An address on the general pathology and serum treatment of plague : delivered at a meeting of the medical profession of Bombay, held under the auspices of the Bombay Medical Union, on March 18th, 1908 : Sir Bhalchandra Krishna, Kt., the president of the Union in the chair / by Khan Bahadur N.H. Choksy, M.D.

With the Author's Compliments.

AN ADDRESS ON THE GENERAL PATHOLOGY AND SERUM TREATMENT OF PLAGUE

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In all ages the search after truth, whether in science or in theology, whether by translation of the Bible, by looking at the stars, by following the life history of pathogenic bacteria in the living animal, or by making an antitoxic serum for the cure of disease, has met with irritated opposition and obstructive prejudice and its supporters have not always escaped calumny. I need not recall to you the invectives that have been applied to some of those most highly esteemed by our profession and by the public.—Mr. Charles A. Ballance in his Presidential Address delivered before the Medical Society of London—*The Lancet*—October 20th, 1906.

AN ADDRESS

ON THE

GENERAL PATHOLOGY

AND

SERUM TREATMENT OF PLAGUE.

Mr. President and Gentlemen,—

The theme of my discourse to-day is entitled the General Pathology and Serum Treatment of Plague. I have advisedly placed the pathology of the affection in the forefront, as apart from its intrinsic importance, it is absolutely necessary to our purpose. Whilst enabling us to understand the essential nature of the disease, as also to grasp the full significance of the grave changes that plague induces in the system, it has a practical bearing upon the application of the serum treatment, inasmuch as it is only by the light it throws upon many obscure problems connected therewith that it becomes possible for us to define its limitations and to estimate its results.

The principal points that I propose to lay before you for consideration are :—

(1) The method of invasion in plague.

(2) The development of the affection.

(3) Its various types, their prevalence and fatality.

(4) The pathological changes which the plague toxin brings about.

(5) The mode of action of the serum and the unfavourable factors it has to contend against.

(6) The results of the application of the serum treatment.

Anything like a full or comprehensive discussion of the above points would take up much more time than is at my disposal, besides entailing too great a tax upon your indulgence. I shall therefore content myself with a brief review of so much as bears upon our principal topic.

1.—THE METHOD OF INVASION IN PLAGUE.

Even in the early days of plague at Bombay, clinical observation tended to show that the channel by which the bacillus pestis gained entrance into the system was through the skin. Careful search for any visible points of infection gave negative results except in about 8–10 % of cases, where pustules, phlyctenules and bullæ were found. Their significance,—as to whether they were the original source of the infection or its after effects,*—could not then be positively determined. And as their incidence was so infrequent, any positive conclusion about their relationship to the disease was then out of the question[1].

The observations of the Russian Plague Commission (1897-1898), however, demonstrated that plague could be induced in monkeys by subcutaneous injections of cultures without leaving any trace at the point of infection; our failure in detecting the same in the human being was thus explained. Further light upon the subject was thrown by the clinical study of a special type of plague, where the effects of the invasion being almost wholly confined to the skin, the progress of the affection could be watched by the naked eye from day to day. I described, for the first time, this type under the name of "Cellulo-Cutaneous Plague" in a paper that I read by invitation before the Medical and Physical Society of Bombay in 1900[2]. I brought forward sufficient evidence, bacteriological and clinical, to entitle it to be recognised as a distinct and at the same time the most benign type of plague. The above and other evidence derived from bacteriological examination of the contents of the cutaneous manifestations abovenamed strengthened the conviction among many workers that infection in plague took place through the skin.[3] "Almost all observers are agreed"—says Major Lamb in the recently published volume on the Etiology and Epidemiology of Plague[4]—"that as far as the common forms of the disease are concerned, man becomes infected through the skin, the primary bubo developing in the gland in connection with the lymphatics which drain the area of skin through which the plague bacilli gain entrance." And that the agent concerned in causing

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* In many instances they escape notice being very minute in the early stages, and when fully developed have been mistaken for after-effects.

the infection, is the rat flea, has been conclusively demonstrated by the extensive series of most elaborate, ingenious and painstaking experiments conducted by the Plague Research Commission. I would refer you to their published reports in the Journal of Hygiene[5].

The actual process by which infection is brought about is thus summarised by Lamb :—

"After careful consideration of all the available evidence bearing on the subject, the Commission were of opinion that it pointed to the conclusion that the bacilli after multiplying in the stomach of the rat flea—Pulex Cheopis—leave its body with the fæces, and then become injected into the healthy animal either by being carried in by the pricker or by being rubbed into the pricker wounds." The flea while sucking has the habit of squirting blood *per anum*. Wounds made by the pricker afford a sufficient avenue for the entrance of the bacilli even when no rubbing is resorted to. It is also possible for infection to take place by contaminated mouth parts or by regurgitation from the stomach. Infection by the eating of infected fleas and by infected saliva can be almost certainly excluded. "The chances of an animal contracting plague after being bitten by a single infected flea are remote." The method of invasion in plague in the case of the bubonic and cellulo-cutaneous types is thus explained.

It has been assumed that in septicæmic plague there is direct infection of the blood. There is however just the possibility, that it might not be always so, as in some instances, whilst the most careful search during life has failed to elicit any evidence of glandular enlargement, the autopsy has revealed bunches of very tiny buboes too deep-seated to be felt, in the axilla and other parts. That can only occur when the lymphatic glands having through some inexplicable cause, failed to arrest the bacilli in their progress, the latter gain an easy entrance into the blood and produce septicæmia. Under such circumstances errors are liable in diagnosis ; a case of the bubonic type with secondary septicæmia is thus likely to be mistaken for primary septicæmic plague. Many observers have noted the presence of very minute buboes in some of the most virulent and fatal cases of plague, and such undoubtedly are of this nature.

Infection in pneumonic plague is contracted by inhalation—especially of the fine spray of the sputum teeming with the bacilli. I would however venture to ask whether it is the only possible channel ? The apparent primary pneumonia might be but a

secondary manifestation of septicæmic plague. Or again it might be caused by the infected finger—so commonly utilised in removing the infective sputum from between the lips—conveying the bacilli to the mouth and establishing an infective focus in the tonsils or the pharynx. These points still require elucidation.

I did not intend to say anything further on this part of the subject, but the recently published report of Dr. Hossack of Calcutta calls for a few remarks. It appears that he has not yet been fully convinced that the rat-flea-to-man theory has been sufficiently well established and he desires further investigation by post-mortem examinations to find out whether there might not exist the possibility of infection through the alimentary canal. Here he appears to follow Hunter and some other observers at Hongkong. So far as our clinical and post-mortem observations go, on this side of India, I am fully convinced that infection does not take place in the way suggested. In not a single instance among over 100 autopsies, at the Arthur Road Hospital, have we come across evidence of primary abdominal infection; the pathological changes noted in the abdominal cavity have been always secondary. Nor does clinical evidence lend any support to this assumption. In the Annual Report of the Maratha Plague Hospital for 1904, I have dealt at length with this theory and the views therein expressed, have, I am gratified to say, met with the approval of Prof. C. J. Martin, F. R. S., Director of the Lister Institute and Member of the Advisory Committee for Plague Investigations in India.

We thus see that bacteriological investigation, has once again corroborated and confirmed the observations made at the bed-side and in the post-mortem room.

2.—THE DEVELOPMENT OF PLAGUE.

Once infection has been brought about by the bite of the flea it proceeds apace; the period of incubation being about three days. The lymph channels take up the bacilli, which the lymph stream conveys to the nearest lymphatic, glands, where it is, that in the words of Ashburton Thompson[6], the first attack is delivered. Except in about 8—10 % of cases, no visible trace is left at the point of infection. The organism soon reacts to the stimulus of this foreign invasion but to no purpose, as it is almost always worsted in the conflict, owing to the normal human blood being devoid of any bactericidal action against the bacillus pestis, just as it is against staphylococci and streptococci as pointed out by Sir Almroth Wright[7]. The immediate result becomes apparent in the enlarged,

swollen and tender gland that we now recognise as a bubo. Its blood and lymphatic supply becomes considerably increased in order to cope with the demand, the vessels becoming dilated and engorged. The bacilli enormously multiply and at the same time disintegrate; and it is to the liberation of the toxin through this disintegration that we owe all the symptoms of the affection. During the period of incubation, no marked symptoms are usually apparent, but no sooner the toxin begins to exert its baneful influence, the whole chain of clinical phenomena comes into view. And here it is, that we recognise the essential difference between an *Intoxication Disease* like diphtheria, wherein the toxin excreted by the microbes as a metabolic product, is free and therefore capable of easy neutralisation, and plague, wherein the toxin is an endo-toxin, confined within the bacterial cell, and necessitating its disintegration before it could be set free and acted upon.

The primary bubo where the attack raged, is seen to be engorged, and becomes, in that expressive German term, "blood-full;" the toxin acting locally upon the medulla causes hæmorrhages within its substance, followed by several foci of necrosis which progress until the entire gland becomes involved. The mischief however does not confine itself to this primary bubo; numerous other glands in the neighbourhood become infected and a conglomeration of such is the usual result. The infection then spreads further along the lymph channels as shown by the infection *e.g.*, in the case of femoral buboes, of the inguinal, the superficial and the deep iliac as also the glands along the course of the abdominal vessels and the mesentric glands. In other cases, not so frequent, the infection travels downwards involving the whole femoral chain, the popliteal glands and glands in the calf upto the ankle. In the upper extremity, the axillary becomes infected, and then the brachial and epi-trochlear glands share the same fate. In the neck, the infection involves the parotid, the submaxillary, anterior and posterior cervical, pre-auricular, and occipetal, sublingual and supra-hyodean through extension from the primary cervical or parotid buboes. The buboes are usually surrounded by peri-glandular œdema or infiltration, generally serous or serosanguinous, and at times hæmorrhagic or gelatinous. Further, direct communication becomes established between the buboes on the one hand, and arterial and venous channels on the other, giving rise to septicæmia with all its attendant evils[8-9]. Such then is the development of the bubonic type of plague.

Now let us see what occurs among those 8–10 % of cases in whom some visible point of infection is apparent. It appears as (*a*) a nodule slightly incurved at the apex; at first hard, but

subsequently surmounted by a tiny vesicle and is called a phlyctenule : (*b*) if seen later, it has become converted into a pustule : (*c*) spherical bullæ having clear cut margins, with serous, or serosanious contents and lastly (*d*) umbilicated bullæ, with a central core suspended from the under surface of the umbilication and attached to the base, with similar contents. Almost pure cultures of the bacillus pestis have been obtained from any of the above, when examined before the contents had become purulent. These cutaneous manifestations precede the symptoms by three to five days. It is often possible to trace the infection from them along the course of the lymph channels, and thus to establish a direct relation between them and the primary bubo. The contents of the phlyctenules and even some bullæ become purulent and if evacuated, the sore left heals rapidly under ordinary treatment. In the case of umbilicated bullæ, a different course is to be noticed. If the bulla is cut open or bursts of itself and the central core removed, its point of attachment to the base, appears as a small dark spot. It gradually increases in size until the whole of its base is encroached upon, and obliterated by a dark scab. This continues to spread at the circumference from day to day, until a period is reached when the medium suitable for the further multiplication of the bacillus pestis becoming exhausted, a line of demarcation appears. The scab assumes a dark greenish hue, feels cold to the touch, is almost hard and leathery and depressed in the centre, as if firmly bound down to the tissues underneath. Its spreading margin, somewhat higher, is conterminous with the surrounding skin which becomes converted into a hard and angry areola studded with minute vesicles. If a little fluid be examined from the margin it invariably shows a pure culture of the bacillus pestis. The destructive process, if limited, becomes a comparatively benign form of plague to which, I have applied the term "Cellulo-Cutaneous Plague." * The buboes, if present—they are not invariably so—are secondary ; and although owing to the slowness of the process, the course of the disease is prolonged from two to three weeks instead of the normal period of 8 to 10 days in all uncomplicated cases of bubonic plague, the recovery rate is higher. Should the necrosis become extensive, as in some cases it does, involving as much as 60 to 90 square inches of the body surface, the infection becomes generalised and the patient succumbs through septicæmia.† Once the line of demarcation has formed, it is not

* Otherwise called carbuncles and hitherto assumed to be a complication of plague ; also known as pest necroses.

† It is also possible for septicæmia to occur through the original bulla, before necrosis developes, as in case No. 129 of 1908, at the Maratha Hospital.

difficult to remove the entire slough *en masse* leaving behind a saucershaped depression in the subcutaneous tissue (often exposing the deep fascia and muscles) of gradually increasing depth from the periphery to the centre, filled with shreds of necrosed tissue, pus and blood; it gradually assumes a healthy aspect under appropriate treatment. Such necroses have been observed on the scalp, neck, face, back, chest, arm and forearm, the abdominal wall, lumbar and gluteal regions, over the mammary gland, the vulva and on the scrotum, the thigh, leg and foot, in fact whenever such umbilicated blisters might be situated. Instead of the necrosis being primary, we occasionally come across cases, where the bubo rapidly comes up to the surface, and infects the skin from underneath, thus producing a secondary necrosis, which spreads in a similar manner. When the slough is ultimately removed, the bubo is found to be firmly adherent to its under surface and comes away with it. For further information upon the subject, I would refer you to my work on the Treatment of Plague with Prof. Lustig's Serum.

The development of the septicæmic type, we have already partially discussed above: once septicæmia has set in, the patient is practically doomed; all the symptoms take on the gravest aspect, but not invariably so. In some instances the patient does not appear to be at all seriously ill and we are apt to be thrown off cur guard. Death however takes place within four to seven days and it is not uncommon for buboes to appear in various parts of the body just before death.

We are all familiar with the extremely insidious development and withal rapid progress of pneumonic plague. I can recall vividly to mind many a case that I had the opportunity to observe from within an hour or two of its onset until the fatal termination. Moderate fever, neither the pulse, nor the respiratory ratio correspondingly higher: no physical signs, and yet marked prostration, and aspect of grave illness; then within a few hours, some scanty pellets of hæmorrhagic sputum, followed by death within twenty four hours. The apparent initial mildness rapidly assuming gravity, even without the appearance of the characteristic sputum is a marked feature of the type. The sputum may be thick, viscid, almost or even purely hæmorrhagic or thin and mucoid tinged bright red; it may be profuse or extremely scanty, and brought up at long intervals. Simple microscopic examination of the sputum is extremely deceptive for purposes of diagnosis as other organisms simulating the morphological characters of the bacillus pestis are not of infrequent occurrence. Many cases so diagnosed have eventually proved not to be pneumonic plague. It is therefore absolutely necessary to make a culture and inoculate animals with it or with the sputum. If the animal becomes ill and dies, and

plague bacilli are recovered from it, then only the diagnosis can be positive. This procedure is however not always necessary, for the rapid progress and fatal termination of the case, leave scarcely any doubt about its nature. The rarity of this type combined with its great infectivity, is of sufficient importance to claim special notice at our hands. One single case is often the focus of a whole series of cases. The case of the late Major Manser, I.M.S. and his attending nurses; that of one of the former House-Surgeons of the Maratha Hospital with its series of 16 cases, that of one of the nurses at the Bai Motlabai Hospital and of the student, both attending upon a case of the pneumonic type, who had miscarried—one and all terminating fatally, is sufficiently appalling. So far as regards Bombay. On the other side of India, Major Green and Dr. Justice[10] have recorded the history of the Baker-gunge epidemic of pneumonic plague, where one case originating at Calcutta in the house of Kaviraj Dwarkanath, led to a series of 19 other cases, all of whom proved fatal. Lieut. Col. Crawford[11] has recorded another similar outbreak involving 20 persons at Hughli in January 1905. In all the above instances the infective agent was the sputum of the patient which induced a similar affection among others. Under other circumstances however, especially if it happens to fall upon an exposed and inflamed mucous surface like the conjunctiva, it gives rise to bubonic plague. The saddest case of the kind that has come under my observation was that of one of the English Nurses, at the Arthur Road Hospital. She had a severe catarrh with injected conjunctiva at the time. Whilst bending over a patient to feed him, he happened to cough and a drop of the infected sputum fell into the eye; three days later, she developed plague with pre-auricular, parotid and cervical buboes with infiltration, on the side of the infected eye and eventually succumbed from œdema of the glottis.

No recovery from pneumonic plague in which the diagnosis has been confirmed as above has been hitherto recorded in this city. I have seen none in the course of eleven epidemics. I am however able to report one instance where there was double infection of the lungs by the bacillus pestis and bacillus pyocaneous. The patient was admitted on the third day of illness—1st July 1907—with moderate fever 101°8, pulse 110, of fair volume and respirations 30: no physical signs and no sputum to indicate the nature of the case, except marked prostration. On the night of the sixth day however, the temperature rose to 104°4, the pulse to 130 and respirations to 35, and he developed symptoms of pain, tightness and constriction in the chest, dyspnœa and cough, with scanty sputum, the naked eye appearance of which was characteristic

neither of pneumonic plague nor of croupous pneumonia. It appeared to be somewhat dark and rusty with a layer of greenish mucus, almost purulent. Physical examination revealed isolated patches of dulness in the middle lobe on both sides: A culture of the sputum was then made and sent to Dr. Ghadially, the Municipal Analyst, who reported three days later the presence of plague bacilli and the bacillus pyocaneous in the culture; a little scraping form which was inoculated subcutaneously into a white mouse and it succumbed within 48 hours and plague bacilli were recovered from it. There was thus no room for doubt as to the nature of the case. The patient remained in a rather precarious condition for three days but improved thereafter, the temperature, pulse and respirations gradually became lower and when the sputum which had in the meanwhile altered its character, was re-examined on the 11th idem, the thirtheenth day of illness, there were no plague bacilli but staphylococcus aureus only: some of the culture from the sputun inoculated into a mouse, did not kill it. In the meanwhile infection from the bronchial glands had spread to the deep abdominal and mesenteric glands, and pain, fixation of the abdominal wall, and tympanites developed, the course being subacute, without much rise of temperature, after the seventeenth day of illness. Recovery however was gradual. In another case, there was double infection from the bacillus pestis, and the pneumococcus and it ended in recovery. Recovery is thus possible in cases of moderate mixed infection.

3.—THE VARIOUS TYPES OF PLAGUE, THEIR PREVALENCE, FATALITY, ETC.

(*a*) *The Frequency of the Various Types* :—Among the 13,023 plague cases that have passed through my hands at the Arthur Road and Maratha Hospitals during the 11 epidemics, I found that the bubonic type was by far the most prevalent accounting for 92.8 % of all admissions. The other types, whatever their pathological, clinical or epidemiological importance were of insignificant frequency. The cellulo-cutaneous was present among 3·7 % and the septicæmic in 2·4 %. The most infective and virulent, the pneumonic, was noticed among just 1 % of all cases. I am, however, inclined to believe, that it prevails to a somewhat greater extent and the Plague Research Commission corroborate :this when they lay down the ratio at 2·5 % :—

Table showing the Frequency of the Various Types of Plague.

Types of Plague.	Frequency.
Bubonic *	92·8 %
Cellulo-Cutaneous	3·7 %
Septicæmic	2·4 %
Pneumonic	1·0 %
Pestis Ambulans	0·1 %

(*b*) *Their Fatality* :—The mortality rate varies from practically nil in pestis ambulans to 98·07 and 99·25 % in the septicæmic and pneumonic types respectively. Happily for us, these most virulent forms do not contribute much to the mortality owing to their rarity. The bubonic type is therefore principally responsible for our heavy death roll. The cellulo-cutaneous type is comparatively benign, the case mortality rate being 63·77% as compared with 74·06 in the bubonic. The following statement indicates the incidence of attacks, deaths and recoveries among these types :—

Table showing the Number of Attacks, Deaths, Recoveries and Percentage of Mortality among various Types of Plague.

Types.	No.	Died.	Recovered.	Case mortality rate per cent.
Bubonic	12,080	8,947	3,133	74·06
Cellulo-Cutaneous	497	317	180	63·77
Septicæmic	312	306	6	98·07
Pneumonic	134	133	1	99·25
Total ...	13,023	9,703	3,320	74·50

* Includes about 1 o/o of cases of Mixed Infection of Plague with Malaria, Relapsing Fever, Small-pox, Chicken-pox, Venereal Infection, etc.

(*c*) *The Buboes* :—Following the classification adopted by Drs. Polverini and Mayr[13] in their report on the serum treatment in 1901, I have grouped the buboes into four main divisions according to their distribution. All buboes in a continuous chain *e.g.* femoral, inguinal and iliac ; or again axillary, brachial and epi-trochlear or parotid and cervical with or without further extension have been grouped under "Multiple Contiguous." When more than one bubo existed in two widely separated parts of the body, *e.g.*, one in femoral and one in axillary, etc., they have been grouped as "Multiple Distal": single axillary buboes on account of their well-known gravity form a class by itself and lastly single buboes in all other situations *e.g.* single cervical, or femoral or inguinal, etc., are placed under one class[14] :—

Table showing the Classification of Buboes and their Frequency.

Buboes.	Frequency.
Multiple Contiguous	63·0 o/o
Multiple Distal	12·5 o/o
Single Axillary	16·5 o/o
All other Single Buboes	8·0 o/o

The case mortality rate also varies, but not within very wide limits, single buboes having the lowest rate—66.30% and single axillary the highest—77.92% as the following statement shows :—

Table showing the Mortality Rates according to Position of Buboes.

	No.	Died.	Recovered.	Case mortality rate per cent.
Multiple Contiguous	7,559	5,698	1,861	75·38
Multiple Distal	1,519	1,029	490	67·74
Axillary	1,975	1,539	436	77·92
All other Single Buboes	1,027	681	346	66·30
Total ...	12,090	8,947	3,133	74·06

(*d*) *Racial Mortality* :—One of the peculiar characteristics of plague is that the incidence of mortality shows wide variations between various races, depending mainly upon their social environment. Among the 13,023 patients above referred to, all the principal races of Bombay were fairly represented. All were treated under the same conditions, under identical methods of treatment and practically under one hand. And yet they exhibited great diversity in results indicating that better stamina, better social conditions and consequent better methods of living have all their due share in modifying these results. Among the Indian patients the Parsees had the lowest mortality rate of 50 % and Hindus of all classes the highest—76·57 % ; the Mahomedans, Native Christians (almost all Goans) and Beni-Israelites standing between the two extremes with 65 to 68 % :—

Table showing the Incidence of Mortality from Plague among Various Races.

Races.	No.	Died.	Recovered.	Case mortality rate per cent.
Hindoos	10,315	7,899	2,416	76·57
Mahomedans	1,450	998	472	68·82
Native Christians	1,088	716	372	65·80
Parsees	126	63	63	50·00
Beni-Israelites	38	26	12	68·42
Eurasians	3	...	3	...
Japanese	2	...	2	...
Chinese	1	1	...	100·00
Total ...	13,023	9,703	3,320	74·50

(*e*) *Mortality by Sexes* :—Another point of some importance is the variation in the mortality rates among the sexes. There is

scarcely any difference between males and females, but children have a lower mortality rate by nearly 10 per cent.:—

Table showing the Mortality Rates by Sexes.

Sexes.	No.	Died.	Recovered.	Mortality rate per cent.
Males	9,126	6,908	2,218	75·69
Females	2,636	1,967	669	74.62
Children	1,261	828	433	65·66
Total ...	13,023	9,703	3,320	74·50

4.—PATHOLOGICAL CHANGES IN PLAGUE.

It is to the post-mortem room that we have to turn for the study of the special pathology of the disease. Here we see that the chief characteristic departure from the normal is hæmorrhage, diffuse, extensive, and wide-spread over almost every tissue and organ, involving many, sparing but a few. The cause is probably not dissimilar to what obtains in the toxæmia from snake venom, but underlying a different condition. Whilst snake venom contains a cytotoxin or endotheliolysin exerting a direct solvent action upon the capillary endothelium and thereby causing hæmorrhages and extravasations, the bacillus pestis produces in culture, a hæmolysin which has the property of dissolving the blood corpuscles. Like the typhoid bacillus, it also produces hæmagglutinins which Welch thinks, are responsible for thrombi from coalesced red corpuscles in the small blood vessels in typhoid and probably also in plague. Let us now consider the macroscopic changes visible to the naked eye under the various systems[16-17]:—

The Brain and the Meninges:—Injection of the cerebral, as also spinal meninges; effusion of lymph (rare) if meningitis be present; excess of fluid in the arachnoid sac; the ventricles full of fluid; the choroid plexuses and the convolutions œdematous and swollen and occasionally hæmatoma of the dura mater. Passive congestion is thus the keynote of these changes.

The Respiratory System :—The larynx injected : occasionally inflamed : hæmorrhages beneath its mucous membrane ; which is also œdematous : aryténo-epiglottidean fold swollen and œdematous : The lungs engorged and œdematous full of sero-sanguinous fluid ; lobular pneumonia in isolated mottled grey patches surrounded by areolæ of intensely congested lung tissue; occasionally lobar pneumonia from pure pest infection ; hæmorrhagic infarcts ; and infarcts from masses of pest bacilli ; multiple embolic abscesses studded over different lobes ; and atelectasis pulmonum. Bronchitis and bronchiectasis. Fibrinous pleurisy, hæmorrhages on the parietal, visceral and diaphragmatic layers of the pleura. Hæmorrhages in the loose connective tissue of the anterior and posterior mediastina. The bronchial glands tumefied, swollen and hæmorrhagic from pest infection.

The Heart and Blood-Vessels :—Pericardial fluid in excess, sometimes sanious, hæmorrhages in the epicardium, pericardium and endocardium, also in the substance of the myocardium : the latter acutely degenerated, soft and friable ; heart cavities generally dilated ; fatty degeneration of the heart muscle, acute endocarditis. Thrombi in the large veins and hæmorrhages in the intima of blood vessels, especially the veins lying adherent to the infected glands.

The Alimentary Canal :—The pharynx congested, rarely a pseudo-diphtheritic membrane covering the tonsils and extending downwards ; the tonsils acutely inflamed : occasionally abscesses and hæmorrhages within the parenchyma. The œsophagus generlly marked out with punctate and sometimes with diffuse hæmorrhages. The mucous membrane of the stomach usually bile-stained : intense injection ; and punctate, stellar or diffuse hæmorrhages with acute erosion. The intestines similarly hæmorrhagic from the pylorus to the rectum, with swollen Peyer's patches and occasional ulceration. The mesenteric glands tumefied, from rosy to dark purple when infected and hæmorrhages in the mesentery ; also in the retro-peritoneal connective tissue and the loose connective tissue surrounding the viscera ; hæmorrhages on the inner aspect of the abdominal wall and within the recti muscles. Hæmorrhages around the deep iliac glands.

The Spleen :—Acute tumor of the spleen from engorgement ; acute degeneration of the substance ; the capsule adherent ; substance deep chocolate almost rusty brown, soft and pulpy like a bag of homogeneous jelly ; hæmorrhagic and embolic infarcts and small abscesses or cysts. Malpighian bodies swollen and distinctly visible.

The Liver :—The liver swollen and enlarged : acute infective degeneration, soft and friable ; necrotic patches within the substance and on the capsule ; fatty degeneration ; multiple embolic abscesses sometimes amyloid degeneration with the surface marbled.

The Kidneys :—The kidneys show parenchymatous and hæmorrhagic nephritis with acute parenchymatous degeneration ; the capsule adherent, stellate and other hæmorrhages ; and hæmorrhagic infarcts ; the cortex thin ; the pyramids swollen and so also the Malpighian capsules ; hæmorrhages in the pelvis of the kidneys; amyloid degeneration ; and profuse hæmorrhage in the connective tissue surrounding them so that the kidneys are found actually embedded in a mass of partly coagulated blood. Embolic infarcts, abscesses and cysts.

Hæmorrhages are found in the ovaries. The skin occasionally shows subcutaneous patches of hæmorrhage, petechiæ and the necroses above described. There is acute red degeneration of the marrow of long bones ; the synovial fringes of joints are found to be infected.

Such in brief are the various lesions that the plague toxin sets up in the system ; they are to be observed in all autopsies performed from the third day of illness and onwards. They impress upon us a very important lesson, *viz.*, that plague is not concentrated solely in its outward and visible manifestations, *viz.*, the buboes. Once the pest bacillus, has succeeded in annihilating their defensive action, they sink into comparative insignificance. It is to the above pathological changes and to them alone that our attention should be directed, for the ultimate fate of the patient depends, not upon the suppuration of the buboes as so often imagined by many and also popularly believed, but upon the extent to which the important organs have become involved and upon the rapidity with which the system is able to throw off the effects of the toxin from them. We thus realise how recovery becomes practically impossible once such grave and fundamental changes have occurred in the normal constituents of the organs. How futile and puny then must our efforts appear when we attempt to control the same by internal antiseptics and drugs and even by serums. The latter however potent, cannot influence the tissue changes nor alter them, if existing, though they do prevent further increase. Hence the necessity of the early application of the serums to forestall the combination of the toxin with the tissue cells.

The symptoms during life but partially reflect these conditions ; their gravity however is enough to demonstrate the extent of the intoxication. I lay before you a tabular statement of the grave

complications and sequelæ encountered among the above 13,023 cases which will not fail to interest you. It gives us a fair idea of the malignant nature of the infection, as also of the ways in which it manifests itself. Among the most fatal complications must be accounted hæmorrhages from the stomach ; secondary or terminal pneumonia, subacute pulmonary œdema ; acute cardiac failure, etc., etc. I do not propose to weary you with the detailed consideration of the various symptoms as you are just as familiar with them as I am. But perhaps you would like to know how they struck a lay observer during the early days of plague in London, about 1625.* George Wither, the Puritan poet of the English Revolution who died the year after the Fire of London, 1667 and who had once been himself a victim to the disease, thus describes the symptoms :—

"On some this plague doth steal insensibly,
Their muddy nature stirring secretly
To their destruction. Some it striketh so
As if a mortal hand had with a blow
Arrested them, and on their flesh hath seen
A palm's impression to appearance been.
One man is faint, weak, sickly, full of fear,
And draws his breath where strong infections are
Yet scapes with life. Another man is young
Light hearted, healthy, stout, well-tempered, strong
And lives in wholesome air, yet gets a fit
Of this land-calenture, and dies of it.
Some are tormented of it till we see
Their veins and sinews almost broken be
The very soul distracted, sense bereft
And scarce the smallest hope of scaping left
Yet soon recover. Other some again
Fall suddenly, yet feel so little pain
When they are seized, that they breathless lie,
Ere any dying symptoms we espy.
On some an endless drowsiness doth creep
Some others cannot get a wink of sleep.
This useth, every day, preservatives,
Yet dies; another taketh none, yet lives,
Even thus uncertainly this sickness plays
Spares, wounds and killeth many different ways."

The above lines show that neither the lapse of time, nor the differences of climate have altered the fickle characteristics of the disease. What it then was, it remains to this day.—

* The Great Plague year was 1665.

Table showing the Principal Complications and Sequelæ in Plague :—

	Number.	Died.	Recovered.
HÆMORRHAGES.			
Coffee-Ground Vomiting	493	490	3
Hæmatemesis	30	30	...
Hæmaturia	91	67	24
Melæna...	45	38	7
Hæmoptysis	42	40	2
Epistaxis...	40	30	10
Sub-Conjunctival Hæmorrhage	100	85	15
Sub-cutaneous Hæmorrhage	35	33	2
Petechiæ...	51	48	3
Menorrhagia	111	96	15
RESPIRATORY SYSTEM.			
Secondary Pneumonia	453	389	64
Subacute Pulmonary Œdema	690	684	6
Œdema of Glottis	125	123	2
Laryngitis	21	15	6
Pleuro-pneumonia	26	26	...
Inflammation of Thyroid and Abscess ...	10	6	4
CIRCULATORY SYSTEM.			
Acute Cardiac Failure	785	785	...
Endocarditis	38	38	...
Pericarditis	27	27	...

Table showing the Principal Complications, &c.—(continued.)

	Number.	Died.	Recovered.
ALIMENTARY SYSTEM.			
Glossitis	12	10	2
Tonsillitis	115	60	55
Pharyngitis	78	50	28
Diarrhœa (Profuse)	85	81	4
Hiccough	250	210	40
Tympanites (Grave)	108	88	20
Icterus (Grave)...	60	60	...
Peritonitis (Localised)...	33	30	3
Mesenteric Infection	265	185	80
Suppression of Urine and Uræmia	20	19	1
NERVOUS SYSTEM.			
Marasmus (Acute and Sub-acute)	230	205	25
Aphasia	55	47	8
Meningitis and Meningeal Irritation... ...	231	221	10
Tetanus	36	35	1
Epilepsy	34	32	2
General Convulsions	105	104	1
Peripheral Neuritis and Paralysis	186	140	46
Glosso-Labio-Pharygeal-Paralysis	70	50	20
Insanity	30	26	4
Coma Vigil	50	50	...

Table showing the Principal Complications, &c.—(concluded.)

	Number.	Died.	Recovered.
GENERAL.			
Hyperpyrexia	35	20	15
Pest Pyæmia	64	62	2
CUTANEOUS SYSTEM.			
Acne (General)	31	22	9
Herpes (Face and lips)	60	35	25
Gangrene	24	23	1
Bullæ and Blisters (Foul)	47	47	...
Necroses...	497	317	180
THE SPECIAL SENSES.			
Keratitis...	161	131	30
Iritis and Hypopion	85	70	15
Panophthalmitis (Single and double) ...	75	67	8
Otorrhœa...	35	27	8
GENERATIVE SYSTEM.			
Abortion and Miscarriage	121	118	3
Mammary Abscess	25	17	8
Orchitis and Epidydimitis	30	25	5
Priapism—(Persistent)	15	7	8
OSSEOUS AND ARTICULAR SYSTEMS.			
Periostitis	45	20	25
Suppurative Arthritis	21	10	11

5.—THE MODE OF ACTION OF THE SERUM AND THE UNFAVOURABLE FACTORS INFLUENCING THE SAME.

(*a*). Various theories have been propounded from time to time to explain the processes of active and passive immunisation. Two theories have however long held the field. The first was the phagocytic theory of Metchnikoff and the second the side-chain theory (Seitenketten-theorie) of Ehrlich. Whilst the former assigned all the functions to the phagocytes in attracting to themselves, englobing and destroying the bacteria, the latter attributed the greater portion of the role to the body fluids. Recent researches have however shown that the two theories are not incompatible. The literature of the subject has become so vast that I can but merely allude here to accepted facts, asking those interested in the subject to study the writings of Bulloch, Wright, Ehrlich, Metchnikoff, Pfeiffer, Bordet, Wassermann, Von Dungern, Welch, Martin, Muir, Ritchie, Macfayden, Rowland and a host of other observers. The latest resume of the subject is by Dean of the Lister Institute in the discussion on phagcytosis at the British Medical Association Meeting at Exeter [18].

The factors concerned in the process of bacteriolysis are complex and require the presence of two substances :–(*a*) The immune body or amboceptor and (*b*) the complement or alexin. In the case of purely "Antitoxic" serums such as the antidiphtheritic the immune body which is contained in the serum directly neutralises the soluble and free diphtheria toxins. The process is simple and takes place in definite chemical proportions. When however, as in the case of plague, the bacterial toxin is contained within the cell of the organism, necessitating its breaking up or disintegration before it could be acted upon, the immune body alone is not capable of bringing this about. What takes place is this. The immune body according to Ehrlich possessing as it does a double affinity, firstly attaches itself to the bacterial cell and thereby sensitises it ; and secondly the combination so formed. attracts to itself by virtue of the other affinity, the leucocytes which contain the complement or alexin. Ultimately it is this dual action of the immune body and the complement that brings about first phagocytosis and the subsequent solution or destruction of the bacterial cell. The same process applies in the case of hæmolysis. Its complexity and double nature are the chief causes which interfere with the success of the therapeutical application of bacteriolytic serums against plague, typhoid, cholera, etc. According to Metchnikoff two processes are involved in phagocytosis– (*a*) the

attraction of the leucocytes by the bacteria and the killing and digesting of the latter by the former. In natural immunity, the protoplasm of the leucocytes produces both the immune body and the complement which act upon and destroy the englobed bacteria without leaving the cells. But in artificial immunity, the immune body escapes in the plasma and the complement similarly. Both are found in the immune serums, the complement escaping from the leucocytes by the breaking up of the dying phagocytes or by the latter liberating it in the process of dying. The subject however is so full of complexities that nothing like a definite agreement on the relative roles played by the plasma and the leucocytes can be determined, as both are so inter-dependent. I have therefore indicated here the barest outline and cannot do better than quote the concluding part of Dr. Dean's paper. "In the discussion of such a question as this, nothing could be more out of place than dogmatism"—says Dean. "At the same time the bulk of the evidence sifted from the literature and derived from my own experiments drives me to the conclusion that the opsonizing (*bacteriolysing in this case*) action is due to two substances;—the one thermostable, the substance sensibilisatrice or amboceptor; the other thermolabile, the alexin or complement. The thermostable substance is the essential one and it may act alone, but its activity is increased by the presence of free complement. The amboceptor is present in relatively small quantities in normal serum, hence the apparent thermolability of the opsonin in normal serum, whereas in the case of an immune serum the amboceptor is present in a larger amount and perhaps with heightened specific properties and plays a predominant part and though heating results in a loss of activity, this is only partial. In both cases the loss is due to destruction of complement."

(*b*). The unfavourable and adverse factors militating against the successful application of serums in plague are:—

I. The complex nature of the affection necessitating two distinct and separate processes before recovery can ensue as above stated. In the first place, the bacillus pestis must be bacteriolysed and secondly, the endotoxin liberated by the former process must be neutralised and eliminated.

II. The great virulence and high mortality of the disease as demonstrated by a series of epidemics. In Bombay, we have had recorded 51,472 attacks and 44,955 deaths from plague during the last four epidemics, equivalent to a case mortality rate of

87·33 per cent. If we exclude hospital treated cases, and add a certain proportion that have either escaped detection or been misregistered, we can safely say that it is 90 per cent ;—which means that the natural expectation of recovery from plague in this city is but 10 out of every hundred attacked.

III. Early and grave septicæmia as noted by Mayr, Berestneff, myself, Greig and the Plague Research Commission. It has been estimated that from 55* to 60 per cent of hospital admissions at the Maratha Hospital are septicæmic and therefore practically not amenable to any treatment[19]. Almost all succumb within three to four days ; if any survive, the ultimate result is death from toxæmia and marasmus.

IV. Multiple foci of infection exist in the numerous buboes and owing to direct communication between the lymphatics on the one hand and veins and arteries on the other, a constant stream of blood infection is kept up.

V. The rapid course of the disease and late treatment, carrying off the larger proportion of cases by the sixth day, with the period of maximum mortality from the third to the sixth day. As most of the hospital cases are admitted between the third and the sixth day of illness they are already too late for treatment. The Plague Research Commission lays down the average duration of fatal cases at 5½ days[20].

6.—THE RESULTS OF SERUM TREATMENT.

I.—Serums prepared by seven different workers have been tested during some of the epidemics. The largest number of observations have however been made with Lustig's and Yersin-Roux' serums. The following table gives a total of 1,739 cases treated at the Arthur Road and Maratha Hospitals with the above with a

* The ratio arrived at by the Plague Research Commission is 58.5 per cent. among 94 patients examined at the Maratha Hospital.

mortality rate of 64·9 per cent. as compared with 75·9 per cent. among 11,284 cases not so treated :—

Table showing the Results of Treatment by Various Serums.

Serums.	No.	Died.	Recovered.	Case mortality rate %.
Lustig's (1899-1901)	1,089	715	374	65.6
Yresin-Roux' (1905-1907) ...	449	273	176	60.8
Do. (1904)	80	55	25	68.7
Brazil's	50	41	9	82.0
Tavel's	28	18	10	64.2
Terni's	16	12	4	75.0
Haffkine's	15	11	4	73.3
Paltauf's	8	4	4	50.0
Japanese	4	1	3	25.0
Total ...	1,739	1,130	609	64.9

I propose to confine my remarks to-day to the later series of cases treated with Yersin-Roux' serum only from 1905-1907.

The method adopted during the last 4 years consisted in rejecting all those patients who appeared to have hardly any probability of benefiting by the serum-treatment as clinically indicated. Convalescent or semi-convalescent cases were further eliminated, as well as those in whom the illness had lasted for six days or more. The latter were excluded, since experience has shown that patients who are alive by the above period are either too far advanced for treatment, or are just beginning to improve spontaneously. The observations were thus restricted to the most acute cases within the first five days of illness and comprised 249 cases. On the suggestion of Professor C. J. Martin, Director of the Lister Institute and Member of the Advisory Committee for Plague Investigations in India, who by the way approved of the above procedure, observations with another series of 400 cases were conducted in such a way that after rejecting the unfit, every

alternate case was treated with the serum, so that 200 cases received the serum and 200 served as controls. In the first series of 249 cases the case mortality rate was 58.60 per cent and among the 200 cases treated alternately with the controls it was 63.5 per cent. as contrasted with 74.5 per cent. among the latter. There was thus a difference of 10.50 per cent in favour of the serum cases :—

Table showing the Results of Treatment with Yersin-Roux' Serum, (1905-1907).

		No.	Died.	Recovered.	Case Mortality per cent.
Serum Cases ...		249	146	103	58.6
Alternate Series	Control Cases	200	148	52	74.0
	Serum Cases	200	127	73	63.5
	Difference in favour of Serum Cases.				10.5 per cent.
Total of Serum Cases ...		449	273	176	60.8

The above figures indicate that under the conditions of hospital practice as existing in Bombay, whilst but 26 patients out of every 100 recover under ordinary treatment, the serum treatment is capable of bringing round 39, that is, the ratio of recovery is increased by 33 per cent. Apart from this, the serum treatment prolongs life considerably as was indicated by comparison with the control cases, which showed that whereas 79 per cent of all deaths among the controls occurred within 4 days after admission, the proportion among the serum cases was 58·2 per cent. only.

The rejected cases which numbered 589 require a few words. They comprised 404 cases between the first and the fifth day of illness ; only 11 out of them recovered, although they received the same remedial measures as the above, except of course the serum. Their exclusion was therefore justifiable. Similarly the exclusion

of cases over 6 days duration, as also of those over 10 days was equally justified by their larger ratio of recovery without the aid of the serum. 7 cases of Pestis Ambulans were rejected because they are extremely mild and always end in recovery, and among the 3 recently inoculated cases who were rejected, 1 died and 2 recovered.

Table showing the Analysis of the Rejected Cases.

Rejected Cases. — Duration of Illness.	No.	Died.	Recovered.	Case mortality per cent.
Between 1st and 5th day	404	393	11	97·2
,, 6th and 9th ,, ...	127	78	49	61·4
10 days and over	48	15	33	31·2
Pestis Ambulans	7	.....	7	...
Inoculated within a week of illness	3	1	2	33·3

I do not propose to enter into the details of the above cases as I have dealt with them fully elsewhere[21].

All the serum as well as the control cases belonged to the bubonic type of plague, received the same general drug treatment but without alcohol in any shape. Hæmorrhages, terminal pneumonia, cardiac failure and maramus contributed to the heaviest mortality among them. Marasmus is due to the rapid bacteriolysis induced by the serum and consequent surcharging of the system with the toxins so liberated and their combination with the tissue cells of the body. It is in cases like these that the want of a purely *Antitoxic* serum is badly felt which alone could avert the fatal issue, for as Wright[22] and his collaborators say, death may supervene in bacterial infections independently of any breakdown in the machinery of immunisation, and plague marasmus is a striking instance of the same. The

antitoxic power of the Yersin-Roux' serum being small its utility becomes therefore limited. The proportion of first day cases treated with the serum was 8·4 per cent only.

II. RECOVERY OF SEPTICÆMIC CASES UNDER SERUM TREATMENT.

The fact that in the earlier observations no amount of serum injected either intravenously or subcutaneously had been effective among septicæmic cases, led the investigators to believe that such cases are necessarily hopeless. The investigations of the Plague Research Commission, however, have shown that such is not invariably the case. Among the cases examined by them, 7 which were under the serum treatment were found to be septicæmic and 2 of these recovered; one of them having no fewer than 500-600 pest bacilli per c. c. of blood. The patient, a child of 7 had received 270 c. c. of the serum in six injections from the second to the sixth day of illness. The other patient a female aged 25 had received 420 c. c. in six injections between the third and the seventh day.

III. THE SERUM TREATMENT AMONG THE INOCULATED. THE INFLUENCE OF INOCULATION ON THE GENERAL MORTALITY FROM PLAGUE.

There were 10 inoculated patients among those treated with the serum at Bombay and Poona, of whom 9 recovered. This shows that the chances of recovery increased as they are by inoculation, become greatly enhanced, if the inoculated are subjected to the serum treatment after infection. I would in this connection make a slight digression with regard to the reduction in mortality among those who become infected after inoculation. We have had numerous statistics and figures placed before us from time to time to illustrate the beneficial effects of inoculation, but sufficient stress has not been hitherto laid upon our experience in this city during 1899–1900. It appears that 175,747 persons (about one-fifth of the then total population)

were inoculated between 1898–1900 ;–16,850 in 1898–99 and 158,897 during 1899-1900 and the influence of this was, I contend, perceptible in the mortality rate for the latter year as indicated by the following statement :—

Years.	Attacks.	Deaths.	Case mortality rate per cent.
1896	2,544	1,936	76·10
1897	13,314	11,003	82·64
1898	22,130	18,185	82·12
1899	19,451	15,796	81·20
1900	17,913	13,285	77·90
1901	21,006	18,736	89·19
1902	16,423	13,820	84·15
1903	23,349	20,788	89·00
1904	15,488	13,538	87·40
1905	16,308	14,198	87·06
1906	12,323	10,830	87·88
1907	7,353	6,389	86·88
Total ...	187,602	158,504	84·48

We observe that the average mortality rate for the city was 82 % before inoculation was undertaken on the above scale. We also note that from 1901 onwards the mortality rate has averaged 88 %, and it was only during 1900, when the largest number of inoculations were performed, that the case mortality rate dropped to 77.90 per cent. The cause and effect are sufficiently striking, and the conclusion patent that the benefit was due to inoculation. As regards the incidence of mortality among the inoculated who have come under treatment at the Bombay hospitals, I have been able to collect about 250 cases, with the low mortality rate of 46 per cent.

IV.—RESULTS OF SERUM TREATMENT IN PRIVATE PRACTICE AT BOMBAY.

In addition to the above observations conducted by myself at the Maratha Hospital, 9 Parsee patients were treated at the Parsee Fever Hospital by Dr. Sorab Nariman of whom 4 died and 5 recovered. There were simultaneously treated in private practice, 245 patients by six observers (Drs. Pais, Heredia, Alfons Mayr, Engineer, Childe and myself) of whom 99 died and 146 recovered, the case mortality rate being 40·4 per cent. as contrasted with 60·8 per cent among hospital cases. This great difference in results was due mainly to early treatment, inasmuch as whilst the proportion of first-day cases treated at the hospital was 8·4 per cent., it was 47·0 per cent. in private practice,—nearly six times as much.

V.—RESULTS OF SERUM TREATMENT AT INDORE, POONA, CALCUTTA AND KARACHI. [25]

The following statement shows the results of treatment at Bombay, as also at the above places :—

Table showing the Results of Serum Treatment at Bombay and elsewhere.

1905-1907.	No.	Died.	Recovered.	Case mortality per cent.
BOMBAY CASES:—				
(*a*) Maratha Hospital	449	273	176	60·8
(*b*) Parsee Fever Hospital	9	4	5	44·4
(*c*) Private Practice	245	99	146	40·4
Indore Cases	218	78	140	35·7
Poona ,, ...	125	62	63	49·6
Calcutta ,, ...	23	13	10	56·5
Karachi ,, ...	34	17	17	50·0
Total	1,103	546	557	49·5

The Indore cases exhibit the best results. I have discussed these at length elsewhere and it would suffice here to state that the epidemic was milder than at Bombay, and the proportion of first day cases treated was 64 per cent. among hospital and private cases combined, as compared with 21 per cent. at Poona and 22·4 per cent. at Bombay.

7.—SUMMARY.

The above statement gives us a total of 1,103 cases with 546 deaths and 557 recoveries equivalent to a case mortality rate of 49.5 per cent. We thus see the beneficial influence of the serum treatment when compared with the average mortality rate from the affection. The above cases are divisible into two groups hospital and private. The difference in results between them is indicated by 16·8 per cent., owing chiefly to early treatment.

Table showing the Results of Serum Treatment in Hospital and Private Practice.

	No.	Died.	Recovered.	Case mortality per cent.
Hospital Cases	624	355	269	56·8
Private ,, ...	479	191	288	40·0
Total ...	1,103	546	557	49·5

This point is still more strikingly brought out in the following table where the mortality rates are compared according to the duration of illness at the time of treatment.

Table showing the Mortality Rates according to the Duration of Illness at the Time of Treatment with Serum.

Duration of Illness.	No.	Died.	Recovered.	Case mortality per cent.
1st Day ...	323	98	225	30·3
2nd ,, ...	311	164	147	52·7
3rd ,, ...	248	155	93	62·5
4th ,, ...	106	60	46	56·6
5th ,, ...	52	32	20	61·5
6th ,, ...	14	8	6	57·1
7th ,, ...	4	4	.....	100·0

We note that among 323 patients treated on the first day of illness, the mortality rate was as low as 30·3per cent. I would venture to enquire, from your vast experience of plague in Bombay, whether you can point to any series of cases that have come under your observation with such a low mortality rate. I greatly doubt the possibility. If we turn to the second-day cases, we see that among 311 cases, it has increased to 52·7 per cent. and by the third day to 62·5 per cent. Thereafter there is some irregularity in results, but in no instance is the mortality rate any near that of the first or second day cases. These figures tell their own tale ; any comment is superfluous. No words are needed to commend to your acceptance the crucial and important fact, that early treatment, *at as early a stage as possible* in the words of Kitasato,[24] is the essence of serum treatment. Treatment on the first day cuts short the normal duration of plague by half, averts grave complications of the circulatory, nervous and other systems, and as the buboes almost invariably become absorbed, recovery is speedy. Such marked effects are hardly to be noticed after the second day and not at all after the third.

The serum treatment has been freely applied among all the principal communities in India, except Europeans, whose number is too small for purposes of comparison. Parsees, Mahomedans, Native Christians and Hindus are the principal races concerned. The Hindus, although numerically largely represented forming as they do more than half of those treated, head the list

with the mortality rate of 55·0 per cent. Native Christians (mostly Goans) stand next with the mortality rate of 44·7 ; then Mahomedans with 43·7, and lastly the Parsees with the extremely low rate of 38·6 per cent.

Table showing the Results of Serum Treatment among Various Races.

Races.	No.	Died.	Recovered.	Case mortality per cent.
Europeans	15	5	10	33·3
Parsees	119	46	73	38·6
Mahomedans	153	67	86	43·7
Native Christians (mostly Goans)	217	97	120	44·7
Hindus	561	309	252	55·0
Japanese	1	.....	1	.....
Jews	4	2	2	50·0
Eurasians...	1	1	.....	100·0
Chinese	1	.....	1	.....

These figures might well be compared with those given in the earlier part of this address in order to estimate the benefit derived by each community from the application of the serum treatment.

8.—DOSAGE OF THE SERUM.

Next in importance to early treatment, comes the question of the dosage of the serum. All my later efforts have been directed towards obtaining the best results with the smallest possible dose, and I am glad to be able to announce that the time is not far distant when we shall be able to achieve good results *with early treatment and moderate doses*, and thus deprive the serum treatment from the stigma of its being the rich man's treatment, as alleged by some. I emphatically dispute this assertion ; even were it true, I submit that where human life is concerned, the question of cost must be subordinated to the result ; I would put it you, whether you would consider any sum between 30 to 50 rupees too much to save one life ?

I find from the last series of hospital cases, that among the 68 patients who recovered, the quantity of serum injected subcutaneously per patient averaged 285 c.c. only. That the quantity required varies very greatly according to the duration of illness and the virulence of the infection is shown by the following table from which we observe that 25 patients received between 100 to 200 c. c., 17 between 200 to 300 c. c. and 16 between 300 to 400 c. c.

Number of patients.	Quantity Injected.
	c. c.
25	100–200
17	200–300
16	300–400
4	400–500
2	500–600
3	600–700
1	700–800

In fact 58 patients out of 68 received under 400 c. c. But at the same time, we notice that the above limit was exceeded, and that was due, either to late treatment, or to extensive infection. It is expected that by intravenous injection more rapid and lasting effects would be obtained, but the method is not easy of application on a large scale, knowing as we do, the great reluctance of the people to such procedures. The Plague Research Commission is however about to investigate by this method ; I have also in train at present a series of observations, where one single injection of 200 c. c. is administered on admission and the progress of the case carefully watched. With the data available from these sources, we shall not be very long, I trust, in arriving at a definite conclusion.

CONCLUSION.

Now, gentlemen, my task is done. If I have been so fortunate as to be able to arouse any interest among you in the serum treatment, and should any of you be desirous to adopt it, I would refer you to my writings wherein I have laid down full, precise and definite directions. The wards of my hospital are open to those who prefer actual demonstration. The treatment is not at all difficult of application, although I must admit, it entails a greater sacrifice of time than a busy practitioner can afford. His success however must be his reward, apart from the gratification of the good that is done. And finally if I can presume to offer you a few closing words of advice, after twelve years of continued observation and experience with plague, I would say :—

(*a*) Avoid alcohol ; it is a cellular poison, it inhibits phagocytosis ; it does not stimulate the heart in the way you require it, and besides does positive harm in many a case.

(*b*) Avoid antiperiodics and antipyretics ; the disease being self-limited, none of these will curtail even by one single hour its normal course.

(*c*) Avoid internal antiseptics, for in the doses in which they are usually administered, they do not reach the plague bacilli in the same form, and become inert. Pure carbolic acid, even 100 grains per day, has failed to show any result.

(*d*) Avoid free and violent purgation at the outset, lest you lower the pulse tension and thus further embarrass the circulation, already being depressed by the cardio-vascular paresis, from the action of the plague toxin, and lastly.

(*e*) Avoid all active interference like incisions into the buboes ; except it be extirpation in the early stage as recommended by Kitasato, in combination with the serum treatment or injections of germicides into them ; avoid irritant applications ; avoid very vigorous fomentations or very hot poultices.

These are some of the lessons that I have gleaned from the study of plague, and I lay them before you for your consideration. Clashing of views and opinions there will always be ; were it otherwise, there could be no progress. We are all however actuated by the same ideals and impelled by the same motives for the common weal, that can only be achieved by co-operation, and mutual good will. And as the last Harveian Orator Dr. Frederick Taylor says[25] "Life is too short for disagreement and by united action alone we can effect what it is our life's work to accomplish." I would conclude by quoting, as he has, what Wagner makes Faust to say in this regard, which is not at all inapplicable in relation to our efforts to acquire some knowledge of plague :—

"The search of knowledge is a weary one and life how short !
How often have the heart and brain overtasked,
Shrunk back despairing from inquiries in vain !
Oh, with what difficulty are the means
Acquired ; that lead us to the springs of knowledge
And when the path is found, ere we have trod
Half the long way—poor wretches we must die !"

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