IX. ON THE QUANTITATIVE ESTIMATION OF THE SEPTICAEMIA IN HUMAN PLAGUE.

The plague bacillus has been discovered in the blood of a large proportion of patients suffering from the disease by every observer. The frequency with which it has been found has increased with the quantity of blood withdrawn for examination. The Austrian Commission (1898) by cultivation from a few drops of blood found the bacillus present in 40 p.c. of the cases examined. Calvert (1903) by cultivation from two or three drops of blood discovered it in 100 % of cases 24 hours before death, but the proportion of cases in which it was found rapidly diminished as the time before death increased. Choksy, Berestneff and Mayr (1903) found *Bacillus pestis* in the blood in 45 % out of 1014 cases examined at the Maratha Hospital, Bombay. Greig (1906), who withdrew 1 c.c. of blood from a vein, found the bacillus in 60 p.c. All observers agree in the conclusion that an extensive septicaemia is very unusual until within a few hours of death, and some roughly quantitative observations were made by the Austrian Commission on this point. So far as we are aware, however, no attempt hitherto has been made to obtain an accurate quantitative estimation of the degree of septicaemia at various stages of the disease. Our primary object in undertaking an investigation of this kind was to test, for purposes of comparison, the infectivity of the excreta of plague patients, especially of the urine and faeces, in addition to the examination of the blood. From this point of view the preliminary series embodied in this paper is incomplete, since the excreta were not examined, for the reason that it was considered necessary, first of all, to gain an idea from the results of a number of blood examinations of the extent of the septicaemia on different days of the disease.

Before commenting on the more important results which emerge

from an analysis of the data brought together in the various tables, an outline may be given of the methods employed throughout.

The blood was withdrawn from a suitable vein at the bend of the elbow by means of a sterilised syringe of 5 c.c. capacity containing 2 c.c. of sterile sodium citrate solution. The surrounding skin having been well cleansed, and washed with a 1—1000 solution of perchloride of mercury, 2 c.c. of blood were drawn from the vein, thus making a 1 in 2 dilution of the blood. The blood and citrate solution were mixed in the syringe and then transferred to a small sterile test-tube. Samples of blood obtained in this way were removed to the laboratory, the subsequent examination being carried out with the least possible delay. In the latter half of the series the test-tubes containing the samples of blood were at once placed in a suitable ice-box in which they were kept till the dilutions were made. The necessary dilutions were effected in a similar manner to that already described in the section on the estimation of the septicaemia in plague-infected rats. Each quantity of diluted blood when measured off was sown into an 100 c.c. flask of neutral broth, and the presence or absence of stalactites was noted in every case where growth occurred. If a culture was obtained in a number of flasks corresponding to a series of dilutions of a particular sample, a portion of the culture given by the highest dilution, *i.e.* by the smallest measured quantity of the blood, was in every instance injected subcutaneously into a guinea-pig as a confirmatory test. In a good many cases in which the stalactite test proved negative or doubtful two or even three of the cultures furnished by one sample were injected into guinea-pigs. The blood was examined microscopically at the same time as the dilutions were being made.

The blood of 28 patients was examined, 74 samples having been taken in all. Of the 28 cases five recovered. The *B. pestis* was found in sixteen of the twenty-three fatal cases.

The cases which recovered do not call for any special remark. It may be mentioned, however, that on the occasions when the blood of these patients was examined it did not contain any plague bacilli.

Of the fatal cases no growth was obtained in any of the quantities taken in seven cases. The main facts are summarised in Table I, and further reference to them is unnecessary.

TABLE I. *Fatal cases in which* B. pestis *was not found.*

Serial No.	Hospital No.	Result of blood examination	Time reckoned from hour of death	Time reckoned from date of attack	Estimated duration of illness
2	1585	less than 1 per c.c.[1]	132½ hours	not known	not known
		,, 10 ,, [2]	60½ ,,		
		,, 1 ,,	36½ ,,		
		,, 10 ,,	12½ ,,		
4	1589	,, 10 ,,	27 ,,	8 days	9 days
8	1611	,, 1 ,,	3 to 14 days	4 to 16 days	19 ,,
16	1647	,, 1 ,,	3 days	26 days?	29 ,, ?
19	1666	,, 1 ,,	28 ,,	4 ,,	32 ,,
		,, 1 ,,	25 ,,	7 ,,	
25	1683	,, 1 ,,	65 hours	5 ,,	8 ,,
		,, 1 ,,	41 ,,	6 ,,	
		,, 1 ,,	17 ,,	7 ,,	
27	1688	,, 1 ,,	6 days	4 ,,	10 ,,
		,, 1 ,,	5 ,,	5 ,,	
		,, 1 ,,	3 ,,	7 ,,	
		,, 1 ,,	9¼ hours	10 ,,	

[1] *i.e.* no growth obtained from 1 c.c. which was the largest quantity examined.
[2] *i.e.* no growth obtained from 0·1 c.c. which was the largest quantity examined.

Cases in which a culture of B. pestis *was obtained from the blood.*

The principal points of interest may be dealt with under the following headings: 1st—comparison of the cultural and microscopical examination of the blood; 2nd—extent of the septicaemia at various intervals before death; and 3rd—relation of the degree of septicaemia to certain factors varying in every case, *e.g.* the age of the patient, the situation and number of the buboes, &c.

Of the 74 samples of blood taken 30 were proved to contain plague bacilli. In 26 of these the stalactite test was positive, and the cultures killed guinea-pigs with typical appearances of plague. In four (13 per cent.), although proved to be plague by the animal test, no stalactites were observed in any of the cultures obtained from several dilutions of the blood. An appearance simulating stalactites was noted in one or two flasks although no growth of *B. pestis* had taken place. These were instances in which either 1 c.c. or 0·1 c.c of blood was added to the culture flask and the explanation doubtless is that the pseudostalactites were simply threads of fibrin suspended

TABLE II. *Fatal cases in which* B. pestis *was recovered from the blood.*

Hospital No.	Quantitative estimation of septicaemia		Time reckoned from hour of death	Time reckoned from date of attack	Estimated duration of illness	Microscopical e of blo
1584	10 but not 100	per c.c.	45 hours	9 days	11 days	negative
1588	>200	,,	20 ,,	3 ,,	4 ,,	,,
1605	100 but not 1000	,,	4½ ,,	6 ,,	6 ,,	,,
1606	100 but not 1000	,,	28 ,,	Unknown	Unknown	,,
	100 but not 1000	,,	4 ,,			moderate num
1609	100 but not 1000	,,	48 ,,	2 days	4 days	negative
	>100	,,	24 ,,	3 ,,		,,
						¾ hrs. p. m., n
1612	1 but not 10	,,	48 ,,	4 ,,	6 ,,	negative
	less than 1	,,	24 ,,	5 ,,		,,
1617	> 100	,,	56½ ,,	Unknown	Unknown	,,
	> 100	,,	32½ ,,			,,
	>1000	,,	8½ ,,			2 bacilli seen
1625	>100	,,	67 ,,	2 days (definite)	5 days (definite)	negative
	>100	,,	43 ,,	3 ,,		,,
	>100	,,	19 ,,	4 ,,		,,
1636	less than 10	,,	73 ,,	3 ,,	6 ,,	,,
	10 but not 100	,,	49 ,,	4 ,,		,,
	10 but not 100	,,	25 ,,	5 ,,		,,
1638	>100	,,	32 ,,	2 days (definite)	3 days (definite)	1 bacillus seen
	1000 but not 10,000	,,	8 ,,	3 ,,		numerous
1660	10 but not 100	,,	53 ,,	4 ,,	6 ,,	negative
	1 but not 10	,,	29 ,,	5 ,,		,,
	100 but not 1000	,,	5 ,,	6 ,,		,,
1676	>10,000	,,	11 ,,	4 ,,	4 ,,	,,
1677	>10,000	,,	81 ,,	4 ,,	7 ,,	,,
	>10,000	,,	57 ,,	5 ,,		,,
	>10,000	,,	33 ,,	6 ,,		,,
	>10,000	,,	9 ,,	7 ,,		a few
1678	>10,000	,,	20 ,,	3 ,,	4 ,,	negative
1680	10 but not 100	,,	75½ ,,	3 ,,	6 ,,	,,
	1 but not 10	,,	51½ ,,	4 ,,		,,
	less than 1	,,	27½ ,,	5 ,,		,,
	less than 1	,,	3½ ,,	6 ,,		,,
1687	>1,000,000	,,	20 ,,	3 ,,	4 ,,	fairly numerou

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in the broth. In some of the flasks stalactite formation was delayed for a considerable time, *e.g.* in a sample containing 10 but not 100 *B. pestis* per c.c. growth and stalactites were first noticed in the "0·1 c.c." culture on the eighth day.

In six only of the 30 positive samples were bacilli observed on microscopical examination. These are shown in the following table:

Serial No.	Microscopical examination	Period before death	Extent of septicaemia
10	2 *B. pestis* seen	8½ hours	>1000 bacilli per c.c.[1]
21	few	9 ,,	>10,000 ,, ,,
6	fairly numerous	4 ,,	100 ,, ,,
26	fairly numerous	20 ,,	>1,000,000 ,, ,,
15	1 *B. pestis* seen	32 ,,	>100 ,, ,,
	numerous	8 ,,	1000 ,, ,,

[1] The sign > indicates that growth occurred in the highest dilution which was made, and that therefore the figure given does not necessarily represent the limit of the degree of septicaemia.

It would appear then that microscopical examination alone gives little indication of the extent of the septicaemia. As a matter of fact by relying too much on the results of microscopical examination in the early part of our work we were frequently misled as to the number of dilutions which it would be necessary to make to reach the limit of the septicaemia.

The degree of septicaemia in each case is shown in Table II, where also will be found the time of examination of each sample with reference to the hour of death and to the reputed date of attack. Most observers, heretofore, have sought to bring their results into relation with a certain day of the disease reckoning from the first day of illness. This of necessity must be in many cases uncertain, at least in India where there is considerable difficulty in obtaining from hospital patients or from their friends an accurate account of the beginning of the illness. For this reason we prefer to state our results in terms of the number of hours before death the sample was examined. It is remarkable that in one case (No. 21) >10,000 bacilli per c.c. were present 81 hours before death and that in No. 26 >1,000,000 bacilli per c.c. were found 20 hours before death. Again, it may be pointed out that in two cases furnishing definite information as to the date of attack, one (No. 11) gave a result of >100 bacilli per c.c. two days from this date, and the other (No. 15)

1000 bacilli per c.c. on the third day. Case 18 is deserving of notice in that it appears to afford an illustration of an irregular or fluctuating septicaemia which increased considerably within a few hours of death. An apparent diminution in the septicaemia, judging from the results obtained from a limited number of examinations, is exemplified in cases 9 and 23.

Lastly from an analysis of our results we have sought to determine whether or not a relationship exists between various factors in each case, *e.g.* the estimated duration of illness, the temperature of the patient, his age and the situation and extent of the buboes, but from the comparatively small number of cases which have been investigated nothing definite can be established on these points.

Summary and Conclusions.

An investigation of the blood of 28 patients suffering from plague has been made, involving the examination of 74 specimens. The *B. pestis* was not found in the blood of five patients whose illness ended in recovery; nor was it found in seven of the fatal cases. The salient facts ascertained from an analysis of the remaining 16 fatal septicaemic cases may be recapitulated thus:

(1) Microscopical examination of the blood cannot be regarded as a trustworthy criterion of the degree of septicaemia.

(2) A severe septicaemia may be present at a comparatively early stage of the disease and for a considerable number of hours before death.

(3) The septicaemia may be of an irregular or fluctuating type.

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