The Milroy lectures on industrial anthrax : delivered before the Royal College of Physicians of London on March 7th, 9th, and 14th, 1905 / by T.M. Legge.


COLLEGE OF MEDICINE

The Milroy Lectures

ON

INDUSTRIAL ANTHRAX

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BY

T. M. LEGGE, M.D. Oxon., D.P.H. Cantab.

HIS MAJESTY'S MEDICAL INSPECTOR OF FACTORIES.

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INDUSTRIAL ANTHRAX.

LECTURE I.

Delivered on March 7th.

MR. PRESIDENT AND GENTLEMEN,—Knowledge of the incidence of industrial anthrax in this country has been greatly increased as the result of Section 73 of the Factory and Workshops Act, 1901 (previously Section 29 of the Act of 1895), requiring every medical practitioner attending on, or called in to visit, a patient whom he believes to be suffering from anthrax contracted in a factory or workshop to notify the case forthwith to the chief inspector of factories at the Home Office. The notification of the practitioner usually states merely that the case is one of anthrax. Further data are obtained in every case by inquiry a few days later both by the certifying surgeon and by the inspector of factories. During the six years 1899 to 1904, both inclusive, there have been thus reported at least 261 cases of anthrax contracted in factories or workshops or so intimately connected with such conditions that I have not thought it wise to exclude them. I have commenced with the year 1899 because since then information has been obtained of the great majority of cases which have occurred. Between the years 1896, when the enactment first came into force, and 1898 cases were reported—13 in 1896, 23 in 1897, and 28 in 1898—but there is little doubt that owing to ignorance of the requirements of the section there was failure to notify some cases which occurred. Taking the figures as a whole they can be distributed in four main divisions.

TABLE I.

Industry.	Males.	Females.	Total.	Fatal.	Per cent.
Worsted and wool	70	18	88	23	26·1
Horsehair and bristles ...	53	17	70	17	24·3
Hides and skins	86	—	86	21	24·4
Other industries	15	2	17	6	35·3
—	224	37	261	67	25·6

Going more into detail as to industry the bulk of the cases in wool have occurred in the processes of wool-sorting, wool-combing, and spinning carried on as independent industries or as preliminary stages in the manufacture of carpets, blankets, and rugs, and of felt; in horsehair they have occurred principally in hair-combing for stuffing purposes and in brush-making; in the hide and skin industry, while the incidence has been mainly at the docks, in warehouses, and tan-yards, isolated cases have been noted in the making of leather articles. The cases included under other industries are interesting. This heading includes isolated cases among workers of horn and persons employed in rag-sorting, in unloading corn, in carrying sacks of potatoes, in a fruit warehouse, in the railway station, and in the manufacture of chemical manure. The total number of persons employed in wool, worsted, and shoddy in the United Kingdom in the year 1901 is stated to have been 259,909 (106,598 males and 153,311 females).[1] Of this large number, however, only 1171 (1164 males and seven females) are classed as being engaged in sorting, and 3093 (1882 males and 1211 females) in combing, the dangerous kinds of wool under the special rules for wool-sorting and wool-combing (Van mohair, mohair, alpaca, pelitan, cashmere, Persian and camel hair), making a total of 4264 persons incurring special risk. At least 64 of the cases occurred among persons employed in the sorting and combing processes of the scheduled dangerous classes of wool. I have excluded from this number cases of outside infection conveyed to others by workers manipulating these wools and cases among spinners and weavers, even when these occurred in factories where dangerous wools were manipulated and were possibly the result of infection from insufficient separation of one process from another. On the number (4264), therefore, exposed to risk, taking these 64 cases, the figure of attack is 1·3 per cent. or 0·21 per cent. per annum. In horsehair factories, in all processes, the total number employed in the year 1901 was 2206 (724 males and 1482 females). The number of cases of anthrax in horsehair factories was at least 40. I have excluded from this figure altogether the cases which occurred from the use of horsehair and bristles in brush factories. Estimated in the same way as for wool, the figure of risk in the horsehair industry is 1·8 per cent., or 0·3 per cent. per annum. The risk in horsehair factories generally, therefore, stated in this way shows itself to be greater than in wool, when the figures dealt with are limited to those manipulating the scheduled dangerous classes. For particular factories, both of wool and horsehair, a very much higher attack rate could be given.

[1] Supplement to the annual report of the Chief Inspector of Factories for the year 1902 (Cd 1979), dated 1904.

Knowledge of the population of the workers throughout the kingdom is necessary to see whether incidence of anthrax follows closely the lines of relative density of population in the particular industry. This is brought out in the following table, where for each of the counties in England the numbers employed in wool, in horsehair, and in leather are inserted. The figures for horsehair do not include persons employed in brush-making. The number of these is 5365. So far as I have been able to ascertain, however, only three or four of the cases included under horsehair can be attributed to bristles. The figures as to persons employed are least satisfactory for the hide and skin industry. They include all the tan-yards but it is probably that only a very small number of those employed in docks or in wharves and warehouses, among whom incidence of anthrax is greatest, are included. Table II. shows the number of persons employed in : (1) wool, worsted, and shoddy factories ; (2) horsehair factories ; and (3) leather in the several counties of England ; and the number of cases of anthrax in the six years 1899–1904. (The figures for (1) and (2) are those of 1900 and for (3) of 1898.)

In the whole of Scotland among 29,256 persons employed in wool three cases of anthrax were reported in the corresponding six years (two in Ayr and one in Lanark) ; among 794 employed in horsehair nine cases (all in Glasgow) were reported. No cases were reported among the 15,563 persons employed in leather. One case from manipulation of hides occurred in Swansea.

Incidence of anthrax on persons employed in wool is centred almost entirely round the Bradford district of the West Riding and in Worcestershire. No case at all has occurred in the woollen factories of the Stroud Valley in Gloucestershire, Wiltshire, Somerset, and Devon, representing a population of 7000 ; and again in the whole of Scotland, where nearly 30,000 are employed, only three cases have been reported. This is explained by the fact that, except in the two counties named, the nature of the manufacture does not involve the use of dangerous classes of wool in the raw state from Asia Minor and Persia to be described presently. In the cloth factories of the Stroud Valley and in Scotland colonial wool chiefly is manipulated. Distribution of the cases from manipulation of horsehair follows much more closely the population so engaged which suggests that the dangerous classes of hair from China, Russia, and Siberia are more generally used. Discrepancies in incidence of anthrax and number of persons employed in leather are to be observed similar to those noted in wool. The counties of Northampton, Somerset, Devon, Surrey, Stafford, Cheshire, West Riding of Yorkshire, and Lanarkshire show practically no cases, although the number of persons employed is fairly large. Anthrax in this industry is mainly confined to the ports of London and Liverpool.

TABLE II.

—	Wool.		Horsehair.		Hides and skin.	
	No. employed.	No. of cases in six years.	No. employed.	No. of cases in six years.	No. employed.	No. of cases in six years.
ENGLAND.						
Bedford	—	—	—	—	107	—
Buckingham...	—	—	—	—	28	—
Cambridge	—	—	—	—	189	—
Chester	280	—	—	—	824	—
Cornwall...	57	—	—	—	92	—
Cumberland	896	—	—	—	390	—
Derby	754	—	—	—	437	—
Devon	1224	—	—	—	757	—
Dorset	—	—	—	—	35	—
Durham	809	—	—	—	100	—
Essex	35	—	—	—	123	—
Gloucester	3275	—	—	—	436	3
Hants	—	—	5	—	304	—
Hereford...	5	—	—	—	123	—
Hertford...	—	—	—	—	169	—
Huntingdon	—	—	—	—	—	—
Kent...	—	—	—	—	657	—
Lancaster	11832	6	117	5	3052	23
Leicester...	2869	—	—	—	214	3
Lincoln	—	—	—	—	425	—
London	227	1	214	30	3869	49
Middlesex	—	—	18	—	58	—
Monmouth	51	—	—	—	20	—
Norfolk	129	—	145	1	83	—
Northampton	—	—	—	—	1061	—
Northumberland	34	—	1	—	308	1
Notts	220	—	—	—	775	—
Oxford	945	—	—	—	—	—
Rutland	—	—	—	—	—	—
Salop	585	—	—	—	155	—
Somerset	1961	—	121	8	896	—
Stafford	32	—	—	—	898	1
Suffolk	—	—	469	2	321	—
Surrey	45	—	—	—	698	—
Sussex	12	—	—	—	126	—
Warwick...	1101	—	—	—	346	—
Westmorland	498	—	—	—	46	—
Wilts	2140	—	—	1	252	3
Worcester	7263	12	122	4	689	—
York, East Riding	27	—	5	—	852	—
,, North Riding	4	—	—	—	101	—
,, West Riding	187204	66	195	10	4268	2
Total	224514	85	1412	61	25038	85

The fatality of the reported cases (25·6 per cent.) is probably higher than would be expected by medical men having knowledge only of cases treated in hospital and less than that expected by the general lay public which believes it hardly possible for recovery from anthrax to take place. It seems, however, to be that which is to be anticipated of anthrax when all cases are included and when the type is mainly external. In Italy,[2] where anthrax is notifiable, in the 11 years 1880–1890 there is record of 24,052, of which 5812 proved fatal—24·1 per cent. In St. Denis and the department of the Seine,[3] between 1886 and 1893, among 123 cases there were 35 deaths—28·4 per cent. Of 91 cases in the horsehair industry in Germany 29 proved fatal—31·6 per cent. Wilhelm Koch[4] collected particulars of 1473 published cases of malignant pustule in which the result was stated and of these 472 died—32 per cent. He adds, however, that these figures must relate to many cases where diagnosis was not made until late and treatment was therefore deferred. Of the 261 cases only six, all of which occurred in Bradford and were all fatal, appear to have been of the internal type. In 248 of the cases the situation of the pustule is stated and this may be grouped as follows:—

TABLE III.

Situation.	Number.	Per cent.
Head and face	108	43·5
Neck	103	41·5
Upper extremity	31	12·5
Lower extremity	3	1·2
Trunk	3	1·2

According to the occupation so in a measure does the situation of the pustule vary. The above list represents cases where infection arises mainly from dust. In the hide and skin industry, however, the pustule was situated on the neck in 49·4 per cent. of the cases as compared with 29·5 per cent. in wool—a difference to be accounted for perhaps by carrying of the hides on the shoulder. The arm, as might be expected, is much more frequently selected as the site of the lesion when the disease is contracted from work connected with the disposal of a carcass, although even then, apparently, it is less frequent than on the face. In 923 cases

[2] Sullo Stato presente della Sieroterapia Anticarbonchiosa, by A. Sclavo, Turin, 1903, p. 28.
[3] Maladies Professionnelles, Paris, 1903, p. 83.
[4] Milzbrand und Rauschbrand, 1886, p. 112.

particulars of which were collected by W. Koch[5] this is brought out (Table IV.).

TABLE IV.

Situation.	Number.	Per cent.
Head and face	447	48·4
Neck	45	4·8
Upper extremity	370	40·0
Lower extremity	26	2·8
Trunk	35	3·8

He further states that of the cases on the upper extremity the situation occurred most frequently on the fingers and the hand. In only one of the list I have prepared was the finger affected. In the anthrax districts of Thuringen, in 209 cases the pustules were situated 74 times on the face, 53 times on the arm, and 51 times on the hand and the fingers. The accident of situation is of considerable moment in determining the severity of the disease. Thus in the cases under review of 13 on the upper eyelid six were fatal—46 per cent.; of 103 on the neck, 31—30 per cent.; of 19 on the forehead, 2—10·5 per cent.; and of 31 on the upper extremity (including the shoulder), 4—12·9 per cent. Inability often to venture on an operation, absence frequently of the diagnostic sign of local necrosis, and the looseness of the cellular tissue account for the high fatality where the upper eyelid or the eyebrow is affected. And even in recovery from the local lesion in this situation extensive sloughing of the eyelid often results. Other figures,[6] based on 180 observations, give the mortality on the head and the face as 26·3 per cent., on the trunk as 22·7, on the neck as 18·5, on the upper extremity as 13·8, and on the lower extremity as 5·1.

The figures which I have given for this country exclude the cases which have occurred to the numerous class of persons who come into contact with animals infected with anthrax during life or have taken part in their slaughter and disposal of the carcass. Unfortunately, in no country can more than a guess be made of the number thus engaged who suffer. In Great Britain the annual returns of the causes of death published by the Registrar-General are of material help. Table V. shows the number of registered deaths from anthrax since 1882 and since 1899 the large share of them borne by those due to factory or workshop conditions.

[5] Loc. cit.
[6] Nassarow, quoted by Sclavo, loc. cit., p. 29.

In 1901 deaths not due to factory conditions were those of a butcher and a fireman in the merchant service ; in 1902, of two farmers, a shepherd, and an auctioneer and valuer (the latter had assisted in dressing a dead carcass) ; and in 1903 of a grocer's assistant, a farm labourer (contracted from bone manure), a butcher, and a gamekeeper. The figures show a marked increase in the decade 1894–1903 (140 deaths) as compared with the previous one (90 cases). Comparison with other countries is not possible as I cannot find that deaths from anthrax are tabulated separately in either France or Germany. Some information on the point, however, is given in the annual reports on diseases of animals in Germany[7] where it is stated (although the figures do not profess to be complete) that in the decade 1894–1903 901

TABLE V.

Year.	Males.	Females.	Total.	Year.	Males.	Females.	Total.	Deaths due to factory or workshop conditions.
1882	10	5	15	1893	6	1	7	—
1883	5	3	8	1894	7	3	10	—
1884	13	5	18	1895	11	2	13	—
1885	7	4	11	1896	8	1	9	—
1886	8	3	11	1897	16	2	18	—
1887	10	1	11	1898	16	2	18	—
1888	11	1	12	1899	16	5	21	17
1889	6	1	7	1900	10	—	10	7
1890	3	1	4	1901	11	1	12	10
1891	1	2	3	1902	12	1	13	9
1892	5	1	6	1903	15	1	16	12

cases of human anthrax occurred, of which 128 were fatal. In 442 of these only can the occupation of those attacked be made out, this number including 312 employed in disposing in one way or another of carcasses of animals which had died from the disease—51 farmers or farm labourers, 25 shepherds or cowherds, 26 horsehair workers, 9 tanners, 7 veterinary surgeons, 4 meat inspectors, 6 butchers, a gamekeeper, an estate agent, a shoemaker, and a person employed in a foreign lamb-skin store. In Austria of 250 cases treated by Graef[8] and two other surgeons nearly all were employed on the land.

[7] Jahresberichte über die Verbreitung von Thierseuchen im Deutschen Reiche, Arbeiten aus dem Kaiserlichen Gesundheitsamte.

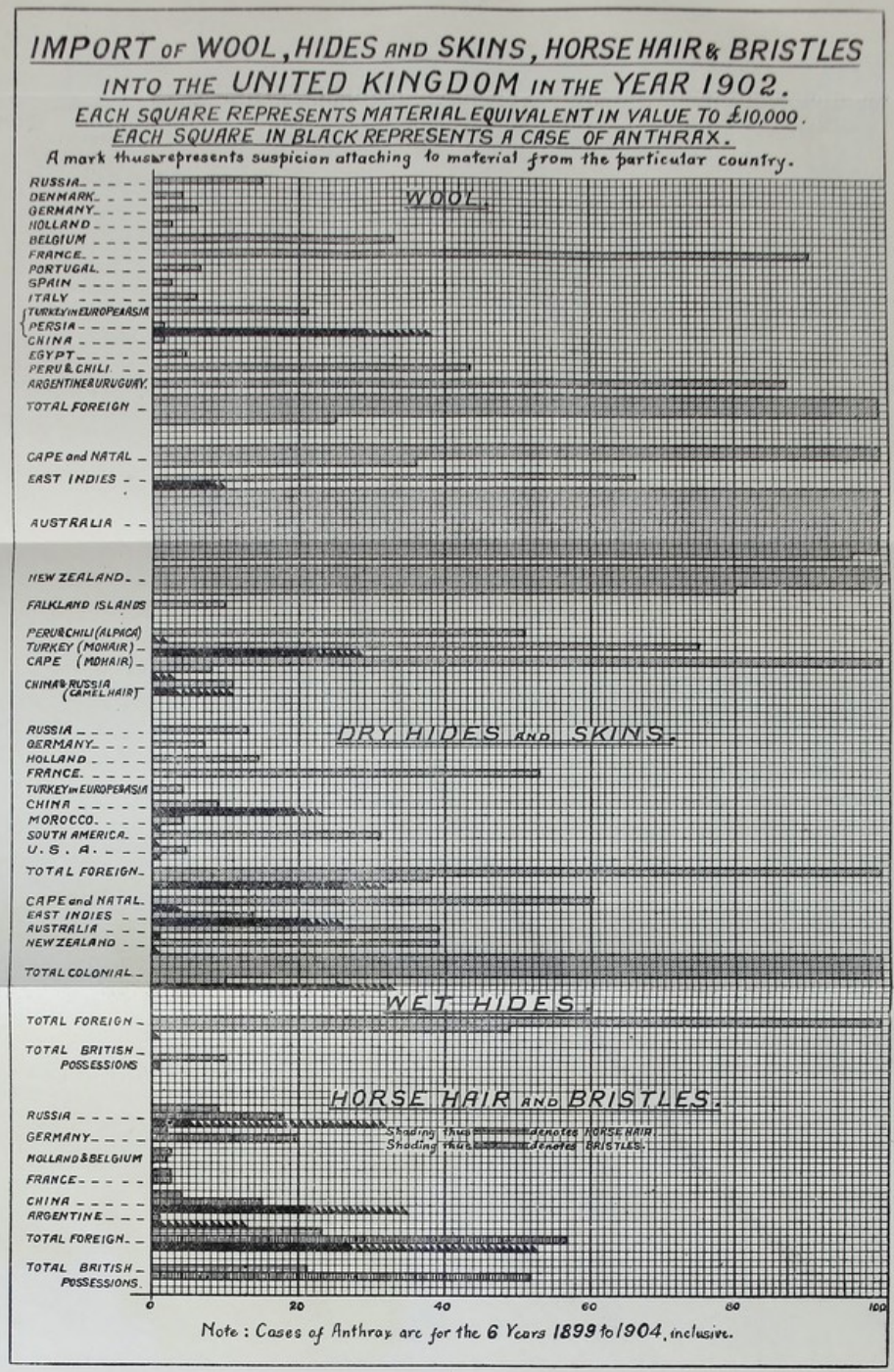
[8] Wiener Klinische Rundschau, Band x., 1903.

With the exception of this country, in all other countries of the world probably anthrax in the human subject is derived much more from contact with the carcass of a dead animal than from the spores contained in the wool, horsehair, hides, and skins of animals imported from distant countries. It is important therefore to ascertain as nearly as can be done the country of origin of the material which conveys anthrax to the factory workers in Great Britain. The source of the suspected material so far as it can be shown is brought out in Table VI.

A mere statement of the source and origin of the infected material which gave rise to the cases in the last six years conveys little information that is surprising unless this is interpreted in the light of the amounts imported from the various countries. The diagram I have prepared [9] shows the value of the amounts of wool, of horsehair, and of hides and skins imported in 1902 in pounds sterling from every country exporting more than an amount equivalent to £10,000. The diagram relates solely to imports and regard has not been had to the very considerable quantities which are re-exported. In the case of wool this is nearly one half, but it would have been impossible for me to have prepared a table showing the amount of material from each country which was consumed in this. The figures show the values of the material shipped from the various ports in the different countries. (See Fig. 1.) There can be no doubt that the considerable amounts from France, Belgium, Holland, and Germany include material which, so far as the country of origin is concerned, ought to be added to that from Persia, Turkey, &c. While I have taken the value of the imports for one year only the number of cases of anthrax attributed to the material from the countries are those of six years. Notwithstanding these limitations to be put upon the diagram it is at once apparent that in the case of wool a small fraction of the total quantity imported has conveyed all the infection. No single case has with certainty been traced in the six years to wool from Australia and New Zealand which in the year 1902 amounted to 417,442,529 pounds, valued at £13,537,457. On the other hand at least 30 cases with certainty, and possibly 40, have occurred from use of Persian wool valued in 1902 at £13,159. At least 21 cases again have occurred from use of mohair and Van mohair imported from European and Asiatic Turkey, the value of which in the same year was £746,818. In horsehair at least 22 cases are traceable to material from China, valued in the year in question at £40,758, or, if bristles be added, at £188,650, and several cases also to Russian or Siberian material valued at £266,497.

[9] Based on the Annual Statement of Trade of the United Kingdom with Foreign Countries and British Possessions in 1902, vol. i.

FIG. 1.


IMPORT OF WOOL, HIDES AND SKINS, HORSE HAIR & BRISTLES
INTO THE UNITED KINGDOM IN THE YEAR 1902.
EACH SQUARE REPRESENTS MATERIAL EQUIVALENT IN VALUE TO £10,000.
EACH SQUARE IN BLACK REPRESENTS A CASE OF ANTHRAX.
A mark thus represents suspicion attaching to material from the particular country.
WOOL.
RUSSIA
DENMARK
GERMANY
HOLLAND
BELGIUM
FRANCE
PORTUGAL
SPAIN
ITALY
TURKEY IN EUROPE & ASIA
PERSIA
CHINA
EGYPT
PERU & CHILI
ARGENTINE & URUGUAY.
TOTAL FOREIGN
CAPE and NATAL
EAST INDIES
AUSTRALIA
NEW ZEALAND
FALKLAND ISLANDS
PERU & CHILI (ALPACA)
TURKEY (MOHAIR)
CAPE (MOHAIR)
CHINA & RUSSIA (CAMEL HAIR)
DRY HIDES AND SKINS.
RUSSIA
GERMANY
HOLLAND
FRANCE
TURKEY IN EUROPE & ASIA
CHINA
MOROCCO
SOUTH AMERICA
U. S. A.
TOTAL FOREIGN
CAPE and NATAL
EAST INDIES
AUSTRALIA
NEW ZEALAND
TOTAL COLONIAL
WET HIDES.
TOTAL FOREIGN
TOTAL BRITISH POSSESSIONS
HORSE HAIR AND BRISTLES.
RUSSIA
GERMANY
HOLLAND & BELGIUM
FRANCE
CHINA
ARGENTINE
TOTAL FOREIGN
TOTAL BRITISH POSSESSIONS.
Shading thus denotes HORSE HAIR
Shading thus denotes BRISTLES.
0
20
40
60
80
100
Note: Cases of Anthrax are for the 6 Years 1899 to 1904, inclusive.

In hides and skins imported in the wet condition (mainly from Italy and South America through the ports of Germany, France, Holland, and Belgium) only two cases could with any certainty be traced, although such material in 1902 was valued at £1,595,109. In dry hides, on the

TABLE VI.

Wool.		Horsehair.		Hides.	
Persian (Bagdad)	29	China	22	China	19
Persian or camel hair	7	Russia, Siberia, or China... ...	13	China or East Indian, &c.	5
Persian or alpaca...	1	Siberia or Russia	5	Madagascar, East India, or China...	1
Mohair or Persian	1	South America or Siberia or Russia	13	Bombay, East Indian	20
Mohair	13	All kinds except Chinese	5	East Indian or Russian green hides	1
Van mohair	8	Indefinite	12	Cawnpore goat skins	1
Mohair or cashmere or camel hair	2		—	Cape or Singapore	1
Cape mohair or Turkey mohair...	3	Total	70	Cape...	3
Mohair or alpaca ...	1			Australian	1
Pelitan or mohair	1			South American or New Zealand ...	1
East Indian... ...	8			Arabian	1
Native, Colonial, or East Indian... ...	2			Morocco	1
Camel hair	3			West African... ...	2
Finished tops ...	1			Buffalo hides... ...	1
Probably Persian or East Indian ...	2			Madras and Bombay tanned hides	1
Indefinite	6			Tanned sheep skins	2
	—			Tanned boot leather	1
Total	88			Native	1
				Colombia	1
				Persian goat skins	3
				Indefinite	19
					—
				Total	86

other hand, 19 cases were due to manipulation of material from China valued in 1902 at £87,989, and a similar number from Bombay and East Indian raw dry hides valued at £265,422.

Having thus shown the part played by the introduction

of raw foreign material in the production of anthrax in man I turn to the information available which will throw light on the occurrence of anthrax in animals in these countries, especially in Asia, and on the conditions which favour its spread. These will be found, I think, in conditions of soil, of climate, and equally also in the primitive nomadic life of many of the inhabitants which takes no thought of rational preventive measures. Anthrax in animals is common in all parts of the world. Official figures[10] showing the gross number attacked in such countries as make returns are set down in Table VII. for the years 1901 to 1903.

TABLE VII.

Country.	Cases of anthrax in animals.		
	1903.	1902.	1901.
Great Britain	1,143	1,032	971
England	792	706	674
Scotland	324	307	281
Wales	27	19	16
Germany	4,626	4,852	5,843
Netherlands	409	356	261
Belgium	512	512	541
Norway	595	537	467
Denmark	15	155	69
Switzerland	237	300	210
Italy	3,959	6,099	2,604
Roumania...	452	104	192
Bosnia and Herzegovina	241	166	273
European Russia and the Caucasus	47,300	42,423	54,731
Asiatic Russia...	4,200	6,802	6,886

In France, Hungary, and Sweden the returns are made, not of the number of animals attacked, but of the number of infected farms, and of those in France there were in the three years 416, 395, and 491 respectively; in Hungary 1974 2158, and 2754; and in Sweden 224, 218, and 179. From one other country in Asia statistics of the prevalence of cattle diseases are given—namely, in India. The numbers of animals that died from anthrax in the North-West Provinces and Oude, North and South Punjab, the Bombay

[10] The figures, except those for Great Britain, are taken from Jahresberichte über die Verbreitung von Thierseuchen.

Presidency, Bengal, Burma, Sind, Rajputana, Madras, and Berar are stated to be as follows :—[11]

TABLE VIII.

—	1899	1900	1901	1902	1903
All animal diseases	343,906	304,931	249,691	228,606	258,419
Anthrax	33,667	36,070	25,997	28,081	30,715

Although these figures may be, and probably are, inaccurate the statement remains in the report that rinderpest and anthrax are the "two most prevalent fatal diseases of Indian cattle." There is an inclination always to doubt the accuracy of statistics on anthrax inasmuch as all sudden deaths of animals which cannot be otherwise accounted for are often ascribed to it. Still, the figures which have been given are separated from the other recognised animal diseases such as rinderpest, cattle plague, foot-and-mouth disease, &c. In the recent Tibetan mission[12] it is stated that anthrax chiefly reduced the number of yaks which accompanied the force from 3000 to 1450. Too much stress must not be laid on the greater number attacked in one country over another in the absence of knowledge of the number of animals in each country. Table IX. shows the actual incidence of the disease per 10,000 of each class of animal. I can only give the figures for Germany and Great Britain.

TABLE IX.

Country.	Year.	Horses.	Cattle.	Sheep.	Goats.	Swine.
Germany ...	1903	0·36	2·11	0·35	0·03	0·08
Great Britain	1903	Not stated.	1·2	0·02	Not stated.	0·8

Although this is the average for the whole of the countries named, incidence in particular districts is far greater. Thus among cattle in the district of Düsseldorf it was 11·15 per 10,000, in Zwickau in Saxony 8·8, in Chemnitz (also in Saxony) 8·5, and in Anhalt 6·6. In this country in 1903

[11] Annual Administration Report of Civil Veterinary Department in India.

[12] Report on the Working of the Army Veterinary Department with the Sikkim Tibet Mission, by Lieutenant-Colonel R. Moore, Simla, 1904.

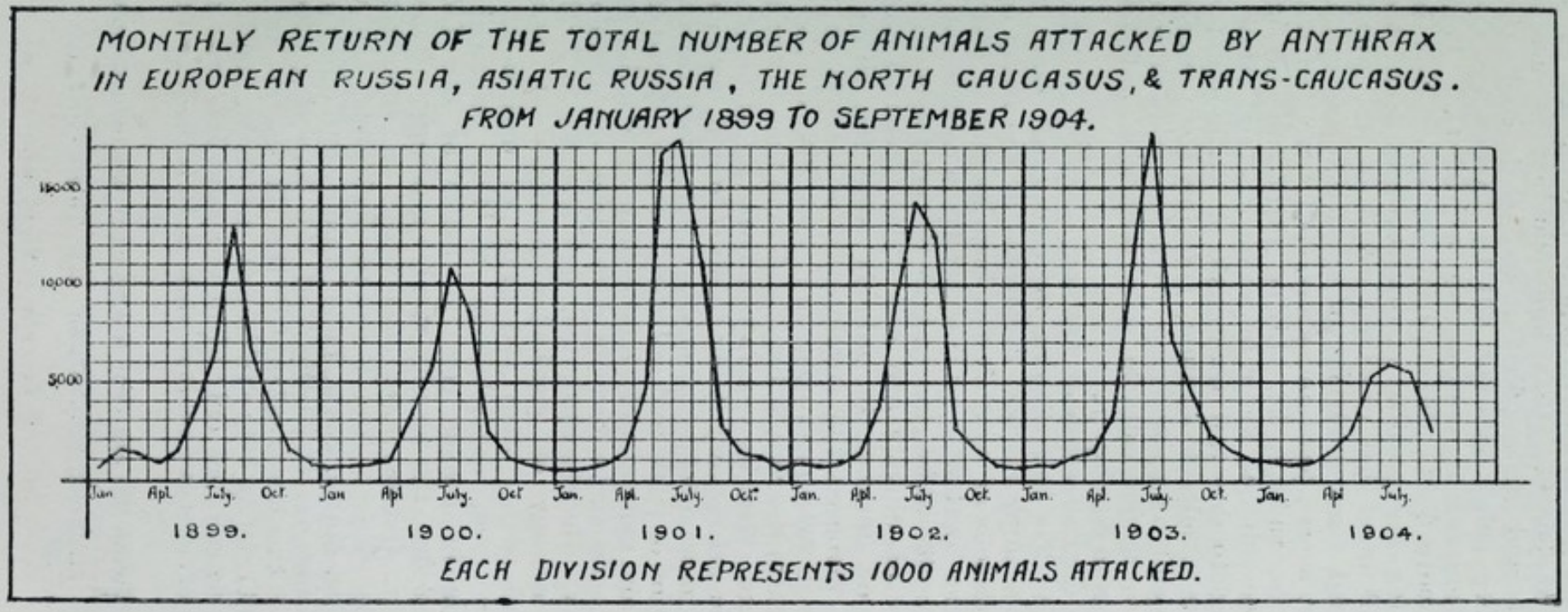
in Haddington it was 15·4 per 10,000 and in Aberdeenshire 4·9. Interest to us centres round the large figures obtained from Russia. In the 59 districts in European Russia from which returns were received in the month of August, 1904, cases of anthrax were only absent from three of them and in the 13 districts of Asiatic Russia they were absent from four. The importance of the figures in establishing the law which I believe underlies the whole question of the incidence of anthrax among animals in Asia and in man in this country is brought out by distributing the cases month by month over a period of years as has been done in the following curve. (See Fig. 2.)

Until March of each year there is practically no change in the incidence ; there is then an enormous development of the disease, reaching its maximum in July and August, followed by a rapid fall in September and October ; in November and December the same figure as that for the early months of the year is reached. This same curve of seasonal influence is apparent, though less marked, in the figures showing incidence of anthrax in Germany since 1885. In contrast to this figures taken quarterly in Great Britain show least incidence of anthrax in the third quarter, July, August, and September. Thus, of a total of 4250 outbreaks in the six years 1899–1904 there occurred in the first quarter 1114, in the second 1166, in the third 850, and in the fourth 1120. As is to be expected in countries where incidence of anthrax is greatest in the hot summer months and where industrial conditions are not predominant incidence on man is subject to the same law and is dependent on direct transmission from animals to man. Thus in Italy of 11,102 cases of malignant pustule reported in Italy in the five years 1892–96 there occurred in the first quarter of the year 1482 cases, in the second 1398, in the third 5286, and in the fourth 2936.

It is interesting to see whether in this country there is any corresponding fluctuation of the disease in man such as occurs in animals in Asia (for what holds good of seasonal influence in European and Asiatic Russia may be assumed to be the same in all countries in Asia exposed to like high summer temperatures). Any close relation between the two must be interfered with, firstly, because factory work at home is continuous all the year round, and secondly, material is stored for varying periods both in Asia and in this country and such as is collected in the summer months in Asia will not necessarily be handled at a corresponding later date here in the factory. The fact that the average number of cases in each of the four months—July to October—is 15·1 and for each of the eight other months is 25·7 points slightly to reflection of the lessened incidence among animals in the winter months in Asia.

The simplest explanation of the facts stated is seasonal variation in temperature and all that this means in changes in the soil and vegetation. We know of the anthrax bacillus

FIG. 2.


MONTHLY RETURN OF THE TOTAL NUMBER OF ANIMALS ATTACKED BY ANTHRAX
IN EUROPEAN RUSSIA, ASIATIC RUSSIA, THE NORTH CAUCASUS, & TRANS-CAUCASUS.
FROM JANUARY 1899 TO SEPTEMBER 1904.
15000
10000
5000
Jan Apl. July. Oct. Jan Apl July. Oct Jan. Apl. July. Oct. Jan. Apl. July Oct. Jan. Apl. July. Oct. Jan. Apl July.
1899. 1900. 1901. 1902. 1903. 1904.
EACH DIVISION REPRESENTS 1000 ANIMALS ATTACKED.

that its greatest development takes place at a temperature of 35° C., that multiplication is arrested below 12° C. and above 45° C., and that cooling below the freezing point does not kill it. Spores are most readily produced at a temperature of 32° C. Below 18° C. and above 42° C. the capacity for sporulation ceases. In studying the possible saprophytic growth of the bacillus Koch[13] found that excellent media for its growth could be obtained from emulsions of seeds rich in starch, such as barley, wheat, peas, and grass, and from the fresh juice of potatoes, turnips, &c. Living plant cells do not form a suitable soil but water in which hay and straw have been allowed to decay, if neutralised or made slightly alkaline, became a suitable medium. Possibly the presence of chalk in the soil by neutralising the acids produced in decay may help to render suitable soils otherwise unfitted for the bacillus to develop in.

The characteristic of anthrax specially to infect certain districts has been known for centuries. Long before the bacillus anthracis was discovered as the *causa causans* the epidemiology of anthrax had been studied in many different countries by Hewsinger,[14] especially in Siberia and Germany, with results which led him to the conclusion that the conditions of climate and soil which favoured the development of anthrax in animals were the same as those which favoured the development of malaria in man. In Siberia it was most commonly met with on the salt grass steppes, in the river valleys, and round the bitter lakes. He had noted that its occurrence never failed on land rich in organic matter and liable to putrefaction, such as is found in the impervious peaty moorland soils with tendency to the formation of pools and marshes. The existence of brackish water and generally of water containing alkaline salts which favours decomposition favoured also the development of anthrax. He observed, too, that the use as fodder of the grass or hay of particular meadows or districts was believed to be often the cause of outbreaks. Wilhelm Koch,[15] from consideration of the principal anthrax districts in France (on the banks of the Loire, Oise, Aisne, Saône, the marshy low-lying country of the Gironde, &c.), in Germany (on the banks of the Danube, the swampy sides of the Bavarian Highlands, the valleys of the Elbe, Mulde, Saale, Bode (which are all liable to flood), and elsewhere, concludes that the favouring conditions of soil for the development of the disease as an epizootic are: (1) fairly impervious soils of chalk, marl, or clay; (2) sandy soil, but only when the sand lies in a thin layer on impervious ground and when it is intimately mixed with

[13] Mittheilungen aus dem Kaiserlichen Gesundheitsamte, Band i., p. 77, 1881.

[14] Die Milzbrand-Krankheiten der Thiere und des Menschen, Erlangen, 1850.

[15] Loc. cit., p. 91, et seq.

decomposing animal and vegetable matter; and (3) peaty soils rich in organic and mineral substances, such as prairies, steppes, and moor and marsh land. Height above the level of the sea matters little, but a definite temperature must be reached at which the growth of the bacillus and formation of spores can take place—i.e., between 18° and 40° C. For a typical anthrax district are required only, in addition to the bacillus, a degree of moisture in the soil greater than that of the surrounding country, periodical high temperatures, and profuse vegetation. The moisture must not be so great as to constitute a bog, because the bacillus will not multiply in land thus saturated. As Billings[16] expresses it, "Places liable to be flooded and drying out to a considerable degree in summer and often exposed to the full action of the summer's sun" are those which describe the anthrax district. In America he describes some of the most marked centres as "cups" in high prairie lands, which retain the spring rain but tend to dry out in the summer. The flooding of low-lying lands, followed by drying from great warmth, make certain parts of the valley of the Mississippi markedly anthrax districts. There during the spring and summer of 1895 of a total of 103,507 horses, cattle, sheep, and pigs 6655 were attacked. In the Bavarian Alps in Switzerland Billings further says: "The people know almost to a day how long they dare let cattle graze on the anthrax districts before they must remove them." Factors which must not be left out of consideration, as they form important links in the chain of the creation of anthrax districts, are the insect bird and animal life and the occurrence of dust storms. Marchoux and Salimbeni[17] have shown, for example, the part played by vultures in South America in the spread of anthrax, first by observing them devour the carcasses of animals which had died from the disease and subsequently finding the bacilli in the excreta.

If we consider for a moment the conditions under which the sheep and animals are reared in Asia, especially in Central Asia, the likelihood for occurrence of anthrax among them is apparent. The central plateau of Asia Minor, the home of the Angora goat, is characterised by a climate of severe winter followed by a sultry summer. A prominent feature of this plateau is the existence of numerous fresh and salt water lakes, such as Lake Van, the brackish waters of which have no outlet. Wool is grown in all parts but the quantity produced is dependent on the character and modes of life of the inhabitants. Most is exported from Mesopotamia, where the nomadic inhabitants have no other occupation than to take care of very numerous flocks of sheep migrating with them according to the climate and foraging conditions. These districts are the warmest in Asia Minor and the reason why the wool from the districts of Bagdad and Bassorah

[16] Twentieth Century Practice of Medicine, Article, Anthrax, p. 422
[17] Annales de l'Institut Pasteur, 1903, p. 564.

is considered of such fine quality is attributed to the fact that the flocks, owing to the mild climate, can pass the winter outside, whereas in the northern mountainous regions the sheep have to be kept under peculiar roofs which are always inadequate to cover the animals which often lie in dirt. Still, the wool from the plains, though of finer quality, contains much more dust than that from the north. Even among the principal family of sheep inhabiting Mesopotamia the character of the wool differs according to the regions whence it comes and various names such as Karadi, Awassi, Mendelli, and Kerkouk are assigned to the qualities. A vast lacustrine region dotted over with lakes or tarns, many of them brackish and with no outlet, or strewn with them like beads on a string, best describes huge districts in Persia, Tibet, Kurdistan, the Kirghiz Steppes, Mongolia, and Northern China, and it is throughout these districts that varieties of the same fat-tailed Persian sheep is found and where the tending of them and of camels, horses, and cattle is the main occupation of the primitive nomadic tribes. Innumerable wild boars haunt the thickets surrounding the salt lakes and swampy delta of the Oxus and Aral.

The number of recorded instances in which the presence of anthrax bacilli has been demonstrated in imported material is not large. This must be because search has not often been made. Andrewes [18] has cultivated bacilli from the dust shaken from a few strands taken at random out of a hydraulically packed bale of China hair weighing five hundredweights. Buchanan [19] found them in Siberian hair used for brushmaking in an asylum for the blind in Glasgow and Balfour Stewart [20] in a piece of a Kurachi hide in Liverpool. Other instances are given by Silberschmidt,[21] Gruber,[22] Frank,[23] and Berka [24] in horsehair and by Heim [25] in goat hair. The most important, however, of such experiments are those of Webb and Duncan made at the factory of the former in Worcester. Of eight cases of China mane hair four contained anthrax; of four bales of the same material all were infected, as were also both of two samples of dust taken from large bulk quantities. From these experiments they draw the conclusion that all bales of China mane hair must be regarded as infected. Whether further development of bacilli occurs inside a bale after it has been packed has never been determined.

If then the conditions of soil, temperature, moisture, and decomposing vegetable matter play so prominent a part in

[18] Annual Report of Chief Inspector of Factories, 1899, p. 263.
[19] Ibid., 1900, p. 471.
[20] Ibid., 1901, p. 239.
[21] Zeitschrift für Hygiene, vol. xx., p. 455.
[22] Oesterreichisches Sanitätswesen, 1896, p. 60.
[23] Münchener Medicinische Wochenschrift, 1899, No. 9.
[24] Wiener Klinische Wochenschrift, 1904, No. 13.
[25] Arbeiten aus dem Kaiserlichen Gesundheitsamte, 1901, vol. xviii.

the development of outbreaks of anthrax among animals it becomes unnecessary to insist that the contagium must invariably be conveyed directly from animal to animal and from an animal that has died from the disease to man. Dirt and sand adhering to the fleeces of healthy Bagdad sheep and Angora goats may contain spores picked up in anthrax districts. In many outbreaks from manipulation of wool, horsehair, and hides no evidence of a fallen fleece or of damaged material is forthcoming. This view is supported by the fact, well known in the trade, that mane hair is considered much more likely to be infected than tail hair inasmuch as the mane hair comes most in contact with the earth. It explains also most readily the remarkable conclusion of Mr. Webb that it would be unsafe to assume that a single bale of horsehair from China was free from risk. The conditions under which animals are herded together in winter "under roofs always inadequate to cover the numerous animals," as is the custom in Kurdistan,[26] or the shelter given to the sheep in caves by the Bedouins in the vilayet of Aleppo might be expected to be much more productive of anthrax once a case occurred than the conditions of soil and temperature described. There is, however, no evidence pointing in this direction

Several outbreaks of anthrax in animals have been directly traced to spores which have escaped from factories in which raw animal products are dealt with either through pollution of streams or through refuse dust used as manure on fields. Sometimes, however, infection is even more direct. Thus two horses at grass in a field on to which dust from Persian wool used in the manufacture of blankets was blown died from the disease in 1901 in Yorkshire. In a series of outbreaks near Zürich [27] eight out of 22 animals were infected by dust blown from the chimney of a horsehair factory and at least seven other cases were due in one way or another to conditions in this factory. Almost the first recorded outbreak of splenic apoplexy in cattle,[28] as the disease was then called, occurred in the valley of the Yeo in Somerset and the existence of a considerable glove industry at Yeovil suggests that the outbreak had relationship with factory conditions. I mention this outbreak because recently Houston [29] has demonstrated the presence of anthrax (1) in the general effluent from the final catchpit in a hide factory in Yeovil; (2) in the septic tank liquor, the sludge, and the washings of coke from primary and secondary coke beds; and (3) in mud from the banks of the river Yeo and Yeo brook. That the spores of anthrax would, he says,

[26] S. P. Sweeney in Wool and Manufacture of Wool, by W. C. Ford, Washington, 1894.

[27] W. Silberschmidt: Zeitschrift für Hygiene, vol. xx., p. 455.

[28] Duguid: Transactions of the Seventh International Congress of Hygiene, vol. iii., p. 213.

[29] A. C. Houston: Anthrax in Yeovil Sewage, Second Report of Commission on Sewage Disposal, 1902, p. 31.

"be swept from the banks in time of flood and carried when present in the mud or river bank down the river to be spread over low-lying land bordering the river hardly admits of any doubt." He guards himself against magnifying the danger thus apparent by saying that "flood water, 'while widening the potentially infective anthrax area,' might affect so wide a separation of the individual spores of anthrax one from the other as to largely remove the element of danger." The fact that there is no increased incidence of anthrax in the hottest season of the year in this country points to the absence of the peculiar and special conditions of temperature and soil which are necessary for the germination of the spores into bacilli and further multiplication of the latter.

On the corporation sewage farm at Kidderminster since 1897, where incidence on the workers from the use of Persian wool during the same period had been high, there have been 11 outbreaks. An outbreak on the sewage farm at Market Harborough in October, 1904, synchronised with the occurrence of three cases of malignant pustule in men employed at a tannery where previously no case had been known to occur. Illustrative outbreaks of a similar nature have been described by Mr. J. Spear,[30] the one traced to washings of Van mohair, manipulation of which had given rise also to cases of malignant pustule in man, and from the refuse sludge from a tannery in London which was used on the farm of the occupier of the factory. Similar outbreaks are reported from Germany[31] and the United States. Thus, in 1901 15 cattle, and in 1900 23 cattle, were believed to have contracted the disease in Marbach on the Neckar by eating grass infected by the water of a stream used in washing foreign hides. At Kirchhain in Hesse-Nassau, an important tanning centre, in 1901 and previous years several outbreaks in animals had been traced to the use of hay from meadows manured with the hair and refuse from tanyards. In 1899 on the Black River, Wisconsin,[32] the distribution of the cases along the river bank for a distance of ten miles below a tannery receiving hides from South America and China indicated the river water as the carrier of the virus. The influence of tanneries in spreading anthrax among the operatives and cattle on pastures watered by streams carrying off the refuse from them was made the subject of inquiry in Pennsylvania during 1897.[33] The deaths of 12 men and 60 head of cattle in that year were attributed to the manipulation of Chinese dry hides in the tanneries of that State. While in some cases, therefore, the association of outbreaks

[30] Tenth and Twelfth Reports of the Medical Officer of the Local Government Board, 1881 and 1883.

[31] Jahresberichte der Thierseuchen im Deutschen Reiche.

[32] Wisconsin Station Report, H. L. Russell, 1900, pp. 171–84.

[33] Influence of Tanneries in Spreading Anthrax, by M. P. Ravenal, M.D. Paper reprinted in the Veterinary Journal, 1899, vol. xlix. p. 23.

of anthrax in animals with factory and workshop conditions is clear, the evidence when closely examined in this country fails to show that incidence of outbreaks of anthrax in cattle is greatest in counties where industries connected with wool or with raw animal products are mostly carried on. Elsewhere[34] I have shown that the number of outbreaks and the number of cattle attacked in each county worked out as a proportion on the number of cattle in each of the counties over a period of five years, negatives so far as can be done by this means, any close association. Indeed, incidence on animals appears to be greatest in counties where danger from factory conditions appears most remote, as, for example, in Cornwall, Westmorland, Northumberland, Hertford, Aberdeen, Banff, Elgin, and Haddington. Incidence of anthrax on animals is twice as great in Scotland as it is in England, yet incidence on the human subject from wool is negligible in Scotland as compared with England. No doubt the direct influence of a particular factory in causing anthrax in animals operates over an extremely limited area, but the use which it is well known is made of refuse dust from wool and horsehair factories as manure is an unknown quantity and may be the cause of many outbreaks the origin of which cannot be traced. Most cases are rightly attributed to the consumption by cattle of infected fodder either from direct grazing on fields where previously cattle had died from the disease, or from grass which had been cut from places where animals have died, or where the carcasses have been buried at an insufficient depth.

As showing the probable relation of the bacillus to the soil I would cite as instructive the tracing of outbreaks in 1903 and 1902[35] to the feeding of cattle on turnips grown near the place where an animal suffering from anthrax had been slaughtered, similar feeding on turnips in the digging up of which dead bones were exposed, and of the death of six oxen out of a shed containing 100 animals from consumption of raw potato skins to which the spores of anthrax must have been attached, as only the six oxen thus fed succumbed. But recital of such cases does not explain sufficiently all the outbreaks in animals, particularly those erratic instances occurring on farms hitherto free from the disease. To account for these McFadyean[36] suggests two possible sources : (1) artificial manure and (2) imported feeding stuffs. Against the view that artificial manure can be the cause he states "the erratic way in which outbreaks occur throughout the country apparently quite unconnected with the more or less liberal employment of artificial manure." In analysing 39 consecutive outbreaks, in 29 of which there was no previous history of anthrax on

[34] Transactions of the Epidemiological Society, vol. xxiii., p. 181.
[35] Jahresberichte von Thierseuchen.
[36] Extraneous Sources of Infection in Outbreaks of Anthrax. Journal of Comparative Pathology and Therapeutics, vol. xv., p. 346.

the farm, he found that in 26 of the 39 outbreaks the animals were receiving a diet into which artificial food in different forms entered. He says: "The circumstances connected with the series of outbreaks deepen the suspicion which already existed that a considerable number of cases of the disease in this country have an extraneous source of infection and that the vehicle of infection is not infrequently some artificial food stuff of which the raw material is derived from a foreign country." In one outbreak amongst cattle which caused the death of six valuable shorthorns he isolated the bacillus from linseed cake and in this instance as soon as the linseed meal was stopped the outbreak ceased. In another outbreak among horses in London similarly the bacillus was isolated from the oats. Of the outbreaks in Germany in 1903 Russian bran was believed to have been the cause in several instances. In 1902 fodder consisting of bran, barley or hay from Russia is cited as having been believed to be the cause of the outbreaks in seven instances. In 1901, in addition to fodder imported from Russia, reference is made to two farms believed to have been infected from fodder grown in the tropics. This view makes intelligible the source of infection in the case of a corndealer, a person unloading corn in a warehouse, and a person carrying sacks of potatoes mentioned at the beginning of this lecture. If the soil under certain conditions is recognised as a suitable medium for the growth of the bacillus it is no longer necessary always to seek for the material cause in raw animal products alone.

LECTURE III.

Delivered on March 14th.

MR. PRESIDENT AND GENTLEMEN,—To follow the incidence of anthrax on the workers in the different processes in the three main industries concerned, wool, horsehair, and hides and skins, it is only necessary to remember the following points. In the case of wool, with the exception of Van mohair, the material is unwashed until after the fleeces are opened to examine their condition, sorted according to colour and quality, cleansed from dust in the willow machines, and blended in large heaps to obtain a uniform shade of colour in bulk. Dust is inseparable from each operation. It next passes through three separate tanks or wash bowls containing soap solution kept at a temperature of about 130° F., so that the effect of washing may be expected to lessen the risk from anthrax in the later processes after drying—namely, carding, combing, finishing, and gilling—to which it is subjected prior to spinning. In considering danger from horsehair distinction must be made between the short mane hair to be curled for stuffing purposes and the long tail hair to be woven into hair cloth and, again, between material that is dyed and that which is undyed. Were all material dyed I believe that the incidence of anthrax in the industry would be materially lessened, because for this process to take effect the hair must be left for some hours in the dyeing solution heated by passage of steam through it. Although in the trade this process is described as "boiling" it is rare for a temperature of 212° F. to be reached throughout the solution. Dirt, however, is mechanically removed and probably the virulence of the anthrax spores is diminished. Specifications unfortunately require at times that horsehair shall remain undyed and shades of a grey colour are demanded. Manufacturers allege that to obtain these grey natural colours material must be used from countries like Siberia in which anthrax is rife. Be this as it may, frequently all the early dusty processes of opening, sorting, willowing to free from dust, and drawing into bundles according to length are done with material that has undergone no preliminary washing process. Finally, to set the curl the hair is exposed to dry heat at a temperature of 250° F. for 24 hours or is exposed to steam under pressure, so that risk after

leaving the factory is not worth consideration. Long hair for weaving purposes is always soaked in a warm soda solution and danger is minimised, as the process of heckling to separate the individual hairs is done while the material is wet. Bristles undergo only a process of dry heckling—frequent drawing of the hair through upright steel pins—before they are used in brush-making. As a rule they arrive sorted and cleaned except in the cheaper kinds, notably "Chinese riflings," which are of low quality and too short to be properly bundled according to length. Large quantities of China mane hair are also used in the manufacture of scrubbing and other brushes and this, although it frequently has undergone no cleansing preparation in China, undergoes no treatment other than that described in the case of bristles. In hides and skins evolution of dust and consequent danger are greatest in the early process of sorting and throwing into heaps according to quality. The precise occupation at which the affected persons were employed is shown in Table XII. arranged in the order of the processes of manufacture from the arrival of the material at the factory to the time when it leaves in a finished condition.

Table XII.

Wool.

Handling bales at wharf... ...	1	Drying	1
Vanman	1	Carding and combing	16
Warehouse	4	Finishing, gilling, and preparing...	6
Overlooker	1	Spinning and weaving	6
Occupier	1	Waste pulling	1
Woolsteeping	1	Sweeping floors	1
Opening bales	3	Dyeing	1
Sorting	16	Engine-house	1
Willowing	13	Infected outside factory	3
Blending	3		
Wool-washing and wool-running	7	Total	88
Mechanic	1		

Horsehair.

Vanman...	1	Yarn winding	1
Clerk in office	1	Stuffing boxing-glov	1
Warehouse	4	Stuffing mattresses	1
Opening, weighing, and carrying	9	Emptying sacks	1
Sorting and mixing	3	Wet heckling	1
Willowing	7	General work	1
Drawing and dressing	9	Infected outside factory	5
Curling and carding	11		
Brushmaking	14	Total	70

HIDES AND SKINS.

Dock labourers	16	Portmanteau-making	1
Wharves or warehouses	41	Leather seller	1
Fellmonger	1	Picker strap-making	1
Tanyards	24		—
Boot-making...	1	Total	86

OTHER INDUSTRIES.

Docks	2	Worker in harness furniture...	1
Fruit and vegetable warehouse	2	Vanman...	1
Horn manufacture	2	Worker in mother of shell ...	1
Rag sorting	1	Knife hafter...	1
Linen weaver	1	Unloading grain...	1
Chemical manure	1	Grain dealer...	1
Saddler	1		—
Railway porter	1	Total	17

ANTHRAX IN RELATION TO THE WOOL AND WORSTED TRADES.

There is interest in comparing the facts now known of the incidence of anthrax in wool and worsted as regards type of the disease, class of persons attacked, supposed dangerous material, and other circumstances with those brought to light a quarter of a century ago when the disease first came prominently into notice by the report of Mr. J. Spear in 1881.[2] He dealt with 32 cases (21 fatal) which occurred during 11 months, November, 1879, to September, 1880, in the neighbourhood of Bradford. Of these nine were typical cutaneous anthrax (two fatal) and the remaining 23 (19 fatal) fully developed internal anthrax. Internal anthrax was, he wrote at that time, "the form of the disease which is the much more common one, at all events the more commonly recorded one amongst wool-sorters," and if there were added cases which were considered mild or rudimentary attacks of the internal form the fatality would appear correspondingly less. During the six years 1899 to 1904 only six cases of the internal form have been reported and there would thus appear to have occurred a remarkable change in the type of the disease prevalent in Bradford, the external and internal form having changed places as regards frequency of appearance. As to the diminution of internal anthrax there is no doubt. Some explanation of the change may be found in the more frequent diagnosis of external anthrax now but this is insufficient to explain the very great reduction in cases of true wool-sorter's disease. Moreover, mild or rudimentary attacks of the constitutional form of the disease are never reported now. Several of the cases investigated

[2] Annual Report of the Local Government Board, 1880-81, Supplement containing Report of the Medical Officer, p. 66.

by Mr. Spear followed on manipulation of gravely infected Van mohair. More recent cases of internal anthrax in 1898 and 1899 similarly followed one another quickly on manipulation of badly infected Persian wool. With our knowledge of the greater virulence of the bacillus under certain conditions it is not unreasonable to assume that variations in type may be due to this cause and that at some future time there may be recrudescence of the severer form.

The principal circumstance, however. which has altered since the time when Mr. Spear wrote is that under which the manipulation of the wool takes place. Now, in addition to regulations requiring care in the opening of the bales and removal of the damaged wool or hair, fallen fleeces and pieces of skin, none of the dangerous specified wools (Alpaca, Pelitan, Cashmere, Persian, Camel hair, and Mohair) may be opened or sorted except at a place where a constant draught of air maintained by a fan carries the dust away downwards. While it cannot be said that introduction of exhaust ventilation at the sorting tables has removed the danger entirely, as the table shows, claim can be made that it is a material safeguard. Instances could be cited in which occurrence of anthrax seems to have followed as cause and effect on cessation or impairment of action of this fan exhaust. Changes in type of the disease therefore may be due to these altered conditions of working. 25 years ago Mr. Spear insisted also on the fact that "with rare exceptions only those suffered who were employed in the first manipulation—in the sorting process,"[3] qualified, however, by the statement that "the power of the wool for mischief cannot be said to be exhausted here, for in the combing-room the material may possibly prove infective." For several years later there must have been the same absence of cases among the carding, combing, and spinning hands, for in a Home Office Report in 1897,[4] charged especially with suggestion of remedial measures, the later wool-combing processes are not specially referred to. Since then, as shown in the table, cases have been most numerous in the processes subsequent to the washing of the wool. Had the scope of the earlier inquiry covered a longer period than one year and extended to other industries such as the carpet and felt manufacture, no doubt cases in departments other than sorting would have been found to occur more frequently than was supposed. So frequent did these cases become that regulations were introduced requiring as perhaps the most important provision isolation from other processes and mechanical exhaust ventilation for the removal of the dust in the process of willowing or cleaning of the material. Cases, however, still continue to be more frequent in the rooms where the carding and combing processes are carried on. I say rooms advisedly because personally I believe some,

[3] Ibid., pp. 78 and 83.
[4] Conditions of Work in Wool-sorting and other Kindred Trades, 1897.

perhaps most, of them are due to infection from unwashed wool, because though combing and carding and spinning are the principal, they are not the exclusive, operations carried on in them. The wash bowl occupies a portion of this room or is connected by a passage and along this a current of air may pass from where the unwashed material is being treated. In the few factories in which incidence on workers in the combing processes has been most frequently observed this absence of separation of the processes connected with washed and unwashed material has been noted. This explanation is insufficient, however, to account for all the cases arising during the later processes. In the year 1904, for instance, two persons at least were attacked in factories where no raw material but only finished "tops" (probably of Persian wool) were used. These tops must have passed through all the various stages of cleaning, washing, and the minute separation of one fibre from another in the combing machines at one factory before they were conveyed to the other where infection occurred.

Although the pulmonary type of the disease was first noticed in Bradford after the introduction of alpaca and mohair as textile materials in 1837 several deaths occurred in later years (1846, 1853-4, 1867-8, and 1874) from manipulation of these materials [5] the danger from Van mohair (introduced about 1863) seems to have overshadowed that from other material such as Persian wool at the time of Mr. Spear's inquiry. He gives the following list of foreign wools in the order of their apparent noxiousness as it was at that time considered to be: (1) Van mohair, (2) Persian, (3) Camel hair, (4) Alpaca, (5) Turkey mohair, (6) Pelitan, (7) Cape mohair, and (8) Cashmere. Now the order would be: (1) Persian, (2) Turkey mohair, (3) Van mohair, (4) East Indian, (5) Camel hair, (6) Alpaca, (7) Pelitan, and (8) Cashmere. Possibly the disappearance of Van mohair from the position of greatest noxiousness is due to the fact that Van mohair alone is required by the regulations to be washed and sorted while damp if at all. The list does not take account of the amount of the various materials used. Danger from East Indian wool which, although very sandy, is believed to be exported in a washed condition, does not appear to have attracted attention, no doubt because its use is much larger in the felt manufacture than in the worsted. Probably the use of Persian wool has increased since 1880. The explanation why it is so largely in demand arises from the fact that this breed of sheep is one of the few in which the wool is naturally of a black, brown, or fawn colour. Thus it is stated that in the Chipal breed in the districts round Bassorah, Bagdad, and Mosul only 20 per cent. of the flocks contain white sheep, the remainder being black, grey, fawn, or brown; and the wool is of a finer quality than that

[5] Bell: Article on Anthrax in Clifford Allbutt's System of Medicine, vol. ii., p. 539.

of other breeds exported from Mesopotamia. With the demand for cloth of khaki colour there is no likelihood of a diminution in the supply of this Persian wool. Fresh openings for its manipulation in the worsted factories are constantly sought. Thus the consul reporting on the trade of Nanking [6] alluding to the uselessness of trade catalogues in general says: "The only one which appeared to me to have possibilities in it was addressed by a firm in London making khaki uniforms. I wrote to the senders pointing out that as the Chinese army was now being reorganised if they would appoint an agent in China it might be possible for them to obtain a contract to supply uniforms for the foreign troops."

It is customary to attribute the absence of anthrax from manipulation of the immense supplies of Australian and New Zealand wool to the fact that such wool has a larger proportion of natural grease or "yelk" in it, the presence of which would tend to stop diffusion of dust. To me this reason is not sufficient to account for the facts and I attribute the immunity mainly (1) to comparatively small incidence of the disease in animals; and (2) to the precautions taken to prevent the spread of disease and to secure proper disposal of the carcass. The existence of similar precautions would explain why the disease is apparently transmitted so rarely from countries such as the Argentine Republic where anthrax among animals is common. Thus in New South Wales [7] in 1902 "the sheep were free from disease except some few cases of anthrax and the losses from it were very slight." In 1901 no outbreaks were reported. The total number of sheep and lambs shorn in 1902 exceeded 25,000,000. In South Australia [8] in 1902 the list of diseases among sheep does not include anthrax. In the report of the chief veterinary officer of New Zealand for 1899 four outbreaks of anthrax are recorded—the first appearance of the disease since 1895.[9]

Still in seeking for means to render safer manipulation of wool and horsehair from Asia the practice of washing the sheep prior to shearing, willowing it from dirt, and discarding the fallen fleeces in the country of origin would be the next best thing to disinfection of the material were that possible by means of steam. This is what some manufacturers would wish to see done and in March, 1903, the chambers of commerce of Bradford, Halifax, and Kidderminster issued a circular letter pointing out the unsatisfactory condition in which Persian wool was received in the country. Nearly every bale is falsely packed—i.e., the fleeces contain locks (inferior wool), skin, fallen wool, and cotton rags, besides soil, sand, dirt, and dust. They urge especially that persons consigning Persian wool should endeavour, first, to keep out

[6] Trade of Nanking, Annual Series, No. 3004, 1903.
[7] Department of Mines and Agriculture, 1903.
[8] Report of Minister of Agriculture, 1903, p. 38.
[9] Veterinarian, 1901, vol. lxxiv., p. 519.

of the bales extraneous matter, and, secondly, to pack locks, fallen wool, and skin in separate bales. Any loss on locks sold at lower prices would be more than recouped by higher prices obtained for honestly packed bales. All the evidence shows, however, that wool is washed less frequently before shipment than it used to be. Thus in 1869 158,000 bales of greasy unwashed wool were sold as compared with 681,500 in 1902, the figures for washed fleeces in the same years being 266,000 and 2500 respectively and for scoured wool 114,000 and 314,000.[10] The reason for this diminution in the quantity of washed fleeces is that the extra cost of washing was not made up to the growers by reduction in freight or the slightly increased market price obtained for it in London.[11] Moreover, the users of wools in this country desire to scour the material themselves in the manner most suited to their particular trade and object to scouring carried out in the colonies and elsewhere. In the report of 1897 already referred to the committee expresses the wish that it were possible for H.M. consuls to report anthrax-infected districts so that by the ear-marking of the bales from such localities imported infection might be traced and arrested.

Mr. Spear[12] was informed that it would not be difficult in Constantinople, where the classification of wools from Asia Minor was made, to secure that fallen fleeces should be classed apart. Pressure in this direction by combined action on the part of manufacturers or of the legislature might have the effect on dealers and native growers abroad of making them take steps to keep apart these fallen fleeces or to separate them in Constantinople. This would of course merely shift the risk from the workers at home to those in Constantinople. The difficulties in the way of carrying out such proposals are many. In the absence of official records based on veterinary reports knowledge of anthrax-infected districts would be untrustworthy and such evidence might tend to grow less when it became realised that knowledge of the incidence of anthrax was followed by stigma attaching to the wool or other material. Other diseases besides anthrax are rife among animals in Asia and it is unlikely that, in the absence of discriminating veterinary reports, the consuls would be in a position to say what bales were infected. The practice, too, of storing wool dependent on the needs of the market, or on fluctuation in price, would equally tend to make such protection illusory. That the matter, however, has not escaped the attention of some of the consuls is apparent from the following quotation from the consular report from Kermanshah in Persia[13]: "In reply to an inquiry as to why more care was not taken in washing and sorting the wool, the Kerman-

[10] Schwartze and Co.'s Report, 1902.

[11] Principles of Wool Combing, by H. Priestman. G. Bell and Sons, 1904.

[12] Loc. cit., p. 110.

[13] Annual Series, No 3189, 1904.

shah wool merchants declared that no skins, cotton rags, or pieces of string were contained in the wool exported by them. They did not wash the wool so well for export as for spinning in the country, as well-washed wool scarcely fetched a better price in Bagdad than the usual wool exported there." If in this country, with all the precautions which are taken to check the spread of the disease and to prevent the flesh of anthrax-infected animals from coming into the market, illicit dealing is still practised and every year carcasses thus infected are found in the meat markets and butchers' shops exposed for sale, what hope is there that in other countries where there are no regulations, where cupidity is not less marked than at home, and where the disease is probably a hundredfold more rife, material good could be achieved by the branding of bales or by reliance on the exclusion of fallen fleeces in the sorting carried on in Constantinople?

The tariff duties of the United States[14] touch on this point by classifying in three divisions the different kinds of wool imported and levying customs dues of varying amounts according to the quality and previous treatment to which it has been subjected. Thus wools of the first class, including that from Bagdad and China and British colonial wool, among others; and of the second class (including camel hair, angora goat, and alpaca) if imported scoured pay thrice the duty; and if imported washed twice the duty they do if imported unwashed. The duty on these wools also is doubled if the value is increased by sorting or rejection of any part of the original fleece, or, again, if it be reduced in value by the admixture of dust or other foreign substance. High duties are placed on any fraudulent attempt to pass an inferior material as of high quality wool. In the inferior wools of Class 3, including South American, native Smyrna, Russian, camel hair, and "wools of like character such as have been usually imported into the United States from Turkey," the classification is based on an increase in the duty on material containing less than 8 per cent. of dirt. These duties apparently have no reference to the prevention of anthrax, nor is it easy to see, apart from pressure from buyers in the United States, what inducement there is for the removal of dirt in the third class when reduction of the amount of dirt to 8 per cent. increases the amount of duty paid. In the first and second classes certainly twice the duty (24 cents per pound) by reduction in value by admixture of dirt would be an incentive to cleaning the wool. That an effect in the cleaning of the wool from China, however, is produced by these duties is shown by the following extract from the report on the trade of China in 1903. "The best wool comes from the flocks of the petty chieftains outside of China proper, who only shear

[14] Customs Tariff Act, 1897, R. F. Downing and Co., New York.

their sheep once a year. The clip is therefore longer in staple and freer from dirt than that obtained from Chinese sheep, which are shorn two or three times a year. All attempts to prevent more than the ordinary amount of dirt which a fleece must collect have proved ineffectual and wool containing 30 per cent. of real estate still continues to be sent down. The cost of carriage is some £1 6*s*. per cwt., and there is quite sufficient dust in Tientsin to render it unnecessary to pay at this rate for transportation thither of the sand of Central Asia. The imposition by the United States of the heavy import duty on wool of 4c. gold per pound led to its being thoroughly winnowed prior to shipment and although the quantities recently shipped appear to be less than were shipped, say, ten years ago, the actual amount of clean wool which now goes forward is in reality greater."

Wool in Asia Minor is collected annually at fairs in centres such as Bitlis, Djezireh, and Mogoul. The nomad tribes of Kurdistan bring their flocks to be sheared there and the small dealers bring the wool that they have collected in different parts of the country.[15] Hair and hides in China are collected by Chinese agents in the interior. No foreigners deal directly with the seller in the interior. 50 per cent. of the horsehair comes from Mongolia and 50 per cent. from near Mukden in Manchuria. Tail hair is washed by the Chinese in the interior but manes and combings undergo no treatment as the price at which they are sold would not pay for cleaning. Bristles are collected as follows. The pig when killed is placed in boiling water and the bristles are scraped off. They are washed in hot water, dried in the sun, and roughly bundled according to length and packed in baskets. These baskets are sold to the interior buyer who opens, cleans, and resorts the bristles which he sells to the foreigner who packs them for shipment. No disinfectant of any kind is used. Hides and goat skins are sold by gross weight which includes the mud and the dirt. If the demand is great anything having the appearance of a hide or a skin is included; if slight the bundles contain good skins, for the interior Chinese buyer knows that then the foreigner will be particular and refuse bad skins. These will be stored up until the market improves. It is entirely a question of price.

Anthrax in Relation to Hides and Skins.

The history of anthrax in this country in relation to hides and skins can be best traced from the reports of Mr. Spear[16] and of Dr. W. H. Hamer[17] on the occurrence of cases in London. Mr. Spear's report dealt mainly with an outbreak in a Bermondsey tanyard which occurred in 1882–83 due to a

[15] Spear: Loc. cit., p. 85.

[16] Annual Report of the Local Government Board, 1882-83. Supplement containing the Report of the Medical Officer.

[17] London County Council: Report of the Medical Officer on Anthrax in London, April 5th, 1894.

consignment of bales shipped from Shanghai. In the space of a few months nine men were attacked, of whom three died. Owing to the danger attaching to the manipulation of the bales several were disposed of in Paris and various ports in Italy and subsequently news arrived that seven men, who had handled these hides in Paris, had been attacked, of whom two had died. Dr. Hamer dealt with a total of 90 cases which had occurred between the years 1873 and 1893. In 86 the occupation was ascertained. Of these 63 handled the hides while in the possession of the hide broker and 23 (of whom 15 were tanners) after removal to other industrial premises. Infection was believed to have been conveyed from China hides in 26 cases, from East Indian in 12, from other specified kinds in nine, and in 34 the source could not be ascertained. The later records which have been obtained since 1899 show that, although the area from which infected hides may arrive has been widened, material from China and East India is now, as it was a quarter of a century ago, the principal source of danger. And later information agrees with the conclusion arrived at by Dr. Hamer that infection from wet hides is very rare. In only two out of his list of 90 cases was there suspicion that wet hides were the cause. Apart from the lessened diffusion of dust by the wet-salting process, Dr. Hamer suggests that the presence of moisture would tend to cause the spores to assume the bacillar form in which they would be more likely to succumb. The cutaneous type of the disease has remained the same, evidence of pulmonary anthrax being as absent now as it was in previous investigations. Dr. Hamer found some ground for the hope that substitution of wet for dry hides which the trade appeared to encourage would, if continued, lessen the risk of anthrax to those manipulating foreign hides in London. He gives the figures of the amount and value of dry and wet hides imported in the years 1882 and 1892. I have added the figures for 1902 (Table XIII.).

TABLE XIII.

Year.	Dry hides.		Wet hides.	
	Cwts.	£	Cwts.	£
1882	576,196	2,098,895	614,471	1,645,786
1892	368,191	946,354	541,286	1,138,903
1902	286,334	845,484	661,198	1,595,109

From this it appears that the total consumption of hides remains the same in 1902 as in 1892; the increase in wet hides balances the reduction in dry. I believe, however, that any conclusions drawn from the above figures are illusory, as the amount and value of dry hides imported are

subject to very considerable fluctuation in the trade returns from year to year.[18] If, for instance, the figures for the year 1900 are taken the amount of dry hides imported would be found to exceed those even for 1882 by 171,551 cwt. Again, while from Bombay and Bengal respectively in 1900 dry hides to the amount of 279,045 and 217,787 cwt. were imported the figures in 1903 dropped to 5261 and 41,619 cwt. It is instructive to show for each year side by side the number of cases of anthrax in which strong suspicion attached to Bombay and East Indian hides and the varying amounts imported from Bombay, Madras, and Bengal in the same years (Table XIV.). Famine prevailed over large districts in India in 1899 which accounted for the enormous quantities of inferior hides shipped to this country in the following year. China hides are recognised in the trade as particularly dangerous and assurance is freely given that this risk has diminished the trade in them. Thus the outbreak in Liverpool in 1900 was attributed to the first introduction of China hides to that port. No diminution is reflected in the Board of Trade returns from year to year which would point to the fact that if imports are reduced at one port they are increased at another. Thus, the value of China hides was estimated in 1899 at £21,455, in 1900 at £12,907, in 1901 at £11,053, and in 1903 at £17,131. The reduction in 1900 can be accounted for by the increased supply of cheap East Indian hides and in 1901 by the great flood in the Yang-tze valley. In 1903 the amount of dry hides imported from China stands only below that from Russia, Holland (of

TABLE XIV.

Year.	Dry hides imported from Bombay, Madras, and Bengal (cwts.).	Number of cases of anthrax attributed to East Indian hides.
1898	117,805	1
1899	144,749	3
1900	507,131	7
1901	127,464	9
1902	51,301	3
1903	49,677	3
1904	—	2

which much may be Chinese), and the East Indies. Evidence from consular reports leads me to suppose that the supply will be increased with the opening up of fresh treaty ports. Thus the consul at Nanking[19] writes: "The export of goat skins has made steady progress since the opening of the port.

[18] Annual Statement of the Trade of the United Kingdom with Foreign Countries and with British Possessions.

[19] Annual Series, No. 2907, 1902.

The value of the trade in 1899 was only £1800, as compared with £32,840 last year. There is undoubtedly a future in Nanking for this class of goods as the supply in Honan is enormous. The same remark applies to hides as to untanned goat skins." Again, the British commercial attaché[20] at Peking writes : "The export of hides has increased in volume 347 per cent. since 1891. Large as is this increase the export of hides does not begin to compare with that of India where conditions governing the supply are almost the same as in China. In both countries cattle are solely bred for agricultural purposes and it is only when they get sick or die of old age that their hides are available for commerce. The export of skins is also a large and growing one, having increased 457 per cent. in value in the last decade." In a later year he says: "Some 40 years ago skins and wool were only remotely thought of ..... and the skins of goats from Honan and Shanghai, which are all converted into the smart American boot, have gone a long way towards building up the wealth of Tientsin."

The hide and skin industry of Germany appears to be greater than that of this country. Thus the number of hides imported into Hamburg in 1903 is stated in the consular report[21] to have exceeded that of Antwerp, Havre, and the United Kingdom combined. Reports of the factory inspectors give no account of incidence on dock labourers or on those manipulating the material in warehouses prior to tanning processes. They have contained every year from 1891 to 1902 references to cases in tanneries but without attempt at complete returns. The number in tanneries and leather factories thus referred to is 65 with 13 deaths—20 per cent. In three tanneries at Kirchhain in 1898 there were 11 cases and in 1902 six. Here sheep skins only are dealt in and of one consignment of 2000 skins 60 were believed to be infected with anthrax. In France information is still scantier than that obtainable in Germany. In the district of St. Denis, near Paris, record of the cases has been carefully kept since 1875 by Dr. Le Roy des Barres.[22] During the years 1875–97 he has seen 72 cases distributed as in Table XV.

TABLE XV.

—	No. employed.	Cases.	Per cent.	Fatal.	Fatality per cent.
Horsehair ...	160	15	9·3	3	20·0
Fellmongers	760	57	7·5	7	12·3
—	920	72	8·8	10	14·0

[20] Trade of China for the Year 1901, by J. W. Jamieson, No. 2912, and for 1903, No. 3127. [21] Annual Series, No. 3186, 1904.
[22] Annales de l'Hygiène Publique, 1897, vol. xxxviii.

All but one of the 57 cases occurred in the only premises where foreign material was dealt in, although there are at least three other important tanneries. Chauveau[23] describes isolated outbreaks in tanyards at Morlaix and the neighbourhood in which the incidence on eight men and 23 animals coincided with the first use in the district of hides imported from China.

There seems no reason for doubt that anthrax can be conveyed by completely tanned material. Apart from the cases tabulated from tanned hides, where possibly infection may have been conveyed from raw hides present on the premises, anthrax has been conveyed to horses apparently through the harness. Thus two horses contracted anthrax, the lesion in both cases being on the flank where a quite new pair of reins came in contact with the body.[24] Experiments have shown that the tanning fluids are insufficient to destroy the vitality of the spores. Thus Ravenal found spores still virulent after immersion for 224 days in the seven tanning fluids of different strength ordinarily used, nor could he suggest any efficient disinfection of the hides which was not likely to injure them. Houston's[25] experiments demonstrating the presence of anthrax spores in the effluent from the catch-pit of a hide factory show that they must be able to survive also the arsenicating, liming, and other processes. In an outbreak in Wisconsin,[26] America, dried hides were placed in solutions of formaldehyde varying in strength from 1 in 500 to 1 in 10,000. At the end of 11 days the anthrax bacillus was cultivated from the solutions containing from 1 in 10,000 to 1 in 2500. The formaldehyde combined gradually with the hide and damaged the material. Success in this direction has been claimed for certain patent preserving fluids of one of which it is reported that anthrax spores are killed in hides and skins soaked for an hour in a 4 per cent. solution. Houston[27] has, however, tested it with disappointing results. During the outbreak in Liverpool the use of hypochlorite of soda was recommended and practised, but cases occurred after as well as before its use. An order of the German Government, dated May 9th, 1902, describing the precautions to be taken in manipulating certain hides, states that no method of disinfection is known which is at the same time certain in its action, easily carried out, and not injurious to the material. Obviously to be of real benefit disinfection of hides if practicable should be done before the material is opened in the warehouse where most of the cases occur and to secure this is impossible at present. In this country consequently the precautions adopted in handling hides and skins coming from China and East India are slight, and

[23] Sur Divers Cas de Charbon, Annales de l'Hygiène Publique, 1892, vol. xxviii., p. 160.

[24] Obrichof: Ein Fall von Ubertragung des Milzbrands durch Leder. Archiv für Veterinärwissenschaften, 1903, p. 1030.

[25] Anthrax in Yeovil Sewage, p. 41. Second Report of Sewage Commission.

[26] Wisconsin Station Reports, 1900.

[27] Loc. cit., p. 41.

directed solely to protection of the workers' clothing by overalls, of their food by prohibition of meals in rooms where the above-named hides are manipulated, provision of washing accommodation, and simple means for dressing wounds. A brief summary of the symptoms of the disease and the necessity for prompt attention are also given.

Anthrax in Relation to Horsehair.

The occurrence of cases in a hair factory at Glasgow in 1878,[28] described by Dr. J. B. Russell, first drew prominent attention to the danger of anthrax to the workers from this material. In his report Dr. Russell cites numerous published reports in France, in one case dating as far back as 1777, in which workmen had been attacked with charbon and boils in opening and sorting bales imported from Russia. In France and Germany, indeed, use of this material appears to have contributed by far the largest share of cases of anthrax. The outbreak in Glasgow in 1879 was due to virulent infection from Russian horsehair. Nine persons were attacked, of whom seven died. Seven of the cases were of the internal type. In 1893 Chauveau[29] described a small outbreak from horsehair in a village in France which has many points of resemblance to that described by Dr. Russell. In less than four months there were seven cases with six deaths. Two of the cases were of the gastro-intestinal type and two of malignant anthrax œdema without external development of a malignant pustule. In this case China horsehair was believed to have been the cause. Since 1878 no case of anthrax was known to have occurred in Glasgow until an outbreak of five cases in 1900. During this second outbreak the particular factory in which all the early cases had occurred escaped, the firm having since 1878 discarded the use of Siberian hair altogether.

The possibility of steam disinfection suggests itself as the only effective means of removing the danger from manipulation of dangerous wool and horsehair. In the case of wool no thorough and minute inquiry as to whether this method is practicable has ever been undertaken. In 1880 a manufacturer in Bradford for the space of 12 months placed all bales of alpaca and mohair in a steaming apparatus at a pressure of five pounds for 12 hours. No experiments were made to see how far sterilisation was accomplished. The firm did not find that the material was injured for spinning purposes. Subsequently the firm discontinued the use of Van mohair wool and the need for steaming disappeared. To obtain certain effects, such as

[28] Annual Report of the Local Government Board, 1878. Supplement containing the Report of the Medical Officer, p. 321.

[29] Annales d'Hygiène Publique, vol. xxix., 1893, p. 224.

the fixing of a dye material on the wool, mohair after it has been carded is still exposed for one and a half hours to steam at five pounds pressure without injury. When high pressures, such as are commonly employed in disinfecting machines in this country, are used, with the increased temperature, there is increased tendency to damage the material. Thus Dr. W. A. Evans,[30] medical officer of health of Bradford, has on several occasions tried to disinfect dangerous wools by means of a Washington Lyons apparatus and says :— "Although my disinfection may have been successful the wool has almost always been irretrievably ruined, altered in texture and very much in appearance."

The practicability of steam disinfection of horsehair has been thoroughly tested in this country and in Germany. The problem of steam disinfection when applied to horsehair and bristles is presented perhaps in its most difficult form. The natural resistance of the spores is increased by the dirt and grease of the material in which they are imbedded. The hair is tied tightly together and in the case of mane hair or combings the bales weighing about five hundredweights are hydraulically press-packed. Recent experiments by Proskauer and Elsner[31] have shown, too, that anthrax spores artificially placed on horsehair are killed with greater difficulty than when on silk. The experiments in this country by Webb and Duncan[32] have been carried out with known infected material, that is with horsehair in its natural condition in which the presence of anthrax had been demonstrated. The experiments were made in a Washington Lyons apparatus. They found that dust shaken from China hair subjected to a temperature of about 245° F. for 20 minutes appeared sterilised. When, however, the horsehair thus treated had been subjected to the process of carding and one horsehair fibre separated from another the anthrax bacillus was cultivated from the dust so produced. From this the conclusion was drawn that the process of carding liberated the spores which had escaped the first disinfection owing to its environment of grease and dirt. Nevertheless, numerous experiments with dust from combing machines showed that the disinfecting process had killed the great bulk of the bacilli and lowered the vitality of those which had survived. They could not sterilise horsehair in bulk by exposure to steam at about 24 pounds gauge pressure (253° F. actual temperature), even for 45 minutes. When the results of the German experiments became known Mr. Webb reduced the pressure at which he worked and found that equally satisfactory results were obtained with temperatures of 226° and 230° F.

The German experiments conducted in the Imperial

[30] Transactions of the Epidemiological Society, 1903-04, vol. xxiii., p. 186.

[31] Zeitschrift für Hygiene, vol. xliii., 1903, p. 504.

[32] Annual Report of the Chief Inspector of Factories for the Year 1900, pp. 472 and 473, and for 1902, pp. 278-81.

Health Office extended from 1894 to 1900.[33] They have been very thorough owing to statements made by manufacturers that the hair made to undergo the preliminary steam disinfection was reduced in quality and, therefore, a source of loss. In the German experiments reliance is based on current saturated steam and not on superheated steam. Anthrax spores are killed by exposure to current saturated steam at 100° C. in five minutes, whereas 20 minutes' exposure is required when superheated steam at from 110° to 120° C. is used. With use of superheated steam spores in the centre of objects to be disinfected may be killed, while those lying on the surface and directly exposed survive. The temperature recorded in these experiments in the centre has been from 99° to 101° C. and in the latter from 105° to 141° C. The only explanation is that the superheated steam as it penetrates into the object gives up its latent heat and acts on the spores in the form of saturated steam.

Leaving out of consideration hair white or light grey in colour, which would be turned yellow, the general conclusion arrived at by the experimenters is that provided the pressure does not exceed two and a quarter pounds, equivalent to a temperature of 219° F., and due precaution is exercised in the management and regulation of the apparatus during the time of disinfection, no injurious effect is produced in the hair which could be considered as diminishing its value or causing it to be a source of loss. Success, however, is only to be attained by minute care in detail: (1) in the construction of the apparatus designed so as to allow the steam to enter from above and to find its exit at the lower part of the apparatus; (2) provision of pressure gauges marking clearly the point when the pressure of two and a quarter pounds has been reached and the provision of thermometers to control the temperature indicated by the pressure gauge; and (3) constant attention to the apparatus during the time disinfection is in progress.

Frequent occurrence of cutaneous anthrax among brush-workers in Belgium has recently caused inquiry to be made there also as to the possibility of removing danger in manipulation of the material. Satisfied of the impracticability of making steam disinfection obligatory in the numerous small workshops throughout the country (a feature of the industry everywhere which adds to the difficulty of controlling the danger) Dr. Glibert, principal medical inspector, has directed his attention mainly to experiments to determine how far simple boiling might be regarded as efficient. Using spores of anthrax which resisted a 5 per cent. solution of carbolic acid for one month, in none of his experiments could he find them capable of developing even after only 15 minutes' exposure. At

[33] Arbeiten aus dem Kaiserlichen Gesundheitsamte, vol. xv., pp 456-99, and vol. xviii., p. 1.

the same time special precautions must be taken to secure penetration of the heat throughout the material because a thermometer placed in the centre of a closely tied bundle of horsehair 15 centimetres in diameter never registered 100 °C., although the liquid in which it was immersed was maintained constantly at this temperature for one and a half hours. These experiments seemed to him the more satisfactory as they followed on unsuccessful results with similar resistant anthrax spores subjected by him (under rigorous conditions) to the accepted procedure of steam disinfection in one of the best equipped continental factories.

To secure certain destruction of all anthrax spores in horsehair absolute reliance cannot be placed on either steam disinfection or simple boiling. Adoption of one or the other is a very material safeguard and steam disinfection is practicable for all kinds of hair except that which is of white colour provided due care is observed. Risk, however, must always be run by those persons who prepare the hair fordisinfection.

LECTURE II.

Delivered on March 9th.

MR. PRESIDENT AND GENTLEMEN,—The treatment of anthrax has been conducted on three lines. The first is based on the fact that man is naturally possessed of a considerable degree of resistance to the disease, as spontaneous recovery from external anthrax is not infrequent. Treatment has, therefore, been conducted on expectant lines only. Secondly, and by far the commonest method, is removal or destruction of the pustule in the belief that the process is at first a local one, the bacilli developing at the seat of infection and only after lapse of time causing serious and it may be fatal effects either by intoxication or by a more widespread distribution of bacilli in the body. I include under this head such methods as excision, cauterisation, and injection into the tissues round the pustule of 5 per cent. carbolic acid, as they all have for their object either the direct destruction of the bacilli or the setting up of a barrier against further extension outwards from the central nidus. Thirdly, following on the successful results obtained in the treatment of certain infective diseases by inoculation with the serum of immunised animals, similar success has been claimed in the case of external anthrax also and, in Italy and South America notably, this method of treatment is coming more and more into practice. The fact that external anthrax is so frequently the subject of spontaneous recovery makes it difficult to compare the respective merits of one and another method of treatment when the only criterion taken is the proportion of deaths to the number attacked. But in the case of external anthrax there are other means of comparison which do not obtain equally in other diseases when this the chief is left out of account, namely—(1) the relative amount of scarring or of deformity left; (2) the applicability of the form of treatment to the differing types assumed by the disease and the stage which it may have reached; and (3) the length of time which elapses from the beginning of the treatment to resumption of employment. All these are fundamentally important in judging of efficacy and the third especially is of moment where industrial considerations enter.

Müller[2] bases a series of articles on the success attending

[2] Deutsche Medicinische Wochenschrift, vol. xx., 1894, pp. 515, 535, 688, 706, 916, 955, 977.

13 consecutive cases treated intentionally in Jena by the most conservative of methods—namely, rest, fixation, and elevation of the part affected, stimulating diet, and the local application of grey ointment. Ramstedt[3] from the same hospital more recently has adduced other seven consecutive cases (one a very severe one of anthrax of the tongue) in which nothing but the same expectant treatment was pursued. And, similarly, Fr. Schultze[4] of Bonn cites also a case of extremely severe malignant pustule of the cheek with extensive œdema of the eyelid, neck, and chest, so extensive as to suggest the gravest prognosis, which recovered (after a plastic operation on the eyelid) without operative treatment on account of the situation of the pustule. Müller's view is that the bacilli multiply slowly at the point of inoculation and that the œdema set up is due to toxins liberated by them. In itself this œdema up to a certain point is to be regarded as a healing process in that it is injurious to the existence of the bacilli already present and is unfavourable to their further development. The fact that bacilli are very rarely found in the blood and then only within a very short period prior to death shows, he thinks, that the blood is not readily infected. Unless the blood-vessels, therefore, are cut through the bacilli will not enter the blood stream except by the devious path of the lymphatic vessels and in the lymphatic glands the bacilli meet with obstruction and are held back. He assumes that generalisation of the infective organisms can only occur after the cells at the point of local infection have been weakened either by actual struggle with the bacilli or by the action of toxins and effort therefore should be directed to maintain the cells at the point of entry in such a state as to prevent best the further spread of the bacilli. Hence the reason for the conservative treatment. It is possible to deal with 11 of the 13 cases he describes, the data in two being insufficient for the purpose. Several were, he says, extremely severe but in all the temperature had sunk to normal and the œdema had considerably diminished within a few days of the date of commencing treatment. The duration of treatment varied from three to 45 days (so long a period in one case being necessary on account of necrosis of both upper and lower eyelids), the average duration being 16 days. But in seven of the 11 it is definitely stated that further attendance in the out-patient department was necessary—in one case for considerable loss of the skin of the arm. He regards as almost a crucial experiment the occurrence of death in the fourteenth case where incisions had been made into a malignant pustule which up to then had been doing well, with the result that after 12 hours the inflammation had extended widely and death ensued in 55 hours. The cases are too few to draw the sweeping conclusion Müller does but they are instructive in

[3] Münchener Medicinische Wochenschrift, vol. xlvi., 1899, p. 517.
[4] Deutsche Medicinische Wochenschrift, vol. xl., 1901.

emphasising the difficulty in sifting the evidence of different methods of treatment. His view that obstacle is placed in the way of generalisation of anthrax by the lymphatic glands is supported by the experiments of Wyssokowitch[5] who found in one case of anthracæmia in man that he could cultivate 52 colonies of anthrax bacilli from a drop of blood from the finger, but similar cultivations from the vesicles, superficial and deep portions of the excised pustule, remained sterile. Following this observation up by injection of bacilli into rabbits in the region of the foot and watching the length of time which elapsed before the different glands and the blood became infected he concluded that the bacilli passed from the primary centre in the subcutaneous tissue into the blood chiefly through the lymph glands, which act as stations and hold up the bacilli until these grow through the glands and pass into the efferent lymph vessels. But seeing that as a consequence of the necrotic process many small veins must become thrombosed and be the seat of development of bacilli Müller gives no sufficient reason why these bacilli should not become detached and pass into the blood stream as readily as they would do were the blood-vessels cut through.

In the first lecture I showed that the mortality of the disease generally was at least 25 per cent. For cases treated under favourable conditions this figure is too high and by this is to be understood primarily excision not later than the fourth day after the initial symptoms have shown themselves. Unless the persons affected have knowledge of the nature of the disease or apply for treatment to a hospital the absence of pain and of constitutional disturbance often causes the lesion to be unheeded. That the general high death-rate is due to ignorance of the symptoms and neglect in applying for early treatment is shown, I think, by study of hospital records in districts where the disease is well recognised. Thus in the hide and skin warehouses round Tooley-street the symptoms are known and patients apply usually in good time at Guy's Hospital. Of 56 cases of malignant pustule treated there between 1896 and 1904 four were fatal—7·1 per cent. Of 20 treated at St. Bartholomew's Hospital two were fatal, and of 39 treated between 1896 and 1904 in the Bradford Royal Infirmary there were six deaths, 15·4 per cent. Study of these records leaves no doubt on the mind that in early cases, and frequently also in advanced, as soon as the local centre of infection has been removed or destroyed there is usually a rapid fall in temperature, the œdema commences to disappear and menace to life is over, although several days may elapse before all glandular swelling has subsided. Fatal cases are those in which excision is practised late and in which the symptoms are already severe on admission. This statement must be regarded as a general

[5] Reference in Centralblatt für Chirurgie, 1892, p. 6.

one only, because examination of the notes on 64 cases treated in St. Bartholomew's Hospital and Guy's Hospital shows that in ten œdema increased after excision and in a small number of the deaths in London hospitals generalisation of the disease followed so quickly after excision as to raise suspicion that they were connected. Surgical interference in external anthrax usually takes the form of free excision, dissecting out the pustule from the healthy tissues beneath, swabbing the wound out with pure carbolic acid, and allowing the wound to granulate up from the bottom. Frequently, also, or in substitution altogether of excision, into the subcutaneous tissue around the margins of the malignant pustule 5 per cent. carbolic acid is injected. At Guy's Hospital, based on the experience of Davies-Colley,[6] which again was based on that of Muskett in South Africa, in addition to excision powdered ipecacuanha is dusted on the wound and ipecacuanha in ten-grain does is given internally. Muskett[7] himself in 15 years treated 50 cases without fatal issue, using locally ipecacuanha mixed with water to the extent of a cream and did not practise excision. He believed the remedy was as much a specific for anthrax as quinine is for ague and mercury for syphilis. Davies-Colley did not feel justified in omitting excision and believed that internal administration of ipecacuanha was useful in acting specifically on the small black sloughs not infrequently found in the intestinal tract in fatal cases, the cause probably of the vomiting so frequently complained of. Washbourn found, too, that ipecacuanha has the power of destroying bacilli but not the spores of anthrax and in the body sporulation does not take place. Muskett cites only four of his 50 cases, all of them affecting the forearm, hand, or finger. The treatment initiated by Davies-Colley is still that carried out most frequently at Guy's Hospital. Russian surgeons[8] appear to have used largely injections of carbolic acid round the pustule. Scharnowski has treated in this manner 50 cases with 2 per cent. of deaths and their severity may be judged from the fact that 25 affected the face and neck. Cases are recorded where very large amounts of carbolic acid have been injected in cases of anthrax when the œdema has been extending without production of symptoms of carboluria. Such a case is reported in the *Guy's Hospital Gazette* of Oct. 8th, 1904. Country practitioners make frequent use of the caustic potash stick alone. Graef[9] describes 384 cases of malignant pustule treated thus by himself and two other physicians since 1856 with 20 deaths—5 per cent. Of his own 75 cases four were fatal and ten were eventually cured after more or

[6] Guy's Hospital Reports, vol. xlvii., 1890, p. 1.
[7] THE LANCET, Feb. 11th, 1888, p. 269.
[8] Reference in Centralblatt für Chirurgie, 1882, 1890, and 1892.
[9] Wiener Klinische Rundschau, vol. x., 1903, p. 165.

less local necrosis (in one case amputation of the arm). In the remaining 61 within 24 hours of the cauterisation the symptoms diminished and the threatening anthrax pustule was converted into a harmless eschar. The situation in these was about equally distributed on the face and neck, on the one hand, and the upper extremity on the other. The eschar commenced to detach itself in from ten to 14 days and became finally detached in the third or fourth week. In the neighbourhood of the eye sometimes plastic operation was necessary. Failure by this method he attributes to delay in application for treatment. He considers that the favourable result of the expectant treatment as shown by Müller does not justify the omission of destruction of the local centre, as he believes by that means the generalisation of the disease can be prevented. Excision as a preliminary to the use of caustics is allowable but, in his opinion, quite unnecessary.

The great objection, however, to be urged against excision is that in some situations—as, for instance, on the eyelids—operative treatment is impracticable or, if practised, must inevitably lead to disfigurement and necessitate subsequent plastic operation or skin-grafting to repair the loss of tissue caused; indeed, it may be said that subsequent treatment of external anthrax after excision is more concerned with remedying the conditions thus produced than by concern for the disease itself. Further, there is the objection that in a few cases it may lead to generalisation. Examination shows that of 15 cases treated by excision at St. Bartholomew's Hospital the average stay in hospital was 20 days and that in not one is it stated the wound was quite healed at the time of discharge. Similarly in Guy's Hospital of 43 cases the average duration of treatment was 15·7 days; in the London Hospital of 38 cases, 16·1 days; and in the Bradford Royal Infirmary of 32 cases, 22·6 days. I draw no inference respecting the average duration of stay in one and another hospital, for this necessarily is dependent on the pressure there may be for beds, causing in some cases an earlier discharge to the out-patient department than in others.

In view of the importance of examining the method of treatment by anti-anthrax serum closely I have set down the details of all the published cases that I can find [10] without selection (see Table X.). All but two of the cases have been treated in Italy with Sclavo's serum. Those numbered 1 to 23 are consecutive cases treated by Dr. Lazzeretti [11] of Siena and 28 to 53 by Dr. Cicognani [12] of Santa Croce. Of

[10] This was written before the cases in the Brit. Med. Jour. of Jan. 7th and Feb. 11th and in THE LANCET of Feb. 4th were published.

[11] Lazzeretti: Ventitre Casi di Pustola Maligna curati col Siero Anticarbonchioso Sclavo, Siena, 1902.

[12] Cicognani: Quattordici Casi di Pustola Maligna curati e guariti col Siero del Professore Sclavo (Gazzetta degli Ospedali e delle

TABLE X.—DETAILS OF 67 CASES OF EXTERNAL ANTHRAX TREATED BY SCLAVO'S SERUM.

Number.	Sex.	Age.	Occupation.	Situation of pustule.	Date of admission.	Probable stage (days).	Treatment (quantities of serum injected in cubic centimetres).	Result.	Resulting condition at site of lesion.	Date of falling off of eschar.	Date of discharge.	Duration in days after commencement of treatment.	First day.	Second day.	Third day.
1	M.	17	Tanner.	Chin. Œdema of neck.	1/3/00	Third.	30	Recovery.	Slight scar.	12/3/00	13/3/00	13	Marked diminution of œdema.	Further diminution.	—
2	M.	18	,,	Neck. Œdema extending over neck.	18/3/00	,,	30	,,	,,	30/3/00	31/3/00	13	Local condition unchanged.	Œdema still extensive.	Marked diminution of œdema.
3	M.	27	,,	Lower eyelid. Œdema involving upper lip.	30/3/00	Second.	30	,,	No visible scar.	9/4/00	10/4/00	12	Œdema increased.	Unchanged.	Œdema disappearing.
4	M.	22	,,	Forehead. Œdema of scalp.	14/4/00	—	20	,,	,,	After seven days.	Not stated.	—	—	Local signs improved.	—
5	M.	47	Peasant.	One on the right forearm; another on the left thumb. Marked œdema and enlargement of the axillary glands.	14/5/00	Third.	40 on the 14th and 20 on the 15th.	,,	Completely cured.	A few days.	26/5/00	12	Œdema increased in both arms.	Œdema disappearing.	—
6	F.	17	Tailoress.	Upper lip. Œdema extending to the cheek and eyelid.	23/5/00	,,	20	,,	No deformity.	31/4/00	28/5/00	5	Œdema diminished.	Complete disappearance of œdema on the eyelid.	—
7	M.	37	Tanner.	Back. Œdema of shoulder and arm.	6/8/00	,,	20	,,	Completely cured.	11/8/00	11/8/00	5	—	—	—
8	M.	39	Butcher.	Neck. Great œdema; difficulty of deglutition.	15/8/00	Sixth.	40	,,	,,	A few days.	28/8/00	13	Diminution of œdema.	Further diminution.	—
9	M.	22	Tanner.	Lower eyelid. Much œdema of both eyelids.	14/8/00	Second.	20 on the 14th and 20 on the 16th.	,,	No interference with function from slight scar.	25/8/00	25/8/00	11	Œdema increased.	Unchanged.	Improvement commencing.
10	M.	60	Hide merchant.	Upper eyelid. No pustule; rapidly extending diffused redness and swelling.	22/8/00	,,	Suspected at first to be diphtheritic inflammation of the conjunctival mucous membrane and treated on the 23rd with antitoxin. On the 24th 20 c.c. of Sclavo's serum and on the 26th 20 c.c.	Fatal.	—	—	—	—	—	—	—
11	M.	39	Milkseller.	Right forearm.	28/12/00	Sixth.	40	Recovery.	Scar hardly visible.	4/1/01	4/1/01	7	Œdema diminishing.	—	—
12	M.	16	Tanner.	Clavicular region. Much swelling.	20/6/01	Third.	40	,,	Completely cured.	About seventh day.	28/6/01	8	—	—	—
13	M.	45	Butcher.	Back of thumb.	1/6/01	Fifth.	30	,,	—	About seventh day.	About 7 days.	7	—	—	—
14	M.	23	Labourer.	Neck. Œdema extending over the clavicle.	3/8/01	—	40	,,	No trace of scar.	8/8/01	12/8/01	9	—	—	—
15	F.	19	Peasant.	Cheek. Œdema of eyelids, forehead, and lip; dyspnœa; difficulty of deglutition.	2/8/01	—	40 on the 2nd and 40 on the 4th.	,,	,,	15/8/01	15/8/01	13	Unchanged.	Unchanged.	—
16	F.	44	Peasant.	Middle finger. Œdema of arm.	3/8/01	—	20	Recovery.	Completely cured.	12/8/01	12/8/01	9	—	—	—
17	M.	5	—	Chin. Œdema of lip and cheek.	4/8/01	—	30	,,	No trace of scar.	16/8/01	16/8/01	12	Unchanged.	Œdema disappearing.	Œdema disappearing.
18	M.	48	Peasant.	Ear.	4/8/01	Eighth.	20	,,	Completely cured.	—	12/8/01	8	Œdema disappearing.	—	—
19	F.	58	,,	Nose.	5/8/01	—	20	,,	No trace of scar.	—	11/8/01	6	Unchanged.	Marked improvement.	—
20	M.	22	,,	Elbow. Much œdema above and below lesion.	18/8/01	—	40	,,	Completely cured.	—	31/8/01	13	—	—	—
21	M.	44	,,	One on the right arm and one on the left arm.	18/10/01	Third.	40	,,	,,	—	28/10/01	10	—	—	—
22	M.	54	Butcher.	Back of hand.	27/10/01	Seventh.	40	,,	—	6/11/01	6/11/01	9	—	—	—
23	M.	61	Labourer.	Cheek.	26/11/01	—	40 on the 26th and 20 on the 27th.	,,	—	—	—	—	—	—	—
24	M.	32	Porter.	External angle of the eye. Eyelid closed by œdema.	13/10/02	Fourth.	20 and 10 on the 13th, 10 on the 14th, and 10 intravenously on the 15th.	,,	Some loss of tissue but function unimpaired.	—	—	—	Œdema diminishing.	Œdema increased; delirium.	—
25	M.	30	Tanner.	Bridge of the nose. Eyelid closed with œdema, which extended over chest.	21/4/03	Fifth.	40 on the 21st and 20 on the 22nd.	,,	Scar hardly visible.	—	Probably not later than 4/5/03	14	Condition improving.	Marked improvement.	—
26	M.	17	Sausage-maker.	Cheek. Much œdema.	1/3/03	Fourth.	22 on the 1st and 11 on the 2nd.	,,	Rapidly healed.	—	—	—	Œdema increasing.	,,	—
27	F.	14 months.	—	Cheek. Œdema of the whole face.	17/8/98	—	28 in three separate doses on the 17th.	,,	Scar hardly visible.	20/8/98	20/8/98	3	Œdema markedly diminished.	—	—
28	M.	33	Tanner.	One on the neck and one on the nose. Persistent vomiting.	15/6/99	Fourth.	40 on the 15th and 20 on the 16th.	,,	No trace of scar.	A few days.	—	Not more than 7.	Œdema disappearing.	Œdema disappeared.	—
29	M.	7	—	Temple. Œdema of neck.	9/8/99	Second.	20 in two doses on the 10th.	,,	—	15/8/99	15/8/99	6	Slight diminution of œdema.	Unchanged.	Marked diminution.
30	M.	69	Tanner.	Root of the nose. Œdema of eyelids.	14/10/99	—	30	,,	—	20/10/99	20/10/99	6	Slight improvement in local condition.	—	—
31	M.	2	—	Cheek.	4/11/99	—	10 on the 4th and 10 on the 5th.	,,	Completely cured.	9/11/99	9/11/99	5	Unchanged.	Improvement.	—
32	M.	20	Tanner.	Cheek.	8/11/99	—	30	,,	No trace of scar.	A few days.	Probably very early.	—	Œdema diminished.	—	—
33	M.	14	,,	Internal angle of the eye with great œdema.	7/2/00	—	20 on the 7th and 30 on the 8th.	,,	Complete loss of upper eyelid.	—	—	—	Œdema increased.	Further increase.	Improvement commenced.
34	F.	13	Tanner's daughter.	Chin. Much œdema of neck.	17/12/00	Fourth.	30 on the 17th and 30 on the 18th.	,,	No trace of scar.	21/12/09	21/12/00	4	Unchanged.	Improvement commencing.	—
35	M.	29	Tanner.	Neck. Slight œdema only.	29/12/00	—	40	,,	Slight scar.	4/1/01	4/1/01	6	—	—	—
36	F.	40	Peasant.	Thigh.	16/1/01	—	40	,,	—	—	—	—	—	—	—
37	M.	39	Tanner.	Shoulder.	30/1/01	—	40	,,	—	—	—	—	—	—	—
38	M.	—	Peasant.	Internal angle of the eye. Great œdema; delirium.	14/4/01	—	Had been cauterised on the 12th, when 40 c.c. were given, 45 c.c. on the 13th, and 40 c.c. on the 14th.	,,	—	—	—	8	Marked improvement.	—	—

DETAILS OF 67 CASES OF EXTERNAL ANTHRAX TREATED BY SCLAVO'S SERUM—(*Continued*).

Number.	Sex.	Age.	Occupation.	Situation of pustule.	Date of admission.	Probable stage (days).	Treatment (quantities of serum injected in cubic centimetres).	Result.	Resulting condition at site of lesion.	Date of falling off of eschar.	Date of discharge.	Duration in days after commencement of treatment.	First day.	Second day.	Third day.
39	M.	20	Tanner.	Angle of the lower jaw. No œdema.	12/3/01	—	40	Recovery.	Completely cured.	Some days.	Some days.	—	—	—	—
40	M.	16	,,	Chin. Extensive infiltration of tissues.	20/3/01	—	40 on the 20th and 40 on the 21st.	,,	—	,,	—	—	Œdema increased.	Unchanged.	Slight improvement.
41	M.	36	,,	Angle of the lower jaw.	21/5/01	—	40 on the 21st and 20 on the 22nd.	,,	—	—	—	—	—	—	—
42	F.	50	Milk-seller.	Cheek. Great œdema.	12/8/01	—	Cauterised on the 10th. Condition became so much worse that the patient was admitted on the 12th, when 40 c.c. were given, and 40 c.c. on the 13th.	,,	Necrosis of upper and lower eyelid.	—	—	—	Condition improved.	—	—
43	M.	35	Tanner.	Eyebrow.	13/9/01	Third or fourth.	40	,,	No loss of tissue or deformity.	21/9/01	21/9/01	9	Slight improvement.	Œdema rapidly disappearing.	—
44	M.	16	,,	Forehead.	27/11/01	Third.	40	,,	Surface healed.	4/12/01	4/12/01	7	Improvement.	—	—
45	M.	45	Porter.	Neck.	13/2/02	Sixth or seventh.	40 on the 13th, 40 on the 14th, and 40 on the 15th.	,,	Completely cured.	Some days.	—	—	Unchanged.	Unchanged locally but general symptoms improved.	—
46	M.	22	,,	Root of the nose.	25/2/02	Fifth.	50	,,	—	5/3/02	At work some days before 5/3/02	6	Œdema diminished.	—	—
47	M.	15	Tanner.	Chin.	20/3/02	—	50	,,	—	27/3/02	27/3/02	7	Œdema increased.	Œdema less. General condition very good.	—
48	M.	24	Sorter of hides.	Cheek.	30/4/02	Third.	50	,,	—	—	5/5/02	5	Œdema diminished.	—	—
49	F.	55	Mother of tanner.	Lower jaw. Much œdema.	20/4/02	Fifth; seventh when treatment commenced.	Excision and cauterisation done on the 20th as there was no serum at hand. On the 21st the condition was worse and more so on the 22nd. On the 23rd 20 c.c. were injected intravenously and 20 subcutaneously.	Fatal.	—	—	—	—	Marked improvement after serum injection on the 23rd.	—	—
50	M.	50	Hide sorter.	Eyelid.	17/6/02	—	50 on the 17th and 50 on the 18th.	Recovery.	Slight scar but no deformity.	29/6/02	29/6/02	12	Œdema increased.	Unchanged.	Improvement.
51	M.	16	Tanner.	Cheek.	31/8/02	Fourth.	40	,,	—	7/9/02	7/9/02	7	—	—	—
52	F.	7	—	Cheek.	24/10/02	Third.	20	,,	Scar hardly visible.	2/11/02	2/11/02	9	—	—	—
53	M.	19	Tanner.	Neck. Œdema of cheek.	16/3/99	Fourth.	Paquelin's cautery and 30 c.c. on the 17th and 10 on the 18th and the 19th.	,,	—	—	25/3/99	9	—	—	—
54	M.	22	,,	Cheek.	16/3/99	Fifth.	Paquelin's cautery and 10 c.c. on three successive days.	,,	—	—	25/3/99	9	—	—	—
55	F.	30	—	Forearm. Severe general symptoms.	19/3/99	Eighth or ninth.	Paquelin's cautery and 190 c.c. in seven days.	Recovery.	—	—	—	Probably 10 or 12	—	—	—
56	M.	18	Tanner.	Neck.	25/10/97	Sixth.	20 in two separate doses on the 25th, 10 on the 26th, and 5 on the 28th.	,,	Small scar.	—	1/11/97	7	Œdema diminished.	—	—
57	M.	17	,,	Neck.	5/1/98	,,	40 in three separate doses.	,,	Scar hardly visible.	19/1/98	12/1/98	7	Marked increase in œdema.	—	—
58	M.	14	,,	Eyebrow. Eye closed by œdema.	7/2/98	Fourth.	55 in two doses on the 7th and 20 on the 9th.	,,	No impairment of function or deformity.	19/2/98	18/2/98	11	—	—	—
59	M.	18	,,	—	28/2/98	Second.	30 on the 28th and 10 on March 1st.	,,	—	—	7/3/98	7	Œdema diminished.	—	—
60	F.	8	—	Two on the neck. Much œdema.	6/5/04	,,	20	,,	Completely cured.	—	17/5/04	11	,,	—	—
61	F.	28	Peasant.	Thigh.	7/6/04	Sixth.	40	,,	,,	—	20/6/04	13	—	—	—
62	F.	35	,,	,,	2/7/04	—	Had been cauterised before 40 c.c. of serum were injected.	,,	—	—	—	—	—	—	—
63	M.	4	—	Neck. Œdema closing eyelids and extending over the chest; difficulty of deglutition.	15/7/04	—	10 and 20 on the 16th.	,,	No trace of scar.	—	25/7/04	10	Œdema increased.	General condition improved.	—
64	M.	63	—	Cheek. Œdema general over the face and neck. General symptoms grave.	10/8/00	Sixth.	40 on the 10th, 10 intravenously on the 11th, and 10 on the 12th.	,,	No deformity.	—	17/8/00	7	Improvement.	—	—
65	M.	30	Cattle-dealer.	Forearm. Great œdema. Temperature 105°.	8/8/03	Fifth.	Thermo-cautery on the 5th. No improvement. On the 8th 150 c.c. were injected intravenously, 50 c.c. intravenously after 12 hours, and 40 c.c. on the 9th subcutaneously.	,,	—	—	About 14/8/03	About 7	Œdema diminished.	—	—
66	M.	27	Butcher.	Forearm. Œdema. Temperature 103°.	2/10/03	—	Thermo-cautery, followed by 80 c.c. intravenously and 30 c.c. subcutaneously.	,,	—	—	6/10/03	In four days returned to work.	—	—	—
67	F.	36	—	Hand. Pulse 150; temperature 104°. Vomiting.	12/8/02	Fourth.	Fuming nitric acid and chloride of zinc. 2 per cent. injections of carbolic acid had been tried. 40 c.c. were given on the 12th, 20 c.c. on the 13th, and 10 c.c. on the 14th.	,,	After 15th concern only for local injuries.	—	—	—	Diminution of œdema.	—	—

REMARKS.

Case 7.—Local symptoms diminished rapidly in a few days. Case 10.—The patient improved until the 29th when he had a rigor, was seized with vomiting and delirium, followed by collapse and death. Case 15.—Entire disappearance of œdema in three days after second injection. Case 20.—By the third day the œdema had greatly diminished. Case 22.—Improved rapidly in a few days. Case 24.—Symptoms and local signs markedly improved by the 18th. Case 28.—Up and about on the 19th. Case 33.—Plastic operation necessary. Case 35.—Remained in bed for only a few hours after injection. Case 36.—Pustules followed normal course. Case 37.—Œdema disappeared in a few days. Case 38.—Got up on the 20th. Case 41.—Got up on the 25th. Case 49.—Continued to improve until suddenly seized with collapse and death on the 28th. Case 55.—Bacilli found in blood and urine on the first and third day but not on any later date.

the 67 cases 56 were treated by serum alone and in 11 this serum treatment was subsequent to other treatment which in ten cases had been excision or cauterisation or both. In 44 of the 56 treated with serum alone data are given precise enough for practical purposes to determine the time which elapsed from the commencement of treatment until complete recovery. In several instances it is the same as the time given for the separation of the eschar but many days before that stage has been reached the patient is to all intents and purposes quite well. Excluding the fatal cases, in every instance but one by the third day marked improvement, not only in the general symptoms but in arrest of the further development of the pustule and in diminution of the œdema, had taken place. Taking the time thus given or to be inferred in these 44 cases the average duration of treatment was eight days. In none was it more than 14 days. I can affirm, too, that in the 12 cases treated with serum alone in which the details are not precise enough to allow of the number of days being given the evidence all points to rapid healing, except in Nos. 24 and 33 where there was loss of tissue. The exact description, so far as it is given, of the final condition at the site of the pustule itself may be summarised as follows: No visible scar, 10; scar hardly visible, 5; slight scar, 10; completely recovered, 15; some loss of tissue in eyelid but function unimpaired, 1; and complete loss of the upper eyelid, 1; total, 42. The situation of the pustule in these cases is indication enough of their severity, the high proportion on the eyelid being especially noticeable. (Table XI.)

In the list are two fatal cases, Nos. 10 and 49. In the first the patient was the subject of malaria, was addicted to alcohol, and had had syphilis. The upper eyelid was affected with œdema extending rapidly over the face and chest and there was no necrotic patch to assist in the diagnosis. The condition was suspected to be diphtheria of the conjunctival mucous membrane and diphtheria antitoxin was injected. A day later some vesicles appeared on the eyebrow, on which date 20 cubic centimetres of the serum were administered. Improvement in the local and general conditions ensued shown by reduction in the œdema, subsidence of fever, and regained appetite Four days later, improvement during that time having been continual, he was seized with a rigor, violent headache, vomiting, rise of temperature, and delirium, on which followed profound collapse, coma, and death. Post mortem there were found extensive submeningeal effusion and hæmorrhage in the substance of the brain. Anthrax bacilli were

Cliniche, No. 14, 1901). Ibid., Pustola Maligna e Siero Anticarbonchioso Sclavo (Gazzetta Medica Italiana, Nos. 51-52, 1902). Garzia: La Sieroterapia Anticarbonchiosa, Quattro Nuove Osservazioni Cliniche (Rivista d'Igiene, 1904). For further literature, see Sclavo, Sullo Stato presente della Sieroterapia Anticarbonchiosa (Rivista d'Igiene, anno xiv., 1903).

found in the submeningeal effusion. In the other case, also affecting the eyelid, serum treatment was delayed owing to the impossibility of obtaining it, so excision was practised. When the serum was obtained and injected intravenously immediate improvement took place. Two days later the œdema had diminished so much that the woman was able to see out of her eye, took her food well, and the pulse-rate dropped from 140 to 104. A few hours later she was seized with sudden collapse, cyanosis, and died. No post-mortem examination was held. Of the nine other cases treated with excision or cautery as well, in one there was complete necrosis of the upper and lower eyelid and in two others it is stated that after four days' treatment the local injury was the only concern, although one was of such exceptional gravity as to have received 200 cubic centimetres of the serum intravenously within 24 hours. In another case in which the bacilli were found in the blood and urine 190 cubic centimetres were administered in the course of seven days.

Particulars are given as to the amount of serum injected in each case. In the early days of the treatment the doses were comparatively small, no more than 20 or 30 cubic centimetres being given at the initial injection. In later cases the initial dose is generally 40 cubic centimetres and those who have experience of the treatment strongly advocate big initial doses. In 39 of the cases the initial dose sufficed. These cases, however, by no means exhaust the list of those in which serum treatment has been adopted. Sclavo[13] himself in 1903 reviewed the subject in a paper in which he tabulated all the cases known to have been treated by means of it in Italy whatever the stage of the disease. These totalled 164 with ten deaths—6·09 per cent. as compared with 24·1 per cent. for the whole of Italy. The facts stated by him he believes are very far from showing accurately the therapeutic value of the anti-anthrax serum. In the early days of a new treatment holding out a possible hope there is always temptation to use it in the most desperate cases. To two of the fatal cases I have referred already. In another, affecting the upper eyelid, the disease was not diagnosed until too late when the woman presented herself with a high temperature, very weak intermittent pulse, difficulty of respiration, and œdema of the face, the neck, and the chest. Death took place within nine hours of commencing treatment. In the fourth the pustule was situated on the neck with marked cyanosis from dyspnœa caused by the œdema. 25 cubic centimetres were injected with little hope of benefit and death followed within 20 hours. In the fifth the pustule was situated on the neck with œdema of the greater part of the thorax. Death took place within 11 hours of admission. 20 cubic centimetres only

[13] Sullo Stato presente della Sieroterapia Anticarbonchiosa, Rivista d'Igiene et Sanita Pubblica, Anno xiv., 1903.

were injected. In the sixth no record was kept except that death took place within 30 hours of admission. In the seventh the pustule was on the neck with œdema rapidly extending to the thorax. Bacilli were found in the blood. There appears to have been no reaction to injection of 45 cubic centimetres on the first day and 30 cubic centimetres on the second. Of the eighth, particulars are not given except that the patient was admitted to the hospital in a serious condition, the victim of alcoholism and suffering from disease of the heart. The ninth had œdema of the neck and chest, and 20 cubic centimetres were injected. On the following day there was marked improvement. 20 cubic centimetres were again injected but death occurred suddenly on the morning of the next day with symptoms of hemiplegia.

TABLE XI.

Situation.	Serum treatment alone.	Excision and serum treatment.
Neck (including angle of jaw) ...	13	2
Cheek (including ear)	11	2
Eyelid	5	2
Eyebrow	2	—
Other parts of face	13	—
Upper extremity...	8	4
Lower extremity	2	1
Trunk	1	—
Not stated	1	—
	56	11

Since July, 1904, serum treatment has been tried in England either alone or in connexion with excision in 12 cases of external anthrax. In one case of so-called malignant anthrax œdema also on the tenth day after the initial symptoms and when the patient was in a comatose condition 30 cubic centimetres were injected subcutaneously four hours before death at a time when bacilli were found present in the blood. In four of the 12 cases of external anthrax serum treatment alone without excision was adopted. The situation of the pustule in these cases was: (1) the malar eminence of the cheek; (2) the forehead; (3) the upper eyelid; and (4) the forearm. Cases 1 and 2 were treated at St. Bartholomew's Hospital.[14] An initial dose of 40 cubic centimetres sufficed

[14] Brit. Med. Jour., C. B. Lockwood and F. W. Andrewes, Jan. 7th, 1905. A. Bowlby and F. W. Andrewes, Feb. 11th, 1905.

in both cases to arrest further "development of vesicles or other indications of the necrotic process." There was increased œdema but this was associated with improvement in all other respects. In one of the cases no colonies of anthrax could be cultivated 19 hours after the serum had been injected although previously the fluid of the vesicles yielded abundant colonies. "Cultures were repeated on the third day again with negative result ..... only a few disintegrating bacilli were found, mostly enclosed in leucocytes." In both cases hardly any scar was left. Case 3 was treated by Dr. W. Mitchell of Bradford. The patient was a mill worker. Already by the second day both eyelids were closed with œdema, which extended to the clavicle on the left side, and the right upper and lower eyelids were dark coloured and appeared as if about to necrose. In four days 100 cubic centimetres were injected, 20 on the first, 50 on the second, 30 on the third, and ten on the fourth. By the fifth day the œdema had almost all disappeared except such as would readily be accounted for by the presence of a necrotic area on the left upper and lower eyelids. Although the local symptoms here were very severe the general condition of the patient remained good. Case 4 was treated at the Royal Infirmary, Bradford. The type of the disease was described as very malignant, with œdema rapidly extending to the shoulder. The patient received 140 cubic centimetres in the course of three days (30 cubic centimetres intravenously on the morning of the day of death). There appeared to be reaction at first in rise of temperature to 103·6° F. but the œdema continued to spread; he became insensible and the diagnosis of meningeal hæmorrhage between the pia mater and arachnoid was made by Dr. J. H. Bell. Post mortem the brain was found to be surrounded with blood between the pia mater and arachnoid and nowhere else.

Six of the eight cases in which excision was practised as well as serum administered (treated in Guy's Hospital, Bradford Infirmary, Kidderminster Infirmary,[15] and by Mr. E. G. Peck of Queensbury, Bradford) made rapid uninterrupted recovery. In the seventh, treated at the North Stafford Infirmary, excision of the pustule on the hand and incisions in the brawny œdema had been made on the twelfth day of the disease. Administration of serum was commenced 24 hours later when the patient was already in a comatose condition. Death took place 24 hours later, there having apparently been no reaction to the serum treatment (except in diminution of the œdema). In the eighth the pustule was situated on the neck with rapidly extending œdema. Two injections only of ten cubic centimetres at 12 hours interval were given. Death occurred within 30 hours of excision.

The claims which have been made as to the effect of serum

[15] THE LANCET, Feb. 4th, 1905, p. 292.

treatment can be summarised by saying that: (1) even in very large doses it is innocuous; (2) it can be well borne even when introduced into the veins; (3) no case taken in an early stage or of moderate severity is fatal if treated with serum; (4) with the serum some cases are saved when the condition is most critical and prognosis almost hopeless; (5) when injected into the veins the serum quickly arrests the extension of the œdematous process so as to reduce notably the danger from suffocation which exists in many of the cases where the pustule is situated on the face or neck; (6) if used soon enough it reduces to a minimum the destruction of the tissues at the site of the pustule; (7) in some situations of the pustule, as the eyelid, serum treatment must be used in preference to any other as it alone can hold out hope of success without permanent injury; and to these may be added (8) that in internal anthrax it is the only treatment which holds out any hope of benefit. In almost all cases injection of the serum is followed by a rise in temperature often to over 105° F. and with it there is an improvement in the general condition of the patient. In the same way the necrotic process itself is to be regarded as a sign that the organism is making effort to resist the anthrax infection.

A few facts may emphasise the value and importance attached to the serum treatment in Italy. In Santa Croce,[16] a small town on the Arno of about 5000 inhabitants, are 36 tanneries employing 350 workers. Danger of anthrax is recognised as being practically limited to hides coming from the east and especially from China, so much so indeed that some manufacturers had ceased to use them. Anthrax among the workers had been frequent, of which the series of cases 28–53 in four years is sufficient evidence. Dr. Cicognani has adopted the serum treatment exclusively since 1899, having had experience that the other methods of treatment did not always prevent a fatal issue and when successful the sufferers could not resume their occupation until after a long period of convalescence. The workers now insist on having this treatment to the exclusion of every other and he states that the manufacturers are so certain of its efficacy that they hesitate no longer to use even Chinese hides. The workers, too, are now so willing to undergo treatment, since operative treatment is uncalled for, that they present themselves when there appears the smallest pimple or boil suggesting anthrax. Dr. Lazzaretti of Siena, a town with many tanneries, has much the same story to tell and says that the efficacy of the serum is known so well in the country round about that peasants come from a distance to receive treatment. Recently in Milan I visited the large horsehair factory of Pachetti Brothers, employing some 700 workers. There, in addition to the

[16] Quattordici Casi di Pustola Maligna, by Dr. Cicognani, Gazzetta degli Ospedali e delle Cliniche, No. 14, 1901.

steam disinfection of horsehair, a physician attends every morning to treat accidents and slight ailments, keeping careful watch for conditions or appearances suggesting anthrax. The surgeon's room is fitted up as a bacteriological laboratory for verification of anthrax, a supply of serum is kept, and thus cases in the earliest stages are caught, treated, and recover without cessation of work for more than a day or two. Signor Pachetti states that he has no fear whatever of the disease among his workpeople, as he has seen so many successes in dealing with it by this method. It was, indeed, this last piece of information communicated to me a year ago by Mr. Albert Webb, of the firm of Edward Webb and Sons, carpet manufacturers, Worcester, which led me to inquire into the method of treatment.

So far I have said nothing of the source or preparation of the anti-anthrax serum. The whole of the cases which I have tabulated with two exceptions have been treated with serum prepared by Sclavo in the Pathological Institute of the University of Siena.

Attempts to protect animals, especially sheep and cattle, from contracting virulent anthrax by producing in them a mild form of the disease which rendered them immune against virulent bacilli date back to the year 1880, when Toussaint [17] suggested inoculation by means of attenuated cultures of the bacillus which had been kept at a temperature of 55° C. for ten minutes. Pasteur and Chamberland elaborated this method, very uncertain in its results, on such practical lines that since the crucial experiments made in May, 1881, it has been the principal means adopted, more especially in France, for preventing the spread of the disease to the unaffected animals of a herd. Culture of anthrax bacilli at a temperature of from 42° to 43° C. caused them to lose the power to produce spores and lessened the virulence independently of their power of multiplication. Inoculation of cultures kept at this temperature for 24 days sufficed to kill mice but not guinea-pigs (the first vaccine), while kept at the same temperature for only 12 days the second vaccine killed both mice and guinea-pigs but not rabbits. Sheep inoculated with a small quantity (one-tenth of a cubic centimetre of Vaccine 1 and subsequently after one or two weeks inoculated with a similar small dose of Vaccine 2) were found to resist inoculation with virulent anthrax. Cattle and horses could be protected in a similar way, the doses of the two vaccines in their case being doubled. Numerous experiments have since been made by the addition of chemicals or interaction of other bacteria to modify the method but without material success. Considerable difficulty was found in maintaining the two vaccines at proper strength. Sometimes the first vaccine in relation to the second was too weak and death

[17] Comptes Rendus, vol. xci., p. 303.

occurred immediately after the second inoculation. In other cases both were too feeble and failed to afford sufficient protection.

The most damaging criticism against Pasteur's method was, however, that made by Koch who showed that the method of inoculation did not protect animals from infection derived through the intestinal tract, the manner in which, under natural conditions, the disease is most prone to arise. The duration of the immunity, moreover, from inoculation does not last longer than one year, so that repeated inoculations become necessary. Still, the following figures[18] show the scale on which Pasteur's inoculation is practised and the results obtained during the 12 years 1882–93. During that time 3,296,815 sheep were vaccinated, with a mortality either after the first or second vaccination or during the subsequent 12 months of 0·94 per cent., as contrasted with the ordinary mortality in all the flocks in the district of 10 per cent. During the same time 438,824 cattle were inoculated, with a mortality of 0·34 per cent., as contrasted with a probable mortality of 5 per cent. if they had been unprotected.

The successful efforts made by Behring in obtaining a protective serum against diphtheria and by Kitasato against tetanus stimulated inquiry in a similar direction as regards anthrax by Behring, Hankin, Metchnikoff, and Roux. All experiments, however, failed to show that by means of the blood of animals either naturally immune or only slightly susceptible passive immunity in other animals could be produced with any degree of certainty. By immunity is to be understood an acquired insusceptibility to the disease, of strictly specific character, variable only within narrow limits, and to be recognised as a condition of striking and lasting character. Marchoux in 1895[19] first succeeded in immunising actively rabbits and sheep, using Pasteur's Vaccines 1 and 2, and then injecting virulent cultures subcutaneously, at first in small and then in greatly increased doses. The serum was taken from the insusceptible animals from 15 to 20 days after the last inoculation, and of four rabbits which received serum in amounts varying from 2 cubic centimetres to 9 cubic centimetres, followed by injection 24 hours later of one-third of a cubic centimetre of an anthrax culture (sufficiently potent to kill two control animals in 48 hours), one survived and death was delayed in another until the seventh day. In a later series of experiments he found that seven out of 24 rabbits which had been first inoculated with anthrax cultures and then treated with serum survived. Already in 1895 Sclavo was able to assert from his experiments that (1) sheep brought to a high degree of

[18] Quoted from Muir and Ritchie's Manual of Bacteriology, 1902, p. 300.

[19] Annales de l'Institut Pasteur, 1895.

active immunity can furnish a serum against anthrax; and (2) this serum shows prophylactic and curative power against anthrax when inoculated into rabbits; and we can trace the germ of the further development of the treatment to man in the last sentence of his paper in which he refers to the hope of being able by means of serum-therapy to combat anthrax both in man and in the domestic animals, from the fact that they are less susceptible to anthrax than are rabbits. He next sought to obtain a more powerful serum and as he recognised that species and individuality were features of considerable moment in this respect, he instituted comparisons as to the efficacy of the serums obtained from the sheep, the goat, the ox, the horse, and the ass. From the last-named animal the most powerful serum was obtained without marked differences in strength from among the five animals experimented on and it is serum from the ass which he uses. This was contrary to the opinion of Behring that the strongest antitoxic sera are obtained from animals which are most susceptible to the particular pathogenic organism, in that the ass is much less susceptible to anthrax than is the sheep or the goat. Even with the ass, however, it is desirable to immunise three or four animals and to select from among these the one producing the most active serum. In order to expedite the immunising effect he instituted simultaneous active and passive immunising treatment and by so doing was able to protect guinea-pigs (in cases where the control animals died on the third day) by simultaneous injection of cultures of anthrax and of the serum into the peritoneal cavity. He then tried to see whether the serum did not succeed better if injected into the veins and whether it was not possible to immunise sheep against anthrax with smaller doses than those used by Sobernheim (to be described later), taking advantage of this co-temporaneous active and passive immunising method. This he found he could do and thus developed a new process of immunisation against anthrax—namely, the injection of a small dose, five, ten, or 15 cubic centimetres, of anti-anthrax serum, together with a culture of slightly attenuated bacilli, followed from 12 to 14 days later by a further injection of virulent anthrax cultures. In 1898 he succeeded in protecting sheep from anthrax of a very virulent nature by injection into the veins of small doses and satisfied himself of the curative properties of the serum by proving that ten cubic centimetres administered 24 hours after inoculation of virulent anthrax cultures protected sheep in cases where one of the control animals died three hours and the others 14 hours later.

In view of the experimental results showing the curative power of the serum and its innocuousness when injected in very large doses into animals Sclavo next turned his attention to treatment of malignant pustule in man and the first case was treated in June, 1897. I have had the opportunity, through the kindness of Dr.

Sclavo, of seeing all the stages in the preparation of the anti-anthrax serum in the Pathological Institute of Siena. On August 10th from an ass which had undergone the process of immunisation during a period of two years about 150 cubic centimetres of blood were taken from the left jugular vein. Similar bleeding had been practised on more than 50 previous occasions for obtaining the serum. On the 13th the clot having separated the serum was decanted and ether was added to the extent of 3 per cent. of the whole bulk. On the 13th to test the efficacy of this serum six rabbits, three to act as controls, were inoculated subcutaneously in the abdomen with 0·5 cubic centimetre of a suspension of a culture of anthrax (grown on agar on August 11th and kept at 36°–37° C.). Three of the rabbits received also at the same time ten cubic centimetres of the serum injected in one of the auricular veins. All the control animals were dead in 36 hours with extensive œdema at the point of inoculation and anthrax bacilli were found in the blood and tissues post-mortem. The three which received the ten cubic centimetres of serum remained well except for slight induration at the point of inoculation until the 16th, when further opportunity of observing them ceased. The efficacy of the serum thus having been proved the serum was then introduced with antiseptic precautions into the ten cubic centimetre tubes in which form it is used. To maintain the immunisation of the ass on August 14th ten cubic centimetres of a culture of anthrax in bouillon containing 2 per cent. gelatin were injected subcutaneously into the right and left side of the neck. This culture was made on the 13th and was mixed with an old culture prepared in the same way a month previously. The use of gelatin in the fluid injected is believed to prevent the formation of an abscess at the point of inoculation. There were much swelling and tenderness which had in great part disappeared by the morning of the 16th. The following is the protocol of the treatment of an ass undergoing the immunising process. May 21st, 5 P.M.: Bled freely; immediately afterwards ten cubic centimetres of serum injected subcutaneously; temperature 38·2° C. May 22nd, 4 P.M.: Injection subcutaneously of one cubic centimetre of a 24 hours' culture in broth (second vaccine). May 23rd and 24th: Temperature 37·8° C. May 30th: Inoculation into the neck of ten cubic centimetres of serum plus one cubic centimetre of a culture of virulent anthrax (for this a 24 hours' agar culture had been emulsified with five cubic centimetres of bouillon). June 1st: Temperature 38·5° C.; marked local reaction. June 14th: Complete recovery; inoculation of one cubic centimetre of virulent anthrax prepared as before. July 8th: Two and a half cubic centimetres of similar culture. August 10th: Ten cubic centimetres of similar culture. August 27th: 20 cubic centimetres of similar culture. Sept. 14th: 20 cubic centimetres of similar culture. Sclav

stated that this treatment might without detriment have been made more rapid by inoculating at intervals of ten days.

Before leaving the subject of the history of serum treatment it is desirable to state what stage has been reached in similar serum treatment of the large domestic animals. This can be best done by study of the work of Sobernheim,[20] because although Sclavo's serum can be, and is, used for this purpose it has never been tried on anything like the same scale. Sobernheim's first series of experiments were carried out in 1897 with serum of cattle which had been subjected to Pasteur's treatment and with the serum of one cow which, after recovery from spontaneous anthrax, had been further treated by Pasteur's method. The results, so far as concerned the production of immunity in rabbits, guinea-pigs, and mice, he considered so variable that they were contrary to any idea of specific action of the serum. Some of the animals lived, others died with the usual rapidity, while in others again death was delayed for several days. He inclined to attribute such success as he obtained merely to increased resistance, as the same sort of result was obtained after inoculation with normal serum. More satisfactory results were obtained from immunising two sheep, one slowly, the other rapidly, to such a degree that they could stand enormous doses of anthrax culture without inconvenience. The serum of the one that was rapidly immunised showed remarkable protective properties in retarding a fatal issue in rabbits for from six to eight days. But even here no certainty in action could be formulated, as sometimes it was not the largest dose which appeared to confer the greatest immunity. The main conclusion which he drew from his experiments at this time (1898) was that in the blood of animals brought to a high degree of immunity against virulent anthrax no specific immune bodies in any "degree worth naming" are present. He held out little hope that serum-therapy would be used as a curative agent in anthrax in animals because of the rapidity of the disease and to be prophylactic it must be certain in its action (variable only within narrow limits), it must be durable, and lastly, it must be effective against inoculation of spores.

In a later series of experiments Sobernheim used the same sheep as were used in the previous experiments but which had received repeated subcutaneous injections of very virulent cultures at fortnightly intervals for nine months. Blood was taken from 12 to 14 days after the last injection and 24 hours after treatment with the serum anthrax cultures were inocu-

[20] Experimentelle Untersuchungen zur Frage der Aktiven und Passiven Mitzbrand-Immunität, Zeitschrift für Hygiene, vol. xxv., 1898. Weiterer Untersuchungen über Milzbrand-Immunität, ibid., vol. xxxi., 1899. Berliner Klinische Wochenschrift. No. 22, 1902. Deutsche Medicinische Wochenschrift, Nos. 26 and 27, 1904

lated into rabbits. Some were saved from what would certainly have been a lethal dose by this serum treatment and in others death was delayed; but the same uncertainty in the result was found as sometimes small doses of three, six, or nine cubic centimetres were as successful as doses of 15 cubic centimetres. Sometimes it protected against inoculation with spores. Sometimes the animals died even when there were no spores. The immune bodies were found present in the blood in sufficient amount to prevent death or to delay a fatal issue when inoculated with cultures of anthrax four or five days after the serum treatment was commenced. He obtained much better results when sheep were treated with serum. Of five sheep treated with the serum in large quantities of from 200 to 500 cubic centimetres and then inoculated with virulent anthrax cultures all survived, while two control animals died within 24 hours. In a further series of experiments on sheep he obtained still more successful results by using the combined active and passive immunising method already described—simultaneous inoculation of anti-anthrax serum and virus or inoculation of them each separately within a short interval of time. He used for the virus anthrax cultures of about the strength of Pasteur's second vaccine, believing that with this strength injurious action would not result in the presence of the immunising serum. As a matter of fact, it was found to be non-injurious and the immunising effect was far greater than that obtained from serum alone.

Subsequently, to test this combined method of producing immunity Sobernheim carried out experiments over a period of two years—1900–1902—with the support and encouragement of the Chamber of Agriculture of Saxony. 33 sheep, 18 oxen, and some horses were treated first with attenuated anthrax cultures and later with highly virulent cultures in increasing doses until a degree of immunity was reached so great that inoculation of enormous quantities of most virulent anthrax cultures could be borne without material ill effects resulting. The serum and culture were not mixed together but five, ten, and 15 cubic centimetres of serum were inoculated into the left side and immediately after from 0·5 to 1 cubic centimetre of the slightly attenuated anthrax culture into the right. After from 12 to 14 days inoculations with virulent anthrax cultures were made. The results of laboratory experiments were entirely satisfactory as ten cubic centimetres of the serum sufficed to protect while the control animals died in from 24 to 36 hours. The immunity, too, thus conferred protected three out of four sheep from contracting the disease through the intestinal tract. Its curative power was also shown in that of five sheep inoculated with virulent anthrax and then subcutaneously treated at intervals of from ten minutes to six hours later with 40 cubic centimetres of the serum, two survived while death was delayed in the others from four to eight days. The control animals were killed in one and a half

days. It was necessary to apply the method on a much larger scale in order to determine its general applicability in veterinary practice. Districts in which outbreaks of anthrax were occurring were therefore selected and 2700 cattle were treated, almost all of them by means of the combined method. No deaths were attributed to the inoculation and no serious injury to health, even when the animals were only two or three weeks old. There were a rise of temperature and slight loss of appetite. From the moment the inoculations began cases of anthrax ceased to break out afresh. The immunity produced was lasting, as for a further nine months (up to the time of reporting), in spite of many outbreaks in untreated animals, none of the treated suffered. With larger doses animals already affected with the disease recovered. The following are examples of the success of the treatment.

1. On one farm in November, 1900, in consequence of outbreaks of anthrax all the cattle had been inoculated with Pasteur's vaccine. Despite this in the following year many died. In January and February of 1902 12 animals had died, three succumbing the day before treatment commenced. On the day itself two died and five became seriously ill. The five which were manifestly ill and others showing fever received 150 cubic centimetres of the serum. Of the remainder 80 received 25 cubic centimetres of the serum alone and 50 received 15 cubic centimetres of the serum plus one cubic centimetre of culture. 60 were not treated as there was not enough material. Of the five seriously ill four completely recovered. The one which died did so after six days. None of the others became ill and only among those which received no treatment did cases occur.

2. On another farm in March, 1901, in consequence of from six to eight cases since the commencement of the year, following on several others the year before, 318 cattle were inoculated at the beginning of April with 15 cubic centimetres of serum plus one cubic centimetre of culture. No more cases occurred.

Sobernheim feels himself, therefore, in view of these results, justified in speaking of anthrax serum as possessing not inconsiderable prophylactic and curative powers. The combined immunising method, he says, is capable of giving an extraordinarily powerful and lasting protection and he summarises its advantages over Pasteur's method as follows: (1) that it is free from danger; (2) that it is effective in one day and has not to be repeated; (3) that a stronger dose and more active cultures are used than is the case with Pasteur's vaccine and probably a more lasting protection is conferred; (4) that it protects from infection by way of the intestinal tract; and (5) that it can be used for curative purposes.

Sobernheim's latest contributions on this subject give further details of the success which has attended his method in Europe and in South America. At the time he wrote (March, 1904) the number of animals treated was about 75,000, of which from 12,000 to 13,000 were sheep, 2000 horses, and the remainder cattle. He himself in 1903 superintended the injection of large herds infected with anthrax on the *estancias* in Argentina. Slight rise of temperature, diminished desire for food, and transitory lessening in cows of the production of milk are observed in some cases where the injection follows a normal course. He refers to the failures experienced in some of the earlier cases treated on three different farms. In one instance of 60 animals about one half developed more or less extensive infiltrations at the point of inoculation and four died. Of the total 75,000 animals treated nine deaths are attributable to the inoculations. Serious illness and death in almost all cases occurred to draught oxen which before and after the inoculations were subjected to hard work. 40 cows inoculated with the same material on the same day and by the same veterinary surgeon showed none of the symptoms present in the draught oxen. Sobernheim cites, in support of his contention that fatigue increases sensibility to anthrax, the experiments of Charrin and Roger on the rat. Further, variability in the virulence of the anthrax vaccine would account for the failures, and since the time that attenuated cultures of the same degree of virulence only have been used there has been no catastrophe among the last 50,000 animals treated.

I have now stated the facts as to the preparation of, and the results from treatment by, anti-anthrax serum. When attempt is made to explain its action we are still almost totally in the dark. The anthrax poison is not comparable with that of diphtheria or tetanus because never yet satisfactorily, despite numerous experiments, has any toxin been obtained from filtered cultures of the bacillus the injection of which produces the specific effects of the disease such as are obtained from injection of diphtheria and tetanus toxins. It is customary from its tendency to generalisation on inoculation to describe the anthrax bacillus as an exciter of septicæmic processes, but the evidence from the manifestation of the behaviour of the bacillus in the human body undoubtedly points to the production of toxin of some sort. The presence of an excessive leucocytosis at the point of inoculation, the local necrosis, the œdema, the effects extending to distant organs, and the constitutional symptoms point to such toxic action. When, therefore, we recognise the absence of toxins from filtered cultures grown in artificial media it must not necessarily be supposed that this holds good for the life processes of the bacillus when developing on its natural soil in the body. Further, the poverty of the blood in bacilli until immediately before death is inconsistent with the view

that the extent of the symptoms is due to the multiplication of the bacilli apart from toxic production. Sobernheim cannot speak positively on the subject. He regards the artificially acquired immunity from the use of the serum as probably due to bactericidal processes rather than to antitoxic, on the ground that the whole character of anthrax infection is septicæmic in nature, but he does not consider that specific bactericidal effect of the anti-anthrax serum has been definitely proved either inside or outside the animal body. The serum does not decrease the development of, much less kill, the bacilli *in vitro* any more than does normal serum, nor does it bring about definite morphological changes in them. For days and sometimes weeks after subcutaneous inoculation of large quantities of anthrax bacilli into highly immunised sheep the bacilli can be found at the point of inoculation. On the eighth or twelfth day after inoculation he has found them in the blood which, in his opinion, points to the likelihood of the development of antitoxic properties. He is convinced that the animal organism must intervene and adapt the specific protective or anti-bodies in some way suitable to its needs. One animal may thus impress more of its own character upon the immune body which it evolves than another. Otherwise it would be impossible to explain, on the supposition that the serum was antitoxic alone, why the same quantity of serum in one case confers immunity on sheep and not on rabbits, and in another on sheep and rabbits both but not on guinea-pigs. This he thinks is explained by the complexity of bacteriolysins.

Ivo Bandi [21] states that the serum which he prepared from the sheep and used successfully in two cases in man possessed considerable bactericidal and antitoxic properties. To test its bactericidal power he followed Bordet and Gengou's method of determining the presence of immune body—namely, the addition, to fresh serum containing a sufficient quantity of complement, of anthrax bacilli sensitised by exposure for some time to the influence of the specific serum heated to 55°C. If there be immune body in the latter the complement in the fresh serum will be seized upon by the immune body and bacteriolytic power will be shown. He adds: "There is no experimental method by which to determine exactly the antitoxic power shown by the anti-anthrax serum, mainly because we have not yet succeeded in preparing a true anthrax toxin and are ignorant how far the products derived from cultures of the anthrax bacillus resemble in constitution and in effect the toxic products elaborated by the same bacillus in the living organism. Anyone, however, who has had occasion to make use of a properly prepared anti-anthrax serum in exceptionally severe cases of anthrax in man can easily assure himself of the existence in this serum of energetic antitoxins. In serious

[21] THE LANCET, August 6th, 1904, p. 372.

cases of this kind the toxic phenomena are evident and very distinct but after the use of the serum they diminish and disappear with remarkable rapidity." Sclavo, however, has not found that heating his serum to 55° C. for one hour in any way prevented its power of conferring immunity on rabbits. Thinking that possibly the rabbit's blood itself might contain sufficient complement to take the place of that excluded by the heating to 55° C. he prepared an anti-complement serum and treated rabbits with a mixture containing five cubic centimetres of his own anti-anthrax serum (heated to 55° C.) and 10 to 15 cubic centimetres of anti-complement serum (similarly heated). At the same time injection subcutaneously of virulent anthrax cultures was made but again the rabbits survived an otherwise certainly fatal infection. Metchnikoff,[22] from his own numerous experiments and those of several others working in his laboratory on the natural and acquired immunity of the dog, the white rat, rabbits, &c., believes that phagocytosis is the main factor in ridding the organism of the bacilli but that the act is dependent on the degree of virulence of the bacilli, and as a consequence of this varying degree of virulence, on the nature of the exudation set up as regards the presence of microphages or other leucocytes. Thus inoculation of attenuated cultures into one ear of a rabbit and of virulent cultures into the other calls forth in the first case circumscribed inflammation with presence of microphages in abundance, which quickly devour the bacilli and set up a leucocytic wall against further invasion; whereas in the second there is an abundant serous exudation containing but few leucocytes in which the bacilli remain free, multiply without interference, and ultimately cause death by septicæmia. Almost precisely similar differences are manifested when anthrax bacilli are inoculated under the skin of a vaccinated and unvaccinated rabbit. The exudation and resulting phenomena in the vaccinated resemble those following on inoculation of attenuated virus. This he explains by saying that a positive chemiotaxis is set up in the one case and a negative in the other. Finally, to explain the passive immunity conferred on rabbits he relies on Marchoux's experiments which he had the opportunity of watching. These showed that simultaneous introduction of bacilli and of immune serum into the peritoneum was followed by rapid englobement of the bacilli, so much so that in a few hours the peritoneal exudation was sterile and, further, that when, artificially, the arrival of microphages at the point of inoculation was hindered, and phagocytosis therefore delayed, the rabbits succumbed to fatal anthrax. The absence of phagocytosis observed by Sobernheim he explains on the ground that immunisation was not as complete as in Marchoux's experi-

[22] L'Immunité, 1902.

ments and consequently the conditions of negative chemiotaxis were set up. Thus immunity against anthrax in the animals experimented on, whether natural, acquired, or passive, is due to phagocytic action, which, however, is only able to manifest itself when the bacilli are introduced in an attenuated form or when they have been weakened in the body by contact with a substance contained in the microphages.

Sclavo will not allow further expression of opinion than that the bactericidal substances of the anti-anthrax serum do not correspond in structure with those present in other bactericidal sera and that in his experience they have only a secondary importance, notably inferior to that of the substances contained in it which stimulate the defensive action of the phagocytes. Facts which, in his view, confirm the stimulating influence of the serum on the phagocytes he adduces from the following experiments. The serum of sheep killed by intravenous injection of anthrax cultures was nevertheless capable of protecting rabbits inoculated subcutaneously with anthrax. Bacilli, therefore, thus injected into the veins and carried to organs where they are bathed in the blood fluids are probably not so favourably situated for allowing phagocytosis to take place as when they are present in the subcutaneous connective tissue. This may serve to explain why the dog, the natural immunity of which to inoculation is considerable, succumbs at once to intravenous injection. In rabbits, too, the action of the serum is more pronounced when it has been injected into the veins from 12 to 24 hours before rather than simultaneously with the cultures. Were the serum merely antitoxic it would not be possible for such differences to occur as are shown in the potency of the serum obtained from different animals. However big the doses of a weak serum, no such good results are obtained as from moderate doses of a powerful serum, probably from the fact that the weak serum insufficiently stimulates the leucocytes. On the other hand, Sobernheim and Radziewsky [23] found that when anthrax bacilli were introduced into the peritoneal cavity or developed there from the spore stage phagocytosis was present in a very small degree and at a late stage, while the swelling up and granular disintegration of the bacilli were obvious. Kisskalt [24] also, distrusting the results on this point obtained by so rough a method as removal by means of capillary pipettes of material from the peritoneal cavity, tested the same point and came to the same conclusion by means of sections. While in white mice phagocytosis was found by him to be pronounced with inoculation of many kinds of non-pathogenic organisms, living and dead, and with all kinds of inanimate foreign particles, it was absent with organisms markedly pathogenic. It was not that the

[23] Zeitschrift für Hygiene, 1901, vol. xxxvii., p. 33.
[24] Ibid., 1903, vol. xlv., pp. 18, 19.

leucocytes took no part in the reaction against the pathogenic organisms. On the contrary, the latter appeared to act chemiotactically on the leucocytes, which not only formed an inclosing wall round them but often lay quite close to the bacillus and only the last act of phagocytosis failed. In this respect his result is comparable with the view of Metchnikoff on inoculation of virulent germs.

The simplest explanation of these differing views is to assume the action of an intracellular toxin, which in slight amount attracts, and in large amount keeps back, the leucocytes. We get less confused if, dismissing phagocytosis from our minds, we still retain the idea of the cells of the body and accept the principle of immunity to be the fabrication by these cells of the bactericidal substances which, passing into the intra- and extra-vascular fluids, destroy the bacilli. And in the case of anthrax it is not difficult to imagine the formation of the bactericidal substances to be stimulated from the intracellular poisons or from other substances liberated by the death and disintegration of the bodies of the bacilli themselves. Radziewsky [25] has shown by special staining methods that all the time the development of an anthrax infection is proceeding the multiplication of organisms is accompanied by death and destruction of others. Introduction of spores of anthrax on threads into the peritoneal cavity of guinea-pigs is followed up to the ninth hour by enormous increase in number so that a thick network of them is formed, all staining well. Between that and the eleventh hour the reverse process goes on, during which an extraordinary destruction takes place, and by the fourteenth almost all are dead. This helps much to explain the negative bacteriological find in several cases of anthrax, as the number of bacteria which may be found at the end of an infection may not correspond in the slightest degree with the number that may at one time or another have been present. If there was no formation of bactericidal substances as the vital powers became exhausted there would be no sufficient reason to explain the decrease rather than increase of bacilli. And it is probable that the bactericidal substances which kill the bacillus are the same as are produced in the organism during the process of immunisation. A fatal issue in anthrax is to be explained on this view of Radziewsky by assuming that as the microbes increase so the cells of the body react to destroy them. The bactericidal substances thus produced destroy so many bacilli that the substances liberated at their death exceed the minimum lethal dose. The use of the serum, therefore, would be to assist in the destruction of the bacilli before the number was such that from their death so much poisonous substance was produced as to be fatal. If this view explained everything its use would be limited to early cases and in late

[25] Loc. cit., p. 34.

cases might even be a direct cause of death. From consideration of the cases treated in man by the serum we can hardly believe that its only effect is to cut short the capacity of the bacilli to increase at a time when the amount of the intracellular poisons has not yet reached a lethal dose. Recently Macfadyen and S. Roland,[26] by special methods consisting in the use of very low temperatures, have obtained extracts from the bodies of typhoid bacilli or, in other words, their intracellular toxin. Injection of this into monkeys, rabbits, and goats over a period of from four to six weeks produced a serum which showed (1) marked bactericidal and antitoxic properties; and (2) curative and preventive properties as regards the typhoid bacilli and their intracellular toxin. This is the first instance where a serum has been obtained which was found to be bactericidal against a particular organism and antitoxic as regards the toxin contained in its substance.

The work of Wright and Douglas,[27] with its proof that the blood fluids by means of certain substances, "opsonins," contained in them modify bacteria in a manner which renders them a ready prey to the phagocytes, may be expected to throw light on the action of the anti-anthrax serum. The anthrax bacillus unfortunately, owing to thread formation, does not appear to lend itself well to the particular method of experiment employed by them—namely, averaging the number of bacteria ingested by a certain number of leucocytes—but in experiments on the opsonic power of human blood in its relation to the anthrax bacillus when unheated serum was used they say, "Although enumeration was impossible there was everywhere evidence of phagocytosis. In the few cases where the leucocytes had not ingested bacteria they were found to have extended themselves in a characteristic manner along the bacterial thread." Repeating the experiments with heated serum "there was practically no sign of phagocytosis." The presence of opsonins in quantity in the blood after inoculation of serum would account for the observation of Andrewes in the case already referred to in which no anthrax colonies could be cultivated 19 hours after injection of serum although their presence had previously been abundantly proved, such few disintegrating bacilli as were found being mostly inclosed in leucocytes.[28]

[26] Centralblatt für Bakteriologie, vol. xxxiv., 1903, p. 765.

[27] An Experimental Investigation of the Rôle of the Blood Fluids in Connexion with Phagocytosis, A. E. Wright and S. R. Douglas, Proceedings of Royal Society, 1904, vol. lxxii., p. 357, and vol. lxxiii., p. 128.

[28] Sclavo's serum can be obtained from Elia Coli, chimico-farmacista, Siena, price 2 francs per tube of 10 c.c. Messrs. Martindale and Messrs. Allen and Hanburys also keep a supply.

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