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Clinical Observations

UPON THE

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AND

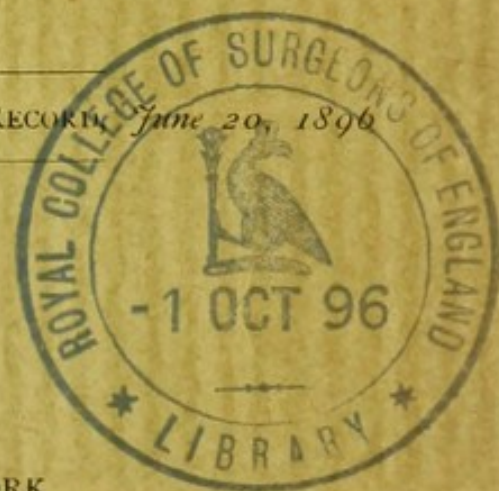
A REPORT OF A PERSONAL INVESTIGATION OF
THIS TREATMENT IN THE PRINCIPAL FEVER HOS-
PITALS OF EUROPE DURING THE SUMMER OF 1895

BY

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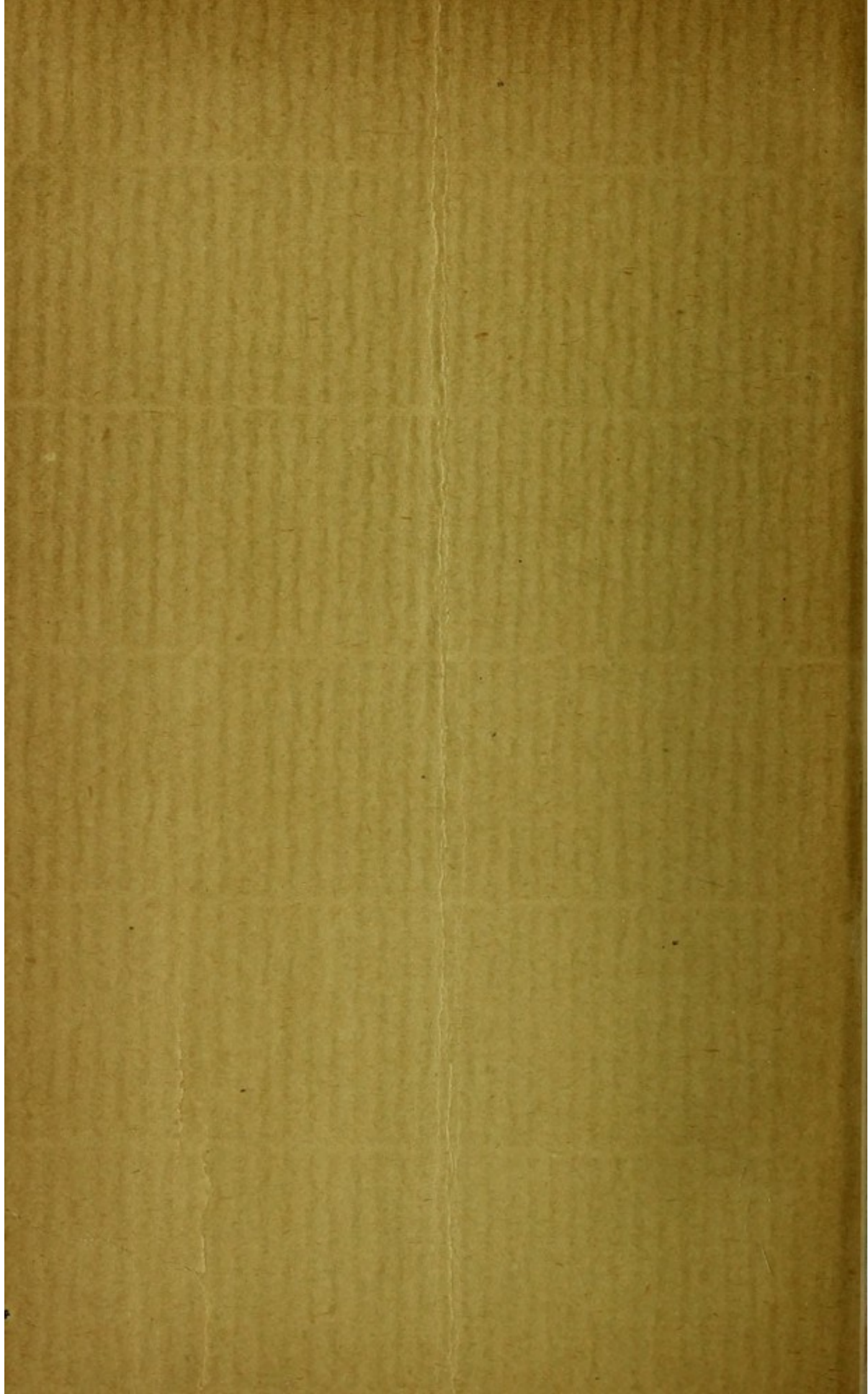


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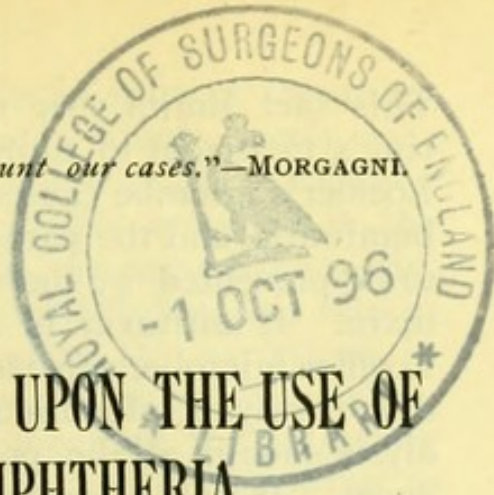
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"We should weigh, not count our cases."—MORGAGNI.



CLINICAL OBSERVATIONS UPON THE USE OF ANTITOXIN IN DIPHTHERIA

AND A REPORT OF A PERSONAL INVESTIGATION OF THIS TREATMENT IN THE PRINCIPAL FEVER HOSPITALS OF EUROPE DURING THE SUMMER OF 1895.*

By JOSEPH E. WINTERS, M.D.,

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SINCE Behring's treatment for diphtheria was proclaimed to the medical profession by Roux at the Buda-Pest congress in 1894, sufficient time has elapsed to warrant our taking a careful analytical review as to what has transpired with reference to it.

Behring's antitoxin was given to the world as a specific against the toxins of the diphtheria bacillus. It has no action on the bacillus; this is not destroyed by the antitoxin, it is not rendered less virulent, it is in no way influenced by the treatment.

Behring has told us that his remedy has no influence on the poisons of other bacilli. Diphtheria in man scarcely ever occurs from pure infection by the Loeffler bacillus. Almost invariably we find in addition to the specific diphtheria bacillus, streptococci, staphylococci, etc. The poisonous substances of the latter bacilli are in no way influenced by antitoxin.

* Read before the New York Academy of Medicine, May 21, 1896.

This fact limits very much the application of Behring's treatment to diphtheria in man. The toxin of Loeffler's microbe causes the cardiac paralysis, the albuminuria, and the paralytic phenomena. These were to be prevented by the neutralizing effect of the antitoxin. If antitoxin is an antidote to the toxin of the Loeffler microbe, cardiac depression, death from cardiac paralysis, albuminuria, and post-diphtheritic paralysis should all be prevented by the action of this agent. It was to remedy these manifestations of the disease that Behring gave to the world his antitoxin.

Behring told us his treatment to be effective must be applied early in the disease; to get the maximum effect, toxin and antitoxin must be applied at the same moment and at the same spot.

Armand Ruffer¹ states that if you inject toxin on one side of the body and antitoxin on the other side at the same time, fourteen times as much is required to protect the animal; if there is a delay of one hour, one hundred times as much is required to protect the animal, and if there is a delay of eleven hours five thousand times as much is required to protect the animal.

In diphtheria in man we can never apply the antitoxin at the site of infection, nor at the moment of infection. A period necessarily intervenes from the time of infection until there are sufficient symptoms to call attention to the illness, and, as the result of this, there is a great limitation to the application of Behring's remedy to diphtheria in man.

Another consideration of prime importance is: if we are to attribute the reported decrease of mortality of diphtheria to the action of a specific, this decrease must be uniform and constant. There must be the same reduction in mortality in all parts of the world where the remedy is applied. For instance, a mortality of eight per cent. in Paris and twenty-eight per cent. in London does not mean that the low mortality in the former city is due to the treatment, but that it is due to a difference in the character of the epidemic, and that when Paris is visited by an epidemic of the same severity as the one that exists in London

it will have the same mortality in spite of the treatment. If there is at work but a single factor, viz., antitoxin, in the reduction of mortality, that reduction must be below the lowest mortality recorded in the natural history of the disease in any part of the world, and it must be steadily maintained below this rate in all parts of the world; otherwise, the variations in mortality may be said to be due to the epidemic character of the disease. We find recorded the following divergences in the deaths from diphtheria, owing to differences in the type of the disease:

	Deaths from Diphtheria.
In New York in 1884,	1,090
“ “ “ “ 1887,	2,167
Again in 1890, only	1,262
“ “ 1894,	2,359
In Boston in 1891,	232
“ “ “ 1894,	817
In Philadelphia in 1888,	350
“ “ “ 1889,	375
“ “ “ 1892,	1,425
In London in 1891,	1,361
“ “ “ 1893,	3,265
In Berlin in 1866 (croup and diphtheria),	813
“ “ “ 1867,	904
“ “ “ 1868,	2,154
Again in 1877, with an increase in population of nearly half a million, only	1091

The same variation in the type of the disease is shown in the mortality returns from hospitals in different years. Thus, we find that in the Children's Hospital in Basel the mortality from diphtheria in 1876 was 34.1 per cent., in 1886 6.2 per cent.²

In the Crown Prince Rudolph Hospital³ (Vienna) we find that the mortality in 1887 was 27.1 per cent., and in 1888 62.8 per cent. These normal variations in the type of the disease must be given due consideration when estimating the value of a mode of treatment.

The rule of uniformity of results applies to reports by individual observers. If one hundred physicians report five thousand cases of diphtheria treated with

antitoxin with a mortality of five per cent., and ten physicians report five hundred cases treated with antitoxin with a mortality of fifty per cent., the only logical conclusion is that there was a difference in the character of the cases in the two series, and that when the one hundred physicians meet with a series of cases of the same type as those treated by the ten physicians, they, too, will have a mortality of fifty per cent.

The most misleading part of the antitoxin literature is the constantly quoted percentage of mortality. The mortality from diphtheria in the city of Boston in 1895 was 14.48 per cent.; in 1893 32.49 per cent., and yet there were one hundred and twelve more deaths from diphtheria in the city of Boston in 1895 than there were in 1893 (four hundred and seventy-six in 1893 and five hundred and eighty-eight in 1895). The percentage mortality in 1895 is less than one-half as much as that of 1893, and yet the actual number of deaths was increased about one-fourth. The percentage reduction of mortality is due to the fact that in 1895 four thousand and ninety-five cases were reported, and there were only one thousand four hundred and sixty-five cases of diphtheria reported in 1893 in the city of Boston. The percentage mortality from diphtheria in the Boston City Hospital in 1893 was 48.44 per cent., and in 1895 13.21 per cent.; and yet we find that there were two hundred and three deaths from diphtheria in the Boston City Hospital in 1893 and two hundred and seven deaths in 1895.

BOSTON CITY HOSPITAL.

Year.	Cases.	Deaths.	Per cent.
1893.....	419.....	203.....	48.44
1894.....	598.....	266.....	44.48
1895.(Antitoxin).1,566.....		207.....	13.21

From the foregoing it is readily seen that percentage mortality is not only misleading, but is absolutely worthless unless accompanied by the actual number of cases reported and the actual number of deaths; and the report must also include a series of years, in order to enable the reader to compare present

results with the results in previous years when there was a mild type of the disease. Reports on the anti-toxin treatment have ingeniously compared years of highest mortality instead of including all years.

The necessity of taking into consideration the character of the prevailing epidemic in order to have a clear understanding, is shown by the following. At Gratz Escherich⁴ treated:

	Cases.	Deaths.	Per cent.
By injection of serum,	51	5	9.8
By non-injection,	36	3	8.3

Kohts⁵ mortality in tracheotomy cases treated with serum is 29.41 per cent.; without serum, twenty-five per cent. For cases not operated on, with serum, 7.6 per cent.; without serum, 6.9 per cent.

At the beginning of the antitoxin treatment Behring told us all cases treated on the first day of the disease could be saved; of those coming under treatment on the second day, nearly all, and of those brought under treatment on the third day, the larger part of them. Behring's words were: "We have it in our hands to reduce the mortality from diphtheria to one-tenth of its former rate" (three to five per cent.). Let us see how this promise of Behring's has been verified.

At the Willard Parker Hospital⁶ during the first nine months of 1895, the results were as follows:

DAY UPON WHICH TREATMENT WAS BEGUN, 1895.

	Cases.	Mortality, per cent.
First day.....	108.....	10.09
Second day.....	130.....	25.19
Third day.....	116.....	34.19

We will cite a few cases showing actual results when treatment is begun in the earlier part of the disease:

CASE I.—Six years old; admitted to scarlet fever ward February 1, 1896; recovered from scarlet fever and was ready for discharge.

March 19th, at 11:30 A.M., she complained of sore throat. The diagnosis of diphtheria having been

made by bacteriological examination, she was injected with 2,000 units of antitoxin, March 21st, at 3:30 A.M., just forty hours after the disease began. In spite of treatment croupy symptoms, which manifested themselves early, increased, and intubation was done at 10 A.M., forty-six and one-half hours after the beginning of her illness. On the evening of the same day, intubation not affording sufficient relief from the stenosis, tracheotomy was performed at 9:40 P.M. The child died at 9:45.

In this case we have an instance of a child developing diphtheria in the hospital and being put upon the serum treatment as soon as the diagnosis was confirmed. Notwithstanding this, the local process extended, even intubation not affording sufficient relief, the whole course of the illness being a repetition of what has been frequently seen in the Willard Parker Hospital service.

CASE II.—Aged two and one-half years; admitted April 22d; ill one-half day. Throat clear; tonsils red and somewhat swollen; croup, some retraction, no cyanosis. Under the head of clinical notes I find: "Child rather croupy on admission." Antitoxin, 2,000 units, on admission. Patient admitted April 22d, about midday.

April 23d, 8:55 A.M., intubation necessary; 2,000 units of antitoxin.

Temperature on admission, 100.8° F. April 23d, temperature, 103.2° F. April 27th, temperature, 99° F. April 28th, temperature, 105° F. April 30th, temperature, 101.6° F. Afternoon of same day, 105.2° F.

May 10th, the baby died, 2:25 A.M.

This is an extraordinary record. The child had been ill one-half day on admission. Clinical notes state: "Child rather croupy on admission." About the only evidence of disease, then, was croup. In spite of antitoxin, 2,000 units, croup increased during the night; intubation became necessary the following day, about twenty-one hours after admission. Next observe the common temperature range which occurs

when the patient shows unusual susceptibility to the influence of antitoxin.

CASE III.—Aged two years; admitted October 22d; one day sick. Marked injection and swelling; dirty white membrane on left tonsil, croup. Prognosis doubtful. Antitoxin, 2,000 units, on admission. Admitted, 9:30 A.M.; intubated, 4:15 P.M.

October 23d, antitoxin, 2,000 units; 9:45 A.M., tube coughed up; 10:05 A.M., intubated. Temperature, 2 P.M., 104.6° F.; hypodermics of brandy and nitroglycerin, hot bath, etc.

October 24th, antitoxin, 1,200 units, 11:45 A.M.; temperature, 104° F.; sponging, etc.

October 27th, temperature, 105° F.; sponge baths nearly every hour.

October 28th, rash.

October 29th, tube removed.

November 1st, temperature went to 105° F.; sponge baths almost hourly.

November 3d, temperature reached 105.8° F.; sponge baths nearly every hour.

November 5th, temperature ranged from 102° to 105° F.

November 6th, temperature, 105.8° F.; sponge baths constantly kept up.

November 7th, temperature ranged from 101.2° to 106.2° F.; sponge baths used almost constantly.

November 8th, temperature, 102° to 106° F.

November 9th, patient died 6:40 P.M.

Here we have a baby two years old, taken sick October 21st, admitted to hospital October 22d at 9:30 A.M., given antitoxin immediately (in all, 5,200 units), and the result is shown by the clinical history. If antitoxin has any possible effect in neutralizing the poison of diphtheria, in relieving or preventing stenosis, or in any way allaying laryngeal symptoms, only a very small part of the clinical history here recorded would have manifested itself.

CASE IV.—Aged two years; admitted February 18th; illness began February 17th. Patient well nourished, pulse good, small amount of membrane on

tonsils and uvula; K. L. B.; complication by bronchitis. Prognosis favorable. Temperature on admission, 101.8° F.; temperature ranged between 99° and 102° F. from time of admission until March 5th, when it rose to 103.6° F., the following day to 105.2° F.; temperature fluctuated until March 18th, when patient died. Antitoxin, 20 c.c., 1 to 300, injected on admission; February 2d, antitoxin injected, 20 c.c., 1 to 300.

CASE V.—Aged seventeen months; admitted February 4th; illness began February 3d. Well nourished and in good general condition; no membrane visible; tonsils and uvula normal in color; large, irregular ulcer on face, involving lid of right eye, right side of nose, and right cheek; suppuration and considerable inflammation at periphery; lids of right eye badly swollen. Prognosis favorable. Antitoxin, 21 c.c., 1 to 300, injected on admission. Temperature on admission, 101.8° F.; following day, 102° F.; from that time practically normal until February 13th, when the chart was stopped. February 22d the temperature suddenly rose to 105° F., and fluctuated between 105° and 106.8° F. until March 7th, when the patient died.

CASE VI.—Aged one year; admitted May 23d; illness began May 22d. Throat dull red with slight tumefaction; thin white membrane on both tonsils and base of uvula and soft palate; much anterior and posterior nasal secretion; K. L. B. Prognosis favorable. Antitoxin, 6.5 c.c., 1 to 1,000, injected on admission. Patient died May 31st.

CASE VII.—Aged four years; admitted February 11th; illness began February 10th. Well nourished; pulse good; few thin streaks of membrane on tonsils; tonsils much enlarged; but little discharge from nose; right-sided cervical adenitis fairly well marked; slight swelling also on left side. Prognosis favorable. Antitoxin, 15 c.c., 1 to 600, injected on admission; February 12th, 15 c.c., 1 to 600; February 13th, 15 c.c., 1 to 600. Temperature on admission, 101° F.; slight variation until February 19th, when temperature

rose to 103° F., on the 20th to 105° F., fluctuating between 102° and 106.5° F. until February 27th, when patient died.

CASE VIII.—Aged sixteen years; admitted May 20th; illness began May 18th. Well developed and nourished; glands of neck enormously swollen; throat much congested; swelling and implication of left tonsil; right tonsil and right peritonsillar space and whole area back into pharynx covered with a dirty white deposit; nares partially obstructed; K. L. B. Prognosis favorable. Antitoxin, 10 c.c., 1 to 1,000, injected on admission; May 21st, 9 c.c., 1 to 1,000; May 25th, 7 c.c., 1 to 1,500.

May 26th (Sunday), pulse 26 to 30 per minute. Patient died May 26th, 10:30 P.M.

This was a remarkably large, strong, well-developed young lady, who was brought to the hospital as soon as the diagnosis of diphtheria was made. If antitoxin has any specific influence over the toxæmia of diphtheria, this patient should have been saved. As the report of the hospital shows, she died from the effects of the toxins on the heart and nerve centres—the pulse having ranged during the last twenty-four hours of life from 26 to 30 per minute, even with the foot of the bed elevated and with the use of all possible stimulants.

CASE IX.—Aged thirteen months; admitted May 16th; illness began May 14th. Well developed and nourished; no apparent anæmia; marked injection and tumefaction; thin white membrane on left tonsil; K. L. B. Prognosis good. Antitoxin, 5 c.c., 1 to 1,500, injected on admission. Patient died June 12th. June 1st rash appeared, with numerous areas of bronchial breathing and fine crepitant râles.

CASE X.—Aged five years; admitted November 11th; two days sick. Necrotic membrane on left tonsil, extending forward to soft palate; grayish membrane on right tonsil; no nasal discharge. Antitoxin, 1,000 units, on admission.

November 12th, antitoxin, 1,000 units.

December 16th, patient died.

CASE XI.—Aged fourteen months; admitted March 25th; two days sick. Speck of membrane on each tonsil; croup rather marked. Antitoxin, 1,000 units, on admission; later, same day, 2,000 units. Intubated at 12:05 P.M., twelve hours after admission. Afternoon of 25th, 1,500 units of antitoxin. Tube coughed up at 9:35 P.M.; intubated at 1:25 A.M., March 26th; tube coughed up immediately after. Intubated at 2:10 A.M.; very restless. At 12:35 P.M. of 26th, tube removed; at 12:45, intubated. At 1 P.M., temperature 106.2° F.

March 27th, 9:30 A.M., tube removed.

March 28th, temperature, 104.2° F.; pulse, 140, very weak.

April 4th, died.

CASE XII.—Aged two years; admitted February 15th; two days sick. Good-sized patch on each tonsil; croupy, husky breathing, and retraction. Antitoxin, 2,000 units, on admission.

February 16th, antitoxin, 1,000 units; 6:10 P.M., intubated.

Admitted February 15th at 2:30 P.M., not having very marked croup, and yet had to be intubated twenty-eight hours after admission and after having had 3,000 units of antitoxin.

February 17th, 3:20 P.M., tube coughed up; 6:30 P.M., intubated; 10:30 P.M., tube removed; 10:40 P.M., intubated.

February 18th, 1:30 A.M., tube removed; 1:40 A.M., intubated, wide calibre; 1:50 A.M., tube coughed up; 2 A.M., intubated, wide calibre. Note states that "urine is scant." 7:30 P.M., tube removed; 11 P.M., intubated; 11:10 P.M., coughed up tube. Urine still scant.

February 25th, 9 P.M., intubated twice.

February 26th, 2:30 A.M., tube removed; 9:30 P.M., intubated twice.

February 27th, 4:40 P.M., tube coughed up.

February 28th, intubated twice; 11 P.M., tube coughed up.

March 5th. Note is found: "Marked retraction."

At 2:40 P.M., intubated; 9:25 P.M., tube coughed up plugged; 10 P.M., intubated.

March 6th, 4:45 A.M., tube coughed up plugged; 5 A.M., intubated; 5:05 A.M., tube coughed up plugged; 5:10 A.M., intubated; 8:50 A.M., tube coughed up.

March 7th, 7:45 A.M., intubated; tube coughed up; 8 A.M., intubated; 11:50 A.M., tube coughed up.

March 8th, 7:25 A.M., intubated.

March 10th, child died at 10:55 A.M.

CASE XIII.—Aged fourteen months; admitted February 20th; two days sick. Membrane on both tonsils, croup. Prognosis doubtful. Antitoxin, 2,000 units, on admission. Admitted at 6:30 A.M.; intubated at 7 A.M.; tube removed at 12:40 P.M.; intubated at 1:30 P.M.

February 21st, antitoxin, 1,000 units, 10:20 A.M.; tube removed at 4:30 P.M.

February 23d, rash appeared; extreme restlessness. Note: "Is very sick this morning; temperature, 105° F."

February 24th: "Very restless and excited all night."

March 5th, temperature, 104° F. Temperature ranged from this point to 105° F. until March 7th. Baby died at 1:45 P.M.

CASE XIV.—Aged four years; admitted December 2d; two days sick. Throat dull red in color, considerable naso-pharyngeal discharge, no membrane, croup. Prognosis unfavorable. Antitoxin, 3,000 units, on admission; intubation immediately after admission.

December 3d, antitoxin, 3,000 units.

December 6th, tube removed, 3:30 P.M.

December 7th, had a bad night; intubated at 9:35 A.M.

December 8th, tube removed.

December 12th, intubated.

December 13th, tube coughed up at 4:30 A.M.; intubated at 6:30 A.M.

December 15th, tube coughed up at 3 A.M.; intubated at 10 A.M.

December 21st, tube removed at 10:10 A.M.; rein-

tubated at 10:50 A.M.; tube removed at 4:05 P.M.; reintubated at 4:15 P.M.

December 23d, rash appeared.

December 24th, tube coughed up at 2 P.M.; reintubated at 2:10 P.M.

December 28th, tube coughed up at 7:10 P.M.; reintubated at 7:15 P.M.

January 6th, antitoxin, 3,000 units. Then I find notes for strychnine, whiskey, cream-of-tartar water, diuretin.

January 28th, when patient died, uncontrollable diarrhœa.

CASE XV.—Aged two years; admitted December 5th; two days sick. Thick yellowish-white membrane on both tonsils and uvula, croup. Prognosis unfavorable. Antitoxin, 3,000 units, on admission; intubation on admission.

December 6th, antitoxin, 3,000 units; cream-of-tartar water, diuretin, poultice to kidneys, mustard bath, glonoin, whiskey, strychnine, calomel.

December 18th, patient died.

CASE XVI.—Aged two years; admitted December 19th; two days sick. Thin white membrane on both tonsils and uvula, croup. Prognosis unfavorable. Antitoxin, 3,000 units, on admission. Admitted at 12:40 P.M.; intubated at 3:35 P.M.; tube coughed up at 3:45 P.M.; reintubated at 7 P.M.

December 20th, antitoxin, 3,000 units; tube removed at 3:30 A.M.; intubated at 3:35 A.M.

December 20th, 11 A.M., temperature, 106.8° F.; pulse, 162. Sponge baths. At 8:30 P.M., temperature, 106° F.; 11 P.M., 103° F.

December 21st, 2:30 A.M., temperature, 102.6° F. Patient died at 5:45 A.M., from exhaustion and cardiac failure.

CASE XVII.—Aged three years; admitted April 19th; two days sick. No membrane in throat, very mild croup, no stenosis, no retraction, slight croupy cough. Child admitted in good condition. Croupy symptoms increased when disturbed; when quiet, breathing normal. Prognosis good. Antitoxin, 1,000 units, on admission.

April 20th, child had only one dose of antitoxin. Second dose not given, as condition of child was good.

April 23d, temperature, 98° F. in forenoon; 102.4° F. in afternoon.

April 24th, temperature, 98.5° F. in forenoon; 103° F. in afternoon.

April 27th. Under clinical notes I find: "Patient not doing very well this morning. Child pale, temperature high."

April 28th, 1:30 P.M.: "Cause of death, heart failure."

CASE XVIII.—Aged one year; admitted April 22d; two days sick. Minute speck on right tonsil. Antitoxin, 600 units. Clinical note states: "Child admitted in pretty poor condition."

April 23d, forenoon, urine scant.

Temperature on admission, 103.8° F. April 23d, 100.8° F. in forenoon; afternoon of same day, 105° F. April 24th, 99.5° F. in forenoon; 104° F. in afternoon. April 25th, 104.8° F. April 26th, forenoon, 99.8° F.; afternoon, 103.8° F.

April 28th, patient died at 2 A.M., from exhaustion and heart failure.

CASE XIX.—Aged fifteen months; admitted April 27th; two days sick. Considerable amount of membrane on tonsils, uvula, and soft palate; membrane was beginning to exfoliate. Prognosis doubtful. Antitoxin, 1,000 units, on admission. Piece of membrane was very loose and washed away when irrigated for the first time.

April 28th, antitoxin, 1,000 units.

May 3d: "Until to-day the child's condition was very satisfactory; she was bright; temperature, pulse, and respiration were fair. She was apparently on the road to recovery, when suddenly during the night the pulse became very feeble, respiration went up to 78 per minute, and she died two hours later of heart failure."

CASE XX.—Aged fifteen months; admitted October 28th; illness began October 26th. Prognosis doubtful. Throat dull red, slight tumefaction, small patch

on right tonsil, larger on left, considerable croup. Antitoxin, 2,000 units, on admission. Patient admitted at 1:30 P.M.

Clinical note states: "In spite of poulticing, intubation became necessary and was performed at 3:20 A.M., October 29th," fourteen hours after antitoxin.

October 29th, antitoxin, 2,000 units.

November 1st, forenoon, tube coughed up.

November 2d, antitoxin, 2,000 units, at 12:30 P.M.; 2 P.M., temperature, 105° F.; pulse, 200; 6 P.M., temperature, 105.2° F.; sponge baths, carbonate of ammonia, caffeine, strychnine, ice pack to head.

November 3d, 6 A.M., temperature, 106° F.; pulse, 190; 9 A.M., temperature, 106° F.

November 4th, 7:45 A.M., patient died, bronchopneumonia.

Another death after seven days of treatment, which was begun on the second day of disease; 6,000 units of antitoxin; child of fifteen months.

CASE XXI.—Aged seventeen months; admitted October 2d; second day of disease. Prognosis doubtful. General swelling and injection of throat; thin necrotic membrane on both tonsils and palate, extending into pharynx; considerable nasal discharge, croup, stenosis, and retraction. Antitoxin, 2,000 units, on admission. Admitted October 2d, 2:30 P.M.; 10:40 P.M., fumigated.

October 3d, 1:15 A.M., it became necessary to intubate; 10:20 A.M., tube removed; 10:50 A.M., intubated; 10:53 A.M., tube coughed up; 11:10 A.M., intubated; 11:35 A.M., antitoxin, 2,000 units; strychnine, caffeine, nitroglycerin, carbonate of ammonia, whiskey, sponge bath, dry cupping. Temperature at 4 A.M., 102° F.; 8 A.M., 107° F.; 11:30 P.M., 108° F.

October 4th, temperature at 12:20 A.M., 107.6° F.; 12:30 A.M., 107.8° F. Died at 12:40 A.M.

Several of the following histories are undoubted instances of the bad effects of antitoxin on nerve centres:

CASE XXII.—Aged fourteen months; admitted November 6th; illness began November 3d. Small patch of membrane on right tonsil; K. L. B.; no complication. Antitoxin, 1,000 units, on admission.

November 9th, slept at intervals quietly, but was very restless when awake.

November 10th, extremely restless most of the night; temperature, 104° F.; sponge bath.

November 12th, pulse very weak.

November 20th, rash appeared.

November 6th, antitoxin, 2,000 units, at 5:30 A.M.; intubated at 1 P.M. Very restless during the day. Respiration, 60 to 70. At 5 P.M., temperature, 105° F.; sponge bath; 8:15 P.M., temperature, 106° F. Child failed to respond to stimulants; temperature became more and more elevated, in spite of sponge bath.

December 7th, died at 12:30 A.M.

According to the record this child had almost no illness on admission. It became very restless after first injection of 1,000 units of antitoxin. Restlessness reappeared in exaggerated form after the injection of antitoxin, 2,000 units, along with high temperature and rapid respiration, until death.

CASE XXIII.—Aged seven months; admitted February 4th; three days sick. Nothing in throat, slight laryngeal symptoms. Clinical note states: "Slight croup, otherwise good condition."

February 5th, antitoxin, 2,000 units.

February 6th, antitoxin, 2,000 units; 4 A.M., temperature, 104.2° F.

February 11th, temperature suddenly rose and erythema appeared in patches over the body. Temperature in evening reached 105.4° F.

February 12th, morning, rash more marked since midnight. "Marked opisthotonos and stiff neck."

February 12th, temperature, 106° F. all night.

February 14th, glands and right side of the neck swollen. Temperature ranged from 104° to 106° F. till March 18th, and patient had convulsions during the night.

March 19th, child died at 9 P.M.

CASE XXIV.—Aged thirteen months; admitted October 13th; three days sick. Marked swelling and injection, no membrane, croup. Intubated on admission.

October 13th, antitoxin, 2,000 units.

October 14th, antitoxin, 2,000 units.

October 14th, tube coughed up at 4:10 A.M.; had to be reinserted at 8:30 A.M.

October 15th, tube coughed up at 10:30 A.M.; intubated at 12:30 P.M.

October 16th, tube coughed up at 7:10 A.M.

October 19th, temperature suddenly rose to 104° F.; temperature remained high but somewhat fluctuating until the 21st, when it reached 105.4° F., and the baby had slight convulsions. In the afternoon respiration became very superficial; patient failed to respond to any stimulants.

October 21st, child died at 5:25 P.M.

CASE XXV.—Aged fourteen months; admitted February 20th; five days sick. Rather thick patch on right tonsil, cry and breathing croupy, no retraction. "Patient admitted in croupy condition, not bad enough to require intubation." Prognosis good. Antitoxin, 2,000 units.

February 21st, antitoxin, 2,000 units, at 10:15 A.M.; intubated at 2:10 P.M.; 5:45 P.M., tube removed.

February 22d, 8:30 A.M., temperature, 104.5° F.; 12 M., 105° F.; pulse, 184; respirations, 84; 11 P.M., temperature, 106.2° F.; opisthotonos. Plunge bath for ten minutes.

February 23d, temperature down, but still opisthotonos and great prostration.

February 29th, opisthotonos; eyes rolled up, with lids half-closed when asleep.

March 3d, opisthotonos and rolled-up eyes.

March 6th, died at 8:15 P.M.

CASE XXVI.—Aged three years; admitted February 17th; four days sick. Much membrane on either tonsil and on pillars of fauces; nose plugged. Prognosis doubtful. Antitoxin, 2,000 units, on admission.

February 18th, antitoxin, 2,000 units.

February 19th, antitoxin, 2,000 units.

February 21st: "Patient seems better to-day. This evening he gave a peculiar cry, heard by the nurse, and was dead on arrival of the physician a moment

later. There were no heart sounds, but artificial respiration was kept up for ten minutes and stimulants were also given. Patient gasped several times and died."

CASE XXVII.—Aged twenty-one months; admitted September 28th; illness began September 25th. Antitoxin, 1,000 units, on admission. Thick white membrane on uvula and both tonsils; slight nasal discharge. Child became cyanosed, apparently from accumulation in the throat; turpeth mineral given, resulting in free vomiting and relief.

September 29th, antitoxin, 1,000 units.

September 29th, became cyanotic from slightest exertion, and was very restless, seeming to indicate a considerable cerebral irritation; considerable retraction and stenosis—so much so that it was thought advisable to see if intubation would give any relief. The result of operation was unsatisfactory and the tube was removed.

September 30th, still more stenosis; restlessness even more marked. Patient almost pulseless.

September 30th, 9:40 P.M., patient died.

This child had no evidence of croup nor of laryngeal complication on admission. According to the record its illness was certainly slight and unimportant. After each injection of antitoxin there were restlessness, weakness, and feeble, imperfect respiration. The bad breathing, for which intubation was tried without relief, was undoubtedly due to the action of the antitoxin on the nerve centres and not due to croup.

CASE XXVIII.—Aged three and one-half years; admitted December 25th; four days sick. Dirty necrotic membrane on both tonsils, palatine arches, and uvula. Prognosis good. Antitoxin, 2,000 units, on admission.

December 26th, antitoxin, 2,000 units.

December 27th, urine scant; cream-of-tartar water, diuretin.

December 30th, strychnine.

January 2d and 3d, thirty per cent. of albumin, granular casts; aromatic spirits of ammonia, tincture

of digitalis, whiskey, etc. In spite of active stimulation the child grew weaker and weaker, and died of heart failure and nephritis, at 10:45 A.M., January 3d.

CASE XXIX.—Baby; admitted April 1st, 12:40 A.M. Antitoxin same hour; intubated at 12:50 P.M. Second dose of antitoxin, 2,000 units, in afternoon of same day. Temperature on admission, 99.8° F.

April 2d, temperature, 104° F.; wet pack, etc.

April 3d, 11 A.M., tube removed; 11.25 A.M., reintubated; 1:30 P.M., temperature, 105.2° F.; 6:45 P.M., extubated; tube found plugged; reintubated, 7:15 P.M.

April 4th, tube removed at 1:15 A.M., plugged; reintubated at 1:50 A.M.; tube removed immediately after; intubated again at 1:55 A.M.

April 4th, 10:20 P.M., temperature, 101.6° F.

April 5th, temperature, 106° F. Child died at 8:07 A.M.

This child had been ill, according to the record, but one day when admitted to the hospital. Antitoxin was immediately injected; twelve hours later intubation became necessary. According to the record, a second injection of antitoxin was given at about the time of the intubation. The following day the tube was removed at 11 A.M. Notwithstanding the influence of 4,000 units of antitoxin on a child who had been ill but one day when admitted and who did not have severe croup, the tube had to be reinserted within twenty-five minutes. The rest of the record shows that in every instance after the removal of the tube it had to be reintroduced. In other words, antitoxin did not have the slightest influence on the diphtheritic process in the larynx.

CASE XXX.—Aged four years and five months; admitted February 26th; illness began February 23d. Strong, well nourished; tonsils very red and much enlarged; numerous small patches of dirty membrane on tonsils and uvula; abundant and slightly foul discharge from nose; slight nasal obstruction; K. L. B. Prognosis favorable. Antitoxin, 20 c.c., 1 to 200, injected on admission; February 28th, antitoxin, 20

c.c., 1 to 200, injected. Temperature on admission, 99.5° F.; temperature ranged between 98.5° and 102° F. until March 18th, when it suddenly rose from 99° to 104° F.; on the 19th to 105° F. High but fluctuating temperature continued until March 28th, when patient died.

CASE XXXI.—Aged two years; admitted February 2d; illness began January 31st. Patient well nourished; small irregular patch of thin light grayish membrane on each tonsil; mucous membrane only slightly hyperæmic; tonsils and uvula about normal in size; K. L. B.; very slight dyspnœa; cough and cry croupy. Prognosis favorable. Antitoxin, 7 c.c., 1 to 400, injected on admission.

February 3d, condition of case satisfactory.

February 4th, antitoxin, 21 c.c., 1 to 400, injected.

Temperature on admission, 99.8° F.

February 15th, temperature, 99° F.; 16th, 103° F.; 17th, 104° F.; 18th, 106° F. Temperature fluctuated until March 25th, when the child died.

CASE XXXII.—Aged nineteen months; admitted March 13th; illness began March 9th. Patient well nourished; white patch well defined on left tonsil, posterior pillar, and uvula; K. L. B. Prognosis good. Antitoxin, 14 c.c., 1 to 500, injected on admission.

March 14th, antitoxin, 10 c.c., 1 to 500, injected.

March 16th, very little urine passed.

March 22d, patient died.

CASE XXXIII.—Aged two years; admitted April 27th; illness began April 23d. Thin white membrane on each tonsil, which were large and infiltrated; K. L. B. Prognosis good. Antitoxin, 8 c.c., 1 to 1,000, injected on admission. Albuminuria, enteritis, pulmonary symptoms, convulsions.

June 7th, patient died.

This child had almost no illness on admission to hospital, according to hospital record.

CASE XXXIV.—A. F.—, aged seven years; admitted June 4th; illness began June 1st. Well developed and nourished; thick dirty white membrane on both tonsils extending to uvula and soft palate; glands

of neck moderately enlarged; slight nasal obstruction, K. L. B. Antitoxin No. 6, 6 c.c., 1 to 1,000, injected on admission.

June 5th, antitoxin, 9 c.c., injected.

June 12th, patient died.

CASE XXXV.—Aged seven months; admitted February 5th; illness began February 2d. General condition only fairly well nourished; no membrane on tonsils and very slight hyperæmia of tonsils and uvula; slightly croupy cough and cry; K. L. B. Prognosis favorable. Antitoxin, 17 c.c., 1 to 300, injected on admission.

February 6th, antitoxin, 10 c.c., injected.

February 20th, patient died.

CASE XXXVI.—Aged one year; admitted January 13th; three days sick. Throat much swollen; membrane on both tonsils and base of uvula; naso-pharyngeal discharge. Prognosis doubtful. Antitoxin, 1,000 units, on admission.

January 16th, temperature suddenly rose to 105° F.; remained high until January 19th, when child died at 12:30 P.M.

This child, one year old, admitted to hospital when three days sick, died after six days' treatment without a complication.

CASE XXXVII.—Aged three years six months; admitted December 13th; one day sick. Small patch of membrane on left tonsil, croup. Antitoxin, 3,000 units, on admission. Admitted at 3 A.M. and antitoxin given immediately; intubated at 3:15 A.M. Antitoxin, 3,000 units, at 6 P.M.

December 16th, tube removed at 4:30 P.M.; intubated at 5:20 P.M.

December 29th, tube removed at 11:47 A.M.; reintubated at 12:10 P.M.

January 4th, tube removed at 1:30 P.M.; had to be reintubated immediately.

January 8th, tube removed at 9:23 A.M.; reintubated immediately.

January 14th, tube removed at 10:10 A.M.; reintubated immediately.

January 17th, tube removed and immediately replaced.

January 24th, tube removed at 10:10 A.M.; replaced immediately.

January 25th, tube coughed up at 3:30 A.M.; reintubated at 3:35 A.M.

January 28th, tube coughed up at 11:15 A.M.; reintubated immediately.

January 28th, tube coughed up at 12:10 P.M.; reintubated immediately.

February 5th, temperature, 104.2° F.; rash over whole body; patient restless.

February 6th, temperature, 102.8° F.; free perspiration.

February 7th, had a restless night. Antitoxin was given, two doses of 3,000 units each.

December 17th, patient was transferred to North Brothers Island, and subsequently died.

CASE XXXVIII.—Aged five years; admitted November 14th; illness began November 13th. Croup. Prognosis unfavorable. Antitoxin, 3,000 units, on admission, poultices to neck, calomel, fumigation, etc.

Admitted at 12:35 P.M.; croup, in spite of treatment, increased. Patient was intubated at 3:30 P.M.

November 15th, antitoxin, 3,000 units; tube removed at 2 A.M.

November 15th, died at 7 P.M. Cause of death, heart failure.

CASE XXXIX.—Aged sixteen months; admitted May 19th; illness began May 18th. Dirty white membrane on each tonsil, general hyperæmia, moderately croupy; K. L. B. Child well developed and nourished. Prognosis doubtful. Antitoxin, 7.5 c.c., 1 to 1,500, injected on admission.

May 20th, 7.5 c.c., 1 to 1,500, injected.

June 12th, child died.

CASE XL.—Aged eleven months; admitted December 16th; two days sick. Dirty white membrane on both tonsils, thin white membrane on uvula, nasopharyngeal discharge, croup. Prognosis unfavorable. Antitoxin, 2,000 units, on admission.

Decemer 17th, intubated at 1:50 A.M.; 6 A.M. a note states on chart: "No urine since admission."

December 17th, antitoxin, 2,000 units; 5:25 P.M., tube removed; 6:35 P.M., intubated; poultices to kidneys constantly. Cream-tartar water, diuretin, etc.

December 18th, child died at 2:30 A.M.

CASE XLI.—Three years old; admitted June 30th; illness began June 28th. Nasal obstruction, thick dirty white membrane covering both tonsils, uvula, and soft palate, extending back toward pharynx; glandular enlargement. Prognosis good, no complication. Antitoxin, 13.5 c.c., 1 to 1,500, injected on admission.

July 2d, 13 c.c., 1 to 1,500, injected.

These histories are of cases brought under treatment in the early part of the disease—many of them on the first and second day. They had full doses of a supposed specific, and yet we do not find recorded in the clinical history one statement which would indicate that this specific modified in any particular a single manifestation of the disease, either in the laryngeal or non-laryngeal cases. Not one item in the clinical records can be found to indicate that any one of these patients was in any way benefited by the antitoxin. This is particularly noticeable in the laryngeal cases. Patients brought in without evidences of very marked croup and after receiving full doses of antitoxin had to be intubated twelve and twenty-four hours after hypodermic use of this so-called specific. The clinical records of these cases are totally against the use of antitoxin in the treatment of diphtheria. A careful study of these records will, it seems to me, convince one who is familiar with diphtheria that there are clinical features here recorded which are due to the treatment and not to the disease. These features are referable to the kidneys, nervous centres, temperature, and respiratory organs.

Injurious Effects of Antitoxin.—At the beginning of this treatment Behring told us that an injection of his serum was as little injurious as an injection of a physiological solution of chloride of sodium. The records of serious complications and results which

have followed the injection of antitoxin in many known cases warrant careful consideration. In certain individuals who show a special susceptibility to antitoxin, the gravest symptoms or death may result from a relatively small dose. The predominating symptoms of these cases are referable to the nervous centres, kidneys, heart, pulmonary organs, and the temperature of the body. One feature of these untoward manifestations following the use of serum, especially when the respiratory organs are involved, is the lateness of their appearance.

The cases of Professor Langerhans' sixteen-months-old son, and Miss Valentine, of Brooklyn, are too well known to need more than mere mention here. In neither of these was any cause for death found by post-mortem examination. In the case of Miss Valentine, the coroner's physician, Dr. John M. Clayland,⁷ reported "Cause of death, convulsion, due to the injection of diphtheria antitoxin."

In the *Journal of the American Medical Association* is reported an instance which occurred in the practice of Dr. Halderman, of Portsmouth, O., in which a sleeping boy, five years old, was given a preventive dose of Behring's serum. Up to the time of the injection he was in perfect health; five minutes afterward he was dead. The account in the *Journal* states that the doctor had withdrawn to another room to refill his syringe for use on another child, when the mother noticed the boy's lips puff up, and called to him that something was wrong with "Willie." By the time the doctor had reached him, the child was dead.

Dr. C. C. Gratiot, of Shullsburg,⁸ Wis., advised a woman in apparently good health to take a preventive dose of antitoxin, as she was nursing her husband and daughter who were ill with diphtheria. Six hundred units of Behring's serum were administered. In a few minutes the woman complained of feeling faint; her pulse was almost imperceptible, she became very pale, her feet and hands were cold, breathing rapid and shallow, pupils dilated, and face covered with cold perspiration. It was six hours before she rallied.

Johannessen⁹ states that on December 9th eight patients of a hospital ward were immunized with six hundred units each of Behring's serum; seven of these children had no reaction, but the eighth, a boy of two years, with spastic spinal paralysis, had diarrhœa on the four following days. On the fourteenth day there were traces of albumin and indican, with a temperature of 103° F. The boy died on the tenth day after injection from collapse.

Alfoldi¹⁰ relates a case of a girl, three years old, who received a preventive injection of two cubic centimetres of Behring's serum, January 16th. January 18th her temperature rose to over 104° F. On the 19th there were severe albuminuria and hæmaturia, petechiæ appeared over the whole body, and on the twentieth day the child died. Alfoldi attributes death to antidiphtheritic serum.

Drs. Moizard and Bouchard¹¹ report the case of a girl of six years, who had a slight angina. Without waiting for the result of the bacteriological examination they injected ten cubic centimetres of Roux's serum. Bacteriological examination proved that the trouble was not diphtheria. On the sixth day after the injection the child's temperature suddenly rose to 105° F. and over, there being at the same time perspiration and insomnia. During the next four days scarlatinoid eruption appeared, which extended over the whole body. On May 12th, after a very restless night, when the throat had been well for a long time, the patient was seized with general convulsions and died four hours later. Dr. Moizard states that "death in this case appears to me certainly to have been due to the preventive injection of serum, administered before the result of the bacteriological examination was known. The dose of serum was decidedly small, and as the source from which it was obtained is above suspicion death can only be attributed to the action of the serum toxins on the cerebral nervous system. The conclusion to be put upon this occurrence is that preventive injections of serum are inadmissible, and that no intervention should be permitted before the result of the bacteriological examination is known."

Dr. Le Gendre stated: "I fully agree with Dr. Moizard, and I have long ago expressed my views as to the inadvisability of resorting to preventive injections of serum."

Guinon and Roufilange¹² have reported a case which ended fatally in a child three years old, with mild diphtheritic angina. Fifteen cubic centimetres of Roux's serum were injected on the third day of the disease. The following day eruption appeared on the body and lower extremities, and mild albuminuria; the second injection, of five cubic centimetres, was followed by diminution in amount of urine and increase of albumin; the tongue and lips swelled. On the next day, after the third injection of serum, there were anuria, swelling of the eyelids, and fetid diarrhœa; three days after the third injection a fourth was given, which resulted in renewed suppression of urine. During the following day and night there were coma and convulsions, and death ensued.

Dr. Thibierge's¹³ four-year-old daughter had a benign diphtheritic angina; serum was injected and urticaria appeared on the third day, and again on the sixth and eighth days, with vomiting, articular pains, and scanty urine. On the fourteenth day there was severe vomiting, and on the eighteenth day suppression of urine, critical relapse, fetid diarrhœa, and pseudo-meningitic disturbances due to serum. The child finally recovered.

Professor Mya¹⁴ (Florence) states that serum injections frequently have no effect on simple follicular tonsillitis associated with a marked degree of hypertrophy of the glands. "I have had under observation five of these patients, in whom the renal functions were absolutely normal before treatment, who on the sixth day of the disease suddenly presented manifest symptoms of intoxication, such as anuria, etc. At the autopsy I found fatty degeneration of the viscera, incident with grave pathological changes in the lymphatic tissue."

Galler¹⁵ has reported similar cases in which on the ninth day miliary eruption appeared; two days later

multiple petechiæ appeared, with œdema of hands and face and subconjunctival hemorrhages; two days later there were drowsiness, intense pain in the left leg with paralysis, petechiæ on the body, pains in the muscles of mastication and of the abdomen, effusion in the left knee-joint, with intermittent pulse. The child could not move on account of intense pain.

A similar case has been reported by Springorum¹⁰ in a girl of four years, which ended fatally.

Variot¹⁷ reports the case of a child of eighteen months who was suffering from slight pharyngeal diphtheria, followed by croup; the child was treated by injection, two doses of twenty cubic centimetres of antitoxin, and died forty-eight hours later in a state of hyperpyrexia. Variot says "this death could not be accounted for by any of the lesions found at the autopsy. There was not a trace of membrane in the throat, which appeared to be perfectly healthy. The same was true of the pharynx. The cause of death is consequently a mystery. Whether in the absence of organic lesions we are to attribute it to serum-hyperthermia is a question which it would be difficult to answer unhesitatingly in the affirmative, seeing that we have no means at our disposal for uniformly detecting toxic substances possibly existing in the serum. This goes to prove the necessity of exercising great care in the use of this treatment in diphtheria, and strengthens me in my opinion that it should not be employed for preventive purposes."

Variot¹⁸ further states: "The serum prepared by Aronson has always produced fever, and as it caused, in a great city of Europe [probably Berlin] nine deaths, one after the other, its use had to be discontinued."

Engel Bey,¹³ in a report of his clinical observations in Cairo, uses the following words:

"There was a frequent impression that the already present weakness is greatly increased by the injection, and that the children fall into a state of prostration, of which they will never recover."

Lennox Browne²⁰ states that of five patients who were treated with antitoxin, two died thirty-five and forty-

five hours respectively after injection, with complete suppression of urine.

Soltmann²¹ states that in nearly all cases the pulse remained frequent, small, and irregular. In four cases collapse followed immediately after the injection of serum and proved fatal.

Körte²² states that of forty patients who died early in the disease and were treated with serum from the start, no less than nineteen died from paralysis of the heart.

Trimmer²³ reports cases of collapse after injection in five cases, but all eventually recovered.

Hagenbach²⁴ reports a case of a little girl who, three days after injection of ten cubic centimetres of serum had petechiæ in the skin, which began first at the neck and were distributed over the whole body; on the seventh day there was profuse vomiting, which could not be controlled. Death by collapse followed three days later. "During life we thought the petechiæ had a relation to the serum injection, and the autopsy, showing hemorrhages into the mucous membranes of the intestines, and the changes in the heart and kidneys, did not change our views."

The resident physician in the diphtheria ward of the Children's Hospital at Strassburg said to me during my visit there last year: "I have seen three children who, I think, were killed by the serum."

Korach²⁵ has reported a fatal termination in the case of a three-year-old who died on the fourth day from an immunizing injection of two cubic centimetres of Behring's serum No. 1.

Hutinel²⁶ states that the rise of temperature which occurs after the injection of antitoxin is often a great danger, especially for tuberculous children. Among the deaths of children treated with serum are a great many showing tuberculosis of the lungs and pulmonary glands, and it is probable that the tuberculous process, which had been latent, became an acute process by the fever-producing injection.

Sevestre²⁷ reports a case of a little girl of five, who, two weeks after an injection of twenty cubic centi-

metres of serum, presented symptoms of extreme gravity—vomiting, fever, enormous swelling of the glands, marked pain in the vertebral articulations, wrists, knees, and ankles, offensive diarrhœa, anuria, severe cardiac disturbances, alternating attacks of delirium, and collapse.

Two of the internes of the Children's Hospital at Frankfort,²⁸ Drs. Gallus and Körte, were injected with Behring's serum the 24th and 25th of October respectively. They were ill with what appeared to be catarrhal angina (one had the Loeffler bacillus). Both were seriously ill afterward with high temperature, repeated attacks of urticaria, swollen glands, pains in joints, sleeplessness, headache, great prostration, sweating, and rapid loss of flesh (five and seven pounds each). These symptoms came on after the disappearance of local evidence of the disease and continued for about three weeks, when both young men were sent to their homes to convalesce and regain their strength.

A child aged four years²⁹ was desperately ill after an injection of thirty cubic centimetres of Roux's serum for an angina with a small white patch on either tonsil. The first injection of serum was given October 24th; October 28th the submaxillary glands commenced to enlarge, the false membrane on the right tonsil increased, and there was albuminuria. October 30th these glands continued to enlarge and the post-occipital glands began to increase. There was intense albuminuria. October 5th red spots appeared on buttocks and abdomen. November 6th the urine was scanty and still albuminous. October 7th the child was in a state of collapse the whole day with complete anuria. The child ultimately recovered.

A child of five years was admitted to Crown Prince Rudolph Hospital,³⁰ Vienna, November 15, 1894, having been ill two days with uncomplicated diphtheria. Four injections of Behring's serum were given. November 23d the child died of paralysis of the heart.

Professor Gnandinger, Crown Prince Rudolph Hospital, told me personally that he had seen more cases of paralysis of the heart in diphtheria since the use of

serum treatment than he had seen during the entire eight years of his connection with the Crown Prince Rudolph Hospital.

Dr. Hutinel³¹ states: "There can be no doubt of the gravity of post-sero-therapeutic ill-effects, for I have met with two cases of death from this cause in children. The injection of Roux's serum was followed in both cases by albuminuria, anuria, etc."

Dr. C. F. Withington³² says: "In private practice I had a case in which I had a great deal of anxiety, not to say alarm from the use of antitoxin. It was a case of a lady with diphtheria involving one tonsil. She received fifteen hundred units of Behring's serum. Two days later the other tonsil began to be involved, with rapidly increasing membrane, and she again received fifteen hundred units. Four or five days after this she was in a condition of a great deal of gravity for about a week. There was first erythema, then intense urticaria; then purpura of a great deal of severity involving both legs and severe pains accompanying the course of the nerves. Her condition was one of high fever, delirium, and great prostration. She is now convalescing. The gravity of the symptoms referable to antitoxin in this case will cause me in the future to be a little conservative in its use."

One of the best practitioners on Staten Island, Dr. Scales, stated to me that he had never in all his experience been so alarmed as he was after an injection of antitoxin in a woman suffering from diphtheria. For six hours after the injection prostration was so extreme that he felt she was likely to die at any moment.

Vierordt³³ reports that "in one case of a girl of two and a half years we thought of the possibility of a bad effect from the serum. The child came in with moderately severe diphtheria of the throat. She received forty-two hundred immunizing units of Behring's serum. There was collapse and stupor. The stupor remained till death, which resulted from heart failure. The autopsy revealed several points of hemorrhage of the mucous membrane of the intestines and the pericardium, and nephritis." Vierordt concluded that the case was not one showing harmful results of

the serum, because it could be explained in different ways; but the case is an exact counterpart of numerous cases reported by other observers, in which the only explanation of the symptoms was the ill-effects produced by the serum.

Dr. Martin J. Fleming, of this city, has reported to me a case of a child, who after an injection of serum had repeated eruptions; finally eczema appeared, which persisted for two months. There was nothing in the family history or in the child's general condition to account for the eczema, the only cause being the use of antitoxin.

At the April (1895) meeting of this academy I stated that the pneumonia of the antitoxin cases of diphtheria differed from the pneumonia we were in the habit of seeing in diphtheria; that it was a totally different disease from that seen before in the course of diphtheria; that it occurred as a sequela and not as a complication.

Dr. J. W. Brannan³⁴ in a report before the Society of Alumni of Bellevue Hospital, has shown that pneumonia was the cause of death in 53.22 per cent. of the fatal cases of diphtheria in the Willard Parker Hospital; whereas, before the antitoxin treatment, pneumonia was a cause of death in only 16.90 per cent. in this hospital. His report further shows that the average duration of stay in the hospital in fatal cases of pneumonia before antitoxin treatment was two days; but since the introduction of antitoxin, the average time of stay in the hospital in fatal cases of pneumonia was 13.7 days, bearing out the statement made by me in April, 1895, that the pneumonia of the antitoxin-treated cases occurred as a sequela and not as a complication of the disease. All conditions in the hospital were precisely the same in 1895 as in 1894, with the exception of the addition of the antitoxin treatment. The enormous increase of pneumonia as the cause of death in the Willard Parker Hospital during the antitoxin treatment has no other explanation than the hypodermic injection of serum albumin. These pneumonias are, as I stated in April

last, septic pneumonias; clinically they have the stamp of a septic process.

In New York and elsewhere it has been claimed in defense of the serum that the unfortunate ill effects in the form of high fever and suppurations are due to streptococcus infection; but if this were really the case they should supervene while the morbid affection is in process of evolution in the throat, whereas they usually supervene after the disappearance of all throat lesions. It is now stated that the bad effects which formerly resulted from the use of antitoxin were due to the amount of serum injected, and that with the use of a more concentrated serum there will be less pneumonia and bad after-effects than formerly. This is a very weak admission. It is an admission that there are bad effects from the serum. Last year it was asserted most positively by the advocates of this treatment that there were no bad effects; that it was absolutely harmless in doses of any amount.

Antitoxin in Private Practice.—The experience of physicians in private practice is of much service in estimating the value of antitoxin.

Dr. Edwin B. Tefft (New Rochelle), a most careful and experienced practitioner, communicated the following cases to me:

CASE I.—Child, aged five years; antitoxin on first and second days; died suddenly on the third day from heart failure. Peroxide of hydrogen and salt solution locally to throat and nose. Other treatment consisted of bichloride of mercury, iron, and stimulants internally.

CASE II.—Aged forty; treated without antitoxin; good recovery.

CASE III.—Aged twenty-seven; treated without antitoxin; good recovery.

CASE IV.—Child, aged fourteen; treated without antitoxin; recovered with slight paralysis as a sequel, which soon passed off.

CASE V.—Child, aged six, sister of Case IV.; antitoxin on second, third, and fourth days; died on fifth day.

CASE VI.—Child, aged four years, brother of Cases

IV. and V.; antitoxin on first and second days; recovered.

CASE VII.—Child, aged ten years; antitoxin on second day; recovered. Other treatment in both of these cases the same as in Case I.

CASE VIII.—Child, aged twelve; antitoxin on second, third, and fourth days; died on seventh day. Other treatment same as in Case I.

CASE IX.—Child, aged twelve; treated without antitoxin; good recovery.

CASE X.—Boy, aged sixteen, brother of Case IX.; also treated without antitoxin; good recovery.

“These were all bad cases. In Case VII. I am confident recovery would have followed without the use of antitoxin. From my experience and from cases I have seen in connection with other physicians, I am not favorably impressed with the utility of antitoxin in the treatment of diphtheria.”

Dr. Tefft reports five cases treated with antitoxin on the first and second day of disease, the youngest being a child of five, the oldest twelve. Three of the five died; mortality, sixty per cent. During the same period there were five cases, stated by Dr. Tefft to be equally severe, treated without antitoxin; all recovered. Cases treated with antitoxin had the same internal and local treatment as those treated without antitoxin. These antitoxin cases had a so-called specific at the very beginning of the disease, and in addition such tonic, stimulating, and local antiseptic treatment as one of our best physicians could devise—and yet show a mortality of sixty per cent., as contrasted with no deaths in five other cases treated without antitoxin.

Dr. de Kraft recently had three cases of diphtheria in one family. Two patients were treated with antitoxin at the beginning of the disease and both died. One treated without antitoxin got well. Another patient in Dr. de Kraft's practice died one hour after the injection of antitoxin.

During the spring of 1895 Dr. de Kraft saw a very severe case of diphtheria in the lower portion of the

city, with another physician, in which it was decided to give antitoxin. Neither, however, having antitoxin, and not knowing just where it could be procured at the time, a physician who was known to have the serum was sent for. When he saw the child he refused to inject, saying that it would surely die and that it would do harm to the cause of serum treatment. He was willing that the child should not have a possible chance of benefit which might arise from the use of the so-called specific fluid, but he was not willing that the fame of the serum treatment should be jeopardized. The baby, however, recovered, on the ordinary medicinal treatment without antitoxin.

Dr. J. C. Shanon recently treated two patients in one family with antitoxin at the very outset of the disease and both died.

Dr. Koempel reports the case of a child taken ill on the night of April 22d. Antitoxin was given during the first twelve hours, and a second dose the following day. The child died twenty-four hours later.

Dr. J. H. Bache reports three patients treated at the beginning of the disease, two of whom died; the third patient, the child of a physician, barely escaped death from the after-effects of the antitoxin.

Dr. P. H. Ernst³⁶ reports twelve cases treated with antitoxin, seven deaths, mortality 58.3 per cent; sixty-five cases treated without antitoxin, eleven deaths, mortality 16.9 per cent.

In all these the clinical diagnosis was confirmed by bacteriological report of the health department.

Dr. John Dorning, who is known as a careful and skilful practitioner, employed antitoxin in his private practice in seven consecutive cases of diphtheria, treated in the early part of the disease—in some of the cases during the first twelve and eighteen hours—and all the patients died. He was compelled to give up the use of antitoxin more than a year ago because of the results in private practice.

Every member of this academy has the highest regard for the opinion of Dr. Francis Huber on anything pertaining to clinical medicine or therapeutics.

Two weeks ago I asked him what he thought of antitoxin, knowing that he had a large experience with diphtheria. His answer was, "Dr. Winters, it is a humbug." That is the impression of a man who used it in private practice in conjunction with his brother, each anxious to get the best possible results and do the most he possibly could in every case. These are the results obtained by "Heilserum," a so-called specific against the toxin of the diphtheria bacillus, when used in private practice at the very beginning of the disease.

The percentage mortality in the Willard Parker Hospital during the year 1895 is very misleading, owing to the mild character of many of the cases received.

Dr. J. W. Brannan³⁶ has reported five hundred and ninety-three cases admitted to the Willard Parker Hospital during the first nine months of 1895 and treated with antitoxin; mortality 26.1 per cent. During the first nine months of 1894 there were four hundred and sixty-nine cases in the hospital, or one hundred and twenty-four less than in 1895. Every practitioner knows there was much less real or clinical diphtheria in New York City in 1895 than in 1894, and yet we have as the result of bacteriological diagnosis one hundred and twenty-four more cases received into the hospital during the first nine months of 1895 than there were during the corresponding months in 1894. The mortality in four hundred and sixty-nine cases in 1894 (non-antitoxin) is reported as being 35.1 per cent., but the report of the resident physician of the hospital to the health board gives the mortality for the first quarter of 1894 as 24.5 per cent.; second quarter, 26.5 per cent.; third quarter, 19.9 per cent.; fourth quarter, 26.8 per cent.; for the year, 29.3 per cent. The mortality of 35.1 per cent. in the report referred to was obtained by including all patients who developed or contracted scarlet fever or measles and were transferred to North Brother Island, and there died of mixed infection. The mortality of the Willard Parker Hospital is recorded as follows:³⁷

WILLARD PARKER HOSPITAL.

Year.	Cases.	Deaths.	Per cent.
1888 . . .	258	60	23.25
1889 . . .	383	79	20.62
1890 . . .	292	67	22.94
1891 . . .	289	85	29.41
1892 . . .	295	79	26.77
1893 . . .	343	108	31.48
1894 . . .	699	205	29.32
1895 (antitoxin) .	778	190	24.42

Could those cases be eliminated which gave no clinical evidence of diphtheria, the mortality of twenty-four per cent. for 1895 would be greatly increased.

The report of Dr. James Ewing³⁸ gives fifty-three cases of diphtheria in which his investigations were carried on. Fifty of these patients were injected with antitoxin, nineteen died, mortality thirty-eight per cent.

Dr. Ewing's investigation in the Willard Parker Hospital was in cases in which there was clinical evidence of diphtheria, and my impression is that this report (thirty-eight per cent. mortality) would fairly well represent the actual mortality of the Willard Parker Hospital at the present time, under serum-therapy, if patients who have clinical evidence of diphtheria were subjected to this treatment, to the exclusion and elimination of those cases which have no clinical data to warrant the diagnosis of diphtheria.

In order to determine the results with reference to larger or smaller doses of serum it was decided in the autumn of 1895 to give to alternate cases as admitted into the hospital, doses of serum of one thousand, two thousand, and three thousand units respectively. There were two series of cases, known as mild and severe, having one thousand and two thousand units respectively, and another series of cases of mild and severe having two thousand and three thousand units respectively.

RECORD OF DOSE IN PARALLEL CASES.

—Lesser Amount.—		—Greater Amount.—	
1,000 Mild.	2,000 Severe.	2,000 Mild.	3,000 Severe.
Case 1	Case 1*	Case 1	Case 1
Case 2*	Case 2	Case 2	Case 2*
Case 3*	Case 3	Case 3	Case 3*
Case 4	Case 4	Case 4	Case 4
Case 5	Case 5	Case 5	Case 5*
Case 6	Case 6	Case 6	Case 6
Case 7*	Case 7	Case 7	Case 7*
Case 8	Case 8	Case 8	Case 8*
Case 9	Case 9	Case 9	Case 9*
Case 10	Case 10	Case 10	Case 10*
Case 11	Case 11	Case 11	Case 11*
Case 12	Case 12*	Case 12	Case 12*
Case 13	Case 13	Case 13	Case 13
Case 14	Case 14*	Case 14	Case 14*
Case 15	Case 15*	Case 15	Case 15
Case 16*	Case 16*	Case 16	Case 16*
Case 17	Case 17	Case 17	Case 17
Case 18	Case 18	Case 18	Case 18*
Case 19	Case 19*	Case 19*	Case 19
Case 20	Case 20*	Case 20	Case 20
Case 21	Case 21	Case 21	Case 21
Case 22	Case 22	Case 22*	Case 22
Case 23	Case 23	Case 23	
Case 24		Case 24	
Case 25		(24—2 died)	(22—11 died,
(25—4 died)	(23—7 died,		50 per cent. ;
	30.4 per cent.)		one died after
			return home.)

94 cases, 24 deaths, mortality 25.5 per cent.

In the two series marked "severe" the cases were probably of nearly equal severity, inasmuch as they were alternate cases as received into the hospital. There were twenty-three severe cases which received two thousand units—seven deaths, mortality of 30.4 per cent., and twenty-two severe cases which received three thousand units—eleven deaths, mortality fifty per cent., the mortality being higher with the larger dose of serum in a series of parallel cases. It may be stated that since these experiments no child has received doses of three thousand units.

The mortality in children of two years old and

* Died.

under, with and without antitoxin, is most interesting and instructive:

1894.

163 cases of children two years old and under.

84 deaths..... 51.5 per cent.

1895.—ANTITOXIN.

153 cases of children two years old and under.

95 deaths..... 62.1 per cent.

Thus we see that at the very time of life when the disease is most dangerous we have in the Willard Parker Hospital a mortality of 10.6 per cent. greater with antitoxin treatment than without.

New York Foundling Asylum.—Prof. J. Lewis Smith³⁹ reports thirty-one diphtheria patients treated with serum in the New York Foundling Asylum, twelve on the first day of disease, seventeen on the second or third day, two on the fourth or fifth day; seventeen died; mortality, 54.8 per cent. All but two of the thirty-one cases were treated on or before the third day of the disease, and twelve on the first day, and yet the mortality was nearly fifty-five per cent. Certainly the antitoxin showed no specific influence in these cases.*

Results in Municipal Hospital in Philadelphia.—During the year 1895 there were 706 cases of diphtheria treated in the Municipal Hospital, Philadelphia. Three hundred and two of these received serum treatment, 404 were treated without serum. In the serum-treated series, 16.88 per cent. were intubation cases. In the non-serum treated series, 17.57 per cent. were intubation cases. The patients in whom antitoxin was used were injected at an early stage of the disease, from the first to the fourth day. No patient was injected who had been ill more than four days at the time of admission to the hospital. Cases that were considered hopeless on admission did not receive serum treatment. All patients that were considered hopeless when brought to the hospital were placed with the

* Mortality in N. Y. Foundling Asylum, 1894 (non-antitoxin year), 24 per cent.; mortality in 1895 (antitoxin year), 45.7 per cent.

non-serum-treated cases, and some of these died within an hour of their admission. This makes the serum-treated cases a far more favorable series than those that did not receive serum. There were more children under five years of age in the non-serum-treated cases, more intubation cases; all cases considered hopeless and late and neglected cases were in the non-serum-treated series. The mortality in the 302 cases treated with serum was 28.1 per cent.; in the 404 cases not treated with serum, 25.9 per cent. Had these 302 serum-treated cases of diphtheria received the same treatment that was given to the 404 cases that did not receive serum, they certainly should have shown a lower death-rate than the 404 cases treated without serum. They were by far a more favorable series, and should have shown under the same treatment better results. It should be stated that the cases treated with serum had the same local antiseptic treatment and the same internal medication and stimulation that were given to the series of non-serum-treated cases; and yet with a so-called specific added to the treatment there is a higher death rate.

Results in Blegdam Hospital (Copenhagen).—Professor Soerensen⁴⁰ reports 51 cases of severe diphtheria treated with serum, and 46 cases of severe diphtheria treated without serum, during the same period; mortality, 33 per cent. in both series. During this period the total number of cases treated in the hospital was 385, with mortality of 16 per cent., showing that the epidemic was a mild one; but for comparison these severe cases were selected for treatment with and without serum. There was no choice of cases unfavorable to the serum, but it depended upon the supply whether it was used or not. The average age of those treated without serum was lower than those treated with serum, four to five years against five to six years. The youngest (six months old) was in the group of those not treated with serum. Among those who died who were treated with serum two were admitted on the first day of the disease, two on the second, and five on the third day of the disease. Of those treated without

serum none were admitted on the first day of disease, four on the second, and one on the third day. Therefore, those who received serum were admitted earlier to the hospital than those who were not so treated. At the time of admission to the hospital complications were more pronounced in the cases treated without serum, the air passages being affected in eight cases, while with those treated with serum the air passages were affected only three times. Severe complications of the kidneys (after admission to hospital) were observed only in those treated with serum. Rise of temperature to a high point occurred in injected cases only. The serum was used earlier in the fatal cases than in the cases which recovered; that is, the day of the first injection was on an average earlier in the fatal than in the successful cases. [This is the most extraordinary part of the report: that the serum was used earlier in the fatal cases than in the cases which recovered.] "From our experiments we cannot see any favorable action of the serum. On the other hand, we observed more severe hemorrhage, albuminuria, nephritis, toxic anuria, fever, eruptions, and more frequent and more pronounced paralysis in those treated with serum.

"The serum was also used in croup cases complicated by severe diphtheria, and in mild cases of croup for the purpose of preventing stenosis. The mortality in all cases (operated and not operated) was 28 per cent. and for operated cases 40 per cent.; but during this same period there were 87 cases of croup that were not injected; the mortality in these, for all cases (operated and not operated) was 25 per cent. and for operated cases 38 per cent.—therefore lower than in those treated with serum. The serum was generally used in mild cases to prevent possible operative interference. The serum could not prevent laryngeal stenosis. Severe diphtheria complicated with croup did very badly with this treatment. All such patients died, and the good result in milder cases is explained by the good type of the present epidemic. The mildness of the epidemic reached a height formerly unknown."

Springorum, Magdeburg Hospital (*Münchener med. Woch.*, Nos. 31 and 32, 1895), says: "We find a remarkable improvement during the last year against former years, even the most favorable, 1890-91; but it is my opinion that the cause of this cannot be due altogether to the serum therapy, but principally to the changed character of our material. The children are admitted at present earlier and in larger numbers."

Years.	Cases.
1889-90.....	105
1890-91.....	139
1891-92.....	165
1892-93... ..	205
1893-94 (antitoxin).....	563
1894-95 (antitoxin).....	688

We began the use of antitoxin in August, 1894, and from that period until April 1st we treated in all with serum (Behring's) 206 children; 78 deaths, 37.9 per cent. mortality. There were 482 cases treated without serum; 122 deaths, 25.3 per cent. mortality. Cases considered hopeless at the time of admission were not injected with serum, and mild cases were not injected with serum. There were 113 tracheotomy cases treated with serum; 52 deaths, 46 per cent. mortality. In 1891-92 there were 107 tracheotomies; 52 deaths, 48.6 per cent. mortality.

It is very striking that in the largest proportion of the fatal cases treated with serum the patients died from paralysis of the heart, and that in those recovering the convalescence was frequently interrupted by affections of the heart. Causes of deaths in the fatal cases treated with serum: descending croup, 17; broncho-pneumonia, 21; sepsis, 16; paralysis of the heart, 24. Of the 122 fatal cases not treated with serum, paralysis of the heart was the cause of death in only 4 cases.

"Either paralysis of the heart occurs now in children who would have died earlier without serum treatment, or the serum has a toxic effect upon the structures of the heart; and the latter is nearly confirmed by a good many observations." When the child is

seemingly on the road to recovery, there regularly occurs from the eighth to the twelfth day a change in the picture of the disease. The children are tired, listless, without appetite; rise of temperature occurs, frequently with an eruption, and if we feel the pulse we find it is small, nearly imperceptible, either very slow or very frequent and irregular; the extremities are cold, the skin is livid. These symptoms sometimes disappear in a few days and recovery follows; but frequently during these periods nephritis arises, and in tracheotomized children bronchitis, which retard their convalescence. Not a small number, however, cannot stand the heart attack, and die of paralysis of the heart. The children fail more and more in spite of large doses of alcohol or camphor; the extremities get colder and colder, the pulse gets feebler, the skin blue; older children complain of headache. In two children I observed spasmodic conditions shortly before death.

“Another picture of heart failure is the following: The children are seemingly well shortly before death, but suddenly they get restless and cyanotic, toss about, and before the physician can arrive death has occurred. We had three such cases.” (See Willard Parker cases, Nos. 19, 22, 24, 26, 27, 28, and 33.)

Report of the Medical Superintendents of the Metropolitan Asylums Board (London), 1895.—

This report embraces 2,182 cases of diphtheria treated with antitoxin; 615 deaths; mortality, 28.1 per cent. The medical superintendents compare this result with that of 1894, when 3,042 cases of diphtheria were treated in all the hospitals of the board (without antitoxin), 902 deaths; mortality, 29.6 per cent.*

There are divergencies in the mortality in the individual hospitals during the antitoxin and non-antitoxin years which show that the 1.5 per cent. reduc-

* In this antitoxin report it is stated: “In a certain number of patients, being moribund at the time of their arrival and beyond the reach of any treatment, no antitoxin was given.” These cases are therefore all eliminated from the report. There were 1,347 patients in the hospitals during the year who did not receive antitoxin treatment; of these 181 died; mortality, 13.4 per cent.

tion in mortality in 1895 over 1894 is not due to a single or specific factor.

In the Southwestern Hospital in 1892 there were 463 cases of diphtheria; 93 deaths; mortality, 22.5 per cent. In 1895, 316 cases treated with antitoxin; 94 deaths; mortality, 29.7 per cent.

In the Southwestern Hospital in 1893, 585 cases; 159 deaths; mortality, 27.1 per cent. In 1895, mortality in antitoxin-treated cases, 29.7 per cent.

In the Southwestern Hospital in 1894, 546 cases; 156 deaths; mortality, 28.5 per cent.

S. W. HOSPITAL.			N. W. HOSPITAL.			
	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.
1892	463	93	22.5	682	138	21.8
1893	585	159	27.1	1,249	332	26.5
1894	546	156	28.5	1,147	309	26.9
Total,	1,594	408	25.5	3,078	779	25.3
	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.
1895 (antitoxin)	316	94	29.7	363	117	32.2
IN S. W. AND N. W. HOSPITAL.						
	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.
1892, '93, '94	4,672	1,187	25.4			
ALL THE HOSPITALS.						
	Cases.	Deaths.	Per cent.	Cases.	Deaths.	Per cent.
1895 (antitoxin)	2,182	615	28.1			

An examination of the above table shows the following:

1. In the Southwestern Hospital a lower death rate obtained in each of the years 1892, 1893, and 1894 in unselected cases treated without antitoxin than existed in 1895 with selected cases treated with antitoxin.

2. In the Northwestern Hospital a lower death rate also obtained in each of the years 1892, 1893, and 1894, in unselected cases treated without antitoxin than existed in 1895 with selected cases treated with antitoxin.

3. The table also shows that in each of the three years 1892, 1893, and 1894 the mortality rate in the Northwestern Hospital was a little lower than it was in the Southwestern Hospital for the corresponding year.

4. The mortality rate for 1895 in the Northwestern Hospital was 2.5 per cent. higher than it was in the Southwestern Hospital.

Such a reversal in mortality rate shows plainly the pernicious effect of selection on statistics.

5. If, with selected cases, the mortality rate under antitoxin is not lowered, it is difficult to say what the rate might have been had all the cases received uniform treatment.

At the Northwestern Hospital in 1892, 682 cases, 138 deaths, mortality 21.8 per cent. In this hospital there were 363 antitoxin-treated cases in 1895, 117 deaths; mortality, 32.2 per cent.

At the Northwestern Hospital in 1893, 1,249 cases, 332 deaths; mortality, 26.5 per cent. Mortality in 1895 in antitoxin cases, 32.2 per cent.

At the Northwestern Hospital in 1894, 1,147 cases, 309 deaths; mortality, 26.9 per cent. Mortality in 1895 in antitoxin cases, 32.2 per cent.

Diphtheria cases were not admitted to the Metropolitan Asylums Board Hospitals until October 23d, and it should be noted that during the seven years that diphtheria patients have been received into these hospitals the mortality has steadily and uniformly declined from 59.3 in 1888, 47.7 per cent. in 1889, 33.5 per cent. in 1890, 30.6 per cent. in 1891, 29.3 per cent. in 1892, 30.4 per cent. in 1893, 29.2 per cent. in 1894. The one exception was in 1893, the explanation for this being an insufficient number of beds to accommodate the diphtheria patients; hence it is stated in the report for 1894, page 203: "The attention of the managers is specially directed to the fact with regard to diphtheria, a most unsatisfactory deficiency of beds has existed during a considerable portion of the year (1893) and that for many weeks the ambulance department was very frequently compelled to defer the removal of diphtheria cases." In the autumn of 1894 a new hospital (Fountain) for fever patients was opened with about five hundred beds. Hence, we find in the London *Lancet* the statement that 3,529 cases of diphtheria were treated in 1895 in the hospitals of

the board as against 3,042 cases in 1894. The natural reduction of mortality which has taken place in these hospitals from year to year since 1888, owing to the board hospitals receiving a larger percentage of the notified cases in London and dealing with a better class of the population, was not even realized from 1894 to 1895. Indeed, it seems probable, when one studies carefully the reports of the Metropolitan Asylums Board from 1888 to 1894 and compares them with the mortality in the Managers' hospitals in 1895, that the mortality was higher with antitoxin than it would have been without.

The age of the patients brought under treatment is an important factor for consideration in determining the value of any method of treatment for diphtheria, the mortality being progressively less with the increasing age of the patient. We find that there were 244 children under two years of age in all the hospitals of the Metropolitan Asylums Board in 1894 (without antitoxin), whereas there were only 219 under two years of age in 1895 (with antitoxin). There were 1,171 children under five years of age treated in the board hospitals in 1894; 1,013 in 1895. There were 2,246 under ten years of age in 1894, and only 1,829 under ten years in 1895. The children under ten years treated in 1894 exceeded the total number of cases treated in all the hospitals with antitoxin in 1895. Had the ages been equal in the total number of cases treated during these two years, the mortality would in all probability have been higher with antitoxin in 1895 than it was in 1894 without antitoxin, seeing that the difference was only 1.5 per cent. even with the enormous age factor in favor of antitoxin-treated cases. The excess of children under two, under five, and under ten years in 1894 (non-antitoxin year) greatly vitiates the value of the report of the antitoxin treatment.

We find in the report of the medical superintendents on antitoxic serum a lack of uniformity in the results which is opposed to the theory of there being any single or specific factor at work in the inferred reduc-

tion of mortality under antitoxin treatment. For instance, at the Northwestern Hospital the mortality in those treated on the second day was 28.9 per cent. and at the Southwestern Hospital 3.8 per cent. There was but one hospital where the mortality was as high among the patients who came under treatment on the second day of the disease in 1894 (non-antitoxin) as it was in the antitoxin cases treated on the second day of the disease at the Northwestern Hospital. The mortality among those brought under treatment on the second day of the disease in all the hospitals of the board during the year 1894 (non-antitoxin) was only 27 per cent.; whereas at the Northwestern Hospital the death rate in 69 cases brought under treatment with antitoxin on the second day of the disease was 28.9 per cent. Had these 69 children received a specific, it certainly must have given a lower death rate than occurred in 539 cases during the year 1894 under ordinary methods of treatment.

Laryngeal Cases.—The most interesting portion of the report of the medical superintendents refers to tracheotomy cases. The mortality in these cases shows the same variation that is seen in the cases as a whole. At the Western Hospital the mortality in tracheotomy cases treated with antitoxin was 40.5 per cent.; at the Northwestern Hospital, 64.2 per cent.

There were 225 tracheotomy cases in all the hospitals treated with antitoxin; 113 deaths; mortality, 50.2 per cent. During the year there were 30 tracheotomy cases in all the hospitals that did not receive antitoxin; 12 deaths; mortality, 40 per cent. The mortality in all the hospitals in the tracheotomy cases treated with antitoxin in 1895 was 50.2 per cent. The mortality in all the hospitals in the tracheotomy cases not treated with antitoxin during the year 1895 was 40 per cent. Where is the specific influence of the antitoxin here? It cannot be said that the tracheotomy cases which were not treated with antitoxin were mild cases. The tracheotomy cases treated with and without antitoxin during the year 1895 were cases of the same degree and offer a very good field for comparison of re-

sults. The mortality in tracheotomy cases treated with antitoxin in 1895 was 10.2 per cent higher than it was with those not treated with antitoxin. This is just the result to be expected when a depressant like antitoxin is added to the treatment of cases of diphtheria so serious as to require tracheotomy.

At the Northwestern Hospital in 1895 28 tracheotomy cases were treated with antitoxin; 18 deaths; mortality, 64.2 per cent. In 1892⁴² there were 58 tracheotomy cases in this hospital; 33 deaths; mortality, 56.8 per cent. In 1893⁴³ 78 tracheotomy cases, 44 deaths; mortality, 56.4 per cent. (One patient cured was a child thirteen months old.) In 1894 79 tracheotomy cases; 47 deaths; mortality, 59.4 per cent. There were in the Northwestern Fever Hospital during 1892-93-94, 215 tracheotomy cases; 124 deaths; mortality, 57.6 per cent. The mortality in this hospital in tracheotomy cases treated with antitoxin in 1895 was 64.2 per cent. During the year 1895 four tracheotomy cases in the Northwestern Hospital were treated without antitoxin and all recovered; as compared with mortality of 64.2 per cent. in the tracheotomy cases treated with antitoxin. Nothing could be more conclusive of the depressing and dangerous effect of antitoxin in that severe form of diphtheria of the larynx and trachea which necessitates tracheotomy than the records of the Northwestern Fever Hospital for the years 1892-93-94-95.

Antitoxin in Laryngeal Diphtheria.—About the only claim made for antitoxin at the present time by its advocates is that it has a favorable influence in laryngeal diphtheria, that it relieves stenosis, that it obviates the necessity for operative interference, that the mortality is lower in non-operated and operated cases treated with serum, and that the tube can be removed earlier when operation becomes necessary. If antitoxin does not cause a "melting away" of the membrane, as was first claimed, and does not lessen the duration of the membrane in the visible portions of the throat, what reason have we for supposing that

it influences the duration of the membrane in the larynx?

Roux does not believe that serum is of any use in pseudo-membranous bronchitis. If it is not of use in pseudo-membranous bronchitis, how can it be of use against pseudo-membranous laryngitis?

Soltmann⁴⁴ (Leipzig) states that in 89 cases of diphtheria treated with serum the diphtheritic process extended downward in 13 cases, even to the involvement of the smallest bronchi.

The mortality in the Willard Parker Hospital for the first nine months of 1895 in intubation cases treated with antitoxin was 68 per cent., and for the last quarter 76.9 per cent. During the first quarter of 1896 there were 31 intubation cases; 21 deaths; mortality, 67.7 per cent. In April there were 11 intubation cases; 8 deaths; mortality, 72.7 per cent.* In May these were 16 intubation cases; 12 patients have died; mortality, 75 per cent. Two patients were discharged; 2 are in hospital. One of these was tracheotomized June 12th, intubation not having been successful.

In the Municipal Hospital, Philadelphia, 71 intubation cases were treated without serum in 1895; 40 deaths; mortality, 56.3 per cent.

Dr. P. H. Ernst⁴⁵ has reported nine cases of intubation treated without serum; two deaths; mortality, 22.2 per cent.

Dr. W. W. Seymour⁴⁶ recently stated before the Academy of Medicine that in his last ten intubation cases he had eight recoveries. In three of these cases antitoxin was used and one of these proved fatal. In seven cases antitoxin was not used, and of these only one was fatal. His mortality in intubation cases treated with antitoxin was 33.3 per cent., and in

* It has been stated (New York Med. Jour., February 15, 1896) that the mortality for operative cases in 1894 was 85 per cent.; but it is impossible to give the exact mortality of the operative cases in the year 1894, because many of the histories of the institution are missing and are not available.

intubation cases not treated with antitoxin 14.2 per cent.

Widerhoefer⁴⁷ gives a mortality of 43 per cent. for intubated cases (before serum treatment).

Von Ranke⁴⁸ gives in 326 intubation cases a mortality of 57.4 per cent. (before serum treatment).

Meisenbach⁴⁹ reports a mortality in tracheotomy cases of 57 per cent. (before serum treatment) in the Philadelphia Children's Hospital.

In Strassburg⁵⁰ in 397 tracheotomies (1891-94) the mortality was 44.3 per cent.

In Geneva⁵¹ from 1872 to 1888 the mortality in tracheotomy cases was 49 per cent.

In Basel⁵² in 333 tracheotomy cases there were 197 deaths; mortality, 59.2 per cent.

In the University College Hospital⁵³ (London) the mortality in tracheotomy cases in 1894 (non-antitoxin year) was 47 per cent.

Sonnenburg⁵⁴ states that in 13 tracheotomy cases treated with serum the mortality was 37.8 per cent., but during a period when serum could not be obtained the mortality in 35 tracheotomy cases was 37.1 per cent.—slightly better without serum. This statement by Sonnenburg shows the very great importance of taking into consideration the character of the epidemic in estimating the value of a mode of treatment.

Kohts⁵⁵ (Strassburg) reports a mortality of 29.1 per cent. in tracheotomy cases treated with serum, and a mortality of 25 per cent. in tracheotomy cases treated without serum.

Is not the very high mortality in intubation cases treated with serum in the Willard Parker Hospital when compared with the results in intubation cases without serum in the Municipal Hospital, Philadelphia, and in intubation cases reported by Widerhoefer and Von Ranke before serum treatment, and in tracheotomy cases in Philadelphia and in all parts of the world before serum treatment, a most positive warning against the use of this treatment in this serious and dangerous form of diphtheria? The divergencies in the results in laryngeal cases treated with serum

is opposed to the theory of there being a specific agent at work. For instance, in Soltmann's ⁵⁶ intubation cases treated with serum the mortality in June was 16.7 per cent.; in May it was 88.9 per cent.; in February 22.2 per cent.; in March 28.6 per cent.; in April 42.9 per cent. If serum had any influence on the low mortality in June of 16.7 per cent., it should be shown as well in the month of May; whereas, during that month we find a mortality of 88.9 per cent. The low mortality of June is due to the character of the cases (see Dr. Ernst's results without serum) and not to the serum treatment. If the antitoxin could bring about this low mortality in one month it certainly could in another.

In Soltmann's report we find the same variations in mortality in diphtheria of throat and nose. The mortality in these cases treated by serum was in February, 5 per cent.; March, 60 per cent.; April, 7 per cent.; May, 21.4 per cent.; June, 14.3 per cent.; July, 25 per cent. If the mortality of 5 per cent. in February were due to the action of a specific agent, we should find the same mortality in all uncomplicated cases of diphtheria of throat and nose throughout the entire period reported by Soltmann; whereas we find a variation ranging from 5 per cent. to 60 per cent., which variation is due to the character of the cases. I mean the low mortality of 5 per cent. was due to the character of the cases treated, and not to the treatment applied. It must be necessary to a method of treatment for it to be accepted as a specific, that its results be uniform in all parts of the world when applied to severe as well as to mild epidemics. Any considerable lack of uniformity of results in a method of treatment shows that the treatment fails to exert any influence when applied to severe cases, and we may suppose that the good results are due to the character of the epidemic and not to the treatment.

A very striking feature of the serum treatment is a lack of uniformity of results, according to the day of disease on which treatment by serum is begun. Heubner ⁵⁷ reports that in cases in which treatment was be-

gun on the second day the mortality was 6 per cent.; Soltmann, 4 per cent; The Southwestern Hospital⁵⁸ (London) in 52 cases, 3.8 per cent.; Seigert,⁵⁹ 20 per cent.; the Willard Parker Hospital⁶⁰ in 130 cases, 25.1 per cent; the Northwestern Hospital (London) in 69 cases, 28.9 per cent. In cases in which treatment was begun on the third day, Heubner's mortality was 4.5 per cent; Willard Parker Hospital in 116 cases, 34.1 per cent.; Southwestern Hospital (London) in 45 cases, 33.3 per cent. From these varied results we are led to believe that the day of disease in which the patient is brought under treatment has much less to do with the results than the character of the epidemic. The individuality of the patient, individual susceptibility and resistance to the action of the toxin, has far more to do with the results than the day of disease on which the patient is brought under treatment.

Why Antitoxin is Popular.—Why is it that antitoxin has to-day the hold on the profession which it has? Certainly many prominent members of our profession have a strong affection for antitoxin. The fame of antitoxin is largely due to the influence of two hospitals, viz., the Empress Frederika Hospital, Berlin (Baginsky's), and the Hospital for Sick Children in Paris (Roux and Martin). Baginsky⁶¹ reports 525 cases treated with serum; 83 deaths; mortality, 15.6 per cent. From March 15, 1894, to March 15, 1895, Baginsky had 525 serum-treated cases and during the same period 126 cases not treated with serum. Before serum treatment began in 1894 224 cases of diphtheria were admitted to the hospital, or 875 cases of diphtheria received into the Empress Frederika Hospital in fourteen and a half months. Comparé these figures with the previous records.

During the years 1890-93 there were 1,063 cases of diphtheria in this hospital (Empress Frederika) and during the serum period 875 cases in fourteen and a half months. It must also be borne in mind that this enormous increase in number was at a time when, as was stated to me in Berlin, diphtheria was not epidemic but existed only in sporadic form. The Em-

press Frederika Hospital is a general hospital for children, with medical, surgical, and contagious disease departments, there being separate pavilions for the contagious diseases. We find recorded in Baginsky's monograph on diphtheria serum the case of a boy brought to the surgical department of the hospital February 25th with a fractured femur; March 19th there was a yellow coating on the left tonsil and Loeffler's bacillus was found. He was transferred to the diphtheria ward, and 4.5 c.c. of antitoxin were given. March 20th 4.5 c.c. were again given. March 23d he was perfectly well. Again, a baby seven months old was brought to the surgical department March 15th on account of club foot. March 24th there was a white coating the size of a lentil on the right tonsil, and the Loeffler bacillus was found. She was transferred to the diphtheria ward and 5 c.c. of antitoxin were given March 25th. March 26th the dose was repeated. March 31st she was perfectly well. Case III. was that of a girl of five years, whose throat was red, but without membrane. The Loeffler bacillus was found. She was transferred to the diphtheria ward July 13th and 5 c.c. of antitoxin were given. She was discharged July 17th.

Of the first hundred cases in Baginsky's book the average time of stay in hospital was ten days. Should statistics to influence the profession and the public be made from such cases?

When I visited the Empress Frederika Hospital while in Berlin, I was first invited to attend the Dispensary Clinic for diseases of children, which opportunity I availed myself of. Such care in the management of cases of slight illness I do not think can be seen anywhere else in the world. The waiting-room for children is under the charge of a trained nurse. Every child has its temperature, pulse, and respiration taken by the nurse and its clothing removed; it is then carefully wrapped and taken before the physician. There again you see the same minute, painstaking care in every case. Noticing this great care and that not in a single instance was the throat examined, I thought

it strange. The doctor told me that the throat was not examined in this room, because the throat of every child was examined before being brought to this room, and if there was any affection of the throat the child was referred to the diphtheria polyclinic. A clinic for walking cases of diphtheria was a revelation to me. The next hour I visited the room where the diphtheria polyclinic is held, under the supervision of the same physician. Every child brought to the dispensary department of the Empress Frederika Hospital, if it presents any throat lesion, is placed in an isolation room of the hospital which they now have for these cases; it is immediately injected with antitoxin, and if Loeffler's bacillus is found, it is placed in the diphtheria pavilion and receives further serum treatment. It is in this way that the enormous number of cases, as compared with previous years, is taken into this hospital for serum treatment. When there is a lack of serum or when there is no serum, these walking cases of throat affection are not detained in the hospital, as it is not deemed safe to do so when they cannot be immunized and protected against their surroundings. It is this method of conducting the diphtheria department of the Empress Frederika Hospital which accounts for the reported low mortality and for the difference in mortality during periods when serum is used and when it is not used. It was this very feature of the reports from the Empress Frederika Hospital which made the strong impression on Virchow. But Virchow had not studied the details; he accepted the percentage mortality without knowing how such percentages were obtained.

At the hospital for sick children in Paris, it was impossible to ascertain the number of cases treated before and since the use of antitoxin; but we find at the Trousseau Hospital that the number of cases admitted before the antitoxin treatment averaged about eight hundred a year; the highest nine hundred. During the first year of antitoxin treatment there were between fourteen hundred and fifteen hundred.

In connection with the subject of Paris statistics,

the following from the *Paris Medical Week*, January 10, 1896, page 24, is interesting: "The most remarkable fact of the last month of 1895 is a sudden increase in the number of deaths from diphtheria [in Paris] to twenty-three, which is identical with the average of the last five years. The number of cases of this disease reported, however, does not differ materially from the number notified during the weeks immediately preceding." The *MEDICAL RECORD* (February 15, 1896) in commenting on this report says: "This naturally brings up the question again: have we been passing through a period of mild diphtheria and will antitoxin prove less efficacious when the virulence of the epidemic is pronounced?" The mortality in Paris has been as high as thirty-two per week during some weeks of 1896.

Variot (Paris) states that bacteriology has included a great number of cases which previously were not considered as cases of diphtheria.

Von Ranke⁶² (Munich) reports 102 cases; mortality, 18.6 per cent. Von Ranke had 162 cases of diphtheria in six months, whereas in the same hospital they have averaged 146 yearly during the last seven years.

Landau⁶³ (Frankenberg) reports 448 cases treated by serum in six months; 100 deaths; mortality, 22.3 per cent. In this same hospital they had averaged $132\frac{1}{3}$ cases per six months for the last fifteen years, whereas during the serum period (from February to July inclusive) 448 cases were admitted.

Rauchfuss (St. Petersburg) reports 101 cases treated with serum in four months; mortality, 34 per cent., previous mortality, 55 per cent.; but he had 101 cases in four months under serum treatment, or at the rate of 303 per year. During the previous twenty-five years they have averaged in this hospital but 142 cases per year.

Vierordt⁶⁴ (Heidelberg) reports a mortality of 25.4 per cent. in diphtheria treated by serum. Serum treatment was begun October 31st, and in four months he received into the hospital 70 cases of diphtheria. I

find from the hospital report that they had received into this hospital during the previous ten months but 56 cases.

The interne at the Children's Hospital (Heidelberg) told me that there was a great influx of cases from the Neckar Valley after the serum treatment began. Many apply to the hospital now who on account of the expense of the serum would not hitherto have applied. During the first ten months of 1894, without serum, 56 cases were received into the hospital, and during the succeeding four months, under the influence of serum treatment, 70 cases; and this at a time, as I was personally informed when in Heidelberg, when diphtheria was sporadic and not epidemic.

For increase in the number of cases during the serum period it remained for Dr. Ernest Germonig, of Trieste, to outdo all others.

Germonig⁶⁶ reports that from the 24th of August, 1894, to the 31st of January, 1895, a period of a little over five months, 362 cases of diphtheria were treated with serum in the Civil Hospital (Trieste). In this hospital they had in 1892 78 cases of diphtheria; in 1893 110 cases; the first eight months of 1894, 149 cases (before serum treatment). In five months and one week (serum treatment), 362 cases.

In 75 cases of diphtheria treated with antitoxin in the University College Hospital,⁶⁶ London, the mortality was 28 per cent.

Two hundred and forty-five patients treated with antitoxin in the American Urban Hospital,⁶⁷ Berlin, gave a mortality of 28 per cent.

Kossel⁶⁸ reports 233 cases; 54 deaths; mortality, 23.1 per cent. Some of these patients had flecks the size of a pinhead on the tonsils; no swollen glands; no fever.

Soltmann⁶⁹ (Leipzig) reports 181 cases of diphtheria with the Loeffler bacillus, treated with serum; 44 deaths; mortality, 24.3 per cent.

Contrast this with Heubner's⁷⁰ statement: "The mortality at my polyclinic (Leipzig), for fifteen years, for children of all ages and throughout the entire

year, through severe and mild epidemics, was 22.5 per cent. This experience was with the same population as that from which hospital patients are drawn. Therefore the mortality was higher than it would have been in good private practice."

Report after report might be quoted, showing that the mortality at the present time under serum treatment ranges from 23 to 28 per cent., and even to 33 per cent. (Copenhagen) and 45 per cent. (New York Foundling Asylum).

Behring promised us that his serum would reduce the mortality to one-tenth of its former rate.

Albuminuria and Post-Diphtheritic Paralysis under Antitoxin Treatment.—If antitoxin is a specific against the toxin of the Loeffler bacillus, the cardiac paralysis, the albuminuria, and the paralytic phenomena of diphtheria should no longer be seen. Albuminuria occurred in 40.9 per cent. of the cases treated with antitoxin in all the hospitals of the Metropolitan Asylums Board ⁷¹ during 1895. Albuminuria occurred in 24.1 per cent. of the cases in all the hospitals of the Metropolitan Asylums Board in 1894 (non-antitoxin year), and in 25.4 per cent. of the cases in 1892.

Soltmann ⁷² found albuminuria in 72 per cent. of cases after the injection of antitoxin, which did not have albuminuria before the injection.

Post-diphtheritic paralysis occurred in 23.2 per cent. of the cases treated with antitoxin in all the hospitals of the Metropolitan Asylums Board in 1895; post-diphtheritic paralysis occurred in 13.2 per cent. of the cases treated in all the hospitals of the Metropolitan Asylums Board in 1894 (non-antitoxin year).

Heubner (Berlin) reported that in cases treated by him in which 1,100 immunizing units had been given, post-diphtheritic paralysis occurred in 7.5 per cent.; whereas, in cases in which 1,700 immunizing units were given, post-diphtheritic paralysis occurred in 12 per cent. of the cases.

Complications and sequelæ, which should be prevented by antitoxin, are greatly increased since the use of this treatment, and to an extent never before known.

Perregeaux ⁷³ has reported of cases at the Trousseau Hospital that articular manifestations were observed at the hospital in eleven cases; after patients had returned to their homes, in nineteen. Diphtheritic paralysis occurred at the hospital twice; among patients who had left the hospital, twenty-one cases were found. Persistent and permanent albuminuria was found in six cases. In other words, it is not known when patients are free from a liability to after-effects from the disease or its treatment when antitoxin is used.

A child at the Willard Parker Hospital, which had recovered after an intubation and was sent home, within forty-eight hours after arriving at its home was taken with convulsions; it was seen by three physicians, but all treatment proved unavailing, and the child died in convulsions. This case is an exact counterpart of a case reported by Moizard (Paris). It is not known when after ill-effects of this treatment will supervene.

Dr. Chantemesse ⁷⁴ states: "I have endeavored to ascertain whether it is not possible to avoid the ill-effects due to hypodermic injections of serum in general, by having recourse to some other method of introducing the remedy. For this purpose I have in twenty patients tried sero-therapy by means of intestinal injection. The effects of this injection appear to be as marked as those of hypodermic injection. In the twenty cases treated in this manner the preventive power of the same dose of serum was substantially the same, whether it was introduced under the skin or by the rectum."

Certainly it is not possible to get any therapeutic properties from the injection of antitoxin into the rectum, and yet here we have the statement that in twenty patients the results were precisely the same as when given hypodermically. The inevitable conclusion is that it has no curative properties when administered in either manner. From the beginning of this treatment at Buda-Pest, until the present time, not one fact has been presented which would tend to

show that the serum treatment has any exact scientific value or scientific basis. We have, after all this period, no information to enlighten us as to the nature or the action of Behring's remedy. The theory of this treatment based on laboratory work assumes that the result of infection by a specific bacillus is always the same, and independent of the organization of the individual; whereas the exact opposite is true. The same causes produce essentially different results in different individuals. Again, inasmuch as streptococci, staphylococci, etc., play a prominent part in every case of severe diphtheria, it is useless to treat the disease with a remedy which can at best be useful only in cases of pure Loeffler infection. Even in these cases of pure infection, to be thoroughly effective, it must be applied at the time or during the first twenty-four hours of infection. A positive clinical diagnosis is nearly impossible during the first twenty-four hours. A bacteriological diagnosis cannot be obtained in less than twenty-four hours, and then the mere presence of Loeffler bacillus in the throat is no proof of the existence of diphtheria.

Kohts⁷⁶ (Strassburg) sums up his conclusions on the serum treatment at the Congress für Innere Medicin, München, April, 1895, as follows:

"The mortality of patients treated with Behring's heilserum is for tracheotomy cases 29.4 per cent.; for those not operated on, 7.6 per cent.

"This result is less favorable than in the year 1891, when the mortality of tracheotomy cases was 25 per cent. without antitoxin; for those not operated on, 6.9 per cent.

"Secondary affections, as disease of the kidneys, affections of the heart, and paralysis, are not prevented by the serum. The result by injection of heilserum during the first two days of the disease does not differ from the results obtained without serum when the patients come under treatment within the first two days of disease. When there was coincidence of severe case of diphtheria with severe chronic and acute disease, pneumonia hæmorrhagica, thrombosis of the heart, and sub-pleural hemorrhages were observed."

After a thorough study in various hospitals in Berlin of the use of diphtheria serum, Passed Assistant Surgeon F. J. B. Cordeiro,⁷⁶ U. S. Navy, in a report to the surgeon-general of the navy, concludes that, so far, proof is lacking of the value of the antitoxin in the treatment of diphtheria:

“1st. A large number of children treated with both small and large immunizing doses have, within a few weeks, acquired diphtheria, and some of them have died of it. We do not possess a single scientific proof that a case of diphtheria was ever prevented by the immunizing process.

“2d. Children, who during the first sickness have been treated with large doses of serum, have a short time after acquired diphtheria anew. They were not rendered immune either by their sickness or by the largest doses of the antitoxin.

“3d. In a large number of cases, children have been treated on the first or second day of their illness with the fullest dose of the antitoxin, and have died.

“4th. It is certain that a large part of those who have died, notwithstanding the serum treatment, did not die from the effects of a mixed infection, but directly from the specific effects of Loeffler's bacillus.

“5th. Heart and other post-diphtherial paralyses are also seen in early and fully treated cases, and they occur as often as they did before the serum treatment.

“6th. Of a fever fall by crisis in the first twenty-four hours, and of a pronounced antipyretic effect of the serum, most observers have seen nothing or next to nothing.

“7th. The separation of the membranes follows in the cases that run favorably in the customary manner; but often there is an extension of the local process and a renewal of the already separated membranes during and after the serum treatment.

“8th. The burden of proof lies with Behring and his coworkers. The world will eagerly and too willingly receive this proof. We know that the former extravagant promises are out of the question; but we should be grateful to have it demonstrated that the serum can

reduce the mortality by even one per cent. As yet we have not the slightest basis on which to found an expectation that fewer children will die in the future of this disease on account of the serum treatment."

One of the strongest arguments against the antitoxin treatment of diphtheria is the attitude of those who are living in hospitals and watching its results, who formerly were earnest advocates of the treatment, and who, after experience, have from conviction become opposed to it.

Dr. William M. Welch (Municipal Hospital, Philadelphia), who has injected over three hundred patients, stated to me that he would not have antitoxin used on himself if he had diphtheria; that if his children had diphtheria of any type, he would not allow them to be injected; and if left to act independently and from his own conviction, he would never inject another patient.

Dr. Steinsieck (North Brothers Island Hospital) says he would not have antitoxin used on himself; that recently he has thought it all over as to what he would do in case his children had diphtheria, and he has decided he would not have them injected with antitoxin, no matter how severe or what the form of the disease might be.

Dr. Warmuth, Dr. Tyler, and Dr. Bemis, of the Municipal Hospital, Philadelphia, were believers in antitoxin, and are now opposed to it.

Dr. Hardin, of Washington, and Dr. Levy, of Richmond, came to the Willard Parker Hospital thorough believers in antitoxin, and are now opposed to it.

Dr. Warmuth (Municipal Hospital, Philadelphia) had diphtheria and refused to have antitoxin used on himself.

Dr. Levy and Dr. Hess, of the Willard Parker Hospital, had diphtheria and refused to have antitoxin.

Not one of the nurses of the staff of these hospitals would have antitoxin used on themselves for immunizing purposes.

Variot states that the doctors and nurses of the Trousseau Hospital (Paris) would not have antitoxin

used for immunizing purposes, though one of the doctors had a severe diphtheria.

It has been said that I have been prejudiced against the use of antitoxin. My impressions with reference to the use of antitoxin were gained first in the autumn of 1894, when I saw Dr. Halliday come under treatment at the Willard Parker Hospital. He was brought to us as soon as the diagnosis of diphtheria was made, partly for isolation and partly to get the benefit of the antitoxin. He had an uncomplicated, but severe, diphtheria, involving most of the throat. He was a strong, healthy young man of perfect habits. He was given antitoxin as soon as admitted—given the full dosage, I understand—and in addition, every other possible treatment, of course, that could be suggested. At the end of two weeks and one day he died of a straight, uncomplicated diphtheria, the antitoxin not having had the slightest influence on a single symptom from beginning to end. This made me wonder, for the man seemed to have every possible chance to be saved by this specific. I was so impressed by it that I went to Dr. A. L. Loomis, and talked over the matter with him on three different occasions. He wanted me to come out then and express my opinion, but I said: "No; there is a possibility that I am mistaken, and I do not wish to deprive any one of the use of it." In that autumn only five patients with diphtheria were treated with antitoxin. Four out of the five died, and the fifth was desperately ill. He had a peculiarly long and tedious convalescence. It was these five cases that led me to study with the greatest care and anxiety—an anxiety such as I have never experienced in connection with any other subject—the action of antitoxin.

With reference to a prejudice, it is monstrous to speak of it—a prejudice against anything which could do any good in such a disease as diphtheria! A man who would have a prejudice against a specific for diphtheria, should not be allowed to practise medicine. If there is a specific for diphtheria, I want it; no member of this academy, no member of the profes-

sion in any portion of the world needs it more than I do; and every man who knows me, knows that it would not be possible for me to cast a word of doubt upon any remedy which could be of the least possible use in the treatment of diphtheria. I could not possibly have brought myself to the position in which I find myself to-night had it not been for my strong conviction regarding the injurious effects of antitoxin. Could I have found that antitoxin did not do any harm, even though it was valueless in the treatment of diphtheria—even though it did not reduce the mortality—I would never have said anything against it. It is because I believe that it is dangerous that my convictions compel me to speak. The time will come, gentlemen, when every member of this academy will feel with reference to it as I do to-night, and you will come to it from conviction, as various members have already.

25 WEST THIRTY-SEVENTH STREET.

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**Additional Fatal Cases after Injection of Anti-
 toxin.**—Dr. A. Chas. Dogge, Helena, Montana, re-
 ports (*Pediatrics*, vol. 2, No. 1, p. 12) a case of sud-
 den death in a child three years of age, after an
 injection of 10 c.c. of antitoxin. The autopsy showed
 nothing abnormal.

“This method (introduction into the circulatory
 system of artificial serum) is entirely different from
 and not to be confounded with serotherapie, which
 has received some terrible blows lately (in Paris), one
 case having resulted in death within an hour after the
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Additional Fatal Cases after Injection of Anti-toxin.—Dr. A. Chas. Dyer, Helena, Montana, reports (Pediatrics, vol. 2, No. 1, p. 17) a case of sudden death in a child three years of age, after an injection of 10 cc. of antitoxin. The autopsy showed nothing abnormal.

"This method (introduction into the circulatory system of artificial serum) is entirely different from and not to be confounded with serotherapy, which has received some terrible blows lately in Paris) one case having resulted in death within an hour after the injection."—Medical Record, June 27th, 1892, p. 922.

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