The treatment of plague with Prof. Lustig's serum / by N.H. Choksy.

THE TREATMENT OF PLAGUE WITH PROF. LUSTIG'S SERUM.

BY

N. H. CHOKSY,

M.D., Honoris Causâ, Freiburg, Germany.
Corresponding Member of the Medical Society of Munich.
Special Assistant Health Officer in charge of Arthur Road and Maratha Plague Hospitals,
Bombay.

BOMBAY:
PRINTED AT THE
"Eagle" Printing Office, Dalal Street, Fort.

1903.

THE TREATMENT OF PLAGUE WITH PROF. LUSTIG'S SERUM.

BY

N. H. CHOKSY,

M.D., Honoris Causâ, Freiburg, Germany.

Corresponding Member of the Medical Society of Munich.

Special Assistant Health Officer in charge of Arthur Road and Maratha Plague Hospitals,

Bombay.

BOMBAY:

PRINTED AT THE

"Eagle" Printing Office, Dalal Street, Fort.

1903.

PREFACE.

Numerous enquiries from various quarters having reached me from time to time, about the observations conducted at the Arthur Road Hospital in the treatment of plague with Lustig's serum, I decided early last year to reprint my papers and reports in the shape of this pamphlet. It has, however, far exceeded its original limits, inasmuch as the subsequent sudden closure of the laboratory for the preparation of the serum in June 1902, on financial and other considerations, and the consequent cessation of all work connected therewith rendered it incumbent to collect together all the information on the subject upto date.

In addition, therefore, to the papers above mentioned, comprising the first four sections of the pamphlet, the remaining sections contain new matter :—

Section V describes some further observations made with the serum during 1901 and 1902.

Section VI gives an account of the discussion on serum-therapy in plague on a paper read by Dr. J. A. Turner, the Health Officer of Bombay, at the Bombay Medical Union.

Section VII furnishes a tabulated statement of the correct statistics relating to all the observations from 1898 to 1902.

Section VIII deals with the treatment of plague with Lustig's serum in private practice and gives the results of the same.

Section IX details the opinions of those conversant with the subject on the value of the treatment of plague with Lustig's serum.

Section X summaries the conclusions arrived at from the foregoing study.

Three appendices have been added :—

A. Describes the histories of 23 cases of plague treated with Lustig's serum under varying conditions and is illustrated with 25 charts.

B. Gives a brief résumé of some recent studies in immunity and their bearing on serum-therapy.

C. Relates to Professor Kolle and Dr. Otto's comparative study of Lustig's, Yersin-Roux' and Tavel's anti-plague serums, and Dr. Polverini's reply to their criticisms.

Had it been possible to foresee when the pamphlet was projected that the closure of the laboratory would necessitate its expansion to its present length, the matter would have been re-cast and re-arranged in another shape, but that could not be done as more than half of it was in print when it happened.

It is, therefore, with some reluctance that this disjointed record is placed before the profession, pieced up together, as it has been, during some brief intervals between three successive epidemics of plague and in the midst of exigencies of other duties; and it is to be hoped that it will be looked upon with indulgence as but an imperfect contribution to the study of serum-therapy in plague.

N. H. C.

Arthur Road Hospital:
Bombay, 1st August 1903

INTRODUCTION.

Observations extending over four successive epidemics of plague, and comprising over 1,500 cases, have most indubitably shown that in serum-therapy we possess the only treatment that holds out any hope of reducing the excessively high case mortality that has so markedly characterised the epidemics at Bombay. It is this extreme virulence of the affection, with an average case mortality rate of 80 per cent. and over, in our public hospitals, that forbids anything like the anticipation of startling results in the treatment of plague in India—be it by the ordinary line of treatment or be it by any serum. The results have to be judged, therefore, not from a comparative standard, but subject to certain reservations and limitations in the light of our knowledge of the disease. We know that plague is extremely rapid in its course; that it produces profound organic and toxic changes in the system within an extremely short period—in many cases within a few hours; that its greatest mortality is between the third, fourth, and fifth days of illness; that the largest number of hospital admissions fall within the time-limit of its maximum mortality; and that scarcely any, except the most virulent cases, seek hospital aid on the first or second day. The most essential and primary consideration in serum-therapy being *early* treatment*—treatment at the earliest possible moment *after* diagnosis (and even *before* diagnosis is confirmed, as is now the rule in the case of diphtheria) —it becomes self-evident how even the best of serums would be powerless to avert death if patients are not treated early. Unless and until this is realised, it will not be possible to achieve good results.

These difficulties in the way of success in serum-therapy, great as they previously were, have become considerably enhanced since compulsory isolation, except in the case of the friendless, the homeless or the most destitute, has been abolished. This procedure has necessarily restricted the

---

* Grünbaum thus sums up (*The Practitioner*, November 1902) the results of recent serum-therapy :—"They all point to the necessity of—

1. Early application of the curative serum.
2. Administering a sufficient dose or doses.
3. Administering the serum at the right place.
4. Using undeteriorated serum."

scope of hospital work, firstly, by reducing the number of admissions into our hospitals; and, secondly, by sending to them a large preponderance of only the gravest cases, instead of a fair admixture of mild, severe and grave cases, as before. The case mortality of the hospitals has also increased *pari passu*—from 80 to as high as 93 per cent. in some instances,—and those who do not, or will not, carefully study these considerations rush to the conclusion that the virulence of plague has enormously increased or that serum-therapy has been a failure. The reports for the years 1900-01 and 1901-02 show this clearly, and further indicate how these factors have contributed to the less favourable results. Under such circumstances, it would be simply futile to waste serum upon such patients in the public hospitals, where its field of action has become so greatly contracted.

Such, however, is not the case in private practice, and the use of the serum should be encouraged, if not among all, at least among the better classes of patients treated at their homes and also in the private hospitals. The results of 130 cases—including Europeans, Parsis, Hindus, Mahomedans, and Native Christians—detailed in the following pages are much more encouraging, and indicate that in the cases treated within a few hours of the onset of the symptoms, or on the first or second day of illness, not only is it possible to obtain a greatly better rate of recovery, but that the normal course of the disease (nine to ten days) could be curtailed by half, thus saving the strength of the patient, and ensuring speedy recovery, without entailing serious damage to the system.

CONTENTS.

APPENDICES.

I

LETTER TO THE "LANCET" ON LUSTIG'S SERUM IN THE TREATMENT OF PLAGUE.

The following letter appeared in the *Lancet*, September 1900, in reply to certain criticisms on the subject, from its Special Correspondent in India :—

Professor Lustig reached Bombay in June, 1897, after the first epidemic of plague had run its course. A few sporadic cases, however, existed, and these were placed at his disposal for treatment with a curative serum he had brought with him from Florence. The results proved extremely satisfactory. As material for further observation was not available in Bombay, he proceeded up-country and treated some thirty cases with results equally satisfactory. When, some time after his return to Florence, he learnt that another epidemic had broken out, he offered to prepare and send down some serum with a view to test its efficacy on a sufficiently large scale, and it is needless to say that his offer was thankfully accepted by the Corporation. Early in March, 1898, Dr. (now Professor) Galeotti and Dr. Polverini arrived in Bombay with a quantity of serum, and as the epidemic was at its height, arrangements were made to begin at once with the serum treatment. As the supply of serum was to reach Bombay from time to time and at irregular intervals, and was to be limited, and as the objects then in view were to test its value on a clinical basis and to watch its effects from day to day on the more pronounced symptoms of plague, the following procedure was adopted in treating the cases. All moribund cases (those in whom the action of the heart had become gravely impaired and exhibited signs of failure or impending failure) and as also all convalescents and semi-convalescents were excluded from the treatment.

The first series of observations lasted from March to November, 1898, and again from February to May, 1899. During the course of this period 403 patients received the serum treatment and 1,190 patients were treated by ordinary methods. The clinical effects of the serum were watched from day to day, and although in some very grave and advanced cases the patients ultimately succumbed, the immediate effects on the general condition of the patients were extremely well marked, and this indicated either that the dose of the serum was too small, or that it was not strong enough, or that the treatment was commenced too late. But on the whole the improvement was quite perceptible and gratifying. When at the termination of these observations the results were tabulated, it was found that the serum-treated cases had a recovery rate of 38·2 per cent., whereas in those not so treated it was 19·5 per cent. only. The latter rate was, however, not less than that of the other large public hospitals, and the combined admissions numbering 4,762 in two of the largest during the same period had a recovery rate of 19·7 per cent., and thus it becomes apparent that the exclusion of

moribunds and convalescents did not tell in favour of the serum by reducing to any extent whatsoever the mortality rate in those treated by ordinary methods. In fact, this system of "selection" so-called or rather mis-called, was so strict and accurate as to eliminate even all mild cases, for had it been otherwise the mortality rate in the serum-treated cases ought to have mounted up much higher than the average of the other hospitals.

The second series of observations was commenced in May, 1899, and is still being continued. The object with which this series was started was to determine the statistical value of the serum, and hence it was resolved to conduct observations on 1,000 cases of plague, 500 to be treated with the serum and 500 by ordinary methods, the latter acting as controls, and the cases were to be taken for treatment *alternately* in the order of admission and *without any attempt at exclusion of any sort.* But objection to this method of treatment was the preponderance of either moribunds or convalescents in either set vitiating the final results. It was, however, anticipated that in two such large sets of 500 cases each, these would equalise at the end, and thus no undue advantage would accrue to one side or the other. We shall see further on whether and to what extent this anticipation was justified by practical experience. Further, in order to arrive at strict accuracy and to eliminate all errors, some standard had to be fixed as to what cases should be classed as moribunds and as convalescents. It was therefore determined to fix the limit for the former at 24 hours, and all patients dying within 24 hours of admission were considered as moribunds, but it was subsequently found that a large number died between 24 and 27 hours of admission, and hence 27 hours was adopted as the standard. As regards convalescents,* all those that had gone over the acute stage of the disease and had a normal temperature or thereabouts and had suppurating or suppurated and open buboes were considered convalescent.

And now as to the results. Up to the end of June, 480 cases have been treated with the serum, and 480 cases have become their controls, under ordinary treatment :—

	No.	Died.	Recovered.	Percentage of mortality.	Percentage of recovery.
Serum cases	480	328	152	68·33	31·67
Control cases	480	382	98	79·58	20·42

The serum cases show a recovery rate of 31·67 per cent., whereas the controls have a rate of 20·42 per cent., a difference in favour of the serum of 11·25 per cent. But the above results are not strictly accurate, and have been rendered fallacious by the undue preponderance of moribunds and convalescents in each series. The anticipation at first entertained about the equalising of these has not been realised in actual practice, and thus an

* All those that were taken as convalescents in both the series ultimately recovered, and there was not a single death amongst them.

element of error has been introduced into the statistics. The 480 serum cases were found to include 139 moribunds and 28 convalescents, whereas the controls had 145 and 38, respectively. The former had an advantage over the latter of six less moribunds, whereas the latter were better off in convalescents by 10. Hence, for a strictly accurate comparison, the only course open is to eliminate all the moribunds and all the convalescents from either series, and then deduce results from those remaining. If that is done, the results stand as below :—

	No.	Died.	Recovered.	Percentage of mortality.	Percentage of recovery.
Serum cases	313	189	124	60·38	39·62
Control cases ...	297	237	60	79·79	20·21

The percentage of recovery stands thus at 39·62 per cent. for the serum cases, and 20·21 for the controls, a difference of 19·08 per cent. in favour of serum. These results clearly indicate the value of serum treatment in those cases that are really acute and fit for treatment, and show that in these it is possible to very nearly double the recovery rate by the use of serum. These differences in the percentages do not, however, show the full value of the serum treatment, and that could only be arrived at by following the method adopted by Professor Haffkine in determining the life-saving value of his prophylactic inoculations against plague. That system is based on calculating the relative ratios of mortality amongst the inoculated and non-inoculated, and if the same system be adopted for the serum treatment, the ratio of recovery in the serum cases as to control cases would be as 1 of control to 1·55 of serum in *all* cases, and 1 to 1·96 when the moribunds and convalescents are excluded from both the series. Or, to put it in another way, if 100 cases out of a given number recover under ordinary treatment, the same number if treated with the serum would give 155 recoveries. And therefore the percentage of recovery is enhanced in one case by 55 per cent. and by 96 per cent. in the other.

These, Sirs, are the plain and unvarnished facts with regard to the use of Professor Lustig's serum in the treatment of plague, and they place before the reader the truth, the whole truth, and nothing but the truth. We have no reason to be dissatisfied with the progress made within two years of its application. Neither the mode of its preparation, nor its application at the bedside have yet been finally determined, and it is only by further research, experiment, and prolonged clinical observation that we shall be enabled to place it on a proper basis. So far as we have gone, we have been able to prove that the serum treatment is the only treatment that can in any way appreciably reduce the high mortality of plague, and we abide by our experience. When the diphtheria antitoxin required more than a decade for its perfection, is it not reasonable that sufficient time should be allowed for the application of a serum against a much more rapidly fatal and more deadly disease like plague ?

II

SOME OBSERVATIONS ON PLAGUE AND ITS TREATMENT WITH LUSTIG'S SERUM. *

MR. PRESIDENT AND GENTLEMEN,—Your Secretary having kindly extended to me an invitation, through Lieut.-Col. Wilkins, to read a paper on the application of Lustig's serum in plague, before this Society, I have with pleasure acceded to his request, inasmuch as I hold that no discussion on the subject would be without its due weight and value in finally assigning to this serum its proper place in Sero-therapy. Before entering into the subject of the serum treatment, I would crave permission to preface a few general observations on the nature and types of plague, its mortality, and the influence of race, age and sex, etc., on the same. All these have an important bearing on the results of the serum treatment. With this purpose I shall draw upon the records of the Arthur Road Hospital, which has received nearly 6,000 plague patients during the four epidemics of plague, about 4,000 of whom have been under my personal observation, and the rest under those of my various assistants, but under my general supervision. And I shall supplement these with some facts derived from the records of the Maratha and Modikhana Hospitals that receive—more especially the former—a better class of patients, belonging mostly to the labouring classes and mill-hands, than those admitted in the institution under my charge, and who consist mainly of the lowest stratum of Hindu society,—the waifs and strays of the city, the ill-fed and the half-starved, picked up from the road-side or drawn from the alleys and bye-lanes where they do most congregate. The bulk of the following observations may, therefore, be assumed to be typical of plague as seen in its worst and most fatal aspects, and they do not apply to the better classes of Hindus, or to other communities, who suffer less in proportion to their numbers, and in whom the mortality is comparatively low.

THE TYPES OF PLAGUE.

For purposes of clinical observation, plague may be divided into the seven following types:—(1) Pestis Minor, (2) Pestis Ambulans, (3) Simple Bubonic Plague, (4) Septicæmic Plague, (5) Pneumonic Plague, (6) Cellulo-Cutaneous Plague, and (7) Non-typical forms of Plague such as those associated with relapsing fever, malaria, small-pox, measles, cholera, phthisis, etc. The proportion in which these types occur in

* Paper read before the Medical and Physical Society of Bombay in September, 1900.

Hospital practice is found from an analysis of 11,600 cases of plague to be as follows :—

(1)	Pestis Minor	0·00 per cent.
(2)	Pestis Ambulans	0·50 „
(3)	Simple Bubonic Plague	77·65 „
(4)	Septicæmic Plague	14·25 „
(5)	Pneumonic Plague	4·10 „
(6)	Cellulo-Cutaneous Plague*	2·50 „
(7)	Non-typical and mixed Plague	1·00 „
		100·00

PESTIS MINOR AND PESTIS AMBULANS.

Pestis Minor and Pestis Ambulans, however interesting they may be from an epidemiological point of view, do not call for any special remarks. No cases of the former ever seek hospital aid, and in the latter they occasionally resort to hospitals if the buboes happen to suppurate—as they sometimes do—and relief is required.

SIMPLE BUBONIC PLAGUE.

Simple Bubonic Plague forms 77·65 per cent. of all cases, and is by far the most important type of plague. It is characterised, as its name implies, by the development, of buboes in various parts of the body, and runs a definite course extending from 8 to 11 days. And any subsequent rises of temperature after the eleventh day are generally due to suppuration of buboes or other complications.

The temperature curve, which practically consists of 2 curves, with an apyrexial interval, which may extend from a few hours to twenty-four or even more in some cases, is very peculiar, and is so unlike that of any other disease, that it is quite characteristic, and it has an important bearing on the behaviour of the serum, as I shall point out later on. There is usually a steady rise of temperature, till the evening of the third or fourth day, followed by a drop of two, three or more degrees on the morning of the fourth or fifth day respectively. The first curve ends here. The second curve begins a few hours after, and generally on the evening of the same day, the temperature rises suddenly high, to the same extent as on the evening previous, or even higher, and coincidently with this, all the symptoms become grave, and death generally supervenes after this secondary rise or reaction. If the patient is, however, going to recover, the reaction is not so high; or if high, it soon subsides, the temperature drops again the next morning,

* During the last epidemic (1899-00) the proportion was 3·61 per cent., *i.e.*, about one per cent. higher than the average.

and it goes down steadily by gradually decreasing morning remissions and evening exacerbations until the normal is reached on the morning of the 8th, 9th, 10th or 11th day. There are many deviations from this, as in every other disease that runs a well-defined periodic course, but it would take up too much of time to discuss them in detail. It would be quite enough to state here that the prognosis of the case greatly depends upon the termination of the first curve. The later it is, the better for the patient, and *vice versâ*. And it has been found that or the serum to be effective, the patient must receive a large dose before the termination of the first curve, and the longer the injection is delayed, the less the chance of recovery. The timely use of the serum before the temperature falls, contributes to lessening the shock consequent on the fall, which sometimes is very rapid and great, and may vary from 4 to 7 degrees or more and moderates the secondary reaction, which is so dangerous and so fatal a feature of plague. The buboes that develop in different parts of the body have great influence in determining the mortality in this type. An analysis of 9,500 cases of buboes shows that they exist in the following relative frequency :—

Femoral...	30·87 per cent.
Inguinal	23·25 „
Axillary...	21·85 „
Multiple...	13·95 „
Cervical...	6·72 „
Parotid	1·68 „
Other situations	1·68 „
	100·00

The average mortality rate in Simple Bubonic Plague is 77·25 per cent., but in individual position of buboes it may vary from 70 to 81 per cent., as follows:—

	Mortality.
Axillary...	81·29 per cent.
Cervical...	78·87 „
Inguinal...	77·62 „
Multiple...	75·87 „
Femoral...	72·56 „
Other situations	71·42 „
Parotid	70·34 „

The above mortality rates are again considerably influenced for the worse by the development of secondary pneumonia, or the occurrence of acute œdema of lungs—one of the most common causes of death in bubonic plague,—and in the case of cervical and parotid buboes by extensive infiltrations, serous, or hæmorrhagic in the tissues of the neck, pharynx and larynx. Axillary buboes, again, if accompanied with extensive infiltration, are more fatal than the average of 81·29 per cent.

SEPTICÆMIC PLAGUE.

Septicæmic plague is a type of plague in which the bacillus pestis gains a direct entrance into the blood, and in which the patient succumbs before any buboes can develop. Its course is more rapid than that of simple bubonic plague, extending at the utmost to six or seven days—usually from three to four,—and if the patient survives after the sixth or seventh day, a bubo generally appears shortly before death. The temperature curve is also different to that of simple bubonic plague. The temperature, as a rule, rises sharply and suddenly to 104° to 106°, or even higher, on the evening of the first day, and drops to normal or subnormal the following morning: and these morning and evening remissions and exacerbations may continue until death supervenes. In some cases the temperature remains high after the first rise, and the fluctuations between the mornings and evenings do not exceed a degree or so, whilst in other cases the tendency is to remain between 97° and 101°. There are no buboes in this type, and plague bacilli can be obtained in abundance from a drop of blood. If the patient's resisting power is so great as to tide him over the first four or five days, buboes appear simultaneously on various parts of the body. Hæmorrhages from the lungs, stomach, intestines and kidneys are very common in this type. The mortality rate in 1,562 cases was found to be 89·62 per cent.

PNEUMONIC PLAGUE.

This form of plague, to which Major Childe, I. M. S., drew our attention in 1897, is the most fatal; the mortality in 514 cases was found to be 96·69 per cent. It exists variably in different epidemics, and in no two does it appear in anything like a fixed ratio. Its duration is short, from four to seven days—usually about four to five,—and it is characterised by high fever, rapid and distressed breathing, absence of buboes; localised lobular pneumonia in isolated greyish patches, distributed over one or more than one lobe, with hæmorrhagic sputum, which may be frothy and copious, or scanty, and in small pellets of almost pure congealed blood, or at times it may be totally absent. Almost pure cultures of plague bacilli can be easily obtained from the sputum, and it is obvious that it is not only, therefore, the most fatal, but also the most dangerous and highly infecting type of plague.

CELLULO-CUTANEOUS PLAGUE.

In the clinical report on plague, which I published in 1897, I described, under the heading of *Cellulo-Cutaneous Necrosis*, large necrotic patches involving the skin and the subcutaneous cellular tissue. Their origin was then obscure, but I surmised that they originated in the small umbilicated blisters which are occasionally seen, and sometimes constitute the only

external evidence of plague. Further observation during the last three epidemics has not only confirmed this, but has led to the knowledge that these necrotic cases form by themselves, not only a distinct type, but also a comparatively milder type of plague, and which I propose to call *Cellulo-Cutaneous Plague.*

It is now an accepted belief that in most cases of plague one of the principal channels of infection is through the skin. The bacilli, soon after they gain an entrance thus, are conveyed to the nearest lymphatic glands without leaving any trace at the point of entrance. In this instance, however, they remain *in situ*, and proliferate, and give rise to the large advancing necroses. A blister, with or without an umbilication, generally the former, forms at the point of infection. Its contents are at first serous, and perfectly clear: they may become, however, turbid and purulent, and even hæmorrhagic. Suspended from the central umbilication is a core which reaches to the floor of the blister. The cuticle breaks, the contents are discharged, and a reddish, angry-looking circular patch remains. Within a few hours it becomes of a dark-greenish hue, cold to the touch, hard and almost leathery, the margin being conterminous with the surrounding healthy skin. The patch then begins to enlarge and advances from the circumference, and its size increases day by day, until a line of demarcation forms. The necrosis appears to be tied down firmly in the centre, which appears depressed, the edges being elevated. Around the circumference a hard, red, angry-looking and raised areola is formed, sometimes covered over with minute vesicles. The necrosis might go on advancing till large areas of the body surface may be involved, the largest hitherto seen covering nearly 80 square inches. The size may vary from an inch or even less in diameter to eight or twelve inches. Large necroses covering the whole of the gluteal region, the entire calf of the leg, or the interscapular space, have been noticed, and they have been found also on the scalp, neck, face, chest, abdomen, loins, thigh, leg, dorsum of foot, vulva, scrotum, etc. After the line of demarcation has formed, removal of the necrosis is fairly easy, if the sloughs underneath have separated, and when the whole of any such necrosis is removed *en masse* by the knife or scissors, a large unhealthy-looking saucer-shaped depression is left, with long and irregular shreds of necrosed tissue, pus and blood, and which under appropriate treatment becomes healthy-looking within three or four days, and heals fairly rapidly by granulation, and without the aid of skin-grafting. If the necrosis goes on, however, steadily enlarging, and the line of demarcation does not form by itself, it is possible to restrict its further spread by subcutaneous injections of sublimate.

The appearance of buboes in this type of plague is variable and depends upon the situation of the blisters and the period when the plague bacilli gain entrance into the lymph channels from the local seat

of mischief. If the latter is somewhat removed from the neighbourhood of the large lymphatic glands, and some time elapses before the bacilli enter the lymph current, the buboes appear later as secondary buboes (from 6 to 10 days after the necrosis); the systemic reaction is not so acute as in simple bubonic plague, the fever is moderate and the case runs a somewhat protracted but a comparatively favourable course in spite of extensive necrosis. If, on the other hand, the blister is in the neighbourhood, the necrosis is moderate in size, buboes develop within two or three days and the case becomes, to all intents and purposes, of bubonic type, but milder in intensity. In the latter case the mortality, though generally determined by the position of the bubo, is less than the average of bubonic type, whereas in the former it may range from 50 to 60 per cent. In fact, this type of plague has the lowest mortality, the average rate being about 62 per cent. only during the last epidemic, *i.e.*, 18 per cent. less than the average, and 15 per cent. less than in the simple bubonic type. It is possible to abort cellulo-cutaneous plague, if seen sufficiently early, and before necrosis has been set up by subcutaneous injections of sublimate near the seat of mischief, and I have been able to do so in three or four cases.

That the process above described is the result of the local action of the bacillus pestis has been demonstrated often and often. Almost pure cultures of the bacillus have been obtained from the blisters and from the advancing margin of the necrosis. And a timely confirmation of this local necrotic action of the bacillus pestis comes from Klein.* In his introductory remarks, as President of the Section of Pathology at the Annual Meeting of the British Medical Association last month, he describes the share which microbes have in determining inflammation, which, he says, is brought about (1) by the toxic products of the microbes, or (2) by the protoplasm of the microbes themselves. The diphtheria bacillus, the tubercle bacillus, the tetanus bacillus and the typhoid bacillus possess the property of setting up inflammatory phenomena, locally and generally, through the action of their toxic products. The tubercle bacillus, the cholera vibrio, the bacillus pestis, etc., act similarly through the action of their dead protoplasm. In addition to producing inflammation and progressive or retrogressive changes, of tissue elements, some of these pathogenic germs, along with pathogenic cocci, possess the property of causing progressive local necrosis, such as the diphtheria bacillus, and the microbes associated with tubercle, glanders, leprosy, etc., to which I would beg to add the *bacillus pestis*. Klein says that this progressive necrosis of the tissues, following typical symptoms of inflammation, is the result of the local action of the bacilli, 'and so long as they are in sufficient numbers and of sufficient virulence, and so long as their multiplication proceeds, the necrosis of the tissues spreads into larger and larger areas. This accounts for the necrosis of very large size that we see in plague. A further

---

* *Vide British Medical Journal*, August 4th, 1900.

confirmation that the dead protoplasm of the bacillus pestis brings about the necrosis, is furnished by the horses immunised for the preparation of Lustig's serum, as they show the same necrosis after injection with the immunising substance or the nucleo-proteid, which is nothing but the dead protoplasm of the plague bacillus. And so also in monkeys, the same local effects can be observed, after injection with the nucleo-proteid.

If I have devoted a little more time to this curious but minor phase of plague, my excuse is its great clinical and pathological importance, and the fact that attention does not appear to have been hitherto drawn prominently to it.

NON-TYPICAL AND MIXED FORMS OF PLAGUE.

These cases form about 1 per cent. of total admissions. In my report of 1897, I had referred to the association of relapsing fever, malaria and phthisis, and the same has been confirmed by further observation. In several instances plague bacilli form the bubo, and spirilla from the blood of the same patient have been demonstrated. Malaria has often and often been proved to exist in association with plague; during the epidemic of measles in 1898-99, several cases of plague with a distinctly measly rash were noted; and during the present year small-pox and cholera have been observed associated with plague. Small-pox developing in a case of plague and plague appearing during the progress of small-pox have been noted and latterly a mixture of plague (pneumonic, as well as bubonic type) and cholera has also been observed. Plague has also been noted to be associated with acute venereal infection, and some fatal cases with hard and soft chancres have been observed.

MORTALITY IN PLAGUE AND THE INFLUENCE OF RACE, AGE, AND SEX.

The mortality rates in the principal types of plague may therefore be put down as follows:—

	Mortality.
Simple Bubonic Plague	... 77·25 per cent.
Septicæmic Plague	... 89·62 „
Pneumonic Plague	... 96·69 „
Cellulo-Cutaneous Plague	... 62·00 „

The average mortality in plague has not been what it is to-day. During the epidemic of 1896-97 it stood at about 61·53 per cent. at the Arthur Road Hospital, and 64·5 per cent. and 68·28 per cent. at the Government House and Grant Road Hospitals respectively. The second epidemic of 1897-98 showed a higher rate, from 78·55 per cent. at the Arthur Road Hospital to 79·26 per cent. at the Grant Road Hospital. The third epidemic of 1898-99

gave a still higher rate, the lowest being 78·97 per cent. at Arthur Road Hospital, and the highest 81·40 per cent. at the Modikhana Hospital. The average mortality in 5,836 cases treated at the Modikhana, Maratha and Arthur Road Hospitals during 1898-99 was 80·39 per cent. During the fourth epidemic of 1899-00 the Maratha Hospital shows a mortality of 80·95 per cent. in 2,599 cases, and the non-serum cases at the Arthur Road Hospital have a mortality of 79·54 per cent. So that, for all practical purposes, the normal mortality rate of plague in our *public hospitals* may safely be put down at 80 per cent. The influence of race, age and sex may be gathered from the following data:—

Race.	*Mortality rate.*
Europeans	30 to 40 per cent.
Eurasians	35 to 45 „
Parsees	45 to 55 „
Mahomedans (Higher classes) ...	50 to 60 „
Mahomedans (Lower classes) ...	60 to 65 „
Native Christians (Goanese) ...	60 to 65 „
Hindus (High caste)	65 to 70 „
Hindus (Low caste)	75 to 85 „

An analysis of 6,000 hospital cases gives the following mortality rates according to sex and age amongst Hindus, Mahomedans and Native Christians. More than 5,000 of them were Hindus:—

	Males.	Females.	Children.	Total.
Hindus	79 71	77·47	69·57	75·33
Mahomedans	64·76	78·04	58·82	65·73
Native Christians... ...	63·77	68·36	58·97	64·34

The mortality in males of all the races is the highest, and in children the lowest, the difference varying from 5 to 10 per cent. between them. The mortality in Mahomedan and Christian females is apparently higher than in males, because of their smaller number.

LUSTIG'S CURATIVE SERUM.

It is unnecessary to detain you here with any detailed account of its preparation, as the same has been published in several medical journals. The observations with the application of the serum were begun in March 1898, with the object of determining whether it possessed any value, and if so what, and whether its use was limited or could be extended to all cases? It may be noted in passing that this inquiry was approached in a spirit of wholesome scepticism, borne of our knowledge of plague during the preceding two epidemics, and the high mortality and rapidly fatal termina-

tion that characterised it. Nor was there any eagerness or undue zeal displayed in either prematurely pushing its claims, or parading the early results. And it was only after long and patient observation, exceeding over a period of more than three months, that it was possible to formulate any opinion as to its value. The clinical effects of its action were so well marked, that it left no doubt in our minds that it had some specific influence on the course of plague.

THE SO-CALLED "SELECTION" METHOD.

It is customary, whenever a new method of treatment has to be tested, to make observations on patients that are fairly typical of the disease, and have fairly reasonable chances of recovery. It is not customary, on the other hand, to test it in those that are in the throes of death, or that have crossed the Rubicon. It is also usual to exclude, from such preliminary investigation, all those disturbing factors that would in ordinary course obscure the results. And as it was found from our previous experience that patients in whom the circulation had become so feeble as to show signs of impending heart failure, as well as those in whom heart failure had already commenced, and the pulse had become imperceptible at the wrist, were not amenable to any treatment that we could apply, it was decided to exclude them from these observations. So also did we exclude the later day cases—convalescents and semi-convalescents—as they were practically on the high road to recovery, and did not require any adventitious help. Eliminating, therefore, the above cases, there remained for observation the really acute cases, which have been called the "selection" cases. It was said that the favourable results of these preliminary observations were due to the selection of *mild* cases. Allow me to point out, that the term *mild*, in connection with a disease like plague with a normal mortality rate of 80 per cent., is quite incompatible and a misnomer. There is no grosser libel on plague than to characterise a plague case mild. For the mildness or otherwise is not to be, and cannot be, determined when the patient comes under treatment, but after the disease has run a certain course, and I hold that it would be certainly bold of any one, however wide and varied his experience of plague may be, to declare a case *mild* within the first three or four days of illness. And if I have been credited with selecting *mild* cases, I cannot certainly lay claim to any such super-human prescience. In no disease is it easier to tell what patient is going to die, and in none more difficult as to who is going to recover. Under these circumstances, I submit, the words, "selection" and "mild," were hardly appropriate.

The clinical phenomena that manifested themselves after the injection of serum were :—moderation in the intensity and duration of fever, improvement in the state of the circulation as shown by increase of arterial pressure, diminution in the size of, and lessening of pain, in buboes, cessation in the progress of advancing lymphatic infection, clearing of the mental

faculties, and a general improvement in the condition of the patient. In those cases where it did not ultimately save the life of the patient, it produced great amelioration in his condition and prolonged life, and time after time patients in semi-comatose condition have been observed to improve to such an extent as to be scarcely recognizable. It was also noted that the effects of the serum were not so evident in cases of septicæmic or pneumonic plague, or in those cases that have a naturally very high rate of mortality. On the other hand, its value was quite apparent in those cases that have a comparatively lower mortality rate, and which was still further reduced by its use.

The observations on the above lines were intermittent on acccunt of the supply of serum being limited, as well as irregular, and there were long intervals during which no serum was available. They extended from March to October 1898, and again from February to April 1899, during which period 403 patients were treated, of whom 249 died and 184 recovered, the recovery rate being 38·21 per cent. During the same period 1,190 patients, were under ordinary treatment, of whom only 233 recovered, the recovery rate being 19·5 per cent. The difference, therefore, in favour of the serum-treated cases was nearly double. The Maratha and Modikhana Hospitals received during the above period 4,762 patients who had a recovery rate of 19·7 per cent. There is thus a remarkable coincidence in the recovery rate between the non-serum cases at the Arthur Road Hospital and all the cases at the two latter hospitals. If it be conceded that the type of the disease, and the nature of the cases admitted into these hospitals, were the same—as they actually were—to what should we ascribe the enhanced recovery rate of the serum cases? It could not be ascribed to the so-called "selection" cases or "mild" cases, for, were it so, the recovery rate in the non-serum cases ought to have reached a vanishing point, whereas it was not lower than the average recovery rate of the other hospitals. It would be beside the purpose of this paper to enter into any lengthy argument on these points, and to those interested in the subject I would refer to the able report of Dr. Polverini, published last year, as it contains all the replies to any arguments that may be advanced.

PRELIMINARY CONCLUSIONS.

The following preliminary conclusions were deduced from the above observations :—

1. That the serum exerted a distinctly favourable influence on the course of plague.
2. That where it failed to avert death, it prolonged life, and temporarily ameliorated the condition of the patient.
3. That it did not exert much effect in those types of plague that are characterised by an extremely high mortality rate.

4. That its application therefore was mainly, though not exclusively, limited to the bubonic type of plague.
5. That there were limitations to its use in hospital practice, as about 50 per cent. of all admissions die within 48 hours, 20 per cent. recover naturally, and there remain about 30 per cent. that can be influenced by the serum treatment.
6. That its use would be more effective in private practice, as early cases would be treated, and that encouraging results, giving a recovery rate of 59·37 per cent. in 32 patients, have been obtained up to now.
7. That it exerts no deleterious influence on the patient, and could be injected into the healthy not only without any ill-effects, but with positive good, as it is capable of conferring *immediate but temporary immunity* against plague ; this immunity may last from 10 to 15 days.

THE ALTERNATIVE METHOD.

Some doubts having been expressed on the validity of the results of the above observations, and the conclusions they led to, and as it was anticipated that more accurate data would be available if no attempts were made to exclude any class of cases, and by treating every alternate patient in the order of admission into hospital, it was resolved to conduct a series of 1,000 observations,—500 cases to be treated with the serum and 500 alternately with them by ordinary treatment. There were certain objections and fallacies involved in this method, to which I drew attention before the observations were begun. Whilst discussing this method of treatment with Professor A. E. Wright of the Indian Plague Commission, I had the honour to draw his attention to the complex nature of the affection, and the number of wide and varied factors that contribute to influence its mortality rate and to point out by actual data furnished from the hospital records, how race, sex, age, the type of plague, the position of buboes, the date of illness at commencement of treatment, and the general condition of the patient, including the state of his circulation, influenced plague mortality. I further contended that for any set or sets of observations on the alternate system, it is quite indispensable, in order to secure accurate results, to so arrange that a serum case and a control case should be,—if not identical, at any rate approximately so, as regards the above important factors, and that so long as these did not equalise, so long would the results be the less accurate. Professor Wright had to admit the force of these contentions, but said that, under the conditions prevailing in the Bombay hospitals, it would not be feasible to have such exact controls, but the probabilities were that in a series of 1,000 cases the conditions would fairly equalise. We shall see later on how this anticipation has been realised in actual practice. Moreover, it was also thought that the moribund and convalescent patients would balance each other in either series.

The observations on the alternate system extended from May 1899 to end of July 1900—June 1899 being excepted. During this period 484 cases were treated with the serum, and 484 were taken as controls and were under treatment by ordinary methods. The former had 155 recoveries, equivalent to a recovery rate of 32·03 per cent., whereas the latter had 99 recoveries, that is, a rate of 20·46 per cent. ; there was thus a difference of 11·57 per cent. in favour of the serum cases. It would take me too long to enter here into any detailed analysis of these 968 cases, and as my friends, Drs. Polverini and Mayr, have just completed a comprehensive report, which will soon be published, I would refer you to the same. All that I need state here is that the fallacies to which we drew attention before the alternate system was begun, appear themselves most glaringly in the results, and, in fact, Drs. Polverini and Mayr have been enabled by these very statistics of the alternate system to expose the errors incidental to such a system when dealing with such a complex disease like plague, and thus to confirm our prognostications. The factors to which I drew your attention above as likely to influence and vitiate the final results, have not become equalised in either series, and to take one instance alone, the serum cases included 139 moribund patients that died within 24 to 27 hours of admission, and 29 convalescents that recovered, as against 147 moribunds, and 38 convalescents on the control side. If, for purposes of argument, we ignore the moribunds from our calculation, as they were bound to die under any case, and take stock of the convalescents only, that tended to obscure the results, and eliminate the same from either series, the serum cases show a recovery rate of 27·70 per cent., whereas the controls have a rate of only 13·68 per cent. only, *i. e.*, nearly half that of the serum cases. If both the moribunds and convalescents be excluded, the recovery rate for the serum cases would stand at 39·88 per cent., as against 20·41 per cent. in the controls. Or to put it in other words, the recovery rate is enhanced by 56 per cent. in all cases treated alternately : by 95 per cent. if the moribunds and convalescents be excluded, and by over 100 per cent. if the convalescents alone be eliminated. A curious confirmation of the beneficial effects of serum is demonstrated by the cellulo-cutaneous type of plague, which occurred somewhat to a larger extent during the last epidemic. Thirty-nine cases of this type came under observation, and of these 18 received the serum treatment and 21 were treated by ordinary methods. Of the former 9 died and 9 recovered, the recovery rate being exactly 50 per cent., whereas of the latter 13 died and 8 recovered the recovery rate being 38·10 per cent. ; that is the difference between the recovery rates of the two sets of cases was 11·90 per cent.—about the same as the difference shown on the total of all observations. And thus even this small series of a peculiar type of plague proves beyond a shadow of doubt the influence of serum in reducing the mortality rate.

It may be added that, during the above period, there were 38 cases that could not be included in one series or the other on account of the difficulty of diagnosis during life, or rapid death when kept under obser-

vation. All these cases were subsequently verified to be plague after death —and in only six that recovered out of them, the course of the affection left no doubt as to their nature. These were called extra cases and have remained totally unconnected with the above.

The results of these observations have confirmed the preliminary conclusions above stated, and a great step in advance has been made by the further knowledge gained during this enquiry. That the influence of the serum treatment is demonstrable as a whole in reducing the total mortality of a hospital, can be shown by a comparison with the records of other hospitals. The total mortality rate of the above 1,006 cases (serum, control and extra) at the Arthur Road Hospital was 74·15 per cent. During the same period the Maratha Hospital had 2,599 cases, and the mortality rate was 80·95 per cent. So that, with less than half the number of patients treated with the serum at the Arthur Road Hospital, the mortality rate of the institution was 6·80 per cent. lower than that of the Maratha, that receives a certainly better class of patients,—that is to say, that if all the patients at the former had been treated with the serum, the difference in the mortality rate between the two institutions would have been over 13 per cent..

MODE OF APPLICATION OF THE SERUM—GENERAL TREATMENT, ETC.

I will not weary you with all the details that we had to work out for ourselves, and without any previous experience as regards the application of the serum, the best method for the same, &c., &c. The results of our experience have been embodied in the accompanying copy of instructions prepared for private medical practitioners, to whom it is intended to issue the serum for use in private practice. I would only add that, subsequent to the date of the framing of these rules, some further observations have been made, which tend to show that two or three large doses of the serum, injected early, and within short intervals, are productive of greater good. In one very severe case of plague, seen on the evening of the fourth day, with a temperature of 105° and feeble pulse, with double sub-maxillary, double posterior cervical, supra-hyoidal, and supra-sternal buboes accompanied by infiltration in the soft parts of the neck, and in the pharynx, with œdema glottidis, dyspnæa and dysphagia, I administered 240 c.c. (in 4 doses of 60 c.c. each) within 36 hours, with the happiest results. The patient made a steady recovery, without any untoward complications, and without suppuration. So also in some cases treated within a few hours of the onset of the symptoms, big initial injections of 100 c.c. have almost cut short the attack. In a recent case treated at the Arthur Road Hospital, a Hindu female dwarf, aged about 20, received about 80 c.c. in two injections within 24 hours with very satisfactory results. The following are the instructions above referred to, and with them is attached a special chart for filling in the necessary particulars :—

INSTRUCTIONS FOR THE TREATMENT OF PLAGUE WITH PROFESSOR LUSTIG'S CURATIVE SERUM.

I. THE SERUM.

1. Each phial contains 20 c.c.

2. No antiseptic is added to the serum.

3. The presence of coagulum, flakes or blood, is no contra-indication to its use.

II. THE SYRINGE.

1. The syringe and needles should be boiled before injection and washed out with 3 per cent. carbolic lotion after use. They should be kept scrupulously clean.

III. METHOD OF INJECTION

1. Injections should be made subcutaneously and on the outer side of thigh or arm, as far as practicable.

2. It is preferable not to give a second injection on the same limb till at least 48 hours after the first.

3. Cleanse the skin thoroughly with soap and water, and carbolic, sublimate, or lysol lotion before injecting.

4. After withdrawing the needle, seal up the puncture with collodium and cotton wool.

IV. MODE OF APPLICATION OF THE SERUM.*

1. As soon as the diagnosis has been made, inject 60 to 80 to 100 c.c. in adults; for children under twelve, half the dose. For infants, 10 c.c. *The patient must be injected as early as possible. Much valuable time is lost in waiting.*

2. Injections should be given in the morning and repeated after 8 to 12 hours.

3. The quantity to be injected on subsequent injections should depend upon the range of the temperature on the previous evening and the general condition of the patient. If the temperature is the same as on the evening of the day of the first injection, may again be injected; if lower, then the same quantity less.

4. The quantity of the serum injected should be gradually decreased day after day, as above, until the temperature reaches to normal in the morning.

5. There is a drop in temperature of one to three degrees or more during the course of plague, and it may occur on any day from the second to the seventh. The injections should not be discontinued when this happens.

---

* These directions have been modified and two injections are now given daily, morning and evening.

6. If the temperature on any evening is found to be lower than in the morning, it is a favourable indication, and the quantity of serum injected the following morning may be safely reduced.

7. Six to eight more injections may be required to effect a cure.

8. The total quantity required for a cure may vary from 150 to 500 c.c. depending upon the severity of the case, complications, &c., and the strength of the serum used.

V. GENERAL AND LOCAL TREATMENT.

The following lines of general and local treatment are suggested for cases treated with the serum :—

1. *Stimulants* :—Brandy or rum in doses varying from 2 drachms to half an ounce or more, and well diluted, should be administered every 2 hours. The quantity of alcohol required for each case would depend upon the habits and the general condition of the patient.

2. *Nourishment* :—Milk or milk and conjee should be given every 2 hours in quantities varying from 4 to 8 ounces.

3. *Cardiac Remedies* :—If the patient's condition when first seen is very low, or if it becomes so in the course of treatment, and if the heart's action is impaired as shown by a weak, thready, readily compressible pulse, or if the pulse is intermittent or fluttering and imperceptible, cardiac remedies should be administered *hypodermically* in addition to the serum injections ; but these should be used with great caution and at intervals of 6 to 8 hours or longer.

4. *Control of Temperature* :—Avoid, as far as possible, any drug treatment. Ice-bag to the head, sponging or wet pack should be the means of reducing high temperatures.

5. *Complications* :—Treat all complications on general principles.

6. *Local Treatment* :—Avoid all irritating applications to the bubo ; apply ice over the same.

The above facts comprise all the data we have at hand up to now on the influence of Lustig's serum in the treatment of plague, and they have so far satisfied the authorities concerned, that preparations have already been made to make it on a larger scale for the next epidemic, and it has now been determined to revert to the former method of treatment, but on a larger scale, *i.e.*, to treat all, exclusive of the moribunds and convalescents.

COMPARISON WITH SERO-THERAPY IN DIPHTHERIA.

The only disease in which sero-therapy has given encouraging results up to now is diphtheria. But for purposes of comparison, diphtheria and plague stand wide asunder. They are so dissimilar in their duration, fatality, and

mode of death,—plague being by far the graver of the two, that comparison can only be instituted under large reservations. Dr. Alexander Anderson of Sheffield has given* some interesting data of mortality statistics in diphtheria, both before and after the introduction of the antitoxin treatment. The average mortality in the Metropolitan Asylums Board Hospitals during the pre-antitoxin period (1888 to 1894) was 30·3 per cent. in 11,598 cases; from 1895 to 1898 it became reduced, under the antitoxin treatment, to 18·4 per cent. in 20,382 cases—a reduction of 12 per cent. And I would put it to you, which is the greater achievement,—a reduction of 12 per cent. mortality in a disease with a natural mortality of only 30 per cent., after over a decade of observation and research, or a reduction of 12 per cent. in a disease with a natural mortality rate of 80 per cent., within 3 years of the inception of sero-therapy in the same? There could be but only one reply to this, and that is sufficiently obvious.

In this connection I should like to quote a few remarks of Dr. Anderson's on sero-therapy in diphtheria, which are so apposite to sero-therapy in plague and which *mutatis mutandis*, word for word might be made applicable to plague :—

"I am strongly of opinion," says he, "that antitoxin ought to be given in every case, however mild, unless it is seen too late for the remedy to be of any value. The objection urged against the use of antitoxin in mild cases, that by other methods of treatment 60 to 70 per cent. of cases will recover, and that there is, therefore, no necessity to give antitoxin in these sixty or seventy cases, does not seem to me to be sound reasoning. In any individual attack of diphtheria, we are dealing with an unknown quantity, with bacilli whose potentiality for mischief cannot be estimated. It does not follow that because a case appears mild at the onset it will remain mild, and that any time grave symptoms may supervene in an apparently mild attack. In judging of the severity of an attack of diphtheria, two factors have to be taken into consideration—(1) the susceptibility of the patient, and (2) the virulence of the organism. Of these factors in any individual patient we know next to nothing. The personal equation is too often lost sight of. One is often surprised to find symptoms of cardiac failure, nephritis and paralysis occur in cases where one would have least expected these complications. The cells of certain individuals are peculiarly susceptible to the diphtheria toxins, and as we cannot gauge the resisting power of any patient beforehand, we are not justified in withholding the antitoxin." Would you not apply these remarks to plague, enhanced three-fold in their serious import and gravity, and would you not then realise what measure of success can attend the lot of one whose labours are cast in the field of plague therapy?

---

* *Quarterly Medical Journal* for Yorkshire and the Adjoining Counties :—February, 1900.

CRITICISM.

Like every other new method of treatment, Lustig's serum has had to undergo criticism. We invite criticism in matters scientific, but at the same time we stipulate that the criticism should be intelligent, that it should be informing, and that it should be honest and straightforward. At the same time, if it does not fall within these requirements, we discard it. I have to say it with great regret that almost all the criticism levelled at the serum treatment lacks one essential element, *viz.*, personal observation and personal interest; and that, instead of inquiring into the subject as a matter of scientific interest, the critics have been led away by a certain amount of prejudice and distrust engendered, no doubt, by the glowing expectations with which another serum was received in Bombay early in 1897, and its limited results and the failure of sero-therapy in other diseases. But the conditions under which we work our public plague hospitals, the material with which we have to deal, and the complex nature and rapidity of death that characterise plague, forbid any such glowing expectations. We have to be thankful for such small mercies as are vouchsafed to us by any line of therapeutics, and if we succeed in enhancing the ratio of recovery rate by 50 per cent. in all cases, as we do with Lustig's serum, we should consider our labours amply repaid. Under such circumstances I trust you will agree with me when I say that if I do not attach any importance to certain criticism, directed without personal experience, and from a safe and respectful distance, I am perfectly justified in adopting the course.

There have been some critics who have reared up a fetish, to which they ask us all to bow down in all humility. Armed with a microscope, a few tubes of agar, a box of paint and a gas jet, with a rabbit or two thrown in, they consider themselves competent to solve all the mysteries of disease in our complex human organism. They look down upon clinical observation, and a clinician is to them a creature to be tolerated as an inevitable, but necessary nuisance, and whom they would readily cast aside if they could. A human being is much too large an object for their study, and with a rat or a rabbit, and perhaps occasionally a monkey, they are well content. They are apt to apply bodily, and without due reservation, the results of their observations on lower animals to man, forgetting, at the same time, the essential differences in the vital processes of the man and the brute. Protests have been frequently raised against this tendency on the part of bacteriologists, by bacteriologists themselves, and by none so emphatically as the members of the Indian Leprosy Commission, that included such noted bacteriologists as the late Professor Kanthack, and the late Dr. Beaven Rake, and the late Major Barclay, I. M. S. They say :—" We regret that, without in the least under-estimating the importance of bacteriological and animal experiments, the modern advance in these have led observers to take a one-sided view to the disregard of the evidence derived from clinical and epidemiological experience. The bacteriologist, in experimenting upon

highly susceptible animals, easily runs the risk of arguing beyond his premises and of drawing conclusions from his experiments, which he applies without sufficient reserve to the natural mode of infection. We believe that it is quite impossible for bacteriology alone, without the aid of clinical and epidemiological observations, to deduce the ætiology of an infectious disease." And yet, after all, our clinical experience of plague in Bombay, during four epidemics, we are calmly told that the clinician is not to be trusted to diagnose plague, and that his opinion and diagnosis do not count for much, so long as the bacteriologist is not at hand with his paraphernalia. I do not wish to be misunderstood. I have the greatest respect for the bacteriologist and his valuable work, so long as he remains within his proper sphere ; but the moment he forgets himself, and oversteps functions that do not legally and equitably belong to him, he becomes an hindrance instead of a useful help, which I readily admit he most undoubtedly is, and it is against this tendency of the bacteriologist to trench upon and usurp the rights that justly belong to the clinician, that I beg most emphatically to protest on this occasion. I have been led to make these remarks because some persons, having no other weapon or argument against the serum treatment, have gravely advanced, one, *viz.*, that the better results of the serum treatment could be explained away by the fact of cases that were not plague, having been taken as such, and that no case should be considered as one of plague unless and until the examination of blood reveals the presence of the bacillus pestis. Now, those who advance these arguments forget that if there are any errors of diagnosis, they ought to be on both the sides, the serum as well as the control, for it is not human for any clinician to so contrive that all his diagnostic errors should fall under one category and not the other. If there were any errors on the serum side, the controls should have shared equally in the same. They also forget that, time after time, the most exact and painstaking examination of the blood, both by the microscope and by culture, have failed to reveal the presence of the bacillus in the most undoubted cases, and even fatal cases of plague, and that it is only just prior to death that in many cases it may be detected. The Austrian Plague Commission, who made daily exhaustive investigations into this matter extending seriatim over 150 cases, confirm this. If, then, bacteriology fails to help us at the most critical moment, and the clinician is not to be trusted to make proper diagnosis, to whom should we turn for guidance ?

A false analogy has been introduced by some in this controversy. Because in every case of diphtheria it is necessary to verify the diagnosis by bacteriological examination, *ergo*, they argue, the same should be done in plague. They obviously forget that, unlike as in diphtheria, there is no other disease that can be mistaken for plague, just as croup—a comparatively benign disease—is often mistaken for diphtheria. In the absence, therefore, of any other disease in our whole nosology that can be mistaken for plague, I fail to see the necessity of imposing bacteriological examination in every case, or distrusting the results in those cases in which it has not been done.

No other affection presents the typical cardinal symptoms of plague which are evident, more or less, in every case, and during epidemic times there is no disease of which the diagnosis is so easy. And yet, in spite of this evident fact, it is often regrettable to observe that woful want of common sense, that fatal hesitancy, and that perverse inability to look things squarely in the face, that characterise the diagnostic efforts of some, who ransack the heavens above and the earth below, for some cause or causes, probable and improbable, of the clinical phenomena they see, whilst self-evident facts appeal to them mutely but in vain and indicate what course to pursue. To this, and to this source alone, I am inclined to attribute the high mortality rate that is so often observed in private practice, especially among the better classes of people. Much valuable time is thus lost, and what timely assistance could have done in the early stages, becomes unavailing later on. The essence of plague treatment by serum lies in its immediate, early and free use, and every hour that is wasted in futile diagnostic antics or self-deception adds to the danger of the patient. It is said that whilst 2,000 units prove beneficial in a case of diphtheria on the first day, even 50,000 are powerless on the third or fourth day; and so also in plague. A good dose on the first day and, perhaps, a second one on the day following would, I believe, eventually suffice to arrest the progress of the disease, although it would not be possible to undo the mischief already done, and which no serum is capable of doing.

Then, again, it has been said that the personal bias of the clinician has much to do with the results. Nothing could be further from the demonstrable facts. However much this aphorism may be applicable to fields of laboratory research and animal experiment, it does not bear upon clinical observation, for there could be no personal bias in clinical medicine, and no observer can convert into plague a case that is not plague and *vice versâ*. The question becomes narrowed down to only a single issue. Were the cases treated with the serum, plague or not plague? If the former, then no personal bias could enter into the inquiry : if the latter, then it shows that no clinician, however wide or varied his experience, is trustworthy. No physician is infallible, and I do not claim to be one. This much would I permit myself to say, that the greatest care and circumspection was exercised in eliminating all sources of errors consequent on faulty diagnosis, and all that skill, experience and constant and daily vigilance could do to secure accurate results was done. If, after that, there were any errors, I may add *humanum est errare*.

And now I shall conclude this paper in the same words with which I closed a recent communication to the *Lancet* : " We have no reason to be dissatisfied with the progress made within two years of its application. Neither the mode of its preparation nor its application at the bedside, has yet been finally determined, and it is only by further research, experiment and prolonged clinical observation that we shall be enabled to place it on a

proper basis. So far as we have gone, we have been able to prove that the serum treatment is the only treatment that can in any way reduce the high mortality of plague, and we abide by our experience."

Lieut.-Col. Wilkins said :—Mr. President and Gentlemen,—We owe Dr. Choksy many thanks for the very carefully thought-out paper he has read, and regret that time did not allow of its being fully read. In connection with this subject I may say that the Municipal Commissioner has kindly consented to 15 more horses being utilized for the purpose of making fresh serum to meet the next epidemic, by which time we hope that serum, enough for 1,250 cases, will be ready. I hope that private practitioners will learn the value of this form of treatment, but I have asked that none but those practitioners who are fully competent to use the serum be allowed to do so, as the serum must not be used unscientifically or at haphazard, but methodically. The serum will be kept at the Arthur Road Hospital, and can be obtained either day or night, with full directions for use with temperature charts.

Dr. Temulji B. Nariman thanked Dr. Choksy for his very able and interesting paper. He said that he agreed with all that was said by Col. Wilkins, and was glad to know that arrangements were made to supply Lustig's serum to private practitioners who, he had no doubt, would give the results of their experience and enable us to judge of the utility or otherwise of Lustig's serum.

Dr. Choksy, in the course of his reply, thanked Col. Wilkins for the great interest he had shown in the serum treatment, and the constant assistance and encouragement he had given him in the course of his investigation. He attributed the success of the results of the treatment with Lustig's serum to Col. Wilkins' cordial co-operation in the work.

III

ANALYSIS OF THE 480 CASES TREATED WITH LUSTIG'S SERUM ON THE ALTERNATIVE METHOD.

Drs. Polverini and Mayr who were engaged in the preparation of the serum, kindly undertook to analyse the cases treated with the serum on the "Alternative Method," and submitted a separate report on the same to the Municipal Commissioner for the City of Bombay. The following extracts have been derived from the same, and deal with the various factors incidentally referred to by me in the foregoing paper :—

"The alternate treatment was properly commenced on the 1st of July, 1899, and was continued until the 31st of July, 1900, when it was abandoned by order of the Municipal Commissioner in favour of clinical selection. As already in May, 1899, the patients had been alternately treated, the record for this month has also been included in this report, although it is incorporated in that of the last year. July, 1900, has been excluded, as the results were not known when the report was taken in hand. Only 4 cases were treated on either side in that month. Three of the serum patients recovered and three of the controls died. The records of each individual bleeding as well as those for the single months are seen from the following tables :—

Table showing the Records of each Individual Bleeding.

Series.	Horse.	Bleeding.	Serum Patients. Number of Patients.	Died.	Recovered.	Percentage of mortality.	Control Patients. Number of Patients.	Died.	Recovered.	Percentage of mortality.	Total. Number of Patients.	Died.	Recovered.	Percentage of mortality.
1	No. 1	2nd bleeding ...	23	15	8	65·21	23	15	8	65·21	46	30	16	65·21
2	„ 4	2nd do. ...	6	2	4	33·33	6	5	1	83·33	12	7	5	58·33
3	„ 3	2nd do. ...	16	12	4	75·00	16	9	7	56·25	32	21	11	65·62
4	„ 1	1st do. ...	6	5	1	83·33	6	5	1	83·33	12	10	2	83·33
5	„ 5	3rd do. ...	16	11	5	68·75	16	12	4	75·00	32	23	9	71·87
6	„ 3	3rd do. ...	24	16	8	66·66	24	21	3	87·50	48	37	11	77·08
7	„ 1	3rd do. ...	36	26	10	72·22	36	32	4	88·88	72	58	14	80·55
8	„ 4	3rd do. ...	37	23	14	62·16	37	29	8	78·37	74	52	22	70·27
9	„ 1	3rd do. ...	4	3	1	75·00	4	3	1	75·00	8	6	2	75·00
10	„ 2	2nd do. ...	15	8	7	53·33	15	12	3	80·00	30	20	10	66·66
11	„ 5	4th do. ...	23	15	8	65·21	23	18	5	78·26	46	33	13	71·73
12	„ 1	4th do. ...	35	25	10	71·42	35	33	2	94·28	70	58	12	82·85
13	„ 3	4th do. ...	25	18	7	72·00	25	19	6	67·60	50	37	13	74·00
14	„ 8	1st do. ...	26	20	6	76·92	26	17	9	75·38	52	37	15	71·15
15	„ 4	4th do. ...	24	13	11	54·16	24	18	6	50·00	48	31	17	64·58
16	„ 2	3rd do. ...	34	23	11	67·64	34	28	6	82·35	68	51	17	75·00
17	„ 9	1st do. ...	16	10	6	62·50	16	11	5	68·75	32	21	11	65·62
18	„ 5	5th do. ...	25	21	4	84·00	25	20	5	80·00	50	41	9	82·00
19	„ 10	1st do. ...	25	18	7	72·00	25	23	2	92·00	50	41	9	82·00
20	„ 7	2nd do. ...	11	8	3	72·72	11	9	2	81·81	22	17	5	77·27
21	„ 1	5th do. ...	17	12	5	70·58	17	11	6	64·70	34	23	11	67·64
22	„ 6	1st do. ...	19	13	6	68·42	19	18	1	94·73	38	31	7	81·57
23	„ 12	1st do. ...	10	6	4	60·00	10	8	2	80·00	20	14	6	70·00
24	„ 9	2nd do. ...	7	5	2	71·42	7	6	1	85·71	14	11	3	78·57
		Total ...	480	328	152	68·33	480	382	98	79·58	960	710	250	73·95

Table showing the Details by Months.

MONTHS.	ARTHUR ROAD HOSPITAL.															MARATHA HOSPITAL.			
	SERUM PATIENTS.				CONTROL PATIENTS.				EXTRA PATIENTS.			TOTAL.				ORDINARY TREATMENT.			
	Number of Patients.	Died.	Recovered.	Percentage of mortality	Number of Patients.	Died.	Recovered.	Percentage of mortality.	Number of Patients.	Died.	Recovered.	Number of Patients.	Died.	Recovered.	Percentage of mortality.	Number of Patients.	Died.	Recovered.	Percentage of mortality.
1899.																			
May	23	15	8	65·21	23	15	8	65·21	6	4	2	52	34	18	65·38	121	96	25	79·33
July	21	13	8	61·90	21	14	7	66·66	6	6	...	48	33	15	68·75	48	34	14	70·83
August	15	12	3	80·00	15	10	5	66·66	...	...	...	30	22	8	73·33	47	39	8	82·97
September	17	9	8	52·94	17	16	1	94·11	4	3	1	38	28	10	73·68	69	56	13	81·16
October	26	21	5	80·77	25	22	3	88·00	7	5	2	58	48	10	82·75	77	58	19	75·32
November	15	10	5	66·66	16	12	4	75·00	...	...	...	31	22	9	70·96	83	71	12	85·54
December	25	14	11	56·00	25	23	2	92·00	6	5	1	56	42	14	75·00	220	171	49	77·72
1900.																			
January	59	38	21	64·40	59	45	14	76·27	2	2	...	120	85	35	70·83	336	275	61	81·84
February	86	64	22	74·41	85	68	17	80·00	5	5	...	176	137	39	77·84	504	416	88	82·54
March	74	45	29	60·81	75	59	16	78·66	...	...	...	149	104	45	69·79	596	487	109	81·71
April	80	61	19	76·25	79	62	17	78·48	1	1	...	160	124	36	77·50	356	294	62	82·58
May	31	21	10	67·74	32	29	3	90·62	1	1	...	64	51	13	79·68	142	107	35	75·35
June	8	5	3	62·50	8	7	1	87·50	...	...	...	16	12	4	75·00	...	...	...	...
Total ...	480	328	152	68·33	480	382	98	79·58	38	32	6	998	742	256	74·34	2,599	2,104	495	80·95

In the table are included the extra cases in order to allow a comparison with the records of the Maratha Hospital, which are also given for the last official year. With regard to this table, it may not be superfluous to mention that the mortality amongst the serum patients, and the total mortality, compared favourably with that of the controls, when the serum treatment had to be discontinued in March last, and that the total mortality for the first half of the month, when the serum was used, was more than 5 per cent. less than for the second half, when it was not employed. The comparison with the Maratha Hospital shows that the monthly mortality at the Arthur Road Hospital, except during October, 1899, and May, 1900, was lower than at the former, and that the lower mortality was maintained during the four months, January to April, 1900, when the epidemic was at its height. It is of special interest to observe how the mortality at the Arthur Road Hospital followed the fluctuations of the death-rate at the other hospital during the above-mentioned months. In February and April the disease showed the highest virulence, and the difference of the mortality of the two hospitals is 5 per cent., in January and March the virulence was a trifle less, and the difference increased to 11 per cent. The higher figures on which the mortality works out during these months are a safeguard that the increase was not accidental, and we shall see later on that it corresponds to a law of serotherapeutics. The mortality for the period of the alternate treatment was less by 6·5 per cent. at the Arthur Road Hospital, although only half the patients received the serum treatment. If all the patients had received it, the reduction of the mortality would have to be calculated at 13 per cent. The difference between the mortality of the serum patients and the controls at the Arthur Road Hospital itself is 11·25 per cent., and, therefore, fairly conforms with the calculated difference of the mortality of both the hospitals. It is this conformity which gives the proof that the reduction of the death-rate on the serum side is real. It might be suggested that the mortality at the Arthur Road Hospital is generally lower than at the Maratha Hospital. Although there seems to be no apparent reason for this, the Maratha Hospital receiving the higher Hindu castes, we thought it useful to meet this suggestion with facts and figures. The Maratha Hospital opened on January 21st, 1898, as we find from Sir James Campbell's Report of 1897-1898. The plague mortality up to the 30th of April, 1898, amongst 738 patients under English treatment, was 73·44 per cent. During the same period, also including one month and a half of the serum treatment, which was commenced on the 13th March, the Arthur Road Hospital had 1,231 admissions with a mortality of 74·16 per cent. It had 273 admissions with 222 deaths, equal to a mortality of 81·31 per cent. in November and December, 1898, and January, 1899, when no serum was available. During these months the Maratha Hospital had 557 admissions with 453 deaths, equal to a mortality of 81·32 per cent. The mortality during the time when no serum was used was, therefore, somewhat higher at the Arthur Road Hospital.

It follows from the last table that the mortality amongst the serum patients was 68·33 per cent. and amongst the controls 79·58 per cent., the difference being 11·25 per cent. in favour of the serum. The alternate treatment was started under the impression that this difference would be the expression of the efficacy of the serum. We have been obliged to demonstrate that such might, or might not, be the case, and to undermine thus the very ground on which we were to base our arguments for the efficacy of the serum. Truly, not an enviable position in which we find ourselves. There is only one way out of this difficulty. The results obtained by the alternate treatment might be accepted as essentially correct if the three classes in which we have divided the patients with regard to the effects of the serum and non-serum treatment were evenly distributed on both sides. That cannot be ascertained directly, but we might find it out indirectly by going into the details of the distribution of the patients as regards caste, sex, age, individual resistance, duration, mode and virulence of infection. If the patients were fairly distributed according to these factors, we could be certain that the same was the case also with respect to three classes mentioned. We shall, therefore, compare in the following the details of the distribution one by one in the order given above, so far as it is statistically feasible. The material for the statistics is taken from the charts of temperature of our patients, which we have gone through carefully ourselves. We begin with the statistics of the distribution according to the caste :—

Race.	Hindus.	Mussalmans.	Native Christians	Parsees.	Total.
Serum patients	404	21	47	8	480
Control patients	405	27	40	8	480

No comments are necessary on this table. The same can be said of the following, showing how the patients were distributed according to the sex :—

Sex.	Males.	Females.	Total.
Serum patients	350	130	480
Control patients	353	127	480

The next table gives the distribution with regard to the age period :—

Age period.	0-10 years.	10-20 years.	20-30 years.	30-40 years.	40-50 years.	50 years and more.	Total.
Serum patients ...	50	129	162	81	37	21	480
Control patients ...	60	127	159	99	25	10	480

The distribution is here in favour of the controls which have 10 more children, among whom the mortality is about 12 per cent. lower than the average, and 23 fewer patients over 40 years, among whom the mortality is higher than the average.

The individual resistance is dependent on caste, sex, age, and previous immunisation. The benefit of the latter was identical, as on either side eleven patients had been inoculated with the plague prophylactic.

With regard to the day of illness on admission the patients were distributed as follows :—

Day of illness on admission.	1st day.	2nd day.	3rd day.	4th day.	5th day.	6th day.	7th day.	8th day	9th day.	10th day and more.	Unknown.	Total.
Serum patients ...	18	121	136	79	32	17	4	16	4	19	34	480
Control patients ...	20	120	100	67	38	25	13	20	4	26	47	480

The advantage lies here again with the controls. It is well known that the mortality from plague in our hospitals is highest amongst the admissions of the earlier days. A marked reduction of the mortality only takes place in the patients admitted after the fifth day of illness. If we divide the cases accordingly, we find on the serum side 386 patients of the first 5 days of illness with a mortality of 71·76 per cent., and on the control side 345 such patients with a mortality of 86·08 per cent. The patients of the sixth and the following days of illness are 60 on the serum side, with a mortality of 45·00 per cent. and 88 on the control side, with a mortality of 51·13 per cent. The serum side had thus 41 more patients who had under the ordinary treatment a mortality of 86·08 per cent. and 28 fewer patients who had a mortality of 51·13 per cent. These facts represent a material advantage for the controls, and they demonstrate at the same time that Dr. Choksy estimated correctly the number of convalescent patients on both sides. We see, moreover, that the reduction of the mortality due to the serum was almost entirely obtained in the patients in the acute stage of the disease.

We come now to compare the distribution according to the manifestation of the disease which indicates to some extent the mode and virulence of the infection. For statistical purposes, the manifestations of the disease have been brought in such groups as show generally a distinct difference of the mortality between each other, the single femoral or inguinal, or other single buboes of more rare occurrence with the lowest mortality heading the columns in the following table. Contiguous buboes are such as femoral and inguinal, femoral and iliac, etc. Only the buboes present on admission were taken in consideration :—

Manifestation of disease.	Single inguinal, femoral buboes.	Single Cervical buboes.	Single Axillary buboes.	Contiguous buboes.	Multiple buboes.	No buboes.	Pneumonia.	Total.
Serum patients ...	170	52	88	131	32	3	4	480
Control patients ...	157	46	100	128	20	16	13	480

The advantage is here on the serum side, which has 13 more cases of single inguinal or femoral buboes, showing the lowest mortality, and 34 fewer cases with axillary buboes, without buboes or with pneumonia, which have the highest mortality. Also, without calculating numerically the statistical value of this advantage, this much can be said with certainty that it cannot have preponderated over the benefit the controls derived from the distribution according to the days of illness where every second patient of the later days represented a recovery.

The following table gives the distribution according to the temperature on admission ; for a fraction of a degree the next lower degree has been recorded.

Temperature on admission	100° F.	101° F.	102° F.	103° F	104° F.	105° F. and more.	Total.
Serum patients	141	79	97	88	54	21	480
Control patients... ...	127	78	112	95	47	21	480

The temperature on admission gives little information as to the severity of the attack, high temperatures being frequently due to the excitement of the transport, whereas low ones in the acute stage of plague are often signs of collapse and impending death. All we can guess from the table is that there are no differences worth mentioning.

There are no more items allowing of a statistical comparison and we can review the facts as follows. The distribution, according to the caste, sex, previous immunisation, and temperature on admission, was practically the

same for both sides. With regard to the age period and the days of illness on admission the distribution has favoured the controls, and with respect to the manifestation of the disease the serum treatment. There is no aim in urging that clinically the advantages on the control side were more important, and we are satisfied if it be admitted that the distribution was *not in favour of the serum.*

Now we can accept the results at the Arthur Road Hospital as correct without fear of being contradicted by anyone whose syllogisms are directed by the principles of logic, and we can say that cures have been effected by the serum treatment which could not have been effected by any other known means. Compared with that fundamental fact the percentage of the cures is of minor importance, as it is a variable quantity which can change only in one direction—in the direction of progress. The treatment of plague with Professor Lustig's serum has thus passed once for all the stage of experiment : its efficacy has become an established fact, against which scepticism would no longer be legitimate.

Hence the serum treatment of plague will be an acknowledged implement in the armoury of the physician, restoring life and health to many, and will rank side by side with that of diphtheria as a great achievement which represents a further and important step towards the solution of the problems of serotherapeutics, it being the second instance in which indisputable evidence has been brought forward for the efficacy of serotherapy in human beings.

Having demonstrated the efficacy of the serum, we shall analyse the results obtained in order to solve a question of practical importance, *viz.*, under what circumstances the serum was most efficacious. From *a priori* considerations we have to expect that the mortality under the serum treatment followed on a lower level closely the fluctuations of the general mortality from plague. Indeed, should we not find any indication of this principle in the course of our investigations, we could even doubt the proofs furnished hitherto. On the other hand, we cannot exclude that there might be considerable deviations from that rule, due to the peculiarity of the remedy or the disease, or to other influences which it would be necessary to trace. If we find such deviations, we shall have to ascertain whether they were accidental or the expression of a law governing the application of the serum. In order to answer our query we shall resort again to the statistics. With regard to them we have to remember that the information we may get might not always be of an absolute but only of a comparative value, or even valueless owing to the small number of observations on which the statistics might be based in single instances. In such a case we might be obliged to control our statistics by those drawn from larger figures. On the whole, we shall find that the results on the serum side are more congruous with those of the general statistics, as the action of the serum and the larger number of recoveries tended to neutralise disturbing influences, of which the distribution of the convalescents was the most important one on the control side. We shall

go through our statistics in the same order as before and begin with that showing the results according to the caste :—

Race.	Serum Patients.				Control Patients			
	Number of patients.	Died	Recovered.	Percentage of mortality.	Number of patients.	Died.	Recovered.	Percentage of mortality.
Hindus	404	282	122	69·80	405	326	79	80·49
Mussalmans	21	14	7	66·66	27	20	7	74·07
Native Christians ...	47	26	21	55·32	40	29	11	72·5
Parsees	8	6	2	75·00	8	7	1	87·5
Total ...	480	328	152	68·33	480	382	98	79·58

The results shown in this table fulfil our expectations, the mortality of the serum patients repeating the fluctuations on the other side. We note here that the reduction of the average mortality of the controls by 7 per cent. in the case of Native Christians corresponds to a reduction of 24 per cent. on the serum side.

The next table gives the results according to the caste and sex :—

Race and Sex.	Serum Patients.				Control Patients.			
	Number of patients.		Recovered.	Percentage of mortality	Number of patients.	Died.	Recovered.	Percentage of mortality.
Hindus.								
Males	291	207	84	71·13	293	236	57	80·54
Females	113	75	38	66·37	112	90	22	80·35
Mussalmans.								
Males	18	13	5	72·22	22	16	6	72·72
Females	3	1	2	33·33	5	4	1	80·00
Native Christians.								
Males	37	19	18	51·35	33	22	11	66·66
Females	10	7	3	70·00	7	7	...	100·00
Parsees.								
Males	4	2	2	50·00	5	5	...	100·00
Females	4	4	...	100·00	3	2	1	66·66
Total ...	480	328	152	68·33	480	382	98	79·58

Considering only the larger figures we see that Hindu males have the highest mortality on both sides. Contrary to the facts of the general statistics, which show that Hindu females have a distinctly lower mortality than Hindu males, there is hardly any reduction in Hindu females on the control side. It is otherwise under the serum treatment. Already, during the time of the selection of the patients, it was observed that females answer better to the serum treatment than males. In the cases of Native Christians it is interesting that the chief reduction of the mortality shows itself on both sides in males. This is correct, Native Christian males having generally a much lower death-rate than females.

The results, according to the age period, are seen from the following table :—

Age period.	Serum Patients.				Control Patients.			
	Number of Patients.	Died.	Recovered.	Percentage of Mortality.	Number of Patients.	Died.	Recovered.	Percentage of Mortality.
From 0-10 years ...	50	25	25	50·00	60	40	20	66·66
,, 10-20 ,, ...	129	90	39	69·76	127	95	32	74·80
,, 20-30 ,, ...	162	105	57	64·81	159	135	24	84·90
,, 30-40 ,, ...	81	62	19	76·54	99	84	15	84·84
,, 40-50 ,, ...	37	28	9	75·67	25	22	3	88·00
,, 50-60 ,, and more ...	21	18	3	85·71	10	6	4	60·00
Total...	480	328	132	68·33	480	382	98	79·58

Children had also during the time of the selection a mortality of 50 per cent. They give the best results under the serum treatment. That the mortality from plague is generally lower among children than in adults is noteworthy, as in other infectious diseases the full-grown individuals are more resistant. The two following periods show, especially on the control side, differences of the mortality which are not to be found in large statistics, from which we learn that the mortality is much the same for both the periods and scarcely lower than the average. This discrepancy might be partly accidental and in part due to the inaccuracy of the patients in stating their age. The later periods show an increased mortality in the right proportion.

Concerning the patients who were prophylactically injected, it will be sufficient to say that 7 such patients recovered on the serum side and 6 amongst the controls.

We pass now on to the table showing the results according to the days of illness on admission :—

Day of illness on admission.	Serum Patients.				Control Patients.			
	Number of Patients.	Died.	Recovered.	Percentage of mortality.	Number of Patients.	Died.	Recovered.	Percentage of mortality.
1st day	18	11	7	61·11	20	18	2	90·00
2nd ,, ...	121	95	26	78·51	120	103	17	85·83
3rd ,, ...	136	96	40	70·58	100	84	16	84·00
4th ,, ...	79	55	24	69·62	67	57	10	85·07
5th ,, ...	32	20	12	62·50	38	35	3	92·10
6th ,, ...	17	13	4	76·47	25	17	8	68·00
7th ,, ...	4	2	2	50·00	13	7	6	53·84
8th ,, ...	16	6	10	37·50	20	11	9	55·00
9th ,, ...	4	1	3	25·00	4	1	3	25·00
10th ,, ...	19	5	14	26·31	26	9	17	34·51
Unknown	34	24	10	70·58	47	40	7	85·10
Total ...	480	328	152	68·33	480	382	98	79·58

The figures in this table have only a relative value as they are chiefly based on the statements of the patients or their friends. In general, we may say that they are more reliable for the earlier days, and that the duration of illness is, if anything, given as too short. Only four per cent. of all the patients were admitted on the first day, and only two amongst twenty recovered on the control side. The statistics corroborate thus the clinical observation that only the severest cases are brought to the hospital on the first day. Still the mortality on the serum side is well below the average. It rises by 17 per cent. for the patients admitted on the second day. Then a marked falling-off for those of the third day, and a steady decline for the patients of the following days. The mortality amongst the controls is practically the same on the first 5 days of illness, the excessive mortality on the first and fifth day being accidental. We have to record here an essential difference of the results. The curve of mortality of the patients admitted on the first 5 days forms an angle on the serum side and is a straight line on the control side. It was irrelevant for the controls on what day they came to the hospital, whereas it made a considerable difference whether a patient received the serum treatment on the first day or on the second day. So long as the necessity of the early treatment is not fully appreciated and acted upon by the public and the medical profession, the results of the serum treatment will never be as satisfactory as they could be. A famous surgeon was wont to tell his pupils that if they be called to an incarcerated hernia in day-time they should not allow the sun to set, and if at night not allow the sun to rise, without having liberated it. *Mutatis mutandis* that must be the principle of the physician in the serum treatment of plague. *One hour lost might be a life lost.*

The next table gives the results according to the manifestation of the disease :—

Manifestation of Disease.	Serum Patients				Control Patients.			
	Number of Patients.	Died.	Recovered	Percentage of mortality.	Number of Patients.	Died.	Recovered.	Percentage of mortality
Single inguinal, femoral, &c., buboes ...	170	97	73	57·05	157	122	35	77·70
Single Cervical buboes	52	38	14	73·07	46	33	13	71·73
Single Axillary buboes	88	64	24	72·72	100	88	12	88·00
Contiguous buboes ...	131	102	29	77·86	128	99	29	77·34
Multiple buboes ...	32	21	11	65·62	20	12	8	60·00
No buboes ...	3	2	1	66·66	16	16	...	100·00
Pneumonia ...	4	4	...	100·00	13	12	1	92·30
Total ...	480	328	152	68·33	480	382	98	79·58

We note here the considerable reduction of the mortality effected by the serum in single femoral or inguinal buboes, and also in axillary buboes. It can be seen from the list of the recovered patients that this reduction was not due to the distribution of the convalescents, which has materially interfered with the correctness of the results in cervical and multiple buboes. Here again the serum has singled out for its action certain patients, *viz.*, those in whom the disease was localised.

The statistics of the results, according to the temperature on admission, did not promise much information, and we have substituted a table demonstrating not the saving of life, but the prolongation of life :—

Died after admission.	Within 12 hours.	Within 24 hours.	Within 48 hours.	Later on.
Serum patients	12·50%	8·95%	18·33%	28·54%
Control patients	16·87%	12·50%	20·65%	29·58%

The influence of the serum made itself felt even in patients who in the common course died within 12 hours after admission. Comparing the percentage of the total deaths within 48 hours after admission, we have 191 patients, or 39·79 per cent., dying under the serum treatment, and 240, or 50 per cent., amongst the controls, this being the usual percentage of deaths within 48 hours after admission occurring in our plague hospitals. In 20 per cent., therefore, of those who would have died within 48 hours after ad-

mission life has been prolonged by the serum treatment. The serum patients lived on an average 4·3 days and the controls 3·2 days. That will reassure those who might still be afraid that in certain cases the serum might be injurious. Careful observation on nearly 1,000 patients has shown that it never does harm, either to moribunds or others.

There are no more statistics available, and we can summarise the information we have gained as follows:—

In general, our anticipations have been justified: the mortality under the serum treatment following the fluctuations of the death-rate on the control side closely on a lower level save for being disproportionately lower in —

(1) Patients of the 1st, 3rd, 4th, and 5th day of illness.

This is in accordance with the first law of serotherapeutics: that the earlier the treatment the better the results. It is no contradiction that the patients of the third and the following days had a lower mortality than those of the second day. A similar observation was made in the selected patients, and it has been commented upon in our previous report to which we refer. The plague, as already stated by the German Plague Commission, is characterised by subsequent attacks of a few days' duration, the first attack being the most fatal.

(2) Native Christians.

(3) Hindu females.

(4) Children.

(5) Patients with single buboes.

The disproportionate reduction in these four classes, which have also under the ordinary treatment a lower mortality than the average, corresponds to another law of serotherapy, which we might formulate thus: "Under those conditions where the average mortality from an infectious disease decreases naturally, the decrease under the influence of a serum treatment takes place in a much higher ratio". Thus a serum of a given strength, which would reduce an average mortality of 80 per cent. to 70 per cent., would not give the same difference of the percentages, or the same proportion of the reduction, if the average mortality were 70 per cent. to begin with. A mortality of 70 per cent. might be reduced to 50 per cent. and less. That is, in the last instance, due to the fact that the germs of an infectious disease multiply in geometrical progression, and that the serum becomes more effective in the same ratio as the germs become less in numbers. Following

on this law, we understand not only the deviations in our statistics, but also why the serum treatment gave so much better results in 1897, when the mortality was considerably lower, than it has been in the following years. We understand also the exceedingly favourable reports which came from places where the mortality from plague was much lower than it is in Bombay. A lower mortality means a less virulent infection; a less virulent infection a less rapid course of the disease, viz., a longer interval between the infection and the fatal issue and an enhanced possibility of timely intervention. Here the two laws of serotherapeutics meet; they are indeed one; and we are at the old argument again—*ceterum censeo curam non esse differendam.*

The deviations we have found in the statistics are not striking, and cannot be so, considering that the mortality was 80 per cent. and the reduction 11 per cent. Each one of them could well be accidental. But what cannot be accidental, what excludes every possibility of an error, is their concurrence, their harmony with the laws of serotherapy and with the clinical observations. With regard to the latter we can say that they are fully borne out by the statistics. We point in this relation to the statements made in last year's report, viz., that the serum gives the best results in children, in patients with simple bubonic plague, that it is effective also on the fourth and fifth day of illness, that the buboes reabsorb oftener, and that life is prolonged. The analysis of the results obtained has thus not only answered our query when the serum is most efficacious: it has also furnished another and most convincing proof for the efficacy of the serum. Whereas the conditions of the patients were originally the same on both sides, the results were different, on the whole, and in the details, and the differences were not irregular but governed by a law, and must logically be ascribed to the one new factor that was intentionally introduced on the one side, viz., to the serum treatment.

Practically, the outcome of the analysis is important in two directions. It is obvious that a Hindu male with contiguous buboes, all other conditions equal, will have a worse prognosis and will require larger doses than a Native Christian male with a single inguinal bubo.

There is nothing more to be said about the alternate treatment, and we have only to mention that four selected cases were treated with the serum in June, 1899, at the Arthur Road Hospital and had one recovery, whereas the 14 remaining patients had two recoveries.

We turn now to the Modikhana Hospital, where in February last an attempt was made to treat patients alternately with the serum. Owing to the pressure of work and the great distance of the hospital from the laboratory at Parel, the undersigned were unable to visit it in order to control the carrying-out of the experiments, which was entirely left to the Medical Officer

in charge, who had received the necessary instructions. The results are seen from the following table :—

Modikhana Hospital 26th January to 27th February 1900.	Number of Patients.	Died.	Recovered.	Percentage of mortality.
Serum patients	66	54	12	81·81
Control patients	66	48	18	72·72
Doubtful cases	43	32	11	74·41

Although the failure of the serum treatment might have been merely due to the distribution of the patients, it seemed strange, and stranger still, the large number of doubtful cases.

A minute investigation elicited the following facts :—

(1) That 21 of the so-called doubtful cases were undoubted cases of bubonic plague, with buboes either on admission or developing buboes in the hospital, and that the greater part of the others were either suffering from plague pneumonia or showed other undoubted symptoms of plague. These cases were, for various reasons, some through inadvertence, excluded from the alternate treatment.

(2) That the serum treatment was neither always begun in proper time nor continued regularly.

(3) That the doses were insufficient, the average quantity of serum used for a patient having been 55 c.c. against 100 c.c., as given in the instructions.

(4) That the total quantity of serum put down as having been injected was in excess of that actually supplied to the hospital.

It appeared, therefore, that the alternation was frequently and arbitrarily interfered with at the Modikhana Hospital; that the serum was administered in a manner and in doses by which curative results could not be expected ; and that the registration of important items was defective. The proofs for these facts and the conclusions drawn from the facts were submitted to Lieutenant-Colonel J. S. Wilkins, Special Medical Officer, Plague Operations, who, after examination, concurred in the opinion that the experiments as conducted at the Modikhana Hospital were valueless and not to be included in the statistics of the alternate treatment.

Six patients were treated with the serum at the Parsee Fever Hospital by Dr. S. Nariman, the Medical Officer in charge of it, two of whom recovered. Eight patients, treated during the same period without serum, had also

two recoveries. Dr. S. Nariman stated that all the cases were equally severe, and added that from the few observations he can infer with certainty that the serum treatment prolongs life.

Ten patients were treated in private practice and had four recoveries. Except one, the cases were all of the third or fourth day of illness and all were very severe.

After having rendered a full account of the patients treated during the last official year, we shall bring in conclusion the statistics of the serum treatment since March, 1898, except those of the Modikhana Hospital, and also other records necessary for comparison.

Period.	Hospitals and private practice.	Treatment.	Number of patients.	Died.	Recovered.	Percentage of mortality.
March 1898 to 31st of October 1898 and 1st Feby. to 30th April 1899.	Arthur Road Hospital.	Serum treatment, selected patients.	380	234	146	61·57
		Ordinary treatment, remaining patients	1,167	942	225	80·71
	Maratha Hospital	Ordinary treatment	3,257	2,636	621	80·93
1st of November 1898 to 31st of January 1899	Arthur Road Hospital.	Ordinary treatment, no serum available.	273	222	51	81·31
	Maratha Hospital.	Ordinary treatment	557	453	104	81·32
1st of May 1899 to 30th of June 1900 (June 1899 excluded).	Arthur Road Hospital.	Alternate treatment serum patients.	480	328	152	68·33
		Alternate treatment control patients.	480	382	98	79·58
1st of May 1899 to 31st of May 1900 (June 1899 excluded).	Maratha Hospital.	Ordinary treatment	2,599	2,154	495	80·90
13th of March 1898 to 30th of June 1900.	Different Hospitals	Serum treatment, partly selected patients.	50	33	17	66·00
	Private Practice.	Serum treatment, not selected patients.	42	19	23	45·23

From the table it appears that on the whole 952 patients were treated with the serum, and that the results have been uniformly in its favour. If we compare those during the periods of the selection and alternation, we find a difference of 7 per cent. Does that prove a diminished efficacy in the second instance? Not necessarily so. No direct comparison between the results is possible. The mortality in the alternately-treated cases is the average mortality which may be obtained by the serum treatment, whereas that in the selected cases is a minimum mortality. A comparison is only possible between the total mortality of the hospital during the periods of the selection and alternation. This comparison shows that the total mortality of the hospital was 1·36 per cent. lower during the second period. From this and from the small difference between the mortality in the selected cases and in those alternately treated, and from the clinical observation, we are convinced that the treatment as practised during the period of the selection would not have given a reduction of 11·25 per cent. if the cases had been treated alternately. This is not due to an improved manufacture, but to the progress made in the administration of the serum. The possibilities in this direction, apart from the intravenous injections, are by no means exhausted. We admit that partly out of imposed economy the doses have not been pushed for some time past as far as might have been done with advantage, as further experience has taught us. It is certain that with larger doses more cures could have been effected. Moreover, the serum was usually injected in repeated small doses, whereas in all probability one large dose would have been more effective. It might turn out that the first dose, necessarily a large one, decides the question of life or death, and that the subsequent doses are of little value. But experience, where human life is concerned, is not gained so quickly as in the laboratory. Still, the increase of the doses can only be a stopgap until improvement is made in the manufacture of the serum, which must be the task of the future. That the task is not an impossible one probably nobody doubts. What we may hope for from an improved manufacture and application of the serum has already been alluded to in our previous report. The results in private practice will depend on the promptness with which the public and the practitioners will avail themselves of the remedy. The chief responsibility rests with the latter, who must be quick with the diagnosis and therapy. The germs of the disease double their number in half-an-hour; there is not a minute to be wasted. Better to inject 100 patients erroneously, who are not sick with plague, than to miss the injection in one who is suffering from it. Unfortunately the probability of a faulty diagnosis is infinitesimal. *In time of an epidemic every swollen and tender gland which cannot be accounted for by other obvious causes must be looked upon as a manifestation of the plague.* The same axiom holds good during epidemics generally with regard to the characteristic symptom of an infection; why, therefore, should it be otherwise in the case of plague? To delay the treatment until the case turns out to be severe would be even worse than to lose time with the diagnosis. When a man is

struggling with the waves, who would wait in going to the rescue until he is sinking ? In our hospitals, where 50 per cent. of the patients die within 48 hours after admission, the limit of our expectations is more restricted than in private practice.

Notwithstanding the lesson of modesty the plague has taught us with regard to " stamping it out " by sanitary measures, there may still be some who are as yet unwilling to draw the obvious inference also with respect to the curative efforts, and who view with scanty satisfaction the promise we are holding out and esteem slightly the results we offer. Only 11 per cent. ! Could it be that such contempt is prompted by the comparison with the results obtained by the serum treatment in other diseases ? There is only one disease in which the efficacy of serotherapy has remained undisputed although it has been claimed for many. What then are the results in diphtheria ? We have at hand the latest statistics of the Metropolitan Asylums Board, based on many thousands of observations, which give the mortality from diphtheria at 30 per cent. previous to the serum treatment and at 18 per cent. after its introduction. Only 12 per cent. ! And to obtain this the most eminent scientists have been working in the best-equipped laboratories for nearly a decade. Yet the results are considered as highly satisfactory, and the serum has become a remedy the public and the physician would be loath to be without. The percentage of the cures is the same in diphtheria and plague, but what a difference of the conditions under which it has been obtained ! There the accumulated experience of the whole scientific world, unlimited means, selected horses, selected serum, the public fully aware that time is life, the patients with healthy organs, the disease of relatively slow course, and with a mortality of only 30 per cent. ! Against it here, manufacture and treatment on their trial, the horses selected with regard to their cost, the serum used regardless of its strength, the patients of the lowest classes in an advanced stage of the disease, their vital power undermined by previous or concurring illness, the disease of a fatal rapidity, and with a mortality of 80 per cent. Truly, it is the case of two vessels : the one steaming in smooth waters and with a favourable breeze, and the other against a hurricane and heavy seas, yet both make the same headway ; but can there be any doubt which one has the more powerful en gines ? We see we are wrong. It cannot be the comparison with the results in other diseases that makes our 11 per cent. not acceptable. Then perhaps the costs are out of proportion to the gain ? Although to the humanitarian such a consideration might be repulsive, we cannot overlook the fact that in practice this must carry weight, and we think it not without advantage to discuss the matter from this point of view.

With the manufacture of the serum, as with any other manufacture, the cost decreases when the output rises. The cost of the experiments were necessarily disproportionately larger than the manufacture on an adequate

scale would be. Moreover, the cost could be considerably reduced if only suitable patients be treated and a charge be made for the serum in those cases where the patients can afford it. We think the last point of importance also, because the charge would do away with the impression that the serum is still on its trial. Provided the above conditions be fulfilled, the costs of the manufacture of the serum will not be out of proportion to the gain, and we can safely say that the results of the serum treatment of plague, as they are at present, will be acceptable also from a pecuniary standpoint."

List of the Serum Patients who Recovered.

Current Number.	Hospital Number.	Caste.	Sex.	Age.	Days of Illness on admission.	Manifestation of Disease.	Highest Temperature.	Bubo suppurated.	Number of Injections.	Quantity of Serum injected.	Remarks.
1	1608	Hindu ...	Male ...	35 years	4	Femoral bubo	102°	1	5	60 c. c.	
2	1617	Do. ...	Do. ...	6 do.	5	Axillary do.	102°	.....	4	30 c. c.	
3	1619	Do. ...	Female.	28 do.	4	Inguinal do.	103°	.....	4	50 c. c.	
4	1627	Do. ...	Male ...	22 do.	4	Femoral do.	100°	.....	1	10 c. c.	
5	1660	Do. ...	Do. ...	20 do.	8	Axillary do.	103°	1	3	55 c. c.	
6	1666	Do. ...	Female.	6 do.	5	Inguinal do.	101°	.....	2	20 c. c.	
7	1688	Do. ...	Do. ...	30 do.	2	Cervical do.	105°	.....	3	60 c. c	
8	1744	Do. ...	Male ...	14 do.	4	Femoral do	104°	.....	2	35 c. c.	
9	1825	Do. ...	Female.	13 do.	4	Axillary do.	103°	1	10	140 c. c.	
10	1829	Do. ...	Do. ...	8 do.	4	Inguinal do.	105°	.....	4	45 c. c.	
11	1843	N. Christian	Male ...	12 do.	2	Do. and Iliac bubo	102°	.....	6	72 c. c.	
12	1824	Hindu ...	Do. ...	30 do.	3	No bubo	103°	.....	8	145 c. c.	
13	1868	Do. ...	Do. ...	3 do.	5	Femoral bubo	103°	.....	8	40 c. c.	
14	1880	Do. ...	Female.	35 do.	2	Do. do.	105°	.....	7	210 c. c.	
15	1891	N. Christian	Male ...	10 do.	1	Do. and Inguinal bubo ...	100°	.....	1	10 c. c.	Twice Haffkinised.
16	1912	Hindu ...	Do. ...	25 do.	3	Parotid and Axillary do. ...	104°	.....	4	140 c. c.	
17	1959	Do. ...	Female.	7 do.	2	Axillary bubo	102°	.....	6	30 c. c.	
18	1988	Parsee ...	Male ...	19 do.	2	Femoral do.	104°	1	8	280 c. c.	
19	1997	Mussalman.	Do. ...	50 do.	12	Do. do.	100°	.....	1	10 c. c.	Convalescent.
20	2040	Hindu ...	Do. ...	20 do.	3	Do. do.	102°	.....	7	200 c. c.	
21	2042	Do. ...	Do. ...	20 do.	6	Inguinal and Iliac bubo	103°	1	7	190 c. c.	
22	2045	Do. ...	Female.	30 do.	3	Axillary bubo	104°	.....	6	230 c. c.	
23	2083	Parsee ...	Male ...	32 do.	4	Femoral and Inguinal bubo ...	101°	.....	2	50 c. c.	Haffkinised.
24	2081	Hindu ...	Female.	10 do.	4	Do. and Iliac bubo	101°	.....	3	80 c. c.	
25	2105	N. Christian	Male ...	30 do.	3	Axillary and Cervical bubo ...	103°	.....	4	90 c. c.	
26	2126	Hindu ...	Do. ...	25 do.	2	Femoral bubo	105°	.....	7	180 c. c.	
27	2135	Do. ...	Do. ...	30 do.	11	Inguinal do.	100°	1	2	20 c. c.	Convalescent.
28	2142	Do. ...	Do. ...	25 do.	4	Do. do.	101°	.....	1	10 c. c.	
29	2196	Do. ...	Female.	45 do.	5	Femoral do.	103°	1	7	150 c. c.	
30	2209	Do. ...	Male ...	40 do.	Unknown.	Do. do.	102°	.....	6	140 c. c.	

List of the Serum Patients who Recovered—contd.

Current Number.	Hospital Number.	Caste.	Sex.	Age.	Days of Illness on admission.	Manifestation of Disease.	Highest Temperature.	Bubo suppurated.	Number of Injections.	Quantity of serum injected.	Remarks.
31	2250	Hindu ...	Male ...	50 years	6	Inguinal do.	100°	1	2	30 c. c.	
32	2253	Do. ...	Do. ...	22 do.	3	Femoral do.	103°	.....	4	95 c c	
33	2297	Mussalman..	Do. ...	12 do.	1	Inguinal, Femoral and Iliac bubo ...	102°	.. ...	6	80 c. c.	
34	2323	Hindu ...	Female.	18 do	4	Femoral bubo	104°	1	6	110 c. c.	
35	2339	N. Christian	Male ...	20 do.	3	Do. do.	104°	1	7	180 c. c.	
36	2356	Hindu ...	Do. ...	12 do.	5	Axillary do.	102°	1	6	75 c. c.	
37	2386	Do. ...	Do. ...	28 do,	15	Do. do.	99°	.....	1	10 c. c	Convalescent.
38	2474	Do. ...	Do. ...	35 do.	5	Femoral, Inguinal and Iliac bubo ...	103°	1	5	110 c. c.	
39	2614	Do. ...	Do. ...	13 do.	4	Do. bubo	103°	1	2	20 c. c	
40	2654	Mussalman..	Female.	10 do.	10	Inguinal do.	98°	1	1	10 c. c	Convalescent.
41	2664	N. Christian	Male ...	12 do.	3	Cervical do.	104°	.....	3	35 c. c.	
42	2679	Hindu ...	Do. ...	28 do.	8	Femoral and Axillary bubo ...	101	1	2	20 c. c.	Convalescent.
43	2698	Do. ...	Do. ...	30 do	10	Do. Inguinal and Iliac bubo ...	101°	1	1	10 c. c.	Do.
44	2714	N. Christian	Do. ...	22 do.	2	Do. bubo	103°	1	8	165 c. c.	
45	2724	Do. ...	Do. ...	12 do.	2	Iliac do.	104°	.....	11	110 c. c.	
46	2733	Hindu ...	Do. ...	10 do.	3	Inguinal do.	103°	1	8	85 c. c.	
47	2777	Do. ...	Do. ...	60 do.	4	Double Axillary bubo	102°	.....	5	80 c. c	
48	2814	Do. ...	Do. ...	3 do.	2	Femoral bubo	102°	1	6	50 c. c.	
49	16	Do. ...	Female.	25 do.	3	Axillary do.	104°	.....	9	170 c. c.	
50	50	Do. ...	Male ...	50 do	5	Inguinal do.	104°	1	7	130 c. c.	
51	74	Do. ...	Do. ...	25 do.	4	Femoral and Inguinal bubo ...	104°	1	8	150 c. c.	
52	106	Do. ...	Do. ...	30 do.	Unknown	Cervical and do. do. ...	98°	.....	2	20 c. c.	Convalescent.
53	204	Do. ...	Do. ...	10 do	9	Inguinal bubo	101°	1	1	10 c. c.	Do.
54	223	Do. ...	Female.	15 do.	10	Femoral do.	100°	1	1	10 c. c.	Do.
55	264	Do. ...	Male ...	30 do.	4	Supra trochl bubo	101°	.....	1	15 c. c.	
56	314	Do. ...	Female.	10 do	3	Double Axillary bubo	101°	.....	6	82 c. c.	
57	354	N. Christian	Male ...	20 do	2	Do. Femoral do.	102°	.....	3	50 c. c.	
58	383	Hindu ...	Female	22 do.	3	Iliac bubo	104°	.....	9	160 c. c.	
59	398	Do. ...	Do. ...	70 do.	11	Cervical bubo	100°	1	1	5 c. c	Convalesce
60	426	Do. ...	Male ...	45 do.	4	Inguinal do.	105°	.....	6	110 c. c.	

61	442	Do. ...	Female.	25	do.	2	Axillary do.	105°	1	15	300 c. c.		
62	447	Do. ...	Male ...	32	do.	2	Do. do.	102°	.....	9	160 c. c.		
63	454	Do. ...	Female.	12	do.	3	Inguinal do.	102°	.....	5	55 c. c.		
64	464	Do. ...	Do. ...	20	do.	9	Femoral do.	100°	.....	1	10 c. c.	Convalescent.	
65	515	N. Christian	Male ...	30	do.	3	Axillary do.	102°	.....	7	120 c. c.		
66	576	Hindu ...	Do. ...	8	do.	3	Double Inguinal bubo	102°	1	6	80 c. c.		
67	602	Do. ...	Female	40	do.	5	Femoral bubo	102°	.....	6	90 c. c.		
68	618	Do. ...	Male ...		do.	6	Cervical do.	103°	.....	4	60 c. c.		
69	686	Do. ...	Do. ...	25	do.	2	Femoral do	103°	.....	10	200 c. c.		
70	752	Do. ...	Do. ...	25	do.	3	Do. do.	104°	.....	9	200 c. c.		
71	772	Do. ...	Female.	2	do.	2	Sub-Lingual bubo	103°	.....	6	50 c. c.		
72	792	Do. ...	Do. ...	30	do.	8	Pectoral bubo	98°	.....	1	10 c. c	Convalescent.	
73	845	Do. ...	Male ...	35	do.	4	Femoral do.	102°	.....	7	120 c. c.		
74	817	Do. ...	Female.	25	do.	1	Do. do.	103°	.....	2	60 c. c.		
75	869	Do. ...	Male ...	49	do.	8	Do and Inguinal bubo ...	100°	1	1	10 c c.	Convalescent.	
76	896	Do. ...	Do. ...	26	do.	8	Inguinal	99°	1	1	5 c. c	Do.	
77	929	Do. ...	Do ...	30	do.	15	Do. and Femoral bubo ...	98°	1	1	5 c. c.	Do.	
78	977	Do. ...	Female.	4	do.	8	Femoral bubo	97°	.....	1	5 c. c.	Do. Haffkinised	
79	883	N. Christian	Male ...	21	do.	7	Inguinal do.	100°	1	3	25 c. c		
80	991	Hindu ...	Do. ...	32	do.	5	Femoral and Inguinal bubo ...	103°	1	6	125 c. c.		
81	1055	Do. ...	Do. ...	25	do.	3	Inguinal bubo	102°	1	6	115 c. c		
82	1097	Do. ...	Do. ...	14	do.	8	Cervical do.	99°	1	1	10 c. c.	Convalescent.	
83	1118	Mussalman	Do. ...	10	do.	3	Axillary do.	104°	1	6	100 c. c.		
84	1131	Hindu ...	Do. ...	30	do.	8	Femoral, Inguinal and Iliac bubo ...	100°	1	1	10 c. c.	Convalescent.	
85	1163	N. Christian	Do. ...	19	do.	15	Inguinal bubo	100°	1	1	10 c. c.	Do.	
86	1172	Hindu ...	Female.	14	do.	3	Cervical do.	100°	1	4	70 c. c.		
87	1194	Do. ...	Male ...	15	do.	5	Axillary do.	103°	1	7	115 c. c.		
88	1237	Do. ...	Do. ...	35	do.	4	Do. do.	100°	.....	2	50 c. c.	Haffkinised.	
89	1252	Do. ...	Do. ...	25	do.	5	Femoral and Iliac bubo	100°	.....	4	75 c. c.		
90	1267	Do. ...	Female.	8	do.	2	Cervical bubo	103°	.....	4	50 c. c.		
91	1289	Do. ...	Male ...	24	do.	3	Femoral, Inguinal and Iliac bubo ...	104°	1	8	175 c. c.		
92	1295	Do. ...	Do. ...	25	do.	3	Axillary bubo	105°	.....	8	145 c. c.		
93	1311	Do. ...	Do. ...	28	do.	3	Supra Clavicular bubo	101°	1	7	135 c. c.		
94	1315	Do. ...	Do. ...	28	do.	1	Cervical bubo	104°	.....	6	85 c. c.		
95	1321	Do. ...	Do. ...	5	do.	2	Do. do.	99°	.....	3	20 c. c.	Convalescent.	
96	1330	Do. ...	Do. ...	30	do.	3	Femoral do.	102°	.....	4	60 c c.		
97	1332	N. Christian	Do. ...	20	do.	1	Inguinal do.	100°	.....	4	60 c. c.		
98	1336	Hindu ...	Do. ...	30	do.	1	Axillary do.	104°	1	8	140 c. c.		
99	1338	Do. ..	Female	23	do.	2	Inguinal and Iliac bubo	105°	1	6	110 c. c.		
100	1358	N. Christian	Do. ...	18	do.	2	Double Axillary bubo	101°	.....	6	96 c. c.		

List of Serum Patients who Recovered—contd.

Current Number.	Hospital Number.	Caste.	Sex.	Age.	Days of Illness on admission.	Manifestation of Disease.	Highest Temperature.	Bubo suppurated.	Number of Injections.	Quantity of serum injected.	Remarks.
101	1361	Hindu. ...	Female.	55 years	2	Iliac bubo	104°	.....	7	115 c. c.	
102	1384	N. Christian	Male ...	25 do.	2	Inguinal bubo	105°	1	11	210 c. c.	
103	1385	Hindu. ...	Do. ...	8 do.	2	Cervical do.	101°	1	6	60 c. c.	
104	1404	Do. ...	Do. ...	25 do.	4	Axillary do.	103°	.....	6	120 c. c.	
105	1443	Do. ...	Do. ...	40 do.	9	Femoral do.	101°	.....	2	20 c. c.	Convalescent.
106	1452	Do. ...	Male ...	20 do.	12	Do. do.	98°	.....	1	10 c. c.	Do.
107	1456	N. Christian	Female	20 do.	3	Axillary do	102°	.....	6	140 c. c.	
108	1460	Hindu. ...	Male ...	23 do.	Unknown	Inguinal do.	104°	.....	7	140 c. c.	
109	1464	N. Christian	Do. ...	18 do.	3	Femoral do.	105°	1	10	230 c. c.	Haffkinised.
110	1468	Hindu. ...	Do. ...	32 do.	4	Inguinal do.	104°	.....	8	190 c. c.	
111	1474	Do. ...	Do. ...	25 do.	3	Axillary do	99°	.....	3	60 c. c.	
112	1493	Do. ...	Do. ...	10 do.	8	Do do.	98°	.....	1	10 c. c.	Convalescent.
113	1510	Do. ...	Female.	12 do.	21	Femoral, Inguinal and Iliac bubo ...	98°	1	1	10 c. c.	Do.
114	1515	Do. ...	Male ...	35 do.	3	Cervical bubo	102°	.....	5	120 c. c.	
115	1521	N. Christian	Do ...	40 do.	Unknown	Do. and Maxil bubo	101°	.....	6	150 c. c	
116	1550	Hindu. ...	Do. ...	24 do.	4	Femoral bubo	104°	.....	5	130 c. c.	
117	1568	Do. ...	Female.	20 do.	3	Inguinal do.	101°	.....	7	160 c. c.	
118	1577	Do. ...	Male ...	40 do	6	Femoral do.	99°	.....	4	80 c. c.	Haffkinised.
119	1594	N. Christian	Do. ...	32 do.	5	Cervical do.	103°	1	9	225 c. c.	
120	1602	Hindu. ...	Do. ...	12 do	4	Do. do.	103°	1	5	100 c. c.	
121	1833	Do. ...	Female.	30 do.	3	Femoral do.	105°	.....	7	170 c. c.	
122	1864	Do. ...	Male ...	20 do.	1	Do. and Iliac bubo	104°	.....	9	270 c. c.	
123	1886	Do. ...	Do. ...	11 do.	15	Inguinal and Femoral bubo ...	99°	.....	1	10 c. c.	Convalescent.
124	1892	Do. ...	Do. ...	40 do.	Unknown	Femoral bubo	101°	1	1	40 c. c.	
125	1942	Do. ...	Do. ...	6 do.	8	Do. and Inguinal bubo ...	99°	1	1	10 c. c.	Convalescent.
126	1954	Do. ...	Female.	23 do.	3	Inguinal and Iliac bubo	103°	1	5	160 c. c.	
127	1937	Mussalman.	Male ...	35 do.	Unknown	Do. bubo	100°	.....	2	40 c. c.	
128	1987	Hindu. ...	Do. ...	20 do.	3	Femoral do.	99°	.....	3	40 c. c.	
129	2047	Do. ...	Female.	25 do.	4	Inguinal do.	101°	1	4	110 c. c.	
130	2045	Do. ...	Do.	12 do.	3	Axillary do.	101°	.....	4	110 c. c.	

131	2057	Do. ...	Do. ...	18	do.	3	Cervical do.	103°	1	6	160 c. c.		
132	2065	Do. ...	Male ...	20	do.	3	Femoral and Iliac bubo	103°	.....	3	90 c. c.		
133	2126	Do. ...	Do. ...	25	do.	7	Do. bubo	101°	.....	1	10 c. c.	Convalescent.	
134	2156	Do. ...	Do. ...	25	do.	3	Inguinal do.	105°	1	6	200 c. c.		
135	2152	Do. ...	Do. ...	21	do.	3	Do. and Cervical bubo ...	103°	.....	4	120 c. c.		
136	2186	N. Christian	Do. ...	13	do	2	Axillary bubo	105°	1	8	220 c. c.		
137	2245	Hindu. ...	Do. ...	25	do.	2	Femoral do.	105°	1	9	300 c. c.		
138	2269	N. Christian	Female.	25	do.	3	Inguinal and Iliac bubo	105°	.....	6	210 c. c.		
139	2303	Hindu. ...	Male ...	50	do.	2	Femoral bubo	103°	.....	5	160 c. c.		
140	2314	Do. ...	Do. ...	50	do.	20	Axillary do.	99°	.....	1	10 c. c.	Convalescent.	
141	2337	Do. ...	Do. ...	16	do.	Unknown	Inguinal do.	104°	1	5	160 c. c.		
142	2396	N. Christian.	Do. ...	8	do.	2	Do. and Femoral bubo ...	102°	.....	4	55 c. c.		
143	2422	Mussalman ..	Do. ...	40	do	11	Femoral bubo	98°	.....	1	10 c. c.	Convalescent.	
144	2466	Hindu. ...	Do. ...	25	do.	2	Do. do.	105°	.....	6	200 c. c.		
145	2475	Do. ...	Female	8	do.	3	Do. do.	103°	1	4	65 c. c.		
146	2483	Do. ...	Do. ...	8	do.	3	Axillary and Cervical bubo ...	103°	1	4	80 c. c.		
147	2552	Do. ...	Male ...	9	do.	Unknown	Do. and Femoral do. ...	102°	.....	3	40 c. c.		
148	2572	Do. ...	Do. ...	30	do.	4	Femoral and Inguinal do. ...	103°	.....	4	140 c. c.		
149	2589	Do. ...	Do. ...	28	do.	4	Axillary bubo	104°	.....	6	190 c. c.		
150	2658	Do. ...	Do. ...	32	do.	4	Double Inguinal bubo	103°	.....	6	210 c. c.		
151	2765	Mussalman ..	Female.	12	do.	Unknown	Do. Cervical do.	105°	.....	7	120 c. c.		
152	2772	Hindu. ...	Male ...	22	do.	Do.	Pepliteal bubo...	101°	.....	5	160 c. c.		

List of the Control Patients who Recovered.

Current Number.	Hospital Number.	Caste.	Sex.	Age.	Days of Illness on admission.	Manifestation of Disease.	Highest temperature.	Bubo suppurated.	Remarks.
1	1615	Hindu ...	Male ...	33 years	5	Femoral bubo	03°	.....	
2	1618	Do. ...	Female.	4 do.	15	Do do	98°	.....	Convalescent.
3	1623	Do. ...	Male ...	40 do.	8	Sub-Maxil do.	100°	.....	Do.
4	1631	Do. ...	Do. ...	30 do.	6	Axillary do.	101°	.....	
5	1674	N. Christian	Do ...	22 do	9	Inguinal do.	103°	.....	
6	1708	Hindu ...	Do. ...	30 do.	2	Do. Femoral and Iliac bubo. ...	104°	1	
7	1723	Mussalman..	Do. ...	50 do.	22	Double Inguinal bubo	99°	.....	Convalescent.
8	1748	Hindu ...	Do. ...	12 do.	7	Cervical and Femoral bubo	99°	.....	Do.
9	1828	Do. ...	Female.	7 do.	3	Femoral bubo	103°	.....	
10	1881	Do. ...	Do. ...	45 do.	5	Axillary do.	103°	.....	
11	1885	N. Christian	Male ...	15 do.	1	Femoral do.	99°	.....	
12	1886	Hindu ...	Do. ...	25 do.	2	Pneumonia	103°	.....	Twice Haffkinised.
13	1893	Do. ...	Do. ...	20 do.	4	Double Inguinal bubo	103°	.....	
14	1914	N. Christian	Do. ...	8 do.	2	Do. Femoral do.	104°	.....	
15	1916	Do. ...	Do. ...	10 do.	3	Femoral, Inguinal and Illiac bubo ...	103°	.....	Twice Haffkinised.
16	1941	Hindu ...	Female.	65 do.	4	Do. bubo	101°	.....	
17	1961	Do. ...	Male ...	18 do.	Unknown	Inguinal do.	104°	1	
18	1991	Mussalman.	Do. ...	25 do.	3	Cervical do.	103°	.....	
19	1998	Hindu ...	Do. ...	18 do.	3	Inguinal and Femoral bubo	100°	1	
20	2007	Parsee ...	Female	14 do.	2	Do. Femoral and Illiac bubo ...	105°	.....	
21	2041	Hindu ...	Male ...	35 do.	3	Axillary bubo	104°		
22	2159	Mussalman..	Do. ...	55 do.	12	Inguinal and Femoral bubo	99°	1	Convalescent.
23	2212	Hindu ...	Do. ...	18 do.	4	Cervical bubo	103°	.....	
24	2226	Do. ...	Do. ...	16 do.	8	Inguinal do.	101°	.....	Convalescent.
25	2322	Do. ...	Female	8 do.	3	Axillary do.	103°	1	
26	2365	Do. ...	Male ...	60 do.	14	Femoral and Inguinal bubo	100°	.....	Convalescent.
27	2384	Do. ...	Do. ...	30 do.	7	Inguinal bubo	101°	.....	
28	2398	Do. ...	Do. ...	7 do.	12	Femoral and Cervical bubo	100°	1	Convalescent.
29	2749	Do. ...	Do. ...	3 do.	4	Cervical bubo	102°	.....	
30	2802	N. Christian	Do. ...	20 do,	3	Inguinal and Femoral bubo	103°	1	

31	73	Hindu ...	Female.	11	do.	12	Cervical bubo	102°	.....	Convalescent.	
32	75	Do. ...	Male ...	15	do.	4	Do do.	102°	.....		
33	117	Do. ...	Female.	20	do.	Unknown	Inguinal do.	102°	1	Convalescent.	
34	240	Do. ...	Male ...	20	do	22	Axillary do.	101°	.....	Do.	
35	248	Do. ...	Female.	30	do.	7	Femoral and Iliac bubo...	101°	.....	Do.	
36	259	Do. ...	Male ...	20	do.	4	Double Axillary do.	102°	.....		
37	282	Do. ...	Do. ...	18	do.	9	Cervical bubo	103°	1	Convalescent.	
38	318	Do. ...	Do. ...	12	do.	9	Axillary do.	101°	1	Do.	Haffkinised.
39	399	Do. ...	Female	8	do.	12	Femoral and Iliac bubo	104°	1	Do.	
40	446	Do. ...	Do. ...	7	do.	6	Double Cervical do.	104°	1	Haffkinised.	
41	575	Do. ...	Male ...	30	do.	8	Femoral bubo	101°	.....	Convalescent.	
42	599	Do. ...	Do. ...	1	do.	2	Do. and Cervical bubo	103°	.....		
43	669	Do. ...	Do. ...	22	do.	8	Double Inguinal bubo	101°	1		
44	685	Mussalman..	Do. ...	30	do.	7	Femoral bubo	101°	.....	Convalescent.	
45	710	Hindu ...	Do. ...	45	do.	6	Inguinal and Iliac bubo...	102°	1		
46	886	Do. ...	Do. ...	12	do.	Unknown.	Femoral and Inguinal bubo	101°	.....		
47	1031	Do. ...	Do. ...	5	do	Do.	Axillary bubo	98°	.....	Convalescent.	
48	1059	Do. ...	Do. ...	35	do.	2	Femoral and Inguinal bubo	103°	1		
49	1056	Do. ...	Do. ...	30	do.	3	Inguinal bubo	104°	.....		
50	1111	Mussalman..	Do. ...	35	do.	12	Cervical do	99°	1	Convalescent.	
51	1138	Hindu ...	Do. ..	40	do	Unknown.	Double Femoral bubo	101°	.....	Do.	
52	1140	Do. ...	Do. ...	24	do.	2	Supra hyoidal bubo	105°	1		
53	1164	Do. ...	Do ...	20	do.	3	Cervical bubo	104°	1		
54	1211	Do. ...	Do. ..	8	do.	4	Inguinal do.	104°	1		
55	1168	Do ...	Female.	30	do.	6	Femoral do.	104°	.....		
56	1228	N. Christian	Male ...	13	do.	8	Cervical do.	101°	1		
57	1256	Hindu ...	Female.	6	do.	6	Supra hyoidal bubo	99°	.....	Convalescent.	
58	1250	Do. ...	Male ...	23	do.	2	Axillary bubo	104°	.....		
59	1270	Do. ...	Do. ...	22	do.	1	Inguinal do.	106°	1	Haffkinised.	
60	1273	Do. ...	Female.	20	do.	6	Femoral do.	105°	.....		
61	1282	Do. ...	Male ...	15	do.	2	Inguinal do.	104°	1		
62	1293	Do. ...	Female.	25	do.	2	Do. do.	104°	1		
63	1316	Mussalman..	Male ...	20	do.	2	Double Inguinal bubo	99°	.....	Haffkinised.	
64	1357	N. Christian	Do. ...	15	do.	11	Inguinal and Cervical bubo	100°	.....	Convalescent.	
65	1349	Hindu ...	Do. ...	32	do.	3	Pectoral bubo	103°	.....		
66	1386	Do. ...	Female.	12	do.	2	Femoral and Iliac bubo	103°	1		
67	1395	N. Christian	Male ...	35	do.	10	Inguinal and Iliac do.	98°	1	Convalescent.	
68	1405	Do. ...	Do. ...	30	do.	2	Axillary bubo	104°	.....		
69	1420	Hindu ...	Do. ...	5	do.	Unknown.	Cervical do.	101°	.....	Convalescent.	

List of the Control Patients who Recovered—contd.

Current Number.	Hospital Number.	Caste.	Sex.	Age.	Days of Illness on admission.	Manifestation of Disease.	Highest temperature	Bubo suppurated.	Remarks.
70	1433	Hindu ...	Male ...	8 years	6	Femoral, Iliac and Inguinal bubo ...	104°	1	
71	1455	Do. ...	Female.	16 do.	5	Cervical bubo	105°	.....	
72	1485	Do. ...	Male ...	35 do.	2	Femoral and Iliac bubo	103°	1	
73	1489	Do. ...	Female.	35 do.	4	Cervical bubo	105°	.....	
74	1543	N. Christian	Male ...	52 do.	3	Inguinal do.	100°	.....	
75	1562	Hindu ...	Do. ...	35 do.	10	Cervical and Axillary bubo	101°	1	Convalescent.
76	1588	Do. ...	Female.	7 do.	4	Femoral and Inguinal do.	104°	.....	
77	1590	Do. ...	Male ...	10 do.	4	Femoral bubo	103°	.....	
78	1825	Do. ...	Do. ...	36 do.	8	Inguinal do.	99°	1	Convalescent.
79	1829	Do. ...	Do. ..	12 do.	20	Femoral do.	99°	1	Do.
80	1849	Do. ...	Female	20 do.	3	Do. do.	104°	1	
81	1877	Do. ...	Male ...	30 do.	8	Do. do.	104°	.....	
82	1897	Do. ...	Do. ...	6 do.	8	Cervical do.	98°	.....	Convalescent.
83	1936	N. Christian	Do. ...	40 do	8	Femoral and Inguinal bubo	101°	.....	Do.
84	1943	Hindu ...	Do. ...	30 do.	6	Do. bubo	105°	1	
85	1995	Do. ...	Do. ...	22 do	3	Inguinal and Iliac bubo...	105°	1	
86	2035	Do. ...	Do. ...	40 do.	10	Double Inguinal do.	103°	.....	Convalescent.
87	2103	Do. ...	Do. ...	25 do.	Unknown.	Femoral and Iliac do.	103°	1	
88	2169	Do. ...	Do. ...	20 do.	15	Femoral and Cervical bubo	104°	1	Convalescent.
89	2184	Do. ...	Do. ...	25 do.	10	Inguinal bubo	102°	1	Do.
90	2191	Do. ...	Do. ...	20 do.	7	Femoral do.	102°	1	
91	2231	Do. ...	Do. ...	25 do.	3	Do. do.	104°	1	
92	2243	Do. ...	Do. ...	15 do.	3	Do. do.	100°	.....	
93	2286	Do. ...	Female.	28 do.	2	Axillary and Cervical bubo	103°	.....	
94	2300	Do. ...	Do. ...	9 do.	7	Do. bubo	103°	1	
95	2382	Do. ...	Do. ...	35 do.	3	Femoral and Inguinal bubo	103°	.....	
96	2494	Mussulman.	Do. ...	25 do.	26	Axillary bubo	98°	.....	Convalescent.
97	2584	Hindu ...	Male ...	8 do.	2	Inguinal do.	104°	1	
98	2779	Do. ...	Do. ...	16 do.	2	Axillary do.	105°	.....	

IV

REPORT SUBMITTED TO THE MUNICIPAL CORPORATION OF THE CITY OF BOMBAY ON THE TREATMENT OF PLAGUE WITH PROF. LUSTIG'S SERUM DURING THE EPIDEMIC OF 1900-01.

1. As some recent researches in bacterio-therapy have contributed to enhance our knowledge of the subject, and at the same time to demonstrate with some accuracy the mode of action of sera in various infections, a brief résumé of the same would not be out of place, inasmuch as these investigations have an important bearing on (1) the serum treatment of plague, (2) the limitations that must be placed on our expectations and (3) the lines along which improvements must be sought for, in order to perfect Lustig's serum.

I. A BRIEF RESUME OF RECENT RESEARCHES IN BACTERIO-THERAPY.

2. Dr. W. Bulloch of the London Hospital has recently summarised the work of various observers, in a series of communications to the medical press* and also before the Pathological Society of London, and the following data have been derived mainly from his contributions, his wording in many cases having been retained intact as it expresses the facts so lucidly and tersely :—

Sero-therapy has shown some successes and notably in the case of diphtheria, the antitoxin has more than realised all expectations. The same, however, cannot be said in favour of tetanus antitoxin, as its curative powers have been found to be but feeble, and even massive doses, after the tetanic symptoms have commenced, have failed to bring about a cure in man. Anti-typhoid, and anti-cholera sera possess the property of killing the living bacteria and of dissolving them (bactericidal or lysogenic action) but they are not able to neutralise the poisons generated by the bacteria, and therefore are not antitoxic sera. As despite the most varied attempts in their preparation, bactericidal sera have not hitherto shown any good results, experimenters have been thrown back on their old resources, *viz.*, the creation of an active immunity in the system, against the specific poison, as in cholera, typhoid, and plague, (Haffkine's Anti-cholera Inoculation, Wrights' Anti-typhoid Immunisation and Haffkine's Plague Prophylactic).

3. The reason why serum treatment has not been so satisfactory in the latter diseases is that they differ essentially in their nature from diphtheria and tetanus, which are *intoxication diseases*, in which the bac-

---

* The *Practitioner* ; December 1900 and May 1901. The *Lancet*, March 23rd, 1901.

teria remain *in situ*, at the point of inoculation, the symptoms being almost exclusively due to the action of a toxine excreted by the microbe as a sort of metabolic product. Such however is not the case in affections like influenza, typhoid, plague, cholera, &c., because the specific poisons of these bacilli are not excreted by them, but are retained in the protoplasm forming the substance of the microbes—in some cases in the living protoplasm. These endo-protoplasmic poisons are named "Proteins." And curative properties can only be expected if the anti-bodies or immune bodies (in the sera) are capable of destroying the infecting bacteria, whether living or dead.

4. The researches of Pfeiffer on cholera vibrios have elucidated many important points in connection with sero-therapy and the experiment called "Pfeiffer's Phenomenon" has now become classical in bacteriological literature. He found that if active cholera vibrios were introduced into the peritoneal cavity of a guinea-pig actively immunised against cholera, they rapidly lost their mobility and disappeared entirely : if the same procedure were adopted in a normal (unprotected) animal, they multiplied and caused death. If the serum of the immunised animal is mixed with a certain quantity of active cholera vibrios and introduced into the peritoneal cavity of a normal animal, the solution of the vibrios (bacteriolysis, lysogenesis) also ensues. But it appears that such action does not go on indefinitely, and is limited, *e. g.*, if ·001 cc. of a typhoid immune serum is capable of protecting a guinea-pig against 2 milligrammes of a living typhoid culture, three times as much serum (·003 cc.) will not protect against 6 milligrammes of culture.

A certain dose of culture having been reached, it is of no consequence whatsoever how much serum is given—the result is the death of the animal. It is apparently these extraordinary phenomena which explain why it is that even with very high grade anti-typhoid sera, successful curative results have not been obtained in man.

5. In the elucidation of these phenomena, a number of investigators have been engaged. Metchnikoff says that the bacteriolysis of cholera vibrios is possible *in vitro* if to the cholera immune serum, a few drops of the normal peritoneal fluid of a guinea-pig be added. Bordet showed that the immune serum *by itself* will produce Pfeiffer's Phenomenon *in vitro* if perfectly fresh, and that it becomes inactive if allowed to stand for a short time, but that it can be activated by the addition of a small quantity of normal serum.

Pfeiffer himself explains the phenomenon thus. His theory is that the serum contains an immunising substance, immune body—anti-body, "substance sensibilisatrice" of Bordet, which possesses only slight inhibiting properties on the cholera vibrio, and that bacteriolysis is produced by its combining with certain substances normally present in the peritoneum of

the immune animals. The animal elaborates these substances in an inactive but stable form, but in certain cases they are rendered active by the agency of the cells of the body. As normal serum is also capable of converting the inactive into active form, it is presumed that it must also contain a something in very minute quantity. Inside the body of the animal this something is reproduced, whereas *in vitro* it is rapidly used up and bacteriolysis cannot be brought about unless peritoneal fluid or normal serum is added. The substance is probably of the nature of a ferment, and its action appears to be selective as in this case it acts upon the protoplasm of the cholera vibrio.

6. The experiments of Pfeiffer, Metchnikoff and Bordet explain why the blood serum of an animal actively immunised against cholera is *insufficient or unable to cure a human being* for example, and the same argument applies to typhoid, plague, etc. In such a serum we have only a part of what we want, and the desideratum is the addition of the ferment-like labile body—the "addiment" or "complement" of Ehrlich and Morgenroth, "alexines" (Buchner) which will induce the condition of bacteriolysis and destruction of the given infective agent. Wassermann experimenting with cultures of bacillus typhosus has shown that in order to increase the healing properties of a bactericidal serum one must add not only a "complement," but one which is not destroyed in the animal body.

7. To what extent the complements "addiments" or "alexines" exist in the system and whether it is possible to increase their amount by artificial means are important questions bearing upon practical bacterio-therapy. Metchnikoff's researches on phagocytosis confirmed and extended by Buchner show that the alexines are secreted by the phagocytes, and that it has been experimentally proved that even if the leucocytes be killed, the fluid containing the alexines is capable of bactericidal action.

And Dr. Bulloch has found from his own observations that artificial leucocytosis, brought about by the action of Sodium Cinnamate increased the amount of alexines. To what extent these complements or alexines increase or diminish under the influence of the poison of the plague bacillus, and whether they become constantly reproduced in sufficient quantities to combine with the immune body in the anti-plague serum are questions still awaiting investigation. It appears according to Wassermann that congenital immunity against infections, is to a large extent due to the defensive action of the complements or alexines. And whenever they have been specifically neutralised by an anti-body in experiments on animals, their congenital resistance is at once lowered, and a dose that is sublethal under normal conditions, proves lethal. Wassermann thinks that attention should be paid to two questions :—First whether the amount of these complements can be increased, and secondly whether an easy and accurate method can be devised for the quantitative estimation of the

specific complements. Dr. Bulloch's observation shows that the first is possible by inducing artificial leucocytosis, and attempts have been made by him and others to solve the second. Prof. Wright of Netley submitted* recently before the Pathological Society of London his observations on the *Bactericidal Action of Normal Blood*, and these have also an important bearing on the subject. He found that on plague bacilli the blood had no bactericidal power and similarly on staphylococci and streptococci. With typhoid and cholera bacilli the blood was very powerful, one 1 cc. of blood would kill about 10,000,000 cholera bacilli, and after a dilution of about 20 the blood would still be able to kill off typhoid bacilli. Prof. Wright's observations therefore show what a difficult battle the system has to fight against plague infections of the blood and also against streptococcus infection which is by no means an infrequent concomitant of plague.

8. An interesting series of observations on the solutions (hæmolysis) of the red blood corpuscles has thrown considerable light on the action of immune sera and Bordet has been able to demonstrate that the laws which apply to the specific bacteriolytic action of immune sera also apply to the phenomenon of hæmolysis. He has found that just as the agglutinating properties of serum exist independently of its bacteriolytic powers, so also in hæmolysis where the agglutinative and hæmolytic powers are not identical and one may exist without the other. The researches of Ehrlich, Morgenroth and others now leave no doubt that the process of hæmolysis like that of bacteriolysis consists of 2 parts and depends upon 2 substances :—(1) a specifically active resistant body—the "immune body," and (2) a highly unstable body—the "addiment" or "complement."

9. In order to find out the laws which govern the behaviour of the immune body, and the complements in the presence of infecting bacteria, Ehrlich formulated a theory, called the "Side-Chain Theory" (Seitenkettentheorie) which has received experimental proof at the hands of Wassermann in the case of tetanus.

According to this theory the possibility of the formation of anti-bodies occurs if any body possesses the property of uniting with the side chains which Ehrlich considers to exist in the ultimate chemical structure of the proteid molecule. As Behring puts it "*that substance which when lying in a cell induces an intoxication, is the cause of the cure of the intoxication if it gets into the blood stream.*" If such a substance is soluble, *e. g.*, a toxine, a chemical neutralization takes place in the solution (serum). If the substance is not directly soluble (*e. g.*, a blood corpuscle, bacterial cell, etc), it is not possible for the anti-bodies themselves to induce a solution or neutralization, but it can be experimentally shown that they become attached to the insoluble body, and the latter becomes ultimately dissolved by the subsequent action of the "complement." Ehrlich assumes

---

* The *Lancet*, March 31, 1901.

that the immune body possesses a specific combining " haptophoric " complex and therefore must possess two points of attachments—one haptophoric group possessing great chemical affinity for the red corpuscle (or bacterial cell), the other haptophoric group possessing an affinity for the ferment-like complement present in the blood serum. Under the influence of the two, the red-blood corpuscle is hæmolysed, the immune body in virtue of its haptophoric complex becoming attached to the complement which is normally present in the blood stream. The complement thus becomes indirectly attached to the body (bacterial cell—red blood corpuscle or erythrocyte, etc.) for which the immune body has a specific affinity.

10. It is not known with certainty whether there is one complement or many. If the complement is a unity then there must be an infinite variety of immune bodies, the only thing common to them all being the possession of a definite haptophoric group for the complement. Ehrlich suggested that these side chains had different functions. They are relatively simple as when uniting with toxines which are probably simply, excretory products of the bacteria. In the case of huge proteid molecules like the blood corpuscle or bacterial protoplasm, the process must be more complex on account of a ferment being requisite for its breaking up, and hence two sets of haptophores are necessary, one to attach the poisons, and the other, the complement,—a ferment, which deconstitutes the complicated bacterial protoplasm and renders it inert. The complements are again thermostable or thermolabile depending upon their behaviour in the presence of heat. Von Dungern has, by further experiments, confirmed this Seitenkettentheorie of Ehrlich's.

It has been found that the " complement " of one animal has the property of giving rise in the body of another of an anti-complement, and this anti-complement if injected into the animal from which the complement had been derived, reduces the ability of that animal to deal with a disease which it could safely do under normal conditions, and thus a sub-lethal dose kills an animal, in which the normal complement had been antagonised.

11. Dr. Bulloch thus concludes his interesting article :—

" From the experiments and results which have been thus briefly summarised some idea may be obtained of the wonderful possibilities which have been opened up both theoretically and practically. With these experiments begins undoubtedly a new era in bacteriological science, an era which in all probability will lead to great events. Before, however, much practical advance can be made, it is certain that a vast amount of laborious laboratory work will have to be done for the elucidation of the principles which underlie the destruction of foreign protoplasm introduced into the living body, before the knowledge can be elevated to the rank of

practical therapeutic means. Already, however, the classical work of Bordet, Ehrlich. and Metchnikoff shows that there is a similarity in the method by which toxic cells are dealt with. In all cases as the result of injection, a specific anti-body is produced, insufficient in itself, however, to compass the destruction of the cell which called it into existence. In this discovery alone one can recognise a marked advance upon previous work, and one can realise why it is that sero-therapeutic results, apart from diphtheria and tetanus, have been so disappointing. Where protoplasm itself is toxic, its dissolution takes place by highly labile bodies (alexines, complements) present in the normal circulating blood, and without doubt it is produced and reproduced through the agency of cells which are probably leucocytes. It may be that the alexines are also in the interior of such cells (phagocytes in Metchnikoff's sense). But even the alexines, if unaided, are powerless. The coalition, however, of the alexine and the immune body reacts on the toxic protoplasm and deprives it of its pathogenic effect. Whether in all cases the protoplasm leaves the body of the cells containing it, like the hæmoglobin of the erythocytes, or whether it is destroyed *in situ* cannot yet be definitely stated. Whether even the process of hæmolysis is a vital process or a purely physical one depending on changes in the permeability of the erythrocytic wall through the agency of the alexine is still a matter of doubt. Still, so much has been done, and so much still remains, that the new field must for years be fruitful soil for workers, who are interested in the development of therapeutic means which may be of service in combating the possibilities and the effects of infection."

12. This then is the present position of sero-therapy and it explains why the success with Lustig's serum in the treatment of plague has not been so encouraging as anticipated, and why also the results obtained during the epidemic of 1900-01 have not been so gratifying as during previous years. There is, however, no cause to be discouraged, and it is only by further observation, experiments and research that it would be possible to perfect the serum treatment of plague, which has hitherto given results which are by no means to be despised, when we realize how high the normal mortality from the disease is. It is, therefore, absolutely necessary that further research and experiments should be directed towards the following or analogous lines :—

(*a*) The perfection of a serum of a very high grade—the highest possible attainable, according to our present knowledge and methods of work.

(*b*) An investigation with a view to find out, whether there is any increase or decrease of the alexines in the human or animal body under the influence of plague poison, and whether they are being constantly reproduced under these conditions, and if not, whether there are any means of increasing their production, so that they may be able to keep up constant coalition with the immune body in the serum in order to effect bacteriolysis.

(*c*) An investigation to show whether it is necessary that any normal horse serum should be added to the anti-plague serum in order to increase its potency by supplying some "complements," and, if so, under what circumstances and in what proportions?

Unless an extended and extensive series of observations have been made on the lines above indicated, no progress would be possible in the successful treatment of plague with Lustig's or any other serum, especially now that we realise how complex are the processes that are involved in the process of bacteriolysis, and how difficult the problem that has to be solved in dealing with the successful treatment of plague by serum. It is to be hoped that the Municipal Corporation of Bombay would stint no efforts in encouraging the perfection of the only known means for the cure of a disease for the prevention of which by Haffkine's Prophylactic they had given such encouragement in the early days of its discovery. And it has to be borne in mind that no advance in serotherapy is possible unless, and indeed, by long, patient, and laborious laboratory work, in conjunction with experiments on animals.

II.—THE EPIDEMIC OF 1900-1901.

13. In the report on serum treatment for January last, I had drawn attention to the increasing virulence of plague in the early days of the epidemic, and attempted to show how far the cases differed from those observed in the previous epidemic. These remarks were intended as a forecast, which became fully confirmed as the epidemic advanced. And, now that the epidemic is practically over, a general review of the cases treated with and without serum would not be without interest.

14. The principal characteristics exhibited by the cases were the following:—

(*a*) *Rapid extension of the local infection with multiple contiguous buboes.*

(*b*) *Intense and rapid septicæmia.*

(*c*) *Irregular course, prolonged duration, frequent relapses due to reinfection, or extension, indolent buboes remaining enlarged for a long time or suppurating very late and numerous complications.*

(*d*) *Tardy convalescence, or marasmus from secondary infections, or death from plague pyæmia and consequent toxic degenerations of the internal organs.*

(*e*) *Greater resistance to the action of serum.*

A detailed consideration of the above characters would explain the gravity and nature of the cases treated :—

(a). Rapid Extension of the Local Infection with Multiple Contiguous Buboes.

15. This was perhaps the most noticeable feature observed. Whereas in previous epidemics, multiple buboes (distal and contiguous) existed in a comparatively small proportion, about 13·95 per cent. (as shown by an analysis of 9,500 cases of the bubonic type), the ratio became greatly increased, and the proportion in which they existed in only 411 cases was 63·01 per cent. In this connection, I made the following remarks in the report for January 1901 :—

" It is not implied from the above that such cases did not exist in the previous epidemics. All that is contended here is that, whereas in former epidemics they were fewer in number, and were observed during the height of the epidemic only, they have appeared now in larger numbers—in fact constitute the bulk of the admissions—and at the beginning of the present epidemic."

This statement was confirmed as the epidemic advanced, and multiple buboes did eventually form the bulk of admissions by attaining the unprecedented proportion of 63 cases out of every 100, and *pari passu* the ratios of single buboes declined. Single axillary buboes, that prevailed to the extent of 21·85 per cent. in former epidemics, showed a rate of 17·77 per cent. and single buboes in other positions (femoral, inguinal, cervical, parotid, &c.) dwindled down from 65·20 per cent. to 14·11 per cent. Pneumonic plague had a ratio of only 2·44 per cent. against 4·10 per cent. and plague *without apparent buboes* a ratio of 2·67 per cent. against 14·25 in previous epidemics. It is apparent from the above that the normal proportions of the different clinical varieties of plague showed a marked divergence from what existed in the four previous epidemics, and the multiplicity of buboes increased the virulence of the disease by multiplying the foci of systemic infection and consequent general toxæmia.

16. Triple buboes in the groin—femoral, inguinal, and iliac—were a constant and by far the most predominant feature, and on *post-mortem* examination it was found that almost invariably the deep iliac, lumbar, and retro-peritoneal glands were infected on the same side, and often and often the infection was found to have travelled over to the opposite side of the body. The mesenteric glands became also infected secondarily, and so also the deep femoral and poplitical. It may be mentioned here that distal multiple buboes (*i. e.*, buboes far removed from each other and in different parts of the body), which result from secondary infection in plague septicæmia of a mild type, are not so fatal as contiguous buboes, like the femoral, inguinal, iliac, deep iliac and lumbar, that so often form a chain

extending from the Scarpa's triangle almost up to the diaphragm. The former appear somewhat late in the course of the affection, and at times after the most acute symptoms have subsided, whereas the latter begin with the beginning of the disease, and the "trinity" may be observed within a few hours of the onset of the symptoms. And again in apparently mild cases that had proved fatal and had shown scarcely any external signs, *post-mortem* examination revealed deep-seated buboes in unusual positions : *e. g.*, in two or three cases, a large bubo, hæmorrhagic and infiltrated, was found wedged in perpendicularly in the connective tissue between the wall of the bladder and the pelvic bones. Sometimes the faintest trace of swelling or infiltration in the neck or axilla would be noticed after a most careful examination during life, and yet on *post-mortem* examination numerous and deep-seated buboes would be found. And as many as 20 to 30 tiny buboes have been removed from the deep cellular tissue of the axilla in a case where during life the only visible sign of plague was a faint and painless infiltration. In most of these cases where the buboes were small and almost imperceptible, rapid and intense septicæmia existed. And cases which were apparently mild, and showed only a single bubo externally, revealed similarly after death deep and unsuspected infection. Another curious feature revealed on *post-mortem* examination in 2 female patients was the following :—Both had triple buboes in the groin, and on *post-mortem* examination about 50 to 60 small suppurating buboes were found over the adipose tissue and between it and the subcutaneous cellular tissue. All these contained pus and plague bacilli, and were probably secondarily infected; cutting deeper, the original buboes were observed encapsuled in a bag of pus, partly necrosed, and partly infiltrated with hæmorrhage.

17. The subjoined table gives an analysis of the cases and their rate of mortality. Multiple buboes had a mortality rate of 79·53 per cent., single axillary buboes 76·71 per cent., single buboes in other situations 50·00 per cent., pneumonic plague 100·00 per cent. The total mortality rate in 411 cases was 75·91 per cent. The only redeeming feature in these figures is the comparatively low mortality in single buboes other than axillary, because of the fact that all these cases were non-septicæmic on admission, and some of them were extremely mild :—

1901.	Multiple Buboes.			Single Axillary. Buboes.			Single Buboes in other Positions.			Pneumonic Plague.			Plague without Apparent Buboes.			Total.		
	No.	Died.	Recovered.	No.	Died.	Recovered.	No.	Died.	Recovered.	No.	Died.	Recovered.	No.	Died.	Recovered.	No.	Died.	Recovered.
January	32	21	11	6	4	2	9	6	3	1	1	...	...	...	...	48	32	16
February	81	64	17	27	18	9	20	13	7	1	1	...	3	3	...	132	99	33
March	95	78	17	24	22	2	13	6	7	4	4	...	5	5	...	141	115	26
April	40	33	7	15	11	4	13	3	10	3	3	...	2	2	...	73	52	21
May	11	10	1	1	1	...	3	1	2	1	1	...	1	1	...	17	14	3
Total ...	259	206	53	73	56	17	58	29	29	10	10	...	11	11	...	411	312	99

(*b*). *Intense and Rapid Septicæmia.*

18. Systematic examination of the blood both by the microscope and, but more specially, by culture (greater reliance having been placed on the latter) confirmed the idea entertained in my report of January last that blood septicæmia was the cause of the intense gravity and virulence of the cases. In all the cases admitted during February, March, April, and May, blood was examined at the time of admission, but unfortunately on account of pressure of work the examination could not be kept up from day to day. Cultures showed that 45 per cent. of cases were already septicæmic at the time of admission, and that out of 165 such septicæmic cases there were only 4 recoveries is sufficient to show their gravity. As to the extent of the septicæmia, it varied very greatly, and the colonies were divided for purposes of comparison into 3 classes—few, numerous, and innumerable. In the two latter, death was very rapid, in the former it was somewhat late.

19. Of the cases that became septicæmic *after* admission, no observations could be separately recorded; in some instances blood was examined from time to time and generally confirmed the clinical inference that septicæmia had set in; whilst in others the appearance of secondary buboes in other parts of body, or secondary pneumonia, left no doubt as to the state of the patient. It is probable that the proportion of septicæmic cases was greater, but could not be detected on account of the small quantity of blood examined. It is absolutely necessary, says Dr. Symes,* that at least 2 cubic centimetres of blood should be taken from a vein for examination for blood infection. This was not possible in our cases, firstly from the difficulty of fixing the veins in dark skins, on account of sluggish circulation, and secondly from want of time. We had to content ourselves with making cultures from 2 or 3 drops of blood taken, after proper precautions, from finger-tips, and with the result, above stated. Had the direction given by Dr. Symes been followed, the results would have been still more significant. He says that failure to detect micro-organisms cannot be accepted as a proof of their absence for the quantity of material is relatively small. And, as this refers to 2 c.c., it is obvious that with 2 or 3 drops of blood the results would be still less satisfactory. The bacteriology of plague is further complicated by secondary infections—streptococcus and staphylococcus—and at times plague bacilli as well as cocci are found in cultures. At other times, in most undoubted cases of plague, examination of blood some time prior to death reveals cocci only, but no plague bacilli. I am greatly indebted to Dr. N. Berestneff, of the University of Moscow (late Russian Sanitary Delegate at Bombay), and to Dr. Alfons Mayr, of the Municipal Laboratory, for their cordial co-operation in making blood examinations, but for whose aid it would not have been possible to examine so many cases systematically.

* The Margin of Error in Bacteriological Diagnosis—By Dr. J. Odery Symes: British Medical Journal, February 23rd, 1901.

(*c*). *Irregular Course; Prolonged Duration; Frequent Relapses due to Reinfection or Extension; Indolent Buboes, remaining enlarged for a long time or suppurating very late; and Numerous Complications.*

20. (*i*). *Irregular Course, Prolonged Duration, and Frequent Relapses*:—

These three may be considered together. On account of the multiplicity of buboes, and extension of the infection, the normal temperature curve of plague was found to be greatly altered, and even in cases where the extension was within moderate limits the temperature did not reach to normal till the thirteenth or fifteenth day. Irregularities in the temperature curve were due to infection of new glands, and at each fresh infection the thermometer gave a clear and unmistakeable indication, although there may have been scarcely any external signs. Secondary and tertiary buboes appeared at long intervals, and kept up the patient's temperature, and at the same time sapped his strength. It was contended by some that some of these late buboes were not due to infection by the plague microbes, but were the result of toxæmia, but this was not borne out by investigation. Under these circumstances, the course of the disease became very irregular and prolonged, and, whereas in former epidemics a patient was considered practically safe if he passed over the tenth day of illness, there was no limit in this epidemic, and although life was prolonged from day to day, especially under the serum treatment, it was almost impossible to declare a patient convalescent within a definite period, and patients have survived in hospital for more than eight weeks without there being any hope of their ultimate recovery. Temporary improvements in the condition of the patient were extremely delusive, and no favourable prognosis could be given for a long long time.

21. (*ii*). *Indolent Buboes, and Late Suppuration.*—This was marked specially in the case of iliac buboes. They varied in size from a pigeon's egg to a cricket-ball, and would neither resolve nor suppurate for long periods. Symptoms would occasionally point to localised peritonitis around them, and if resolution did come about eventually it was extremely slow, and would take weeks, and if the patient exerted himself in any way or tried to walk, when in this state, acute or subacute symptoms would appear, causing pain, tension and tenderness, and again confining him to absolute rest in bed. When they suppurated, they had to be incised through the walls of the abdomen and drained. Such buboes have been opened as late as on the 48th day of illness,* and the pus has been found to contain plague bacilli in an active state and capable of growth by cultures. In another case, the bubo was opened on the 27th day of illness, and although plague bacilli were absent in the pus, only a few cocci being found, the blood of the patient gave distinct agglutination. The former cases give rise to a question which has long been debated, viz.:—*Whether a plague patient could himself be free from all acute signs of plague and yet be capable of infecting others and, if so, up to what period?*

* In two instances.

In the light of the above cases and others, where the suppurated buboes seem to remain encapsuled and dormant for a long time, it must be assumed that, although the patient himself remains immune, the encapsuled bubo containing plague bacilli is capable of infecting others if it bursts of itself or is opened, and that the period of infection may be as late as 50 days after the initial attack of the disease. And perhaps in this condition the patient himself is not free from the risk of auto-infection, if through any cause his standard of immunity becomes lowered and the plague bacilli gain an entrance into his system from such a focus.

22. (*iii*). *Complications.*—The extent and severity of the complications bore no relation to what was observed in the previous epidemics. They existed in greater frequency, were graver in their import, and contributed greatly to the heavy mortality. Often and often more than one serious complication co-existed in the same patient, and carried him off. Amongst those more frequent were coffee-ground vomiting, meningitis, secondary pneumonia, secondary infections and marasmus. No note has been taken here of the minor complications like delirium, aphasia, paralysis of the extensors from peripheral neuritis, bulbar paralysis, ascending and descending lymphangitis and lymphadenitis, etc., which, although not necessarily fatal, retarded the progress of the cases.

The following statement gives an approximate idea of the nature of the graver complications and their fatality in the 411 cases admitted from January to May 1901 :—

Complications.	No.	Died.	Recovered.
Coffee-ground Vomiting	25	24	1
Meningitis	19	18	1
Secondary Pneumonia	28	24	4
Hæmaturia	2	2	.....
Secondary Infections	9	5	4*
Do. + Marasmus	9	6	3
General Convulsions	2	2	.....
Tympanites	8	7	1
Peritonitis	3	2	1

* These were cases of extremely mild secondary infections with only a few colonies of cocci in the blood and had single buboes.

(*d*). *Tardy Convalescence, or Marasmus from Secondary Infection, or Death from Plague Pyæmia and Consequent Toxic Degeneration of the Internal Organs.*

23. In one of the preceding sections, the causes of the prolonged and irregular course of the disease have been discussed, and the same causes operated in those patients who became convalescent to retard their recovery. Either fresh complications in the shape of new buboes developed, or secondary infections—streptococcus or staphylococcus—brought them again on the verge of death. After the patients had gone on to a certain hopeful stage, they suddenly retrograded, and marasmus set in, accompanied by prostration and break-down of the nervous system, rapid and great wasting, enfeeblement of mental faculties, localised paralysis, inability to swallow food, &c.: in fact the patient who looked bright and cheerful and on the high-road to recovery became a physical and mental wreck. This was generally found to be due to intense toxæmia or secondary infections, and only a third of the patients that got into this state could be brought round with extreme difficulty—and eventually two of them were discharged in a fairly satisfactory condition after having been in hospital nearly 4 months, and one is now almost well.

24. In other cases, although life was considerably prolonged, death eventually supervened, and it was found to be due to plague pyæmia and toxic degeneration of the internal organs. Hardly any organ was free from degeneration, parenchymatous, adipose or amyloid, and infection and suppuration of almost the whole lymphatic system was evident. On *post-mortem* examination, however, no plague bacilli could be found in one of these late cases, and all that was observed was the degeneration.

(*e*). *Greater Resistance to the Action of Serum.*

25. In the report for January 1901, above quoted, reference was made to the larger doses of serum needed, the average having been 400 cc. in the cases that recovered during that month. As the epidemic progressed, it was found that even 400 c.c. had but temporary effect, and it was considered advisable to make further observations with a view to determine whether large doses would have the desired effect, and the limit to which the serum could be safely pushed. The doses were accordingly increased and the limit to which the serum could be pushed determined. But it will be noted, from what has preceded in this report, how hopeless was the struggle against such rapid and intense septicæmia and an infection of this extensive nature and the results fully justify the conclusion that, however strong the serum, there is a limit to its efficacy, and if the infection goes beyond a certain stage, there is no possibility of cure. There is no doubt that often and often life was prolonged by the serum, by controlling to a great extent the septicæmia and also the extension of

local infection, but art was unable to overtake nature, and had to step aside, letting nature take her own inevitable course. The experiments and conclusions related in the first section of this report explain why even with such massive doses of the serum it was impossible to save life in the majority of cases and the two desiderata laid down above, *viz.* :—that enormous doses of even high grade sera fail in cholera, typhoid, and plague, because there is a limit to their action on account of the peculiar nature of the intraprotoplasmic poison, and that in these sera we do not possess *all* the means that are necessary to neutralise the effects of these poisons, have been confirmed by the results of the serum treatment during the epidemic of 1900-01.

26. However gratifying were the results obtained on the alternate system during the epidemic of 1899-1900, the same cannot be said of the last epidemic, and this itself shows that there must be, as there actually are, limitations to the use of serum in plague, and that in cases where septicæmia had already set in before the treatment was begun or where a multiplicity of buboes existed, it was almost a hopeless struggle against fate, and no amount of serum could save the patient, although it was capable of prolonging life, and ameliorating symptoms. Nothing could illustrate this better than a short synopsis of the 19 cases, each of whom received over 1000 c.c. of serum. Fourteen of them died and five only recovered and as we were enabled to make *post-mortem* examinations on some of them, considerable light has been thrown upon the nature of these cases and the extent of the infection (local and general) in them.

27. *Case No.* 503.—The patient, a Hindu boy, aged 15, came under treatment on the 5th day of illness (March 14th 1901), with right axillary infiltration. The quantity of serum injected morning and evening day after day has been marked on the accompanying chart. After some temporary improvement he developed secondary buboes (double femoral, inguinal and iliac) on March 17th ; secondary pneumonia appeared on the 23rd idem, and on the 30th, left parotid and iliac buboes were observed. From the 25th of March to the 10th of April he was in the marasmatic condition above described, and his life was despaired of. So long as there was any indication of fresh infection, the serum injections were kept up and within 20 days, the total quantity injected subcutaneously was 1580 c.c. The patient eventually made a good recovery, and was discharged from the hospital 2 months and 4 days after admission.

28. *Case No.* 516.—This patient was a sweeper, aged 30, and was admitted on the third day (March 12th, 1901) of illness with left femoral, inguinal and iliac buboes. On the 13th, he developed right femoral : on the 15th, right iliac, on the 22nd, secondary pneumonia, and on the 29th, left femoral and iliac buboes appeared to be soft and suppurating. The left femoral bubo was incised on the 6th of April, but the iliac became again hard, and remained indolent and enlarged but painless till the 29th follow-

ing ; it then became gradually smaller, and when the patient was discharged on the 5th of May it had shrunk considerably, but could still be felt. This patient received the enormous amount of 2405 c.c. of serum—all subcutaneously, within 20 days, and he had to be kept so long under its influence, as there were distinct signs of deep abdominal infection, and so long as they persisted it was not deemed advisable to stop the serum. All the other buboes resolved. The largest quantity of serum injected on a single day was 400 c.c. in 4 injections of 100 c.c. each at intervals of 4 hours, the day after his admission.

29. *Case No.* 654.—The patient, a Hindu female famine emigrant, was admitted on March 27th with left femoral, inguinal, and iliac buboes. She received within seven days 1150 c.c. of the serum subcutaneously, the buboes resolved, and she was discharged cured on the 5th of May. In this case plague and malaria were combined, and as soon as the acute plague symptoms subsided, there was elevation of temperature. Anticipating some extension of infection, the serum was continued four days longer, but as there was total absence of all local signs, and the patient's condition no worse, except for the evening rise, malaria was suspected, and she was put upon quinine ; the effects of this were soon apparent, the fever became less, and eventually subsided altogether.

30. *Case No.* 677.—A Hindu male, aged 25, was admitted on the 5th day of illness (March 31st, 1901) with a large bubo in the right iliac fossa, and small femoral, and inguinal buboes on the same side, together with cellulo-cutaneous necrosis (about 3" in diameter) on the loin. There was localised peritonitis in the right illiac fossa, the day following, and he developed secondary pneumonia on 2nd April. The total quantity of serum injected was 1880 c.c. within 12 days. On April 14th he developed an abscess on the back of the thigh at its upper third, and when it was opened on the 20th, it was found to discharge very offensive pus, and communicating with the hip joint ; the bone was denuded of periostem and exposed. This did not completely heal up till the end of June. The iliac bubo remained as a large hard mass of the size of a cricket ball till the end of the month. It became soft thereafter and was eventually opened on the 48th day of illness ; the pus was found to contain plague bacilli capable of growth. The convalescence of the patient has been very tardy and he is still in hospital on the 30th of June. The necrosis separated, and was removed and the ulcer healed up rapidly. This patient remained for 3 weeks in marasmus.

31. *Case No.* 805.—The patient, a Purdeshee syce, was admitted on the 6th (?) day of illness with right femoral, inguinal, and iliac buboes, and a pimple over the hypogastrim, he developed secondary pneumonia on the 4th day after admission. The total quantity of serum injected subcutaneously was 1020 cc. within 11 days. All the buboes resolved, and he was discharged cured on the 25th of May.*

---

* All of these cases were not septicæmic on admission.

32. *Case No.* 182.—The patient, a Hindu male, aged 25 years, was admitted on the 3rd day of illness (29th January 1901) with left inguinal and iliac buboes. He was placed under Roux's serum and received 900 c.c. in four days, but as the quantity of this serum became exhausted, it was supplemented by 600 c.c. of Lustig's serum within the four days following—the total quantity injected thus came to 1500 c.c. The buboes became large, hard and infiltrated, and the whole of the Scarpa's triangle and iliac fossa apeared to be filled by a hard stony mass. Some fluctuation having been felt, the inguinal bubo was incised, but with temporary relief; the patient got steadily worse, and died on the 10th of February. *Post-mortem* examination was made by Dr. Dürck of the University of Munich, and the deep iliac, lumbar and abdominal glands were found to be infected: there was a thrombus in the left femoral vein, and multiple embolic abscesses, containing plague bacilli, were found in the liver and both the lungs.

33. *Case No.* 467.—The patient, a Hindu male, aged 25, was admitted on the second day of illness (March 4th) with left axillary bubo with infiltration. He was not septicæmic on admission. After receiving 470 c.c. of the serum within 3 days, he improved so much, that the serum was stopped and he was considered semi-convalescent. He remained in this condition for 5 days and then relapsed on the 12th; he developed double femoral, inguinal, and iliac buboes; on the 16th, right posterior cervical with infiltration; on the 17th, infiltration on the abdominal wall, side of the thorax; on the 20th, secondary pneumonia and on the 24th, he sank into marasmus. When the secondary buboes developed, the serum was resumed and he had 675 c.c. more during six days. He died from secondary infection, on the 34th day of illness, the temperature rising to 108°·4 a few hours before death. *Post-mortem* examination was made by Dr. Berestneff of the University of Moscow, and death was found to be due to marasmus from secondary infections: fatty degeneration of the heart, and liver, œdema of the lungs, hypostasis, bronchitis and hydrothorax were also noticed. No traces of plague bacilli could be found anywhere.

34. *Case No.* 471.—The patient, a Mussalman female, aged about 20, was admitted on March 5th on the second day of illness with left inguinal bubo: she was septicæmic; she had a miscarriage the same morning at 1 a.m. She had 10 injections of serum within 5 days, amounting to 1070 c.c., 100 c.c. of which was given intravenously on three occasions, in doses of 30, 30, and 40 c.c. She died of heart failure on the fifth day after admission. No *post-mortem* could be made.

35. *Case No.* 478.—The patient, a Hindu female, aged about 20, was admitted on the 5th (?) day of illness with left axillary bubo. She was non-septicæmic on admission: she received in all 1160 c.c. of serum in eleven injections, but in spite of this, she developed a secondary bubo (left femoral) five days after admission. She died of heart failure on the eighth day after admission.

36. *Case No.* 572.—The patient, a Christian convert child, aged about 11, was admitted on the fourth day of illness (18th March) with left femoral, inguinal and iliac buboes. She was not septicæmic on admission. She had coffee-ground vomiting on the day of admission ; on the 20th, right femoral, inguinal and iliac buboes developed, on the 22nd, she had general convulsions and the temperature rose to 107°·8, and on the 26th she sank into marasmus, and died in the same condition on the 1st of April, on the 15th day after admission. She had altogether 1090 c.c. of serum in 23 injections.

37. *Case No.* 588.—The patient, a Native Christian, aged about 15, was admitted on the 2nd day of illness (18th March) with right axillary bubo ; she was septicæmic on admission and innumerable colonies of plague bacilli were found on culture. Within four days, she had received 450 c.c. of serum, and had so far improved that the dose of serum was reduced. This was, however, followed by a relapse, for, on the evening of the same day, she developed double femoral buboes, the iliac appeared on the 25th and left axillary the day following. From the 29th she sank into marasmus, and died ultimately on the 24th day of illness, with hyperpyrexia, from secondary infection, the temperature reaching to 109°. The total quantity of serum received by her was 2205 c.c. in 24 injections.

38. *Case No.* 613.—The patient, a Hindu female, aged about 30, was admitted on the third day of illness (22nd March), with right femoral, inguinal and iliac buboes. She was septicæmic on admission. On the day following, she had coffee-ground vomiting, and on the 24th, intense tympanites set in. After it was relieved by appropriate treatment, the patient improved very greatly, but it appeared as if the deeper glands were getting infected. The serum was kept up, and she received 2150 c.c. in all in 21 injections. On the first day she had 400 c.c. in four injections of 100 c.c. each at intervals of four hours. She died from heart failure eleven days after admission. On *post-mortem* examination, femoral, inguinal, iliac, lumbar and mesenteric buboes were found suppurated. Multiple abscesses and emboli in the lungs, fatty degeneration of the myocardium and liver, &c., were noticed.

39. *Case No.* 644.—A Mahomedan, aged about 23, was admitted on the fifth day of illness, with left femoral, inguinal and iliac buboes. The patient was not septicæmic. He had in all 1150 c.c. of serum in nine injections, 160 of which were given intravenously on four occasions in doses of 40 c.c. each, but he developed secondary pneumonia, and died on the fifth day after admission.

40. *Case No.* 685.—The patient, a Hindu female, aged about 25, was admitted on the second day of illness with left axillary bubo. She was not septicæmic ; she received in all 2070 c.c. of serum in 19 injections, 600 cc. having been injected on the first day in doses of 150 c.c. each at intervals of 3 to 4 hours. She did not develop any evident secondary buboes, and repeated examination of blood failed to show plague bacilli : she succumbed

on the thirteenth day after admission. On *post-mortem* examination the following was noticed :—atelectasis pulmonum ; bronchitis ; old pleuritic adhesions ; acute degeneration of the heart muscle : parenchymatous nephritis, melanosis in spleen ; lymphatic abscesses in the axilla, on the right side, and hæmorrhagic buboes—inguinal and femoral—thrombus in the right saphena vein, subcutaneous hæmorrhage in the skin of the leg, and œdema of the right lower extremity, etc.

41. *Case No.* 759.—The patient, a Hindu male, aged 20, was admitted on the third day of illness (11th April) with right axillary bubo and infiltration. He was septicæmic. On the 16th right femoral, inguinal, and iliac buboes appeared, and similarly on the 22nd those on the opposite side. The patient received 2000 c.c. of serum in 19 days, but died ultimately from secondary streptococcus septicæmia.

42. *Case No.* 806.—The patient, a Hindu female, aged about 20, was admitted on (?) day of illness (18th April). She was not septicæmic, and had left axillary and righ tpectoral buboes : secondary pneumonia developed on the 23rd, and the patient died on the eighth day after admission. She received in all 1420 c,c. in nine days.

43. *Case No.* 799.—The patient, a Hindu male, aged 20, was admitted on the 4th day of illness (18th April) with double axillary buboes. He was septicæmic and had double blood infection—plague and staphylococcus. He received 1260 c.c. of serum in 13 days ; on the 21st, he developed secondary pneumonia and on the 27th, left femoral and iliac buboes. He died on the 17th day after admission.

44. *Case No.* 829.—The patient, a Hindu male, aged about 20, was admitted on the third day of illness (20th April) with double axillary and double femoral and inguinal buboes. Though clinically septicæmic, plague bacilli were not found in the blood. Secondary pneumonia developed on the 21st, and then infiltration on the right and left sides of the neck on the 27th and 28th respectively. He received 2280 c.c. of serum in 21 days, and died on the 22nd day after admission. On *post-mortem* examination the following was noticed :—General lymphatic infection with abscesses, degeneration of heart, and liver, extensive hæmorrage from the pelvis of the kidney and parenchymatous nephritis.

45. *Case No.* 853.—A Hindu child, aged 6, supposed to be ill for 10 days, was admitted on April 25th with a primary blister over the shoulder, left axillary, double femoral and right inguinal and iliac buboes. She was septicæmic and double blood infection was present—plague and streptococcus. She had 1300 c.c. of serum in 16 days and died on the 19th day of illness.

46. On comparing the course of events and *post-mortem* appearances in the non-serum cases with the above, no striking differences could be observed, and a few random selections from them repeat almost the same tale.

Case No. 419.—Death on the fourth day. *Post-mortem* appearances : atrophy of myocardium, œdema of lungs, amyloid degeneration of kidneys.

Case No. 323.—Death on the third day. *Post-mortem* appearances : pneumonia, atelectasis pulmonum, multiple abscesses in liver, parenchymatous, and hæmorrhagic nephritis, fatty degeneration of myocardium.

Case No. 362.—Pestis hæmorrhagica : almost universal hæmorrhage in all the organs.

Case No. 463.—Death on the thirty-eighth day : abscesses, femoral, iliac and lumbar, degeneration of organs : subcutaneous abscess in the thyroid region.

Case No. 785.—Embolic abscesses in lungs, kidneys and in pancreas, general icteric condition of organs and tissues.

Case No. 776.—Multiple hæmorrhagic polyadenitis : degeneration of organs : profuse hæmorrhage from pelvis of kidney (in the sub-peritoneal cellular tissue).

47. The total number of *post-mortem* examinations made during February, March and April was 38, of which 15 were made by Privat-Docent, Dr. Herman Dürck of the University of Munich : 20 by Privat-Docent, Dr. Nicolas Berestneff of the University of Moscow, and 3, by Dr. A. Mayr of the Municipal Laboratory, to all of whom I take this opportunity of tendering my best acknowledgments for their cordial co-operation and assistance. It is obvious from the foregoing, how essential these examinations were, and in their absence, much that has been learnt during the last epidemic would have been left in the dark.

48. The chief and essential difference between the case treated with and without the serum was the undoubted prolongation of life, and comparatively fewer cases died at such a late stage of illness amongst the latter. There was a marked difference even in the deaths that took place within 48 hours of admission, the non-serum cases losing many more than the serum. So that in both directions, there was ample evidence of prolongation of life.

49. The reason why there was greater resistance to the action of serum is therefore quite apparent from what has been stated above, and in the presence of the multiplicity of the foci of systemic infection must be traced the origin of the same. Time after time plague bacilli were found to disappear from the blood, both after intravenous and subcutaneous injections, but they again almost invariably appeared. Intravenous injections had a more decided effect and after every injection there was a fall of temperature, and improvement in the condition of the patient. But it was not possible to continue intravenous injections indefinitely, and in no case was it possi-

ble to give more than two injections within twenty-four hours. The difficulties connected with this method were very great ; the dark colour of the skin combined with a weak and almost failing circulation, made it no easy task to fix a vein, and sometimes after repeated efforts, the attempt had to be given up. In fact, the latter was a great bar to anything like an extensive use of this method of treatment. Its effects were, however, well marked in some cases and as an instance No. 133 may be quoted :—The patient, a Christian girl, aged about 13, was admitted on the second day of illness with right femoral and inguinal buboes. The temperature on admission was 101°·4 ; at about 10 a.m. she was given 40 c.c. of serum intravenously, and soon after 60 c.c. subcutaneously. Within half an hour she had a rigor and temperature rose at once to 106°·4. This was due probably to the serum having not been sufficiently warmed before injecting intravenously. The temperature did not remain high very long, the patient commenced to perspire freely within a short time and it fell to 101°·6 by 2 p. m.* In the evening it was 100°·2 and the following morning 97°·4. She received 50 c.c. and 30 c.c. subcutaneously, on the two days following, but it appeared that there was no necessity for the second injection. Both the buboes had almost disappeared within 24 hours of the intravenous injection : there was no pain or swelling, and except a slight rise of temperature on the evening of the second day, she was convalescent. The patient made an uninterrupted recovery. And similarly in cases that eventually proved fatal, both intravenous and subcutaneous injections showed a marked influence on the condition of the patient, and especially as regards buboes, which became smaller, hard, and less painful.†

50. Another point that was noticeable as regards the action of serum was this :—It was found that although the effect of the serum on blood infection was marked, re-infection took place so often, and so rapidly, that unless a constant stream of serum was kept, there was no possibility of counteracting the re-infection, and as the channels of infection were multiple, and their connection with the veinous and arterial systems intimate, it is not difficult to realise how futile were the efforts to keep it under check. Dr. Leaf has described how direct connection exists between the lymphatic vessels and veins, and even in some cases arteries, especially in the thoraic region, axilla, and groin. Such being the case direct blood infection would be extremely easy with multiple infection of lymphatic glands. And the frequent association of septicæmia and secondary pneumonia with axillary buboes, leading to the high rate of mortality in them is readily explained by such direct connection between the lymphatic vessels of the axilla and the veins in the same region.

* This crisis has also been observed in other cases without rise of temperature, profuse perspiration, frequent sneezing with a thin watery discharge from the nose, profuse lachrymation.

† The average quantity of serum injected intravenously at one time was 40 c.c.; in some cases however 60 to 80 to 100 c.c. even were injected.

A similar connection has been shown to exist in the femoral and inguinal regions. Dr. Leaf's observations have led him to formulate the following conclusions* :—

1. The azygos veins normally receive a great many lymphatic vessels.

2. Some of the smaller arteries in the thoracic region open directly into lymphatic vessels : some of the smaller veins open directly into large lymphatic trunks, and these two factors help to quicken the movements of the lymph.

3. Direct communications are found to exist between arteries, lymphatic vessels and veins.

4. The communications between veins and lymphatic vessels have been observed to take place in a great many regions in the body (the vena cava, the portal, the renal, axillary, internal illiac and the azygos veins,—all directly communicate with the lymphatic system.)

5. Owing to the presence of these communications, the cells of a malignant growth (and the plague bacilli as well—N. H. C.) can pass either from the lymphatics into the veins or *vice versa* and hence not only in the sacromata but also in the carcinomata the cells as well as the lymphatics should always be regarded as channels along which the cells may at any moment be conveyed to distant parts of the body.

   It is sufficiently clear from the above how constant infection and re-infection of blood is possible with multiple infection of lymphatic glands, and how difficult, nay almost impossible it would be to keep the blood stream constantly charged with enough serum to bring about bacteriolysis. And thus Dr. Leaf's important contribution helps us to understand how with even massive doses of sera it was not possible to overtake the rapid and recurring septicæmia of plague.

51. And again, it has been found that although in many cases the serum was able to counteract the blood infection, it was not possible for it to affect the source from which the infection originated, *viz.* :—the buboes. On account of the inflammatory and necrotic processes that generally co-exist and also the state of partial or complete encapsulation in which they have been found on *post-mortem* examination, the serum does not seem to reach them

* On the Relation of Blood to Lymphatic Vessels. By C. H. Leaf, M. B.—*Lancet*, 3rd March 1900.

and hence it is that bacilli have been found to be active in the buboes, whilst none are to be found in the blood. And therefore so long as they remain active in the buboes, they are capable of setting up fresh mischief, even though the outward manifestations of infection may have been temporarily neutralised by the serum. The local action of the serum on the centres of infection is not much under the above circumstances and therefore it has been suggested by some, that subcutaneous injection of serum should be made as near the bubo as possible, so as to envelope it in the injected serum. This has been done in some cases, but without marked effect. There is no doubt that certain conditions exist locally in the buboes, which whilst not interfering with the multiplication of the plague bacilli, are able to retard the action of the serum, or render it ineffectual in its topical action. And so long as this condition may exist, so long the patient remains in danger of auto-infection or extension of mischief.

52. The above facts fully explain why sero-therapy did not give such good results as during the previous year. Had the conditions been the same, as in the previous epidemics, the results would have been still more encouraging, inasmuch as the serum that was used was stronger than that of last year. But under the altered circumstances of the last epidemic, we had to contend against factors which were practically not existent previously and hence our difficulties were greatly enhanced, and in the light of our present knowledge it appears, that if we had to deal with another epidemic of the same nature, the results would be the same, unless, indeed, it were possible to so perfect the serum on the lines indicated in a former section, as to make it effective against general blood infection.

III.—THE RESULTS IN 1900-01.

53. From August 1900 to February 1901, the serum treatment was again conducted on the selection method. As no serum was available in February, only five patients were treated with it and the rest 127 as detailed further.

During the seven months comprised in the above period, 52 patients were treated with the serum, of whom 35 died and 17 recovered. The non-serum cases numbered 162, and 125 of them died and 37 recovered. The mortality rate in the former was therefore 67·30 per cent. as against 77·16 per cent. in the latter. The difference in the mortality rate between these two sets of cases would have been greater, had there been sufficient serum in February to treat all the cases that were fit for serum treatment.

The following table shows the details of the cases treated month by month :—

Months.	Serum Cases.			Non-Serum Cases.		
	No.	Died.	Recovered.	No.	Died.	Recovered.
August 1900	4	3	1	...	...	...
September ,, ...	9	6	3	2	2	...
October ,, ...	5	4	1	...	...	...
November ,, ...	...	...	...	4	4	...
December ,, ...	8	6	2	5	5	...
January 1901	21	12	9	24	19	5
February ,, ...	5	4	1	127	95	32
Total ...	52	35	17	162	125	37

54. Under instruction from the Special Medical Officer the alternate system of treatment was resumed from March, and the following table summarizes the results for March, April and May. In order to save the serum as much as possible, it was arranged that all moribund patients falling in the serum group, as well as any convalescents, should not receive the serum, and deaths or recoveries among them should count as if they were so treated. And hence out of the 104 cases that came under this group, 32 did not receive any injections—24 because they were moribund or very late and all of whom died, and 8 because they were convalescent or semi-convalescent and all of whom recovered :—

Months.	Serum Cases.			Non-Serum Cases.		
	No.	Died.	Recovered.	No.	Died.	Recovered.
March 1901	62	49	13	60	52	8
April ,, ...	34	26	8	35	22	13
May ,, ...	8	6	2	7	7	...
Total ...	104	81	23	102	81	21

From the foregoing table it will be noticed that out of 104 cases treated with the serum, 81 died and 23 recovered, whereas out of 102 non-serum cases, 81 died and 21 recovered. The mortality rate, therefore, works out at 77·82 per cent. in the former, and 79·42 in the latter, a difference of 1·53 per cent. in favour of the serum, which may be ignored for all practical purposes. The combined mortality of the serum and non-serum cases works out at 78·64 per cent. which, though high as it is, would have been higher still, but for 16 convalescent cases that were included in them. If they were eliminated, there would remain 190 cases, with 162 deaths and 28 recoveries, equivalent to a mortality rate of 85·93 per cent.

55. If the above results are analysed with reference to the presence or absence of septicæmia in the patients, on admission, the results become sufficiently striking and again point to the fact, that when a patient comes to the hospital in the septicæmic condition, he has practically no chances of recovery, however he may be treated. As no systematic examination of the blood was conducted during January, 27 cases not treated with the serum have been excluded from that month, and the following analysis includes 384 cases only out of 411 total admissions :—

Serum Cases.

Months.	Septicæmic Cases.			Non-Septicæmic Cases.		
	No.	Died.	Recovered.	No.	Died.	Recovered.
January	9	9	.....	12	3	9
February	3	3	.....	2	1	1
March	28	26	2	36	24	12
April	15	15	.....	19	11	8
May	2	2	.....	7	4	3
Total ...	57	55	2	76	43	33

The above table shows that out of 57 cases that were treated with the serum, in the septicæmic state, 55 died and only 2 recovered, the latter being comparatively mild cases as they showed scarcely a colony or two in the cultures. The mortality rate in them was therefore 96·66 per cent. There were 76 cases, however, on the other hand who were not septicæmic on admission and they lost only 43, and had 33 recoveries, which was equivalent to a mortality rate of 56·59 per cent. It thus appears that whereas only 3·33 per cent. of septicæmic cases recovered under the serum treatment, the percentage of recoveries in those not septicæmic was 43·41 per cent. under the same treatment, that is there was a difference of 40 per cent. in favour of the latter.

56. Turning now to the cases not treated with the serum and analysing them according as they were or were not septicæmic on admission, the results may be stated as follows :—

Non-Serum Cases.

Months.	Septicæmic Cases.			Non-Septicæmic Cases.		
	No.	Died.	Recovered	No.	Died.	Recovered.
February	48	46	2	79	49	30
March	38	38	.....	39	27	12
April	16	16	.....	23	10	13
May	6	6	.....	2	2	.....
Total ...	108	106	2	143	88	55

The non-serum septicæmic cases numbered 108, of whom 106 died and 2 recovered : the mortality rate being 98·14 per cent. There were 143 non-septicæmic cases, of whom 88 died, and 55 recovered, the mortality rate being 61·53 per cent., that is a difference of 36·66 per cent. in favour of the latter. On comparing the mortality rate in these two sets of cases they stand thus :—

	Septicæmic Cases Mortality rate.	*Non-Septicæmic Cases Mortality rate.*
Serum	96·66 per cent.	56·59 per cent.
Non-serum	98·14 „	61·53 „

It is unfortunate that for purposes of accurate comparison, the complete figures for January are not available on account of 27 cases having been excluded for non-examination of blood, otherwise the difference between the non-septicæmic serum and non-serum cases would have been greater than 4·94 per cent. And it has to be remembered in this connection that this difference of nearly five per cent.was obtained in an epidemic that was characterised by such virulence and multiplicity of buboes as described above.

57. If the influence of serum is compared on the multiple and single buboes, the utility of the serum becomes self-evident as shown below :—

	Serum.			Non-Serum.			Total.		
	No.	Died.	Recovered.	No.	Died.	Recovered.	No.	Died.	Recovered.
Multiple Buboes	95	71	24	164	135	29	259	206	53
Single Axillary	19	17*	2	54	39	15	73	56	17
Other Single Buboes	18	8	10	40	21	19	58	29	29
Pneumonic	3	3	...	7	7	...	10	10	...
Without Apparent Buboes ...	...	...	...	11	11	...	11	11	...
Total ...	135	99	36	276	213	63	411	312	99

* Almost all of these cases did not receive any serum as they were moribund, and 15 of them had secondary pneumonia as a complication.

The recovery rates may be compared thus :—

	Serum	*Non-serum.*
Multiple Buboes	25·26 per cent.	15 24 per cent.
Axillary Buboes	10·53 „	27 77 „
Other Single Buboes	55·55 „	47·50 „

Except, therefore, in the case of single axillary buboes where, for the reason stated above, the recovery rate is higher than in the non-serum cases, the serum group shows better results—in multiple buboes by 10 per cent., and in single buboes by 8 per cent. And although, at first sight, the results taken as a whole did not show any difference, an analysis of the cases as above at once reveals, whether the serum has been useful or not, and to what extent.

TABLE showing the details of cases treated with Lustig's Serum for the Month of February 1901.

Register No.	Date of Admission.	NAMES.	Age.	Sex.	Caste.	Duration of Disease.	Bubo.	Quantity injected c.c.	RESULT.		REMARKS.
									Died.	Cured.	
	1901.					Days.					
206	1st Feb.	Roza Rebello ...	25	Female.	Christ	5	Left femoral & inguinal.	630 c.c.	...	Recovered.	
210	1st do.	Vishram Khemjee..	45	Male ...	Musal.	3	Right inguinal... ...	300 „	Died ...	.....	Death from gradual heart failure.
215	2nd do.	Baptista Lobo ...	25	Male ...	Christ.	2	Left femoral, inguinal and iliac	200 „	„ ...	.....	Death within 12 hours of admission from heart failure.
214	2nd do.	Asharabai Nana ...	18	Female.	Hindu	4	Left femoral, inguinal and iliac	200 „	„ ...	.....	Do. do.
219	2nd do.	C. P. Cardoz ...	35	Male ..	Christ.	3	Left femoral, inguinal and iliac	300 „	„ ...	.....	Death from sudden heart failure.

TABLE showing the details of cases treated with Lustig's Serum for the Month of March 1901.

No.	Register No.	Date of Admission.	NAMES.	Age.	Sex.	Caste.	Duration of Disease.	Bubo.	Non-Septicæmic — Septicæmic :— Few colonies + Many colonies++ Innumerable+++ + after =	Quantity injected c.c.	Result.	REMARKS.
		1901.					Days.					
1	451	3rd Mar.	Casimir Fernandes.	20	Male ...	Christ.	3	Right femoral, inguinal and iliac.	+ +	400 c. c. ... 200 c. c. ...	Died ...	Coffee-ground vomiting, secondary bubo, left iliac.
2	456	,, ...	Rudka Sukhai ...	19	,, ...	Hindu.	3	Right femoral, inguinal and iliac.	+ + +		,, ...	Secondary bubo, right axillary.
3	461	4th Mar.	Francis Minguel ...	8	,, ...	Christ.	3	Left posterior, cervical and submaxillary.	+ +	200 c. c. ...	,, ...	Secondary bubo, right posterior cervical.
4	463	,, ...	Purshotam Govind.	25	,, ...	Hindu.	30	Left femoral (open)	+	Not injected	,, ...	Lumbar and iliac abscesses. On P. M. examination; plague pyæmia.
5	467	,, ...	Puran Ghashoo ...	35	,, ...	, ...	2	Left axillary ...	=	1145 c. c. ...	,, ...	Marasmus.
6	471	5th Mar.	Mariam Mohomed..	20	Female.	Musal..	2	Left inguinal ...	+	1070 c. c. ...	,, ...	70 c. c. intravenous ; had miscarriage before admission ; life prolonged for 5 days.
7	474	6th Mar.	Govind Mahadoo...	24	Male ...	Hindu.	3	Left femoral, inguinal and iliac.	=	170 c. c. ...	Recovered.	
8	478	7th Mar.	Zingi Khandoo ...	20	Female.	,, ...	3 ?	Left axillary ...	=	1160 c. c. ...	Died ...	Life prolonged for 7 days, secondary bubo, left femoral.
9	481	8th Mar.	Mohamad Saheb ...	12	Male ...	Musal.	10	Double sub-maxillary, submental and left parotid.	+	Not injected	Recovered.	

TABLE showing the details of cases treated with Lustig's Serum for the Month of March 1901—*contd.*

No.	Register No.	Date of Admission.	NAMES.	Age.	Sex.	Caste.	Duration of Disease.	Bubo.	Non-Septicæmic— Septicæmic:— Few colonies + Many colonies + + Innumerable + + + + after =	Quantity injected c. c.	Result.	REMARKS.
		1901.					Days.					
10	488	9th Mar.	C. P. Pinto ...	45	Male ...	Christ.	3	Right axillary infiltration.	+ +	420 c. c. ...	Died ...	
11	492	10th „	J. P. Almeida ...	60	„ ...	„ ...	3	Right femoral, inguinal and iliac.	—	200 c. c. ...	„ ...	Death from œdema of lungs; subcutaneous hæmorrhage in large patches on trunk & back.
12	498	„ ...	Pascol Rodrigues ...	25	„ ...	„ ...	2	Double femoral, inguinal and iliac.	+ and also staphylococcus septicæmia.	400 c. c. ...	„ ...	Double infection; meningitis.
13	500	„ ...	Janabai Balkrishna	20	Female...	Hindu	1	Left axillary very small,	+ +	850 c. c....	„ ...	Secondary bubo, double posterior cervical.
14	501	11th Mar.	Chandri Babia ...	22	„ ...	„ ...	8?	Left femoral, inguinal and iliac	+	Not injected	„ ...	Moribund on admission; not injected.
15	506	„ ...	St. Anne J. DeCosta	30	„ ...	Christ.	4	Right posterior, cervical and necrosis on cheek.	—	550 c. c. ...	Recovered.	Plague and small-pox.
16	510	„ ...	Shantaram Annunt..	12	Male ...	Hindu	3	Left axillary with infiltration.	—	470 c. c. ...	Died ...	Meningitis.
17	516	12th Mar.	Soma Poonjia ...	30	„ ...	„ ...	2	Left femoral, inguinal and iliac.	—	2405 c. c. ...	Recovered.	Injections continued for 21 days on account of secondary pneumonia and secondary buboes, right femoral, inguinal & iliac.
18	504	11th Mar.	Sonoo Luxman ...	16	„ ...	„ ...	3	Left supratrochlear and necrosis on elbow.	+ + + and also staphylococcus septicæmia.	500 c. c. ...	Died ...	Secondary pneumonia and double axillary.

19	525	13th Mar.	Balla Naroba ...	35	„ ...	„ ...	7	Left femoral, inguinal and iliac, necrosis over hip joint.	+ +	Not injected	„ ...	Moribund on admission ; not injected.
20	527	„ ...	Nabai Raghoo ...	35	Female..	„ ...	?	Right femoral, inguinal and iliac.	+ + +	„ ...	„ ...	Moribund on admission ; not injected.
21	503	14th Mar.	Shiveram Deoji ...	15	Male ...	„ ...	5	Right axillary infiltration.	=	1580 c. c. ...	Recovered.	Secondary buboes and pneumonia, marasmus and secondary infection.
22	530	„ ...	Eneas St. Anne Cardoz.	25	„ ...	Christ.	3	Right axillary infiltration.	—	Not injected	Died ...	Moribund on admission ; not injected.
23	534	„ ...	Domingo Borges ...	50	„ ...	„ ...	4	Left axillary and brachial,	=	600 c. c. ...	„ ...	Secondary pneumonia.
24	538	15th Mar.	Tatia Narayen ...	20	Male ...	Hindu	5	Left femoral, inguinal and iliac.	—	950 c. c. ...	„ ...	Life prolonged for 7 days.
25	543	„ ...	Jani, wife of Harji.	30	Female..	„ ...	2	Right axillary ...	+	500 c. c. ...	„ ...	Secondary buboes, left femoral, inguinal and iliac.
26	545	„ ...	Rowji Krishna ..	25	Male ...	„ ...	2	Right axillary with infiltration.	=	500 c. c. ...	„ ...	Coffee-ground vomiting, left femoral, inguinal and iliac
27	547	„ ...	Hari Bhayaji ...	22	„ ...	„ ...	2	Left femoral, inguinal and iliac.	+ +	Not injected	„ ..	Moribund ; not injected.
28	553	„ ...	Tookaram Nathiaram.	30	„ ...	„ ...	3	Right femoral, inguinal and iliac.	—	„ ...	„ ...	Do. do.
29	556	16th Mar.	Lawrence Fernandez.	50	„ ...	Christ	2	Left femoral, inguinal and iliac.	—	550 c. c. ...	„ ...	
30	559	„ ...	Narayen Dowlatia	30	„ ...	Hindu	4	Pneumonic plague..	+	Not injected	„ ..	Do. do.
31	560	„ ...	Bhikoo Baloo ...	25	„ ...	„ ...	6	Right femoral, inguinal and iliac.	—	„ ...	„ ...	Moribund ; not injected ; sub-conjunctival hæmorrhage.
32	562	„ ...	Kaloo Behari ...	20	„ ...	„ ...	8	Right femoral, inguinal and iliac.	+?	„ ...	Recovered.	Convalescent, not injected.
33	568	„ ...	Sayamma Pochaya	7	Female .	„ ...	2	Right fomoral, inguinal and iliac.	=	630 c. c ...	„ ...	
34	572	18th Mar.	Esther Nathaniel...	11	„ ...	Christ	2	Left femoral, inguinal and iliac.	=	1090 c. c. ...	Died ...	Coffee-ground vomitting ; general convulsions, secondary bubo, right femoral, inguinal and iliac. Death from exhaustion and marasmus.

TABLE showing the details of cases treated with Lustig's Serum for the Month of March 1901—*contd.*

No.	Register No.	Date of Admission.	NAMES.	Age.	Sex.	Caste.	Duration of Disease.	Bubo.	Non-Septicæmic— Septicæmic :— Few colonies + Many colonies + + Innumerable + + + + after =	Quantity Injected c. c.	Result.	REMARKS.
		1901.					Days.					
35	574	18th Mar.	Hanook Harjee ...	12	Male ...	Hindu	3	Left femoral, inguinal and iliac.	—	480 c. c. ...	Died ...	Coffee-ground vomiting.
36	557	„ ...	Divali Hanook ...	7	Female .	„ ...	3	Left posterior cervical.	=	650 c. c. ...	Recovered.	Secondary bubo, double femoral, inguinal and iliac.
37	578	„ ...	Suleman Ismail ...	50	Male ...	Musal.	2	Left axillary with infiltration.	+ +	400 c. c. ...	Died ...	Secondary pneumonia, coffee-ground vomiting.
38	570	„ ...	Rama Mahadoo ...	30	„ ...	Hindu	2	Left posterior cervical.	—	610 c. c....	Recovered.	Tympanites ; very violent delirium.
39	576	„ ...	Balla Sakharam ...	25	„ ...	„ ...	4	Rightposteriorcervical & left femoral, inguinal and iliac.	+?	620 c. c, ...	„ ...	Old case of relapsing fever with plague infection.
40	581	„ ...	Govind Mahadoo ...	33	„ ...	„ ...	2	Right femoral, inguinal and iliac.	=	680 c. c....	Died ..	Secondary bubo, left femoral, inguinal and iliac.
41	586	„ ...	David Isaac ...	25	„ ...	Jew ...	3	Left femoral, inguinal and iliac.	—	200 c. c. ...	„ ...	Coffee-ground vomiting.
42	588	„ ...	Matilda Almeida ...	15	Female...	Christ.	2	Right axillary.	+ + +	2250 c. c. ...	„ ...	Secondary buboes; marasmus.
43	592	„ ...	Ramchandra Narayen.	35	Male ...	Hindu	4	Left femoral, inguinal and iliac.	+ +	Not injected	„ ...	Moribund ; not injected.
44	594	19th Mar.	Sonabai Soma ...	25	Female..	„ ...	3	Right femoral, inguinal and iliac.	—	300 c. c ...	„ ...	
45	599	20th Mar.	Mahipaty Canoo ...	20	Male ...	„ ...	4	Left axillary with infiltration.	—	400 c. c. ...	„ ...	
46	603	„ ...	Mahadoo Dhondoo	10	„ ...	„ ...	2	Right femoral, inguinal and iliac.	—	Not injected	„ ...	Moribund and not injected.

47	608	21st Mar.	Krishna Sakharam..	30	Female..	„ ...	3	Double femoral, inguinal and iliac.	+	500 c. c. ...	„ ...	Coffee-ground vomiting ; tympanites.
48	613	22nd Mar.	Gangabai Badai ...	30	„ ...	„ ...	2	Right femoral, inguinal and iliac.	+	2150 c. c. ...	„ ...	Coffee-ground vomiting ; tympanites.
49	618	„ ...	Dattaram Bapoo ...	23	Male ...	„ ...	8	Left posterior cervical and sub-maxillary.	=	200 c. c. ...	„ ...	Late case ; secondary buboes, right femoral, inguinal & iliac.
50	624	23rd Mar.	Ratnia Dhondoo ...	8	„ ...	„ ...	2	Right posterior cervical.	—	160 c. c ...	„ ...	Hyperpyrexia before death, Temp, 107·4.
51	631	24th Mar.	Govind Cannoba ...	28	„ ...	„ ...	1	Right inguinal and iliac.	—	690 c. c. ...	„ ...	
52	634	„ ...	Manuel Correa ...	58	„ ...	Christ.	4	Right axillary with infiltration.	+ +	330 c. c. ...	„ ...	80 c. c. intravenous.
53	637	„ ...	Krishni Mahadoo...	30	Female..	Hindu	...	Left axillary ...	+?	Not injected	„ ...	Moribund ; not injected.
54	644	25th Mar.	Hussein Heerawan.	23	Male ...	Musal.	5	Left femoral, inguinal and iliac.	=	1150 c. c. ...	„ ...	Secondary pneumonia; 160 c.c intravenous.
55	649	26th Mar.	Chimaji Bhawoo ...	40	„ ...	Hindu	5	Right femoral, inguinal and iliac.	—	850 c. c. ...	„ ...	Tympanites.
56	651	27th Mar.	Conceicao L. Dias...	12	Female..	Christ.	2	Right axillary with infiltration.	+ + +	400 c. c. ...	„ ...	80 c. c. intravenous.
57	654	„ ...	Ponam Kanji ...	25	„ ...	Hindu	2	Left femoral, inguinal and iliac.	—	1150 c. c. ...	Recovered.	
58	663	28th Mar.	Bhoota Padma ...	30	Male ...	„ ...	2	Double femoral, inguinal and iliac.	+ + +	Not injected	Died ...	Moribund ; not injected.
59	665	29th Mar.	Kandahising Pratipalsingh.	45	„ ...	„ ...	5	Left femoral, inguinal and iliac.	+ +	650 c. c...	„ ..	Tympanites.
60	675	31st Mar.	Savatribai Sadhoo...	50	Female..	„ ...	10	Right femoral, inguinal, iliac and left femoral.	+	Not injected	„ ...	Moribund ; not injected.
61	677	„ ...	Dhondoo Rajoo ...	25	Male ...	„ ...	5	Right iliac.	—	1880 c. c. ...	Recovered.	Secondary ; pneumonia, peritonitis.
62	671	„ ...	Budhoo Sukali ...	35	„ ...	„ ...	2	Left femoral, inguinal and iliac.	—	900 c. c. ...	„ ...	Secondary staphylococcus, infection in blood ; meningitis.

N.B .—Where Septicæmia was confirmed sometime after admission, the cases are marked=in the column for Septicæmia.

TABLE showing the details of cases treated with Lustig's Serum for the Month of April 1901.

No.	Register No.	Date of admission.	NAMES.	Age.	Sex.	Caste.	Duration of Disease.	Bubo.	Non-Septicæmic— Septicæmic :— Few Colonies + Many Colonies + + Innumerable + + +	Quantity injected c. c.	Result.	REMARKS.
63	681	1st April.	Mahadoo Babaji...	36	Male ...	Hindu	5	Right axillary with infiltration.	+ + +	Not injected	Died ...	Moribund ; not injected.
64	685	2nd April.	Naba Chokoo ...	25	Female.	,,	2	Left axillary.	=	270 c. c. ...	,,	Secondary pneumonia.
65	692	3rd April.	Yesoo Krishna ...	20	Male ...	,,	7	Left femoral, inguinal and iliac.	+ + +	Not injected	,,	Moribund ; not injected.
66	696	,,	Battosi Gokhran ...	40	Female.	,,	3	Left axillary with infiltration.	=	200 c. c. ...	,,	Secondary pneumonia.
67	700	,,	Rahimbux Mahomdi.	40	Male ...	Musal.	25	Right iliac.	—	Not injected	Recovered	Convalescent ; bubo very large, soft and fluctuating.
68	689	,,	Shekh Ali Abdul Kadir.	50	,,	,,	3	Left inguinal and iliac.	—	400 c. c. ...	Died ...	
69	705	4th April	Durga Homaji ...	5	Female.	Hindu	8	Right inguinal.	—	Not injected	Recovered.	Convalescent.
70	710	,,	Ibrahim Haji ...	24	Male ...	Musal.	3	Right axillary with infiltration.	+ + +	,, ,, ...	Died ...	Moribund ; not injected.
71	721	6th April.	Ratno Vithoo ...	33	,,	Hindu	4	Right axillary with infiltration.	+ + +	400 c. c. ...	,,	
72	717	,,	Krishna Luxman...	14	,,	,,	6	Left axillary with infiltration.	=	Not injected	,,	Moribund; secondary pneumonia ; not injected.
73	725	7th April.	Bhanoo Ramji ...	30	,,	,,	4	Right femoral, inguinal and illac.	—	500 c. c.	,,	Tympanites.
74	742	8th April.	Datto Yeshvant. ...	30	,,	,,	5	Right femoral, inguinal, iliac and necrosis on calf.	+ + +	100 c. c.	,,	Secondary pneumonia.
75	745	9th April.	Dugroo Krishna...	8	,,	,,	10	Left posterior cervical,	—	Not injected	Recovered.	Convalescent ; bubo open.

76	752	11th Apl.	Magdelena Kilgamo.	45	Female.	Christ.	3	Left femoral, inguinal and iliac.	—	700 c. c. ...	Died ...	
77	764	12th Apl.	Anna Mary Fernandes.	40	„ ...	„ ...	3	Left femoral, inguinal and iliac.	—	840 c. c. ...	Recovered.	
78	759	„ ...	Dhakoo Govind ...	20	Male ...	Hindu	3	Right axillary with infiltration.	+	2000 c. c. ...	Died ...	Secondary buboes. double femoral, inguinal and iliac. Death from Staphylococcus septicæmia.
79	756	„ ...	Augustine Dias ...	13	„ ...	Christ.	3	Double iliac and right axillary.	+	100 c. c. ...	„ ...	Secondary right posterior cervical.
80	768	13th Apl.	Dhondoo Ganoo ...	30	„ ...	Hindu	5	Right femoral, inguinal and iliac.	Cocci	180 c. c. ...	„ ...	Semi-moribund on admission.
81	771	15th Apl.	Kanee Kalia ...	30	Female.	„ ...	?	Left femoral, inguinal and iliac	+ + +	Not injected	„ ...	Moribund, not injected.
82	797	18th Apl.	Bholaram Shanker.	30	Male ...	„ ...	4	Left femoral, inguinal and iliac.	+ + +	„ „ ...	„ ...	
83	801	„ ...	Sadoo Luxman ...	30	„ ...	„ ...	5	Left axillary and left posterior cervical.	+ +	„ „ ...	„ ...	Not injected because almost pulseless on admission. Secondary buboes, double femoral ; Right submaxillary.
84	803	„ ...	Savi Bhavoo ...	9	Female.	„ ...	2	Left posterior cervical.	+ +	220 c. c. ...	„ ...	
85	805	„ ...	Bachoo Chiloo ...	22	Male ...	„ ...	3	Right femoral, inguinal and iliac.	=	1020 „ ...	Recovered.	Secondary pneumonia.
86	808	„ ...	Harnee Bheema ...	30	Female.	„ ...	4	Right supratrochlear.	+	260 „ ...	Died ...	Do. do.
87	810	„ ...	Gunee Govind ...	30	„ ...	„ ...	5	Pneumonic ...	+ +	Not injected	„ ...	
88	806	„ ...	Shitee Krishna ...	20	„ ...	„ ...	6	Left axillary and right pectoral.	=	1420 c. c. ...	„ ...	Secondary pneumonia.
89	799	„ ...	Luxman Krishna ...	20	Male ...	„ ...	4	Double axillary ...	+ and cocci	1260 „ ..	„ ...	Plague and staphylococcus septicæmia. Secondary pneumonia; left femoral and iliac buboes secondary

TABLE showing the details of cases treated with Lustig's Serum for the Month of April 1901— *contd.*

No.	Register No.	Date of Admission.	NAMES.	Age.	Sex.	Caste.	Duration of Disease.	Bubo.	Non-Septicæmic— Septicæmic— Few Colonies. + Many Colonies ++ Innumerable +++	Quantity injected, c.c.	Result.	REMARKS.
90	822	19th Apl.	Abdool Khan Nur Khan.	50	Male ...	Musal.	49	Left inguinal and iliac.	—	Not injected.	Recovered.	Convalescent.
91	829	20th Apl.	Govind Bhagia ...	20	„ ...	Hindu	3	Double axillary ...	=	2280 c. c. ...	Died ...	Double femoral and inguinal ; secondary pneumonia.
92	845	23rd Apl.	Sakoo Gopal ...	12	Female..	„ ...	15	Left axillary ...	—	Not injected.	Recovered.	Semi-convalescent.
93	853	25th Apl.	Kashi Baloo ...	6	„ ...	„ ...	4?	Left axillary and right femoral, inguinal and iliac.	Cocci	1300 c. c. ...	Died ...	Plague and staphylococcus septicæmia on admission.
94	859	„ ...	Bhairoo Nowjee ...	28	Male ...	„ ...	3	Left femoral, inguinal and iliac.	—	620 „ ...	Recovered.	Plague and small-pox.
95	862	26th Apl.	Keroo Ooma ...	11	„ ...	„ ...	1	Right femoral, inguinal and iliac.	++	220 „ ...	Died ...	Sudden heart failure.
96	872	29th Apl.	Janee Yella ...	6	Female .	„ ...	2	Left femoral, inguinal and iliac.	?	200 „ ...	„ ...	Pulse almost imperceptible on admission.

TABLE showing the details of cases treated with Lustig's Serum for the Month of May 1901.

No.	Register No.	Date of Admission.	NAMES.	Age.	Sex	Caste.	Duration of Disease.	Bubo.	Non septicæmic— Septicæmic— Few colonies + Many colonies + + Innumerable + + +	Quantity injected.	Results.	REMARKS.
		1901.					Days.					
97	875	1st May	Kondibai Bandoo ...	25	Female.	Hindu.	4	Left femoral, ingcinal and iliac.	=	Not injected	Died ...	Secondary phneumonia.
98	881	,, ,,	Bhagoobai Rama ...	30	,, ...	,, ...	6 ?	Right axillary with infiltration.	+ + + & cocci	,,	,, ...	
99	888	2nd ,,	Salvador Louis ...	25	Male ...	Christ.	12	Right femoral ...	Cocci	,,	Recovered.	Semi-convalescent.
100	899	5th ,,	Mahadoo Ittoo ...	19	,. ...	Hindu.	6	Left axillary double femoral.	+ + +	,,	Died ...	
101	902	6th ,,	Dowlatia Pandoo ...	36	,, ...	,, ...	7 ?	Right femoral, inguinal and iliac.	—	440 c. c.	Recovered.	
102	916	8th ,,	Raghoo Ramjee ...	32	,, ...	,, ...	8 ?	Left inguinal and iliac.	—	720 c. c.	Died ...	Meningitis.
103	925	13th ,,	Govind Namia ...	18	,, ...	,, ...	4	Pneumonic plague	=	650 c. c.	,, ...	Plague and diplococcus Pneumonia.
104	986	16th ,,	Hussin Mohidin ...	13	,, ...	Musal.	7 ?	Right femoral, inguinal and iliac.	—	240 c. c.	,, ...	Commencing heart failure on admission.

V

FURTHER OBSERVATIONS WITH LUSTIG'S SERUM DURING 1901 AND 1902.

Sometime prior and also subsequent to the completion of the foregoing series of cases, other observations were conducted at the *Maratha Hospital* during 1901 and 1902, partly under the supervision of Dr. Mayr of the Municipal laboratory, who has kindly placed all the information at my disposal.

The first series comprised 38 cases, observed on the Selection Method from November 1900 to January 1901. The results were, that 32 of the cases treated with the serum died, and 6 only recovered, the mortality rate being equivalent to 84·21 per cent. The mortality rate among the cases treated under the ordinary English treatment during the same period was 88·8 per cent. With regard to this series, Dr. Polverini observes* "that the number of recoveries in the cases under the serum treatment would have been 9, but for the fact that 3 patients died in full convalescence from avoidable complications." Major W. E. Jennings, I. M. S., the then Special Medical Officer, Plague Operations, says† "that these results were not to be despised, especially when it is remembered that the advantage gained at the Maratha Hospital was at a time when the percentage of mortality amongst cases treated by other methods was 88·8." Further, with the view to illustrate how observations with the serum treatment have laboured under grave and serious disadvantages at the other hospitals—including those at the *Modikhana Hospital*, referred to in a previous section—as compared with those at the *Arthur Road Hospital*, it would not be uninteresting to quote here what the Medical Officer, who was mainly responsible for the above series of cases, has himself to say. He observes‡ "that owing however to the quantity of serum being limited and the fact that *he was so busy as to be unable to devote sufficient personal attention to ensure that the experiments were being conducted scientifically*, it was decided to abandon them for a while at this hospital." And yet, strange as it may appear, the critics of the serum treatment have relied mainly upon such imperfect observations in order to belittle its value.

---

* Municipal Commissioner's Report on Plague in Bombay for the year ending 31st May 1901, page 254.

† Ibid, page 152.

‡ Ibid, page 166.

The second series of observations extended from 31st July to 17th December 1901, and comprised 44 patients. In undertaking these observations, Dr. Mayr introduced a modification in the method of selection adopted, *viz* :—that only the most acute cases up to the fifth day of illness were selected for treatment. Of the 44 patients under the serum treatment, 31 died, and 13 recovered, the rate of mortality being equivalent to 70·45 per cent. On the other hand 203 patients on the ordinary English treatment showed 161 deaths and 42 recoveries, the mortality rate being 79·31 per cent. The serum-treated cases had thus an advantage of 8·86 per cent. in their favour. But if, in order to equalise the conditions for comparison in both the groups, we eliminate from the latter all the cases after the fifth day of illness, we find that there remain 179 cases with 32 recoveries, with a mortality rate of 82 per cent., and the difference in favour of the serum cases thus increases from 8·86 to 11·5 per cent.,—the latter being the true index of its value. Dr. Mayr analysed the above series and found that the proportion of septicæmic cases was nearly 41 per cent. in the serum group as against 32 per cent. in the non-serum. There were 24 cases in the latter group admitted after the fifth day of illness, of whom 14 died and 10 recovered, the rate of mortality being 58 per cent.

The last series of observations at the Maratha Hospital was conducted during April and May 1902. The object was to determine the comparative value of Lustig's serum, Roux-Yersin's and ordinary treatment, and, with this view, the first case was treated with Lustig's serum, the second with Roux-Yersin's, the third was under ordinary English treatment and the fourth again with Lustig's, and so on. Unfortunately, however, the observations could not be carried out on a sufficiently large scale, as the admissions fell off considerably, and the cases that were admitted were so grave and in such an advanced stage of illness as to preclude any hope of recovery under any line of treatment. Under such circumstances no inference can be drawn from such scanty materials, as only 31 cases were treated under each head. Had it been possible to treat at least 300 cases, under each system, some reliable conclusions would have been possible. And hence this series of cases is included here, for completing the account of all the observations up to date, rather than to indicate what serum or what line of treatment is superior.

Of the 31 cases under Lustig's treatment, all died; of a similar number under Roux-Yersin's, 29 died and 2 recovered, and of those under the ordinary English treatment 29 also died and 2 recovered. Analysing these results, Dr. Mayr found that, of the two recoveries under the ordinary treatment, one was in a semi-convalescent patient, and the other in a very mild case of a convict admitted from one of the local

prisons. Further, the following statement indicates the relative position of the cases treated :—

	Lustig's Serum.	Roux-Yersin's Serum.	Ordinary English Treatment.
1. Total number treated	31	31	31
2. Admitted dead	2	1	...
3. Septicæmic Cases	16	15	13
4. Septicæmic Cases not injected with the Serum because moribund on admission (included in Item 3).	9	7	...
5. Non-Septicæmic Cases not injected because moribund.	3	2	...
6. Total of Items 2, 3, and 5	21	18	13
7. Deducting Item 6 from Item 1, there remained for actual treatment.	10	13	18
8. Recovered	...	2	2

The foregoing table indicates how out of the 62 cases under the serum treatment it was possible to treat 23 only, 10 with Lustig's and 13 with Roux-Yersin's,* if we eliminate those received dead, and also the septicæmic cases for whom, as we now know, there is no possibility of cure, and the moribund non-septicæmic cases. The cases under the Lustig's serum were placed at a comparatively greater disadvantage and with proportionately less favourable results, but, as explained above, such a small series of cases possess very little value one way or the other. As in other similar observations, distinct prolongation of life under the serum treatment was also observed in these cases, grave as they were. Whereas all cases under the ordinary treatment,—except 3·4 per cent.,—succumbed within six days of illness, the ratio of those who lived longer than six days, but ultimately succumbed, was 19 and 17 per cent. respectively in the cases treated with the Lustig's and Roux-Yersin's serum respectively.

Dr. Costello's Observations at Poona.

Dr. Mayr has also communicated to me the results of some observations made at Poona during 1901 by Dr. Costello with Lustig's serum. The idea was to treat the patients on the alternate system, but it was not strictly adhered to, and in a series of 28 cases in the serum group, and 27 in the control, arbitrary interference with the natural sequence of cases was intro-

* It would be interesting to note here that the Roux-Yersin's serum used for these observations was from the same stock with which Dr. Mayr had conducted some observations at the Modikhana Hospital from December 1901 to February 1902 with far better results. 35 cases were treated with this serum, and a similar number alternately with ordinary treatment; the former had 11 recoveries as against 6 in the latter group. And the fact that this very serum failed to give anything like the same results only a couple of months later indicates that it was due to a decided change for the worse in the type of the cases treated and not to the deterioration of the serum. For witness the 6 recoveries under ordinary treatment out of 35 cases at the Modikhana Hospital, as contrasted with 2 only out of 31 at the Maratha Hospital only two months later, when the epidemic had far advanced.

duced by the exclusion of some five cases. Three cases that ought to have gone to the serum group were excluded : two, because they were moribund, and one, because it was a convalescent case. Similarly two cases were excluded in the control group : one because it was moribund, and the other, because the patient had had an attack of plague in 1899. Dr. Costello was able to show 8 recoveries in the control group, and 6 only in the serum. Dr. Mayr has been at pains to redistribute the cases in their natural order of alternation, and demonstrates that had the same not been interfered with, and assuming that the serum had no curative effects, there would have been 6 recoveries in the readjusted control group of 30 cases, and 10 in the serum group with a similar number. The above series indicates the errors to which observers are liable according to the interpretation they may happen to place on the term "alternate system", and shows how two different observers may bring out divergent results from the one and same series of cases according to their interpretation of the term. As has been indicated in a previous section, no exclusions are allowable in this system, and the moment they are made the system ceases to be alternate.

Referring to the type of the disease prevalent at Poona at the time, and the nature of the cases treated, Dr. Mayr observes that three of the recoveries in the serum group were in very grave cases, two of whom had received over a litre each of the serum, and the third was a pregnant female in whom abortion was prevented. The charts examined by him show that there was distinct prolongation of life in the serum-treated cases inasmuch as 20 of the fatal cases in the control group had an average duration of life of 1 day and 14 hours after admission into hospital : whereas in the serum group it was 2 days and 20 hours. Dr. Mayr thinks that the average mortality rate at the period was about 80 per cent., and concludes that from the great virulence of the epidemic he had under-, rather than over-, estimated the benefit derived from the serum treatment.

Concluding Remarks.

A careful and impartial perusal of the account of the observations conducted at the Modikhana Hospital (66 cases), at the Maratha Hospital (38 cases 1900-1901), and at Poona (27 cases 1901) should lead to but one conclusion, *viz* :—that, apart from the difficulties inherent in the nature of the cases themselves, other and extraneous factors, that were avoidable, tended to vitiate the results, and that the treatment with Lustig's serum was not conducted in these instances with that rigorous care, scientific precision, and strict exactitude that are so inseparable from similar investigations. As to what those factors were, and how they obscured the real results, has been already discussed, and all that now remains is to express the hope that, should any similar observations be conducted in the future, they would be placed under better auspices, and may show more favourable results.

VI

THE WITHDRAWAL OF GOVERNMENT SUBSIDY.

CLOSING OF THE LABORATORY.

PROTEST BY DRS. POLVERINI AND MAYR.

DISCUSSION ON LUSTIG'S SERUM.

THE HEALTH OFFICER'S ADDRESS.

CRITICISMS ON LUSTIG'S SERUM.

DR. CHOKSY'S REPLY.

THE RESOLUTIONS PASSED.

The Municipal Commissioner for the City of Bombay, having decided to close the laboratory for the preparation of Lustig's serum, addressed the following communication to Prof. Lustig on 15th May 1902 :—

" I have the honor to inform you that it has been decided to discontinue the further preparation of Plague Curative Serum at the Municipal Laboratory at Parel from the next month. This decision was arrived at chiefly on financial ground, inasmuch as the subsidy that Government hitherto gave towards the expense has been now withheld and a considerably smaller sum has been sanctioned by the Corporation for expenditure on plague measures in the current year. The Government of India having abolished the compulsory removal of plague patients to Hospitals, the field for work in our plague hospitals has been much curtailed, and the cases that are now available for observation are not suitable for obtaining encouraging results. It is these circumstances that have compelled me to arrive at such a decision."

DRS. POLVERINI AND MAYR'S PROTEST.

On learning the above decision Drs. Polverini and Mayr submitted a protest to the Municipal Commissioner. They contended that the sudden closure of the laboratory, entailing as it did the cessation of all research work in connection with sero-therapy of plague, would deal a fatal blow to the cause of sero-therapy not only in India but also elsewhere. They sub-

mitted that the opinion of the Indian Plague Commission was entirely in favour of sero-therapy and the continuance of further research in India, and further explained under what circumstance the later results of the treatment with Lustig's serum in a smaller series of cases had not been so satisfactory as the previous ones conducted on a much larger scale. They referred to the much more satisfactory results obtained in private practice and suggested that, inasmuch as the conditions of work in the public hospitals had considerably altered since the abolition of compulsory segregation, the preparation of the serum may be continued on a smaller scale. And finally they protested against the discontinuance of the preparation of the serum for the following reasons :—

1. " Because there is no prospect at present of the preparation of Lustig's serum being taken up elsewhere, so that much of the experience gained here will be lost."
2. " Because the preparation of Prof. Lustig's serum is less dangerous and requires less trained assistance than that of other anti-plague sera."
3. " Because there is here the opportunity of obtaining fresh cultures from plague patients for the purpose of immunisation, a desideratum which we think of great importance."
4. " Because there is here the possibility of testing the serum immediately on man. It is the collaboration of the laboratory and the hospital which promises the best results."
5. " Because the experiments made during the last year make us confident that the manufacture of the serum is still capable of considerable improvement."
6. " And because many problems which suggested themselves in the course of the manufacture and application of the serum are still awaiting solution."

DISCUSSION ON LUSTIG'S SERUM.

THE HEALTH OFFICER'S ADDRESS.

As the outcome of the above proceedings, the Bombay Medical Union took up the consideration of the subject, and invited a meeting of the local medical profession, at which Dr. J. A. TURNER, the Executive Health Officer, opened the discussion with an address. He gavea brief history of the subject and placed before the meeting the results in hospital and private practice, supplementing the same with some observations on the bacteriology of plague, its infectivity, and the difficulties incidental to the preparation and use of serum in the treatment of plague. The circumstances under which the observations were conducted were detailed, and he observed that the class of patients on whom it was tried

and the conditions of the hospital treatment were against successful results, even if the serum was the best obtainable. He contended that in Bombay, where plague had existed for six years, scientific investigation into the cause and cure of the disease ought to be carried out, and expressed the hope that the Municipality, that had all along been the pioneers of prophylactic and curative remedies, would see to the continuance of these observations, subsidised of course by Government, as the plague had now become an Imperial instead of a local question. Dr. Turner then related some of the difficulties incidental to the preparation of the serum and said that Drs. Polverini and Mayr had worked laboriously under great difficulties, and their reports showed that by the results of their labours, both in the preparation of the serum and its clinical use, our knowledge of the serum treatment had been increased. He said that it had been urged by Dr. Choksy, Dr. Polverini, and Dr. Mayr, three gentlemen who had the most intimate acquaintance with the preparation and use of the serum, that we should not be discouraged by the results. And that they pointed out that, because the serum prepared here had failed to produce good results in patients who were practically moribund, it was unfair to condemn it altogether, and that he agreed with them. Dr. Turner concluded his address with the observation that patient and laborious work, unfettered by official red tape and constant inquiries into results, was required before we could say that serum-therapy as a curative for plague was or was not possible.

Dr. Choksy, having been asked to speak, placed before the meeting the particulars of the private patients, and pointed out that the effects of early treatment were extremely well marked. He described how all the acute symptoms rapidly ameliorated in the cases treated on the first day: the buboes did not suppurate and the convalescence was rapid. He concluded with the following statement, prefacing it with the remark that he laid it before the profession not with the object of seeking any ephemeral notoriety, nor for engendering hopes foredoomed to failure, but with the full consciousness of the responsibility he incurred and in the light of his experience during the six epidemics, *viz.*:—

Should those who are conversant with the application of the serum in plague be entrusted with 100 patients on the first day of illness—provided the cases are not septicæmic—they would be able to bring round at least 60, if not more, by the use either of Lustig's or Roux's serum, of the strength that has been used in Bombay during the last two epidemics.

Dr. Choksy was followed by Drs. K. S. Engineer, S. S. Batlivala, J. P. Nicholson, C. Fernandez, Rajabali V. Patel, B. S. Shroff, J. J. Cursetji, C. T. Master, R. Lakhdir and others, all of whom related their personal experiences of the use of Lustig's serum, and expressed favourable opinions of its value, more especially in early cases.

Unfavourable Criticisms.

Dr. Sukhia opened the debate for the opposition with the statement that he had no personal experience of the treatment of plague with Lustig's serum and that he had not much personal experience of plague also, and that he had derived some knowledge from consultations with hakims (Mahomedan quacks). He went at some length into the past history of the serum treatment, and contended that he was not against Lustig's serum or sero-therapy on principle, but that it appeared to him that the serum prepared locally had proved an absolute failure, although that which came from Florence was somewhat successful. He compared various disjointed statistics of the serum treatment in hospital and private practice with a view to support the above contentions. The comparative mortality rates of the Municipal and private hospitals were adduced in proof of the above assertions, and he stated that the ordinary treatment in the private hospitals was more successful and showed even better results than the treatment with Lustig's serum. He criticised adversely the various systems of treatment adopted in testing the serum and alleged that the treatment during the alternate system was left in the hands of ignorant hospital assistants and therefore errors were liable and the results unreliable. He complained about the dose being large and observed that it was cruelty to inject large doses; it was cruel and inhuman; it was a torture. Dr. Sukhia raised numerous important and unimportant points which had been already amply discussed in the various papers published on the subject and concluded by saying that the closure of the laboratory was quite justifiable on account of the failure of the serum treatment and that it was not closed on financial grounds, as alleged, as the expenses connected with the laboratory could have been well borne by the Municipal treasury.

Dr. S. K. Nariman said that his experience of the serum treatment of plague was limited to but six patients, who were all intelligent Parsees. He contended that there were several drawbacks to the use of the serum. As the dose was large it was difficult to keep the needle sterile when more serum had to be drawn from the bottle; there was local tension and stiffness and joint-pains even after convalescence. His experience was too limited to give any definite opinion on the value of Lustig's serum, but he was inclined to think that the treatment tended to prolong life, though he did not say so with certainty. He also criticised the methods adopted, almost reiterating the arguments of the previous speaker, and observed, after quoting some statistics for various periods, that the ordinary treatment was as good as the serum treatment, and the ratio of mortality almost equal. He referred to the later statistics of 1901 and 1902 and said that they showed that the serum treatment had no value, and that the explanation given of the less satisfactory results during 1901 were not convincing, as there was no increase in the normal mortality rate of the cases under ordinary treatment at the Arthur Road and other hospitals. It was criminal,

said Dr. Nariman, on the part of the Municipality and Government to force the treatment on the poor illiterate, and he assumed and asked were not the patients forcibly treated with the serum when they resisted.

The above proceedings extended over two meetings and at the third meeting the debate was concluded with a reply from Dr. Choksy.

DR. CHOKSY'S REPLY.

Dr. Choksy observed :—To reply seriatim to the various arguments placed before the meeting by the last two speakers would require an essay, inasmuch as they have, between them, ranged over the whole field of serotherapy. I do not propose, however, to inflict one upon you, but would content myself with replying to such observations as are relevant.

Results in Private Practice.

The statement that I laid before the first meeting with regard to the cases treated in private cases was, it appears, incomplete, as some further data have been supplied to me subsequently, and they show that the total now stands at 130 cases, with 58 deaths and 72 recoveries, the mortality rate being equivalent to 44·61 per cent. The statistics quoted by Dr. Sukhia refer to a portion of the above only, and that, too, for a limited period whereas the figures that I submit are up to date, and complete so far as I could make them ; I have also been able to supplement the details of 26 patients, so that instead of 90 only, as on the last occasion, they now relate to 116 :—

Race.	Number.	Died.	Re-covered.	Percentage of Mortality.
Europeans	... 6	2	4	33·33
Parsees	... 52	21	31	40·38
Mahomedans ...	... 22	10	12	45·45
Hindus	... 29	17	12	58·62
Native Christians ...	... 7	5	2	71·42

The mortality rates, you will observe, are progressive, the Europeans heading the list with the minimum of 33·33 per cent. ; the Parsees show 40·38 per cent., the Mahomedans 45·45, the Hindus 58·62, and Native Christians 71·42. It is strange that no exact figures should have been placed before the meeting by the previous speakers to enable you to compare the results under ordinary treatment in private practice, and hence we have no data to judge whether their results have been better or worse ; I think the above would not compare unfavourably.

Early and Late Cases.

The next point to which I would beg to draw your attention is with regard to early treatment. Much confusion has, it seems, arisen with regard to what are called *early cases* and *late cases*. These terms have been applied

to plague, not in their absolute sense, but only relatively. As the mortality from plague is highest between the third and the fifth days of illness, patients admitted on those days are comparatively *late* for treatment and in regard to their chances of recovery. If admitted on the first or second day, they are called *early*, and if after the fifth day, when there is a natural decline in the mortality rate, they are *later cases* and also more favourable. And hence it is, that if the best results from serum treatment are to be observed, they can be obtained only in the earlier cases, and or, in the far more favourable but less interesting or useful ones, after the fifth day. But so rapid is the effect of the plague poison, that the contrast between the first and second day becomes startling, and we find, that whereas of the 26 cases in private practice, treated on the first day, only 4 died, and 22 recovered, of the 34 treated on the second, 20 died and only 14 recovered. The mortality rate on the first day was, therefore, 15·38 per cent. and on the second, 58·82 per cent. This, surely, could not have been accidental, and here at least there were no ignorant hospital assistants to vitiate the results. This meeting would certainly like to know, whether any line of treatment has shown, or can show, such a low mortality rate as 15·38 per cent. in the cases treated on the first day of illness.

Major Childe's Report.

Dr. Sukhia next refers to Major Childe's report, to the stimulants used in conjunction with the serum treatment, and to Surgeon-General Bainbridge's observations on hospital mortality. That is all ancient history. If he had not referred to this episode, it would have saved me from the painful necessity of noticing it. But as he has thought fit to do so, and if there be no reply, he would assume everything to be right. The report to which Dr. Sukhia refers, was made by Major Childe *without personally observing a single case under treatment, or treating one himself!* He was asked by Government to make a report, and as he was otherwise engaged, an assistant surgeon was deputed to go round the Arthur Road Hospital instead, and from the information, figures, etc., supplied by him, he framed the report, which the Surgeon-General backed up. Now, can you conceive of such a procedure in any civilized country, where a report on a highly scientific subject is made by proxy, and accepted in good faith by the powers that be? But as you are aware, many things are possible in this country. Dr. Sukhia has, perhaps, overlooked the fact, that Major Childe, in spite of these disadvantages, was constrained to observe as follows:—"It cannot be said . . . . that the serum treatment of plague shows any marked curative results . . . the most that can be claimed is a 10 per cent. reduction in mortality." Professor TANNER HEWLETT, of King's College, London, in reviewing this report in the *Practitioner* of September 1901, says:—"'Only 10 per cent. reduction!' says Childe, and seems to regard this as of no consequence; yet, with diphtheria antitoxin, the mortality from diphtheria has only been reduced by 12 per cent. or so."

Surgeon-General Bainbridge on High Mortality.

With regard to Surgeon-General Bainbridge's remarks about the high mortality in plague cases in our public hospitals, there has been no change up to now, and the rates have varied very little. No remedy for reducing it has been suggested or applied; it has now been acknowledged that, under the conditions existing in this city, no marked reduction is possible, and we must recognise the inevitable.

The Use of Stimulants.

The use of stimulants was, I hold, perfectly justifiable. We are all physicians first, and experimenters afterwards, and it is incumbent upon us to do all that we can, for the interests of our patients, first, and for science or experiment, afterwards. Here, then, was a new remedy placed in my hands for trial, about which I then knew very little, and was it safe, in the interests of patients—"of the poor illiterate patients"—to rely upon it alone and to withhold the judicious use of alcoholic and other cardiac stimulants, the efficacy of which was so well known? You can well realise the immense responsibility thus thrown upon me, and if I therefore used these agents, as subsidiary adjuvants to the serum treatment, I did no wrong. If the serum cases received any extra benefit by their use, the same benefit similarly accrued to the patients under ordinary treatment also, and if there was a gain in favour of the serum, that should be attributed to the serum only.

The Florence and the Locally-made Sera.

And now I come to that distinction without a difference, that *Florence brand* of the Lustig's serum as contrasted with *the Local brand.* For, mind you, Dr. Sukhia has taken good care to enlighten us, that he is not against the original Lustig's serum or sero-therapy; Oh, no! not he; it is only that particular mischievous little brand of local manufacture that he so cordially detests. Unfortunately, Dr. Polverini and Dr. Mayr, who are responsible for its preparation, are not here to defend themselves, and I do not find myself in a position to say what they would have said had they been present. To this much would I commit myself, that so far as my information goes, no violent or radical changes in the method of preparation of the serum, according to Professor Lustig's original method, were made by them, and that the serum made locally was not inferior to that made by Professor Lustig himself at Florence. Nay, it was to some extent improved upon and rendered more effective, and samples submitted but lately to an independent authority, Professor Tavel, of the Institute of Infectious Diseases, at Berne, elicited a favourable opinion of its quality. It was frequently tested and compared with the Yersin-Roux's serum, to many samples of which the locally-made serum closely approached in strength, and in one instance the latter was found to be even superior. Professor Lustig, who was made fully conversant,

week by week, with what was going on in Bombay, has had no cause to complain that his method had been deviated from, or that the serum made here was of inferior quality. It is also alleged that climatic causes may have interfered with the efficacy of the locally-made serum. The Indian Plague Commission do not think so; they believe rather that the reason why Lustig's serum gave *conclusively favourable results* was, because it was prepared in India, and was thus presumably comparatively fresh serum, and unaltered by heating or lapse of time, like Yersin-Roux, obtained from Paris. So much then for the method of preparation.

The Results.

The Selection Method.

Let us now turn to the results. The Florence serum was used at the Arthur Road Hospital on 257 patients, on the so-called Selection Method, and compared with the ordinary treatment; it showed a difference of 22·70 per cent. That was in 1898. No serum was available in Bombay between October 1898 and end of January 1899, when those engaged in its preparation were asked to bleed the horses and supply the serum, although they were not fully prepared; the serum was not of adequate strength, and was still awaiting testing on animals. Weak as the serum was then known to be by the authorities, it was still tried in the hospital and also given to the Indian Plague Commission for testing. And what was the result? From the 28th of Jauuary to 30th April, 189 cases were treated on the same method as before, and they showed an advantage of 17·43 per cent. over those treated with ordinary treatment—that is, about 5 per cent. less than the Florence serum, and which difference could be accounted for on the above grounds.

The Alternate System.

Here ended the so-called Selection Method, and we entered upon the second phase of our enquiry—*viz.*, the Alternate System. It has been assumed that we were either the originators of the system or were so enamoured of it, that we were blind to its faults. The facts are the reverse. When the system was thrust upon us, at first by a lay authority, and subsequently by the Indian Plague Commission, we strenuously opposed it, and exposed the fallacies and pitfalls incidental to it. I reiterated the arguments contained therein officially in my evidence before the Indian Plague Commission, and also in private conversation with Professors Sir T. R. Fraser and Wright and Dr. Ruffer. They replied, that in a series of 1,000 cases, up to which they wished us to carry the observations, the conditions would equalise, and that in order to obtain the statistical proof of the value of the serum this was the only system, and that we must proceed with it. The conditions imposed upon us were that every other patient in the order of his

admission *into the plague ward*—mind you, not into the hospital—was to be treated with the serum; that no exclusion whatsoever was to be made; and that the patient, whose turn it was, was to be promptly injected, as soon as the diagnosis was made. I carried out these instructions to the best of my ability, ably assisted as I was by Drs. Fraser and Sethna and by the much-abused hospital assistants. Let me say here in fairness to these men, that they were men of exceptional ability, who had worked under me from the very beginning and on whose judgment I could fully rely. Errors, of course, would be inevitable, but they were comparatively few and we were fortunately able in all cases without exception to rectify the same. Infallibility is not one of our prerogatives, and no medical man will presume to say that he is infallible, and much less would an hospital assistant. But the oportunities for diagnostic errors were extremely limited, on account of our constant presence, and often and often, if I was not on the premises when the patients were admitted, one or both the Assistant Medical Officers or Dr. Mayr would be. No suspicious cases were taken into the plague wards, and all elements of doubt were thereby eliminated. There is, however, one serious flaw in the argument of the critics when they talk of diagnostic errors. If such errors there were, they would fall naturally on both the sides, for, unless an observer was actually dishonest, he could not so contrive that all the diagnostic errors should fall to his own side and to his own advantage and not to the opposite. Is any one here prepared to say it was so? And again, if the favourable results in this extensive series of alternate system are assumed to be due to the diagnostic errors of hospital assistants, will the critics tell us why, in the subsequent series of 1900-01, the same beneficent influence was not in evidence? I may therefore reiterate that the greatest care and circumspection were exercised in eliminating all sources of errors consequent on faulty diagnosis, and all that skill, experience and constant and daily vigilance could do to secure accurate results, was done. If after all that, there were any errors, I may add *humanum est errare*. What were the results of this series which ended on 31st July 1900? 484 cases were treated on either side,—that is, a total of 968 cases,—and the serum cases showed a difference in their favour of 11·5 per cent. The Indian Plague Commission was satisfied. The Commissioners observe in their report:—"We have here at last a result obtained by a method which satisfies the demands formulated in a previous section. The diminution of plague mortality by 11·5 per cent., in such an extensive series of cases, treated with the serum, seems to us—assuming, as we presume we may do—the correctness of the records, conclusive as to benefit having been derived from the administration of the serum." Does this appear to you like that failure of the local brand of Lustig's serum as has been alleged?

In August 1900, the new regulations about compulsory segregation in hospitals were issued, and they had a marked influence in reducing the number of patients and also in sending an uniformly worse class of cases,

and simultaneously with it, we received orders that as the Alternate System had proved the statistical value of the serum, we should revert to the Selection Method, so as to give the benefit of the treatment to the curable cases and not waste it upon the moribunds. From August 1900 to the first week in February of 1901, 55 cases were thus treated, and they showed an advantage of 12·81 per cent. in favour of the serum. I would specially invite your attention to this result, and I may add that the serum used at this period was, if anything, stronger than that used during the Alternate System, in the previous year.

The Results of 1901.

In March 1901 the last order was countermanded; we were told to revert once again to the Alternate System, so that during the three months ending 31st May 1901, 104 cases were treated with the serum and 102 with ordinary treatment. The difference then in favour of the serum treatment was only 1·53 per cent. or practically negligible, and this was the first occasion during five years that the results had come so low. Under such circumstances, what would sensible men do? Would they forthwith proceed to doom the serum as a failure or adopt the only rational course, *viz.*, to enquire as to the reasons that had brought about such results? I adopted the latter course, and my investigations fully demonstrated that the above were due, not to inferior serum,—for, had it been so, it could not have become so deteriorated, after four years' constant work, as to be incapable of doing any good in twice or even three times the original dose, and I came to the conclusion that the causes were to be sought for in the cases treated. But I had anticipated such a contingency from what I had observed at the bedside so early as January 1901, and thus long before this Alternate Method was again adopted, and had warned the authorities in my report for the month what to expect. My warning was not too late, nor uncalled for; for, as the epidemic advanced, we found the cases graver and graver, clinically and bacteriologically, and the timely opportunity that we had of performing 38 *post-mortem* examinations soon cleared all doubt and indicated why the serum had not given the same results. These *post-mortem* examinations were conducted not in secrecy, nor did the malign shadow of the hospital assistant cast its spell over the corpses, showing them up to be more malignant than they really were. And Professor Hahn, Drs. Dürck, Berestneff, Mayr and myself were simply appalled at what we saw. For, apart from septicæmia, multiple buboes that are so fatal in their effects and contribute to the constant replenishment of the blood with the supply of plague bacilli had increased in frequency from about 13 per cent. as in the previous epidemics, to 63 per cent. in that of 1900-01.

Special Report of 1901.

The records of these *post-mortem* examinations and notes of cases were submitted to Professor Lustig, and he fully realised our difficulties, but

did not say that these poorer results were due to inferior serum. I embodied these and other observations in a separate report, with charts, etc., and you will be interested to know, what others, more capable of appreciating the value of our work and the difficulties in our way, have had to say about it. The *Lancet* in an annotation referring to this report says :—" The pamphlet affords interesting reading . . . Dr. Choksy ascribes the partial failure to the peculiarities of the epidemic which are mentioned above, especially the marked tendency to re-infection, and the large number of septicæmic cases. Factors had to be contended with which were practically non-existent previously, and he believes that if another epidemic occurred of the same nature, the results would be the same, unless, indeed, it were possible to so perfect the serum as to make it effective against general plague infection." Well, another epidemic has passed, and my prognostications of twelve months ago have not been falsified, as witness the results at the Maratha Hospital during 1902. The same results have been obtained under similar conditions, and will continue to be obtained so long as the present conditions last. I, at all events, had nothing to do with observations at the Maratha Hospital. The *Indian Medical Gazette*, whilst not agreeing with our conclusions, has the fairness to give us credit for our reports, which, it says, " are exactly what they should be : they are careful, honest, and impartial, and every fact and argument for and against the special efficacy of this treatment is clearly detailed and discussed." . . . . . Referring to the above report, it observes " Dr. Choksy's pamphlet is a very able one, and he deals honestly and impartially with the evidence for and against the use of Lustig's serum in plague. But the most remarkable, as well as the most interesting, portion of his recent pamphlet is the careful account Dr. Choksy gives of the unusual and special virulence of the epidemic of the past year in Bombay. There can be no doubt in the mind of the reader, after a persual of this pamphlet, that the epidemic of 1900-01 was exceptionally virulent, not in the numbers attacked, but in the intensity of the clinical symptoms." It proceeds :—" In view of the above it will scarcely be surprising that the results of the use of Lustig's curative serum were more disappointing than the previous experiences of it seemed to warrant." In the *Medical Press* and *Circular* of the 4th ult., Dr. Drury, Physician to Sir Patrick Dun's Hospital at Dublin, writes a critical note on the same report, and observes : " Indeed, a hasty glance at the figures might lead one to the impression that little or nothing had been attained by this treatment, but the analysis of the cases at once reveals whether the serum has been useful or not, and to what extent. Dr. Choksy appears to have no doubt about its utility, and he goes to considerable pains to show why the results have been so disappointing." Now, let us see what other competent and impartial observers have to say. Dr. W. Bulloch, Physician to the London Hospital, whom I have quoted in this report, writes to me : " I have read with great interest your reports on the epidemics of plague which you sent me. I am indebted to you for your friendly mention of my

work and for the reference to the articles in the *Practitioner*. The latter cost me a deal of labour, and I thought that no one read such heavy stuff. Still the importance of the subject led me to write about it, as a great deal of ignorance on such subjects is constantly recurring in medical reports. I think your report, which I have read carefully, is extremely judicious and an important contribution to the subject of plague. As the work proceeds, the difficulties associated with bactericidal sera seem also to increase, and we seem, so far, a very long way off from a practical result." Major Semple, R.A.M.C., the Director of the Pasteur Institute at Kasauli, writes to me : " It is certainly a most interesting report ; I am afraid that there are still many points to be cleared up in connection with the anti-plague serum. You mention several of them in your report, so I see you are also of this opinion."

Criticism on the Results of 1901.

You have heard the above opinions, and you have also noted what our learned critics have brought forward. Instead of studying this report, as they should have, carefully and intelligently—a report which has been characterised as careful, honest, impartial, and as an important contribution to our knowledge of the subject—they have failed to realise its value and have brushed it aside so contemptuously. The only allusion made to it is by Dr. Nariman, who has permitted himself to make one sagacious remark. It applies to the systematic examination of the blood of the patients—which, by the way, he does not call cruel—and he sagaciously says it was rightly made. Will he tell us what he found from a similar examination of the blood at the Parsee Hospital, for that would help this meeting in solving the vexed question of the virulence of plague during 1900-01. And this meeting would also like to know from Drs. Sukhia and Nariman their personal experience of *post-mortem* examinations so as to set all doubts at rest. For no physician, however able he may be, can possibly have a thorough knowledge of the diseases he has to treat, unless his experience at the bedside is supplemented with work in the *post-mortem* room and the laboratory. But, whatever their personal experience in this regard, I ask, Sir, whether they are justified in totally ignoring the report, inasmuch as it fully explains the very circumstances under which the serum failed to give satisfactory results. They ask how it was that the mortality rate in the non-serum cases during 1901 was not higher than before if the epidemic was more virulent ? The reply is :— Refer to the report, study it intelligently, and without bias or prejudice, and you will find the explanation for this apparent discrepancy, *viz.—in the presence of the cases with single buboes with lower mortality that preponderated so largely in the non-serum group.**

One single table is all that they could pick out from this report, and evidently they had not the fairness to appreciate our difficulties, nor did they state, as they ought to have, that there existed certain qualifying and un-

* *Vide* paras. 17 and 58 and the tables included with them.

favourable circumstances that altered the previous state of affairs, and that, therefore, the results were so disappointing. One of the critics' experience of plague in general is derived, as he himself admits, "from consultations with quacks," and the others from observation on "the six intelligent Parsee patients." Are you prepared to accept their testimony against—not mine,—but that quoted above—the testimony of men who have no interest in the subject beyond the honest desire to arrive at the truth, and who are qualified by their training and experience to be impartial judges, capable of appreciating, at their true value, not only the limitations of serotherapy, but also the difficulties we had had to contend against. For you must know *that we can only cure cases that are curable* and that the serum is not an *elixir vitæ* that would put life into the incurable or the moribund. When the infection has gone beyond a certain limit, even the strongest serum would not avail. We cannot achieve the impossible even with the strongest serum; and, because we have failed to achieve it, is that the reason why the serum should be discarded? Could anything be more irrational? There are limitations to every art, and so has medicine. What serum, or what treatment, could possibly achieve success when nature claims her victims at the rate of 93 out of every 100, as she did but two months ago at the Maratha Hospital?

The Alleged Drawbacks.

I now come to the drawbacks mentioned by Dr. Nariman. He complains of the dose being large, the difficulty of keeping the needle sterile when more serum has to be drawn from the bottle, of the local tension and stiffness, and of joint-pains. The obvious duty of a physician, when confronted with obstacles in his path, is not to run away from it, or to forsake it altogether, before he is satisfied after due inquiries whether ways and means do or do not exist to circumvent them. There is nothing to show that Dr. Nariman did anything of the kind: he was apparently satisfied with the intelligence of his patients, forgetting the common truth that the more intelligent the patient the worse for the physician, and gave up the use of serum. That ways and means do exist is apparent, and we have tried them with success, otherwise we would not have been able to go on so long. And what are they? They are—a little extra care, a little of common sense, a little change in the technique, the timely application of some of the common laws of physics and simple medical adjuvants; these are all that are needed to obviate most, if not all, the difficulties, and are easily learned. If Dr. Nariman had applied at the Arthur Road Hospital, he would have received some useful hints. It is, indeed, surprising that this should not have struck him. Not only joint-pains but actual arthritis occur in meat-eaters, but not in all cases, and vegetarians do not suffer from it. This probably depends upon the chemical constitution of the blood.

The Large Dose.

The question of dose now remains, and I admit that it is large, and would wish it were capable of material reduction. But is it? Professor

Roux, the Director of the Pasteur Institute at Paris, than whom there is no, higher authority living, says that large doses are absolutely necessary. In a communication to Dr. Mayr, he observes: "The physicians who direct the treatment of plague patients must first of all be convinced *that large doses must be used if good results are to be obtained.* The plague is not a disease which can be compared with diphtheria. In plague the germs thrive in the whole body, and enter the blood, whereas in diphtheria the bacilli are localised and act through their toxin. *Small quantities of serum are sufficient in diphtheria; they would be useless in plague.*" Professor Sir T. R. Fraser, the President of the Indian Plague Commission, says at page 444 of the report: "The results with the several antitoxin sera designed to accomplish this (*i.e.*, rendering the specific virus innocuous within the body of the patient), which have been used in India, are certainly encouraging, and justify the hope that, with sera of greater bactericidal and anti-toxic power than those hitherto prepared, more definite therapeutic benefit will be obtained. *To obtain the best results, the serum should be injected at as early a stage in the illness as possible, the quantity should be large,* and the injections should be repeated for several days, even although the temperature of the patient and the general conditions have been much improved by the previous injections. In severe cases, and certainly in the pneumonic and septicæmic forms of plague, the serum should be injected directly into a vein, for the therapeutic power of a serum is much greater when it is injected into a blood vessel than when it is injected into the sub-cutaneous tissues. At the same time it is not probable that a serum will ever be prepared which is capable, even by intravenous injection, of preventing death in pneumonic or septicæmic plague after grave symptoms have become developed, and, therefore, when the virus is already diffused in large quantities throughout the body. On the reasonable supposition that in bubonic cases the plague bacilli are for a time concentrated in the primary buboes, it is advisable to inject the serum into the buboes or the tissues immediately surrounding them; and it is probable that the last results will be obtained [I may add they have been obtained] by this plan of administration, which, however, does not appear to have been employed in practice." It was employed before Professor Fraser's report was out on the recommendation of Professor Calmette of Lille.] This, then, is our justification for the large doses that we use, and if you think, Sir, that we err at all, we may say, we err in good company. Such large doses have been declared to be absolutely necessary by the highest authorities, and if the patients' life is not to be trifled with must be used.

The Allegations of Cruelty, Inhumanity, and Torture.

Of the many curious, strange, and sad episodes in connection with plague in this city, the saddest appears to me to be the spectacle of the two medical men who now pose before you as the champions of the poor and the illiterate, whom a cruel Government and still more cruel Municipality have been

entrusting to the tender mercies of their inhuman medical officers to be tortured at their sweet will. This is nothing if not melo-dramatic ; and one touch only is needed to complete the picture ;—a few tears brushed away at the appropriate juncture on behalf of sufferings of the poor dumb creatures, for whom their heart is overflowing with sympathy ! ! ! But is this true ? It were monstrous were it ; if not, I shall leave it to you what to call it. *It is criminal*, says Dr. Nariman, *on the part of the Municipality and Government to force the treatment on the poor illiterate*, and he assumes and asks *were not the patients forcibly treated with the serum when they resisted ?* Dr. Sukhia says *it is cruelty to inject large doses; it is cruel and inhuman ; it is a torture.* These are, as you will perceive, serious allegations, made not at any anti-vaccination or anti-vivisection meeting, where they would pass muster and go unchallenged, but before a body of intelligent medical men, and that they should have been made at all, passes my comprehension. You will rightly assume that these gentlemen were fully prepared to substantiate them with evidence. Have they produced any ? Is there an iota of evidence laid before you that would justify you in accepting these grave indictments ? I see none. All that you have before you is the *ipse dixit* of a gentleman who admits that his knowledge of plague is comparatively limited, and the opinion of another whose personal experience of serum treatment is limited to but six cases, and who evidently was not familiar with the proper technique at the time he treated those patients. Is this the testimony on which you would accept the allegations of cruelty, inhumanity, and torture ? These gentlemen do little credit to your intelligence if they think that you will take them at their word. I trust you will estimate them at their true worth. To place before a body of scientific men such serious allegations and to ask them to accept them as gospel, without any proofs, appears to me to be not far short of playing to the gallery ; and, as you are aware, it takes but little in this country to raise a loud cry of cruelty, inhumanity, and torture against Government or the Municipality. Have these gentlemen weighed the import of their words and do they realise of what incalculable mischief they are capable ? The Government and the Municipality have had to answer much for their sins of commission and omission in connection with plague measures, but it never entered the heads of even their most rabid detractors to charge them with criminal participation in forcing a cruel and inhuman treatment on the poor illiterate. That unique distinction, it seems, was reserved for these two medical men, and you have seen how well they have acquitted themselves ! I protest, Sir, and protest most vehemently against these insinuations, which are just as baseless as they are unjustifiable, and I assert that it is no more cruel, if it be so, to inject the serum in large doses than it is to vaccinate against small-pox, and certainly less so than the prophylactic inoculation against plague, cholera and typhoid and also intra-venous and sub-cutaneous saline injections in cholera, serious hæmorrhages, *etc.* And, whereas the local effects of vaccination against small-pox do not wear off till a fortnight or later, the local

effects of serum injections disappear, or can be made to, under capable hands within a few hours. I deny that it is either cruel, inhuman, or that it is a torture to inject large doses of the serum. I deny, without the slightest fear of contradiction, that the treatment with serum was forced on the poor illiterate. I deny that, when the patients resisted, they were forcibly injected. I never met with any opposition on the part of patients or their friends, and if in some cases they were reluctant—and who would not be under such distressing circumstances when their near and dear ones are so afflicted—their reluctance was soon overcome,—not by force as has been alleged, but by judicious persuasion, and by the actual demonstration of the larger number of recoveries amongst cases that had their charts marked with a big red "L", showing that they were treated with the serum. These people, poor and illiterate as they were, and who so willingly submitted themselves or their near and dear ones to the treatment after this, exhibited minds more open to conviction and reason, and greater intelligence, and they realised better where their best interests lay, than some of those who presume to be intelligent and literate men. And finally it seems to me that it is nothing short of libellous to allege, as it has been, that when the patients resisted the serum treatment they were forcibly treated. Will you, Sir, call upon Dr. Nariman for his proofs, for he it was who made this statement, and will you also call upon him as well as Dr. Sukhia to produce their proofs of cruelty, inhumanity, and torture?

Comparative Results of Private and Public Hospitals.

Dr. Sukhia has opened up the vast question of the comparative results of public and private hospitals for purposes of contrasting the serum treatment. I maintain that his position here is entirely untenable, as he institutes comparisons between things that are in no way comparable. The public hospitals, with their more or less uniform class of patients, belonging mostly to the Hindu labouring classes and the lower and lowest castes, with a few Mahomedans and Native Christians, are not to be compared with the different strata of Hindu and other society that resort to their private hospitals, and, whereas the public hospitals have, throughout the last six epidemics, maintained an almost uniform rate of mortality varying from 75 to 81 per cent., there has been great diversity of results between the various private hospitals, and these depend, as I and most others conversant with plague believe, mainly on the racial incidence and power of resistance in the various classes. I have compared and tabulated the results of the larger private hospitals from 1898 to 1901, and I find that the mortality rates in the various Hindu hospitals vary from 70 per cent. to 81 per cent.; in the Mahomedan hospitals from 49 to 56 per cent.; the Parsee hospital, 55 per cent.; and the Beni-Israel 44 per cent. And I also find that the variations among Hindus and Mahomedans, *inter se*, are so marked that they could be accounted for only by their racial incidence. And yet you see that Dr. Sukhia groups these heterogeneous elements into one whole and compares

them with the results of the serum treatment in public hospitals. Not content with that, and obviously ignoring these vital differences in mortality rates ranging from 44 to 81 per cent. in private hospitals, he holds up before us, for admiration, the quacks and the untrained nurses who were in charge of the Mahomedan hospitals as the patterns we qualified men should imitate, and he seriously contends that they know more of plague, its diagnosis, and treatment than we do. Could anything be more preposterous? I have had some experience of the quacks, for during the first two epidemics they were inflicted upon me in large numbers and were allowed to visit the hospital, and I, too, have learned something from them. I learned that their ignorance was equalled only by their impudence, and that both were exceeded by their gross mendacity.

Conclusion.

This finishes my defence. I have tarried rather long at it, but the blame, if any, rests not so much with myself as with those who have compelled me to be so. And yet I find that, though I have considered most of the principal points brought berore you, some minor ones have been left untouched. Let them remain in peace. I believe I have met the principal arguments placed before you clearly, honestly and impartially, and without withholding anything. I have demonstrated how the largest number of observations have shown the advantages of sero-therapy by the various methods adopted for testing it, and I have explained how, under altered circumstances and conditions, a very much smaller series has been disappointing. Are you prepared to ignore the larger and better results for the smaller and less favourable and to doom the serum as an absolute failure? If you do, the responsibility is yours, and it is a very serious one indeed; if not, then I trust you will express your opinion without fear or favour, and state your honest convictions in this regard. To me it appears that the outcome of these proceedings will have far-reaching effects, inasmuch as you are called upon not only to declare your views on this subject, but also to pronounce judgment upon my coadjutors and myself, and to express your opinion whether you consider our figures and statistics correct and reliable or otherwise; whether we are honest men, striving to do our duty to the best of our ability in the cause of humanity and science, or that we are the cruel and inhuman monsters we have been depicted to be; and whether we delude ourselves and also possess the capacity of deluding others in a matter fraught with such vital consequences. The verdict rests with you. In conclusion, I would add that such is my firm conviction and belief in the efficacy of the serum treatment that I would reiterate what I said at the first meeting, *viz*:—"*Should those who are conversant with the application of the serum in plague be entrusted with 100 patients on the first day of illness, provided the cases are not septicæmic, they would be able to bring round at least 60, if not more, by the use either of Lustig's or Roux' serum of the strength that has been used in Bombay during the last two epidemics.*

And, now, let me thank you for the great patience with which you have heard me through, and repeating, as I do, what I said on the first occasion I do not suppose you would wish me to alter anything, to qualify anything, or to retract anything. I have said what I have said : the onus is mine.

RESOLUTIONS AND AMENDMENTS.

The Hon'ble Sir Bhalchandra Krishna rose next to move certain resolutions and spoke at length in support of the same, criticising the action of the Government in withdrawing the subsidy in the face of the recommendations of the Indian Plague Commission. Drs. Katrak, Nariman, and B. S. Shroff moved three several amendments to the resolutions proposed by Sir Bhalchandra Krishna, and eventually after protracted discussion the meeting unanimously adopted the last amendment (Dr. Shroff's) and resolved that the President of the meeting be requested to communicate the same to Government and to the President of the Municipal Corporation :—

That this meeting is of opinion that in the interests of science and humanity, and with a view to afford medical men opportunities of trying the efficacy of, and using as remedial measures against plague, curative sera, either free of cost or otherwise, as may be found expedient, it is necessary that some arrangements be made whereby research work in connection with sero-therapy in Bombay be continued either on the plan of Dr. Lustig or any other plan or plans that may be suggested.

DISCUSSION AT THE MUNICIPAL CORPORATION.

On the above resolution and the protest of Drs. Polverini and Mayr coming up for discussion before the Municipal Corporation (14th August 1902), the following motion was carried by a majority :—

Moved by the Hon'ble Sir Bhalchandra Krishna, and seconded by Dr. K. E. Dadachanjee :

"That all the papers relating to the subject be forwarded to the Government with the expression of the Corporation's hope that the Government would see their way to make suitable arrangements for continuing research and experiments in sero-therapy in Bombay"

Thus ended another chapter in the history of sero-therapy of plague in Bombay,—which like every other new line of treatment, has had to suffer a greal deal, not so much from honest, impartial and intelligent criticisms as from the ignorance, prejudice and bias of its self-opinionated critics, who would not be convinced at any cost and who would take no pains to convince themselves by personal observation or study.

VII

CORRECT STATISTICS OF THE SERUM TREATMENT.

As the method adopted by the opponents of Lustig's serum in quoting the statistics of the treatment before the meeting of the profession has led to considerable confusion, it has been considered advisable to give here a complete and accurate statement showing the different periods during which the serum was utilised at the various hospitals, the systems adopted, and the results. Corresponding statistics for the cases not treated with the serum are also given, period for period, with a view to enable accurate comparison. As regards the figures for the Maratha Hospital, only the patients under exactly similar conditions are given, *i.e.*, those that were under the English treatment: all those treated by the native doctors (vaid and hakim) have been eliminated. The rest of the statement explains itself:—

STATEMENT OF THE RESULTS OF THE TREATMENT OF PLAGUE PATIENTS WITH LUSTIG'S SERUM IN THE MUNICIPAL HOSPITALS OF BOMBAY FROM 1898 TO 1902.

Arthur Road Hospital.

Period.	System of Treatment.	Serum-Treated Patients.			Patients under Ordinary Treatment.			Difference in favour of the Serum Patients; per cent.
		Number.	Deaths.	Case Mortality per cent.	Number.	Deaths.	Case Mortality per cent.	
March to Oct. 1898 ...	Selection ...	257	145	56·4	752	595	79.1	22·7
Jan. to April and June 1899..	Do. ...	189	124	65·60	884	734	83.03	17·4
May 1899 and July 1899 to Aug. 1900...	Alternate ...	484	329	68·00	484	385	79·5	11·5
August 1900 to Feb. 1901 (3 extra cases).	Selection ...	55	36	65·45	184	144	78·26	12·81
March, April and May 1901...	Alternate ...	104	81	77·82	102	81	79·42	1·53

Maratha Hospital.

1898	Selection ...	28	17	60·71	...	...	80·7	20·0
Nov. 1900 to Jan.1901	Do. ...	38*	32	84·21	...	...	88·8	4·59
August to Dec. 1901..	Do. ...	44†	31	70·45	203	161	79·31	(11·5) 8·86
April and May 1902...	Alternate ...	31‡	31	100·00	31	29	93·54	*Nil.*

*1. With regard to this series of cases Dr. Polverini observes (*vide* Municipal Commissioner's Report on Plague in Bombay for the year ending 31st May 1901, page 254) :—" The number of recoveries under the serum treatment would have been 9 but for the fact that 3 patients died in full convalescence from avoidable complications."

2. Major W. E. Jennings, I. M. S., Special Medical Officer, Plague Operations, also says (*vide ibid*, page 152) :—" These results, however, are not to be despised, especially when it is remembered that the advantage gained at the Maratha Hospital was at a time when the percentage of mortality among cases treated by other methods was 88·8."

3. The Medical Officer in charge of the Maratha Hospital says (*vide ibid*, page 166) :—" That owing, however, to the quantity of serum being limited, and the fact that *he was so busy as to be unable to devote sufficient personal attention to ensure that the experiments were being conducted scientifically*, it was decided to abandon them for a while at this hospital."

† Dr. Mayr conducted these observations and states that he selected for treatment the most acute cases,—*i.e.*, cases admitted up to the fifth day of illness. He found that, whilst nearly 41 per cent. of the serum-treated cases were septicæmic, the ratio was 32 per cent. only among those under the ordinary English treatment. On comparing the admissions upto the fifth day of illness, it was observed that, whilst the 44 serum-treated patients had a mortality rate of 70·45 percent., 179 patients similarly situated, under the ordinary English treatment, showed a mortality rate of 82 per cent., and the lower rate (79·31) shown in the above table is due to the inclusion of 24 later cases, of whom 10 recovered. So that the actual difference under more or less identical conditions was 11·5 per cent. in favour of the serum cases, and not 8·86 per cent.

‡ These observations were also under the supervision of Dr. Mayr, but the method was different. The system adopted was to treat one case with Lustig's, the next case with Roux', the third with ordinary English treatment, and the fourth again with Lustig's serum, and so on. The 31 cases under Lustig serum included 16 septicæmic cases, 2 were received dead in their turn, and 3 non-septicæmic cases who were not injected because they were moribund. Thus 21 cases became excluded as incurable and there remained only 10 cases fit for treatment, all of whom died.

Of the 31 Roux' serum cases, 15 were septicæmic, 1 was received dead, and 2 non-septicæmic were not injected because they were moribund. Thus 18 cases were excluded, and of the 13 who remained 2 recovered. There were 13 septicæmic cases among those under ordinary English treatment, and no cases were received dead. Of the 18 thus remaining, 2 recovered—one a semi-convalescent case and another a mild case.

It will be noted, therefore, that the Lustig cases laboured under proportionately greater disadvantages, 10 only being actually treated, as against 13 of Roux' cases and 18 other ordinary treatment.

Prolongation of life was, however, noticeable in the serum-treated cases, and it was found that, whereas only 3·4 per cent. of the total deaths under the ordinary English treatment occurred after the 6th day of illness, the ratio was was 19 and 17 per cent. in the Lustig and Roux cases respectively.

Modikhana Hospital.

February 1900 ...	Alternate ...	66§	54	81·81	66	48	72·72	*Nil.*
1901	Selection ...	2	1	50·00	...	...	...	...

Government House (Parel) Hospital.

1898	Selection ...	12	3	75·00	...	...	...	...

§ The observations at the Modikhana Hospital were to be conducted on the alternate system, but, instead of there being an equal number of patients on both sides, it was found that there were 66 serum cases, 66 control cases, and 43 "doubtful cases." This matter was investigated by Lieut.-Col. J. S. Wilkins, I.M.S., Special Medical Officer, Plague Operations, who observes—(*vide* Municipal Commissioner's Report on Plague for the year ending 31 May 1900, page 154):—"I regret to have to add that I think the results obtained by the serum treatment at the Modikhana Hospital valueless. The question has been thoroughly gone into by myself, and I cannot help saying that, for all intents and purposes, the observations are useless, as they were carried on without any system."

N.B.—The above statement comprises all the cases treated in the Bombay Hospitals, except 8 cases treated in the Parsee Fever Hospital (during 1899 and 1900), of whom 5 died and 3 recovered.

VIII

THE USE OF LUSTIG'S SERUM IN PRIVATE PRACTICE.

Compared to the observations in public hospitals, the cases treated in private practice were limited and numbered 130 only. Conservative as the local profession must be and undoubtedly is, borrowing as it does, its traditions from the English profession, it speaks well for its liberal-mindedness, that it should not have hesitated to resort to the serum treatment of plague, and should have encouraged patients to place themselves under it. For, no sooner was it known that the locally-made serum was available, there was a constant demand, which unfortunately could not be always complied with, without entailing the risk of interrupting the observations in hospitals. And hence the benefit that could have been derived from it in private practice has not yet been fully demonstrated. Sufficient indications have however been afforded, bearing out the anticipations of the beneficial effects of sero-therapy in plague in private patients, and especially so in the cases treated within the first twenty-four hours of the onset of the symptoms. Whatever other considerations might enter into the discussion of the factors contributing to such favourable results—*e. g.* the greater power of resistance among the better classes from whom the private patients were mainly derived, better surroundings, careful nursing, &c.—the effects of the early application of the serum were too well-marked to be attributable to these alone. Nor were they always present. By far the larger proportion of patients came under observation at a later stage of the disease, and often when other measures had failed to stem the tide of septicæmia. And in several very advanced cases medical men had to inject the patients in deference to wishes of their friends, whereas if left to their own inclinations, they would have desisted from doing so. It cannot, therefore, be contended that the better results as a whole in private practice were due to ideally favourable conditions for the application of the serum.

Whenever it was applied on the first day, it was noticed that the rapidly rising temperature became arrested in its upward course, and remained either stationary or but temporarily elevated; it fell to about the normal the following morning; and after a moderate secondary rise, with but slight oscillations—so characteristic of plague—for a day or two, it again reached the normal on the fourth or fifth morning. The gradually enlarging buboes became hard, painless, less tender, and could be freely handled within a day or two; and subsided slowly without suppuration. The general condition of the patient also considerably improved, the mind and expression cleared; hardly any nervous prostration or enfeeblement of the circulation could be noticed: sleep became natural and the patient was generally cheerful, scarcely realising that he was afflicted with such a grave infection as plague. The fear of any serious complications or danger to

life ceased practically from the fourth or fifth day ; the normal course of the disease was thus curtailed by half, convalescence was hastened, and all serious or lasting mischief to the system thus averted.

In regard to cases treated on and after the second day, the above effects were not so well marked, although there was considerable amelioration in the symptoms ; the course of the disease was not always shortened and suppuration of the buboes was the rule ; convalescence was however not protracted. But the grave changes in the circulatory and nervous systems that follow upon the enormous and rapid multiplication of the plague bacilli within a day or two made themselves evident, and enhanced considerably the difficulties to be contended against ; and, if once septicæmia set in, the chances were almost always against a favourable termination of the case.

The cases treated in private practice extended over four epidemics, and numbered 130 in all. The following statement shows by whom the serum treatment was used and with what results :—

	Number treated.	Died.	Recovered.
The present writer in consultation with medical practitioners	74	40	34
The late Dr. Ismael Jan Mahomed	18	5	13
Dr. Rajaballi V. Patel	16	7	9
,, B. S. Shroff	6	3	3
,, K. S. Engineer	4	...	4
Prof. Galeotti	4	1	3
Dr. Polverini	4	...	4
,, S. S. Batliwala	2	...	2
,, A. Mayr	1	1	...
,, N. F. Surveyor	1	1	...
Total ...	130	58	72

It will be noted from the above that there were 58 deaths and 72 recoveries among the 130 patients, equivalent to a mortality rate of 44·61 per cent. If the mortality rates between the cases treated by the present writer and those treated by other medical men were to be compared, a somewhat striking difference becomes apparent, which may be expressed thus :—

	Number treated.	Died.	Recovered.	Case-mortality per cent.
Present writer	74	40	34	54·05
Other medical men	56	18	38	32·14
			Difference ...	21·91

A difference of nearly 22 per cent. is thus observed, and the reasons for this are not far to seek. The assistance of the present writer was not generally sought till at a later stage of the disease, and, in about half a dozen cases, he had had to use the serum against his own wishes, and in order "to give the patients the best chance" as required by their friends. On the other hand, the medical men who used the serum independently of him had, in the large majority of cases, the advantage of commencing the treatment very early, *i. e.*, on the first day, and were therefore more successful in their results. This evidence fully harmonises with the anticipations of the benefit to be derived from early treatment.

The above patients included all the principal races in this city and they were distributed as follows :—

Race.*	Number.	Died.	Recovered.	Case Mortality per cent.
Europeans	6	2	4	33·33
Parsis	60	22	38	36 66
Mahomedans	26	11	15	42 30
Hindus	31	18	13	58 06
Native Christians...	7	5	2	71·42
Total ...	130	58	72	44·61

The mortality rates, as will be noticed, are progressive, but as the numbers treated in the highest and lowest ratios are limited, no deductions can be drawn from them. Both the European and the five Native-Christian patients who succumbed were septicæmic at the time the serum treatment was applied. And yet the mortality among the former is lower than the average. The mortality rate of 71·42 in the latter is higher than the average recorded among the *hospital patients* of the same class, where it closely approximates to that in Mahomedans. The Parsi, the Mahomedan, and the Hindu mortality rates stand respectively at 36·66, 42·30, and 58·06 per cent., and are considerably lower than under other methods of treatment. The influence of race, so well marked in hospital cases, becomes also evident in private practice and indicates what an important share racial incidence has in modifying the disease and reducing its high mortality.

The benefit of early treatment, above referred to, was well marked. Of the 26 patients treated on the first day of illness, 4 succumbed and 22 recovered, whereas, of the 34 treated on the second day, 20 died and 14 recovered. The mortality rate in the former case being equivalent to 15·38 per cent. only, as against 58·82 among the latter. And this clearly indicates what a few hours' delay would mean in the treatment of such a rapidly fatal infection as that of plague.

* This statement has been revised subsequent to the meeting of the local profession, where particulars for 116 patients only were submitted.

IX

SOME OPINIONS ON THE VALUE OF THE TREATMENT OF PLAGUE WITH LUSTIG'S SERUM.

It has been alleged that high scientific and expert opinion was unfavourable to the treatment with Lustig's serum. What weight or importance should be attached to such statements would be best indicated by the following extracts from the opinions of those who have had the advantage of personal acquaintance with the serum treatment, and who alone should be considered competent to express opinions as to its utility or otherwise :—

SIR THOMAS R. FRASER,

PRESIDENT, INDIAN PLAGUE COMMISSION.

Professor Sir T. R. Fraser, the President of the Indian Plague Commission, observes (page 444 of the report):—

"The results with the several antitoxin sera designed to accomplish this (*i. e.*, rendering the specific virus innocuous within the body of the patient) which have been used in India are certainly encouraging, and justify the hope that, with sera of greater bactericidal and anti-toxic power than those hitherto prepared, more definite therapeutic benefit will be obtained."

REPORT OF THE INDIAN PLAGUE COMMISSION.

Referring to the results of treatment of plague with Lustig's serum at the Arthur Road Hospital on the "alternate system" (May 1899 to August 1900) the Commissioners observe at page 317, para. 565 :—

"We have here at last a result obtained by a method which satisfies the demands formulated in a previous section. The diminution of plague mortality by 11·5 per cent. in such an extensive series of cases treated with the serum seems to us—assuming, as we presume we may do, the correctness of the records—conclusive as to benefit having been derived from the administration of the serum."

At page 319, para. 570, they say: "To sum up, we think we may, not only in view of the facts summarised above, but also of the unequivocal opinion expressed by Dr. Simond, Captain Mason, R.A.M.C., Dr. Choksy and Dr. Nazareth, as to an improvement having been witnessed by them in the clinical symptoms of patients treated with the serum, conclude that, on the whole, a certain amount of advantage in all probability accrued to the patients, both in the case of those injected with Yersin's serum and of those injected with Lustig's serum."

In paragraph 571, they state that, "with regard to the *future preparation* and *therapeutic employment* of *anti-plague sera in India*, they offer the following suggestions :—

1. They opine that, although the results of the serum treatment in plague have not been so successful as in diphtheria, none the less, the method of serum therapy is in plague, as in other infectious diseases, the only method which holds forth a prospect of ultimate success.

2. They suggest that, instead of striving after treating with the serum the largest number of patients possible, efforts should be made to *perfecting the preparation and application of* the *serum*, and with that object the blood changes that occur in the animals that are immunised for preparing the serum should be studied. And similarly the blood of plague patients should be examined *before* and *after* injecting the serum.

3. That in the future preparation of sera in India the simpler methods of Yersin and others should not be neglected.

DR. J. A. TURNER D. P. H.,

EXECUTIVE HEALTH OFFICER, BOMBAY MUNICIPALITY.

The following extracts are derived from Dr. Turner's address at the meeting of the Local Medical Profession :—

"At the present stage of serum treatment we are not in a position to say that it is a total failure. It has shown proofs of its efficiency by facts and figures. At times the results may not fulfil all our expectations, yet serum carefully prepared and administered under proper conditions cannot but produce some good effect. It has, in very many cases, prolonged life and ameliorated the conditions of the patient."

* * * * * * *

"From the experiments which have been performed much knowledge has been gained, but much labour and time will still be required before any practical result can be obtained. The object for which the Municipality instituted the laboratory for the preparation of an anti-plague serum has only partly been accomplished. The results so far as obtaining an antidote for plague have not been successful ; but that many valuable lives have been saved cannot be denied, and it has supplemented the knowledge obtained by the most recent observers. Results of scientific investigations of the most delicate and tedious and dangerous description cannot be made to order. In the time of panic the preparation of serum began ; immediate demand was made for serum, of which great things were expected ; the results were hurried ; the serum was used before it was ready. The class of patients on whom it was tried and the condition of the hospital treatment were all against successful results. Even if the serum was the best obtainable, I do not ask you to accept all or any of the figures as promising that Lustig's plague serum is the antidote for plague. I maintain, however, that here in

this city of Bombay, where plague has existed for six years, scientific investigation into the cause and cure of the disease ought to be carried out. The Municipality have all along been the pioneers of both curative and prophylactic remedies, and that body has shown much public spirit in providing ways and means for investigation; it cannot be expected to continue to spend such large sums on what is practically an Imperial question. I submit to you, therefore, that in the interests of the public health not only of Bombay, but the whole of India and the world, further research should proceed in the direction of serum therapeutics. I believe that the Corporation of Bombay, which has done so much hitherto, would be glad to assist in this, and that the Government of India should be requested to continue research work in the serum treatment of plague in Bombay, which is the largest city in India, and where more material is at hand to carry on the work."

* * * * * * *

"Drs. Polverini and Mayr have worked laboriously under great difficulties, and their reports show that by the results of their labours, both in the preparation of the serum and its clinical use, our knowledge of the serum treatment has been increased. Naturally they raise a voice of protest against the discontinuance of the serum preparation for the following reasons:—(1) Because there is no prospect at present of the preparation of Professor Lustig's serum being taken up elsewhere so that much of the experience gained here will be lost; (2) because the preparation of Professor Lustig's serum is less dangerous and requires less trained assistance than that of other anti-plague sera; (3) because there is here the opportunity of obtaining fresh cultures from plague-patients for the purpose of immunisation, a desideratum which we think of great importance; (4) because there is here the possibility of testing the serum immediately on man. It is the collaboration of the laboratory and the hospital which promises the best results; (5) because the experiments made during the last year make us confident that the manufacture of the serum is still capable of considerable improvement; and (6) because many problems which suggested themselves in the course of the manufacture and application of the serum are still awaiting solution. This then is shortly our knowledge of the preparation and treatment by serum in Bombay. It has been urged by Dr. Choksy, Dr. Polverini and Dr. Mayr, three gentlemen who have the most intimate acquaintance with the preparation and use of the serum, that we should not be discouraged by the results. They point out that because the serum prepared here has failed to produce good results in patients who are practically moribund it is unfair to condemn it altogether, and I agree with them."

* * * * * * *

"Patient and laborious work, unfettered by official red tape and constant inquiries into results, is required before we can say that serum-therapy as a curative for plague is or is not possible."

COLONEL T. S. WEIR, I. M. S.,

LATE EXECUTIVE HEALTH OFFICER, BOMBAY MUNICIPALITY.

Colonel Weir who strongly supported the serum treatment, has stated that even a 10 per cent. reduction in mortality was not to be despised or discarded in a disease that killed 80 patients out of every 100, and that it meant the saving of 100 more lives out of every 1,000 cases. Is this a matter of no consequence?

PROFESSOR MAX SCHOTTELIUS,

PROFESSOR OF HYGIENE, UNIVERSITY OF FREIBURG, BADEN, GERMANY.

Professor Schottelius visited Bombay during the height of the epidemic of 1899-1900, and made observations on plague at the various hospitals. He published the same in the Journal of the Hygienic Institute of Freiburg, in the course of which he stated :—

"More accessible (than Haffkine's results of preventive inoculation against plague) to scientific criticism and control are the results of Lustig's curative plague serum which is prepared at the Municipal Laboratory at Bombay."

Professor Schottelius accepts, without the least hesitation, the results of the alternate method of treatment as absolutely correct, and further observes :—"The French (Roux-Yersin's) serum is no doubt unlucky in India, and more discredited than it deserves. It should be possible to make in Bombay another extended trial. Lustig's serum is also not yet perfect, but it is capable of improvement if both the laboratories, whose sera up to now have given the best results, were to work in collaboration ; and, if that is done, the best results can be expected."

PROFESSOR MARTIN HAHN,

EXTRAORDINARY PROFESSOR OF HYGIENE, MUNICH.

Professor Hahn, who was in Bombay during March and April 1901, had an opportunity of observing the treatment of plague with Lustig's serum at the Arthur Road Hospital, and, in a lecture that he delivered before the Medical Society of Berlin, expressed himself thus on the subject :—"The serum is almost exclusively used in the Arthur Road Hospital, where, by the personality of the officer in charge and the organisation of the hospital, guarantee is given for the correct observation of the results obtained. If we consider that chiefly grave cases only are brought to the hospital, the reduction of the mortality by 12 per cent. obtained during the alternate treatment in 1900—which might be improved upon in future—seems relatively favourable. Still it cannot be denied that at present (1901), owing to the large doses which are needed, the serum cannot as yet be considered as a means of combating plague *on a large scale.* This, however, does not imply that

further investigations, which are already supported by Government and which ought to be supported more liberally, may not lead to still more favourable results."

COLONEL J. S. WILKINS, I. M. S.,

LATE SPECIAL MEDICAL OFFICER, PLAGUE OPERATIONS BOMBAY.

Colonel Wilkins thus concludes his remarks on the serum treatment (page 405, Report of the Municipal Commissioner on the Plague in Bombay for the year ending 31st March 1899):—

"I am personally of opinion that the manufacture of this serum should be continued as long as the results given are hopeful, which they decidedly are; or until some other and more potent remedy is found to act on this most fatal disease."

Referring to Dr. Choksy's method of selection of cases for treatment with the serum, Colonel Wilkins observes (page 393 of the above report): "I think it ought to be noted that, although there is an idea that the cases selected for inoculation must have been favourable ones, and that the unfavourable cases were not inoculated, the mortality among the non-inoculated which, one would think, ought in consequence, to be higher than the general rate of mortality in other hospitals, is as a matter of fact almost the same. This perhaps shows that Dr. Choksy's selections were fair and unbiassed, and that the serum did account for the difference between the inoculated and non-inoculated on its own merits."

Again Colonel Wilkins in the report for the year ending 31st May, 1900, (page 154) states :—

"In summing up the results of the effects of Lustig's serum, I am of opinion that it is of the greatest value as a curative agent if employed in the early stages of the disease. . . The serum "is a valuable curative agent, but a great deal depends on the conditions in which the patient is situated."

MAJOR W. E. JENNINGS, I. M. S.,

LATE SPECIAL MEDICAL OFFICER, PLAGUE OPERATIONS BOMBAY.

Major Jennings observes at pages 152-153 of the Report for the year ending 31st May, 1901 :—"We are not in a much better position, further, regarding the effects of Professor Lustig's curative serum this year than we were last year, owing to the fact that only a limited number of experiments was possible during the period under report. . . . . The unusual virulence in the type of the disease during this epidemic rendered it necessary that at least three times the quantity of serum as was found to be sufficient for each case last year was required this year before any visible result could be obtained." Referring to the comparatively smaller results in favour of the serum treatment at the Arthur Road and Maratha Hospitals, he observes:

"These results, however, are not to be despised, especially when it is remembered that the advantage gained at the Maratha Hospital was at a time when the percentage of mortality among cases treated by other methods was 88·8. The treatment acts best in cases where there are not multiple buboes and which are not septicæmic in character on admission. . . . . Although the percentage of cases, however, in which death was averted by the serum was less than in previous years, yet the clinical histories show that, in many of the fatal cases in the serum group, life was prolonged, and acute symptoms ameliorated to a considerable extent."

Major Jennings, in the preface to a compilation of papers in connection with Lustig's serum (23rd July 1901), concludes :—

"A careful study of these statistics will indicate that this form of treatment has given more encouraging results than any other, even in an epidemic in which the type was more severe than in previous years, and during which it was possible to conduct a limited number of experiments."

X

CONCLUSION.

The study of the preceding papers indicate that we have arrived at that stage in the progress of sero-therapy in plague when we can summarise our knowledge and experience for future guidance and further research. The last two epidemics have been fruitful of interesting and not less useful observation, in the course of which we have had to unlearn something, to learn a great deal, and to find that much yet remains to be learnt.

We now know, for instance, that plague is a much more complex and deadly disease than what it had been considered to be during its earlier visitations. That it does not exist in or take on the same form, or exhibit the same virulence, year after year or even during the progress of a single epidemic. That, in its variability of type and virulence, it stands apart from other infectious or contagious disorders. That it is not comparable to diphtheria, with the results of sero-therapy in which it has been usual to compare the results of sero-therapy in plague; and that there exist such essential and radical differences between the nature, course, and fatality of the two affections that they would not admit of such comparison in strict conformity with the usual and accepted canons of scientific investigation. That, as, in the words of the Indian Plague Commission, we cannot have a comparison between things that are not in any respect comparable, the comparison of diphtheria with plague is at once placed out of court. And, finally, that the expectations of brilliant results from sero-therapy in plague that were once entertained in some quarters were premature and dictated by the want of proper appreciation of the nature and gravity of the disease.

We have learnt—

1. That, for purposes of serum treatment, plague-patients are divisible into two main groups : the non-septicæmic and the septicæmic.

2. That the serum—Lustig's or Roux-Yersin's—is capable of considerably reducing the case mortality of plague in the non-septicæmic cases, but that in the septicæmic (when bacilli are found in blood by culture) both are equally of no avail; they cannot avert death; all that they do is to prolong life.

3. That the above applies to the patients treated at Bombay only, as, from the published records of the epidemics at Oporto and Glasgow, we find that Europeans even with grave septicæmia recovered there under the Roux-Yersin's serum.

4. That any hope of achieving better results in septicæmic cases by systematic intravenous injections of the serum must be abandoned, inasmuch as it has not been found advantageous or practicable to adopt largely this procedure in hospital practice and it is next to impossible to introduce it in private practice in India.

5. That, for success in non-septicæmic cases, reliance must be placed solely on sub-cutaneous injections, and that the only way to achieve good results is to subject the patient to the serum treatment as soon after the disease declares itself as possible.

6. That time is the essence of successful sero-therapy in plague, and it must not be wasted in futile efforts at self-deception when once the disease has declared itself by clear and unmistakeable symptoms.

This then is the present position of the serum treatment of plague. Along what lines investigations should be extended has been already suggested. But whether, even supplemented by the results of these and other similar observations, we would eventually succeed in preparing a serum capable of curing cases of septicæmic plague is more than one can predict; the probabilities appear at present to be anything but hopeful, and Professor Sir Thomas R. Fraser, the President of the Indian Plague Commission is of the same opinion.

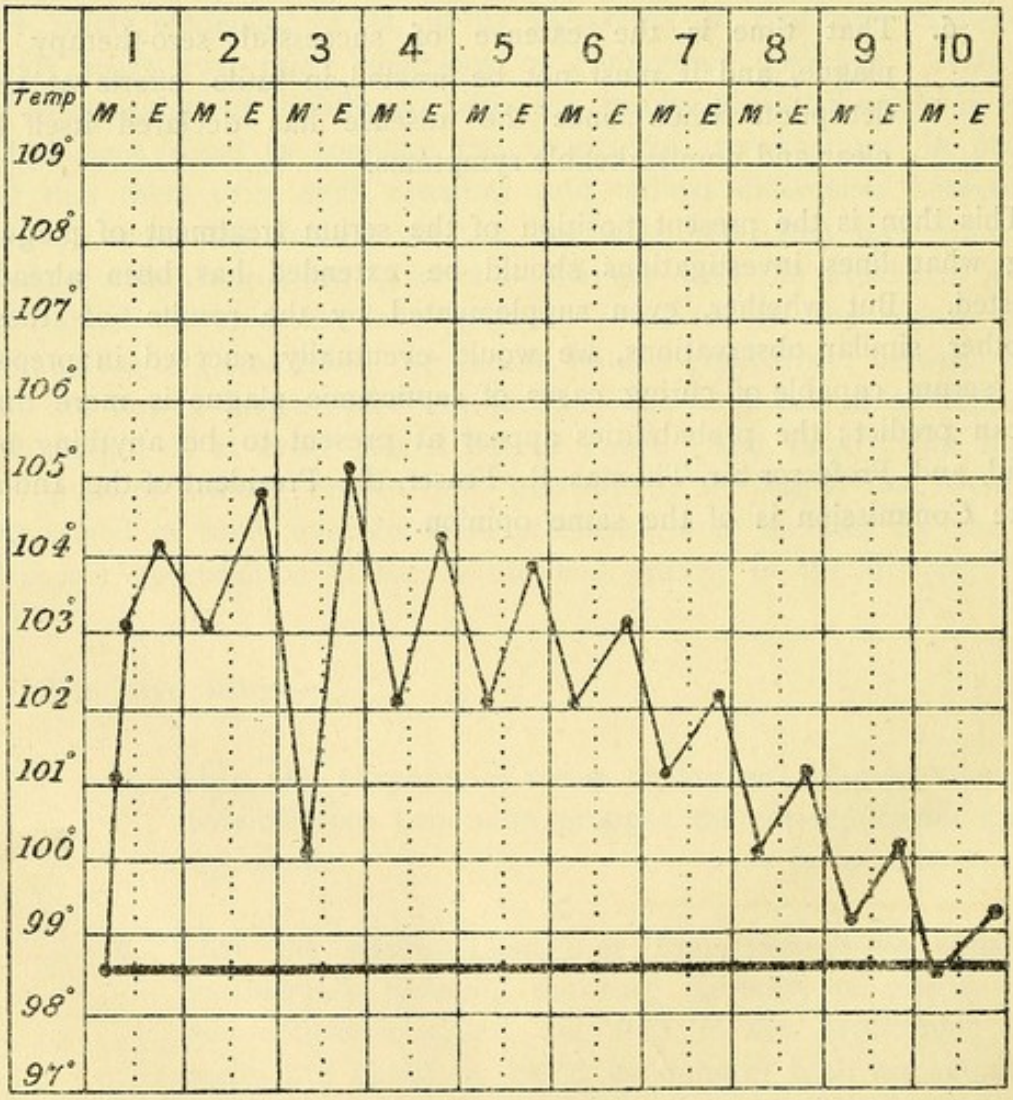
APPENDICES

A.

ILLUSTRATIVE CASES.

The preceding account of the observations with Lustig's serum would not be complete without a few illustrative cases demonstrating its action under the various conditions under which it was employed. With this view 23 cases have been selected, and, in order to allow of comparison between them and the cases naturally ending in recovery and death, one chart of each of the latter has also been included.

The normal plague chart of a patient recovering under ordinary treatment and without any unusual complications is quite characteristic of the disease. The temperature curve is divisible into at least two, if not three,



A normal plague chart.—(Somewhat schematic).

separate curves. The first curve begins with the initial symptoms, attains its maximum intensity on the evening of the second or third day, and terminates with a drop of two, three, or more degrees on the morning of the third or fourth days respectively. And although the temperature may be 97° or even lower, there is no corresponding improvement in the pulse or in the general condition of the patient.

Within a few hours, the second curve begins its upward course; the temperature attains to the level of the preceding evening or mounts higher, and all the symptoms become coincidently grave. It falls by two degrees or more the following morning, and thereafter morning and evening remissions and exacerbations continue, although on a lower plane, till the sixth or seventh day, when the second curve may be said to terminate. Both the first and second curves are liable to many variations, and in no two cases are they exactly alike But the above chart, somewhat schematic though it is, indicates fairly the normal course. The third curve begins on the sixth or seventh morning and takes one of two courses:—there is either a gradual step-like fall by lysis from day to day until the normal is reached on the morning of the tenth day, or the oscillations may continue for two or three days, though lower than in the second curve, and the temperature falls to normal by crisis on the same day. The former is the more usual course, although the latter is by no means infrequent. The range of the crisis is not great and does not generally exceed three degrees or so. The normal course, therefore, of a case of plague ending in recovery may be taken to be ten days: this time-limit is liable to be reduced to eight days or may become extended to twelve or more in uncomplicated cases, everything depending upon the severity of the infection and the suppuration or otherwise of the buboes; deep-seated suppuration, or local sloughing, may also contribute to a more extended curve. Comparing the above chart with those that follow, it will become apparent that the normal course of the disease is considerably shortened under the timely application of the serum.

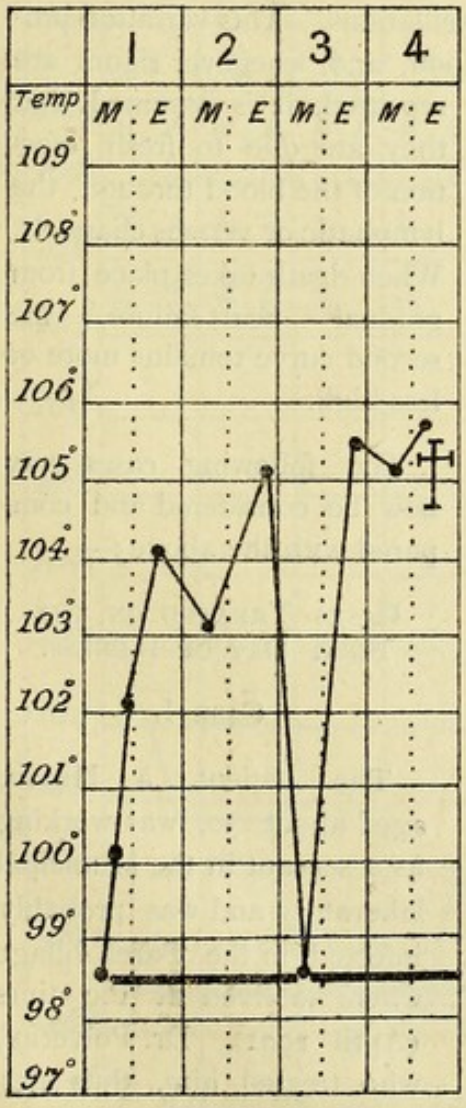
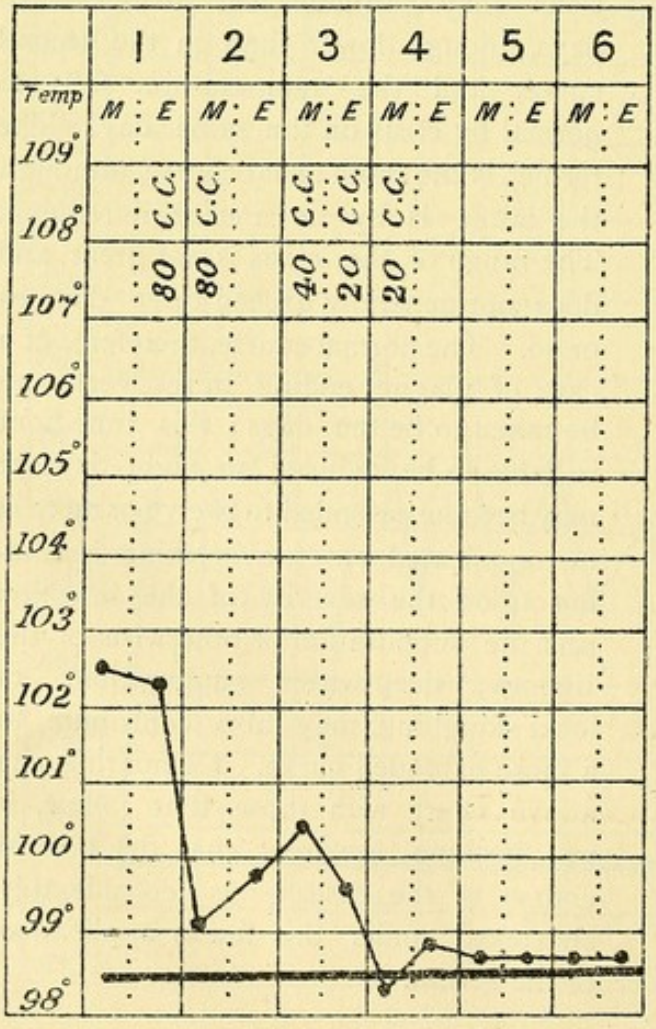


Chart of a plague case who died on the evening of the fourth day.

The next chart shows the temperature curve in a patient who died on the fourth day. In this connection it has to be remembered that, except in the most virulent and malignant form of infection,—which has been happily so rare in this country,—plague does not carry off the patient on the first or second day. The heaviest mortality takes place from the third to the fifth day, and thereafter the rate becomes gradually less as the duration of illness is prolonged. Here, too, it will be noticed that the temperature curve consists of two curves. The first is similar to that in the case ending in recovery, but the second curve, that begins on the morning of the third or fourth day, is liable to considerable variations according as to whether the patient becomes septicæmic or dies from heart-failure. For, not every case that dies on the fourth or fifth day is necessarily septicæmic, and in many instances repeated examinations and cultures from blood taken shortly before death have failed to reveal the presence of the plague bacilli. In the former case, the temperature curve takes on the usual features associated with any kind of septicæmia, with frequent remissions and exacerbations, the latter generally accompanied with rigors, or the temperature remains more or less sustained until death with but slight oscillations. This variation probably depends upon the infection of the blood, and, whenever rigors are repeated, it is assumed that they are due to fresh infection of the blood through the lymphatic or venous channels. When death takes place from gradual heart-failure, the second curve remains more or less high.

I.



The following cases may now be considered and compared with the above :—

Cases Treated on the First Day of Illness.

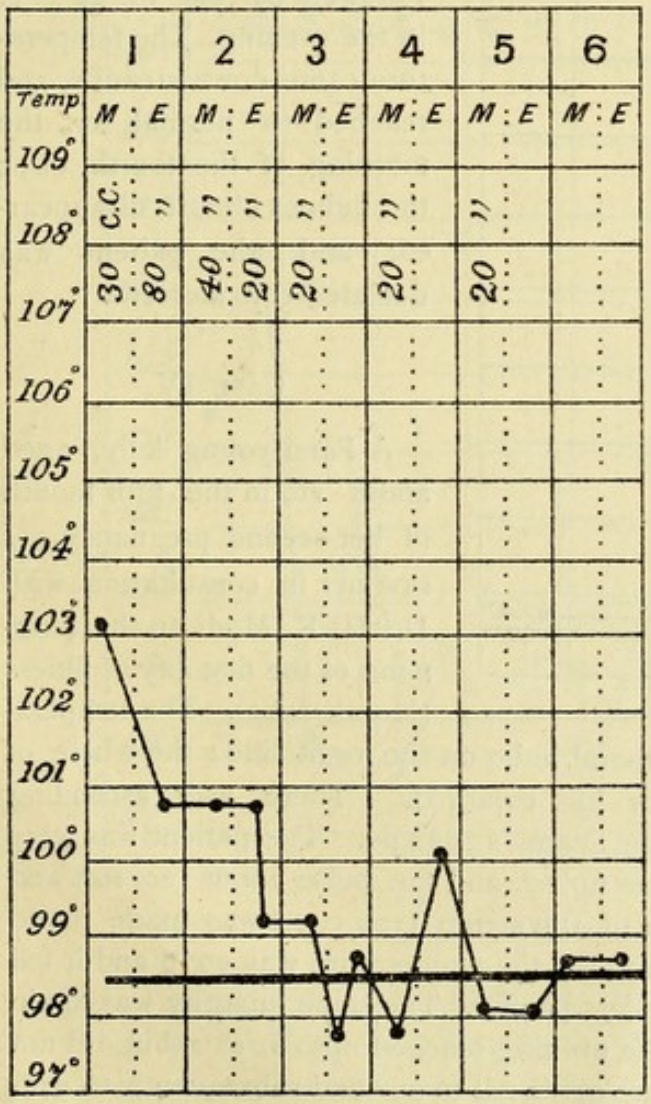
Case I.

The patient, a Hindu, aged about 30, was working as a servant in the Municipal laboratory and was probably infected in the Parel village where he lived at the time (April 1901). Dr. Polverini, who treated him, thus describes the case :—"The most remarkable thing in this case

was the rapidity of absorption of the bubo (left axillary). The patient was all right at 9 A.M., got fever at about 10-30, and at 4 P.M., when first I saw him, had a very large tender bubo in the left axilla with extensive infiltration. The first serum injection of 80 c. c. was made all round the bubo; on the following morning the pain was found to be much less, the infiltration had diminished, and the bubo smaller; another 80 c. c. were injected; and also 40 c. c. on the morning of the third day. By this time, the pain, tenderness, the bubo, and the infiltration were hardly noticeable. Two more injections of 20 c. c. each were made on the evening of the third and morning of the fourth day respectively, and the patient was practically convalescent on the fifth day." The temperature curve shows an immediate fall after the first injection, followed by a second curve of short duration, and final drop to the normal on the morning of the fourth day.

CASE II.

II.

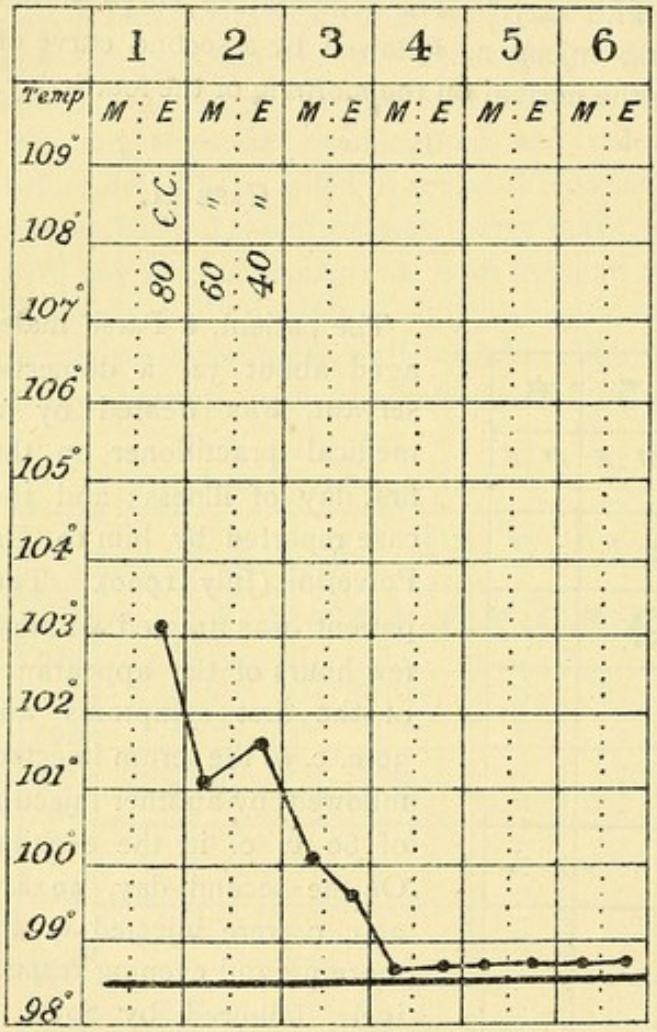


The patient, a Parsi male, aged about 32, a domestic servant, was treated by a medical practitioner on the first day of illness; and the case reported by him to Dr. Polverini (July 1900). The patient was treated within a few hours of the appearance of the first symptoms and 30 c. c. of the serum injected, followed by another injection of 80 c. c. in the evening. On the second day, 40 and 20 c. c. were injected in the morning and evening respectively, followed by 20 c. c. each on the morning of the third, fourth, and fifth day. The temperature curve indicates a gradual but steady decline and the second curve is scarcely evident. The patient was practically convalescent on the fifth day. The bubo (femoral ?) became rapidly absorbed.

Case III.

Dr.——,European, who was working with Dr. Polverini in the Municipal laboratory for the preparation of the serum, became infected in the course of his work. (July 1901). Whilst in the laboratory (about 3 P.M.) he got a rigor, followed by rise of temperature, which went up to 103° in a few hours, and femoral and inguinal buboes developed on the left side. Within five hours of the initial symptoms Dr. Polverini injected him with 80 c. c. of the serum round about the buboes. When I saw him the following morning, the temperature was 101°, the buboes distinctly smaller, and less painful. Another injection of 60 c. c. was made and was followed by one of 40 c. c. in the evening. The temperature came down steadily and reached to normal on the morning of the fourth day; the buboes almost disappeared, and the patient was declared convalescent.

III.

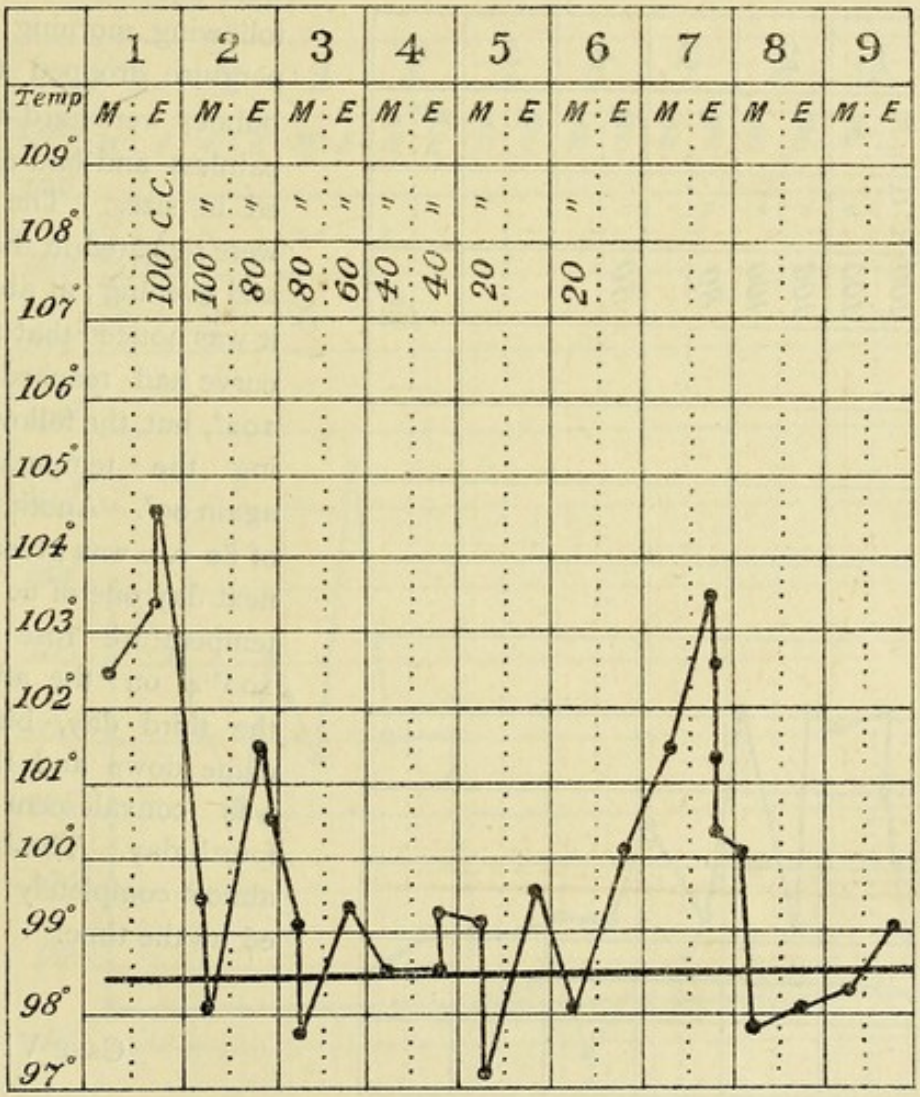


Case IV.

A Parsi young lady, aged about 26, in the fifth month of her second pregnancy. I saw her in consultation with Dr. H. R. Modi on the afternoon of the first day of illness (March 1902). The temperature was 104°·4; there was a femoral bubo on the right side; the whole of the femoral chain was more or less enlarged. There was ascending lymphangitis from the ankle to the Scarpa's triangle. The patient was very restless, flushed in the face, tongue furred, and the pulse about 120, soft and compressible. The first injection of the serum (100 c. c.) was made round about the bubo; the following morning the temperature was 99°·6 and it fell gradually to 98°·2; the bubo was less painful. The same quantity was again injected. The second curve in the evening reached upto 101°·2 but did not continue long, and the temperature again fell to 99° and subsequently to 97°. The further injections are shown in the chart, and were continued as a matter

of precaution; the patient was practically convalescent on the fifth day, when the bubo had almost disappeared. A bilious crisis supervened on the seventh day, and led to a temporary rise of temperature; from the ninth to the twenty-fourth day the patient suffered from general arthritis, and almost every principal joint of the body, not excluding even the tempero-maxillary articulation, was affected one by one. Some erythema also developed. Eventually she made a good recovery, and abortion, which is almost invariably the rule in plague cases, leading generally to a fatal termination, was no doubt averted by the timely application of the serum.

IV.

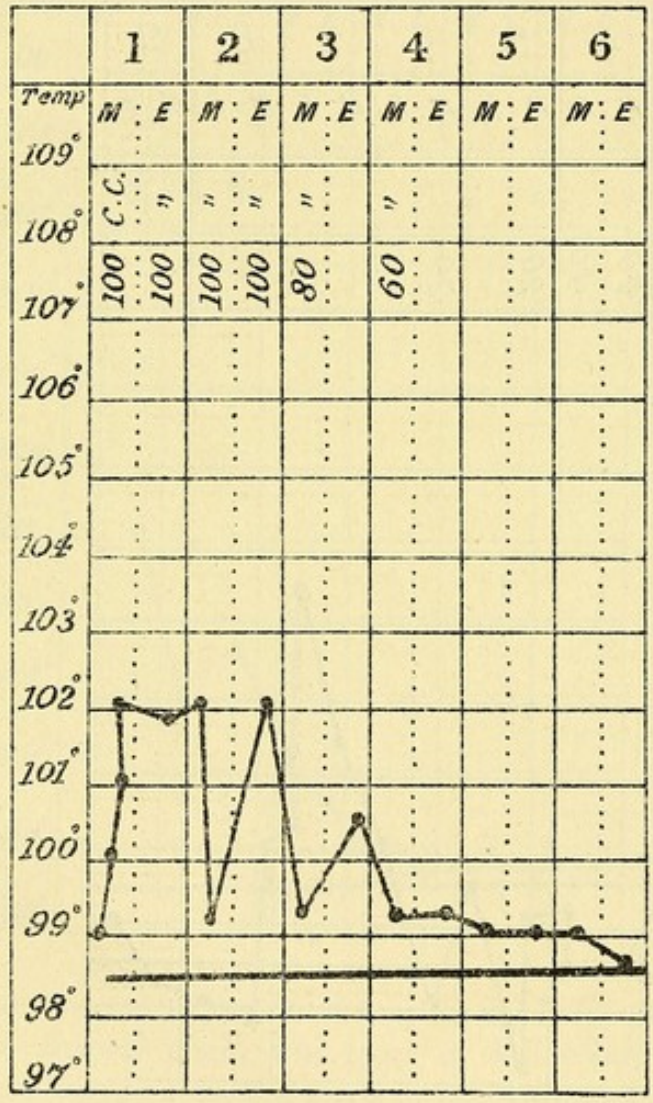


Case V.

The patient, a Parsi male, aged about 33, I saw in consultation with Drs. De Silva and Bomonjee Framjee on 13th April 1902. He was all right the previous day and had attended to his work. On that morning he got up with slight pain in both the groins, which was preceded by

rigors some hours previously. The temperature at 8 a. m. was about 99° and rose steadily, and when I saw him at about noon it was 102°. The face was flushed, pulse about 100, of good tension and volume; he had developed femoro-inguinal buboes on both the sides, which were tender and painful. There was also some infiltration around the buboes, which had been gradually enlarging in size with the rise of temperature. The first injection of serum was made contiguous to the buboes, and 50 c.c. were injected on either side. Soon after the injection it was noticed that the upward course of the temperature was arrested, and in the evening it was found to be stationary, when another 100 c. c. were injected as before. The following morning the temperature dropped to 99°, the buboes were hard and almost painless and had not increased in size. The injections were repeated in the morning and evening; at about 6 p.m. it was noticed that the second curve had reached to about 102°, but the following morning the temperature was again 99°. Another injection of 80 c.c. was given and the next day one of 60 c.c. The temperature rose to about 100°·4 on the afternoon of the third day, but it soon came down and the patient was convalescent on the fourth day. The buboes had almost completely disappeared by the time.

V.

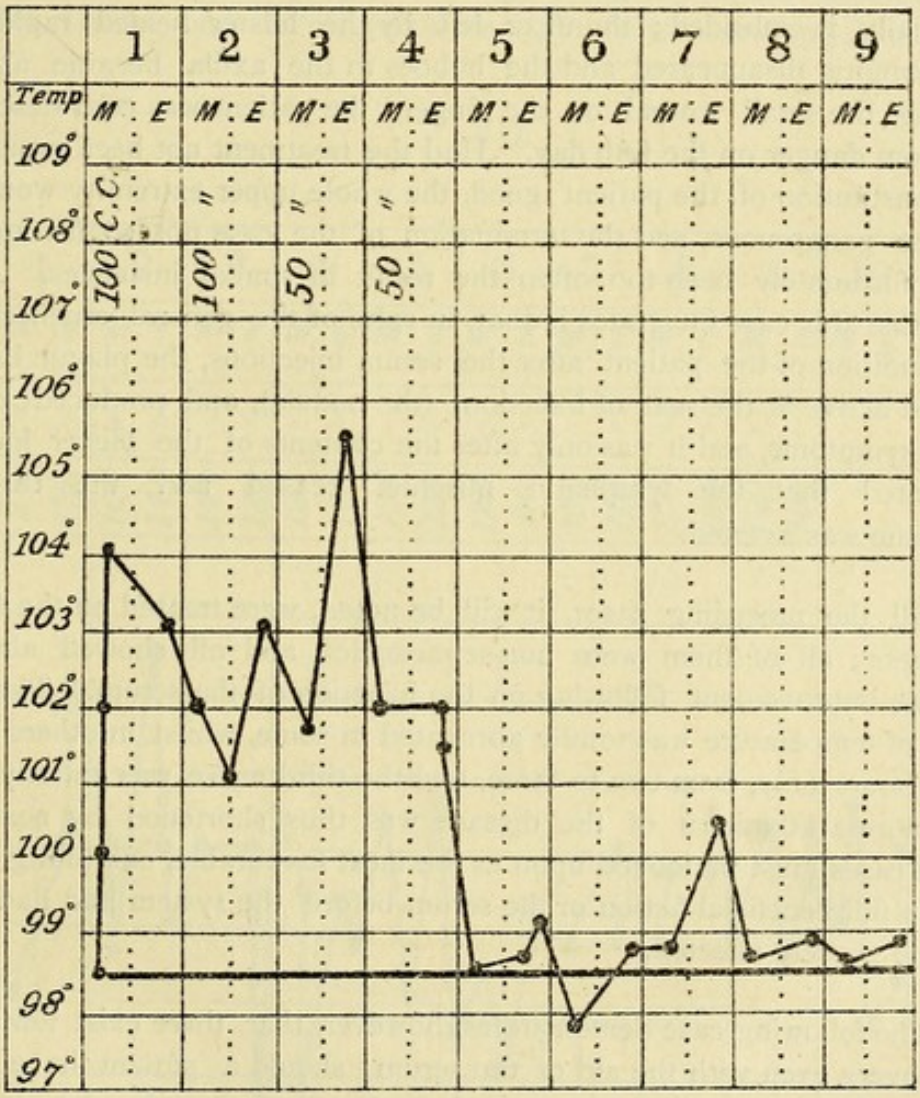


CASE VI.

Assistant Surgeon——, European, aged 40, House Surgeon of one of the local hospitals. I was asked to see him by Lieut-Colonel Henderson, I. M. S., and Lieut-Colonel Wilkins, I. M. S., the then Special Medical Officer, Plague Operations, Bombay. The patient was attending to his duties in the out-patient department till 10 A. M. (30th September 1900), when he was seized with sudden rigors and took to bed. When seen about two-and-a-half hours later, the temperature had risen to 104°, the face

flushed, eyes injected, and he was rather excited and restless. A hard nodule, the size of a small pea, was noticed on the tip of the index finger of the left hand; the superficial lymphatic vessels were found to be inflamed, and could be traced up from the spot along the dorsum of the hand up the fore-arm and arm to the axilla. In the axilla, a bunch of tender buboes was noticed. The case was diagnosed as plague, although the patient most vehemently protested, as plague patients usually do, that he was not suffering from the affection and that he needed no serum injections. After some persuasion he was prevailed upon and 100 c. c. were

VI.



injected. The temperature in the evening was found to be 103°. The following morning it was 102° and at about noon it was a degree less. The buboes in the axilla were less painful and the nodule on the finger-tip remained much the same. Another injection of 100 c. c. was given. The temperature on the evening of the second day (the second curve) was 103° and on the following morning it fell to 101°·8. As there was steady improvement,

the dose of the serum was reduced to 50 c. c. on the third day. That evening the temperature rose again to 105°·4, the patient passed a very restless night and complained of intense burning pain at the tip of the finger. The nodule when seen on the morning of the fourth day (temperature 102°) was found to have developed into a blister, which was incised, and cultures on sloped agar were made from its contents, which were sero-sanious. Another injection of 50 c. c. was made; he felt very comfortable after the blister was opened. The temperature remained steady that evening; he passed a good night, and on the morning of the fifth day the temperature was normal. The agar tubes showed a pure growth of plague bacilli within 24 hours. An irregular patch of skin on the dorsum of the left hand assumed a rather dusky hue on the third day, as if localised gangrene was threatened, but eventually it subsided; the ulcer left by the blister healed rapidly; the lymphangitis disappeared and the buboes in the axilla became absorbed. Barring the small wound on the finger, the patient was convalescent and free from danger on the fifth day. Had the treatment not been prompt, and the constitution of the patient good, the whole upper extremity would have become gangrenous, and the termination of the case not so favourable as has unfortunately been too often the result in similar instances. Another point that this case illustrates is that, in spite of the general amelioration in the condition of the patient after the serum injections, the plague bacilli remained active at the seat of infection, (the nodule), and produced constitutional symptoms, and it was only after the contents of the blister had been evacuated that the lymphatic mischief ceased and the threatened gangrene was averted.

All the preceding cases, it will be noted, were treated on the first day of illness; all of them were non-septicæmic; and all showed almost immediate improvement following on the injection of the serum. The second curve of temperature was totally abrogated in some, whilst in others it lasted a few hours only, from two to three, and the third curve was entirely absent. The normal duration of the disease was thus shortened by nearly half. These cases must be looked upon as the most favourable, exhibiting, as they do, the full beneficial action of the serum before the system had had time to become gravely affected.

The following case demonstrates, however, that there exist few chances of recovery even with the aid of the serum should a patient have become septicæmic within a few hours; and further that, though such cases end fatally within from 24 to 48 hours, the serum treatment is capable of prolonging the life till the tenth or eleventh day.

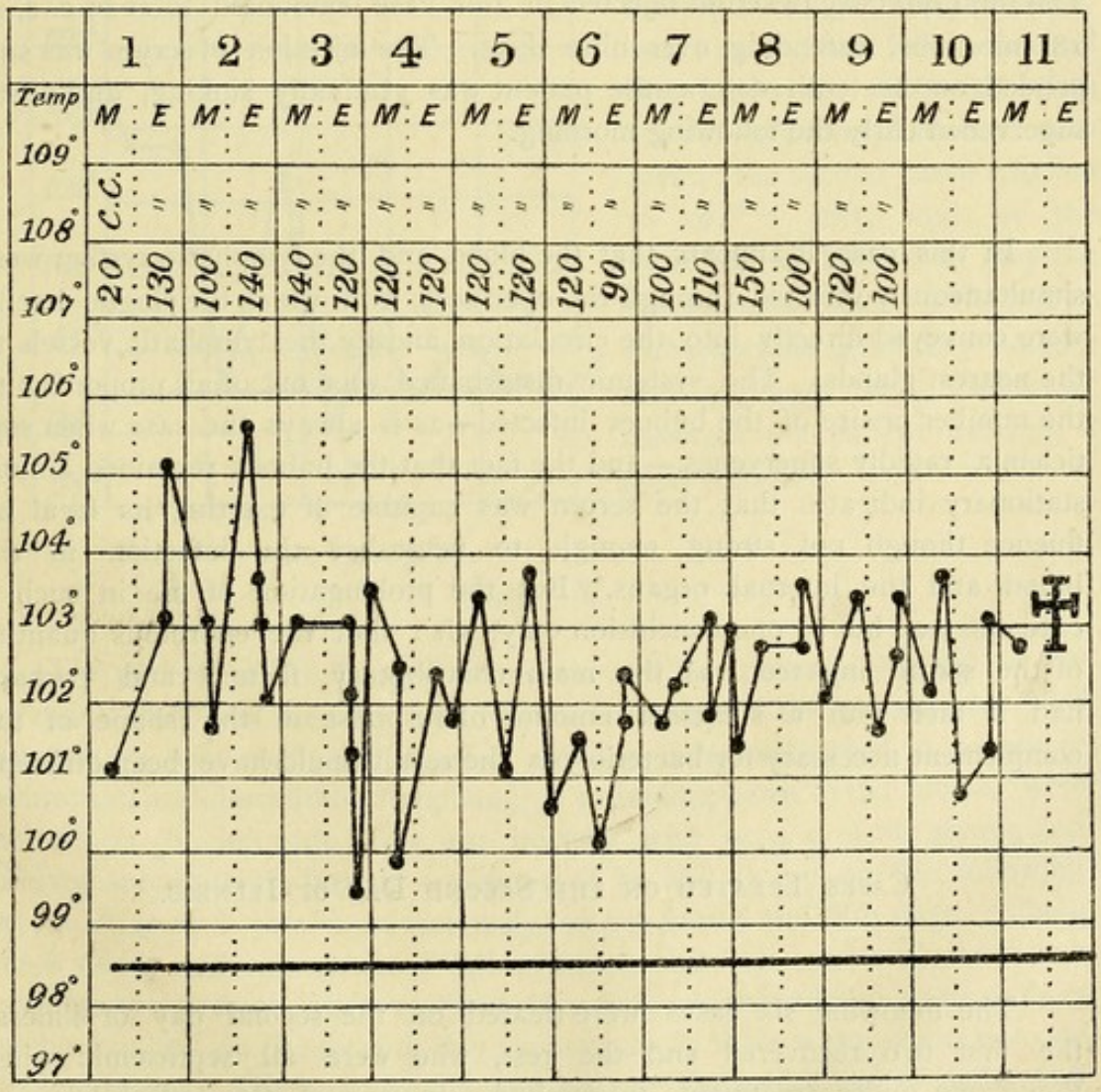
Case VII.

The patient was a Parsi lady, aged about 38, well built, though rather anæmic, on account of some ovarian trouble, for which she was under the

treatment of Dr. Jehangir J. Cursetjee. She had had an open sore, the result of a blister on the abdomen, over the ovarian region, and in this state she went to nurse some relatives suffering from the plague in a badly-infected quarter of the city.

What with constant anxiety, want of proper rest and food, consequent on the demise of some of them, she felt rather feverish and returned home, and it was found that she had a temperature of 101°. Although there were no indications of plague, she was injected with 20 c.c. of the serum as a matter of precaution. When I saw her the same evening, the patient had an extremely anxious and frightened look, breathing was shallow and rapid, and the pulse irregularly intermittent, thready, and often almost imperceptible. Two tiny buboes had developed in the right femoral and inguinal region.

VII.



There was now no doubt that the patient was suffering from plague, with grave cardio-vascular paresis, foreboding rapid cardiac failure. In fact, all the symptoms pointed to a rapidly fatal termination, probably during the course of the night. Cardiac stimulants were freely resorted to, both hypodermically and by the mouth, and 130 c. c. of serum injected in the neighbourhood of the buboes. It will be noticed from the chart that the serum injections were continued although the temperature curve indicated septicæmia.

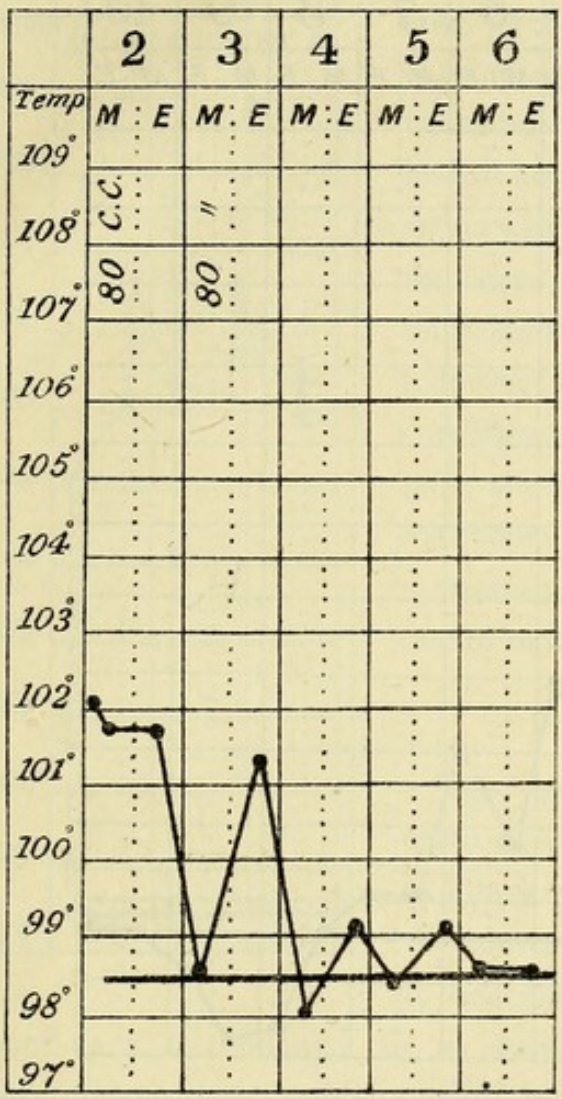
There was considerable improvement in the condition of the patient, following after the serum injections; the heart's action was kept up, and the buboes remained small and painless up to the eighth day, when they became visibly larger, swollen and tender; they again subsided by the evening after further injection of the serum in their neighbourhood; on the ninth day, there was noticed some infiltration on the thigh, the buboes remained stationary, and, on the tenth, a deep iliac bubo could be felt on the same side. The total quantity of serum injected in this case amounted to 2020 c. c, in 18 injections, extending over nine days. The injection of serum was suspended on the tenth day, as the patient was gradually sinking, and death supervened early the following morning.

In this case, it appears that the blood and the lymphatic system were simultaneously infected through the open sore, from which the plague bacilli were conveyed directly into the circulation, and by the lymphatic vessels to the nearest glands. The systemic disturbance was out of all proportion to the number or size of the buboes infected—as is always the case when septicæmia rapidly supervenes,—and the fact that the buboes remained almost stationary indicates that the serum was capable of exerting its local influence though not strong enough to neutralise the infection in the blood and the internal organs. But the prolongation of life in such a case can lead but to one conclusion only, viz: that the enormous quantity of the serum injected was the main contributory factor, and perhaps had it met with a sufficient amount of response in the shape of the complement necessary for bacteriolysis the result would have been different.

Cases Treated on the Second Day of Illness.

The following six cases were treated on the second day of illness; the first two recovered and the rest, who were all septicæmic when they came under treatment, succumbed. In one of the latter, life was prolonged for nine days.

VIII.



Case VIII.

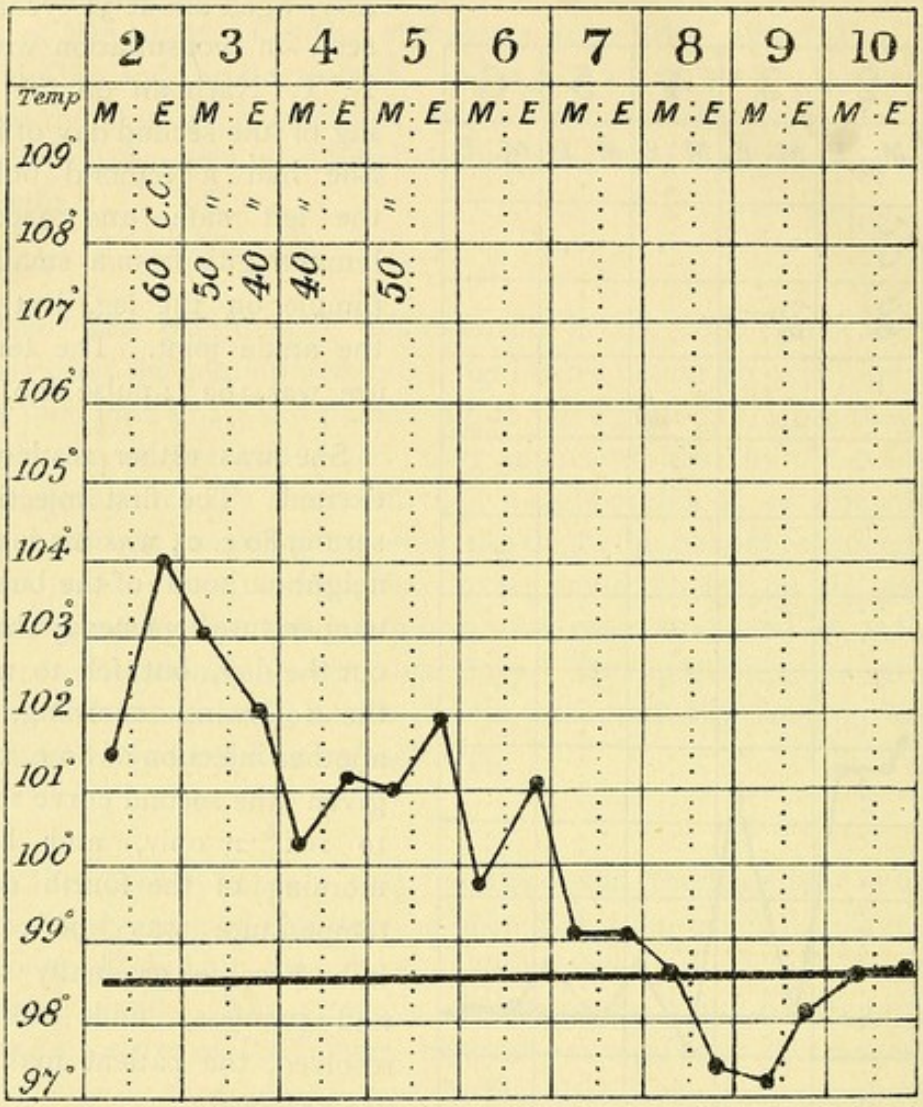
The patient, a Parsi young lady, aged about 30 years, was seen in consultation with Dr. R. T. Nariman on the morning of the second day of illness. She had a femoral bubo on the left side, and ascending lymphangitis from a small open pimple on the leg, just above the ankle joint. The temperature was 102°; pulse 120.

She was rather restless and excited. The first injection of serum, 80 c. c., was made in the neighbourhood of the bubo, the temperature kept steady throughout the day, but fell to normal the following morning, when another injection of 80 c. c. was given; the second curve reached to 101°·2 only, and by the morning of the fourth day the temperature was 98°. The bubo became gradually smaller and painless, and eventually resolved, the patient making a good recovery.

Case IX.

The patient, a Hindu, aged about 28, was the personal servant of Dr. Polverini, and was seen by him on the evening of the second day; the temperature was 104°, and a small axillary bubo embedded in extensive infiltration, and descending lymphangitis extending down to the elbow, were noticed on the left side. He was injected with 60 c. c. of the serum, and received subsequently further injections of 50 and 40 c. c. on the following day, and 40 and 50 c. c. respectively on the fourth and fifth days. There was a steady and uninterrupted fall of temperature to 100°·2 till the fourth morning, the second curve reached to 102°, and extended over three days reaching to 99° on the seventh day; subsequently there was a slight rise due to suppuration. The bubo was incised on the fourteenth day of illness and the patient made a good recovery.

IX.

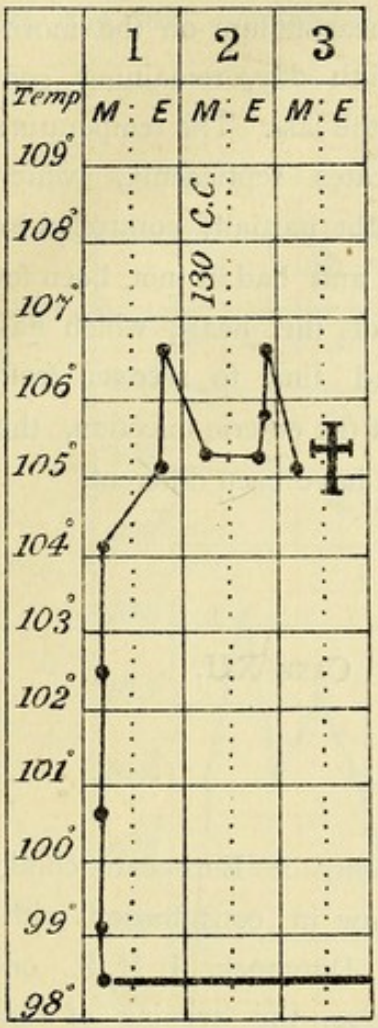


The above case extended longer than those treated on the first day of illness, the second curve took its full course, though the third was entirely absent. The bubo suppurated, and had to be incised, and thus the duration of illness became prolonged.

Case X.

The patient, a young Hindu, aged 23, a recent arrival in Bombay, was seen in consultation with Dr. C. Fernandes on the morning of the second day of illness (3rd November 1900). He was taken ill the day previous, and the temperature had gone up to 106°4 in the

X.



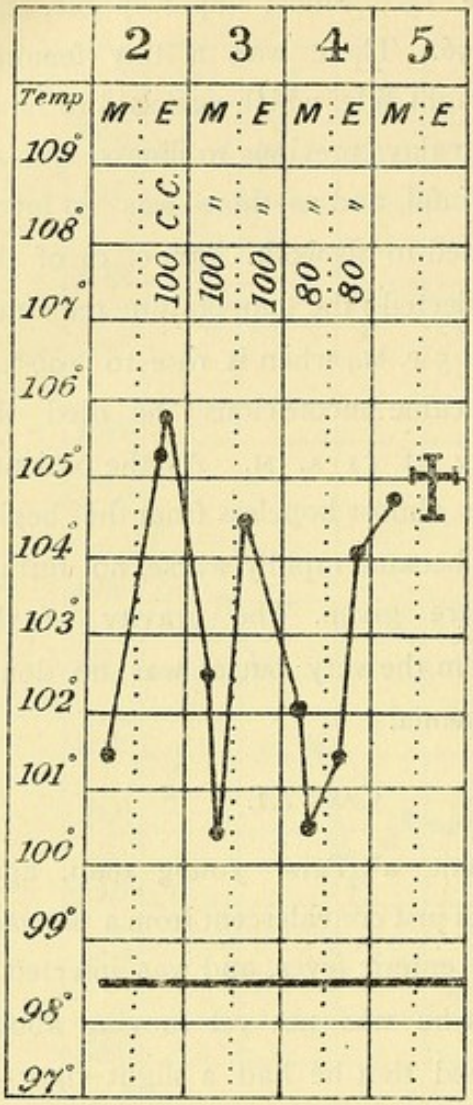
evening. He was semi-conscious, temperature 105°·4, pulse 150, almost imperceptible, and respirations 56. There was a tiny femoral bubo on the right side, which was said to have developed two days previous to illness, but as it was not painful, and as there was no fever, he had attended to his work. 130 c. c. of the serum were injected; the temperature remained the same till 5 P. M., when it rose to 106°.4, the patient became unconscious; he died the following day at 11 A. M. As the patient's condition was almost hopeless from the beginning, and he became rapidly worse, no further injections were given. The gravity of the symptoms from the very outset was no doubt due to septicæmia.

Case XI.

The patient, a Parsi young man, aged about 21, was just convalescent from a protracted attack of enteric fever, and was infected in the house, as he was not yet moving about. It was noticed that he had a slight rigor at about 11 P. M. followed by a succession of rigors, with a steadily rising temperature, which had attained to 105°.4, when I saw him first with Dr. Sethna, at about 7-30 P. M. the following evening. The pulse was 140, extremely weak and almost thready; rigors had continued throughout the day; there was some cough with bronchitic sputum tinged with blood; the stomach was very irritable, vomiting being incessant, and left femoral and deep iliac buboes, with upward extension. The condition of the patient was critical, and the prognosis extremely unfavourable, as all the symptoms pointed to profound septicæmia with rapid cardio-vascular paresis.

Under these circumstances I did not consider it advisable to treat him with the serum; but at the desire of Col. Dimmock, I.M.S., who was also jointly in consultation with me, and at the earnest solicitations of the parents, I had to give in, and administered the first injection of 100 c. c.

XI.



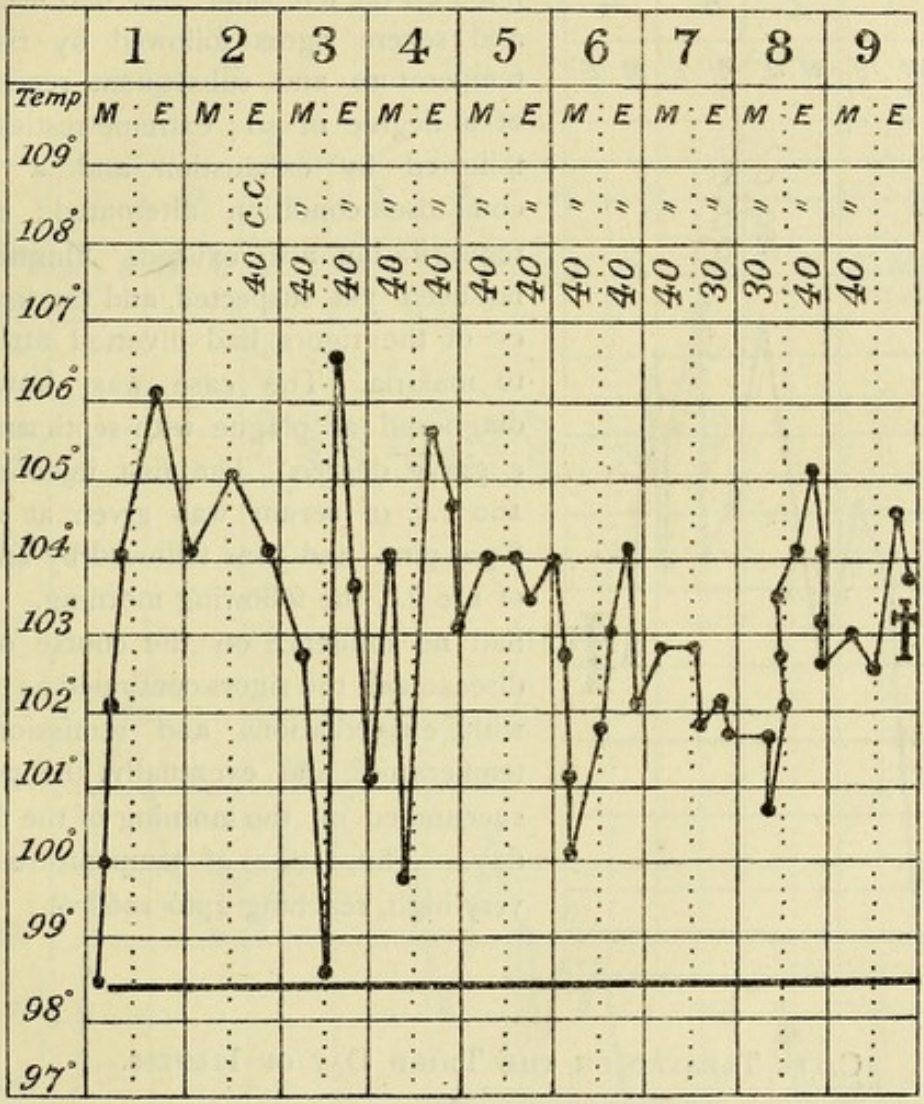
Four more injections followed, but the patient's condition became worse, and he died of heart-failure on the morning of the fifth day, remaining conscious up to the last. The temperature curve indicates septicæmia, which was no doubt partially controlled by the serum, and had it not been for the state of the heart, which had scarcely had time to recover from the effects of the enteric infection, the result would have been different.

Case XII.

The patient, a European child, aged 9, I saw in consultation with Col. H. P. Dimmock, I. M. S., on 1st April 1902, the evening of the second day of illness. Her temperature was 106° on the previous evening, it had dropped to 104° on that morning, but risen again to 105° at midday, and was 104° at about 5-20 P. M. She had a femoral bubo, on the right side with extension upwards, and the deep iliac glands were also found enlarged. There was some tenderness along the course of the iliac vessels, indicating that the glands along their course had become infected. The pulse was 140, soft and compressible. The heart's action had become considerably impaired by this time, and it was thought desirable to resort to cardiac stimulants hypodermically. The first injection of 40 c. c. was made in the neighbourhood of the buboes. The following morning the temperature fell to 98°·4, and by the afternoon it rose again to 106°·4. The septicæmic character of the temperature curve then became well marked. The serum injections were continued in the doses as marked on the chart. Petechiæ on the sacral region and buttocks developed on the third day. On

the sixth, seventh, and eighth days, secondary buboes developed; right and left anterior, and posterior cervical; the heart continued failing from day to day, and eventually the patient expired on the ninth day at 4-30 P. M.

XII.

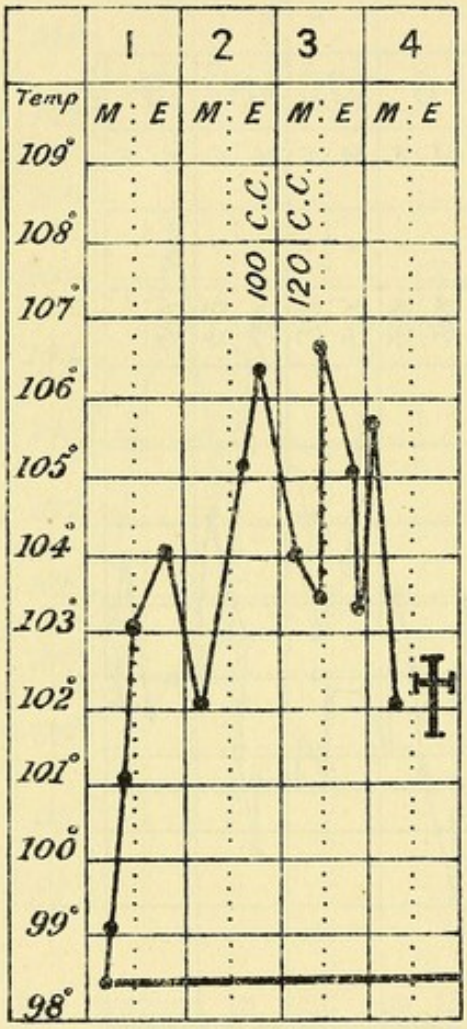


The patient was violently delirious for two nights, and, although somewhat dazed at first, brightened up considerably from the fourth to the seventh day. Cardiac failure was repeatedly threatened, but timely intervention with stimulants kept her going on till the ninth day. Had the patient not been treated with the serum, she would have in all probability succumbed on the third, or at the very most on the fourth, day. The serum appeared to control the septicæmia to a certain extent, but, when the blood current became repeatedly replenished with the plague bacilli from the numerous buboes, it became powerless.

Case XIII.

The patient was a young Goanese male, aged 18, whom I saw in consultation with Drs. Fialho and Fernandes on the evening of the second day of illness; the temperature was 106°·4, pulse feeble and almost imperceptible; there was a tiny femoral bubo on the left side. He had frequent and severe rigors followed by rise of temperature and subsequent remissions of a degree or so; extreme restlessness followed by exhaustion and a semi-comatose condition alternated; mitral regurgitation also existed. Plague had not been yet suspected, and the frequency of the rigors had diverted attention to malaria. The case was, however, diagnosed as plague with septicæmia of a grave degree. The first injection of 100 c.c. of serum was given at about 8-30 p.m. and was followed by another of 120 c.c. the following morning. They had no influence on the course of the disease and the rigors continued as before with exacerbations and remissions of temperature, and eventually the patient succumbed on the morning of the fourth day. The range of temperature was very high, reaching upto 106°·6.

XIII.



Cases Treated on the Third Day of Illness.

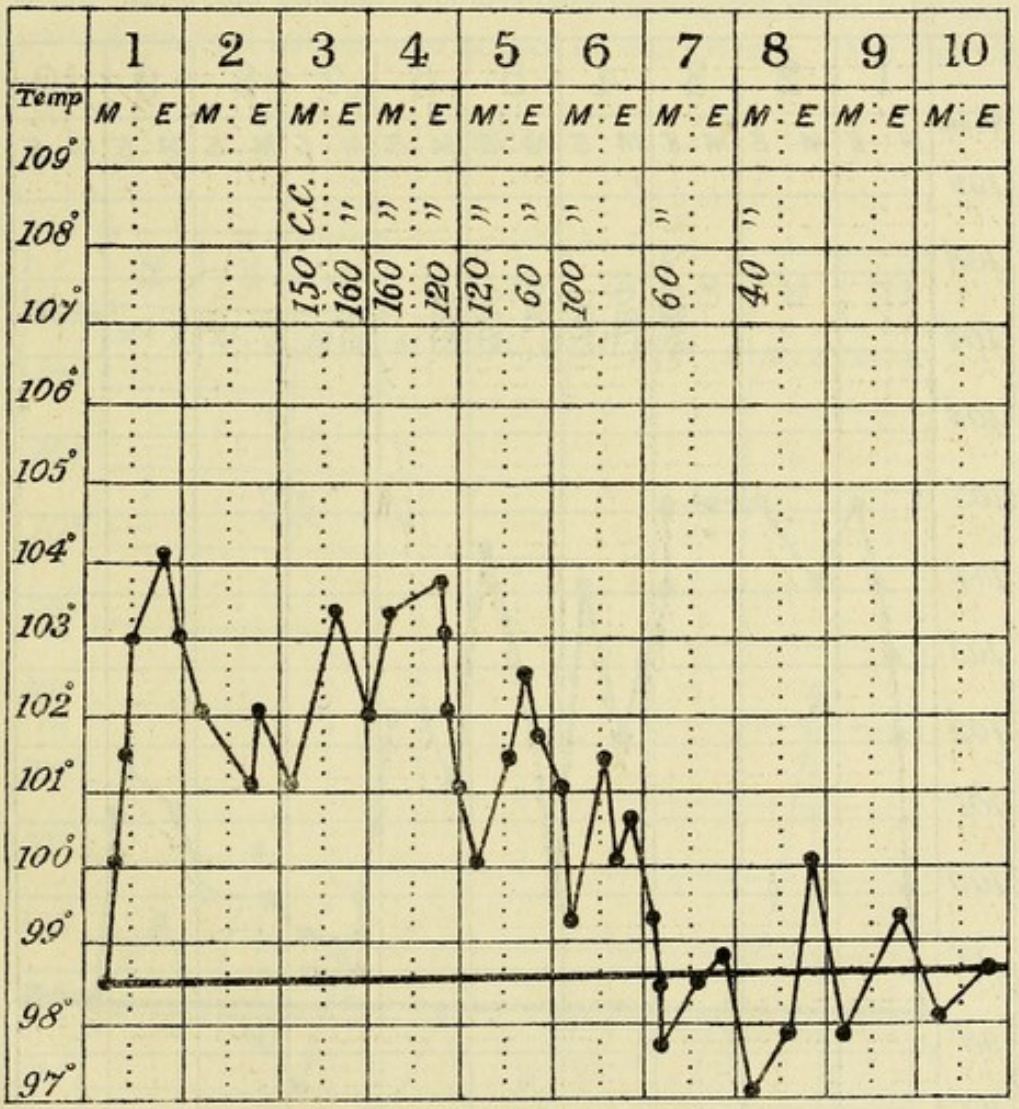
The following five cases were treated on the third day of illness; the first three were non-septicæmic and recovered, the total duration of illness ranging from 7 to 8 days. The rest were septicæmic and succumbed—life having been prolonged in one to ten days.

Case XIV.

The patient was a Parsi young man, aged 36, whom I saw in consultation with Drs. Rozario and Patel on the morning of the third day of illness. The temperature was 101° but the state of the heart gave rise to consider-

able anxiety, as the pulse was very compressible, and irregularly intermittent. He was a nervous patient and very anxious to know what he was suffering from. The presence of femoral and inguinal buboes on the left side, coupled with the previous range of temperature and the state of the circulation, led to the diagnosis of plague; and, as the virulence of the-then prevailing epidemic (March 1901) was severe, it was decided to inject him with larger doses of the serum than usual. The first injection of 150 c.c.

XIV.



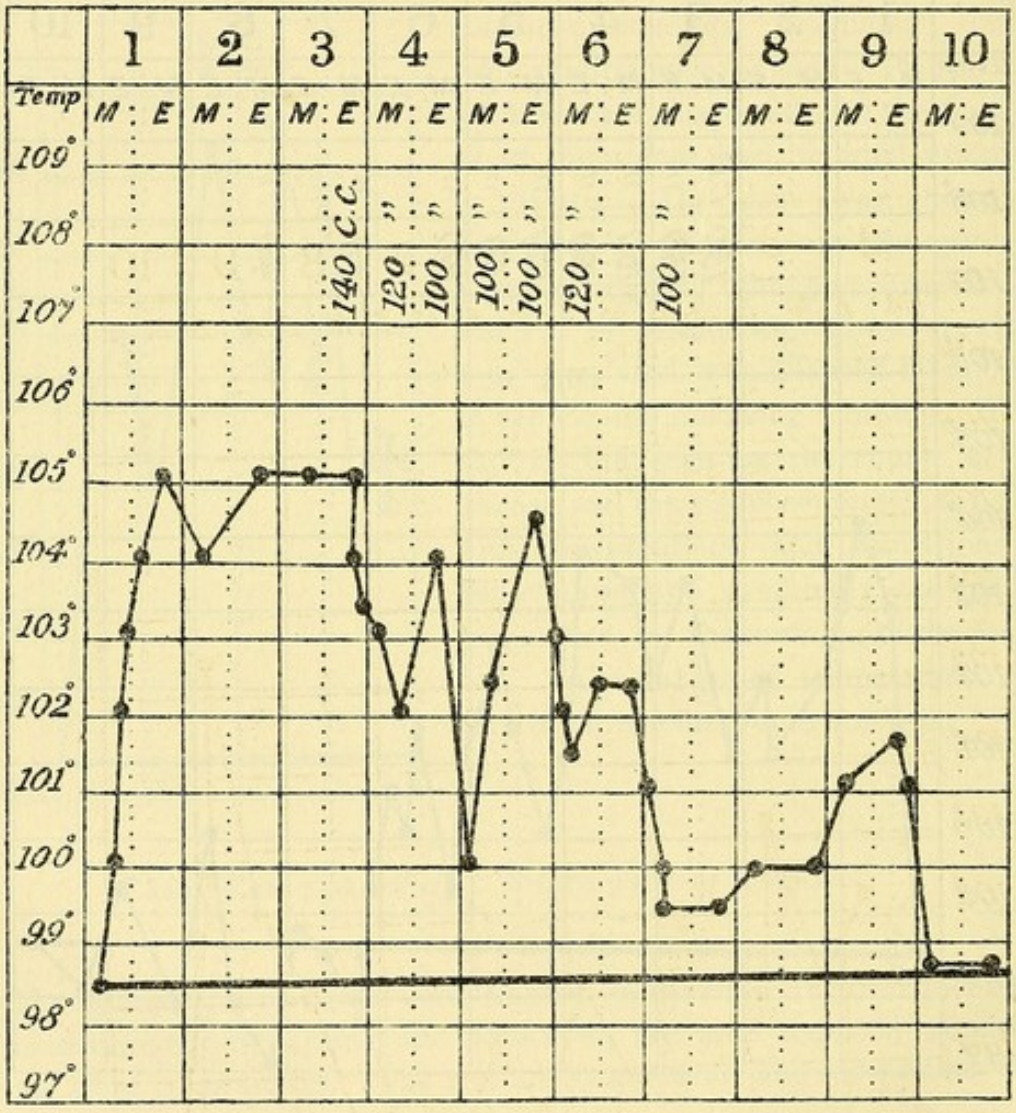
was given in the neighbourhood of the buboes and it was followed up by 8 more injections distributed over six days. The progress of the patient was slow but uninterrupted, although cardiac failure was very imminent on the evening of the sixth day, and was averted in time by the exhibition of cardiac stimulants hypodermically and by the mouth. Although the temperature fell to normal on the morning of the seventh day and even lower on the eighth, one injection daily of the serum was continued as a matter of

precaution. The buboes resolved, but the recovery was extremely tardy on account of the weak state of the circulation. The chart shows all the three typical curves, though somewhat shortened.

Case XV.

The patient was a Christian male, aged 20, whom I saw in consultation with Dr. Fernandes on the evening of the third day of illness. There existed femoral and iliac buboes on the right side, and the temperature had remained more or less at 105° since the afternoon of the first day. This was

XV.



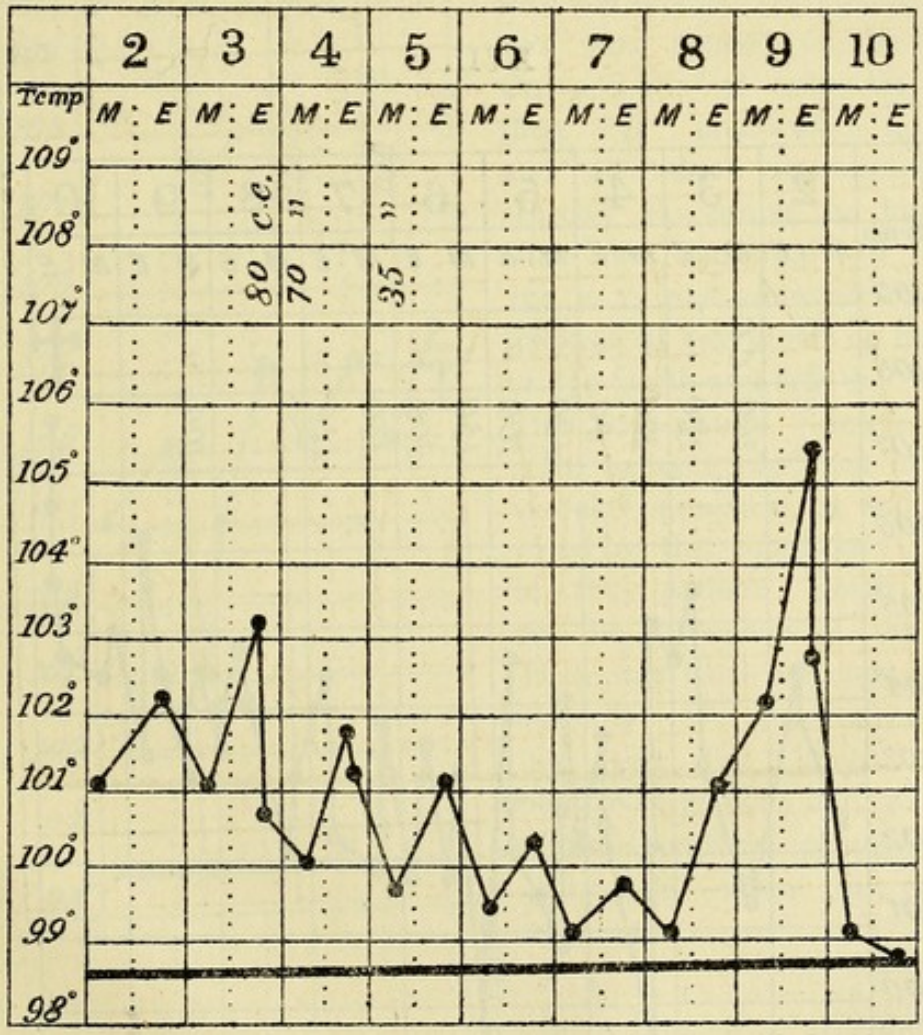
by no means a favourable indication, showing, as it did, either septicæmia or extension upwards along the deep iliac glands. The circulation was, however, not gravely affected; the pulse rate was but 104, and it was steady and of good uniform volume. The patient was rather excited and restless. The first injection of serum 140 c.c. was then given and followed up by six more, distributed over four days. Up to the morning of the fifth day, the

progress was favourable, but on that evening the temperature registered 104°·2, and another bubo along the femoral chain developed. It soon subsided, however, and further progress was not interrupted except by suppuration and subsequent incision of the primary femoral bubo. Recovery was fairly rapid, and the other buboes gradually resolved.

Case XVI.

The patient was a Mahomedan lady, aged 57, of good vigorous constitution, whom I saw in consultation with Dr. B. S. Shroff at about 11 p. m. on the third day of illness. The temperature had gone up to 103°·2; pulse was about 120 of fair volume; she was very restless and difficult to control, axillary and pectoral buboes were noticed on the left side. The first injec-

XVI.



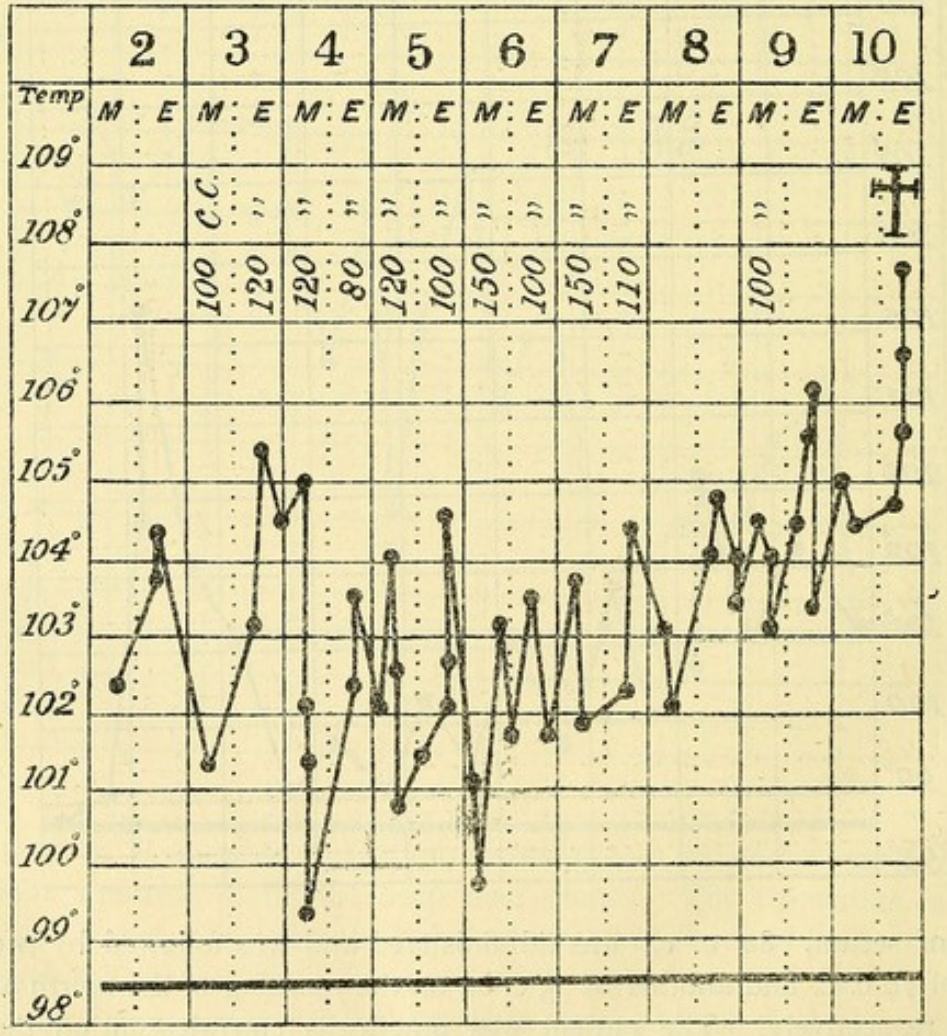
tion of serum, 80 c. c., was administered and was followed by two more, one of 70 c. c. and another of 35 c. c., on the morning of the fourth and fifth days respectively. The patient was practically convalescent on the morning of the seventh day and the buboes had almost disappeared. She per

sisted however in sitting up, with the result that the temperature again rose to 104° on the evening of the eighth day and mounted up to 105°·2 on the following evening, but without any serious consequences, and it fell to normal on the morning of the tenth day.

Case XVII.

The patient, a thin and delicate European lady, aged 42, I saw in consultation with Dr. DeMonte at midday on the third day of illness. She had inguinal and deep iliac buboes on the right side and also posterior cervical buboes on the same side, indicating a septicæmic condition. The temperature curve shows clearly the nature of the disease and the prolongation of life till the tenth day. Frequent rigors, in the course of the treatment, demonstrated that the blood was being repeatedly infected with plague bacilli, and there were unmistakeable local signs on the fifth day of illness

XVII.

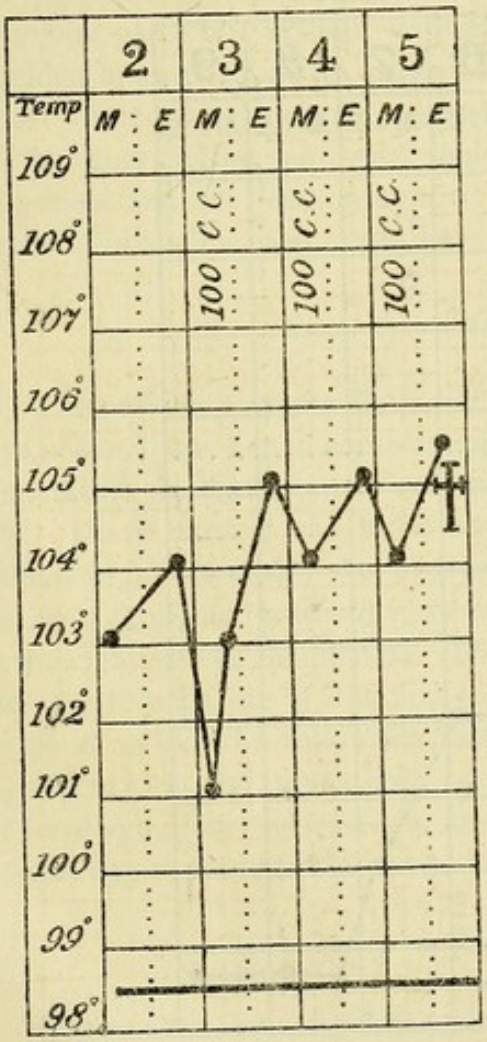


pointing to the extension of the infection along the deep iliac, lumbars and retro-peritoneal glands, as well as the mesenteric. The action of the heart was much enfeebled from the very outset and cardiac stimulants were required hypodermically. The temperature rose to 107°·4 before death and the patient was unconscious for about two days previous. The ordinary termination of such a case would have been death on the third or fouth day.

Case XVIII.

The patient was a young Hindu, aged 26, whom I saw on the morning of the third day of illness with Colonel Dimmock, I. M. S. He was a well-built and well-nourished man, but very restless and difficult to control. The temperature was 103°, and had been a degree higher the previous evening; the pulse was soft, easily compressible, occasionally intermittent, and varied 130 to 140. Femoral and iliac glands with considerable periglandular infiltration were noticed on the right side. On account of religious prejudices there was practically no nursing, and all the circumstances were scarcely favourable to his recovery. The first injection of serum of 100 c. c. was administered, and was followed by two others on the morning of the fourth and fifth day repectively. The temperature however persisted high, between 104° and 105°; cardio-vescular paresis set in, and was aggravated by the continuous restless-ness of the patient. Death supervened on the afternoon of the fifth day. There was local evidence of extension upwards of the infection along the deep iliac lumbar and retro-peritoneal glands; and it is probable that the condition of the patient was septicæmic when he came under treatment.

XVIII.



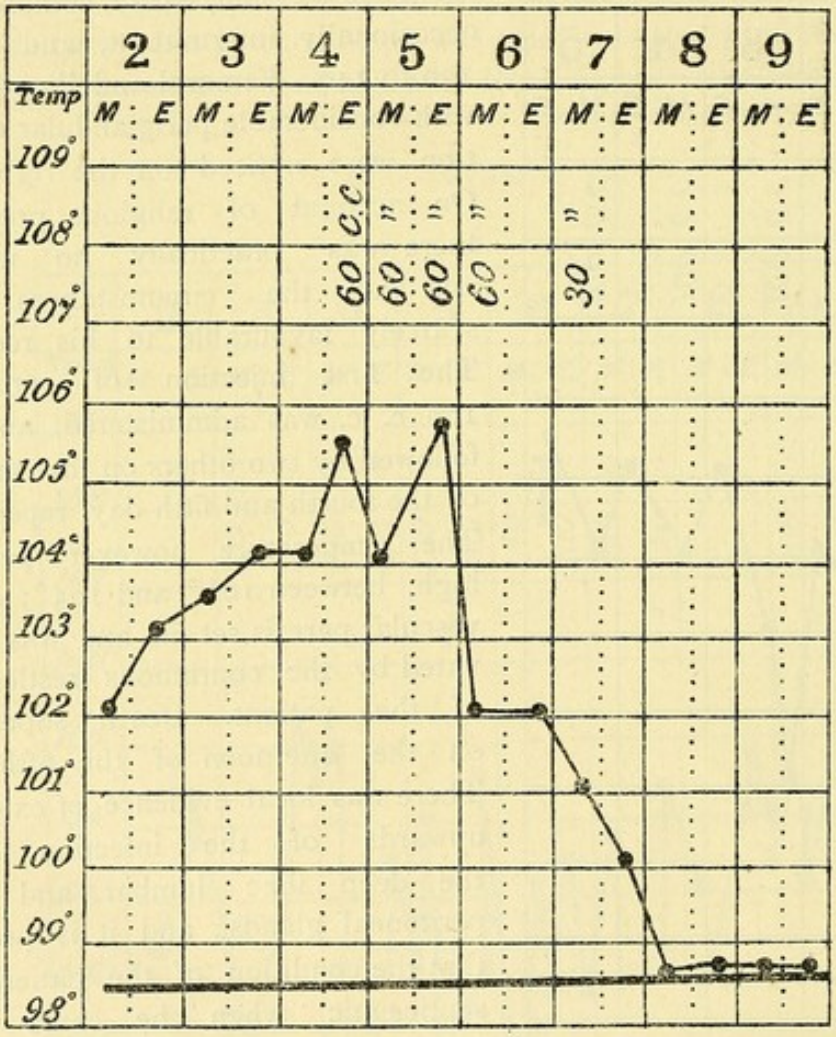
Cases Treated on the Fourth Day of Illness.

The following three cases were treated in the fourth day of illness and they all recovered. One of them was septicæmic and in the two others the cervical glands were infected.

Case XIX.

A Parsi gentleman, aged 42, of rather stout build, I saw in consultation with Dr. J. P. Nicholson late one evening (about 10-30 p. m.) in May 1900. He had left Bombay from an infected house about five days previously for a hill station, a few hours' journey from here, and within two days developed fever with right parotid bubo, which was followed within a few hours by the left, and subsequently by double sub-maxillary, sub-mental, supra-hyoideal median, with extensive infiltration in the neck and face. As his condition became grave, and he was getting steadily worse, he was brought down to Bombay on the evening of the fourth day of illness. The

XIX.



temperature was 105°·4; pulse 146, extremely feeble, soft and compressible. He was propped up in bed, and the condition of the head and neck was as above. There was œdema glottidis, dyspnœa and dysphagia; the voice was scarcely audible, hoarse and rasping; and the patient's efforts to work even a few drops of fluid down the throat were agonising and painful to watch. His

condition was extremely critical and the prognosis by no means hopeful. The serum was, however, injected in a single dose of 60 c. c., and the following morning his condition was almost unchanged, perhaps a trifling better. There was no increase in the infiltration or buboes, and he could breathe easier. Another injection of 60 c. c. in the morning and a similar one in the evening followed. The temperature on the fifth varied from 103° in the morning to 105° in the evening. On the morning of the sixth day, the temperature dropped to 102°; there was considerable amelioration in his condition; the infiltration had almost disappeared, and the buboes could be distinctly felt. Breathing was much easier, and fluid nourishment could be taken without much effort. The same dose of the serum was injected; the temperature remained at 102° throughout the day, and dropped to normal on the morning of the seventh day, when another injection of 30 c. c. was given. The patient made an uninterrupted recovery, with but slight erythema and some joint-pains but without suppuration of buboes. One serious incident—a sudden attempt to sit up in bed—during the early days of convalescence almost precipitated acute cardiac failure and probable death. Help was however on the spot, and remedial measures restored the patient. If the patient had not been brought to Bombay and the serum applied in time, the result in such a case would have been fatal.

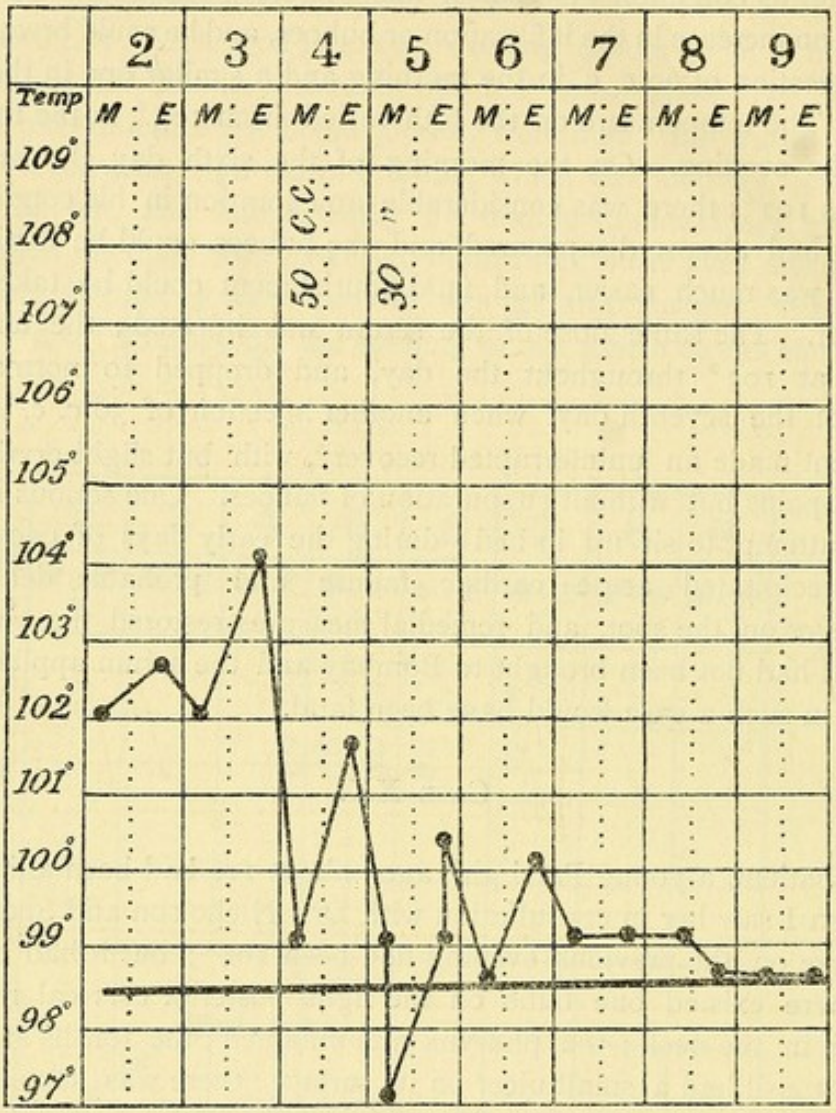
Case XX.

The patient, a young Parsi girl, aged about 11, had been ailing for four days, when I saw her in consultation with Drs. Nicholson and Spencer. The temperature on the previous evening had been 104°; but it had dropped to 99°. There existed one bubo on the right posterior cervical region with infiltration in the neck; the pharynx was inflamed; the tonsils swollen, and the right tonsil had a small ulcer on its surface; there was some infiltration on the right side of the larynx. The serum treatment was thus commenced after the termination of the first curve, and 50 c. c. were injected, followed by 30 c. c. on the following morning. The second curve did not rise beyond 101°·8, and, after slight oscillations for three days, it fell to 99°; all the local symptoms soon abated and the patient made an excellent recovery without any suppuration of the buboes.

Case XXI.

The patient, a young Hindu, aged 17, the son of a medical man, I saw in consultation with his father and Drs. Engineer and Mehta on the morning of the fourth day. His temperature had gone up to 106° the previous evening and was 102°·2. He had left femoral and femoro-inguinal buboes with some infiltration. The pulse was weak and thready, and heart-failure had been threatened the day previous, but he had recovered after injections of cardiac stimulants. The prognosis of the case was naturally grave and it was feared that the time for the application of serum had past. 100 c. c. of the

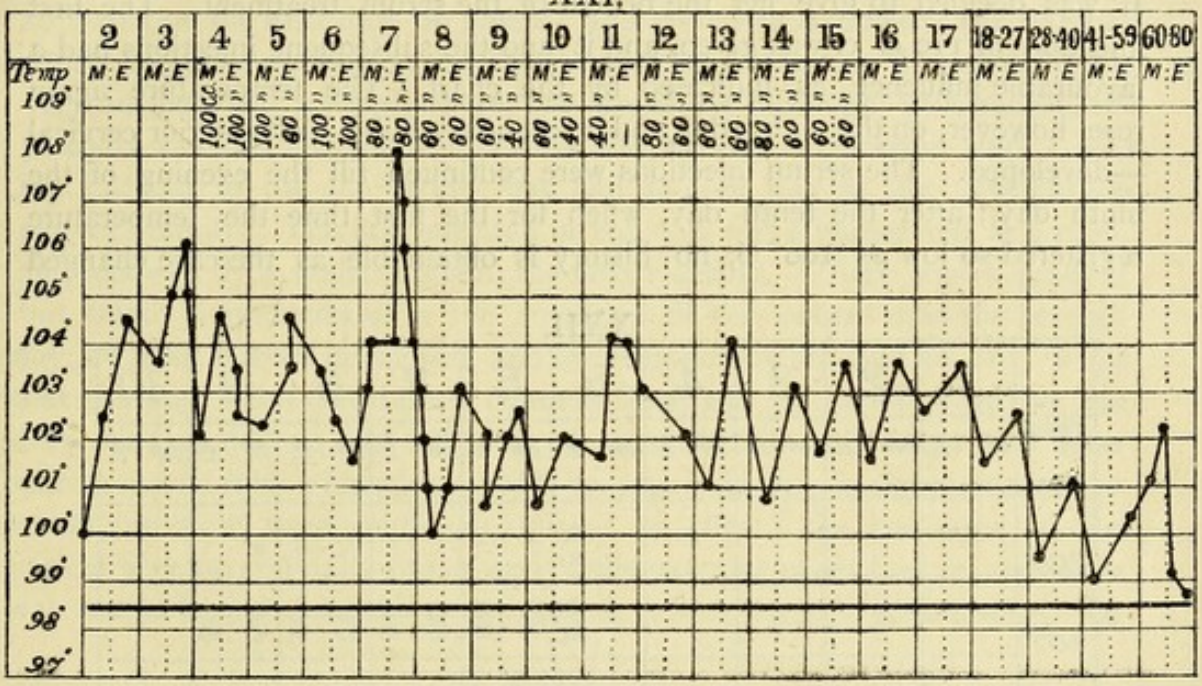
XX.



serum were, however, injected in the neighbourhood of the buboes. The patient's progress was fairly hopeful up to the evening of the sixth day; but, on the morning of the seventh, the temperature took an upward course, rose to 104°, and simultaneously with it the deep iliac glands on the opposite side were found infected. There was retention of urine, and instructions were left with the doctors in attendance to use the catheter with due aseptic precautions. Unfortunately for the patient, there was some flaw in carrying this out and it resulted in bringing on a sharp attack of urethral fever. The urine became ammoniacal; the temperature rose to 108° after violent rigors; he became unconscious, general convulsions set in, and the heart began to fail and no pulse could be felt at the wrist. He was immediately packed in ice, stimulant cardiac injections were given (three within an hour), and after some time the temperature began to fall until it came to about 100° in the morning. That all the above symptoms were due to urethral fever, and not to plague, became evident from the subsequent course of the

case till the tenth day, when the temperature, that had been gradually declining, rose again to 104·°4 and right deep iliac and left axilliary buboes developed. The dose of the serum which had been reduced was again increased, and there was considerable improvement till the morning of the thirteenth day, when there were further indications of the infection spreading upwards from the right iliac bubo. The serum was continued till the evening of the fifteenth day. On the tenth day the left femoral and inguinal buboes were found to have suppurated and were incised. Further injections

XXI.



of the serum were discontinued as no fresh buboes appeared; fever, however, continued in a more or less remittent type for about three weeks longer, and as it was not malarial, and there were no signs of phthisis, it was assumed that it was due to the irritation caused by the gradual absorption and elimination from the system of the products of plague infection from the numerous secondary buboes. This has also been noticed in other cases. The convalescence was naturally long and tardy, and an attack of acute dysentery retarded it. Ultimately he made a good recovery, though he was not able to leave the bed till the twelvth week.

Cases Treated on the Fifth Day of Illness.

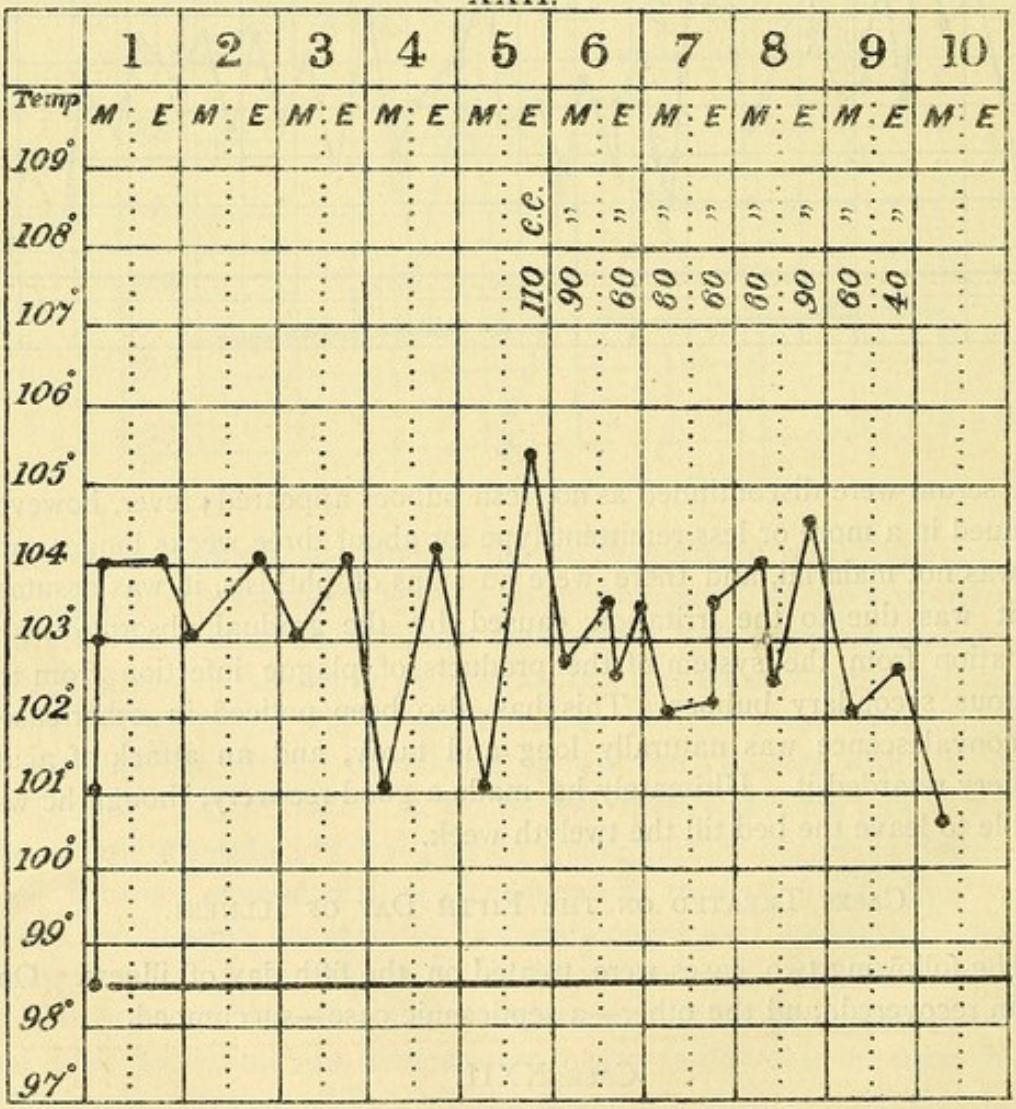
The following two cases were treated on the fifth day of illness. One of them recovered, and the other—a septicæmic case—succumbed.

Case XXII.

The patient was a young Parsi girl, aged 18, whom I saw in consultation with Drs. R. T. Nariman and Kapadia on the afternoon of the fifth

day of illness. There was previous history of persistent fever for three days, that had subsequently become markedly intermittent and accompanied with rigors; a supra-trochlear bubo had developed on the right arm with considerable infiltration from the shoulder to the elbow that day. A small umbilicated blister—the seat of infection—was noticed on the back over the left scapula, and it is probable that the system was being gradually infected from it; this also accounted for the prolonged course and late appearance of the bubo. The temperature was 105°·4; the patient was very restless and extremely nervous. The base of the right lung was found to be affected. It was decided to give her the benefit of the serum treatment. The first injection of 110 c. c. was given, and it and the subsequent injections had a favourable influence, as indicated by the chart. The temperature again rose, however, on the eighth day and a secondary bubo—left anterior cervical—developed. The serum injections were continued till the evening of the ninth day; after the tenth day, when for the first time the temperature registered so low as 100°·6, no history is obtainable as the case changed

XXII.

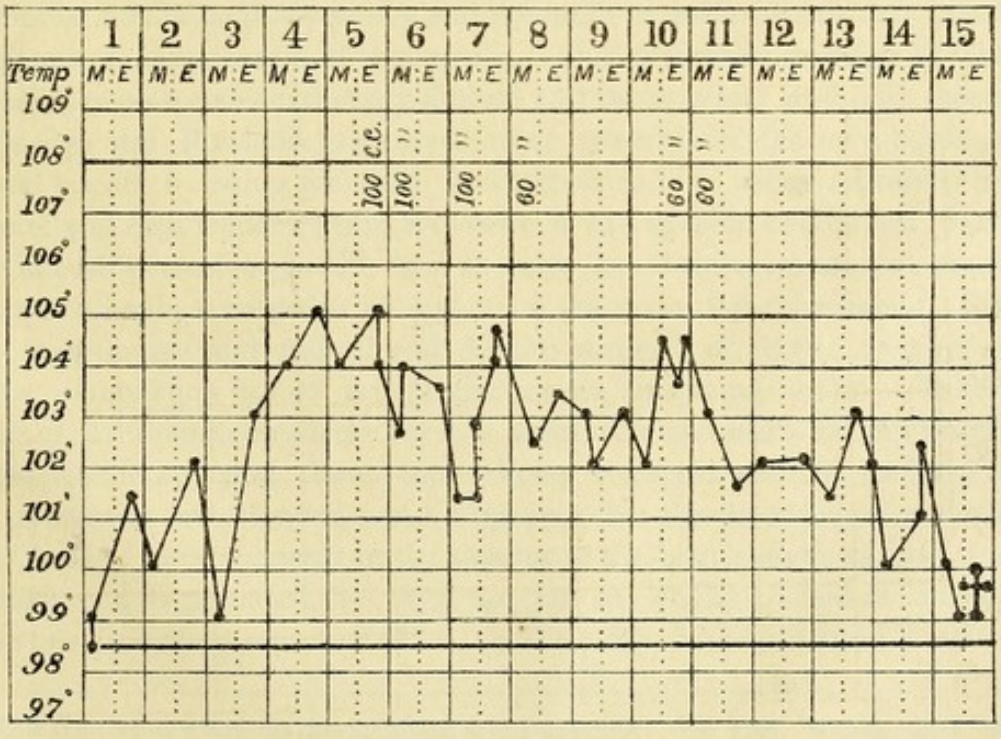


hands, except that she recovered. In this case the secondary bubo developed not as the result of septicæmia, but from extension of the infection upwards from the scapular region to the neck through the lymph vessels.

Case XXIII.

This patient was a young Hindu, aged about 35, and had been ill five days, when I saw him in consultation with Dr. Velkar late that evening. The temperature chart indicates his previous condition. The temperature was 105°, and he had two buboes—one primary in the left axilla, that had appeared on the first day of illness; and the other secondary, left inguinal, which had been noticed on the afternoon of the fifth day. The patient was very restless and excited, there was persistent hiccough with nausea, the pharynx was also inflamed. The case was already septicæmic, and I was not inclined to use the serum, but had to give way at the desire of the patient's family. The first injection of 100 c. c. was administered at 9 p. m. and followed by a similar amount the next morning. There was a gradual but steady improvement in the condition of the patient upto the seventh day; no fresh buboes developed, and the temperature reached to 101°·6 on that morning. But this did not continue long, and on the following day the deep iliac glands on the left side became infected, and a large hard mass with considerable infiltration could be seen and felt in the region. The serum injections were continued, but to no effect; the condition of the patient became gradually worse, and cardio-vascular paresis set in, and there was marked and distressing tympanites, which further embarrassed the

XXIII.



heart. Deep fluctuation was felt in the inguinal bubo, and it was incised on the tenth day, but without any relief. The patient succumbed on the morning of the fifteenth day of illness. Septicæmic as this case undoubtedly was with multiple buboes, the serum prolonged his life, and, had heart-failure not set in, the result would have been different.

All the above cases have been selected from among the patients treated in private practice, as accurate histories were available from the beginning of illness in every case.

B

SOME RECENT STUDIES IN IMMUNITY AND THEIR BEARING ON SERUM-THERAPY.

Extra- and Intra-Cellular Toxins.

In the brief résumé of recent researches in bacterio-therapy in one of the preceding sections, reference has been made to the *intoxication diseases* like diphtheria and tetanus, in which their respective antitoxic serums are capable of neutralising the free soluble toxins generated in the body by their microbes. In marked contrast with the above, it was also noted that in by far the larger group of infective diseases, comprising some of the most important and widespread affections, like influenza, typhoid, pneumonia, cholera, plague, and pyogenic septicæmia, the microbes do not secrete or excrete or form free soluble toxins. Their poisons are intra-protoplasmic or intracellular, and are retained within the dead protoplasm of their cells and at times in the living protoplasm also. They are set free only when the microbes degenerate or die.* There is always an enormous destruction of these microbes in the body, and what we see by the microscope or culture is only but a fraction of the whole existing in the body, living and dead. (Welch). The question whether these microbes produce soluble toxins within the organism, although they do not do so in the ordinary artificial culture media, has yet to be investigated ; so far as at present , no definite results have been reached. But it is presumed that living bacteria in the infected body, and under suitable nutritive conditions, not analogous to those in artificial media, actively produce and secrete receptors which may become the means of intoxication of body cells. Our present knowledge of these intracellular poisons is extremely limited and incomplete, and only recently Macfayden and Rowland have made some progress in the investigation of typhoid bacilli by using for their investigations the juices expressed from the bacterial cells under certain well-defined and specific conditions. Lustig and Galeotti's neucleo-proteid, derived from the disintegration and solution of plague microbes, may also be said to be the toxin of plague bacilli. It has been investigated and utilised both for the purposes of plague prophylactic and for immunising horses for producing an antiplague serum. Professor Welch of Baltimore considers that it is absolutely necessary for any progress in bacterio-therapy that these intracellular toxins should be isolated and their properties investigated, and he believes that the knowledge so derived would lead to improvements in the quality of the bacteriolytic serums, some of which as now prepared, he says, are not so wholly devoid of antitoxic properties as is often represented or, shall we say, misrepresented in spite of

* The Huxley Lecture on Recent Studies in Immunity. By Prof. Welch. *Brit. Med. Jour :* Oct. 11th, 1902.

proofs to the contrary. He thinks that these investigations would help us in solving the localization, or rather the selective affinity, of bacteria in disease, *e. g.* in the intestines in typhoid and cholera, in the lymphatic glands in plague, etc. Welch suggests that, within certain limits, the less closely related the two species of animals the more powerful is the antagonistic effect of the specific serum, especially so in cytotoxic (bacteriolytic) and hæmolytic sera. This opinion differs from that of some other observers, who think that the more closely related the species the better, and who, for instance, suggest the monkey as the proper animal for producing antiplague serum for use in man. But considering the nature of the plague infection, and the amount of serum that would be necessary, the use of the monkey for such purposes does not appear to be practicable.

Bacteriolysis; Ehrlich's Side-Chain Theory.

In the section above referred to, it was shown that the factors concerned in the process of bacteriolysis were complex and that they consisted of two parts, and depended upon two substances :—(1) *the immune body* or *intermediary body** ; (2) *the complement.* Both are absolutely necessary for the purpose and must exist in suitable proportions to bring about the solution or destruction of the red corpuscle or the microbe. Ehrlich's side-chain theory was formulated to investigate the laws governing the behaviour of the immune body and the complement in the presence of the infecting bacteria, or, to state more correctly, the mechanism of antitoxic and bacteriolytic actions. Ehrlich assumes that in the case of purely antitoxic serums the immune body in the serum directly neutralises the soluble free toxin (diphtheria) like a chemical neutralization ; the process is extremely simple, the action taking place in definite chemical equivalents. But if the substance to be acted upon is not directly soluble, like a blood corpuscle or a bacterial cell, the immune body itself is powerless to dissolve, or destroy, it, and then what happens is this :—The immune body on account of its double affinity, firstly, attaches itself to the red corpuscle, or bacterial cell, and thereby sensitizes it ; and, secondly, the combination so formed attracts by virtue of the other affinity the leucocyte containing the complement, and ultimately it is this dual action of the immune body and the complement that brings about the solution or the destruction of the blood corpuscle or the bacterial cell. Ehrlich, therefore, holds that the intermediary or immune body possesses a specific combining *haptophoric complex* with two points of attachment : one haptophoric group possessing receptors having great affinity for the red corpuscle, or the bacterial cell, and the other similarly for the complement present in the blood serum. And it is in the possession of the two affinities and under their resultant action that hæmolysis or bacteriolysis is brought about. The process is, therefore, complex and of a

* Also called amboceptor, sensitizer, etc. Ehrlich calls the normal immune body zwischenkörper, or go-between, to distinguish it from that produced in artificial immune sera, which he calls amboceptor.

double nature, and hence it is that, according to Welch, the successful therapeutic application of bacteriolytic serums meets with difficulties which have yet to be overcome. The above facts explain why it is much more difficult to produce and apply an anti-typhoid or anti-plague serum than one associated with a simpler disease like diphtheria.

The Nature of Snake-Venom.

Cognate to the above subject of bacteriolytic and antitoxic action and the essential presence of the immune body and complements, Professor Welch gave in the Huxley lecture an account of the researches of Flexner and Noguchi on the nature of snake-venom. It was hitherto believed that the action of snake-venom was like that of simple intoxication as in diphtheria and tetanus, but the above researches have shown that cobra-venom is of a amboceptor nature, *i.e.* possessing two kinds of affinities. "Flexner, Noguchi, and Keys teach that, in poisoning by venom, human and animal bodies contain in the form of complements the substances which are most directly concerned in the act of poisoning. The snake-venom contains only one-half of the complete poison, the other, and the really destructive, half is widely distributed in the blood and cells of man and animals. The venom contains the intermediary bodies, and therefore it serves to bring into the necessary relation with constituents of the body cells poisons we already harbour, or may generate, but which are harmless without the intervention of the intermediary bodies. These poisons within us are powerful weapons, which when seized by hostile hands may be turned with deadly effect against our own cells, but which are also our main defence against parasitic invaders. We see here, as everywhere, that nature is neither kind nor cruel, but simply obedient to law." It was also hitherto believed that the hæmorrhages observed in snake-venom poisoning were due to its hæmolytic action, but it has now been determined that snake-venom contains a cytotoxin which has the property of inducing hæmorrhages through its power of dissolving endothelial cells—an *endotheliolysin*. It exerts a direct solvent action upon the capillary endothelium and hence produces hæmorrhages and extravasations. *

An immense amount of practical work in connection with the immune or intermediary bodies and the complements, their seat of production and reproduction, mode of action, etc, has been accomplished by a number of observers. This has been lately expounded in a most able, exhaustive, and

---

* In the case of plague bacilli it has been found that they produce in culture hæmolysins which dissolve the blood corpuscles. This hæmolytic property does not, however, stand in definite relation to virulence. Clinical observation has, however, shown that almost all cases attended with hæmorrhages terminate fatally. Normal human and other blood serums contain anti-hæmolysins.

Besides the hæmolysins, the bacteria produce hæmagglutinins and Welch thinks that the thrombi in the small blood vessels in typhoid (and plague?) are due to coalesced red corpuscles from the action of their bacterial hæmagglutinins.

masterly survey and analysis* by Professor Ritchie of Oxford. No apology is, therefore, needed to quote in this connection a few of his principal conclusions in so far as they relate to serum-therapy :—

The Immune Body and the Complement.

It has been experimentally proved that an immune serum can be inactivated by heat, but that it is possible to restore activity to it, or to reactivate it, by the addition of some normal serum from an unimmunised animal of the same species, as also of another species. In some cases, however, the normal serum from an immunised animal of the same species is incapable of bringing about the result and the normal serum from an unimmunised animal of another species is essential. All the immune sera do not contain the immune body and the complement in equal proportions. Von Dungern has succeeded in isolating them and measuring the amount of each present in the immune sera. Ehrlich believes in the multiplicity of the immune bodies and complements, and holds that the complements present in the same serum may be thermolabile (destroyed by heat) or thermostable (resistant to heat). Bordet is inclined to believe the same of the immune bodies also. The immune bodies are, therefore, specific for the particulate bacterium or hæmolytic process. With regard to the specificity of complements, Bordet thinks that they are non-specific, but at the same time admits that there ought to exist some kind of differentiation—although all of them must be possessed of one common property, viz :—the ability to bring about bacteriolysis or hæmolysis by combining with a bacterial cell or erythrocyte (red blood corpuscle) already sensitised by its specific immune body. The main question of the multiplicity of complements cannot be settled at present.

A deficiency either of the immune body or of the complement in an immune serum results in incomplete reaction, and the bacteria will not be thoroughly destroyed. Wassermann found in animals that had died in spite of treatment with immune sera that the immune body was so much in excess as to protect another animal against the infection, but that death took place from the deficiency of the complement. This might possibly explain why even with the massive doses of the serum that were used during the plague epidemic of 1900-01 we could obtain no satisfactory results in cases of plague septicæmia. Neisser and Weschberg state that the injection of more than a certain quantity of immune body is injurious. Ainley Walker has recently stated that bacteria growing in immune sera produce anti-immune bodies and thereby become more virulent. Is it possible for this to happen in the living infected organism under the influence of plague septicæmia and excess of immune body from the serum injected? Clinical observation supplies the answer that excess of immune body did no harm. The complement disappears from the immune serums if kept for some

* The Journal of Hygiene—April, July, October 1902.

time, and (also if heated) therefore different sera show different results. (Ainley Walker). Is it possible to make up the deficiency of the complement? It is not an easy matter to do so, although the addition of fresh normal serum of animals of the same species to the immune serum or its simultaneous injection suggest themselves naturally. Wassermann found that the serum of the same species of animals does not supply the complement in the case of anti-typhoid serum, and in guinea-pigs the serum of a non-immunised horse was required.. Walker has also observed that anti-typhoid serum can be sensitised by the serum of the rabbit, the ox, and the pig. It must naturally occur that complements thus derived from various sources would act differently and hence the most active (avid) should be used for this purpose. So far as plague is concerned we are still in the dark on this subject, as unfortunately the observations that I suggested on similar lines in 1901 could not be carried out on account of the closure of the laboratory. We do not know what amount of complement exists in Lustig's or Yersin-Roux' serum when fresh, neither the period of its disappearance, nor the mode of sensitizing it. And, finally, the reproduction of complements in plague infection must be a matter for future investigation.

Metschnikoff's Adaptation of the Phagocytic Theory to Ehrlich's Observations.

It was surmised that the phagocytic theory, which, in the words of Professor Welch, Metschnikoff has defended for two decades against severe assaults with a large measure of success, would require fresh modifications in order to fit it in with Ehrlich's researches. But such has not been found to be the case. According to Metschnikoff two processes are involved in phagocytosis—(*a*) the attraction of the cells by the bacteria and (*b*) the killing and digesting of the latter by the cells. The protoplasm of the cells produce the immune body and the complement, and these act upon and destroy the englobed bacteria. In natu ral immunity these do not leave the cells but in artificial immunity the immune body escapes in the plasma, though no evidence exists at present to show that the complement behaves similarly. But both are found in the immune sera, because the latter escapes and becomes free by the breaking up of the dying phagocytes or by the latter liberating it in the process of dying. Prof. Welch says that the phagocytic school fully recognise the doctrine of Ehrlich as regards the action of an intermediary body and complements, and on the other hand the humoural or the German school recognise the cells, especially the leucocytes and other cells of the blood-forming organs as the immediate source of the proctective substances. Many differences in detail still exist. The essential difference between the two schools concerns the place where the intermediary body and the complement unite. All are agreed that the intermediary body exists free in the blood plasma, but Metschnikoff holds that the complement is within the leucocytes from which it is not secreted, but can be liberated only through damage to the cells.

The Bactericidal Power of Normal Blood and the Mechanism of Artificial Immunity.

Is the bactericidal power normally possessed by the blood the same as that which is present in the sera of immune animals? It is probable that the same factors are concerned in bringing about the same result. The bactericidal effect of an immune serum is inimically affected by an excess of immune body, so that if a serum naturally possessed bactericidal properties, and if at the same time it was capable of supplying the complement to an immune body, the addition of an excess of the latter robbed the serum of its bactericidal action (Neisser and Weschberg). The observations of Gengou show that, whereas the serum of non-immunised animals gave definite bactericidal action, the plasma sometimes showed very little and sometimes not at all. The physiological processes involved in bringing about artificial immunity are the same as those employed for the assimilation by the cells of food. (Ehrlich). Metschnikoff comes to the same conclusion although from a different point of view. But the idea is that the reaction in the system is but an exaggeration of the normal functions of the cells under the altered conditions brought about by injection of substances for producing artificial immunity. The cells do not become invested with any new functions for the purpose.

The Immune Body and the Complement Free in Liquor Sanguinis.

The presence of the immune body and the complement in the free state in the liquor sanguinis has been discussed by Wassermann, who thinks that the complement is not confined within the cells, but naturally exists free in the blood of the guinea-pig. Metschnikoff holds that although the immune body may escape, and be free in the body fluids, the complement remains always associated within the cells, and also that both these bodies are formed in the same class of cells, and that under ordinary circumstances bacteria are destroyed only when they are taken up by these cells. This question, however, requires to be settled by further investigation.

Where are the Immune Body and the Complement Formed?

The sites of the formation of the immune body and the complement have been variously suggested. Experiments indicate that the leucocytes are concerned in the formation of the complement, and probably also of the immune body. But the leucocytes are not the only cells of the body capable of manufacturing these substances, for the reaction of the body against infection may not be confined to cells which act as actual phagocytes, *e. g.*, eosinophile leucocytes, but that other cells enter into the struggle against an invading agent and may discharge from their protoplasm substances having bactericidal or bacteriolytic functions.

Agglutination and Immunity.

The relation of agglutination to immunity is neither constant nor important. Whilst normal sera sometimes possess agglutinating properties

the latter are not essential factors in the action of immune serums. A serum may be agglutinative and yet not bacteriolytic, and whilst the bactericidal properties are destroyed by heating to 55° C. the agglutinative action remains unaffected. Evidence exists in favour of the view of Nicolle that two substances are necessary for agglutination, one in the bacterium and one in the immune serum, although Bordet contends that the action is due to molecular interchange, and Ehrlich that it is due to the formation of special substances in the immune serum, analogous to, but distinct from, those concerned in bactericidal action.

Ferments in Bactericidal Action.

There is no evidence to show that anything in the nature of a ferment is concerned in bacteriolysis. There is, however, no doubt that ferments can be formed by leucocytes and it is quite conceivable that, by virtue of one set of powers, a phagocyte may kill a bacterium, and by virtue of another set of powers it may digest it; and that the latter process may be the same as ordinary proteolysis as it occurs in connection with the intestinal glands of an animal.

Chemiotaxis.

Metschnikoff having accepted Ehrlich's explanation that two bodies are concerned in bactericidal action, the question arises whether this action is entirely extracellular, or whether bacteria may be saturated with the immune body extracellularly and meet the complement only intracellularly. Another question is as regards the nature of the chemiotaxis, positive and negative—the attraction of the phagocytes by the bacteria, which is necessary for recovery after infection, or their repulsion, which accompanies susceptibility. What factors bring about this attraction? Metschnikoff explains this on a chemical basis, and states that the immune bodies contain substances (stimulines) which lead to chemiotaxis; stimulines, he says, exist in normal as well as immune sera. Savtchenko says that the stimulation of the phagocytes is due to the impregnation of the bacteria by the immune body of the immune serum. The evidence, however, in favour of Metschnikoff's views is scarcely convincing. At present it is extremely difficult to differentiate between a stimulating effect and a bactericidal action. It may be possible that the action may be due not to a chemical but to a physical stimulus.

Leucocytosis and Artificial Immunisation.

What processes actually underlie the so-called education of the leucocytes during immunisation? Are the same leucocytes as those that first englobed the small dose of the bacteria concerned in the subsequent action of phagocytosis when a larger dose is injected, and if so what do we know of the duration of the life of leucocytes? And, if this period is to be measured by days, then on what does the immunisation process exert its lasting effect? It is a well-known fact that the hyperleucocytosis that

occurs in many infective diseases is but temporary and the swelling of the spleen generally noticed may be due to the over-activity in that great organ of leucocytic destruction. The aggregation of leucocytes at the seat of infection has drawn away attention from the part played by the phagocyte-producing tissues, viz :—great germinative activity is noticed (Roger and Muir) in the precursors of the leucocytes—there is polymorphonuclear hyper-leucocytosis in bone-marrow, and so active is the process of division in the parent cells that the red marrow increases in amount and encroaches on the yellow; proliferation also occurs in the fixed cells lining the sinuses of lymphatic glands; in the hyaline cells living free in the lymph sinuses. Similar hyaline cells, endothelial and connective tissue cells, and wandering cells proliferate during infection. In different infections, different groups of cells proliferate, *e. g.*, in typhoid fever, there is no polymorphonuclear cell proliferation, but endothelial cells and hyaline cells in lymphatics do. In plague, Row and Surveyor* have reported the complete abolition of eosinophile cells in the majority of cases and increase in the large hyaline mononuclears as compared with the lymphocytes. There is a general chemiotactive effect in infections, which draws the polymorphonuclear leucocytes from the bone-marrow, and these and other proliferative changes during infection appear to be a beneficial exaggeration of normal functions brought about for resisting the infection. The changes are due to a stimulation by the toxins of the bacteria, even in those cases where no soluble toxins are found *in vitro*, and it is possible that bacteria might emit physical influences. The conclusion arrived at at present appears to be :—It is possible that on the fixed cells of the body and the fixed precursors of the wandering cells are impressed qualities which perpetuate immunity in an animal which has survived an infection.

The foregoing principal conclusions from Professor Ritchie's admirable analysis, quoted almost verbatim, convey but an imperfect idea of the main issues involved in the process of immunisation, natural and artificial; they indicate the enormous amount of work that has been done, and still remains to be done, in connection with the subject. The investigation of the nature, properties, and action *in vitro*, and in animals of the intra-cellular toxins, has been but just begun, and, until full and complete knowledge of the subject is available, the difficulties in preparing potent bacteriolytic serums will not be overcome. These difficulties will vary with the action of the various toxins and will be greater in the case of rapidly-fatal diseases, like cholera and plague, than in typhoid, pneumonia, influenza, etc. And any serum to be effective in the former group must be possessed of great potency, and even then it could give satisfactory results only if used early.

---

* Transactions of the Bombay Medical and Physical Society, April 1902.

C.

PROF. KOLLE AND DR. OTTO'S COMPARATIVE STUDY OF VARIOUS ANTI-PLAGUE SERUMS.

In Professors Koch and Flügge's journal * there lately appeared an article from Prof. Kolle and Dr. Otto giving the results of a comparative study in animals of three different anti-plague serums, *viz*:—1. Lustig and Galeotti's (called by them the Indian serum); 2. Yersin-Roux' (called French); 3. Tavel's (called Berne). Two samples of the first-named serum were examined: one received by them from the Health Officer of Bombay and dated 9th January 1902; and the other, dated 21st March 1902, it appears from a local medical man. It will be noted that none of the samples was despatched to Prof. Kolle direct by Dr. Polverini, who was in charge of the preparation of Professor Lustig's serum. In fact, Dr. Polverini assures the writer that he was not aware that the serums issued by him to the Health Officer and to the Municipal Secretary, who seems to have passed it on to the medical man, were intended for such important investigations. As serums of varying degrees of activity had to be made at the laboratory, on account of the absence of facilities for discarding horses, once purchased, but found to be unsuitable for the purpose after trial, it is more than probable that the serum tested at Berlin was not the best that Dr. Polverini could supply. This presumption is strengthened by the fact that one of the samples was found to contain carbolic acid, the use of which had been abandoned already in 1900, and it must, therefore, have been at least two years old; whereas the other sample showed some agglutinating properties, which were generally totally absent, as Dr. Polverini states, in the serum prepared by him. As the French and Berne serums represented no doubt the best specimens of their kind that the respective laboratories could supply, and as there was no guarantee that the same was the case with the serum sent from Bombay, all that could be said in favour of Prof. Kolle's results is that those particular samples of the Indian serum tested by him were less efficacious in animals than the others, but they prove in no way that Professor Lustig's method of preparation is inferior to the French or Swiss methods.

Prof. Kolle and Dr. Otto's results may be summarised as follows:—

(*a.*) Almost no agglutinating properties were found in Lustig's serum, whereas the French and Berne serums possessed the same in higher degree and in almost identical proportions. But it is a fact well known to all bacteriologists that agglutinating and curative properties are not the same and that they bear no casual relation. (*Vide* Appendix B.)

* Zeitschrift für Hygiene und Infections Krankheiten. IV. Bd., 1902.

(*b.*) All the serums tested did not act well in mice on account of rapid and general septicæmia, whilst, on the other hand, the effects were better in rats, in whom the infection was more localised.

(*c.*) In experimenting by various methods they found that Lustig's serum gave 50 per cent. of protection if injected 24 hours before infection in guinea-pigs; in other experiments life was not saved, but only prolonged.

(*d.*) The details of observations are given by them as follows:—

Serums.	Number of Observations	Percentage of Recovery.
Lustig's	62	20·00
French	90	39·00
Berne	120	57·00
Control	68	3·00

There were, besides, 48 observations with mixed infections without a single recovery. The above table indicates that that particular sample of Lustig's serum was the weakest of the three.

Lustig's serum was also used in guinea-pigs, and the observations made numbered 23: the percentage of recovery was found to be 17·40.

The details as regards the effects on mice and rats of these serums were as under:—

Serums.	Mice.		Rats.	
	No.	Percentage of Recovery.	No.	Percentage of Recovery.
Lustig's	26	0 00	36	33·3
French	50	20·00	40	60·0
Berne	50	31·00	70	75·7

Lustig's serum had no effect on mice, and as to its influence on rats it was found to be the weakest of the three. It is not surprising that the inference Prof. Kolle and Dr. Otto draw from the above tables is unfavourable to Lustig's serum. But it may be pointed out that, apart from the unauthenticated quality of the serum tested by them, the tests applied seem to have been scarcely fair to Lustig's serum, inasmuch as the number of animals experimented upon with it was the smallest, 124, whereas 180 animals were used for the experiments with the French serum and 240 for those with the Berne serum. The results might have been totally different, and more in favour of

the Indian serum, had the same number of experiments been made in each case. We can, therefore, state in this respect, as well as in others that follow, that the conditions of experimenting were not so equalised as they ought to have been in order to guard against and exclude material sources of errors. As to the somewhat startling conclusion—that Lustig's serum should not be used in man—that Prof. Kolle and Dr. Otto have arrived at from the somewhat inexact experiments on animals, we would remind them that they themselves caution us against the application in man of experiences gained in animals. As to their advocating the alternate method of treatment in order to test plague serums in man, it is rather surprising that they should have been so ignorant of the fact that the very method has been adopted with Lustig's serum on over 1,200 patients with conclusive and favourable results.

Dr. Polverini's Reply.

Dr. Polverini in the course of his reply* says that divergent results from experiments in animals are due to different methods of work in various laboratories, to differences in the value of the specimens of the same serum, and even in serum drawn from the same horse at varying periods. He lays great stress on the methods of testing the serum adopted by the critics and he divides his arguments as follows :—

Experiments on Animals.

(*a.*) *The Quantity Injected*:—The results of experiments on animals depend mainly on the absolute exactness of the quantity of the cultures injected, and which should be reasonable in amount and not more than double the minimum lethal dose. For it is now well established that, if any quantity beyond a certain dose is injected, fatal results cannot be averted, even if the quantity of serum injected was many times greater.

(*b.*) *The Mode of Injection:*—The method of injection adopted by Drs. Kolle and Otto is open to serious objection inasmuch as in pricking the tails of mice or rats with a needle dipped into a culture it is not possible to state how much has been injected. The method was, therefore, unsafe and inexact.

(*c.*) *The Cultures Employed:*—The cultures employed should always be of uniform virulence, grown in the same medium, and under the same conditions. Emulsions of internal organs are not safe, nor reliable, on account of variations in virulence and quantity. There is nothing to show that any special care was taken in order to observe the above safeguards in the experiments made at Berlin.

---

* Münchner medizenischen Wochenschrift No. 15, 1903.

(*d.*) *Experiments made in Bombay:*—In his experiments in Bombay, Dr. Polverini says he took special care to eliminate all these sources of error. The cultures used were grown on agar under identical conditions for 48 hours, and their virulence was exactly known, as the material was invariably derived from cultures made from the blood of septicæmic plague patients. A normal loop was used for taking up the cultures; an emulsion of known strength was made in normal saline solution; and the quantity injected was thus definitely known,—more than the m.l.d.; the injections were made subcutaneously with a graduated syringe. Experiments made under the above rigorous conditions showed good results, and Dr. Polverini found that not a single control animal remained alive.

Preparation of the Serum.

In preparing serum for use in the human being it is essential that the cultures should be obtained from plague patients and not from animals in whom the virulence has been artificially kept up. Both the French and Berne serums have, however, been made from cultures of bacilli passed through animals, in order to keep up the virulence, and the serums so made naturally give better results in the same species than one in which the immunising substance has been derived from man. In Kolle's and Otto's experiments, therefore, the conditions were not fair, as a serum prepared from human cultures was used in mice and rats infected from cultures derived from animal sources, and hence their inferences cannot be said to be in any way conclusive.

The Species of Animals Experimented Upon.

The anti-plague serum is not equally efficacious in all species of animals; and, whereas in one species it may give good results, in another there may be absolute failure. Dr. Polverini found in experimenting with a sample of serum from the Institute Pasteur, Paris, that, whilst it was most efficacious in white mice, it completely failed in red-haired rats from Gujarat, although the quantity of culture injected in the latter was much smaller and the dose of the serum proportionately greater. And any conclusion drawn from such observations would, therefore, be erroneous. *Failure in mice or other animals does not necessarily mean failure in the human being.* Whether a plague-serum is curative in man or not can only be ascertained by the treatment of plague patients. Dr. Polverini finally refers to the large series of observations made on plague patients at Bombay; and concludes that Lustig's serum is the only one that has hitherto been tested with good results on an extensive scale by the alternate method advocated by Prof. Kolle and Dr. Otto themselves.

FINALE.

The final chapter in the history of Lustig's serum has been closed so far as this city is concerned. To the representation of the Municipal Corporation, Government replied to the effect that their interest still continued and that it would be looked after by the Imperial Research Laboratory, and that the subject would receive further and more extended consideration on the establishment of a Central Bacteriological Institute at Bombay. All that we have been permitted to know of the interest of the Research Laboratory is that within the last twelve months it has treated some hundred and odd patients with a new serum hitherto unused in man, whilst extensively-used serums, like those of Lustig and Yersin-Roux, have been relegated to the background.

We have passed through seven epidemics of plague at Bombay, and our clinical experience, extending over several thousands of cases, has demonstrated that cases of septicæmic and pneumonic plague, and those who attain to a temperature of 107° or have a pulse-rate ranging to about 160, are almost invariably fatal.* The total number of recoveries in such cases during the above period may be counted on the fingers of one hand. And yet, when we are deliberately told that a serum should be used only in such cases, and the results compared with similar cases not so treated, we are reluctant to believe that such advice is either seriously meant or warranted by any known or accepted principle of serum-therapy. It does not appear to take sufficient cognizance of the rapidity and gravity of the disease, of the difficulties we have to encounter, and the conditions under which we have to work, apart from the difficulties associated with the preparation of a bacteriolytic serum of high potency. In practical therapeutics we have not yet been able to achieve miracles, but that is what we are told to do in connection with the plague-serum. No one can possibly object to keeping always in view the high ideal embodied in the above advice, and to strive one's best to attain to it; but, because with our present knowledge we are unable to do so, does it stand to reason that we should forsake what little we may have in search of the unattainable? Progress in all matters scientific has been from the lesser to the greater and not *vice versâ*, and we fail to see why this universally-accepted canon should be denied to us in the case of plague serum-therapy.

---

* Dr. Alfons Mayr of the Municipal Laboratory examined the blood (by culture) of 1014 patients on admission at the Maratha Hospital during 1902, and found that 437 (43·09 per cent.) were septicæmic: *not one* out of this large number recovered.

At the Arthur Road Hospital in 1901, 43·79 per cent. of patients were found to be septicæmic on admission; and out of 180 so found there were *four* recoveries, two in doubtful cases and two in whom only one or two colonies were found on culture.

No recovery in any authenticated case of pneumonic plague (*bacteriologically verified*) has been hitherto reported in Bombay, and I have seen none in the course of seven epidemics.

We had in this case a serum that had been investigated in man and animals for over four years with comparatively encouraging results. We say comparatively, for it must be so, regard being had to the high mortality-rate of the disease in Bombay. We had applied it to over 1,500 patients and we were just able, after a great deal of laborious and patient work, to see our way to increasing its potency and perfecting its action when all of a sudden the work was put a stop to, and all the knowledge and experience gained practically lost. Whilst at Paris and Geneva, at St. Petersburg and Moscow, and even in far-off Brazil, investigations on plague serum-therapy are in progress and pushing forward, not Bombay alone,—the home and habitat of plague,—but all India, must rest content with such vicarious assistance as any foreign country may be pleased to extend to them!