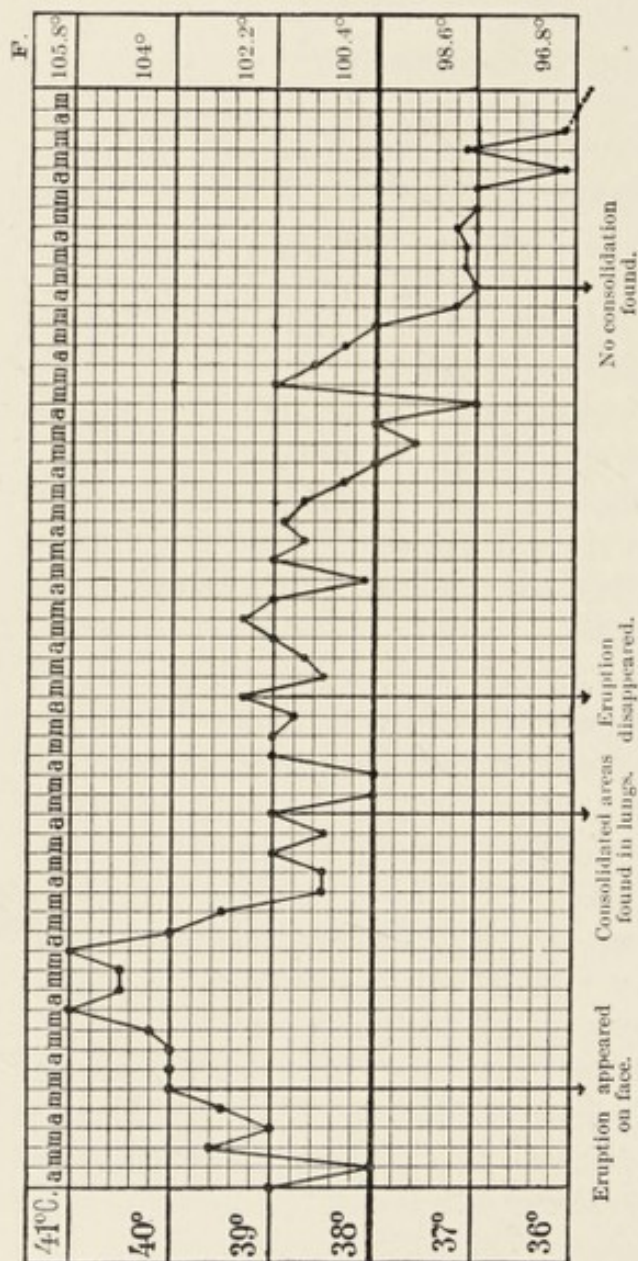
The above was a light case of bronchopneumonia, with rapid recovery.

CASE 12.—Marie B., four years of age. Symptoms of cough, sore throat, and pain in the eyes developed on February 16, 1888. When first seen, on February 19th, she had a slight conjunctivitis, coryza, severe bronchitis, and enlargement of the spleen. There was an eruption on the mucous membranes and on the face. Up to the 25th the bowels remained normal; on this day and the one following there was diarrhea. On the 24th an area of consolidation was found posteriorly, at the base of the right lung, and on the 26th a similar condition developed at the base of the left lung. The consolidation spread until the 4th of March, then disappeared rapidly. Pulse and respiration rate reached their maximum height on March 3d, when the record showed a pulse of 174 and a respiration of 63. On February 29th the temperature rose to

41° C. (106° F.). From March 6th on it was normal or subnormal. The daily record is given in the chart (Fig. 41).

The severity of the pulmonary involvement is shown by the effect on the temperature. If we compare the two parts of the double curve, we see that the fever was considerably higher in the second, after the rash had faded, than it was at its height.

The **mild forms of measles** now remain to be discussed. These are of frequent occurrence, and give rise to such trifling symptoms that medical advice is seldom asked, at least among the poorer classes. It is for this reason, probably, that the mildest forms are very little known. Even so experienced a practitioner as von Leube states* that "although there may be but very little fever in mild cases, it is never entirely absent." Now, it so happens that the outdoor department of the Tübingen policlinic takes charge of even the mildest cases of measles, and in its records I find two

Fig. 41.

which ran their course without any fever whatever. The histories are as follows:

CASE 13.—Adolf K., four weeks old. Two other children in the family were sick with measles. There were no prodromata. The infant

* "Specielle Diagnose der inneren Krankheiten," Leipsic, Vogel, 1893, vol. II, p. 358.
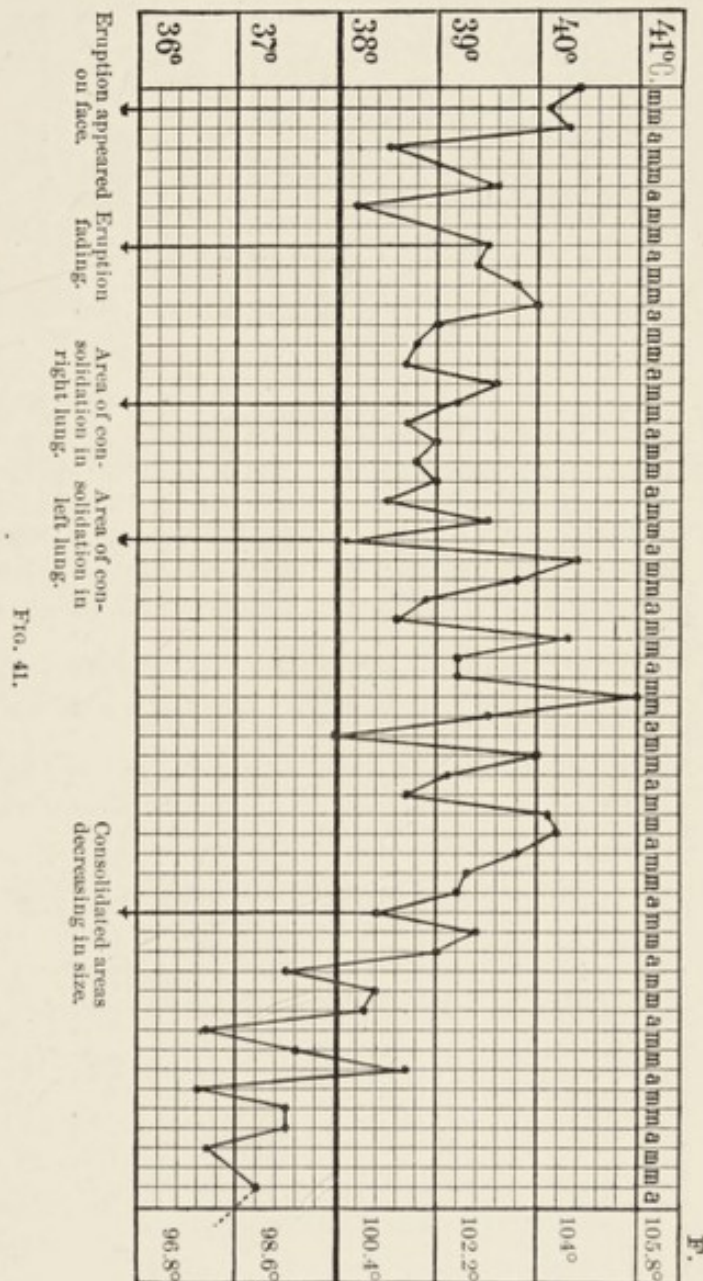
was first seen on October 21, 1891. It had no conjunctivitis, no coryza, and no enanthema, but was suffering from a slight bronchial catarrh, and had rather thin stools. The skin eruption was well developed, and remained visible until the 24th. The maximum temperature was 37.3° C. (99° F.). The daily record is shown on the chart (Fig. 42).

Eruption appeared   Eruption
on face.   fading.

FIG. 42.

Eruption appeared   Eruption
on face.   faded.
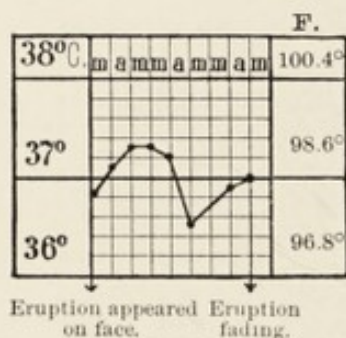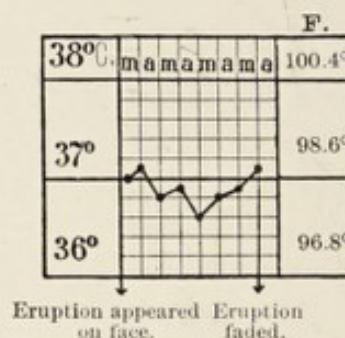
FIG. 43.

CASE 14.—Friedrich K., twenty-one months old. The infant had been in contact with measles cases. For a few days it had seemed listless and had lost appetite. It was seen on September 19, 1893, when the following symptoms were noted: conjunctivitis, enanthema, and bronchial catarrh. The bowels were regular. The skin eruption appeared first on the face, and lasted until the 23d. The highest temperature was 37.1° C. (99° F.), as is shown in the chart (Fig. 43).

These cases serve to demonstrate that measles is not necessarily accompanied by fever; it is true that the temperature was not taken before the eruption broke out, but this, again, is usually the time of the highest fever. If fever is absent at this stage, and the temperature, indeed, is rather inclined to be below normal, it is certainly improbable, to say the least, that a rise took place earlier. The mildness of the other symptoms of infection, or their failure to develop at all, is in accordance with the behavior of the temperature.
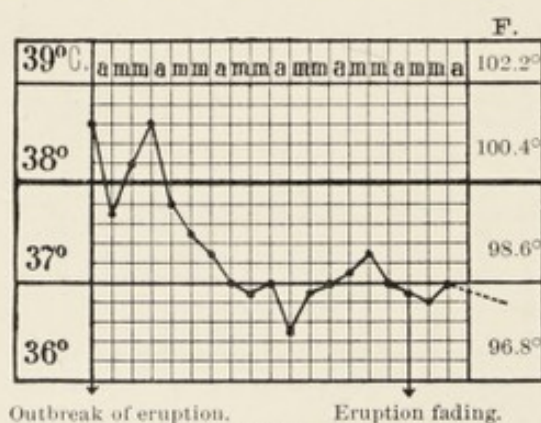
Outbreak of eruption.   Eruption fading.

FIG. 44.

I add a few cases illustrative of the intermediate form between the above and the fully developed type of the infection.

CASE 15.—Hermann S., two years of age. Three other children in the family were taken sick with measles about two weeks previously. The patient displayed a loss of appetite before the attack. He was seen on September 18, 1891, and found to be suffering from conjunctivitis, coryza, and enanthema. The rash was beginning to show on the skin, and remained distinct until the 24th. The highest temperature was 38.6° C. (101° F.). For details, see the chart (Fig. 44).

Case 16.—Emma L., three and a half years of age. Contact with an infected person could not be proved, but an epidemic was in progress at the time. On July 15, 1891, she began to lose appetite, and to have headache and a cough. She was seen on that day, and the following additional symptoms were noted: conjunctivitis, coryza, enanthema, diarrhea, and bronchial catarrh. The external rash did not develop until July 18th, fading on the 21st. The highest temperature was 39.6° C. (103° F.), on the day before the rash broke out. The temperature curve (Fig. 45) shows the daily record.
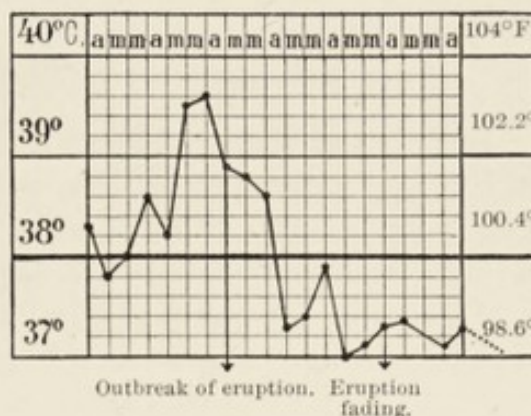
Case 17.—August Sch., six years of age. The other children of the family were sick with measles. On the 13th of July, 1891, he began to complain of headache and cough and to lose his appetite. He was seen on the 17th, when conjunctivitis, coryza, and enanthema were found to be present. The rash broke out on the skin on the 19th, but faded one day later. The maximum temperature was 40.3° C. (104.5° F.), occurring after the rash had begun to fade. The chart (Fig. 46) supplies the daily record.

Outbreak of eruption. Eruption fading.

Fig. 45.

Outbreak of eruption.
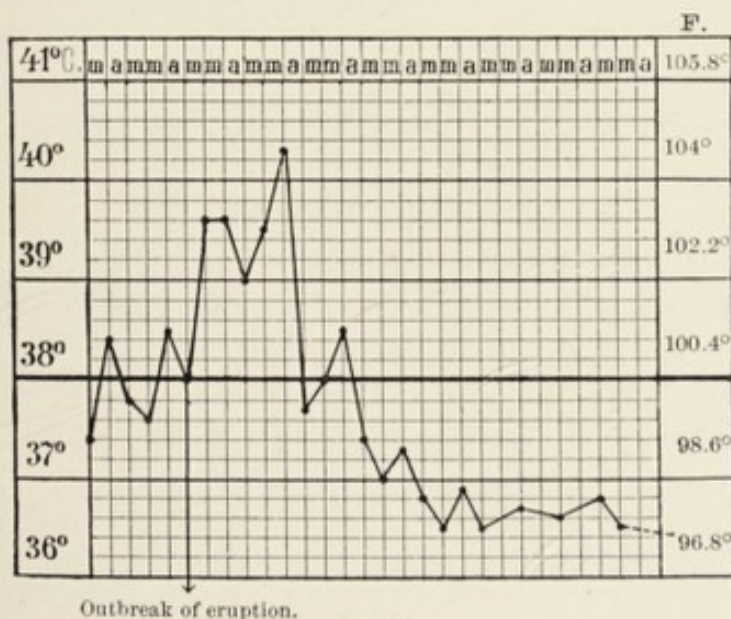
Fig. 46.

Mild cases of infection are accompanied neither by symptoms of systemic intoxication nor by well-marked inflammations of the mucous membranes; for the prognosis, therefore, we must depend on the course of the temperature, which is a fairly reliable guide.

I think the several histories cited will serve to give a general conception of the pathologic conditions produced by the measles poison

alone.   Complications must be considered separately, and for the sake
of clearness I shall take them up in connection with the lesions of the
different organs.   The so-called sequels of measles will be treated
under the same headings.

THE SYMPTOMS CONSIDERED SEPARATELY.

Duration of Different Stages.—Reference was made in the section
on Etiology to the fact that the only period definitely known to us is
that lying between infection and the outbreak of external eruption,
covering from thirteen to fifteen days.

This period is a constant one, but is composed of two factors, each
of which is subject to considerable variation.   The main point is, how-
ever, that their sum is unchanging.   To state the question differently
—the measles poison may cause almost no disturbances until the rash
develops, or may give rise to constitutional symptoms soon after in-
fection occurs.   This conception of the case seems to me most in
accordance with the facts.   Although the course of measles conforms
in general to certain known rules, and the disease is very properly
classed among those which allow of a "typical" description, it no
more follows fixed lines of development than does any other form of
infection.

A distinction must be drawn between constitutional and local
symptoms in considering early manifestations of the infection.   If we
study the reports of different recognized authorities, we find a great
divergence of opinion as to the phenomena of the period of incubation.
This can be explained in part, no doubt, by the different source of
their data, gathered in one instance chiefly from private, in another
chiefly from hospital, practice, and also, I think, by the varying char-
acter of the epidemics observed.   Let us consider the views of Bohn
and Thomas, for example:

Bohn writes *: "Constitutional disturbances are rarely altogether
absent from the incubation period of measles, whereas in the other
acute exanthemata this is almost always a latent stage.   An infected
individual usually feels generally indisposed for days before the actual
outbreak of the disease, though seldom ill enough to stay in bed.
Children look pale, lose interest, are listless and sleepy, often complain
of headache or pain in the stomach, feel nauseated, and have a poor
appetite.   At times they are feverish.   Catarrhal symptoms do not
regularly belong to this period.   .   .   .   This much is clear—if we

* See Gerhardt's "Handbuch," vol. II., pp. 297, 298.

deduct all the time in which any indisposition is manifested, we leave an average of only a few days for the absolutely latent germinating period of measles,"

Thomas says*: "In the period of incubation, the infection normally remains completely latent; this period is distinguished, therefore, by an absence of fever as well as of local symptoms."

I will endeavor to show that both statements are correct and both at the same time incorrect. Fever is an unfailing manifestation of constitutional disturbances caused by infectious processes. After studying the many temperature records made in our Tübingen policlinic, I have come to the conclusion that we cannot properly speak of signs of an infectious disease, whatever its order may be, in the absence of all local symptoms and of fever. The rule in the children's hospital at Heidelberg, the Luisen-Heilanstalt, is to take the temperature of all patients twice a day, no matter what their trouble may be. Oscar Embden,† in a thesis written under the direction of Herrn v. Dusch, gives a chart (in No. 8) showing one of the children under observation to have had no rise of temperature before the outbreak of the rash. Nor were any local symptoms noted. In another of his cases the rash developed only twenty-four hours after the first rise of temperature.

It seems to me that these cases clearly prove the possibility of a greatly prolonged period of incubation, during which the infection remains entirely latent. It is not quite so easy to find conclusive evidence in support of Bohn's position, for it may be questioned whether temporary disturbances evidenced before the regular development of the disease are necessarily the direct result of the action of the measles poison.‡ It is not impossible that the presence of the latter may make the body more sensitive to the other influences. Systematic temperature records with a view to determining these points have never been published. Thomas states, however, that he has observed temporary fever, up to 39.8°, accompanied by slight constitutional symptoms and trifling catarrhs of the upper respiratory passages, during the time when the individuals in question were "under the influence of the measles infection." These disturbances were followed by several days of normal temperature and improvement in local conditions, before the ordinary symptoms of measles began to develop in their regular

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* See v. Ziemssen's "Handbuch," *loc. cit.,* p. 76.

† "Eine Masernepidemie in Heidelberg im Jahre 1888." (Published in 1889.)

‡ Compare Thomas, "Beiträge zur Kenntniss der Masern," *Archiv der Heilkunde,* 1867, pp. 390, 391; also Henoch, "Vorlesungen über Kinderkrankheiten."

sequence. He frequently found the temperature slightly over normal —from 37.9° to 38.3°—during the period following infection, although no other signs of bodily derangement were present.

Unless we choose to make a sharp distinction between period of
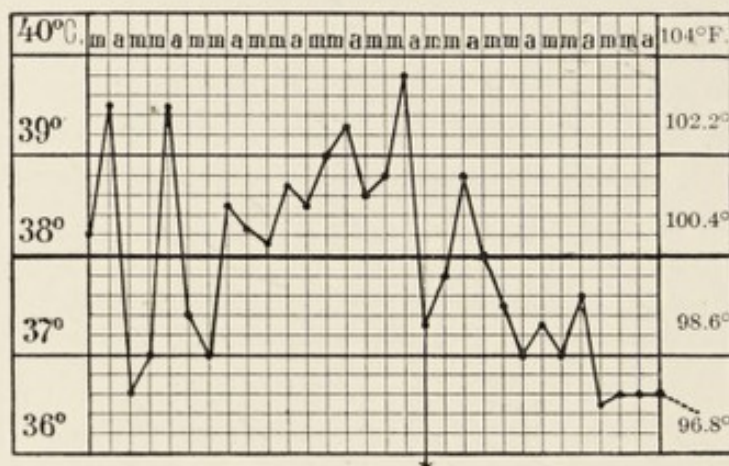
Outbreak of eruption.
Fig. 47.

incubation and period of commencement, or, let us say, as seems to me more correct, period of development of the disease, it is easy to find examples in opposition to the two presented by Embden. We have, indeed, only to refer to his own statements; his temperature chart No. 2 (Fig. 47), which illustrates a case of recurrence in the patient whose

Outbreak of eruption.
Fig. 48.

original attack is followed in chart No. 1 (Fig. 48), shows fever to have been present for a long time before the eruption broke out.

The two following cases of my own furnish similar evidence:

CASE 18. — Anna W., eight months old. Her three-year-old brother was suffering from a mild attack of measles, the rash in his case having developed on the 16th of March, 1893. The little girl began to feel sick on March 23d; she was feverish, restless, and coughed frequently. During the following day she developed conjunctivitis, coryza, bronchitis, diarrhea, and an eruption on the buccal mucous membrane. These symptoms were of only moderate intensity. The rash did not break out until the 29th of March, the fever going down almost simultaneously.
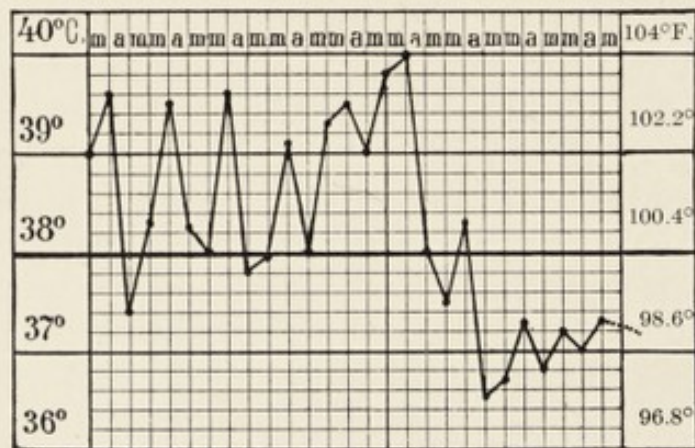
CASE 19.—Emil K., five years of age. On July 15, 1891, he began to lose appetite, and to suffer from headache and cough, these symptoms being followed by coryza, conjunctivitis, bronchial catarrh, and the development of a buccal enanthema. The rash did not appear until July 20th, and lasted only two days.

The occasional very early development of the ordinary catarrhal symptoms is admitted on all sides, and is doubtless to be explained on the same ground as was suggested for an early rise of temperature.

It is customary to divide the course of measles into different stages, for the sake of greater clearness in describing the disease. Each stage has a fixed length, and is distinguished by special symptoms.

There is no objection to the division into stages, if we bear in mind that they represent the course of an average case, determined from the comparison of a large number of cases, embracing, of course, the maximum and minimum of duration and intensity of infection.

Since in fully developed cases we find the poison manifested in its completeness, we have only to consider how the symptoms are distributed over the period under the sway of the measles poison in order to gain a clear conception of the typical course of the disease. The accepted lengths of the several stages, marking, as they do, the progressive development of an average infection, furnish us with a standard by which we are aided in judging the course of any given case, both in respect to its general symptoms and its local inflammations.

Deviations from this standard will often be noted, but—and I wish to lay emphasis on this point—this does not necessarily imply that they are deviations from the "normal," since what we call "normal" only represents the *average* course. Physicians of limited experience sometimes fail to grasp this point fully, and are in consequence inclined to hold too strictly to set rules and to speak of "normal" and "anomalous" cases of measles when the distinction is really not warranted. This would not matter except that the individual patient is liable to suffer from the non-appreciation of certain features of his "normal" case on the one hand, and the exaggeration of his "anomalous" course of infection on the other. *Dixi et salvavi animam.*

The several stages are known as follows:

1. *Incubation.* This stage is entirely free from symptoms, or at any rate exhibits none peculiar to measles. Its duration is from nine to ten days.

2. *Prodromal, initial, or enanthemic stage.* All these terms are in use. Its duration is from three to four days. Symptoms: Fever, conjunctivitis, coryza, pharyngeal and bronchial catarrh. The eruption develops on the mucous membranes—enanthema.

3. *Exanthemic stage.* Its duration is from four to five days. Symptoms: The fever is higher and more continuous, and the general condition is worse. The inflammation of the mucous membranes

18

increases, and the measles rash breaks out on the skin. The disease is now at its height.

Some writers distinguish eruption from efflorescence, thus subdividing this stage into two. I consider this unnecessary, and, indeed, hardly feasible.

4. *Stage of desquamation.* Its duration is somewhat uncertain. It is marked by subsidence of the fever, the disappearance of constitutional symptoms and of the inflammation in the mucous membranes, by the fading of the rash, and by the appearance of a branny desquamation. When this stage is completed, the patient is considered to have recovered.

The Fever.—In the majority of cases the fever, which of course is simply one of the symptoms of the general infectious process, is ushered in by a succession of chilly sensations; an actual chill is observed only exceptionally.

Ziemssen and Krabler, for instance, state that only 5 out of 311 cases occurring during the epidemic of 1861 at Greifswald gave a history of a chill at the onset.*

A great deal has been written about the course of the temperature and the various degrees of fever to be observed. I do not consider that the facts warrant us in speaking of a firmly established and typical temperature curve in measles. Every extensive set of cases comprises a number which so evidently deviate from the standard in this respect as to preclude our adherence to any strict rule.

Wunderlich, past master of thermometrics though he be, has succeeded in leading us somewhat astray in regard to measles in his desire to discover a definite law for the course of the temperature in all infectious diseases,† although he himself sounded a note of warning. The following sentences certainly make a contradictory impression on the mind of an unprejudiced reader ‡: "The fever which in measles precedes the eruption and accompanies it up to its complete development is quite strictly typical in character. Since measles, however, is a disease the course of which is particularly subject to irregularities, certain epidemics being distinguished by their eccentric type of infection, we must of course be prepared to meet with many deviations

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* "Klinische Beobachtungen über die Masern und ihre Complicationen," u. s. w., *Greifswalder med. Beitr.*, vol. ii, pp. 117 *et seq.*

† See Wunderlich, "Ueber einige Verhältnisse des Fieberverlaufes beiden Masern," u. s. w., *Archiv der Heilkunde*, 4th year, 1863, p. 332, 3d paragraph.

‡ "Das Verhalten der Eigenwärme in Krankheiten," Leipsic, Otto Wiegand, 1870, 2d ed., p. 326.

from the usual temperature curve. Measles, furthermore, is in the main a disease of childhood, when the temperature is more easily disturbed by accidental influences than at any other time of life. It is only natural, therefore, that cases should frequently display more or less well-marked deviations from that type of temperature record which characterizes the uncomplicated action of the measles contagium on previously healthy, susceptible, and not overirritable or sensitive individuals."

He gives clear expression to all the conditions on which the phenomena in question depend, but proceeds, nevertheless, to present a typical curve, which, however, as exemplified by Figs. 27–29 in Wunderlich's work, hardly gives an impression of uniformity.

Here, again, it is a question of principle, of how far to go in distinguishing "normal" from "anomalous" cases of measles. I believe, as I have already stated, that we should exercise greater reserve, and not lay too much stress on deviations from the average course.

Wunderlich and his pupils represent the opposite point of view. Which side more nearly approaches the truth is open to discussion, but one thing is certain—an attempt to "formulate a law," or, to put it better, to establish a rule of experience, should be based on the study of a large number of cases. If this foundation be lacking, such a "law" can have but a very limited applicability, if, indeed, it can be relied on at all.

The reasonableness of this demand can scarcely be disputed; it is essential to the critical analysis of any formula for the temperature changes in measles, which should precede its acceptance as a standard.

Little is known of the temperature during the incubation period proper. As was stated above, this question calls for systematic investigation.

The facts are somewhat better understood in connection with the prodromal stage. Eight cases described by Embden are entirely above criticism; next in value are those cited by Thomas.* I myself have the records of a limited number of cases in which the temperature was taken regularly from the beginning. The data at our disposal increase in number the nearer the time of incubation approaches the outbreak of the eruption. We can, at least, be said to know more of this period than of the one preceding it.

Thomas † describes the **normal course of the fever** as follows: "The temperature rises rapidly, and as a rule uninterruptedly, to a

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* "Beiträge zur Kenntniss der Masern," *loc. cit.*, p. 390.
† See v. Ziemssen's "Handbuch," *loc. cit.*, pp. 77, 78.

considerable height, certainly high enough to constitute true fever (102°
to 104° F.); it seldom remains below 102° F. The fever symptoms
usually abate very appreciably on the following morning,—that is, on
the second day of the prodromal stage,—the temperature frequently
even falling to normal; exceptionally, it remains high for another
twelve or twenty-four hours before the remission takes place. This
initial fever, lasting on the average one day, is succeeded in most cases
by two days of very light fever. On the first of these two days—that is, on the second day of sickness—the fever is particularly apt to remain low, whereas on the following day, the third, this applies at the most only to the morning hours, a further more or less well-marked rise of temperature seldom failing to occur in the evening."
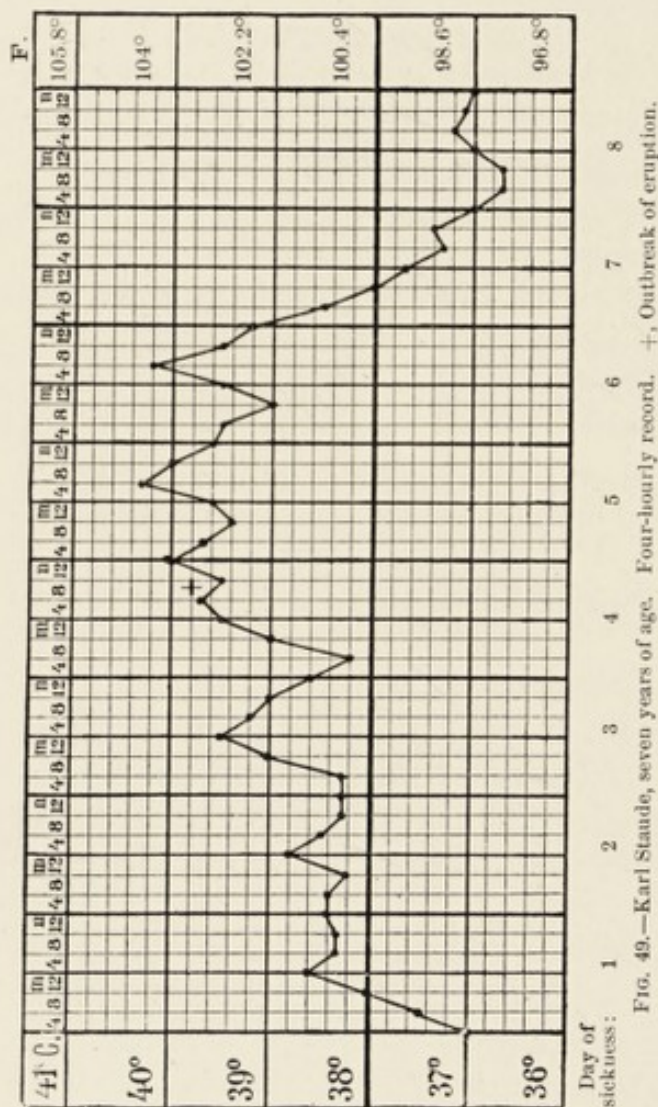
FIG. 49.—Karl Staude, seven years of age. Four-hourly record. +, Outbreak of eruption.

This description undoubtedly fits many cases, perhaps the majority. But another and no less pronounced a type of fever development is also met with. It is characterized by the same rapid initial rise, but not by the well-marked remission. The peculiar fluctuations of temperature corresponding to night and day observed in health are not effaced, on the whole, though the fever continues to increase. This is well illustrated in Embden's cases. Figure 49 is a reproduction of his temperature curve No. 3.

In some instances the prodromal fever merges into that of the eruptive stage without any remission to speak of.

The above comprise the main well-defined phenomena of tempera-

ture with which we have to deal during the period under discussion. There are, of course, numerous modifications, but I do not consider it desirable to give prominence to too many details. (See the foregoing charts.)

We next come to the period beginning with the **outbreak of the rash.** Here we find ourselves well supplied with temperature records.

To quote first from Thomas [*]: "With the onset of the eruptive stage, the remittent and intermittent character of the fever during the prodromal period undergoes a change. The temperature, heretofore only moderately raised, and at times even normal, mounts upward, and the 'fastigium'[†] of the measles begins.

"It is in the eruptive stage that the temperature reaches its maximum height, usually about thirty-six hours after it commences, thus coinciding in normal cases with the full development of the rash or just preceding it. In exceptional cases the fever may be at its highest point soon after this stage sets in. The normal duration of the 'fastigium' is from one and a half to two and a half days; it is shorter in proportion to the length of the prodromal period and vice versâ, hence in any case the maximum temperature can be looked for at the end of the fifth or sixth day of sickness (fever) with considerable assurance.

"In mild cases the rash develops early on the fourth day of fever; in more severe ones it is not seen until the latter part of the same day. The earlier appearance of the rash is usually marked by a higher morning temperature than is otherwise observed on this day. If the first decided rise of temperature (to 39° C. (102.2° F.) or over) takes place during the morning, a further rise usually follows in the evening; the next morning is marked by a moderate or only slight remission, or this may be altogether absent, and on the evening of this, the fifth day of sickness (fever), the temperature touches its highest point. When the rash does not develop until the evening of the fourth day, there is usually only a slight remission on the following morning, or none whatever, and the fever continues its course as in the first instance, reaching its maximum height on the evening of the sixth day. Sometimes a regular remission occurs on two successive days, followed by a rise of temperature, the maximum not being developed until the second exacerbation. In still other cases, although the rash breaks

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[*] Von Ziemssen's "Handbuch," pp. 79 *et seq.*

[†] Wunderlich defines fastigium as "that time of the disease when the fever remains at its height and in full force without any decided abatement, though subject to some fluctuation." *Archiv für Heilkunde,* 1863, p. 345.

out in due season, the height of the fever, instead of being reached in the evening, is delayed until the next morning, or, in other words, until the sixth day.

"The maximum of temperature and eruption coincide, as above stated, in cases of measles running the most normal course.

"In a decided minority of cases, which in respect to eruption and defervescence present a no less normal course, the height of the fever is reached somewhat earlier in the eruptive stage, although not quite at its onset, the rash not coming to its full development until after the temperature has gone down a little. This condition frequently heralds the development of some complication. The highest rise of temperature in the 'fastigium' usually represents the height of the fever in the disease as a whole; in rare instances it is exceeded by the initial rise on the first day of sickness (fever). As a rule, it takes place during the evening. The average maximum rise is to 40° C. (104° F.), but it frequently approaches or even slightly exceeds 41° C. (105.8° F.), without there being any other influence at work than the measles eruption."
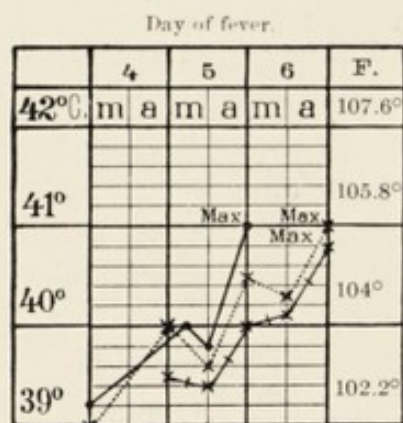
Day of fever.

Outbreak of eruption.

FIG. 50.

In reading this description, which is unquestionably true to life, the impression is easily gained that the rules governing the phenomena under discussion are exceedingly elastic.

The accompanying diagram (Fig. 50) seems to me to present the facts more clearly. The point to be emphasized is the more or less rapid rise of temperature with more or less well-defined but never very considerable remissions, the fever reaching its height in three times twenty-four hours at the longest. Whoever is willing to take the trouble, will have no difficulty in finding a number of temperature records at variance with this rule. I would refer him, among others, to the charts shown in different parts of this article. It is important to remember that the height of the rash usually coincides with the height of the fever. Usually, but not always.

The course of the temperature in the final stage (that of defervescence or desquamation) is given thus by Thomas [*]:

"After the rash attains its full development in the stage of efflo-

* Von Ziemssen's "Handbuch," p. 83.

rescence, the temperature, which usually reaches its highest mark at the same time, begins to fall. If the maximum should have been passed somewhat earlier, though this is not the normal course, the fever will be found to abate more rapidly after the rash begins to fade than before. The rapidity of defervescence varies in different cases; in the majority the temperature sinks to normal within twenty-four or thirty-six hours after attaining its highest point, if not sooner. Frequently, indeed, it is found to be normal on the morning after the evening of its maximum rise; less frequently its subsidence occupies two or two and a half days. It falls most rapidly during the night, an abrupt decline being only exceptionally observed at any other time. When defervescence is completed within a short time, the temperature sinks without any appreciable break; if extended over a day and a half or longer, its downward course will present remissions. The fever in the latter case abates only moderately between the evening on which the eruption is at its height and the following morning, frequently falling to about one degree (C.) above normal, though a lower mark is sometimes reached. After this fall there is a period of exacerbation, but in normal cases the temperature never rises as high as on the previous evening. It soon begins to sink again, before the night is well advanced, and becomes normal by morning at the latest, remaining so if nothing occurs to delay the progress toward recovery. Sometimes a subnormal temperature is observed on the first few days of convalescence; occasionally there is a very slight degree of fever, only a few tenths of a degree, or the two conditions may alternate. As a rule, these trifling anomalies are seen only in cases in which the local symptoms were severe; they have no further significance, and are succeeded in a few days by perfectly normal temperature."

The facts here presented also admit of no dispute; they are well illustrated in charts Nos. 46, 49, etc. In all cases there is a fall of temperature, coinciding with the disappearance of the greater part of the rash. It is quite true, too, that it usually becomes normal in a comparatively short time, but I am of the opinion that it is a mistake to set too narrow boundaries to the period of defervescence. It may be over three days before a normal temperature is reached, and yet the case be one of "normal" measles. It is a fact, furthermore, that the temperature may be found subnormal for days or even weeks after defervescence.

In order to grasp the significance of the temperature changes in measles, we must consider them from both a practical and a theoretic

standpoint, from the point of view of the practitioner as well as from that of the pathologist.

Speaking broadly, we have to deal with a disease process, which, leaving aside the stage of incubation, is divided into two parts, one characterized by the enanthema and the fever accompanying it, the other by the exanthema and its high temperatures. The infection of measles is usually of a benign type. This is proclaimed throughout the course of the fever induced by the measles poison by the continued efforts of the heat-regulating centers to reduce the temperature to normal, the effect of their activity being observed as follows:

1. The normal temperature phenomena in respect to day and night are preserved, the temperature rising during the day and falling at night.

2. The nightly falls of temperature are comparatively well marked; the remissions of the fever due to the infection always take place at night.

The measles poison does not display the same intensity throughout its course, as is best seen in the abatement of the fever which usually accompanies the invasion. The action of the regulating centers is also less hampered at this time.

Again, the poison remains effective for only a short period, a fact sufficiently evidenced by the rapid fall of the temperature after but a few days of high fever. These characteristics of the measles poison seem to me to afford all the explanation necessary to an understanding of the temperature changes, and serve at the same time, I think, as an argument against a fixed type of temperature curve.

I cannot quite agree with Wunderlich * in the following statement: "The course of the temperature must be individual and characteristic in each separate infectious disease; each must possess its typical curve, and if we fail to recognize it, the fault certainly lies with us and our methods of observation. It is chiefly a question of our inability to distinguish the accidental from the essential, and so to evolve the pure law of nature from out the play of manifold individual phenomena."

It should never be forgotten that in all infectious diseases we really have to deal with biologic processes. Living beings are in conflict; on the one side the human body, composed of countless cells joined together to form a unit, on the other separate cells, also in unlimited number, but each acting for itself, living its individual

* "Ueber einige Verhaltnisse des Fieberverlaufes bei Masern," u. s. w., *Archiv der Heilkunde*, 1863, p. 332.

life. However simple the life-process of micro-organisms may be, we know it to be subject to variations, which are expressed by the greater or less amount of injury done by the invading bacteria to the body of their host at different times. During the conflict the virulence of the infectious organisms usually seems to vary at very short intervals. Now, even assuming the resistance of the human body, as far as it affects the individual organisms, to undergo no material change, then a "typical" temperature curve can portray the battle going on within only to the extent of representing the life history of the micro-organisms, when this is limited to a definite period and subject to certain laws during the same. Malarial fever, in which we have to do with the plasmodium, and typhoid fever* belong to this class; in both these processes the bacteria are under strict military discipline, to make use of a simile. But how the temperature curve varies in different cases of sepsis or tuberculosis. Here we can have no typical curve, for the reason that the micro-organisms at work seem to be governed by no fixed laws, to spread and multiply within the body, sometimes with greater, sometimes less rapidity, without regard to stated periods of time. There may be a sudden and stormy rise of more than four degrees, succeeded by only slight fever of less than one degree, and all without any reference to the normal twenty-four-hour curve, the fever sometimes developing during its upward, sometimes during its downward, slope. The part invaded by the microscopic enemy is frequently, if not invariably, betrayed by local lesions.

Nor is it possible to discover a type when the disease sets in with such virulence as to end fatally in a short time. The temperature, in common with all other symptoms, is completely dominated by the poison; the regulating centers are powerless to combat it. The phenomena of an overpowering infection are the same in all such cases; there is nothing characteristic of a specific bacterium to be seen.

Destructive outbreaks of this kind are certainly rare in connection with measles. As the course of the disease goes to show, we have to deal, in all probability, with a poison which develops gradually, and not, as a rule, all at one time, some of the infectious material becoming active before the rest. This is plainly shown by the interval separating the enanthemic from the exanthemic manifestations, and in cases where such an interval is to be observed, it seems proper to

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*See Jürgensen, "Die Körperwärme des gesunden Menschen," Leipsic, F. C. W. Vogel, 1873, pp. 55, 56.

speak of a double invasion. The fever which is sometimes noted during the incubation period, too, can most easily be explained on the theory of the early development of small quantities of the infectious organisms.

The greater the number of organisms acting at any one time, the less can the regulating centers make their influence felt, and vice versâ. Consequently the temperature curve appears more or less notched, and varies decidedly in different cases. Although its main features may be reproduced with a fair degree of regularity, it illustrates the special points of individual cases very clearly.

Wunderlich himself states his conclusions in rather a guarded manner as follows *: "The most essential and characteristic features of this typical curve are the continual fever of short duration and its rapid and decisive fall when the eruption is fully developed." Even this statement calls for modification, since, as I mentioned above, defervescence may be extended over more than three days, without any apparent outside influence being at work. It strikes me that, according to Wunderlich's own words, his "type" of fever has not much ground to stand on.

From a practical standpoint, the importance of the temperature record lies mainly in its relation to the eruption. It should particularly be borne in mind that a high temperature persisting after the rash fades indicates the development of some complication. The cause of the complications occurring in measles is not thoroughly understood. Bronchopneumonia is well known to be the one most often met with, but we are ignorant of its cause.

Is the measles contagium still active? It is hardly probable. Is it a question of secondary infection, perhaps involving different micro-organisms in different cases? This is quite possible, but there is nothing to prove it. The explanation generally adduced in former days, that the inflammatory process set up by the measles is continued as an independent affection, is hardly worth discussing at the present time; or, at any rate, cannot be accepted without some supporting evidence. The question can only be decided in the light of bacteriologic investigations which are yet to be made.

The temperature changes connected with the complications of measles will be considered in the proper place.

The Eruption.—No distinction can be drawn between the eruption appearing on the mucous membranes (the enanthema) and that

* "Ueber einige Verhältnisse des Fieberverlaufes bei den Masern," u. s. w., *loc. cit.*, p. 334.

PLATE 23
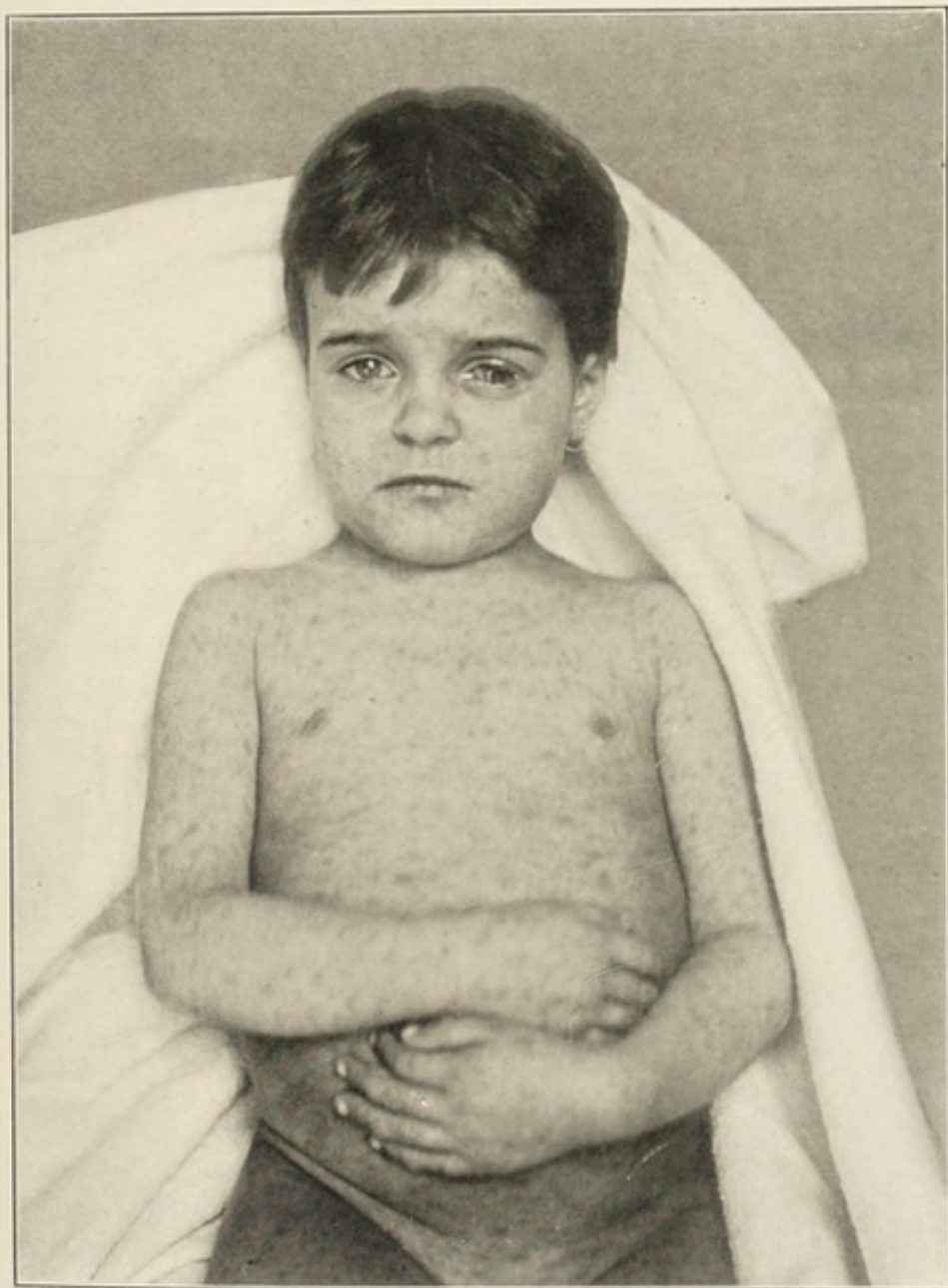
From a case of measles. (Photograph by Dr. Jay F. Schamberg.)
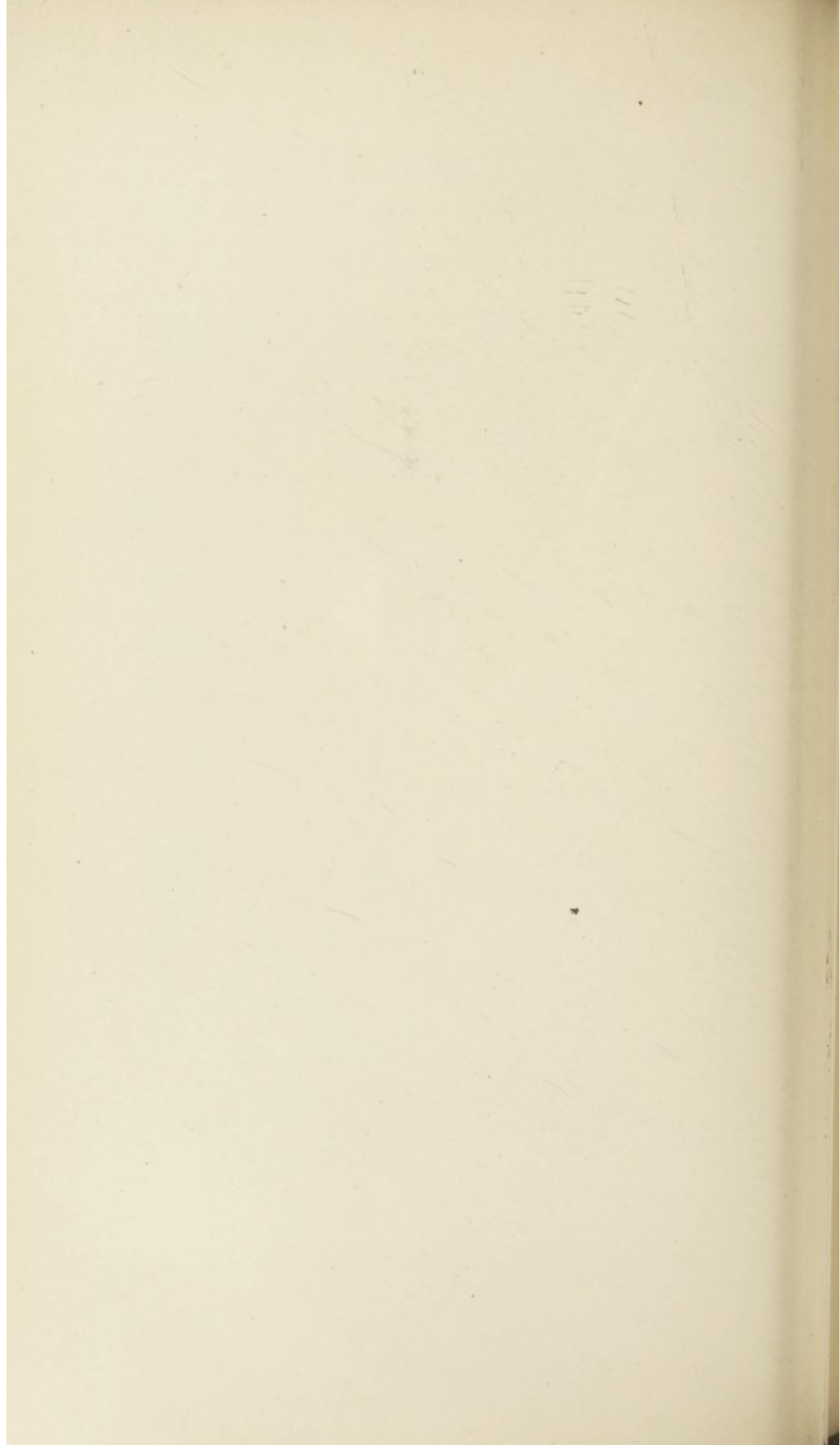
which is seen on the skin (the exanthema). The two are alike as to origin—undoubtedly a genuine localized infectious process—and form. Dissimilarities in appearance are solely the result of dissimilar local conditions, of the different power of resistance displayed by the several varieties of tissue attacked.

While the phenomena of the exanthema were so striking to physicians and laymen alike as to give the disease its name (red spots, measles), it was long before the full significance of the enanthema received recognition.

I think it proper to give a brief survey of the history of the latter, from the time of Willan on. He had observed its occurrence and writes of it thus *: "I would further call attention to the fact that on the fourth day [from the onset of the fever; the same day on which, according to Willan, the external rash also develops] small dark red spots, in form closely resembling those just described, make their appearance on the hard and soft palates, the uvula, and the tonsils. In the course of the fifth day they become coalescent, and finally take the form of a general diffuse redness spreading over the fauces and behind the soft palate."

Heim,† that excellent German observer, noticed the enanthema to develop earlier that the external rash, as we see from the following extract: "On the second day of fever, small light red spots usually appear in the mouth." He looks on these as quite similar to the spots on the skin.

As far as I can discover, there was less attention paid to the enanthema later on. Trousseau,‡ to be sure, thoroughly understood the matter, describing the enanthema and its appearance prior to the exanthema with great clearness. In his treatise on the disease § Franz Mayr casually mentions that spots may also be seen on the mucous membranes, but denies the development of an enanthema in his principal work on the subject. Ziemssen and Krabler‖ look upon it as an exceptional feature. Barthez and Rilliet** also maintain that it does not appear regularly. They state that Dr. d'Espine has observed it as described by Heim, but that they themselves have repeatedly looked for a buccal eruption in vain, and under the most favorable conditions. If this be so, it would almost seem that the enanthema must sometimes be absent, for I fail to understand how it could escape a practised eye which was bent on seeing it.

At the present time, at least, the eruption on the mucous surfaces is usually to be observed. To Rehn †† belongs the credit of being the first to

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* "Die Hautkrankheiten und ihre Behandlung." Translated by F. C. Friese, Breslau, Korn, 1806, vol. iii, Pt. 1, p. 166.

† "Bemerkungen über die Verschiedenheit des Scharlachs, der Rötheln und der Masern," u. s. w., *Journal der praktischen Heilkunde.* Ed. by C. W. Hufeland and K. Himly, 1812, Pt. 4, pp. 86 *et seq.*

‡ "Medicin. Klinik," u. s. w. Translated by Culmann, Würzburg, Stahel, 1866, vol. i, p. 139.

§ *Loc. cit.,* p. 10.   ‖ *Loc. cit.,* p. 201.   ** *Loc. cit.,* p. 238.

†† "Zur Symptomatologie und Kritik des Prodromalstadiums der Masern." By Dr. H. Rehn of Hanau. "Jahrbuch für Kinderheilkunde," u. s. w., new series, 1st year (1868), pp. 97 *et seq.*

call attention to the great significance of this phenomenon in the study of the morbid processes peculiar to measles. Other important articles followed his, among which that by Alois Monti* is particularly valuable.

Before entering into details, let us consider the **anatomic changes** which take place in the tissues immediately affected by the measles poison. The latter has a mild inflammatory action on the skin and mucous membranes, which, however, are not equally involved throughout. One essential point of difference lies in the form in which the inflammation presents itself, becoming diffuse in the case of the mucous membranes, while on the skin it always remains circumscribed. The more intense inflammatory lesions seen in places on the background of a generally inflamed mucous surface—the enanthema —give evidence of the identity of the two processes. It is quite reasonable to suppose that a diffuse inflammation would also develop on the skin were it not for the more compact arrangement of its tissues.

The histologic examinations thus far reported have been limited to the skin. The most minute description is that given by Unna,† whose observations coincide, in the main, with those previously published by Gustav Simon.‡ I will not attempt to decide as to the correctness of the conclusions which Unna draws from his studies. He writes as follows:

"The clinical symptoms point to a spastic paralysis of the blood-vessels of the skin, following close upon the primary active hyperemia which develops in the neighborhood of the infectious organism after it lodges in the capillaries of the skin. This spastic condition of the vessels explains the cyanotic appearance, the papular form, and the urticaria-like edema of the center of the eruptive spots, also the frequent escape of hemoglobin. It is not to be wondered at, therefore, that on cutting across a measles papule, either on the living or the dead subject, we fail to detect any evidences of hyperemia or to discover any dilated blood-vessels. Other signs of the edematous stage, however, are regularly present. The rapidly forming, spastic edema always collects at the points of least resistance, which, in the early years of childhood, when the disease usually occurs, are represented by the adipose tissue, the sweat glands, and the sheaths of the larger

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* "Studien über das Verhalten der Schleimhaute bei den acuten Exanthemen," "Jahrbuch für Kinderheilkunde," new series, vol. VI (1873), pp. 20 *et seq.*

† "Die Histopathologie der Hautkrankheiten," p. 625.

‡ "Die Hautkrankheiten durch anatomische Untersuchungen erläutert," 2d ed., Berlin, C. Reimer, 1851, pp. 122 *et seq.*

blood-vessels supplying the muscles of the skin and the hair follicles. Accordingly, in specimens hardened in alcohol we find the ducts of the sweat glands highly edematous, looking like great gaps in the tissue, partly filled with distended areolar tissue and thin-walled connective-tissue cysts, while the corresponding sweat glands compressed by the edema lie in an angle at the end of the ducts. Individual sweat glands, hair follicles, and muscle-fibers all seem to be floating free in broad cleft-like lymph spaces. In addition, the middle and deep layers of the skin contain spaces and channels, round, oval, or irregularly shaped, which we must regard in part as distended lymphatics, in part as enormously dilated lymph spaces. In a few places, more especially in the neighborhood of the hair follicles, these dilated lymph channels can be traced upward to the papillæ of the corium. . . . The signs of an intense edema of skin and subcutaneous tissue as here described are equaled in importance by the almost complete absence of a cellular exudate. The emigration of white blood-cells does not exceed that to be observed in any simple passive hyperemia; indeed, is rather less than is usual in such cases. For this reason only a few leucocytes are to be seen in the epidermis. The rete mucosum does not appear thickened: the edema does not extend to the lymph channels of this layer. I have found no indications of mitosis at the height of the inflammatory process; this is rather an accompaniment of desquamation. Some slight anomalies of cornification are presented, however. The stratum granulosum is missing in places, while the basal lamellæ of the stratum corneum are thickened. At the time of desquamation the superbasal corneous lamellæ become separated from the basal, and, together with the middle and outer lamellæ, fall off in the shape of measles scales. This loss of epithelium is made good by mitotic cell proliferation."

This, then, is the picture of the ordinary flat, or slightly papular type of measles eruption.

According to Neumann and Catrin, Unna describes more far-reaching changes in the cases where the eruption takes the form of small nodules. They consist of well-developed inflammatory lesions of the blood-vessels, and marked degenerative changes in the epithelium. The theory of earlier days: "The measles eruption consists of an inflammation of the follicles of the skin, with a slight degree of exudation,"* was not based on microscopic examination, but solely on external appearances. It was adhered to in spite of Simon's studies, but must now at last be discarded.

* Franz Mayr in his treatise, p. 11; also in Hebra's " Handbuch."

Let us return to the eruption on the mucous membranes.

First, in regard to its situation. We are chiefly concerned with its appearance in the buccal cavity, if only because this is so easily inspected. The eruption is not evenly distributed over its surfaces. The best detailed description, which also takes account of the time of development, is that from the pen of Dr. N. Flindt. It really deserves to be taken from its grave in the "Reports of the Danish Board of Health," and I herewith give it in almost literal translation:

"First day of fever: The pharynx shows a slight diffuse redness.

"Second day of fever: On inspecting the throat, the posterior pillars of the fauces and the tonsils are seen to be considerably injected, but not perceptibly swollen; the anterior pillars and the soft palate are also injected, but the redness is less marked and is unevenly distributed. On the evening of the same day the tonsils and posterior pillars of the fauces appear generally reddened, as in the morning, and slightly swollen, and, in addition, an eruption is seen on the anterior surface of the soft palate and the posterior portion of the hard palate. The mucous membrane of these parts is otherwise normal in color. The eruption consists of round or somewhat irregularly shaped light red spots, not very distinctly circumscribed, and only just raised above the level of the mucous surface. The spots vary in size from a pinhead to a lentil, are in part isolated and in part collected into groups, quite irregular in shape, and in some places coalescent. At the center of the small red spots, and giving them a peculiar appearance, are situated numbers of tiny, whitish, shiny raised points, apparently vesicular in character, and irregularly grouped according to the arrangement of the spots on which they lie. These tiny miliary vesicles can be both seen and felt as distinct elevations. The palpebral conjunctiva is reddened throughout, and besides the net-like injection dependent on the distribution of its blood supply, it sometimes appears spotted, and covered with miliary, pearl-colored, raised points similar to those on the mucous membrane of the palate.

"Third day of fever: The buccal mucous membrane is for the most part normal in color, except for the eruption above described, which now covers the entire anterior surface of the soft palate, and, as a rule, all but the anterior third of the hard palate. The spots are still isolated in part, and in part have joined to form irregular figures; their color is deeper than before, and here and there they are slightly elevated. They are covered by the vesicles already described, and in some cases the latter are also seen on apparently normal mucous membrane. Similar groups of spots and vesicles can now also be perceived

on the mucous membrane of the cheeks, especially on the parts corresponding to the space between the upper and lower molar teeth. The gums and inner surfaces of the lips usually preserve their normal color, or, at the most, appear slightly injected; they almost never show an eruption at this time. The tonsils and pillars of the fauces remain diffusely reddened as before. The injection of the palpebral conjunctiva is now so intense as to obscure the spots, but the vesicles are still visible. The eruption now begins to develop on the skin. In the evening the condition is about the same.

"Fourth day of fever: On the hard and soft palate and cheeks the eruption is very prominent, and in the latter situation more thickly developed. In places the spots have become coalescent for a considerable distance. The eruption has disappeared from the conjunctiva. No change to be noted in the evening.

"Fifth day of fever: The eruption in the mouth is more distinct than at any previous time. Faint red spots are now often to be seen on the inner surface and even on the outer border of the lips; less frequently, and only in indistinct outline, on the gums. The congestion of tonsils and fauces is unaltered. The external rash is fading, and the temperature going down.

"Sixth day of fever: The eruption is no longer perceptible, but the mucous surfaces of the palate and cheeks often show a more or less distinct diffuse redness. The temperature is normal."

The foregoing statements are confirmed by all physicians who give the subject their special attention.

I would further add that the eruption on the mucous membranes may appear darker in consequence of hemorrhagic effusion into the separate spots and surrounding tissue. The process of absorption is carried on as usual, light-colored spots sometimes marking the points of hemorrhage for a short time afterward.

The mucous membrane of other parts may also be involved. Gerhardt * found an eruption in the larynx, trachea, and bronchi; he emphasizes its identity with that seen on the skin and the fact of its earlier development. According to Thomas and Bohn, Steiner has observed red spots on the intestinal mucous membrane, resembling the external rash. I have not been able to find the original article; Thomas, usually so accurate in his references, has made an error in this instance, for at the pages which he mentions in volumes LXXXIV and CVI of the "Prager Vierteljahrsschrift," there is nothing bearing on measles.

* "Lehrbuch der Kinderkrankheiten," p. 63.

Circumscribed red spots are also said to appear on the mucous membrane of the genitals and the bladder (Fuchs, Henoch, and Chomel, cited by Thomas).

[**Koplik's Spots.**—For a description of the characteristic appearance and the diagnostic value of the "buccal spots" it is but just to refer to the writings of Dr. Koplik on the subject,* as follows: "Scant attention is given to the most important elements of the eruption as it appears on the mucous membrane on the inside of the cheeks and on that of the lips. A thorough understanding of the eruption on the buccal mucous membrane will aid in separating an invading measles from a mass of eruptions resembling measles which appear on the skin in infancy and childhood.

" If we look in the mouth at this period (invasion), we see a redness of the fauces; perhaps, not in all cases, a few spots on the soft palate. On the buccal mucous membrane and the insides of the lips we invariably see a distinct eruption which consists of small, irregular spots, of a bright red color. In the center of each spot there is noted, in strong daylight, a minute bluish-white speck. These red spots, with accompanying specks of a bluish-white color, are absolutely pathognomonic of beginning measles, and when seen can be relied upon as a forerunner of this eruption. . . . No one has, to my knowledge, called attention to the pathgonomonic nature of these small bluish-white specks and their background of red, irregularly shaped spots. They cannot be mistaken for sprue, because they are not as large nor as white as sprue spots. These specks of bluish-white surrounded by a red area are seen on the buccal mucous membrane and on the inside of the lips, not on the soft or hard palate. Sometimes only a few red spots, with this central bluish point, may exist—six or more; and in marked cases they may cover the whole inside of the buccal mucous membrane. If these bluish-white specks on a red spotted background are at the height of their development, they never become opaque, as sprue, and in this respect, when once seen, are diagnostic, nor do they ever coalesce to become plaque-like in form. They retain the punctate character.

"The eruption just described is of greatest value at the very outset of the disease, the invasion. As the skin eruption begins to appear and spreads, the eruption on the mucous membrane becomes diffuse and the characters of a discrete eruption disappear and lose themselves in an intense general redness. When the skin eruption is at the efflorescence, the eruption on the buccal mucous membrane

* *Archives of Pediatrics*, vol. XIII, No. 12, pp. 918 to 920.

PLATE 24.

FIG. 1.
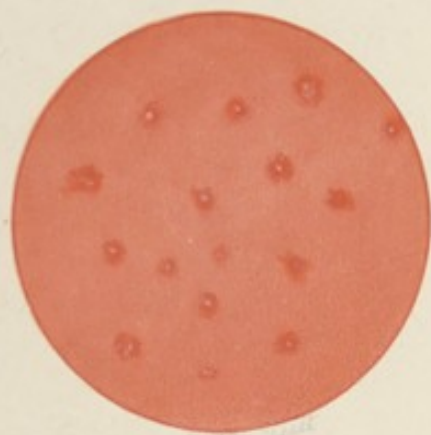
FIG. 2.
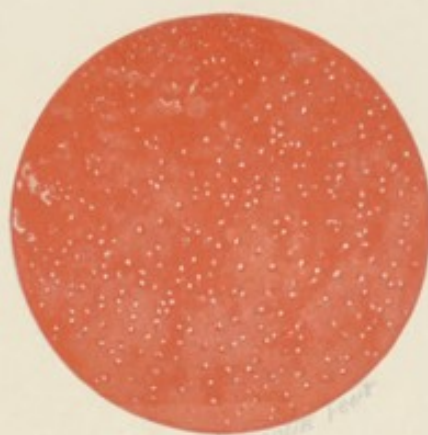
FIG. 3.
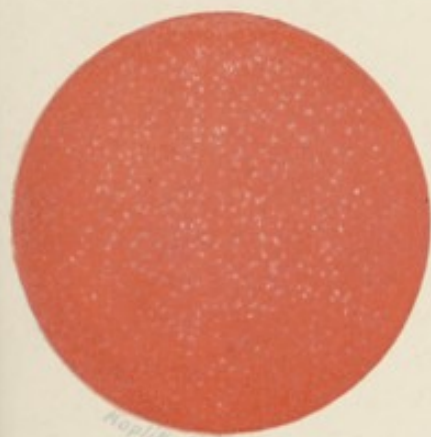
FIG. 4.

The pathognomonic sign of measles (Koplik's spots).

FIG. 1.—The discrete measles-spots on the buccal or labial mucous membrane, showing the isolated rose-red spot, with the minute bluish-white center, on the normally colored mucous membrane.

FIG. 2.—The partially diffuse eruption on the mucous membrane of the cheeks and lips; patches of pale pink interspersed among rose-red patches, the latter showing numerous pale bluish-white spots.

FIG. 3.—The appearance of the buccal or labial mucous membrane when the measles-spots completely coalesce and give a diffuse redness, with the myriads of bluish-white specks. The exanthem is at this time generally fully developed.

FIG. 4.—Aphthous stomatitis, likely to be mistaken for measles-spots. Mucous membrane normal in hue. Minute *yellow points* are surrounded by a red area. Always discrete.

(The Medical News, June 3, 1899.)
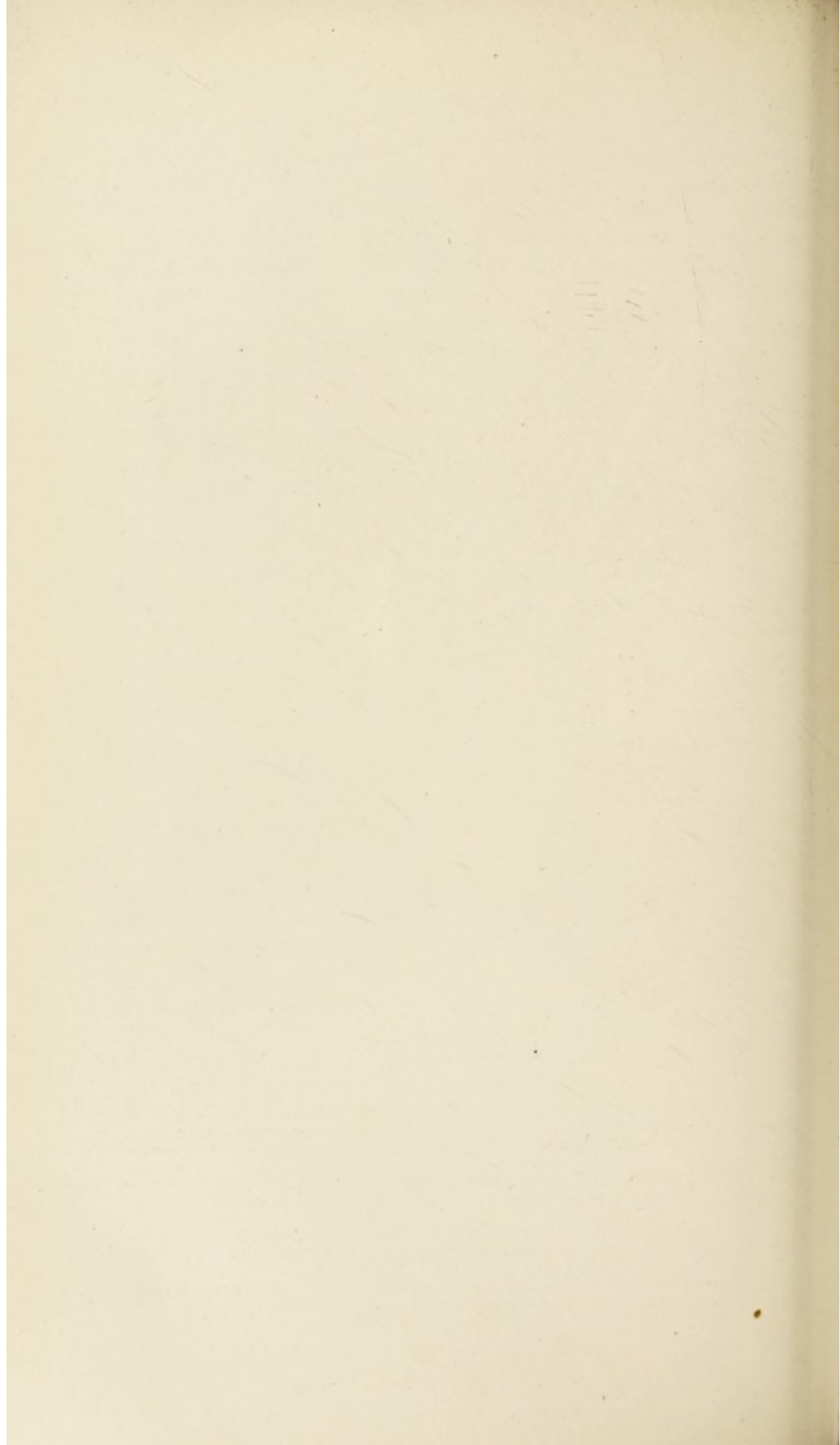
has lost the characters of a discrete spotting and has become a diffuse red background with innumerable bluish-white specks scattered on its surface. . . . The mucous membrane retrogrades to the normal appearances long before the eruption on the skin has disappeared."

Libman* has looked for these spots in 50 cases, and found them in every instance. As a rule, the more marked the rash, the fewer in number the spots. In the course of daily examination of the mouth on general principles in healthy children who had been exposed, the spots were recognized in a number of cases, so that early isolation was possible. The exanthem, coryza, etc., are fallacious in some cases, and the spots are, all in all, the most unequivocal symptom we have. This author has never seen any counterpart of Koplik's spots in other diseases, although lesions of purpura and secondary syphilis have resembled them roughly.

Knöspel† states that many of the older pediatrists have described an exanthem of the mucous membranes in measles. Flindt has given a very full account of these spots. But since Koplik has shown a new feature, their early appearance before the outbreak of the rash, he is deserving of the credit for the diagnostic significance of the spots. Slawyk was the first to take up the study of the latter after Koplik's description.

Knöspel has seen 41 patients with these spots in Ganghofner's clinic. In other ambulatory cases the notification card was made out as soon as the spots were noted without waiting for the exanthem. Knöspel shows by a number of clinical histories the great benefit derived in diagnosis from the recognition of the spots.

Finckelstein‡ has seen 5 cases of Koplik's spots in Heubner's pediatric clinic as described by their discoverer. The sign is of value in discriminating between measles before the appearance of the rash and influenza. It was present in each one of 5 cases examined.

Slawyk§ examined 52 children with measles for Koplik's spots and found them in 45 cases. He describes them as round, bluish-white, slightly raised, and having a reddish center. He usually saw from 6 to 20 on a side, but exceptionally the number ran up into the hundreds. Occasionally he saw them on one side only. He found them more numerous near the lower molars. Under the microscope they are seen to be composed of buccal epithelium in fatty degeneration.

* *Med. Record*, June 11, 1898.   † *Prag. med. Wochenschrift*, Oct. 13, 1898.
‡ *Berl. klin. Woch.*, p. 605, 1898.   § *Deutsch. med. Wochenschr.*, 1898, No. 27.

19

Havas* investigated 16 children with measles for the presence or absence of this symptom, and discovered it in all but one case. In some instances the spots appeared larger than as represented by Koplik. Many times they attained the size of a lentil. In some situations, especially upon the gums, a sort of bluish-white deposit formed upon the spots. The favorite localities were the buccal mucosa opposite the lower posterior molars, the region of Steno's duct, and the gum of the lower jaw. The differential diagnosis is always guaranteed by the presence of this sign.

Manasse† states that he has seen Koplik's spots without consecutive measles, and measles without preceding Koplik's spots. Hence he thinks the sign, while of some value, is by no means unfailing.

Hirsch ‡ has seen Koplik's spots in every one of some 40 or 50 cases of measles thus tested. He has found the sign of great value in the negro, in whom it is often difficult to detect the exanthem.

Cotter § studied 187 cases of measles in reference to Koplik's spots, the material coming from an epidemic at the New York Foundling Hospital. The first point tested was the regularity of the appearance of the spots. These appeared in 169 out of 187 cases, while 8 patients presented no spots, and in 10 the result was in doubt. The second point referred to the question of priority of appearance of the spots. Cotter found that the appearance was synchronous in 78 cases, while in 88 the spots preceded the eruption (from one to five days before). Finally, in 2 cases the rash came out before the spots. In not one of the cases was this symptom the sole evidence of measles.

Ross‖ investigated 15 cases for Koplik's symptom, and pronounces it of great value in differential diagnosis, both in regard to other exanthemata and to non-eruptive febrile conditions. Its trustworthiness is almost absolute.

Lorand** has studied Koplik's spots under the direction of Prof. von Bokay. In 175 cases of measles the spots were absent 11 times. Of the entire material, 92 cases were seen in the prodromal period; and of these, 3 had no spots.

In another series of 348 cases the spots were absent in 19. Lorand admits, however, that special facilities for illumination might have shown the presence of the spots in these apparently negative results.

* *Wien. med. Presse*, 1899, No. 24.   † *Münch. med. Wochenschr.*, June 5, 1900.

‡ *Phila. Med. Jour.*, 1900, vi, 343.   § *Arch. of Pediatrics*, 1900, xvii.

‖ *Columbus Med. Jour.*, xxiv, 1900.

** "Jahrb. f. Kinderheilk.," 1901, iii, 658.

Advantages of the discovery: (1) Diagnosis; (2) differential diagnosis; (3) prophylaxis. All the profession should be able to recognize these spots.

Priority: Weiss * awards this to Flindt (Nothnagel's "Handbuch," 1896); Slawyk to Filatow, in his "Acute Infectious Diseases," 1895; the author quotes Bohn, in Gerhardt's "Handb. d. Kinderkr."; Gerhardt himself cites Reubold ("Virchow's Arch.," 1853, Bd. vii).

Falkener † entitles his article "Filatow's Spots in Morbilli," giving this authority full priority over Koplik. He has studied 76 cases, every one of which exhibited the spots. This sign is of great value in excluding rötheln, croup, and measles without eruption.

Sobel ‡ has made a special study of the buccal mucosa in dermatoses of all kinds, eruptive fevers, and drug rashes, but in no instance did he ever see anything resembling Koplik's spots.]

In considering the **eruption on the skin,** we will first speak of its outward characteristics and then take up its manner of spreading.

The measles eruption consists of circumscribed, slightly raised spots, varying in color from light to dark red; and in part presenting a slight central elevation; as each develops separately, the skin is never completely covered at any one place. The spots are not always round, but vary greatly in shape; they appear long-drawn-out, notched, crescentic, etc. It is a peculiarity of the eruption, at least at first, that it is sharply outlined against the unaffected surrounding skin. The individual spots measure from less than 1 mm. to nearly 1 cm.; most frequently they have a surface area of about 2 or 3 mm.

The fact that the eruption is actually raised above the normal skin can be demonstrated both by sight and touch. This is the case from the beginning, and continues until desquamation is completed, but is particularly marked when the eruption is at its height.

The rash may be very light in color, and is very apt to be so at first if it develops only scantily. It is seen in all shades up to a deep purple, and, as a rule, increases in depth of color as the individual spots go on to full development. For a time the color disappears entirely on direct pressure, or, better still, on stretching the skin at that point; next, a slight yellowish discoloration remains when this is done, finally becoming brownish in tone. The presence of a hemorrhagic effusion, confined to the area covered by the spot, gives it a distinctly bluish tinge, which, of course, persists when the skin is stretched over it.

The central elevation which especially marks the individuality of

* *Wien. klin. Wochen.*, 1899, 251.   † *Lancet*, 1901, i, 315.
‡ *N. Y. Med. Jour.*, 1898, lxviii, 556.

the spots composing the eruption is not always present. The heavier
the rash, the more papular is its character. The condition of passive
edema described by Unna, and by him referred to a previous spastic
contraction of the muscular coat of the blood-vessels, induced by the
action of the disease poison, explains the papulation very satisfactorily.

The fact that each spot of the measles eruption develops inde-
pendently is of the greatest importance in giving it a distinctive char-
acter, since no matter how close together they may lie, there are
invariably some islands of normal skin left between them. This is also
the case when primarily circumscribed spots become coalescent in
places, as always occurs when the rash is at all thick. Intervals of un-
affected skin are found in every case without exception, even when the
rash is everywhere of the confluent variety. They may be very small,
but they are present nevertheless. This gives the skin a peculiar ap-
pearance where the rash is thickest, the whitish streaks looking like
very irregular winding channels in the dark red surface of the skin.
Nor is the contrast between morbid and healthy skin effaced when it
is generally swollen, as happens not at all infrequently in confluent
measles, in places where the underlying tissue has a loosely woven tex-
ture, as in the face, for instance.

The fact that the eruption develops in independent spots seems to
me to throw a strong light on the whole process. I think we are obliged
to conclude the eruption to be produced by some form of organic life
circulating in the blood, which can work harm only to those tissues
in which it comes to lodge. This would explain the circumscribed
character of the affected areas. If the poison were simply in solution
in the blood, the morbid changes would necessarily be evenly dis-
tributed throughout. The demonstration of the presence of typhoid
bacilli in the roseola spots of typhoid fever helps to corroborate this
theory.

The eruption is not evenly distributed over the body, some parts
being involved earlier and more intensely than others. Occasionally
a tiny punctate rash is seen here and there on the body quite early,
even before the eruption develops on the mucous membranes, but it
soon disappears again. Rashes of very short duration, covering a
rather larger area, may also be observed in some cases, just before the
outbreak of the general eruption. It is an open question whether
these phenomena are referable to the products of metabolism of the
specific bacteria. Sometimes a true measles eruption develops later
in the same place.

The face is first attacked in the great majority of cases; the rash,

too, is usually thickest in this situation. Opinions vary somewhat, as to the part of face or head where it is first to be seen. Heim says, between the ears and nose; Gerhardt, on the cheeks and about the temples; Mayr, on the temples and neck; Bohn, on the cheeks and about the lips; Barthez and Rilliet, first the chin, then the lips and cheeks; Thomas, the chin, forehead and temples, over the mastoid process, and on the scalp, especially at the back of the head, while N. Flindt names the cheeks, the region below the eyes, the forehead, chin, and temples, behind the ears, the bridge of the nose, or about the nostrils and the upper lip.

I think that from all this different testimony we may safely conclude the location of the first spots to be of no great importance, and hardly subject to a general rule. It suffices to remember that the eruption is first to be looked for on the face and the adjacent portions of the scalp. Next it appears on the neck and throat and the upper part of the back and chest, and soon afterward on the wrists. The general rule for its further development is that the lower parts of the body are attacked last, extensor and flexor surfaces being fairly equally involved. The palms of the hands and soles of the feet do not escape.

In respect to the development of the rash, I would also call attention to the different stages represented by the spots on any one part of the body (quite apart from the difference as to time of outbreak between any two given parts of the body), some always appearing in advance of others. This is most noticeable when the rash is first coming out and when fading; it is less apparent, of course, when it is at its height. On the whole, the rash may be said to develop less thickly on the parts last involved than elsewhere, but here, too, perfectly fresh spots can often be seen beside fully matured ones. The confluent form of rash is decidedly most often exhibited on the face, at least when covering an extensive area; small confluent patches, comprising a few spots only, may be observed on any part of the body.

The following forms of eruption are distinguished according to their external characteristics.

Morbilli læves, red spots showing a small central elevation—the usual form.

Morbilli papulosi, in which the central elevation is nodular and the spots are colored a deeper red.

Morbilli vesiculosi s. miliares. Here the spots are covered with tiny vesicles, resembling "goose-flesh."

Morbilli confluentes s. conferti. As its name expresses, this form represents extensive coalescence of separate spots.

Morbilli hæmorrhagici, characterized by hemorrhagic effusion into and around the individual spots.

These several forms simply represent different degrees of local disorders of nutrition in the skin, and have no bearing on the disease proper. I entirely agree with the following statement of Fürbringer [*]: "They (the various forms of the eruption) are of considerable interest to the dermatologist, and in their more striking manifestations make a great impression on the young practitioner. The experienced clinician or pediatrist gives his attention chiefly to the general course of the disease and is not much influenced by the appearance of the eruption."

This applies, above all, to the hemorrhages, which of course are to be sharply distinguished from those attending the so-called "dissolutio sanguinis." The differentiation can only be made, however, by taking the general condition into consideration, since the local distribution of the effusion in the skin is the same in both cases.

Otto Veit,[†] who has written a very excellent article on the subject, presents the following conclusions from his studies:

"Several different forms of hemorrhagic effusion into the rete Malpighii and corium are met with in cases of hemorrhagic measles. There are the isolated, sharply circumscribed, blackish tinged, small, round petechiæ, the κατ' ἐξοχήν; but far more frequently we see larger ecchymoses, preserving the shape and size of the former spots of rash. Sometimes the effusion takes the form of long, irregular streaks (vibices), sometimes that of large plaques (purpura hæmorrhagica). Any one of these different forms may be seen alone, or two or more may occur in the same individual. Only a few parts of the body may be involved, or the hemorrhages may be distributed over more or less of its entire surface. The color of the affected areas when fully developed varies from purple to black, subsequently passing through the changes characteristic of the absorption of extravasated blood. They may last for a few days or several weeks. In four of my cases the ecchymoses were accompanied by nosebleed, otherwise there were no hemorrhages from other parts.

"The early appearance of the hemorrhages, usually within the first few days, is an especially important indication of their dependence on the measles eruption, and calls for a strict differentiation from a petechial process which may develop some weeks later, after the rash has entirely disappeared."

Veit states very positively that, according to his observations,

[*] "Measles," in Eulenburg's "Real-Encyklopädie," u. s. w., Vienna, Urban & Schwarzenberg, 1887, 2d ed., vol. XII, p. 555.

[†] "Ueber hämorrhagische Masern," *Virchow's Archiv*, vol. XIV, p. 86.

when the formation of petechiæ was preceded by high fever, it would abate when they appeared, while the patient's general condition would at the same time improve decidedly. The more detailed histories of the cases which he cites—unfortunately, no temperature records are given—unquestionably bear out this statement. It is therefore apparent that we have to consider two forms of hemorrhagic measles, a benign and a malignant form.

As Thomas very correctly states, the rapidity with which the eruption spreads over the body depends to a certain extent on whether it begins to develop close to the time when the fever sets in or somewhat earlier. Thus, if the rash appears on the face at the beginning of the invasion (prodromal or enanthemic stage), it will not at once proceed to spread, but will temporarily remain moderately developed and stationary. But when the temperature begins to rise higher rapidly a little later, the rash, too, proceeds to develop quickly over the whole body, and grows much thicker on the face. On the other hand, when the eruption first breaks out close to the time when the fever is approaching its height, it will cover the body with great rapidity and intensity. The total duration of the rash depends, of course, on this point.

As a general rule, the rash fades first from the parts where it first appeared, and last from those last attacked. It sometimes happens that after it has begun to fade it again takes on a brighter hue. This indicates, however, nothing more than a rise of temperature, whereby the circulation of the blood in the skin becomes more active and the rash in consequence appears more distinct than before. There is no renewal of the eruption. This is Thomas' opinion, and I entirely concur in it.

The further course of the process, the slight temporary pigmentation, and the desquamation have already received sufficient consideration.

Perspiration is usually observed in the course of the measles fever, beginning before the rash breaks out, accompanying its development, and increasing during the remissions of the fever. The skin is seldom quite dry either, when the temperature is rising.

All thus far said in regard to the eruption applies to the great majority of cases, in which we have to deal with a simple uncomplicated measles infection. We have been speaking, therefore, of the average case. Let us now take up the more important of the irregular forms.

The possible occurrence of **morbilli sine exanthemate** is accepted

by many physicians. I myself must say with Henoch and Fürbringer that I have never seen an undoubted case. Bohn * very properly urges that special attention be paid to the enanthema in order to make a positive diagnosis. He says: "Perhaps this fragment of the eruption, at least, is always to be found, and if so, the cases could of course not be referred to as examples of measles without eruption." A review of the literature bearing on the subject seems to me to show that the majority of careful observers express themselves on this point with considerable reserve. To warrant a diagnosis there must be opportunity for infection, marked catarrhal symptoms of the usual type, and fever similar to that of measles cases. Thomas † writes: "Sometimes, even in primary attacks, we meet with cases where the disease runs its ordinary course in respect to catarrhal symptoms and fever up to the time when the eruption should appear, and then comes to an end without showing either an eruption or the fever characteristic of the eruption period; these cases are distinguished, therefore, by the presence of the first half of the regular measles fever from others which present an irregular course of temperature." I should not hesitate to pronounce a case which really presented these features to be one of true measles, but I have in vain sought for histories of individual cases of this description.

Embden states that in the Heidelberg epidemic described by him no less than 20 (4.3%) of the 461 cases which came under medical observation failed to display any eruption, which is, indeed, an unusually high proportion. Most of these cases, he says, were of a mild type, but severe complications occurred in a few instances. But here, again, we have nothing but the general statement—not a single history is given.

The history of a case of measles of a severe form, in which no eruption appeared, is reported by Rilliet.‡ Two children in one family were taken with measles which ran a normal course. Twelve days later a third child of the same family, twenty-one months old, began to cough and sneeze and to have fever. The looked-for eruption did not appear, but a lobular pneumonia involving both lungs developed on the fourth day and spread very rapidly. This was followed by a keratitis, and the child died on the eighth day of the disease. Even though there is no absolute proof that this was a case of measles, the possibility is not to be disregarded.

* See Gerhardt's "Handbuch," *loc. cit.*, p. 307.

† See v. Ziemssen's "Handbuch," *loc. cit.*, p. 85.

‡ See Barthez and Rilliet, *loc. cit.*, p. 249.

Some authors assert that desquamation has been known to follow in non-eruptive cases, a statement which Thomas is inclined to credit on the ground of the analogy with instances of such desquamation after scarlatina, and the observations recorded by Fr. Seitz. The latter, however, are of little value as evidence on this point, being summed up by Seitz * in the following brief statement: "A few times I saw cases presenting all the characteristic symptoms of measles except that no eruption was visible on the skin, but which were followed, nevertheless, by *partial* desquamation." The criticism which naturally suggests itself here, and which is apparent to Thomas himself,—namely, that it is difficult to understand how a skin affection sufficiently severe to cause desquamation should not have been recognizable previously,—is most plainly voiced by Mayr, who gives it as his opinion that the eruption had been simply overlooked. This would certainly seem the most plausible explanation, *since the desquamation is stated to have involved certain parts only.*

Different opinions exist as to the import of the so-called **irregular form of eruption** in measles. Formerly much weight was laid upon it. A remnant of this earlier view still lingers in Henoch's writings, as follows †: "When the rash, instead of spreading in the usual manner, from the face downward toward the feet, first breaks out on the chest or back, and then develops irregularly in all directions from

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*"Statistics of Disease in Munich from May, 1841, to July, 1843, Read at a Meeting of the Local Medical Society," etc., *Medicinisches Correspondenzblatt bayerischer Aerzte,* 1844, No. 12, p. 181. I am obliged to assume that it is this paper only to which Thomas refers. He also mentions the *Prager Vierteljahrsschrift,* vol. v (1845), in which, on page 85 of the "Analecten," there is to be found a short note and reference, but containing nothing in regard to the principal point in question, that of "partial" desquamation. The other reference given by Thomas, *Bayerisches Intelligenzblatt,* 1873, p. 756, is incorrect, measles being in nowise under discussion at that place. I have not the slightest desire to attack Thomas, whose method of dealing with his subject by drawing from the plentiful storehouse of past experience is highly to be recommended to those writers who treat to-day of yesterday's events, their field of vision being restricted to their own cases. But even old Homer may sometimes be caught napping, and when such points as that now under discussion are involved, it is perhaps permissible to awaken him, since if the fact in question were really established, it would be of considerable interest from the standpoint of general pathology. But just for this very reason we should demand more reliable evidence than has yet been presented, and not rely on simple general statements, however trustworthy the observers responsible for them may be. The following, taken from Romberg, is an example in point: "A diagnosis of measles without eruption seemed to be justified in a number of cases in which symptoms of lassitude, sneezing, lacrimation, but no cough, were displayed; in many of these cases a desquamation involving the entire surface of the body and lasting some time was noted." (See the reference on page 301.)

† "Vorlesungen über Kinderkrankheiten," p. 671, 3d ed.

this point, the course of the disease is very apt to be unfavorably influenced by complications or by a previously existing general bodily weakness." He adds, however, that this sign does not apply in all cases.

My own opinion coincides with that of Thomas and Bohn, who believe the outcome of the disease to be quite unaffected by the first appearance of the rash on some other part than the face. I think, indeed, that this mode of development is quite often observable in certain epidemics, and in such instances it is the neck and upper part of the chest which are most likely to be attacked first.

In other cases, the rash is entirely or almost entirely limited to certain regions, leaving other parts which it usually covers quite unaffected. Bohn even asserts that the face may show no rash, although the skin everywhere else is covered.
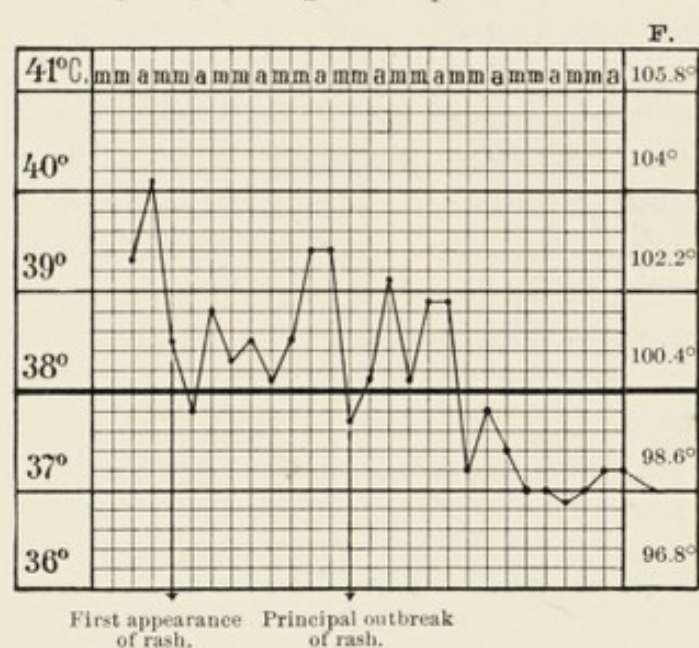
The eruption never develops over the entire body at once, but always appears in successive stages. Cases in which these stages are separated by well-defined intervals simply express this

First appearance Principal outbreak
of rash. of rash.
Fig. 51.

general rule in an exaggerated or, let us say, in a particularly pronounced manner. I have already (page 297) referred to Thomas' remarks on the subject, and will now only add the history of a case in point, which is peculiar, however, in showing no rise of temperature at the time of the principal outbreak of the rash, which was separated from its earliest appearance by more than three days.

CASE 20.—Paul J., two and a half years of age. The other children of the family were ill with measles. On the 10th of July, 1891, the patient began to show symptoms of cough, conjunctivitis, coryza, and bronchitis. The highest fever on this day was 40.1° C. (104.1° F.). On the 11th of July a few spots of eruption became visible on the face, and the skin of the body showed slight "marble-like" tracings. A well-defined and extensive rash was not seen until the 14th, when the mucous membrane also showed the characteristic spots. The general course of the disease was quite light.

The temperature chart (Fig. 51) shows that the fever bore no relation to the eruption. In this case the days preceding the definite outbreak of the eruption can, to be sure, be looked upon as belonging to the prodromal stage, which, as we know, may be marked by the appearance of a few spots. This is a matter of no importance to any one who lays but small weight on a strict systematic division into stages. The main point is the fact that the general course of the disease is entirely unaffected by such very apparent deviations from the ordinary.

Another phenomenon which calls for consideration is the so-called **"retrogressive form"** of measles, in which the rash either fades, when normally it should be spreading further, or disappears too quickly after reaching its height. This, according to traditional belief, drives the measles poison inward from the skin, thereby causing severe inflammation of the internal organs. It seems hardly necessary to argue the subject from this standpoint.

Experience has shown that when the general circulation is seriously interfered with—usually in consequence of the extension of the catarrhal inflammation to the small bronchi and the secondary involvement of the lungs—the blood supply of the skin is diminished; the latter becomes paler all over, the spots of rash which were previously sharply outlined grow less distinct, but still remain visible, and both the eruption and the skin in general take on a somewhat bluish tinge.

One almost feels tempted to dismiss the question with this simple mechanical explanation, and would probably be justified in doing so in many cases. There is, however, another possible cause. We know in general that the poison of an infectious disease circulating in the blood of the various tissues of the body may be stored up in one or the other of these according to its individual proclivities, where sooner or later it is excreted or rendered inert as a result of the activity of the cells with which it comes into direct contact. In the case of measles, the effects of the poison are seen in the skin and the mucous membranes, in which tissues it is also probably destroyed. The infectious stream is conveyed in both directions, first, indeed, as a rule, to the mucous membranes, and then to the skin, but the inflammation of the former is not in the least decreased, in most cases, by the outbreak of the external rash. It is conceivable that under certain circumstances a larger proportion than usual of the poison may be diverted to the mucous membranes, causing an excessive inflammation of this tissue, while the skin is left comparatively unaffected. The point to be noted in such cases is less the so-called retrogression of the rash than how much it spreads at the time severe respiratory symptoms have begun to manifest themselves. The latter may appear very early in the dis-

ease, and this class of cases calls for more careful observation than it has thus far received. Nor will the true explanation of the phenomena in question be easily arrived at, for it is plain that the circulatory disturbances in the skin dependent on the bronchitis can curtail the action of the measles poison on the skin only, as manifested by the less severe reaction of the latter than normally occurs. Only the future can decide the question. The contrast between the above suggestions and the formerly accepted theory, which I discredit, is well marked; it is not a question of the poison already present in the skin being driven out of it, but of the exclusion from this tissue of part of the quantity which ordinarily is carried into it.

A fact of minor importance to be noted is the irregular distribution of the rash in cases of nervous disease on parts of the body affected by the latter. F. Mayr,[*] for instance, mentions that in one case of spinal disease with paralysis of the lower limbs the latter "showed very little or no eruption." Thomas asserts that the opposite condition is sometimes to be observed; he also speaks of a case of hemidrosis in which the measles rash appeared only on the affected side.

Since the true nature of the phenomena is still in doubt, it is proper to refer here, also, to the **development of bullæ** on the skin, and probably on parts of the mucous membrane, which may occur in connection with measles. Notwithstanding the appellation "morbilli bullosi sive pemphigoidei," chosen by Steiner[†] to describe this condition, it is probably due to the accidental conjunction of another infectious process with measles, as Henoch[‡] has pointed out. These cases are very rare; Steiner saw only four, all in the same family and developing in short succession, among a total of nearly 6000 cases of measles, while only one has come under Henoch's observation in all his practice.

The appearances in Steiner's cases may be summed up as follows: The bullæ varied in size from a pea to a pigeon's egg; they were stretched tense by their contents, which at first consisted of a clear or slightly turbid fluid of alkaline reaction, increasing in turbidity later on. The skin of the affected parts seemed little altered, sometimes showing a red border around the base of the bullæ. Crusts formed after the bullæ broke, but there was no cicatrization. The process attacked any part of the body, sometimes one, sometimes another,

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[*] See Virchow's "Handbuch," *loc. cit.*, p. 85.

[†] "Morbilli bullosi," etc., "Jahrbuch für Kinderheilkunde," new series, vol. VII, pp. 346 *et seq.*

[‡] "Zur Pathologie der Masern," *Berliner klinische Wochenschrift*, 1882, pp. 193 *et seq.*

without reference to the presence of the measles eruption; of the mucous membranes, those of the mouth, the nose, and the inner surfaces of the labia majora were affected. The bullæ appeared in successive crops, not at all in connection with the measles eruption, sometimes developing before the latter, sometimes at the same time or following it, but always persisting at the time of desquamation. The bullous process was accompanied by fever, independent of that due to the measles infection.

In Henoch's case the bullæ were of much larger size, so that a single one covered each cheek, and they were so plentifully distributed over the body that the epidermis was lifted up as if it were the seat of extensive burns. Two of the above-mentioned five cases proved fatal, apparently as a result of pneumonia. Henoch regards the condition as due to a complication of measles with acute pemphigus, which is to be ranked among the infectious diseases.

The disease ran a somewhat different course in a case described by Romberg,* in which the skin under the bullæ became gangrenous. The patient, however, recovered.

Gangrene of the skin occurring subsequent to or during an attack of measles has also been observed in other cases. Thomas † has collected several from the literature of the subject. He also tells of the occasional development of ecthyma, furuncles, impetigo, etc. The question is really of no great importance, and the connection of these disorders with measles is probably often very doubtful, the latter being so common a disease as to make it hardly strange for an individual whom it attacks now and then to acquire another affection at the same time. If there were a relation of cause and effect, such "sequels" would surely be met with more often. At the most, it can be said only that in measles, as in any severe infectious disease, the bodily resistance is lowered, and in case of children who from their earliest years have lived under unfavorable conditions, the consequences of such secondary infection may indeed be serious, even in respect to parts of the body quite unaffected by the original disease.‡

For the sake of completeness, it should also be stated that herpes facialis occasionally is seen while the eruption is breaking out.

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* "Die Masernepidemie in Tübingen im Sommer 1838." Thesis by F. C. v. Gmelin, 1839, pp. 19 *et seq.*

† See v. Ziemssen's "Handbuch," *loc. cit.*, p. 91.

‡ See article by Fr. Mayr, *Zeitschrift der k. k. Gesellschaft der Aerzte zu Wien, loc. cit.*, p. 209.

RESPIRATORY PASSAGES.

It is very unusual for the catarrhal inflammation of the nasal mucous membrane to become of serious import. Where infants are concerned, the occlusion of the nasal passages by the swollen membrane may necessitate mouth-breathing, and so interfere considerably with their nourishment, since the latter mode of breathing and nursing are not compatible. When recognized in time, this difficulty can, of course, be met.

Hemorrhages from the nose, occurring in the enanthemic stage, or probably more often at the time the rash is developing on the skin, are, as a rule, of no great moment, seldom becoming severe enough to make the loss of blood a serious question. Indeed, patients often feel somewhat relieved of their headache.

It is quite another matter when nosebleed occurs as a result of a hemorrhagic diathesis. In such cases the loss of blood from this, as from any other mucous membrane, may be so great as to threaten an immediate fatal ending.

It is, of course, possible for pathogenic bacteria to plant themselves upon the inflamed mucous membrane of the nose, there setting up their specific processes, but this certainly does not happen often, nor do membranous exudates in the pharynx, whether due to true diphtheria or some other severe inflammation, spread to the nasal passages, except in unusual cases. Here we have a marked distinction from scarlatina.

The pharyngeal mucous surfaces are always involved to a certain degree in measles. The eruption and the accompanying inflammation have already been considered. As a rule, however, the inflammation remains superficial, though complications in the form of other morbid processes are of occasional occurrence, diphtheria being the most important of the latter. The diphtheritic inflammation does not necessarily extend further into the respiratory passages. Embden's * 461 cases seen during the Heidelberg epidemic included 10 complicated by pharyngeal diphtheria, only one of which ended fatally, as a result of extension to the larynx. The individual features distinguishing any particular epidemic, which so largely determine the outcome in diphtheria, always play a prominent part in these cases, really governing the situation in fact; hence it is not to be wondered at that observations made at different times and places are apt to disagree. It may be stated, however, that to all appearances measles produces no special predisposition to diphtheritic infection.

* *Loc. cit.*, pp. 20 *et seq.*

The larynx presents more serious points for consideration. Its mucous membrane is usually affected by the catarrhal inflammation accompanying the enanthemic stage, and the eruption itself may be said to develop frequently, and possibly always, in this situation. As laryngeal examinations have been made in only a small number of cases, it is impossible to speak with authority on this score.

It is the rule for the voice to be somewhat husky or even decidedly hoarse at the onset of measles, nor does this symptom cause any uneasiness. Anxiety is at once aroused, however, by the onset of attacks of pseudo-croup, which are of the ordinary type—a barking cough, often coming on in paroxysms, accompanied by dyspnea with the well-known signs of laryngeal stenosis. The attacks, especially in early childhood, are often due to a temporary occlusion of the larynx by an unusually plentiful mucous secretion, and in such instances they are usually free from danger, the alarming symptoms of occlusion being dispelled by a powerful cough and a moment or two of strangling, the symptoms not reappearing for some time, although the barking cough and hoarseness may persist. The outcome is not always so favorable, however, since the anatomic cause may be of quite a different nature.

In Barthez and Rilliet's autopsy reports,* although the facts are somewhat indefinitely stated, we find that ulcers or erosions were present in somewhat less than one-half the cases, pseudomembrane in one-fifth, simple inflammation in one-sixth, and no lesion whatever in a further one-fifth.

These pathologic findings are, in my opinion, in harmony with clinical experience, although the figures will vary on different occasions, especially in regard to the frequency of membranous deposits.

Gerhardt's † reports of laryngeal examinations on living subjects furnish us with valuable information, demonstrating the presence of superficial ulcers, especially on the posterior wall of the larynx, in cases manifesting severe symptoms of stenosis: "They are formed as a result of the very vulnerable mucous surfaces being pressed and rubbed during the frequently repeated movements of coughing."

In connection with this ulcerative process the opening of the larynx may be narrowed by the development of circumscribed edema, either of inflammatory origin or due to local disturbances of circulation in the blood- or lymph-vessels. As soon as this takes place (and it is the more likely to do so the younger the child, since the anatomic conditions improve with increasing years) the dyspnea will

* *Loc. cit.*, p. 269.   † "Lehrbuch der Kinderkrankheiten," p. 63.

be found to change in character. It will still come on in the form of severe suffocative attacks, but—and herein lies the distinction—in the intervals, when all seems quiet, the symptoms of stenosis will persist, though to a lesser degree. This should put the physician on his guard. The symptoms may diminish when the eruption breaks out, thereby giving more ground for a diagnosis of "pseudo-croup," as Embden states it. My own clinical experience gives me no reason to doubt that this is possible, but such improvement cannot be depended upon to determine the issue.

A differential diagnosis between the croupous and the less dangerous form cannot be made in the beginning. I know of no one positive indication, unless it be the presence of a pseudomembrane in the pharynx or the coughing up of bronchial casts. The pharyngeal exudate is very often absent, however; of Embden's * six cases observed during the Heidelberg epidemic, not one presented this sign, yet all died, and the autopsy revealed the croupous nature (in an anatomic sense) of the inflammation.

The dislodgment of fibrinous casts by coughing is also an uncertain matter, possibly because the lungs, hampered by the narrowed lumen of the swollen bronchi and their own insufficient inspiratory dilatation, are unable to expel a current of air forcible enough to loosen the membrane, however violent the action of the abdominal muscles may be.

The body-temperature is usually of no value as a diagnostic sign. Apart from the fact that well-marked fever is by no means a regular accompaniment of diphtheria, the temperature at the time of early laryngeal involvement is entirely governed by the measles infection. Later on it is affected by various other causes, in especial by inflammatory processes in the bronchi set up by one or another variety of pathogenic bacteria which have found their way thither. At any rate, the temperature cannot be depended on as a guide. There is still another difficulty in the way of diagnosis. Long and severe attacks of laryngeal stenosis, in the intervals between which the condition is not entirely relieved, may closely simulate genuine croupous attacks, although in reality caused only by a spastic contraction, possibly even by a slight contraction, of the muscles closing the glottis, their antagonists having become paretic.† This can properly be assumed to be the case when the dangerous symptoms are almost immediately relieved by a warm bath, leaving only a trace of the stenosis. Sooner or later the trouble increases, but can again

* *Loc. cit.*   † See Jürgensen, v. Ziemssen's "Handbuch," vol. v, p. 232, 2d ed.

be dispelled by a warm bath. The frequency of attacks of this nature seems to vary considerably in different epidemics. In Kiel I saw a few cases, enough, at least, to make me familiar with the condition when it developed, as it often did, during the Tübingen epidemic of 1874. I distinctly remember how experienced practitioners at that time would get everything in readiness for a tracheotomy, and that a warm bath would then be found effectual in overcoming the danger. I occasionally met with similar cases in subsequent years, but they were very rare as compared with those of 1874.

The fact that the course of the measles infection furnishes no clue to a diagnosis greatly increases the difficulty of reaching a conclusion as to the true state of affairs in the larynx. This applies, at least, to the critical period; later on, when the measles infection has come to an end and all has so far gone well, if the patient is attacked by symptoms of severe laryngeal stenosis, it is a comparatively easy matter to know with what we have to deal. Embden had a number of such cases (Nos. 3 and 5), and I could add others out of my own experience. But in the beginning, during the enanthemic as well as the exanthemic stage, after bronchopneumonia has made its appearance, the stenosis may be due to any one of the causes already discussed. It has seemed to me that the spastic variety frequently showed itself in connection with fully developed bronchopneumonia.

Laryngeal stenosis, when it persists for any length of time, is always a grave symptom in measles cases, quite apart from the formation of a pseudomembrane.

[In New York city, where diphtheria is endemic, it would not be safe to consider any persistent laryngeal stenosis as other than due to an added infection through the Bacillus diphtheriæ. Especially is this true in large institutions. I am speaking within my own knowledge when I say that all laryngeal stenosis and all pseudomembranous pharyngitis in institutions here would be at once considered to be diphtheria, would be given antitoxin, and, if the critical symptoms could not be tided over, would be intubated.

It is at present the established custom in these institutions to give immunizing doses of antitoxin (250 to 500 units) to infants and young children in the stage of invasion of measles. This practice has much improved the later results in measles epidemics.]

Of the causes to which this fact is attributable, the bronchitis deserves the first place. Narrowing of the glottis, as is true of well-marked dyspnea of any origin, leads to a change of action on the

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part of the muscles of respiration, as a result of which those belonging to the sternoclavicular and scapular groups assume the chief rôle.* The consequences are that the anterior portions of the lungs come to contain a great deal of air and very little blood, while in the posterior portions there is much blood and but little air. Thus the conditions become more and more unfavorable for the even expansion of the lungs, the lower lobes collapse posteriorly, the walls of the bronchi, covered with tenacious mucus, are pressed together and can be reopened only with difficulty, and areas of inflammation soon appear in the atelectatic portions as a result of the activity of bacteria which are ever present in the bronchial secretions, and which are carried into the affected parts by the violent respiratory movements as well as the no less violent attacks of coughing.

An autopsy report, together with a short history of the case, will serve to make these points clear:

CASE 21.—Frederick K., eighteen months of age. Taken under treatment May 4, 1893. According to the patient's mother, the rash first appeared on his face on April 30th. When he was first seen, it was still distinct, but disappeared completely by May 6th. There was a well-marked conjunctivitis, especially on the right side. Other symptoms were angina, accompanied by considerable pharyngeal secretion, which was easily removable, however, and bronchitis. The bronchitis extended on the 5th to the fine bronchi, and on the 6th areas of consolidation were demonstrable in both lower lobes. Laryngeal stenosis set in on the 8th and death took place on the evening of the 9th. The course of the temperature is shown in the accompanying chart (Fig. 52).
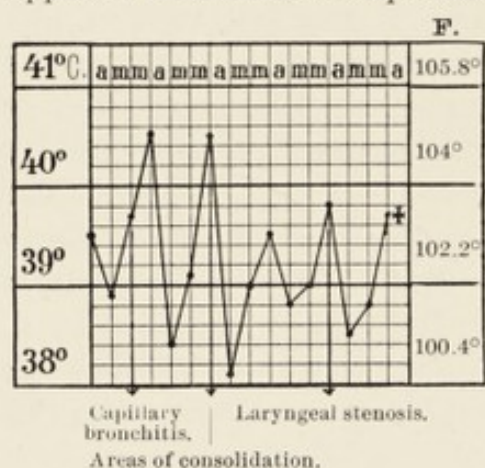
Capillary bronchitis. Laryngeal stenosis.
Areas of consolidation.

FIG. 52.

The following are extracts from the autopsy report (by Prof. v. Baumgarten): "In the nasopharyngeal space as well as covering the entire mucous membrane of the pharynx is a large quantity of mucopurulent secretion, which completely fills the pouches of the pyriform sinus and the opening of the larynx. On removing the secretion, the entire posterior surface of the soft palate and uvula and the neighboring portions of the pharynx are seen to be covered with a firmly adherent grayish-yellow membrane. A similar membrane, of tubular shape, is also present in the larynx and extends downward into the trachea almost to its bifurcation.

"On removing the sternum the lungs press forward, and appear greatly dilated; they are completely in contact in the median line and so nearly

* See Jürgensen, "Lehrbuch der spec. Path. u. Ther.," 3d ed., Leipsic, Veit & Co., 1894, p. 510.

approximated at the lower border of the anterior mediastinum as to expose only a small portion, about a finger's width, of the pericardium. The lingula of the left upper lobe forms an exception to this general condition of dilatation of the anterior portions of the lungs; it is dark red in color and exhibits a few areas of atelectasis. The external borders of the lungs correspond to the anterior and inner portions in condition, and are so swollen and arched outward as to lie close against the chest-wall, especially on the left side; on the right side there is still sufficient space between the lung and the thoracic wall to admit a finger. The pleura covering the anterior surface of the lungs is normal in appearance.

"When removed from the thorax, the most posterior portion of the left lung, especially of the lower lobe, is seen to be greatly collapsed, in marked distinction to the anterior and middle portions. Only a small area of the upper lobe, in its lower part, is thus affected. The collapsed areas are sharply outlined against the dilated parts; the latter are of a dark blue color, are firm to the touch, and emit an indistinct crepitant sound on pressure, while their surface is evenly covered by a fibrinous exudate. A quantity of ecchymoses are seen extending from the consolidated areas to the other parts of the lung tissue. The finely fibrinous pseudo-membrane covering the pleura stretches across the interlobular space onto the upper lobe.

"On forcing a current of air into the lower lobe of the left lung it is possible with some effort to completely expand the collapsed area so that it does not appreciably differ in appearance from the other parts, and on section shows no dark consolidated spots, but an entirely even surface of a brick-red color from which small, purulent, cork-like masses of secretion can be pressed. The above-mentioned atelectatic portion of the upper lobe, however, contains an infiltrated area, rather larger than a pea, which protrudes slightly from the surrounding tissue, and is further distinguished by its compact composition.

"The right lung shows in its general features an entirely similar condition, with the same contrast between the dilated anterior and middle portions and the collapsed posterior portion. A slight fibrinous exudate is seen only on the sharp posterior border of the middle lobe, at which point the lung tissue feels thickened and leathery, while the collapsed portions are softer and crackle distinctly between the fingers. Without artificial dilatation small lobules containing air are visible on the generally dark surface of the latter. On careful palpation, an indurated, airless area is found in a second situation—viz., in the posterior third of the upper lobe looking toward the interlobular space. Here the lung tissue is not only firm to the touch as a whole, but also shows the presence of a number of infiltrated areas. The tissue in all these places can be expanded by a strong current of air. At one point in the middle lobe, however, bordering on the interlobular space, and lying somewhat anteriorly, there is a triangular area, about 1.5 cm. ($\frac{5}{8}$ inch) in diameter, which admits no air and is hard to the touch."

It should be added that both sides of the heart were dilated by a large quantity of blood.

The above case is well calculated to illustrate the determining mechanical conditions under discussion. At first there was a comparatively light attack of measles, then an extension of the catarrhal

inflammation to the small bronchi took place after the rash had begun to fade, areas of consolidation soon afterward forming in the usual situation, posteriorly and inferiorly on both sides. The rise of temperature was marked on the two days during which these changes in the lungs were observed, especially on the first of the two. The diphtheritic infection, to which the pseudomembrane in the pharynx and the upper portion of the air-passages nearly down to the bifurcation of the trachea was due, brought about a considerable **reduction** of the fever.

The autopsy findings, which are so carefully described, show the conditions for oxidation of the blood in the lungs to have been most unfavorable. I would especially call attention to the condition of the anterior and posterior portions of the lungs, for in this case we are concerned with a pseudomembrane on the mucous membrane of the larynx which did not even extend into the large bronchi, not to mention their smaller ramifications. Apart from this, and a general catarrhal inflammation of the small bronchi, the lung tissue exhibited only a few small areas of genuine inflammation; the lesion was chiefly one of atelectasis.

We have in this case, therefore, a fairly characteristic picture of the havoc wrought by laryngeal stenosis in conjunction with a bronchial catarrh. Nor should the cardiac dilatation be overlooked, proving, as it does, how seriously the general circulation was affected.

The bronchial inflammation is the most important factor in determining the outcome of an attack of measles. It is an inherent feature of the infectious process, and whether it is ever entirely absent from a case, as is sometimes taken for granted, is really an open question. The mere circumstance that no bronchial râles can be heard does not by any means prove the bronchial mucous membrane not to be inflamed.

The symptoms of bronchial inflammation as manifested in measles are similar to those of an attack of ordinary bronchitis. When only the large tubes are involved, there is a cough, which often, however, has a more spasmodic character and sounds more barking and hoarse than in simple bronchitis cases, a peculiarity due to the additional inflammation of pharynx and larynx. The sputum, too, as far as it can be spoken of in connection with young children, is from the first rather more plentiful; it is probably derived chiefly from the upper respiratory passages, since the coarse moist mucous râles produced in the bronchial tubes are not heard to any extent until later in the disease, say, on the third or fourth day of fever. There

is hardly any danger so long as the catarrhal inflammation does not attack the small bronchi. The situation becomes serious, however, as soon as these become involved, more especially if broncho-pneumonia develops. I have already described the general features of the affection (see page 264), hence I will now proceed to discuss its separate features.

The fact that capillary bronchitis may set in very early, even at the very onset of the infectious process, deserves special attention. This is, to be sure, of quite rare occurrence, but the possibility is illustrated by the following case:

CASE 22.—Karl K., five years of age. The other children of the family were ill with measles. The patient began to show signs of lassitude and loss of appetite at the beginning of the month and also complained of headache. He was first seen on the evening of February 9, 1888, when his temperature was 38° C. (100.4° F.). Signs of capillary bronchitis appeared on the 10th, and areas of consolidation were noted on the 19th, remaining distinct until the 20th of March. When the patient was discharged from treatment, on

FIG. 33.—1+, The capillary bronchitis is already extensively developed; 2+, outbreak of rash; 3+, beginning of desquamation; 4+, beginning of bronchopneumonia demonstrable.
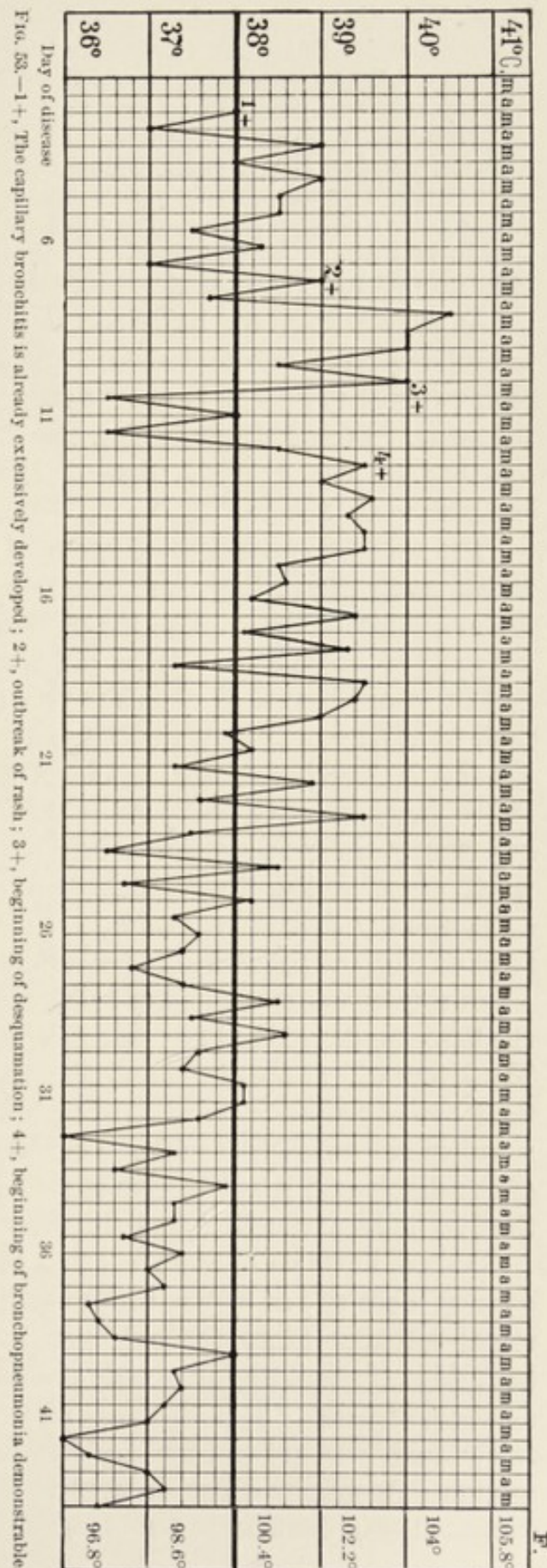
March 25th, these areas had not completely cleared up. The measles erup-
tion did not break out until February 14th, spreading from the face over
the body in the usual manner; it remained visible until February 16th. Its
development was preceded by coryza, conjunctivitis, and a spotted rash
on the buccal mucous membrane. The temperature chart is appended,
showing the slow course of the bronchopneumonia; it serves also to com-
plete the set of cases already presented. (Figs. 39, 40, 41, 52.) It is, of
course, impossible to disregard the possibility of a tubercular complica-
tion in this case. An examination made in March, 1895, however, failed
to reveal any structural changes in the lungs.

As a rule, capillary bronchitis develops later in the disease; it
is less frequently observed toward the end of the enanthemic stage
than when the eruption is at its height, or in the days immediately
following. During desquamation this complication occurs with less
and less frequency as the time of onset of the measles infection
becomes more remote.

The same may be said of areas of consolidation in the lungs,
which, appearing as they do in connection with the bronchial inflam-
mation, must be regarded as the sequence of the latter. It is most
desirable to make a differential diagnosis between *simple atelectasis*
and *bronchopneumonia*, but this is very often a difficult matter. At
first, to be sure, it is only a question of discovering the signs of local
changes in the lung tissue; that is, of demonstrating a more or less
airless condition of certain parts of the lungs. Since extensive areas
are usually involved simultaneously, or at least within a compara-
tively short period, the examination does not present any very
extraordinary difficulties, but it is never an easy task unless one is
familiar with the percussion of a child's thorax.

In respect to the method of examination, it is best first to outline
the lower border of the lung, determining the level of the diaphragm.
The latter will always be found abnormally high as a result of the
rapid and superficial respiration which without exception accompanies
a widely developed bronchitis. On the right side this high position
of the diaphragm is apt to give rise to the gross error of mistaking
the liver in its unusually raised situation for consolidated lung tissue.

It should also be remembered that the consolidated areas usually
develop more or less symmetrically in both lower lobes close to the
spinal column. Since the condition is almost exactly similar on
both sides, it cannot be accurately determined by comparing the two
during percussion. It is therefore better to percuss each side sepa-
rately from the anterior axillary line backward toward the spinal
column. Anteriorly there is always some normal or even over-
expanded lung tissue to be found, which makes it easier to define the

limits of consolidation. When the anterior boundary of the consolidated area is thus determined, its longitudinal diameter can best be demonstrated by percussion from above downward. In this way even small collapsed areas can be discovered, and their further extension from the spinal column toward the side of the chest, and from below upward, in which directions it always takes place, can be accurately followed. The finger, which in this instance is decidedly preferable to the pleximeter, should be laid straight across the ribs, pressing lightly, not firmly, against them. Then percussion may be practised as forcibly as desired, but the stroke should always be a short one, in order to bring out the sound differences clearly. This does not occur if the finger be pressed firmly, because the vibrations will spread too far through and along the elastic thoracic wall of the child patient, rendering it impossible to outline the collapsed area sharply.

The boundary between the airless and air-containing portions of the lung almost always follows a plane perpendicular to the transverse diameter of the chest; hence, if the finger be laid obliquely across the ribs it will cover areas representing both these conditions; both will simultaneously be brought into vibration by the percussion strokes, thus precluding a sharp distinction between them.

The above rules should be strictly adhered to by all who lack experience in such examinations; a trained practitioner can better afford to disregard them, since he is guided by his highly cultivated tactile sense as well as by his ear.

The presence of a consolidated area proves nothing beyond the fact that at that particular point the lung tissue contains a reduced quantity of air.

Even by auscultation it cannot immediately be determined whether we have to do with a simple atelectasis or a bronchopneumonia. In the former case, to be sure, the breath-sounds are usually very weak, of the type very properly termed "indefinite." But how is it when bronchopneumonia is present? The bronchial tubes are filled with a varying quantity of mucus; any degree between indefinite, weak, vesicular respiratory sounds and loud bronchial breathing, so loud as actually to be painful to the ear, may therefore be heard. After a hard fit of coughing bronchial breathing may be heard at a point where just previously hardly any respiratory sounds at all were perceptible. The same is true of vocal fremitus, which where crying infants are concerned is well known to be a valuable guide. The following is therefore the most definite statement per-

missible: If loud bronchial breathing be heard over a dull area, a diagnosis of pneumonia is established; if this sign be absent, pneumonia may exist or the case may be one of atelectasis only.

Small circumscribed spots of pneumonia within an area of atelectatic lung tissue are hardly determinable by physical signs.

The presence of peculiar fine mucous râles, resembling crepitant râles, but heard in expiration also in contradistinction to the latter, does not establish the diagnosis. Such râles are a product of the capillary bronchitis, and being transmitted for some distance from their point of origin, may be heard even over moderately large areas of atelectasis. Atelectasis is positively shown to be the sole, or at least the predominating, lesion, if the dulness clears up more or less perfectly, as a result of deep respiratory efforts, whether voluntary or produced by therapeutic measures. After death atelectatic lung tissue can be completely inflated, and the same result can be accomplished in the living subject, at least in part, and where the condition is largely recent, by cold douches administered while the patient is in a warm bath.

[In our experience the best early signs and symptoms of a developing pneumonia are:

1. Apathy, mental dulness, and prostration-toxemia.

2. Fever, increased beyond the normal measles curve.

3. Disturbed respiration-pulse ratio. The normal being 1 to 4 (for example, 20 to 80, with a temperature of 99° F.), the ratio in oncoming pneumonia often approximates 1 to 3; for example, with a temperature of 104° F. the respirations rise to 40, the pulse to only 120.

4. Râles, fine and localized, in addition to the coarse râles of general bronchitis.

5. Diminished respiratory murmur over the affected portion of the lung.

6. Bronchovesicular respiration.

7. Dulness.

The general view concerning capillary bronchitis has changed somewhat. At the New York Foundling Hospital, for instance, the term capillary bronchitis has fallen out of use. Autopsy findings have brought us to the habit of considering that there are but two stages of pulmonary inflammation that it is practicable to recognize: one a general bronchitis, the other bronchopneumonia. Theoretically, the inflammation may be thought of as advancing to the finer bronchi and stopping there; practically, this is not to be considered.

It is our opinion that the rational way is to consider a slight bronchitis of the coarser bronchi as normal to measles, a pronounced general bronchitis as a complication which will disturb the normal temperature curve, and a group of phenomena enumerated above as indicating a very serious complication—bronchopneumonia. Capillary bronchitis and collapse of the lung are but steps in the advance toward a bronchopneumonia, and cannot be separately considered.

It is to be expected that the pulmonary tissues of young children, who are in a stage of rapid physical transition and who have been to a varying degree depressed by the infection (measles), will react very differently under different circumstances; the kinds of micro-organisms present in the lungs and their virulence vary greatly. The changes seen at autopsy, and likewise the clinical signs, will therefore be most varied; but it is impracticable to recognize these variations, in making a diagnosis, to any further degree than that indicated above.]

Bronchopneumonia occurring in the course of measles usually first involves the lower lobes on both sides; in the great majority of cases, if other portions of the lungs are attacked at all, it is as a result of some mechanical obstacle in the way of their expansion, such as circumscribed pleuritic adhesions, small areas of consolidated or cicatricial tissue of earlier date, etc. The process is always the same; the inflamed and swollen bronchial walls become stuck together, thus increasing the resistance offered the entrance of the air; this is followed by collapse, and, if infectious bacteria happen to be present, by bronchopneumonia. It is a point to be noted, however, that in measles the inflammation may very rapidly supervene on the condition of collapse, or even play so prominent a part from the first that atelectasis can hardly be spoken of at all.

In my opinion, which is borne out by my personal experience, the question of whether atelectasis or bronchopneumonia is present, in addition to the capillary bronchitis, cannot be positively decided on the ground of general symptoms.

Two points are here concerned: the body-temperature and the interference with the respiratory function and its consequences.

Between the time when the measles fever commences and when it reaches its height it is impossible to say whether a given rise of temperature is or is not due to the original infectious process itself. No one can tell. Again, if at a later period, when the measles infection is dying out—as shown by a fall of temperature—and the fever normally runs lower, the temperature nevertheless remains high, are

we justified in drawing any conclusion as to the pathologic process then going on in the lungs? I think not, for the chief question is not whether we have to do with a catarrhal inflammation of the small bronchi, with atelectasis or pneumonia, but what agent of infection is responsible for any or all of these processes. The height and character of the fever are determined not by the anatomic lesion produced, but by the nature of the causative agent of the same. The fever may be high, although only bronchitis be present, while it may run low in spite of a well-developed pneumonia. Since the collapse of the lungs is unquestionably favored by high fever, necessitating, as it does, frequent superficial respiration, an infectious agent whose growth induces this symptom will more easily cause the development of consolidated areas than one not possessing this characteristic. But this does not at all imply that the germ producing the fever must necessarily cause a corresponding degree of inflammation. Take, for instance, the behavior of the pneumococcus; it may induce consolidation of small areas in an apex, with fever up to 42° C. (107.6° F.), or an extensive inflammation involving an entire lobe, with a rise of temperature hardly reaching 40° C. (104° F.), or certainly not much higher. And yet the organism in both instances is the same. However little we may know of the details of the etiology of measles-pneumonia, it behooves us to hold fast to this general pathologic principle, especially since its truth as applied to measles is supported by clinical experience.

To sum up: neither the height nor the course of the temperature serves to indicate whether a wide-spread bronchitis or a bronchopneumonia is in progress.

The following very instructive case is taken from Ziemssen-Krabler *:

Case 23.—The patient was a girl, eight and a half years of age. Hoarseness and cough were noted for several days preceding the acute onset, which took place on November 7, 1861, with symptoms of headache, weakness of the limbs, anorexia, coryza, and pain in the eyes. The eruption appeared on November 10th.

November 11th: The general symptoms appear severe; there is a well-developed cough and labored respiration, accompanied by fine râles audible at a considerable distance. Medium-sized dry râles are heard over the entire chest, respiration nowhere retaining its vesicular character.

November 12th: The patient's general condition is improved; the eruption on the face and body is very pale, but is still of a light red color on the extremities. The respiration is easier and there are no tracheal râles. Posteriorly and inferiorly on both sides there is a small area of

* *Loc. cit.*, p. 232, History No. 56.

slight dulness, over which a number of small, non-resonant râles are heard, diminishing toward the anterior and upper regions of the chest.

November 13th: The general condition is worse; coughing is violent and frequently paroxysmal in character. The patient is extremely hoarse. The posterior dulness reaches upward on both sides to the spine of the scapula, being more marked on the right side; there are no respiratory sounds, these being replaced by small non-resonant râles.

November 14th: There is a tendency to somnolence and cyanosis. Desquamation of the face is marked. Respiration is labored; the cough sometimes takes the form of separate, short coughs, sometimes of paroxysmal attacks. Repeated examinations show the dulness on both sides to be unevenly outlined and changeable; sometimes percussion elicits a tympanitic note. Small, moist, non-resonant râles are heard.

November 15th: The patient passed a very restless night, with convulsions and delirium, which gave way to a somnolent condition during the day. She had an attack of great prostration in the evening. The respiration is superficial and the cough lacking in power and accompanied by a plentiful sputum.

November 16th: During the night there was delirium, followed by somnolence during the day. The cough is weak. In the evening the patient grew extremely restless and passed into a condition of extreme collapse. The respiration is regular but superficial. There are no well-marked areas of dulness discoverable on percussion of the chest posteriorly. Coarse non-resonant râles are heard all over the chest.

November 17th: During the night the patient was delirious and jactitation was marked. This morning she is in a somnolent condition. Loud tracheal râles are heard. In the evening a slight dulness is demonstrable on both sides posteriorly, with tympanitic resonance under the right scapula. There are many moist râles.

November 18th: The patient died this morning after an extremely restless night, during which she coughed a great deal without raising any sputum.

The patient had rapidly lost flesh and strength from the 14th on, and edema of the feet appeared before death.

On autopsy, the left lung was found distended anteriorly; posteriorly there were some limited areas of consolidation both above and below. The right lung was greatly distended anteriorly, the upper lobe exhibited a few spots of atelectasis; the greater part of the middle lobe and almost the entire lower lobe were consolidated and airless. The bronchi were dilated on both sides and filled with a plentiful mucopurulent secretion. Signs of catarrhal pneumonia were visible in a few places; the rest of the lung was found dilatable artificially.

Notwithstanding the changes in the lungs present in addition to the bronchitis, v. Ziemssen and Krabler count this case among those in which the bronchitis is the controlling factor, and to my mind their position is fully justified. The accompanying chart (Fig. 54) shows very graphically the similarity as to main features in the course of pulse, respiration, and temperature, while the curves bear no apparent relation to the presence of consolidated areas in the lungs. The lines fall both on the 13th, at which time the areas of

dulness on both sides were found most extensive, and on the 16th, when they had nearly disappeared; this condition, indicating the presence of atelectatic areas and possibly of small foci of inflammation, certainly did not dominate the situation. It was the catarrhal inflammation, which in consequence of its wide distribution, and probably also of the powerful fever-producing action of the bacteria causing it, acted the leading part.
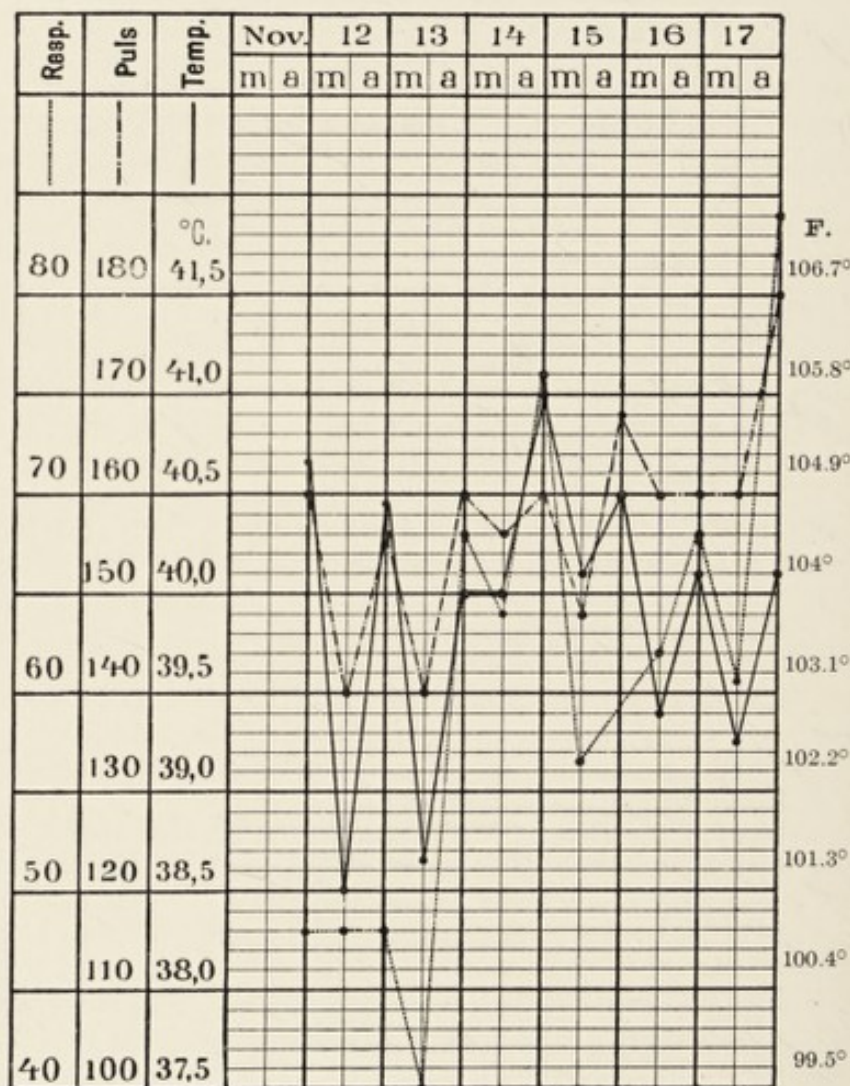
Fig. 54.

The general symptoms of a measles patient attacked by a serious pulmonary inflammation are those of a severe toxemia. Of the toxic agents here concerned, carbon dioxid, retained as it is in the tissues because of insufficient oxidation of the blood passing through the lungs, is undoubtedly one of the most important. In addition, we probably have to deal with some of the metabolic products of the bacteria which flourish on the soil so well prepared for their growth

by the measles poison. It is as yet impossible to decide just what effects to ascribe to one or the other of the agents in question. We can only bear in mind under what extreme disadvantages the circulation and the interchange of gases are carried on in the lungs, in consequence of the partial occlusion of the air-passages by the general catarrhal inflammation. The assistance rendered the circulation by the changes in thoracic capacity during inspiration and expiration is reduced to a minimum, and, as in the case of laryngeal stenosis, the anterior portions of the lungs are dilated and anemic while the posterior portions, even if they do not collapse, remain well filled with blood, but poorly supplied with air. The whole work of maintaining the pulmonary circulation therefore falls on the heart, and were it not for the fact that this organ is, comparatively speaking, very vigorous in childhood, the percentage of mortality would be still more unfavorable.

This is not the place for a detailed description of the anatomic phenomena of bronchopneumonia in measles; for such the reader is referred to the writings of Bartels * and of v. Ziemssen,† who have entered into the subject very fully. Nor are we here concerned with the minute features of the development of this complication.

A few words as to its course are, however, in keeping with our purpose. In the great majority of cases it is the very acute form of bronchopneumonia which is observed during the actual course of the measles infection or immediately following it. The consolidated foci are more widely distributed, firmer, and in all ways more like those of a croupous pneumonia than in the more slowly developing form. The fever, too, is decidedly high. In favorable cases, however, this acute form of bronchopneumonia clears up in the course of a few weeks at the most, the fever always falling by lysis (see Figs. 40 and 41). It is far less common for the inflammation to take a slow course; I have, however, already given an instance of this form (Fig. 53).

Bronchopneumonia of the type which makes its appearance after the measles infection has come to an end, and bearing only an indefinite relation to the latter, belongs to a different category. It undoubtedly represents a secondary process due to infection by bacteria for whose growth the soil has, to be sure, been made more favorable by the attack of measles, but whose action is altogether

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* *Virchow's Archiv, loc. cit.*, pp. 76 *et seq.*

† "Pleuritis und Pneumonie im Kindesalter," Berlin, Hirschwald, 1862, pp. 293 *et seq.*

an independent one.   This statement holds good in spite of the fact that the catarrhal inflammation due to the measles infection has meanwhile persisted, but without giving rise to serious consequences, for it is hardly reasonable to suppose the measles poison as such to retain its virulence for so long a time.   Positive conclusions are inadmissible in view of the paucity of the facts thus far ascertained. In addition to the tubercle bacillus, which unquestionably plays a leading part, we shall probably learn of other bacteria here concerned when this field of inquiry, to which but scant attention has heretofore been paid, is investigated.   Perhaps we shall then be in a position to distinguish between the different forms in which the disease manifests itself clinically with reference to their specific causative agents.

The frequency of the occurrence of bronchopneumonia as a complication of measles varies greatly in different epidemics, as the following examples will suffice to show:

According to Bartels, among 573 cases, bronchopneumonia occurred 68 times = 11.9%; according to v. Ziemssen-Krabler, among 311 cases, bronchopneumonia occurred 50 times = 16.1%; according to Embden, among 461 cases, bronchopneumonia occurred 27 times = 5.9%.

There is nothing special to be said of the sequels of bronchopneumonia complicating measles; any and all of those which may manifest themselves under ordinary circumstances have been observed, especially the various forms of chronic interstitial pneumonia.   A detailed discussion of this point is not in place here.   It is sufficient also to mention in passing that occasional instances of pulmonary gangrene and putrid bronchitis following measles are on record— chance disease processes which might supervene on any severe bronchial inflammation.

Tuberculosis developing in the course of measles merits, on the other hand, closer attention.   Although this form of inflammation, too, has only a distant connection with the original disease, still its comparative frequency as a sequel to the latter calls for a word of explanation.   The bronchitis is the connecting-link between the two infectious processes, or in exceptional instances this rôle is assumed by an intestinal catarrh of extended duration.

Autopsies on children who have succumbed to tuberculosis following measles frequently show—to speak first of recognized facts— the thoracic lymph nodes (bronchial, tracheal, and mediastinal nodes) to be the seat of a former tubercular inflammation; they are found filled with caseous masses, and often contain fresh tubercles in addi-

tion. This is the picture most frequently presented. Auto-infection from such a focus of earlier inflammation takes place in the manner usual with children, manifesting itself as a general miliary tuberculosis, but chiefly involving the brain and its membranes, death being due to the cerebral process. The lungs remain comparatively unaffected, pulmonary symptoms certainly not playing a prominent part in the disease. It is unnecessary to enter into details, since the phenomena of the leptomeningitis infantum here in question nowise differ from those observed when the affection is excited by any other cause.

The above statements, however, do not apply to tuberculosis arising in connection with the less acute form of bronchopneumonia following measles. I at least have not seen many such cases, and am unable to find more than a few carefully described. The following history may, therefore, be of some practical interest *:

CASE 24.—Caroline S., two years of age; family without tubercular taint. The patient was always in good health until November 24, 1876, when she was attacked by the prodromal symptoms of measles. The rash appeared on the 26th, remaining visible for two days. There were no abnormal symptoms at this time. As the temperature, however, rose still higher after the rash faded, a careful examination was made of the chest. On December 2d consolidated areas were found anteriorly in the upper part of the left lung, and posteriorly in the upper part of the right lung— in unusual situations, it will be observed. During the next few weeks, in addition to the capillary bronchitis, by which the lungs were still generally affected, areas of dulness, persisting for a short time, appeared first in one place, then in another. The chief changes were observed in the left upper lobe. The pulse-rate remained close to 150, respiration at 70 to 80, while the temperature ran from 38° to 39° C. (100° to 102° F.), only exceptionally passing beyond these limits.

By January 1st signs of consolidation of the right lower lobe also developed; the condition remained otherwise about the same.

By January 15th retraction of the thorax on the upper part of the left side became noticeable. The general condition of the patient, however, showed improvement, and the fever decreased.

On January 25th the patient began to suffer from symptoms of leptomeningitis of the usual type, to which disease she succumbed on February 4th.

The autopsy (by Schüppel) showed the following condition:

A tubercular meningitis of moderate intensity; no cheesy nodules, but everywhere fresh, gray tubercles, and a large quantity of fluid in the ventricles.

There were signs of bronchopneumonia of considerable standing in the posterior portion of the upper lobe and in the entire lower lobe of the right

*This case is reported in detail by Eugen Kommerell, in his article entitled "Ueber Phthisis und Tuberculosis," from the Tübingen Policlinic, *Deutsches Archiv für klinische Medicin*, vol. XXII, pp. 179 *et seq.*

lung; the bronchi throughout the lung were dilated and filled with plugs of thick pus.

The upper lobe of the left lung showed a cirrhotic condition, with saccular dilatation of the bronchi and cheesy peribronchitis—of comparatively recent origin. Half of the lower lobe was infiltrated with bronchopneumonia, and the condition of the bronchi was similar to that on the right side. A few small unmistakable groups of tubercles were present in a few isolated situations in the upper half of the lower lobe. These tubercles were firm, prominent, and varied in color from gray to grayish-white. A number of small, white, tubercle-like nodules were found under the capsule of the liver.

The thoracic lymph nodes, as well as the mesenteric nodes, all showed an entire absence of tubercles or old caseous masses.

This case is interesting in more than one aspect. First, in respect to diagnosis. Not a single sign pointed to a tubercular complication up to the time when the cerebral symptoms were first manifested. The patient's whole condition was similar to that observed in a bronchopneumonia running a slow course, improvement even taking place between the fifth and the eighth weeks, when the tubercle bacilli must certainly have already been present and in process of development. The improvement was plainly expressed by a diminution in the fever

Fig. 55.— ·········· From December 12 to 19, 1876. —.—.— From January 2 to 9, 1877.

as also in the pulse- and respiration-rates; the general state of nutrition of the patient, too, was raised, and she appeared brighter. There was not a single sign, therefore, to betray the tubercular infection.

The accompanying chart (Fig. 55) shows the course of the temperature in the third to fourth, and again in the sixth to seventh, weeks, and gives a clear picture of the whole process.

The fact that in this instance the tubercular infection did not take its origin in an old focus of inflammation is of still greater importance. It might seem reasonable to regard the cheesy peribronchitis in the cirrhotic left upper lobe as the original seat of the

disease, but apart from the evidence furnished by the physical examinations, which were made with great care, the progress of the pulmonary inflammation being accurately followed and recorded from day to day,—even so it is, of course, possible to overlook an old lesion of small size,—this view is not supported by the autopsy findings. Professor Schüppel, who is surely entitled to an opinion in questions involving tuberculosis, positively declared against it; according to him, the cicatricial process was of recent origin, the result of the bronchopneumonia and the subsequent tubercular infection.

The fact that the lymph nodes were not involved effectively supports his opinion. Therefore, unless the existence of an old focus of infection at some point, which was simply overlooked, be urged, the explanation of the tubercular process must be sought in the entrance of the bacilli from without the body at a time when the inflamed mucous membrane of the bronchi offered a favorable site for their reception and multiplication.

The development of tuberculosis subsequent to measles therefore falls under two heads:

1. *The lymph stream draining the inflamed portions of the bronchial mucous membrane,* and flowing through the corresponding lymph nodes, increased in volume as in case of any inflammatory process, may set free some of the tubercle bacilli contained in the nodes, and carry them into the circulation.

2. *Tubercle bacilli may enter from without* and implant themselves on the inflamed parts of the bronchial mucous membrane.

Clinically, we can hardly expect ever to succeed in distinguishing between the two modes of infection, but we may be able to do so postmortem.

Tuberculosis following measles does not by any means always make steady progress toward the end; temporary cures, or, if the expression be preferred, remissions of the disease, may be observed as in ordinary cases.

It is a noteworthy fact that many, though not all, measles epidemics cause a high mortality among children already having foci of cheesy degeneration. Nor is the number small of those who, succumbing to consumption in later years, received their first demonstrable pulmonary lesion as a result of bronchopneumonia complicating measles.

It goes without saying that statistics as to the frequency of *tuberculosis after measles* can, at the most, possess significance only

for the special locality to which they refer. And it is a question whether they have even this limited value, conditions being so very complicated. To give an instance: a severe epidemic of pertussis, complicated to a large extent by bronchopneumonia, preceding an outbreak of measles, may have already wrought such havoc among the children with old tubercular lesions as to leave but little opportunity for the later infection to do much harm. Just the contrary occurs when measles breaks out first in a community containing a large number of children among whom no bronchitis of infectious origin has held sway for a considerable period. It is such considerations as these which deprive statistics of any real value.

Genuine croupous pneumonia must, like tuberculosis, be looked upon as a chance complication of measles. Perhaps in this instance, too, the bronchitis of the measles infection furnishes the connecting-link, by giving the pathogenic bacteria an opportunity to implant themselves in the lungs.

Since we have learned to differentiate between broncho- and croupous pneumonia, it is generally agreed that the latter form does not often accompany measles. Von Ziemssen and Krabler * state the matter very correctly as follows: " It is not unusual, especially in the pneumonic complications of measles, for the physician to find it impossible to decide whether the inflammation be of the croupous or the catarrhal form, in spite of the most careful consideration of all the points in the case." I also entirely agree with them as to the possibility which they suggest, of the coexistence of both forms in a given case, as the result of which the points of differentiation would necessarily be obliterated.

The whole question has become more and more complicated as the years have gone by. From a pathologic standpoint we are still in duty bound, indeed, to distinguish between a confluent bronchopneumonia, even when it involves a large part of the lungs, and a pneumonia in which the lesion consists of an evenly distributed inflammation of the whole part affected. But we cannot always hold to the rule of differentiation which is supposed to be decisive, and base our conclusions on the smooth or granular aspect of the lung on section, and on the presence or absence of a fibrinous exudate. The objections to this rule are especially marked in case of children's lungs, in which the granular character of the fibrinous exudate is well known to be less distinct, necessitating the use of the microscope to decide the question. Occasionally, too, a few groups of bron-

* *Loc. cit.*, p. 238.

chioles and alveoli filled with fibrin are found within an area of inflammation which, as a whole, is unmistakably of the broncho-pneumonic type.

The same infectious bacteria are found in both forms of inflammation, the diplococcus of Fränkel being the one most frequently concerned. The conclusion seems almost inevitable that the effects produced by the infectious bacteria vary with their mode of entrance into the lung tissue, depending on whether they are carried by the blood stream or implant themselves on the bronchial mucous membrane. This leaves the question out of discussion of whether in true pneumonia the bacteria are originally taken into the body by way of the bronchi.

In consequence of the difficulties above mentioned, the clinician is brought somewhat into conflict with the pathologist if, from his standpoint, he insists on the necessity of differentiating between broncho-and croupous pneumonia, as, in my opinion, he is unquestionably forced to do. Perhaps an agreement can be reached by which the diagnosis will depend on the presence or absence of a wide-spread capillary bronchitis. This certainly decides the course and the outcome of the case, at any rate, and therefore justifies the clinician in claiming its importance as a guiding sign. We are gradually leaving our childhood days behind us, when the picture of the horse in our books represented *the* horse, just as the conception of pneumonia in olden medical days was limited to the *typical* picture of pneumonia. But I will break off here, since to pursue the subject further would lead me into uncalled-for digressions. The infrequent occurrence of a pneumonia which in its clinical symptoms is distinctly distinguishable from bronchopneumonia, however, leads me to give the following interesting case, taken from v. Ziemssen-Krabler *:

CASE 25.—The patient was a boy, three and a half years of age. He had shown symptoms of cough and coryza for several days before coming under observation. He was first seen on November 21, 1861, when his symptoms appeared quite severe: in addition to coryza, cough, and conjunctivitis, he was suffering from vomiting, diarrhea, and sleeplessness, alternating with somnolency. There was a painful aphthous inflammation of the buccal mucous membrane.

The rash did not appear until the afternoon of November 24th. Its development was accompanied by severe general symptoms—delirium, jactitation, and somnolence, also tenesmus with frequent watery, brown stools. These symptoms began to decrease on the afternoon of the 26th. The rash had disappeared by the morning of the 27th; the fever rose on the afternoon of that day, the patient's thirst increased, and he passed a very restless night.

* *Loc. cit.*, pp. 238 *et seq.*, History No. 57.

The chest examination on the morning of the 28th showed some suspicious signs in the upper part of the right lung posteriorly, but consolidation could not be definitely determined until the 30th.

On December 4th consolidation of the lower lobe of the left lung from its root down to its base was demonstrated. At the lower border of the right lung there was a narrow strip of dulness with diminished respiratory sounds.

By the 5th a zone of dulness at the base of the right lung had developed
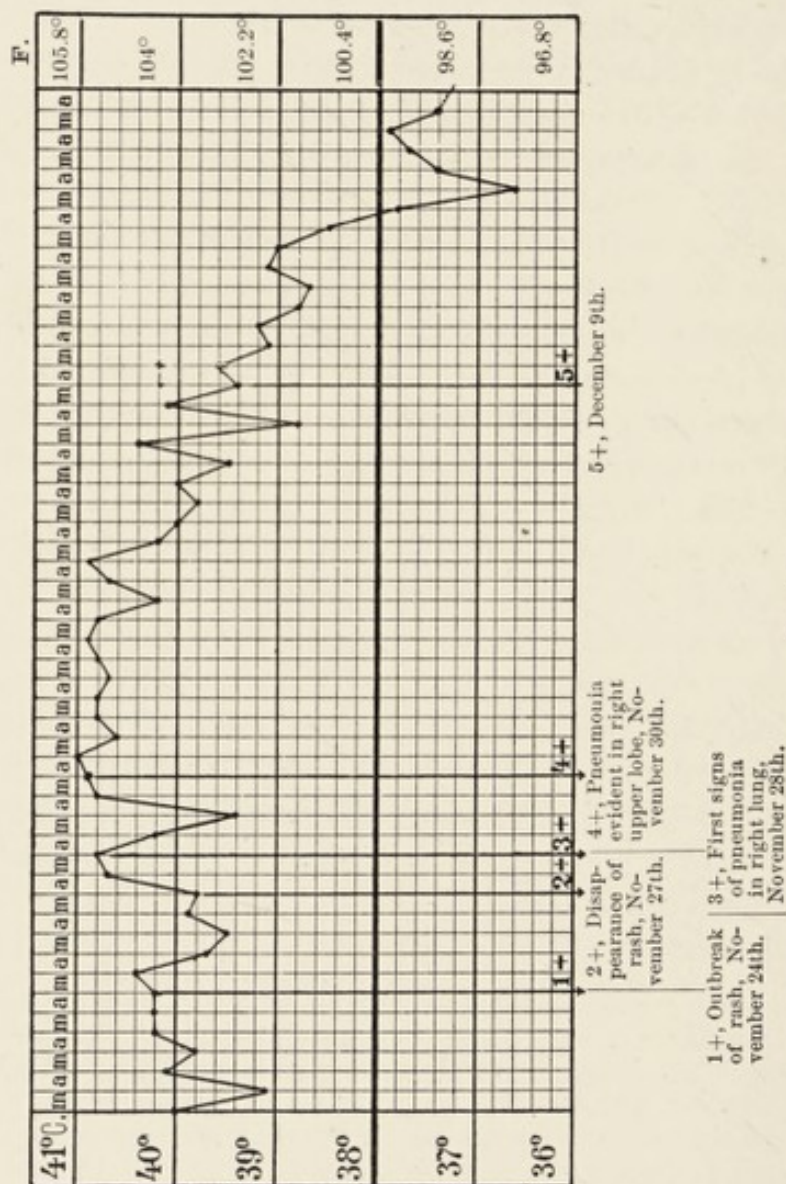
Fig. 56

(pleural exudate?). The dulness below on the left side extended moderately high up, and pulmonary resonance could be obtained only at the root.

On the 6th the dulness at the right apex began to diminish, but it continued to spread downward and laterally. On the left side it had entirely disappeared.

On the 10th an area of consolidation appeared on the right side along the spinal column extending downward nearly to the lower border of the

lungs; it also extended laterally toward the axilla, but only to the axillary line, where its boundary was distinct in a perpendicular line.

By the 25th this dulness had entirely disappeared. It should be added that on the right side more or less well-marked resonant râles of various sizes were always audible over the several areas of consolidation.

While the general symptoms were severe, they showed none of the characteristics of a true intoxication. The patient frequently went into a condition of collapse, and lost flesh and strength to a very marked degree, for which the frequent recurrences of severe diarrheal attacks were undoubtedly in part responsible. On the 14th a plentiful growth of Oidium albicans was noted. In spite of the high fever neither pulse- nor respiration-rate was exceptionally rapid. The former was about 120 at the most critical period, and was subject to comparatively slight variations. The temperature did not rise as high as 40° C. (104° F.) after the 10th, and on the 14th fell to normal. There were, therefore, twenty-four days of fever in all, of which seventeen were ascribable to the pneumonia.

The course of the temperature is shown in figure 56.

In the above case there was undoubtedly a severe pneumonic infection with extensive pulmonary consolidation. Since the bronchi of the unaffected parts remained patent, however, and the heart was vigorous, the disease ran a favorable course. If a bronchopneumonia had been present, the outcome would probably have been different.

THE PLEURA.

Inflammation of the **pleura** over the areas affected by bronchopneumonia is limited, in the overwhelming majority of cases, to the formation of a slight fibrinous exudate, or in light attacks the membrane may only appear clouded. Very often no importance attaches to the pleural inflammation. But in bronchopneumonias of long duration this is not so. Extensive adhesions are very apt to form between the pulmonary and the costal pleuræ, always a serious matter from a mechanical standpoint alone, as such adhesions interfere with the expansion of the lung.

Effusions into the pleural cavity are not often observed in connection with bronchopneumonia, no matter in what way the latter may arise, and the pneumonia of measles furnishes no exception to this general rule.

Fürbringer,* on the other hand, has lately again called attention to the development of an independent pleuritis with effusion as an unusual but by no means very rare complication of measles. He himself has seen quite a number of such cases, for the most part running an exceedingly acute course, and probably genuinely purulent in character from the first. Only in one instance did the exudate

* See Eulenburg's " Real-Encyklopädie," vol. xii (2d ed.), p. 559.

have a moderately serous character, but, as Fürbringer himself suggests, the similarity of the cases in this respect may have been only due to coincidence.

In my opinion, the occurrence at all of a pleuritic effusion during or following measles is a matter of chance,* for the measles infection can hardly be thought to have anything to do with the pleuritis except through the medium of the bronchitis and its immediate consequences. This statement does not, to be sure, quite harmonize with a report by v. Guttceit † of a measles epidemic among the peasantry in the vicinity of Orel in 1840. He tells how at the time the rash had mostly faded, or in a very few instances as early as the end of the stage of efflorescence, a fluid exudate would form, usually in both pleural cavities, the process being accompanied by a renewal of the fever. *All patients* thus attacked died on the fourth day from the beginning of the "acute hydrothorax." At least three out of every five measles patients fell prey to this complication, young people in their sixteenth to eighteenth year as well as children, and succumbing with equal rapidity. At a later period v. Guttceit again observed the same phenomena in two children of five and seven years of age, respectively. He practised aspiration and withdrew large quantities of a light yellow, clear serum, but to no effect; not even the dyspnea was relieved, and both children died on the evening of the day on which the operation was performed.

The pleuritic involvement in these cases may have been the result of some secondary infection, but no conclusions can be drawn as to its nature from the brief report above referred to.

THE HEART.

It would be incorrect to speak of an injurious effect on the **heart** as being directly due to the measles poison. If the organ as such be naturally vigorous, a child's heart will adapt its action to the height of the fever, and, if necessary, to the degree to which the patency of the bronchi is interfered with. It may, however, be otherwise involved during an attack of measles, although this does not often occur. It is, indeed, a rare exception to have one's attention called to the comparatively great frequency of heart complications, as was the case in the report of the Würzburg epidemic of 1883.‡

* See Bibliography in Thomas's article in v. Ziemssen's "Handbuch."

† "Dreissig Jahre Praxis," Vienna, W. Braumüller, 1873, Pt. 1, p. 251.

‡ Breyer, "Mitth. über die Masernepidemie der Stadt Würzburg," u. s. w. Thesis edited by Gerhardt.

Some complicating infection may have been at work; indeed, the author of the report openly states that he has in mind a "specially modified measles contagium" which, circulating with the blood stream, possessed the peculiar characteristic of causing morbid processes of the endocardium, a part to which the ordinary contagium of measles is but little adapted.

In order to avoid diagnostic errors it is necessary always to remember the conditions caused by superficial respiration in feverish children, more especially when their bronchial tubes are partly occluded. The retraction of the lungs by reason of their elasticity, and their effort to preserve as far as possible a state of equilibrium, exposes the heart, allowing an unusually large portion of its surface to come in contact with the chest-wall. The area of cardiac dulness is thereby abnormally extended upward and to the right, and the diastolic heart sounds over the pulmonary artery become louder in consequence, lying, as this artery does, nearer to the chest-wall than the aorta and being covered only by the thin border of the lung. If under any circumstances any sounds are to be heard accompanying the heart movements, then the inexperienced practitioner is convinced of the existence of an endo- or peri-carditis. A determination of the level of the diaphragm on both sides, showing the limits of the lungs, will be likely to prevent such an error at this, which is not made so seldom as one might suppose.

THE DIGESTIVE ORGANS.

Although no anatomic changes are demonstrable in the **intestines**, the occurrence of frequent evacuations during an attack of measles bears a close relation to the underlying infectious process. Diarrhea may appear as an early symptom, ushering in the enanthemic stage or even preceding it, but may also persist until after the conclusion of the eruptive stage. It is probably most frequently observed when the rash is at its height, though opinions differ on this point. Barthez and Rilliet, and Thomas, too, state it to occur chiefly in the early part of the disease, up to the beginning of the exanthemic stage, while others, Henoch and Bohn, for instance, express themselves less positively.

The diarrhea is ascribed to the specific inflammation of the intestinal mucous membrane, to the eruptive process by which it also is affected. Thomas,* however, reports that in one epidemic which he had occasion to observe, Peyer's patches were found swollen in every case without exception in which a postmortem examination was made of those who died during the eruptive stage or soon afterward. The condition was similar to that seen in typhoid fever cases. The swelling of the patches began to diminish at the close of the

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* See v. Ziemssen's "Handbuch," *loc. cit.*, p. 104.

eruptive stage and was only faintly discernible later on in the disease. He failed to find any instance of ulceration.

In light attacks of diarrhea, which are by far the most frequent, the symptoms are limited to a greater or less number of fluid passages containing feces mixed with mucus, and not always accompanied by colic. No danger attaches to the condition unless the passages become abnormally large, which is said sometimes to occur, especially in hot weather when the affection assumes a choleraic form (Bohn). In addition to these forms of diarrhea, the symptoms of which are referable chiefly to the small intestine, we occasionally have to deal with a catarrhal inflammation of the large intestine in which the lymph follicles also take part. The diarrhea is then accompanied by tenesmus and the stools contain blood and large quantities of mucus.

Although the diarrhea is in itself of but slight importance at first, the most experienced clinicians very properly lay stress on the well-marked tendency to persist which this symptom manifests. It is therefore well to be cautious and not to wait too long before beginning active treatment.

Other forms of intestinal inflammation occurring during or subsequent to measles are on record, but their development at that time was probably only a matter of chance. Bohn,* in fact, makes a direct statement to this effect: "When Asiatic cholera is raging simultaneously, the diarrhea of measles often passes directly into the former disease."

It is more difficult to form an opinion as to the cases presenting the anatomic changes characteristic of diphtheria of the large intestine. If a whole group of such cases develops as a sequel to measles, as described by v. Guttceit,† manifesting all the symptoms of true dysentery, the cause may, in all probability, be sought in a fresh infection by the contagium of dysentery. Where sporadic cases, however, are concerned, especially in a district free from dysentery, we are brought face to face with the question, as yet unsolved, of whether the phenomena characteristic of dysentery, clinical as well as pathologic, are necessarily always produced by the same specific bacterium.

The whole matter of the relation between the measles infection and intestinal inflammations developing late in the course of the disease seems to me rather confused; for if it be true that an intestinal complication is the more dangerous, the later it appears in the course

* See Gerhardt's "Handbuch," *loc. cit.*, p. 313.   † *Loc. cit.*, p. 252.

of measles (as stated by Barthez and Rilliet, and also by Thomas), it would surely argue against any direct relation between the two processes. The most probable explanation, to my mind, is that the action of the measles poison simply lays the mucous membrane of the intestine, like that of the bronchi, open to attack by some other form of bacterial disease.

It is admitted on all sides that the **stomach,** apart from symptoms of functional disturbance, which accompany every acute infectious process, remains practically unaffected in measles.

The **mouth,** on the other hand, may be the seat of lesions from which serious consequences may proceed. Leaving the processes already described—the enanthema, etc.—out of consideration, our attention is first called to that peculiar localized affection of the buccal mucous membrane consisting of the formation of aphthæ. It is quite often seen in measles, though its frequency varies in different epidemics, as does also the time of its appearance, for which it may choose the days preceding the eruptive stage or the period during which the eruption is developing. The troubles directly due to the aphthous inflammation, such as an increased flow of saliva, and pain on taking nourishment, etc., need hardly excite apprehension. It may, however, lead to serious complications in measles cases. The complication may take the shape of a similar inflammation in the larynx, causing laryngeal stenosis, which the case previously referred to (Case 5) shows to be not an entirely remote possibility, even though it is but seldom observed. Still more weight attaches to ulcerative processes in the mouth, which sometimes supervene on the aphthous inflammation, sometimes develop simultaneously. The clinician does not always find it easy to draw a practical distinction between the several processes here concerned, however desirable it undoubtedly is to maintain a systematic classification of the same. It is proper to state, I think, that the presence of an aphthous inflammation should put the physician on his guard, and that it calls for especially careful treatment of the mouth, without reference to the question of what relation exists between aphthæ, ulcerative stomatitis, and noma, which last-named affection has also been known to occur in measles.

A detailed description of these symptoms will be found in other parts of this manual, hence I will not refer to them here. It should be borne in mind, however, that poorly nourished children and all who live in unfavorable surroundings display a decided tendency to develop severe inflammatory lesions of the tissues within the mouth.

THE NERVOUS SYSTEM.

The opinion is quite generally accepted that the measles poison does not, as a rule, cause symptoms indicative of severe cerebral intoxication. This does not in the least imply that functional disturbances of the brain are unknown; on the contrary, convulsions, unconsciousness, and delirium frequently accompany an attack of measles, and are, indeed, to be expected, for the reason that it is preëminently a disease of childhood.

The distinction rests on the following points: **Cerebral symptoms** in a measles patient, developing in connection with a sudden and marked rise of temperature, may be explained on the ground of the "mechanical" changes, if I may so term them, which the fever induces in the tissues. If the symptoms subside, as is usual, when the temperature again falls, even if its reduction be brought about by the direct abstraction of heat, as by a cold bath, it is safe to conclude that there is no serious underlying condition. When the measles contagium causes a true toxemia, however, the cerebral symptoms no longer depend on a rise of temperature. Some of the cases previously cited (page 261) serve to illustrate how this condition manifests itself. It is rare, however, for the infection to display such extreme virulence. The cerebral disturbances known as anemic delirium, consequent upon a sudden reduction of the fever, are met with only very exceptionally in measles cases, and are, indeed, not often observed in children under any circumstances.

It is important to remember that the form of bronchopneumonia which runs a slow course is sometimes accompanied by cerebral symptoms in many respects suggestive of tubercular meningitis, such as apathy, retraction of the head, slight muscular twitchings, vomiting, and finally violent convulsions followed by coma. The slow, intermittent pulse, a sign which is seldom absent from a case of tubercular meningitis, may be missed here, but may, on the other hand, be present. I regard it as impossible in such a long-continued attack of bronchopneumonia to draw a positive conclusion as to the presence or absence, in addition, of a moderate number of tubercles in the brain and its membranes, unless it be on evidence furnished by the ophthalmoscope. Nor is this at all strange, since the main symptoms of the cerebral affection are aroused not by the tubercular inflammation, as such, but by the circulatory disturbances accompanying it and manifested in the form of edema and effusion. I once even had a case of wide-spread miliary tuberculosis which dis-

played all the characteristic clinical symptoms of a meningitis, and yet on autopsy no trace of tubercles in the brain could be discovered in spite of very careful search. The conditions which develop during measles are similar; the changes in the composition of the blood—it suffices to refer to the diminished quantity of oxygen and the excess of carbon dioxid which it contains—make the walls of the cerebral blood-vessels more permeable, and as a result we find the same edema of the tissues and the same effusion in the ventricles as in cases of tubercular meningitis—but nothing further.

This covers the subject as far as the direct effects of the measles poison on the cerebrum are concerned. Indirectly, however, measles may undoubtedly be responsible for various **other forms of nervous disease;** for the·miliary tubercular processes, for instance, which have already been referred to. Fürbringer speaks of having once seen a case of purulent cerebrospinal meningitis develop in close sequence with the stage of eruption, but although a connection between the two diseases is conceivable, it is certainly less distinct.

In respect to the list of various forms of cerebral involvement given by Thomas * as related to measles, I agree with Henoch and Bohn, who are inclined to doubt the responsibility of the latter disease.

THE KIDNEYS.

The **urine** of measles patients often contains albumin, just as it does in fever of any origin, without necessarily indicating an involvement of much importance.

True nephritis, on the other hand, is rare, as is admitted by all authorities. Even Henoch, with his very large clinical opportunities, reports having seen only two unmistakable cases. He cautions against a possible error of diagnosis which might lead to false conclusions, as it well might if the underlying infection were taken for measles when in reality it was scarlatina. It should be added that a nephritis following an attack of measles complicated by diphtheria cannot be attributed to the former disease. The statement made by Reimer,† that he found amyloid degeneration of the kidneys in 5 out of 51 autopsies on children who had died during an attack of measles, are of course meaningless as far as the pathology of measles is concerned. It is probable—although no definite conclusions can be drawn from the report itself—that the degeneration in question

* See v. Ziemssen's "Handbuch," *loc. cit.*, p. 105.

† "Casuistische und pathologisch-anatomische Mittheilungen aus dem Nicolai-Kinderhospital zu St. Petersburg," "Jahrbuch für Kinderheilkunde," vol. x, p. 3.

was the result of a chronic tuberculosis, as signs of this disease were evident in quite a number of the autopsies which he performed.

The following statements are taken from the carefully prepared article by Plagge,* which also contains references to the authorities quoted:

Attention must be called to the similarity in general features between the facts as herein given and those observed in scarlatina. The resemblance is apparent even as to the manner in which the complication develops. Certain epidemics are accompanied by nephritis, but the form which the latter affection takes is not at all especially malignant. The nephritis usually develops during the stage of desquamation, but may do so either sooner or later in the disease. In symptoms and course it does not appreciably differ from an ordinary acute nephritis; for a description of these points the reader is referred to the section on "Scarlatina." The prognosis is favorable. It is a question, I think, whether the antecedent infection can be held responsible for the case of chronic parenchymatous nephritis following measles which Plagge † cites. The history shows the •patient to have suffered from various previous ailments, and the early church-going, during the coldest season of the year, too, may very possibly have had something to do with the case, particularly as the child was not overstrong.

THE LIVER, SPLEEN, AND LYMPH NODES.

In the most severe forms of measles the **spleen** and **liver** are affected just as in intense infectious processes in general, whether caused by the contagium of measles or of any other disease. As a rule, there are no demonstrable clinical symptoms, such as enlargement, or pain due to tension and inflammation of the capsule. It is hardly necessary to state that serious disturbances of circulation, accompanying wide-spread capillary bronchitis, and the pulmonary lesions to which it leads, may cause congestion of these organs, as of any other part of the body.

[**Focal Necrosis.**‡—"Focal necrosis of the liver may be a lesion of measles. This condition is due to the local action of bacterial toxins usually at a distance from the seat of the bacterial growth. It has been observed resulting from the toxins of diphtheria, acute lobar

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* "Ueber Nephritis bei Masern," Würzburg Thesis, edited by Gerhardt, 1885.

† *Loc. cit.*, p 24.

‡ R. G. Freeman. "Result of Work at the New York Foundling Hospital," *Archives of Pediatrics*, Feb., 1900.

pneumonia, malaria, streptococcus infection, and Asiatic cholera. Two toxalbumins of vegetable origin have been found to produce similar lesions. The lesion is not confined to the liver, but involves other organs.

"In the liver only the larger areas of focal necrosis are visible to the naked eye. The appearance of these larger areas is fairly characteristic, although they may be mistaken for tubercle. The microscopic lesion, when well marked, consists of a sharply circumscribed roundish area of necrosis, in which the cytoplasm fails to stain, and there is fragmentation of the nuclei.

"The writer found this lesion of focal necrosis following measles in 4 out of 14 consecutive autopsies on measles cases. All of these were very carefully examined. In 2 of the 4 cases the lesion was evident on gross examination, while in one case only one microscopic area of marked necrosis was found. So far as the author knows, this lesion has not previously been described as a lesion of measles. A more complete report of this work has already been made.*]

The superficial **lymph nodes** appear somewhat swollen, but not sufficiently so to warrant a belief in their direct involvement by the measles poison circulating in the blood. It is much more probable that the lymph stream, somewhat increased in volume, which drains the inflamed skin is responsible for their enlargement. The nodes of the anterior and posterior cervical and submaxillary regions are somewhat differently affected. When the inflammation of the nasal and pharyngeal mucous membrane is severe, the lymph nodes into which the lymphatics of these parts empty are found swollen in proportion to the severity of the inflammation, and it is hardly possible to decide whether the action of the measles poison on the nodes is direct or indirect. The same may be said, it seems to me, of the tracheal, mediastinal, and bronchial lymphatic system. The intense swelling of the lymph nodes within the abdominal cavity in very severe measles cases (see Case 9), when no pathologic changes take place in the mucous membrane of the digestive organs, must assuredly, on the other hand, I think, be directly due to the action of the measles poison. The well-marked enlargement of the spleen which is also observed in these cases goes to support this view. Unless the lymph nodes are the seat of old tubercular (scrofulous) degenerative processes, the swelling usually subsides entirely. Abscesses may occasionally form, but this is a very uncommon sequel.

*New York Medical Record, vol. LIV, 1898, p. 135.

JOINTS AND BONES.

The swelling of the **joints** and inflammatory lesions of the **bones** which are occasionally reported probably stand, for the most part, only in distant relation to the measles infection, although this is not necessarily the case. The possibility of the joints * now and then being affected as in scarlatina must be admitted, but as a rule the arthritis is dependent on an antecedent localized tuberculosis. The occurrence of septic inflammatory processes is also on record.

THE EXTERNAL GENITAL ORGANS.

These organs are occasionally attacked by gangrene, and where female patients are concerned, by noma. Henoch is undoubtedly correct in stating that gangrenous processes, whatever parts of the body they involve, are seen only in wretchedly nourished, sickly children, and in questioning whether measles can really be held responsible for their development.

Gangrene was formerly much more often observed than nowadays, a change which Henoch attributes to the adoption of protective therapeutic measures in place of the energetic antiphlogistic procedures which used to be in vogue. I would suggest, in addition, that mercurials, especially calomel, held a prominent place among the remedies of the antiphlogistic method.

THE BLOOD AND THE HEMORRHAGIC DIATHESIS.

Not much is known in regard to the changes which take place in the **blood** during measles. Apart from a few reports of blood examinations in individual instances, which are of comparatively small value, our present information chiefly rests on a series of observations made on 18 cases at the Children's Clinic in Graz.† As the Fleischl hemometer was used in these tests, only relative figures were obtained. Since the work was conducted with great accuracy,—under the guidance, I presume, of R. v. Jaksch,—it gives a general idea of the phenomena in question, in spite of the unavoidable shortcomings of the method employed.

The following points were noted in uncomplicated cases: The hemoglobin was diminished after the temperature fell to normal; it

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* See article by Dr. Kompe, of Grossalmerode, "Kniegelenksentzündung als Complication der Masern," "Jahrbuch für Kinderheilkunde," vol. XXIX, p. 420.

† "Hämoglobingehalt des Blutes gesunder und kranker Kinder," by Dr. J. Widowitz. "Jahrbuch für Kinderheilkunde," vol. XXVIII, pp. 25 *et seq.*

increased during the last week of convalescence, in many cases reaching the figure observed in the stage of efflorescence.

There is nothing peculiar to measles in the above; according to Widowitz, the same changes occur in scarlatina. Complications developing in the course of measles produce very marked changes, but it is unnecessary to pursue the subject further here.

[There are differences of opinion among recent writers on the blood in measles, possibly because most of the observations have been made upon adults and in the stage of eruption, at least of fever. A. Renaud * states that during the stage of incubation, commencing at the beginning of this period, there is a hyperleucocytosis which increases rapidly, reaching its maximum about the sixth day before the appearance of the eruption. After this it diminishes. There is a relative and an absolute increase in the number of the polynuclear cells and an absolute increase, but relative diminution, in the number of lymphocytes. During the period of the enanthem there is, in normal measles, a diminution in the proportion of the polynuclear cells, while in cases of measles which are or are to be complicated with other diseases this diminution does not exist. During the eruptive period there is a characteristic hypoleucocytosis due to the diminution, both absolute and relative, of the polynuclear cells; and a relative but not absolute increase of lymphocytes. The hypoleucocytosis generally reaches its maximum on the second day, about twenty-four hours after the appearance of the eruption. The number of leucocytes is at that time reduced to about half, and the diminution is almost entirely in the polynuclear cells. From this time on, the leucocytosis rises again to the normal, ordinarily from the first to the fifth day of the exanthem, provided there are no complications. If there are complications, however, the total number of leucocytes increases again at once, the polynuclear cells also increasing absolutely and relatively.

During the post-eruptive period, if there are complications, there is a hyperleucocytosis which is due to the increase in the number of polynuclear cells. In normal measles there are no alterations in the erythrocytes.

Renaud believes that these modifications in the blood are of importance for both diagnosis and prognosis in measles. When the so-called prodromal signs of measles are developed, as is well known, it is too late to avoid contagion. The most important point as

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* Thése de Lausanne, "Valeur diagnostique et pronostique de la leucocytose dans la rugeole," Paris, 1900; and *Rev. mens. des mal. de l'enfance*, 1901, xix, 229.

regards diagnosis, and the earliest, is the *hyperleucocytosis of the period of incubation.* As already noted, this hyperleucocytosis begins with the infection and increases rapidly, reaching its maximum eight or nine days before the eruption—that is, four or five days before the contagious period. This is its value in prophylaxis, but especially in cases of measles breaking out in school or hospital and in large families. Examination of the blood will, he considers, show whether the children are or are not in the stage of incubation of measles. If the leucocytosis is normal, they have not contracted the disease; if the number of leucocytes is increased without any apparent cause, they have contracted it. Hyperleucocytosis of the incubation stage of measles should not be confounded with that of the catarrhal stage of whooping-cough. In the latter the increase in the number of leucocytes consists in increase in lymphocytes. The diagnosis of measles in the catarrhal and eruptive stages will be assisted by the examination of the blood—in differential diagnosis. Drug-eruptions are never accompanied by hyperleucocytosis, but sometimes by an increase in the number of white corpuscles. Antitoxin rashes are accompanied by hyperleucocytosis. In scarlet fever there is hyperleucocytosis with an increase in the number of eosinophiles—the opposite condition to that found in the eruptive stage of measles. As regards prognosis in measles, the examination of the blood also gives valuable information. In the hyperleucocytosis of the period of eruption the diminution in the number of leucocytes is about one-half; in measles which are or are to become abnormal this diminution may be greater or less. The hyperleucocytosis which is too large and continues too long is of bad prognostic import. The hypoleucocytosis which is slight and which changes rapidly to a hyperleucocytosis indicates a complication or the approach of a complication. A conjunctivitis, however, or a simple bronchitis, may show an increase in the number of leucocytes.

Cabot * states that "in mild cases the blood shows no changes at all; where bronchitis, conjunctivitis, and coryza are very marked, fibrin may be increased. . . . The value of the blood examination is considerable in excluding scarlet fever, diphtheria, and syphilitic roseola, all of which show leucocytosis. It cannot, apparently, be distinguished by the blood count from rötheln (German measles).

"**White Cells.**—There is no leucocytosis, often a leucopenia, during the eruptive stage. In convalescence the lymphocytes, and especially the large mononuclear forms, are increased."

* "Clinical Examination of the Blood," 1901.

Cabot classifies measles and rötheln among the diseases showing absence of leucocytosis.

Ewing * summarizes our present knowledge of the blood in measles as follows: "The red cells have been found in the great majority of cases to suffer little or no change, but a loss of Hb is usually demonstrable after defervescence.

"In adults, uncomplicated measles never causes leucocytosis, but is characterized rather by hypoleucocytosis, reaching in one of Rieder's cases 2700 cells. From 4000 to 6000 cells are commonly seen. This fact was first noted by Pee, and has been confirmed by Pick, Rieder, Rille, Felsenthal, and others.

"Normal or slightly reduced numbers of white cells are found at the onset of the disease. At the height of the exanthem they are usually at their lowest figure (Pee, Turk), and return to the normal within a few days or a week after defervescence. When the bronchitis is severe, there may be a moderate leucocytosis, Hayem finding 10,000 to 14,000 cells in such cases occurring in children. Rieder observed slight leucocytosis in a case complicated by catarrhal pneumonia. Cabot observed 9000 cells in two cases, one hemorrhagic. The writer found no leucocytosis in three cases occurring in malarious subjects. The malarial parasites reappeared with the chills during convalescence.

"The proportions of the various leucocytes show no distinctly abnormal variation. Turk found a rather high percentage of polynuclear cells during the fever, with diminution of small lymphocytes. Pee, Klein, and Turk noted an excess of large mononuclear cells. The eosins are usually in low normal proportions during the early febrile period, but tend to diminish as the eruption declines; yet Turk found nearly 5% during the second week of the disease.

"**Bacteriologic examination of the blood** was negative in ten cases examined by Barbier. Weber claims to have found in the blood of measles a protozoon which he has also seen in variola.

"**Applications in Diagnosis.**—Typical cases of measles and of scarlet fever may sometimes be distinguished from each other in their early stages by examination of the blood. Yet, as Turk says, the blood in measles strongly resembles that of a mild scarlet fever, as both show a nearly normal number of leucocytes and normal proportions of eosins. Yet equally severe constitutional disturbance should give on the second or third day leucocytosis if scarlatinal; normal or diminished leucocytes if for measles."

* "Clinical Pathology of the Blood," 1901.

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In **German measles** there was no leucocytosis in two cases mentioned by Cabot.]

I will also pass briefly over the phenomena which, although their nature is not yet clear, are grouped together under the name of **hemorrhagic diathesis.** They are only rarely met with in measles, a fact which is only in part explained by the rarity of severe toxemia in this disease. Neither do they often develop as a sequel to measles. Occasional cases are seen by all practitioners of wide experience, but there is no question of any close relation between measles and the hemorrhagic phenomena.

Scorbutus, as a disease entity, appears as a complication of measles just as often or as seldom as the local endemic conditions provide for.

ORGANS OF SENSE.

The eyes and ears are exposed to inflammation during an attack of measles. Conjunctivitis is a regular feature of the disease, and the inflammation of the mucous membrane of the nose and pharynx extends along the Eustachian tube and may finally reach the middle ear. For practical purposes it matters little whether the inflammation thus induced be the direct result of the measles poison or whether other infectious agents are responsible. Although it usually displays a more or less benign character unless the patient be the subject of scrofula or tuberculosis, the condition calls for careful treatment. Let us take up the separate points involved.

The Eyes.—It is extremely important that the most careful attention should be paid to the eyes in severe attacks of measles, whether their severity be due to the virulence of the infection itself, or develop later as a result of bronchopneumonia. In such cases, as in all acute diseases accompanied by diminished cerebral activity, the eyelids fail to close as quickly and tightly as they should, and the lacrimal secretion is insufficient. Foreign bodies are apt to enter and remain in the eyes, causing an inflammation which may develop into a panophthalmitis and finally lead to destruction of the eyeball. These complications can be avoided by proper and timely care.

Eversbusch * states that the following eye affections occur during and subsequent to measles:

Blepharospasm, in consequence of a highly developed photophobia. This may give rise to subsequent short-sightedness.

* "Behandlung der bei Infectionskrankheiten vorkommenden Erkrankungen des Sehorgans," "Handbuch der speciellen Therapie innerer Krankheiten," edited by Pentzoldt and Stintzing. Jena, G. Fischer, 1894, vol. i, pp. 605 *et seq.*

Inflammation of the lacrimal gland.

Hyperemia of the conjunctiva and catarrhal conjunctivitis. This lesion is characteristic of the measles infection, but not infrequently persists after the latter has subsided, and takes on a severe form.

Necrosis of the cornea and central purulent infiltration. These lesions are ascribed to poor circulation and bacterial embolism, or to the implantation of bacteria from without on the cornea, which in its reduced state of nutrition offers a favorable site for their growth.

Marginal ulcers of the cornea.

Weakness of accommodation; paralysis or spasm of the ocular muscles.

Affections of the optic nerve, taking the form of amblyopia or amaurosis; atrophy of the nerve may develop later.

I have here omitted the affections belonging to some other disease process running its course simultaneously with measles, such as tuberculosis, diphtheria, sepsis, uremia, etc.

The Ears.—The forms of inflammation to which the ears are subject are much fewer in number. The following are met with, according to Burkner *:

Acute catarrh of the middle ear. This is the form most commonly observed; it is seen in a large percentage of cases in some epidemics, sometimes developing early in the disease, but usually not until the stage of desquamation.

Severe purulent otitis media. This is not at all a rare complication.

The author also states that "an invasion of the labyrinth by cocci, causing necrosis, has been repeatedly demonstrated of late. The lesion results in a very serious loss of functional power."

This fairly well completes the list of ear affections which stand in more or less close relation to measles. It must be added that measles confers no immunity against any other disease, whether of infectious origin or not; chance may therefore bring about any conceivable combination. The term "secondary" was formerly applied to measles when it developed during the course of some other disease. Such a distinction seems to me uncalled for. The question which presents itself to the physician, whatever other disease be present, is, How will the course of the case be affected by this special combination of different processes? The answer varies in every instance, and

* "Behandlung der bei Infectionskrankheiten vorkommenden Ohraffectionen." *Loc. cit.,* p. 581.

depends on the personal equation of the patient no less than on the physical diagnosis.

Occasionally a whole group of cases of some other infectious disease, which happens to be endemic or epidemic in that locality, is observed to develop in close sequence with measles. Does this argue a relation of cause and effect between measles and the other disease, in the sense that the measles poison predisposes to the latter? It will be difficult to decide this question positively. The effect on all the mucous membranes involved in measles being to reduce their power of resistance, it becomes easier for other pathogenic bacteria to implant themselves on or to penetrate the same; the development of a new infectious process consecutively to measles is therefore not hard to understand. It is not only possible, but probable, that this explanation is correct, but the great number of cases of measles which occur during an epidemic of any considerable size makes it impossible to present statistical proofs capable of bearing critical analysis.

The infectious processes which supposably develop as a result of the "predisposing influence" of measles chiefly involve the intestines, such as dysentery and cholera. Croupous pneumonia, however, also belongs to this group.*

Let us consider the effects of measles from the opposite point of view. Thomas says †: "When measles develops during the progress of an affection to which it does not usually give rise, it sometimes exerts a favorable influence on the course of the latter." He bases this statement on the experience of a considerable number of physicians of repute, and there is undoubtedly some truth in it. The two classes of lesions here referred to should, however, be considered separately.

First, chronic skin diseases, which are stated to disappear after an attack of measles, even in case of adults. This may well be, since measles causes a temporary change in the conditions of nutrition in the skin, which may supply the stimulus necessary for overcoming the existing disorders.

Secondly, in respect to an improvement in the general bodily nutrition and curative effects of measles on local affections of long standing (of the bones, joints, etc.). Clinical experience has undoubtedly shown such cures to occur as the result of acute infectious processes in general, a phenomenon which is probably to be explained as follows: Every active disturbance of the ordinary routine process

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* As during the epidemic at Griefswald, v. Ziemssen-Krabler, *loc. cit.*, p. 234.

† See v. Ziemssen's "Handbuch," *loc. cit.*, p. 113.

of metabolism clears out old decayed tissue, making room for newly formed cells developing from nuclei which have escaped destruction. It is truly an example of the "survival of the fittest."

Cases showing the favorable influence of measles in causing the subsidence of various forms of nervous disorders are also on record. I fail, however, to see the possibility of any connection, as alleged, between measles and the disappearance of round-worms, or the cure of a gonorrhea.

DIAGNOSIS.

IT is, of course, easy to make a diagnosis of measles when the disease is epidemic, but quite a different matter where sporadic cases are concerned, particularly when the symptoms are not well marked. Under such circumstances even a physician of wide experience may be forced to reserve his opinion for a time.

[**Meunier's Sign.***—"There exists during the phase called incubation of measles a phenomenon which we have constantly observed and which consists in a marked lowering of body-weight independent of every kind of morbid troubles—digestive, secretory, or other."

That diminution of weight, or pre-measles fall, is all the more striking as it contrasts in the child with the ascending curve of physiologic growth. It begins about the fourth or fifth day after contagion—that is to say, five or six days before the appearance of the first catarrhal or febrile symptoms, eight or ten days before eruption. It lasts several days, more often even to the beginning of invasion. Its intensity varies with the case, but seems independent of the age of the subject and of the severity of the later measles. The loss of weight is about 300 grams (10 ounces), or 50 grams (1½ ounces) a day in a child of one to four years. It may reach 700 grams (22 ounces) and has not been observed less than 90 grams (3 ounces).]

It is a mistake to attach too much weight to the appearance of the skin eruption, and to regard it as a conclusive pathognomonic indication. In measles, as in all other diseases, the diagnosis should be based on the manifestations of the disease in their entirety. If the essential characteristic features are present,—the catarrhal inflammation of the mucous membranes and the accompanying enanthema, the skin eruption, developing somewhat later, and the fever,—the diagnosis is assured. I have already discussed the details of the symptomatology so thoroughly as to make it unnecessary to review them now.

[For a discussion of the conditions of the blood in measles and in other diseases with which it may be confounded, see the immediately preceding pages.]

* "Sur un symptôme nouveau de la période précontagieuse de la rougeole et sur sa valeur prophylactique." M. le Dr. Henri Meunier, *Gaz. Hebd. de Med. et de Chirurg.*, n. s. Tome III, No. 89, 1057, 1898.

The question of differential diagnosis, however, calls for special consideration. The following diseases must be thought of in this connection:

1. Rötheln ; Roseola.—An error in diagnosis between this disease and measles may easily arise, as is admitted by all who look upon the former as an independent infection. The main distinction lies in the comparative mildness of the general and local symptoms of rötheln, as in all other respects the two diseases are, or at least may be, similar. This being the case, it is naturally impossible in a given sporadic case to decide between them on the ground of symptoms. The probabilities point to rötheln, if a wide-spread epidemic happens to prevail at the time, attacking large numbers of those who have previously had measles, and if, in the case in question, the patient is known to have already had the latter disease. For a fuller discussion of this point I would refer the reader to the section on "Rötheln."

2. Scarlatina.—The chief differential points here are: The sudden stormy onset of scarlatina after a short prodromal period, or without any appreciable prodromal symptoms whatever; the high fever which accompanies it from the beginning; the angina; and the enlargement of the glands, not only of the cervical region, but also in other parts of the body, notably in the groin.

The scarlatinal rash is first seen below the clavicles, the face being only attacked later; the region about the mouth remains comparatively unaffected, and presents a strikingly white appearance in contrast to the rest of the face, which is highly injected. The rash spreads over the whole body, leaving no free intervals of skin such as are seen in measles. In measles, when the finger is lightly passed over the skin, the surface of the latter feels slightly uneven, the sensation being due to the prominence of the individual spots of eruption; in scarlatina the skin is evenly swollen, and this sign is therefore absent. If the scarlatinal rash is of recent development, the skin, when firmly stretched, takes on a general yellowish hue, whereas in measles this change of color is seen only over the spots of eruption and is only faintly marked.

The "strawberry tongue" observed in scarlatina patients has, when fully developed, a very characteristic appearance, such as it is difficult to imagine could be duplicated in measles. But the tongue in measles may closely resemble it in the beginning, when the red and swollen papillæ rise up above the yellowish-gray level of the surrounding epithelial layer.

When we further consider that the catarrhal inflammation char-

acterizing measles is absent in scarlatina, a confusion of the two diseases would certainly seem almost out of the question. And yet such a confusion is quite possible, the more so, the earlier the case is seen. Other symptoms help to furnish a clue later on,—I refer chiefly to the course of the fever and the form of desquamation,— but I must admit that I belong among those who, as Fürbringer and v. Leube have lately done, openly confess that a positive differential diagnosis of scarlatina and measles may present insuperable obstacles. The physician whose sense of smell equals that of Heim may perhaps form an exception. Heim himself says, by the way,* that he knows of no absolutely reliable sign which can always be depended upon except the odor. The odor perceptible in scarlet fever, according to him, is somewhat similar to that of carnivorous wild animals when kept in cages, whereas in the early part of measles (up to the seventh day) there is a sweetish odor, such as attaches to freshly pulled goose feathers. Later a sour odor takes its place, but Heim seems to lay less stress on this. I do not in the least doubt the existence of such a keen sense of smell, and envy every physician who possesses it. One of my friends was thus gifted, and it enabled him, for instance, to recognize typhoid fever at an early stage.

3. Smallpox.—An error in diagnosis is possible at an early stage of the disease. Like measles, the eruption of smallpox first appears on the face in the form of circumscribed, light red prominences in the skin, only later developing into papules and finally into pustules. Too much stress should not be laid on the fact that in measles the spots are usually somewhat larger (Curschmann †).

The same mucous membranes which are involved during the initial stage of measles sometimes become inflamed during the corresponding period of smallpox, as manifested by the symptoms of conjunctivitis, coryza, angina, and bronchitis, and may even exhibit a red macular eruption. Similarly, the inflammation may involve the larynx, in which case hoarseness and the characteristic cough will also be added.

The conditions would thus seem very favorable for a mistake in diagnosis as far as local symptoms are concerned. But it is otherwise in respect to general symptoms. First of all, it is important to remember that a smallpox patient feels much sicker than one suffering from measles; there is a greater sense of lassitude and weakness, and the headache is much more severe. The onset of smallpox, too, is accompanied, as a rule, by one or more chills, which drive the tem-

Loc. cit., p. 74.

† See v. Ziemssen's "Handbuch," vol. II, 2, p. 443 of 2d ed.

perature higher and with greater rapidity than is usually the case in measles. These toxic symptoms may, however, be manifested also in severe attacks of measles. The course of the fever is of greater importance. In measles it rises at the time the eruption breaks out, and remains high while this is spreading; in smallpox it begins to fall from the moment the eruption appears, though not always to normal, it is true. Curschmann is doubtless right in laying great emphasis on this point. Another valuable sign is the lumbar pain peculiar to smallpox. All doubt vanishes with the further development of the smallpox eruption, but it is of the greatest importance to make a positive diagnosis at the earliest possible moment.

[Blood examination shows no leucocytosis in the early stage, in which diagnosis is to be made. In the suppurative stage leucocytosis is present (Ewing).]

4. Typhus Fever (Spotted Fever).—According to those who are familiar with both diseases, it is possible to confuse the two. An error is favored by the fact that a catarrhal inflammation of the nasal, buccal, laryngeal, and bronchial mucous membranes, as well as of the conjunctivæ, precedes the outbreak of the typhus rash by several days. It is true that the general symptoms are much more intense during this period than in measles, but it must be remembered that this is an uncertain sign. The onset is more sudden than in measles, the temperature rises higher at once, the spleen becomes much enlarged, but these points do not necessarily furnish a positive indication in a given case. Another distinction to be noted is the behavior of the eruption toward the face, which, when it breaks out, on about the third day, at first taking the form of a roseola, it leaves entirely or in great part unaffected. Still more emphasis may be laid on the hemorrhagic exudation which takes place in the separate macules two or three days after their appearance, transforming them into petechiæ. This would to my mind seem a definite differential point, as by this time a careful observer ought surely to be able to exclude hemorrhagic measles. I cannot speak from personal experience, however, as I have never seen a case of typhus fever.

5. Septic Infections.—The pus-forming cocci have the power of causing a rash which very closely simulates that of measles, in the same way that a septic rash may on occasion resemble any of the various forms of eruption. The physician who is not familiar with the symptoms of septic infection of unknown origin may thus well be misled in his diagnosis. The following is a case out of my own practice:

MEASLES.

CASE 26.—Louise H., ten years of age, was taken ill on November 7, 1894, with diarrhea, abdominal pain, dysphagia, and pains in the right side and left arm. These symptoms, for the most part, subsided during the next two days, and when I first saw the patient, on November 9th, only the high fever and quite a well-marked angina were noted. By the 12th all the symptoms had disappeared except the fever, which still remained high. On this date the face appeared somewhat cyanosed and
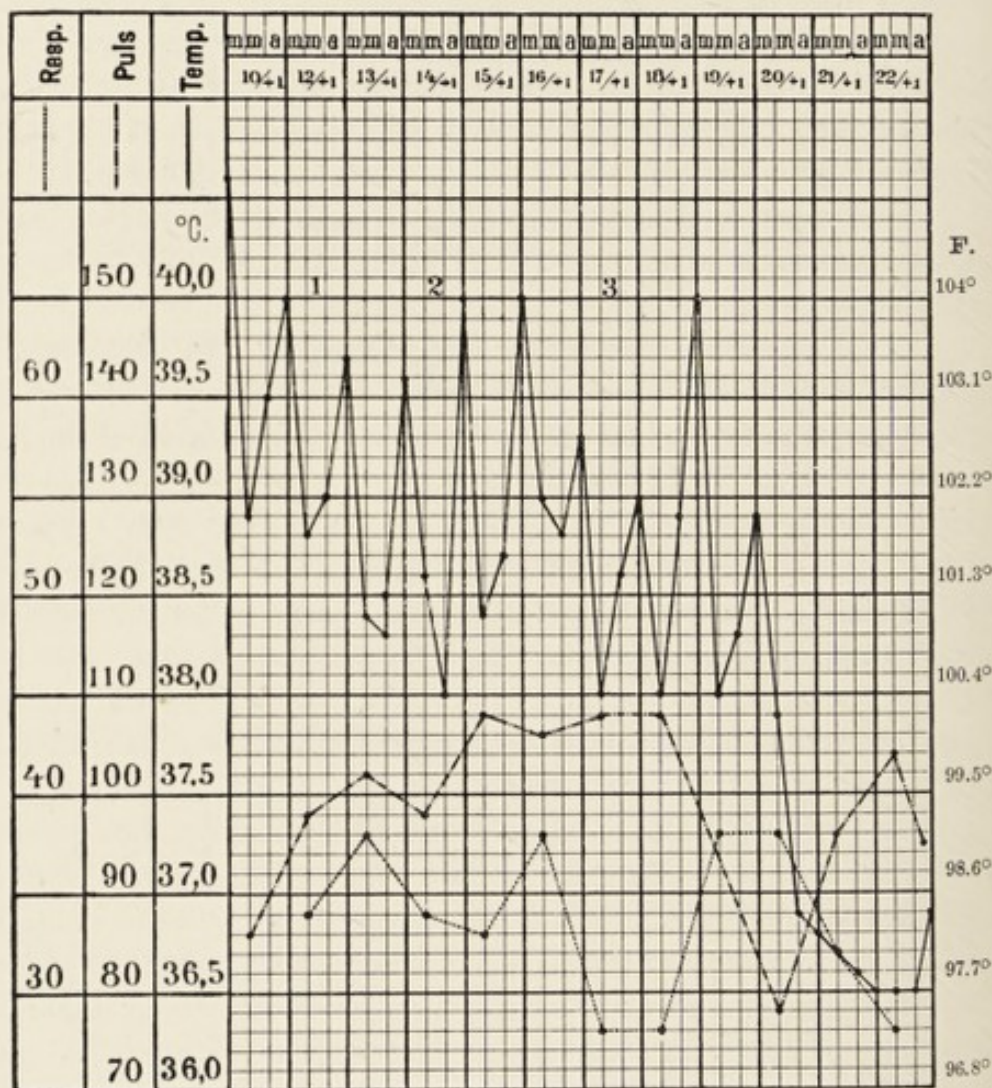
FIG. 57.—1, Outbreak of the measles-like rash; also first signs of pulmonary consolidation; 2, development of the erysipelatous rash on face; 3, desquamation completed. Pulse and respiration noted only once daily, in the morning; the temperature record dates from second day of disease.

slightly swollen, and a rash broke out over the entire body, with the exception of the face. It consisted of red spots, the largest the size of a lentil, distinctly raised above the surrounding surface; it became confluent in some places, but, on the whole, remained circumscribed. It resembled the rash of measles. The redness disappeared entirely when the skin was put on the stretch. There was no itching and no pain. In the upper portion of the right lung early signs of consolidation were detected, but there was no general bronchial catarrh. The spleen was

enlarged; it measured 7 to 7.5 cm. (2.75 to 3 in.). The patient again complained of pain in the limbs and sensitiveness to pressure.

On the 13th the rash was still in evidence, but disappeared except for a faint yellowish-brown discoloration at the site of the spots when the skin was put on the stretch. The pain in the limbs was more severe; sensitiveness to pressure was manifested in both humeri, in the bones of both forearms, in the right tibia, and in the left ankle, which appeared swollen. The consolidation of the lung was more distinct, the area of cardiac dulness was somewhat increased, and the heart sounds were less clear.

On the 14th desquamation of the fine-scaled variety began on the body and legs. The lower third of the left femur also was sensitive to pressure on this day. The consolidation of the right lung now included its whole posterior surface, but was most marked at the apex. The râles were everywhere somewhat louder. At midday the skin on the upper part of both cheeks and over the bridge of the nose was observed to be red and swollen, the inflammation extending into the surrounding skin in the shape of sharply notched prolongations. In appearance this reddened area stood midway between erysipelas and phlegmonous inflammation.

By the 15th all sensitiveness to pressure had subsided, except over a small portion of the left astragalus. The skin was still scaling in circumscribed spots, and the superficial inflammation of the face was subsiding.

As to the further course of the case, it suffices to say that the patient suffered from severe headache and was slightly delirious during the night of the 17th to 18th. The temperature fell to normal on the 19th, and was afterward at times subnormal (it was taken three times a day up to the 5th of December). By the 26th all the local symptoms had disappeared.

In this instance the resemblance to the measles rash was as striking as I have ever seen it. Due consideration of the other symptoms, however, could leave no doubt as to the real nature of the sickness. I attach no less diagnostic significance to the pains in the bones and the peculiar pulmonary involvement than to the course of the fever and the behavior of pulse and respiration. If such a case were under observation only for that part of its course connected with the development of the eruption, the only point which would make the attending physician hesitate in making a diagnosis of measles might very probably be the absence of catarrhal symptoms—of the conjunctivitis, coryza, and bronchitis which he would expect to find. Nor would it have helped him much to note the temperature a few times only, and the real condition might have been overlooked, in spite of the patient's complaints of indefinite "pains in the limbs," since such pains are apt to be taken very lightly, and to be set down to "rheumatism" without careful investigation.

6. Von Leube is perfectly right in stating that "since the eruption in measles represents one form of roseola, it is natural that roseolas of all kinds should be mistaken for it, especially when the patient is seen for the first time in the eruptive stage of the disease." *

* *Loc. cit.*, p. 361.

Attention has over and over again been called to the fact that it is impossible to make a diagnosis of measles on the appearance of the eruption alone. The most frequent sources of error are probably the various **drug eruptions,** developing in connection with a general disorder accompanied by well-marked catarrhal inflammation. Of the disorders in question, influenza presents the most striking example. I saw a case of this kind only a few weeks ago, in which the rash disappeared within one day after discontinuing the use of spirits of turpentine. It had looked very much like a measles rash when examined over a limited field. In addition to the drugs which, pharmacologically speaking, are classed as ethereal oils, it is chiefly the group of modern antipyretics, and antipyrin itself in particular, which are responsible for errors in this direction. If any of these drugs have been employed in a case presenting diagnostic difficulties, its use should be discontinued until the point can be decided. Iodin is another medicine causing a suspicious rash, especially since conjunctivitis and coryza are then present in addition.

Gerhardt * lays emphasis on the following fact: "The roseola of syphilis simulates the measles rash more closely than any other form of roseola, the resemblance being especially marked when prodromal fever is present."

Taking all the possible difficulties referred to into consideration, we have to admit that, except during an epidemic, the diagnosis of measles is by no means a simple matter.

[**Koplik's Spots.**—The present-day experiences in American practice justify the following conclusions:

1. Measles cases regularly show buccal "spots," usually early enough to be of corroborative diagnostic value (91% approximately).

2. Typical "Koplik spots" are seen in measles only.

3. The presence of buccal "spots" without other symptoms of measles cannot be considered a guarantee of immunity against the infection of measles.

4. The average time of appearance of buccal "spots" before the general exanthem is one to three days. A few cases have been reported as early as the fifth day.

5. Buccal "spots" lead to an early diagnosis, but unfortunately the diagnosis is, even then, not early enough to antedate infection in this extremely contagious disease. It does not suffice to prevent the spread of measles in the schools, hospital wards, and asylums.

6. Buccal "spots" serve in differentiating measles from: (*a*)

* "Lehrbuch der Kinderkrankheiten," p. 65.

Scarlet fever, in which the buccal mucous membrane is of normal color. (*b*) Simple aphthæ, which do not show such bright red spots and the bluish-white specks characteristic of measles "spots." (*c*) Rötheln. A pronounced case of German measles is often extremely difficult to differentiate from measles. The buccal "spots" here serve a useful purpose. In measles approximately 91% show buccal "spots." In rötheln the mucous membrane is normally pale pink. Rötheln as observed in the United States is reported to be regularly without buccal "spots." (*d*) Antitoxin rashes, erythema multiforme, common cold, influenza, etc.

Dr. R. G. Freeman at the New York Foundling Hospital has observed a few cases in which typical "spots" were present and yet no symptoms of measles followed. One would not feel justified in the present collected experience in considering such cases immune and exposing them to infection.

Dr. Rotch, of Boston, justly summarizes as to the present estimate of the value of this sign as follows: "The presence of Koplik's spots helps in a large majority of cases. The consensus of medical opinion seems to be that, while their absence does not exclude measles, their presence is pathognomonic of measles."]

PROGNOSIS.

THE serious import which attaches to measles as an epidemic disease has already been discussed (see page 255). As a rule, it does not rank as a malignant disease, for the reason that it chiefly attacks young children and breaks out so often as to preclude very large numbers from being attacked at any one time. The disease assumes a different aspect, however, under certain conditions, such as existed, for instance, on the Faroe Islands or in Iceland. Then it becomes a sweeping pestilence, with all its attendant horrors. The details of the epidemics just referred to have already been given.

The **prognosis of measles,** as of diseases in general, rests in large part on two factors: viz., on the severity of the special epidemic in progress and the power of resistance displayed by the affected individual.

[I have discussed this point in an article on " A Recent Epidemic of Measles in the New York Foundling Hospital: Its Relation to Immunization with Diphtheria Antitoxin."* It is to be noted that this is a most favorable report. The season of the year was October and November. The temperature during these two months was mostly uniform and mild, allowing efficient ventilation. The children had had a summer of abundant recreation in the open air, and were in a good state of physical health.

March and April would offer a contrast both in conditions and consequent mortality.

"In all, there were 258 cases and 36 deaths (13.9%). Of the 258 cases, 53 were complicated with bronchopneumonia (20.5%); of these, 31 terminated fatally (58%). Autopsy showed the presence of complicating bronchopneumonia in 31 of the 36 fatal cases."

Ages of patients, up to four and a half years. Previous illness or condition of nutrition is not taken into consideration. It is to be remembered that these are institution children. They had the usual characteristics, but were at the time in their best possible form.

Systematic immunizing with diphtheria antitoxin was practised on all exposed children except nurslings. To this precaution is thought to be due the favorable results. Previous experience leads to this belief.

* W. P. Northrup, *Medical News,* vol. LXXI, No. 26, 1897, p. 817.

To formulate measles statistics of mortality has seemed to the editor, after much consideration of the subject, no better than worthless.

It is only a question of how much besides measles is killing the child. Children in private families under favorable surroundings have a small percentage of fatality, but this is not to be determined: they are not fully reported. Children in crowded hospitals, children with lowered vitality from poor food and insufficient air, develop complications which make their percentage abnormally high. Such statistics for measles as the Hospital for Scarlet Fever and Diphtheria Patients (private patients from thirty families) have furnished for the two several diseases have a value as compared to which all measles statistics in New York city are worthless.

A child which may be capable of passing through measles may be heavily handicapped in the race when weighted with complications, or if it enter in an enfeebled condition.

There remains, now that diphtheria is removed from the list, but one scourge in institutions for children—a plague—and that *plague is measles.*]

The severity of the infectious process does not vary so greatly in different epidemics of measles as in similar outbreaks of scarlatina, but this point is nevertheless of distinct importance. And whoever asserts that measles is essentially a benign disease, to which only weaklings at the most succumb, only shows his lack of personal experience as well as his unfamiliarity with medical literature.

Although they refer only to a small place, my policlinic statistics are well fitted to illustrate the different character of various epidemics, since the population from which the patients were gathered remains very uniform. For the city of Tübingen by itself I find the average mortality (53 fatal cases among a total of 868) to have been 6.1%. It varied as follows in different epidemics:

1874	133 cases,	8 deaths	= 6.0%
1880	109 "	4 "	= 3.7%
1884	213 "	10 "	= 4.7%
1888	152 "	10 "	= 6.6%
1891	117 "	6 "	= 5.1%
1893	90 "	8 "	= 8.9%

The ratio between the lowest and highest mortality in the above table equals that of 100 : 242. If the small epidemic of 1877 be added (42 cases with 6 deaths), the ratio changes to 100 : 389.

The following are the death-rates of various epidemics in other places; the lowest are for Munich and Stuttgart:

Munich *: the average mortality for four epidemics was 1.7%; the figures for the separate epidemics were 0.7%, twice 1.5%, and once 2.7%. (From data of the Hauner Children's Hospital and Children's Policlinic; total number of cases, 1907.)

Stuttgart †: From 1852 to 1865, 380 cases of measles were treated by the physicians attached to the city free medical service; the conditions for recovery were therefore unfavorable. Of these patients, only 7 died, or 1.8%, an extremely low death-rate.

The mortality was higher in the epidemics enumerated below, which may be classed as of medium severity, if such a classification, indeed, has any real meaning:

Heidelberg, 1888, reported by Embden ‡: 461 cases, with 31 deaths, giving 6.7%. (From data obtained at the Policlinic and the Children's Hospital.)

Kiel, 1860, reported by Bartels §: 573 cases with 39 deaths, giving 6.8%. (From data of the Policlinic.)

Greifswald, 1861, reported by Ziemssen and Krabler ‖: 311 cases with 21 deaths, giving 6.8%. (Chiefly from data of the Policlinic, with the addition of those noted in v. Ziemssen's private practice and a few cases treated in the hospital.)

Würzburg, 1883, reported by Breier **: 1896 cases, with 153 deaths, giving 8.1%. (The figures cover all the cases under medical treatment.)

The last figures approach the truth more nearly than any of the others, because they refer to all classes of the population, a most important point in judging mortality tables. It should be remembered, by the way, that in measles more than in other diseases many cases are allowed to run their course without medical treatment, because the lower classes look upon it as a comparatively innocent disease. Such cases are, of course, chiefly of a mild type; thus the mortality is made to appear higher than it really is.

Physicians in private practice, who deal with patients of all classes, have much better results in measles cases than can be obtained

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* H. Ranke, "Epidemiologische Skizzen aus München," "Jahrbuch für Kinderheilkunde," new series, vol. II (1869), p. 36.

† Prof. O. Köstlin, "Zur Geschichte der Masern," u. s. w., *Archiv des Vereines für Wissenschaftliche Heilkunde,* 1866, vol. II, p. 342.

‡ *Loc. cit.*, p. 4.   § *Loc. cit.*, p. 66.

‖ *Loc. cit.*, p. 119.   ** *Loc. cit.*, pp. 11 and 15.

by the physicians connected with policlinics. For one thing, their patients have a better constitutional power of resistance; for another, they are sent for early in the disease, even in mild cases. The truth of this statement is so generally recognized that it is not worth while to cite many points in proof. It will suffice to mention that during the Heidelberg epidemic of 1888 the mortality among the patients of the Policlinic was 6.7%, while among those treated in private practice it was only 2.6%. According to Fürbringer,* the rate in an epidemic at Jena of which he had personal knowledge was 8.1% for Policlinic cases, and only 3.3% for private patients. The difference in mortality becomes more striking the nearer the patients approach the upper and lower limits of the social scale. The figures obtained by a physician who, like a neighbor of Für-bringer's at a meeting of the Berlin Medical Society, cries out, "No patient of mine must die from measles!" present a marked contrast to those of physicians whose results refer to hospital wards.

Henoch † states that 294 measles patients were treated in his children's division of the Charité Hospital between April, 1888, and October 1, 1890. Of this number, 89 died, or 30.3%. In Fürbringer's service at Friedrichshain from 1886 to 1890 there were 453 cases of measles with 103 deaths, or 22.6%. In 1886 to 1887 the mortality there even reached 30.4% (181 cases, with 55 deaths). Of the patients in his charge, however, Fürbringer declares that "almost all who succumbed were in miserable condition and were suffering from severe complications when brought to the hospital." ‡ Henoch makes a similar explanation, saying that the majority of those under treatment were rachitic and suffering from various atrophic condi-tions, and that many were tubercular.

Apart from the influence of general condition, the prognosis depends to a large extent on the **age of the patient.** The facts may be summed up as follows:

During the first six months of infancy the mortality is compara-tively low; it then rises, reaching its maximum during the child's second year, and becomes low after the completion of the fifth year.

The great importance of age as a factor in prognosis is generally agreed upon. I give on the following page an English mortality table, which covers a broad field.

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* *Berliner klin. Wochenschrift,* 1891, p. 103.

† "Ueber die Masernepidemie der letzten Jahre," *Charité-Annalen,* vol. XVI, 1891, pp. 608 *et seq.*

‡ *Berliner klin. Wochenschrift, loc. cit.*

23

MORTALITY FOR MEASLES IN ENGLAND FROM 1868 TO 1872.*

IN 1000 FATAL CASES THE AGE OF THE PATIENTS WAS RESPECTIVELY:

0-1	1-2	2-3	3-4	4-5	5-15	15-25	25-45	45-65	Over 65.
200	376	190	101	53	72	3	4	1	0

Another table illustrating the point in question refers to the epidemic at Würzburg.† The total number who died from measles in all classes of the population was divided as follows in respect to age:

In their first year 23.5%
" " second year 35.3%
" " third to fifth year...............................33.3%
" " sixth to twentieth year......................... 7.8%

Of the 36 infants who died during their first year, 5 were under six months of age, or 14%; 31 were from six months to one year of age, or 86%. This goes to show the comparatively great immunity of early infancy; only a few take measles at this period of life, and with those attacked the disease runs a mild course. The foregoing proportional mortality at different ages applies with a fair degree of accuracy to the ordinary conditions of life as brought about by modern industrial and social relations, but the statistics of sweeping epidemics in places where the disease breaks out only at widely separated intervals may make quite a different showing. During the extremely mild epidemic on the Faroe Islands in 1875, for instance, Hoff reports that while only 8 out of 1123 cases ended fatally, 5 of those who died were healthy, vigorous individuals from twenty to thirty years of age. Hoff states that the infection took a more severe form among the adult population, especially as to general symptoms, death in all cases occurring when the disease was at its height and not as a result of sequels.

Panum's report ‡ of the Faroe epidemic of 1845 also shows the danger to have been greatest for adult patients, and for infants under one year of age, whereas of those between one and twenty years of age, on the other hand, a strikingly small proportion succumbed. The following table is especially valuable for statistical purposes because it includes the average mortality for each different age-division.

* From a work by Dr. John W. Tripe, cited in the "Jahrbuch für Kinderheilkunde," vol. IX, p. 412.

† Breyer, *loc. cit.*, pp. 15, 16.   ‡ Panum, *loc. cit.*, p. 287.

Average Annual Mortality on the Faroe Islands.		Mortality During Epidemic of Measles. (During the early months of the year 1846.)	
Age-divisions.	Mortality of different age-divisions.	Mortality of different age-divisions.	Ratio of mortality during epidemic to average mortality. (The latter = 1.)
Under 1 year	10.9	30.0	1 : 2.8
1– 10	0.6	0.6	1 : 1.0
10– 20	0.5	0.4	1 : 0.8
20– 30	0.55	0.75	1 : 1.4
30– 40	0.85	2.1	1 : 2.4
40– 50	1.1	2.8	1 : 2.6
50– 60	1.0	4.5	1 : 4.5
60– 70	2.0	7.8	1 : 3.9
70– 80	6.0	13.1	1 : 2.5
80–100	16.9	26.1	1 : 1.5

The figures cited by Panum for the mortality from measles in Iceland in 1846, which he takes from Schleisner's report, are somewhat at variance with the above. While the rate is also high for the first year of life, and for adults over twenty years of age, the Iceland epidemic also told heavily on children from one to three years of age.

The facts are less clear with reference to the Iceland epidemic of 1882; still, quite a large number of fatal cases occurred among the adult population. Different portions of the island, however, were very differently affected.

It is hard to give a definite reason for such a high mortality at the most vigorous time of life. It is quite possible that the body tissues at that time offer the measles contagium a more favorable soil for luxuriant growth, as a result of which the infectious process becomes especially virulent. This would more than counterbalance the advantage to be expected from the larger size of the air-passages, even of the smallest ones, and the greater power exhibited by the respiratory muscles in the adult.

It will not do to urge the effects of unfavorable conditions of life in connection with the epidemics in those far-away northern islands, the Faroe group, for they are inhabited by a hardy, long-lived race *; 350 out of every 1000 deaths on these islands occurred, on the average, in individuals over seventy years of age, whereas in Denmark only 150 out of 1000 represented this period of life. In Iceland the figures are somewhat different; there the total mortality is so high that the population has rather decreased than increased in the course of several centuries, in spite of the unusual fecundity of the women. This fact is chiefly due to the large number of infants who perish

* Panum, *loc. cit.*, p. 287.

during their first year. In Denmark 569 out of every 1000 reach the age of thirty-eight, while in Iceland the same number live only to the age of fourteen. The figures given by Schleisner for ordinary years (1844 and 1845) in Iceland give a good idea of the conditions prevailing there. The total number of deaths, 1365, was divided as follows with respect to age:

Up to 1 year	557	40.8%
1 to 20 years	139	10.2%
20 to 50 "	283	20.7%
50 to 100 "	386	28.3%

It would appear from this table that when the dangerous period of early infancy is once passed, the Icelanders acquire a considerable power of resistance.

Sex has no influence whatever on the prognosis of measles.

Let us now take up the separate points on which the prognosis does depend.

The degree of virulence displayed by the infectious process is a most important factor in measles. In judging this, we are better guided by the rapid development of general symptoms of collapse than by the height of the fever. The significance of the latter must, of course, not be underestimated, but in some cases the fever is unusually high at the onset and yet it soon subsides. An abnormally high temperature is in itself seldom a serious menace, less so to children than to adults. The course of the temperature, however, often furnishes the first indication of unfavorable developments. This point has already been discussed, and it is unnecessary to review it here.

Capillary bronchitis, together with its sequel, bronchopneumonia, is the most frequent cause of death in measles. These bronchial complications will always be found to occupy so much the most prominent place in a list of deaths during measles, wherever obtained, as to give them the importance of the controlling factor. "These lesions form the foundation, the background, so to speak, for the various other changes exhibited" is Henoch's * conclusion in reviewing the results of postmortem examinations, and its truth is so well authenticated as to make statistical evidence appear superfluous.

According to one estimate, which, to be sure, is not based on sufficiently extensive and accurate data, one-third of the children attacked by bronchopneumonia during measles succumb to this complication.

* *Charité-Annalen, loc. cit.,* p. 610.

Laryngeal affections, also, exert a decidedly unfavorable influence. The prognosis here depends on whether the process in the larynx simply represents a local manifestation of the measles poison, or whether it is due to secondary infection by diphtheria bacilli. In the latter case it is more a question of the prognosis of diphtheria than of measles.

The same may, of course, be said of all other diseases of microbic origin developing in connection with measles. Of these, tuberculosis is the most notable example. An attack of measles may perhaps imply greater immediate danger to a tubercular child than to one not so affected,—at least if it is sickly, or its lungs are already seriously involved,—but the subsequent development of the tubercular process is still more to be feared.

As to the intestinal disorders of measles, they do not often form an element of real danger when dependent on the latter infection alone, except where sickly children are concerned. I have already pointed out the possibility of secondary pathogenic processes developing in this connection. (See page 327.)

I think that the foregoing covers all essential points, and that I may therefore properly close this section here.

TREATMENT.

THE first questions to be met are those relating to **prophylaxis.**

In view of the universal extreme susceptibility to measles, and of the fact that it does not diminish with increasing years, almost every individual must expect sooner or later to be attacked by this disease. This is unavoidable. It is possible, on the other hand, to protect a given individual temporarily, but only by means of complete and early isolation. (See pp. 229, 230.)

When should this plan be pursued? Certainly in case of especially malignant epidemics, as it is extremely probable that an individual who has never had measles will fare better if attacked during an epidemic characterized by a less severe form of the disease.

Age is another consideration. And since the outlook is more favorable after the third year is completed, it is well to avoid exposure until then.

In a given case the question will, of course, depend on the physical condition of the individual concerned. Scrofulous, tubercular, rachitic children, those whose state of nutrition is below the normal from any cause, or who have just recovered from some severe infectious disease, must be treated differently from healthy children in this respect.

The prophylactic rules applicable to schools have already been referred to. (See page 222.)

The dangerous possibility of the outbreak of a sweeping epidemic of measles, should the number of those who have never had the disease become very large in a community, has actually led to a discussion on the advisability of importing measles cases at regular stated intervals. Nor can such a plan be regarded as altogether unjustifiable with respect to the conditions existing in Iceland. Even here at home [Tübingen] the same idea is given expression, though in a different form. It is not at all unusual during an epidemic of a universally mild type for children to be intentionally brought into contact with measles patients. If asked for one's opinion as a physician, the parents should be warned that although a case contracted under such circumstances will probably also run a mild course, this cannot be counted on with certainty. The results of

inoculation experiments with smallpox may be taken as a guide in this connection. *I earnestly advise every physician to conceal none of the possible dangers from those who seek his opinion, and certainly not to suggest the plan of his own accord.*

When a case of measles once develops in a family, an attempt to protect the other susceptible members seldom meets with success, especially if the disease is not recognized until the eruption appears. It is often amusing to the initiated to see a "conscientious" mother turn the whole house upside down to this end—and all for nothing.

If there are children in the family whom it seems advisable to protect from contagion, they should be sent away to some other place which is free from measles before any one in the family is attacked; in no other way can even comparative safety be assured. This may be difficult to carry out for various reasons, but the physician should repeatedly insist on the great uncertainty of maintaining complete isolation at home, unless all communication whatever with the outside world be prohibited. It is very doubtful whether there is anything to be gained from isolating a child who apparently already shows the initial symptom of the disease, in the shape of a "slight" cold in the head. It is, of course, possible that such an attempt may prove successful, and as far as school life is concerned, the advantage of excluding a suspected child is manifest, but it is a different matter in the narrower circle of the home. The question of employing such prophylactic measures in the home on the first development of suspicious symptoms naturally does not present itself except at the time of an epidemic. Unfortunately, however, there are always some people, men as well as women, who insist that their physician should under all circumstances be able to give a definite name to a cold in the head. It would be considerably easier to give a definite name to those who make the demand. They would certainly be surprised to learn that their standpoint is not unlike that of those despotic rulers who used to have their physician killed if he failed to save the life of some favorite.

[Hutinel,* in prophylaxis and therapy of bronchopneumonia in relation to measles, goes far in painstaking precautions which are well worth adding to further illustrate modern views.

1. Children suffering from bronchopneumonia should be isolated; should not be near children having simple measles.

2. Not only developed cases, but cases that show bronchitis or

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* "Complications Broncho-pulmonaires de la Rougeole," *La Presse Medicale,* vol. v, No. 38, 1897.

those that have been exposed to the contagion, may be said to be threatened with bronchopneumonia.

3. Children should not be grouped; neither those in full eruption of measles, nor those in the stage of incubation.

4. The child should be kept in a condition of cleanliness most extreme. If the skin is not in satisfactory condition, is excoriated, eczematous, or simply dirty, the child should be given a sublimate bath without hesitation, using 1 : 5000 solution, and be made thoroughly clean.

5. Sores, crusts, ulcers, impetiginous patches, or eczematous surfaces should be antiseptically dressed with surgical minuteness.

6. There are normally micro-organisms in the mouth, the pharynx, the nasal fossæ, etc., which are capable of becoming virulent and provoking bronchopneumonia. One should take care of the mucous membranes covering these regions not less carefully than the external tegument.

7. Nasal lavage is more often harmful than useful. It is liable to irritate the delicate epithelium, and often leads to otitis media. Boric acid in vaselin or in tepid water may be gently applied. Hutinel's results have justified this method of antisepsis.]

The duties of the attending physician may in most cases be limited to watching the course of the disease; under ordinary circumstances he will have done his part after giving the necessary orders for the sick-room. The question of nursing, indeed, calls for the most careful attention.

First of all, in respect to the **sick-room itself.** The air which the patient has to breathe should always be kept as pure and uncontaminated as possible. The condition of the bronchi depends largely on this point; it is a fact that severe bronchitis and bronchopneumonia develop much more frequently and run a much more threatening course where the sick-room is poorly supplied with fresh air. Bartels'[*] very positive assertion to this effect has never been contradicted, although the explanation which he offers is unsatisfactory. He believes that carbon dioxid accumulates in such quantity in an ill-ventilated room as to interfere with the excretion of this gas by the lungs. Such an excessive accumulation of the poisonous gas can surely only take place in very unusual cases, if ever. The evil consequences of poor ventilation are more probably due to the irritating effects of the organic and inorganic dust particles which the air contains on the inflamed mucous membrane of the bronchi, more or less

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[*] *Virchow's Archiv*, vol. XXI, pp. 135 *et seq.*

stripped as they are of their protective layer of ciliated epithelium. The chief source of the trouble may at least be sought here; added to, perhaps, by the unknown materials which make themselves so unpleasantly appreciable to our sense of smell.

However this may be, it is a fact that a patient ill with measles needs fresh air in even greater measure than one suffering from some other acute infectious disease accompanied by fever. The most favorable conditions for the patient are attained by keeping the room at a temperature of about 17° to 20° C. (63° to 68° F.), by avoiding strong drafts, and by supplying sufficient moisture to the air by means of steam. This is easily managed in the better class of homes; but how about poor patients? In order to accomplish the main point and admit plenty of fresh air, we are often compelled to relinquish the advantages to be derived from an even temperature and an exclusion of drafts. Nor does the patient suffer in consequence; it has been conclusively shown that drafts do no harm to a fever patient; there is no danger whatever of his taking cold. In winter time if the room grows too cold and the patient complains of feeling chilly, this can be remedied for the time being by additional bedding. It is not necessary to keep the windows open day and night, but simply to supply a sufficient quantity of fresh air, which it is possible to do under any and all circumstances. The same may be said of the saturation of the air by steam. The floor of the sick-room, too, should be wiped up daily with a damp cloth, never with a dry one.

How is it in regard to lighting the room?

I earnestly and unreservedly advise against darkening the room to any appreciable degree. It is quite sufficient to see that the light does not shine directly into the patient's eyes, by turning the bed so that it stands with its back to the windows. Slight shading of the windows is permissible in case of a too brilliant side-light, but over-darkening must be carefully avoided. At night the room should be kept dimly lighted.

It should not be left to ophthalmologists to warn against the injurious effects of darkening the sick-room. We general practitioners should see to it that patients suffering from infectious diseases are not deprived of light. Light is a necessity of life, an imperative condition. I am convinced of the great advantage which the carrying-out of the above simple rules alone is to measles patients. I have seen enough of the conditions so graphically and truthfully described by Bartels to appreciate and fear their harmful influence, since only two years after his article appeared I was appointed to the

position of assistant physician to the Policlinic in Kiel, where the prejudices of the people at large could only be gradually overcome. I found the opposition to improved methods much less marked here in Tübingen, and nowadays it has altogether disappeared. The orders of the attending physician are now carried out unhesitatingly, and as fully as circumstances permit. How this is in other places I do not know, but I am convinced that the attainment of the desired end only calls for sufficient firmness on the part of physicians in general; for the blessing which light and air prove to those who are ill with measles soon becomes apparent to even an ignorant observer. This was Bartels' experience, too, as shown in the following statement: "It was not until the high mortality among those attacked by measles had stirred the hearts of the people that they lent a willing ear to our commands, and from that time on the death-rate began visibly to decrease."

Nothing in particular need be said as to the arrangement of the bed, except that from the first the patient's head should not lie too low, on account of the catarrhal pharyngitis which is always present. Many a distressing attack of coughing can be avoided by keeping the patient raised in bed, since in this position the upper aperture of the larynx is not unnecessarily irritated by the plentiful secretion of mucus and the swollen and elongated uvula. If a severe bronchitis develops, the patient should be raised up on pillows almost to a sitting posture, this being a great assistance to respiration.

What is to be said in regard to **treatment of the fever?**

I do not consider a systematic course of antipyretic treatment to be indicated in the great majority of cases. The fever is usually of short duration, and is not high enough to demand such treatment. Experience has positively shown, to be sure, that it can do no harm to lower the temperature by careful hydropathic measures, and it becomes imperative to do so under certain circumstances. The indication for such measures depends more on the patient's general condition than on the temperature *per se*. On the whole, therefore, it is not desirable to give a general order for a bath whenever the temperature reaches a certain degree.

The special indications for antipyretic treatment are:

1. When the sudden development of high fever is accompanied by severe cerebral symptoms, such as unconsciousness, delirium, and convulsions.

The best method is to give a short douche of cold water, not warmer than 15° C. (59° F.), and lasting from one-half to two minutes. The

water should be applied to head and neck in particular. If the cerebral symptoms do not thereupon improve, if their severity does not even temporarily diminish, and the temperature remains at the same point or goes even higher, more active measures of heat abstraction should be adopted. If the patient is a young child, as is usually the case, it should be given a bath, from 20° to 25° C. (68° to 77° F.) in temperature, at first limited to about five minutes, and completed by a short douche of the head and neck, using for this purpose water which is as cold as can well be borne. Vigorous friction of the skin must be practised during the bath, and it must afterward be well rubbed with dry cloths. The bath and douche are to be repeated as often as the cerebral symptoms demand, as it is by the latter and not by the fever that we must be guided.

The temperature of the baths should be lower for older children and adults, and the baths perhaps be somewhat prolonged. Personally I prefer the former modification as less unpleasant to the patient.

In carrying out any active measures of heat abstraction in measles cases we must remember the possible occurrence of temporary heart failure, as a result of the rapid fall of temperature. This is explained by the fact that in measles the infectious process does not show any special inherent tendency to maintain a high degree of fever, as it does, for instance, in scarlatina. It is very important, therefore, to take the temperature, per rectum of course, about fifteen minutes after the bath. This precaution should certainly not be neglected, at least after the first bath.

An excellent plan is to give a dose of wine before the bath—in case of little children, say, 20 to 40 c.c. (5 to 10 fluidrams) of strong sweet wine about fifteen to twenty minutes beforehand, and again immediately after the bath.

According to my belief and experience, our only hope of saving the patient's life in severe malignant cases lies in hydrotherapy. All hesitation should be put aside, and the treatment be carried through unfalteringly. If it is only a question of overcoming temporary cerebral disturbances in patients who have a tendency to develop the same on comparatively slight cause, a few cold douches will usually be found sufficient. The manner in which the patient reacts to the douches is often of great, and sometimes of conclusive, significance from the standpoint of prognosis.

2. When, in addition to the high fever, there is a wide-spread bronchitis.

With reference to the reasons for advising hydrotherapy in this

connection, it should be remembered that respiration grows more rapid and superficial as the temperature rises; the expansion of the lungs is consequently diminished, atelectasis is more likely to develop, less of the lung surface is actually used for breathing purposes, and there is danger of carbon dioxid poisoning as well as of insufficient oxidation of the blood.

Occasionally signs of severe bronchitis are manifested at the onset, in which case the rise of temperature accompanying the eruption is greatly to be feared. Here the baths are of the greatest value. They should be prescribed in accordance with the height of the fever, and always accompanied by cold douches applied to back and chest. They need be kept up only as long as the fever remains high. The temperature, together with the rate of respiration, furnishes the indication for their repetition. If respiration becomes rapid out of proportion to the fever, the lungs should be examined at once, as signs of diminished expansion can then often be detected over certain areas and the condition be remedied by the use of cold douches or some other method of inducing deep respiratory efforts.

The same indications exist for hydropathic treatment, of course, when capillary bronchitis attended by atelectasis or bronchopneumonia develops later in the course of measles. The methods to be pursued are the same; the main point to be considered, however, is how to cause the lungs to expand to the greatest degree possible, and this will determine the method employed.

3. When the patient is feverish, even in light cases of measles, it is not necessary, but it relieves discomfort, to give one or, if desired, two baths during the evening, the temperature of the same being only slightly below the normal temperature of the body. I do not like to have the bath below 28° C. (82° F.), or higher than 33° C. (91° F.), and it should last for from ten to fifteen minutes. The patient sleeps more quietly after such a bath, and is usually less inclined to cough.

The question of the treatment to be recommended for the affections of the respiratory passages is one of greater importance, for the reason that measures of relief are more often called for in this connection.

We have first to consider the affections of the larynx. I have already called attention to the manifold forms which laryngeal involvement may take in measles, and have pointed out the difficulties in the way of a differential diagnosis. It is fortunate that, although we may as yet often be unable to distinguish between the various forms in question, the plan of treatment, at least in the beginning, is very much the same in all cases.

As soon as a hoarse, barking cough is noticed the patient's head should be raised higher; young children may be given warm milk to drink; older ones should gargle, if possible, with a demulcent (such as decoct. altheæ or a solution of gum acacia). The mucus which collects in the mouth must be removed, and the nasal passages frequently cleansed with a soft camel's-hair brush moistened in luke-warm water, in order to keep them as open as possible. When the nose becomes stopped up, the mouth and pharynx become dry, as a result of mouth-breathing, and this is to be avoided as far as may be. It is of some advantage to keep the mouth covered with a wet cloth; this should be of fine linen, of not more than two thicknesses, and be renewed very often. Little children, however, especially when feverish, are apt to object to it. The percentage of moisture in the air must be increased, and it is a good plan to let the stream of vapor from an inhalation apparatus containing a weak salt solution (0.6%) play against the mouth and nostrils. This should be kept up day and night. As an additional aid, a wet compress (Priessnitz) should be applied to the throat, and changed only three times in twenty-four hours at most. It is better to use hot water, as hot as can be borne, rather than cold, for the compress, not only for the first application, but when it is renewed, which should be done very rapidly.

A constant cough, due to pharyngeal irritability, can sometimes be rendered less troublesome by applying a weak solution of cocain to the pharyngeal mucous membrane. I have not employed the measure myself frequently enough to venture a positive opinion, but I would call attention to the dangers which, in case of children, may possibly attend the use of a strong cocain solution,—up to 20% has been recommended,—although the latter can be depended upon to give relief. Opiates are still more objectionable, although I find them very useful for adult patients under the above-mentioned circumstances.

[Laryngeal spasm is such a pronounced feature of both catarrhal and diphtheritic laryngitis that Dover's powder is frequently given to allay it in order to relieve the patient and ascertain the urgency of the need of operation. O'Dwyer frequently resorted to this after introduction of antitoxin.]

If the symptoms increase in severity, and signs of laryngeal stenosis develop, a warm bath should be given, the patient's temperature furnishing no contraindication. Even with a fever of 40° C. (104° F.) or over, the bath should be of about the same temperature. It should last from fifteen to twenty minutes, vigorous skin friction being prac-

tised meanwhile. If symptoms of cerebral congestion should appear, —redness of the face, muscular twitchings or possibly even convulsions,—the difficulty can usually be overcome by applying cold compresses or an ice-bag to the head.

If the stenosis is entirely or largely a nervous manifestation, it will disappear as a result of the bath. But even when it depends more upon the swelling of the inflamed mucous membrane,—nervous influences can seldom be absolutely excluded,—the patient often feels relieved by the bath, and also seems to breathe more easily. The attempt is at any rate justifiable, unless the symptoms point to immediate danger of suffocation. In the latter case there is still a question as to whether a tracheotomy is really unavoidable. We must not forget that the bronchitis plays an important part in measles, and that the mucus will be none the easier to expel from the bronchi after the tracheotomy. An important point to be considered in treating young children is the small size of their respiratory passages, making it possible for even the trachea to become temporarily plugged with mucus. For this reason I believe the administration of an emetic to be not only advisable, but imperative, but for one dose only. If reliable apomorphin is at hand, at least one-half a hypodermic syringeful of the following solution should be injected subcutaneously:

 ℞. Apomorphin. hydrochlorat..................0.1
   Glycerini pur. 0.5
   Aq. dest. ....9.4.   M.

This method gives the most rapid results and causes the least exhaustion. Tartar emetic also does good service if given in sufficient quantity. Too small a dose, one which does not act within a few minutes, has an injurious effect on the stomach, and, in proportion to the amount absorbed, upon the whole system also. I am in the habit of prescribing as follows, without respect to age:

 ℞. Antimonii et potassii tartratis...............0.05
   Pulv. radicis ipecacuanhæ..................1.0
 M. Ft. chart. d. tal. dos. No. iv.
 Sig.—One powder every ten minutes until effective.

If the emetic fails to act, or if its action does not relieve the stenosis, or if this possibly should even increase, an operation then becomes necessary. In hospital practice we may perhaps choose between intubation and tracheotomy; in private cases the latter procedure seems to me the only one to be considered. Almost every physician has probably known a patient to recover, even when a tracheotomy was refused, and this may be more likely to happen

in cases of laryngeal stenosis accompanying measles than otherwise, but such lucky chances cannot be counted on, and it is our duty as physicians to advise the operation. If the stenosis is supposed to be due to a true diphtheritic infection, the injection of antitoxin may come into question, but further evidence in this direction is requisite.

[Hospital experience in New York would lead one to fear any laryngeal hoarseness as the first step to symptoms of pneumonia or of diphtheritic stenosis. Intubation would be the procedure in New York, and antitoxin would be given while considering the subject.]

Let us now consider the treatment of the bronchitis. As long as the inflammation is limited to the larger bronchi, no special treatment is called for. I do not prescribe mistura solvens, which is still largely used, because I have never become convinced of its efficaciousness, nor of its entire harmlessness under all circumstances. The same may be said, in my opinion, of the decoction of ipecac (0.5 to 200). It seems to me better, in treating older children and adults, to try the effects of apomorphin, but only if the condition of the heart makes it seem advisable.

R. Apomorphini hydrochlorat................... 0.02
Ac. hydrochlorici dil. 1.0
Succ. glycyrrhizæ 5.0
Aquæ.............................q. s. ad 100.0.   M.
Sig.—One teaspoonful every hour.

The above is the dose for children; for adults it may be doubled.

This class of remedy is indicated when in spite of a violent cough the sputum remains scanty and tenacious.

A constant irritating cough may prove so annoying, and possibly even so exhausting, as to demand relief. Morphin can be relied on for adult patients, but in common with most other physicians I regard it as contraindicated in case of young children. In treating the latter we should rather confine ourselves to the more general measures already discussed.

Every effort should be made to insure an early recognition of the extension of the inflammation to the small bronchi and the consequent pulmonary lesions, since it is extremely important to begin treatment at once. The aim of the treatment is to keep the air-passages as open as possible for the admission of air to the respiratory surfaces, and hydropathic procedures of various kinds furnish the means to this end. The main points in connection with the treatment have already been gone over (see p. 362); as a rule, any serious bronchial involvement in measles is accompanied by high fever. Occasionally, how-

ever, the temperature is found to be subnormal. This phenomenon
is almost entirely confined to cases in which the disease has been in
progress for some time, and in which the blood has become insufficiently
oxygenated and the patient is already well under the influence of
carbon dioxid. Heat abstraction is, of course, contraindicated under
these circumstances; the patient's condition, indeed, rather demands
additional warmth. Deep respiratory effort, however, must be in-
duced. A thin stream of cold water only 1 cm. in diameter, but as
cold as can be obtained, is allowed to play against the back of the
head, in the region over the medulla oblongata, just below the external
occipital protuberance. The douche should last a few seconds only,
and be repeated at intervals of fifteen to twenty seconds, for ten
times at the most. Care should be taken that the water does not
come in contact with any considerable area of chest or back. If the
worst danger for the patient be thus happily averted, more extensive
douches can be employed later during a full bath, which is to be
prescribed with reference to the patient's temperature. As long as
the temperature remains subnormal, heat abstraction is absolutely
to be avoided. Instead, a warm bath, from 38° to 40° C. (100° to 104°
F.), is strongly to be recommended. The patient should be kept in
it for some time, and be vigorously rubbed meanwhile. The superfi-
cial circulation is stimulated by both the bath and the friction, thus
relieving the heart, and the heat supplied by the water is a further
advantage. The patient's bed, too, should be warmed. When it is
impracticable to give a bath, it is well to wrap the patient's limbs
in hot cloths; this will supply a certain amount of heat, or, at least,
prevent a further loss of the same from the body.

If the case has been under medical supervision from the first, the un-
favorable condition just described will seldom be met with. It develops
quite frequently, however, in neglected cases. I have been called to many
such in the past, and have learned by personal experience that it is impos-
sible to save the patient's life, unless a further loss of body-heat be pre-
vented. It is unnecessary to argue at length how greatly the end is
hastened by this loss.

When capillary bronchitis complicating measles is treated from
the first according to the principles here laid down, it is usually
unnecessary to administer medicines. The essential point, or at
least the most important point to be gained by additional treatment,
is to stimulate and increase the expulsive power of the cough, so that
no further stoppage of the bronchi may be caused by retained secre-
tion. This is sufficiently accomplished by the douches, and much

more effectually than by drugs. Among the latter, however, I still place some reliance on the following old-time prescription:

R. Infuso decoct. senegæ (rad. 10)............95.0
  Strain and add:
    Liq. ammonii anisat....................... 5.0.   M.
  Sig.—One teaspoonful every hour.

For adults the separate ingredients are to be doubled and the mixture given in tablespoon doses. It is seldom indicated, however, for adult patients, unless they are unusually weak or very old, as otherwise the cough hardly ever grows sufficiently weak to necessitate artificial stimulation.

When coarse mucous râles are heard over a large portion of the lungs in addition to the fine râles already present, it becomes evident that mucus has also accumulated within the larger bronchi, and a last effort must be made toward its removal by means of an emetic. The effects of a douche should always be tried first, however, and I recommend its repetition immediately before or immediately after giving the emetic, before the latter has time to act. A patient in the condition here described will necessarily always exhibit the symptoms of advanced carbon dioxid intoxication, and, among these, a greatly reduced reflex excitability. Sometimes a few deep breaths alone will suffice to restore the nervous equilibrium sufficiently to admit of vomiting, and, in consequence, of the expulsion of the mucus collected in the larger bronchial tubes. A douche directed against the back of the neck will often prove efficacious in this connection.

Unfortunately, circumstances do not always permit of the use of warm water in large quantity, and in such cases a cold pack must be substituted. I make use of the latter when forced to do so, but am no great admirer of the procedure. O. Vierordt * goes too far, though, I think, in calling it "utterly valueless"; the experience which Bartels and v. Ziemssen had with its employment disproves such an assertion. And there is often enough no other method open to physicians whose practice lies among the poorer classes—it is important to bear this in mind.

I will not deny that the measure in question involves certain possible dangers, but believe that they can to a certain extent be avoided by observing the following precautions:

1. The arms should always be left free; the pack need, as a rule, cover only the chest and back. If it seems necessary, because of high fever, to include the legs, and the entire body, the feet must not

* "Behandlung der Masern," Pentzoldt-Stintzing's " Handbuch," vol. I, p. 184.

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be allowed to become chilled. To prevent this, they may be wrapped in warm cloths or kept warm by a hot bottle or be briskly rubbed. All this demands at least a woolen blanket and sufficient fire to heat water or sand in a suitable vessel of some description. If these essentials are not obtainable, all one can do is to apply cold wet cloths to the chest and abdomen. Happy the physician who does not need to face the external miseries of life, to be hampered by want and poverty in caring for his patients!

The compresses should never be drawn so tight as to interfere with the expansion of the chest.

2. Where young children are concerned, a considerable degree of heat abstraction takes place as a result of a pack, even when applied only to the chest and back, and this may constitute a possible source of danger. Bartels and v. Ziemssen have found that unless closely supervised by the physician, the pack is sometimes kept up too long and may cause threatening symptoms; v. Ziemssen even considers it necessary to visit a child which is under this treatment every two to three hours. When those intrusted with the nursing are unskilled in the use of the thermometer and it is impracticable for the physician to see the patient sufficiently often, it is a good plan to leave orders for the pack to be discontinued as soon as respiration becomes deeper. The following rules are of service at such times: The linen cloths are to be thoroughly wet in cold water, but very carefully wrung out, and applied in double thickness at most to chest and back. They are to be renewed every half hour only. If the child's breathing grows less rapid, if its forehead and abdomen no longer feel burning hot to the hand, and it goes to sleep, the cloths are not to be changed again until these symptoms reappear. Such rules furnish, of course, only a poor guide, but the physician can often do no better.

If it seems desirable to bring about a considerable reduction of temperature within a short space of time, it can be done by wringing out the cloths less thoroughly and changing the same every ten minutes. The orders for such a measure should be given very carefully and minutely.

The condition of the **heart** does not usually call for special treatment, as this organ is rarely directly affected by the measles poison, and in case of severe general toxemia it suffers only in common with all the other organs of the body. But, as at such times it is impossible to determine how far the threatening symptoms are due to the effect of the toxins on the nerve-centers, and how far to the direct toxic influence of the blood, or to what extent the muscular system,

including, of course, the heart-muscle itself, is involved, there is little to be hoped for from treatment. I agree with O. Vierordt,* who strongly recommends hypodermic injections of camphorated oil, although I have but slight confidence in its power to exert a favorable influence on the general course of the case. My advice is to make the separate doses large,—for children 1 gm. = 0.1 gm. of camphor, for adults 5 gm. = 1.5 gm. of camphor,—but never to repeat them oftener than every ten hours. My experience in regard to the action of camphor, which is quite extensive, has made me deem it inadvisable to repeat the injections at intervals of a few hours only.

The strength of the heart is undoubtedly highly taxed when the bronchi and lungs are severely involved, and in such cases treatment may become very necessary. Let us not forget, however, that better results can be obtained by combating the fever and the bronchitis— in other words, by preventive measures—than by direct stimulation of the heart. This is certainly true of children, at least, who manifest quite a different degree of cardiac vigor and resistance from adults.

The administration of wine in connection with the bath treatment has already been spoken of. Coffee or tea, with or without the addition of a strong alcoholic, is also a valuable stimulant. If the patient shows symptoms of collapse, indicating a rapid diminution of cardiac action, camphor may be given hypodermically, either in oily or ethereal solution, or hypodermic injections of ether alone may be used instead. Collapse may occur under such a large variety of conditions as to make an enumeration of the same almost meaningless. It is simply a question of carefully observing the action of the heart, especially if respiration is any in way interfered with, and of not waiting too long before resorting to stimulation.

Organs of Digestion.—In measles, as in all other infectious diseases accompanied by fever, the condition of the mouth should receive careful attention. In children aphthous inflammation is of frequent occurrence, and the growths due to the pressure of Oidium albicans are very often a source of trouble. For this the catarrhal inflammation of the nasal mucous membrane is responsible, by necessitating breathing through the mouth, whereby the mucous membrane of both mouth and pharynx, which itself is already the seat of an inflammatory process, becomes dry and cracked, offering a favorable opportunity for the entrance and implantation of the oidium, and undoubtedly of other varieties of microbic life as well. The lower the constitu-

* *Loc. cit.*, p. 181.

tional power of resistance displayed by the patient, the more likely are we to meet with this class of complications.

Under the circumstances it is naturally impracticable to direct the treatment toward the improvement of the general nutrition; there is no time for this, and all we can do is to keep the mouth and pharynx in a condition as unfavorable as possible to microbic development, by the most conscientious and careful methods of prophylaxis and antisepsis. And additional care is necessary in dealing with a patient of weak constitution. The mouth should regularly be cleansed after nourishment has been taken, and the nostrils kept as patent as possible. If oidium patches or aphthæ have already developed, chlorate of potash and biborate of soda are indicated— but I will not enter further into the special therapeutics of diseases of the mouth. If the most careful prophylaxis fails to prevent the development of an ulcerative stomatitis, or even noma, the complication in question will then determine the further method of treatment to be pursued. This has already been described in another place.

Severe forms of gastric disturbance need hardly be spoken of in connection with measles, as they differ in nowise from similar affections seen in any other acute infectious disease accompanied by fever.

It is important, on the other hand, to take a definite stand with regard to the intestinal disorders of measles.

I would, in the first place, point out the possibility that the frequent evacuations may serve the purpose of carrying off injurious matter of some description.

Although I have no desire to appear as a defender of the old-time theory of intestinal crises, and all that goes with it, I am forced to admit the kernel of truth which it contains, however thick the shell of absurd generalizations in which it lies incased and concealed. The improvement which manifests itself in the patient's entire general condition coincidently with the frequent diarrheal passages, an improvement which is especially noticeable in severe cases, is evidence in favor of this assumption. It is no less a fact that the evacuations produced by the action of purgatives fail to exert any such beneficial influence. This has been tested so often as to make it more than superfluous for the individual physician to repeat the experiment at the expense of his patients. In view of these points I would suggest the following plan of treatment:

1. Diarrhea during measles calls for no treatment unless there is danger of too great a loss of fluid from the body. As to when this

danger arises, it is better to judge each case individually than to be guided by any general rule as to the number and size of the evacuations. Generally speaking, a patient whose tissues normally contain a considerable quantity of fluid is able to bear the loss of a larger amount than one who is less plentifully supplied in this respect, but this is not necessarily the case.

2. If a diarrhea which develops when the measles infection is at its height continues to persist subsequently, treatment should not be too long delayed.

3. If symptoms appear indicating the development of an intestinal disorder, not directly related to the measles infection, the complication is to be treated just as if it occurred independently.

The last statement seems self-evident, and needs no explanation. It applies equally to the intestinal disorders which are met with as sequels of measles.

The treatment of the diarrheal affections of measles in the narrower sense of the words—if I may so express myself—consists, first, in irrigation of the bowel with physiologic salt solution (0.6%) at the normal body-temperature. The irrigation is to be practised immediately after an evacuation, and is to be repeated two or three times in the course of twenty-four hours. A solution of gum acacia (1 : 200) may be used in addition, as it serves to protect the intestinal mucous membrane from the irritating effects of the materials coming from higher up in the canal. Its sufficiency is more marked if it is preceded by an irrigation with one to two liters of the salt solution, $\frac{1}{4}$ to $\frac{1}{2}$ liter of the gum acacia solution, according to the age of the patient, being injected a half hour or less afterward, under low pressure (from a height of 18 or 20 inches).

Opium may be used without hesitation in case of adults and of children who have passed the period of secondary dentition. It may occasionally seem imperative to employ this drug in treating younger children, but the very frequent idiosyncrasy manifested against it at an early age must never be forgotten.

If the main indication is to prevent further loss of fluid by the intestinal evacuations, the treatment must be directed toward decreasing the peristaltic action of the large intestine, and to this end opium should be administered locally. For young children laudanum is the most preferable form, in doses in accordance with their age, using a demulcent decoction or a solution of gum acacia as a vehicle, and injecting it under low pressure. For older children suppositories containing the extract of opium are to be recommended.

The application of warm cloths or Priessnitz compresses to the abdomen is a useful measure, unless contraindicated by the general condition of the patient.

A suitable diet must be prescribed, and small doses of a dry strong wine or of cognac are especially serviceable.

As already stated, severe secondary intestinal disorders demand special appropriate measures of treatment, which, as a rule, call for no modification with reference to the measles infection, as they usually develop only after the latter has run its course.

Itching of the skin, if troublesome, can be partially relieved by inunctions of oil, vaselin, and the like.

Nephritis is to be treated as in cases of scarlatina.

For the therapeutic measures best adapted to overcome the complicating diseases of the sensory organs reference should be had to the works of specialists.

A few words are necessary in regard to diet. In ordinary cases the usual rules applicable to fever patients are sufficient. As the sickness is normally expected to be of short duration only, it is unnecessary to force much nourishment upon a patient whose appetite is naturally impaired. Milk, diluted with an equal quantity of water and slightly salted, is always a suitable article of diet for a fever patient, whether child or adult. Wine is not necessarily indicated, but I am personally in the habit of prescribing it because my patients, as a class, are accustomed to its use and are then willing to do without any other medicine.

The appetite usually returns soon after the temperature falls to normal, and if stomach and intestines are in good order, the convalescent's desires in the way of food, unless very extreme, may safely be complied with.

When bronchopneumonia develops, complete recovery cannot be expected for many weeks, even in favorable cases, and the general nutrition will necessarily suffer greatly in consequence. Under these circumstances, the patient should be given as much nourishment as possible from the first—not at all an easy task. Fluids alone should be prescribed, and given in small quantities. The extreme dyspnea precludes mastication altogether, and it is very difficult for the patient even to swallow a good mouthful of a fluid substance at once. Often it is impossible even to give water per rectum, on account of the violent attacks of coughing. We can simply try to do our best in each case.

How long should a measles patient be confined to bed? In an

attack of medium severity I do not permit the patient to get up for from one to two weeks after the last rise of temperature. The difference of time depends on the surroundings of the patient: children living in well-warmed houses may be allowed greater latitude in this respect than those belonging to the poorer classes, who are better off in bed. During the summer the rules may be somewhat more relaxed than is advisable in winter. The condition of the respiratory organs is by far the most important point to be considered in this connection. As long as the catarrhal symptoms persist, I usually prescribe a daily bath at the temperature of the body, followed by a very short cold douche. The patient should be kept in bed all the time until the symptoms of respiratory irritation have entirely disappeared. Nor should the marked tendency to recurrences of bronchitis which is manifested by the patient for years after a severe attack be forgotten, and the necessity which it imposes of taking suitable precautions against exposure.

With reference to the care of the skin during convalescence, it is customary to prescribe one or more warm baths during this period. O. Vierordt has lately sounded a note of caution as to such baths, as, according to his experience, a cold is easily contracted immediately after a fever. My own observations do not support this statement, possibly because I always order a cold douche after the bath.

The supposed virtue of baths as a means of lessening the danger of infection to others, because the epidermal scales are thereby thoroughly removed, hardly deserves special comment, as it is chiefly an expression of the old-time belief which made the stage of desquamation responsible for the transmission of the disease. Apart, however, from the advantages, the particulars of which are as yet hardly clearly understood, to be derived from a careful toilet of the skin, convalescents usually enjoy the warm baths as well as the douches, or sometimes in spite of the latter. I make it a rule, therefore, to prescribe one a day up to the time of complete convalescence, when the patient is again about the house.
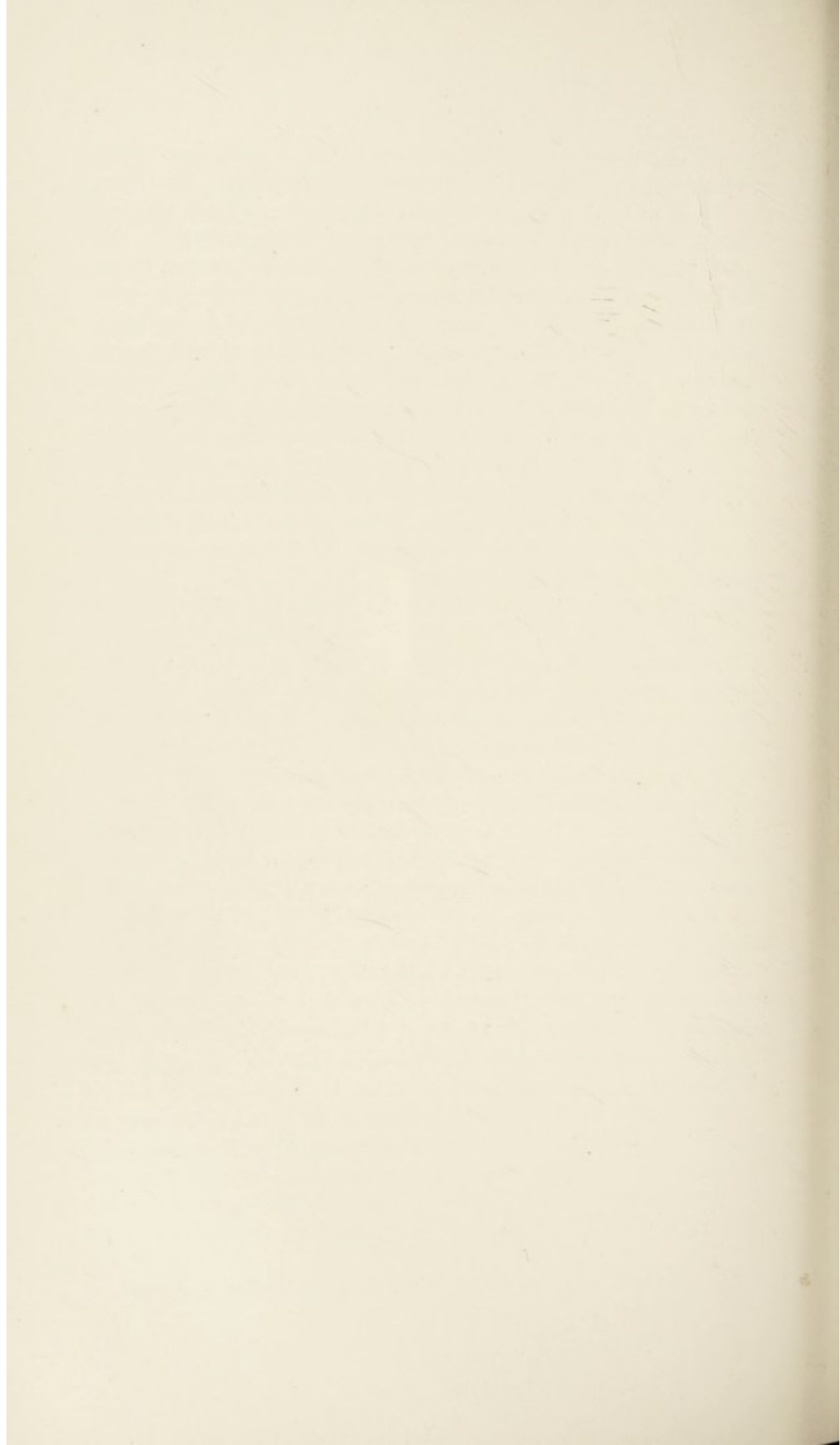
SCARLATINA.

SCARLATINA.

ETIOLOGY.

IN none of the acute exanthemata does our lack of knowledge of the cause of the disease prove so disturbing a factor as in scarlatina. A clear conception of the processes that take place in the body in its course is, on account of this fact, rendered in every respect considerably more difficult, and in many particulars altogether impossible. The outward manifestations of the disease are very various, and its inward nature must be an analogous one. Otherwise it were hardly conceivable why, far more frequently than in any other infectious disease, at one time the patient promptly yields to the destroyer, and again, under what appear to us to be similar conditions, he experiences hardly any grave consequences. Between these extremes lies a wide territory of an endless number of disorders, that can involve nearly all the organs of the body. It is certainly an important consideration that other infections show a more marked tendency to complicate the course of scarlatina; this being especially true of the septic processes. This fact, however, only renders certain features a little more intelligible.

If we add, now, the consideration that the incubation period is of such a varying nature, the theory becomes still more firmly grounded of the existence of a cause that must itself act under very varying conditions. The statistics of individual experience that follow will affirm this opinion in a forcible way.

I wish only to add that so excellent and acute an observer as Gerhardt * has seriously considered the question as to whether that which we call scarlatina is not rather *a group of diseases* than a single disease.

How far can we trace the earliest certain history of scarlatina?

* Section on Diseases of Children, 48th Congress of German Naturalists and Physicians, Graz, 1875. Report of Soltmann, "Jahrbuch für Kinderheilkunde," N. F., Bd. ix, S. 322.

According to Haeser,* from the thirteenth century on; and as proof he quotes a passage from Michael Scotus (d. 1250) that warrants this assumption.

Hirsch † holds a more conservative ground, and refrains from a definite statement or date. He argues, however, that scarlatina must have existed as a disease long before it was described by the medical profession as a separate affection. This at all events is most probable.

Whoever wishes to consult the early literature on this question will find an excellent recapitulation, with citation of the important passages from the various authorities, by Willan.‡   The conclusion is—and is likely to be an accurate one—that scarlatina had been described by many physicians, and had also been observed by them; just as surely, however, that few could speak from an actual acquaintance with the disease. Apart from measles and erysipelas, which have been repeatedly and intentionally classed with scarlatina (as when one wished, for theoretic reasons, to make no distinction, or when he was unable, through lack of careful observation, to distinguish), those diseases which can occur in conjunction with scarlatina have been considered as types of the genuine disease; of course, with special mention of their own nature; but in so far as they were considered to be modified forms of scarlatina, they exceeded their right. In this manner diphtheria especially was without warrant connected with scarlatina, and Willan himself still shows a tendency in this direction.

Among many others may be named as physicians who have earned for themselves great distinction in the study of scarlatina: Ingrassia (Beobachtungen aus Palermo im 1560); Gregor Horst, 1624; Döring (Breslau) and Sennert (Wittenberg), 1627. Still more valuable have been the works of Sydenham and Morton, by means of which an intimate acquaintance with scarlatina has spread generally among medical men.

The affection has been given various names, which, although describing the changes caused by the disease of the skin, helped in no way to avoid the confusion: *e. g.,* "rossania," "rossalia," "robelia," and "rubiola" by the Italians; presumably derived from the robia root (*Rubia tinctorum*). The French spoke in the same way of "rubeola" and "rubiola." Among the various authors the terms "morbillus ignei," "erysipelata," and "purpura" were in current use, while "scarlatina" is said by Haeser to have been used among the Italians as early as the Middle Ages.

From this condition of affairs it passes without further remark that we know nothing of the real origin of scarlatina; although one circumstance indicates that the affection claims as its own a certain locality in the world. Europe and North America are at present the

* "Geschichte der epidemischen Krankheiten," 3d revision, p. 67, Jena, G. Fischer, 1882.

† "Handbuch der historisch-geographischen Pathologie," 2d revision, Bd. I, S. 122, Stuttgart, Enke, 1881.

‡ "Hautkrankheiten," translated by F. G. Friese, Bd. III, I. Abtheilung, S. 193, Breslau, Korn, 1806.

mother-ground; though scarlatina may occur in any locality sporadic-
ally or even in a passing epidemic form. It has, however, not made
for itself in such places a permanent home. It is always a possibility
that a new infection, brought from elsewhere, may cause a reappear-
ance of the disease. In the absence of such an event, and in such
regions, mankind is free from the scourge of scarlatina. This cannot
be based upon the existing business relations and the changing
conditions of daily life, because the continually afflicted portion
of the earth, and still more that which only exceptionally suffers,
covers too great an area. How much of man's existence is spent
upon the highway, how wide his travels, how varying his conditions
of life! And a further, still more forcible argument: measles no
less than smallpox recognizes no limits to its distribution. Where
they attain a footing, there they remain. Then, after the first attack
of the disease, the soil, so to speak, exhausts itself, or man may
render himself artificially immune. One cannot, however, depend
upon the conditions presented on the one hand by the Faroe Islands,
on the other by vaccination, to explain the limited extension of
scarlatina. There is surely some feature involved that is peculiar to
the nature of the infection.

*Scarlatina does not attack every individual that is exposed to the
contagion.* The reason for this fact we cannot explain. I will
endeavor in the following to present a sketch of the facts as already
ascertained, and I consider it proper to begin with the simple con-
ditions of the Faroe Islanders. Possibly no case of scarlatina
had appeared upon these islands during the time covered by historic
records. There is still a question as to the nature of the epidemic
of the years 1815 and 1816, then termed "Friesel"; but from that
time on, certainly nothing was observed that was even suggestive
of scarlatina. When in 1873 to 1875 an epidemic of scarlatina did
appear, it attacked a people which for fifty-seven years had certainly
never come in contact with the contagion. I have already spoken of
the business relations and conditions of daily life among the Faroe
Islanders, that render so exceptionally favorable the exact observation
of the cause of the epidemic, and need only state that the observers
were among the foremost and most conscientious physicians. The
following table presents a full insight into their conclusions. Hoff
secured the statistics for the chief city of the islands, Thorshavn, so
that we have before us an accurate abstract of the subject. The
headings of the various divisions of the table will make clear their
contents.

SCARLATINA IN THORSHAVN.

AGE.	TOTAL NUMBER OF INHABITANTS.	TOTAL OF THOSE LIVING IN DWELLINGS INFECTED WITH SCARLATINA.	TOTAL NUMBER OF THE LATTER ATTACKED.	PERCENTAGE OF TOTAL NUMBER OF SCARLATINA PATIENTS.
0- 1	17	12	8	66.6
1- 5	74	65	44	67.1
5-15	184	155	99	63.9
15-20	68	56	42	75.0
20-40	299	171	40	23.4
40-60	193	105	3	2.9
Over 60	90	55	1	1.8

The chief conclusion: that from a population comprising all ages, and certainly not protected by a previous attack against scarlatina, only 38.3% suffered from the epidemic.

A comparison with the statistics of measles furnishes an opportunity for the recognition of the difference in man's susceptibility to the two acute exanthemata.

Of the 930 inhabitants of Thorshavn, there were in 1875, when measles attacked the place in epidemic form, 418 protected by previous occurrence of the infection, and yet 506 were at that time prostrated by the disease.

Thus there were more than 99% of the same population susceptible to the infection of measles, whereas only 38% yielded to the infection of scarlatina.

These statistics are unique in that such favorable conditions for the observation of the disease have either never previously presented themselves, or have not been taken advantage of. The consensus of medical experience agrees in its verdict. Further discussion of the cause of immunity of individuals against scarlatina I prefer to reserve until later, and at present only state the further important conclusions obtained from the Faroes epidemic.

Unfortunately, we cannot state with the certainty that was possible in the measles epidemic the manner in which the infection was admitted to the islands. Hoff expresses the opinion in his report to the Sundhedscollegium that the scarlatina epidemic had its origin either in the Shetland or the Orkney Islands. In a later communication* he designates Kirkwall (in the Orkneys) as the probable birthplace of the outbreak. Only the seat of its appearance, however, is certain—the island of Sudero, where the first cases

* "Remarks on the Climate of the Faroe Isles," *Journal of the Scottish Meteorological Society,* 1882.

appeared in February, 1873. From October of the same year on, occurred a spread of the infection to Thorshavn, and then it extended completely over the island.

This required a comparatively long space of time—from February, 1873, until April, 1875; in short, twenty-seven months. The particulars can be gathered from the following statistics.

If we reason from the supposition (and there appears no other so suitable) that the infection dates from a single importation of the disease, we can see how continually the scarlatina epidemic retained its hold upon Sudero, the place of the first attack. It began and ended upon this, one of the largest of the 24 islands. The preponderance of those afflicted were attacked in the seventeenth month (reckoned from the beginning). After an intermission of the following three months, there was a relighting of the disease.

It is reported that from other portions of the group of islands the infection was carried back to Sudero, although nothing is said in regard to particulars. Even though one considers this fact (if we take it for granted that it is already assured), the conclusion remains even more positive, that a general susceptibility to the infection of scarlatina does not exist. In regard to Thorshavn the fact is of importance that its people live crowded together, and come in constant contact with one another in daily traffic. The number of victims in this place very soon reached its maximum. Out of 237 cases, 211 (89%) occurred in three consecutive months, of which the first leads with 118 (50%). I will later on demonstrate the fact that the proper inference is not one of an exhaustion of the disease.

How irregular the extension of scarlatina appears to be, has been clearly shown by the records of its behavior in the various inroads upon the Faroe Isles. I mention only the figures that comprise the rather more marked local epidemics, together with their relative percentages. They are as follows: Haldersvig, 161 inhabitants and 58 scarlet fever cases (36%); Eide, 305 inhabitants and 6 scarlatina cases (2%). Of the latter (Eide) it should be mentioned especially that it is a thickly settled place.

Let us now consider the main points in the observations in the Faroe Islands in relation to the nature of the transference of the scarlatinal poison.

It must be stated in the beginning that this cannot by any means be determined with the certainty that was possible in measles. The length of the period of incubation cannot be so sharply defined. Hoff states, it is true, that its duration comprises with regularity

SCARLATINA IN THE FAROES.

DISTRICTS.	1873.						1874.												1875.	Total from March, 1873, to April, 1875.
	March to June.	July to August.	September.	October.	November.	December.	January.	February.	March.	April.	May.	June.	July.	August.	September.	October.	November.	December.	January to April.	
Sudero	9	.	2	4	.	.	.	.	2	9	9	4	21	8	6	.	.	.	6	80
Thorshavn	.	.	.	4	118	72	21	5	12	2	2	1	.	.	.	.	.	.	.	237
Cases within the district of Thorshavn	.	.	.	.	38	85	72	28	35	29	27	24	23	16	1	12	6	2	3	401
Norderöerne	.	.	.	.	.	.	.	5	27	37	11	19	16	9	7	.	.	.	.	131
All the islands together . .	9	.	2	8	156	157	93	38	76	77	49	48	60	33	14	12	6	2	9	849

eight or nine days, and presents considerations that must be called indicative of the truth of his assertion; as, for instance, the following:

1. A peasant girl on the 11th of November consulted a physician in Thorshavn, which town was then suffering severely from the epidemic form of scarlatina. At her home there was no sign of the disease. She herself became ill on the 19th of November, and later on the 27th and 28th two others of her household.

One may object to the first of these three cases on the ground that we know only of the girl as having been in an infected locality, not as having come into contact with persons ill of the disease. This somewhat trifling objection does not, however, hold with the two following cases.

2. On May 2d a sailor in whom the eruption appeared on this very day was admitted to the Thorshavn hospital. Nine days before he had been in Klakswig, where scarlatina was wide-spread. Before and since he had without intermission been on the sea, and busy at his occupation as a fisherman.

3. The one-year-old daughter of an inhabitant of Kollefjord went to bed with scarlatina and diphtheritis. Her four-year-old sister, who up to that time had lived in a distant healthy dwelling, was brought home on June 15th, and at five o'clock in the morning was placed in bed by her sick sister. Dr. Hoff, who visited the place at seven o'clock, two hours later, had the children separated at once, and the well child kept, as far as possible, from the sick one. Both, however, remained in the same house. On June 24th the four-year-old girl also broke out with the scarlet rash.

This case also we must accept, even though it is not absolutely certain that the infection did not occur at a later moment, since outside intercourse was not entirely prevented.

If we admit that the possibility of an eight- or nine-day incubation period is conclusively demonstrated by these observations, we must straightway include the fact that the duration also may be of different lengths. Hoff is of the opinion that the apparent exceptions to the rule can always be explained: as in cases where the occupants of a house in which scarlatina has obtained a footing are attacked at intervals of one or several days. This may depend upon the varying susceptibility of the individual; in addition to which must come into consideration the persistency and tenacity of the infection.

The foregoing is certainly a plausible theory. It is just as possible, however, that the incubation period is one of varying duration, and the limitation of the incubation to eight or nine days is not so frequent an occurrence that one must accept it as the rule. Hoff himself, as is indubitably shown by these observations, has seen exceptions, as well as the other physicians at work with and near him. Of these, Petersen speaks of variations in the incubation period of nine and eleven days; Lund also mentions the same fact, and refers to 9 cases that he considers applicable. Of these, he shows a nine-day incubation period in only 1, a ten-day period in 5, and in 3 a duration of eleven days.

In forming a decision as to the time of the infection by scarlatina, and as to whether a third person, himself remaining well, or fomites, can transmit the infection, the Faroes epidemic affords useful evidence.

In the summary of the sanitary report the following concise statement is made: "The transmission of the infecting substance occurred undoubtedly in the majority of cases by direct contagion, and usually during the stage of desquamation. Lund reports the occurrence of infection in isolated cases, even during the incubation period, three to six days after the infection of the patient, who from this time on transmitted the disease. Contagion also appears to have occurred repeatedly, in isolated cases, during the period of eruption." But as statistics are lacking, discussion is of no advantage.

As evidence for the theory that scarlatina can be transmitted by means of fomites, and by persons who themselves remain healthy, may be mentioned the following:

1. Articles of clothing were taken from a house in which there had been, three months before, two cases of scarlatina to a house in

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a locality free from the infection, whereupon this locality became the seat of the disease.

2. Furniture from a house in which there had been scarlatina is said to have been the contagion bearer.

Since no definite statements are presented, one must not place too great reliance upon these claims.

3. "An instance of the transference of the infecting substance through the medium of one or even two persons who themselves escaped infection seemed to cause the first appearance of the disease in Videro, one of the northern islands. The disease appeared in two houses on the ninth day after Petersen (the attending physician) had passed the night in one, and was then consulted by a patient from the second dwelling. This patient himself, an adult, was not attacked, but the children in the house occupied by him received the infection."

4. "A servant traveled from an infected dwelling in Thorshavn on November 5th to his employer's in Kollefjord, where the disease had not previously made its appearance. The journey (several miles) was made in an open boat, in a pouring rain, and against a strong headwind. The man came, therefore, in all probability in first contact with the children of his employer on the next day; yet the exanthem appeared on them nine days later, on November 15th" (Hoff).

5. "A sailor left his home, which was infected by scarlatina, without himself having suffered from the infection. He then remained more than three weeks at sea on board a fishing-vessel. On his home journey he spent the night of March 28th in the locality of Nordskaale after he had put on his best clothing, which had up to that moment been kept, with the contagion probably clinging to them, in his ship's chest. In the village, where previously no scarlatina had been known, there appeared on the 5th of April, and in the house in which the sailor had passed the night, an outbreak of the exanthem" (Hoff).

The foregoing reports are a literal translation. They appear to be conclusive, although it seems to me that their authors repeat them mainly from hearsay, and do not seem inclined to shoulder the full responsibility. The possibility of infection by even another way is established by various facts. Thus, it is mentioned in the report that, besides the 849 cases that came to publication through their physicians, "probably not so very seldom light cases had escaped recognition by the attending physician."

The people evidently did not fear the disease, as was the case with measles, and this fact is emphasized in the report of the district physician, Petersen. And it is easily comprehensible, *when one considers the different manner in which the two diseases showed themselves to the inhabitants of the Faroes.*

In the *severe measles epidemic* of 1846 nearly three-fourths of the *entire population were attacked, many died, and all cases occurred within a comparatively short space of time. In contrast, the mild scarlatina epidemic, which, in such a length of time, attacked only about one-eleventh of the population, and proved fatal in not more than 4% of cases, must have appeared of far less importance in the minds of the people.*

Moreover, the fact has not been overlooked that so little attention was paid to the exclusion of all communication with the outside world; nor is it sure how much attention was paid to remembering what persons entered the house. And if it be still further considered that those who were mildly attacked exhibited fewer signs of their ailment,—for we know how, often enough, in adults scarlatina may pass by with a mere angina,—one is inclined to withhold definite conclusion as to the transmission of the disease.

If this is true of conditions in general, it must be applicable to a greater degree in those that are offered by a life in which the cases of scarlatina appear at short intervals; and an active business life allows little probability that the time of infection can be recognized. Naturally it will be necessary to gather together our combined experience. I wish to begin with the consideration of **the immunity of the individual.**

We may consider it an established fact that the period of life has a very considerable influence, in the sense that—drawing only a rough boundary-line—after puberty there is a markedly diminished susceptibility to the infection as compared with earlier life. In the schedule of Hoff, which I quoted above, and which, although merely a synopsis, is accurate, there will be seen the following figures: Out of 343 inhabitants of Thorshavn up to twenty years, 193 were attacked with scarlatina (56.3%); out of 582 inhabitants of Thorshavn over forty years of age, 44 suffered from the disease (7.6%).

This is a proportion of about 7 to 1, and since it concerns a population not rendered even partly immune by a previous epidemic, the conclusion is of marked import. The foregoing, which is recognized as a fact on all sides, ought to be corroborated by two great series of compilations formed of statistical figures. And even with the present estimation, though only approximate conclusions can be

formed and there are no absolute figures, it is none the less a satis-
factory one, in my opinion.

Norway: The proportion between those who died of scarlatina
(1872–78) and the total population, arranged by ages and accord-
ing to the sex, is presented in official form in the diagram of
Dr. Axel Johannessen.* This shows that after the tenth year
there occurs a very considerable decrease in the mortality of scar-
latina. After the fifteenth year the mortality scarcely enters into
consideration. The same conclusions are obtained from the fol-
lowing tables of mortality in England from scarlatina between 1868
and 1872 †:

SCARLATINA IN NORWAY.

Age.	Male Population.	Number of Male Casualties.	Percentage of Male Casualties.	Female Population.	Number of Female Casualties.	Percentage of Female Casualties.	Total Population of Both Sexes.	Casualties in Both Sexes.	Percentage Mortality in Both Sexes.
0– 1 year	26,906	389	2.1	25,801	310	1.7	52,707	700	1.9
1– 5 years	87,835	1892	3.2	85,634	1824	3.0	173,469	3806	3.1
5–10 "	102,267	820	1.1	99,490	667	1.0	201,757	1487	1.1
10–15 "	100,189	181	0.3	97,012	145	0.2	197,201	326	0.2
15–20 "	89,184	33	0.06	90,661	48	0.08	179,845	81	0.07
20–30 "	131,015	18	0.02	152,295	14	0.01	283,310	32	0.02
30–40 "	97,021	6	0.01	109,488	12	0.02	206,509	18	0.01

Of 1000 that died as a result of the scarlatina, the ages were, in
years:

0–1;	1–2;	2–3;	3–4;	4–5;	5–16;	15–25;	25–45;	45–65.
65	147	165	149	120	316	22	14	2

No one of the number was older than sixty-five. From fifteen
years on, the mortality rate decreases so rapidly that from the 1000
only 38 deaths fall in the later years of life.

The conclusions to be drawn from the above figures admit of a
double significance. There may be indicated a less frequent infection
at the corresponding age (after puberty), or there may also be a
lessened virulence in the infection itself. In the case of scarlatina
probably both factors exist side by side. Should any one wish to

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* " Die epidemische Verbreitung des Scharlachfiebers in Norwegen," "Acade-
misches Preisschrift," S. 144, Christiania, Jakob Dybwad, 1884.

† Dr. John W. Tripe. Quoted from the "Jahrbuch für Kinderheilkunde,"
N. F., Bd. ix, S. 412.

extend the distribution of the mortality over the various years of childhood, the following may be learned from the comprehensive analysis by Murchison,* which covers 148,829 fatal cases in England:

0–1	year of age	9,999	= 67	per 1000			
1–2	years " "	20,975	= 141	" "			
2–3	" " "	23,842	= 160	" "	}	Total number of	
3–4	" " "	22,528	= 151	" "		fatal cases.	
4–5	" " "	17,726	= 119	" "			

Total mortality for the ages 0–5 = 638 per 1000.

The figures further show:

5–10 years of age 38,591 = 259 per 1000
10–15 " " " 8,676 = 58 " "

The small remainder of 45 in a thousand distributes itself over the different ages of life. A list of the "very old folk" is made by Thomas, one of whom is said to have been one hundred and forty-one years of age.

Still more exact are the statistics reported by Johannessen † in regard to the fatal cases of scarlatina in Christiana during the first year of life. They comprise 1040 cases occurring between the years 1862 and 1878, and of these there died at the:

1st month 0	}	The first year of life:
2d and 3d months 3		Total mortality =
4th to 6th " 12		98 per 1000.
7th to 12th " 78		
2d and 3d years............................430 per 1000.		
4th and 5th years.............................226 " "		
From 5 to 10 years ....205 " "		
From 11 to 15 years............................ 23 " "		

One sees thus how, in spite of the smaller figures, and notwithstanding the very different outward conditions, the essential principles of the conclusions remain the same.

Also the *communis opinio*, the general view held by the medical profession, which does not rest upon figures for its basis, is in perfect accord with the more exact findings. Thomas quotes a number of statements of individuals that one may read if one wishes.

The question as to whether the immunity conferred by a certain age in life is lessened under certain conditions is of such practical importance that I would like to discuss it thoroughly.

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*These statistics are taken from Thomas's "Scharlach," in v. Ziemssen's "Handbuch," Bd. ii, 2, S. 188, 2d edition.

† *Loc. cit.*, p. 86 (Tabelle VI).

We will start again from conditions that are the most simple and uncomplicated. Such are to be found in the so-called "surgical scarlatina." * I follow the findings of Hoffa, who has weighed the facts under consideration with excellent judgment. It should be pointed out at the start that many have been too comprehensive in their limitation of the diagnosis. For what cannot be included in such a definition as: "If an exanthem resembling scarlatina develops in a traumatic case, or after an operation, whether at the site of the injury or at a point distant from the same, we call the condition surgical scarlatina"?

Hoffa properly excludes such cases as are not certainly scarlatina, and these fall into three classifications:

1. *Erythema congestivum.* A local whealing of the skin, appearing a few hours after a trifling operation, such as circumcision, and just as promptly disappearing, leaving no trace behind. It appears most frequently in injuries of or interferences with portions of the body that are rich in nerve-supply, and we may look upon the condition as in a measure a sensory phenomenon dependent upon the vasomotor nerves, and partly as a reflex symptom.

2. *Erythema toxicum* conforms in all particulars to the nature of the erythemata that occur after the use of certain drugs: *e. g.,* the balsams, etc. We take it for granted that in such cases there are present in the blood certain secretions from the wound, or destroyed tissue materials due to the injury, and consider (it appears to me with insufficient reason) the fibrin ferment to be the cause. Certain it is that after the use of anesthetics, and in cases of poisoning with phenol or mercuric chlorid, these erythemata can manifest themselves. One in especial presents an extraordinary resemblance to scarlatina in the form of a finely punctate reddening of the skin. Other forms show more of the well-known larger spots, separated by unaffected areas. Only the trunk and limbs are affected, the eruption lasts about twenty-four hours, and no desquamation ensues. It is very remarkable, moreover, that general symptoms, a suddenly oncoming high fever, in certain cases with brain symptoms and gastric disturbance, accompany the appearance of the erythema.

3. *Skin affections that are associated with septic conditions* are named in this connection with great appropriateness, since they are by far the most difficult to exclude.

* Compare Dr. Albert Hoffa in Richard v. Volkmann's *Sammlung klinischer Vorträge,* Section on Chirurgie, Nr. 90, S. 2679 (1886 and 1887).—Dr. Konrad Brunner: "Ueber Wundscharlach," *Berliner klinische Wochenschrift,* 1895, Nr. 22.

Hoffa takes the following position after discriminating between the conditions that show a degree of resemblance to scarlatina that requires no very marked consideration: "I consider the diagnosis of scarlatina assured only when, in addition to the characteristic exanthem, at least one or other of the signs that make up the symptom-complex of the disease is present, as angina, swelling of the sub-maxillary glands, desquamation, or nephritis. It becomes absolutely certain if other patients that have come in contact with such a case also become infected."

Whoever observes in his diagnosis of the individual case this method of procedure will certainly stand on safe ground. We have now gone so far that we may ask the question: *Is the tendency to scarlatina increased in any way by trauma?*

English surgeons, as Sir James Paget, seem disposed to answer in the affirmative, and to attribute the condition to an alteration of the nervous system due to the trauma itself or to an inflammatory process. Nothing can be made out of such general statements. Much more practical seem the conclusions of Hoffa, who has determined the fact that **scarlatina can originate from wounds.** To be sure, the number of cases that are capable of proof is small. But one exists among them before which, it appears to me, every criticism that confines itself within the bounds of reason must yield. I refer to the study of his own case by W. von Leube—for he unfortunately was the sufferer.

I give his own statement,* Hoffa's account differing from it only in insignificant details. Von Leube says:

"I have surely had a very slight tendency to scarlatina, since neither as a child, when several of my brothers and sisters were ill of the disease, was I attacked, nor later on, in my treatment of my patients. One day I wounded the index-finger of my left hand during the autopsy upon the cadaver of a case that had died of an unusually severe case of scarlatina. On the seventh day after the injury to my finger the wound, which had only imperfectly healed, began to pain. Then early in the tenth day I became unwell and angina appeared. On the eleventh day vomiting, and a decided fever followed, and at the end of the same day the scarlatinal exanthem appeared. This, contrary to the usual procedure, spread first *from the original lesion, following the lymphatic vessels up to the left arm, in the form of a broad red stripe, and then rapidly extended over the rest of my body.* The course of the disease was one of medium severity; the desquamation began also upon my left arm."

I would call attention to the fact that the beginning of the fore-

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* "Specielle Diagnose der inneren Krankheiten," Bd. ii, S. 364, 2d and 3d editions, Leipzig, F. C. W. Vogel, 1893.

going case, as far as the general symptoms were concerned, corresponded throughout to the usual form; that the angina was not lacking, but that the eruption—the skin involvement—began at the seat of injury, and that at this point the reorganization process also began. So that I consider it a fact established by the experience in this case, that the infection of scarlatina can have its origin in a wound, and that this actually occurred is witnessed by the mode of extension of the skin affection.

This theory of Hoffa, that every open wound offers a more ready means of entrance to the infection of scarlatina, just as to any other infection, will not be doubted in its broad application. The body, which is in itself not more than at other times susceptible, finds itself, owing to the presence in large quantities of the toxic substance, unprepared to withstand an influence which when it was a weaker force it had resisted; and if it were still less potent, it would still overcome. The principle holds even in matters that do not concern the human constitution, and especially when the organic and inorganic natural poisons are under consideration. If I understand von Leube correctly, he holds in this matter a similar opinion.

An established footing will be obtained for the theory provided the fact is verified that, in the event of a scrupulous antiseptic treatment of wounds, such a condition as *surgical scarlatina in the strict sense of the word does not exist.* In favor of this speaks, in addition to Hoffa's own observations, the epidemic of scarlatina in the surgical ward of Guy's Hospital, reported by the English surgeon Howse. His final conclusion is that antiseptic treatment is a complete and perfect protection against such infection by scarlatina.

To sum up, we may say *that wounds perhaps render their victim liable to somewhat more ready infection by scarlatina than otherwise were the case.* This possibility is, however, so small that it, in point of fact, seldom comes into consideration.

That we should not ascribe to wounds in a general way an interruption of the immunity given by the age in life is just as certain.

On the other hand, it must be admitted that, once scarlatina has made its way into a hospital, its inmates are somewhat more in danger of infection because of the fact that they present in these wounds wider gates of entrance for the poison. This pertains to all wounds, no matter what the outward condition, that come into proximity with scarlatina.

The question is not so simple a one as to the importance of the

relation between the childbed and scarlatina.* ¶I am of the opinion that two tendencies, professionally speaking, rule among medical men, the one exerting itself more along specialistic lines, the other more in sympathy with the general views of the day.

R. Olshausen is at present one of the most decided representatives of the specialistic school, and an article † by him contains the reasons · supporting the theory that during the puerperium scarlatina is an infection especially to be dreaded. I must go more into detail in regard to the matter. It is of the first importance to differentiate between genuine scarlatina and other forms of eruption that occur during the childbed, but which, apart from a more or less marked, and sometimes deceptive (Litten), outward resemblance, have nothing in common with the true infection of scarlatina. Hoffa's classification of surgical scarlatina more than likely covers the question, and essentially the same conditions come under discussion. Erythema congestivum and erythema toxicum are, again, of minor importance, *special stress resting upon eruptions resulting in consequence of sepsis.* It has been a misfortune that any one (Malfatti) should, even at the beginning of our observation of scarlatina, have emphasized the skin features of the disease, and from them have chosen the name for the entire condition. The character of the disease was indicated by the name, and thus the whole study of the subject was given a preconceived idea as its basis, which must have and has hindered its gradual, healthy development. Let us consider Malfatti's ‡ description of the disease, whose work was of such great value, and inquire, " Was this in fact an epidemic of genuine scarlatina during the puerperium?"

I would like to call attention to the fact that Malfatti by the word "scarlatina" did not mean that which we call by the same name. He widely *extends the application of the term, including even the "pest" of Thucydides.*

"Can we, after an attentive reading of this artistic description (a reproduction of the passage referred to precedes in Latin translation), still doubt that we have before us the picture of that disease that was called

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* Compare Litten's "Ueber septische Erkrankungen," *Zeitschrift für klinische Medicin*, Bd. ii, S. 431 (1881).—"Beiträge zur Lehre von der Scarlatina," *Charité-Annalen*, Bd. vii, S. 173, 1882.

† "Untersuchungen über die Complication des Puerperium mit Scharlach und die sogenannte Scarlatina puerperalis," *Archiv für Gynäkologie*, 1876, Bd. ix, S. 169.

‡ An account of a malignant scarlet fever which was prevalent among the women in confinement in Vienna in 1799, with some remarks by Dr. Johann Malfatti, *Journal der praktischen Heilkunde*, by C. W. Hupeland, Bd. xii, Part 3, S. 120, Berlin, Ungar, 1801.

scarlatina? And can it not be concluded with all probability that in the infectious conditions that were often called *pest*, and which used to appear under all sorts of forms, scarlatina was the real disease?"

The real character of the "Athenian pest"* has not been presented with convincing certainty, and will in all probability hardly so be shown; *but scarlatina, in our sense of the word, it certainly was not.*

In considering the condition seen and described by Malfatti the following appears to be an important point:

1. Without doubt the cases continually present a local disease of the genitalia, especially of the uterus. Moreover, this condition preceded the general symptoms.

"After a pregnancy, and then, as a rule, after a normal delivery, our puerperal case passed the following day entirely free from untoward signs, except that the lochia were in unusually large quantity and had far more odor than was the case with the other patients. †

"The first symptom that appeared was an extraordinary stench from the lochia.‡

"A slight, but deep-seated pain arose from palpation of the lower portion of the uterus. Otherwise the abdomen was painless and soft. §

"The belly remained soft and insensitive, except for occasional pains in the region of the uterus." ‖

His first statement refers to the beginning of the illness; those following refer to the later course of the disease.

The autopsy showed the following:

"The uterus was more or less full of blood, yet sufficiently contracted. Its substance presented unusual features, but at the cervix were seen traces of outspreading inflammation, a small quantity of purulent material, and on its border a livid blackish color, which penetrated to a greater or less distance the uterine substance, and in some cases disseminated everywhere the odor of gangrene. The genitalia appeared also inflamed; all the other abdominal organs were, however, unaffected."**

He speaks somewhat more exactly in another passage ††:

"The peritoneum throughout the course of the disease showed no evidence of involvement, and at the autopsy presented no traces of inflammation or of any other pathologic process. The uterus was the only organ in which one could find any such change.

"The opinions of the prosectors were various in regard to the special involvement of this organ. Some said that they had discovered nothing more than an unusual degree of extravasation and indications of a previous inflammation accompanied by a purulent exudate. Others found the condition to be a deeply penetrating gangrene. But the variance of their judgment, to my mind, was due to the varying constitutions of the subjects themselves.

"Many autopsies, especially of those who died in childbed in my own

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* Compare Haeser, *loc. cit.*, p. 4.   † Malfatti, *loc. cit.*, p. 186.

‡ *Ibid.*, S. 137.   § *Ibid.*, S. 127.   ‖ *Ibid.*, S. 128.

** *Ibid.*, S. 130.   †† *Ibid.*, S. 135.

ward, convinced me that gangrene could not have been overlooked in any of those who died on the third or fourth day of the disease. The blackish color of the whole cervix; the purulent exudate covering it; the facility with which one could tear the tissue, of which a portion swam lightly on the surface of water; then the extraordinarily offensive stench coming from it;—all left no room for doubt.

" In the case of those, however, whose illness ran a longer course, and who lived until the tenth or fourteenth day of the disease, we noted on the cervix a marked suggillation of a livid appearance, with a distinct softening of the tissues, which already showed a gangrenous change."

Olshausen * takes exception to these statements in the following fashion: " If we picture to ourselves the appearance of the interior surface of the puerperal uterus, and consider the pathologic anatomy at such a time, we may express the belief that these were changes that take place with special rapidity and ease after death from scarlatina or other of the exanthemata. At most, the lochial stench spoken of by Malfatti awakes the suspicion that a *gangrenous endometritis* was present in not a few cases. The possibility of the occurrence must be of course admitted, but it would be impossible to characterize such a process, in the absence of all other symptoms, especially in the absence in every case of peritonitis, as a symptom of puerperal septicemia. Much more natural would it be to consider it a condition consequent upon the severe constitutional disease."

In reply I may say:

1. The extraordinary foulness of the lochia was the first indication, and this made itself evident before a single feature of the general disturbance became noticeable. Further:

" *The more marked the odor of the lochia was in the beginning, the more serious proved the disease.*" †

Therefore it seems clearly indicated that the putrid lochia—a symptom of gangrenous endometritis—*preceded the general condition.*

2. The findings of the autopsies seem to be so clear that one is not entitled without excellent reasons to doubts that involve generalities, such as those expressed by Olshausen.

Many autopsies were made during the Vienna epidemic, and this very fact warrants the conclusion that sections were made there at a still earlier period. Have we won the right to set aside the statements of the prosectors, on the ground that they differed so completely in their observations? Especially when we have before us the positive assertion of Malfatti, that the pathologists reported in the various cases different findings, but that this was due to the character of the disease in the individual case.

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* *Loc. cit.,* pp. 179, 180.   † Malfatti.

Certainly, the reports from the autopsy cannot be measured by our standards, and their comprehension is made especially difficult by the fact that nothing is reported in regard to the time that elapsed between death and the postmortem examination. We have no information, moreover, as to the time of year at which the epidemic appeared. Nevertheless it appears to me certain that *grave pathologic changes were present in the uterus.* We know well that there need be no involvement of the peritoneum present in an endometritis that causes a general infection. The distinctly mentioned observation, "tenderness in palpation of the uterus as a regular symptom," indicates, moreover, that the peritoneal uterine covering was, in fact, not in perfect condition. With regard to the condition of the cervix, the "purulent exudate," etc.,—though I shall lay no stress upon it,— I do not wish entirely to pass it by without mention.

3. *What right have we to consider the exanthem as that of scarlatina?*

I will epitomize the description of the entire disease.*

At the end of the second, or often between the sixth and seventh days after delivery, there appear shivering, chilliness, moderate headache, and ringing in the ears, a dry, hot skin, and nervousness. The pulse becomes somewhat quicker and weaker than normal.

"*There appeared a slight flushing of the face and neck, especially on the eyelids, and the eyes showed a tendency to secretion.*" Then a light, dry cough, and very seldom an insignificant soreness of the throat. The act of swallowing was not obstructed and the chest remained clear. Appetite was diminished, the urine showed no abnormalities, there was neither diarrhea nor vomiting. A moderate swelling of the mammæ. "*The following night was quiet, and the next day, usually its evening, the redness of the face increased and allowed the recognition of the spreading exanthem through its gradual extension over the breast.* At the same time the nervousness and the cough increased, without there being at any time pain in the throat. The pulse, which at first was almost normal, became rapid, rather hard, and irritable; the skin was often moist, the headache increased, and occasionally a slight nosebleed took place. Otherwise, everything remained as before, except that the patient complained of weakness, and was very restless. During the night sleep was interrupted and disturbed; the rises of temperature increased by several degrees; the eruption came more and more into evidence, the thirst became greater, but the tongue remained for the most part soft and moist. During the morning was noted a remission of the fever, the cough was silent, *the act of swallowing remained unimpeded, and if in the beginning there had been a slight angina, it also disappeared entirely. The exanthem disappeared as entirely as though it had never been present.* Toward evening, however, it was *always* seen reappearing with a more marked redness than on the preceding day, then spreading over the limbs and assuming a distinct miliary appearance. The attacks of fever increased, yet with a decrease in the nervous symptoms. The pulse became more rapid and weak, the skin dry, the patient remained conscious, complained almost never of pain in the

* Malfatti, *loc. cit.,* p. 126.

abdomen, yet the restlessness increased, and the outlook became dark. . . . . The pulse in general remained more or less weak, and rose in certain instances to 110 per minute, in others was little above the normal rate. In such a condition our patient reached the end of the third, fourth, or at the most the fifth day, when suddenly the exanthem, which was in full blow or had already begun to desquamate, took on a dark bluish appearance. There were noted here and there, especially on the extremities, single blue spots. Without warning a feeling of intense cold came over the patient, a temporary wandering in the speech, and slight twitchings; the pulse became all at once irregular, very rapid, or disappeared altogether. The expression was hippocratic, the limbs cold, and within one or two hours sudden death overtook the patient.''

I am of the opinion that from this description no form of proof can be obtained to show that the disease was a genuine scarlatina. Neither was the onset so stormy as it usually is in scarlatina, nor was there a high fever,—the frequency of the pulse being taken as the measure, —nor, finally, did the eruption conform to the rules of scarlatina. It is an unheard-of thing for the exanthem of scarlatina to disappear with the morning remission of fever "as though it had never been present." The fact that either no angina, or only in very slight degree, was present cannot be too strongly emphasized, since its occurrence in genuine puerperal scarlatina may be also said to form the rule, according to the experience of trustworthy observers.*

4. *Scarlatina is said to have been transmitted from one of the patients to the nurse.*

We read from Malfatti†: "It was not rare for the scarlatina which was then epidemic in Vienna to assert itself by no other symptom than sore throat and fever, without an evident eruption.

"In my wards in the Allgemeinen Krankenhaus was a nurse who attended the puerperal cases of scarlatina and was herself attacked by the disease. *The angina was in her case very severe, the eruption barely evident, the fever far higher than that which the puerperal case showed*—of all of which, without treatment, she became entirely well, as did all of those who were attacked, except the puerperal patients."

The fact is that we have nothing further here than that a nurse has had an angina in connection with a marked fever. That this was caused by scarlatina is conceivable, but by no means sure. Therefore the final conclusion as to whether the whole epidemic was one of genuine scarlatina is more than doubtful.

I have instituted a thorough examination of the first description of supposedly genuine scarlatina because it seems needful to me to again and again call attention to the fact that a conception of the

* Compare statements by Hervieux and Braxton-Hicks, in Olshausen, pp. 172, 178.
† *Loc. cit.*, p. 133, 134.

course of a disease that depends entirely upon the outward features only renders impossible an actual insight into the method of its causation. Malfatti has, it seems to me, drawn the picture as accurately as his time warranted; and has, because his patients became red, named the whole condition scarlatina. Olshausen, forming his opinion somewhat too exclusively from a principle that is for the most part no longer held by his professional colleagues, will not agree to the diagnosis of sepsis, because peritoneal involvement was discovered.

His attempt to give true scarlatina its due has led him, I think, too far upon the thin ice, so to speak, upon which the English obstetricians are prone to walk.

It will be sufficient to quote the following: " We are also impelled to the belief that the incubation period tends to lengthen itself out during the time of pregnancy, and lasts months even, under certain circumstances, until with delivery the contagion springs forth into active eruption." *

I refrain from discussion. If in the year 1875 (or 1876) it had been possible in the London Obstetrical Society still to defend the claim that infection with scarlatina caused puerperal fever, and that scarlatina could again be transferred to others from the puerperal cases, we would also have no objections to raise against the theory that an attack of scarlatina may be precipitated by the delivery—the germ having been transmitted and come to maturity with the fetus.

The extreme rarity of scarlatina during *pregnancy*, a fact generally accepted as fixed (Olshausen having been able to discover only seven cases), makes necessary this remarkable supposition of an indefinitely lengthened incubation period. The delivery of the woman is then said to form its termination—and why? *Deus ex machina!*

Litten † expresses an entirely different opinion: " When infection occurs there usually follows an abortion, and the more surely so, the younger the state of pregnancy." He himself saw in two cases of pregnancy in the sixth month, in one of them abortion occurring on the second day, in the other a few hours before the appearance of the eruption. Then he continues: " It appears, according to the occasional statements that I have found in literature, that in a large number of cases abortion or premature delivery is the final outcome." These are facts that place scarlatina in the same class and position with the other acute infectious diseases.

* Olshausen, *loc. cit.,* p. 188.   † *Charité-Annalen,* Bd. vii, S. 173.

The theory has recently been advanced and supported by a number of writers that scarlatina is nothing more or less than a streptococcus infection. I will consider this question at another point. Were it so, as Babes, Sörensen, and, although with greater reserve, Konrad Brunner hold, then the discussion in regard to the character of surgical and puerperal scarlatina would have to shape its course from an entirely different standpoint. It is, however, my own belief that the evidence against an identity of the scarlatinal poison with the streptococcus is overwhelming.

How composed and clear in contrast to such statements sounds the following: "The writer cannot refrain from calling especial attention to these rather characteristic statements of the English * in regard to puerperal scarlatina. Every one will say it is possible that here and there a woman in childbed has had scarlatina. But (and I refer to an assertion by Braxton-Hicks) out of 87 puerperal cases with fever, 37 are characterized as scarlatina, although 17 had absolutely no exanthem and almost none of the patients showed marked throat involvement—and this cannot but do damage to the facts. Where, then, remain the characteristic symptoms, since those already mentioned correspond just as fittingly with septicemia? This fact, only, appears indisputable, *that in England patients in childbed more frequently than is the case with us exhibit an erythema of the skin. One rests in doubt in regard to the significance of the fact. The remaining symptoms, however, point one and all to the same septic processes that we daily see in our own country.*"

The author of the foregoing is the same Olshausen.† I would like to place myself in his attitude of the year 1872, and express myself in accordance with it.

1. *Epidemics of scarlatina among women in childbed, such as might indubitably be referred to the specific poison of the infectious disease, to which alone we ascribe the name scarlatina, have never been observed. The number of sporadic cases is also a very limited one.*

Litten gives statements in evidence, of which I mention only a few: According to A. Martin, there were among 16,000 puerperal patients in the Berlin Obstetric Clinic only three cases of scarlatina; and this, too, in a large city, where scarlatina is never absent.

2. *The fact that now and again a puerperal case can be attacked by scarlatina ought to be questioned.*

3. *The condition described as puerperal scarlatina is, in the vast*

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* Winckel, "Die Pathologie und Therapie des Wochenbettes," 3d edition, p. 530, Berlin, Hirschwald, 1878.

† "Jahresbericht über die Leistungen und Fortschritte in der gesammten Medicin" (Virchow-Hirsch), VI. Jahrg., Bd. xvii, S. 598, Berlin, Hirschwald, 1872.

majority of cases, a septic infection, an involvement of the skin similar to scarlatina.

4. *Scarlatina, in the strict meaning of the word, is of slight significance as a factor in the mortality of the puerperium.* If we grant that the disease termed "scarlet fever" was actually scarlatina, and not a septic infection, then we find that during the five years 1874 to 1878 in Norway, *out of 1461 women that died in childbed there were only 3 that were affected with "scarlet fever":* viz., not more than 0.2% * of the total number. It may also be said that the prognosis of genuine puerperal scarlatina is by no means unfavorable.†

To epitomize: *The immunity which is afforded against scarlatina by increasing age is lessened neither because of external wounds, nor by the childbed, to any considerable degree.‡*

In regard to epidemics occurring among adults, we have few reports. Of great importance are the statements of Vogl,§ of the General Medical Staff of Bavaria. Twice scarlatina appeared in the garrison of Munich in epidemic form.

In 1884–85 in the course of one hundred and seventy-eight days, 125 out of 7442 men from the effective force became ill = 16.7 per 1000.

In 1894–95 in the course of one hundred and fifty-five days, 311 out of 9608 of the effective force were attacked = 32.3 per 1000.

The first epidemic had a fatality of 4%, the second of only 1.2%, both being, of course, mild in their nature.

I must again frequently refer to this work.

Whether **internal diseases,** be they of whatever nature, carry with them a special predisposition to scarlatina has not been determined. If a person who has been afforded immunity against the disease by his time of life exposes himself to the influence of the poison by continual contact with scarlatinal subjects, he may also be infected. In the case of mothers who nurse their children during scarlatina this frequently occurs; every physician of wide experience has instances of this kind to report. *In such cases the immunity of age invariably makes itself still evident,* however, in that those who are infected in this manner show, at least in the great number of cases, either light forms of the disease that are not fully developed, or even *a simple angina.*

My meaning may be thus expressed: The poison enters in far greater quantity and with a greater toxic influence than when it occurs under the usual conditions. Because of this fact the resisting power of the body

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* Johannessen, *loc. cit.,* p. 204.

† Fehling, "Die Physiologie und Pathologie des Wochenbettes," S. 172.

‡ Compare *Deutsche med. Wochenschrift,* 1891, S. 153, 154.

§ *München. med. Wochenschrift,* 1895, S. 949.

may, at least partly, be set aside or overcome. My experience in smallpox cases may properly be called in to support this theory, and is, in my opinion, altogether convincing. I had once the following experience: A nurse in the smallpox ward was revaccinated by me at the time of appearance of the first cases, and unusually large, fully developed pustules appeared. During the epidemic of 1866 this nurse, who was true to her duty, cared for her patients without experiencing any damage to her own health. In 1870–71 a revaccination was made without result, and toward the end of the epidemic her sweetheart was admitted to the hospital with "black" (malignant) smallpox. Extended pneumonia soon set in with severe dyspnea. The nurse now spent her time, when her duties allowed it, by his bed, and supported the air-hungry man with her arm, his head lying upon her breast or her shoulder. In this way she was naturally in an unusual degree exposed to the atmosphere poisoned by a smallpox subject. This continued several days, until death ended the scene. The nurse, who had up to this time remained free from infection, was now herself taken with smallpox. The infection continued light in character,— the immunity of the vaccine making itself still evident,—and after a high and long-continued prodromal fever there appeared a very few tiny nodules in the skin, that quickly disappeared.

This experience needs no elucidation or comment.

Let us now turn our attention to the general conditions, which have been mentioned only in connection with the narrow limitations of the epidemic in the Faroe Isles.

Personal peculiarities have a slight significance in comparison with the period of life that tends to eruptive conditions.

The **sex** also plays no important part.

So as to avoid the errors that are necessary when small figures are used, I append the following testimony of statistics.

Scarlatina Cases in Norway.[*]—During the twelve years, 1867 to 1878, there were officially noted: Males, 30,425 = 49.2%; females, 31,427 = 50.8%.

According to the census in 1875 there was a population in the kingdom: Males, 888,571; females, 930,282.

The relative number per thousand between the scarlatina patients and the total number of inhabitants of both sexes stands for the twelve years as follows: Males, 2.85%; females, 2.82%.

The fatal cases of scarlatina in England,[†] including all ages, amounted to a total of 148,829: Males, 75,373 = 50.7%; females, 73,456 = 49.3%.

The distribution of the fatal cases of scarlatina in regard to age can be carried out only for England, and has a limited importance

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[*] Johannessen, *loc. cit.*, p. 105.   [†] Thomas, *loc. cit.*, p. 188.

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only, since the actual number of those belonging to the different ages of both sexes is not known. The conclusions are these:

Under five years, 51.7% males, 48.3% females; from five to fifteen years, 49.2% males, 50.8% females; from fifteen to fifty-five years, 45.6% males, 54.4% females.

If we study the figures of the mortality still more closely, the male sex appears at a disadvantage up to the fifth year of life (51 : 49), the tendency showing itself most decidedly in the first year (56 : 44). Certain conditions play a part here that have no connection with the disease itself, in so far as it depends directly upon the nature of the poison, or upon the idiosyncrasy of the individual. The greater number of male children born accounts for the earlier period of life, and for the later period the fact that women, on account of the greater length of time spent in the sick-room, are more exposed to infection (Johannessen)—they follow the life of the nurse far more assiduously than men.

There has been an attempt to ascribe special weight to **racial influences;** and even to such a degree as to characterize the Anglo-Saxon family as especially disposed to scarlatina. How lightly the theory has been considered, however, appears from the fact that more often in England than anywhere else the mild forms of the disease have been noted, and for a longer time than elsewhere only a trace of the disease was to be found.

According to the evidence collected by Hirsch,* racial peculiarities can be assigned no influence in the matter of immunity.

He mentions, for instance, writings by Frick, of Baltimore, which state that in the epidemics there between 1850 and 1854 the relative numbers of those attacked with scarlatina were 13.8 white and 10.8 colored people, from a population of 10,000. According to Mantegazza, the Creoles suffer more severely than the whites.

Moreover, the social position of the individual exerts no important influence. One must always understand that the advantages of good food and favorable surroundings, etc., assert themselves in a general way, so that a man in comfortable circumstances is, on the whole, more resistant to disease than the poor man. This, however, is all that can be said, and scarlatina tends less than many of the other infectious diseases to draw distinctions between those whom it attacks.

Hirsch brings considerable evidence from England. It will be sufficient to mention the following from the report of the London epidemic of 1868: "The officials of the city sanitary department unite in the statement that the wealthy suffered as much and more than the poorer portion of the population." A few observations at variance with this view come

* *Loc. cit.,* p. 137.

from certain parts of Norway, but they alter the force of the general rule in no particular.*

The question as to the **length of the incubation period** is a very difficult one.

Let us attempt a review of the observations that appear to meet the strict demand of the case. We must accept the premise that the patients have had no opportunity of contact with the infection besides the one mentioned by the author of the report, as given in all good faith, for there can be no thought of an absolute control in the matter.

Trousseau † states that: "A merchant had taken his daughter from London to Eaux-Bonnes in the Pyrenees, and then passed the winter with her in Pau. On his return journey to England he stopped in Paris, intending to pass several days there. His eldest daughter had remained in London, where she had charge of the household. Full of impatience to embrace her father and sister, she started toward Paris, was taken with fever and sore throat on the way across the Channel, and arrived six or seven hours later with a severe attack of scarlatina. She arrived at the hotel almost at the same moment that her father and sister came from Pau. Her sister occupied the same room with her, and exhibited twenty-four hours later the first symptoms of a fortunately light case of scarlatina. *At that time, moreover, scarlatina was epidemic in London, and not in Pau.*"

Murchison,‡ whose name likewise calls for respect, has in his wide medical experience found only thirteen cases that allowed him to draw any certain conclusions as to the true incubation. Among these it was:

Less than 24 hours....twice.		Less than 3 days....twice.	
" " 31½ " ....once.		" " 3½ " ....once.	
" " 36 " ....once.		" " 4 " ....once.	
" " 40 " ....once.		" " 5 " ....three times.	
Less than 6 days.....................once.			

The details in the different cases are withheld, and all is omitted from the following that does not bear upon the question.

CASE I.—A twenty-two-year-old woman was admitted on April 22, 1858, into the London Fever Hospital. She came from *Oxfordshire* on the 19th, *where there was no scarlatina, to see in London a sister who was very ill*

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* Johannessen, *loc. cit.*, p. 141.

† Medicinische Klinik, Bd. I, S. 98. Translated into German by Culman.

‡ "Contributions to the Etiology, Pathology, and Treatment of Scarlet Fever," *The Lancet*, 1864, vol. II, pp. 176, 177.

of this disease. On the following morning she fell ill, with a chill, headache, angina, and on the 21st the eruption appeared. Fatal outcome.

CASE III.—A family had sent out invitations for a child's party. The day previous one of the children was taken with scarlatina. So as still to be able to give the entertainment, the sick child was placed in the attic. Monday, the invited children were in the house from 9 to 4 o'clock. *On the next day,* between 11 P. M. and midnight, one of them, living in a distant part of London, broke out with the symptoms of scarlatina, and died in a few days.

CASES XII AND XIII.—On January 10, 1864, a child returned to a sailor's house from a visit in a house where there was scarlatina. *The little girl was herself not attacked, but on the 15th and 16th two other children in the same house with her showed the disease.*

"The only discoverable source of the infection was that already given here."

These examples will suffice. One can see from them that convincing reasons for the correctness of the conclusions that are drawn are *not always* at hand; Case I is not to be questioned; Case III, however, is rather doubtful; Case XII and XIII appear to me devoid of proof. This is true to a still more marked degree of the report made by Dr. W. Tonge Smith * from the London Fever Hospital.

He considers it as certain that the incubation period is never longer than three days. But how does it stand in regard to the proof?

CASE III.—J. O'B. was transferred as a scarlatina patient from a respectable hospital with which a medical school is combined, and in which he was for several days isolated, to the Fever Hospital. He was there admitted on November 4, 1879, at 11 A. M. Although no symptoms of scarlatina or any other acute disease were present, Dr. Smith had him taken into the scarlatina ward, trusting fully in the authority that had diagnosed the case. On the 7th of November the disease first made its appearance; at 9 A. M., angina and fever; at 1 M. the exanthem. "*Length of incubation period, seventy hours, not more.*"

CASE IV.—G. W. was admitted with Case III at the same hour, from the same place, and under identical conditions, sent by the same authority without presenting a single symptom of the disease. "Credulously," Dr. Smith placed this patient also in the scarlatina ward. Until November 17th the patient was well. During the afternoon appeared suddenly vomiting, angina, fever, and the exanthem. *Incubation period,* by unprejudiced interpretation, thirteen to fourteen days.

Dr. Smith, however, is of the opinion that this case proves only that one can live about fourteen days among scarlatina patients without being infected; for he has repeatedly seen individuals lying among scarlatinal subjects in well-aired rooms who were attacked only at the end of the third day after they had gotten out of bed, and had so come into closer contact with them.

It is unnecessary to add even a word of comment.

* "The Incubation of Scarlet Fever," *The British Medical Journal*, January, 1883, pp. 150, 151.

E. Hagenbach-Burkhardt weighs his experience with greater judgment. In his first article* the conditions are so thoroughly discussed that one is in a position to form his own opinion. He reports four cases, *with an incubation period of about three, seven, eleven, and fourteen days.*

His conclusions can hardly be objected to. A later article † submits still larger figures. Hagenbach himself, however, remarks that he considers them only approximately exact.

They appear to me especially worthy of notice because he has taken the pains to so carefully criticize his own work.

His figures show an incubation period of:

Under 1 day ......once.	Under 10 days......once.
" 2 days......once.	" 11 " ......five times.
" 3 " ......four times.	" 12 " ......once.
" 4 " ......five times.	" 13 " ......four times.
" 5 " ......once.	" 14 " ......twice.
" 6 " ......seven times.	" 15 " ......five times.
" 7 " ......three times.	" 17 " ......twice.
" 8 " ......four times.	" 18 " ......once.
" 9 " ......twice.	" 19 " ......twice.
Over 20 days ......six times.

The possibility that a seemingly long incubation period might have been simulated because of an indirect transmission of the disease, Hagenbach considers already taken for granted. And properly so. But it should be pointed out, on the other hand, that the number of cases with an incubation longer than twelve days amount to no less than 38% (22 out of 58). It were a curious occurrence if indirect infection had a toxic power for these only. Of no less importance are the conclusions from the Munich garrison epidemic. One may always say that special conditions were present here that differ considerably from those affecting the majority of people. On the other hand, Vogl's rule, that the appearance of the exanthem occurs three, or at the most five, days from the time of the infection, seems to be one that is well grounded as far as the material that he had was concerned. There has been an attempt to make it appear probable that the incubation can last for even six weeks.‡ This is as difficult to prove, however, as to disprove, since we are concerned always with individual cases, that cannot be made to conform to rule.

*"Zur Aetiologie des Scharlach," "Jahrbuch für Kinderheilkunde," N. F., Bd. VIII, S. 288.

†"Ueber Spitalinfectionen," "Jahrbuch für Kinderheilkunde," N. F., Bd. XXIV, S. 105.

‡Johannessen, *loc. cit.*, p. 166.

In all probability, the shorter period of incubation—somewhere up to twelve days—stands on a more sure footing than that of a longer duration. In favor of this view I wish to mention the cases in Norway,* which answer to no rule, and which are taken from the "Medical Report." It shows at least a decided conservatism that only 19 cases have been submitted as capable of proof, 17 of these showing an incubation period of eight days or less, and one each of ten and twelve days.

Here and there physicians, on the ground of their own experience, consider themselves entitled to fix upon middle figures for the length of incubation, always granting, however, the possibility of variations from these figures. Thus, Fürbringer mentions three to six days; von Leube, four to seven, and Thomas makes a similar statement.

There exist also writings that indicate distinct conditions that may influence the length of the incubation.

The already mentioned theory of Hoffa,† that "a wound offers to the scarlatina poison a wider portal of entrance," is utilized by some in the claim that, in the case of the wounded who have been exposed to the infection, there is a shortening of the period of incubation.

E. Hagenbach-Burkhardt ‡ says: "It appeared to me a very striking fact that the incubation was very short in most of the cases that I have just described (scarlatina after tracheotomy), and I would add that in all these cases the origin was fairly certain." In v. Leube's own case the time that elapsed between the injury and the outbreak of the eruption was eleven days, and the comments of v. Leube himself on this unusually extended incubation are worthy of attention. They demonstrate to what a high degree the resistance of the subject comes into play, in proportion to the virulence of the entering poison. I coincide entirely with v. Leube's view.

Sörensen§ writes in the same vein from Copenhagen.

Gerhardt says‖: "It appears that the infection from a beginning case of scarlatina more frequently has a long, while that from a convalescent case has a short, period of incubation."

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* Johannessen, *loc. cit.*, p. 165.   † See page 390 of this volume.

‡ "Jahrbuch für Kinderheilkunde," N. F., Bd. xxiv, S. 115; see also Emil Koch, "Ein Beitrag zur Kenntniss des chirurgischen Scharlachs aus dem Kinderspital zu Basel."

§ "Jahrbuch für Kinderheilkunde," N. F., Bd. xxxii, S. 95.

‖ "Lehrbuch der Kinderkrankheiten," 4th edition, S. 96, Tübingen, Laupp.

Johannessen * claims that the Norwegian statistics warrant the conclusion that the severity of the epidemic has an influence in deciding this question; and, in this respect, that the severe epidemic is characterized by a shorter, the light one by a longer, period of incubation.

" By way of example may be mentioned the fact that the incubation in the mild epidemic in Oestlofoten in 1783 lasted ten days; in an epidemic of medium severity in Follo in 1875, six days; in an epidemic in Nordmoere in 1875 in which the disease began with marked initial symptoms, thirty-six hours; in three cases ending in death in Romsdalen in 1878, twenty-four hours; and in a mild epidemic in Soertersdalen in 1877, eight days The incubation in a bad epidemic in Grong in 1878 was one, two, and two and one-half days in duration; and eight to fourteen days in an epidemic in Drontheim in 1865, with a mortality of 10.1%."

The actual observations can hardly have been as exact as the figures seem to indicate. Otherwise the statements in regard to the incubation period, which here limit themselves to nineteen cases, would have been made much more comprehensive, through the medical reports of Norway. Their real significance is not likely to be denied, however, from the view of the case obtained in a general way by the attending physician.

Without attempting to answer the question in regard to the incubation period, for that is at present impossible, and in order to understand the difficulties that stand in the way of such an answer, we must call certain other just as dubious matters into consideration.

First of all, what is the state of affairs with regard to the **active life of the scarlatinal poison**—*how long does it last, what about its persistency, its liability to transmission by means of articles of utility, or by means of persons either themselves not infected or becoming ill at a later period?*

All these things can without any difficulty be distinguished in discussion, but in actual life not so easily; for in the cases that come under our observation these questions are more or less interwoven and involved with one another. Moreover, the information obtained from the comparatively one-sided observations in the Faroe Isles (see page 385) is not conclusive.

One must, in any event, hold to the belief that the *life period of the scarlatinal poison is by no means an unlimited one.* Else it were hardly conceivable that in any locality the disease, when once introduced, could for a long time be absolutely wiped out, and only again reappear when a new infection is introduced. And this rule holds

* *Loc. cit.*, p. 166.

not only for the far-reaching conditions existing in those parts of the earth that are now and then subject to scarlatina, but also for the narrower conditions offered by the home country, by the permanent dwelling-place of the disease,—Europe and North America,— by the lowlands, and by small and medium-sized cities. Why do I mention these self-evident facts? Because statements are constantly appearing that ascribe to the poison of scarlatina, if not an immortality, at least an improbable longevity.

W. Boeck,[*] the well-known Norwegian syphilographer, relates the following:

"The children of a colleague of mine had obtained permission to play with some things in an old writing-desk *In a drawer lay some hair that had been cut from two children that had died twenty years before;* since that time the drawer had not been touched. Now it was opened, and the children took scarlatina. These cases were the first in the city, so that the probability is evident that the infection was transmitted in this way." It may not be hypercriticism to call attention to the fact that these cases, although the first, occurred at the time when scarlatina appeared as an epidemic in the same place. For it is expressly stated that they were the first, and from this follows the inference that they were not the only cases."

The lengthy persistence of the poison in a certain locality is affirmed with great positiveness by different trustworthy physicians.

Thus, one reads in Murchison: "Dr. Elliotson gives an example: The patient, ill of scarlatina, was brought into a room of St. Thomas' Hospital, and during the following two years *nearly all the children and young people* that lay in the same room contracted the disease, although the apartment was every year thoroughly cleaned and whitewashed."

E. Hagenbach-Burkhardt [†] states that in a certain room in the Children's Hospital at Basle, that was never allowed a thorough airing, infection by scarlatina had frequently occurred. *In the course of almost a year and a half, there were not less than nine cases* (of scarlatina), *while at the same time—another half year is included in this estimation—in the rest of the entire house there were only four cases.*

The observations of Vogl in regard to the Munich garrison epidemic have been accurately reported, and are of great value. In both of the two great epidemics that were separated by a period of ten years, the "Türkenkaserne" suffered from the disease in a measure altogether out of proportion. In 1884–85 their roll showed

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[*] According to Johannessen, *loc. cit.*, pp. 161, 162.

[†] "Jahrbuch für Kinderheilkunde," N. F., Bd. xxiv, S. 115.

a mortality of 24.1 per thousand, as against 9.9 per thousand in the Hofgartenkaserne. In 1894–95 their mortality was 80.5 per thousand, as against (maximum) 15.2 per thousand in the Marsfeldkaserne.

Vogl expresses himself with great discretion in his statement "that the disproportionate mortality in certain barracks during sporadic as well as epidemic attacks of scarlatina indicates that local conditions can furnish the required soil for the infection; likewise that one must take for granted an occasional tendency for the disease to appear in epidemic form."[*] I consider this reservation a wise one, and one that is necessary because of the facts already known. As yet we have no clear conception how it is possible that a poison for whose complete development we must consider the human body necessary can be so influenced in its power of infection by any such external conditions as are dependent upon the living apartments.

That there is *not a simple adherence of the poison to a place* in this case can be inferred from the fact that in the Munich "Türken-kaserne" *a fresh infection occurred from outside,* the source of which was discovered. *And only when it had already made its appearance did the influence of the locality show itself.*

I will also remark that all attempts to institute a change through the recognized means of disinfection were of no avail.

From private dwellings comes the same story. One seemingly conclusive case is mentioned by Murchison [†]: Dr. Richardson tells the story that a married couple occupied a country house with their four children. One of the children was there taken with scarlatina, of which it died. The other children were at once taken to a village several miles away, but after several weeks one of them was allowed to come home. *In the course of twenty-four hours this child also was attacked,* and died of scarlatina in just as short a time as the first child. The house was then thoroughly cleaned, the walls whitewashed, and all clothing either washed or destroyed. After four more months the third child was brought to the house, and again, *after twenty-four hours it was attacked by scarlatina and died.*

It was believed that the poison was retained in the straw covering that lay in a thick layer on the beds of the children. And this is possible; though I am also inclined to take into consideration the floors, in view of the hospital investigations on the subject. The fateful influence of the so-called false floor has at other times shown its influence.

Murchison gives still another example, but it is altogether unnecessary to go further in the matter. The facts are certain, and every active physician has something to relate of the kind.

Much more difficult is the reply to the question *whether scarlatina is transmitted by means of articles of utility, or through a third person, who himself remains immune.* Reports in regard to this particular form of infection are very numerous *: Letters, books, photographs, and once even a violin was considered to be the medium of transmission. *The clothing and the linen of scarlatina patients are of special note.* It is not appropriate to introduce individual statements, since their scope is too narrow to allow accurate criticism. Whether one will at once allow credence to a report, or whether one tends in advance to refuse belief in it, and if there is not a perfect sequence of proof accompanying, depends upon the individual. One must make sure in regard to what he receives from a certain source, whether he considers it trustworthy or not. I am of the opinion that this is a case where we cannot go out of our way on account of our belief in the authority or because of an oath on the word of the Master. It is especially important to learn whether any other possibility of infection must be excluded, and in regard to this question only he is able to decide who is in the midst of affairs. It makes a marked difference whether there has been a sufficient examination of the existing conditions; also whether the author of the report is capable of an unbiased judgment. Even if one admits both these things, he may still call into question the conclusions, if he believes himself entitled to do so from sound reasons. I have taken this liberty myself in the case of the apparently unanimous observations in the Faroe Isles, because of certain facts; namely, the frequent occurrence of light cases from which the physicians, as a rule, learned nothing. I will simply quote the story of v. Hildenbrand †:

"*A black coat, in which I once attended a scarlatina patient in Vienna, and for a year and a half I had not worn, and which, without putting it on, I carried from Vienna to Podolia, gave me myself the disease in the latter province. Scarlatina had been previously in the place an unheard-of disease, and one which I transmitted still further from my own person.*"

Who can prove that this was impossible? or who can prove that it really was the case?

If one considers the fact that the poison of scarlatina can adhere for a long time to a dwelling, he tends perhaps, without further

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* Murchison, Thomas, Johannessen, and others.

†"Ueber den ansteckenden Typhus," 2d edition, S. 118, Wien, Camesina, 1815.

hesitation, to share the view that poisons that cling to certain objects can also be transmitted from them. But this conclusion is not a convincing one. We must distinguish in the matter of the cause of disease between an adherence to a locality, or to persons, or to surrounding objects of utility. Thus, malaria is intimately associated with certain localities, but that it can be transmitted in the manner under discussion no one has as yet proved. The same is true of croupous pneumonia.

One is led still further from a different point of view.

We can say with a probability bordering on certainty that the scarlatina poison is an entity that goes out from the body of the patient, mingling with the air in the finest particles. This scarlatina dust—to coin a term—becomes thicker, the nearer the atmosphere in question is to the body of the patient, its source and origin. Just as does every dust, this also settles upon all fixed objects. This is to state at the start that it can adhere to these objects, and if, now, the enduring nature of the poison is admitted to be a fact, the conclusion becomes necessary that a spread of the disease can occur in this way. We must, however, in this case, as well as in all others, consider "quantity proportions"; we must think "quantitatively," as Karl v. Vierordt has happily expressed it.

Von Kerschensteiner has done this in his discussion of the question,* and it seems to me has thereby essentially simplified the matter. He differentiates definitely between:

1. *Objects that have been in close contact with the patient* (his clothes, his linen, his bed) and contain great quantities of the poison, and can transmit it.

2. Persons who dust the clothing of others who have been in close contact with the patients can be infected. This is, for example, possible in the case of the clothes cleaner of a doctor who has attended many patients during an epidemic.

3. *A simple visit in the bedroom of a scarlatinal subject becomes the less important, the further the visitor remains from the patient.*

For the transference of the infection through a third person, himself healthy, the following conditions are required:

(*a*) The poison, in the form of dust, must be carried in the air from the patient to the visitor.

* "Ueber die Vertragbarkeit der Masern, des Scharlach, und der Blattern durch dritte Personen," *Aerztliches Intelligenzblatt* (*Münch. med. Wochenschrift*), 1882, S. 447; and "Verbreitung von Masern, Scharlach, und Blattern," "Vorträge über Gesundheitspflege und Rettungswesen während der Hygiene-Ausstellung zu Berlin," 1883, S. 16.

(*b*) It must attach itself to the clothing, the skin, or the hair of the visitor.

(*c*) It must be given off from its bearer in the direction of a stream of air that moves toward the person to be infected, so that there may be an entrance portal by which it can be received, still in an active condition. To this end it must also be in sufficient quantity, and its ability to infect—and this must be noted especially in the case of scarlatina—must be so thoroughly exercised upon him who is exposed to the contagion that it can be well said to be a very considerable force.

"*How many favorable conditions must combine to enable such a transference to become effective!*" forms the conclusion to the remarks of v. Kerschensteiner.

It appears to me that we can in this way obtain a comparatively thorough insight into the matter, and especially with regard to the question how far an infection is possible through physicians who, in treating scarlatina patients, go from them to others who require their services. And this is a matter of great consequence to life. What position should a conscientious physician hold in regard to visiting other patients after seeing those sick of scarlatina, if he is compelled to say to himself that it is probable that he will transfer the same disease to them? The truth is that our knowledge in regard to the matter will set us in a measure at rest. Under ordinary circumstances the transmission is so very rare that we have hardly to consider the possibility. When it occurs,—and the possibility cannot be absolutely denied,—there are present such special conditions as are not usually to be met with.

As an instance of this I would like to give this case, whose story is told by Dr. M. Loeb in Worms *:

His three-year-old daughter became ill of a marked case of scarlatina. "As I have seen no scarlatina patient in my practice, and my colleagues, of whom I inquired, knew of no cases in the city, the etiology of the disease remained for a long time a riddle, since my daughter at that time associated with no children, and was constantly under observation. The solution of the riddle was evident to me later on. My colleague, Dr. W. v. Essinger, who was in Mannheim on a visit, had attended there and repeatedly examined the three children of a relative all seriously ill with scarlatina; this was on the morning of March 3d. In the afternoon of the same day he made me a visit, and repeatedly and for a long time held my little daughter on his lap. His suit of clothing he had not previously changed while in Mannheim."

* "Die Incubationsdauer des Scharlachs," "Jahrbuch für Kinderheilkunde," N. F., Bd. ix, S. 174.

The period of incubation was hardly twice twenty-four hours.

In this case the physician came into freer and much longer contact both with the scarlatina patient from whom he received the poison, and also with the child to whom he carried it, than is usual in practice, and therefore we cannot raise any question in regard to the case.

There remains to be mentioned the introduction of the poison of scarlatina by means of cow's milk, which for some time caused considerable discussion. It was believed that a direct transference was possible from the cow, herself sick with scarlatina, to human beings, and the cause of the disease was then said to have been found. From this it followed that the latter (the "Streptococcus scarlatinæ") was nothing other than the Streptococcus pyogenes; and, further, that the diseased cow had suffered from cow-pox, not from scarlatina.* And yet the possibility is not excluded that scarlatina can be transmitted by means of the milk. The observations in question came mostly from England,† and it is for the most part stated that the subjects either have come directly or indirectly in contact with the milk, which was the contagion-bearer. The cream is said to have been especially dangerous, though only when great quantities of uncooked milk were drunk did the disease make its appearance.

As an example I give the latest news from Rostock, which shows that, even if transmitted in this form, the state of affairs is by no means simple. Rostock had had for a number of years a considerable number of cases of scarlatina. In 1885, up to the end of May there were only 28 cases reported. June, however, brought 36. "Very striking in this sudden flaring up of the epidemic in June was the limitation to certain streets leading down to the Warnow without there being any discoverable connection between the not very large number of indisposed families, or among the cases of the children themselves, while the other cases of illness during May were scattered over the entire city. The majority became ill in the last three days of May and the first ten days in June, and, this proving a clue, it was learned that the attacked families (with two or three exceptions, in which such a connecting-link was not discoverable) had obtained *their supply of milk from a single isolated 'fee farm' of the village Gehlsdorf, lying on the other side of the Warnow. On this farm, since the middle of May, without there having been elsewhere in the village either scarlatina or any similar illness, six more or less severe cases of scarlatina and a series of throat disorders occurred in the family of the tenant and among the day workers belonging to the farm.* Besides two or three adults, only one two-and-a-half-year-old child of the proprietor of the farm remained free. *A number of those who were taken ill had attended to the milking and to the further care of the milk itself;* which, however, was not kept, as is in small households frequently the case, in the living or sleeping rooms, but in a

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* Fürbringer in Eulenburg's "Real-Encyklopädie," 2d edition, Bd. xxvii.

† A. Baginsky: "Zur Verbreitung von Infectionskrankheiten durch den Genuss roher Milch," *Deutsche med. Wochenschrift,* 1886, S. 494.

separate apartment. It was then brought by the proprietor himself, and, after his illness, by a servant, to the customers in the city. *The former had in the early part of June a mild angina;* the latter escaped entirely. The first to be taken ill in Rostock did not, as far as is known, come into contact with the carrier of the milk, since the latter was regularly received by the domestics, or later by others of the family who were not infected. *According to the investigations of the physicians who observed the epidemic at that time, which were instituted as soon as possible (after the 9th of June), 8 of the 36 cases could be referred with certainty to the Gehlsdorf milk as the source of the infection;* while of the other cases, a considerable number must be attributed to infection from those who were first taken ill.

"The *milk* was also considered infectious, because only those who had drunk, without first boiling it, became ill; while those escaped the infection who had taken only boiled milk, as, for instance, two children, of four and two years of age, in another family, but in the same house, where through the milk (not boiled) many cases of infection had occurred."

It may also be added that the Rostock physicians agreed unanimously in the opinion that the milk was the contagion-bearer.

We can see that the investigation extended, and from an early period, into all the details that were of importance. The conclusions of the Rostock physicians are well grounded. A doubt is, of course, still possible. But what a favorable opportunity for the development of the scarlatina poison (what the cause was we know as little as ever) presented itself in Rostock follows from the fact that the epidemic furnished in the last half year (July to December) 172 cases, against 64 in the first half. In the whole previous year (1884) there were only 165 cases reported.

[The importance of milk as an agency in the conveyance of disease, and in particular scarlet fever, has often been referred to and made the subject of special investigations. One of the most valuable of these is that of R. G. Freeman,* who studied 53 epidemics of typhoid fever attributed to milk, 26 of scarlatina, 11 of diphtheria, 2 of foot-and-mouth disease, 3 of throat affections, 2 of acute poisoning by milk, and 1 of cholera. All of these epidemics occurred since 1880, up to which time a tabulation had been prepared by Earnest Hart. In all of the diseases referred to, milk may serve as a vehicle of conveyance of infection; and as infants constitute the great majority of the consumers, they are particularly liable to infection carried in this way. Freeman divided the diseases conveyed by milk into three classes: (1) Those in which the pathogenic micro-organisms are conveyed by the milk from the diseased cow, as in the case of tuberculosis, anthrax, foot-and-mouth disease, and acute enteritis. (2) Those in which the organisms are introduced into the milk during or after milk-

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* *Medical Record*, March 28, 1896.

ing, from outside sources, as in the case of cholera and typhoid fever, scarlet fever, and diphtheria. (3) Those in which the milk contains poisons developed by bacteriologic growth.

Although typhoid fever, cholera, and scarlet fever epidemics have been attributed to milk, in no case could Freeman find evidence that the particular organism causing a disease had been demonstrated in a sample of milk. This negative evidence has led some to deny the conclusiveness of the proof, since the organisms of the two first-named diseases are well enough known to have been isolated.

Among the general characteristics of milk epidemics, whatever the special disease may be, are the following:

1. The cases appear suddenly, many new ones each day, and the subsidence is equally prompt after the contaminated milk-supply is stopped.

2. The houses invaded are often quite distant from each other, and not restricted to a particular part of the town.

3. The houses of the rich are more apt to be seriously invaded than those of the poor.

4. Those members of each family who are milk-drinkers are most liable to be infected. In an epidemic reported by Freeman, 78% of the special milk-drinkers were affected, while only 27% of those not special milk-drinkers were affected. This, of course, is of particular importance in the case of diseases such as typhoid fever, which are more commonly met with among adults.

5. Those who have used the milk of a certain milk-supply will be found affected, while others escape.

6. In many instances the epidemics have been preceded by disease among the milk-dealers themselves or their families.

With regard to scarlatina, Freeman states that there is conclusive evidence that certain epidemics have been caused by contaminated milk. In 26 recent epidemics, all occurring in England, there were 15 in which contamination from a case of the disease in man was evident. The occasional occurrence of an epidemic without evidence of such contamination has led to a careful examination of the cows furnishing the milk, and the source of some epidemics has been attributed to lesions about the udders of cows. This view, put forward by Klein, has not been confirmed. No epidemic has been traced to the milk supplied in America; not, according to Freeman, because such epidemics do not exist, but rather because the milk-supply is not inquired into.

Hall* has found upon investigation that scarlet fever does not

* *Medical Record*, 1899, vol. LVI.

occur to any extent in countries where cow's milk is not used as food, or where children live wholly upon the breast until three, four, or more years of age. If milk is used as food, but comes solely from the ass or goat, this affection is also unknown. The increasing number of cases and epidemics which are traceable to milk infection would appear, in connection with the above facts of immunity, to render contamination through the milk the principal source of the spread of scarlatina.]

Where is the poison of scarlatina contained in the body of the patient? and with this question I would like to consider also the two following: *At what time in the disease can infection occur? and how does it usually take place?*

It may be stated with certainty that the scarlatina patient, even in the beginning of the attack, is capable of transmitting the infection. A large number of individual experiences indicate this fact; of these, however, I mention only the case of Trousseau, previously mentioned (page 403).

Vogl * goes much further, and closes his description of his experience in the Munich garrison epidemic with the statement that *" the contagion, as a rule, occurs through direct contact during the period of incubation, i. e., three to five days before the active appearance of the disease."*

The array of proof cannot be well produced in epitome. Certainly, however, the facts advanced by him are worthy of the closest consideration, and whoever is interested in so important a question may himself study the article.

The attempt to build still further upon similarly fixed principles, and to establish certain fixed facts in regard to the later periods of the disease, is at the start devoid of prospect. For if it be proved that the scarlatinal poison is formed so early in the body of the patient, and if it is further sure that in adhering to the person it remains still active, one cannot with certainty decide whether the poison that comes into evidence in the latter part of the disease originated from the former or not. At least we may count on the possibility that the quantity of the poison increases with the further development of the disease, and in this way infection may perhaps result from the height of a previous infection.

The views of medical men as to *when the scarlatina patient is most dangerous to those about him* differ very decidedly. For the most part there is at present a tendency to the opinion that the early stages are

* *Loc. cit.,* p. 985.

the most important; but there are still sufficient supporters of the old teaching, which especially emphasizes the desquamative period; as, for instance, Hoff, in his observations in the Faroe Isles (see page 385).

It would be of great value if we could determine the exact time *when the patient ceases to be able to transmit the disease,* when he becomes free from danger to others. This is usually said to be as soon as the desquamation is complete. And if we count in the exfoliation of the epidermis from the soles of the feet and the palms of the hands (some consider this unnecessary), the termination is long enough postponed. Cases such as these are probably, however, very rare.

Medical Director Dahl[*] reports that a servant-girl was detained in the Reichshospital in Christiana a month after the end of the disease; yet on her return, and in spite of the fact that her clothing was disinfected, she carried the infection to the children in the house where she served. "It appears, therefore, as if the infectious substance had adhered to her person."

If there is really no other interpretation possible, then the scarlatina poison must be a still more wonderful entity than it is already considered to be.

Recently Wood [†] has reported a similar case. *The idea that the poison of scarlatina accumulates especially in such places in the body where the outward symptoms are predominant lies ready at hand.* And, in accordance with it, the skin is regarded as the most important influence in transmitting the infection, though proofs, of such a nature as exist in smallpox, are not to be had. Inoculation has had only a limited trial, and its results have not all coincided. Before I discuss the matter, however, I wish to say that *without question, according to the unanimous opinion of the profession, people who suffer merely from an angina, and have no exanthem, can transmit scarlatina.*

Murchison speaks as follows [‡]: "It is well known that *when adults, who years before have had scarlatina, come into close contact with scarlatina patients, they easily contract angina, with little or no fever, and no eruption.* I have frequently found that when one or two children in a house have had scarlatina, every adult in the same dwelling has suffered from a severe angina."

Now, *such an angina is scarlatina in a modified form,—called scarlatina faucium or scarlatina latens* by certain writers,—and it is probable that

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[*] Johannessen, *loc. cit.,* p. 167.

[†] Fürbringer in Eulenburg's "Encyklopädische Jahrbücher der gesammten Heilkunde," 1893, S. 602.

[‡] *Loc. cit.,* p. 431.

those who are attacked in this way can transmit the several forms of the disease.

Förster* says: "*The advance of a scarlatina epidemic escapes us in not a few cases through the fact that many persons become infected, and are therefore infectious for others, who give no thought to the matter.* Measles without an exanthem forms a very rare occurrence; on the contrary, scarlatina without the exanthem is a rather frequent one." Among 230 cases of scarlatina he has classified, besides 7 cases of diphtheritic angina, 19 as apparently simple cases, because their origin could be traced in a clear manner from the scarlatina infection. Four of the latter were complicated with nephritis, and one of the two died.

Förster goes so far as to characterize in the same fashion even the *scarlatinal rheumatism*, and the *nephritis* (?) which occurs in epidemic form, apparently without any other local affection.

"It remains, indeed, still unproved how truly such forms can transmit scarlatina. We must, however, in the mean time consider them suspicious."

Finally, we have the observations of the Norwegian †:

"Attention is called to the fact that scarlatina can appear merely as a simple angina, especially in the case of adults and grown children.

"There exists a whole line of such reports, as appears from the following diagram (comprising a great number of places and embracing the years 1837 to 1878, but giving no statistics), and often there is the distinct statement that such cases (angina scarlatinosa, febris scarlatinosa sine exanthemate, angina scarlatinosa sine exanthemate), just as the more pronounced forms, have carried the infectious substances with them."

That the transmission of the disease can occur even in the very beginning of the disease, E. Hagenbach‡ brings positive proof:

"The boy Stich (infected in the hospital) showed symptoms of the disease during the one and a half hours that he still lay among the other children—fever (100.7° F.), pain in the throat, redness and swelling of the tonsils and the surrounding parts, nausea, but *no trace of an exanthem, in spite of repeated examinations*, since scarlatina had been assumed to be the condition.

"The boy Haass, infected from Stich, during two hours that he remained among the other children showed fever (102.2° F.), headache, nausea, trouble in swallowing, redness of the throat, *but at this time no exanthem.*"

From this boy still another was infected at this time.

One should compare with these cases the reports by Vogl already mentioned (see page 416).

We meet here with a great difficulty in interpreting the evidence correctly. We teach nowadays, and the lesson is founded on good ground, *that very finely divided dust can pass into the air and spread itself broadcast only when it is in a dry state. Now, the toxic substance*

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* "Jahrbuch für Kinderheilkunde," N. F., Bd. x, S. 170.
† Johannessen, *loc. cit.*, p. 181.
‡ "Jahrbuch für Kinderheilkunde," N. F., Bd. viii, S. 293.

of scarlatina is an actual substance, not a vapor. How, then, should it go from the moist mouth cavity into the vicinity of the patient, and from here spread still further? In the individual case we may always take it for granted that the secretions from the mouth have lodged and dried somewhere on the body or clothes of a patient with scarlatina angina—though this explanation serves only for a makeshift, which one can hardly make use of in a general way. I know of no explanation that can be given that will be satisfactory, but will at least bring the subject into discussion. The reports in regard to the transmission of the disease by inoculation of the skin with nasal or bronchial mucus are also insufficient. Results, perhaps, will first be obtained from the blood.

Murchison [*] states his facts with a detailed declaration of the sources from which they are obtained. These have been for the great part impossible for me to obtain; therefore, I confine myself to reproducing the main statement as given by Murchison himself.

Stoll is said to have successfully produced infection by rubbing into the skin the epidermal scales from a case of scarlatina, but all particulars are omitted.

According to Dr. Robert Williams, Sir Busick Harwood has inoculated well children with the contents of the vesicles that occur with the eruption of the exanthem upon the skin. The attempt succeeded often, but the aim to secure a mitigated form of the disease was not fulfilled. The disease lost none of its dangerous character. Therefore the attempt, which had also been taken up by other physicians, was carried no further. The matter appears to have been related by one doctor to another, and a positive basis for the facts is lacking.

Murchison remarks, in the connection, that he found only one statement worthy of consideration, that takes an absolutely different position. This was a case of a scarlatina patient who had such an active delirium that it was necessary to restrain him in bed by force. His attendant was a poor man, who had injured his hand on a broken bottle. The hand came in constant contact with the patient's skin, which was covered with secretion from the vesicles, during his efforts to restrain him. On the following day the attendant's hand became much more inflamed, and his arm was swollen. After five days he was taken with scarlatina, and after a short time died from the disease.

Murchison comments, with propriety, *that the attendant was exposed to the poison of the disease in the customary manner as well.*

Miquel d'Ambroise reported in the year 1834 to the French Academy of Medicine that he had inoculated a number of children with the fluid from the scarlatina vesicles. After thirty hours a red areola appeared about the puncture openings, which resembled in all respects the eruption of scarlatina. This redness increased for three days, and disappeared first on the fifth day. It was not a traumatic inflammation, because a second inoculation in the same individual produced no effect. The operation afforded *complete immunity against scarlatina.* Two children, one and a

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[*] *Loc. cit,* p. 175; also Thomas, in v. Ziemssen's "Handbuch," Bd. ii, 2, S. 169.

half and nine years old respectively, who had never before had the disease, were not attacked, although they occupied the same bed with a child suffering from scarlatina.

It may, indeed, be true that in these cases the inoculation actually had its effect. *The evidence is hardly conclusive*, and certainly the last-mentioned fact is not, since the same occurrence has often enough been observed in the case of children who have not been inoculated.

Rostan reports two cases in which the exanthem appeared seven days after the inoculation.

Copland treated a severe scarlatina case which received its infection from a small quantity of sputum from a patient with malignant scarlatina.

So much for Murchison: one sees that the ground gained is not a marked one.

Dr. Rupprecht reports * a further observation on the infection through the secretion from the pharynx or the bronchial passage. He performed a tracheotomy on a twenty-year-old girl suffering from scarlatina and diphtheria, following the procedure with artificial respiration. This was carried out as follows: A thick elastic catheter was cut, and placed in the silver tracheal cannula. Through this the surgeon forced in his breath in regular rhythm, the air then being expressed by rhythmic pressure upon the chest. "I was so busy with the breathing process that several times I failed to remove my mouth from the catheter quickly enough, and received some of the expressed air and mucus from the patient in my own mouth." About sixty hours later angina showed itself in the form of pain in the angle of the left lower jaw, and seventy-eight hours after the infection there was a *severe chill*. Although the exanthem appeared in unusual fashion, the diagnosis of scarlatina was certain.

There are also other cases, as that of v. Leube, observed by himself (see page 391). The manner of transmission, however, remains an open question; for what is there that cannot force entrance through a wound that is obtained during an autopsy of a case of scarlatina?—blood, particles from the skin, any of the juices of the tissues, all come into consideration together. The fact that the toxic substance circulates in the blood, and is contained in it, would hardly admit of doubt if one could discover that during the intrauterine life of the fetus a scarlatina infection occurred through the mother. The existing authorities on the subject are, it seems to me, too uncertain to warrant us in calling the matter an assured fact.† Opinions are divided on the question, Bohn, Fürbringer, Murchison,

* "Ein Fall von Scharlach," *Wiener med. Wochenschrift*, 1862, Hauptblatt, S. 435.

† Report by Thomas, *loc. cit.*, p. 191.

and Thomas taking a negative stand. Thomas,* however, expresses himself reservedly, and says:

"Whether or no children are born with scarlatina is hard to ascertain, because most of them arrive in the world with a redness of the skin, or a yellowish redness similar to that of scarlatina, and after birth also desquamate. Since, however, there is no question that children may be born with smallpox of women suffering from the disease, or who have only been exposed to it, why should this not also be possible with scarlatina?"

In truth, the possibility does exist; but how in regard to the proofs? Let us consider a number of cases.

Tourtual † reports the case of a thirty-year-old woman who, in the eighth month of pregnancy, and until shortly before her delivery, constantly nursed her sick husband and her ten-year-old son. According to her parents' statement, *she had never had scarlatina,* and at this time did not have the disease. Shortly before the delivery, however, an exhausting diarrhea set in, which after the childbirth ceased of itself. The child would accept neither the breast of the wet-nurse nor any form of fluid nourishment. This continued until the fifth day, on the evening of which "nature made an attempt by vomiting to rid itself of a quantity of tenacious mucus and purulent material. This increased so in quantity on flushing the mouth with sugar-water that the nurse had constantly to keep wiping it from the mouth. From then on, the child swallowed more easily, but did not yet improve in sucking at the breast, especially because of a 'stopping up' of the nose. *Early on the sixth day,* when the throat and nose had thoroughly cleansed themselves by repeated vomiting and sneezing, it began to be anxious to take the breast."

On the day after the birth there appeared "an unusual redness over the whole body, which the mother feared was scarlatina. I found, in truth, the rash characteristically developed. At one time the lips, the mouth-cavity, and the tongue were a shiny red color, like sealing-wax; otherwise there was nothing unusual, and nothing in the form of an obstruction."

"My attention was now directed especially to the desquamation period in order to obtain a positive knowledge in regard to the eruption. This showed itself upon the ninth day by a gradual diminution of the redness and by a crinkling of the skin. The scaling then took place in pieces nearly as large as in older children, and, as occurs only in rare instances, there was later a complete shedding of the nails from the hands and feet." The child made a complete recovery.

This is the story. I lay no weight upon it, because the authority is somewhat a credulous one. This I infer from the fact that he reports as a sequel—*scarlatina metastasis,* he calls it—the case of a nineteen-year-old girl, who had attended a "dangerous" case of scarlatina through

* *Loc. cit.,* p. 190, almost literally quoted from Stiebel, "Ueber den Scharlach," *Journal für Kinderkrankheiten,* Bd. xxxiii, S. 164.

† "Bemerkungen über die Scharlachepidemie zu Münster vom Jahre 1822–1823," *Journal der praktischen Heilkunde,* 1826, S. 16.

four weeks, and then had fever and angina, "but no eruption." He observes the following:

"The fever continued for nine days without a crisis, while all sorts of symptoms, as choking, vomiting, hiccup, etc., appeared." On the ninth day of the disease pain in the back with stiffness, then with paralysis of the limbs, also retention of the urine and feces, frequent vomiting, and later a difficulty in swallowing." "*At the end of the third week* were perceived the first signs of the desquamation of the atypical and hardly evident exanthem" (previously it was stated in so many words that an eruption was not present). "The inability to swallow grew worse every day, so that within a short time not the smallest quantity of fluid could be ingested. This condition *continued three months, and during the whole time neither urine nor feces passed from the patient.*" Then came the "crisis." Marked twitching and shaking of the whole body were noted, and, according to the mother's statement, a loud cracking in the spinal column—then all went well.

Manifestly, this was a severe case of hysteria; the writer has not even proved himself a good observer. But, apart from this consideration:

If we must consider the possibility of a period of incubation of less than twenty-four hours in scarlatina (see p. 403), then the fact cannot be excluded that a child born at 6 o'clock of the previous day can have been infected in the course of the following one. Otherwise the supposition cannot be denied that a mother who remains well can herself transmit the poison of scarlatina to the fetus.

This case of Tourtual appears to be the most conclusive of all that are accessible to me. I will mention a few others.

D. M. Williams [*] states that four children of a mother who had had scarlatina became ill. She herself was attacked on September 22d, and on November 4th (forty-three days later) was delivered of a "fine girl," whose skin went through a desquamation. Nothing further is brought in the way of evidence that the child developed the disease *in utero*, and after birth went into a desquamative process. It died on December 6th in consequence of an erysipelas originating in the umbilicus, and followed by abscesses.

Gregory [†] reports: "On April 28, 1839, my youngest son was born at the time of a scarlatina epidemic, and evidently suffering from some form of fever. On the following day his throat was affected, and plainly by angina maligna. An exanthem never appeared. The child wasted away, and died on May 1st." The case is hardly one that can be utilized until we ascertain what Gregory means by *angina maligna*.

Stiebel [‡] gives the short statement that: "A twenty-five-year-old woman toward the end of her pregnancy took scarlatina with a severe eruption. . . . When the child was born, it could not swallow for several days. It was scarlet-red in color, and the skin separated in larger patches than usual." Also in this case I can see no convincing evidence. Cases dating from the time when scarlatina, as such, was not intimately known, such as those repeated from Ballonius (1538–1616), are, of course, to be excluded.

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[*] "Scarlet Fever during Pregnancy," *The British Medical Journal*, January, 1875, p. 37.

[†] "Vorlesungen über die Ausschlagsfieber," 1845, S. 134.   [‡] *Loc. cit.*

The cases reported by Ferrario in Pavia * are also doubtful, and only one is reported in a source accessible to me. Besides "red flecks upon the skin," the mucous membranes of the stomach and intestines were also covered, as does not usually occur in scarlatina. The eight months' fetus was born dead.

These illustrations will be sufficient to enable every one to form his own opinion.

That women sick with scarlatina may bear children who are free from the disease has been often observed.

If the view held by Döhle † should be verified, which claims to find in the blood of scarlatina patients similar pictures to those in the blood of measles subjects, and which he considers to be the specific microbes, then without any question the presence of the poisonous substance would be proved. His short statement is as follows:

"I have been able so far to examine the blood of five scarlatina patients. There have been repeatedly present two different forms of parasites. The first presents small active cocci of a faint, clear appearance, and on which frequently there is a flagellum to be seen. The size of the coccus varies up to 1 μ, as does also the length of the flagella. Usually the latter are short, and frequently have on their extremity a little knob-like swelling. Sometimes one can see diplococci, surrounded by a clear zone, and also twice or three times as large protoplasm bodies of various formation. This protoplasm is very finely granular, and contains, as a rule, brown pigment granules, which are of a very striking appearance with the open diaphragm. The movements of these bodies consist essentially of contraction of the protoplasm, while changes of position are very meager. These occur just as in measles, both inside and outside the red blood-corpuscles. I have also succeeded in cultivating the different forms."

In what manner does the poison of scarlatina force its way into the body of the patient?

We cannot help admitting that the poison contained in that portion of the atmosphere surrounding the patient is taken up directly from the air. But it always remains undecided, where the gate of entrance stands. We must think of the mucous membranes of the upper air-passages, also of the bronchi; but the infection may also occur through the pharynx, and perhaps from the surface of the tonsils. Finally, the possibility is not to be excluded that the poison has been swallowed with the saliva, and has then entered by the digestive passages. We know nothing, however, of the facts of the case.

* Cited by Naumann, "Handbuch der med. Klinik," Bd. III, Erste Abtheilung, S. 782, Reutlingen, Ensslin, 1832.

† "Zur Aetiologie von Masern Pocken, Scharlach, Syphilis," *Centralblatt für Bacteriologie und Parasitenkunde*, Bd. XII, S. 909.

Everything consists in the weighing of possibilities, which must present themselves in this way or that, in order to produce an infection.

The same points come into consideration in the discussion of an *infection from the poison that adheres to different objects.* The less frequent forms of infection have already been mentioned. If we would surmise, we must say that *our understanding of the scarlatina poison is by no means a deep or thorough one.*

The same is true of the behavior of the individual *toward the poison.* Certain things are at this point deserving of remark. First, *that even in the case of an unusually favorable opportunity for infection, the latter does not necessarily ensue,* although the subjects be children even, to whom their age affords no immunity.

Thus, it is reported from Norway[*]: In the epidemic at Modum in 1876 only a single one of ten children was attacked, all of whom ranged from one-half to fourteen years in age, and none had had scarlatina before. In this case the apartments were so confined that all lived in the same room and slept in the same bed.

The epidemic was a malignant one, and the mortality in the whole kingdom was the highest for more than a century.[†]

Every medical man has had an opportunity for similar experience, and if he is busy among the poorer classes, it is by no means a rare occurrence. I have, therefore, only mentioned this case because it appears ready at hand.

It is worthy of attention that *certain individuals act differently in regard to the poison at different times,* and can have a temporary, changing susceptibility. For this fact a remarkable case, related by a good observer, stands sponsor.

R. Förster,[‡] in Dresden, states that: "In the family of a foreigner living here, one after another of four children took scarlatina, and *one of them ran a severe and long-drawn-out course.* The father nursed this child with the greatest self-sacrifice, undertook nearly all the measures necessary during the illness, and remained free from the disease, although he had previously not had scarlatina. It is, of course, possible that the poisonous substance had not come in contact with him, but this is hardly conceivable.

"*A year later he visited a friend whose child lay ill of scarlatina. He merely asked after its condition, in the vestibule, and yet a few days later became moderately ill with the same disease.*"

Adults thus, with their lessened susceptibility corresponding to their time of life, have at one time exposed themselves freely to the

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[*] Johannessen, *loc. cit.,* p. 168.   [†] *Ibid.,* p. 40.

[‡] "Einige Bemerkungen über die Verbreitungsweise der Masern und des Scharlachs," "Jarhbuch für Kinderheilkunde," N. F., Bd. x, S. 171. Further observations by Thomas, *loc. cit.,* p. 183.

influence of a poison without result (as in the case of a nurse's work); and then, again, have been infected at a time when far slighter quantities of the contagion can have come in contact with their persons.

It has also been stated that in certain families there exists an *unusual susceptibility to scarlatina:* almost all their members have been attacked as soon as the opportunity for infection has presented. Moreover, and this is especially to be noted, the *cases are severe;* they run a less favorable course, even when the infecting poison originates in a light case of the disease.

This view does not seem plausible to me, and my own experience does not confirm it.

That a great number of persons who dwell together can be attacked by scarlatina is altogether certain. But that *blood relationship* plays a rôle in the matter remains an open question.

Thomas[*] brings forward a few points of evidence—mostly second-hand —after the "Jahresberichten." But his array seems to me poorly adapted to satisfactorily support the principle first advanced by him of a "family disposition."

Copeman[†] at least offers a personal observation of the year 1844. "In one family four children died so suddenly that the suspicion was excited of possible poisoning. The fifth child had a regular case of scarlatina." The epidemic was extremely severe, with many fatalities.

The same Copeman reports also a well-to-do countryman's family: "One son came home with a mild attack of scarlatina, and went through a light case. A short time afterward a child and its nurse fell ill, then a second child, the mother, and a third child, and all five died in one week." This is certainly an example of a severe *house*—but not *family*—disease; for that the nurse was a relative is not stated.

Also Trousseau,[‡] to whom Thomas refers, has still something else to say: "Scarlatina epidemics may be full of danger for an entire general population, or they may assume this character only for a single family. *The malignancy limits itself in a measure to a single hearth,* and in such cases the disease is malignant *for all persons that live within its circle.*" By this is meant, I take it, only "family" in the wider sense; *i. e.,* those living together in the same dwelling. And this meaning need hardly be altered on account of the following remark, that "I wish to take the opportunity to recall the sad case, recently reported in the English papers, of a clergyman of York, who within one week lost all of his six or seven children."

Trousseau refers to a newspaper communication, which is to be considered even the less a sufficiently scientific source of knowledge in that not once is there an exact statement as to the number of the children that died.

[*] *Loc. cit.,* p. 182.

[†] "Jahresbericht über die Leistungen und Fortschritte in der Gesammten Medicin," R. Virchow und Aug. Hirsch, VI. Jahrgang, Berlin, Hirschwald, 1871, Bd. ii, S. 247.

[‡] *Loc. cit.,* p. 122.

Härlin's* observations from Stuttgart are in every way worthy of consideration, but will they serve here as a means of proof? The case was that of an *epidemic form of exanthem:* "On account of its slight development it was inexactly termed 'rötheln.' Its course in every respect was benign: slight or no rises of temperature; mild catarrhal symptoms, occasionally early vomiting, an eruption of the appearance of measles extending over the entire body, only a moderate indisposition, and a termination of the whole illness in a few days, a persistence of the eruption during twenty-four to forty-eight hours, then a hardly perceptible, fine desquamation;—all characterize the picture of the disease. One might call it the lightest form of measles. Many children who had already had the latter disease were attacked. *Scarlatina and measles at that time appeared only in scattered cases*, and one death occurred in December from scarlatina." Such was the character of the prevailing disease.

The disease began in the early part of December, 1860, in a *family numbering eleven persons*. After the end of the month other cases appeared. Only six had angina, two of these being mentioned as having had a spotted redness of the pharynx. *Two of the six cases had already had scarlatina*. Of the five others, *one case had an exanthem markedly resembling scarlatina* (Case 9); in all the others, there is either no special mention of the nature of the eruption, or else it is characterized as similar to measles. Härlin says in his summary: "It appears worthy of note that the exanthem was strikingly analogous to that of measles, in Case 6 going even as far as the peculiar papular appearance." Branny desquamation was the rule; that actual fragments of skin were cast off is distinctly stated in regard to only one case (No. 4). It should be mentioned, moreover, in this connection that in one of the cases (Case 3), which was rather severe, "the desquamation went to such an unusual degree that the patient appeared covered with *thick layers of bran*."

The sudden onset of the disease, frequently with vomiting, may be worthy of mention, but is of less significance than the fact that three times dropsy with albuminuria was noted, twice (Cases 2 and 9) where the probability of a scarlatinal affection was marked; once—the mildest case—in Case 6, in which the exanthem most closely resembled measles.

I will not absolutely deny the possibility that all these cases were scarlatina, but would like at least to submit the question whether they ought to be used as complete proofs of a "family tendency."

The "Nachricht aus Württemberg" referred to by Thomas is an unauthentic newspaper article taken from the "Schwäbischer Mercur," and deals with a small but severe epidemic of scarlatina (1857).

The additional communication of Corson† possesses small value. He criticizes severely the treatment of a colleague who in a short space of time lost seven members out of a family of twelve. How far measles and diphtheria are to be considered in this connection cannot be decided. The physician in attendance mentions them as the explanation of the large number of deaths, and, in any event, at the time in question they were epidemic in this portion of the United States. *Whether Corson saw these cases himself seems doubtful.*

I will also mention a short statement by Johannessen‡: "As an in-

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* "Eine Familienepidemie von Scharlach," *Med. Correspondenzblatt des Württemberg'schen Aerztlichen Vereins*, Bd. xxxi (1861), S. 155.

† Virchow-Hirsch's "Jahresbericht," für 1871, ii, S. 249.　　　‡ *Loc. cit.*, p. 167.

stance of a '*family susceptibility*' a pastor's family may be mentioned. Out of five children, four took scarlatina; and of these, three died." (An epidemic in Romsdalen, 1878, which was characterized as rather malignant—*mehr bösartige*).

From this evidence it appears to me that a "family susceptibility" is not an altogether improbable thing. That the children of a family under certain circumstances are infected more easily than the servant portion of the same household explains itself easily by the immunity conferred on the latter by their age. The parents, moreover, spend much more time with their sick children than the servants, and are therefore also in a greater degree exposed to the infection than they. But in cases where—unfortunately, it is always growing rarer—a servant belongs permanently to a family, and where she in unselfish faithfulness acts as nurse, she is in no less degree exposed to the infection and will no less frequently be attacked than the father and mother. Every physician has learned this fact who has been busy among such conditions. I am one of these, and for this reason consider that the opinion *that certain families, as such, offer an especially fertile soil for the scarlatina poison*—this being the kernel of the discussion—remains at *least not proven.*

[Seitz* states that family disposition plays a part in scarlet fever which is not in evidence in other acute exanthematous diseases. Many families show a heightened tendency to contract the disease, while others show a corresponding immunity.]

Henoch † gives still another interpretation: "Striking to me appeared the fact, noted undoubtedly by many other physicians, that if scarlatina breaks out in a family, and one of the children dies of the malignant form, very frequently also a second and a third child are taken off under similar conditions, and in this way whole families can die out. It appears probable to me that under such conditions the case is one of a mixed infection." Henoch considers the possibility of a sepsis with scarlatina. The question, I think, can only be answered by bringing together all the statistics, and by weighing them with reference to all the conditions that enter into consideration —and their number is by no means small. For lack of space I must, of course, give up all thought of such a procedure. For how far could we not extend the meaning of blood relationship? In the case of a population such as is presented by the Tübingen vine-dressers, who form by their intermarriage a—so to speak—great family, an accurate

* " Kurzgefasstes Lehrbuch der Kinderheilkunde," Berlin, 1901.
† "Vorlesungen über Kinderkrankheiten," S. 654, 3d edition.

conclusion appears to me unattainable. The same is true of many closely bound village communities. One were thus confined to such places as offer a changing composition of their population, and chiefly to the great cities.

I must also, at this point, reject the inference drawn by Thomas from the supposition that a family tendency exists: that *"the fact affords sufficient reason for anxiety in regard to other members of the family if two or more children are in rapid succession attacked by scarlatina."*

The deductions to be drawn from this premise, however, seem to me to be not unworthy of consideration in the practice of medicine; whoever knows the anxious care that exerts its influence over men during a severe epidemic of scarlatina will agree with me. "I have lost my children" carries with it idle despair on the one hand, aimless overactivity on the other.

For the most part it can be said that whoever has once had the disease is from that time on immune to the poison. Notwithstanding this, repeated infections do occur, and with all their sequels.

It goes without saying that relapses—*i. e.*, those features of the disease or a part of it that repeat themselves during the course of one and the same infection—do not belong to this class. They will be treated of in the section devoted especially to pathology. The credit undoubtedly belongs to Thomas * of calling attention to this fact.

The distinction is demonstrated, so far as practicable, in the statistical compilation of Körner.†

Maiselis ‡ has *used the same cases extensively* (to put it mildly) *as Körner, and without referring to the latter.* We will therefore refer mainly to Körner's "Arbeit." It is very thorough, and yet errors have nevertheless crept into its pages. This is also true of Gillespie's, who is said to have seen cases of scarlatina occurring a second time in the same person in not less than twenty-one instances.

There were two epidemics in the Edinburgh Donaldson Hospital, an educational institute for poor and deserted children, that was erected in 1850. The first epidemic § began on September 17, and continued until December 19, 1852. In all, 72 children were attacked and 8 adults, out of 123 and 33 respectively who dwelt in the building.

Every child at the time of its admission had to bring a medical certificate

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* *Loc. cit.*, p. 198.

† "Ueber Scharlachrecidive," "Jahrbuch für Kinderheilkunde," N. F., Bd. IX, S. 362.

‡ "Ueber die durch das Ueberstehen von Infectionskrankheiten erworbene Immunität," *Virchow's Archiv*, Bd. cxxxvii, S. 472.

§ *Journal für Kinderkrankheiten*, Bd. XXIII, S. 152.

in regard to its previous condition of health. From this procedure it was learned that 23 of the children had already had scarlatina. Of the adults, this was the case with five, and these remained immune. *In contrast to them,* 11 *children were attacked out of the 23 who had already once had scarlatina.*

This is an instance, if the statements of the physicians who provided the certificates were accurate,—a thing that cannot be tested,—of genuine fresh infection with its resulting conditions. The case was even different in the second epidemic,* which began on November 6, 1861, and ended January 31, 1862. In all, 39 children and 4 adults became ill out of 177 and 32 respectively occupying the house. *"Ten children took scarlatina for the second time,"* we read in the report. From the latter we are unable to determine whether the illness was in the form of a relapse, or of a genuine fresh infection. Murchison alone, who describes this epidemic, states that in most of the eleven cases the *eruption was to be found in only one of the attacks.* Murchison himself does not discriminate between the two conditions, and they may easily have been cases of relapse.

We have already spoken of Trojanowsky's † observations, which must be considered in relation to their own conditions, and may hardly be utilized in such a connection as this. Maiselis states an incorrect number—23 instead of 18.

Thomas ‡ asserts, and with propriety, that *it is difficult to entirely avoid confusion with the condition called rötheln.* Statistics, therefore, have only a limited value. This becomes still smaller if one takes the gound held by Murchison,§ who says that the *rudimentary* form of scarlatina, which shows itself possibly by a mere angina combined with some fever, may repeatedly attack a man who has much to do with scarlatina patients. If we include these cases, and this is undoubtedly proper, then a repeated infection is by no means rare; much more frequent, certainly, than the forms that show a complete display of the symptom-complex of the disease.

Well-authenticated second occurrences of the complete course of the disease have been described by trustworthy observers in no inconsiderable number of instances. Körner's "Arbeit" contains his conclusions in regard to the subject, in which he gives the following summary ‖:

The first attacks occurred usually in childhood, before the tenth year; the second attacks about two to six years later. Only in six cases did less than a year intervene. *The second attacks were usually not milder than the first; rather often they were severer.* Although the actual figures may not at once agree with the foregoing, the final result may be counted upon as accurate.

[That scarlatina may recur is to be taken on sufficient authority.

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* Cannstatt's "Jahresbericht," 1862, Bd. iv, S. 125.

† See Introduction to "The Acute Exanthemata," page 214 of this volume.

‡ *Loc. cit.,* p. 196.   § *Loc. cit.,* p. 431.   ‖ *Loc. cit.,* p. 381.

I have never seen an undoubted case. Lay and professional sources are constantly quoted as proving the possibility of second attacks. When physicians gravely recount examples of scarlatina occurring three to six times in the same individual, the natural skeptic returns to his original attitude. A few men on whose judgment I am willing to rely have been convinced that they have seen such recurrence. All that I can say is that in all the cases I have investigated, one attack has been light and open to doubt.]

A *third attack of scarlatina* in the same person is still more rare, and in regard to such cases there is usually only a brief statement.

Thus, Murchison* reports that Sir Gilbert Blane had seen in one young woman three attacks of scarlatina "without the slightest suspicion or possibility of a doubt." From my location the source of information is inaccessible, but it is not to be presumed without further knowledge that the individual attacks were distinctly separated in point of time. Again, there is the following remark, that Dr. Richardson has, according to his story, himself suffered three different times from scarlatina.

Körner presents other more or less authentic observations.

Striebel † reports: "In the case of a woman, about fifty years of age, *I have seen scarlatina run its complete course four years in succession*, the skin desquamating in certain areas in parchment-like pieces a half-shoe in length." From the latter circumstance I take the case to be a genuine one.

A still more frequent repetition, as far as I can learn, has not been observed with any degree of certainty.

Jahn ‡ accompanies his report of the case of a forty-two-year-old woman with a well-founded doubt. The case was one *of an exanthem that outwardly resembled scarlatina with mild fever and angina*, followed by a partly branny, partly shreddy desquamation of the skin. The patient stated that *she had had scarlatina when a child of six years, and had now had an attack similar to the present one seven times*. Jahn concludes with the words: "I admit freely that I am able to suggest no suitable name for the condition in question. It cannot be called *urticaria, essara, erysipelas universale, erythema*, or *ignis sacer*, and the option only remains either to christen it with the above-mentioned name (*scarlatina*), accompanied by a question mark, or *pseudo-scarlatina*."

Not much can be made out of the following note of Jahn's: "In addition to these observations there is, it appears, one of Henrici's, namely, that during the epidemic of scarlatina that extended from the autumn of 1797 into the year 1798 at Kiel, a woman, who had already had scarlatina sixteen times, with all its symptoms, was attacked for the seventeenth time." No authority is cited, and if one wished to find it, he must consult the periodicals of that time for assistance, for a more extensive work by Henrici is not mentioned in Engelmann's "Bibliotheca Medica."

* *Loc. cit.*, p. 431.   † *Loc. cit.*, p. 154.
‡ "Scarlatina habitualis?" *Rust's Magazin*, Bd. xxviii, 1. Heft., S. 69.

Let us now take up the consideration of the **general conditions** relating to the spread of scarlatina.

Climatic influences of themselves are probably of minor importance. Scarlatina is found in the tropics just as in the more northern latitudes.

How, then, in regard to the *seasons of the year?*

Hirsch * has collected the reports from 435 scarlatina epidemics in the average latitudinal distribution. His articles represent "the time of their influence, and especially with reference to their acme."

Of 100 epidemics there were: In the autumn, 29.5; in the winter, 24.7; in the summer, 24.0; in the spring, 21.8.

An additional compilation shows the mortality—London (1838 to 1853) with 55,287, Sweden (1864 to 1873) with 11,630 deaths from scarlatina, distributed as follows:

	LONDON.	SWEDEN.
Autumn	32.1%	29.4%
Winter	22.8%	24.6%
Summer	25.2%	23.9%
Spring	19.9%	22.1%

The figures given by Johannessen † for Norway are exact. He gives them first for the *beginning of the epidemic according to the months.* "So as to be able to study the relation of the appearance of the epidemic to the season of the year, I have *arranged the great and more wide-spread* epidemics with reference to the years, whose monthly reports may be considered somewhat trustworthy, wherever such are stated accurately, or at least allow of an easy estimation."

Johannessen classifies the 52 epidemics of Norway, which correspond to these requirements, as occurring: In the autumn (22), 42.3%; in the winter (13), 25.0%; in the summer (8), 15.4%; in the spring (9), 17.3%.

In answering the question as to the month in which scarlatina appears with the greatest frequency, Johannessen made use of 51 *epidemics.* The conclusions obtained are: Autumn (13), 25%; winter (25), 49%; summer (6), 12%; spring (7), 14%.

There is still another estimation of the *total number of cases of scarlatina in Norway* ‡ treated by physicians from 1867 to 1878. It includes 65,785 cases *with* 8608 *deaths.* The figures for the various years vacillate between 1776 (1874) and 12.590 (1876), with respectively 220 and 1760 deaths: In the autumn, 24%; in the winter, 31%; in the summer, 20%; in the spring, 25%.

* *Loc. cit.,* p. 131.   † *Loc. cit.,* p. 97.

‡ Tabelle VII von Johannessen, *loc. cit.,* p. 87.

The following curve of Johannessen (Fig. 58) shows the distribution (percentage of the total number) according to the months.

Everything being considered, there is observed a *not overwhelmingly strong, but evident influence of the season of the year, in this sense—that autumn and winter (September to February) are more prone to the disease than the spring and summer (March to August).*

Even if we attempt to ascertain upon what condition this fact depends, the result obtained is of no great value. It is of the first importance, however, to consider the conditions of temperature.

Johannessen has found a certain *connection between* the temperature of the air and scarlatina, through a comparison of the two curves, and in this sense, that during the ascent of the temperature curve the relative frequency of scarlatina falls, or vice versa. He utters a warning, however, with great propriety against hasty conclusions.

His countryman, Magellsen,* is bolder, and claims that he has found a distinct relation between the two. He states in so many words "*that the mortality curve presents a mirror of the curve of the temperature.*" A critical consideration of the question would lead us too far, since it must needs, in order to be intelligible, go into the general theoretic views developed by Magellsen. I wish still to mention the observations of E. Hagenbach,† who found that the total number of fatal cases of scarlatina in the years 1824 to 1873 so distribute themselves that there fall in the colder months (November to April), 65%; in the warmer months (May to October), 35%.
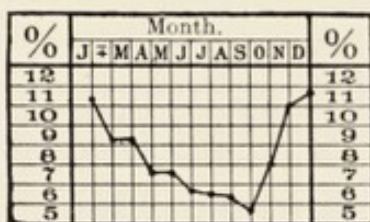
FIG. 58.

Here is certainly a considerable difference, which, however, apart from the fact that the figures are small (160 cases), has only a local significance; for even in Würzburg the general conditions are of a very different nature.

Hagenbach calculates, from the statements of Voit in regard to Würzburg (280 fatal cases): The colder months, 54.6%; the warmer months, 45.4%.

In regard to the relative influence of such other forces as the weather, the wind, the atmospheric pressure, etc., nothing is known.

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* "Wetter und Krankheit," "Lufttemperatur und Scharlachfieber," Christiania, 1893 (Selbstverlag), 1 Heft.

† "Epidemiologisches aus Basel," "Jahrbuch für Kinderheilkunde," N. F., Bd. ix, S. 52.

According to Julius Gutmann:* "The idea that scarlatina epidemics make their appearance with certain directions of the *wind currents,* mostly west-southwest, and disappear with their cessation, appears by no means well founded." The following view expressed by Hirsch † may at once be considered as correct:

"*Just as the local distribution of scarlatina is independent of climatic influences, so is also the time for the appearance of the disease independent of the time of year and the weather; at any rate, it is influenced far less than that of smallpox and measles.*"

Moreover, the foundations upon which the dwellings are built are of no discoverable significance with regard to the occurrence or the severity of scarlatina. Attempts to find a connection must therefore be relinquished because now this, now that, position has been characterized in the individual case as especially favorable or unfavorable. There is something essential to the disease that does not allow of discovery.

Just as little causal influence has the altitude. Wherever man lives, whether it is on the seacoast, or on the highest mountain, or on the flat land, scarlatina can make its way, if once its germ obtains a footing.

The extension of scarlatina differs materially from that of measles. Measles never disappears altogether from the great cities, but in the moderate-sized cities, that have a not too actively changing population, the disease can disappear completely and for years at a time. Still more is this true of the lowlands. Scarlatina, however, behaves differently. There seems in a much more marked degree to be a regular connection between the different cases. Scarlatina much less easily submits to a complete disappearance for a length of time.

Hirsch ‡ chooses another form of expression for the same fact, and says: "While isolated cases of measles are usually the forerunners of the epidemic, or continue for some time as its scattered remnants, sporadic cases of scarlatina have been observed comparatively frequently and in greater or less numbers."

If one compares the table on page 434 with that previously given for measles, § the difference is at once apparent: in the former there were no less than ten measles-free years in Tübingen and Lustnau; in the latter, a single one.

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* "Ueber die Gesetze der Epidemien des Scharlachfiebers," Würzburger Dissertation von 1859, S. 19.

† *Loc. cit.,* p. 130.   ‡ *Loc. cit.,* p. 129.

§ Compare "Measles" in this volume, page 254.

28

SCARLATINA IN THE TÜBINGEN UNIVERSITY POLICLINIC, 1873–1894.

547 Cases, with 45 Deaths = 8.23%.

YEAR.	1873.	1874.	1875.	1876.	1877.	1878.	1879.	1880.	1881.	1882.	1883.	1884.	1885.	1886.	1887.	1888.	1889.	1890.	1891.	1892.	1893.	1894.	REMARKS.
Tübingen .	2	2	16	5	8	21[1]	20[1]	0	7	30[2]	0	1	4	2	1	23[3]	131[3]	32	6	6	11	2	Total number 329, with 22 deaths = 6.69%.
Lustnau . .	0	3	33	0	30[4]	32[5]	18[5]	2	7	2	0	0	0	4	0	42[6]	28[6]	12	0	0	0	5	Total: 218, with 23 deaths = 10.55%.

Duration of the epidemic in days from the admission of the first to the last case:

[1] From March 19, 1878, until September 4, 1879.

[2] From December 3, 1881, until March 21, 8 cases ; then from May 5 to June 26, 26 cases.

[3] From December 5, 1888, until May 27 (unbroken connection).

[4] From March 2 until September 17, 1877.

[5] From June 11 until April 14, 1879.

[6] From August 31, 1888, until November 29, 1889, continuously. Then a short succession of cases (10) from June 25 to July 25, 1890.

The little place Lustnau has been free from scarlatina for nine years, and the city Tübingen, which has nearly eight times as many inhabitants, only one year, and probably never, for the policlinic clientelle forms only a fraction of the total population.

The validity of the rule is easily discoverable over narrow as well as wide areas. I give here a graphic description of the *mortality of scarlatina and measles*, both for the narrow conditions of the Tübingen Policlinic (Fig. 59) and also for the extensive ones of the kingdom of Norway (Fig. 60). One can see how much more decided the departure of measles is from the average (mean) line, than is that of scarlatina.

The mortality in Basle * during the fifty years from 1824 to 1873 shows the same result ; twelve years being free from fatal cases of scarlatina, as against seventeen years in which no fatal cases were recorded from measles. Figure 61 (to be compared with Fig. 37 †) gives an insight into the matter.

Scarlatina is also a more permanent disease in those regions continually visited by it than is the case with measles.

The connection between the individual cases is not altogether easy to recognize. Possibly the tenacity of the poison is the causal factor, and its adherence to inanimate objects in company with which it is brought into conditions favorable to its transmission is of great importance. *It must not, however, be forgotten that an apparently simple angina may be nothing else than a subdued expression*

* From Hagenbach, "Epidemiologisches aus Basel," "Jahrbuch für Kinderheilkunde," N. F., Bd. IX.

† Compare "Measles," in this volume, page 256.

of the scarlatina poison. May the continuous connection be inter-
preted in this way? I am of the opinion that we have just as little
right to deny this, as to assert it as a fact.

We are concerned here, as in many of the infectious diseases, with
an unsolved problem. What causes the spreading of the disease
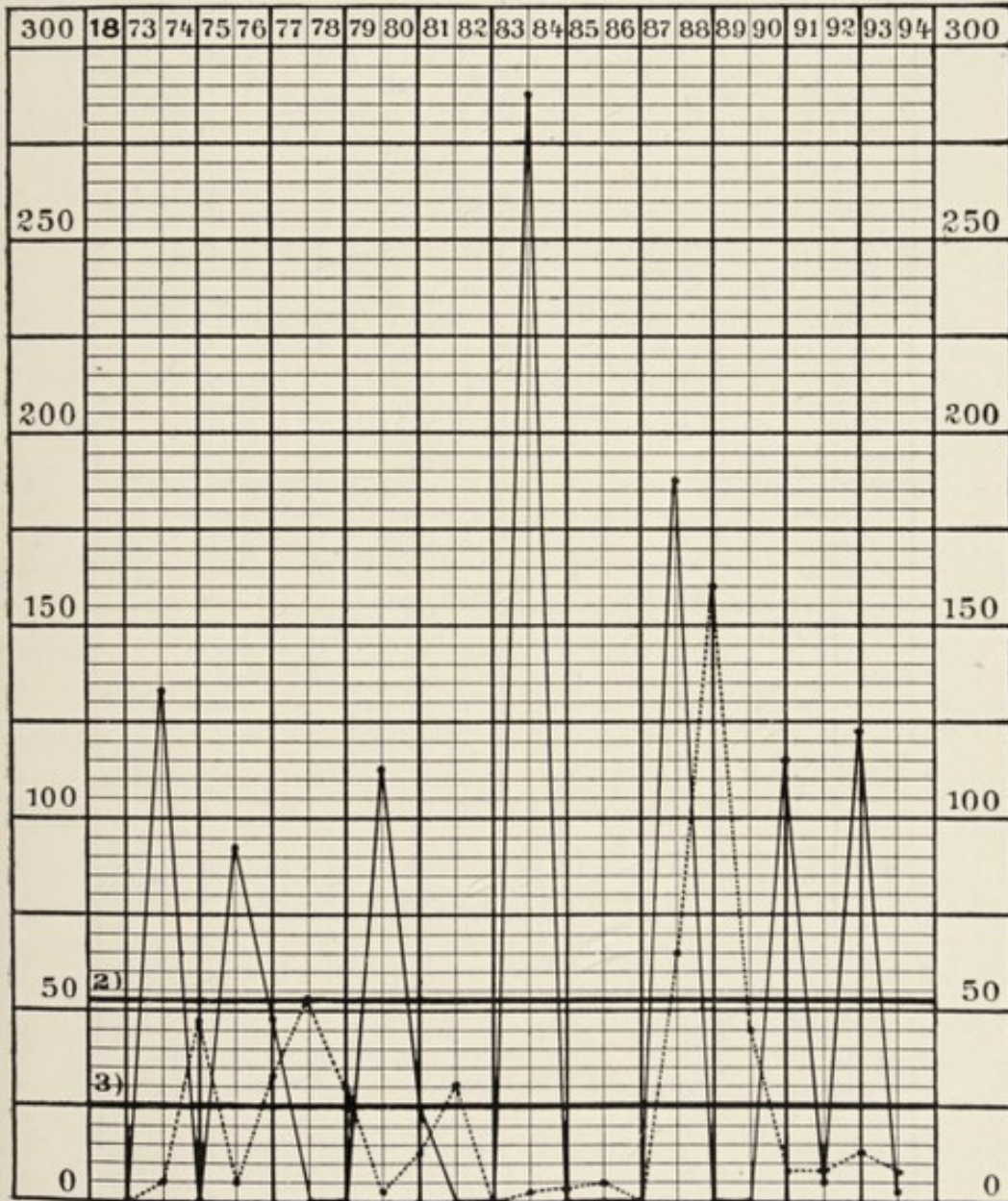
FIG. 59.—Scarlatina cases (. . .) and measles cases (━) in the Tübingen Policlinic in 1873-1874. 2, The
line of the year's average for measles ; 3, the line of the year's average for scarlatina.

beyond all bounds—its appearance in the form of a plague? How
does it come that certain living principles, which have certainly
existed as such for a long time, now and then assert themselves in
overwhelming force, destroying other forms of existence?

Since we have learned to recognize the causes of the infectious diseases as living principles, they must be considered as such: grasshoppers, butterflies, cockchafers, mice,—and whatever else may fall as a plague on mankind,
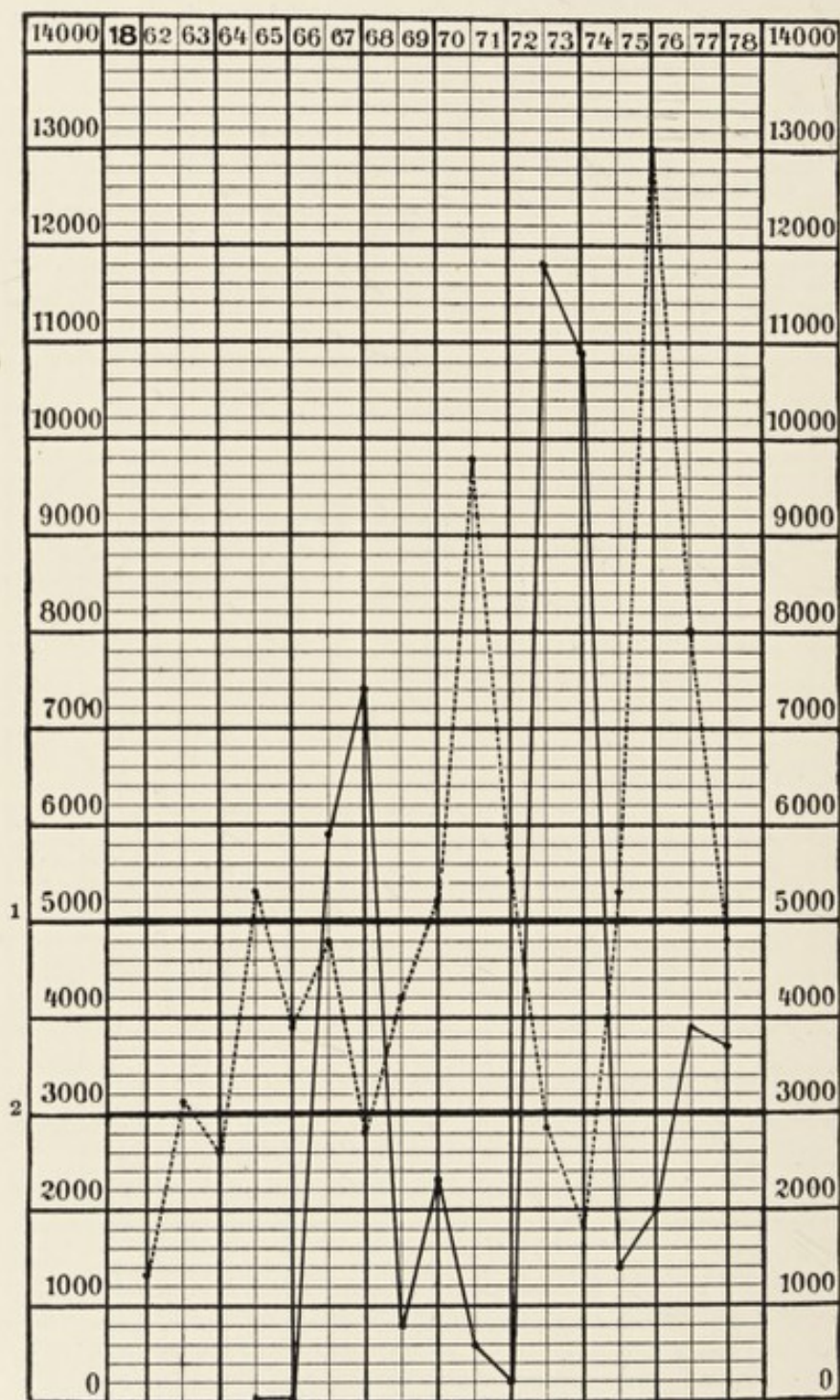
FIG. 60.—Scarlatina cases (. . .) and measles cases (━) in Norway from 1862 (1865) until 1878. 1, The yearly average for scarlatina (5000) ; 2, the yearly average for measles (3000).

—must be treated in the same fashion. Therefore it was highly proper to make the attempt in Norway to study the influence of the tormentors, the field-mice (Hypudæus), and the traces they leave behind in connection

with the spread of scarlatina, which is also a plague upon the people. Of course, such an investigation must be carried on with all the discretion required by the difficulty of the question. Johannessen,* who interested himself in the subject, gives the following facts: The years in *which the field-mice (Lemminge) have been evident, have in fact frequently been scarlatina years.* He brings as evidence of this the period from 1852 to 1877. Zoologic studies by Robert Collet are also adduced, which conclude "that unknown conditions presented in certain years that are favorable to an enormous progeny from a single pairing,—viz., of field-mice,—also the simultaneous generation from other and entirely independent pairings, bring it about that the cause cannot lie in the specific conditions of one pairing, rather must be sought for in the general condition of affairs."

If we wish, now, to condense the matter, we obtain the conclusion *"that in certain years especially favorable conditions present themselves for the development of organic forms that possess temporarily a strong vitality"* (Johannessen).

This view is certainly interesting, but takes us not much further on our way. So far, we must admit that we know absolutely nothing *of the causes that are responsible for the extension, and for the dangerous nature of scarlatina epidemics.* We are only in a position to assert *the unique nature of the scarlatina epidemic.* Hirsch † well says with reference to it:

1. *" When once the disease has attained to the epidemic form, it continues not rarely for several years in more or less extensive circumference, and then frequently secures an extension reaching over a wide territory."*

Fig. 61.

He offers as evidence a series of incontestable facts.

This was the order of things in the following years of scarlatina:

1825 and 1826 in Denmark, England, Germany, and France.
1832 to 1835 in the above countries, and also Ireland and Russia.
1846 to 1849 in Denmark, England and Scotland, and Germany.
1821 and 1851 in North America.

In the occasionally afflicted regions, in the east of South America, 1831 to 1837.

One cannot discuss the *recurrence in relation to certain periods,* as has been claimed for certain localities. So soon as we deal with the more general conditions, it becomes evident that accident alone has
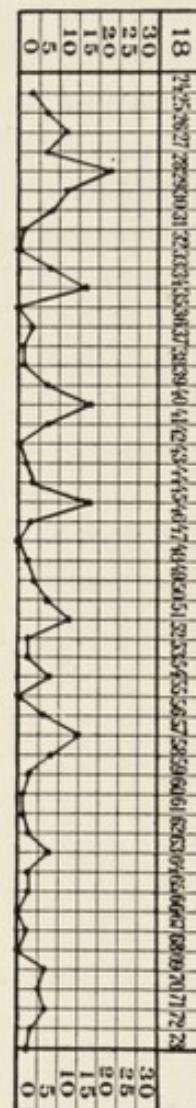
* *Loc. cit.,* p. 130.　　　　　　† *Loc. cit.,* p. 129.

been at play, where we had believed that we might find a positive principle.

2. "*A peculiarity of scarlatina shows itself in the varying intensity of the disease, most pronounced in the height of the relative mortality, which is almost zero, or involves a small number of all those attacked (3% to 5%) in certain epidemics, while in others it reaches 3% and over.*

This changeability in the severity of the disease shows itself, moreover, not only in the single consecutive local epidemics; rather within wider limits embracing a number of epidemics. It also becomes evident in pregnant fashion by a comparison of the intensity of the disease in neighboring localities or in wider territories that are simultaneously afflicted."

We need not seek for proofs of the correctness of these statements. It sounds remarkable to us coming from England, a land that later was so severely infected, to hear Sydenham,* one of England's best-known physicians, in describing his form of treatment, say: "Simplici hac et naturali plane methodo, hoc morbi nomen (vix enim altius assurgit) sine molestia, aut periculo quovis facillime abigitur."

The condition of affairs in Norway has been made intelligible by Johannessen.† Scarlatina takes an important place among the causes of death in the population, there being credited to the disease (1867 to 1878) 6.6% *of all the deaths.* The mortality varies, however, in the different years between 2.1% (1874) and 12.5% (1876) of the total number of deaths.

Still more marked was the variation in Basle. Out of every 1000 deaths during the fifty years from 1824 to 1873, there was an average of 5.1 deaths from scarlatina.

Apart from the fact that fourteen years presented *no fatal cases of scarlatina,* the relative proportions in the epidemic years were as follows: From 1000 deaths, the epidemic of 1828 gave 24.4; from 1000 deaths, the epidemic of 1872 gave 3.9. The difference is more than a sixfold one.

Hagenbach demonstrates by statistics apropos of Basle, the fact that within longer spaces of time embracing a number of epidemics the malignancy of the disease also shows a variation.

In the first twenty-five years (1824 to 1848) there were 6.2%, and in the second twenty-five years (1849 to 1873) 4.1%, fatal cases of scarlatina per 1000 dying from all causes. These facts have been confirmed, moreover, by the most prominent physicians, although they submit no direct evidence with their statement.

* Opera omnia, Tom. prim., Sectio septa, Cap. secund.   † *Loc. cit.,* p. 137.

Trousseau * reports the following: Bretonneau had for a quarter of a century seen only light epidemics of scarlatina—"then it suddenly altered its character and struck grievous blows."

Graves relates that in Dublin from 1801 to 1804 severe epidemics had arisen, and during the following twenty-seven years the disease was most benign; then followed again malignant epidemics, which reached their climax in 1834 and 1835.

Johannessen cites many examples from the Norwegian reports, which assert how *various the character of simultaneous epidemics can be in localities lying close to one another.*

It would be worthy of marked consideration *if in the same district, and in the same year, two different infections could produce two epidemics of dissimilar nature.* Johannessen gives instances even of this, though I consider them not a convincing proof. For even were it admitted that the infection succeeded, according to the supposition, we must always raise two objections:

1. The possibility has not been excluded that the previous epidemic has again flared up, without a new infection. In this way it can alter its nature—and from a malignant become a benign epidemic, or vice versa.

2. Since we can by no means—Johannessen himself offers proofs of this —say that a light attack is transmitted from a lightly involved scarlatina patient, or that from a severely ill scarlatina subject a severe illness follows, the authority is lacking to form a judgment even when the right to do so appears to be present; as if, for instance, a light epidemic had passed by, and now a severe epidemic follows infection through a serious case.

Under the ordinary conditions of civilized life the schools play a foremost rôle in the transmission of the disease. The conditions are practically the same as in measles. A difference perhaps consists in the fact that on account of the tenacity of the scarlatina poison, it is difficult to drive it out of the schoolrooms into which it has once entered. And yet I have found no observations applying directly to the schools.

The *temporary gathering together of large bodies of people* may, if the germ of scarlatina is carried among them, of course favor the spread of the disease to the same degree as occurs in the schools. But the great immunity afforded by advancing age always retards, and in a marked manner, the infection of the masses.

Johannessen † cites several writings on the subject. In many localities in Norway which are thickly populated observations of this kind can be instituted with a degree of accuracy.

The attempt has been made to discover certain relations between scarlatina and other infectious diseases, but without success. The

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* "Medicinische Klinik," Bd. i, S. 95.   † *Loc. cit.*, p. 159.

comparison of the reports of the disease yields far better results: "*Scarlatina epidemics form the conclusion for no other epidemics, and are not driven out of existence by any other contagion.*" *

The significance of scarlatina as one of the *general infections* is certainly very great. We must always call attention to the fact, however, that especially the child-world suffers from the disease. Such serious catastrophes as measles has called forth in Iceland throughout the entire population seem to be an impossible thing for scarlatina. On the other hand, one must not forget that many a man has brought out of his attack of scarlatina permanent lesions, and borne many forms of disturbances far into old age.

[**Bacteriology of Scarlet Fever.**—Pearce,† after a very complete study of the pathology of scarlatina, has nothing new to advance as to the actual cause of the affection. The secondary inflammatory lesions are due to the Streptococcus pyogenes, Staphylococcus pyogenes aureus, and pneumococcus, in this order of frequency. The streptococcus, in addition, is found most frequently in the throat and nose and in general infection. We are unable to state whether the toxins formed in this disease are due to its essential cause or are the products of the secondary infecting organisms.

Baginsky ‡ states that it is difficult after his experience to recede entirely from the position that scarlatina is due to the streptococcus, and that the latter by no means represents a secondary infection following in the wake of some other germ-disease. In discussion (the paper was read before the Berlin Medical Society) Heubner admitted the constant presence of the streptococcus, but was not satisfied with the results of animal experiment. Slawyk had failed to find this micro-organism in some cases at the outset of the disease. Wassermann stated that if Baginsky is correct, scarlet fever is always a septic process. The possibility that the exciting cause of the disease may be an extremely minute micro-organism should not be lost sight of.

Class's "Diplococcus scarlatinæ."—Class § holds that the diplococcus described by him in a series of papers is the actual cause of scarlatina, because it is invariably present in the throat secretions, blood, and scales of patients with the disease; because it possesses an individuality which differentiates it from all other micro-organisms; because it is pathogenic to experiment animals, and in one species

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* Gutmann, *loc. cit.*, p. 19.　　　　　† "Boston City Hospital Reports," 1899.
‡ *Deutsch. med. Zeitung*, 1900, No. 50.
§ *Jour. Amer. Med. Assoc.*, Feb. 24, 1900.

of animal (the pig) the resulting disease corresponds closely to human scarlatina; because the blood of scarlatinous convalescents inhibits the growth of the germ; because it can induce nephritis in some animals (guinea-pigs).

In Class's paper he shows that injection of convalescent blood into an experiment animal apparently protected the latter from contracting the disease.]

PATHOLOGY.

OUTLINE OF THE DISEASE; SEVERE AND MILD FORMS.

The symptom-complex of scarlatina is so little that of a single affection that I consider it proper to describe it in its general outline, and then to give single pictures of what we observe directly from the sickbed.

Simple scarlatina (I wish to reserve this title for those cases in which all the disturbances are produced by the poison itself, but in which no one symptom, predominating over the others, rules the case) runs approximately the following course:

The period of incubation presents no symptoms worthy of mention. Usually it is altogether undisturbed, only now and again appearing a slight indisposition, a tired feeling, depression, loss of appetite; in the case of children, a loss of the desire to play, and, in short, they are "not up to the mark," according to the common expression. The mothers say to the physician that there must be something the matter with the little one—but what? That, not even he is able to ascertain. Only when an epidemic is in progress is one likely to think of scarlatina.

The invasion almost always then appears suddenly with marked changes in the condition, that assert themselves in short order—repeated chilly sensations, or a severe chill, headache, dizziness, and confusion increasing even to stupor, perhaps even convulsions, vomiting, and rises in temperature, which in a few hours reaches a high level. As accompanying symptoms of the general disturbance are heard complaints of the dryness of the skin, burning sensations, and actual pain in the throat that is increased on swallowing. The pharyngeal mucous membrane is red and swollen and the tonsils and submaxillary glands soon become somewhat enlarged.

With rising temperature and increasing nervous symptoms the *exanthem begins to appear*, first showing itself under the clavicles and on the upper portions of the chest, and then extending continuously. The neck, the extensor surfaces of the limbs, the joint areas, the hands and feet, are the most vigorously attacked, the face and the hairy portions of the head the least. The face is, however, as a rule, markedly puffed up and flushed; only the portion around

the mouth appears pale. All this presents a picture peculiar to itself.

The eruption consists in the very beginning of tiny red elevations about the size of a pinhead, which appear in close arrangement upon the skin, which is, on the whole, still of a natural color. This rapidly puffs up, however, and becomes flushed, the single foci run together, and there appears the uniform, almost scarlet, more or less dark color, which, because of the tiny elevations that have been present from the beginning, does not appear altogether regular.

The inflammation increases upon the mucous membrane of the pharynx, and there appears an eruption similar to that of the skin. The alteration in the tongue is pathognomonic. It has already become swollen, and has, especially in the middle, a grayish-yellow coating of closely adherent, overgrown epithelium. It is now red on the edges and at the tip, and over the remaining portions the swollen papillæ project their red points, breaking through the grayish-yellow layer from beneath. In a comparatively short time this appearance changes. The coating entirely disappears, the whole tongue is of a scarlet-red color, the papillæ as a whole are swollen and project above the surface like little uvulæ. This is the *raspberry,* or *cat's tongue.* It is invariably dry. Upon the *tonsils,* and perhaps also upon the arch of the mouth, appears now a coating of gray, often tinged with brown, and quite adherent. In the beginning this consists of separate patches which promptly run into one another. The nares are frequently slightly swollen, there is a slight reddening and secretion of the conjunctivæ, slight râles are heard in the larger bronchi, and there is a tendency to a cough that has now and then (at least for a time) a croupy sound. The latter is not an invariable symptom, but is of frequent occurrence. On the other hand, it is a constant rule that, in addition to the glands of the neck, the other lymph glands become markedly swollen to the touch—especially those in the groins and the axillæ. These appear slightly tender on pressure. The *urine* often gives a trace of albumin, and epithelial cells from the renal tubules may be noted.

When the eruption has once spread over the entire body, the changes in the mucous membrane and in the glands reach their height. The general symptoms, and the fever in especial, have subsided at a somewhat earlier time.

Now begins the *desquamation of the skin,* which, starting from the neck at the point at which the eruption first appeared, proceeds just in the sequence that the eruption has followed. On the neck,

the face, the head, and the trunk, and on the upper portion of the limbs, only small fragments of skin are separated; on the hands and feet, however, and particularly on their inner surfaces, large, continuous pieces come away. At the same time the involvement of the pharynx and the swelling of the glands subside. *The fever disappears, but, like all the other symptoms, gradually, and only in exceptional cases by crisis.*

A more accurate timing of cases that we may characterize as "normal" can hardly be given. A complete return to health requires a considerable period. It is important for the physician to know that not only during the gradual disappearance of the symptoms of the disease, but as well during the convalescence, many forms of disorders can appear. Slight, temporary rises of temperature often occur without any recognizable cause.

Edema and nephritis, frequent as they are, do not belong necessarily to scarlatina. They need, therefore, only be mentioned here.

First of all, an instance from the sickbed:

OBSERVATION I.—Paul B., ten years of age. This great, strong child was perfectly well on July 1, 1878. In the night of July 1st he came crying about daybreak, between two and four o'clock, to his parents, hardly able to speak, and complaining of a severe sore throat.

When first seen, his temperature was 40.5° C. (104.9° F.),—8 A. M. of the same day, about four hours after the invasion,—the eruption of the chest and back already developing. Tongue thickly coated, but still free at the back and on the edges. Papillæ not visible.

Second day of the disease: Very high fever, up to 41.2° C. (106.1° F.). Marked swelling of the glands of the neck. In the evening, vomiting.

Third day: Continually high fever, up to 41.0° C. (105.8° F.). Thick coating on the right, much less on the left tonsil.

Fourth day: The thermometer registers only 40.4° C. (104.7° F.). The tonsils are considerably swollen; the coating, however, has nearly disappeared. Complains of pain in genitals; objectively, nothing abnormal. Urine, examined at once, is normal.

Fifth day: Maximum temperature only 39.7° C. (103.4° F.), minimum 38.8° C. (102° F.). The exanthem developing as usual, begins to pale.

Up to the eighth day of the disease the fever has gradually subsided. The mean was lower, the maximum 39.7° C. (103.4° F.), minimum 38.5° C. (101.3° F.). The general condition was good. The patient had been well enough to be taken out of bed, and examined standing. Tonsils markedly swollen. Complains of pain in elbows and shoulder-joints; objectively, no signs. Desquamation begins.

In the morning still pain in the elbows and shoulders; in the evening only in the axillæ. Swelling has left the glands, even in the latter region. Only the tonsils remain large.

Up to the sixteenth day there is a diminution in all the painful symptoms. "The patient is kept in bed with difficulty." From the twelfth day, again, evening rises of temperature to 38.5° C. (101.3° F.). The urine always free from albumin. Discharged twenty-eight days after

the beginning of the disease. Everything normal subsequently. The temperature readings, taken at first every two hours, are shown in figure 62.

The case may be termed a moderately severe one, and corresponds to the requirement that none of the symptoms should predominate over that of the genuine scarlatina. The pains in the limbs were of too little moment to warrant our speaking of them as a complication. I wish, however, to call attention to the behavior of the temperature —one that is very frequent in the somewhat severe cases of scarlatina. After the attack has been overcome there is for some time a tendency to a rise above the normal.

Let us now proceed at once to the severe cases, ending in death

Seventh day of the disease.
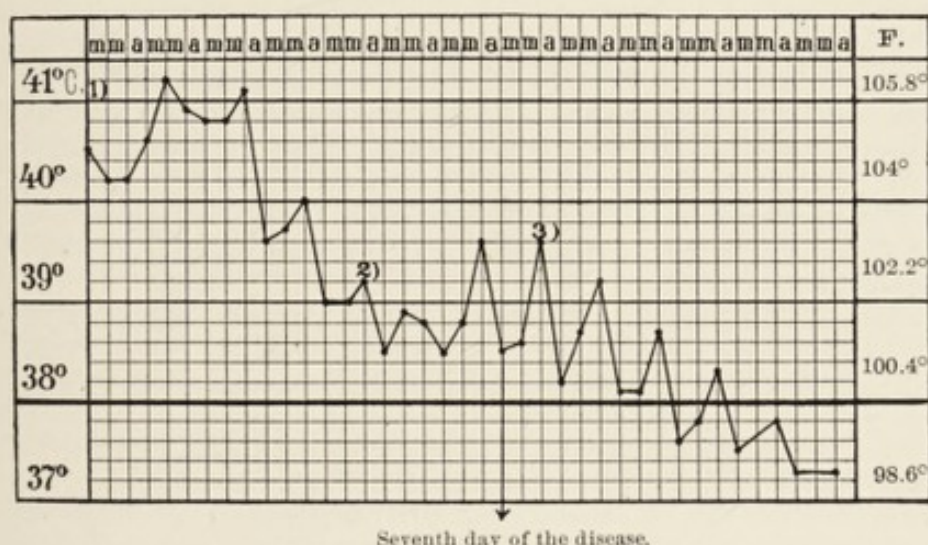
FIG. 62.—1, Eruption already apparent; 2, exanthem begins to fade; 3, joint pains.

in a short time, and in which the poison shows its presence otherwise than by its local changes.

I give here a number of cases from my own experience:

OBSERVATION II.—Gustav M., two years old. His father died of tuberculosis. His ten-year-old brother has been treated since November 19th for scarlatina.

Beginning of the disease on December 12, 1888, in the morning about 8 o'clock, with repeated severe vomiting, and fever. Seen by me at 11.30 A. M. Child is well nourished. Entire face is red and somewhat bloated. On the thorax, especially posteriorly between the shoulder-blades, is the scarlatina exanthem in its first stages. The inguinal lymph glands, and rather more markedly the glands of the neck, especially in the neighborhood of the angle of the jaw, are swollen.

Marked redness of the pharyngeal mucous membrane, moderate swelling of the tonsils and tongue, corresponding to the beginning of scarlatina.

The child remained sitting on the table during the examination and gave by no means the impression of being severely sick.

This continued until evening, when, on the physician's visit, only the

faint pulse, with a temperature of 39.8° C. (103.6° F.), appeared worthy of attention.

In the night the little one got out of his bed into that of his mother, slept there with interruptions, but otherwise quietly, drank wine eagerly, and in doing this carried the glass in his hand to his own mouth.

In the morning, at 7.30 o'clock, he had, on asking for it, wine and milk. The temperature, taken at 8 o'clock A. M., was only 38.4° C. (101.1° F.). From 9.30 o'clock on, the mother noticed that the breathing was shallow; at 10 A. M., following several convulsive movements of the arms, death quietly took place, twenty-six hours after the beginning of the disease.

And what did the autopsy show?

(Extract from the protocol: prosector, Prof. Nauwerck.) Ecchymoses in great numbers upon the skin, pleura, and epicardium. The lymph glands throughout the body moderately but distinctly enlarged, moist, and violet in color. The blood only slightly coagulated, mostly fluid. The right heart somewhat dilated, the cardiac muscle pale. Spleen one-third larger than normal; liver moist, anemic, grayish-red and grayish-yellow in color. The kidneys somewhat anemic, moist, otherwise entirely unchanged. Gastric and intestinal mucous membrane anemic, otherwise normal. Pharynx and throat: "Mucous membrane of the pharynx, and of the entrance to the larynx, of an intensely red and violet-red color. The aryepiglottidean folds somewhat edematous, the entire mucous membrane somewhat swollen, and especially that of the uvula.

"The tonsils moderately enlarged and, on section, appear a spotted grayish-yellow and gray-red color; a purulent fluid can be scraped from the cut surface of the section. The surface is discolored a turbid, greenish-yellow, or rather a dirty brownish-black, to the depth of a millimeter. Moreover, the reddened mucous membrane of the uvula, the arch of the mouth, the pharynx, the ostium laryngis, are covered with firm, opaque, gray scales, that can be partly separated, whereupon the intensely red mucous membrane comes better into view. On the epiglottis there is, and especially on the free edge, a grayish-yellow eschar penetrating into the tissues. The mucous membrane of the larynx and the trachea is reddened; the vocal cords are uninvolved."

In regard to the lungs it is noted that their bronchi, even to the finest subdivisions, are intensely red, and filled with a dense grayish-red fluid. This extends on both sides over the bronchial tree.

Brain: The sinus longitudinalis contains considerable clotted and fluid blood. The dura shows nothing of interest. On the right the gyri are flattened, the sulci obliterated, the larger and medium-sized veins are full, the remaining surface is also flattened. To the left the same condition, as also at the base of the brain. The soft membranes of the brain everywhere normal. The lateral ventricles are not markedly enlarged. The brain substance is moist, shiny, edematous, and its consistence decidedly lessened. A moderate number of extravasations. Edema is also markedly in evidence on the basal ganglia, the latter being somewhat anemic. The cerebellum likewise is highly edematous.

OBSERVATION III.—Marie V., eight years old. Previous history: When two or three years old had measles, afterward typhoid fever. In her fourth year diphtheria. Since then perfectly well. On June 17, 1878, she was with her parents in the fields, happy and cheery, without a sign of present or impending illness. Next day at noon she ate five or six unripe

apples and drank a good deal of new cider. The child then went to bed well, and slept soundly the entire night.

At 4.30 A. M., June 18th, she waked with a desire to stool, went to the closet, and then lay down again in bed.

A short time afterward the bowels moved twice in the bed. The passages were quite yellow, like "scrambled eggs," contained neither much mucus nor any blood. Pain in the belly was entirely wanting. The mother gave her camomile tea.

At 9 A. M. again a copious movement in the bed, and again at 10 o'clock.

At this point she came into my charge: The child lies rather limp, the face is pale, there is no exanthem upon the skin. Marked swelling of the tonsils, but no membrane. The tongue is highly coated, its papillæ are hardly swollen.

Nothing noteworthy in the lungs; only posteriorly, above and on the right side, an impaired percussion resonance, but no abnormality on auscultation.

The patient in spite of the high fever (40.4° C.; 104.7° F.) is fully conscious: replies intelligently to questions, stretches out the tongue when told, etc. After the examination the child was again put to bed.

Repeated diarrhea at 12 M. and 2 P. M., the last being of a very foul odor.

Up to this time the child was fully conscious, speaking with its mother. From 2 to 5 o'clock it was unconscious, lying for the most part with closed eyes, opening the same when spoken to, but giving no response.

At 5 o'clock it recovered consciousness, took milk and wine, and even played with flowers that had been brought to it. This continued only until 5.30 o'clock.

At this time the physician made his visit. The history sheet reads: "The child appears much changed from the morning. Especially marked is the cyanosis of the face and lips. The nose is cool, and the pupils still react, though contracted. The pharynx is very easy to examine, the introduction of the spoon producing no choking or gagging. The tonsils, especially the left, are covered with yellow areas, as in follicular tonsillitis. Everywhere over the abdomen is a loud rumbling. The lungs are in the same condition as in the morning.

"The patient shows marked stupor, responding to questions either not at all, or only with an unintelligible answer. She does not know what day it is, though she seems to recognize her mother, and stretches out her tongue when told, though very slowly, and evidently with difficulty. At times there is rolling of the eyeballs.

"There is no exanthem present, the left leg alone appearing slightly red in comparison with the right. As the temperature remains high (at 4 o'clock, 40.5° C.; 104.9° F.), baths are ordered, and at the same time champagne. At 6 o'clock the first bath is given, lasting eight minutes, in water taken directly from the spring. During the bath the child recovered itself so far as to say repeatedly that it wished to get out; further than this, however, it said nothing. Immediately afterward a little wine was taken without difficulty, but soon the condition of stupor returned.

"At 8 o'clock, with a temperature of 41.9° C. (107.4° F.), the second bath had the same result. At 8.30 the father came home. He spoke to her, but she did not recognize him and talked only in an incoherent

fashion. Then she tried several times to spring out of the bed. The respiration was at times quiet and restful, then again hurried, and audible throughout the room.

" From 10 o'clock on a decided change for the worse. The child twisted itself and raised itself up, and again severe diarrhea set in, together with active vomiting; the face and hands became cold, and the hands blue. The thumbs were turned in, the pulse became inappreciable. Delirium appeared. Champagne, given in smallest quantities, was, like everything else, immediately vomited, the vomitus containing bile and mucus. Toward 11 o'clock the limbs again became warm and the pulse perceptible, but too fast to count. From this time on the patient uttered no sound. The diarrhea increased steadily. Vomiting now only followed paroxysms of choking. In the early morning hours she ceased swallowing, there were several convulsive movements of the arms, a half hour before death the whole body raised up, then perfect quiet—the pulse barely perceptible, the respirations weaker and weaker. At 8 A. M. death came, *twenty-eight hours after the invasion.*" Figure 63 shows the progress of the fever.
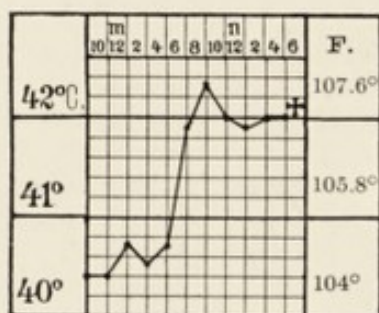
Fig. 63.—Taken from about the fifth hour of the disease on.

It remains to state that in the same house, though in another family, a six-year-old girl fell ill on June 16th, of scarlatina, with a marked eruption. The course of the disease was one of moderate severity, which recovered in four weeks without interruption.

The autopsy (Prof. v. Schüppel) showed: The body poorly nourished, the skin a deep brown, with extensive bluish-red death spots appearing on the back, the neck and shoulders, to a certain extent on the breast, also on the back of the legs and on the feet. In these spots a number of dark petechial points were to be seen. No typical eruption was present. Marked rigor mortis of the lower extremities; this had already disappeared from the upper. The feet decidedly extended owing to contraction of the calf muscles. The muscles pale, but presenting nothing further of interest.

The lymph glands in the neck considerably swollen. The cervical veins full of firmly coagulated blood. The mucous membrane of the mouth and pharynx covered with turbid mucus and with reddish spots. The tonsils project as pale red masses, the size of a cherry, their follicles filled with yellowish, somewhat solid, and to a degree membranous masses; otherwise no membrane on the surface. The follicular gland tissue on the dorsum of the tongue is very prominent, and especially the follicles on the posterior pharyngeal wall, and still more marked is the swelling of the so-called pharyngeal tonsil. This is so decided that it half closes the upper portion of the pharynx and forms a layer of tissue almost a half centimeter thick, which appears to separate into distinct leaves, or longitudinal folds.

From the cut surface of the tonsils the swollen follicles project distinctly; the lacunæ are full of thick plugs of caseous material.

The cervical lymph glands are fully the size of a cherry, firm and very juicy, the tissue pale brownish-red, partly whitish-yellow, but moist, and full of small lymphoid vesicles.

The mucous membrane of the larynx and trachea shows only a moderate swelling and redness.

The thyroidea and thymus are normal.

The lungs are extremely distended, collapse very slowly, and their anterior edges are in opposition. The pleural cavity empty.

In the visceral pleura a number of fresh ecchymoses; several lobules, especially in the lower lobe, are collapsed or infiltrated with inflammatory exudate. The upper lobe of the left lung full of air, moderately full of blood, more congested from behind forward. The lower lobe is in much the same condition, except that a number of the superficial lobules are poor in, even to absence of, air; there is a solid infiltration, dark blood-red in color, and the tissue itself, as well as the overlying pleura, shows fresh ecchymoses.

In the larger bronchi is a quantity of tenacious, turbid mucus, the mucous membrane being a light red. The smaller bronchioles and the bronchial glands normal.

The right lung corresponds to the left. It is everywhere full of air; at the base a few collapsed, dark bluish-red lobules, and on the posterior portion of the lower lobe a small, air-empty, hemorrhagic, infiltrated focus, with a pale area in the center.

The bronchi similar to those of the left side.

The pericardial sac normal. The heart contracted. The left ventricle empty; in the left auricle some partly coagulated blood; in the right heart, large, white, moist fibrin clots. The valves and great vessels in all respects normal.

The cardiac muscle pale brownish-red, firm, and hard.

The abdominal cavity devoid of fluid.

The liver of normal size. On its surface are seen, besides a number of very pale, anemic spots, also numerous, thickly arranged, sand-grain-sized white nodules, which in part follow the course of the capsular vessels in the form of a sheath, and give the appearance of lymphomata. These nodules, and especially their arrangement in columns following the course of the vessels, are noticed also in the liver tissue itself. The hepatic tissue is, moreover, in a measure congested, of normal consistency, and, according to the irregular distribution of the contained blood, is of a pale yellow to a dark reddish-brown color. The gall-bladder is distended.

The spleen measures 13 cm. (5¼ in.) on its convex surface. It is correspondingly broad and thick, its capsule distended. The splenic tissue is of normal consistency, contains the normal quantity of blood, the follicles are closely arranged, and there is a marked lymphatic infiltration.

The kidneys are somewhat swollen and slightly flabby. The venous network on the surface highly injected, and here and in the capsule fresh ecchymoses. The organs are throughout anemic, the cortex yellow-brown, giving off quantities of epithelium. The pyramids are anemic. In the mucous membrane of the pelvis a number of small ecchymoses.

The mesenteric lymph glands are invariably considerably swollen, to the size of a hazelnut, and are soft, juicy, and of a whitish color.

The mucous membrane of the esophagus is intensely red and excoriated.

In the stomach is a small quantity of grayish-green fluid. The mucous

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membrane is slightly swollen, pale gray in color, somewhat ecchymotic, and covered with bile-stained mucus.

In the small intestine very many ascarides and scanty fecal masses. The smaller worms are actively motile; the mucous membrane is in these places of a catarrhal red color, and ecchymosed. Peyer's patches and the solitary follicles are large, swollen, and ecchymosed. The mucous membrane of the large intestine is everywhere grayish-red and highly injected. Also in the beginning of the large bowel a packet of ascarides, as well as innumerable trichocephali.

The roof of the skull normal in blood supply.

The dura mater very fragile, dry, and its sinuses, as well as the veins of the pia mater, distended with blood. The convolutions of the brain distinctly flattened from pressure; their surface likewise is dry. At the base of the brain, as well as at the entrance of the spinal canal, the membranes appear perfectly normal.

The brain substance is soft, markedly edematous, almost of pulpy consistence, altogether anemic, and only the larger vessels are filled. The cortex likewise markedly swollen. The ventricles moderately dilated and containing clear serum.

The ependyma normal. The fornix macerated.

The large ganglia and the cerebellum likewise edematous.

OBSERVATION IV.—Marie H., three and three-quarter years old. Besides measles, no previous illness. No tuberculosis in the family.

On July 1, 1890, the child was brought home at 2 P. M. from school, where it had suddenly become ill, with severe vomiting. This continued at home, and once there passed a thin stool.

When seen by the physician (7 P. M.—five hours after the invasion) the following was noted:

Child well nourished, with slightly cyanotic appearance. The abdomen is markedly distended. Heart and lungs normal (respirations 22, pulse 166). The child seems dull; is, however, perfectly conscious, and says that she has no pain. Since her younger sister is ill of scarlatina, she is examined for an exanthem, but nothing is found. (Nothing is noted in the history sheet in regard to the pharynx, the glands, etc.)

From the prescription (small doses of calomel) it may be assumed that summer diarrhea was suspected.

On the morning of July 2d: During the night a distinct scarlatinal exanthem has appeared. The glands of the neck are slightly swollen, the tongue covered with a yellowish-white coat, from which the follicles project like red asparagus tops. Slight angina.

The temperature falls at 8 o'clock (A. M.) to 37.6° C. (99.6° F.), the child feeling well. "The case is considered a light infection" is found on the history sheet. But it turned out differently. At 3 P. M. suddenly convulsions appeared, very severe and recurring; also active vomiting. This continued, so that at 10 P. M. the physician was called. At this time the pulse was 166, the respiration 46. The child lay unconscious, with wide-open eyes. The pupils were widely dilated, no longer reacting to light. There were tonic and clonic contractions in the muscles of the upper extremity; the thumbs were turned in, the remaining fingers in "claw position." The feet were extended. The mouth closed, and without force impossible to open (*trismus*). In a warm bath the convulsive movements became suddenly more active, so that the whole back was contorted into a posteriorly convex arch (*tetanus*). The attack gradually

subsided, though during the half hour that the physician was present the child was never free from convulsive movements, which only ceased a quarter of an hour before death. Loud rattling in the trachea. At 11.45 o'clock death took place, about thirty-four hours after the beginning of the disease, and about nine hours after the appearance of severe symptoms.

Figure 64 shows the progress of the fever.

The autopsy showed (Pathologisches Institut, extract): The skin is still a distinct scarlet-red color, throughout which numberless closely arranged red nodules project. The pharyngeal mucous membrane intensely red and swollen. The tonsils swollen, their lacunæ filled with viscid plugs of purulent material. Nowhere are diphtheritic eschars or erosions. The membrane of the larynx and trachea is pale. The lungs everywhere full of air, in the lower portions markedly congested; moderate edema.

Pericardial sac and heart normal.

Spleen rather large, of firm consistence, its follicles distinctly swollen.

The liver without special abnormalities; also the kidneys, which are somewhat pale. Stomach and intestines show a pale membrane.

Marked swelling of the glandular elements in both large and small intestine.

The cervical lymph glands and those of the mesentery are enlarged—the latter to the size of a walnut, the former to that of a hazelnut, and of a grayish-red color.

The brain was not examined.

With regard to the result of the bacteriologic examination compare page 469.

Fig. 64.—1, Evening temperature of July 1st. The following temperatures are of July 2d.

I would like now to stop for a moment to consider these cases, because they present a clear picture of a scarlatinal poisoning, which, without any local involvement, leads to a rapid end. Each one is taken from a different year, representing 1878, 1888, and 1890. No one can therefore object on the ground of an "epidemic peculiarity" that has exerted an influence.

The sudden invasion offers no new feature, occurring in all, even the lightest forms. It must, however, be stated that the height of the fever by no means keeps pace with the severity of the infection. In Case II the temperature had a maximum of 39.8° C. (103.6° F.), and several hours before death of only 38.4° C. (101.1° F.). In Case IV a maximum of 40.6° C. (105° F.) was recorded, but after a short time, as death approached, the temperature fell to 39.4° C. (102.9° F.). Only in Case III was a high point suddenly attained—maximum 42.3° C. (108.1° F.)—and held until death.

Attention should also be called to the great variation in the symptoms.

This is true even in Case III. The child is at first fully conscious, is then for three hours unconscious, and recovers itself so far, though only for a short time, as to play with flowers. Throughout, the body-temperature remained at about the same point.

In both the other cases the sudden transition from an apparently mild case to one of the severest type is very striking. In Case II the exact time limits cannot be fixed; but it surely was of shorter duration than Case IV, and in any event lasted only a few hours. Then an absolutely peaceful death, free from all signs of the storm. During the nine hours that in Case IV came between the change for the worse and the demise, one convulsion followed another, and the excitation of the centers increased even to producing trismus and severe tetanus.

The local lesions that are peculiar to scarlatina, as such, were more or less completely developed in the same short time. The processes must be located preeminently in the lymphatic system: besides the swelling of the spleen, that of the glands in the various portions of the body; in Case III even the formation of lymphatic new-growths (first described by E. Wagner *) in the liver and spleen.

Then the involvement of the pharynx, in all the cases markedly shown, and especially permanent in the case (No. II) lasting for the shortest time.

The eruption on the skin was absent in Case III, but there is no justification for not including it as one of scarlatina. Apart from other reasons for this view, we have the presence of scarlatina in the same house, the features of the disease, its course, the report from the autopsy, and there is especially noted in the postmortem records a "spotted reddening of the mucous membranes of the mouth and pharynx."

The exanthem was therefore present here, also, although there was in truth only an atypical prodromal erythema upon the skin, as may occur in all the acute exanthemata. In Case II the eruption is slight; in Case IV, on the other hand, markedly developed, so as to be still visible on the corpse.

Of the organs that stand in direct relation to the sudden end, the brain should be mentioned before the heart. Certainly marked lesions were not discoverable in the latter, and although cardiac weakness was evident during the course of the disease, it was not a

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* "Beitrag zur pathologischen Anatomie des Scharlachs," *Archiv der Heilkunde,* 8. Jahrgang, S. 262.

permanent condition. The presence of excitation and also paralytic conditions (of the brain), on the other hand, was emphasized in the most forcible manner. Almost invariably in the infections that become suddenly fatal there is nothing noted in the brain except edema. I will only add that the condition usually classed among the "complications of scarlatina"—inflammation of the bronchial mucous membrane—in Case II was marked, and extended itself to the finer air-passages, while in Case III it was confined to the larger passages, and barely present there.

Bronchitis has taken so prominent a position in other cases of suddenly fatal scarlatina in my experience that it has at least—I will not say directly caused the death—hastened the fatal end. There are of these cases no fewer than four, all with a duration of two to four days. I will shortly enter into their discussion; but first the cases themselves:

OBSERVATION V.—Rosine R., five years old. The child has always been weakly, and has once suffered from an extensive and obstinate eczema of the scalp, repeatedly from bronchial catarrh; from pneumonia; and from bronchopneumonia, in the beginning of the present year. She recovered from measles, but a long-continuing bronchial catarrh followed (treated in the policlinic). Only in the summer had the child begun to get into proper condition.

On November 10, 1888, she was put to bed perfectly well, and cheerful and happy. On the 11th about 2 A. M. restlessness; the child wanted its father. The parents noticed that its skin was already hot. At 4 A. M. for the first time *vomiting*, which was repeated frequently during the course of the day.

Complaints of pain on swallowing, and pain in the upper portions of the chest. Cough—"the cough was not natural, the child giving the impression that it could not properly open the mouth." Thus the day passed. The anxious parents, who were well-to-do, thought that the little girl had again caught cold, although at 6 P. M. the temperature had already risen to 40.4° C. (104.7° F.). The policlinic was then consulted on the morning of November 12th; previously the deaconess had seen the child, as often occurs with us, and the temperatures which we have, previous to its coming into our complete charge, had been taken by the sister.

Result of examination about 11 o'clock:

The patient is by no means in a good condition. Especially striking is the cyanosis of the face; the skin on the other portions of the body is very pale. Respirations 36, pulse about 160.

The child shows a high degree of stupor, is apathetic, and limp; during the examination, which was made outside the bed, it needed to be supported on all sides.

The eyes are half open, staring into space without expression. The face and neck are somewhat bloated. The cervical and submaxillary glands are moderately, and in the inguinal regions not at all, swollen.

Nasal catarrh with seropurulent discharge; slight conjunctivitis.

In response to a loud command the child opens its mouth; the tongue

is covered with a thick, grayish-yellow covering; the papillæ are not visible. The pharynx is everywhere markedly swollen and red; the tonsils meet nearly in the middle of the isthmus faucium; behind them appears the swollen uvula, pushed somewhat backward. In certain areas on the tonsils, separated by large free spaces, a thin yellowish membrane.

The examination of the thorax showed nothing noteworthy beyond the apparently slight bronchial catarrh. Only on the left, a finger's-breadth beneath the nipple, a faint murmur, which it was impossible to designate as either râle or friction rub.

Splenic dulness: 6 to 10 cm. (2½ to 4 in.).

In the following hours, only the picture of a serious illness, without any predominant features.

About 11 A. M., November 13th: The cyanosis has markedly increased, hands and feet are blue and feet cold. The eyes show the same fixed stare. During the examination the child is more restless than yesterday, and offers resistance.

The pulse cannot be counted accurately—about 200; respirations 46.

Upon the tonsils, and especially on the right side, a continuous, dirty grayish-yellow membrane has formed; otherwise the mouth and pharynx present the same appearance as yesterday. The masses of mucus, collecting in the posterior part of the pharynx, impede now and again the breathing.

Fig. 65.—1 and 2, Midday and evening temperatures of the preceding day.

Upon the skin an eruption: not very thickly placed red spots, of the size of a pinhead and somewhat larger, that are slightly raised above the red and slightly swollen skin. The eruption is, on the whole, poorly displayed; the papules are most numerous in the lumbar and sacral regions, and here also the skin is most markedly reddened; also on the extensor surface of the arms. Papules and redness are present also on the face, except the region around the mouth, which remains pale.

The child discharges liquid stools in the bed.

Splenic dulness: 6 to 11 cm. (2½ to 4⅜ in.).

About 12.30 o'clock, without further symptoms, a quiet death—about two and one-half days after the commencement of the illness.

The progress of the fever is shown in figure 65.

Autopsy (Prof. Nauwerck) extract: Unusually marked death spots, especially on the anterior surface; very pale, edematous, bloated face, with cyanotic lips. Spleen double the normal size. The cervical lymph glands, especially about the angle of the jaw, the bronchial glands, and those in the ileocecal region are swollen. The lymphatic elements in the bowel, on the contrary, show no marked swelling.

Marked inflammation with necrosis of the pharyngeal organs.

Extensive adhesions of the pleuræ on both sides. The lungs still contain air, but right and left is an inflammation descending even into the finer bronchioles, with purulent secretion. The inflammation in the larynx and trachea is far milder.

The changes in the organs have reached absolutely no degree worthy of mention, and need not be further discussed.

OBSERVATION VI.—Karl H., four years of age. No previous illness, as far as his parents, themselves healthy, know.

The present illness began suddenly on the morning of December 14, 1888, with vomiting, and, during the course of the day, difficulty in swallowing.

On the 16th instant his family noted that his skin was red. When seen by me in the evening, he showed perfect consciousness, well-nourished condition, face puffed up, somewhat cyanotic. On both sides of his neck a decidedly swollen packet of glands. Slight nasal catarrh, the child breathing through the mouth. The pharyngeal mucous membrane swollen and red; upon the membrane of the markedly swollen tonsils a thin false membrane. The tongue red anteriorly, otherwise thickly coated. On the body a full-blown scarlatinal exanthem.

With every respiration were heard loud râles in the upper air-passages, and on auscultation over both lungs, large moist râles were audible.

On December 17th, A. M.: The patient is stupid. The face is very bloated and cyanotic; decided nasal catarrh with a free, serous discharge. Pharyngeal examination same as yesterday.

Marked dyspnea, with rhonchi in the larger air-passages increased in intensity over yesterday. The bronchial catarrh has extended, and on the right side a beginning consolidation is perceptible. Pulse 160, respiration 44.

During the examination the patient is weak and *prostrated*. A temporary improvement follows a cold douche in the warm bath, but at 7 P. M. death follows, with symptoms of dyspnea, after about three days of illness.

The temperature at its maximum was 39.6° C. (103.2° F.) (noon, December 17th); at its minimum, 38.3° C. (100.9° F.), four hours later, and three hours before death.

From the autopsy (Prof. Nauwerck), extract: Wide-spread death spots, the exanthem distinctly recognizable, mingled with petechiæ. Decidedly bloated, pale features with bleached, livid lips. In the neck the subcutaneous tissue is distinctly edematous.

Cervical lymph glands enlarged, and already infiltrated with pus; bronchial and ileocecal lymph glands only swollen. The spleen markedly enlarged.

The pharyngeal organs much inflamed; *necrosis* of the mucous membrane. The tonsils extensively infiltrated with pus, and in portions gangrenous.

In regard to the respiratory organs, I quote from the protocol:

"Mucous membrane of the larynx and trachea grayish-red, with occasional ecchymoses, and richly covered with purulent collections. The aryepiglottidean folds are slightly swollen. From the left bronchus comes rich, creamy pus, mixed with a few air-bubbles.

"In the pleura, especially that over the lower lobe, many tiny hemorrhages. The pleura at the base of the lower lobe, as well on the posterior and lower portions, is covered with a fibrinous exudate. The fibrin is in the form of transparent tubercles.

"The whole left lung is large, the bronchial mucous membrane intensely red. From the swollen bronchioles protrude everywhere plugs of purulent material.

"The upper lobes still contain air, are edematous and pale brownish-

red in color. Only the lingula is partly empty of air, atelectatic, and bluish-red; from the smallest bronchioles come plugs of pus.

"The lower lobe likewise contains air, more markedly edematous, somewhat more congested, various lobules posteriorly are atelectatic. In the lower lobe, posteriorly, a tubercular caseous focus, encapsulated by white connective tissue, and 1.5 mm. (0.06 in.) in diameter; also a small pea-sized lymph gland is caseous.

"On the right side: purulent contents of bronchus, also present in quantity.

"In the pleura a considerable number of hemorrhages, especially in the lower lobe. At the base of the latter is rather firm, but detachable, moist fibrin. Bronchial mucous membrane similar to the left side.

"The upper lobe presents the same appearance as on the left side.

"The middle lobe is devoid of air, dense, though relaxed to the touch, dark brownish-red with a grayish tinge.

"From the bronchi come profuse plugs of pus, and the fluid from the parenchyma is also turbid.

"The lower lobe contains air, is edematous, the pus-plugs are at this point considerably fewer in number."

The cardiac muscle of the left ventricle appears to show a cloudy change.

The alterations in the other organs are inconsiderable; the brain was not examined.

In Case II death occurred too suddenly for the extensive bronchitis to have been able to make itself evident, and in Case V it played a rôle secondary to the intoxication, though always asserting itself to a certain extent. But in Case VI, I do not hesitate to ascribe to the bronchitis a great, and perhaps deciding, influence upon the termination.

It is probable that the scarlatina poison also contributed its share, and its influence upon the brain must not be underestimated. But the picture that was made evident by the autopsy was one that we see in an extensive capillary bronchitis, with atelectasis and broncho-pneumonia. Just so in the two other cases, which I will not quote in detail at this time.

Such a severe involvement of the bronchi in the beginning of scarlatina is quite rare; at least one may say there are few reports on the subject.

I must call attention to the fact that of my cases, the greatest number fall in the year 1888, and in December. There is no record of severe epidemic catarrhal involvements in Lustnau, but here they were under observation. Yet we may speak of it as a peculiar feature of the poison that only temporarily asserts itself. It is probably only chance that will account for the finding in each case of old tubercular foci in the bodies of the four children.

Another report comes from Tübingen, of a six-year-old girl, July, 1889, in whom old tubercular foci were not present.

I add still another case, with a sudden fatal ending, in which severe gangrene made itself evident at an early date.

OBSERVATION VII.—John George K., eight years of age. No previous serious illness; merely a tendency to throat inflammation, lasting only for a short time. The mother has noticed for fourteen days that the child has "looked badly" and has been altogether less active and buoyant than usual. When she took him with her into the country, he went to sleep, and expressed a wish to go to bed earlier than usual. Attendance upon school was, however, not interrupted.

On June 10, 1878, in the forenoon he took no breakfast. Slept considerably during the entire day. Toward evening he became hot, and very thirsty, and simultaneously had vomiting and diarrhea. At night he was delirious, lost consciousness, and failed to recognize his relatives. If addressed, he turned his head around, but could not be induced to speak.

On June 11th, A. M.: Complete unconsciousness. The physician was able to see him only in the evening, because during the day the house was closed. From afternoon on, the deaconess was with the patient.

Condition in the evening: Wide-spread scarlatinal eruption. Tongue lightly coated, dark red on the edges, the papillæ only slightly swollen. The tonsils markedly enlarged and covered with mucus; no membrane. The cervical lymph glands decidedly, and those of the inguinal region considerably, enlarged. Lungs and heart show no specific changes.

Mind stupid: the patient offers the hand still, when told, but will not respond to a remark. Pulse 156.

June 12th: Cold baths were given during the night, following which the mind became clearer, though only temporarily, and toward evening it was again considerably clouded.

"The examination of the pharynx is difficult, because the patient presses his teeth together, and even by active pressure upon the soft palate inadequate gagging is secured. Still, one may see purulent collections flowing down from the left tonsil; from the right, not much can be seen."

The eruption is in full bloom. Pulse 144.

June 13th: About the same condition. There appears on the left tonsil a membranous coating, and on spraying the pharynx, fragments of membrane come away. On both corneæ there are small, pinhead, white points. Pulse 144.

June 14th: In the morning severe prostration; otherwise an unchanged condition. The pulse small, and 140; the temperature low. Slight twitchings precede death at 1.30 P. M.

The progress of the fever is seen in figure 66.

Autopsy (Prof. v. Schüpple), extract: The child is poorly nourished. The skin almost everywhere, with the exception of the feet and anteriorly on the thighs, is of a dark bluish-red to a rose-red color, of a diffuse and rather uniform appearance, fading only slightly on pressure. Numberless tiny, for the most part faded-out ecchymoses in the skin, both in the pale and in the bluish-red areas. Nowhere edema. Subcutaneous tissue rather rich in fat. Muscular development corresponding to the age. Eyes fixed in a stare.

Cellular tissue in the neck is markedly infiltrated; the lymph glands are here decidedly enlarged. The retropharyngeal cellular tissue is infiltrated in a peculiar manner by seropurulent exudate.

The lymph glands are larger than beans, and are in places infiltrated by firm connective tissue, their cut surface being spotted dark red and whitish. The paler portions are already in a condition of necrosis, and one can press from them a grayish-yellow pulpy material.

The posterior mouth and pharyngeal cavities contain foul, grayish-green mucoid masses.

The mucous membrane itself, as well as the epiglottis, and the entrance to the larynx are discolored a dirty gray to a grass-green color.

Both tonsils are involved in a superficial gangrenous process, most marked on the right side. Its deeper portions show a soft, dark red, almost pulpy mass, which is gradually becoming gangrenous.

Behind the arcus glosso-palatinus on the right side the pharyngeal mucous membrane superficially is necrotic.

The mucous membrane of the larynx is likewise discolored and distinctly swollen.

FIG. 66.
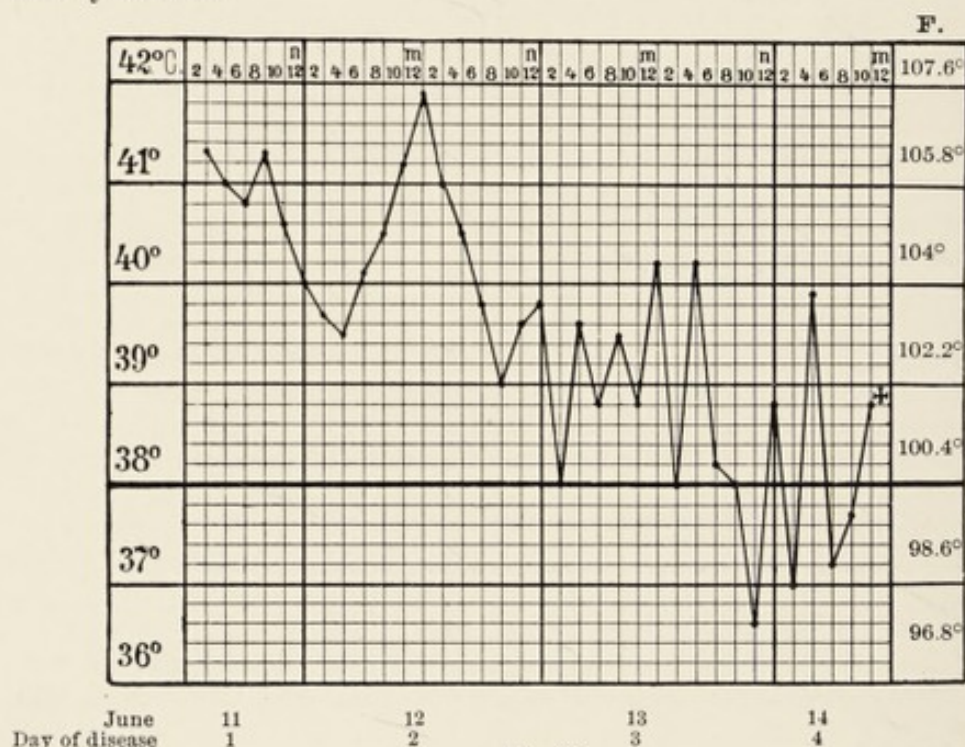
The lungs are not collapsed. The pleural cavities are free from fluid; the pleuræ normal.

The left lung everywhere contains air, posteriorly and anteriorly containing the same quantity of blood, and, on the whole, rather anemic. In the lower lobe a postmortem coloring of otherwise normal tissue is evident in the pleura.

The bronchial mucous membrane presents the same grayish discolored appearance as that of the larynx and trachea.

The right lung corresponds in all particulars to the left. The bronchial glands are not enlarged and are very much congested.

The spleen corresponds to that of a grown man, and is about double its normal size.

The mesenteric glands are generally swollen to twice their size, as are the follicles in the membrane of the small intestine, and the Peyer's

patches. The mucous membrane of the large bowel and its follicles are, on the contrary, normal.

The liver, normal in size, pale, and anemic. On section it shows a distinctly acinous arrangement. The boundaries of the lobules are markedly broad and white, as if infiltrated by lymph, and a number of white nodules with the appearance of small lymphomata are scattered throughout the hepatic tissue.

The gall-bladder full of thin, fluid, pale-colored bile.

The kidneys show cloudy swelling.

The heart is somewhat dilated, its muscle pale brown.

The brain anemic; slight opacity of the meninges; marked edema. Cortex distinctly swollen.

This is evidently not a simple case of scarlatina, another infection having very early appeared as a complicating condition, probably due to pus-producing organisms, perhaps to decomposition bacteria. Let us consider the case entirely from the standpoint of the findings: Suppuration and gangrene in the involved organs characterize it, and the behavior of the temperature also presents a picture fully in accord with the condition seen in severe septic processes. Comparison with figures 63, 64, and 65 brings into prominence the fact that such a rise and fall of temperature as took place on June 13th and 14th—the third and fourth days of the disease—do not occur in simple scarlatina.

Septic infection plays so frequent and so positive a rôle in the course of scarlatina that it appears to me warranted to give it mention in this place.

I wish still to consider the **hemorrhagic form of scarlatina,** which is, to say the least, very uncommon in Germany. Fürbringer * saw it among many hundreds of cases of scarlatina only a few times. In the malignant epidemics of England it is said by Bohn to occur more frequently. Taking it as a whole, the picture is one of a severe intoxication, with hemorrhagic symptoms added. These are usually mere hemorrhages into the skin and into the subcutaneous connective tissue, into the serous membranes, and the mucous membranes, appearing in large numbers, and covering much surface. A small number of these extravasations could be found even in my own cases.

Bohn † denies positively that large hemorrhages occur upon the free surfaces. Fürbringer is of the opinion that they exceptionally occur; while Thomas‡ calls them frequent, though he considers a different condition under the term "hemorrhagic scarlatina."

* Eulenburg's "Real-Encyklopädie," 2 Aufl., Bd. xvii, S. 467.
† Gerhardt's "Handbuch," Bd. ii, S. 265.
‡ v. Ziemssen's "Handbuch," Bd. ii, S. 297, 298.

Thomas gives the most detailed description:

"As a rule, the condition of the patient is from the beginning serious, and characterized by intense fever and brain symptoms. The exanthem is for the most part only imperfectly developed; on the other hand, there appear, to a certain extent continuously for several days, partly at intervals, either everywhere on the body or only in certain portions, millet-grain to hemp-seed in size, distinctly circumscribed, carmine-red or dark purple spots, or finally even great suggillations. The skin, which in the beginning is red and erythematous, becomes later relaxed and shriveled, and the face bloated. The angina, as in all severe cases, as a rule, is very decided, often diphtheritic or gangrenous; the involvement of the lymph glands and tissues of the neck is usually considerable, and an unfavorable outcome, due especially to the latter condition (gangrene) and to diphtheria, is quite frequent.

"Hemorrhages from the cavities of the body and from the mucous membranes are a customary phenomenon, especially where the latter, as is often the case, are essentially involved, and perhaps even to the extent of ulceration. The latter applies especially to the nasal, and intestinal (large intestine) mucous membranes, and can cause hemorrhage of the severest degree. Moreover, sometimes there occurs a severe hemorrhage from a tooth cavity, or from slight chance wounds, and, among others, those from leeching and cupping. Often hemorrhages occur from the urinary passages, so that the urine may have even a black color; their origin is usually the kidney substance, more rarely the renal pelvis, or the lower portions of the urinary tract. In women, genital hemorrhage, with or without diphtheritic involvement of the vagina, is a frequent phenomenon. Also the internal organs, the brain, heart, liver, spleen, stomach, and lungs, may be the seat of hemorrhage; likewise the subcutaneous tissue, especially on the neck; and, finally, there occurs more or less hemorrhagic exudation into the pleura and pericardium." Death is the usual outcome.

We see from this description that Thomas extends the meaning of "hemorrhagic scarlatina," and includes symptoms that may be caused by far different infections in the course of the disease. Whether this is justifiable, I am inclined to doubt. The view held by Bohn appears to me a more proper one: "For the most part very young children in the first and second year of life, but of very dissimilar constitutions, become suddenly ill with a precipitate rise of fever, vomiting, diarrhea, drowsiness, dyspnea, and convulsions, and within ten to twenty hours are corpses, the skin a few hours previous becoming

dotted with extravasations of blood (*Blutfleckig*). Hemorrhages do not occur from the orifices of the body. The spleen is enlarged."

Following Jenner, Bohn sums up the former's description of hemorrhagic scarlatina, as seen in England, in the following: "After several days of angina, severe fever, with or without delirium and unconsciousness, there appears a scarlet-red or even darker eruption, mixed with numerous petechiæ. Death follows after a few days, without the patient again regaining consciousness. In the cadaver, one may see numerous petechiæ in the serous and mucous membranes, an enlarged spleen, the blood very thin, the organs otherwise normal." Adults also seem there to be subject to the condition.

In such cases there is no doubt present a most malignant influence of the scarlatina poison only. Fürbringer seems to consider the probability, in cases that continue for a somewhat longer period, of a complication by sepsis.

Let us now return, by way of contrast, to a *case of the mildest nature.*

We may summarize in the following manner: None of the phenomena peculiar to scarlatina need be lacking; all can occur together in the same case. There may, on the other hand, only a portion of the symptom-complex be apparent. It is certain, however, that a severe disturbance is not troubling the patient, whether it be of a general nature, involving no special organ, or whether one that attacks a single one. Thus a suddenly oncoming and marked rise of temperature (40.0° C.—104° F.—and even higher) may occur, but it disappears within a short time. The inflammation of the pharynx with glandular enlargement may also be present, but without further developments, and hardly becoming troublesome, even when it endures for a somewhat longer period. A fully developed exanthem may appear, and run through its customary course of a week's length. It remains, however, only an eruption upon the skin, and goes no further.

That the scarlatinal toxin is alone to be considered in connection with these mild cases, and that under no circumstances do other causal influences ever become coactive, is a necessary conclusion, proved by actual experience.

The following cases will render this clear:

OBSERVATION VIII.—Karoline St., three and one-half years of age. Except measles, no previous illness.

On November 10, 1889, she became seriously ill, rather suddenly; the two previous days she was also not perfectly well. The child soon

became red, then pale. and several times felt chilly. The mother believed she had taken cold. On the 10th, however, the face was so strikingly red, and remained so, that a physician was summoned.

When first seen: Over the body a wide-spread, scarlatinal exanthem, especially distinct upon the face, the breast, and the extensor surfaces of the lower extremities. The tongue, somewhat coated, showed swollen papillæ, especially toward its tip. Both tonsils markedly swollen, with a thin mucous coating. Slight nasal catarrh. The cervical lymph glands slightly swollen, on the left side more than on the right; the inguinal glands rather decidedly swollen.

November 11th: The exanthem appears plainly on the back.

November 12th: The exanthem everywhere in full bloom, the inguinal glands less markedly swollen.

November 13th and 14th: The exanthem is gradually fading, the angina and glandular enlargement are diminishing.

Further course without event. Observation of case continued until December 10th.

In this case all the symptoms befitting scarlatina were present with the exception of the rise of temperature, which not only was lacking, but in its place appeared for the most part low falls of tem-

FIG. 67.

perature. One sees this distinctly in figure 67, which no one would consider a temperature curve of scarlatina. That it was in fact scarlatina is proved further by the illness of the sister—also a light attack, but with a constantly accompanying fever. The case may be briefly mentioned:

OBSERVATION IX.—Katherine St., eight years of age. Had measles at the same time as her sister, otherwise no previous illness.

The disease began suddenly on November 13, 1889, in the afternoon. The child came from school with headache and difficulty in swallowing, and vomited several times during the night.

Seen on November 14th: Scarlatinal eruption in its very incipiency on the chest under both clavicles. The tongue swollen with distinct papillæ. Severe angina, but no membrane. Nasal mucous membrane covered with dried-up secretion. Cervical lymph glands slightly, and in the inguinal region decidedly, enlarged. On the 15th and 16th the exanthem spread over the entire body, but only reached an imperfect development, and on the 18th began to fade.

Course uneventful. Case observed until December 14th. The temperature was highest in the afternoon of November 16th, with 40.1° C.

(104.1° F.); on the 21st was 38.5° C. (101.3° F.), and from this time 38° C. (100.4° F.) was never again attained. There was a fever of at least eight days' duration.

Still another evidence that scarlatina can run its course without an increase in the temperature.

OBSERVATION X.—Louise L., seven years old. Became ill on January 12, 1879, without subjective symptoms. In the morning her mother noticed that the child's face was red. In the house of her grandmother was at that time a case of scarlatina, still under treatment. Intercourse had continued with the house, though not through the child herself.

Seen and examined on January 12th, in the forenoon.

In the case of Louise the exanthem is slight in the face, upon the entire anterior surface of the trunk, and most evident upon the right upper leg. The tongue is red anteriorly; its papillæ are only slightly swollen. The tonsils are red and swollen, free from membrane; there is a slight redness of the pharyngeal mucous membrane. Edema of the forehead and eyelids is striking. Cervical glands enlarged. Urine free from albumin. First temperature taken at midday—37.8° C. (100.0° F.).
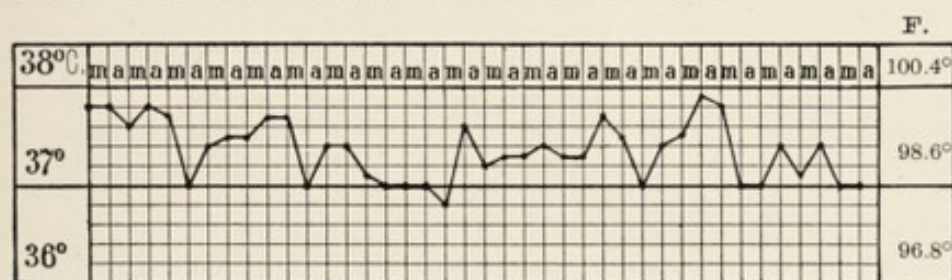
FIG. 68.

January 13th: The exanthem has nearly disappeared, also the symptoms in the pharynx are less marked. The cervical glands still somewhat swollen.

January 15th: In excellent condition. Exanthem entirely disappeared. The further course of the disease uneventful; no severe desquamation took place. The child could hardly be kept in bed until January 31st.

The temperature at no time reached 38.0° C. (100.4° F.), but showed variations, to which I shall refer later. (See Fig. 68.)

The fact that in both cases *scarlatina was present without fever,* or, in short, that it actually was scarlatina, may not well be doubted. For, in addition to the exanthem, there were the other pathognomonic phenomena, even though only slightly developed. In Case VIII the illness of the sister following after four days' time strengthens the diagnosis; in Case X at least the possibility of an infection by means of the other members of the family is assured. Neither occurred as a sporadic case, but appeared at a time when cases of the disease were frequent.

There are most favorable conditions in our Policlinic that admit of such investigations, these being by no means the only ones we have made.

Certain authorities doubt the occurrence of genuine scarlatina without fever, or at least believe that it is not yet placed on the basis of certainty.

Wunderlich* expresses himself as follows: "Whether among these abnormally mild cases there also occur those in which the temperature shows absolutely no or a minimum change, I cannot say from my own experience, because I have never been able in very light cases to observe the beginning of the disease."

The cases that Thomas† has seen, and adduced by him, have also had a continuous though short fever.

Henoch mentions no altogether fever-free cases. Bohn has seen none, and also Fürbringer. Leichtenstern,‡ on the other hand, reports such an one.

Up to this point we have contrasted the pictures as a whole that are presented by scarlatina, and essentially with a view to the danger to the patient himself. The intermediate conditions, the transition from the mild to the severe forms of the disease, are so numerous that it will be almost impossible to adduce all the evidence. It suffices to point out the fact that now this, now that characteristic is more strongly or lightly developed, and that now the one, now the other organ makes evident its involvement.

On the other hand, one must consider briefly those cases that have been given a special name with reference to the absence of a symptom usually present in scarlatina. To this class belong such cases as fail to show a fever, and besides *scarlatina sine febre,* we speak also of *scarlatina sine exanthemate,* and a *scarlatina sine angina.* That both the latter do occur is taken for granted by the majority of observers. In regard to the frequency of the occurrence, however, opinions are divided. Fürbringer goes by far the furthest in *classing scarlatinal angina without an eruption* (its presence being assured by the subsequent appearance of nephritis) *among the great rarities.*

[**Scarlatinoid.**—Neurath § describes under this term an affection which occurred in epidemic form in Herzegovina, and which was analogous to the simplest type of scarlet fever. The disease was characterized clinically by an intense erythema, fever of moderate inten-

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* "Das Verhältniss der Eigenwärme in Krankheiten," Leipzig, Otto Wigand, 1870, 2 Aufl., S. 330.

† "Klinische Studien ueber die Nierenerkrankung bei Scharlach," *Archiv der Heilkunde,* 11 Jahrgang, S. 147.

‡ *Deutsche med. Wochenschrift,* 1882, S. 173.

§ *Wien. med. Wochenschr.,* 1901, No. 13.

sity, a mild type of angina, small plaques on the tonsils, strawberry tongue, etc.

The principal difference between this affection and the common type of scarlatina appears to lie in the total absence of all complications in the former. (Compare Fourth Disease, under "Rötheln.")

New Type of Scarlatina.—Robertson[*] calls attention to a very mild epidemic at Paisley which resembled glandular fever. It appeared to have spread largely through the use of swings in a playground, the boys catching the ropes at the same places and often wetting their fingers with saliva before doing so. (Compare Fourth Disease, under "Rötheln.")]

Thomas,[†] on the other hand, says: "*Even an angina that occurs during a scarlatinal epidemic is suspicious.*"

Leichtenstern holds the same ground. He observed frequently during the Cologne epidemic cases of "acute morbus Brightii," often with general edema and uremic symptoms; a fatal outcome was by no means rare. The patients, just as regularly as the attending physician, stated that at no time was there ever a redness of the skin present. In some cases a mild angina was noted, in others a true diphtheritis faucium, but without exanthem, as the precursor of the acute nephritis. The cases comprised, in the main, those of adult years, and repeatedly persons who had come from the dwellings of, or from nursing, scarlatina patients.

In concluding his observations, Leichtenstern expresses the belief that "*the so-called true acute morbus Brightii is frequently an abortive form of a different infectious disease, whose poison in its excretion by the kidneys causes the acute nephritis.*"

Among these infectious diseases scarlatina would take first place.

Here, as in all forms of the disease, it is admittedly of theoretic moment that the absolute absence of an essential symptom may occur. But in practice the significance is a much slighter one. Whether the thermometer rises above normal only for a few hours, or whether it never rises, is of just as little importance as the appearance or non-appearance of a temporary skin eruption. Henoch,[‡] it seems to me with great propriety, remarks that the physician who is called early in such cases of scarlatina may be in doubt whether he has in fact to consider a case of genuine scarlatina or only a passing

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[*] *Brit. Med. Jour.*, April 5, 1901.

[†] v. Ziemssen's "Handbuch," *loc. cit.*, p. 269.

[‡] "Mittheilungen über das Scharlachfieber," *Charité-Annalen*, III. Jahrgang, S. 553.

erythema. How often it occurs that only on account of the increasing severity of the angina the physician is first summoned when the eruption has disappeared! Possibly a close examination of the skin will now show a slight desquamation, perhaps it only appears later: whether it can entirely fail remains for discussion.

All of the foregoing applies especially to children of an age that predisposes to scarlatina.

"On the other hand, one should remember that in the vicinity of a scarlatina patient, febrile indisposition, angina, and catarrh of the different mucous membranes, vomiting, even diphtheria of the tonsils, in the other members of the family that have already had the disease are almost daily occurrences. We must only accept a case as one of scarlatina if, during an epidemic, especially in families where either early or late a distinct scarlatinal case appears, cases occur in which nothing more is lacking from the fully developed picture than the confidently awaited exanthem." Bohn * expresses himself in this fashion, and will, I believe, hardly experience a contradiction.

A fully developed exanthem, with an entire absence of angina, may also occur, but is very rare. It has been stated that such cases are mild in their course.

We must also consider a possible reappearance of the exanthem, either in the course of an attack that is still in progress, or directly following an apparently completed attack of scarlatina. We cannot on principle distinguish between the forms divided by Thomas into relapse ("recidiv") and pseudo-relapse ("pseudo-recidiv"), since in neither of these does a new infection occur from without, as is stated by Thomas † himself.

But that the scarlatinal toxin is able, by flaring up afresh, to relight either the whole disease, even in its convalescence, or a portion only of its symptom-complex, appears to me certain. Körner ‡ gives a report of the literature up to 1876. Henoch § gives still further evidence from his own experience, and he and Körner agree in stating that scarlatinal relapses occur perhaps oftener than is supposed. The former says: "I believe that with closer attention relapses of scarlatina will be more frequently noted than has heretofore been the case. We must expect, however, not a full and perfect picture of the disease. Much rather may only single symptoms, perhaps

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* *Loc. cit.,* p. 265. † In v. Ziemssen's "Handbuch," *loc. cit.,* p. 198.
‡ "Jahrbuch für Kinderheilkunde," Neue Folge, Bd. ix, S. 362.
§ *Charité-Annalen,* Bd. iii, S. 540 u. 559.

fever and the exanthem, make their appearance for a time, so that in private practice, where one does not make regular use of his thermometer, a relapse may be easily overlooked. *A fully developed relapse does not differ in any essential point from the original attack.* It may be more mild or more severe, may appear early or late, but usually occurs in the middle of the third week from the beginning of the disease.

The conditions found in enteric fever may be mentioned as analogous to these cases. Henoch is of the opinion "that the toxin, whose character is not now understood, is not completely eliminated by the first attack, and therefore a relapse must follow, similar to a recrudescence in relapsing fever, in which the reappearance of the spirilla in the blood, which have been missed during the interval, has again been determined." This view is a general one, and I see no reason to question it.

But there is another question, *as to whether the scarlatinal toxin of itself always becomes evident, or only together with a septic infection. I am inclined to seriously consider the possibility that the latter may of itself render the picture similar to one of a relapsing case of scarlatina.* This question comes to me in an especially forcible manner in the consideration of the conditions called by Thomas " pseudo-relapse." *

He describes it as follows: "Sometimes a new and general eruption appears in unexpected fashion, following an attack of scarlatina whose course has been constantly irregular, and ushered in sometimes by a typhoid form of fever without marked local symptoms, sometimes by severe local affections of a most various nature. This may even occur after an uninterrupted illness, at the end of the second or during the third week of the disease."

The character of the eruption presents in many respects departures from its customary form that Thomas describes in detail. He sees in these, however, only " analogues of that which is seen in cases of the ordinary scarlatinal eruption"; a distinct roseola, and a marked involvement of the face, including the vicinity of the mouth, being mentioned as unique exceptions. The constant fever has no special significance.

" An acute but moderate injection of the mucous membrane of the pharynx and mouth is never lacking, and the tongue usually takes on an appearance similar to that of the first invasion (redness, swelling of the papillæ); there is also a moderate swelling of the cervical glands.

* In v. Ziemssen's " Handbuch," *loc. cit.*, p. 295.

"Slight conjunctivitis, nasal catarrh, and hoarseness with cough and the general symptoms of a mild bronchial catarrh are sometimes noted even before the appearance of the second eruption.

"The mucous membranes of the digestive tract are not markedly affected; the liver is normal; the spleen for the most part remains moderately enlarged. Various nervous symptoms seem to be observed only as results of a high temperature."

So much for Thomas. When we read this description, the altered form of the exanthem, upon which I lay little stress, will at the most attract some attention. It is a very different thing, however, when one scrutinizes the histories of the cases by Thomas.* There are, in all, only five cases which are observed and carefully reported by Thomas himself.

Körner adds a few doubtful cases, that retire before criticism. *Excepting in one case (Anna Kind), another "complication is mentioned, which we must in all probability refer to the influence of pus-producing organisms:* otitis, abscess formation, and gangrene following suppuration of the tissues. Twice death occurred, so that it is not quite clear how Thomas can say †: "In general, it may be taken for granted that the course of scarlatina . . . is not rendered decidedly worse; most cases recover."

The course of the fever is—and here I agree with Thomas—not characteristic, and we may assume that it does not exclude sepsis, in that it presents the marked variations that are often seen in that condition. Reports of the autopsies are lacking.

When we consider the question in its entirety, the term "pseudo-relapse" appears to be a happy one, but in another sense than that in which Thomas has used the word. The matter requires, at any rate, a further light, like so many others in the study of scarlatina.

It will be of advantage to discuss at this time the manner in which the so-called complications and sequels of scarlatina exert their influence. These are disorders that prove of serious moment not only in the individual case, but even for entire epidemics, practically shaping the complexion of the disease and its prognosis. *They are not regular attendants upon scarlatina, but so often form a part of the picture that a distinct relation to it is unquestionable.* What is the nature of the relation? Here there arise various possibilities:

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* "Beobachtungen über masernähnliche Hautauschläge," *Archiv der Heilkunde,* 1869, Bd. x, S. 458.

† v. Ziemssen's "Handbuch," *loc. cit.,* p. 297

1. *The scarlatina poison* is able of *itself*, apart from the organs that are customarily attacked by it (*i. e.*, in the majority of cases), to assert itself elsewhere in the body under certain conditions neither understood nor recognized by us. It can extend its special—specific —influence to parts that are rarely, or not to any marked degree, involved in the process.

2. *The toxin can create conditions in tissues attacked by it* that dispose them to offer a ready entrance into the body *to other causes of disease.* •

3. *The toxin can so diminish the resistance of the organism which it attacks*—its vitality—that it is no longer able to withstand successfully harmful influences of any sort, whether they be pathogenic bacteria from within or without, or whether they be conditions of weakness independent of the latter, or dependent upon them; *e. g.,* the impaired functional activity of any organ.

In a general way, I think such a division should be satisfactory and exhaustive. Yet, even though it does satisfy the orderly requirements of the understanding, as a matter of fact it is only to a moderate degree practicable. The reason lies in our lack of knowledge of the cause of the disease; and also in the fact that the latter appears now as a pitiless destroyer, again as an altogether benign influence; the frolicsome kitten, and the hungry tiger.

If we venture the attempt to consider an actual case in this light, we dare not let anything pass without attention. The causes of the septic condition come especially into consideration in regard to our decision as to what is to be ascribed to the scarlatina poison as such, and what to the bacteria that have made their way into the body by means of the way opened by the toxin. Moreover, the conditions caused in disease by sepsis as well as by the scarlatinal toxin, whether general or specific, are exceedingly difficult, if at all possible, to separate from one another.

The attempt has recently been made to cut the Gordian knot by characterizing *scarlatina itself as a streptococcus infection.*[*]

Apart from the important, and it seems to me unavoidable, clinical considerations that stand in the way of this view, represented especially by Babes,[†] there has been carried out in Baumgarten's

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[*] "Eine Zusammenstellung der einschlagenden Arbeiten findet sich bei Konrad Brunneer," "Ueber Wundscharlach," *Berlin. klin. Wochenschrift*, 1895, No. 22.

[†] "Bacteriologische Untersuschungen ueber septische Processe des Kindesalters," Leipzig, Veit, 1889, S. 23 ff.

institute an investigation * that exposes its inaccuracy from the standpoint of bacteriology itself.

The case in question was that previously mentioned (Observation IV) of, at most, a thirty-four hours' duration. In this rapid course it was possible for one to obtain a clear picture of a pure infection by scarlatina. We find that in no other organs than the tonsils were streptococci found. "In the light of the investigations of Kurth, showing that the Streptococcus pyogenes can be obtained from the tonsils also by means of a culture in non-scarlatinal angina, this, our single positive evidence, loses all its significance, and may not be quoted in favor of a closer relation of the Streptococcus pyogenes to scarlatinal processes."

The conclusion is a simple one: *If scarlatina develops fully in the absence of streptococci, then streptococci cannot be the cause of the scarlatina.*

By means of the important investigation of Böhm we may ascribe to the scarlatinal toxin whatever was found in the way of pathologic change in the autopsy reported by him: the involvement of the skin, the buccal mucous membrane, and portions of the lymphatic system —the spleen, glands, follicles of the intestines, and the tonsils. The brain symptoms would be without propriety considered in the same connection.

It is certain that in the later stages of the disease all these are or may be involved by pus-producing organisms, the skin not excepted. One must in such cases, if we wish an accurate description, speak of a real complication, since there is, besides the scarlatinal toxin, another cause of disease present.

It seems also probable to me from the studies already reported (*vid.* Cases II, V, and VI) that the mucous membrane of the air-passages is exposed to the scarlatinal poison; this is, however, not proved. The nasal mucous membrane may first be attacked by the scarlatinal toxin, and then other pathologic organisms, and pus-producing organisms settle upon it, and later sometimes even the exciting causes of decomposition. From, here then, the neighboring cavities may be involved in the disease, and not directly owing to the scarlatinal toxin.

Nephritis is in all probability a result of the influence of the scarlatinal poison upon the kidneys, but, in addition, pus organisms

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* Johannes Böhm, "Beitrag zur Frage nach der Beziehung des Streptococcus pyogenes zur Aetiologie des Scharlach," Tübinger Dissertation praes. v. Baumgarten aus dem Jahre 1892.

may frequently come into consideration, and in a minority of cases the pus organisms may perhaps alone cause the nephritis.

Böhm and Baumgarten express themselves as follows in the matter: "We do not wish to deny that the very frequent scarlatinal nephritis belongs to the inflammatory processes caused by secondary streptococcus infection; *proved*, however, it is not, and not even by the findings of Babes.

"This much only stands proved, that in advanced cases of scarlatina streptococcus elements very frequently, one might say constantly, are present in the more or less diseased kidneys of scarlatinal patients. That these elements cause the condition termed scarlatinal nephritis does not necessarily follow."

It is mentioned separately and with special emphasis that the only case of Babes "which leaves no doubt that streptococci took part in the causation of the renal changes *should not be looked upon as a genuine scarlatinal nephritis*, rather as a complicating *metastatic nephritis*."

To form a general estimate of the origin of that which is called *scarlatinal rheumatism* will hardly be practicable. It is possible that there may be a primary intoxication by the poison, but it is also possible that the pus organisms play a part. This cannot be disputed on the ground of the temporary character of the symptoms; for the involvement of the joints, and of the bones, differs in no way in cryptogenic sepsis from that of scarlatinal rheumatism.

In regard to the *cardiac disturbance*, I would advance the same principle, except that one may in this case hold the scarlatina toxin —at least in the beginning—alone responsible.

Wherever pus formation occurs, there is certainly a secondary in-wandering by pus cocci; the scarlatinal toxin is able to produce the severest forms of necrosis, but is capable of no pus formation. It is probable that the *pharyngeal mucous membrane*, primarily affected by the scarlatinal toxin, and especially *the tonsils*, serve as a usual means of entrance, at least in a great number of cases.

From the pharynx the *decomposition bacteria* force their way into the dead tissue. The death of this tissue the scarlatinal poison is able to accomplish alone, either indirectly, or directly in combination with the pus organisms. *True diphtheria* is certainly a complication, and it is probable that the bacillus finds, at least at times, conditions favorable to its lodgment in the previously affected mucous membranes.

Croupous pneumonia is always a true complication; it remains a question whether its occurrence may be otherwise explained than on the ground that scarlatina furnishes an exhausted condition of the whole body.

In conclusion it should also be mentioned that an extension of the symptoms of tissue disability * that belong to scrofulosis is not seldom found as a consequence of scarlatina. Thus we may see existing affections of the organs, of whatever nature they may be, either during or after scarlatina assert themselves more forcibly than before.

Taking everything into consideration, there will, to my belief, be obtained a better comprehension of the existing conditions if we refrain from giving general descriptions of the processes that may complicate scarlatina. I consider it of greater advantage to consider separately the symptoms appearing in combination with the disease; always, however, with reference to the main condition.

In the same manner I refrain from a descriptive summary of the anatomic changes, which have already been enumerated in full in the above protocols of the autopsies.

* *Vid* Sequels

CONSIDERATION OF THE SYMPTOMS.

COURSE OF THE DISEASE.

As we have already discovered * in discussing the foregoing considerations, a definite period for the incubation cannot be assigned. It varies from less than a day to weeks in length, a limit of about fourteen days, however, being considered the maximum.

During this incubation **symptoms of a pathologic nature** are so completely lacking in such a majority of cases that one may look upon their absence as the general rule. We may even doubt whether a slight preceding indisposition ought really to be ascribed to the scarlatinal toxin.

The **time of the onset** of the disease, however, except in the lightest cases, is marked in a very positive manner.

The invasion of scarlatina is recognized by some sudden change in the condition of the patient. Most frequently, we may say, *vomiting* appears as a general symptom, *angina* as a local one; in addition, there is *fever*, which may be introduced by a severe chill or by repeated feelings of chilliness.

[*Experience Coinciding.*—My experience at the Willard Parker Hospital among adults, who can give their own history clearly, is that the symptoms in the invasion of scarlatina appear in the following order: (1) Sore throat; every adult mentioned this. (2) Headache, which was next in point of frequency. (3) Fever, which was generally described as a feeling of heat in the head or a burning heat all over. (4) Vomiting; adults were not regularly affected with this, it being much more common in children.

My experience among young children in private families indicates that vomiting is the first symptom that is noticed by the mother, and this is usually accompanied by fever. A child of a friend, for instance, was brought into the reception room to be shown to guests. She was taken up by the mother, and, probably as the result of the slight excitement, at once vomited. I took her temperature immediately, and found it 39.7° C. (103.5° F.). She passed through a typical scarlet fever. In another family the grandmother was in bed with scarlatinal sore throat, without skin eruption; a sister was dying, in

* Compare page 403.

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another room, of scarlet fever, with a temperature of 41.7° C. (107° F.); and a servant was in a side room, in the first day of skin eruption. The excitement of the arrival of a consulting physician caused another child, the youngest of the family, to rush into its grandmother's room. She had previously been well, but just at this time was taken with vomiting; her temperature, taken at once, was found to be 39.7° C. (103.5° F.). The servant mentioned had been well until the second morning before. On rising, she had vomited, the first symptom.

In my experience these cases illustrate fairly well the onset of scarlatina as I usually see it. The symptoms, then, are usually as follows: In adults, sore throat, headache, fever, vomiting, or slight chill; in children, vomiting once or twice without apparent cause, fever, sore throat, malaise.]

In my opinion, one does well to place the sudden transition from health to indisposition in the foreground, since it is unique. Variations from a simple indisposition to symptoms of the severest brain disorders may occur.

If we adhere to the customary division, we will then call this the **stadium invasionis,** characterized, at least very often, by fever, inflammation of the pharyngeal mucous membrane, and angina, and sometimes by enlargement of the glands.

It is only of short duration, and in the course of the same, or of the next day at the latest, appears the **stadium exanthematicum,** with the development of an eruption. This period—subdivisions (*stadium eruptionis, florescentiæ*) are of no importance—embraces the culmination of all the symptoms characteristic of scarlatina; fever, with general symptoms, involvement of the pharyngeal organs, the glands, and the skin; duration about four to six days.

Then follows, with a gradual subsidence of all symptoms, the **stadium desquamationis**—as the name shows, called after the disappearance of the exanthem, and the condition of the skin subsequent to it. The duration is several weeks, and is not accurately determinable.

Relapses may occur from the very beginning until late in convalescence. The statistics of their frequency will be discussed with the consideration of the involvement of the organs.

FEVER.

Wunderlich * claims that scarlatina has a less characteristic type of **temperature curve** than many other diseases, and especially than

* "Eigenwärme in Krankheiten" u. s. w., S. 330.

smallpox and measles. In this he is fully justified. Not only the various secondary processes, but the great variation in the virulence of the infecting substance, call forth all sorts of irregularities that can with difficulty be made allowance for. So that we meet with difficulty if we attempt to say what the real temperature curve of scarlatina is.

Wunderlich describes as the average type the following: The temperature rises from the commencement of the invasion very rapidly, and reaches, after a few hours, 40° C. (105.8° F.) to 41° C. (104.0° F.). With slight morning remissions there follows a still further rise from the appearance of the exanthem until the time of its complete extension over the body.

When the eruption is at its height, the fall of the temperature begins, and in such a manner that, though the curve covering the
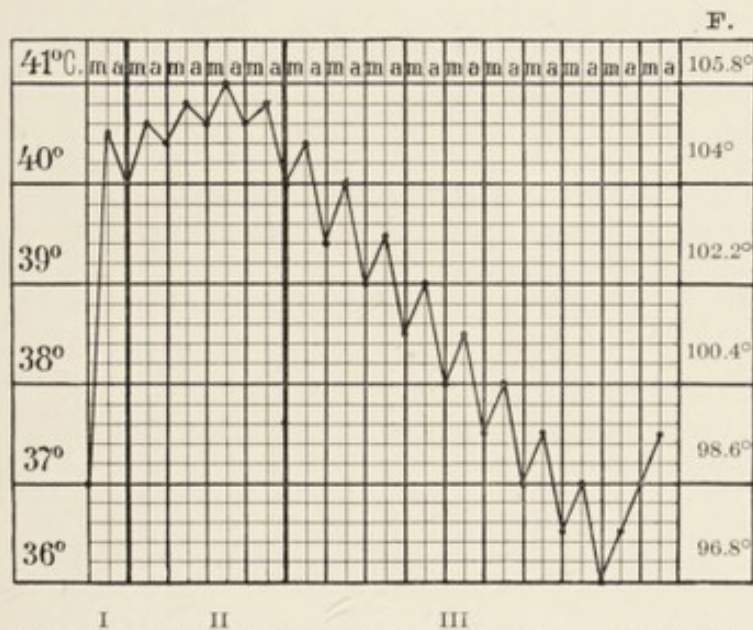
Fig. 69.—I, Invasion; II, development and extension of the exanthem; III, retirement of the eruption.

normal progress of the twenty-four hours retains its form, yet a gradual lowering of the general curve, that had been driven to a high point by the disease, is accomplished. We may then see directly following for several days a subnormal temperature, though not below 36° C. (96.8° F.).

Figure 69 gives a picture of the method of procedure adhered to in greater or less degree in all cases. It is unquestionably dependent in a measure upon the development and behavior of the eruption. Since the latter is, however, only one feature of the infection, one should not expect that it can satisfy all the requirements imposed by a strictly characteristic description that would embrace all the phenomena of the disease.

Moreover, the temperature curve in scarlatina of itself by no means assures a sure insight into the pathologic condition that is present in the body. The action of the toxin does not always reflect itself in the fever.

Leichtenstern* reports a case in which, in spite of an unusually severe development of the exanthem over the whole body, and in spite of the almost afebrile course of the disease, an extraordinary degree of delirium was present. This undoubtedly was a case of toxemia excited by the direct cause of the disease.

Cases with an abundant exanthem and moderate fever are rare (Wunderlich); but they sometimes occur, and afford a proof for the fact that the eruption is not always sufficient to account for the severity of the infection.

My own ten-year-old daughter had suddenly, on the afternoon of June 4, 1894, an angina. Early on the morning of the 5th the exanthem had already fully developed, and extended itself in the course of the day over the whole body. It was very marked, unusually so, as was also the desquamation that followed. The maximum temperature was 38.4° C. (101.1° F.) on the evening of the 4th, and on the evening of the 5th was 38.0° C. (100. 4° F.). During the period from then until July 3d, there was at no time a rise of temperature, and instead, from June 8th on, the thermometer registered constantly under 37.0° C. (98.6° F.) (rectum).

It is not practicable to discuss all the variations in the fever curve of scarlatina, and only the most essential can be considered.

With the greatest regularity there occurs a sudden rise of temperature as an accompaniment of the invasion. Even to this rule there are exceptions, however, and cases occur not only with slight, but with an entire absence of fever.

Emma H., five years of age; admitted to treatment on February 20, 1877; on March 2d became unwell, with *fluor albus*. Evening temperature, 38.9° C. (102.0° F.). Over the entire body a diffuse redness, which at noon was visible on the neck and chest. Tonsils and uvula red and swollen. March 3d, morning, 39.7° C. (103.4° F.); evening, 40.0° C. (104.0° F.). March 4th, morning, 40.0° C. (104.0° F.); evening, 40.0° C. (104.0° F.), etc.

The foregoing is an observation of Henoch's,† and Leichtenstern has also seen such cases.

The height of the fever shows much more frequent variations from the usual type, and this is hardly surprising. We are concerned with one of the processes caused by the scarlatinal toxin, which may find expression in more than one way: through the absolute height

* *Loc. cit.*, p. 173.   † *Charité-Annalen*, iii, S. 512.

of the temperature, as well as by the variations in the daily temperature curve. Both features exhibit themselves in the patient. Cases in which the temperature hardly reaches 40.0° C. (104.0° F.) are so common that they require no evidence to support their claim for existence. Likewise, those that show remissions of 1.5° C. (34.7° F.) and more from a high fever (up to 40.5° C.—104.9° F.—and above).

On the other hand, it is noteworthy that by no means seldom the remission may be slight, in spite of a comparatively lower temperature. As an example of this:

OBSERVATION X.—Johanna Fr., six years old. Previous illnesses— rachitis, pertussis, measles.

On June 16, 1878, the child and her mother went to a cemetery quite a distance from their house; there she became chilly, so that she was brought home. On the 17th she was somewhat better, but about 11 A. M. chilliness again appeared, and in the evening she felt very hot. On June 18th, in the forenoon, an eruption appeared on the entire body, and the child was placed in the care of the Policlinic.

Course.—All the symptoms of scarlatina: Severe exanthem, which faded from June 22d on. From the 29th on, desquamation in patches took place. Angina, with a membrane, lasted to the sixth day. Slight swelling of the glands. Considerable enlargement of the spleen. Slight bronchial catarrh. No other disturbances in the organs. Only moderate rises of temperature until July 17th. Observation of the case continued until August 4th. The maximum temperature on June 19th, at 4 A. M.,

Noon. Evening.
FIG. 70.

was 40.4° C. (104.7° F.). In the following twenty-four hours the temperature curve was as pictured in figure 70. We see that the variations during these days of the climax of the fever did not once equal one degree, so as even to reach 39.5° C. (103.1° F.).
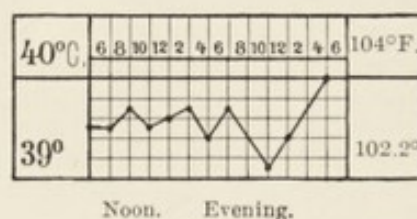
After an acute initial fever, the entire illness was either afebrile, or marked by a very low fever.

Henoch * cites a case of this kind that I do not question, although it admits of a doubt, which Henoch himself does not exclude.

Max P., on March 19, 1875, was treated antiseptically for a great abscess, due to mechanical injury. On the 21st and 22d the temperature rose to 38.5° C. (101.3° F.), the patient feeling perfectly well. On the evening of the 22d, suddenly a temperature of 40.2° C. (104.3° F.), marked redness of the face, of the arms, and the inner surfaces of the limbs. On the 23d the face, thorax, arms, and legs were covered with a distinct scarlatinal eruption; tongue white in the middle, with red tip and edges. Active angina. On the 24th the exanthem paler, many miliary vesicles upon the legs. Tongue red and smooth, but with prominent papillæ. From April 2d on, free desquamation, visible over the

*Charité-Annalen, loc. cit., pp. 512, 513.

entire body, and especially on the hands and feet, appearing in layers, and continuing about twelve days.

On the morning of March 23d the temperature had fallen to 37.0° C. (98.6° F.), and went at no time again over 37.8° C. (100.0° F.); then followed subnormal readings.

With the additional comment, "I incline to the opinion that such cases often occur," I must heartily agree. I do not find any such positive case among my own histories: on the other hand, a large number in which, after the stormy onset of the invasion fever, the temperature has fallen nearly to normal, and there remained.

Then the following:

OBSERVATION XI.—Hermann F., four years old.

For several days indisposition and loss of appetite; a marked tendency to sleepiness. On April 2, 1879, about 2 o'clock the child fell from a wall, about six feet high, and received a slight contusion of the head, without any abrasion of the skin. Toward evening repeated chilliness, the hands and feet shivering decidedly, head hot, no redness observed on the body.

On April 3d (A. M.) marked depression and loss of appetite. Admitted in the afternoon. Scarlatina exanthem on the face, anteriorly on the chest, posteriorly on the back. No angina nor difficulty in swallowing. On April 4th the eruption, deep-colored and showing in certain areas punctate petechiæ, has spread over the entire body. Angina also is now present.

On the fifth the eruption has already begun to fade. The further course uninterrupted.

The temperature on April 3d at 4 P. M., also toward the end of the first day of the disease, was 40.6° C. (105.0° F.). On the second day of the disease it did not rise above 38.2° C. (100.7° F.), and on the third day not above 37.9° C. (100.2° F.). Subsequently a slight fever appeared (see pp. 482 *et seq.*).

The **inverse type of fever** is considered by Henoch as a great rarity, and he has seen only one case. I have personally, as has Fürbringer, often observed it, and rather at the time of defervescence than at the acme.

The period of defervescence and the convalescence are the times when by far the most frequent and decided variations occur. Least often, one may say, and on the whole seldom, we see a rapid defervescence that approaches a crisis, as in this case:

OBSERVATION XII.—Frau Friederike H., twenty-four years old. Has felt poorly for several days; complains especially of weakness.

On the 11th October, 1877, A. M.: Angina, difficulty in swallowing, nausea, chilliness with sensations of severe fever following. The symptoms have increased, and marked headache has toward evening added itself to their list.

Admitted to treatment on the morning of October 12th: Diffuse

scarlatinal exanthem on the thorax; upon both swollen tonsils a slight coating; the tongue distinctly of a raspberry appearance. Symptoms of cardiac weakness that require treatment.

October 13th: Marked restlessness, headache. Eruption uniformly extensive over the entire body. Angina is complained of. The coating more marked on the left tonsil. The cervical glands swollen.

October 14th: The eruption much more active, especially on the left half of the abdomen, which appears a dark, bluish-red color, with distinctly prominent and numerous dark red points, surrounded by an area of a brighter red. The membrane easily removed by spraying. Marked raspberry tongue. Patient complains of headache. Cardiac weakness is less evident.

On October 15th: The eruption has nearly disappeared. The desquamation begins, and is very decided,—from the feet large patches are cast off,—continuing into November.

The convalescence was slow, but free from interruption.

Figure 71 shows the peculiar course of the temperature. We see that from the evening of the fourth day of the disease on, the temperature falls precipitately, and after the fifth day reaches the normal. From that time on for a long time (November) it was frequently taken, and constantly registered normal.

This was by no means a mild attack, and especially the cardiac symptoms were very grave.

It is much more frequent for the defervescence to draw itself out. This can depend upon various causes, which are sometimes possible of recognition, as in the case of

Fig. 71.

an evident involvement of some organ; at other times they remain obscure.

In the case of *some organic involvement*, the constitutional disturbance caused by it will find its expression in the temperature to a degree corresponding to its significance. No general comment is possible. Whatever there is to be said on the subject will be included in the discussion of the localized sequels.

The thermometer becomes a matter of course; every rise of temperature invites a searching examination, though often enough this is without result either for the time being or for the general outcome of the case. A rise of temperature above the normal merely indicates that something is not as it should be—and that is all.
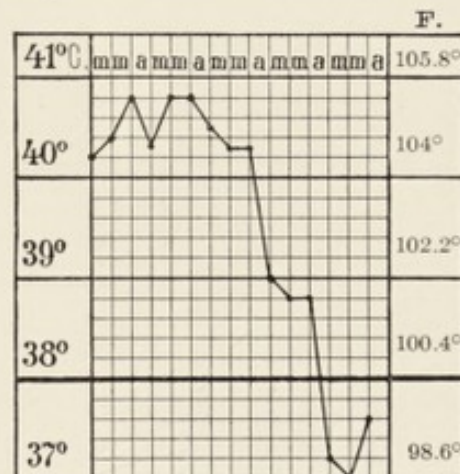
Let us consider the facts in advance, and the attempt at an explanation may follow.

I wish, first, to recall the fact that in the weeks that follow an attack of a scarlatina, characterized by no especially severe local affections that outlast the fever, quite often there appear slight variations from the normal temperature. These are recognized only in the event that one as a matter of principle—this has been the rule in my Policlinic for many years—has daily records made of the temperature for at least four weeks.

Let us recall the case reported in Observation I. Figure 62, which belongs to it, shows that the defervescence, which was synchronous with the fading of the exanthem, was interrupted on the sixth day of the disease. There then appeared jumps to 39.7° C. (103.4° F.), and for the first time, on the thirteenth day, the temperature reached the stage described by Wunderlich as typically normal, though even
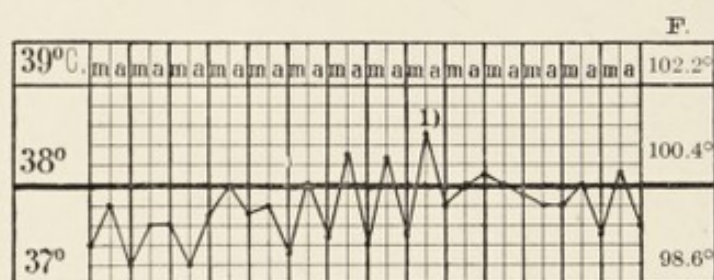
FIG. 72.—1, Swelling of the face.

the two succeeding weeks were not characterized by a truly regular temperature.

Once, after three days, which showed no deviations (twelfth to fourteenth day from the beginning of the illness), further rises of temperature to 38.5° C. (101.3⁷ F.) occurred, and the morning temperature was at times higher than the evening. Figure 72 shows this condition. Locally were found only on the eighth and ninth days slight joint pains without swelling; then, on the twenty-second day, a slight swelling of the face. Both coincided with rises of temperature. Affections of other natures, and particularly nephritis, were absolutely lacking. The recovery from the pharyngeal involvement, and from the evident glandular enlargements, was complete nine days after the invasion. Moreover, nothing occurred in the subsequent period to awaken suspicion. The case was somewhat different in Observation X. Here the temperature never fell to normal: the marked remissions corresponding with the fading of the exanthem appeared to be positive on the seventh day of illness; but

then up to the twenty-ninth day the case proceeded with a slight elevation of temperature, and on several days with the *typus inversus.*

All local disturbances were lacking, with the exception of the splenic enlargement, which remained demonstrable until the twenty-first day of the disease.

We see from Figure 73 that in the course of time the rises became somewhat less high, until finally the normal was attained.

OBSERVATION XIII.—Karl M., two and three-fourths years of age. In the night of the 28th–29th July, 1878, about 12 o'clock, vomiting. On the morning of the 29th, admitted to the Policlinic. Tongue coated, with somewhat swollen papillæ, slight angina, slightly swollen cervical glands, slight bronchial catarrh. During the evening: *scarlatinal exanthem* beneath the clavicle, the tongue characteristic. The exanthem spread until July 31st still further, but was not severe. On August 22d it began to fade. Undisturbed course, desquamation, but no excoriation.

In this case—and it was a mild one—the temperature returned to normal after a course of about fifty-six hours, and continued so for two days, first at a subnormal level, whereupon there appeared again, and without any local symptoms, a short rise to 38.8° C. (101.8° F.).

In the succeeding time there were only subnormal readings, figure 74 showing the outline.

We have now attained a point from which we may more easily consider the condition known as "**secondary fever.**"

FIG. 73.—Recession of the exanthem.

I have given these examples because, in my opinion, they show that the scarlatinal toxin is of itself able to cause such deviations in the temperature curve. This appears to me a proof that the toxin can remain for a comparatively long time within the body, that it is in such a case also more enduring than that of measles. Its tenacity of existence outside the organism makes itself evident also within. Thus an analogy is suggested, in that, just as in the case of an epidemic the gradual attack upon the masses of the people is interrupted by pauses, the same is true of the indi-

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vidual cases that are attacked. How nearly this corresponds with the fact, may remain undecided; to the unprejudiced opinion, however, the comparison is a striking one.

Fürbringer * has chosen this term for a fever "following genuine scarlatina, that is independent of, and certainly caused by no discoverable complication. Its type may be very various: "*recurrent*," "*defervescent*," "*stationary*," "*irregular*"—all these are mere words, for whose significance we must diligently search.

Wunderlich † certainly recognizes the condition, and also Thomas,‡ and, in a measure at least, Henoch.§ Also to me the matter has for a long time been not a new one. More detailed are the descriptions of Gumprecht, ‖ based upon Fürbringer's Berlin material. Gumprecht describes, in addition to light cases of the kind reported here, severer ones also. He places, moreover, the transitional forms, as described by Thomas, among the anomalous varieties of the fever curve.

Thomas recognizes two anomalous types that appear in the connection.

1. "Anomalies can be caused by the fever, in that it may appear after a normal development and course of the exanthem and of the angina, not only to a certain extent in the period of defervescence, but may continue for a time. Sometimes it is of a nature that corresponds with the form of scarlatina that will be described later as lasting for weeks with a typhoid course, and at others it follows an irregular course, with a generally increasing intensity, this being especially true when death occurs at some time between the end of the first and the third, and, as a rule, during the second week; still again, with a varying but marked elevation of temperature and an irregular course, due to new processes that are devoid of direct danger to life, but which always destroy hope of a rapidly favorable outcome.

FIG. 74.—1, Fourteen hours after the beginning of the disease; 2, exanthem fades.

* "Real-Encyklopädie," Bd. XVII, S. 472. † *Loc. cit.*, p. 333.
‡ v. Ziemssen's "Handbuch," *loc. cit.*, pp. 272 und 293.
§ "Vorlesungen über Kinderkrankheiten," S. 633, 3d edition
‖ "Zur Kenntniss des Nachfiebers beim Scharlach," Jenenser Dissertation, 1889.

Finally, it may occur without any further cause, and with a slower defervescence, than is the case in the simple delayed type.

"Not rarely, after a temporary remission, there occurs in cases characterized at first and during the eruptive stage by a slight or moderate degree of fever (such cases may run a more serious course), a temporary pyrexia, either rapid or slow in progress, marked by an unusually severe exacerbation (41° C.—105.8° F.—and over), not always occurring in the evening, and sometimes introduced by chills.

"Usually these cases are accompanied by intense nervous symptoms of all forms, the severity of which corresponds to some extent with the degree of pyrexia, so that they seem to be directly ascribable to the same. The pulse is often unusually high (160 and over), the heart action extremely violent, and the first cardiac tones are either very diffuse or altogether replaced by a murmur."

Thomas adds that these cardiac changes, possibly accompanied by dilatation, can only be *functional disturbances.*

Myocarditis and valvular endocarditis occurring at this period of the disease belong among the complications of scarlatina.

2. "By no means seldom occurs still another form of the disease, characterized by slight or moderate localizations, and by disproportionately severe and a very long-drawn-out fever. The latter feature, together with the considerable intensity of the pyrexia, warrants the term 'scarlatina, with a course similar to typhoid fever.'

"Evidently in this form the fever is of major, and the local affection of minor, importance, although at times nothing more than a protracted local disturbance appears to cause the continuation of the fever into the fourth week and longer.

"The *eruption* in this form of scarlatina appears usually after a hyperpyrexia of several days' duration, which follows a sudden initial fever. It is often unusually slight; otherwise it develops according to rule. The *angina* is second in importance of the local affections, and is also frequently of no consequence. It is, as a rule, present in advance of the exanthem. Notwithstanding these facts, *brain symptoms and fever*, especially in the beginning of the disease, are not infrequently quite marked; the expression is vacant, thirst severe, and the tongue tends to dryness, yet clearing itself in a characteristic manner. Some cough may be present, and the skin, which after the fading of the exanthem has desquamated as usual, remains dry and hot. Later the patient is apathetic, and, in addition to some slight affection of the organs of hearing, is usually deaf; the spleen swells somewhat, *hypostasis may occur in the lungs,* and the *bowel movements*

are of the nature of a diarrhea. As a rule, no local affection other than a moderate enlargement of the cervical lymphatic glands is perceptible in connection with the remittent fever of weeks' duration."

Nephritis may appear in the third week, and, according to Thomas, determines, when present, the character of the fever.

At the autopsies of subjects dying in the later periods of the disease one notes, besides the usual involvement of the pharynx, the lymph glands, the skin, and perhaps also the kidneys, "hyperemia of the brain, slight turbidity of the meninges, catarrh of the air-passages and pulmonary hypostasis, transudations into the serous cavities, the liver and spleen full of blood and often swollen, *marked follicular involvement of the intestinal tract, and infiltration of its mesenteric lymph glands; sometimes also Peyer's patches are swollen in a manner rather similar to typhoid fever.*"

It is by no means certain that in these cases there is a real complication with enteric fever.*

A perfect understanding of the cause of the disease that may be active here or there will be repeatedly denied to us so long as we fail to recognize the cause of scarlatina itself. I feel that we are again concerned in distinguishing a septic infection from one caused by the toxin of scarlatina, and must state, as before, that we are on a very slippery footing.

It must be admitted that the pus cocci are able to cause a very similar picture in the disease. Thus, the form first described by Thomas corresponds almost exactly with that which we see sometimes arising from an obscure septic infection, especially in conditions characterized by cardiac affections.†

It exceeds, however, the authority warranted by the actual facts to ascribe, as Fürbringer and Gumprecht wish to do, everything to streptococcus infection that occurs in the form of a secondary fever.

"Secondary fever is probably a distinct form of secondary infection, and bears in scarlatina a direct relation to the streptococcus findings.

"It is probable that the streptococci can enter even through tonsils that are not diphtheritic.

"The biologic process taking place after the entrance of the

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* Thomas, *loc. cit.*, pp 293, 294.

† Compare my text-book, " Lehrbuch der speciellen Pathologie und Therapie," 3d edition, S. 296, "Kryptogenische Septico-pyämie," S. 441, " Endocarditis." Leipzig, 1894, Veit & Co.

streptococci may, moreover, exhaust itself, and its pyrogenic influence be the only recognizable feature."

These are statements of Gumprecht's,* with which Fürbringer coincides.

On the other hand, it may be said that we have no right to deny the ability of the scarlatina toxin to remain longer in the body than is the rule, and itself to cause the condition. Relapses themselves prove this possibility.†

How often does it actually take place? In my opinion, as already stated, not so very seldom. For if we follow out systematically, as I make it a rule to do, the course of the temperature after the active period of the disease is ended, pictures similar to those furnished by figures 72, 74, and 81 become quite frequent. Moreover, the clinical symptoms do not always coincide with those of the milder septic infections. While the latter frequently affect the temperature in a manner resembling the secondary fever of scarlatina, the former processes differ in that long afebrile intermissions occur,‡ extending over weeks. *Still more weighty appears the fact that the great tendency of the septic infections to a relapse is not realized in this case.* And of the symptoms of the affection, the temporary swelling of the face, with fever, appearing on the twenty-second day of the disease, is not likely to be ascribable to a septic infection, while its peculiar relation to the invasion of scarlatina is well known.

The course of the disease and the autopsy findings in the cases described by Thomas as "scarlatina with a course similar to typhoid fever" hardly coincide with what one sees in sepsis, nor do they correspond perfectly with a general infection running its course without any severe local involvement.

The marked involvement of the follicles in the intestine, to which especial attention is called, we have seen even in those cases that have had a rapidly fatal outcome (compare Observation IV).

Subnormal temperatures not only occur during the several days following the fever, but may continue, even in the mildest cases, for several weeks. This was the case, for instance, with my daughter, six days after the beginning of the scarlatina; then for twenty-two days the evening temperature was constantly below 37° C. (98.6° F.), the morning reading going several times to 35.8° C. (96.4° F.).

We have still to mention the fact that the highest temperatures

* *Loc. cit.*, pp. 21, 22. † See page 466.

‡ Compare Dennig, "Ueber septische Erkrankungen," S. 51, Leipzig, F. C. W. Vogel, 1891.

known may be attained in scarlatina. These are, as a rule, preliminary to death. Wunderlich has seen under such circumstances 43.5° C. (110.3° F.), Thomas almost 44° . (111.2° F.), Leichtenstern 42.8° C. (109.0° F.) and 43.3° C. (109.9° F.). Yet when this does not continue too long, temperature readings of 42° C. (107.6° F.) may occur, and the case still recover.

A satisfactory and perfect understanding of the fever in scarlatina is, to my mind, impossible. The use of the thermometer until late in the convalescence—and this must be repeated again and again—is indispensable, if we would follow out the course of the disease. Sometimes it is only by such measures that we recognize impending dangers, and perhaps combat them.

THE EXANTHEM.

Henoch is undoubtedly correct in the statement that there can be no description that will embrace all forms of the scarlatina eruption. We become convinced of this, both at the bedside and by reading the descriptions of the various authors. I will confine myself to Thomas' description of the skin lesion in the early stages—and I have usually noted about the same conditions.

First of all, one notes on a pallid skin thickly arranged puncta, approximately the size of a pinhead, in the beginning a light red color, but soon becoming darker, and for the most part slightly extending their area. These puncta are arranged at equal intervals, and are of like size, leaving about as much of the skin free as is covered by them. In this way they form a characteristic picture, which continues, however, only for a short time. The skin soon swells in the interspaces, together with the puncta, from which the redness spreads to the surrounding areas. In this way there appears the more or less deep scarlet-red character of the skin. Observed from a short distance (Henoch, Fürbringer), the color is uniform. If one observes more closely, he recognizes the original red puncta, the areas surrounding them, and perhaps even tiny white lines between the latter. In a moderately developed exanthem these are never nearly so broad as in measles.

Fürbringer offers an appropriate simile when he says that in measles the skin appears to be sprinkled with red ink; in scarlatina, as if it were smeared with it.

In order to *understand the process theoretically*, we may state in a general way that in scarlatina, just as in measles, the exanthem springs from individual foci; from a practical point of view, it may be considered that

in a short time there is a complete running together of these foci, and that the skin lesion thus appears a more uniform one.

Not invariably, but very frequently in some epidemics, papules develop upon the scarlet spots, and from these come tiny, discrete vesicles. The name **scarlatina miliaris** (*scharlachfriesel*) has been given to this form, and although previously a special significance was attached to it, it must to a certain extent be looked upon as the same condition.

[Griffith * insists that this clinical form of the disease is not an indication of severity of type; neither is there any parallel between the degree of intensity of the eruption of miliaria and that of the scarlatinous rash; nor is there any consonance between the amount of miliaria eruption and the degree of scarlatinous desquamation. There is no doubt that a profuse miliary outbreak may mask the presence of the scarlatinous rash in certain cases and cause difficulty in making the diagnosis.]

The extension of the scarlatinal eruption over the skin follows certain rules far less than is the case with measles. Bohn expresses the state of affairs as follows: " In scarlatina the exanthem departs frequently from the anatomic sequence followed in measles and smallpox for its extension over the surface of the body. We may, however, fix it as a rule that the scarlatinal eruption appears first beneath the clavicles and on the neck; and then shortly on certain portions of the face—and in regard to this I shall speak in detail. Then follow the skin of the head, trunk, arms, and hands, and, last of all, the legs and feet."

With this description of Bohn's I must coincide. It also agrees with what has been taught by Bartels. Stimulated by these men, I have paid much attention to the method of extension of the exanthem, and therefore venture to refer to my own observations.

With regard to the various details I can state the following:

The region around the mouth is seldom involved by the eruption. In striking contrast to the surrounding parts, the slightly swollen skin appears like a broad, white ring including the lips and to the chin. The cheeks are more generally flushed, and one sees on them only occasional scarlatinal puncta. The latter appear, however, upon the forehead, the scalp, and, as a rule, also on the ears. With the extension of the eruption the face takes on in the very beginning an altogether characteristic appearance. The pale oral ring is caused by a poor supply of blood to the part, and we may with propriety

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* *Phila. Med. Jour.*, 1900, v, 1091.

speak of a spasm of the blood-vessels; on the other hand, the contrast with the deep red of the surrounding areas is also in evidence.

Thomas claims that the finely punctate and more uniform exanthem on the trunk, throat, and neck, like that on the upper halves of the extremities, appears fully developed, "while on the lower limbs and forearms frequently occur wider spaces between the single spots than in most other portions, and even small, and entirely free areas of skin. On the other hand, close beside these are areas of diffuse redness, equal in size. We see not rarely a confluent redness, especially in the neighborhood of the joints." I am of the opinion that, on the whole, this description will meet requirements, but have the impression that individual epidemics present their own differences in this respect, and the statements of the same observers in regard to the character of the eruption on the hands and feet are fully authorized; frequently a papular elevation of the single spots (roseola) with scarlet puncta in the neighborhood on the dorsal surfaces of the hands and feet. On the inner sides of the hand and feet there is a more uniform and often only a slight redness.

It is also worthy of mention that the areas over the joints, and especially their extensor surfaces, are more actively involved than the area around them. There is often an extraordinarily marked eruption in these localities.

There are innumerable transition forms between the fully developed scarlatinal eruption and the form of the disease that runs its course without an exanthem (see p. 464).

More or less extensive portions of the body may remain free, or be so slightly and for so short a time involved that only an unusually careful observation will discover the eruption at all. The order of involvement of the parts may be anomalous; or, finally, in place of a face that is usually either slightly or not at all involved, we may have one covered by a fully developed exanthem. And when we consider scarlatina in its entirety, we fail to see in all of this an anomaly.

[Lemoine * relates that in an epidemic of 200 cases of scarlatina the eruption and desquamation were limited to the face in 23. The claim has been made that in such cases the eruption is only an erythema which accompanies a non-scarlatinous angina. Lemoine therefore took note of the state of the face in 93 cases of simple angina and found that but 6 of the latter were accompanied by erythema. He appears to believe that some of these cases at least were

*Arch. of Pediatrics, xv, p. 178.

examples of atypical scarlatina. (Compare "Fourth Disease," under "Rötheln.")]

The skin nearly always—except, of course, in cases of a slight exanthem—is extensively swollen. Its redness increases gradually from the first appearance of the eruption, and is usually more marked in the evening than in the morning—a fact undoubtedly dependent upon the fever. Quite frequently in severe eruptions there appear small extravasations; these must not be taken for an expression of a general, severe infection, but rather as one of the extreme congestion of the skin. Hemorrhagic diathesis forms an entirely different condition.

Very early in the eruptive stage, and certainly during the first twenty-four hours, the redness disappears with pressure and upon the active stretching of the skin, so that we see in these areas a normal color. It may be that not even the smallest petechiæ have appeared at this time. Later there is a different condition present. The skin now appears on pressure a uniformly yellowish-red color, over the entire extent from which the blood has been displaced.

There is only slight significance in the fact that the skin in scarlatina, when a slight mechanical stimulus is exerted, becomes pallid as far as the influence of the stimulus extends. This depends upon the increased excitability of the smooth muscle-fibers in the smallest capillaries. One can write in white letters on the skin simply by carrying the rounded point of a pencil over the skin; this cannot, however, be utilized in the diagnosis of scarlatina, as Bouchut claims; and Henoch and Thomas have lately taken a well-founded exception to this theory.

The scarlatinal rash is associated with itching, which is most marked when the miliary vesicles are present in large numbers. Sweating usually accompanies the severe itching, and occurs not only at the time of the appearance and at the acme of the eruption, but a little later also, and in increased measure.

I wish to insert here a report by Unna * of the tissue changes found by him in the skin at the height of the disease.

1. Marked wrinkling of the entire epidermis and of the papillary body in contrast to the cutis, which is tense and relatively less extensive, and retracted from its position.

2. True edema is not present in the cutis; the latter is, however, distinguished by an enormous distention of the blood-vessels. The capillaries of the papillary body, and also of the cutis itself, are distended in a uniformly tubular manner, as if forcibly injected.

* "Die Histopathologie der Hautkrankheiten," Berlin, Hirschwald, 1894, S. 628.

Only as an exception is there in scarlatina an interstitial edema of the cutis, and a distention of all the lymph spaces, especially in the neighborhood of the follicles. The condition is rare, and occurs only in certain areas. It would correspond to the form of *scarlatina papulata.*

3. Inflammatory phenomena are altogether lacking, and true inflammation need not be considered.

In the prickle layer (lying immediately over the cutis) there are hardly any changes, and especially are mitoses wanting. Only in the transition layers and on the epidermis itself are they to be found. We can differentiate two forms:

(*a*) *The callous type.* The stratum corneum (outside the prickle layer) remains, but the horny layer lying above it shows no longer the division into layers; rather, the three normal layers, according to Unna,* are melted into one.

(*b*) *The type simulating the mucous membranes.* The stratum corneum has disappeared, and in the imperfectly hornified mass, which is loosely connected, and in which the nuclear remnants are preserved in the form of little rods, the upper layers excoriate in an irregular manner, and the prickle layer is continually being transformed into a desquamation.

4. The puncta of scarlatina correspond only to a hyperemia that is much more marked throughout their areas, and through them can occur a genuine extravasation.

5. No explanation can be given of the tissue changes that lie behind the formation of the miliary vesicles. The further changes suffered by the skin, after the exanthem has passed its height, are as follows:

There follows a desquamation of a double nature: First a branny type, as in measles; this involves the scalp, the face, the neck, and the trunk, as a rule. Then in the form of patches or layers—separation of the skin in considerable fragments, especially on the palms of the hands and the soles of the feet. It can involve the entire surface of the hands, and to a lesser extent the feet. I received once as a present from Ernst Brand (Stettin) an almost perfect glove from the hand of a young girl. The scaling on the other portions of the body is not so severe, although pieces several centimeters long may be cast off in those areas where, as a rule, only the branny desquamation takes place.

The rule is usually followed that the scaling begins on the skin in those areas in which the exanthem first appeared, and in its development it follows still further the original mode of extension. It is by no means rare for the scaling to commence on the upper body, while

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* *Vid.* Unna, " Darstellung der Histologie der Haut," in v. Ziemssen's " Handbuch," Bd. xiv, I, S. 23.

the hands and feet only become redder. It must be stated as a positive rule, however, that the beginning of desquamation takes place at the point where the eruption begins to fade.

Thomas claims that the desquamation may in rare cases follow the exanthem only after a lapse of several weeks. I have never observed this to be the case, and can find no confirmation of it in the literature.

The length of time covered by the desquamation is a varying one, especially after a marked eruption. It may be that it repeats itself in certain areas; and that on both occasions either shreds or small pieces are cast off, or perhaps at one time the former, and at the other the latter.

If now, as Thomas has reported of a case of Jadioux, the desquamation repeats itself five or six times, there is no possible limitation for the time required. In this connection, as in all other questions involving the primary influence of the scarlatina poison, influences are at work that are very difficult of recognition. Thus the degree of desquamation does not always correspond to the extent of the eruption. This is said to be possible to such a measure "that a typical desquamation may occur on portions of the body without any eruption having preceded it,—e. g., on the face,—and that, too, in patients in whom there has been noted only a very temporary and minimum reddening of the skin, or absolutely none at all." Thomas * refers to a large number of writers who confirm his statements; and yet they are not incontestable, as Mayr † implies between the lines. Henoch,‡ on the other hand, asserts himself positively as follows: "I have never seen the desquamation of the epidermis take place except as the result of a more or less fully developed exanthem. In two cases of scarlatina sine exanthemate there was absolutely not a trace of desquamation perceptible."

These were cases of young women who nursed their sick children, and had a febrile angina without an eruption, and then fourteen days later a nephritis, so that the diagnosis was assured. Henoch calls in question the accuracy of the statements made by other men in this regard, and without sufficient reason; for it is only claimed that after an eruptionless scarlatina the desquamation *may* take place, not that it must occur. A negative observation is by no means conclusive against the possibility of occurrence.

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* v. Ziemssen's " Handbuch," *loc. cit.*, p. 225.
† Virchow's " Handbuch," Bd. iii, S. 118.
‡ *Charité-Annalen*, Bd. iii, S. 557.

The matter is made somewhat clearer by Unna's investigations. He found exactly the same histologic changes in the epidermis, only somewhat less fully developed, in those areas of the skin of a scarlatina patient that had not participated in the redness. So that the possibility could not be excluded that in cases where the erythema was totally lacking the processes in the skin that precede desquamation were none the less present. This, of course, remains unproved. For this purpose it is necessary to directly examine the skin from an eruptionless case of scarlatina, and whether Unna has done this, does not appear certain from his account.

Attention should be called to the facts, from the side of the physician, that a slight desquamation may be seen upon the nails of the hands (as well as of the feet) when it is not to be seen anywhere else (Jenner). We must observe this fact in the decision of the foregoing question. In contrast to this slight desquamation, there may be one so considerable that the nails of the hands and feet are shed and the hair falls out.

The histologic examination of the skin at such a time gives, according to Unna, the following:

" In the *callous form* the homogeneous callous, horny layer of the skin is separated by a loose stratum corneum from its juncture with the normal middle layer. This results in a new normal basal layer and stratum corneum.

" In the *form simulating mucous membrane* the loose horny layer passes gradually into a firm basal layer, and the stratum corneum."

To the callous type belong the shreds of skin, and to the form simulating mucous membrane belong the scales, the latter process not rarely passing over after a time into the former.

The nuclear proliferations are comparatively scarce. In the cutis there occur at the commencement of this period, around the vessels and on the papillary bodies, numerous nuclear changes, as usual, but they are confined to the fixed connective-tissue cells. Generally speaking, the procedures that take place are such as lead slowly to the re-establishment of the epidermal tissue, histologically speaking.

All changes that take place in the skin of scarlatinal cases Unna attempts to classify as direct results of the influence of the scarlatinal eruption upon the skin. The intermediate inflammation plays in this light an altogether secondary rôle. The same fact is true in measles, and, it appears to me, it is supported by good reasons. If these conclusions are correct,—and there are no criticisms of them, so far as I know, on the part of the specialists,—then Unna's statements are well worthy of notice.

"The main fundamental difference in the intoxication in the two processes lies in the fact that in scarlatina a pure paralysis of the vessels occurs, while in measles spastic congestive symptoms concur and predominate. The customary inflammatory signs are in both infections very secondary processes, and occur only exceptionally to a marked degree, and are then confined to local areas.

"The processes in the epidemic forms are likewise much more intelligible when considered as direct, specific influences of the poison, than as the outcome of a simple dermatitis. Were they only the latter, the desquamation in scarlatina must needs be slighter than in measles, corresponding with the smaller quantity of exudate in the lymph spaces, whereas the facts are just the opposite.

"Just this last point forms the most pregnant histologic contrast between the two diseases; the blood-capillaries are distended to their widest limit without distention of the lymph vessels in scarlatina, while in measles the lymph spaces and channels appear large in the skin of the cadaver beside the narrow blood-vessels."

Retrocedent scarlatina is talked of less among the laity than retrocedent measles. And with good reason; for even when the heart action has been considerably depressed, one always sees in the much-distended capillaries of the skin a sufficient supply of blood; true pallor does not appear, and there is only a darker color. The blood becomes even richer in CO_2. If now the skin becomes a deeper red after a bath, we hear great joy expressed that the eruption has again appeared. The reason of this lies in the idea that a new eruption has occurred that diverts the poison from the vital parts. This is, however, not to be seriously considered; the blood merely flows more quickly through the skin. A more active cardiac action is always evidenced in this manner, and, in truth, in this measure it is a good sign.

With regard to the external forms taken by the eruption, we differentiate:

Scarlatina lævis, the usual form of uniform redness as seen from a short distance, and of swelling of the skin with its characteristic features. There is no warrant for such a division as *scarlatina lævigata*, which may be and should be classed as merely a more marked appearance of scarlatina lævis.

Scarlatina papulosa, the formation of papules on the skin and a more decided development and swelling of the puncta.

Scarlatina miliaris, the formation of vesicles on a skin that otherwise appears normal.

Scarlatina variegata, the form that tends most easily to confusion. It is not described with great concord of opinion, though every one agrees in the presence of variously formed discrete foci, of different sizes, which first

appear as described, but later run into the surrounding areas and present the customary picture of a scarlatinal skin.

Whether the discrete foci can be recognized as such in the further course of the disease by their color and more divided swelling; whether they extend to the face; whether they appear only here and there on portions of the body that show in other respects the usual involvement; or whether they come and go with varying redness, or remain;—all these matters are of secondary importance.

Scarlatina hæmorrhagica. Small punctiform petechiæ are so frequent, and especially in the region of the joints, that we have been used to term them almost normal in a severe eruption. Also in other localities they belong by no means among the unusual phenomena. There is certainly no justification for the classification. As far as concerns the recognition of purely local changes in the skin, it is devoid of value; while as an expression of a severe infection it is totally useless.

OTHER INVOLVEMENTS OF THE SKIN.

The foregoing skin processes are undoubtedly the direct result of the scarlatina. Besides these, still others sometimes occur, whose relation to the main disease is not altogether clear. I wish in this connection to consider the deeper processes in which the cutis is also involved. The suspicion at once arises that a secondary infection, whether septico-gangrenous or one due to pus-producing organisms, plays a part in such cases.

Experiences in regard to the frequency of these processes differ. Henoch has seen them only rarely, others not so seldom. First of all, one will note decubitus in portions of the skin that have been exposed to severe pressure. Whether also the nutritional disturbance of the skin, caused by the scarlatinal toxin, requires special consideration, is doubtful. Were it so, gangrene from pressure must needs appear more frequently than in other infections, whereas this is not the rule. In certain epidemics it may be the case, and then the destructive process attacks also other portions of the skin. It may appear in quite different ways; as blebs, that remain discrete, or more frequently as extensive elevations of the epidermis, as papules, nodes, etc.

OBSERVATION XIV.—August H., nine years old. Became suddenly ill on the afternoon of July 16, 1875, with severe vomiting, angina, fever, which was first moderate (39.0° C.—102.2° F.) and later rose to 40.5° C. (104.9° F.). Marked eruption, swelling of the glands, gangrene of the tonsils, severe brain symptoms. Death on the eighth day of illness. On the seventh day there appeared on the skin great blebs, in regard to which the autopsy notes state "on the upper extremities the cutis is dry and crusty, following a blebs formation and rupture of the epidermis, and portions are involved in an ulcerative process."

In addition, there was gangrene of the nasal mucous membrane and of the tonsils, as well as of the esophageal membrane.

[Eichhorst * knows of but three cases in literature in which gangrene followed scarlet fever. The lower extremities were the seat of the gangrene in all the cases, while in one (the author's) the arms were affected as well. In the author's observation the origin of the gangrene was an embolus.

Wilson † described a case in which symmetric gangrene extended from the nose upon the rest of the face, a similar phenomenon occurring over the sacrococcygeal region. The process developed about three weeks after recovery from scarlatina.]

This was undoubtedly a case of gangrenous infection. The case, which is reported from Bäumler's clinic by Hildenbrand,‡ looks more like an infection by pus cocci, and is also so considered by the writer. He expresses himself as though considering rheumatic phenomena, and an evident embolic affection of the skin, similar to a purpura hæmorrhagica with gangrene of the skin. I give an abstract of the case.

OBSERVATION XV.—Karoline S., twelve years of age. Became ill of scarlatina on March 2, 1889, in the Freiburg surgical clinic, where she was under treatment for infantile paralysis, and was promptly transferred to the medical clinic. Distinct exanthem. Angina, with membrane formation, which in the next few days covered the tonsils and uvula. Temperature up to 40.4° C. (104.7° F.).

On March 5th: Exanthem slight and hemorrhagic.

March 6th: Pain in the wrists; on the 11th, in the left arm. The temperature from the 5th on, attained at no time 39° C. (102.2° F.).

March 16th: Wandering pains in the limbs, epigastrium, and cardiac regions. In the throat slight remnants of the membrane are to be still seen. On the 17th pain in the interphalangeal joints of the left middle finger.

March 18th: After noon, and lasting for a few hours, multiple and extremely painful swellings of the joints of both arms (fingers, hands, and elbows) developed; moreover, on the elbows and the extensor surfaces of the forearms tiny pea- to bean-sized papular infiltrations of the skin were seen, with hemorrhagic centers and surrounded by a pale area. Vomiting; the eye-grounds normal; the cardiac tones clear.

March 19th: Also on the lobes of the ear as well as on the buttocks similar skin eruptions, partly in the form of tiny petechiæ, partly of larger, hemorrhagic infiltrated nodules; here and there a blebs-like raising of the epidermis; about the involved joints a marked periarticular edema; vomiting; excited heart action; albumin in the urine.

March 20th: Again there is a fresh membrane formation in the throat in different areas with a tendency to confluence. The skin involvement on the extensor surfaces of the elbow-joints has changed into great hemorrhagic, gangrenous patches surrounded by a red inflammatory area. The

* Deutsch. Arch. f. klin. Med., Bd. LXX, 5–6.

† Review in " Arch. f. Kinderheilk.," 1898, XXIV, p. 418.

‡ " Statistical and Clinical Data concerning Scarlatina," reprinted from " Bericht der Naturforschenden Gesellschaft zu Freiburg i. B.," Bd. VII, 2. Heft., S. 34.

joint enlargements are somewhat lessened; vomiting; heart action very excitable.

March 22d: Joint enlargements, especially on the elbows, diminished; on the left side the whole dorsum of the hand edematous. On both thighs a scattered fresh eruption, on the right side an extravasation going as deep as the fascia. Also on the upper arms several fresh hemorrhagic nodules. In the pharynx an extensive necrotic membrane; also on the tongue and oral mucous membrane discolored, gangrenous, and fast-clinging patches; an intense pallor; the gums swollen, bleeding easily; a marked gangrenous serous nasal secretion.

During the further course of the disease there appeared on March 25th a change in the first cardiac tone, resembling a murmur, and then remaining as an indistinct sound. The pulse-rate was always very high in proportion to the temperature, which never went above 39° C. (102.2° F.). The maximum occurred on March 20th—172 and 39.3° C. (102.7° F.). Sometimes the pulse was irregular. Until April 4th the gangrenous hemorrhagic areas on the extensor surface of the elbows were gradually cast off and replaced by large and healthy looking granulation surfaces.

On March 28th there were again considerable brain symptoms, which were, however, of short duration. On April 22d erysipelas appeared on the left thigh, continuing only until the 25th.

The condition of the pharyngeal mucous membranes improved from the end of March on. The elbow-joints were on April 24th freely movable. On May 7th the child, still somewhat anemic, was sent back to the surgical clinic.

In my opinion, the simplest explanation for the rare phenomena is afforded by the presupposition of a *sepsis*, asserting itself very early in the joint pains on the fourth day of the disease. Besides the skin affections there was very probably a local involvement of the heart; also the late pharyngeal complication can be interpreted as a streptococcus diphtheritis.* The erysipelas presents just as few difficulties. According to the rather generally accepted theory that the erysipelococcus of Fehleisen is identical with the streptococcus, the condition is to be characterized as no more than a flaring up of a septic process, which is rather the rule than the exception. In some cases it is hardly, or only with difficulty, possible to decide whether the skin lesions hold a close or distant relation to scarlatina. One must never lose sight of the fact that decided disturbances of nutrition are dependent upon the toxin, and that these can assert themselves through constitutional as well as by localized symptoms; through the former, inasmuch as they are able to effect for a considerable time changes in the functions of the skin—including nutrition and function in the widest meaning; through the latter, because of the fact that temporarily the conditions become more favorable to the entrance and settlement of any of the parasites.

* *Vid.* Dennig, *loc. cit.*, Case 20.

I am inclined to consider from this point of view, also, the **furuncles** that appear by no means rarely after scarlatina, recurring frequently, and spreading in large numbers over the entire body, and also the **multiple abscesses** that may be present. In these cases there is a localized aggregation of streptococci and one, as a rule, limited to narrow foci. Following smallpox, the occurrence is even more frequent, and to be interpreted in the same manner.

In the brief report by Leichtenstern it is stated * that in two cases of scarlatina the previously normal skin suffered long-continuing (chronic) changes, asserting themselves in the form of an exaggerated desquamation, roughness, dryness, and thickness of the epidermis.

Wallenberg's † observation takes an entirely different ground. In the case of a twenty-one-and-a-half-year-old man who, it appears, had a moderate attack of scarlatina, the desquamation followed a curious course:

1. The epidermis was elevated over almost the entire surface of the body—the rete Malpighii lay partly uncovered and in areas the size of the palm of the hand, and was partly covered with a coating of mucoid crusts (*Schleimkrusten*).

2. In certain localities (lids, neck, legs) there was pus formation in the subcutaneous tissue, that required evacuation.

3. The finger- and toe-nails came off; the hair from the head and beard, the eyebrows, the eyelashes, the hair on the pubes, and the fine hair over the entire body was absolutely lost.

The desquamation continued for about four weeks. After its completion there remained a permanent alteration in its place:

4. *The patient, who formerly had a dark complexion and dark brown hair, had now white hair,* which (according to Perl) showed the peculiarities of the newborn, or of that acquired in old age. The skin became almost milk-white, with a shade of reddish.

5. There remained a marked sensitiveness of the skin to external irritation. Wide-spread eczema appeared even when mild irritants exerted their influence.

In this case both influences may have worked together. The abscess formation is hardly conceivable without pus cocci, and since no severe constitutional symptoms are reported, their lodgment in the subcutaneous connective tissue after their entrance into the locality is probable.

The outspoken, severe, and continuous nutritive disturbances of the skin, and their sister complications, we may consider to be evident results of the scarlatina toxin. Dr. Wallenberg holds, and properly, that removal of the pigment cells may be inferred from the albumin, and that the deeper layers of the epidermis were permanently injured.

Urticaria, a condition that I and many other physicians have seen in the course of scarlatina, has no constitutional significance.

* *Loc. cit.*, p. 174.

† "Ein Fall von bleibender Veränderung der Haar- und Hautfarbe nach Scharlachfieber," "Vierteljahrsschrift für Dermatologie und Syphilis," 3 Jahrgang (1876), p. 63.

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It may occur as a chance condition, and it may appear as an accompaniment of some other infectious process.

With regard to the **herpes,** it need only be said that the phenomena may appear early or late in scarlatina, and in severe as well as in mild cases, and usually in the vicinity of the mouth.

Pemphigus has frequently been observed in company with the eruption of scarlatina, both in sporadic cases, and here and there in epidemics; also during the desquamative period.*

INVOLVEMENT OF THE PHARYNX AND ORAL CAVITY.

The toxin of scarlatina holds close relation with the pharyngeal organs, and in them it exhibits its typical lesions.

In this very general statement a principle may be represented as thoroughly established. That exceptions occur has been already stated, but such cases are to be looked upon just as are those in which the exanthem is missing on the skin, and do not alter the actual fact.

On the other hand, opinions differ as to whether the scarlatinal toxin alone comes into consideration, or whether alongside of it other causes of disease are at work.

The latter is a possibility, and must, without question, repeatedly be allowed. But—and this is the essence of the question—*can the toxin itself cause the severe tissue changes in the pharynx, or are these processes which destroy the involved parts always dependent upon the cooperation of other micro-organisms?*

The time will come, we hope, when the answer to this question will aid the physician in curing the condition. This would be already true if we could always combat the pathogenic bacteria by specific means, whether through such as might originate from their own metabolism, or through some other source. We have not yet reached this point; but we will hardly put aside the attempt to see more clearly into the matter as an unwarranted one.

That some disorder is in progress in the pharynx, and that in scarlatina it makes itself evident early in the disease,—this we have known as long as we have recognized the disease as such. But one will often do well, even in including the entire symptom-complex, not to transgress this line: "Disturbances of function are the only tissue changes perceptible to the eye."

There is a feeling of "dryness in the throat," a slight difficulty in, and possibly an increased need of swallowing, a redness of the pharynx, with more or less distinct swelling of the involved portion,

* *Vid.* Thomas in v. Ziemssen's " Handbuch," pp. 292, 305.

apparent to the physician. This is almost always present in the beginning. Whatever further developments occur, however, depend upon the outcome in the individual case. In my opinion, we cannot calculate upon so accurate a course being followed by the inflammatory processes as in measles. At least I have not found myself able to recognize any regularity. It is the varying severity of the infection, whether simple, and caused by the scarlatinal toxin alone, or whether it is complex, and dependent upon other pathogenic influences also, that causes suddenly at one time an exaggeration of the disturbances that progresses externally as well as in the internal organs, and at another confines itself strictly to the previously involved areas. One thing may, however, be looked upon as the rule: the inflammation of the mucous membrane appears at first more as a uniform redness, and is followed later in certain places by a discrete, very marked spotting. The edges of these areas are slightly raised, in this way creating a picture similar to that seen upon the skin.*

Further than this I do not wish to go. Monti † has described all manner of features as characteristics of the pharyngeal disease. He makes a fundamental difference between the angina scarlatinosa simplex, which he terms "the pharyngeal involvement in an uncomplicated scarlatina," and "cases running an anomalous course." This is another attempt to use the strait-jacket of classification where only a difference in the degree of symptoms is concerned, which are all to be ascribed alike to the same cause—the scarlatinal poison. Nature does not recognize such barriers, either in this or other connections. There are always gradual transitions. A single case will not certainly fulfil its conditions, when stamped with its number, which is deposited here or there in the great magazine. And the number of Monti's observations—altogether 105, of which 58 are distinguished as "uncomplicated"—is certainly too small to form permanent rules therefrom.

My own views coincide thoroughly with those expressed by Fürbringer.

We have still to consider an inflammatory condition of the pharynx which, according to Monti, originates perhaps in the majority of cases from the soft palate, and as a rule extends elsewhere from this point. It may be granted to him that the posterior pharyngeal wall is seldom alone involved in the beginning of a disease by its processes. He sees in this an important diagnostic point as contrasted with the condition of affairs in smallpox.

In order to consider the matter, as it lies before us, it is worth

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* *Vid.* page 510.

† "Studien über das Verhalten der Schleimhäute bei den acuten Exanthemen," "Jahrbuch für Kinderheilkunde," N. F., Bd. VI, S. 227.

while to determine our position from an anatomic standpoint. In this light we can say that:

Any form of inflammation may be present, from one that is superficial, limiting itself to the mucous membrane (*angina super-ficialis* of E. Wagner *), to the pus-forming (phlegmonous), the croupous, the diphtheritic, and gangrenous.

Moreover, it should be stated that from the area originally attacked extensive spreading may take place in all directions; first into the nose and its cavities, through the openings leading into the ear and the eye, and less often to the larynx or still deeper into the air-passages.

In such a case the matter is a simple one. It is a different story when the etiologic condition is an obscured one, and there is a question as to what the cause of the disease is in a given case.

Before all, the following question requires discussion: *Is scarlatina alone able to cause a diphtheritis in the anatomic sense of the word?*

Henoch is perfectly right in saying that nothing causes more confusion than the misuse of the anatomic term "diphtheritis" for the clinical diphtheria. The latter infectious disease not only does not require the accompaniment of a diphtheritic inflammation, but it is a gross error for one to speak of diphtheria when nothing more than a diphtheritic inflammation exists.

Henoch proposes, in order to make the matter clear and practicable, that we speak of *necrotic inflammation* in scarlatina, which anatomically either altogether or nearly assumes the appearance of the diphtheritic type.

The process is essentially one of an infiltration of the tissues by an exudate which later on coagulates, and degenerates to a greater or less extent.

The belief is gaining more and more ground that ascribes to the scarlatina toxin, as such, the power to cause necrotic inflammation.

Henoch † is the keenest representative of this teaching, which makes "the eminent tendency to necrotic inflammatory processes" almost the essential feature of scarlatina. Heubner ‡ coincides absolutely with Henoch, and no less certain is Fürbringer §: "It is

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* v. Ziemssen's "Handbuch der speciellen Pathologie und Therapie," 2 ed., Bd. vii, erste Hälfte, S. 142.

† "Vorlesungen," u. s. w., S. 643.

‡ "Bemerkungen zur Frage der Scharlachdiphtheritis," "Jahrbuch für Kinderheilunde," N. F., Bd. xxxi, S. 56.

§ Eulenburg's "Real-Encyklopädie," S. 468 of the indicated volume.

inexplicable that we find even to-day representatives of the view that scarlatinous diphtheria is in no way different from the real diphtheria."

In the "Arbeit" of Sörensen * the same view is held in a very decided fashion.

Sörensen goes even further. He considers the possibility "whether the scarlatinal diphtheritis may form the anatomic basis for the scarlatina, since the process soon involves the entire body, or whether the diphtheritic angina (or coryza) is the primary focus of the disease, the point of entrance for the infection, owing to the changes produced in it by the disease."

According to Johannessen,† the Norwegian, Thoresen, seems to have expressed this opinion before the Dane, Sörensen: "Thoresen emphasizes the idea that the angina is the primary localization of the disease, and the starting-point of the whole process." By way of evidence, his "Arbeit" is cited, for the year 1872 from the "Norsk Magazin for Lagevidenkaben."

Formerly many held the view *that diphtheria and scarlatina were ascribable to the same cause.*

This ground can no longer properly be held. I wish to state, however, that we (in Schleswig-Holstein) who had not known from experience what diphtheria was up to its appearance in the beginning of the sixties, were by no means ready to deny that it was an abnormal form of scarlatina. Cases occurred which ran their course with a slight eruption, in every way similar to the scarlatina exanthem. This was seen in a number of places, and the Norwegian physicians also, as may be seen from the writings of Johannessen, saw the necessity of considering seriously the identity of diphtheria and scarlatina.

Leichtenstern‡ assumes an altogether unique position in regard to the question. He denies the double infection, since in over 600 cases of scarlatinal diphtheria not once has he seen the paralysis ensue that belongs to the genuine diphtheria. He continues: "It has repeatedly been observed that *scarlatinal subjects with diphtheria, or even with only a slight angina without a membrane formation*, have infected individuals in their vicinity (mostly adults) with severe pharyngeal diphtheria without an exanthem." In no instance did the characteristic paralysis appear as a sequel, though nephritis, with all its results, did follow. On the other hand, Leichtenstern saw in the case of a strongly built healthy girl of eighteen years, who had been in a house infected by scarlatina, and was admitted to treatment because of a moderate febrile angina without exanthem, on the fifth day from the invasion sudden death from cardiac paralysis. The cardiac muscle showed a loss of consistency; otherwise, except for the preagonal pulmonary edema, there were present only a slight swelling and redness of the pharynx.

* "Ueber Scharlachdiphtheritis," *Zeitschrift für klinische Medicin*, Bd. xix, S. 538.

† *Loc. cit.*, p. 18?   ‡ *Deutsche med. Wochenschrift*, 1882, S. 175.

Leichtenstern himself states that certain proof of a new infection could not be found; *i. e., genuine scarlatina transmitted from patients suffering from pharyngeal involvement to others.* Thus there remains a well-founded doubt whether in these cases a double infection may not have been present. Certainly only a doubt, however, for it is always possible, in the wondrous variety of the symptoms in a single epidemic, that, without any other indication of infection, necrotic scarlatinal angina may as frequently occur as was the case in Leichtenstern's experience in Cologne.

There remains the following possibility: that the severe forms of pharyngeal involvement in scarlatina are secondary infections; and that the scarlatinal toxin has only opened the door to the entrance of the diphtheria bacilli and the pus-producing cocci. So that, finally, the idea that every pharyngeal involvement similar to diphtheria must have its origin in diphtheria, seems to me untenable. On the contrary, I hold unqualifiedly the ground that, together with scarlatina, but usually following it, both diphtheria and the septic infections may make their appearance and take their origin from the pharyngeal organs.

I believe, still further, that the frequency with which this occurs is one that varies with the locality and the time; and that, directly owing to this fact, the variety of views among different observers, among whom we see our best men, some supporting the one and some the other view, can be clearly understood.

Gerhardt * and Bohn † have contested the teaching of the identity of genuine diphtheria with the diphtheritic inflammation in scarlatina.

Since we cannot expect a general coincidence of opinion, it will be necessary to adduce the facts that come under consideration.

1. It would be surely an important point *if diphtheria and scarlatina were to be found occurring simultaneously with regard to time and place.* Gerhardt has noted this occurrence in detail with regard to Würzburg (an epidemic of both infections over the city), and, in a general way, in the case of a number of German cities numbering over 15,000 inhabitants. It only remains to comment that the Würzburg observation included but the single year 1878; also that the curves of the scarlatina and diphtheria mortalities in the German cities do not run a parallel course, as, for instance, in the year 1880 (diagram of Gerhardt).

The reports from the kingdom of Norway for the years 1862 to 1878 (scarlatina) and 1860 to 1878 (croup and diphtheria), embracing

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* "Verhandlungen des Congresses für innere Medecin," 1883, S. 135.
† *Loc. cit.,* p. 269.

both the morbidity and the mortality figures, do not show a close relation between the two infections. (See Fig. 75.)
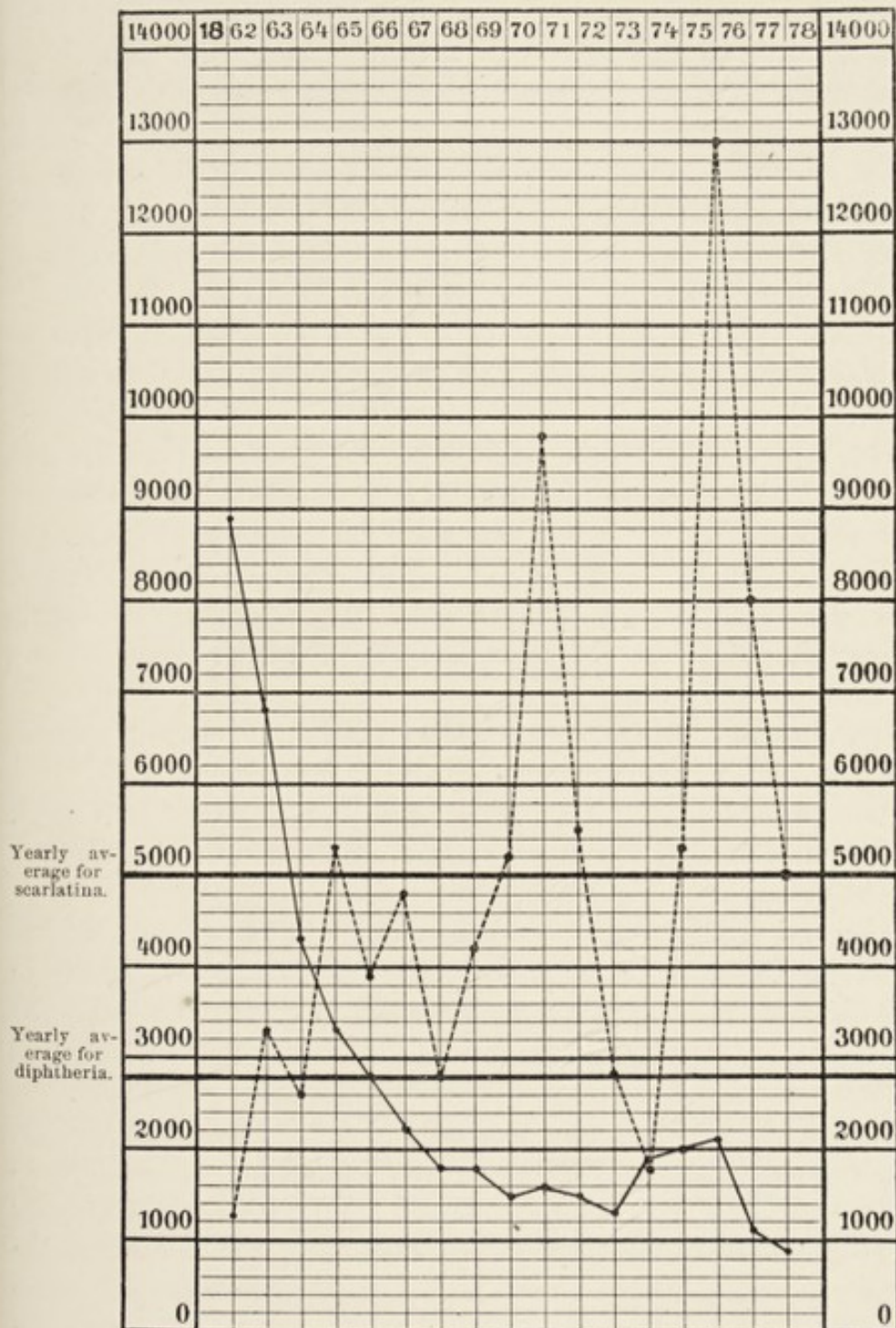
Fig. 75.—(- ⌐ - -), Scarlatina in Norway, 1862–1878; (━━━), diphtheria in Norway, 1862–1878.

I give only the approximate figures of the morbidity, according to Johannessen, and these are altogether sufficient to determine the failure of the connection. From 1862 to 1867 croup and diphtheria are counted together, and from 1868 on separately. For the latter years I have taken

the sum total of both, the figures during this period not being distinguishable. The mortality curve also runs in the same manner.

From this point of view we therefore fail to determine that scarlatinal diphtheritis and diphtheria correspond as to their cause. On the other hand, the question remains undiscussed, whether in localities where both infections hold sway true diphtheria occurs in scarlatinal subjects more frequently, as a complication favored by the pharyngeal involvement due to scarlatina, than where diphtheria is not in evidence. Escherich * goes too far in saying that in the early stages of scarlatina there is actually a lessened disposition to true diphtheria.

2. Since the bacillus of Löffler is looked upon as the cause of diphtheria, one would be inclined to say: Where it is found, we have a case of true diphtheria; where it is lacking, some other condition. And if one proceeds with the necessary care to the examination, and then draws his conclusion from it, this is allowable. But the matter is not such a simple one that we may conclude, merely from the discovery of the diphtheria bacillus in the exudate of a scarlatinal angina, that it is the cause of the disease. The recognized difficulties of identifying the truly virulent bacillus of Löffler come at this point into full evidence.

Investigations have shown that in unquestioned and genuine scarlatinal diphtheritis the Löffler bacillus may be wanting.

I will content myself with referring to the "Arbeit" of Tangl,† who examined five cases from my Policlinic, and two from A. Fränkel's wards at Urban.

Tangl lays special weight upon the fact that in two cases alike, on the first day that the membrane appeared, he made inoculations from the living subjects. Löffler's bacilli failed to appear, as in all the other attempts. Löffler himself has had the same negative result, as well as Babes, Kolisko, Paltauf, Heübner, Sörensen, and others.

Baumgarten ‡ raises the question in this connection whether, since streptococci are so extraordinarily frequent in scarlatinal diphtheritis, the possibility is excluded that "the diphtheria bacillus may have been present in these cases in the beginning, but, because of the especially powerful action of the streptococci, they disappear more quickly than in other instances."

* "Diphtherie, Croup, Serumtherapie." Wien, Leipzig, Teschen, Karl Prochaska, 1895, S. 37.

† "Zur Frage der Scharlachdiphtheritis," *Centralblatt für Bacteriologie und Parasitenkunde*, Bd. x, No. 1.

‡ "Jahresbericht," Bd. v, S. 215.

Just as certainly has the Löffler bacillus been found in scarlatinal diphtheritis. Tangl confirms the findings of Escherich, who did not prove his conclusions in all respects. In all probability this constitutes *a secondary infection*, also a genuine complication, that asserts itself, as a rule, in the later stages, and not in connection with the invasion of the toxin.

It is an important fact that the Streptococcus pyogenes is almost invariably found in necrotic scarlatinal angina, and, as was discovered by Tangl, with Würtz and Bourges, is present very early in the disease. As the Streptococcus pyogenes itself can cause in the pharynx a necrotic process, it is not only possible, but very probable, that it may be active as well in scarlatina. So long as we know nothing of the actual cause of scarlatina, it will naturally be impossible to make any certain statement in regard to its nature, or how the scarlatinal toxin, apart from any influence by other pathogenic organisms, behaves in regard to the severe (the necrotic) form of inflammation. One can now merely express his opinions; and I believe that the scarlatinal toxin *can* itself be the cause.

There is no doubt that, following a genuine diphtheria, sepsis may be caused by pus-producing organisms, and in this connection the streptococcus plays a leading part. On account of this, the boundaries between the local and constitutional affections are wiped out. Scarlatina and diphtheria are brought nearer together in this respect. But it is always possible to determine distinguishing principles, to which we can hold in most cases. And one must not forget that a certain diagnosis is dependent upon the examination of each individual case. One does well, I think, not to separate the clinical and anatomic examinations; they complement one another, and it is not proper to tear them apart.

In the main I agree with Sörensen, whose conclusions, however, I do not in all respects, and without certain reservations, corroborate.

1. Is any one able, by simply inspecting the genuine diphtheritic membrane, to differentiate it from the membranes that occur in a scarlatina that is not complicated by diphtheria? In many cases, yes! In diphtheria there are firm, compact membranes, of a grayish-yellow color, that can be separated in their entirety. In scarlatina the membranes are softer, looser, separable only in portions, and of a more brownish color. It requires a practised eye, and especially one that is sensitive to shades of color, to recognize these differences. He who possesses such an eye, however, will soon learn to depend somewhat upon it.

Of course, this is a matter of purely personal impressions, for which every one will choose his own characterization. Thus, Sörensen calls the scarlatinal membrane yellowish, the diphtheritic, white. For most men the more or less firm attachment of the membrane will prove the better diagnostic distinction. I might further say that I have never seen in scarlatina a rolling up and crinkling of the membrane in separating itself, such as occurs quite frequently in genuine diphtheria.

2. *A deep destruction of the tissues in the vicinity of the parts primarily involved is far more rare in diphtheria than in scarlatina.* Necrosis does occur, especially the suppuration that extends itself superficially, but is far more frequent in scarlatina. This destruction will be seen in its proper significance if one considers the conditions relative to the time in the disease. Earlier in scarlatina, later in diphtheria, forms the rule that is taught by experience.

Such anatomic pictures in the pharynx as my Case 2 presented, which ran a fatal course within twenty-six hours, are hardly likely to be met with in genuine diphtheria. The latter disease is characterized (in cases in which death occurs in a similarly short time, without laryngeal distress, and with symptoms of severe intoxication, and when severe local disturbances arise) by a firm, rigid infiltration of the tissues. If these are cut through, one sees barely a sign of fluid, and certainly nothing that resembles pus.

Moreover, the further course is a different one in the cases that have a less stormy record: The extension of an infiltration to the vicinity, simulating a phlegmon, which, going still further by continuity, involves all the tissues, includes the skin, subcutaneous connective tissue, the cervical glands, and leads to suppuration, often later even to gangrene;—unfortunately, this is not a rare thing in scarlatina.

In diphtheria, as a rule, the phlegmonous inflammation is absent, the degenerated tissues becoming gangrenous without that step coming in between. We may assume with some degree of probability that the ridding of the tissues of the streptococci is rendered difficult in a very different way from that in scarlatina, directly owing to the destruction of the tissues by the diphtheria bacilli, and the simultaneous deposit of a thick layer of necrotic material. In the beginning there is only an inflammatory secretion, that opens the lymph spaces and loosens the superficial epithelium.

The streptococcus easily makes its way into the tissues, and when this has taken place, it causes, either with or without the help of the

scarlatinal toxin, the tissue disturbances. The streptococcus has already attained its position within the tissues, and is not hindered in its further extension.

3. *Embarrassment of the larynx by a membrane formation is a comparatively rare occurrence in scarlatina, and still more rare is a croupous exudate upon the mucous membranes, and extending deep down into the air-passages.*

This fact can hardly be contested, and nearly all observers have made themselves sponsors for its accuracy.

Bretonneau (1824) denied practically any tendency of the diphtheritic inflammation of the pharynx in scarlatina to extend itself to the air-passages. This is, however, as Henoch properly shows,* only in a measure correct. He himself, a decided supporter of the theory that scarlatinal diphtheritis has nothing in common with genuine diphtheria, cites a number of cases to prove that Bretonneau is in error.

The conclusion that is to be drawn from the foregoing is, of course, not forceful, since the bacteriologic examination and reports are lacking. We must always deal with the possibility that a double infection is present, and, accompanying the scarlatina, a true diphtheria. The possibility does not appear to have been excluded in Henoch's observations; and in one case (No. 4) he goes so far as to associate the death which followed in the fourth week of the disease (primarily scarlatina) with an involvement of the larynx that was characterized anatomically as a diphtheritic inflammation. The conditions in Cases 6 and 7 are, in my opinion, to be judged in much the same manner; in both, in a short time after the beginning of the scarlatina, laryngeal embarrassment became evident, though the pharyngeal condition markedly diminished. In addition, we learn that in four out of seven autopsies the esophagus was involved, and in some instances to a marked extent, in one even to the cardia (Case 8). Henoch, moreover, does not deny the possibility of a double infection, and himself cites several cases in which scarlatina appeared after diphtheria.†

There is lacking, of course (these observations having been made in 1878), a bacteriologic report. I will therefore report a case of my own in which the bacteriologic examination was carried out, and in which the genuine Löffler bacilli were discovered:

OBSERVATION XV.—Friedrich Th., four and a half years old. Patient comes from a healthy family, and except for measles in the fall of 1893, has had no previous illness.

For about fourteen days has experienced frequently recurring pains in the head and limbs, and obstinate constipation.

Admitted to treatment on February 18, 1894, in the forenoon. Moderate angina, some of the cervical lymph glands are swollen, temperature above 39.5° C. (103.1° F.).

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* *Charité-Annalen*, Bd. III, S. 533.   † *Ibid.*, S. 525, 526.

On February 19th: Wide-spread scarlatinal exanthem, especially marked on the breast and forearms. Typical scarlatinal tongue, swelling of the lymph glands at the angle of the jaw, on the neck, and in the groin. Some coryza, and some fissures at the opening of the nares. Cough, though the lungs show no abnormalities.

On the 21st the eruption has nearly disappeared, desquamation is already evident on the neck. Marked angina, the tongue still characteristic, the enlargement of the peripheral lymph glands remains unchanged. During the night there was dyspnea, and at the same time the patient complained of pain in the right half of the chest. The physical examination showed a high respiratory rate (56) and the signs of a right-sided pleural effusion.

On the 22d wide-spread urticaria, blotches of the size of the palm of the hand, with severe itching. Scarlatinal exanthem has quite disappeared. Lung condition, etc., unchanged.

On the 23d: Urticaria only in certain areas. The physical signs of pneumothorax on the right side, besides the exudate. The respirations vary between 48 and 68 per minute.

On the 25th: Marked hoarseness. Cyanosis and dyspnea increase, respirations not over 48.

On the 26th: Distinct signs of laryngeal stenosis; the respiration down to 44 per minute. Death with the phenomena of suffocation in the evening about 12 P. M.

The course of the temperature is seen from figure 76.
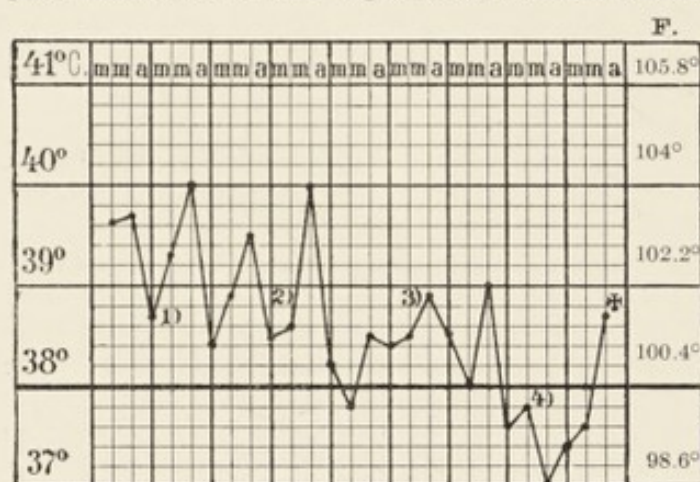
FIG. 76.—1, Appearance of the exanthem; 2, pleuritis; 3, pneumothorax; 4, diphtheria.

Autopsy report (Dr. Henke), thirty-six hours postmortem: Fairly well nourished cadaver, rigor mortis everywhere present, numerous death spots. In the abdomen a small quantity of fluid; the intestines shiny, smooth, somewhat distended. Position normal.

Position of diaphragm: On the right side the sixth, on the left the fifth, intercostal space in the mammillary line. The liver, pushed far below, reaches beyond the edge of the ribs by four finger's-breadths. Upon incision under water great air-bubbles escape from the right pleural cavity. The heart was little larger than the fist of the corpse. The right ventricle was dilated, the valves normal.

The lungs: On opening the thorax one enters on the right side a pleural cavity filled with a large quantity of thick pus. The right lung is completely collapsed, the upper lobe pressed against the mediastinum, the middle portion of the upper lobe attached to the pleura costalis by means of slight adhesions. In the left pleural cavity there is no fluid. The left lung is covered anteriorly by an opaque pleura, coated with a whitish fibrinous deposit. The lung itself everywhere contains air and crepitates on pressure; its bronchi, to the finer divisions, coated with

tenacious purulent mucus; the mucous membrane is swollen and red. The lung substance is full of blood. The quantity of pus in the right pleural cavity about 300 c.c. (10 fl. oz.). The great portion of the lower lobe, the entire upper and middle lobes of the right lung, are completely atelectatic. Besides this, only a small portion, between the middle and lower lobes, still contains air. On the anterior side of the middle lobe, near the surface, is a bronchiectatic cavity the size of a cherry, leading into a bronchus the size of a pencil, and full of pus. In the neighborhood of this cavity there is a sharply cut opening in the pleura pulmonalis, barely the size of a pinhead. When introduced, the probe reaches about 2 cm. (0.78 in.) into the substance of the lung.

On the posterior wall of the pharynx, also including the entire larynx and the posterior portion of the trachea, there is an extensive membrane of a yellowish-green color. The underlying mucous membrane is reddened. The tonsils are free, and only in the right appears a pus focus, the size of a pinhead. The spleen is congested, and enlarged to one and a half times its size.

In regard to the further findings, we may briefly remark that the kidneys were congested, with a slightly cloudy cortex, and scattered extravasations in the renal pelvis.

Streaks of extravasation were noted also in the duodenum; the *solitary follicles*, the Peyer's patches, and the mesenteric lymph glands were freshly though only moderately swollen. The liver pale, of acinous character.

The bacteriologic examination found in the membrane of the trachea very numerous diphtheria bacilli and a few streptococci.

Thus, on February 19th the scarlatinal eruption appeared; on the 25th the first signs of involvement of the larynx; on the 26th distinct signs of laryngeal obstruction; and in the course of the same day, death by suffocation. The pyopneumothorax had, no doubt, hastened the end.

This is not the place to further discuss the many features of the clinically interesting case. I wish only to call attention to the fact that the temperature after the appearance of the diphtheria fell considerably, as happens not rarely in the infection.

4. *I do not wish to lay too much stress upon the fact that in the involvement of the larynx by a diphtheritic inflammation from the pharynx accompanying scarlatina the clinical symptoms have a characteristic type.*

They resemble, according to Bohn's * idea, more the picture exhibited by a "usual inflammatory croup." He refers, in this connection to Mayr,† who is, it seems to me, not altogether clear upon the point.

The question is a difficult one, because it involves a number of uncertain subjects. For is there, indeed, a "true croup," a condition char-

* Gerhardt's "Handbuch," *loc. cit.*, p. 269.
† Hebra's "Hautkrankheiten," *loc. cit.*, pp. 124, 125.

acterized anatomically by a pseudomembrane, and possibly limited to the larynx, that is not due to the active cause of diphtheria? Who can at present answer that definitely with yes or no?

There is the further point that the diagnostic rule does not always hold in cases that must certainly be ascribed to diphtheria, nor in cases of severe involvement of the larynx with stenosis, which certainly cannot be ascribed to it. It is as follows: In diphtheria there is a slower development of the laryngeal embarrassment, therefore a gradual increase of the symptoms; no early, violent, and sudden dyspnea, no barking cough appearing at intervals. In pseudocroup, in a very short time appear the signs of stenosis, and an attack of coughing with its recognized signs, and sudden pallor, and a frequent recurrence of the whole picture.

It is of still less importance that the voice in true diphtheria in the beginning is only less resonant, while in all the other forms it is hoarse.

The whole question depends upon the extent of the inflammatory infiltrations and their rapidity of development, and also upon purely anatomic conditions. We may allow that usually true diphtheria requires more time to cause an obstruction of the larynx, and that it forms membranes upon this area as a rule less quickly, and certainly not such as extend themselves with one stroke over a wide surface. But as really conclusive I am not willing to regard these matters.

It is worthy of mention that Mayr rather presupposes an unfavorable outcome for laryngeal stenosis if the patient has already often suffered from attacks of croup. If this be a fact, one might conclude that the tissues that have been frequently visited by inflammation (pseudocroup) are here, as elsewhere, more accessible to the causes of inflammation and less capable of resistance.

5. *The paralyses that follow genuine diphtheria are absent in the pharyngeal diphtheritis accompanying scarlatina.*

This is an assured fact in the great majority of cases. In the small number in which it does not hold good we must always consider the possibility of a double infection.

Attention should also be called to the following: In the case of a somewhat severe angina, involving the soft palate, an incomplete obstruction of the nasopharyngeal cavity may take place, and as well during scarlatina as in any other condition. It is merely the result of the inflammatory processes in the areas involved by them. When, moreover, coexistent with the scarlatinal angina, fluids pour from the nose and may be swallowed by the patient, there is no proof that a diphtheritic paralysis is present (Henoch). The latter may only be assumed to be present when first the actual symptoms appear—such as anesthesia of the palate, with loss of the reflexes, accommodation paralyses, or more extensive paralyses in the region of the muscles of the body.

Bohn states, to be sure, that paresis of the muscles of the palate by no means rarely follows; but he says that he has never observed other— the more remote—paralyses.

Henoch has seen them just as infrequently. Only Thomas reports several cases.* He advances the hypothesis that their rare occurrence is easily explained "by the peculiar scarlatinal constitution"; a statement, it must be confessed, that carries a very slight meaning.

It appears to me more reasonable to call attention to the recognized fact that in certain epidemics of diphtheria the paralyses are missing; and, further, that where diphtheria and scarlatina exist, many of the subjects yield before the double attack. Thus it may be that we possess comparatively few reports on the paralyses following scarlatina in combination with diphtheria.

6. As to the time required by the course of the disease, Henoch declares very properly, in regard to the condition that he calls the *necrotic inflammation typical of scarlatina*, that it appears, as a rule, on the third or fourth day after the beginning of the disease. This holds good only for the cases that are moderately severe; in severe cases it may be present even in the course of the first twenty-four hours. (See Observation II.)

In order to ascertain an outside time-limit for the later phenomena, such as appear after the complete development of the eruption over the entire body, we will not, in all probability, need to refer to the direct influence of the scarlatinal toxin. In this case there are surely other causes of disease at work, which, whether they be the streptococcus or Löffler's bacillus, may come into evidence at any time.

We are therefore not in a position to form from the early or late appearance of the pharyngeal processes definite conclusions in regard to the nature of the final influence that caused them.

[In order to determine something concerning the nature of the pseudomembranous inflammations occurring in the course of scarlet fever, Chabade † examined the throats of 214 scarlatina patients in the Petrovpavlosk hospital at St. Petersburg in the year ending September, 1898.

Of the patients, 98 had a catarrhal angina; 33 had lacunar angina, a pseudomembrane covering only the crypts of the tonsils; 83 showed a true pseudomembranous angina, the membrane extending over the tonsils and upon the pillars of the fauces and the neighboring parts.

In the first group were found streptococci and sometimes staphylococci, never Bacillus diphtheriæ. In the second group the bacillus of Löffler was noted in two patients only, in one almost in pure culture. Finally, in the third group the presence of the Bacillus diphtheriæ

* v. Ziemssen's "Handbuch," *loc. cit.*, pp. 231, 311.

† "De l'association de la scarlatine avec la diphthérite," par M. I. Chabade, *La Semaine Medicale*, 1899, p. 184.

was established in eleven cases, in three of which it was very nearly in pure culture and eight times associated with streptococcus.

M. Chabade concludes that the subjects presenting a mixed infection, scarlatina and diphtheria, ought to be separated from individuals affected with pure scarlet fever. In order to do this it is necessary to examine bacteriologically all patients with false membranes in their throat. The author furthermore thinks that scarlet fever associated with diphtheria ought to be treated with antidiphtheritic serum.

Variot and Devé* have analyzed a series of 525 cases of scarlet fever, with the following result: In 31 the diagnosis of the type was in doubt, as the patients were seen only in the desquamative stage; of the balance, 432 were examples of scarlatina simplex, while the remaining 62 presented an exudative angina. The total number of cases of angina in the series was 212, of which 150 were non-exudative and 62 (as already stated) exudative; of this last number, 32 cases were diphtheroid, while the remaining 30 were examples of true diphtheria. Of the diphtheroid cases, 8 died (25%), while the mortality of the diphtheritic series was 6 (20%). The death-rate in the scarlatina simplex series was about 3%.

Garratt and Washbourn † advocate a bacteriologic examination of the throats of all scarlet fever patients and convalescents, especially where a number of cases are isolated in common, as a possible means of discovering the presence of latent diphtheria in season to isolate the patient and thus prevent an epidemic of post-scarlatinal diphtheria. Of 666 cases of scarlet fever treated at the London Fever Hospital during 1896 to 1898, over 1% presented the Klebs-Löffler bacillus in the throat upon admission. Only a minority of these cases presented any clinical evidences of diphtheria.]

The **oral cavity** also shares in the changes caused by the scarlatinal toxin, but the latter of itself causes hardly any deep injuries to the mucous membranes of the mouth. Usually it remains a superficial lesion; hyperemia with marked exfoliation of the upper layer of the epithelium, and sometimes, but by no means always, in certain areas a marked redness causing an appearance similar to the skin eruption. The latter is always of short duration.

The **red borders of the lips** may be altered in similar fashion, although the spots resembling the exanthem occur at this point very seldom. On the contrary, there will be seen, especially in severe

* "Soc. méd. d. Hôp.," 1900, xvii, p. 1025.
† "Annales de méd. et chir. infantiles," 1899, t. iii.

cases, accompanying the obstruction of the nasal opening, dryness and the formation of crusts, which are dark colored from extravasated blood; also fissures at the angles of the mouth. This picture differs in no respect from that of all diseases that are accompanied by severe fever.

The processes to be noted on the tongue Bohn * has described accurately and clearly as follows: "The tongue will be found slightly swollen and tooth-marked from the beginning of the disease, somewhat broader and thicker, its hypertrophied papillæ projecting and becoming distinct from one another. While it is covered during the entire first period by the grayish-white layer of epithelium, and only the denuded edges and tips appear a deep red, the epithelium separates more and more every day toward the middle, and is detached in large pieces. Sometimes only the epithelial surfaces of the papillæ are lost at first, and the latter appear to have broken through the gray coating with their excoriated tips."

I may say, here, that this is the *customary procedure.*

The markedly swollen and red papillæ, resembling asparagus tops, and lifting themselves from out their bed over the grayish-yellow surface of the tongue, present in the beginning a no less typical appearance than that shown by the whole tongue at a later period.

Bohn continues: "The tongue, at last entirely denuded, appears a burning red, sometimes a bluish color, dry and shiny as though scraped; and the thickened papillæ, separated by furrows from one another, give it a nodular, even warty appearance, so that the terms *strawberry* (or *raspberry*) *tongue* and, since its peculiarities are found in no other disease, *scarlatinal tongue* are appropriate. It acquires these characteristics early or late, but usually between the third and fifth days, altogether independently, however, of the external eruption, with which it generally bears no relation. Sometimes itching is noted in the mouth and upon the tongue. In case of high fever the furrows may deepen between the papillæ into *rhagades.*"

The latter is, again, by no means a characteristic symptom. In all diseases that run their course with a high fever the same feature is present, if the breathing takes place to any extent with the mouth open.

"The tongue returns to its usual condition rapidly, and on the seventh or eighth day is nearly normal. At this time aphthæ often occur, especially at the tip of the tongue."

I wish especially to emphasize the fact that these are only aphthæ, and that *the condition is not, as often believed, diphtheria.*

* *Loc. cit.*, pp. 260, 261.

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The very marked difference in the pathologic significance of these processes requires detailed discussion.

By some (Betz, for example) vesicles on the papillæ of the tongue (*Zungenfreisel*) have been described, with clear or slightly opaque fluid contents. I have also now and again seen the occurrence, but it seems to me of trifling importance, and represents only a somewhat more marked local disturbance. The same is true of an exaggerated swelling of the circumvallate papillæ.

A. Neumann * gives a still more detailed account of the processes of the scarlatinal tongue that are perceptible to the eye, which presents no essential differences from Bohn's description. It may only be mentioned that in the cases closely watched by him a longer time elapsed before the normal appearance was regained. In 22 observations only nine times at the end of the second week was there a perfectly normal condition of the lingual mucous membrane. *Nine times it was arrived at during the third week, and four during the fourth and fifth weeks.*

In consequence of the oral involvement due to the scarlatinal toxin a number of local disturbances may occur. Apart from the necrotic, diphtheritic processes, which usually extend into the vicinity, and are so intimately connected with the disease of the pharyngeal organs that a clinical deduction has no significance, the lodgment and growth of the *thrush fungus* should be especially mentioned. This should never be underestimated, and requires likewise a full consideration.

INVOLVEMENT OF THE NASAL CAVITIES, THE EARS, AND THE EYES.

These are of great significance in scarlatina, not only because of the local changes caused by them, but because the severest constitutional symptoms can be produced from the nasal cavities as well as the middle and inner ear.

The inquiry should first be made whether the scarlatinal poison itself can cause pathologic disturbances in these structures. This answer must, on principle, be an affirmative one, though one may promptly add: Where there is a serious process, whether a local destruction of tissue or a menace to the whole body, secondary infections perhaps always, at least usually, play their part in the game.

The anatomic conditions ascertained from our knowledge of the

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* " Zur Entwicklung und klinischen Bedeutung der Scharlachzunge," *Deutsches Archiv für klin. Med.*, Bd. xlvii, S. 379 ff.

formation of the portions of the body that come under consideration are determinative.

The nose presents a mucous membrane, often injured, full of folds, with an extensive surface in contrast to a narrow circumference. It offers recesses for pathogenic organisms, which, when once settled, cannot easily be expelled.

If a powerful cause of inflammation makes its way into the middle ear, the exudate excited by its presence is confined within narrow limits, and there arises great pressure, with all its consequences. These become evident first at their point of origin, but the customary febrile conditions in suppurations of the middle ear which do not evacuate themselves indicate beyond doubt that some process is under way in the system that is not beneficial to the general condition. Of the extension of the inflammation to the mastoid process and its consequences nothing need here be said.

The destruction of an eye is generally not accompanied by an evident reaction upon the entire body; this occurs, as a rule, only when the organ has experienced very serious disturbances.

These conditions become evident no matter what the form of origin of the inflammation that is active in their sphere. They therefore excite more of an influence, and cause more danger, than any other feature of the disease. I desire to leave the question open as to what influence the scarlatinal toxin, circulating with the blood, possesses as the sole cause of the inflammation in the previously mentioned portions of the body. For the most part, these are instances of an extension to the neighboring cavities of the tissue processes originating in the pharynx; and that each one communicates the process of its own particular type goes without saying.

The **mucous membrane of the nose** may remain absolutely free in scarlatina. In many cases we observe no swelling, nor redness; the breathing takes place through the normal passages, unobstructed as before; and there is no increase of secretion. At other times there is only a slight disturbance of the passageway with the discharge of small quantities of slightly turbid secretion.

[**Early Purulent Coryza in Scarlatina.**—According to a review in the "Rev. d. mal. de l'enfance," Feb., 1901, some of the physicians at the isolation hospital at Porte d'Aubervilliers appear to look upon this symptom as more pernicious than the worst forms of angina. As it is an example of a highly virulent streptococcus coryza, it is in position to infect the nasal sinuses, middle ear, and cervical glands (the latter usually suppurate under these circumstances), as well as the system at large. Statistics show a marked connection between this purulent rhinitis of the eruptive stage and fatal cases; in fact,

this complication of scarlatina may be termed the most deadly of all, leading apparently to over 50% of the mortality.]

Severe symptoms always accompany severe involvement of **the pharynx.** Usually these do not show themselves during the first day, though it may be that, even as early as this, the deeper involvements of the pharynx make their appearance. First one notes the signs of distress caused by swelling of the mucous membrane—the patient breathes through the open mouth. This may occur for a short time only, without causing a secretion from the nose. Soon there appears, first a turbid, then a distinctly purulent discharge. The nasal openings swell, the skin over the entire organ is tense, slightly edematous, and there form on the red and thickened alæ in the first place erosions, which later develop into superficial ulcerations. When the process reaches this point, it recedes every day until every trace has disappeared.

In less favorable cases severe inflammation with destruction of tissue take place, whether of a diphtheritic nature, or accompanied by gangrene; complete obstruction to the passage of the air; bloody, shreddy secretion, which becomes offensive and transmits a foul odor; always more or less pus—the latter never being absent. The anatomic changes are (and this deserves special mention) the same as occur in secondary infections, only exceptionally involving the deeper structures. Destruction of cartilage, of the bones, or of the soft parts belongs among the greatest rarities.

On the contrary, one sees very frequently, alongside of the severest involvements of the pharynx and nose, **the middle ear** implicated. These processes are usually in scarlatina, though not always, inflammatory processes going hand in hand with pus formation. It is very probable that the cause of infection makes its way through the Eustachian tubes. The possibility that the deeper processes can be caused by the scarlatinal toxin itself cannot be denied, though it is not proved. The aural affections appear before the beginning of desquamation, though they may make their first appearance as late as the third week of the disease.

The phenomena that bespeak a threatening condition are: Increase of temperature, which, when it reaches a high degree, causes brain symptoms, together with severe pain, which never is absent, and is often of the severest type. The brain symptoms may increase in intensity, even to severe convulsive attacks; coma may appear, and in such degrees as to cause the appearance of a sudden meningitis. It is entirely different in childhood. The ear is indicated as the seat

of pain. The neighboring glands swell uniformly; already enlarged, they increase still further in size, and are often sensitive to pressure.

Also symptoms that indicate disturbances of the function of hearing. Difficulty of hearing is invariable, and is noticeable even to those who are not attentive. One must speak louder at first, then almost shout, if he wishes to be understood. The older children and adults say that they have heard everything as if from a distance, this feature becoming more and more prominent within a short space of time. Tinnitus aurium is frequently complained of.

The physical examination in the milder cases, according to Bürkner,* gives the following results: The membrana tympani is injected, lusterless, reddish-gray, and funnel-shaped. The characteristic symptoms of this "sunken-in condition" are a marked projection of the processus brevis and of the posterior fold, and the apparent shortening of the handle of the malleus, which always forms with the posterior fold an acute angle instead of a right angle. If there is present a considerable hypersecretion, we see the exudate in the under portion of the tympanic membrane shining through with a yellowish color, wherefore it depends upon the degree of swelling and the color of the membrane as to whether a niveau-boundary is clearly visible. In case of a very marked collection of secretion, a portion of the membrana tympani, and especially the posterior, upper quadrant, or the entire membrane itself may bulge outward.

The further diagnostic symptoms, discoverable on the introduction of the catheter, followed by inflation with air, I may pass over at this time. Bürkner has given them in their proper place a description that fully satisfies all practical needs. Thus, he gives very exact directions as to the best form of catheter to introduce—not always an altogether easy procedure. I wish only to add his description of the local conditions that are noted in acute suppurative middle ear disease, since they are often enough of importance in scarlatina.

"There is already in the first hours an active injection of the vessels, then a bluish-red, sometimes yellowish-red, color of the membrana tympani. The edges of the somewhat flattened membrane are not always distinctly recognizable, because the neighboring deep-lying portions of the auditory canal are also injected and swollen. The swelling of the tympanic membrane increases rapidly, the handle of the malleus disappears, a serous transudate occurs, and usually a desquamation also, which, when it begins to roll off tiny shreds of

* "Handbuch der speciellen Therapie innerer Krankheiten," Penzoldt und Stintzing, Bd. i, S. 586. Jena, G. Fischer, 1884.

epidermis, can impart a map-like appearance to the membrane. After the constantly increasing bulging, through which one may sometimes see the secretion distinctly shining, there follows after a few hours, or more frequently one to three days, the breaking through of the pus—the perforation. This is, at the start, very tiny, and its position in the majority of cases is the anterior, lower quadrant. In the auditory canal pus occurs sometimes in small, and sometimes in very large quantities."

Middle-ear disease is always a serious condition. Apart from the danger of brain involvement, which can originate from it (see below), the consequences must be considered with regard to the hearing; and in this respect it is a very important consideration that the affection so often is bilateral.

Albert Burckhardt-Merian,* among the 85 ear complications after scarlatina reported by him in 1880, found not less than 72 cases (84.7%) in which both ears were affected. What mournful consequences this can involve, and how comparatively frequent they are, appears from the following: Out of 4309 cases of acquired deafness and dumbness reported by the above-named physician, no fewer than 445 (10.3%) were referable to scarlatina. If we consider, in addition, the more or less marked deafness, which is just as injurious to one's business ability as to his joy in life, we will place the middle-ear disease that follows scarlatina in its proper illumination.

Burckhardt-Merian † was of the opinion that he must oppose the medical men who chose to see in the condition a by no means unwelcome metastasis that leaves free the internal organs. "The time is not so far in the past when scarlatinal suppurations of the ear were greeted by physicians with a curious and comfortable satisfaction. Far from seeing in them a new and grave complication, they held it a favorable prognostic sign if in this manner a diversion occurred. The last traces of the humoral-pathologic ideas remain in this tradition, which, in spite of the earnest warnings from the aurists, has always swayed the masses, and often even the physicians. In this, I find by experience, lies the main reason for the indifference and carelessness with which even to-day, in a general way, abscess of the ear following scarlatina is allowed to take care of itself. Many believe also in the fatalistic idea that scarlatina must always spare something, and the families of the sick ones comfort themselves with the belief that it is better that the organs of hearing should be sacrificed to the disease than the kidneys or some other organs. Against this old notion we must strive with all our energy." These are true words, and I trust that they will meet with more and more hearty acceptation, and the more so since in such cases treatment at the proper time can afford good results.

* "Ueber den Scharlach in seinen Beziehungen zum Gehörorgan," v. Volkmann's "Sammlung klinischer Vorträge," Chirurgie Nr. 54.   † Loc. cit., pp. 15, 16.

Grave consequences are the rule if there is an extension of the process from the tympanic cavity to the dura mater. The anatomic relations favor to a marked degree this extension.* The tegmen tympani and the sutura petro-squamosa are the dangerous points. The thin plate of bone that forms the tegmen is itself easily penetrable by the causes of the inflammation, and in certain localities (the region over the hammer and incus articulation) presents openings where the dura and the mucous membrane of the tympanic cavity are in direct apposition. Through the sutura petro-squamosa, which in children remains wide open, the dura is continuous with the periosteum of the tympanic cavity, and into it pass the vessels from the cranial cavity; so that it is not to be wondered at that meningitis, abscess of the brain, and thrombosis of the sinus can originate in the tympanic cavity.

A. Baader † reports a case observed by Dr. Kunz in which erosion of the sinus transversus with fatal hemorrhages from the ear originated in a purulent otitis media following scarlatina.

Involvements of **the eyes** in scarlatina are only rare cases to be ascribed to the direct influence of the toxin. Inflammatory conditions of the conjunctiva occur early, appearing and running their course in a manner similar to that in measles.

Significant disorders may thus take place in a shorter or a longer time, and we may distinguish between two forms:

1. In all acute infectious diseases, and similarly in scarlatina, there may be severe involvements of the brain, causing an imperfect closure of the eyelids and a lessening of the tear secretion. Foreign bodies of all sorts, instead of being properly washed from the cornea, now cause a disorder that may lead to panophthalmitis and loss of the eye.

2. By means of the tear duct infectious inflammations may spread to the conjunctiva, and from there involve the eyeball. The danger of a loss of sight is by no means a rare one in scarlatina, and we have every cause to be on our guard. The first warning symptoms will the more easily be neglected since we are concerned with a general involvement of so serious a nature that the attention of the physician is completely absorbed in caring for it alone. But the more dangerous the entire condition, the more must the details be looked after.

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*Vid. Merkel, "Handbuch der topographischen Anatomie," Bd. i, S. 535, Braunschweig, F. Vieweg und Sohn, 1885–1890.

†"Acute Verblutung bei Scharlach," *Correspondenzblatt für Schweizer Aerzte*, 1875, Bd. v, S. 617.

Moreover, there can be no doubt that an injurious influence involving the whole system asserts itself in every one of its members; and this must be as carefully guarded against as though it appeared independently and during the perfect equilibrium of the whole system. Thus the apparently trifling inflammations of the conjunctiva, which occur as early symptoms in severe cases of scarlatina, deserve full attention.

INVOLVEMENTS OF THE ORGANS OF THE LYMPHATIC SYSTEM.

These are affected in a direct manner by the action of the scarlatinal toxin, and may be involved by any of the secondary infections occurring in the course of scarlatina. This fact will account for an exceedingly manifold variety of pathologic processes.

The scarlatinal toxin, which exerts to a certain degree a distinct influence upon those who are attacked by it, always causes a disorder of the lymphatic system. This is peculiar to the toxin, and it requires no other influence to cause it.

I consider it necessary to emphasize this statement with great vigor, and to produce the proof of its accuracy. Let us turn back to the findings in the autopsies of those who died in a short period from scarlatina (see Observations II to VI). It is invariably the case that the organs composing the lymphatic system in the most various portions of the body are found to have undergone pathologic changes. And not only the lymph glands,—which are always involved, now more in this locality, again in another, and whether beneath the skin or within the body,—but also the single and multiple follicles, wherever they occur. The spleen shows a marked involvement, often reaching twice its normal size in the early days of the disease. This was the case in Observation V, in which death occurred after two days. In Observation III the spleen in an eight-year-old child measured on its convexity 13 cm. (5.12 in.), and was correspondingly wide and thick. There were also lymphatic new-growths (E. Wagner) in the spleen and liver.

In a secondary infection also the spleen may be severely involved. Besides a simple hyperplasia, infarcts and purulent foci of greater or less size may occur, and this forms no unusual occurrence. Highly interesting, moreover, is the observation of Leichtenstern, that, together with nephritis, very frequently an acute enlargement of the spleen appears with a renewed enlargement of the glands. This seems hardly to have come under consideration before, and yet it is a matter that appears to me of great importance.

It may still be objected that in every case in the beginning there are other injurious agencies active together with the scarlatinal toxin. The precise bacteriologic examination of Case 4 (see page 470) sets aside this objection and allows us to state the principle, which ought to be manifest, as proved.

Experience by the sick-bed leads to the same conclusion. In every severe case of scarlatina a large number of the superficial lymph glands are swollen. In the case of the cervical glands, at the angle of the jaw, in the nape of the neck, we may go back to the fact that their source of origin (the mucous membranes that are connected with them through the lymph stream) is involved in a more or less severe inflammatory excitement due to the scarlatinal toxin; and also to the fact that the lymph, which carries with it the causes of inflammation, sifts through them. This will not be denied, and may, indeed, come into consideration. But it cannot be looked upon as applicable to the glands in the inguinal region, which are frequently much swollen, and at a time when the eruption is not yet to be seen on the limbs. If we now consider the enlargement of the glands within the abdomen, which occurs in scarlatina entirely independently of any disturbance of the digestive system, and is present even in mild forms of the disease, the conclusion must be that the toxin, circulating with the blood and lymph within the body, is of itself able to cause the inflammatory excitement.

Another question is as to whether the scarlatinal toxin of itself, and without the cooperation of other pathologic influences, is able to cause a destruction of the lymphatic system and death of tissue in the patient attacked by it. The answer will be a difficult one, because the cases in which the toxin fully unfolds its evil influences end in a short time in death. One might be able to make an accurate statement, but in order to do this such a careful histologic, and simultaneous bacteriologic, examination must be undertaken as has not been executed to my knowledge up to this time. If we hold to Henoch's opinion that the scarlatinal toxin can cause necrosis in the pharyngeal organs, which are included in the lymphatic system, we must not reject the same possibility of its occurrence in the internal lymphatic glands, though the fact is not proved (compare Crooke's findings in the mucous membrane of the stomach, page 581). No investigation has been carried out in regard to the pathogenic organisms, therefore the possibility that they are the source of the necrosis is not absolutely excluded. We must the rather call attention to the fact that we will certainly see in cases in which other pathogenic influences are active

serious destruction of tissue, whether caused through suppuration, or necrosis, or decomposition; also in cases in which the mucous membranes, robbed of their epithelial coating, and forming part of the causal focus of the glandular involvement, have opened gate and door to the microbes that easily make their way to them and cause suppuration and decomposition. The cervical glands, and *those of the lower jaw and of the pharynx, come almost exclusively into consideration. The nasal, the oral, and the pharyngeal centers form the most important starting-points for these processes, characterized in the most limited sense of the word as sequels (secondary infections). These are the conditions that so often cause death.* In contrast to them, the actual danger of the scarlatinal infection retires into the background. It suffices to mention the fact that septic and gangrenous conditions have involved all portions of the body in the extent of the destruction, both through intoxications of the system and by affecting single organs by means of the blood or through extension to neighboring tissues; also that they are incalculable, and that their results cannot be prevented. We have only the slightest curative influence over them. The difficulties met with by the surgeon and gynecologist before the day of aseptic treatment we have still to experience to-day in dealing with scarlatinal sepsis; we are powerless when once the disease is under way, and are hardly ever in the position to prevent it; for we cannot exclude the air from the inflamed cavities, deprived as they are of their covering and protecting membrane, and just as little can we bring anything to bear locally that will certainly destroy the organisms that have already made their way there. A picture can be drawn of the disease which, in general outlines at least, will represent the condition of affairs. In addition to the swelling of the lymph glands in the region of the lower jaw and the neck, occurs that of the surrounding parts. We can see and feel the enlargement upward, as a rule, and to the middle of the ear, extending downward almost to the clavicle and posteriorly to the mastoid process. If it is, as often enough, double-sided, both areas join in the middle line. Unilateral enlargements merge into the surrounding tissues without a distinct boundary. Usually the enlarged glands can be distinctly seen and felt; more rarely their outlines also disappear in the swollen tissues.

In such cases one usually sees the form of enlargement (firm, unyielding, and hard as a board, involving the whole vicinity of the lower jaw) described as angina Ludovici, which extends very deeply into the tissues, and generally ends in destruction of tissue—true gangrene. Even the floor of the mouth may appear swollen.

The underlying skin is without exception tense, and traversed by distended veins. It is either pale and exsanguinated, or red (bright red to blue red), varying according to the individual case.

The face appears more or less swollen by edema, though the forehead and eyelids (at least the upper) are exempt. The nasal openings are usually obstructed, their edges excoriated, covered with bloody crusts; the skin over the nose is very tense, of a white or light blue color, the entire nose appears enlarged and is sometimes quite deformed.

The lips are swollen, their mucous membrane is dry and furred in many places; especially in the middle and at the outer border there are dry, blood-stained scabs. We find a similar appearance on the swollen tongue, which is covered with a heavy coating mixed with blood.

The mouth and pharynx are in any event lined by a swollen, red, and opaque mucous membrane. Usually there may be found also upon the latter grayish-yellow and, owing to extravasation, brownish-red masses; or there may appear on the palate and on the uvula tenacious and membranous exudates. Such membranes may occur upon the tonsils, which may be extensively involved and even destroyed.

A fetid odor is not lacking. If genuine gangrene supervenes, the breath is almost unbearable. We then see everywhere in the mouth and pharynx a grayish-green discoloration, and shreds of dead tissue are piled up here or there or cast off and ejected with the oral discharge, which is usually copious. The entire area of the mouth is ulcerated, and bleeds easily.

Suppuration of the middle ear, evacuating itself through the destroyed tympanic membrane, is quite frequent. The outlook becomes altogether hopeless if panophthalmitis joins company and runs its invariable violent course with destruction of the bulb.

In the enlarged glands suppuration may occur and extend over a longer or shorter period—and how often one waits longingly for the occurrence! If we have made incisions, or if in the neglected cases rupture takes place, probably a temporary improvement is noted; healing, however, is not yet at hand. It always requires a long time until the focus of suppuration is closed off, and it is by no means a rarity for genuine gangrene to appear soon after this point. We now see the pale yellow or bluish skin,—bare of every vestige of fatty tissue, and appearing a grayish-green color in the ruptured portions,— stretching itself over a space in whose floor muscles, tendons, vessels,

and nerves appear as though dissected out. Everywhere the shapeless remains of destroyed tissues lie scattered between.

The constitutional symptoms are no less severe. Fever; rises of temperature that follow no rule, and are perhaps interrupted by periods of subnormal temperature for a shorter or longer time; degeneration of the tissues attacked by the poison or poisons, and loss of bodily functions in every direction. In addition, there is the insufficient repairing power; the disposition to accept nourishment is as slight as the ability to use and incorporate what is ingested. On all sides the continually increasing emaciation makes itself evident, as well as a weakness that increases from day to day; not only of the whole organism, but of the single members. Light pressure upon the skin may now lead to decubitus; a superficial irritation of the conjunctiva to ulceration; and, owing to the insufficient change of position, pulmonary hypostasis sets in. As distinct indications of the injury suffered by the entire system we have the extravasations under the skin and mucous membranes. All of this we actually see, and the condition is not a very different one in the internal organs. There, also, disturbances of circulation, at other times of little significance, suffice to cause fatal results.

This forms a sketch of the case, though in every instance we will meet with a new arrangement of details. I would like, now, to present two cases that do not differ too much from the average type.

OBSERVATION XVI.—Karl St., five years of age. With the exception of an angina which occurred a few weeks ago and disappeared in six days, he has had no previous illness. On May 23, 1878, sudden appearance of malaise, loss of appetite, and during the following night sensations of heat, restlessness, and mind wandering. On the morning of the 24th severe vomiting, pain in the throat, difficulty in swallowing. Admitted to treatment in the evening.

Child well nourished, with a beginning scarlatinal exanthem. Tongue grayish-yellow, the red, swollen papillæ already visible. Hard and soft palate very red; the tonsils swollen and almost meeting in the middle, their adjacent surfaces covered with a grayish-white, firmly adherent membrane. The lymph glands at the angles of both lower jaws considerably swollen; the axillary and inguinal glands less so. The spleen markedly enlarged. Some bronchial catarrh; otherwise no evident abnormalities.

In the ensuing days the eruption became more distinct. I will only cite in detail the changes in the glands that are of interest. The history reads as follows:

May 27th: Swelling of the cervical glands diminished, likewise the involvement of the pharynx has subsided.

May 31st: Glands on the right side of neck very markedly swollen, and the skin over them reddened.

June 1st: Glands of the neck are still more swollen, and the skin edematous.

June 3d: On the right side over the glandular tumors, indistinct fluctuation.

June 5th: Incision on the right side, from which a fairly large quantity of pus was evacuated. On the left side more marked swelling with red and edematous skin. The involvement of the pharyngeal organs is less and less evident.

June 9th: Incision on the left side, from which only a small quantity of pus was obtained. The tissues on both sides of the neck are markedly infiltrated.

June 11th: On the right side the cervical swelling has almost entirely disappeared; on the left it is much diminished.

June 14th: The comparatively slight suppuration on the left side is evidently growing more marked from below.

June 16th: Discharge of pus from the left ear without warning.

During the night of June 18th–19th extravasations of blood appeared under the skin on the chest and abdomen; the general condition, which up to that time had been tolerable, now became serious.

On June 20th, at 1 o'clock A. M., death occurred, without other symptoms than those of sudden and general collapse.

Autopsy, fourteen hours postmortem (Prof. v. Schüppel): "The body is emaciated to a marked degree. The skin discolored a dirty yellow to brown, with scattered, pale death spots on the trunk. The skin of the abdomen, partly also of the breast, is covered with numerous, sometimes confluent petechiæ, that are also to be noted on the legs and feet, though in small numbers. The lips, especially in the angles of the mouth, are dried up, and on the anterior edge of the sternocleidomastoid there is a round opening, 1 square centimeter (0.4 sq. in.) in size, which leads to the right into a cavity 2 or 3 cm. (0.79 or 1.18 in.) deep, whose edges and base are dry, while on the left side the opening appears to correspond with a more recent incision, shallower and moist with permanent secretion.

"The muscles are markedly atrophic, of a bright red color; the subcutaneous connective tissue is almost devoid of fat. The cellular tissue of the neck is somewhat more densely infiltrated, especially around the region of the pus-cavities. On the left side the gangrenous cavity extends to a point directly over the internal jugular vein. The mucous membrane of the oral and pharyngeal cavities is pale and not swollen.

"The retropharyngeal and still more the peripharyngeal cellular tissue in the region of the nasopharynx is infiltrated with pus, and on the left side joins with an abscess. The latter is not connected with the previously mentioned gangrenous cavity. In the firmly infiltrated cellular tissue of the vicinity there are a number of moderately enlarged lymph glands, which are still soft and juicy.

"Corresponding to the left tonsil, there is a deep funnel-shaped ulcer, which is 1 cm. deep and proceeds toward the outside. On the lower border of this ulcer, whose base is smooth and covered with permanent secretion, lie pulpy fragments of the tonsillar tissue. Also on the right the tonsil is half destroyed, and a similar ulcer appears in place of the upper half. The laryngeal and tracheal mucous membranes are pale, not swollen, and free from pathologic changes. The muscles at the base of the tongue, especially the genioglossus, are full of numerous petechiæ vibices, as is also the tongue substance in the anterior portion."

Pleura and lungs (abstract): A fresh pleurisy with small quantities of exudate; on both sides extravasations into the pulmonary as well as the costal pleura. In the upper lobe of the right lung a sharply circumscribed, brownish-red, moist infarct, half the size of a cherry, which is partly involved in a purulent softening and shows rather plainly a line of demarcation. The parenchyma in the vicinity is full of blood and ecchymosed. Otherwise no pathologic foci in the lungs, which appear partly inflated, partly edematous.

The bronchi and bronchial glands are hardly affected.

In the pericardium a small quantity of very turbid mucoid fluid, containing purulent particles. The pericardium everywhere covered with mucofibrinous exudate, lusterless and opaque. The serosa considerably ecchymosed. The heart is, on the whole, flabby, and in its chambers are scanty, moist, pale clots. The cardiac muscle is relaxed, pale brown, shiny with fat, rather firm to the touch.

In the abdomen, in the dependent portions a mucopurulent, turbid, brownish-yellow fluid, whose total quantity amounts to perhaps half a liter. All the organs covered by the peritoneum are coated with a turbid, smeary, muco-purulo-fibrinous membrane.

The spleen is firmly adherent to the surrounding parts. Its capsule is rough and ecchymosed in many areas. The organ is enlarged to fully twice its normal size, and especially in breadth. The tissue is very pale, grayish-red, of seemingly firm consistence, yet somewhat more relaxed than usual. On section the surface is homogeneous.

The liver is bound down to the diaphragm by an old adhesion. Its serosa is diffusely opaque, pale gray in color. The organ is normal in size, extremely poor in blood, very pale grayish-red in color, its acinous arrangement is faintly evident, the tissue appears somewhat fatty and full of small whitish lymphatic nodes that are hard to distinguish. The bile is thick and dark colored.

The left kidney is swollen to almost double its size, and is flabby and relaxed to the highest degree. The capsule is easily and smoothly separable. On the surface of the kidney are many small hemorrhages, partly brown through metabolic changes, while on the other side of the organ they are blackish, owing to the nearness of the bowel. On section, the pyramids are seen to be colored a faint pink, while the cortical substance is pale yellowish-white to a yellow color. Extreme anemia. The tissues are markedly moist with edema. The medullary substance is very slight compared with the swollen cortex. The latter seems almost homogeneous, and is supplied with few vessels. From the surface can be scraped a slightly turbid pulp. The right kidney does not appear quite so large as the left, but has the same characteristics.

The bladder is completely empty, and its mucous membrane is spotted red.

In the stomach a greenish fluid, the mucous membrane swollen, of a pale gray to a bilious color, with numerous and mostly fresh ecchymoses, which appear as vibices, especially in the folds of the mucous membrane, and also in the serosa. On the posterior wall of the stomach, in the neighborhood of the small curvature, there occur in the mucous membranes three swollen areas, almost like pustules, whose substance is loose and stained with bile; in the center a blackish-gray, sunken-in, and necrotic portion, while on the edge there is a red area caused by extravasation of blood (necrosis?).

The mesenteric glands somewhat swollen and pale. In the large and small intestines, besides a somewhat (here and there) evident swelling of the mucous membrane, there is no essential change.

The temperature shows in its marked features what took place (see Fig. 77). The first portion of the temperature curve corresponds to a medium severity of involvement by the scarlatina; the eruption and its extension over the body being followed by high readings of the thermometer, and the course as a whole showing a decidedly remittent type. This continues for several days; then there occurs simultaneously with the suppuration of the glands, and in the surrounding tissues of the neck, again a marked rise of temperature. Locally, during an apparent regression of the symptoms, and certainly with the condition in the pharynx limiting itself to the already involved portions, there is a corresponding increase of inflammation in the lymph glands and their surrounding territory.

Fig. 77.—1, First day of the disease; the exanthem is developing; 2, marked swelling of the cervical glands, especially on the right side; 3, incision into the glands on the right side; 4, incision into the glands on the left side; 5, hemorrhages under the skin.
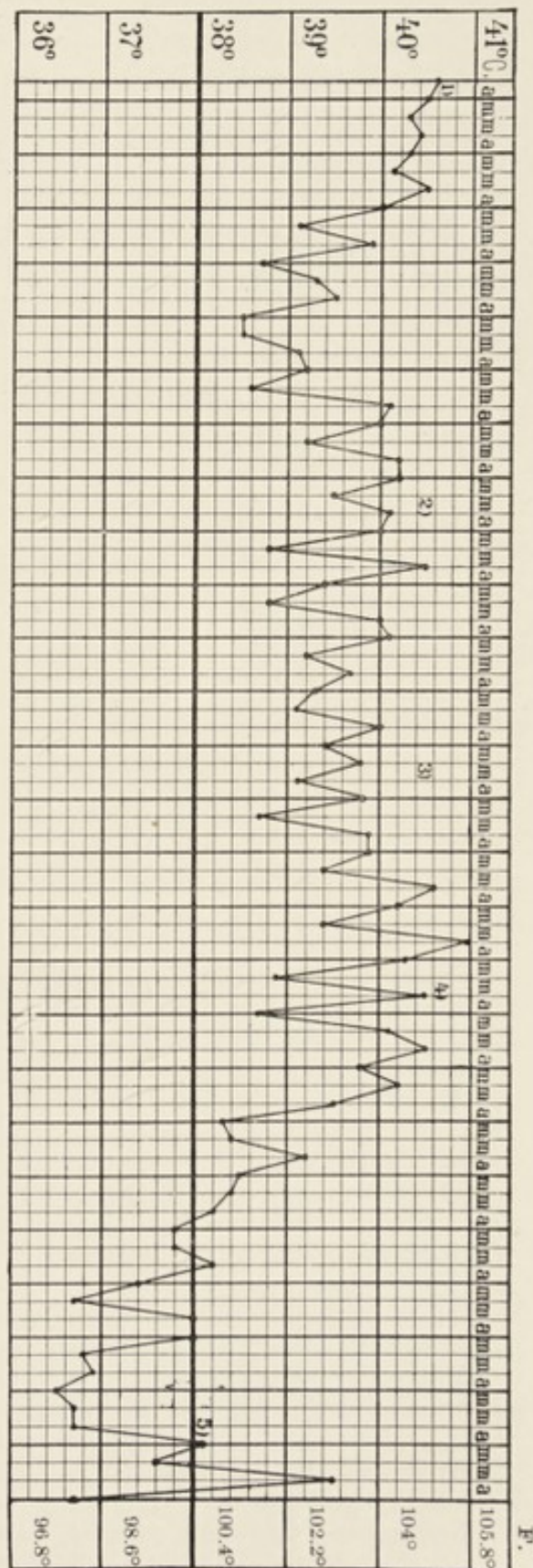
Eight and twelve days, respectively, pass before suppuration occurs in such measure as to warrant evacuation by the knife. All this time the temperature continued at a considerable height,—from the readings, unquestionably remittent in type,—and yet to be characterized as a very considerable fever. The latter was a mark of the extending septic infection of the system, to which the temperature curve corresponded. That the local process of abscess formation was no longer actively in control follows from the fact that *about two hours after the evacuation of the pus on the right side a fall of more than* 1.5° C. (34.7° F.) *in temperature followed, and yet after two hours more the previous height was again attained.*

During the week preceding the death the temperature fell to subnormal, as a result of the exhaustion of the system. The process in the middle ear did not again become evident.

There were no violent symptoms present, only from day to day an increasing failure in nutrition, which finally expressed itself in the form of extravasations into the tissues.

The autopsy teaches how extensive the local processes were, how considerable was the involvement of the internal organs, also the distant influence of the septic infection.

In my opinion, it is essential in the processes following scarlatina that are accompanied by suppuration, in addition to the absolutely necessary attention to all the directly involved organs, to keep a sharp watch for the general picture of sepsis. This is by no means a new fact, but it requires emphasis.

OBSERVATION XVII.—Gottlob H., four years of age. According to statement, has had no previous illness. Together with his six-year-old brother, was suddenly attacked, on November 10, 1888: difficulty in swallowing, vomiting, feeling of heat.

Admitted on November 11th. Well nourished, the face bloated and red. Almost the entire body, especially the trunk, covered by an unusually severe scarlatinal exanthem. Slight swelling of the lymph glands in the groin, more marked on the neck, and especially on and beneath the angle of the jaw. Swelling and redness of the pharyngeal mucous membrane. Swelling of the tonsils, which are covered with a thin veil-like membrane. (No statement in regard to the tongue in the history.)

On the right side the upper and lower eyelids are red, and so swollen that they are closed. A protecting bandage was at once applied.

November 12th: The skin on the body presents a violet-blue appearance. The membrane on the tonsils is more marked, its color grayish-yellow. Discharge of a clear serous fluid from the nose. Slight conjunctivitis of the right eye (in addition to the bandage, a solution of zinc sulphate, 0.5%).

November 14th: The swelling of the eyelids on the right side has

subsided; not the conjunctivitis, however. This has become more severe, and even the subconjunctival vessels are overfilled.

From the mouth and nose comes a disagreeable, insipid-sweet odor. On the still swollen tonsils the membrane is discolored and ragged. In some portions there are ulcerations. The cervical glands, especially on the right side, are swollen in large packets.

November 16th: The discharge from the nose is more and more foul and the fetor increases. The right cornea begins to cloud. More marked nutritive depression. Loss of strength.

November 18th: Beginning of desquamation; the skin is still distinctly cyanotic. The cervical glands on the left side are also much more swollen. Large ulcerous cavities in both tonsils.

November 20th: The right cornea has become necrotic. Slight conjunctivitis also on the left side. Increase of the general weakness, and, in addition, the heart is in poor condition.

November 21st: The right bulb altogether destroyed. The lens appears exposed to view.

Of the further course it requires only to be said that the left-sided conjunctivitis subsided. Prof. Schleich saw the patient and prescribed drops of sublimate solution, 0.5%. The general dissolution took its course: a few days before death a gangrenous ulcer formed on the right side about 2 cm. (0.79 in.) from the anus.

On December 1st, without any occurrences in the mean time worthy of notice, death occurred.

Autopsy (Prof. Nauwerck): "Marked emaciation. In different areas, especially on the neck, desquamation of the epidermis. On both sides of the neck glandular tumors, which show fluctuation in places. The right eye sunken in. The cornea is covered by a black scab, and the surrounding tissues are infiltrated with pus. On incising the skin, on the right side of the neck a glandular abscess connected with the skin is opened, from which is evacuated a considerable amount of grayish-yellow pus.

"In place of both tonsils one sees two large gaps, the edges of the ulcers rounded, grayish-white in color, and the base quite smooth, with a discolored, grayish-yellow membrane. When the membrane is removed, the base appears, as a whole, smooth and of a pale grayish color. On the right side the ulceration is deeper, its base is uneven, here and there necrotic, grayish-yellow, opaque, portions of tissue still sticking fast to the underlying parts.

"The mucous membrane of the pharynx and of the entrance to the larynx slightly reddened. The mucous membrane of the larynx and trachea of a pale, very light red color.

"To the right and outward from the right tonsil there is an abscess, hazelnut in size, with smooth, gray, and fatty, necrotic, opaque walls. This abscess is completely separated from the tonsillar ulcers by a partition about 2 cm. (0.79 in.) thick, and the pus from it has a fetid odor. Further down lies the abscess previously described, and still deeper a number of glands that are in part only swollen and red, and partly involved in a diffuse suppuration.

"In the external jugular vein there is a soft, grayish-red adherent thrombus reaching to the thoracic opening and originating in the deepest of the suppurating glands. The external jugular vein is entirely surrounded by the suppurating glands, which adhere closely to the walls.

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The interior of the vein appears of a grayish-red color. The thrombus in certain areas is in the process of undergoing degeneration. On the left side is the previously mentioned larger glandular abscess, whose walls are infiltrated. In this area no thrombi are to be found. The spleen is twice its normal size, and of a rather dark gray color."

With regard to the remainder of the examination, it need only be stated that the heart muscles appeared anemic and somewhat flabby, and that there was a wide-spread, purulent capillary bronchitis. The pleura and peritoneum were free; the kidneys edematous and anemic; the liver slightly fatty; the gastro-intestinal tract anemic and slightly catarrhal. Finally, there was the gangrenous (decubitus) ulcer in the vicinity of the anus. This case presents several variations from the preceding one (Observation XVI).

If we follow out the main features of the disease as a whole, the course of the temperature will be recognized (Fig. 78), as well as the fact that there is, except for the first days of the illness, which may have been influenced in a measure by the scarlatinal toxin alone, less of the variation to be noted than is compatible with the newly forming foci. Considered in its entirety, it is rather more on the type of a constant fever, to which are added for short periods—for

Fig. 78.—1, Acme of the eruption; 2, gangrene begins in the nasal and pharyngeal cavities; 3, beginning of desquamation; 4, necrosis of the right cornea and, on the following day, destruction of the entire bulb.

hours—marked rises or falls of temperature; the actual extremes of rise and fall, however, not being excessive. How far the early gangrene affected these conditions cannot be ascertained. Septico-putrid infection, or septicemia, forms the best characterization for

the general condition. The involvement of the eyes is well worthy of notice.

It would almost appear as if one must refer the destruction of the right eye to a local influence of specific nature. Strongly in favor of this view is the fact that in the very beginning there was present such a well-developed inflammation of the lids, and that the conjunctivitis developed later. The extension to the cornea could not be prevented, although a protecting bandage was placed over the eye and appropriate treatment employed. We cannot ascribe the condition to an extension of the suppurative and gangrenous process in the nasal mucous membrane through the lacrimal duct, because at that time it was not there. We must also abandon the idea that a general predisposing debility asserted itself especially in the eye; for the conjunctivitis of the left side after a few days entirely subsided, though at a time when the general intoxication was following a very different course.

Further mention must be made of the phlebitis originating from the suppurating glands in the jugularis externa which they surrounded, and of the consequent thrombus formation in the vein.

Destruction of the lymph glands and their immediate surroundings can cause the severest of local consequences. Primarily, the injuries to the great cervical vessels are to be mentioned, including the carotid artery, as well as the jugular vein.

There exists no satisfactory, complete commentary on this subject. Short but exhaustive descriptions of individual cases are given by A. Baader,[*] and also by J. Möller.[†] Then Charles West.[‡] Three fatal cases were observed by Kennedy. Dr. Huber, in Memmingen, has reported a case [§] in which hemorrhage from the eroded artery occurred, showing itself by a moderate-sized tumor on the neck (hematoma scarlatinosum, he calls it), which when opened by incision resulted in death.

I quote as an instance an extract from the article by A. Baader: "A four-year-old child became severely ill of scarlatina with marked pharyngeal diphtheritis. At the end of the third week the cervical glands on the right side suppurated, healing after an incision, in a short time. In the fourth week there appeared swollen glands on the left side, with fever that quickly increased in intensity. The physician found severe

[*] "Acute Verblutung bei Scharlach," *Correspondenzblatt für Schweize Aerzte,* 1875, Bd. v, S. 614.

[†] "Beschreibung einer Scharlachepidemie u. s. w.," *Archiv für physiologische Heilkunde,* Bd. iv, S. 549–552.

[‡] "Pathologie und Therapie der Kinderkrankheiten," 4th edition, Berlin, A. Hirschwald, 1865, S. 464.

[§] *Deutsches Archiv für klinische Medicin,* Bd. viii, S. 422.

symptoms of tracheal stenosis, protracted and difficult respiration, the neck was extended, the head drawn back; especially the inspiration was labored. The epigastrium, instead of being distended, was sunken in. The skin of the face was cyanotic to a high degree."

As the cause of the condition there was a decided tumor noted in the submaxillary region on the left side. "This was so considerable that the edge of the lower jaw and a part of the ascending ramus not only was no longer distinguishable, but the swelling extended even further, reaching the laryngeal region and the Adam's apple. The bluish-red of the skin showed a marbled appearance."

The attending physician, Dr. Rippmann, made an incision in order to relieve the threatened symptoms of laryngeal stenosis by evacuation of the pus. No pus appeared, however, and in its stead came a dark black and firm blood-clot, after the removal of which followed a thick stream of arterial blood. Pressure caused the hemorrhage to cease, after the wound of incision had been sutured. Then four days later a severe hemorrhage occurred from the mouth and nose, with a fatal result.

The autopsy proved that the external carotid had been destroyed by gangrene. The hemorrhage occurred externally only after the removal of the compressing clot by the physician's hand. Then the sac surrounding the carotid—the purulent and gangrenous tissue had constituted the walls for the abscess cavity—ruptured internally. At this point, since there was no longer any resistance, the hemorrhage took place.

This case is an unusually instructive one for the practising physician. The danger involved in the stenosis of the trachea certainly warranted the opening of the supposed abscess. Moreover, the subsidence of the respiratory symptoms proved that the local obstructions had been removed, and the powerful stream of blood showed that an artery had been injured. It is easy to conceive that no one should have thought of the external carotid itself, and the stoppage of the flow and the pulsations of the branches of the carotid gave ground for the belief that it was only a small artery. The point of perforation lay to the inside of the artery, and the flow of blood was thus prevented by the pressure of the bandage from forcing against the external wall of the abscess sac that surrounded the artery. Only when the resisting power of the necrotic tissue had been diminished too far to allow it longer to meet the pressure did the blood make its way from the carotid into the mouth.

For the above reason the carotid was not ligated, though the procedure was earnestly considered. Whether in this way the fatal result could have been prevented no one can say. Under the existing circumstances, however, the procedure was certainly authorized. In one of Möller's cases it was carried out, and, in spite of the operation being in a portion of the neck that was involved in gangrene, the case recovered.

Baader reports in regard to this observation:

A six-year-old child became ill of a severe attack of scarlatina with marked diphtheritis of the pharynx, mouth, and nose. On the thirteenth day of the disease "from the ear to the shoulder, and to the sterno-clavicular articulation, appeared a tumor of phlegmonous character, and everywhere fluctuating. In the lowest portion, about two finger's-breadths beneath the middle of the clavicle, I made a transverse incision. From the opening flowed a blackish, putrid fluid, mixed with many shreds of tissue." The severe constitutional symptoms—40.5° C. (104.9° F.), and an almost unreckonable, small pulse—subsided somewhat, and the child took nourishment, so that there seemed to be hope. On the evening of the twentieth day of the disease, however, the fever was renewed, with signs of a bilateral lobular pneumonia. In the following night, while the child lay in a stupor, a profuse hemorrhage suddenly occurred from the wound, and was stopped by its father by pressure of the finger. The extensive sac of the gangrenous abscess was by the next morning tightly distended, fluctuating at no point, and in the wound appeared a black coagulum.

The autopsy showed the following: The abscess cavity reached anteriorly to the right edge of the sternum, below to the lower edge of the pectorales major, and outward to the outer edge of the shoulder. In the external jugular vein in the supraclavicular fossa there was an irregular and jagged perforation, in which was a coagulum that could be easily removed with the forceps. The lumen of the vein was free.

In this case also the hemorrhage ceased temporarily. No phlebitis had appeared, and possibly life might have been preserved if it had not been for the double-sided bronchopneumonia.

Dr. J. Hamilton [*] relates a case in which the jugular vein was perforated by the extension of the gangrenous process from the necrotic cervical lymph glands on its posterior wall, and yet the patient lived.

Cases have very rarely been reported of the rupture of the pharynx and the extrusion of blood.[†] Henoch also cites two such cases.[‡]

The collection of pus arising from the necrosis of the glands and the surrounding parts, unless evacuated at the proper time, or unless it ruptures outward, makes its way downward. Henoch has seen the apex of the right pleural sac covered with pus. Bartels has seen a rupture into the pleural cavity.

Retropharyngeal abscess has still to be considered. Bokai[§] saw this occur seven times out of 664 cases of scarlatina in the children's hospital. Six times he ascribed it to a retropharyngeal lymph-adenitis arising from the influence of the scarlatinal poison, and only

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[*] Quoted in Canstatt's "Jahresbericht," 1863, Bd. iv, S. 131.
[†] Cremen, in Canstatt's "Jahresbericht," 1863, Bd. iv, S. 130.
[‡] "Vorlesungen über Kinderkrankheiten," S. 634.
[§] "Jahrbuch für Kinderheilkunde," N. F., Bd. x, S. 108.

once did it occur through metastasis. In the case reported by Bokai more in detail (Case 9 of his series), which ran a fatal course, suppuration appeared in a retropharyngeal gland on the fifth day from the beginning of the disease.

The earlier physicians showed a tendency to look on swellings of the cellular tissue in the region of the parotid gland that extend up and posteriorly as affections of the gland itself, and spoke directly of parotitis. Usually the parotid gland is little if at all involved (v. Ammon, Röser, Möller).

It is a different matter in a constitutional septic condition, in which the gland, or, more properly, the gland and the surrounding connective tissue, can be totally destroyed.

INVOLVEMENT OF THE JOINTS AND BONES (THE SO-CALLED SCARLATINAL RHEUMATISM).*

It is true also in the case of these affections that we cannot with accuracy decide what to ascribe to the scarlatinal toxin alone, and what to the accompanying causes of disease.

Without question, if the pus-producing organisms may interfere, the involvement of the joints is merely a symptom of a septic condition, and not a real complication. Such cases are severe and often enough run a course that is characterized by other localizations in the vital organs.

From these cases those of a mild type must be separated, and clinically this presents no real difficulties. But it should be stated here that a case appearing at first to be a mild one may take on a grave character. Moreover, the anatomic forms of the inflammation—serous and purulent—are of marked significance in relation to the involved joint, though they afford no conclusion as to the nature of the direct cause of the condition. The latter fact is evidenced by Case 5, reported by Bokai—ulcerative endocarditis; in the involved joints merely an increased quantity of clear yellow synovial fluid; the cartilages of the joints smooth, pale with a touch of blue color; the capsular membrane injected in places.

It is worthy of attention that **scarlatinal rheumatism**—and I retain this term because it is absolutely a harmless one—in different epidemics shows a remarkable variation in the frequency of its occurrence. Thus, Koren † observed the mild form, called by him

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* Compare the excellent articles by Bokai, Jr.: " Die acute Gelenkentzündun, als eine der Complicationen bei Scarlach," " Jahrbuch für Kinderheilkunde," N. F., Bd. xix, S. 309. " Ueber die scarlatinösen Gelenkentzündungen," Ebendort, Bd. xxiii, S. 304.

† *Vid.* Johannessen, *loc. cit.,* p. 195.

synovitis scarlatinosa, 27 times among 426 cases (6.3%) in the epidemic in Christiana, during the years 1875 to 1877. Henry Ashby,* among 500 cases in the Children's Hospital in Manchester, saw 10 mild (2%) and 2 severe cases.

All observations in regard to the milder affections, wherever and whenever made, thoroughly agree that it is by far the most frequent variety.

The clinical picture associated with the condition may be stated as follows: The beginning of the involvement occurs usually between the early part of the second and the third week and coincides with the desquamation. Meanwhile we have already noted on the third day effusions into the joints. Most frequently the carpal joints and the articulations of the fingers are involved, and, of the large joints, the knees. No joint, however, remains altogether exempt, and it is a noteworthy fact that even the articulations of the spinal column may share in the process. As a rule, more than one joint is involved.

Among the symptoms, pain is hardly ever found missing; swelling may either fail to appear, or may be considerable; and naturally upon both of these depend the disturbances of function that vary within wide limits.

As pathognomonic may be mentioned—as already done by Trousseau †—the great constancy of the symptoms. No sudden variations occur; the joint remains involved over the entire period, neither increasing nor decreasing in size, as so often occurs in acute articular rheumatism.

This may have some connection with the short duration, for in most instances the entire condition has disappeared within three or four days, and, exceptionally only, it may last through a week.

The general condition is very often slightly, and never more than in a slight degree, disturbed, this being also the case with the course of the temperature. As far as I can learn, there is nothing to be found in literature in regard to the relation of the bones to such mild affections. My own experience teaches me that they may also be involved, and just as slightly and for as short a time as the joints.

I append an instance which includes a mild joint involvement:

OBSERVATION XVIII.—William H., fourteen years old. Became ill on January 1, 1879, with sore throat, pain in the ears, and chilly sensations. Admitted to treatment on January 3d, with angina, rather marked

* "On the Nature of the So-called Scarlatinal Rheumatism," *Brit. Med. Jour.*, 1883, II, p. 514.

† "Medicin. Klinik," u. s. w., Bd. I, S. 116.

membrane on the right tonsil, a slight membrane on the uvula. The tongue anteriorly reddened, swelling of the submaxillary and inguinal glands. In the evening the scarlatinal eruption, first visible in the neck and chest.

On the 4th, extension of the exanthem over the chest, abdomen, and thighs. A scarlatinal tongue, the angina and membrane more marked. Cervical glands painful. General condition good.

On the 6th the eruption is fading. Pains, especially at night, in both elbows and in the right ankle. Headache. In the evening the pains in the ankle have disappeared.

On the 7th, pains still continue in the elbows, especially in the deep portions of the joints, and on the anterior surface of the humerus. " Both the legs in the tibial regions are painful, especially on pressure between the bones of the leg; the tibia also at its lower extremity (on the ankle). No distinct swelling."

On the 8th, pains in the limbs have largely subsided. No angina, no longer any membrane, the glandular swelling has retired.
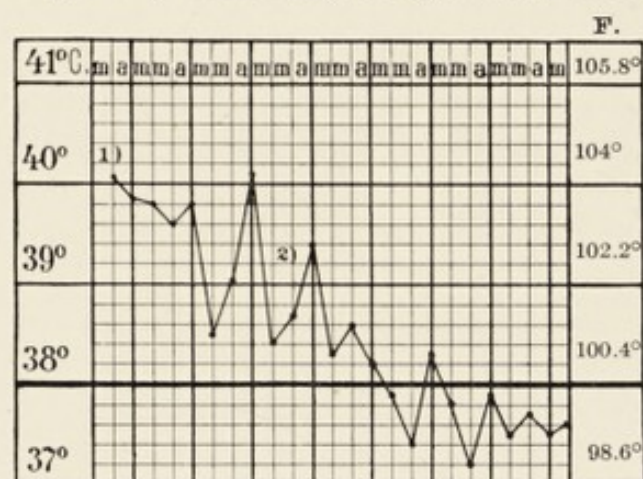
Fig. 79.—1, Appearance of the eruption ; 2, on this and the following days joint and bone pains.

"On the 10th, deep within the bend of the elbow, the humerus is still distinctly sensitive to pressure."

On the 11th there is no longer any tenderness on pressure.

Uninterrupted convalescence. A study of the temperature curve (Fig. 79) shows no disturbance corresponding with the incidents of the illness, which was mild from the beginning and remained so until the end.

The case was precisely similar to that of a five-year-old boy who became ill at nearly the same time.

I am, unfortunately, not able to report how frequently in this small epidemic (Lustnau, from June 11, 1878, to April 14, 1879—altogether, 50 cases) the bone and joint involvement was noted, since the history records are no longer to be found. It is a matter of fact, however, that marked cases of septic infection occurred at the time, and that later they increased so in number that we can almost speak of an epidemic disease. It may be that this has already played its part. Certainly it will be necessary to pay more attention to the phenomena in the bones than has heretofore been the case.

Bokai distinguishes a group, which he designates as " *scarlatinous, serous joint inflammations, which follow an acute, or may be a chronic course,* and sometimes merge into 'white swelling.' "

This is, in all probability, simply a joint tuberculosis which forms as the result of inflammation that is secondary to the scarlatina.

Perhaps those forms also come under observation which are in the beginning purely serous, and later have a purulent exudate. They also belong to the septic processes, and are real complications, just as are those which have been preceded by an acute suppuration.

It is an unquestioned fact * that joint involvements with suppuration do not always accompany sepsis—involvements that are often short in duration, of little significance, and perhaps are simple serous exudates. We have also in them nothing that may be placed in close relation to the scarlatina. Certain physicians, such as Henoch, have seen cases in which the purulent inflammation of the joint originated in an abscess that has ruptured from the vicinity into the joint.

In regard to the frequency of all these latter severe affections, it · can only be said that it is a slighter one than that of the mild types. The characteristics of the disease by no means distinguish themselves from those of sepsis; and, in addition to the more or less severe constitutional disturbance, the local involvement asserts itself in the parts that are attacked.

Just as in the course of scarlatina septic infection may appear, so may scarlatina complicate sepsis. At least it appears to me that the following case admits of no other interpretation:

OBSERVATION XIX.—Karoline Th., fourteen years old. Beginning of illness on December 18, 1878, at noon, with marked chilliness, followed by heat, and pain in the right shoulder.

Admitted in the afternoon of December 19th. Marked dyspnea, respirations 52 per minute, pulse 160. The right half of the chest painful over its entire extent, expands less than the left; the breath sounds are weaker on the right side, especially in the upper portions of the lungs. No symptoms of localization in foci discoverable. Marked pains in the right shoulder. The symptoms continue on the next day; pain now also in the entire right upper extremity.

On the 21st: On the face and in the pharynx a decided redness, which shows also on the tip of the pale red tongue. At noon vomiting occurred twice. The respirations have fallen to 32, the pulse 165 in the morning, 155 in the evening.

On the 22d: A distinct scarlatinal exanthem on the neck, chest, and abdomen, also on the palate; angina, submaxillary and inguinal glands swollen, shoulder-joint painful, swollen, elbow-joint painful.

On the 23d: Marked scarlatinal tongue, the exanthem visible on the legs. Pain in the right shoulder more severe, in the elbows less, but in the wrist and metacarpophalangeal articulations it is distinct—everything right-sided. A slight area of consolidation demonstrable in the right upper lobe, and a sputum similar to that of pneumonia is said to have been expectorated.

Respirations 25 to 28. Pulse in the evening varying between 115

* Compare Dennig, *loc.cit.*, p. 84.

and 130. The desquamation begins on the face with the subsidence of the pharyngeal inflammation; no membrane present on the 27th. On January 30th the exanthem has entirely disappeared. The signs of consolidation still persist in the right upper lobe. Respirations between 32 and 36. Pulse 110 to 120. The joint pains are gradually disappearing. A tumor is forming in the anterior portion of the axilla, though in a way connected with the joint. Incision and evacuation of a considerable quantity of pus (laudable) on January 2, 1879.

Information is lacking as to the further course of the disease. Recovery followed.

Simultaneously with the local affections that have nothing in common with the scarlatina the general condition followed its characteristic course. If we study the temperature curve (Fig. 80), it is apparent that the first four days have the highest fever records; it experiences no further rise on account of the outbreak of the scarlatina.
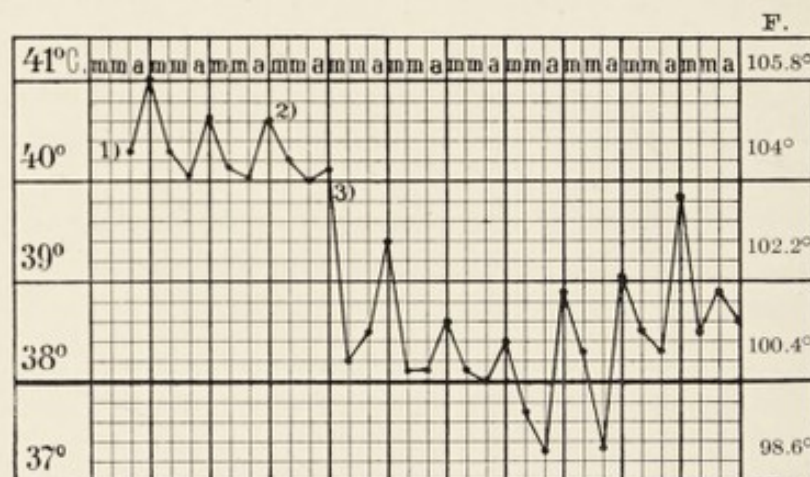
FIG. 80.—1, Second day of the disease; 2, appearance of the eruption; 3, consolidation in the right upper lobe becomes demonstrable.

The scarlatinal infection was not a severe one, and held a position decidedly secondary to that of the preceding septic infection. The non-appearance of other pharyngeal and glandular affections, as well as the absence of nephritis from the further course of the disease, were in accordance with the general conditions in cases of mild scarlatina. The later rises in temperature hold a close relation to the pus formation that was present from the beginning; i. e., the periarticular abscess on the shoulder.

After its evacuation, so far as I can learn from the inadequate history, improvement set in. The question that was frequently discussed, and by even the physicians of earlier times, whether, especially in the milder cases, a real complication with acute articular rheumatism (genuine articular rheumatism) might be present, was answered by them in the negative, Trousseau being the most prom-

inent in the matter. Now that there is a possibility that acute articular rheumatism stands in close relation to the entire group of affections caused by pus-producing organisms, the subject becomes more and more one worthy of discussion, or, rather, one that requires it, and we have still less reason for going deeper into the question just mentioned.

Cardiac involvement, and especially endocarditis, according to the statements of some, may appear in scarlatinal rheumatism, and likewise chorea. I will content myself with the mere mention of these facts. Their significance is as little understood as the general consideration of the affections of the joints and bones.

[**Scarlatinal Myositis.**—Brück * regards this condition as affiliated with scarlatinal arthritis. In the material analyzed by the writer the muscles of the trunk appeared to be the favorite localization (lumbar, intercostal, pectoral, abdominal, etc.). The complication appeared from nine to twenty-one days after the debut of the fever, and was heralded by a rise of temperature. The chief spontaneous symptoms were pain and soreness. When the intercostal muscles were affected, there was a certain amount of interference with respiration; when the abdominal wall was affected, the pain simulated that of colic. As an induced symptom extreme sensitiveness to pressure was noted in some muscles. As a rule, however, massage, with warm baths, appeared to give relief.

Multiple Neuritis Following Scarlatina.—Egis † states that but two cases of this sequence are upon record, including his own. In the latter case both peroneal nerves were paralyzed, and an ataxic gait was present. Careful examination appeared to show that this condition bore no relationship to a possible postdiphtheritic paralysis. In all the localities affected by the latter disease the functions were intact, and in this case the picture of multiple neuritis was evident.]

INVOLVEMENTS OF THE KIDNEYS AND DROPSY, WITH THEIR CONSEQUENT CONDITIONS.

It may be taken for granted that the **affections of the kidney** appearing after scarlatina stand in close relation with the latter disease. We were once accustomed to separate the true inflammations of the renal organs—that occur at a later time, let us say, in general, after the second week of the disease—from those disturbances that the kidneys themselves experience in the beginning. The latter have

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* *Petersb. med. Presse*, 1896, No. 18.
† "Arch. f. Kinderheilk.," 1900, xxviii.

no characteristic features, and may occur alike in all acute infections connected with fever.

C. Friedländer * reports, in regard to the early form, that it appears simultaneously with the exanthem, or soon after, and is only of short duration—at the most, a few weeks. We find anatomically a moderate hyperemia of the kidney, with a slight degree of cloudy swelling of the epithelium in the convoluted tubules. The epithelium here and there shows marked proliferation, and is later cast off entirely. The vessels of the glomerulus are normal, the epithelium of the capsule being usually slightly thickened, and sometimes there is an albuminous fluid between the capsule and the glomerulus. In the convoluted tubules, and now and then in the straight tubules, are found hyaline and granular casts, and often only loose epithelial cells and small round cells. The interstitial substance shows hardly any alteration, merely here and there a number of accumulated round cells.

In the second week there is a complete regression, or at the most there remain microscopic fat granules in moderate numbers in the somewhat enlarged epithelial cells of the tubules. There are also occasional casts in the tubules. Clinically, only the rarest indications of edema; as a rule, albumin and casts in the urine.

Friedländer has chosen for this form the name "*initial*" *catarrhal nephritis*. He describes as characteristic the glomerulo-nephritis that installs itself in the third week and later, as Klebs first described it (1876). He recognized anatomically "kidneys containing the usual amount of blood, or even hyperemic, of increased consistency, and reminding one of a congested kidney. Moreover, while in the congested kidney the glomeruli show distinctly as blood-red areas upon the surface of the cortex, whose normal outline is otherwise well preserved, the glomeruli are everywhere empty of blood, and protrude as gray, more or less markedly enlarged granules over the surface of the corticular substance. Apart from this, the kidney is perfectly normal, and only in rare cases, and in a long persistence of the disease, is there a partial clouding of the corticular substance."

Microscopically there are seen "glomeruli completely empty of blood, and only occasionally a red blood-corpuscle in a convolution. Marked increase in the number of nuclei. The glomeruli are converted from thin-walled spaces, possessing a clear, sharply outlined partition, into sausage-shaped solid masses. The wall and the contents appear hardly capable of separation, the entire picture consisting of a finely granular material in which here and there fat

* "Ueber Nephritis Scarlatinosa," *Fortschritte der Medicin*, Bd. I, S. 81.

granules and many polymorphous granules are deposited. The epithelium of the capsule is only slightly thickened, and only in a few cases is there a marked proliferation of the latter. The scattered and mostly squamous cells of a radiating appearance that are found normally caught between the single loops of the glomerulus may likewise increase in volume and number, though only exceptionally to any marked degree. In any event it is certain, and easy of determination, that the impenetrability of the loops for the blood is not caused by pressure from without; rather, from a stoppage of the lumen."

Friedländer presents the foregoing picture as typical of the nephritis following scarlatina. According to his observations, there may also occasionally be noted:

1. *Slight interstitial infiltrations;* always, however, very local in extent, and especially occurring around the larger branches of the vessels.

2. *Fatty degeneration of the epithelium,* in cases of longer duration, especially in the convoluted tubules, and usually in connection with a proliferation of interstitial tissue (transition to the large white kidney, which Friedländer demonstrates as quite rare).

3. In the arteries and also in the glomerular loops are *hyaline deposits.*

The clinical symptoms are those of scarlatinal nephritis in general (see p. 553).

Friedländer has seen, still further, in scarlatina—though he considers that it was a case of complication with an "especially severe diphtheritic affection, cervical phlegmon," etc.—*the large soft hemorrhagic kidney.* He describes the changes that occur as follows: "The kidneys are enlarged, markedly flabby, and in the cortex the outlines are entirely lost. The latter is of a diffuse, gray color. As a rule, there are no glomeruli to be seen, and in their stead are usually a great number of partly punctiform hemorrhages, partly large hemorrhagic infiltrations."

Microscopically, there is seen an extension of the interstitial tissue caused by a marked collection of small round cells, and usually only slight changes in the epithelial cells. Friedländer considers the term "interstitial septic nephritis" to be an appropriate one. He attempts also to sharply distinguish these forms of kidney involvement: "No causal connection can be discovered. Transition forms are absolutely lacking, and mixed forms are extremely rare."

If we observe his own descriptions closely, however, they show

that this is not the case. In the catarrhal form he mentions changes in the glomerulus; the glomerulo-nephritis, epithelial fatty degeneration, and accompanying interstitial changes that are present at least here and there; and how to characterize and interpret these conditions—as mixed or transition forms—remains for the individual to decide; but present they certainly are.

Among the other investigators, one description agrees in the main with Friedländer, though not in the detailed account. E. Wagner * differs from him to the greatest extent, and then says that he has never seen a genuine " Klebs' nephritis" after scarlatina. " Most frequently the large white kidney of Bright is found after a duration of a day or of a few weeks; sometimes with numerous petechiæ, sometimes without them. The microscope alone makes the process clear and shows in many cases a great variation in the glomerular changes, in the tubules, and also in the stroma."

More rarely occurs the form described by Wagner as *acute lymphomatous nephritis;* there is cellular infiltration of the cortex of the kidney, the cells being not of a uniform size, but either much smaller or much larger than a red corpuscle. The infiltration occurs especially around the glomeruli, which appear small; their capsules are often either symmetrically or irregularly compressed together. Small collections of cells gather in the interstitial tissue between the more or less uniformly compressed tubules, whose epithelium has also suffered from the pressure. In the areas that have been spared from this influence all the structures—glomeruli, tubules, stroma capillaries—are larger and more distended. The cases in which Wagner saw this form were complicated by severe pharyngeal diphtheritis, and with suppurative joint involvements. They were undoubtedly instances of complications with at least a predominant septic infection. The changes in the glomeruli are more prominent in the cases reported by Crooke,† but besides these there are also the same early changes in the tubules and in the interstitial substance. Crooke continually lays the main stress, as does Friedländer, upon the inflammation of the glomeruli.

The findings of Sörensen ‡ are similar. He also emphasizes the

* (a) *Deutsches Archiv für klinische Medicin*, Bd. xxv, S. 529; (b) v. Ziemssen's " Handbuch der speciellen Pathologie und Therapie," 3d ed., Bd. ix, S. 150.

† " Zur pathologischen Anatomie des Scharlachs." By Dr. George Crooke, of London. From the laboratory of Prof. Eberth (Halle). *Fortschritte der Medicin,* Bd. iii, S. 651.

‡ " Ueber Scharlachnephritis," *Zeitschrift für klinische Medicin*, Bd. xviii, S. 298.

significance of the glomerulo-nephritis, and is of the opinion that Wagner has not paid sufficient attention to this feature.

This is, however, not the case. Wagner goes into the question thoroughly enough; moreover, it should be understood, as Sörensen has suggested is possible, that in Wagner's series glomerulo-nephritis was present only to a slight extent. This brought up one of the most important points in connection with scarlatinal nephritis: *Must the kidney affections always show the same anatomic picture?* The answer No! must be given with great positiveness. We may always be confident that the glomeruli are involved when the clinical picture of acute nephritis arises,* but, in addition, all the other structures of the kidney come under consideration, whether it be the glandular portion itself, or the vascular system. One may safely depend upon Cohnheim's † investigations, which demonstrate the general conditions that are eliminative in this connection. Previously we had no understanding of the subject. It should also be mentioned here that the substance which involves the kidneys consequent upon scarlatina circulates with the blood, and with it makes its way to the kidneys. The first badly exposed point is the glomerulus with its epithelial covering (Cohnheim). It is possible that under certain conditions— and we must seek these in the nature of the toxin, which may have a varying selective tendency—now the vessel-walls, and again the epithelium within the glomerule, will be involved. This, however, appears to be of minor importance, because the one must suffer as soon as the other has experienced any considerable injury.

Whatever process takes place in the glomerulus involves the epithelium, and then the convoluted tubules; and if it is an irritant, it may exert its influence here as such. In view of Heidenhain's ‡ investigations, moreover, it is conceivable that the toxin may enter the uriniferous tubules from the capillary network around them, and not involve the glomeruli. It is an essential fact that *normally there is never the same current in all the renal vessels alike, nor are all the uriniferous tubules employed to the same extent.* The consequence is that the toxic influence affects neither the glomeruli nor the epithelium of the uriniferous tubules at one and the same time, and therefore a nephritis cannot well occur in both kidneys in a uniform distribution.

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* Compare Nauwerck: "Ueber acute Glomerulonephritis," "Ziegler's Beiträge zur pathologischen Anatomie und Physiologie," Jena, G. Fisher, 1886, Bd. i, S. 64.

† "Vorlesungen über allgemeine Pathologie," 2d ed., 1882, Bd. ii, S. 326.

‡ *Pflüger's Archiv für die gesammte Physiologie*, Bd. ix, S. 1.

This circumstance seems to me of the greatest significance in the consideration of scarlatinal nephritis. The influence exerted by an inflammatory substance depends not only upon its intensity, but upon the length of time it remains in a position in which it has the power to act. In cases which we can follow clinically an irregular course is manifested for the most part, improvement alternating with loss of ground. The conclusion that the cause of the disease is at the bottom of this circumstance, and that it is present in the blood, and with the latter makes its way to the kidneys, either in increased quantity or in increased strength, is to a certain extent probable. It now becomes dependent upon the secretory conditions existing at that time in the involved portions of the kidney, and the length of time the injurious substance remains there. If this be only a short time, only the directly affected portions of tissue will have to suffer; if it is a longer period, then the process is somewhat more extensive. Since materials in solution in the blood may come under consideration in the question, we may think of a simple diffusion, and perhaps even of a pressure influence. Thus it may be intelligible how the interstitial tissue here and there becomes involved, in addition to the vessels and epithelium, and even in a very mild inflammation.

A deeper insight into the processes caused by scarlatinal nephritis is rendered impossible by the fact that we know nothing of the materials that are influential. It seems peremptory, however, *that it is something other than organic elements, or micro-organisms;* for in individual cases the schizomycetes that have been found may often, perhaps always, have secured lodgment at a later time. Or if they were the actual causes of the disease, then there certainly was no true scarlatinal nephritis; rather, a septic nephritis in the narrow sense of the word, and a true complication. How one should stand in regard to the question, and what significance those (mostly severe) forms have which occur in company with an extensive necrosis in the pharynx, and wide-spread suppuration of the glands, can also not be decided with certainty. It may be that under the term "septic" one may make the matter satisfactorily clear to himself. By this can merely be meant, however, the fact that at the time of its origin something else has been at work, and perhaps an actual visitation and settling of pus cocci. This must be decided according to the individual case.

It is altogether incomprehensible that genuine scarlatinal nephritis should occur with such varying frequency. The fact itself is certain, but it is by no means easy to obtain such trustworthy statistics that

one may depend upon them. Steiner estimates the variations as from 5 to 70%; Johannessen gives little more, and does not wish to give more, than an approximate idea when he places the highest figures obtained from the Norwegian reports as at one time about 90%, and at another about 70%, of the scarlatinal patients who later suffered from nephritis. It has been shown by a number of responsible observers, as Bartels and E. Wagner, that in certain epidemics nephritis may almost, or even altogether, fail to appear.

This teaching requires limitation, if the views held by various medical men, among whom especially Sörensen * may be mentioned, shall be made good. The gist is as follows: *More or less considerable inflammatory tissue changes may be present in the kidney, without causing evident or discoverable symptoms.* The "clinical" symptoms of nephritis appear much later than the anatomic changes take place.

I do not find that the evidence brought by Sörensen for the frequency of this occurrence is conclusive. We may always, considering it as a complement of Crooke's principle, agree with him in saying "the processes are indicated in the early stages of the fever, from which are developed sometimes the severe forms of nephritis."

The facts that lie at the bottom of the matter are these: that renal changes may actually be present in the bodies of those who have died in the early stages, but not as a consequence of nephritis. This, however, need not be the case. Sörensen's investigations, moreover, relate, as it appears, almost exclusively to scarlatinal cases, accompanied by "diphtheritis," or even by pneumonia. One is therefore hardly in a position to say positively what has been caused simply and solely by the scarlatinal toxin.†

The older belief, especially represented by Steiner,‡ is not fully correct: viz., "that the kidney involvement in scarlatina is nothing other than a peculiar simultaneous localization of this infectious disease in the uropoietic system; and that the renal disease in scarlatina forms an essential symptom of the general condition, just as do the exanthem and the angina that is almost never absent." The statement must be characterized as unauthorized "that the kidneys invariably, and at the beginning of the disease, share in the scarlatinal process." Apart from his clinical observations, Bartels § has paid especial attention to this question, and says that in the great majority of cases examined by him neither albumin nor epithelium from the

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* "Ueber Scharlachnephritis," *loc. cit.,* p. 316.
† See page 549.   ‡ "Jahrbuch für Kinderheilkunde," N. F., Bd. I, S. 440.
§ *Loc. cit.,* p. 222.

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uriniferous tubules could be discovered; he could thus also present a contradiction based on anatomic grounds.

Friedländer found among 229 autopsies upon scarlatinal subjects only about half as many cases of renal involvement, and how far he extended the meaning of the latter term, so that an oversight could hardly have occurred, is proved by his descriptions of the light, early forms and of the catarrhal nephritis.

On the other hand, no objections can be made to the fact that the nephritis, as well as the involvement of the skin and of the pharyngeal mucous membranes, can originate from the influence of the specific scarlatinal poison, and in so far we may term it "essential."

This is, however, a word that makes the actual process no more clear to us. In this question all our difficulties lie gathered together.

Let us now run over the acknowledged facts. In addition to the marked variation in the frequency in different epidemics it may be mentioned that:

1. *Whether nephritis makes its appearance in a certain case or not is a matter independent of the general character.* In other words, a mild case of scarlatina may be accompanied by nephritis, and a very severe one exempt. On this point nearly every one is agreed. On the other hand, opinions differ as to whether in epidemics that are not characterized by a great frequency of renal involvements, but are characterized on the whole as malignant, nephritis in general occurs more often than in the milder epidemics.

Bartels and Bohn answer "yes" to the question; Fürbringer takes the opposite view, and I would like to confirm his stand, as far as I may be allowed an opinion. Severe cases, especially those accompanied by diphtheritis, are predisposed, and always somewhat more frequently complicated by nephritis.

Whether this is a nephritis scarlatinosa in the correct sense of the word is not yet certain, and it appears to me that we will have to take pains to place the etiology on a proper foundation if we are to make any further advance in the solution of the question.

2. *The renal inflammation following scarlatina makes its appearance, as a rule, in the course of the third week from the beginning of the disease.* From the clinical standpoint this principle is an incontestable one, yet it should be stated that changes may already have very early occurred in the kidneys. In the present state of our knowledge there appears to be no objection to the belief that the scarlatinal toxin may assert itself in the kidneys in a very short space of time, when once it has attained a footing in the body. And in this regard it is of small im-

portance whether we refer to the elevations of the temperature or to anything else, since the toxin itself always remains the ultimate cause.

The early renal involvement is common to the other, or, we may better say, to most of the other, infectious diseases that are characterized by fever. But the inflammation of the kidneys that occurs at a time when the other symptoms of the disease have for the greater part, or often enough entirely, disappeared is pathognomonic. How this takes place requires explanation.

The termination of the renal affection is assigned to different periods. That its appearance later than the third week is a rare occurrence is in accordance with general experience, and the sixth week has been assigned as its latest limit (observation of Fürbringer).

3. *External conditions have no significance with respect to the occurrence of the nephritis, and this may be emphasized in the matter of "taking cold" as a predisposing influence.*

"The idea, that many are contesting even to-day, that nephritis is the result of a 'cold,' or of a suppression of epidermal perspiration, is shared by me in no degree whatsoever, for almost all of my cases have originated in spite of the most scrupulous care, and only a few children have left their bed a few days too soon" (Henoch).

"I would expressly state that I have seen the most severe involvements of the kidney in the convalescence of scarlatina, although overanxious parents have not allowed the little patients to get out of bed, while neglected children in the Policlinic, who have gone through their scarlatinal processes, so to speak, on the streets, have remained exempt" (Bartels).

So far as I can see, this view is generally held by German physicians. Among the more recent writings I find that the Copenhagen Hospital physician, Sörensen, has mentioned exposure to cold at least as an occasional cause, though in rather ambiguous terms.*

The attempts at an explanation should be briefly considered. A *mechanical theory* has been formulated by Bohn,† as follows:

"The renal inflammation in scarlatina occurs because of the collateral and compensatory flow of blood to the kidneys, resulting from the peculiar conditions under which scarlatina exists. The cutis, as soon as the inflammation has subsided from it, is covered by a double layer of exudate and dead epithelium. Through the vicarious relations between the skin and kidneys a moment can occur that will cause circulatory disturbances in the skin, and as a consequence hyperemia in the kidneys, with its

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* "Ueber Scharlachnephritis," *loc. cit.*, p. 316.
† Gerhardt's "Handbuch," *loc. cit.*, p. 275.

resulting conditions; and this the more easily takes place when during the desquamation the skin, which has grown sensitive, experiences an exposure to cold. In this way nephritis appears frequently after severe eruptions and delayed desquamation, and children who have been too soon exposed to the cool air are especially liable. In regard to the cold-water treatment, it is said with propriety that it disposes the child almost certainly to avoid a later nephritis, and since I have begun to bathe early in the case, and repeatedly after the fever has subsided, I have seen many fewer of the sequels.

"One should take notice of the enormous quantities of dead epidermis floating on the surface of the first and second bath waters (especially when the bath, for external reasons, has only been used late in the case) in order to estimate the disadvantages under which the skin has long suffered."

I must honestly admit that I gather no positive information from these conclusions. It should first be stated that a "collateral and compensatory flow of blood to the kidneys," or "hyperemia" of the same organs, as Bohn later terms it, is in no way capable of producing in them an inflammation. This requires a special irritant; if it is not present in the blood flowing to the kidney, there occurs an increased action of the glands, and an increased excretion of urine. The most that could be thought of, even theoretically, would be the rupture of the capillaries.

Bohn, moreover, mentions certain things as predisposing conditions to a nephritis—a marked eruption, delayed desquamation, improper hygienic surroundings—whose significance he brings into question. It should, moreover, be pointed out that the renal inflammation may follow an attack of scarlatina that runs its course with extraordinarily slight, perhaps very incomplete, skin involvement. In such a case all mechanical disturbances of the skin are lacking. Enough has been said to show that the explanation is unsatisfactory. One can but ascribe it to the influence of the scarlatinal toxin. This exerts an inflammatory irritation upon the kidneys. Since the fact must be met, however, that nephritis occurs with such varying frequency in different epidemics, we are compelled to present a still further consideration: viz., that *personal peculiarities of the patient cannot seriously come under discussion.*

Yet it were very remarkable if the kidneys of scarlatinal patients at one time should almost without exception react so positively to the toxin, while at another they should appear insensible to even a marked quantity.

There remains, therefore, something besides the idea that the causes for the variation in the frequency are to be looked for in the scarlatinal toxin alone. That explanation will be the most easily conceived, it seems

to me, which considers the fact that the nephritis occurs in the later stages of the disease. The following possibilities then come into consideration:

1. The toxin retained in the body for a long time, may be so thoroughly changed, weakened, that its excretion through the kidneys may succeed without producing an inflammation.

2. Or its virulence may have been too considerable, and the diluting force too insufficient; then it may cause nephritis in the excretion.

3. Also the possibility may be considered that while the nature of the toxin that causes the inflammation remains unaltered the same toxin may, by passing gradually and slowly through the kidneys, never attain a sufficient concentration in the renal circulation to become injurious in its influence. If, however, large quantities are excreted at one time, there may be temporarily a sufficient accumulation in the renal circulation, and consequently a possibility of inflammation.

Perhaps this is the most probable theory. And yet with all of the discussion we gain little ground. We know nothing in regard to the actual cause of scarlatina, nothing of the materials produced in the body under its stimulus, that act as the causes of the inflammation. Analogy allows us in the present state of our knowledge only the following form of expression for the unknown: Tubercle bacillus—tuberculin; tetanus bacillus—tetanin, etc.—and nothing more.

Before I discuss the clinical symptoms of nephritis, I wish to speak in general terms of dropsy in scarlatina. In the great number of cases dropsy appears with the nephritis, and in accordance with it shows the characteristics of renal dropsy.

First and foremost, the subcutaneous connective tissue is involved; the edema frequently changes its location, and comes and goes without our being able to discover any certain reason for the procedure. Moreover, effusions may take place into the cavities, and most frequently ascites occurs. Likewise edema of the glottis, or of the lungs, etc., may make its appearance.

The details will be discussed at a later point. An answer must now be given to the question as to *whether dropsy may occur after scarlatina without nephritis.*

In the earlier literature there are numerous statements answering this question in the affirmative. Thus, in the article of Barthez and Rilliet * there are a large number, of which the most noteworthy is that of the Berlin physician, Dr. Phillip. The latter, according to the quotation by Quincke, observed at Berlin during an epidemic of some 100 cases, anasarca as a constant sequel of scarlatina, and "in at least 60 cases" which he ("for the most part, several times during the course of the disease") tested for albumin he proved the absence of the same.

Quincke states truly that writers mention dropsy in scarlatina without

* *Loc. cit.*, p. 179. *Vid.* also Quincke, "Ueber einfache Scharlach-wasser-sucht," *Berliner klinische Wochenschrift*, 1882, S. 409.

nephritis less, the more recent their books are. Thomas * also discusses
the subject, and contradicts the latter statement, succeeding only in
proving that he himself has seen no pertinent cases.

Quincke reports three personal observations, of brothers and
sisters. They were admitted to the hospital from three to four weeks
after the beginning of the scarlatina, with anasarca and ascites. In
the one there never was found a trace of albumin, in both the others
only a faint trace on the day of their admission, and in the youngest
only once afterward. Formed substances (casts, etc.) were never
found, notwithstanding repeated examinations; all were miserable
and poorly nourished; the oldest had a slight fever during the
first day. After the second to the fourth week the dropsy had dis-
appeared from all. That there was any reason in these cases to
assume the presence of nephritis, I would like to deny, in company
with Quincke; and especially the second case, in which albumin was
never present, seems to be incontestable.

But the question has taken a somewhat different aspect, in the
light of the anatomic examinations that have followed the clinical
study. Litten † reports the following case:

OBSERVATION XX.—Ida K., twenty-one years old, tailoress, admitted
on May 24, died on June 12, 1879.

The patient was taken ill four days before admission with a high fever
and angina. On May 23d appeared a scarlatinal erythema, covering
the whole body. Temperature 39.3° C. (102.7° F.); evening, 39.7° C.
(103.4° F.). The course of the scarlatina was comparatively regular,
except that the fever was kept continually above the normal point by
a bronchial catarrh and mild pleurisy. The urine was absolutely normal.
In the succeeding days, while the desquamation developed along its
usual course, there formed a diffuse cervical phlegmon on the right side,
with a coincident swelling of the parotid gland, and of the submaxillary
and cervical glands, which formed pockets larger in size than a walnut.
On the 28th the complete aphonia was striking, and caused a laryngo-
scopic examination, which discovered a total paralysis of the right
vocal cord, continuing until death. We ascribed this to the pressure
upon the vagus by the tumor in the neck.

On June 1st a pericardial rub became audible, which likewise lasted
until the end. A slight edema of the left side of the face, appearing on
June 5th, and disappearing after a few days, was considered to be related
to the swelling of the neck, because of which possibly the venous outflow
was hindered. The pharyngitis increased also. The glandular tumor,
as well as the submaxillary phlegmon, extended further and further, and
over the swollen parotid fluctuation could already be detected.

On June 11th the patient began suddenly to suffer from marked

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* Von Ziemssen's "Handbuch," *loc. cit.*, pp. 247, 277, 279.

† "Beiträge zur Lehre von der Scarlatina," *Charité-Annalen*, 1880, Bd. VII,
S. 162.

dyspnea, the respiratory rate rising from 18 to 60 or 70 per minute. At the same time the pulse frequency increased from 74 to 124 and 140 beats per minute.

In the night of June 12th the patient had not a moment's sleep, owing to the extreme dyspnea. In spite of all the narcotics that were tried, this increased, and led to death about midnight.

The urine, which had during the course of the disease been examined with care several times daily, both chemically and microscopically, showed absolutely no abnormality. Once we found scattered casts without albuminuria—a symptom that has no essential pathologic significance, and may occur in healthy people.

Death followed on the 23d day of the disease.

The autopsy gave the following report from the examination of the kidneys: "Both kidneys extremely large, about 17 cm. (6.67 in.) long, by 9 cm. (3.54 in.) broad, by about 5 cm. (2 in.) thick. Their tissue was markedly relaxed and almost of pulpy confluent consistence. The cortex was very broad and opaque. The glomeruli were not discernible with the naked eye. The whole parenchyma was full of numberless pinhead hemorrhages, and large ecchymoses occurred under the capsule and in the pelvis of the kidney."

From the microscopic examination: "The interstitial tissues are infiltrated with blood, and there are numerous circumscribed areas of inflammation throughout the entire kidney, most profuse under the capsule and around the glomeruli. The glomeruli are swollen and distended; the epithelium of the tubules in many instances has lost its nuclei and is indistinctly limited by the tunica propria; also, within Bowman's capsule the epithelial cells have in many places been cast off (filling the interspace which in portions was quite wide between the convolutions and the capsular membrane) in the form of large epithelial balls. A large number of the uriniferous tubules, especially in the straight portion, are filled with casts; many other tubules appearing distinctly widened." It may, by the way, be mentioned that the pericardium, pleura, and the connective tissue in the anterior mediastinum, were all involved in a hemorrhagic inflammation, which had caused an effusion into the pericardial sac. The right vagus was also extensively involved.

Through this observation of Litten's, certain evidence is afforded that even a severe nephritis may run its course entirely free from clinical symptoms.

With Litten, I should be inclined to consider the slight edema of the right side of the face as of local origin. If we now add the fact that nephritis may occur very early in connection with scarlatina, that it need not be constantly evident, at least in its influence upon the urine as we see it,—in this light we cannot deny there is good ground for objection to the old theory.* Even though in a case of dropsy following scarlatina no change is evident in the urine, it is by no means proved that the kidneys remain unimpaired. The later we begin our observations, and the less systematically they are carried out, the more easy it

* *Vid.* cases by Henoch in his "Vorlesungen über Kinderkrankheiten."

becomes to overlook a mere passing abnormality in the urine. This fact has already been well recognized by Legendre.[*]

As the matter now stands, one must join with Henoch in the warning that care is necessary before assuming the presence of scarlatinal dropsy without involvement of the kidneys. We may go even further in saying that the proof for the occurrence of dropsy in scarlatina without nephritis has not yet been adduced—this being only possible through the autopsy later.

Attention may be called to the fact that the meaning of the term *dropsy*, especially that of anasarca, either cannot be or is not sharply defined. Thomas speaks, for instance, of "simple edemata, which appear without any discoverable affection of the kidneys, and not only in consequence of an anemic condition."

Henoch and Fürbringer take a more definite ground in distinguishing the form of dropsy characterized as "*cachectic*"—and with good authority. Inflammatory edemas in the narrow meaning of the term —*i. e.*, such as extend in the immediate vicinity of a certain inflammatory focus—do not belong in this classification.

How does it occur that in scarlatinal dropsy anasarca is so predominantly frequent and so markedly developed? The thought arises at once that the marked disturbance of the nutrition of the skin, peculiar to the scarlatinal toxin, may prove an essential factor in its causation.

Barthez and Rilliet consider the question in their somewhat exhaustive article, as does Leichtenstern.[†] Without going into the details, I wish to state that these authors have paid special attention to the lymphatic system in their investigations. Cohnheim,[‡] on the other hand, emphasizes the blood-vessels, and his conclusions are as follows:

The skin and subcutaneous tissues suffer changes in respect to their blood-vessels as the result of the scarlatinal toxin that render the latter pervious to their contents. If these disturbances of nutrition become more marked, an exudation of fluid may even now take place, without the blood itself becoming essentially deteriorated in its own composition; up to a certain point this must always take place in a severe scarlatinal infection. A dropsical anasarca without nephritis might thus be explained, and form a parallel with inflammatory vessel changes. If, now, through disease, the functional activity of the kidneys is greatly diminished, so that water is retained in the body, plasma passes out from the diluted blood, and through the per-

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[*] *Vid.* Barthez-Rilliet, *loc. cit.*, p. 179. [†] *Loc. cit.*, p. 247.
[‡] "Vorlesungen über allgemeine Pathologie," Bd. ii, S. 450.

vious vessels of the skin. "In this way the subcutaneous cellular tissue forms a depository for the water that is not excreted, as it should be, by the kidneys."

This interpretation is based upon the well-known investigations of Cohnheim and Lichtheim,* and the anatomic studies of Unna, which have shown such a marked involvement of the vessels of the skin in scarlatina, give them still more importance. As far as I can see, there can be no essential objection raised. It may be that some one will refer to the cases of exanthemless scarlatina that are followed by dropsy. How little this point applies to the question can be inferred from our discussion of the processes suffered by the skin in the exanthemless affection.†

Let us pass on to the *clinical picture of nephritis with its resulting processes.*

One of the first indications of a threatening nephritis I have found to be a rise of temperature. There are epidemics in which this may be of great value, as when a period of normal temperature follows the rise that marks the beginning of the infection and accompanies its usual course. In such a case we learn at an early date, from a second rise that occurs during a succeeding period, that the condition is not as it should be. Accurate observation will thus teach us perhaps to recognize an imminent nephritis earlier than by any other means. I must admit, however, that the affair is by no means always so simple. Very often the temperature, whether from this or that influence, does not subside entirely; in such cases a systematic thorough test of the functional activity of the kidneys and of every other organ is prevented. As a certain warning of the onset of a nephritis, a rise of temperature is in such cases absolutely valueless.

Whenever I have been able to secure regular estimations of the temperature, absolutely exact and continuing over subsequent weeks of time, the procedure has been successful. And, from my own results, I consider that only the foregoing view corresponds with the actual conditions in the case. With this also coincides the fact that our most careful observers either do not mention the temperature in the beginning of scarlatina (Henoch, Bohn) or ascribe little significance to it (Thomas). Moreover, I wish to call attention to the fact that rises in temperature of 0.5° C. (0.9° F.), during the early febrile days, may indicate a developing nephritis. A sudden onset, with chills, shaking, and a slight fever, also may occur (Fürbringer).

* "Ueber Hydraemie und hydrämisches Oedem," *Virchow's Archiv*, Bd. LXIX; Cohnheim's "Gesammelten Ahbandlungen," S. 556, Berlin, Hirschwald, 1885.

† See page 492.

Much greater stress should be laid upon the edema. A swelling of the lower eyelids and their vicinity, which often enough is extremely slight, appearing here more often than on the upper lid, is a customary prodromal sign. The space between the eyelids becomes somewhat smaller, owing to the swelling, and is especially striking to those in the vicinity if it becomes more marked on one side than the other. Slight collections of fluid usually become evident at an early day on the knuckles and on the dorsum of the foot.

In case of a more extensive involvement the swelling involves the whole face, and not rarely reaches the point of a deformity—in men, of the penis and prepuce (the post-horn type, sometimes caused by the passing urine giving to the opening of the urinary tube a curved appearance) and the scrotum, and in women of the labia majora. At the same time or shortly after, the epidermis and the lower layers of the skin also join in the extension of the swelling. If the most extreme degrees are attained, the color of the skin, which has become empty of blood, and strikingly dry, becomes a whitish-yellow; there are no vessels to be seen in it, though one sees on the surfaces that come into contact an inflammatory reddening. The process may go on even to a rupture of the epidermis—only exceptionally elsewhere than on the legs—and the fluid, by working its way through, may cause serious disturbances in the poorly nourished tissues. More or less superficial ulceration may occur, amounting even to gangrene.

Henoch reminds us that during the entire course of a nephritis the edema may fail to make its appearance. This is, however, a rare occurrence.

By no means always do we find collections of fluid in the cavities of the body. Most frequently—and in regard to this matter there is a unanimous agreement—an effusion occurs into the abdominal cavity, forming ascites. Usually, however, it follows, in point of time, after the dropsy.

The influence of the position of the body over the distribution of the effused fluid is unmistakable. Those portions that are most dependent are most affected. This rule not only holds for anasarca; pleural effusions always occur more markedly in the half of the pleura corresponding to that on which the patient lies, either for the most part or altogether.

Symptoms directly attributable to the kidneys, which precede the disturbance of their active functions, do occur, but are by no means regularly present. Among these are pains, or, more frequently, a

feeling of oppression in the lumbar region. The former may extend themselves within certain limits, and especially to the thigh.

Tension of the capsule by the swollen kidneys is supposed to cause these symptoms, and the occasional initial vomiting will likewise be attributable to the overstretching of the capsule. Soon there appear symptoms that point directly to the renal affection. Strangury repeatedly asserts itself, only small quantities of urine being voided at a time. The urinary secretion may, indeed, be slight, and for some days entirely cease. In the great majority of cases this is due to cessation of functional activity—a true anuria renalis. I have nevertheless several times observed an overfull bladder, so that one does well to pay attention to this possibility.

Thomas has studied in detail the **secretion of urine in the course of scarlatina,** and, based on his report, the following statement may be made:

In the beginning of the disease there is no essential disturbance present. The urine shows only those characteristics that appear in every febrile condition. Comparatively often, however, there forms in the otherwise clear and albumin-free urine, soon after the beginning of the affection, a mucous cloud, which contains more or less of cloudy degenerated epithelium, sooner or later cylindroids also, rarely epithelial, still more rarely hyaline, casts.

Only in exceptional cases is there already albumin present in small quantities, and, for the time being, also epithelial and hyaline casts, as well as red and white blood-corpuscles. These changes correspond to the condition termed *catarrh of the uriniferous tubules,* which corresponds with that called *catarrhal nephritis* by Friedländer. Usually these signs of disease disappear from the urine with the subsidence of the fever. They may, however, lead up to the onset of a severe renal inflammation, and it would be a more accurate statement to say that the latter grows out of the mildef phenomena.

We now find that the urine is strikingly diminished in quantity, is turbid, and a rich sediment is precipitated, consisting of more or less altered epithelium from the smaller urinary passages, tube-casts, and white and red corpuscles. The latter, which are sometimes even in the beginning so numerous as to be evident from the coloring-matter liberated from them, soon, as a rule, become still more numerous. The color of the urine, which varies according to the number of the red corpuscles, becomes more and more markedly red. The quantity of albumin also increases more and more, and in this fashion the height of the nephritis is attained.

The following departures from the usual order of affairs may be noted:

1. An increase of the urine quantity may for a short time precede the diminution of the same (Baginsky). This is rare.

2. There may be so little blood in the urine that it may be recognized only with the microscope.

3. Tube-casts may be present in great numbers without the albumin being discoverable by our customary tests.

4. In spite of a marked quantity of albumin, tube-casts may be absent.

5. Normal urine may be evacuated for a time, and even for several days.

In regard to the grosser conditions of the urine composition in the fully developed form of scarlatinal nephritis, Bartels,* after numerous observations, reports the following:

1. The specific gravity varies according to the amount of urine passed; in the beginning it is high, up to 1031; later it may fall to 1006.

2. The amount of urea (percentage) is at first about normal, and seldom goes over 2.5%: with increased diuresis it may fall to 0.8%. The absolute quantity of urea excreted is in the beginning diminished; later on, it increases corresponding to the nourishment given and to the restoration of the renal functions.

3. The percentage of albumin rarely exceeds 0.5.

4. Blood and albumin do not run parallel in their relation as to quantity; a markedly bloody urine may show very little albumin, and vice versâ.

5. The blood disappears from the urine sooner than the albumin.

6. Tube-casts are present during the entire course of the process, but in very varying quantity. In distinctly recent cases nearly all the casts are hyaline, small, and often covered with epithelium from the uriniferous tubules. After some time there appear casts with fat droplets, finally also broad hyaline, and altogether granular dark casts. Blood casts may occur in bloody urine.

7. The remaining forms of organic constituents one sees quite rarely.

8. Uric acid, and also oxalic acid in various combinations, crystalline or amorphous.

In regard to the **output of nitrogen by the kidneys** we have the accurate investigations of Carl v. Noorden.†

At a time when for days no urine or only small quantities are voided, the nitrogen-containing decomposition products remain in the body to a great extent and are only cast off at a later time, to-

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* *Loc. cit.*, p. 244.

† "Lehrbuch der Pathologie des Stoffwechsels," Berlin, Hirschwald, 1893, S. 397.

gether with the newly manufactured waste products, after the reopening of the embarrassed excretory passages. We find also in the earlier periods less, and in the following periods—those of convalescence—more, nitrogen in the urine, corresponding to the nutriment ingested and to the destruction of albumin at the given time.

Instead of describing further these conditions that are thoroughly understood, I give an example:

A child with scarlatinal nephritis excreted in the beginning of the disease 3.2–6.5–4.5 gm. (0.1–0.21–0.14 oz.) N in the urine. When a sudden improvement occurred, the quantity rose (without there having been at any time more than 8 gm.—0.26 oz.—N in the food) in two days to 14.2 and 16.1 gm. (0.46 and 0.52 oz.) of nitrogen.

Carl v. Noorden considers it the rule, according to his own investigations, that the kidneys suffering from an acute inflammation cannot take charge of all the nitrogen. Exceptions may, however, occur.

I will insert here a pertinent observation by J. Prior [*]:

Scarlatinal nephritis in a nineteen-year-old man. In the beginning violent symptoms, which subsided after five days. At the time of observation for eight days there had been no fever, no edema, and the formed constituents of the urine were beginning to disappear. Four times daily the patient ingested 500 gm. (16.07 oz.) of milk, 100 gm. (3.21 oz.) of white bread, and 13.88 gm. (0.45 oz.) of nitrogen. From this approximately the same quantity of nitrogen was excreted.

The average for five successive days follows:

Quantity of Urine.	Specific Gravity.	Albumin.	Nitrogen.	Uric Acid.	Sodium Chlorid.	Sulphuric Acid.	Phosphoric Acid.	Nitrogen in the Feces.	Nitrogen in Feces and Urine.	Difference in the Nitrogen.
1194	1023	16.16	12.57	0.63	10.02	2.01	2.93	0.58	13.15	0.73

Then, with the milk were given two soft-boiled eggs each time (altogether, eight eggs in the day). The amount of nitrogen ingested was now 21.079 gm. (0.65 oz.). What form the conditions now took is shown by the table, which includes the day of the experiment as well as the two succeeding ones:

	Quantity of Urine.	Specific Gravity.	Albumin.	Nitrogen.	Uric Acid.	Sodium Chlorid.	Sulphuric Acid.	Phosphoric Acid.	Nitrogen in the Feces.	Total Excretion of Nitrogen.	Difference between Ingested and Excreted Nitrogen.
1	1240	1031	15.9	18.09	0.74	11.14	2.36	3.69	0.8	18.89	— 2.18
2	1210	1027	16.0	15.92	0.66	10.31	2.03	3.12	1.2	17.12	+ 3.24
3	1250	1028	15.7	13.63	0.60	10.22	2.10	2.99	0.6	14.23	+ 0.35

[*] "Einwirkung der Albuminate auf die Thätigkeit der Niere," *Zeitschrift für klinische Medicin*, Bd. XVIII, S. 119.

Without repeating the conclusions drawn by Prior with respect to the details of metabolism,—to which Carl v. Noorden* takes exception,—I want to say that the experiment in any event shows the relatively great functional power of a kidney under an increasingly severe pathologic condition. Nothing can be said in regard to the remarkable retention of large quantities of urea. Carl v. Noorden considers that proof is not afforded that such a retention actually did occur, and there may, indeed, have been a very temporary accumulation of a portion of the unconverted albumin that had been administered in excess.

The nephritis ends in the great majority of cases favorably. As an average duration we may name four to six weeks. But both shorter, as well as longer, courses will be run by the condition that require special mention.

Leichtenstern unfortunately reports the following very briefly: "Cases of acute hemorrhagic nephritis recurring twice or even several times are of great interest. In one case the nephritis appeared in four acute attacks with hematuria and oliguria, while in the interval the urine passed freely, and was absolutely free from albumin." The lack of particulars as to the time of occurrence does not admit of our discussing the case.

Bartels observed after eighteen months a complete convalescence. The old view, that chronic nephritis can never originate from the acute scarlatinal variety, is no longer tenable. To be sure, it is a rare occurrence, but Aufrecht, Fürbringer, Henoch, Leyden, Litten,† and O. Vierordt have all seen it. The danger is, however, a remote one in comparison with others that threaten in the course of the nephritis. Among the latter, uremia takes first place, and next the dropsy and the suppurative inflammations come into consideration.

[**Modification of Urinary Toxicity in Scarlatina.**—Mazaud ‡ states that during the febrile period the toxicity of the urine is relatively high, producing convulsions in the experiment animal. When the fever curve sinks, there is a urotoxic crisis of short duration, which coincides, as a rule, with the urinary crisis. After convalescence is established the urine becomes hypotoxic, remaining thus for a long time.]

* " Besprechungen einiger neueren Arbeiten über Albuminurie und Nephritis," *Berlin. klin. Wochenschrift*, 1891, S. 543.

† *Vid.* his extremely valuable Observation XXI, page 573 of this volume.

‡ *Revue d. mal de l'enfance*, 1898, t. XVI.

THE HEART.

There still remain the changes that take place in the heart. Since these have a marked significance in all the incidents of the disease, and often enough one of life and death importance, I will discuss them here, in a general way, and put the question as follows:

1. *How does the heart react to the scarlatinal toxin?*

2. *What is the effect upon the heart when a nephritis occurs in a scarlatinal patient?*

That the scarlatinal toxin alone is able to produce serious changes in the entire cardiac system may be considered as certain from the numerous anatomic investigations. Ernst Romberg * has instituted the most thorough and searching investigations, and with them the technique of the methods of to-day came into general application.

In the 10 cases that underwent the most careful examination for the extension of the disease to the organ the involvement was noted, according to the gross anatomic layers, as follows:

IN SCARLATINA:			IN SCARLATINAL NEPHRITIS:		
Myocarditis, Interstitial and Parenchymatous.	Pericarditis.	Endocarditis.	Myocarditis, Interstitial and Parenchymatous.	Pericarditis.	Endocarditis.
Twice severe. Once moderate. Four times slight. Once absent.	Three times severe. Three times slight. Three times absent.	Twice severe. Three times slight. Three times absent.	Twice slight. Once old indurative changes.	Twice slight.	Twice absent.

Let us stop to consider the changes in the **myocardium**. These are, owing to the fact that the muscles form the actual working machine, the final factor that determines the functional activity of the heart.

The **cardiac muscle** is altered not only in its parenchyma, but in regard to its supporting tissue—the interstitial connective tissue. This has great significance, as Romberg has very properly stated. I wish, moreover, to say that the distinction insisted upon by many between degenerations and inflammatory processes can have hardly any importance here. Their origin is the same, and to distinguish between them is to gain nothing in the end. We will do best to speak of acute infectious myosites, with the French (Hayem, Martin), and in this matter Romberg is unquestionably correct.

Pericarditis exerts its influence, when it reaches a marked development, from the visceral layer outward against the parietal layer, but only rarely breaks through the outermost, which is formed by strong connec-

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* "Ueber die Erkrankungen des Herzmuskels bei Typhus abdominalis, Scharlach. u. Diphtherie," aus der Med. Klinik zu Leipzig (Curschmann), *Deutsches Archiv für klinische Medicin*, Bd. xlviii, S. 369, and Bd. xlix, S. 413.

tive tissue. Often, therefore, no cloudy swelling is found, and no fibrinous exudate is to be seen, although the microscope discovers an infiltration of round cells, and occasionally their presence in large numbers.

Endocarditis is, on the whole, a rare condition, though in scarlatina it is more frequent than in diphtheria and typhoid fever; it leaves the valves free and attacks the cardiac walls.

The **cardionervous** system in the cases examined by Romberg showed relatively little involvement. There was an infiltration by round cells of one or more ganglia, involving either the ganglia themselves or their covering of connective tissue only; but the latter was a rare occurrence. Whether other real disturbances occur and present conditions that apparently differ from the ordinary, Romberg does not positively state. In the nerves of the pericardium he has never met with perineuritic changes—and this in contrast to diphtheria and typhoid fever.

The French—especially Martin—have laid great stress upon the **involvement of the arteries.** Romberg, indeed, found a *peri-arteritis* here and there on the large vessels; but *endarteritis* which, because of a narrowing of the lumen and degeneration of the smooth muscle-fibers in the involved areas, can be accompanied by severe local processes, he never with certainty saw.

The entire condition has a general and decisive significance only when it is not to be considered the consequence of a mixed infection due to scarlatina and pus cocci in combination. I am of the opinion that Romberg might have termed the cases examined by him, in accordance with our present powers of discernment, as cases of genuine scarlatinal infection.

The conclusion that the scarlatinal toxin endangers the heart corresponds accurately with our experience at the bedside. Entirely apart from the question as to how far the fever, the hyperpyrexia, and as to how far influences distinctly independent of it—intoxications—come into consideration, we will not be able to deny a disturbance of the functional powers of the heart in scarlatina as the general order of things. As is always the case, it shows itself in various ways: tachycardia, an irregularity both in the rhythm and force of the heart-beats, and, in the later stages, perhaps even bradycardia—symptoms that appear externally to differ, but in their inherent nature are hard to distinguish; signs that the nerves or the muscle-fibers are not in their full power.

Going a little more into detail: According to Ernst Romberg, the scarlatinal toxin may in the early days of the disease cause a *marked cardiac dilatation*, though he has observed this phenomenon only in severe cases.

Henoch properly remarks that, among the disturbances accompanying cases of scarlatina that run a violent course to a sudden death, those involving the heart present the main danger. The pulse

may attain a very high rate, is often uncountable; moreover, the cardiac tones run together, so that one cannot differentiate them or estimate their number. The pulse is, of course, small and irregular, and with the intermittent action of the heart corresponds the distribution of the blood. There is coldness, cyanosis, then pallor, appearing first and most markedly in those portions of the body that are furthest removed from the heart. The picture is exactly that of an acute cardiac insufficiency.

In pure cases of scarlatina during the later stages there is sometimes a slowly and gradually developing cardiac weakness. A marked diminution in the frequency of the pulse (bradycardia) occurs, on the whole, less frequently than in most of the other infections.

Sudden cessation of cardiac action with instantaneous death, preceded by no warning, has been observed very rarely, and not nearly so often as in diphtheria.*

What takes place in the heart when nephritis occurs in scarlatinal subjects?

The recent past has given us important observations on this point, and, first, those of C. Friedländer.†

1. In children there hardly ever fails to be present a hypertrophy and dilatation of the heart; in adults this appears to be a less frequent occurrence.

C. Friedländer has seen only 4 such cases; twice in twenty-year-old patients a slight hypertrophy, which in two adults (in their thirtieth and fortieth years) was not demonstrable.

2. The changes may affect both sides of the heart alike; usually, however, they are developed more on the left side than on the right.

3. The heart increases in weight in children on an average about 40%, the maximum decidedly exceeding this limit in some cases.

4. The increase in size of the heart was in nearly all cases very marked. The ventricles as well as the auricles were much dilated and filled with blood.

A comparison óf the autopsies on scarlatinal subjects in whom nephritis was absent showed that cardiac involvement was not present, so that the latter may also be ascribed to the nephritis. Detailed statements in regard to the time from the beginning of the nephritis

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*Compare the clinical portions of E. Romberg's "Arbeit," *Deutsches Archiv für klinische Medicin,*" Bd. XLIX, S. 413.

†"Ueber Herzhypertrophie." Du Bois-Reymond, *Archiv für Physiologie,* 1881, S. 168. Compare *Verhandlungen des Vereines für innere Medicin,* v, 19 Februar, 1883, in *Deutsches med. Wochenschrift,* 1883, S. 207.

to the occurrence of the cardiac involvement are wanting. We can only infer from general remarks that, as a rule, the latter appears early in the disease. It is also noteworthy that in acute nephritis arising from other causes cardiac hypertrophy is seldom present. Friedländer believes that these other causes occur "almost entirely in adults." This need not necessarily be so, however, and I would suggest the acute renal inflammations following diphtheria as supporting my claim.

Riegel * has studied the development clinically with great detail, and fixes the following principles:

1. In most, if not all, cases of scarlatinal nephritis there are evident from the beginning of the disease, and almost synchronously with the appearance of albuminuria, also the signs of an increased tension in the arterial system.

2. This increased tension of the aortic system is always connected in a marked degree with a slowing of the cardiac action. Frequently there exists also a slight irregularity of action. The more marked the arterial pressure, the more considerable the slowing of the pulse.

3. With the subsidence of the nephritis, the pulse-rate increases in the ratio that the arterial pressure decreases.

4. The cardiac enlargement is a secondary consequence of the increased arterial pressure, and appears only after the pressure has been increased for some time. A clinically demonstrable enlargement of the heart occurs only in cases of arterial pressure. In some cases such an enlargement is already evident a few days after the beginning of the nephritis. (Cases 1 and 2.)

If we examine Riegel's conclusions, we must admit this his evidence is flawless. It may be, however, that some one will not accept the sphygmographic readings as conclusive of the tension in the arteries. For the conditions that are under consideration here, however, I am inclined to value highly the significance of the sphygmographic verdict received from such an experienced hand.

From the combined view of these anatomically and clinically ascertained facts, let us endeavor to gain a more accurate insight into the nature of the occurrence.

With the appearance of the nephritis the heart is burdened with an increased load of work—the tension in the circulation increases, and offers an increased resistance. If the cardiac inflammation caused by the scarlatinal toxin, myositis playing the chief rôle in the process,

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* "Ueber die Veränderungen des Herzens und des Gefässsystems bei acuter Nephritis," *Zeitschrift für klinische Medicin*, Bd. vii, 1884, S. 260.

has been of a marked degree, and if the reserve force of the heart has been in this manner diminished, it becomes unequal to its task, is exhausted, and dilatation follows. This may occur very suddenly, and be so decided that death may occur in a short time. Or if there are enough capable muscle-fibers, and if there is sufficient nourishment to supply them, there develops a hypertrophy adequate to the work at hand. If the influence upon the heart is only slight, a hypertrophy promptly occurs. It is possible that a certain degree of dilatation is always present, but the fact may not be clinically demonstrable.

I give a few examples of the processes commonly observed during the formation of cardiac dilatation *:

Silbermann (Case 4): Boy of three and a half years. Two months ago was very ill with cholera nostras. Previously entirely well. Scarlatina ran a favorable course, on the whole, in spite of high temperature (42.3° C. —108.1° F.) up to the beginning of the third week. Nephritis and dropsy then made their appearance. After four days of continued edema there was a marked tension of the pulse, and a decidedly increased cardiac action without evident extension of the heart dulness, and with merely sharp, accentuated cardiac tones. Within the next few days a slight lessening of the pulse-tension. Then suddenly a softer, but by no means smaller, pulse. At the same time a broadening of the area of cardiac dulness: on the right side to the right edge of the sternum, on the left about 2 cm. (0.79 in.) beyond the mammillary line, above to the second intercostal space. The first initial tone is replaced by a murmur; the diastolic tone over the pulmonalis is loudly accentuated. During the further course a marked loss of cardiac power with extension of the dulness to the left as far as the axillary line, weak apex-beat, a double murmur over the mitral area, lessened intensity of the diastolic pulmonary tone. Pulmonary edema. Death.

The autopsy showed "an enormous dilatation of the left ventricle and apex of the heart, while the right half of the organ appeared to be only slightly dilated. The left ventricular cavity was enlarged to more than twice its size, its wall neither thicker nor thinner than normal." Microscopic changes absent from cardiac muscle. Marked glomerulonephritis.

In addition to the altogether predominant dilatation in this case, a hypertrophy of the left ventricle must be assumed, which in the beginning displayed itself more distinctly in the general picture.

Very different was the course of Case 5 of Silbermann, to which I offer no protest, in spite of there having been no autopsy:

A six-year-old girl, rather sickly from mild rachitis, and later from

* "Ueber die Entstehung der excentrischen Hypertrophie und der acuten Dilatation des linken Ventrikels im Verlauf der Scharlach-nephritis," von Dr. Oscar Silbermann in Breslau, "Jahrbuch für Kinderheilkunde," N. F., Bd. xvii (1881), S. 178.

anemia, but never seriously ill. Very mild scarlatina, which caused a doubt in the mind of the attending physician (Silbermann himself) in regard to the diagnosis. In the beginning of the third week there was slight fever (39° C.—102.2° F.), edema, and nephritis. In the next three days the heart, up to this time sound, was not markedly affected; loud but pure tones, the pulse-tension very high. Urinary excretion barely 100 c.c. (3.38 fl. oz.). In the night patient complained of pain in the precordial region and general weakness; the pulse was fairly full; to the left only did the dulness extend over its limits; no very threatening symptoms. Wine was ordered as a stimulant.

Silbermann then continues: "We left the child without being especially anxious, but on the next morning the picture was entirely changed. At 10 A. M. an enormous extent of dulness was noted, reaching nearly to the axillary line, and the apex-beat was pushed downward to the eighth intercostal space in the mammillary line. The cardiac boundaries above (second interspace) and to the right (middle of the sternum) showed nothing striking. The pulse had meanwhile risen to 120, and had become very weak. Over the mitral region the first tone was replaced by a moderately loud murmur. The apex made a hardly noticeable stroke on the thoracic wall." After injection of ether and large doses of Hungarian wine the condition improved somewhat. "When I saw the child in the afternoon, at 2 o'clock, the pulse was somewhat better. Then all at once, shortly after I had ended the cardiac examination, the child cried out, turned on its right side, and died."

It seems to me that the differential diagnosis of an effusion into the pericardium might come into question. But the absolute limitation of the dulness to the left side of the thorax makes this less of a probability. Silbermann cites similar cases from James Goodhard, with the anatomic findings, published in "Guy's Hospital Reports." The original is not accessible to me.

Still another case, in which the hypertrophy of the left ventricle was markedly developed: A four-year-old boy, previously perfectly well, became ill of a mild scarlatina. At the end of the third week a slight edema of the face and knuckles, which markedly increased up to the beginning of the fourth week. Ascites also. Symptoms ascribable to the circulatory organs now appeared, the latter being up to this time normal. Marked tension of the radial, considerably exaggerated apex-beat, no cardiac enlargement. Nephritis. On the following day the apex-beat passed beyond the mammillary line. The heart tones were loud and somewhat ringing, but clear. After two more days the apex-beat moved still further outward; the systolic mitral tone was replaced by a murmur. This continued until the beginning of the fifth week; again a very loud but clear

tone appeared; now, however, a marked increase of the cardiac dulness: the upper border in the second intercostal space; to the left about 2.5 cm. (1 inch) to the outside of the mammillary line, running from here nearly at a right angle down to the seventh intercostal space. The apex-beat is moved out almost to the axillary line. To the right, the right sternal border. Later uremia set in, finally pulmonary edema, and death. The cardiac tones became loud and clear before the fatal ending.

Autopsy: At the opening of the thoracic cavity the enormous size of the heart struck every one, the left ventricle being at least double as long as the right. Its cavity was markedly dilated, its walls much hypertrophied. The right half of the heart was only moderately dilated; otherwise perfectly normal.

The heart was 7.0 cm. (2.75 in.) long, 6.0 cm. (2.36 in.) broad, and 3.0 cm. (1.18 in.) thick. Its weight amounted to 112 gm. (3.6 oz.) (against 70 to 80 gm.—2.25 to 2.57 oz.—normally). Glomerulonephritis.

This increase in the cardiac muscle occurred within the short time of two weeks.

We will proceed immediately to consider **endocarditis and pericarditis following scarlatina.** That both may occur besides the myocarditis, and be caused by the original toxin itself, has been determined by Romberg. Through this fact the anatomic foundation is afforded for a view long held by me, that the heart, in all of its pathologic conditions dependent upon an infection, is involved in all its parts, though now more in this one, now more in that. We will therefore do best always to speak of a *pancarditis.* Of course, the attempt must be made to ascertain in every case which of the tissues are evidently, and which most severely involved. But this will not often succeed. With regard to the endocardium, the locality of the inflammation itself comes especially into consideration (endocarditis of the cardiac wall).

It must be noted, moreover, that sepsis complicating scarlatina causes in the heart, as its favorite point of attack, clinically as well as anatomically, exactly the same symptoms as those of pancarditis. An etiologic distinction at the bedside I consider is never possible, and not even by the section table with the help of the bacteriologic examination. Entirely apart from the septic affections caused by pus cocci, that may appear distinctly at any point of the body, and which serve as a foci of infection, still others come under consideration. As a result of experimental investigations, we may say that in order to further the permanent settling of pus cocci on and within the endocardium, it is necessary that the nutritive condition be impaired, and in this way a favorable culture-medium furnished.

The scarlatinal toxin can of itself bring this about. It opens at once door and gate to the pus cocci, and in many places. Thus it is

not to be wondered at that septic endocarditis frequently appears when other pathologic foci, due to sepsis, are not discoverable.

I submit the question, which seems to me a very appropriate one, whether the relatively frequent occurrence in scarlatinal nephritis of all the affections of the serous membranes, accompanied by pus formation, does not admit of a similar interpretation.

That the materials which are present in the lymph spaces in nephritis, whether they be only retained waste products of the normal combustion, or whether newly formed toxins, are of no benefit to the protoplasm requires no proof. The generally injurious influence, and the preparation of the soil for the pus cocci everywhere in the body, may possibly be referred to this circumstance.

Endocarditis of the cardiac wall appears to be more frequently present than valvular endocarditis. The former offers practically no possibility of diagnosis; and if the myocardium were not simultaneously involved, or if emboli did not occur, it would present barely any pathologic phenomena. All that we see corresponds with the picture of cardiac weakness. In the further course of the disease, however, and often without being discoverable to the most conscientious observation, the valves may become involved. I am inclined to interpret, along with Curschmann,* cases in which, after the passing of the scarlatina, cardiac disturbances are just as little recognizable as during the original affection, and yet after a year or more display real valvular lesions, as follows:

Mural endocarditis without marked myocarditis, but with slow extension to the valves. In these conditions, I may add, every trace of fever may be lacking. If we include these forms under the term endocarditis, as is right and proper, the severe so-called septic form takes a decidedly back position in point of frequency. We should not be too quick with the diagnosis of *valvular endocarditis*. One becomes more and more aware how easily an affection, essentially limiting itself to the muscle-fibers, may simulate the valvular affection; at least for a short space of time. No dependence may be placed upon the murmur at the mitral area. The physician must be very careful, moreover, to observe the position of the diaphragm if he would avoid grossly deceiving himself.

In children this rule is especially to be observed. Cardiac dilatation, because of its limitation to the left ventricle, is less likely to lead to an error, although mitral murmurs are frequent in the condition.

* *Deutsches Archiv für klinische Medicin*, Bd. xlix, S. 437.

Pericarditis, also, when anatomically present often enough gives absolutely no symptoms. If it involves the surface especially, we have the customary clinical signs, though I wish to call attention to errors—and in scarlatina I have often seen them—that can occur in the dry form as well as in the pericarditis with effusion. A muscle sound may crepitate extremely like the friction rub, and the marked dilatation of the entire heart may simulate an effusion. Great care is required, if one is to be on the safe side, and there are cases in which a positive diagnosis cannot be made.

Pericarditis may be accompanied by a serofibrinous or by a purulent exudate. The latter condition occurs more frequently when nephritis is present than otherwise. But, according to unanimous opinion, pericarditis plays no great rôle, and is decidedly rare, especially in its severe forms.

UREMIA.

Let us turn back to the discussion of **uremia.** The tendency is continually gaining ground to look on uremia neither as a pathologic condition that is complete in itself, nor as having a single cause of existence. I feel that in scarlatina we have every reason to hold to this fundamental belief.

Most prominent among the uremic phenomena, from a clinical standpoint, are the disturbances of the brain, though a number of others appear in addition to the latter. Especially are the cardiac disturbances also to be mentioned, and it seems, at least occasionally, as if the incapacity of the heart formed the cause of the whole condition. The marked perviousness of the vessel-walls, together with changes in the constitution of the blood, favor the occurrence of edema to a decided degree.

I do not wish, with Leichtenstern,* to ascribe the whole symptom-complex of uremia to anemia and to an inflammatory edema of the brain and its membrane. But that scarlatinal nephritis is due to these causes quite frequently, and probably most often, I consider to be true. In addition to these, peculiar autointoxications in some way make themselves evident.

This, however, is not the place to discuss in detail the unwarranted theories as to the originating causes of uremia,† and let us therefore turn to the facts of the case.

* *Deutsche med. Wochenschrift,* 1882, S. 247.

† Compare L. Landois, " Die Urämie," Vienna and Leipzig, Urban and Schwarzenberg.

1. Uremia usually makes its appearance only after the nephritis has become distinctly evident, and especially when a considerable diminution has occurred in the quantity of excreted urine. That this is the rule admits of no doubt, though it has exceptions.

Henoch* reports: "In the case of a four-year-old child taken ill on December 28, 1880, with scarlatina, the scanty urine, examined on January 9, 1881, contained no albumin. Notwithstanding, on the morning of the 10th, suddenly there were intense convulsions of the right side of the face and body, and stupor; the pulse strong and 144. The urine drawn by catheter now contained a considerable amount of albumin." On the 14th the albumin had disappeared. Recovery.

Then the following fatal case†: "Otto S., a twelve-year-old child, admitted on July 22, 1873, with edema of the face and scrotum following scarlatina. No fever. Urine scanty, markedly acid. Contains no albumin and no nephritic elements; only an amorphous uratic sediment which dissolves on heating; also on both following days the same negative result. In the night of the 24th–25th uremic seizures; in the morning cyanosis, failure of the pulse, complete unconsciousness. The urine, which was evacuated by catheter with difficulty, contained large quantities of albumin and many highly granular casts. Death followed on the 27th through collapse and pulmonary edema, after consciousness had been fully regained. Autopsy: Exquisite nephritis, fatty liver, pulmonary edema, bronchopneumonia."

Whether, in these cases, the diminution in the quantity of urine was extreme cannot be determined from the meager statement. If not, they belong to the cases already described as "latent nephritis," and the fact that uremia may also occur in such nephritis is of great practical significance.

I wish to state that Leichtenstern‡ saw in the Cologne epidemic three cases in which the first symptom of the developing nephritis was a uremic attack, followed by complete anuria, up to which time, and even three or four hours previously, the urine had been voided free from albumin and blood. In one case after twelve hours, and in the second only after several days, appeared albuminuria, hematuria, and oliguria.
The same condition was present in these cases.

Such cases are, on the whole, quite rare. Much more frequently it occurs that without any remarkable diminution in the quantity of urine, even with free urine output, uremia makes its appearance. Henoch and Leichtenstern report cases of this kind and nearly every busy physician has seen the occurrence.

2. *The symptoms of uremia:* Vomiting, headache, and a more or less marked disturbance of the brain functions. Some deafness and slight twitchings in the muscles of the face are very often present.

If the condition persists, we may then speak of a mild uremia.

* "Vorlesungen," S. 587.   † *Ibid.*, p. 592.   ‡ *Loc. cit.*, pp. 246–248.

A case of Leichtenstern warns us to use great foresight. He saw a case of uremia with fatal ending, although nothing other than a very gradual oncoming coma manifested itself. At the autopsy: Cerebral anemia, with marked edema.

But often enough the typical attack occurs, which only as an exception is a sudden one, and without any warning. E. Wagner * gives the best description known to me, and, with few abbreviations, I quote him as follows:

Unconsciousness: according to the severity; the sensibility is also lessened in varying degree, or even lost; likewise the reaction of the reflexes of the skin, the conjunctiva, and iris.

In some cases the tonic contractions appear to be entirely lacking; often they are only a second long; again, and more usually, they last for a larger period. The head meanwhile is extended posteriorly or to one side, and the extremities and spinal column are also in extension. The mouth is fast closed, the eyes are fixed, the lids open, more rarely shut, the pupils dilated, rarely narrow, and all reflexes are lost. The respiration ceases for a second. The face appears pale and sunken in.

The clonic contractions show the well-known type that is hard to describe. While unconsciousness continues there occur varying, and as a rule very severe, convulsions of the face, including the lower jaw (gnashing of the teeth) and the eyeball, and also of the trunk and extremities. At one time these extend over all portions alike; at another they are irregularly distributed, but begin in a certain part of the body, and from this point extend still further. The duration varies up to several minutes. Then a diminution, complete relaxation, alternating with clonic contractions—then recovery. The breathing is at first hurried and deep, later on it varies in length at different times. In consequence of this, and on account of the muscular contractions, the veins of the skin undergo a marked swelling, the face and mucous membranes are cyanotic, the eyeballs protrude markedly. Not rarely a bloody froth collects at the mouth; the saliva is filled with bubbles due to the disturbance of the breathing, and with the latter is possibly mixed the blood from any tooth wounds. Inspiration and expiration appear occasionally to be convulsive, and may be accompanied by tracheal rattling.

The temperature rises, sometimes several degrees. The pulse, if at all perceptible, is frequent, small, and usually visible, and palpable only over the cardiac region, or on the carotid; over the latter there is sometimes a marked pulsation.

* "Der Morbus Brightii," *loc cit.*, p. 63.

The skin is dry and covered with perspiration; sometimes the urine and stools are involuntary. The convulsions subside rarely at once, the breathing becomes more regular, and the cyanosis disappears. The pulse may remain rapid for hours, or even permanently. The temperature falls rapidly. The coma, however, still continues, and the more severe the attack, the longer it lasts, up to several days. Consciousness returns only gradually.

Sometimes there is a single attack of this sort, to which after a few days recovery succeeds, or in which, though seldom, death may occur. Much more frequently the attacks repeat themselves, either daily or a number of times on the same day, and even 20 or 30, or more. In the latter case, the patient in the interval usually either remains completely unconscious or partly recovers. In case of improvement the attacks become less frequent, shorter, less general, and consciousness returns more and more. Not rarely marked stupor persists for several days; sometimes between the milder attacks severe, and even the worst forms make their appearance. If the number of attacks is very great, death is the customary result, taking place, as a rule, with the patient still in a comatose state.

If the patient does not die in coma, still other processes may ensue.

Mania: Wagner saw a case in which in one day there were eleven attacks, and every time followed by the wildest mania, with a rise of the temperature in the axilla to $42.0°$ C. ($107.6°$ F.). Notwithstanding this, the patient lived.

Melancholic depression may occur as a sequel.

Only in a few cases are there disturbances of the motility and sensibility.

Leichtenstern saw "two cases of unilateral uremic convulsions with marked deviation of both eyes toward the involved side. In one case *hemiplegia* followed the unilateral convulsions, and on the same side. Autopsy: Uniform anemia of the brain with considerable edema."

Again: "One case with uremic trismus and tetanus with contractures of all the muscles, lasting over several days, following uremic convulsions. Several days of unconsciousness. Later, a markedly slow respiration and heart-beat. Outcome, recovery."

In one case aphasia was present.

Much more frequent is amaurosis. It seldom precedes the attack, and usually the patient notes on returning to consciousness that he is blind. The amaurosis is frequently already pretty well developed; more rarely it reaches its acme later, in a few hours or several days

after the attack, and still more rarely it remains incomplete. It always involves both eyes.

The ophthalmoscopic examination shows no abnormality. The retinitis of Bright is not present. Litten has, however, repeatedly seen swelling of the optic nerve and, as has Reimer,* capillary apoplexies in the retina.

The pupils are rarely dilated and reactionless; usually they react completely but slowly to light. In the latter case the prognosis is good, as a rule; the usual power returns completely after twelve to twenty-four hours, or a few days, or rarely after weeks of time. If the pupillary reaction is absent, a complete recovery is still possible. If the pupils react to light, the cause of the amaurosis cannot be in the retina, the optic tract, nor in the quadrigemina; rather, between these structures just named and the center governing the perception of light, or even in the center itself.

If the attack occur, the patient remains, as a rule, amaurotic in the interval. More rarely the amaurosis disappears, to return with a new attack, and again to disappear.

Tinnitus aurium, difficulty of hearing, amounting even to complete deafness, are rarer conditions; they can also suddenly disappear.

The heart and respirations are frequently influenced from the center. In addition, there is an anatomic disturbance.

Wagner asserts that the pulse, sometimes for several days before the eclamptic attack, shows a marked slowing, even to 40 beats per minute.

In the attack itself there is always an acceleration, even so much, perhaps, as to render it impossible to count the pulse. During the coma the rate continues at the same level, and is neither slowed nor hurried, only a higher tension than usual. The conditions are otherwise so complicated that an accurate interpretation of them is neither in general nor in the individual case successful.

Leichtenstern † states that "one of the most frequent modes of onset of scarlatinal uremia is uremic dyspnea or tachypnea, which is usually seen in combination with tachycardia; the number of respirations may rise to 60, and that of the pulse to 200. In nearly all cases there is an alabaster-white color of the skin, sometimes with a bluish tinge on the lips. The tachypnea and tachycardia may persist unaltered

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* "Casuistische und pathologisch-anatomische Mittheilungen aus dem Nikolai-Kinderhospitale zu St. Petersburg," "Jahrbuch für Kinderheilkunde," N. F., Bd. x, S. 22.

† *Loc. cit.,* p. 247.

for days, and in rare cases for weeks, and with the slightest remissions; or they may appear only exceptionally in severe paroxysms (asthma uræmicum). The patient complains frequently of severe pains in the cardiac region and in the abdomen. The mind is absolutely clear. The jactitation, the restlessness, and the anxious cry of children render this most frequent form of uremic affection full of anguish for the patient as well as for those in the vicinity.

Uremic dyspnea exists, as a rule, with an absence of any discoverable change in the lungs, and without pleural or pericardial exudate. This does not mean, however, that the cardiac muscle or any other portion of the heart remains anatomically unimpaired.

Leichtenstern continues: "The latter may appear, and occasionally general pulmonary edema. In one case this reached such a degree that for hours at a time, with the respirations, white, foamy masses came bubbling from the mouth and ran together in the form of serum in the sputum-cup. There was more than a liter of serum collected in this way." The patient recovered.

Fleischer * found in the expectoration evacuated in this manner in twenty-four hours over 2 gm. (30.86 grs.) of urea.

For this no explanation can be given. We may only look upon the heart which has experienced actual alterations in its substance as a substantial partaker in the entire series of phenomena.

The twitching of the skin surface that disturbs the patient even when unconscious must still be mentioned.

The vomiting may be characterized only in part as a cerebral symptom. It can be caused by the stretching of its capsule by the swollen kidney; or through the excretion of certain elements upon the mucous membrane of the stomach (urea and the ammonium carbonate derived from it have been positively determined in this connection); and perhaps also through edema of the gastric mucous membrane. The so-called *uremic diarrheas* appear, in the light of our present knowledge, to depend upon local irritation of the intestinal mucous membrane.

Of the constitutional symptoms the fever is especially to be mentioned.

A moderate fever (38.0° to 39.5° C.—100.4° to 103.1° F.), according to Wagner, is the rule during the attack, as well as during the succeeding coma. Rises to 42.0° C. (107.6° F.), with or without preceding chills, are rare, as are also the subnormal temperatures that follow them (down to 34.0° C.—92.3° F.). In addition to the

* Quoted by Landois, *loc. cit.*, p. 119.

increased production of heat caused by the severe muscular contractions, a number of other matters come into consideration, such as a diminished or increased external elimination of heat dependent upon the centers that control the lumen of the superficial vessels (Landois). Besides these conditions that are still within the powers of our conception, we must consider also the possible marked influence of intoxications upon the regulation of the temperature. The positive importance of this point remains for the future to decide.

3. The frequency of the occurrence of uremia can be more accurately determined than the duration and outcome, owing to the great variation in the conditions of time and locality.* In studying the reports of epidemics one gains the impression that in this particular, as in every other, the unknown something is playing its part, and that this lends to the fundamental disease its various forms. We can only say with certainty that as long as there is present a renal disease, just so long may uremia make its appearance. Its recurrence, with long intervals widely separated from one another, is a noteworthy feature.

I quote briefly from the following instructive case of Litten's †:

OBSERVATION XXI.—A seventeen-year-old girl, previously well and strong. On the fifth day of the disease, although in the course of a mild attack, nephritis and dropsy. The heart dulness of normal size. The urine measured in the beginning only 380 c.c. (12.8 fl. oz.). It then increased rapidly until the twenty-fifth day, and reached during this time 1560 c.c. (52.7 fl. oz.).

The specific gravity varied between 1008 and 1010. The urine was markedly albuminous, and contained considerable blood, many polymorphonuclear leucocytes, unchanged as well as fatty renal cells, cylindroids, and casts. The dropsy increased decidedly.

On the 26th day repeated vomiting. Urine, specific gravity 1004, quantity 320 c.c. (10.8 fl. oz.) and less, almost transparent, free from blood.

On the 27th day: Marked nausea, three uremic attacks with coma and convulsions. Amaurosis; the optic papillæ on both sides more prominent than usual. The vessels ascend more vertically on its edge, and appear more tortuous than previously. Repeated epistaxis.

Urine, specific gravity 1003, and only 280 c.c. (9.5 fl. oz.) in quantity; free from blood and sediment, and contains strikingly less albumin.

On the 28th day: Complete subsidence of the edema of the papillæ. Normal power of sight. Urine, 1003, 2230 c.c. (68.6 fl. oz.). Except for some blood, no sediment; the quantity of albumin has again increased.

Between the twenty-eighth day and about the beginning of the tenth week a gradual extension of cardiac dulness: to the left, a finger's-breadth over the mammillary line; to the right, extending 3 cm. (1.18 in.) beyond

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* Compare Johannessen, *loc. cit.*, p. 185
† *Charité-Annalen*, Bd. VII, S. 152.

the edge of the sternum. The urine during this time varied in its character, containing now more, now less albumin, and was at times free from blood. In quantity it varied from 1100 c.c. (37.1 fl. oz.) to 1800 c.c. (60.8 fl. oz.). The specific gravity averaged 1007.

On the seventy-first day of the disease the urine was absolutely free from albumin, and in quantity 1350 c.c. (45.6 fl. oz.); the specific gravity 1010. The edema had markedly diminished. On the seventy-fourth day there was again a decrease in the urinary excretion (400 c.c.,—13.5 fl. oz.,—specific gravity 1014), much albumin, some blood. Marked edema. Vomiting, uremic attacks with complete blindness, and the same ophthalmoscopic picture as before.

Asthmatic attacks returned on the seventy-fifth day. The amaurosis was, however, less marked, and on the seventy-sixth day entirely disappeared. Now, however, a bilateral hydrothorax.

Until the death, which followed in the fifteenth week, there were no further uremic attacks, only conjunctival and retinal hemorrhages, and general extravasation into the skin. The heart dulness extends still further (5 cm.—3 in.) beyond the right sternal border.

The urine varied in quantity and character as before. Its specific gravity was, however, remarkably high, 1023 in 1000 c.c. (33.81 fl. oz.). In the last days before death only small portions of the urine excreted. Vomiting appeared afresh, as well as diarrhea and dyspepsia.

Autopsy: Both kidneys of normal size, smooth on the surface, very anemic. The cortex relatively narrow, of an opaque yellow color and covered with many yellow, opaque spots, especially over the columns of Bertini. The medullary substance yellowish and very anemic; no hemorrhages noticeable in the parenchyma.

Corresponding to the yellow opaque spots in the cortical substance, peculiar foci were seen under the microscope in which the renal structure was completely destroyed. In its place was a cicatricial tissue, poor in cells, in which one could distinguish broken-down tubules which were for the most part destroyed. The arterial vessels belonging to these foci were in many instances narrowed by proliferation of the endothelium, and in places entirely occluded. Scattered everywhere throughout the cortex, and even in the medulla, were innumerable collections of round cells in tiny foci, partly in the interstitial tissue, partly following the vessels, and especially around the glomeruli. The latter were in many cases compressed and the loops of the vessels eroded. Between the glomeruli and their capsules were red and white corpuscles, as well as purely granular, of a more homogeneous granular substance that became more distended on heating and surrounded the glomeruli in the form of a half-moon. The tubules were in portions markedly dilated and filled with casts. The epithelium of the tubules in the cortex was turbid with albuminous and fatty degeneration; poorly circumscribed and with few visible nuclei.

The heart was considerably enlarged, superficially smooth, and shiny. The cardiac chambers on both sides dilated, and the walls very thin. The muscles were brownish-red, dry, and firm. In many places one saw yellowish-white and smooth indurations, including the trabeculæ; in the other areas, and especially between the trabecular muscles of the right ventricle, there were extensive parietal fibrin exudations, already losing their color (*dilatatio cordis* and *myocarditis fibrosa*).

This case of Litten's is significant in more than one respect.

First, there is afforded through it a proof *that the acute form of scarlatinal nephritis may run into the chronic form.* For here are foci that represent the same processes as those met with in wider distribution in interstitial nephritis.

The objection that the subject may have had contracted kidney, taken scarlatina, and acquired acute nephritis, and, dying from the old trouble, be wrongly considered to have had contracted kidney as a result of scarlatinal nephritis,—this, I say, certainly does not apply here. Moreover, the long interval between the uremic attacks (twenty-sixth and seventy-fourth days of the disease) should be mentioned as unusual; the progressive but intermittent processes in the kidneys account, to my mind, fully for these peculiarities. This explanation, however, is by no means sufficient to account for the marked variation in the character of the urine.

Litten "holds that shortly before and during the uremic attacks, and perhaps even causing the latter, an intense swelling of the diseased portion of the kidney takes place (possibly a hyperemia, an edema, or an increase in the inflammatory exudate), preventing the renal secretion."

If we accept this hypothesis, we will explain the decided diminution in the quantity of urine excreted, and the fact that, at times, no pathologic products are mingled with the secretion (albumin, desquamated epithelium, casts, blood, etc.). It is, at least, to be considered, and may be the right explanation. In any event it is the simplest.

It seems especially remarkable to me that the specific gravity of the urine during the fourth week fell to 1003, although only 280 c.c. (9.5 fl. oz.) were voided. Later, on one occasion—the eighty-fourth day of the disease—it rose to 1023, as against a day's secretion of 120 c.c. (4 fl. oz.). Are not influences exerted here through the brain centers? Edema of the brain was discovered on the first day through the swelling of the papillæ. The changes in the eye-ground may be characterized as rare.

Brain Symptoms Independent of Uremia.—A great number of these have already been mentioned, such as those belonging to the infections, as such, and those which follow otitis, etc.

There are still other symptoms, that are, perhaps, only indirectly dependent upon the scarlatinal poison itself. In considering such we must again have recourse to the frequent mixed infection due to the pus cocci.

Meningitis requires mention, as well as more or less extensive pus foci in the brain, which may be directly due to organisms circulating in the blood, or to infectious emboli from the heart or from the pulmonary veins. Neither the one nor the other is a frequent condition. Reimer * alone has found meningitis in 48 autopsies not less than seventeen times, and one additional case of tubercular meningitis. Henoch, on the contrary, remarks that he is able to say nothing in regard to meningitis from personal experience.

Litten and Fürbringer have seen the condition, and Leichtenstern also, as it appears, in only one case during the great Cologne epidemic.

Of course, the autopsy alone can give definite information as to whether the suppuration has occurred in the membranes or in the brain itself. And I believe Henoch to be altogether correct in saying that the clinical symptoms of meningitis cannot be distinguished from those that characterize the "malignant" form of the disease itself, and, I wish to add, not even from the symptoms of uremia.

THE AIR-PASSAGES AND PLEURA.

Mention has been made of the larynx and the upper air-passages in another place,† and the processes originating from the scarlatinal poison itself and those from secondary affections (sepsis and diphtheria) have already been discussed. Acute edema of **the glottis** alone needs to be emphasized. It can develop as a local affection as the result of the inflammatory swellings in the neighborhood, and also in consequence of dropsy due to nephritis. It is, of course, invariably a serious menace to life.

[**Perichondritis of the Larynx in Scarlet Fever.**—Kraus ‡ states that this complication is one of great rarity, occurring about once in 200 or 250 cases. In a case reported by himself the angina, which was of severe type, appears to have extended downward into the air-passages, aphonia developing on the sixth day of the disease. The diagnosis was made during life and confirmed upon autopsy. Intubation and tracheotomy both became necessary, and the child did well until carried off by further complications (hemorrhagic nephritis, purulent pleurisy).]

The bronchi are unquestionably involved in the process by the cause that produces the disease itself. I have already submitted a sufficient number of examples (see especially Cases 5 and 6).

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* *Loc. cit.*, p. 17. † See page 507.
‡ *Prag. med. Wochenschr.*, 1899, Nos. 29 and 30.

Henoch, among others, particularly emphasizes the following. He writes *:

"The mucous membrane of the bronchi and the parenchyma of the lungs are excited by inflammatory influences far more frequently than we usually suppose. Not only catarrh, but more or less extensive broncho-pneumonia, occurs in the first and second weeks of the disease. These conditions are frequently overlooked, however, because a whole series of synchronous severe typhoid symptoms disguise them and divert the attention of the physician. We found bronchitis and bronchopneumonia in nearly all the severe cases, and also repeatedly during life."

Leichtenstern † remarks that "in children acute lobar pneumonias, sometimes bilateral, and mostly involving the upper lobes, appear as well at the height of the disease as in the nephritis stage. These are pneu-monias such as in the shortest space of time lead to a complete infiltra-tion of a whole upper lobe (more rarely a lower lobe). They are true lobar pneumonias, as the careful examination of a number of cases has taught; neither croupous nor catarrhal, rather a genuine, acute, des-quamative pneumonia. The infiltrated, solid upper lobe resists the knife, is dense, has a smooth, homogeneous, bluish-red surface on section, contains little serum, but is full of blood. The same process may in rare cases appear to be lobular—*i. e.*, limited to one portion (lobule) of the lobe. True catarrhal pneumonia has never been met with in scar-latina."

As is well known, the term "desquamative pneumonia" is severely contested by anatomists, and few hold to the view advanced by Buhl. On the other hand, there may well be a relative agreement in regard to the fact that it is a sudden, confluent pneumonia that springs originally from a single focus. The bronchi need not necessarily be extensively involved, as is proved by the findings at the autopsy in my Observation III, in which death occurred twenty-eight hours after the beginning of the disease. It is easily conceivable that now and then the infecting substance makes its way in through the blood stream, but remains, in any event, limited to a small circumference.

In the later course of scarlatina foci may originate in **the lungs** from many different sources. Among such conditions may be mentioned the "deglutition pneumonia" in gangrenous processes in the nasal and pharyngeal cavities; the infarcts that result sometimes from the infectious or non-infectious emboli from the veins of the body, though originating more frequently in the right heart; and the many small abscesses that occur in sepsis. Leichtenstern properly calls further attention to the fact that during the nephritis "acute edematous infiltrations, leading to a complete absence of air, and serous lobar pneumonias" (inflammatory edemas) may occur, accompanied by extreme succulence of the infiltrated lobe,—frequently the upper,— and which exhibit a free epithelial desquamation and must be dis-

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* "Vorlesungen über Kinderkrankheiten," S. 642, 3d ed.
† *Loc. cit.*, p. 268.

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tinguished from the desquamative type of pneumonia by the serous exudate. These very pneumonias often present during life acute lobar consolidations, which disappear as quickly as they arise. *True croupous pneumonia*, according to unanimous opinion, is much more rare in scarlatina not accompanied by nephritis than when complicated with the renal condition. Even here it does not occur often. At any time during the entire period of the nephritis pneumonia may make its appearance. Both conditions may occur side by side and simultaneously, and in such cases the question remains open as to whether the renal affection has not been present for a longer time than the symptoms indicated.

I will briefly relate an observation of my own in just such a case*: Mild scarlatina, the temperature only once attaining 40° C. (104.0° F.). Slight pharyngeal involvement. No albumin in the urine. After six days, convalescence. After about three weeks, slight indisposition, but no rise of temperature, and no albuminuria. Then, twenty-eight days after the beginning of the disease, violent vomiting, marked apathy, bloating of the face, the quantity of urine much decreased, with a decided quantity of albumin, the temperature suddenly rising to 41.2° C. (106.1° F.). Consolidation is already evident in the right lower lobe, coming to a full development on the immediately succeeding days. On the fourth day of the disease it spreads to the upper lobe of the same side. Resolution begins from below, and on the seventh day of the disease is distinct also in the upper lobe. On the sixteenth day all lung symptoms disappeared. The nephritis continued only fourteen days. The disease, all in all, was quite severe, this being especially true because of the brain symptoms. Mild uremic symptoms, together with the fever, which remained for eight days, may have caused the latter.

The following observation possesses interest in that, in spite of the pneumonia and its long persistence, accompanied by marked diminution of the urinary secretion, no disturbances of any gravity appeared.

Observation XXII.—A little girl of three years. Unusually mild scarlatina without a special pharyngeal involvement. Maximum of temperature 39° C. (102.2° F.). Sixteen days after the appearance of the eruption the first signs of nephritis. Burning on passage of the urine, decreased quantity of albumin present, though in slight quantities. Besides moderate rises of temperature there were no pathologic symptoms present in the interval. On the twentieth day of the disease a marked decrease in the urinary excretion with rapidly increasing temperature; at 8 A. M., 37.7° C. (99.8° F.); in the afternoon at four o'clock it was 40.9° C. (105.6° F.). The pulse-rate was very high; the respiratory rate far less marked, though difficult and accompanied by pain in the

*Alexander Kees, "Ueber croupöse Pneumonie neben acuter Nephritis," in Jürgensen, "Croupöse Pneumonie," Beobactungen aus der Tübinger Poliklinik, Tübingen, H. Klapp, 1883, S. 192.

lower portion of the chest. On the next day pneumonia, together with all its physical symptoms, became evident in the left lower lobe, and subsequently extended itself still further.

From the same day (twenty-first since the appearance of the eruption) until the twenty-seventh—seven days—no urine was voided; at least, this is stated by the family, who were extremely intelligent, and took special notice of the fecal discharges with a view to this point. We can rest assured that no considerable amount of urine had been voided. Yet there was no edema, and never was there swelling present in the face. It may be doubted whether we should look upon the vomiting, which occurred twice (on the twenty-second and twenty-fifth days of the disease), as uremic. Possibly the free and watery bowel movements that were present from the twenty-first to the twenty-sixth days accounted for the greatest part of the water excretion. In the course of the eighth day from the beginning of the pneumonia and the nephritis (twenty-seventh day of disease) the temperature fell by crisis to normal; in the next eight days the renal and pulmonary affection disappeared entirely, so that the child at the end of the fifth week could be dismissed entirely well.

In spite of the very light attack, as figure 81 shows, and after the retirement of the scarlatina itself, the system was by no means in proper order. This was indicated by the irregular temperature, with slight rises. The renal inflammation caused no fever on the day of its appearance; fever appeared immediately after, however, though, to be sure, only in slight degree. Then came the pneumonia, beginning, according

FIG. 81.—1, First day of the disease; scarlatinal eruption and pain in the throat. 2, Lessened secretion of urine. Albuminuria. 3, Beginning of the pneumonia. 4, Continuous temperature of 38.0° C. (100.4° F.).
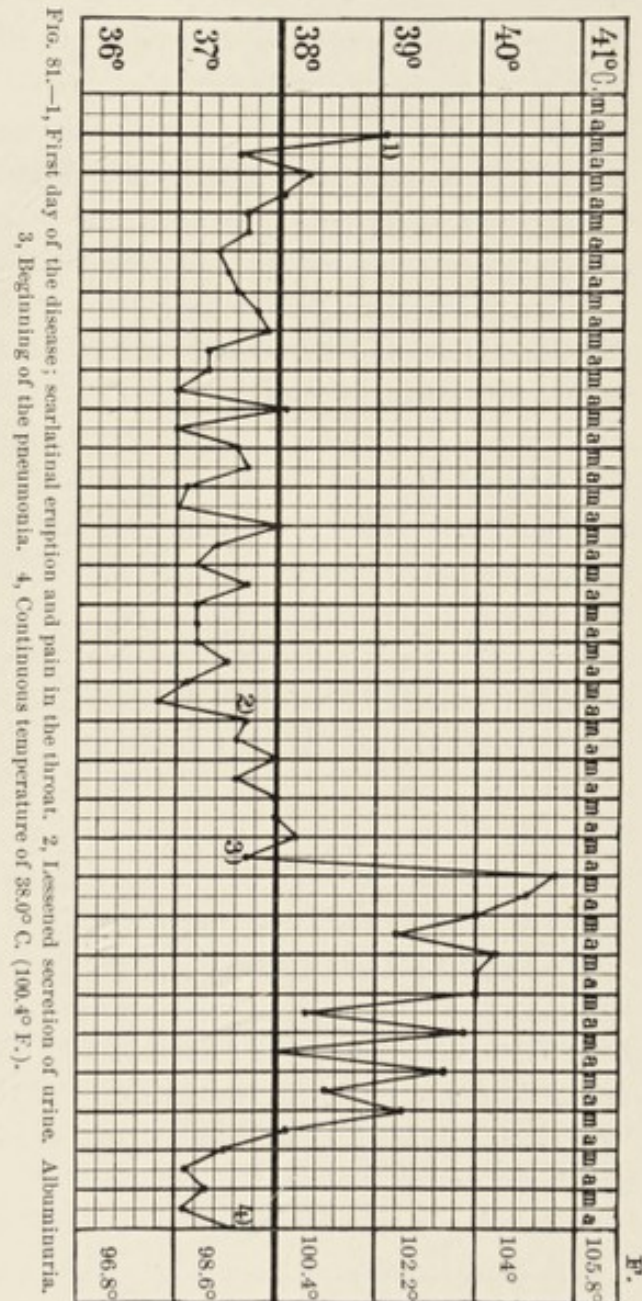
to rule, with sudden and high temperature, and later falling somewhat more slowly. The latter characteristic showed less plainly on a chart registering only the evening and morning temperatures. If we take the average of the second hourly readings, they give during the six days of illness a variation only between 39.9° and 39.4° C. (103.8° and 102.9° F.).

The prompt healing of the local affection is a noteworthy feature. It is clear without further remark that hypostasis may occur in the lungs. *Gangrene of the lungs* may also occur. It may be that in the severe infections, and especially when nephritis is present, pulmonary edema will comparatively often be noted, although it cannot be considered a true pulmonary complication.

Abundant opportunity is given by the severe tissue changes in the lungs for an involvement of **the pleura**. This pleuritis deports itself directly in relation to the extension and nature of the foci in the lungs. It may be a dry pleurisy, or an exudate may be present, the latter being serofibrinous, purulent, or gangrenous. The conditions are exactly those of the pleural disease that usually accompanies inflammations of the lungs. It differs, however, from the pleurisies that are independent of the lung. It appears to me by no means easy to gain a clear understanding in the matter, since the statements of those who have studied the subject show marked discrepancies. And since I myself have not a very extensive experience with such conditions, I must confine myself to the reports of actual cases. In the minority of cases a pleuritic exudate occurs early,—somewhere about the middle of the second week of illness,—and the largest number occur at the time of the nephritis and the accompanying dropsy.

In regard to this there is general unanimity of opinion. We may sometimes in this connection speak, with Leichtenstern, of inflammatory edema, though the dividing-line between exudate and transudate cannot be sharply drawn. The patient who suffers from "scarlatinal rheumatism" is especially exposed to pleural involvement (Henoch).

Fürbringer characterizes the typical exudative pleuritis as a frequent complication (about 5%), which, according to his experience, even when it appears at the height of the exanthem, colors the whole picture of the disease.

Thomas claims that all forms of pleuritis have the peculiarity of a very rapid development, and often cause only moderately severe local disturbances in spite of there being an extensive process. Fürbringer is of the same mind.

All agree that the exudate involves, as a rule, only one-half of the pleural cavity. The majority of observers assert that these pleural exudates are for the most part, and Henoch says "almost always," purulent. Streptococci have been found in them (O. Vierordt). Litten is more reserved in his opinion, and mentions the frequency of serous exudates in scarlatinal nephritides without complications. Litten also calls attention to another possibility: "There are cases of scarlatina in which during the convalescence dyspnea suddenly appears, and without warning. In such cases, then, without any other complication being present, and especially in the absence of joint affections, there may develop in a few days a serous pleuritis with a marked exudate. The prognosis in such cases is always bad. Analogous observations have already been made by Andral."

We see how much there is still to be learned in regard to pleurisy in scarlatina.

In Norway, at least, pleuritis is of slight importance as a fatal influence. Johannessen finds among 688 deaths, only three as the result of pleurisy. It can hardly be supposed that this is everywhere true, though I have not been able to find any statistics in regard to the point.

THE DIGESTIVE ORGANS.

Even the digestive tract is not always exempt from the influence of the scarlatinal poison, although its involvement is not especially severe, nor does it appear as a prominent factor in the disease.

The autopsies in my cases that have been rapidly fatal within twenty-six to fifty-nine hours have shown an intensely red and somewhat excoriated esophagus (Case 3); swelling repeatedly occurred (Cases 3 and 5) with profuse mucus-formation upon the membrane; the intestine frequently presented a more or less marked swelling of the follicular glands, and its mucous membrane was swollen and ecchymosed. Anemia of the mucous membranes was noted in all the cases, even when no other signs of the disease were present.

The thorough study made by Crooke * is well worthy of attention, since he was able to examine **the stomach** immediately after death. He reports a case that lasted only twenty-six hours:

"The stomach showed marked changes. Its entire mucous membrane was much swollen, its surface covered with mucus, and hyperplastic, especially in the region of the pylorus, where the "etat mamelonné" reached a high degree. With the exception of a few hyperemic spots, the gastric mucous membrane was pale and opaque. The microscopic examination showed these changes to be due to an extraordinary hyperemia of the

* "Zur pathologischen Anatomie des Scharlachs," *Fortschritte der Medicin*, Bd. III, S. 653 (1885).

lymphatic tissues in the gastric mucous membrane of children and young people. Some of the hyperplasias were so large that they reached the surface of the mucous membrane and pressed the glands upward and to one side. Many were necrotic in the center and so friable that on section they would easily fall to pieces. From these foci the lymphatic infiltration spread to the interglandular tissues and produced the picture of an interstitial gastritis spreading by foci throughout the entire membrane. The blood-vessels of the interglandular connective tissue are distended, and often there is a proliferation of the nuclei in their walls. The cylindric epithelium of the excreting glands is entirely desquamated and the upper glandular layer is more or less thoroughly infiltrated with round cells. The blind extremities of the glands are dilated and filled with a quantity of swollen, round or polyhedral (vesicular) cells; the latter are devoid of nuclei and are undergoing coagulation-necrosis. The muscularis mucosæ is thickened, infiltrated with small round cells, and shows an increase in the number of nuclei."

In two other severe cases similar changes were less markedly present.

These processes occur, without doubt, as the result of the scarlatinal toxin itself.

I have no knowledge of the existence of more thorough studies of the intestinal mucous membrane.

In the further course of scarlatina changes are also found in the digestive organs that must be looked upon as simply secondary. Thus, Henoch reports cases in which the necrotic process has involved the esophagus, and even the gastric mucous membrane. Likewise, Litten has found diphtheritic ulcers in the stomach. He saw in this case of only five days' duration a wide-spread diphtheritic "process" on the soft palate, in the pharynx, the esophagus, with extension into the stomach, also in the bronchi and lungs; finally, even in the large intestine. When this process takes place in a true case of diphtheria, the extension is most remarkable. Fürbringer properly calls attention to the fact that gastric and intestinal affections may occur as localizations of a septic infection. "Occasionally one is astonished at the autopsy by a dysenteric condition of the large bowel." I want to emphasize the fact that the by no means harmless collections in the nose, the mouth, and pharynx, often enough are swallowed, and that it is truly wonderful that serious tissue changes do not occur as a result much oftener than is actually the case. Besides the diphtheritis of the large intestine, ulceration of the Peyer's patches and of the solitary follicles has been reported, presenting a somewhat similar appearance to the usual picture of typhoid fever.[*]

With regard to the *clinical symptoms*, vomiting is in the beginning

[*] *Vid.* Thomas in v. Ziemssen's "Handbuch," S. 242.

of the disease, as well as later on, to be looked upon only in rare cases as a symptom certainly dependent upon the stomach itself, and caused by the disturbance taking place within it. The phenomena that accompany the invasion of scarlatina, the sudden rise of temperature and the genuine intoxication, cannot be separated. A little later the cough appears, and is due to manifold causes; on account of the abnormal condition of the pharyngeal organs it may produce nausea.

Secondary affections accompanied by sudden rises of temperature may also assert themselves, and, finally, and most important of all, is the fact that vomiting may accompany nephritis, and is almost always present in uremia.

I agree with Litten thoroughly in looking upon the vomiting, as such, as of no great importance; in other words, it will seldom become so severe as to be of itself dangerous.

The **affections of the intestine** assert themselves especially in the very beginning, following the invasion, in the form of a more or less active diarrhea, that is sometimes very severe. In the case cited by me in detail (Observation III) the diarrhea was the very first sign and recurred during the twenty-eight-hour illness so often that the number of stools could no longer be accurately given. Also in two other cases diarrhea appeared, once early and once somewhat later. We often have this symptom in the severest forms of the disease.

Litten * considers the intestinal condition more in detail than other writers. He differentiates three clinical forms:

1. *Simple catarrhal enteritis,* usually with a rapid and favorable course. It may appear at any time during the course of scarlatina, and is absolutely independent of any discoverable pathologic influence. (I wish in this connection to remark that in cases of uremia which have previously shown no disturbance of the intestines a simple diarrhea may occur, even at the beginning of the nephritis. See Observation XXII.)

Litten proceeds: The diarrheas, which are sometimes very obstinate, may lengthen out the disease and hasten the prostration of the case. In two autopsies were seen, once a marked edema of the intestinal mucous membrane, in the second case merely a catarrh of the large intestine with slight ulceration of the follicles.

2. The clinical picture of *dysentery* with tenesmus, and with pus and blood in the stools. Anatomically: diphtheritis with ulceration,

* *Charité-Annalen*, Bd. vii, S. 128.

most frequently of the large intestine, extending into the rectum and into the small bowel.

3. The clinical picture of *typhoid fever* (*scarlatinal typhoid*). Litten's description agrees in its main features with that of Thomas.[*] He calls attention especially to the fact that the abdomen may show marked meteorismus, and that there may be severe and critical hemorrhages from the intestine. The stools were, in his experience, altogether liquid, free from blood and pus, and of a pale color—a bright yellow dotted with white spots and specks. The pulse, in contrast with typhoid fever, was extremely rapid and of high tension.

Litten characterizes this form as one of the severest of scarlatinas. When the patient survives, the convalescence is very protracted. Anatomically we have swelling of Peyer's patches and of the solitary follicles, with follicular erosion of the intestinal mucous membrane, pulpy enlargement of the mesenteric glands, splenic tumor, and a swelling of the splenic follicles. We may preserve this classification for the sake of order, though one should always remember that it merely carries the essential phenomena toward their termination, while in regard to the causes of the condition nothing is or can be said.

With regard to the lymphatic system as represented in the intestines and in the abdominal cavity, as well as in the spleen, discussion has already been had in another place.[†]

Mention must still be made of **the liver,** and of certain anatomic processes that take place in this organ. Litten makes the statement that cloudy swelling is hardly ever lacking in the liver at the autopsy of a scarlatina case. In the course of severe cases this is succeeded by parenchymatous degeneration, which may lead on to destruction of the liver substance and to acute yellow atrophy. He himself describes two cases representing this that are incontestable. Other examples may also be found here and there in literature.

Liebermeister[‡] reports a process seen in the liver of a twenty-six-year-old woman, at the autopsy, which he designates as the early stage of parenchymatous degeneration. Litten coincides essentially with his opinion, although he believes that it was only a cloudy swelling with beginning parenchymatous degeneration. Unquestionably, had the patient lived longer, yellow atrophy would have followed.

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[*] See p. 482.

[†] See pp. 452–520, and the autopsy reports of the severe cases.

[‡] "Beiträge zur pathologischen Anatomie und Klinik der Leberkrankheiten," Tübingen, Laupp, 1864, S. 330.

It was a case of a twenty-six-year-old woman who had been actively in charge of a scarlatinal case. On the fourth day of her own marked case of scarlatina she was admitted with a temperature of 41.9° C. (107.4° F.) and a pulse of 160 into the regular clinic, and died there on the same evening.

The autopsy showed, fourteen hours postmortem: Extensive ecchymoses of the skin, small foci of pus in the markedly swollen tonsils. The heart slightly involved in fatty degeneration. The spleen somewhat enlarged. The epithelium of the convoluted tubules opaque, but not to any marked degree. The urine in the bladder contained some traces of albumin. "The liver weighed 1520 gm. (48.87 oz.) (about normal), was of normal appearance, rather soft in consistency, showed no lobulations on section, was a reddish-yellow color, very anemic, and very friable. The liver cells were almost filled with the finest of granules, and a few of them with medium-sized fat droplets. Many cells contained also granular bile pigment. The scattered cells that contained less fat were decidedly opaque. The size of the cells was, on the average from 42 measurements, 25.0 μ. As a rule, they appeared to contain in the center of the lobules just as much fat as at the periphery. The bile pigment was most marked at the center." The gall-bladder was full of dark-green, thin bile. The intestinal contents were slightly bile-stained. In the stomach was some altered blood.

E. Wagner was the first to observe the new growth of lymphatic tissue in the scarlatinal liver. He presents as evidence a case that terminated in death in forty-eight hours. In a second, diphtheritis was present also; the duration of the illness was twenty-four days. Cases of so-called "puerperal scarlatina" he excludes entirely, because the diagnosis appears to him to be doubtful; certainly this is a praiseworthy reserve. I wish to present also my own Observation III at this time, as a case in which the short duration (twenty-eight hours) and the subsequent autopsy findings made a double infection improbable. In Observation VII, in spite of sequence of death after three days, sepsis unquestionably was present.

Crooke's cases, since they all are of more than seven days' duration, cannot be utilized; also because no further statements are made in regard to their clinical features. He says*: "In genuine cases the lymphatic proliferation does not appear to such a degree as in the complicated cases," and one must therefore assume that he has actually seen pure cases. In Wagner's description it has already been mentioned that microscopic collections of cells occur in the connective tissue in addition to the macroscopic granules. Special emphasis is laid by some writers upon this fact, and the term "acute interstitial hepatitis" has been discussed. After all, we must conclude that the picture presents nothing typical of scarlatina. We see identical ap-

* *Loc. cit.,* p. 654.

pearances in many infectious diseases that run a severe course. They form, moreover, almost the only means of expression of an especially severe toxic influence upon the liver.

The picture of acute yellow atrophy departs in no particular from the ordinary. The lymphatic and interstitial processes are not recognizable during the life of the patient.

The **peritoneum** is only rarely involved in simple scarlatina; much more often in scarlatinal nephritis. One should remember, in connection with paracentesis for ascites, the danger of converting a serous effusion into a purulent one.

THE BLOOD; THE HEMORRHAGIC DIATHESIS.

Accurate photometric estimations by means of the spectroscope have been carried out only in rare instances.

[Ewing, of New York, summarizes the present knowledge of the blood in scarlet fever as follows:

"Hayem gave the first systematic account of the blood changes in scarlatina, finding a loss of about one million red cells after defervescence, and a moderate leucocytosis in average cases, much increased by severe angina or by suppurative processes. Somewhat isolated observations were reported by many of the earlier blood analysts,—Halla, Pee, Pick, Reinert, Sadler,—while extensive series of cases were studied by Rieder and Kotschetkoff.

"The whole blood suffers in a slight degree the usual effects of fever. The formation of fibrin is usually increased, especially when there is extensive angina or suppurative complications (Hayem). Heubner noted hemoglobinemia in one case representing the septicemic type of the disease.

"**Red Cells.**—The gradual loss of red cells noted by Hayem was fully verified by Kotschetkoff, who found a reduction to three millions or less in nearly all cases. The regeneration of the blood was slow, and was complete only after six weeks or longer. On the other hand, Zappert found less than four million cells in only one of six cases; and very slight anemia was noted in a considerable number of cases examined at varying periods by Leichtenstern, Arnheim, Pee, Pick, Reinert, Sadler, and Felsenthal.

"**Leucocytes.**—Kotschetkoff classified the leucocytoses in three groups: the mild cases, showing between 10,000 and 20,000 white cells; the moderately severe cases, with 20,000 to 30,000 cells; and the very severe and usually fatal cases, with a leucocytosis of 30,000 to 40,000 cells; while in some rapidly fatal cases over 40,000 leucocytes

were found. Yet Rieder's ten observations never gave more than 23,000 cells, and usually less than 20,000, although some of his cases were complicated with pneumonia and croupous pharyngitis, and were fatal. Felsenthal's six cases were in children and of moderate severity, and showed 18,000 to 30,000 cells.

"The leucocytosis begins one or two days before the appearance of the rash, reaches its height with or shortly after the full development of the eruption, and while in some cases rapidly falling with the eruption, usually continues for four or five days longer, and very often persists for days or weeks after the temperature has become normal.

"The grade of leucocytosis seems in general to correspond to the severity of the disease, especially of the angina, but not to the height of the temperature. Complications, such as lymphadenitis, otitis, and nephritis, usually have little effect on the leucocytosis (Kotschetkoff); but Pee observed two cases in which the leucocytosis increased when the lymph-nodes began to swell late in the disease. Pneumonia caused but slight increase in some of Rieder's cases.

"**Types of Leucocytes.**—The percentage of polynuclear cells is in all cases much increased, varying from 85% to 98% according to the intensity of the disease, reaching the highest point on the second day of the exanthem, and thereafter slowly declining. In fatal cases the proportion of polynuclear cells falls but slightly, or soon regains or passes into the original figure.

"The eosinophile cells may show characteristic variations. In all but very severe cases they are normal or subnormal at first, steadily increase after two or three days, reaching a maximum of 8% to 15% in the second or third week, and, thereafter declining slowly, reach the normal figure about the sixth week. In fatal cases the eosins may disappear early in the disease.

"The lymphocytes are at first diminished, but later rise to normal proportions.

"The above rules, deduced by Kotschetkoff, while probably representing the average case, are not always applicable. Thus, Weiss found no eosins in one case at the height of the exanthem. Rille observed marked eosinophilia in a fatal case; Bensaude observed as high as 20% of eosins in one instance; Klein reports lymphocytosis during convalescence; and many writers (Rieder and Turk) have described a high, persistent leucocytosis, especially in those cases followed by nephritis or other complications. Turk has called attention to the remarkable change which the leucocytes undergo about the fifth day of the disease, when the polynuclear cells rapidly diminish

and the eosins and lymphocytes rapidly increase. Ths secondary leucocytosis he likens to the somewhat similar phenomenon seen in variola.

"**Bacteriology.**—Raskin found Streptococcus pyogenes in the circulating blood in 2 of 64 cases, while all other culture was sterile. Negative results were obtained in 2 cases by Sittmann and in 4 cases by Kraus."]

Leichtenstern * found in a moderately severe case of scarlatina in a strong seventeen-year-old boy, with high temperature at the start, returning to normal on the seventh day, neither during the course of the disease nor in the convalescence a diminution in the hemoglobin present. Three estimations were made in the first and two in the second.

Reinert† saw a case, also a fairly severe one, of a weakly boy of eleven years, with moderate temperature (not over 39.5° C.—103.1° F.—), in whom there was on the third day a diminution of the hemoglobin. The red corpuscles were also somewhat diminished in number, though only to a slight degree; the leucocytes were somewhat increased. The relative proportion was 1 : 410, as against 1 : 500 or 1 : 800 as the normal. Single estimations, such as these, however, are of little value.

Widowitz‡ instituted a series of examinations in 14 cases, in some of them commencing with the first day of the disease. The hemoglobin was in the beginning, with only one exception, strikingly high in quantity, falling then gradually until the beginning of convalescence, when it again rose. It never, however, regained its previous height. So much for pure cases!

When nephritis appeared as a complicating condition, the hemoglobin diminished gradually with its appearance, or suddenly and decidedly in the event of an exacerbation; at other times less so. Thus, for example, in the severe Case No. 7 (Widowitz), when nephritis appeared (eighteenth day of the disease) the hemoglobin, estimated according to Fleischl, fell from 85% to 79%, on the same day to 74%, and on the following day to 69%. In the exacerbation (thirty-seventh day of the disease) it fell from 46% to 39%.

I do not wish to lay too much stress upon these figures, although the technique may have been faultless—and we have no reason to doubt this fact; still, the distribution of the blood within the body, and the relation between the floating, formed constituents and the plasma, may have be-

* "Untersuchungen über den Hämoglobingehalt des Blutes in gesunden und kranken Zuständen," Leipzig, F. C. W. Vogel, 1878, S. 77 und Tabelle 17.

† "Die Zählung der Blutkörperchen und deren Bedeutung für Diagnose und Therapie," Leipzig, F. C. W. Vogel, 1891, S. 180.

‡ "Hämoglobingehalt des Blutes gesunder und kranker Kinder," "Jahrbuch für Kinderheilkunde," N. F., Bd. xxvii, S. 384; see also my comments on the method, page 509 of this volume.

come altered. There is, moreover, to be considered the temporarily increased concentration in case transudations suddenly take place, or marked diarrheas occur. In the withdrawal of the blood we obtain something one day that is different from that of the next, without there being present necessarily either an increase or a diminution in the actual quantity of the red blood-corpuscles. This was the state of affairs in Case No. 6 of Widowitz. On the twenty-sixth day of his illness a patient of his, suffering from nephritis, showed directly after a uremic attack the following count:

RED BLOOD-CORPUSCLES.

At 3 P. M. 3,550,000	hemoglobin 69% (Fleischl)
At 5 P. M. 2,475,000	" 54% "

Marked edema was already present at the 3 P. M. examination, and the distribution of the blood-corpuscles must also have been altered. But that in the course of two hours such a high degree of change under existing conditions could not have taken place, needs no further discussion. Moreover, the lack of proportion between the number of red blood-corpuscles and the hemoglobin is to me a striking one. In the same case:

	ERYTHROCYTES.	HEMOGLOBIN.
On the first day of illness.	4,437,000	78%
" tenth day of illness.	4,325,000	60%
" eighteenth day of illness.	3,950,000	70%

The conclusion that one would have to draw from the foregoing would be that a sudden change had occurred in the character of the red corpuscles—a new formation and degeneration. The foundation for this theory, however, is hardly a certain one. Whether we will make further progress with more exact methods remains to be seen. It would appear merely that the blood examination has none too great a value.

With the exception of cases caused by sepsis and gangrene intoxications, hemorrhagic scarlatina, in the narrow meaning of the term,* as well as the hemorrhagic diathesis, is quite rare. Barthez and Rilliet† have never seen a case in their hospital work. One of them has alone observed such a case, and in the recent past. An eight-year-old girl began her attack of scarlatina with nosebleed, followed by the appearance of petechiæ. In the course of five weeks there were repeated severe hemorrhages from the nose and occasionally also hematuria,—the origin not being stated,—and the child died with the symptoms of the severest anemia. Rilliet adds that he frequently observed during the epidemic that occurred in Genf in 1853 severe nasal hemorrhages.

Henoch ‡ has seen, altogether, only seven cases of hemorrhagic diathesis. All ran a favorable course, although in one case continuous epistaxis and hemorrhage from the mouth and the external ear were present. In addition, there were many ecchymoses on the skin and

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* See page 459. † *Loc. cit.*, p. 196. ‡ "Vorlesungen," S. 659.

an extravasation into the right upper eyelid. Nephritis also appeared.

It is an interesting fact that Leichtenstern, in his brief description of the severe and extensive (he himself saw over a thousand cases) Cologne epidemic, makes no mention of the hemorrhagic diathesis. Litten also fails to mention it.

THE EYES.

The rule that special attention should be paid to the eyes in severe cases, in order to prevent foreign bodies that remain upon the cornea from causing inflammation, holds still more rigidly in scarlatina than in measles.

Eversbusch * mentions among the affections of the eyes the following:

The skin eruption, when occurring upon the eyelids, can cause excoriations that can go on to catarrh and swelling during the stage of desquamation, and involve the cornea, constituting the so-called "corneal ulcer."

Inflammation of the lacrimal glands and of the lacrimal sac.

Hyperemia and catarrh of the conjunctiva, and croupous and diphtheritic inflammation of the same.

Panophthalmitis.

Failure of accommodation.

Uremic amblyopia and amaurosis.

Neuroretinitis nephritica.

Septic processes in the retina.

Optic neuritis, if meningitis is present.

Hemorrhage into the retina.

Serous infiltration and phlegmon of the orbit.

Paralysis and contractures of the eye muscles.

This list comprises all the processes that may accompany not only scarlatina and follow it, but also those attending and following the secondary infections. The latter subject, so important to the physician, has already been discussed (see p. 514), as have also the affections of the ear, and their far-reaching sequels.

[**Relapses in Scarlet Fever.**—Kennan † concludes, after a review of literature, old and recent, that the alleged relapses of scarlet fever

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* "Behandlung der bei Infectionskrankheiten vorkommenden Erkrankungen des Sehorgans," "Handbuch der speciellen Therapie innerer Krankheiten," Pentzoldt u. Stintzing, Jena, G. Fischer, 1894, Bd. i, S. 605.

† *Dublin Jour. of Med. Science*, 1898, No. 324.

which follow closely upon the primary attack have been noted only of late years. He thinks that this is to be explained by the grouping of scarlet fever patients in separate pavilions, which makes it possible for reinfection to occur after mild cases (in other words, these so-called relapses represent a reinfection from without).

Etiology of " Return Cases " of Scarlatina.—Millard [*] records the fact that 158 out of 4810 patients discharged from the hospital after recovery from scarlet fever were apparently the carriers of infection to 173 new cases. He believes that the discharged patients retained virulent germs in the skin, nasal mucus, otorrheal discharges, etc., despite all attempts to protect the outside world. The interval which elapsed between the discharge of old cases and admission of new ones averaged about eight weeks.

Latency of the Scarlatinous Virus in the Secondarily Enlarged Lymph-nodes.—Stembo [†] recalls the teaching of Leichtenstern, that upon the appearance of scarlatinous nephritis the spleen and lymph-nodes frequently become enlarged. This fact is largely ignored, and Stembo states that this secondary adenitis may readily suggest the presence of Pfeiffer's glandular fever, in cases in which albuminuria has not yet supervened. In cases of benign scarlatina with rapid convalescence it is by no means uncommon, especially in epidemics, to observe an apparent recrudescence of the cervical and submaxillary adenitis, accompanied by high temperature, and followed within a day or two by the worst type of scarlatinous nephritis.

Secondary Rashes in Scarlet Fever.—Griffith [‡] states that this manifestation stands in no necessary relation with " secondary sore throat," which is generally acute quinsy. But during the evolution of a secondary rash the throat may be sore because it is involved in the eruption. He leaves the question open as to whether a secondary rash represents a true relapse (from autoinfection) or a reinfection from an outside source. This question assumes vast importance in a large fever hospital. A patient who contracts a mild type of the disease outside of the hospital might after admission and during convalescence fall a victim to much more virulent germs derived from some of the other patients.]

SEQUELS.

It is easy to understand that more or less serious disturbances may well follow a disease that involves the entire system, as does a severe

* *Brit. Med. Jour.*, Sept. 3, 1898. † *Deutsch. med. Wochenschrift*, May 31, 1900.
‡ *Quar. Med. Journ.*, Oct., 1895.

case of scarlatina; and especially if we recollect the relatively great frequency of sepsis in the course of the disease. This shows itself, first of all, in the general nutrition; a long-continued poverty of blood, a great susceptibility to other pathologic influences, and a slow development of the children themselves, follow the disease by no means seldom.

It is also worth recording that scarlatina may awake into activity a **tuberculosis,** a focus of which has already been present in the body. Such a process may be compared, in a measure, to the far milder ones that involve the mucous membranes in measles, and thus form the ground for infection from the lymph glands which contain the bacilli. On the other hand, death may bring, at times, such a speedy end that tuberculosis has no opportunity to develop.

Barthez and Rilliet * hold a unique position in regard to this question. I cannot quote them at length, but will submit the main points of their conclusions, as follows:

1. Scarlatina, in rare instances, favors a development of tuberculosis.

2. Tubercular children rarely take scarlatina, which then runs an anomalous course.

3. Children with a tuberculosis that has been cured may contract scarlatina, and the latter disease may in such cases follow a normal course.

4. Tubercular children who contract scarlatina are found to have only a few crude tubercles, which are very rarely caseous.

5. In such cases the tubercles tend to calcify within a short time.

"We draw from these facts the conclusion that *the tubercular diathesis and scarlatina are antagonistic.*"

These statements are worthy of remark, and perhaps deserve consideration. They have met with contradiction, as in the case of Mayr,† who could not verify their accuracy. Moreover, Leichtenstern has seen in two cases during the convalescence an acute miliary tuberculosis already present. We have noted the same occurrence in the Tübingen Policlinic.

The assertions of Barthez and Rilliet in regard to the influence exerted by scarlatina over the acute infections are of slight significance. The number is far too small to warrant such far-reaching conclusions as the following: Scarlatina can render more serious the diseases that usually complicate its course; and, on the other hand, render more favorable the course of those that are not usually seen in combination with it.

* *Loc. cit.,* p. 201. † Hebra's "Handbuch," p. 141.

Among the **genuine sequels** I wish to classify such as are caused by the persistence in the body of the causes of sepsis after an attack of scarlatina, providing the patient has taken this opportunity to contract a septic infection. That such influences may remain, and that the occurrence is by no means rare, is already a certainty. It will be sufficient to recall the main facts.

An apparently healed furuncle shows over its cicatrix, sometimes months after, a slight redness. If the part is protected from pressure, this disappears in the course of time, and healing finally becomes complete. As long as the redness persists, even active rubbing—*e. g.*, in drying the skin after washing—suffices at once to cause the appearance of a new furuncle in the same position. From such a focus, through local inoculation, a long-continuing furunculosis can take its start.

Among the sequels must also be considered the development of *valvular lesions from endocarditis,* especially of the cardiac wall, arising during scarlatina (see page 565). Finally, also, the rare cases in which nephritis passes into a chronic type. In contrast with this group stands that in which a complicating condition continues for a longer or shorter time during the course of scarlatina. To the latter belong many different processes; certainly *the disturbances caused by otitis,* which, if bilateral and of such severity as to cause loss of hearing, can result in *deaf-mutism.* From the same cause there has been noted, at times, a *peripheral paralysis of the face.*

If the brain and its membranes have been affected, frequently traces are left behind, if, indeed, the patient actually survives. Fürbringer[*] attributes " a special clinical significance to a peculiar, hemorrhagic encephalitis, which perhaps always requires the presence of an accompanying nephritis." Henoch agrees with this view. Fürbringer says, further: " We saw, as a result of it, a child in the sixth week of the disease become hemiplegic and die within a few days. Likewise, we cannot help but make this process, and the porencephalitis left behind it, responsible for a case, lately reported by us, of the most peculiar athetochoreic movements of a paralyzed arm, lasting over ten years. Also Wildermuth, who has lately directed attention to chronic epileptic conditions as sequels of scarlatina, relates similar cases."

I must also mention the fact that experience differs as to a chorea which is not dependent upon distinct anatomic causes. Henoch[†] has seen it in two instances, together with joint involvements in the acme

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[*] *Loc. cit.,* p. 478. [†] "Vorlesungen," S. 659.

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of a scarlatina; never as a sequel. Gubler and Bouchut, however, call it, as he says, a frequent sequel. Gerhardt * considers the connection between endocarditis and joint diseases an intimate one, but says, in a general way, that chorea may sometimes occur as a sequel. Litten does not admit that there is an involvement of the endocardium, and states that at least it is not present in all instances. There are many items of individual observation that might be discussed without the gain of any special advantage. Only the acute psychosis which occasionally appears during convalescence needs to be considered.

According to Kraepelin,† "the pathologic picture is a uniform one in its general aspects. Almost always, in the desquamation period, and as a rule between the ninth and eleventh days of the disease, there develops more or less suddenly an anxious, confused delirium, with marked excitement, and varying melancholia, more rarely exalted, illusions and hallucinations of one or of all the senses, most frequently that of sight. The anxiety increases so as to cause blind attempts at flight; usually amnesia is present."

Kraepelin considers the exhaustion caused by the foregoing disease as the influence coming most prominently into consideration. But the individual predisposition has a marked share also, and has been evident in 38% of all the reported cases. The earlier years of life are preeminent, and three-fourths of all cases were of the male sex, and only one-fourth of the female. The affection can run its course within a few hours; about 75% of the cases run their course within a week; and in the remainder the time varies up to a month. Usually the predisposed are involved. The prognosis is unqualifiedly favorable. Apart from the changes in the larynx, caused by ulceration, which can produce serious damage through the formation of cicatricial tissue in healing, I wish to call attention to a few observations of Leichtenstern in regard to the possible sequels.‡

He has seen, in one case, far on in the convalescence, chronic edema of the glottis, with pale, transparent, edematous swelling of one aryepiglottidean fold, almost the size of a chestnut, which almost completely closed the entrance of the larynx from above. Threatened suffocation had to be prevented by incisions.

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* "Lehrbuch der Kinderkrankheiten," S. 76.

† "Ueber den Einfluss acuter Krankheiten auf die Entstehnug von Geisteskrankheiten," *Archiv für Psychiatrie und Nervenkrankheiten*, Bd. xii, S. 84. Compare also Thomas in v. Ziemssen's "Handbuch," S. 273, 274.

‡ *Loc. cit.*, p. 175.

"Loss of the voice developing in the stage of convalescence after a scarlatinal inflammation of the pharynx and larynx, laryngeal dyspnea, and the symptoms of stenosis depend, as repeated examinations have taught us, neither upon inflammatory swelling, nor (far less) upon ulceration or membrane formation in the larynx; rather, upon complete paralysis of the muscles. This paralysis, which leads to a position of the vocal cords similar to that seen in the cadaver, is purely myopathic, and dependent upon infiltration by fluid, and the consequent loss of functional power of the laryngeal muscles."

We have, in the foregoing, covered the essential points in connection with the sequels of scarlatina.

Scarlatina may coincide, in point of time, with any of the acute or chronic diseases. There are no exceptions to this rule.

Reports have been made now and then of a favorable influence exerted in this way upon a chronic disease, yet the number of cases is a small one, and far less significant than in measles. This may have some connection with the fact that the more severe scarlatinal infection tends more easily to a fatal ending in subjects whose vitality has been exhausted.

[The statistics of the Hospital for Scarlet Fever and Diphtheria Patients of New York, though comprising a smaller number of cases than those of some older and larger institutions, are particularly valuable because the cases are drawn from a class of society in which debility from improper food and hardships of various sorts does not occur. It is therefore of interest to note the tabulated reports and the conclusions regarding scarlet fever published by this hospital. The onset was marked by a chill in 30.2% of the cases; vomiting was present in 60.4%, and sore throat in 86.8%. In about 10% neither vomiting nor sore throat was present, though the cases were undoubtedly scarlet fever. The typical strawberry tongue was seldom observed, and the filiform papillæ of the tongue were prominent in less than 25% of the cases. The period of invasion varied from five to one hundred and sixty-eight hours, the average being thirty-four hours. The earliest symptom was in most instances bright redness of the throat. This occurred in every case admitted early in the disease. In over 30% of the cases an exudate resembling traces of milk was found in the throat. When this was wiped away, it soon reappeared. Cultures from it always showed some variety of streptococcus. Sometimes it increased to a nondetachable membrane. Follicular tonsillitis was present in 26.5% of the cases. Cervical adenitis was present in every case of scarlet fever in which there was present an exudative inflammation in the naso-

pharynx. Suppuration never occurred. The eruption of the skin in
nearly every case seemed to consist of two factors: These were a dila-
tation of the superficial blood-vessels, causing a pronounced blush;
and an inflammation of the sweat-glands, producing small points of
more intense redness, and sometimes a finely papular or vesicular
roughness. A vesicular miliaria was present in 9.7% of these cases.
With regard to the cases in which these two factors were not present:
No eruption at all was seen in one carefully observed case; in 6% of
the cases no general blush was ever noticed, but a well-defined miliaria
was present, with marked constitutional symptoms and profuse des-
quamation; in 3.9% of the other cases no miliaria occurred. Vascu-
lar rupture was present in 4.9%. As constant a symptom as the red-
ness of the throat was the desquamation of the epidermis. This did
not seem to vary according to the extent or character of the rash, but
rather with the thickness of the epidermis. It usually began upon the
edge of the ears before the eruption had completely faded, and in some
instances during the height of the eruption. In a few cases it was not
noticed until it appeared upon the palms of the hands and soles of the
feet, beginning under the end of the nails and upon the wrists and
ankles. The process required, on the average, until the forty-seventh
day for its completion. Rapidity of the pulse-rate was seldom dis-
proportionate to the temperature in uncomplicated cases, even when
observed from the first. This may have been due to the absolute rest
that was enforced. Albuminuria was present in 31%, but in only
14.5% for more than two days.]

DIAGNOSIS.

WELL-DEVELOPED cases of scarlatina are easily recognized. The fact, however, that one may be in a quandary in regard to the conditions occurring in the puerperium, and in cases of trauma, proves that a certain diagnosis is far from being always possible.

The warning should also be heeded in regard to a narrowness of judgment based exclusively, or in the main, upon the appearance of the eruption. Hebra, the great classifier of the affections of the skin, includes the general phenomena in his definition of the "acute, exudative, contagious dermatitides." "I understand by the name exanthem those diseases which are recognized as much by their involvement of the whole organism, and by the simultaneous appearance of fever-phenomena, as by the distinct and customary symptoms upon the general surface; they show an acute course that can be calculated upon in advance, and develop a contagium."*

Mayr,† his pupil, in discussing the diagnosis of scarlatina, speaks just as positively of the necessity of considering the general phenomena in order to form a diagnosis.

Every one will admit the correctness of the principle; in individual cases, however, it will be violated. I do not know whether I am correct in the statement, but it has occurred in my experience that sometimes a dread of confessing that he is not quite sure of what is before him causes the physician to form a positive diagnosis of scarlatina.

In a disease that appears to the laity to be so easily recognized that they question the knowledge of the physician who expresses himself with reservation, this tendency is clearly understood. There is possibly, therefore, an occasional error in diagnosing scarlatina more often than it is really present, as well as in a failure to recognize the condition. Irregular scarlatina, in a form characterized only by angina, should especially be mentioned, and is impossible of recognition. We have already thoroughly discussed this question.

As **essential signs of an infection by the scarlatinal toxin** we may depend upon:

1. *The sudden invasion and its complete development, in any event, in a relatively short time, and with serious symptoms;* especially a rapid rise of fever; very often vomiting and stupor.

* In Virchow's "Handbuch," Bd. III, S. 79.   † *Ibid.*, S. 146.

2. *Angina with its accompanying phenomena*, pain, difficulty in swallowing, redness and swelling of the pharyngeal mucous membrane, the latter taking a more uniformly red color. Later there is a circumscribed, markedly red swelling. Perhaps, in the future course, necrosis of the tissues, scarlatinal nephritis.

3. *The development of the raspberry (cat's) tongue.*

4. *The eruption* beginning under the clavicles, then extending to the neck, the nuchæ, and the breast, involving the face to a lesser extent, and leaving free especially the region about the mouth. In addition, in the beginning, the circumscribed red nodules, raised slightly above the surface of the skin; then a general reddening of the surface through their coalescence. There are no intervals in the redness until a later period, when the exanthem has disappeared. The desquamation, at least in some places, occurs in patches or fragments.

5. *Enlargement of the lymph glands.* This is of less significance when situated in the neck than when in other portions of the body. Especially should the inguinal glands be mentioned. A comparatively early phenomenon, upon which great dependence may be laid, is the following:

Heim describes several cases in which he found the sense of smell so acutely developed in certain of the laity, who had previously had their attention called by him to the facts of the case, that they recognized[*] scarlatina without a shadow of a doubt. I have already mentioned these things,[†] but wish to refer to them once more, since it is always possible that they may be of significance for some one or other.

After Heim has remarked how difficult it is to describe impressions of smell so that they can be again recognized by others from their peculiar nature, he continues with his description of the odor of scarlatina as follows:

"There are provisioners here in Berlin who sell old herrings, old cheese, etc., in cellars whose doors open on the street. The air in these cellars gives an odor similar to that of scarlatina. Also the smell which one perceives at a short distance from the keepers of carniverous wild beasts, such as lions, tigers, etc., has a resemblance to the odor of scarlatina." Advancing years relieved Heim of the acuteness of his sense of smell, as well as of that of sight, and, as he relates: "Three years ago, at a time when there was no scarlatinal epidemic in evidence, and I had treated no scarlatinal cases for several months, I was called to the nine-year-old boy of Frau Hofräthin Parthey. The patient was hot, thirsty, had some pain, and had a rapid pulse. I diagnosed the affection as catarrhal fever. The mother of the sick boy, however, whose sister several years before had died of scarlatina, and who had seen several others suffering from the disease, asserted positively that the boy had scarlatina, because the perspiration had the odor peculiar to the disease. Since I myself did not perceive it, I

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[*] "Hufeland's Journal," 1812, Part IV, S. 75, 76.
[†] See "Measles," page 344.

considered her opinion a bold one, and especially since it was given so positively. But on the following day I found to my amazement that it was absolutely correct, for the scarlatinal exanthem had made its appearance." In the same family there now occurred other cases of scarlatina. An eleven-year-old son was isolated, had considerable fever, and complained of pain in his throat. Heim took it for granted that he had also contracted scarlatina, and proposed laying him beside his brother and sister, who had the disease. The mother declared, however, that she could not discover the odor, kept them apart, and in fact he continued free from the disease. This was both a positive and negative proof of the ability of the lady to form a diagnosis of scarlatina from the odor.

The course of the fever, its fall by lysis, is of significance in the later periods. But I do not wish to draw too positive conclusions from the temperature, since it shows too great irregularities, and can appear in the same form in many other infections. Of all the sequels that are of great importance in the diagnosis of a rudimentary scarlatina that has not been recognizable during its course, dropsy and nephritis are correctly placed in the first rank.

If an epidemic is known to be extant, and if the patient has been known to have been in contact with those already infected, then any one may easily make the diagnosis of scarlatina, even though only a few of the symptoms are present. We must not forget, however, that this anamnestic assistance is often lacking, as is often the case also in measles.

[**Lymphatic Glands.***—The superficial glands were examined by Schamberg in 100 cases of scarlet fever. The various lymphatic glands were enlarged in the following proportion of cases:

Inguinal glands	100%
(a) pea-sized	23%
(b) bean-sized	77%
Axillary	96%
Maxillary	95%
Posterior cervical	77%
Anterior cervical	44%
Submaxillary	36%
Epitrochlear	26%
Sublingual	25%

"As a diagnostic aid, therefore, in differentiating the rashes in diphtheria from true scarlet fever the study of the glands is perhaps of considerable value. A well-marked enlargement of all the superficial glands, particularly the epitrochlear and axillary, would in

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*"A Clinical Study of the Lymphatic Glands in One Hundred Cases of Scarlet Fever," Jay F. Schamberg, *Ann. of Gyn. and Pediatry*, vol. XIII, Sept., 1900, pp. 191–196.

doubtful cases, I think, tend to throw the balance in favor of scarlet fever.

"In distinguishing between scarlet fever and measles, which task is not invariably easy, an examination of the glands lends but little aid, because in the latter disease there is also a generalized glandular enlargement. It is to be noted, however, that the aden-opathy of measles is not nearly as well marked as that observed in scarlet fever."

The writer observes that enlargement of the glands may serve a useful purpose in differentiating from the "erythema scarlatinoides." In the latter, it is believed, the glands are not usually enlarged.

Cabot gives, in regard to the blood, the following:

Summary.—"Moderate anemia. Leucocytosis beginning before the eruption, and often lasting into convalescence. Eosinophiles said to be increased in favorable cases, absent in bad cases.

"Diagnostic and Prognostic Value.—1. The chief importance of the blood examination is in distinguishing the disease from measles and the eruptions of other diseases. Measles has no leucocytosis.

"2. Whether the prognostic significance attached by Neusser and others to the percentage of eosinophiles is genuine or not cannot as yet be positively stated."]

What may now lead to confusion, and from which other infections must the diagnosis be made? There come into consideration:

1. **Measles**—and in regard to this disease, I may refer to the fore-going conclusions.

2. **Rötheln**—this will be considered further on.

3. Of the greatest importance are the various forms of the **septic exanthemata.**

In our discussion of the extraordinarily important and practical questions with regard to the nature of puerperal and traumatic scar-latina, the points that come under consideration have already been weighed. I will content myself, therefore, with a reference to Litten's* exposition of the matter, since his fundamental principle appears to me incontestable:

"In septic infections an erythema sometimes makes its appear-ance, and spreads in the shortest time over the entire body. It is of an unusually deep purple color. The nature of its development and its appearance resemble so completely the scarlatinal exanthem that I know no differentiating characteristic to distinguish between the two conditions. Even the same localities that usually remain free in scar-

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* *Charité-Annalen,* Bd. vii, S. 178.

latina remain also unaffected in the septic erythema. The face is like-wise markedly congested, the conjunctivæ injected, and the nasal secre-tion is increased. Moreover, the tongue may assume an intense reddish color at its edges. Miliary eruptions often occur also as a complication. If death does not follow upon the acme of the skin affection, desquamation ensues without any simultaneous fall of temperature, fully resembling in this particular the state of affairs in scarlatina."

There follow then a number of histories of cases of genuine scarla-tina in puerperal women, and of septic erythema in similar cases, which are very instructive in their similarity. The skin affection is therefore of little value in the differential diagnosis, and how difficult it can be to recognize the septic infection, especially such as develops from a hidden source, is well recognized.

I wish to call special attention to the fact that in the latter condi-tion frequently the tonsils form the portal of entrance. We then have the pharyngeal involvement as the primary focus of the disease; the erythema follows, and the sudden stormy invasion, with high fever, and the other constitutional symptoms so common to scarlatina, are also present. Then is good counsel valuable. If the hemorrhages in the retina, upon which Litten lays so much stress, were always present, one would have significant ground for a diagnosis. But when they are lacking,—and this is, in my experience, a frequent occurrence,—the matter still remains in doubt. The subsequent course may not solve the question, for it may be a case of sepsis complicating one of scarla-tina. I am of the belief that the diagnosis can be made with certainty only when the cause of the disease not only has been definitely discov-ered, but when its discovery somewhere in the body is rendered possi-ble. Let us not forget that at present even the pus cocci, at least dur-ing life, may escape detection.

4. **Erythemata in general,** of whatever origin, may perhaps lead to confusion, at least of a temporary nature. In such cases the ab-sence of the scarlatinal puncta should attract the attention.

[Antitoxin rashes are at times most difficult to differentiate from scarlet fever rashes. At the Willard Parker Hospital, in New York, where both diphtheria and scarlet fever are cared for, it has been almost beyond the power of experts to pronounce definitely upon certain cases. It is evidently of extreme importance to remove early cases of scarlatina developing in a diphtheria ward, and it is equally important to avoid the removal of a case of diphtheria to a scarlet fever ward merely because of the appearance of antitoxin rash. It

has required the utmost pains on the part of the authorities to avoid mistakes in such decisions.

The blood examination may in future prove to be of great value in differentiating these conditions. At present, however, the testimony indicates that the blood shows leucocytosis in both diphtheria and scarlet fever; and while the administration of antitoxin causes a marked diminution in the number of leucocytes for from twenty-four to forty-eight hours, the leucocytosis returns. At the time of the probable appearance of the rash the effect of the antitoxin upon the blood would therefore have passed off; hence we are not now aided in the diagnosis by blood examination.]

5. Genuine **erysipelas** is without difficulty distinguished by its peculiar distribution. The projections, springing irregularly and to all sides from the original focus of the disease, which contrast themselves against the healthy skin by their slight elevation above the surface as round or pointed arcs, never are seen in scarlatina.

Urticaria will hardly form a cause of error.

In conclusion, I would say, that the more we see of the acute exanthemata, the more we are convinced that the scarlatina cannot invariably be recognized.

PROGNOSIS.

THE prognosis in scarlatina is dependent, to a most marked degree, upon the **character of the epidemic;** everything else takes rank secondary to this consideration. This matter is continually returning for consideration; and has been since we first learned to distinguish the disease from the other acute exanthemata.

Thomas brings an array of evidence, with a few examples of which I will content myself, since they are based upon large statistical figures.

In Hamburg* were attacked: In 1891, 2902 persons, of whom 133 died = 4.6%; in 1886, 3105 persons, of whom 348 died = 11.2%. From 1885 to 1894 (ten years) out of 21,834 scarlatinal patients, 1475 died in Hamburg. The average is 6.8%. The maximum and minimum are given at the same figure.

In Stockholm† were attacked: In 1865, 2019 persons, of whom 56 died = 2.8%; in 1869, 1190 persons, of whom 327 died = 27.5%. From 1865 to 1885 (twenty-one years) out of 15,137 scarlatinal subjects in Stockholm, 2461 died; an average of 16.3%. Against a minimum figure of 2.8% stands the maximum, 28.8% (1870; 565 cases with 163 deaths).

It should also be mentioned that the absolute frequency of scarlatina at a given time, and the extensiveness of the epidemic, do not stand in any definite relation to the severity. The above figures prove this fact conclusively. The objection that a more extensive spreading of scarlatina brings a larger number of cases to notice, because attention is not called to cases that are otherwise of no especial interest, loses some of its force in the light of the small fatality in the largest epidemic that Stockholm has ever had (1865). The masses have no fear of a disease that removes only 28 out of 1000 that are attacked. On the contrary, in the years when only a few fell ill, but many died, many more were brought to the physician.

In England, which has suffered to a very considerable extent from

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* "Bericht des Medicinalraths (Dr. J. Reincke) über die medicinische Statistik des Hamburgischen Staates für das Jahr 1894," S. 58.

† Quoted by Sture Carlsson from Lennmalm: "Nagra Anteckningar om Skarlakansfebern pa Katarina Sjukhus," Stockholm, 1895.

scarlatina, the mortality, according to a recent statement,* amounted at the lowest ebb to 13%, and reached even to 40%.

The sporadic cases of scarlatina are in no way less dangerous than the epidemic form. Thus, out of 11 cases in 1868 in Stockholm, 5 had a fatal termination.

Among the diseases influencing **the mortality among the masses,** scarlatina is one of great significance. The relation between scarlatina and measles appears to be a varying one, dependent upon different times and places. Now the latter, again the former, claims a greater number of victims. Thus, in Bavaria, Majer † states that during the period from 1857–58 to 1868–69 measles was responsible for only 0.76% of the total mortality, while 1.5% was credited to scarlatina. In Hamburg, on the other hand, there was in the decade from 1885 to 1895 the following mortality: From measles, 1987 persons; from scarlatina, 1475 persons.

We have comprehensive statistics in regard to the scarlatinal mortality from different countries, and from the larger cities.

Norway ‡: During the years 1867 to 1878 the mean percentage mortality of scarlatina was 6.6% of the deaths from all causes. The figures varied between 2.12% and 12.5%.

Sweden §: During the years 1861 to 1885 a mean percentage of 3.7% (of the total mortality) in the cities; in the country, 3.8%.

Bavaria †: During the years 1857–58 and 1868–69 a mean average of 1.5% (of the total mortality: out of 1,706,200 deaths, 25,740 were of scarlatina). Variations from 0.8% (1860–61) to 3.2% (1868–69).

For comparison I mention the fact that in London ‖ the mean total amounted to 4.2%, with a variation between 2.4% and 7% (1861 to 1865).

That **the age in life** holds the second place in determining the prognosis, has already been thoroughly discussed.** How the prognosis should be determined for the different years of life does not seem clear to me, if we consider the relative statistics of the cases and of the mortality. Statements by different authors vary in the most decided

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* Moore, "Eruptive and Continued Fevers," Dublin, 1892, p. 161. Quoted by Carlsson, *loc. cit.*, p. 53.

† "Die epidemischen Kinderkrankheiten in Bayern während der Periode 1857–58 und 1868–69." Karl Majer, *Journal der Kinderkrankheiten*, 1871, Bd. LVI, S. 161.

‡ Johannessen, *loc. cit.*, Tabelle V, und S. 137.

§ Lennmalm bei Carlsson, *loc. cit.*, p. 52.

‖ Thomas, in v. Ziemssen's "Handbuch," *loc. cit.*, p. 325.

** See page 388, and the conclusions.

fashion.* Only this much is certain: that adults are in a far less degree endangered than children. The influence of social status, and everything else that brings into consideration the differences in food, nursing, and treatment of the sick, is not a very considerable one. It may, however, make itself felt to a certain degree. Thomas † emphasizes this circumstance, which every one who has had experience among all classes of the people can confirm.

Accurate statistics are hard to secure. Approximate figures, to be utilized with discretion, are furnished by the reports from Stockholm.‡ In the seven years from 1857 to 1863, 927 cases with 210 deaths were observed exclusively among the poorer classes, a mean mortality of 22.7%. Statements in regard to the mortality in the entire population for the same period are lacking. No opinion can therefore be formed in the matter. The question also arises whether the condition of affairs among the poor rendered impossible the securing of medical treatment. In this the mild cases would hardly be reported in full numbers. In the year 1857 there was a great epidemic. Among the poor there were 655 cases and 148 fatalities, or 22.6%, corresponding almost with the mean average.

Let us now pass on to the particular influences that determine the prognosis. It is worthy of mention that **an unfavorable outcome may be caused by the following:**

1. *The virulence of the infection,* which makes itself evident under the appearance of an intoxication with a sudden loss of all vitality, and especially with disturbance of the brain and of the heart. A high temperature may be lacking, but is usually present. Early in the disease —during the six days (at most) following the invasion—it is of itself almost decisive. If the phenomena typical of the intoxication subside, and only fever is present, which may rise to 42.0° C. (107.6° F.), and continue there obstinately, one may then consider the possibility of recovery. Yet the fever must not be depended upon as the criterion for the imminence of the danger.

2. The occurrence of *a septic infection* in the course of scarlatina. Again does the severity of the infection come into question in a very important manner, to say the least. One must not forget how significant the dangers which sepsis can directly excite by its many localizations, and in all of the vital organs. Further, one must consider the fact that the toxin that remains in the body so frequently and for a long time after sepsis may later on excite a new attack of the disease.

In regard to *involvements of the organs,* it must be said that there is always a danger connected with these processes, whatever their direct cause—the scarlatinal toxin or some other influence.

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* Thomas, *loc. cit.,* p. 323.   † *Loc. cit.,* p. 322.   ‡ Carlsson, *loc. cit.,* p. 2.

3. *Necrotic inflammatory processes originating in the pharyngeal organs.* The extension of the phenomena of decomposition to the nose, as shown from the excretion, was very properly by the earlier physicians looked upon as a danger-signal. Apart from the otitis, which can more easily make headway under such circumstances, the possibilities of a septic and gangrenous infection or intoxication, in the presence of necrotic lymph glands in the cervical and postcervical regions, become more real. It will occur more frequently than in an involvement of the pharynx alone, which, when once gangrene has set in, involves the nasal cavity in the process.

I cannot ascribe great weight to the assertion of Carlsson,* since of course the necrotic inflammation in the individual case is only a single phenomenon of the disease. But I want to mention the fact that the total mortality of his 4000 cases amounted to 18.85%, while of those suffering from severe pharyngeal involvement—no less than 49.88% of the total number—28.78% terminated in death.

4. *Nephritis,* with its attendant dropsy, is always a symptom that requires reflection, always decidedly darkens the prognosis; but different epidemics show not only a decided variation in the frequency, but likewise in the seriousness of the affection.

Well-marked uremia demands many victims, and is decidedly the worst sequel of nephritis. The large effusions into the cavities of the body are also not to be underestimated; and the fact that nephritis favors the occurrence of inflammatory exudates which render the prognosis considerably worse must not be forgotten.

5. *Cardiac involvements* are always dangerous. It cannot be determined in advance whether genuine tissue changes are at the bottom of the cardiac failure, but, apart from this, when the disturbance is of marked degree, it increases the danger of a fatal outcome.

A very rapid pulse is an unfavorable sign, in case there is not at the same time a very decided rise of temperature without any typical phenomena of the intoxication. If the pulse is very frequent, small, irregular, with a moderate rise of temperature, or if the hands, feet, ears, and the tip of the nose feel cold, then the case is going badly for the patient.

6. *Affections of the air-passages*—constriction of the entrance to the larynx, and bronchitis, widely distributed and involving the finer air-passages—are of unfavorable omen.

The remaining affections of the respiratory passages, especially the pneumonias, in so far as they are bronchopneumonias, must be

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* *Loc. cit.,* p. 62.

looked upon as very serious conditions. This is much less true of croupous pneumonia. In the latter condition it is a question of great importance whether the patient is much exhausted, and especially whether the heart is in good condition. If there is no longer present a decided resisting power, then the croupous pneumonia, which so usually ends favorably, terminates in death. With respect to all the other conditions that may occur during the course of scarlatina, the involvements of the central organs, the digestive apparatus, etc., the prognosis must be made on general principles according to the severity of the affection.

In conclusion: **In scarlatina we should always be extremely reserved with the prognosis.** Especially should one never forget that a case that appears to be a light one for a longer or a shorter time may run an unfavorable course. At least four weeks must have passed, calculated from the beginning of the attack, before recovery can be discussed with surety. If the physician has the advantage of observing the course of the epidemic, he can then form a somewhat more certain prognosis for the individual case. He is a wise man, however, who remembers the treacherous nature of scarlatina.

TREATMENT.

As the susceptibility to scarlatina is not a general one, and since it becomes less with advancing age, and as the danger to life also diminishes, the lessons of prophylaxis should be made comparatively plain.

To begin with, we lack knowledge as to whether a certain person can contract scarlatina or will remain free from the disease. Nor is there a reason why this should be put to the test. Indeed, every form of contact with scarlatinal subjects should be avoided. This rule holds all the more urgently, the younger the person. Therefore there is no reason, even in the mildest epidemics, for exposing to the danger of infection a person not previously attacked by the disease, as occurred formerly quite frequently in smallpox, and as happens, now and then, with the measles of to-day. The physician must oppose such a procedure with all his power.

The question is full of practical importance to the physician: *What is to be done when a member of a family is attacked with scar atina?*

Although we may have serious doubts as to the real advantages to be obtained by isolation, yet the measure is imperative in my opinion. No attempt must be made, however, with the idea of making it effective with insufficient means. Yet how often are we driven to exactly such a position! If one could promptly remove every scarlatinal patient from the house and transfer him to the hospital, much would be gained. But this is feasible in only the minority of cases, and need hardly be told. And how does it stand in the majority of cases? The direct intercourse with brothers and sisters is interrupted, to be sure, and the scarlatinal child is placed in a room by itself. When all goes well and the conditions of the household render it possible, it is even transferred to another story, and some person is appointed in attendance who shall not come in contact with the other members of the family. Yet will the mother be dissuaded from seeing her loved one, especially if the illness takes a serious turn, or if there is any danger? Sometimes, to be sure, and especially if she remains conscious of her duty to her other children, and is of a strong character. Else she comforts herself with, "Once does not amount to anything, and a few seconds can do no harm." Moreover, often enough the visit in intimate contact with the patient is followed by a return amongst the well

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members of the family and into just as close contact with them. This occurs repeatedly when the storm of feeling bursts over the danger of the patient. In this way the poison may be transmitted, as well as by carelessness in the handling of the patient's linen, which is usually left to the servants. I believe that every physician who has learned the course of affairs with his own eyes will agree with me. Under unfavorable circumstances, in small rooms, where it is impossib'e to secure a special nurse, the prevention of immediate intercourse between the patient and the well brothers and sisters is all that is possible. And among the poor we must even dispense with this safeguard. Were there such arrangements in fact, as have been suggested by v. Kerschensteiner,* by means of which prophylaxis could be brought to bear,—enforced where possible by the laws,—then the extension of scarlatina among the population would be rendered more difficult, though the afflicted family would be exposed to an increased danger.

With regard to provisions governing scarlatinal epidemics in schools, I have already expressed myself † ; this is one of the most difficult problems in the whole study of the disease.

The experience of Staff-surgeon Vogl ‡ in the garrison epidemics is well worthy of attention: "It proved impossible to prevent the spread of the disease, even among the relatively less susceptible soldiers, though everything was done that was in our power." "The first case that was discovered gave the signal, of course, for prompt measures. The patient was immediately transferred to the quarantine, and disinfection carried out systematically and energetically. Intercourse was restricted. The placing of the attendants was entirely within the charge of the physicians."

Vogl ascribes the impossibility of preventing the disease to the following causes: The patient has already entered upon the stage of incubation before exhibiting a sign of indisposition, and is already able to transmit the scarlatina to others. This may (he calculates the incubation at three to five days), at any rate, sufficiently explain the gross extension. If this explanation is correct, the difficulties accumulate in the way of an effective prophylaxis for a community into which scarlatina has made its way, or among whom, as is always the case in large cities, the disease is a permanent fixture. Vogl continues: "If with the first known case of scarlatina in a school it may be taken for granted that for three to five days the case has been infecting others, we must not expect to prevent further cases of the disease by isolating

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* See Introduction, page 220.   † See page 220 of this volume.
     ‡ *Münchener med. Wochenschrift,* 1895, S. 983.

it, even though the scarlatinal child is turned back immediately from
the threshold of the school-room. Moreover, it becomes clear, in the
same way, that a delay in closing the school for even one half-day
must have as its result new infections in ever-increasing proportion.
The closing of the school, from this point of view, cannot take place
too soon." Of course, Vogl requires the strictest isolation of the
family, and especially the children, if in their circle a case of scar-
latina has appeared.

All this is, indeed, well conceived, but is it practicable? How
much time has been lost from the lessons? Indeed, one may well ask,
under the circumstances, how much time remains for the lessons?
The most extended epidemic that I have ever seen here in Tübingen
continued from December 5, 1888, to May 27, 1890—the schools closed
for nearly a year and a half, an apparently inconceivable thing. And
in no event is Vogl himself sure that the result is certain. "The more
frequently medical acuteness is able to discover the source of infection
in its very beginning, the nearer one comes to the longed-for goal of
heading off the epidemic, which otherwise, in spite of all other meas-
ures, continues uninterrupted in its progress."

This principle is correct, but it can just as certainly be made prac-
tical in only the smallest number of cases. I would call attention, by
way of comparison, to the military precautions against cholera, which
are barely protective. The slight intestinal disturbances in cholera
are analogous to the simple anginas in scarlatina.

*What, then, is to be said of disinfection in scarlatina, and what of its
value?*

There is no reason to doubt that the task of destruction, or let us
say rather, in order to be strictly accurate, the disarming of the scar-
latinal toxin as found in the body- and bed-linen, is not only possible,
but practicable. Thorough washing in boiling soap-and-water for a
sufficient time, then a long drying in the air, and perhaps also a subse-
quent bleaching in the sun, appear to be sufficient.

Accurate reports in regard to the disinfection of certain portions of
the bed itself I have not seen. Daily experience seems to indicate that
the usual procedures—active beating in the air and a long-continued
exposure to the sun—are, I will not say sufficient, but that they appear
so to the laity. Careful people make a rule of taking apart the differ-
ent portions of the bedding, and in this way the tickings can also be
cleansed. Unfortunately, it is a different story with the bedrooms in
which the patients have passed their illness. Let us hear several
competent opinions:

Vogl* says: "Success is only to be expected by the limitation and even the discontinuance of outside intercourse. This is at best a difficult and unsatisfactory defensive measure, but it accomplishes more, and is more effective, than the ever so heroic measures with costly disinfecting apparatus, whose limited influence (disinfection of the bed- and body-linen) will not affect the outcome in the slightest degree." Disinfection is therefore given credit for a very narrow usefulness. Vogl reported at a still earlier time that the patient himself, even, had been subjected to the process of disinfection.

E. Hagenbach-Burkhardt† says: "As soon as scarlatina was diagnosed certainly, the patient was removed, with all the bedding, to the isolation department. The entire room was at once emptied, the walls washed, the room disinfected, and, in as scientific a manner as possible, in the following order: chlorin fumes, sulphur, the carbolic spray, and the sublimate spray. Special attention should be paid to the thorough airing of the room, and this may be successfully carried out even in large apartments, provided there are on both sides large window spaces. Such a complete air-cleansing was hardly possible in the smaller rooms." All rooms were treated in this way; only of one small room is it expressly stated that: "It is a fair conclusion that the scarlatinal toxin must be a very persistent one, since after months of inoccupancy of the room, infection repeatedly took place; moreover, our disinfection and absolutely thorough cleansing were unable to drive it from the house; and our precautionary measures were unavailing."

There is little prospect of completely disinfecting infected rooms in a private house. It is somewhat comforting, therefore, that this persistence of the toxic substance seems to have been limited to certain rooms only. We are then safe in saying that disinfection, carried out conscientiously, according to our present lights, may prove of no avail; whether it is necessarily unavailing is another question. And therefore a physician may not take a stand in opposition to an attempt at disinfection. Further than this we cannot go.

[Methods of Quarantine and Disinfection Employed in the Hospital for Scarlet Fever and Diphtheria Patients, New York (from Annual Report, 1901).—Each patient has a private room, there being no wards. The laundry is in a building by itself. The disinfecting plant is also separated from the hospital, and consists of a steam-

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* *Loc. cit.*, p. 984.

† "Jahrbuch für Kinderheilkunde," N. F., Bd. xxiv, S. 111–115. Compare, also, Emil Koch, *loc. cit.*, p. 35.

tank and formaldehyd chamber. In the former the steam is raised
under pressure to a temperature of 110° C. (230° F.) and kept on for
half an hour. If formaldehyd is used, the articles to be disinfected
are exposed to the gas continuously for twelve hours.

Patients are carefully examined before being admitted; and if
there is any question in regard to diagnosis, they are placed in the
observation room. The resident physician before entering the pres-
ence of the patient is required to wash his hands thoroughly with
soap and water, followed by immersing them in bichlorid solution,
1:2000. A gown is supplied which buttons closely around the neck,
covering the collar and enveloping the body completely, just clearing
the floor. To this is added a cap arranged to cover the head and
neck, exposing only the face. This, with a pair of rubber overshoes,
completes the uniform. When he leaves the patient the hands and
face are disinfected thoroughly and the mouth is cleansed with boric
acid solution. All visitors must obey the same regulations. Ladies,
if admitted at all, are required to remove their outer skirts before
putting on the uniform.

Patients are not allowed to leave until free from contagion. They
are examined repeatedly, particular attention being given to the
feet, which are sometimes slow in finishing desquamation. The
scalp requires washing, as does the external auditory meatus, which
is often found filled with desquamating epithelium in cases otherwise
free from contagion. During the week preceding discharge, patients
have their ears irrigated with bichlorid solution 1:8000, and the
scalp shampooed on alternate days.

On the day of discharge the following routine is adopted for
adults (for children, special instructions are given in each case):
(1) The ears are irrigated with bichlorid solution 1:8000; (2) the
scalp is shampooed with soap and water; (3) the scalp is shampooed
with bichlorid 1:2000; (4) a tub-bath is given of soap and water;
(5) a tub-bath is given of bichlorid solution 1:8000 for twenty minutes;
(6) a sponge-bath is given of bichlorid solution 1:2000; (7) the bichlorid
is sponged off with sterile water; (8) a nasal spray is given of bichlorid
solution 1:8000; (9) the mouth is cleansed with saturated solution
of boric acid. There is a suite of discharge rooms, used as follows:
In No. 1 the patient leaves the hospital clothing. In No. 2 he is
disinfected. In No. 3 he puts on his freshly disinfected clothing.

All clothing that can be washed is disinfected with steam. For
other articles formaldehyd gas is used. Books and papers are steamed
after removing the leather binding of the former. The print is slightly

blurred as a result, but no further damage is done. Toilet articles are treated in the same way, but jewels (rings, pins, etc.) are disinfected with pure carbolic acid. Watches are exposed to formaldehyd gas.

In this hospital there has been no history, as far as known, of contagion from a discharged patient.]

With regard to the administration of medicaments as a prophylactic measure, we must admit that we know of none that are qualified for the purpose. This is as true with respect to belladonna, extolled by Hahnemann,* as to the biniodid of mercury and oil of eucalyptus,† recommended to-day by the English physicians. It also applies to the measures that are said to abbreviate and ameliorate the course of scarlatina—the so-called "specifics."

[Speransky ‡ gave Fowler's solution to 12 children who had been exposed to scarlatina, one or two drops twice daily. None of the children contracted the disease, although they continued to mingle with infected cases. Krause, who annotates the original article (which appeared in "Vratsch," 1896, No. 31), states that evidence of this character deserves attention, as more significant than alleged therapeutic results obtained from drugs.]

How should the sick-room be arranged? The general rules, plenty of air, frequently changed, and not too little light, are to be adhered to in scarlatina as in other diseases. During the first week, at least, a continuous current of air through the chamber is of advantage, and even in the later stages I am just as little afraid of open windows. If symptoms appear in the respiratory tract, we proceed as outlined under the treatment of measles.

One thing, however, I have learned to fear in the early stages of scarlatina—viz., a too high temperature of the sick-room, and too heavy a covering for the patient. Sometimes I have seen severe brain symptoms, increasing even to general convulsions, disappear as soon as the patient became cooler. I have gained the impression that with the increase in the temperature of the body,—because of a diminished dissemination of heat,—the temperature naturally exceeds the mark attained by the fever itself, owing to an influence exerted by some other factor.

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* R. Köhler, "Handbuch der Speciellen Therapie," Tübingen, H. Laupp, 1867, Bd. i, 3d edition, S. 87.

† O. Vierordt, "Behandlung des Scharlachs," in Pentzoldt-Stintzing's "Handbuch," Bd. i, S. 193.

‡ "Archiv f. Kinderheilkunde," xxiv, 423.

Whether this is accurate must remain undecided. The temperature of the room should not be above 15° C. (59° F.), if all would be as it should, and the patient should be lightly covered.

Great emphasis should be laid upon the care of the mouth, and from the very beginning, I attempt to give as bountiful a supply of nourishment as possible. We do not know how long the disease will last, and every loss of body-substance must be avoided. It must not, therefore, be overlooked that the hungry fever patient must give up his vital substance—the albumin of his tissues, of which too much already has been destroyed under the influence of the poison.* A lack of nourishment is therefore to be avoided, as far as possible.

It is understood, of course, that there are certain limits to be drawn. In these cases, as in all others, the digestive system should not be called too actively into play. And because of the involvement of the pharynx, liquid nourishment is required for scarlatinal patients. The different cereals (children's food), not too much sweetened, and boiled to a more or less thick mush, seem to me a more suitable food than the milk which is so generally used. The latter has, to be sure, the advantage that it carries with it large quantities of water into the system, which are beneficial to scarlatinal patients.

Whether a practice is to be made of giving wine in the ordinarily severe cases I consider a question that cannot be decided on principle. I give light red Tyrolean wine, according to the age, from 0.2 liter (0.21 pts.) daily and upward, because it is a cheaper remedy and of more use than any of the customary aimless medicaments. When one has to do with teetotalers, he may avoid disagreeable comments without doing his patient any great harm. He can in such cases take even a more positive stand when wine becomes necessary as a medicament.

Should one particular form of treatment always be followed? This question cannot be indiscriminately answered in the affirmative. For often—as, for example, in measles—specific measures become necessary, and in order that these may be instituted at the proper time, a careful and continuous observation of the patient is indispensable.

Let us now proceed to the details of the treatment:

THE SYMPTOMS OF THE INTOXICATION AND THE FEVER.

These two must be distinguished as a matter of principle, but therapeutically a distinction is hardly possible, and, in any event, it

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* Compare Carl v. Noorden, "Lehrbuch der Pathologie des Stoffwechsels," Berlin, Hirschwald, 1893, S. 193.

seems to me of no advantage. The matter in hand is not only that of lowering the high temperature, which is indeed important; but there are other questions in addition, of a different nature. The tasks assigned, then, in so far as they are at all possible, can only be mastered by the employment of water. The heart stimulants also come into consideration.

The brain, the whole circulation, the heart, as well as the vessels, are directly affected by the scarlatinal toxin, and the temperature may still not be excessively high. In case it is high, the same influences, or at least similar ones, are exerted by it upon these same organs. Although everything is not clear in regard to the details, we may fix the following general principles: In every intoxication the danger becomes greater the longer the toxin continues in action in those localities where it is able to exert its influence. A removal of the poison is possible only if in some way it becomes weakened, or perhaps is even destroyed outright, or if a dilution and therefore a diminution in the quantity of the toxin is accomplished by a substance which is itself harmless.

The force that best counteracts the energy of every poison known to us as possessing an active influence upon the human body—happily called their biologic elective affinity (*Wahlverwandschaft*)—is an active circulation and a decided blood current. It is possible that the toxins are excreted from the general circulation; possible, also, that they become transformed elsewhere in the tissues or in the blood. It is also conceivable that the protoplasm, whose vitality has been lessened at the point of localization of the poison, may obtain new vigor from the newly circulating blood, and such a power of resistance that the toxin itself may be destroyed on the spot.

These are all theories that may be applicable to the chemical action of the toxins. If we consider them as fundamental principles, the object of our treatment becomes, to a certain extent, recognizable —viz., to bring, in the shortest space of time, as much healthy blood to the endangered locality as is possible. Water is able to accomplish this task, and the cardiac stimulants have their place beside it.

The following conclusions are based upon certain well-known facts: The difference between the temperature of the body-surface and the water that comes in contact with it are the determining factors. At the very moment that cold water comes in contact with the skin, deep respirations ensue, which not only cause a more complete distention of the lungs, but must have a considerable influence upon the circulation. The heart, which during the superficial breathing, is working under

difficulties, is now relieved of the burden to a considerable degree, and receives more and a better quality of blood. Owing to this, its vitality and functional power increase. If the temperature of the body is increased, the number of heart-beats falls with the cooling caused by the radiation of heat to the water surrounding the body, the intervals between the single beats become longer, the diastolic storing away of blood in the heart becomes greater, and the heart in this way becomes qualified for better work. At this point begins a more rapid and copious circulation throughout the entire system, and with it the possibility of throwing off the toxin.

[Buxbaum * reviews the hydrotherapy of scarlet fever *in extenso*, bringing the subject up to the present day. It does not appear that there have been many advances in this province of late years. The principles of Jürgensen, Leichtenstern, Trousseau, and other well-known clinicians are reiterated.

Buxbaum, who is a pupil of Winternitz, employs the following in all cases: He first uses partial bathing with a cloth dipped in cold water. In this manner he gains the patient's confidence. A quieting and revivifying response to the treatment is evident to all observers. The pulse quickly becomes slower and stronger in action. If partial sponging is well borne, Buxbaum proceeds to the "half-bath" with friction and affusion, the latter manipulations being essential to the success of the treatment.

The duration of the half-bath depends wholly upon its effect, and the moment the desired results are attained the bath may cease. The baths cause deep inspirations, which ventilate the lungs and exert a powerful effect on the circulation, that of the encephalon being especially benefited.

As the effects of the baths persist for a considerable period, not more than two or three need be given daily. If stuporous and convulsive phenomena are present, warm baths with cold affusions are indicated. Hyperpyrexia must be antagonized at all costs. Buxbaum recommends for the purpose the alternation of half-baths with cold packs.

Schill (Wiesbaden) treated 110 successive cases of scarlatina by hydrotherapy, and but one patient of this series developed nephritis. Ssokolow deprecates the use of fatty inunctions, for he holds that the skin eliminates the toxins and that the baths favor perspiration, while inunctions prevent it. Scarlet fever treated hydriatrically is, he thinks, a mild and uncomplicated disease.]

* "Lehrbuch d. Hydrotherapie," Leipzig, 1900.

And now as to the influence of an active temperature stimulus directly applied to the skull-cap. There cannot, in this case, well be an appreciable abstraction of heat, even when very cold water is applied. But there is a relaxation of the local blood circulation, and we know that the vessels of the meninges change their circumference according to the form of heat applied, so that an opportunity is given for an alteration of the distribution of blood in the brain and in the cortex. The relaxation of the sensorium—a symptom that appears after active stimulation of the skull in almost all of the intoxications involving the brain—becomes in this way intelligible for the first time.

Leichtenstern* calls attention to a peculiarity of the cardiac action in scarlatinal subjects when under the influence of the cold bath. A diminution in the pulse-rate appears before a reduction of the body-temperature has taken place, and then outlasts the reduction of temperature. He has observed the former symptom in hundreds of cases and the latter "by no means seldom." The cases he cites demonstrate clearly the facts, showing that there is a decided indication in scarlatina for the use of baths in reducing temperature.

I consider the best form of treatment, from the beginning of the invasion in scarlatina to the remission of the severe general symptoms, to be the **use of the cold bath.** The height of the temperature may be taken as the general index. Thus, we bathe when the temperature in the rectum reaches 40.0° C. (104.0° F.). The temperature of the water may be—and especially in the case of children—20.0° C. (68.0° F.), and the duration of the bath in such cases should be only five minutes. With older children we can reduce it to 15.0° C. (59.0° F.) without lengthening the time of the bath.

The general rule that cold but short baths are to be preferred to the warm baths of longer duration holds all the more in scarlatina since, in addition to the influence of the baths upon the temperature, that upon the circulation, as recently discussed, comes forcibly into question. Leichtenstern, moreover, is perfectly right in noting that there circulates in the relaxed vessels of the skin in scarlatina a large quantity of blood, and that therefore the direct dissemination of heat is freer, while the influences caused at a distance by the thermic stimulation of the skin become more decided.

Since the contraction of the vessels caused by the irritation of the vasomotor muscles and nerves of the skin must be a slight one,—the skin of a scarlatina patient remaining red in the bath,—yet it exists, although a mere temporary increase in the functional activity of

* "Ueber Scharlachtherapie," *Deutsche med. Wochenschrift,* 1882, S. 617, 618, 632.

the heart, caused by increased resistance, is less than ever to be feared.

When the bath is at an end, the patient is lightly dried and returned to bed. Variations in the procedure are required according to the circumstances. If the case is a light one, the severity of the general affection being of greater significance to the experienced physician than the temperature, fewer baths need to be employed, and they may be repeated, according to the case, every four or six hours. Should the temperature not reach 40° C. (104.0° F.) at any time, or should it temporarily fall so far during the day as to warrant the term "remission," lukewarm baths will be sufficient, or even sponging will suffice. In mild epidemics measures such as have just been mentioned are absolutely unnecessary. Only the febrile excitement that appears toward evening during the early days of the disease makes it desirable to give the patient some relief.

The condition of the heart and brain should always be carefully observed, since both organs, exposed as they are primarily to the influence of the scarlatinal toxin, may require antitoxic measures In the severest cases this is hardly possible of attainment by any means, and death pitilessly claims her prey. We need only to look at the above Observations II to VI, accompanied on the one side by the slightest, and on the other by very considerable, rises of temperature.

How is one to act in such a position? I shall not make any definite suggestions, since many points have to be weighed and considered that have little to do with the cases themselves. It always makes a very great difference whether the attending physician has formed the conviction that he is at the death-bed. To arrive properly at such an opinion requires great experience, the optimist thinking at odds with the pessimist. It must also be seriously considered whether the physician really has the confidence of the family. If this is unconditional, he will be able to act more freely than he otherwise might. Finally, the feeling of those around the patient must be considered, for they are at one time ready to anticipate an unavoidable fate, and at another eager to fight until the last second. The physician must calculate in regard to all these things, and I believe that it is not the poorest doctor that does so. One point may still be mentioned: the unconscious scarlatina patient appreciates none of the discomforts that the treatment would cause him were he fully himself. Nor do I believe that the patient runs any risk on account of it; and have neither myself, nor have any of my assistant physicians in the cases treated by them, formed the impression that this is so. Of

course, I presuppose that the treatment is not altogether non-sensical.

The treatment may be instituted as follows:

1. Upon signs of marked stupor and subnormal temperature, a douche of quite cold water, of short duration, chiefly over the back of the neck and head, and given with the patient in the warm bath. If a positive result is obtained, even if only a temporary one, this may be repeated after one or two hours.

2. If convulsions are also present, a long-continued (ten to fifteen minutes) warm bath, and then, at the end of the same, a douche as before. No narcotics are to be used.

3. In case of high fever it is important to discover whether the skin is hot or cold.

(a) If the latter, the condition suggests a considerable weakness. An injection of ether, often followed by camphorated oil, if the condition has improved and the pulse has become stronger, or is only, as is often the case, barely to be felt. Of both these substances, too small quantities should not be used. The ether injection may, in certain cases, be repeated every half-hour, and that of camphorated oil only after a long time—about ten hours. If the skin is cool or even cold, it cannot to any considerable extent give off heat in the cool bath, yet thermic stimulation will awaken a response. The application of cold is justified only when a sufficient quantity again begins to circulate at the periphery. We may attempt, in addition to the cardiac stimulants, to see how far we may obtain a result with a warm bath (about 40° C.—104.0° F.) in which the patient remains up to ten minutes, while his skin is being well rubbed. I do not lay much weight upon this, to be sure, and whatever success is attained will be owing to the stimulation of the heart action. Should the condition so far improve that the worst symptoms would seem to be averted, even in the slightest degree, then the skin, which has become warm, may be douched over the entire body with cold water, though only for a minute. If the skin has not first become warm, this is absolutely contraindicated.

(b) A high internal and external temperature of the body—genuine hyperpyrexia, without marked influence upon the circulation, and accompanied by a hot skin—calls for the earliest and most active measures.

The brain symptoms may be of any type; and on account of this, the attempt to better the condition by means of reducing the temperature is not contraindicated. Close attention must, however, be paid to the heart. If there is a high pulse-rate, as is usually the case, I make

it a custom always in advance to use strong cardiac stimulants, whether in the shape of strong wine or of an injection of camphorated oil. There is no indication here, I believe, for the rapid and brief action of the ether.

If the temperature of the body has suddenly risen to 41.0° C. (105.8° F.) or 42.0° C. (107.6° F.), no one can tell whether, in addition, true symptoms of intoxication are present or not. An attempt to better the condition by reducing the temperature is not only allowable, but necessary, if—and this is indispensable—the heart can do the work that it is called upon to do.

If we decide to act, let it be with vigor. Therefore, quite cold baths of not too long duration, and repeated, according to necessity, hourly or every two hours. In addition, *douching the head and back of the neck* with still colder water when possible, both in the beginning and at the end of the bath.

. The general condition of the patient soon demonstrates whether there is still hope. If there ensues no genuine fall of temperature, and if the readings, taken immediately after the bath and one half-hour later, show no appreciable fall in the thermometer, then there is little improvement to be anticipated. In such cases the hyperpyrexia is only an accompanying symptom of the breaking-down of the nervous system, due to the scarlatinal toxin. No result will be attained (see Observation IV) in cases in which three cold baths, two hours apart, are unable to overcome the rise of temperature. For a brief moment the consciousness may partly return; but brings no real advantage.

4. Severe bronchitis seems to me to justify the attempt to combat it, even when accompanied by severe general phenomena. The principles discussed in connection with the therapy of measles will be adhered to in such cases.

That we may dispense with the internal remedies directed at a reduction of the temperature in scarlatina seems to be more and more generally recognized. I have given them up long since; for even should we depress the temperature by their means (this may succeed in cases characterized by hyperpyrexia as the expression of the extreme brain intoxication, though only through unusual doses), the brain symptoms disappear to no greater extent than the heart recovers itself. On the contrary, the cardiac weakness becomes rather more marked than diminished; especially if a too sudden attack is made upon the body-temperature. In the latter event the blood supply required for the nourishment of the brain is endangered. I recall the anemic delirium following the crisis of a pneumonia. Moreover, attention should be called to the fact that all of these remedies are not acceptable to the living protoplasm. The unwise use of antipyrin by the laity during the last influenza epidemic has, I think, supplied sufficient warning for the time being.

Has the employment of the cold water treatment *an influence tending to the production of nephritis?*

I have previously stated that in not a single instance have genuine colds proved of any significance in the convalescence of scarlatina. Patients in a febrile condition do not take cold; the correctness of this view being, nowadays, hardly contested.

Let us listen to the opinion of Leichtenstern,* who has seen and carefully observed the largest number of cases: "My statistics, based upon a very large supply of material, justify me in the conclusion that the cold-water treatment of scarlatina markedly diminishes the tendency to nephritis as a sequel rather than increases it."

Whether the influence upon the circulation which I have mentioned, which also acts for the good of the kidneys, takes a part in this or not, may remain uncertain; we will be satisfied with the possession of the fact. Nor do we see otitis more frequently under the treatment.

Leichtenstern asserts that there is no ground for a contrary belief. The idea that the exanthem is driven into the internal organs by the cold baths belongs to the world of fables. Leichtenstern has seen a most favorable action upon the skin, in that the itching subsided in his patients. My own observations have not invariably confirmed this statement.

Our discussion upon this point has related only to the symptoms caused by the scarlatinal toxin itself, and the high temperature. Nothing has been said of the simultaneous involvement of the organs. I will consider the latter at the same time with the other infections that complicate the course of scarlatina; for etiologically they can by no means always be separated.

First, with regard to the water treatment and the contraindications that are said to exist to its use.

Intoxication and fever are typical of the septic processes, which take first place among the secondary affections. We are far less frequently concerned with gangrene and its consequent conditions—the septic intoxications.

The statement should be made at once that I place no great confidence in the water treatment in either the former or the latter condition. Whether there actually is any benefit from its use becomes more and more questionable with the passage of time.

I have briefly characterized my position in my book on "The Spinal Pathology and Therapy of Septicopyemia,"† after a rich experience, as follows: "A systematic treatment by cold bathing should be dispensed

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* *Loc. cit.*, p. 616.   † S. 310, 311, 3d edition.   Leipzig, Veit & Co., 1894.

with. The significance of the fever is decidedly secondary to that of the intoxication; if there is a continuous fever present, with high or even very high temperature, the intoxication is of such a grade that it alone causes death. The lower temperatures, frequently of only short duration, and with slight intermittent rises, require no special treatment. Whoever employs the cold baths in high fever of such a nature soon convinces himself that they do no harm, but also no good. There is for a period merely a reduction of temperature, and at no time is the sensorium more clear. Cold spongings are very agreeable to patients that perspire freely.

"In other respects the use of the water treatment has only a symptomatic indication; for instance, extensive catarrh of the bronchi indicates the cold douche in a warm or a lukewarm bath." All of the foregoing applies still more aptly to the putrid intoxications.

I have gained the impression that in sepsis the administration of small quantities of phenacetin is of advantage, at least in so far as the drug lessens the discomfort of the patient.

The influence upon the temperature, even in large doses, is uncertain, and I have never seen the course of the disease favorably influenced by its use in this way. For adults my maximum dose has been 0.5 gm. (7.71 grs.) and upward, four times daily; in children, from 0.05 gm. (0.77 grs.) up, and just as often. As this drug is insoluble in water, it is well to dispense it in the form of pastilles, and especially for children, unless one has to consider the greater expense of the preparation. I write for:

R. Phenacetin . . . . (0.05) 0.5 gm. (7.71 grs.)
    Massæ cacao . . . . (1.0) 2.0 gm. (30.86 grs.)
M. et ft. trochisc. No. xx.
Sig. —One four times daily.

Contraindications to the cold bath treatment are:

1. All markedly developed conditions of cardiac weakness, from whatever cause, in case the attempt to considerably increase the cardiac action by stimulants fails. Since this applies also to scarlatina, as above stated, it comes into prominent consideration in the case of all the sequels. In the presence of evident anatomic and especially inflammatory processes—as a rule, an inflammation involving an entire organ, a pancarditis—I avoid on principle any direct attempt at reducing the body-temperature.

2. All signs of dyspnea accompanied by stenosis of the upper air-passages. Violent respirations can, in such cases, only bring harm to the patient.*

3. Hemorrhage from the nose, the mouth, from eroded vessels in the neck, in hemorrhagic diathesis.

4. All joint inflammations. If no appreciable advantage is to be

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* See the conclusions under " Measles" in regard to this question, pages 305 *et seq.*

expected, we should spare the patient the pain that is unavoidably caused by the exertion involved in the bath.

These are essentially the contraindications as enumerated by Leichtenstern. The absolute rule holds good in the treatment of the sequels of scarlatina as in the long-drawn-out course of any disease, that we must place the greatest importance upon keeping the nourishment, the supply of food, and the strength at a high point. I would lay great stress upon the administration of alcohol, which, often enough, for a time comes into play as our only reserve remedy.

[**Preventive Inoculation with the Virus of Scarlet Fever.**—Stickler [*] attempted to produce a mild type of the disease by inoculating children (exposed?) with mucus from the throats of recent cases of scarlatina, injected subcutaneously. He found that the type of disease produced was too severe to sanction the use of such attempts at securing immunity. Incidentally he proved that the secretions of the mouth and pharynx at the outbreak of the disease are highly virulent. Hardly any incubation period is present in fever thus produced, as the temperature rises within two hours and the rash appears in most cases within the first twenty-four hours.

Serotherapy of Scarlatina.—In 1896 Josias, of the Trousseau Hospital, gave an account of the experience of this institution with Marmorek's serum. The results were disappointing. A comparison of two series of cases, in one of which the serum was employed, appears to show that the latter offers no advantages over a regimen consisting chiefly of milk diet and antiseptic lavage of the throat.

Blood-serum of Convalescents as a Specific in Scarlet Fever.—Roger [†] relates a single case in which he applied this resource with apparent benefit. The patient was in the second day of the disease, and comatose. He did not improve under hydrotherapy and saline infusion. Death seemed imminent, and a serum was rapidly prepared from the blood of a convalescent from scarlet fever. The patient himself was first bled and the convalescent serum (80 c.c.— 2.7 fl. oz.) injected into a vein. Five hours later the patient had rallied, but was still in a grave condition. The cool baths were resumed and the gain in improvement was notably increased. Next day there was a complete absence of unfavorable symptoms, and the patient made a good recovery. Roger does not attempt to generalize from this single case.

Credé's Ointment in Severe Scarlatina.—Baginsky [‡] has em-

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[*] "Trans. Med. Soc. New Jersey," 1897.   [†] *Presse méd.*, 1896, iv, 425.
[‡] "Die Therapie der Gegenwart," 1900, p. 252.

ployed Credé's colloidal silver ointment in numerous cases with a view of antagonizing the septic element in scarlet fever. The cases selected for the trial were of unusual severity. The method of inunction was that prescribed by Schede himself. The results of the treatment were disappointing in every way. Only 3 out of 13 cases survived, and there is no assurance that this termination would not have been secured without the remedy, which failed to prevent the development of certain local lesions (nephritis, otitis media, etc.) and seemed to exert no specific influence at any time.

Eucalyptus Inunction.—Curgenven* writes a paper on the experience of Priestley and other physicians, including himself, on the use of eucalyptus inunctions in scarlatina. A consensus of testimony among those who have used this resource is that the death-rate under these circumstances is very low, the number of complications much fewer in proportion, the duration of the fever less, and the disinfecting power great—as shown by the failure of the disease to spread to other individuals.]

TREATMENT OF THE LOCAL AFFECTIONS.

1. **Pharyngeal Organs and the Nose.**—The specific influence causing the changes in these localities is not known to us. The objects of our treatment, however, are to limit the inflammatory process, to prevent localization of micrococci, to prevent an extension to neighboring tissues, and to remove promptly and thoroughly all necrotic tissue. The limit of our power is already indicated to a certain extent, in that it is by no means clearly enough marked out.

[**Treatment of the Early Purulent Rhinitis of Scarlatina.**—At the isolation hospital at Porte d'Aubervilliers † this much-dreaded complication is treated essentially as follows: Prophylaxis is all-important, for, once the condition is fairly established, it is often impossible to arrest its action; and even when the discharge is checked, the patient may succumb rapidly to general infection.

When the patient is first attacked, the nasal passages should be irrigated at regular intervals. A Nélaton catheter is passed through the nose and out of the mouth so as to bring three small apertures previously made with scissors in contact with the nasal fossa, and later, if desired, with the pharynx. This catheter is then connected with an irrigation apparatus. The fluid escapes externally through the eye of the catheter, as well as through the apertures. The irriga-

* *Med. Magazine*, Lond., IV, 470.   † *Rev. d. mal. de l'enfance*, Feb., 1901.

tion fluid is composed of equal parts of peroxid of hydrogen and solution of sodium bicarbonate (4 : 1000). The reservoir should be from 20 to 30 inches above the patient. The irrigations should be practised three or four times daily and twice during the night. After each irrigation a little mentholated or resorcinized ointment is introduced into the nostrils with a tampon.]

In order to relieve the pain due to the angina, the patient is allowed to let small pieces of ice melt in the mouth, and to wash it out with cold water. Some prefer the ice-collar, others a hot poultice. I tend toward the use of the latter unless a marked swelling of the glands should contraindicate. All other indications are those for the mechanical forms of treatment. The best procedure that I can recommend is the spray, and I believe that Monti has described the method used by us for years in the policlinic. The point of a small syringe is covered with a fairly thin rubber tube, which is filled with ice-cold water, and introduced into the anterior part of the mouth. We then empty the contents with decided force, holding the body of the syringe firm, and repeat the procedure several times. Any separable mucus, or secretion that is not too firmly adherent, will be discharged from the mouth and nose—the latter method being especially emphasized. Nothing enters the larynx, the epiglottis closing at once; though if the latter is no longer able to close, owing to paralysis or necrosis, the method is not permissible. The procedure appears to be a crude one, but it is highly effective, and can be carried out in a short space of time. The relief is such that older children sometimes even ask that it be repeated.

I do not believe that much is to be gained through the so-called disinfectants, whether used in the form of a spray or by direct application to the mucous membrane after cleansing. Concentrated solutions of such substances as have any value, such as mercuric chlorid, cannot be employed. Moreover, it is a question whether they penetrate through the superficial layers of the tissue into the deeper layers, either when painted on the surface or simply touched on different areas. I conscientiously avoid any violent measures. Such torturing of patients as was customary in the beginning of the sixties, when diphtheria again became epidemic, by means of deep cauterization with hydrochloric acid or with caustic potash, in all forms of membrane formation or in membrane-producing affections of the pharynx such as accompanied scarlatina, comes vividly into memory. Hardly any one carries out such heroic measures to-day. But it cannot be expected that mild endeavors will be of any avail where the most active fail. It is

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necessary, therefore, to only remember how quickly the lymph circulation from a focus of inflammation carries the micro-organisms to other parts (Cohnheim) in order to understand how slight the prospects of success are. And what do we know as to the influence of the "mild" disinfectants in destroying the life of pathogenic micro-organisms? Do they deserve their title? Nothing of any importance is to be anticipated from them; they always cause pain and inconvenience. I personally prefer to spare the patient.

Heubner[*] has recommended the injection of a 3% solution of carbolic acid into the substance of the tonsils or into the soft palate. The cannula that is used (which can be attached to every Pravaz syringe) has a point only 0.5 cm. (0.19 in.) in length, so that it is prevented from penetrating the tissues too deeply. Twice daily 0.5 c.c. (8.11 minims) is injected into each side. On the third or fifth day of the disease, if the membrane is extending further, or if it now for the first time makes its appearance, and especially when a marked swelling of the lymphatic glands becomes apparent, with a tendency to a rise in the fever, the treatment should be begun. It is to be continued until every considerable rise of temperature has ceased, and the local pharyngeal affection is completely healed—as a rule, from four to ten days. The result appears in that the membrane ceases to extend further and that which is already present becomes less. There is also a marked diminution in the size of the glands.

On principle, no objection can be raised to this method, if it combats the cause of the disease (Heubner considers the streptococcus discovered by him as such) on the spot, and at once makes its way with the latter into the lymph glands. But the results have not yet become conclusive enough to warrant our standing sponsor for it. Von Ziemssen and Sahli have recently[†] expressed their acknowledgment of its value. Heubner has been able to show a favorable decrease in the mortality from a long series of observations, which, as he properly remarks, are always of limited value; the statistics are so large, however, "that it cannot have been only an accident." In the Leipzig district-policlinic Heubner treated, from 1877 to 1879, 151 cases without the injections, and with 25% of deaths; from 1880 to 1888, 211 cases with injections, and of this number only 8% died. As

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[*] "Ueber Scharlachdiphtherie und deren Behandlung," "Verhandlungen des V Congresses für innere Medicin," 1886, S. 374; also "Bemerkungen über die Frage des Scharlachdiphtheritis und deren Behandlung," "Jahrbuch für Kinderheilkunde," N. F., Bd. xxxi.

[†] "Verhandlungen des XII Congresses für innere Medicin," 1893, S. 192.

the procedure is a simple one and hardly painful, further investigation is very much to be desired.

[Seibert continues to employ ichthyol in scarlatina with much success. He first recommended it in 1894 for the dermatitis only. He has since employed it additionally for the angina in the form of an irrigation (5%) for the throat, applied through the nose (or mouth, if the nose is impermeable).

The author's experience has assured him that the ichthyol thus exhibited is non-toxic. It appears to destroy the streptococcus in the body as it does *in vitro*, to cut short the angina, and to prevent complications due to this germ. He also regards ichthyol irrigations as a prophylactic against the disease.]

2. **The Lymph Glands.**—Only those need be considered that are secondarily infected from the nose and the pharyngeal organs. The glands that owe their enlargement to the scarlatinal toxin circulating in the blood require no attention, unless in exceptional instances. The treatment of the original focus is to be considered a prophylactic measure. If it is neglected,—as frequently happens, I am sorry to say,—*what is then to be done?*

We may apply cold; and ice in rubber bags, closely surrounding the involved parts, furnishes the best means to retard the inflammation and to prevent its proceeding to pus formation. As a rule, if not always, a flannel layer is advisable next the skin of the patient. This local extraction of heat should be continued day and night. It is only allowable, however, when the skin that covers the swollen packets of glands is not blanched and traversed by veins that raise themselves from the white surroundings as thick cords, and there is no edema present depending upon a disturbance of the lymph circulation. Inflammatory edema, on the other hand, and a red, hot, swollen skin, of course present no contraindications.

An error that is by no means infrequently committed in practice is the continuance of the ice-treatment over too lengthy a period, or, if advice is summoned too late, it is often employed when it is no longer of use. It certainly does harm when it disturbs the circulation in the inflamed portions more than is proper, and death of the insufficiently nourished tissue is then the result.

If the symptoms are those of an imperfect blood and lymph circulation, the application of moist heat—the thickest poultices, and as warm as possible—is to be recommended as the best adapted for the case; indeed, absolutely required. One does well, I think, as a general rule, not to let the cold exert its influence too long. If in the course

of a few days the swellings have not markedly subsided, one should no
longer hesitate for fear of suppuration. And if the latter process is
already present, the knife must be called upon for assistance as soon as
it is detected.

Not only the general disturbance, the continually high fever, and
the transference of all manner of toxic substances into the general
circulation, but the tissue necrosis due to the pus which is compressed
within the tissues and encroaches upon them, require an incision. We
should not wait until the abscess appears directly beneath the skin.
The incision itself, as well as the after-treatment, fall naturally under
the domain of surgery.

An attempt to cause the subsidence of the glandular swelling by paint-
ing with tincture of iodin, or by rubbing in iodin ointment, blue ointment,
and ichthyol ointment, is of no avail, only irritating the skin, and may be
entirely dispensed with.

3. **Otitis and its sequels** are to be treated according to the princi-
ples of otology. A doctor of internal medicine is in such matters abso-
lutely incapable.

4. **Nephritis and Dropsy.**—We must deny to every one the power
to prevent renal inflammation. It is, on the other hand, perhaps pos-
sible to regulate its course somewhat and to diminish its severity. I
hold to the old rule, that every scarlatinal patient, whether lightly or
severely affected, should be kept in bed at least four weeks, and longer
if the epidemic is one in which there is much nephritis; not because I
fear his catching cold, but because I am of the opinion that a uniform-
ity of the body-temperature such as is insured by rest in bed may have
a marked significance. A clear conception of the origin of a nephritis
can hardly as yet be claimed. In regard to the nourishment, we avoid
everything that transgresses the cardinal rule that one should give to
scarlatinal convalescents, as rapidly as possible, a substitute for what
they have lost during the disease. For this purpose a milk diet is
hardly suited, and in this opinion I heartily coincide with O. Vierordt's
recent statements.*

Heretofore there has been much fear of giving a diet rich in albu-
min. This is without ground. The functional activity of the dis-
eased kidney has been proved, by means of Prior's† experiments,
adequate for the excretion of the nitrogenous bodies manufactured
from the albumin. It is certain that the normal active principles of
the urine, and especially urea itself, exert a stimulating influence upon

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* *Loc. cit.*, p. 203.   † See page 557.

the kidneys only so long as they augment the renal activity and increase the diuresis.

If we reason from the ever-probable hypothesis that the renal inflammation is due to a substance originating somewhere, perhaps everywhere, in the human body, which by its passage through the organs engaged in its excretion—the kidneys—is able to exert upon them an irritative influence, one conclusion becomes evident, viz., that the hypothetic toxin should be caused to pass through the kidneys in the highest possible dilution. For this purpose urea, which is formed in large quantities, and likewise large quantities of drinking-water, are especially well adapted. The functional irritation or stimulus of the kidneys must be sharply differentiated from that which is inflammatory, and it must not be forgotten that in the former a circulation through the organs of large quantities of healthy blood must have a beneficial influence.

Objections to this form of reasoning are possible if the ground is taken that the toxin in question is itself certainly destroyed, provided it remain for any length of time. In such an event it were unnecessary to float the toxin away; indeed, it would do harm. But to my mind there are no facts that warrant such an interpretation.

Of course, such forms of nourishment must be avoided as tend to cause digestive disturbances. "Bland diet" is the term that is applied to the proper form of food, though it will be well not to extend the meaning of the expression into too great a resemblance to that of former times. Our present understanding of physiology reaches further, and permits of more procedures that have an end in view, and that are suitable to the individual case. Therefore a free diet, even of the albuminous foods, and not too small a quantity of liquid. The acids are very appropriate in this condition, and alcohol is not contraindicated, if there is any need for it, though it is well not to use it in the form of beer.

Daily baths should be given at the temperature of the body, and lasting for a quarter or half an hour, and are, with good reason, quite generally recommended. They have a beneficial influence upon the reproduction of the skin, which has suffered in nutrition owing to the scarlatina. After the bath the patient must be returned into the bed, which, when necessary, should be thoroughly warmed. His skin must first be well dried and rubbed, though not with too much force. The temperature of the room should be kept at about 20° C. (68.0° F.), and the patient not too lightly covered.

The temperature should be taken at least twice daily, and it is

better to estimate it morning and evening, and in the middle of the day. The amount of urine excreted daily is to be carefully observed, and in the policlinic we lend a graduated cylinder to the family, in which the urine can be poured after evacuation. The people can be accustomed to such great accuracy that if they see anything peculiar in the cylinder their attention is attracted to it. It is usually taken care of and seldom broken. It is also recommended that a tablet be kept with it, in which regular notes are entered.

When possible, an examination should be made daily for albumin, and this can be done perfectly well at the bedside. Admixtures of blood, when at all considerable, seldom escape the experienced eye, in case the urine is kept in a glass cylinder. The same may be said of a marked turbidity, which in certain cases, necessitates a microscopic examination. I lay great stress upon this form of vigilance, because it enables one to recognize involvement in the very beginning. It need not be said that one must look just as diligently for the edema which often precedes even the albuminuria, or the hematuria, in point of time; in this respect special attention is to be paid to the eyelids.

As soon as there is a suspicious appearance, I employ hot baths, with a hot pack following. One should begin with water at a temperature of 39° C. (102.2° F.), and leave the patient fifteen minutes in the bath. He is then directly wrapped in a linen sheet soaked in hot water, and with one or more blankets, laid in a warm bed, and well covered up. After one or two hours, during which he is given considerable quantities of hot fluids, the patient is relieved from his wet coverings and rubbed well with warm, dry towels. He is then given fresh, warm clothing, and lies as usual in the bed. Care must be taken that the latter is neither moist nor cold. The patient is also to be warmly covered after the bath.

Usually there is an immediate and free perspiration, which lasts by no means seldom for several hours. In many cases there occurs simultaneously, or soon thereafter, an abundant excretion of urine. In the case of an outspoken nephritis this procedure is to be gone through with twice daily. The temperature of the bath is raised to 40° or 41° C. (104.0° or 105.8° F.), and this is best accomplished by beginning with 39° C. (102.2° F.) and raising the temperature by the gradual addition of hot water. The duration of the bath may be lengthened to an hour, but, as a rule, a half-hour is sufficient. A wet, cold cloth on the head should be frequently changed during the pack; this hinders as far as possible congestion of the brain. I make a regular practice of observing this precaution. A febrile condition does

not contraindicate diaphoresis when instituted in this manner, even when the temperature is very high.

I have gained the impression moreover, that it is a truly advantageous measure. Yet I lay no great weight upon the fact that during a long space of time—more than thirty years—whenever I could use the method from the beginning of the affection I have only in rare cases seen death follow. This may be accident, and we certainly have had in our policlinic no scarlatina epidemics with severe nephritis. Moreover, there is no time when one should be more reserved in his estimation of therapeutic results than in scarlatina and its sequels. For this reason I wish to present my experience just as it occurred.

With regard to the use of hot-air baths, which are now applicable by means of a very simple procedure, I have had no personal experience. Possibly they are as useful or are to be preferred to the warm water baths.

In the further course of scarlatinal nephritis one may attempt the use of diuretics. I have not had much benefit from the potassium acetate, but in the use of diuretin (theobromin-sodium-salicylate), and from the double salt of sulphuric acid with caffein and sodium, I have noted an increase in the amount of urine excreted, though by no means as a regular occurrence. These preparations can hardly work any harm, and I consider them worthy of a more extended trial. On the contrary, it is indeed a question whether calomel is harmless. I have never tried it in this form of nephritis, and the majority of German physicians appear to have used it just as little. Digitalis comes into play as a cardiac remedy in nephritis, as in every case, with its peculiar power, and is often a grateful measure. The general rules for the administration of the drug apply in the cases under discussion.

And now to pass on to the treatment of uremia. In the light of the many meanings involved in this term, or, to express the thought more satisfactorily, with the causes of uremia as various as its phenomena, it will hardly be possible to find a method of treatment that will always be applicable. The more general indications will therefore be appropriate.

There is no question that uremic symptoms may appear, even when there is a copious excretion of urine. This, however, is decidedly the exception to the rule, and the principle may in most instances be counted upon, that a decided diminution of the functional activity ushers in the uremia. It follows, then, that uremia hinders the processes that diuresis favors. Moreover, the treatment that has just been discussed as proper for nephritis is, at the same time, one calcu-

lated to prevent uremia. We may take this opportunity to emphasize more clearly two other distinct forms.

1. With the perspiration certain soluble constituents of the blood can be extracted and cast off. Moreover, it cannot be denied that there may be among the latter certain substances which, by developing poisonous influences, become the direct causes of the uremic attack, although we do not recognize and cannot discover them. The attempt to produce free sweating has always found its justification in this view.

2. The fact that a copious circulation of healthy blood is conclusive of the preservation of the functional activity of all portions of the body has been positively determined. If, now, uremic phenomena depend upon the influence of genuine poisons, and if they may be produced by (inflammatory) edemas of certain portions of the brain, either for this or some other reason an active circulation is qualified in the highest degree to combat them. We must therefore increase the work of the heart and of the respiratory muscles in order to influence the circulation most actively.

In this way we learn to understand why not every diaphoretic may be used as an effective means of cure. Pilocarpin, for instance, has such a limited field of usefulness that some—and I am one of the number—advise against its use in any event. Its depressing effect upon the heart raises a well-founded objection to its use.

The cathartic class of medicines produces effects that are by no means certain; these drugs are not dependable assistants in the time of need. Voluntary evacuations of the bowel we should seek to check only when they are leading to a great loss of fluid from the tissues. This necessity exists only in the rarest and most exceptional cases on account of the dropsical effusions that nearly always are present. The evacuations may be of advantage to the patient, and the symptoms of uremia disappear; still more frequently they may fail to appear in spite of the very localized disturbance of the functional activity of the kidneys, although a large quantity of fluid had been evacuated through the bowel. But to produce this effect artificially is an entirely different matter, and by no means a safe procedure; for ulcers may form, owing to the breaking-up of the urea that has been brought to the mucous membrane into ammonium carbonate, and the result is, to say the least, an unwelcome addition to the general picture; still more, it is an actual and serious danger. I do not recommend the procedure.

The typical uremic attack is in no way dissimilar to eclampsia in its widest meaning. It has, in common with the latter, the serious

hindrance to respiration and to the circulation, also the disarrangement of the supply of blood and air to the tissues. There is also the paralysis resulting from irritation of the brain, and the accumulation of the waste products of exhaustion in the muscles, that have for a long time been actively at work. The necessity of restraining the convulsions needs no further argument. Perhaps in the beginning a warm bath (38° C.—100.4° F.) of long duration will be of advantage, and, if only twitchings are evident, one should always make the attempt. If, however, active convulsions are already present, there is not much to be expected from the procedure. We should not wait too long before beginning the careful use of inhalations of chloroform, continuing them until the muscles are relaxed. In order to render this influence certain, there should be given in severe cases, and according to the age of the child, 0.1 to 0.5 gm. (1.54 to 7.71 grs.) of chloral hydrate in 50 to 100 gm. (1.6 to 3.2 oz.) of decoction of althea; and in the case of adults, up to 2 gm. (30.86 grs.). I would strongly advise against the subcutaneous injection of the drug.

The cardiac condition may call for stimulation, and in such cases ether or camphorated oil may be injected. Musk formerly was in frequent use, but now is seldom employed. I have often tried it, and have not been sparing in its use, but have nothing favorable to report of the attempt.

Blood-letting is recommended by certain individuals. Fürbringer * says in regard to it: " Blood-letting may have a brilliant result, and not so very seldom; but one must be exceedingly careful both in case of a beginning cardiac weakness, or of general anemia, and especially, in small children that have been weakened by the original disease." Also Henoch, in presenting the results of a great personal experience, limits himself to the withdrawal of small quantities of blood from healthy children only.

I do not wish to leave this subject without mentioning the fact that very tiny quantities of tincture of iodin—one drop to a deciliter of distilled water, in teaspoonful doses—often do good service in controlling the vomiting that so frequently forms a troublesome symptom.

Dropsy affords almost no opportunity for further treatment than by the warm bath. Effusions into the cavities of the body must in many cases be left to themselves. Occasionally it may become necessary to take active measures with the ascites, or to puncture in case of double-sided pleurisy, though I have waited even in cases that were marked by a high grade of dyspnea, and finally succeeded without active treatment. It is an important consideration with me that one

*Eulenburg's " Real-Encyklopädie," p. 482.

only obtains from the puncture a temporary result. Moreover, it has recently been pointed out that after such a procedure a serous exudate may become purulent. Should this be true, it would practically forbid the measure altogether.

Unilateral pleural exudates of inflammator·· nature are to be treated just as other pleuritides. If they persist or a long time, one must then proceed to an exploratory puncture, and, according to the outcome, determine his course of procedure.

It must be mentioned that a number of reports have recently been made* of cases in which the simple evacuation of an empyema has resulted in a permanent cure. We would, on principle, choose resection, and especially in children, since they offer such favorable prospects after the operation.

Affections of the heart and pericardium occurring in the course of scarlatina are to be treated in the usual manner. This is true, also, of the joint affections. Salicylic acid has failed me in such cases, as it has in many others.

I cannot second the warning of O. Vierordt in regard to the use of cold baths in a complicating croupous pneumonia, if nephritis is already present. The cases that I have treated throughout according to my own method have run just as favorable a course as all pneumonias in childhood; although they were not light cases. They were not in the slightest degree unfavorably influenced by the reduction of temperature.† Pneumonias with sepsis, or bronchopneumonias, act very differently, and must be treated accordingly.

I have already spoken of the advantage in the use of warm baths for a long time during the convalescence. Nothing further need be said in general of the disease, as every case must be measured according to its own rule.

* O. Vierordt, *loc. cit.*, p. 201.

† See the communication on " Some Accurate Observations," by Dr. Alexander Kees, in " Croupöse Pneumonie," Tübingen, 1883, Laupp, S. 187.

GERMAN MEASLES
(RÖTHELN ; RUBEOLA).

GERMAN MEASLES (RÖTHELN; RUBEOLA).

IDEAS CONCERNING THE DISEASE.

ACUTE exanthematous diseases which are neither measles nor scarlet fever are described as German measles. While this is certain, it is not less certain that we have to deal with things which are essentially different from each other. Single groups are sharply enough distinguished from others, may be clearly differentiated, and hence are easily classified, and this is the justification for the disease which is now called rubeola by leading physicians. But with equal right it may be said that this throws brighter light on only a part of the question, while much remains as before in darkness.

["**Fourth Disease**" **and Scarlatina.**—In an editorial in the "Archives of Pediatrics," Sept., 1901, this alleged new malady is summed up as follows: That form of "German measles" which simulates mild scarlatina is believed by Dukes and others to be an independent disease of a benign type, which derives great interest from the possibility of its confusion, under various circumstances, with scarlet fever. According to Dukes, the "fourth disease" differs from the latter affection in having a much longer incubation period, and in the absence of prodromes—vomiting, high pulse, and severe angina. In the "fourth disease" the eruption begins usually upon the face; otherwise it appears to differ in nowise from the scarlatinal exanthem. Desquamation may be profuse after "fourth disease," and out of all proportion to the severity of the rash. Generally speaking, the new malady is quite destitute of any toxic reaction.

Rötheln is considered at this date a separate disease in America. The following discussion is interesting historically.]

Henoch* makes the following statement: "My own experience does not justify me in giving a positive opinion upon this question;

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* "Vorlesungen über Kinderkrankheiten," p. 685 of the third edition.

even if I have seen here and there in a family a few children sick of a disease corresponding to the 'rötheln' of authors, and have not infrequently observed cases which made me doubtful of the diagnosis, yet I have not had the opportunity of observing great epidemics or endemics of this kind. So long as this is the case, I am not in a position to declare myself in favor of the independence of rötheln."

In fact, it has happened to me in exactly the same way. If I had to decide according to my own observations, I would have to say unconditionally: "I do not know."

Leichtenstern* gives a picture from the practical life of the physician, without contending about the question of rötheln: "The beginning of the scarlet fever epidemic came at a time when measles was also very wide-spread. At this time there also appeared exanthems of such capricious behavior that it was difficult for the most skilful to decide whether he had to do with a case of scarlet fever or of measles." Leichtenstern tells of cases in which an exanthem, which, judged by its character and localization, was undoubtedly measles, with coryza, conjunctivitis, and tracheobronchitis, occurred simultaneously with severe diphtheritic sore throat, which was later followed by an acute hemorrhagic nephritis. There occurred cases in which an insignificant angina was accompanied by severe conjunctivitis and tracheobronchitis, together with a scarlet exanthem which was uniformly distributed over the whole body. There was repeatedly, at this time, heated controversy concerning whether these were cases of measles or of scarlet fever or of both together. There were physicians in Cologne who had only scarlet fever to treat; others, who reported only measles.

[**Rubella, Scarlatina, and the "Fourth Disease."**—Watson Williams† speaks of the apparent indorsement of Duke's new disease by the profession at large, as shown by the constant increase in the number of reported cases. But the question is far from being settled, and before we can admit the existence of "fourth disease" as a separate entity, a more careful study of rubella must be made. Is there such an entity as rubella scarlatinosa? and does it confer immunity against the morbillous type of rubella?

Williams has recently witnessed a school epidemic of what was unquestionably German measles, in which the morbillous and scarla-

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* "Ueber die 1880 und 1881 in Köln herschende Scharlachepidemie." Reported by the author to the General Medical Association of Cologne, *Deutsche med. Wochenschrift*, 1882, S. 174.

† *Brit. Med. Jour.*, Dec. 21, 1901.

tinous types existed side by side. Several cases bore a striking similarity to scarlatina, and therefore incidentally to "fourth disease." One boy thus affected mingled with healthy scholars, but no further cases of this type developed. Owing to the fact that rubella breeds true, we seldom see the two types associated in a single epidemic, yet exceptions to this rule have occurred, not only in the case just related, but elsewhere, as in an epidemic seen by Dr. Fyffe in 1891.

Another phase of this question is the simulation of rubella by scarlatina, as seen in a recent milk-borne epidemic of the latter affection at Clifton, England. Cases which were diagnosticated as German measles were followed by others of what appeared to be typical scarlatina. Physicians regarded the epidemic as one of "fourth disease." Yet the victims had been drinking milk which was clearly infected with the virus of scarlatina. Other patients along the milk-route were sent to isolation hospitals, where they mingled with cases of known scarlatina without contracting the latter, nor did they propagate "fourth disease" to the scarlet fever patients.

Williams next discusses Duke's crucial feature, the incubation period, which is given as from nine to twenty-one days for "fourth disease," as well as other alleged differential points (absence of vomiting, low pulse and temperature, absence of renal complications, etc.). He shows that in the epidemic of scarlatina just narrated all these alleged characteristics of "fourth disease" were present.

It has not yet been shown that "fourth disease" protects from rubella, nor that it occurs in those who have had scarlatina.]

"As soon as the epidemic of measles ceased, the subsequent cases of scarlet fever regained their normal character, and during the year and a half in which the scarlet fever still raged, not the slightest question was raised as to the character of the disease."

Every experienced physician has seen similar things. This suggests the often-expressed thought that there is a mixed form, a double infection perhaps, in which the poison of one disease affects the nature of the other in a peculiar way. This would be a simple and perhaps also an acceptable explanation. As we know that measles and scarlet fever may occur simultaneously in the same individual, no one can deny the premises. But much remains to be explained.

1. The cases of known double infection are rare; these mixed forms occur with great frequency. But, we may say, this is a question of epidemics, in which the conditions are different and the danger of infection is greater. This is hard to contradict; but how satisfactory is the explanation, is another matter.

2. It would be of much greater importance to determine whether a person who had recovered from this mixed form had become immune to scarlet fever and measles. More significant would be the proof of the immunity to measles, because the susceptibility to this disease is nearly unlimited. If one could prove this assertion, then would the idea of double infection be much better supported. On the other hand, the objection might be raised that the coexistence of the two contagions would perhaps render the acquirement of protection futile.

It is asserted by many good observers that the disease which is called "rötheln" offers no protection from either measles or scarlet fever.* But whether among these rötheln cases are found also some which might be considered as mixed forms, occurring during a double epidemic, is another question. In order to reach a conclusion, one would need to pay careful heed to these relations.

3. Knowledge of the pathogenic causes which produce the acute exanthems will decide the question with certainty.

As the meaning of facts may change, it seems premature theorizing to depend on them, and say: If measles and scarlet fever are epidemic at the same time, then a disease may develop which unites in itself certain features of both acute exanthems. Whether it is reasonable to speak in these cases of "rubeola," I will leave undecided, but I would consider it not wise, since the name might lead to confusion.

Older physicians have gone further. Building on this foundation, they have advanced the view that the mixed forms,—the expression "the hybrid forms" was a favorite one with them,—separating themselves from their original progenitors, may win independence.

Thus the younger Hildenbrand† says: "Rötheln is explained as the joint production of scarlet fever and measles, so that now the one and now the other element prevails. The cause of this union, which takes place sometimes before and sometimes after the completed formation of the contagium, is most probably atmospheric influence. The hybrid form may, however, under favorable circumstances, acquire such maturity that it becomes independent and assumes an epidemic character."

How much truth there is in this cannot now be said. Strong adherents of Darwin would perhaps be inclined to favor it. But proof is entirely lacking. The urgent question: "Do recurrences occur?" is then justifiable. At the cost of some knowledge of dialectics and

* See page 645.

† I have not used the original articles, and cite according to the abstracts of later writers. This quotation is from Naumann, "Handbuch der medicinischen Klinik," Bd. III, first edition, Reutlingen, Ensslin, 1832, S. 825, 826. The older literature is here exactly reported, so far as it is important.

with a passion for argument, it would be safe to affirm it. The unprejudiced, however, will not accept it, because the facts in question admit of this simple explanation: Under the name rubeola are grouped certain simple cases of scarlet fever and of measles which become epidemic. This applies to scarlet fever more than to measles.

Conclusive is this representation of Heim,* who stood at the height of his influence at the time when an independent position was said to be given to rötheln right from Berlin†; Selle, professor in the Charité, is named as first combatant.

Heim says as follows: "Rötheln is, like measles, purpura, etc., a disease attended by a macular eruption, but essentially nothing but a variety of scarlet fever. A sufficient reason for this assertion is, I firmly believe, the similarity of the symptoms which are noticed both before the eruption appears and during its continuance.

"The characteristics of this disease which make it a peculiar kind of scarlet fever are the following:

"1. The sore throat is more rarely lacking, more painful and severe than in scarlet fever.

"2. The eruption is constant, which is not true in scarlet fever. When it has appeared, it rarely disappears during the continuance of the disease.

"3. The eruption is generally darker in color than in scarlet fever.

"4. The eruption appears on the whole surface of the body one day after the fever and sore throat, but there are fewer spots on the face and sometimes none at all.

"5. The macule in rötheln is of two varieties. One kind is perfectly formed at the time of its appearance, has a sharply limited but irregular border, with generally obtuse, but occasionally acute or right angles. One macule does not touch another during the whole course of the disease, however severe it may be. Their greatest diameter is from one to one and a half lines.

"The other kind appears as red points of the size of a millet-seed with indistinct, not sharply limited outlines. These either remain discrete and of the same size, or they spread at the periphery, reaching a diameter of one to one and a half or two lines. The former happens in mild cases and when the number of the spots is not large. But if the disease is severe and the eruption extensive, the macules do not so much run together as that the skin between them becomes quite red, so that on the second and some following days such an eruption resembles that of genuine scarlatina.

"But however red the skin may appear, if we observe carefully, we

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* "Bemerkungen über die Verschiedenheit des Scharlachs, der Rötheln und der Masern, vorzüglich in diagnostischer Hinsicht," Hufeland-Himly, *Journal der praktischen Heilkunde*, 1812, Part IV, S. 76.

† "Klaatsch, "Ueber Rötheln," *Zeitschrift für klinische Medicin*, Bd. x, S. 1. The author cites as proof the "Rudimenta pyretologiæ Methodicæ," published by Selle, and the beginning of the eightieth year of the preceding century as time. The quotation is not here quite exact; according to Engelmann's "Bibliotheca medico-chirurgica," Selle's work has appeared in four editions (1770, 1773, 1786, and 1789), the first with the title slightly different.

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can always make out the single red points. If one is in doubt in such cases whether the eruption is that of a true scarlatina or of rötheln, he may use the test of pressure with the finger.* The spot pressed in both cases appears for a moment quite pale. In rötheln, however, the original red point quickly reappears, the flush spreading at the periphery until the pale color has entirely disappeared. In true scarlatina, on the other hand, one never sees the same red point, but the redness returns partly from the periphery or quite irregularly, beginning at the center of the spot pressed upon.

"At times, at the appearance of the rash of rötheln, the whole skin, even that of the face, appears as red as in scarlet fever. Usually, however, the general redness disappears on the second day and the remaining macules present their usual appearance. I never saw both kinds of macules in the same individual. The epidemics in which the former kind is found are rare; the latter is the usual kind.

"6. Every macule of rötheln, with sharply or indistinctly limited borders, is, in its normal condition, quite smooth to the feeling and has not the slightest elevation, either in the middle, as in measles, or at the periphery, as have some spots in urticaria. If such a patient is kept warm in bed and treated with hot drugs, or if the heat of the summer is great, or if the patient is cachectic and inclined to rashes, or if gastric fever is connected with it, then a miliary eruption may be united with it. Such a miliary eruption in children as well as in adults when heated, with or without the fever of rötheln, is very different from the miliary eruption peculiar to scarlet fever and measles; for the former contain no visible fluid, are far smaller, and present in greater number than the latter, which contain a milk-white fluid, are much larger, and only rarely appear over the whole body, but usually only in single parts.

"Many physicians believe that these miliaria correspond to the true rötheln eruption, but this is not true. It is true that, if not two-thirds, at least half, of the rötheln patients, especially of those in whom the macules are not sharply defined, have these miliary spots, and there are epidemics in which the miliary eruption is rarely lacking. But only too often I have found the rötheln rash, especially that with well-defined borders, without miliaria, and there are other times when this disease shows no miliaria.

"7. This last-mentioned miliary eruption, which has a milk-white color and at least the size of hempseed, occurs more frequently in rötheln than in scarlatina.

"8. The rötheln eruption is usually visible for six to eight or even ten days, and when it disappears leaves no redness behind.

"9. When the two diseases, rötheln and scarlatina, appear to be of equal severity, I believe, in spite of the contrary opinion of most estimable physicians, that the former is the more dangerous.

"10. One may have the eruption of rötheln, as well as that of scarlet fever, on only a few places on the body or even not at all. But these cases are, according to my experience, far rarer than in scarlet fever. Thus, I saw in the space of fourteen days in one family six rötheln patients, all of whom had very sore throats and high fever; four children had the eruption over the whole body; the mother had the eruption only on her hands, and the father no trace of it on any part of his body.

* "The eruption is pressed quite forcibly with a finger, which is then quickly lifted."

"11. In some few cases I have seen rötheln combined with scarlet fever, but never with measles.

"12. After the disease is over, the skin desquamates in pieces, which are not so large as those in scarlet fever, but not so small as in measles.

"13. Dropsical sequels may follow, but this does not happen so often as after scarlet fever."

Examination of these statements shows conclusively, it seems to me, that Heim has here described nothing else than scarlet fever in which the form of the exanthem has been different from the usual one. This is shown even more conclusively if we examine his "tabular summary of the points of differential diagnosis of scarlet fever, rötheln, and measles."* In respect to the eruption, the differential points are abundant; in all other respects, only quantitative differences are here and there mentioned; in the first column, "scarlet fever," the symptoms of scarlet fever are given; in the second, devoted to German measles, we find quite regularly "the same here." In spite of the fact that Heim, whose descriptions indicate careful observation, ascribes to his cases of rötheln even his favorite phenomenon, the sign quite peculiar to scarlet fever, yet he considers the separation of the two diseases justifiable on account of the difference in the exanthem. It seems, then, to have been a form of the same disease, differing from the usual form. Physicians have probably diagnosed all their cases more or less by this. Besides this variety, the ordinary scarlet fever also occurred, but was rarely recognized.

This explains how the Berlin physician Formey † for the years 1784 to 1796 reported 1180 deaths in Berlin from rötheln, while only 205 were ascribed to scarlet fever and 103 to measles. Heim ‡ remarks on this point that Formey believed that there were many cases of scarlet fever among the deaths reported as from rötheln. Heim thinks that, as the "ordinary man" often confuses German measles with measles, many of these cases may also have been from measles.

Klaatsch thus briefly summarizes the descriptions of the medical writers of that time: "The disease begins with severe nervous symptoms, delirium, and vomiting, accompanied by inflammation of the throat, often with white patches. With this a uniform or irregular bright red eruption is present. It is followed by edema and desquamation in large pieces."

This is significant. I believe we are fully justified in considering as true scarlet fever the disease which at his time received the name "ru-

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*The same reference, pp. 97–107. † According to Klaatsch, *loc. cit.*, p. 2.

‡ In his review of Henke's "Handbuch der Kinderkrankheiten," *Horn's Archiv*, 1809, Bd. viii, S. 162.

beola'' or ''rubeola scarlatinosa.'' Hebra and Mayr use this latter term for scarlatina variegata, but it cannot be said that this was the form which was always seen and gave occasion for the separation of the diseases. Rather, the story teaches us that many peculiar things may be seen; as, for instance, scarlatina papulosa, a rather rare form, and formation of miliaria on the skin of scarlet fever patients, a phenomenon oftener observed in the past than at present. The warning that one should not lay too much stress on the appearance of the eruption is here again certainly suggested.

It is very probable that in early times, as at present, cases of measles were regarded as German measles. Brief remarks from the early times in regard to this are found in Naumann. But this has not been of great influence in the development of the whole study. We must now discuss the question of the justification for the separation of rötheln, as we to-day understand the term, from measles.

GERMAN MEASLES (RÖTHELN).

ETIOLOGY.

In order to be able to consider an acute exanthem as an independent disease, as a pathologic entity, it is necessary to show that its occurrence lends no protection against any other acute exanthem and that no other acute exanthem protects from it.*

How is it with rötheln? I believe the proof is at hand that neither scarlet fever nor measles grants immunity against rötheln. I select the following from many important observations: Thomas † asserts that in the year 1872 the following diseases occurred among the children of the Nitsche family:

	Rötheln.	Scarlet Fever.	Measles.
Max	February 10.	....	
George	February 27.	March 23.	} All three in July.
Melitta	March 3.	March 26.	

One of the children, who was sick at the same time as the two others, died of scarlet fever. This shows a case in which the three acute exanthematous diseases occurred in quick succession in two children.

Dr. v. Geuser, Vienna, tells of the occurrence of measles soon after German measles, followed later in two of the children by scarlet fever. The day of eruption is given in the following table ‡:

	Rötheln.	Measles.	
Elsa	April 29.	May 9.	
Fritz	May 18.	May 21.	} 1887.
Greta	May 17.	May 21.	

Elsa and Fritz were attacked with scarlet fever simultaneously toward the end of February.

In the discussion of epidemics of rötheln, it has been repeatedly mentioned that those attacked with this disease had, in many cases,

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* See Introduction, p. 203.

† "Neue Erfahrungen über Rötheln," "Jahrbuch für Kinderheilkunde," N. F., Bd. v, S. 346.

‡ "Rötheln und Masern in unmittelbarer Aufeinanderfolge," "Jahrbuch für Kinderheilkunde," N. F., Bd. xxviii, S. 420.

already had other acute exanthematous diseases, especially measles.[*] The objection has been raised that the validity of the conclusions drawn from such facts must be questioned because it is well known that the same individual may have measles a second time. The rarity [†] of this occurrence, however, is a sufficient answer to this objection and destroys its validity.

Examples are not at hand that any one who had had rötheln was again attacked with it. If this is so, then the common sentence, "like protects against its like," would be applicable to it, and another proof of its independence would be presented.

The repeated occurrence of rötheln (one must admit that it may act as an epidemic) would lead to the conclusion that it is an infectious disease. But that is not saying that it may be carried from one person to another. Many earlier observers deny this or reserve their decision. J. Steiner,[‡] in 1869, says: "That rötheln develops a contagium and is carried from one child to another is questioned by most observers, and, according to my experience, I must say that the disease is not contagious."

Later observers, however, assert very positively at least the possibility of its being contagious. I consider this proved, so far as clinical demonstrations go.

Whether the contagion is carried more or less easily, must be decided as in the other acute exanthems. Klaatsch [§] asserts that, like Mettenheimer and Thierfelder, he has repeatedly seen one child of a family sicken of rötheln, while the others were not affected. But he has also known of cases where the opposite was true.

The spreading of rötheln in institutions is of great importance in deciding this question. Thus Emminghaus [‖] gives a report of his experiences in the children's hospital at Jena; Klaatsch, of his observations in a pensionate for young women. The experiences of American physicians bring to our knowledge still more extensive reports from orphan asylums, deaf and dumb institutions, etc.[**]

The period of incubation is considered as rather long. The difficulty of securing quite definite statements of facts is here so great that

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[*] See later views from foreign literature by v. Geuser, S. 429. The rötheln question was discussed in the Seventh Internat. Congress, London, 1881, and the reports of the same contain much that is of interest.

[†] See " Measles," p. 233.

[‡] " Ueber Rötheln," *Archiv für Dermatologie und Syphilis*, Bd. I, S. 244, 245.

[§] *Loc. cit.*, p. 11.

[‖] " Ueber Rubeolen," " Jahrbuch für Kinderheilkunde," N. F., Bd. IV, S. 47.

[**] See v. Geuser, *loc. cit.*

it is necessary to rely on general statements. These show that, as a minimum, the period of incubation is one day (the American physicians, Atkinson and Griffith); as a maximum, however, it is more than four weeks (Klaatsch). On the average, the duration is considered as more than fourteen and less than twenty-one days.

Children are more frequently attacked than adults. Infants show slight susceptibility. The greatest susceptibility is from the time of the second dentition to puberty.

It is assumed that the children of the poor are more frequently attacked than those of the well-to-do. This is because the opportunities for infection are so much greater.*

In addition to the different parts of Europe, rötheln is observed quite frequently in the United States of America. This is not saying that it does not occur in other places, but where the sanitary conditions are less carefully guarded, the disease is only too easily overlooked. Yet Thomas,† who had the public in his power in his Leipzig policlinic, complained much of the indifference of the relatives, which rendered observation difficult for him.

Epidemics are said to occur oftener in the first half of the year.

PATHOLOGY.

General Picture of the Disease.—Thomas ‡ gives the following description of the course of the disease: "After the patient has for a few hours to a day coughed and sneezed and shown some dislike to the light, the beginning of the eruption is observed in the face, either without any further symptoms or with a rise of temperature. While the eruption spreads gradually over the whole body, the temperature, after reaching its height, returns quickly or slowly to normal. The general condition is not disturbed in these mild febrile cases, while in cases of higher and more lasting fever there is a slight indisposition. Most children will not remain in bed, but are found out of bed or even in the open air.

"Local symptoms of the disease other than those of a slight catarrh, and with it some difficulty in swallowing in cases of severe

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* Compare with Emminghaus: "Rötheln," in Gerhardt's "Handbuch der Kinderkrankheiten," Bd. ii, S. 344.

† "Jahrbuch für Kinderheilkunde," Bd. v, S. 345.

‡ In v. Ziemssen's "Handbuch," Bd. ii, 2d edition, S. 155.

angina, as well as temporary and slight disturbance of appetite, do not occur in normal cases of rötheln. Some nervous symptoms, chilliness, heat, thirst, etc., are present only during the fever and are proportioned to this in point of severity.

"After the fading of the exanthem, or even before this fades, the symptoms of irritation of the mucous membranes disappear, either at once or after a temporary mucous discharge. Convalescence usually progresses quite undisturbed."

A severe form of the disease has not been observed in German epidemics. On the contrary, from America* come reports of epidemics of malignant rötheln in which during the invasion the symptoms of a severe infection were observed—vomiting, convulsions, delirium, etc. The temperature during the eruption rose to 40° C. (104.0° F.), the pulse to 150 beats, and even heart failure supervened. Pneumonia, bronchitis, pleuritis, so-called complications, occurred repeatedly. Still oftener, gastro-intestinal disorders, slight albuminuria, and even dropsy were seen.†

It cannot probably be asserted positively whether these were epidemics of true rötheln or of another acute exanthematous disease. Scarlet fever teaches us that we can form no conclusion as to the nature of a disease from its variable severity.

In the year 1863, in the Policlinic of Kiel, I saw a large number of cases, which were not measles and were not scarlet fever, although in most particulars they resembled the former. They were by no means trivial diseases and were often accompanied by capillary bronchitis and bronchopneumonia. I lacked the wide experience necessary to give a positive diagnosis; but Bartels was of the opinion that we were dealing with a special disease. In several cases, according to our opinion, the period of incubation extended to nine days, reckoned from the possible infection to the breaking out of the eruption. This and the circumstance that many of the patients had had measles a short time before (epidemic of 1861) satisfied Bartels. I will give only this brief notice, as I have to depend upon my memory of the cases.

OBSERVATIONS UPON THE SYMPTOMS.

Duration.—There is not much to be said on this subject, as all the symptoms disappear after a very short time.

Premonitory symptoms may be wholly lacking, in which case the

* See v. Geuser, *loc. cit.*, p. 426. The sources are not accessible to me.

† Of 166 cases in an epidemic observed in a Philadelphia hospital, 1881–82, 7 died of these complications. Reported by W. H. Edward, *Am. Jour. of Med. Sciences*, Oct., 1884.

eruption is the first indication of the disease. In other cases the patient presents for days—as many as four are mentioned—symptoms similar to those appearing in the enanthema of measles.

So we have really a slight inflammation of the conjunctiva and of the mucous membranes of the nose, pharynx, and larynx. Swelling of the glands at the angle of the lower jaw may also be noticed. In addition to these symptoms, there may be malaise, with disturbances of the appetite and headache—sometimes pains in the limbs, dizziness, and in children even convulsions have been observed.

Elevation of the temperature, perhaps ushered in by a chill, may be shown. Emminghaus,[*] who describes a relatively long prodromal time, generally three days, gives an increase of one degree above the normal; in later publications he fixes the temperature at 39.0° C. (102.2° F.).

All the symptoms may show vacillations and even disappear before the appearance of the eruption.

The duration of the eruption may be very short, even limited to hours, or it may last for days. The average duration is two to four days; the maximum, six to seven days.

A time limit for the period of desquamation cannot be set; the often very slight desquamation follows no rule.

Temperature.—It often happens that no elevation of temperature is observed at any period of the disease. The number of these cases is not small, but differs materially in different epidemics. Emminghaus[†] observed elevation of temperature in all his cases; Thomas frequently failed to observe it, but adds the limiting phrase, "at least during the period while I was observing my patients. If, then, an elevation of temperature was present, it must have been before my observations began, and must have disappeared soon after the eruption appeared in the face, which, according to the anamneses, is not very probable."[‡] Von Nymann, who, in an educational institution for girls, had considerable opportunity for investigation, had, according to the statement of Thomas, among 119 cases, 53 without and 61 with elevation of temperature, which was thus just about one-half.

The thermometer may show a not inconsiderable rise of temperature. Thomas[§] once found (Louise Proft, a girl of three and a half years) in the afternoon at 5 o'clock a temperature of 40.1° C. (104.9° F.) in the rectum (the eruption had appeared in the morning). This

[*] "Jahrbuch für Kinderkrankheiten," *loc. cit.*, p. 56.
[†] "Jahrbuch für Kinderheilkunde," *loc. cit.*, p. 58.
[‡] In v. Ziemssen's "Handbuch," *loc. cit.*, p. 154.
[§] "Jahrbuch für Kinderheilkunde," N. F., Bd. v, S. 352.

was a case which ended favorably in a few days without any complications.

Emminghaus found once a temperature of 40.2° C. (104.3° F.), but it was in a case, he states, in which there was at the same time bronchitis and probably a pneumonia of short duration.

Von Nymann observed the temperature reach 38.0° C. (100.4° F.), thirty-nine times; 38.5° C. (101.3° F.), fourteen times; 39.0° C. (102.2° F.), six times; 39.5° C. (103.1° F.), twice. The duration of the increase is not great. After, at the most, four days, but usually earlier, the temperature falls to normal or even below normal.

The nature of the temperature curve and its relation to the other symptoms are thus described by Emminghaus*: "The initial fever stands in close relation to the severity of the other prodromal symptoms. If the premonitory symptoms are marked, and the exanthem does not appear until the second day or later, then a morning remission appears, followed by an evening exacerbation, generally indicating the appearance of the eruption.

"With insignificant prodromal symptoms, followed on the same day by the appearance of the eruption, an elevation of temperature occurs only before the eruption. This may disappear so quickly that one cannot get the beginning of the curve, and only the acme and the critical fall of temperature come to view, with a rapid fall below normal or an oscillation about the normal."

If there is a fever lasting through the whole attack, then it is remittent in type, and falls by crisis or lysis in two to four days.

The highest point of the temperature curve never coincides with the maximum of the eruption in this or that part of the body. While the several regions of the body may show the eruption successively, the temperature, with slight exacerbations, which never reach the first elevation, returns to normal, and has reached it when the portion of the body last attacked shows the eruption at its height.

If the temperature rises again, or if it rises above the initial elevation, then a relapse with analogous temperature curve, or a complication, is to be expected.

The Eruption.—The mucous membrane of the palate and pharynx may show changes which, like the enanthem of measles, resemble in form the exanthem of rötheln.

Many observers consider this certain. Thus, Emminghaus † says: "On the mucosa of the pharynx an analogous exanthem could be shown

* In Gerhardt's "Handbuch," *loc. cit.*, p. 351.
† "Jahrbuch für Kinderheilkunde," *loc. cit.*, p. 58.

in some cases. It always had the limited circular form." Likewise Gerhardt * states: "The mucosa of the throat shows the same irregular hyperemic, hemorrhagic red points as in measles." H. Rehn † also writes: "Parallel with the affection of the skin, occurred an eruption on the mucous membranes of the eyelid, nose, mouth, and throat, in which, especially on the soft palate, nodular swellings of the glands and follicles were found."

Thomas,‡ on the other hand, expresses the comparison less strongly. He says: "Partial redness of the mucosa of the palate is never lacking. If this becomes concentrated around a center, especially in the central part of the velum of the soft palate, in which swollen follicles become more or less prominent and it thus spreads not quite uniformly over the palate, it is still far from showing an appearance as characteristic as that presented on the skin. One can class it among the exanthems of mucous membranes, as this condition is usually called, but it is not perfectly analogous to the eruption on the skin. On the skin there is no trace of hyperemia between the single macules, while the whole mucosa is more or less affected and the nearly normal portions by no means exceed the reddened portions, which—at least in the most numerous cases, the children—are divided irregularly into stripes or blotches. In an adult, spots of a deeper red can be discovered in the generally injected mucosa."

The opposing views are so decided that only one conclusion can be reached: Enanthems may be present or they may be lacking.

The appearance and development of the exanthem are vividly described by Emminghaus§ as follows: "When the exanthem followed distinct prodromal symptoms, it began with a just visible light reddish flush of the skin, which disappeared on pressure, and showed no elevation at all.

"From this condition the second step developed within a few hours.

"From the brighter flush circumscribed darker and smaller macules developed, while in part the redness still persisted. On the other hand, amid more intense reddening another form arose out of the common foundation form, also distinguished as macules, but more faded, while the redness of the skin between them is more intense.

"If one examines the one form after some hours or after half a day, he sees simply the further development of the above-described eruption—dark, rose-red to fiery red isolated macules, from the size of a pin-head to that of a small bean. Between them dilated capillaries are often seen. The elevation is now quite distinct. On pressure, the macule disappears, but quickly reappears.

* "Lehrbuch der Kinderkrankheiten," 4th ed., Tübingen, Laupp, 1881, S. 82.

† "Eine Rubeolen-Epidemie," "Jahrbuch für Kinderheilkunde," N. F., Bd. XXIX, S. 282.

‡ In v. Ziemssen's "Handbuch," *loc. cit.*, p. 149.

§ "Jahrbuch für Kinderheilkunde," *loc. cit.*, pp. 56, 57.

"In the diffuse form the skin is redder and the macules, which are surrounded as by a halo, are united to neighboring macules by streaks and stripes. Elevation is not to be so distinctly felt. On pressure, they react exactly as the macules before described.

"These conditions indicate the acme of the eruption, and last not longer than half a day. Then the exanthem begins to undergo meta-morphosis. The red spot, which no longer completely disappears under pressure, is turning to a reddish-brown.

"The circumscribed form begins to lose its regularly circular form and the macules are no longer of nearly uniform size.

"In the diffuse form one sees irregular macules of the same color, and the skin shows paler star-shaped areas. After one-half to one day, the macules have become somewhat paler, though still distinctly reddish-brown; and after the same time, we see only very pale brown-ish areas isolated in the light yellowish skin, while at the same time small elevations, corresponding in size to the point of a pin, appear and after one day have become more numerous and more distinct, and of normal color. They supply material to the minute pores which on careful observation are found in protected regions of the body; for instance, in the supraclavicular space."

The descriptions of Thomas differ not more markedly than generally happens in the representation of the skin changes occurring in the acute exanthems. The following are worthy of mention:

1. Thomas has not seen the introductory erythema.*

2. He distinguishes three types: one with large macules, the usual one with medium-sized macules, and one in which the macules are small. The first is quite rare. The macules are here relatively few, but may reach a square centimeter in size. They are never round, but are angular and serrated, and variously irregular in outline. Though they determine the character of the eruption, they are never present alone, but always mingled with smaller, and especially with the smallest variety grouped around the large macule.

In the type in which the macules are small, the single macules are closer together and at an equal distance from each other. They are of about the size of a bean, but many are smaller and few are larger.

The exanthem thus somewhat resembles scarlet fever, the macules of which are usually much smaller and more closely placed.

In the usual type the macules are most widely separated, and are generally of the size of a bean, although there are larger and smaller ones mingled with these. The type is chiefly characterized by the moderate number of the macules and by the lack of preponderance of either the large or the very small ones.

One might, of course, describe transitional types.†

We can see, from these quotations, that differences are of course

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* "Jahrbuch für Kinderheilkunde," N. F., Bd. v, S. 349.
† In v. Ziemssen's "Handbuch," *loc. cit.*, pp. 146, 147.

present, but they are purely external and quantitative. The term "type" is therefore perhaps not wholly appropriate.

Real confluence, as regularly observed in measles in certain parts of the body, is never present in rötheln. Even in the fine-pointed form, the erythema comparable to that of scarlet fever is not present. After strong pressure we notice, in the return of the redness, that it consists of closely crowded single points. At times miliary vesicles are formed; for instance, on the back when the patient has been kept warm in bed.

Mention is made of petechiæ by only one writer.

Capillary hyperemia of the papillæ and uppermost layers of the corium is regarded as the anatomic basis of the skin affection; this, with slight inflammation and correspondingly slight exudation, passes between the uppermost layer of the corium and the epidermis.

Spreading of the Eruption.—The eruption does not all appear at once, but comes out in crops, which of course are separated from each other by a relatively short period of time.

It is considered as characteristic of rötheln that its exanthem never reaches its highest point, or stage of florescence, in all parts of the body at the same time, but has already faded in one part when it is in full bloom in another part.

The rule for the spread of the eruption is this: It attacks first the scalp and face; then the neck and trunk, from *above* down; then the arms; and last the legs and feet. Variations are rare.

The following details should also be mentioned: Distinct patches are present about the lips—a fact which is advanced as distinguishing it from scarlet fever. Generally the eruption is mostly in the face, the spots growing less frequent from above down. The same is true with regard to color. The eruption may be seen in the palms of the hands and soles of the feet in cases in which it is not too slight.

It has been noticed many times that the spots are closer together in those portions of the body over which the clothing fits rather snugly and thus irritates the skin. This recalls the statement that in the back and posterior part of the thigh of the patient confined to his bed more of the eruption is found than in the same parts when the patient is up.

Klaatsch * tells of peculiar variations: "The strangest appearance was presented by a boy whose body from the girdle down was thickly covered with the eruption, while the upper part was entirely free. A short time ago I saw a patient having the eruption as a red band about

* *Loc. cit.*, p. 10.

the thigh at the same height on both sides." It is not known whether here any external irritation caused the phenomenon.

Emminghaus,* with a prudence acquired through experience, discusses the question: Is there a rubeola without exanthem? In cases of the epidemic observed by him, in all of which the prodromal symptoms were present, no eruption was observed. But he leaves it unsettled whether an exanthem of very short duration might not have occurred in the fifteen hours between his evening and morning visits. Naturally, this question could arise only in the mildest cases.

The fact that the desquamation is in all cases inconsiderable depends upon the slight anatomic changes in the skin in rubeola. At its termination, which is so very different in different cases, just as much as in the development of the eruption, which, although in narrow limits, shows marked differences in severity, the question arises whether the disturbances of nutrition are sufficient to cause desquamation. In many epidemics this was not the case, while in others such desquamation was seen. But even in its highest development it does not reach the severity of the desquamation seen after measles, to say nothing of that after scarlet fever.

Whether by pedantic surveillance, especially in portions of the body protected from rubbing, one can guard a little from shedding, is a question of no moment.

Itching may or may not be associated with the exanthem.

The Other Phenomena of the Disease.—These have usually no great importance. Even the catarrhal irritations of the mucosa of the throat and respiratory tract are extremely limited during the whole course of the disease, and do not continue into the convalescence.

One may meet some catarrh of the mucous membrane of the mouth, and there may be coating of the tongue with slightly enlarged papillæ, which, breaking through the coating, may appear as red points.

The above-described changes in the throat are accompanied by a slight difficulty in swallowing; there may be some hoarseness and even a slight barking cough. All this, with the catarrh, disappears in a short time; even the bronchitis does not extend beyond the larger bronchi, but remains a simple tracheitis.

The enlargement of the lymph glands deserves somewhat more consideration, not on account of its practical, but because of its theoretic importance. Enlarged glands are not always, but, as appears from the representations of most observers, very frequently, present.

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* "Jahrbuch für Kinderheilkunde," *loc. cit.*, p. 56, and in Gerhardt's "Handbuch," *loc. cit.*, p. 350.

The almost exceptionally marked enlargement of the cervical lymph glands and of those near the mastoid process seemed very characteristic. They were found so constantly in the present epidemic that if one knew that he had a case of an acute exanthem, he could make the diagnosis of rötheln in the dark by touch alone. I never found them so enlarged in measles. Also a slight enlargement of the axillary and inguinal glands is present in most cases.*

The glandular swellings may be present in the prodromal stage and last for some weeks until perfect restoration. The glands of the neck and throat are oftenest affected, but those in other parts of the body may be, especially those in the region of the thigh.

The enlargement may be considerable, so that if the glands of the neck and lower jaw are involved, it may hinder the free passage of the lymph and cause the face to become bloated. The glands are soft, not sensitive, and recovery takes place without complications. Suppuration has never been seen.

It is probable that it is not due to an irritation in the region supplying the gland; but the poison of the disease seems to influence the gland directly.

I find no statements concerning the spleen. Serious disturbances in the digestive tract, as little as inflammation of the kidney, belong to the phenomena of this disease. They should be considered as true complications, which may be brought by chance to a patient with rötheln as well as to one previously well. Under this head belongs also the case of pneumonia with fatal termination in an adult, reported by Emminghaus.†

Sequels are now and then mentioned, but they are so few and so uncertain that a relation to rötheln can scarcely be shown.

DIAGNOSIS.

If we collect all the facts, we cannot, in my opinion, recognize the right to independence of this disease which is called rötheln.

["Koplik's spots," which occur regularly (approximately 91%) on the buccal mucous membrane of measles, are absent in rötheln. At the present stating of the subject rötheln is believed in the United States to be a separate disease, and best differentiated from measles by the absence of buccal "spots."]

* Klaatsch, *loc. cit.*, p. 11.
† "Jahrbuch für Kinderheilkunde," N. F., Bd. iv, S. 54.

Somewhat different is it with the diagnosis of an isolated case, which appears alone, not belonging to a group. Here, I maintain that however much our best observers do it, I am not justified in giving a positive diagnosis. In proof, I will present some of my own observations:

Anna G., eleven years old: She has had the diseases of childhood,—more exact information was not to be had,—but has never had a severe sickness.

On the 8th of November an eruption was seen, first in the face, then in the neck and breast region. On the 9th of November she was presented before the clinic. We found: A well-developed girl, with nothing especially noticeable in the internal organs. On the face, neck, breast, and back, less plentifully on the abdomen and on the limbs, numerous red efflorescences, from the size of a bean to that of a twenty-pfennig piece, are seen; these appear as flattened papules, which itch severely and are quite similar to the blotches of urticaria; on pressure, slightly thickened, yellowish-brown skin is seen between them. Slight conjunctivitis; no redness of the mucosa of the mouth and throat. The submaxillary glands are enlarged. Constipation for some days. Temperature, 37.8° C. (100.0° F.).

Further observation showed:

November 10th: The eruption as yesterday, but the spots on the back have become larger, more reddened, and slightly infiltrated. The itching is severe.

November 11th: Regression of the eruption in the face and neck; but in the lower extremities, new eruptions with slight enlargement of the inguinal glands. The submaxillary glands still considerably swollen. The conjunctivitis has lessened.

November 12th: Slight angina with rise of temperature to 38.0° C. (100.4° F.). The eruption on face, neck, breast, and back is scarcely to be seen; on the abdomen and limbs it is slighter. Swelling of glands and angina less marked.

November 14th: Eruption on legs just visible, and everywhere else the skin is normal.

November 15th: Only slight enlargement in the submaxillary and inguinal regions. Nothing is to be seen of the eruption.

The temperature, measured three times a day, only once (12th of November) rose to 38.0° C. (100.4° F.); otherwise it was lower; some mornings it was higher than normal (37.8° C.—100.0° F.). Nothing noticeable in the short convalescence. The recovery of the glands was perfect.

This might have been rötheln, though the eruption appeared somewhat like urticaria, which, according to Thomas, is never the case in rötheln. There were at that time no cases of measles and scarlet fever in our circle of observation.

In March (11th to 23d), 1895, occurred four cases, and in May (15th and 17th) occurred two which are described more exactly.

The picture of the disease corresponds perfectly to that described; but the children belonged to different families and none of their brothers and sisters had been or became sick. Their dwellings, for the most part, lay far apart. Thus a very essential condition for the diagnosis of rötheln was lacking—the epidemic character. Hence my hesitation.

The description of the appearances in rötheln as I have tried to give them, according to the best sources of information, makes a detailed discussion of diagnosis unnecessary.

I will only add that in children, especially in young children, all possible internal and external influences, for the most part unknown to us, may excite changes in the skin, which are of short duration. These erythemata and roseolæ, as one must call them systematically, are very liable to lead to changes. To this our attention has been called by many, but especially by Hebra and his pupils.

The greatest difficulty in diagnosis lies in distinguishing rötheln from a mild case of measles.

PROGNOSIS AND THERAPY.

THE prognosis, according to our present knowledge, is, at least for our European cases, extremely favorable. For the treatment, we may refer to that for measles.

I might repeat a very excellent remark of Klaatsch.* After he had explained how an isolation of the family was unnecessary in cases of rötheln, he adds: It is certainly a fact worthy of recognition in hygienic matters that recently a law arranges that children attacked with acute contagious diseases shall not attend school, and also forbids the brothers and sisters from attending school as long as any danger of infection exists.

But it is, in my opinion, going too far when, as is true in this law, measles and rötheln are treated just alike, and for both the children

* *Loc cit.,* p. 12

must be kept from school for five weeks. The mildness of the disease seems to me not to justify so stringent a law.

If we wish to pass a law against the spread of acute exanthematous disease through a school,—I speak from another standpoint, that of Kerschensteiner,—then should we exclude rötheln. Perhaps the difficulty of distinguishing this disease from measles caused the decision in favor of the above-mentioned regulation.

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