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BUBONIC PLAGUE

MONTENEGRO

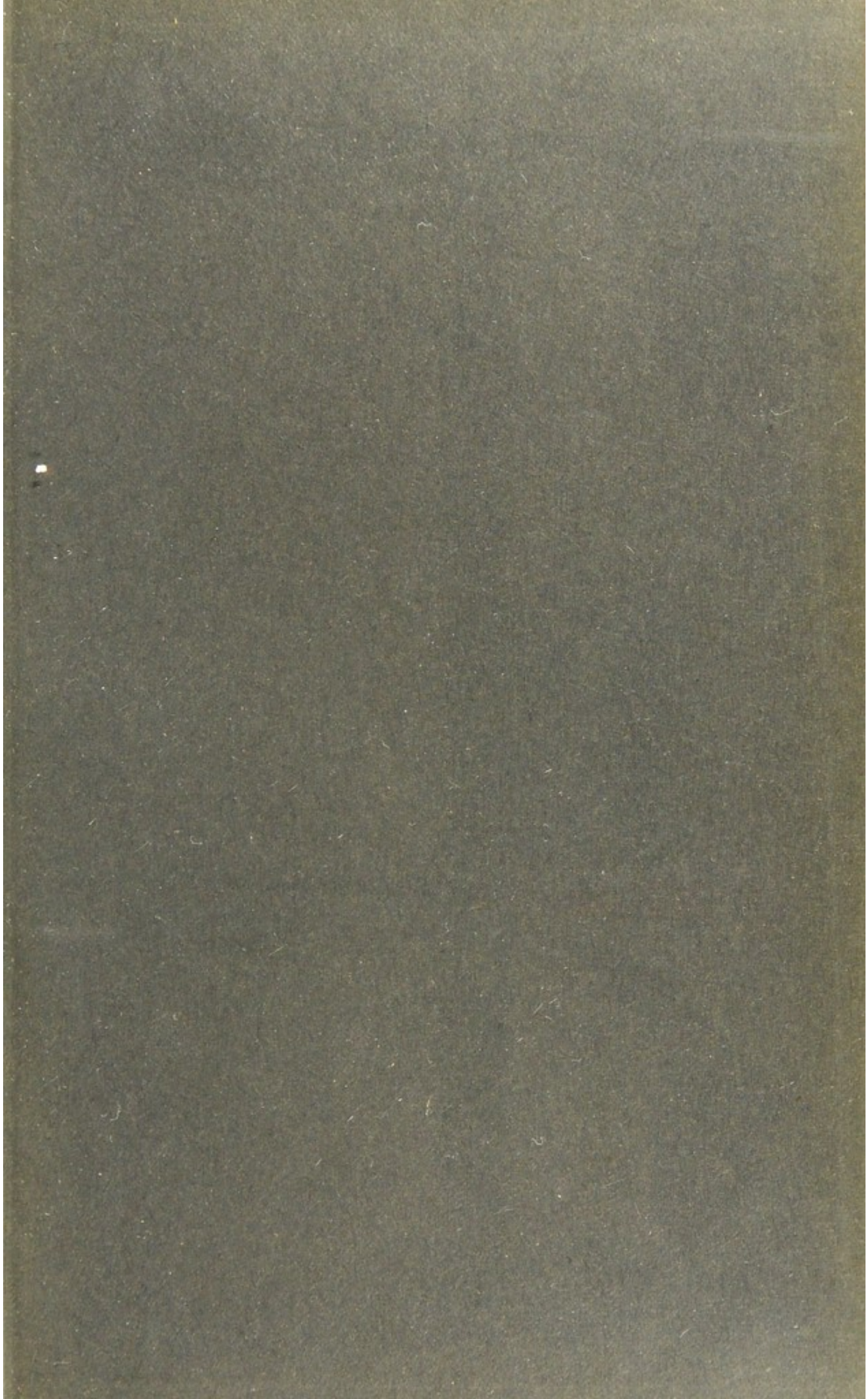


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BUBONIC PLAGUE

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BUBONIC PLAGUE:

Its Course and Symptoms and Means of
Prevention and Treatment,

ACCORDING TO THE LATEST SCIENTIFIC DISCOVERIES;
INCLUDING NOTES ON CASES IN OPORTO.

WITH AN APPENDIX

SPECIALLY WRITTEN BY THE AUTHOR FOR THE ENGLISH EDITION.

BY

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To
THE EDITORS OF THE 'IMPARCIAL,'
WHO HAVE ALWAYS
SHOWN THEMSELVES SO UNTIRING IN THEIR EFFORTS
TO FURTHER THE PUBLIC WELFARE,
AND AT WHOSE INSTIGATION
THE AUTHOR UNDERTOOK THE COMPILATION OF THIS WORK,
HE NOW DEDICATES IT,
IN TOKEN OF HIS WARM APPRECIATION.



PREFACE

THERE is absolutely no book, either in Spain or abroad, which gives a resumé of the important work that has been done during recent years to discover the causes of the propagation of the plague and how to combat its attacks. This scientific material, in enormous quantity, is scattered through reviews, communications, pamphlets and periodicals of all countries. By bringing it together in this work I have tried to make it possible for such of my medical brethren who have not the means of obtaining the information, and the public in general, to make themselves rapidly acquainted with the latest scientific advances.

The epidemic having appeared in Oporto, I have thought it my duty to include the greater part of the data in regard to it obtained from the observations and experiments carried out in that city by the foreign commissions, and can assure Spanish medical men that in this work interesting facts are brought to their knowledge which are of great value in aiding them to form a clear conception of the disease.

I sincerely believe that, as a whole, my work constitutes a complete, though summary, preparation for our struggle against the epidemic if we are compelled to deal with it. Energetic action can only arise from clear ideas, and I do not hesitate to declare, in spite of empiricism and routine,

that so far as I am concerned, my moments of greatest confusion have been those in which I have found myself without the theoretic preparation necessary to interpret correctly the phenomena I was observing.

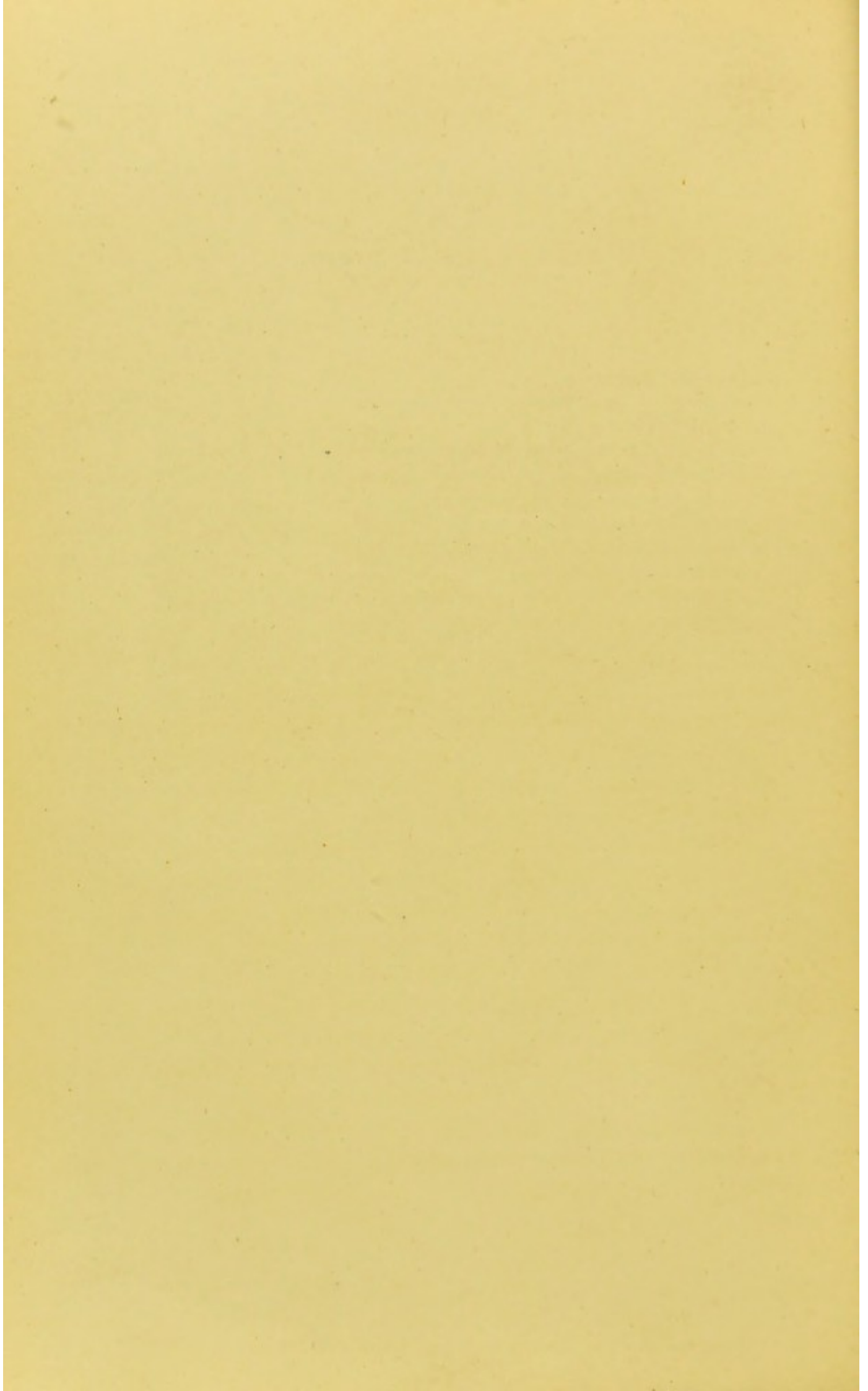
DR. VERDES MONTENEGRO.

MADRID,

September 15th, 1899.

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BUBONIC PLAGUE

BIOLOGICAL CHARACTERS

THE micro-organism which produces plague is a bacillus discovered by Yersin and Kitasato separately in 1894. Its rounded extremities and the shortness of its greatest diameter give it the appearance of a cocco-bacillus. Its form is not constant, its elementary forms being spherical; the largest varieties are those obtained by cultivation in agar (Rebuschini). It is reproduced entirely by subdivision, without the formation of spores.

The Yersin bacillus is aerobic, and grows at somewhat low temperatures, from 35° to 37° (95° to 98·6° F.); it develops so rapidly that at the end of twenty-four or forty-eight hours abundant colonies can be obtained. It is easily coloured by methyl-blue or fuchsine, but not by Gram's method. Almost always the bacilli appear to be surrounded by a capsule. Their extremities are more easily coloured than the centre, in which there generally remains a clear space owing to the absence of colouring.

In cultivations the bacilli appear in groups, forming chains on which are numerous enlargements. When the cultivation is in gelatine, the chains are usually enlarged,

the enlargement being formed by little rods attached laterally. Cultivated in broth, they unite, forming clusters which adhere to the sides of the tube, showing an appearance very analogous to cultivations of streptococcus. At the end of some time the clusters are precipitated, the liquid remaining clear. Solidified serum and gelatine, with or without glycerine, are excellent cultivating media.

The best medium appears to be the 2 per cent. alkaline solution of peptone with 1 to 2 per cent. of gelatine (Yersin). When the pulp from a bubo is sown in gelatine, white, transparent colonies with radiated borders develop.

The conditions of resistance of the bacillus to external influences are not well known, and it is very rash to affirm, as some have done, that its vitality is not strong.

In cultivations its virulence decreases rapidly, but it is easy to strengthen it anew. If the broth is subjected for an hour to the action of a temperature of 58° (136.4° F.), the sowing of a particle of bacillus material remains sterile. The serum of a patient convalescent from the plague checks the development of the cultivations, and produces the phenomenon of agglutination. The agglutinating power of the serum is not manifested before the seventh day of the illness, and continues to increase until the second or third week of the convalescence.

The action for a few minutes of a temperature of 100° (212° F.) destroys the bacillus. Chemical disinfectants, especially the acids, have very great influence over it; it resists very slightly the action of a 1 per cent. solution of carbolic acid. It is very doubtful whether, as some assert, quicklime in water, in the proportion of 1 to 100, destroys the bacillus rapidly enough, and it is more doubtful, however, whether air and the sun kill it rapidly. In special conditions the bacillus can retain its virulence for a long time;

this appears to be shown by cases of infection from infected clothing, of which we shall speak later.

The above is what is really known as to the action of the bacillus; all other assertions in regard to the action of water, of the sun, of desiccation, etc., are entirely arbitrary. Strictly speaking, there appear to be distinct species of bacilli, and among them, while some cultivations lose their virulence rapidly, others preserve it for a long time. Some cultivations exposed to the influence of light and air in the Pasteur Institute showed virulence after three months and a half, and killed a guinea-pig in a little longer time than is required by cultivations of normal virulence.

It is to be taken into consideration, besides, that a weakened cultivation can easily recover its activity. Batzaroff received some broth the virulence of which had decreased so much that a large dose inoculated in a rat did not kill it, nor did it kill a guinea-pig, notwithstanding the exceeding sensibility of this animal to the infection. Depositing a certain quantity of the cultivation in the nostril of another guinea-pig, he succeeded in producing plague pneumonia, and killed the animal, but in eight days (!).

A second guinea-pig being inoculated with sections of the spleen of the first, the duration of the illness was shortened, and, indeed, on the third or fourth transmission death occurred in three days, the usual time.

In cases in which the virulence has been greatly diminished, the association of other microbes, principally streptococci, with the bacillus appears to arouse its activity.

The knowledge of this fact is important, because Yersin has found the plague bacillus in a non-virulent state living as a simple saprophyte at a depth of four centimetres in the soil of places where the epidemic was raging, and also

sometimes after it was over. The facts already mentioned make us believe that the bacillus can easily recover its pathogenic activity under certain conditions, as when placed in a medium exceptionally favourable to its development (the nasal mucous membrane in the experiments of Batzaroff), or on association with other microbes.

It has been said that desiccation rapidly kills the microbe; this is little likely. Prolonged desiccation in vacuo of a part of infected spleen is impotent to destroy it; at the end of three or four weeks a particle of it, powdered and injected with sterilized water, produced the disease in the animal experimented on and caused its death in the usual time. When desiccation occurs in the earth, in three weeks the virulence appears to diminish. The assertion that damp and dark localities favour the development of the disease appears to be equally rash. We will see in the study of the epidemiology how little influence these places have in the propagation of the plague; but besides this, the results of the experiment of Simond are against the supposition. In a plate of very virulent cultivation in gelatine, placed in a dark and damp house, the rapid proliferation of fungus and saprophytes strangled the bacillus in two days, and inoculation produced no result.

Although the bacillus of plague is pathogenic, not only in man, but also in various other animals, as rats, cats, pigs, sheep, oxen, etc., it is not so to an equal extent in all; besides, the infection of an animal by the pathological products from another of a distinct species does not always give any result, and when it does, there appear, in virtue of the transmission, very considerable differences in the intensity of the transmitted disease. This makes it appear that sometimes a different microbe is in question. The experiments of Lawson show that the plague of oxen is

not the same as the human, and thus it will be generally considered that the bacillus met with by Kitasato in an ox dead of plague is the specific bacillus of that disease, which has no direct relationship to that of man.

In cases in which the disease is transmissible from one species of animal to another, although with variations in the intensity, it appears reasonable to attribute these differences to the work of adaptation of the microbe to the new medium, which, so far as it is concerned, the animal of a distinct species from that in which it was developed is to it. Although the rat is thought to be the mammifer to which is to be attributed the most important rôle in the propagation of the plague, the infection of the animal with pathological products from man is not very virulent in the first individual inoculated! If a second animal is infected from the first, the virulence augments, and in a third experiment it actually reaches the normal intensity of the disease in the species in question. It appears, then, that the microbes must adapt themselves to each new species, and take out in it letters of naturalization, so to speak. So that they may reach the normal virulence in the first inoculation, it is necessary, so to say, to acclimatize them by introducing them, enveloped in a covering of collodion, into the peritoneum of an animal belonging to the species on which one is experimenting.

On the other hand, by inoculation from one to another of the same species, bacilli are obtained of a fixed virulence according to the species operated on, so that inoculation causes the death of a guinea-pig in three days or of a mouse in two. If a guinea-pig is inoculated with the bacillus which kills the mouse in two days, the animal does not die until five or six days; a second guinea-pig infected with bacilli from the first dies in less time, and, at the

end of a series of inoculations, bacilli can be obtained which kill the guinea-pig in three days. But then these bacilli are not at all as virulent as they were for the mouse, and it is necessary to have recourse to a new inoculation in this species to kill the animal in two days, as at the beginning (Calmette and Borel). This assertion is, however, only exact within certain limits, and at the end of a number of transmissions the virulence diminishes. The difference of susceptibility of different species has been proved by a multitude of observations and experiments.

Lawson could not infect pigs, either by alimentation or by subcutaneous injection. Experimenting on sucking-pigs, he succeeded in causing tumefaction and œdema at the site of the inoculation, but could not discover the bacillus in the ganglia. Wilm and Ogatta say that they did find them.

Mattei has seen cats dangerously ill of plague, and has found the bacillus in their stools, but the animals recovered their health. The monkey is very susceptible to the infection, and the dog appears almost as refractory to it.

Markl and Rouse, working separately, have succeeded in isolating a soluble toxine from the broth used in cultivations, inoculation with which is mortal to the guinea-pig in the smallest quantities. This toxine has proved useless when tried as an immunizator. The doubt whether the septicæmic symptoms which are observed in plague are caused by the toxine or by other products of the nutritive changes of the bacillus in the organism have, however, had no result. Experiments made by Bandi contradict the first of these suppositions.

MODE IN WHICH THE INFECTION IS MANIFESTED

The agent which produces the disease being known, it appears logical to study in succession the mechanism by which the infection is introduced, and the gates of entrance which the organism offers to the infecting virus. In the present state of our knowledge we must admit that there is no part of the body which may not be infected, though all parts do not offer the same aptitude for receiving the infection. It is possible to put them down in order according to the greater or lesser facility and frequency of contagion; and in this respect it can be said that after the skin, the nasal, ocular, buccal, intestinal, rectal, and vaginal mucous membranes stand in order, the latter showing the least tendency to infection.

It is possible in a certain way to conjecture what has been the gate which has given entrance to the infection, considering the site at which the primary bubo appears, since the relation is usually so direct that the inoculation of the plague would supply an excellent means for the study of the anastomoses of the lymphatic vessels (Batzaroff).

Inoculation in the intestine produces buboes in the mesenteric glands; in the rectum, in the inguinal; in the vagina, in a series of ganglia which follow the direction of the vertebral column. Inoculation in the nose causes swelling of the deep cervical glands; infection of the mouth, tumefaction of the submaxillary, and of the eyes of the parotid glands. When the skin of the limbs has given entry to the pathogenic agent, the glands which are affected in the first place are those situated at the articulation of the limb with the trunk.

Infection through the Skin.

In regard to the possibility of infection through the skin there cannot be any doubt; it is only open to discussion as to whether the microbe of the plague can penetrate the healthy skin. The consideration of what happens with other infections would make us believe that it may be necessary for a solution of continuity to exist, though so small that it escapes notice.

Lawson believes that there is always a noticeable wound; this assertion does not agree with many careful observations. In many cases, however, it is present; and among these may be reckoned those of two Japanese physicians who wounded themselves while making autopsies, and acquired the disease. Simond has seen several times a scratch in the part traversed by the lymphatic vessels passing to the gland in which later on the bubo appeared, but this scratch is not constant. The experiments of Zabolotny throw sufficient light on this point. The distinguished Russian physician infected monkeys, by a slight puncture in the palm of the hand with the point of a needle. Such a wound, imperceptible, sufficed to produce the disease, and did not leave any trace, nor was lymphangitis produced before the swelling of the glands, being in this respect contrary to what happens after anatomical punctures.

The result of this experiment shows that the scratch, wound, etc., which has given entry to the virus may remain unnoticed, so that certainly the apparent integrity of the skin does not justify the conclusion that the contagion has not penetrated and made itself manifest through it.

The action of the skin is different from that of the subjacent cellular tissue; subcutaneous injection of the virus generally provokes in the animals used in the laboratory

œdema of the part affected before the bubo develops. Nor does lymphangitis show itself in these animals. Clinically, Lawson says that he has observed a late lymphangitis in those cases in which the slow evolution of the disease has given time for the production of the phenomenon.

Infection through the Conjunctiva.

A case seen in Bombay in 1897 confirms the possibility of this mode of infection, which experiments had given cause to be thought possible. A nurse received in the eye a particle of the sputum from a patient suffering from pneumonic plague. Next day there was intense conjunctivitis; swelling of the parotid and deep cervical glands then followed, and she died, a victim of the plague.

Infection through the Respiratory Organs.

When a guinea-pig is inoculated in the nose, taking care not to wound the mucous membrane, the first bubo appears in the deep cervical glands, and primary pneumonia occurs. The nasal mucus seems to offer an extremely favourable medium for the cultivation of the bacillus of Yersin, since, as we have seen, bacilli without virulence, incapable of producing any effect by subcutaneous injection, develop the disease when deposited in the nose.

It is not well ascertained whether this infection gives rise to broncho-pneumonia of plague by inspiration of the infecting material or by propagation of the nasal inflammation by continuity to the respiratory tubes. It is probable that it arises in both ways; and perhaps the absence which is sometimes observed of primary bubo of the deep cervical glands shows what was the chief point of origin of the infection. (Intra-tracheal injection of cultivations produces

pneumonia, without primary bubo in the neck.) It would be of great interest to decide this question, since it would assist in clearing up the doubts which there now are as to the possibility of infection through the air, but we have not sufficient data. It is, however, an interesting fact that the nose, far from acting as a filter which checks the virus of the plague, as it does that of tubercle, for example, is really an excellent hot-house in which it can prepare itself for its attack on the organism. Simond made a monkey breathe infected flour, but did not succeed in producing the pneumonia of plague.

Infection through the Digestive Tract.

To form a clear idea of this, the most debated mechanism of infection, we must get rid, in the first place, of the possibility of a simultaneous infection by the nose.

Batzaroff observed that the guinea-pigs who chewed the beetroot on which their sick companions had been feeding acquired pneumonia. In these cases the infection must be attributed to the nasal mucus which covered the snouts of these animals, since, in the first place, there appeared hypersecretion of this mucus, and afterwards infarction of the deep cervical glands and pneumonia, as in the former case.

This cause of error being got rid of, which is possible by taking great care to limit the action of the infecting agent to a definite part of the digestive tube, the difficulties are so numerous that it becomes necessary to take the whole question, so to speak, *en bloc*, and ask if infection is possible by this way, anticipating only the possibility, admitted by all, of infection through the tonsils.

Wysokowitz, in twenty-four autopsies, was never able

to prove infection arising in the intestine or stomach. The lesions discovered in them were the consequences of septicæmia. The primary mesenteric bubo was wanting, even when the ganglia of this region were swollen.

The tumefaction of a group of ganglia signifies nothing, because in autopsies we frequently find that all the lymphatic glands are more or less enlarged. The primary bubo is recognised by its size, by the peripheral œdema, and, above all, by the enormous quantity of bacilli it contains—a quantity so great that its volume appears to be more due to the augmentation of that quantity than to the alterations in its texture.

The introduction of pure cultivations into the stomach has given no results whatever in the hands of this experimenter.

Simond made a rat eat pieces of a diseased spleen, without any result being produced. Twenty days afterwards he repeated the experiment three times *in the same animal* without effect. Fearing that in some way the animal might have acquired immunity, he inoculated it hypodermically, and succeeded in infecting it.

Koch has never seen any case that could be attributed to infection through the digestive tract.

Lawson, whose experiments are cited in the first chapter, is of the opinion, after making numerous observations in Hong Kong, that there is no ground for asserting that the digestive tract is a gate of entry for the contagion.

Batzaroff says that he has infected animals by making them eat contaminated food. As the conditions of the experiment are unknown, it is impossible to judge of it, since the infection might have acted through the nose, the skin, etc. Of all the experiments performed by Simond, only one gave a positive result. The animal which was

the victim of it had a wound in the snout, which had been caused by a spatula. Bandi and Stagnitta, on the other hand, have succeeded in infecting more than forty animals by alimentation, and found in them swelling of the mesenteric glands; but it is not possible to be certain that this swelling was primary, and the experiments have many vulnerable points.

Notwithstanding, since experiments are quoted having positive results, it is prudent to admit the possibility of infection by the alimentary canal. The frequency with which the experimenters failed to carry out their intentions would make us incline to the belief that infection in this way is difficult, and, on the whole, is likely to be rare in practice. It is probable that the acids of the gastric juice on the one hand (p. 13), and on the other the abundance of bacteria in the intestine (p. 14), make infection difficult.

Infection through the rectum is difficult in animals, but has succeeded in many cases. It is very probable that to this mode of infection may be attributed some of the cases that have occurred in Levrée (Bombay). In a tank of dirty water near by Hankin discovered the bacillus. The banks of the reservoir served as a latrine, and the natives used the water to wash themselves after defecation. There were no data of autopsies from which the site of the infection could be judged, but though it might occur through the skin, the nasal mucous membrane, etc., it is possible that some cases arose by infection through the rectum.

Infection through the Vagina.

Infection by way of the vagina only occurs with great difficulty in animals, and gives no result, except in very rare cases, in which perhaps contusions of the organ and

the virulence of the bacillus facilitate the contagion. It is to be believed that this immunity is owing in a great measure to the bacterian flora, which normally develops in the vagina, and to the fluids which moisten it, and check the development of the bacillus. No experiments *in vitro* have been made, so far as I know, to clear up the question.

VEHICLES WHICH CONVEY THE CONTAGION

The morbid agent has been discovered in the pus of the bubos during the first days of suppuration; it afterwards disappears, smothered by the ordinary microbes, of which the micrococcus is the chief. Suppuration is relatively rare. Of 2,300 cases observed by Lawson, 50 suppurated. Koch believes that it only happens in cases secondarily infected by the streptococcus.

The bacillus is so abundant in the sputum of those suffering from the pneumonic form that it has been easy to obtain pure cultivations from it (Childe). The fact is a surprising one, as there is always such a diversity of micro-organisms in the sputum that to obtain a pure cultivation of Koch's bacillus it is necessary to have recourse to the complicated proceeding, with repeated washings, of Kitasato, and even then only one operation is successful among many failures.

The bacilli are not always present in the urine or the fæces, and, when present, not generally in great numbers (Wilm). The presence of the germs may be attributed to the recurrent hæmorrhages which occur in the last stages of the disease; thus it would be an error to suppose that the existence of the bacillus in the fæces indicates infection by way of the digestive tract. Albrecht found none in a series of twenty-four observations.

The bacillus has not been found in the sweat when the skin was not infected by the sputum, pus, etc., of the patient.

In regard to the milk, there are no observations. Lawson had occasion to see a woman who suckled her child during the first two days of the sickness. The child did not fall sick.

In the blood the bacillus is only found in the latest stages of the disease, and then not always. Sometimes the richness of the blood in bacilli is extraordinary. Lustig says that from the fifth to the seventh day he found them in millions. In some of the autopsies performed in Oporto the preparations made with blood from the heart justify the assertion of the Italian physician.

Transmission by Animals.

Rats.—In the order of importance as vehicles for transmission of the plague rats take the first place, and also the fleas which co-operate with the former in the diffusion of the disease in our species.

It may be said that the plague is a disease of rats, which infects man. Generally, before the epidemic breaks out in a city, bodies of rats which have died of plague are found in the streets and houses. This was observed in Karad and Mundra in 1897, and in Kurachee and Bombay in 1898. According to the observations of Simond, the epidemic among rats follows a course analogous to that of the epidemic in man. After a period, during which the cases are not very frequent, the plague becomes suddenly very severe, and claims very numerous victims. On this panic determines the emigration of the majority of the rats, so that the sickness decreases; the sick animals meanwhile,

losing their habitual fear of man, run through the streets in broad daylight as if stupefied, until they fall dead in the drains, in the cellars, or in the middle of the gutter.

Hankin has proved also that generally the first cases in a population occur precisely in those quarters in which the existence of the dead bodies of rats has first been discovered, and on many occasions it has been possible to demonstrate that the propagation of the epidemic from one town to another does not follow the route taken by the fugitives from the infected human population, but that taken by the rats in their flight. In a short time cases appear in the towns situated on this route.

Mr. Snow, Administrator of Bombay, established in the most decided manner that the propagation of the plague to different quarters of the city, from the first focus to the population immediately surrounding that focus, did not follow the panic which was produced in the population when the existence of the first cases became known, but took place long after, when the rats emigrated, and in the direction followed by them.

When fugitive families, flying from an infected city, have invaded a healthy population, the first cases have not always occurred among those families, or those who have given them shelter, but more frequently in grain, flour, leather or cloth warehouses—that is to say, where rats are most numerous—and the first victims are the caretakers of these warehouses. Sometimes, however, the first case is one of the fugitive family, leading us to believe that he was infected previous to leaving his house. When the case does not occur immediately, it can generally be shown that some days before its appearance a dead rat was discovered in the dwelling. An individual living in Bombay who had lost his wife by the plague, fled from the town. The rats of the

house in which he lodged attacked his luggage, which contained his dead wife's clothing; they died, and produced cases of plague in the family of the fugitive, who last of all succumbed to the disease.

But, after all, the relations between the rat and man are not intimate enough to explain the frequency of the contagion. Numerous cases are cited of persons who have contracted plague by touching the dead bodies of rats. At the beginning of the epidemic in Bombay there were found one morning in a cotton warehouse a great number of dead rats. Out of twenty servants who were employed in throwing them away, half suffered from plague. None of the customers who visited the warehouse that morning suffered. A coachman found one day a dead rat in the yard and threw it into the street. Two days later he died of plague. There was no other case in the building.

As is easily understood, these facts are not sufficient to explain the contagiousness of a disease which claims thousands of victims. There is a much greater abundance of observations relating to the immunity with which the corpses of rats may be handled.

Before the epidemic broke out in Mandvi the rats died in thousands, and the street arabs amused themselves by throwing them at each other, without any cases of plague appearing.

Fleas.—Simond has made ingenious experiments to show that plague is transmitted from the rat to man by means of fleas. A healthy rat has very few fleas on him, doubtless because, being careful of his toilette, he gets rid of them as cats and dogs do.

A sick rat becomes absolutely covered by these insects, doubtless because the illness makes him careless and neglectful of himself. The insects which attack the sick

animals charge themselves with microbes and afterwards kindly transfer those to us.

The great importance of a knowledge of these intimate relations between the rat and fleas, of these details of his private life, though they may appear ridiculous and unimportant, is easily seen.

Simond put two rats into a cage, one ill of plague and having fleas on it, the other healthy, having none, and separated them by a wire division. A short time afterwards the sick rat died, and at the end of two days the other became ill and died; the fleas had abandoned the dead body of the former and passed over to the other. The intestines of these fleas were gorged with bacilli; one of these insects was certain to infect with the contents of its intestine the puncture it might make on an animal or man.

Looking at the practical result, another experiment in confirmation of the first was made; he put two rats in a cage, also separating them by a wire netting, one being sick of plague, the other healthy, but both without fleas. Shortly afterwards the sick one died; the other one remained healthy.

The fleas, some time after the rat dies, abandon the body when it becomes cold, so that the servants who touch rats recently dead become ill; the little boys who play with rats which have been dead for many hours remain well (p. 26).

Transmission from Man to Man.

The contagion from man to man is not of great importance. This appears to be shown by the fact that physicians and nurses *very rarely fall victims to the disease.*

In the Parel Hospital 240 patients were daily visited by their relations; none of these, or of those employed at the hospital, of whom there were more than 140, took the disease. There was only one case of a man-servant in the post-mortem room (Thompson). In the Grant Road Hospital the same happened. Only one man-servant, who was in the habit of drinking the remains of the alcoholic potions which were being administered to the patients, took the disease (Dallas). Finally, in Hubli, by the most minute investigation, no relation between the victims could be discovered (Collie).

It is not to be looked on as strange that this should happen, as the bacillus cannot be found on the skin unless pus, sputum, or dejections have contaminated it.

The danger of infection by fleas exists to those near the sick, but this insect does not infect man in great numbers, and besides, it can only gorge itself with bacilli in the last days of the disease, since, until then, as we have already said, these do not appear in the blood.

The most frequent cases of contagion are those of physicians who have made post-mortem examinations, doubtless from coming in contact with the blood and with organs infected by the microbes. Two of Kitasato's assistants acquired the plague in Hong Kong in this way.

Transmission through the Air.

Man does not appear to be apt to convey the infection to great distances. Travellers going from infected localities do not propagate the disease if their clothes have been well disinfected. On the other hand, the patient is himself a most important medium of transmission. A person who

is attacked on his arrival among a healthy population will certainly infect that population if special care is not taken to destroy the primary focus of the disease as indicated above. Thus it is shown that imported cases always precede those among natives of the locality, and when these are attacked, a space of time elapses between the first and second cases; that is just the time during which the different mechanisms of infection we will study in succession come into play. In breathing, the air which surrounds the plague-stricken patient might be expected to be very dangerous. A multitude of people have lived in Hong Kong in the hospitals, or in dwellings where ten or twelve patients were being attended to, breathing an atmosphere which the bad ventilation tended to make insupportable, and sleeping beside the beds occupied by the patients without any grounds arising for the belief that the overcrowding gave rise to a single case (Lawson).

We know, besides, that the inspiration of air charged with powder contaminated with the bacillus by a dry cultivation did not infect the monkey. The result agrees with that obtained by Beninde, Lastchenco, Sticker and Heyman, in their experiments in regard to the transmission of tubercle by the powder of dried sputum, and, taken as a whole, suggests the idea that the fresh sputum may transmit the plague, as it has transmitted tuberculosis and probably pneumonia. The great richness in bacilli of the sputum of those suffering from pneumonia pestis has caused it to be believed that when the patients speak, cough, sneeze, etc., they may throw off very fine particles of sputum loaded with germs which will infect those breathing the same atmosphere—in a word, that the same conditions of transmissibility as in phthisis in regard to the powder of fresh sputum, discovered by the disciples of

Flügge, and which will produce such a decided sensation in the scientific world, obtain in plague.

Transmission to great distances is not probable. In Bombay it was believed that the air carried the germs from a grain warehouse in a suburb where there were cases; there was no reasonable foundation for this suspicion.

Transmission by Objects.

Both for short and long distances, clothing, textile fabrics of various kinds, dirty objects, etc., act as important vehicles of contagion. This is well known from antiquity, and in regard to this matter only a short explanation is necessary, which we will give in the following chapter. We have no data as to the probability of transmission by water and food.

MECHANISM OF DIFFUSION OF THE PLAGUE

The rats which emigrate from an infected locality to a healthy one, or from an infected to an uninfected district in a town, would be likely to infect the rats of the place invaded by them. This infection, however, will only occur rarely, because the healthy rats devour the sick and dead ones (p. 11), but for the fleas, which, abandoning the dead bodies, pass to the living (p. 27). It also frequently occurs that contagion takes place through the nose, the sick having contaminated the food on which all are feeding. This is indicated by observations made in Calcutta, in which were noticed severe conjunctivitis, submaxillary swelling, and pulmonary lesions in a great number of the bodies of these animals. The rats having died, the fleas conveyed the plague to the living.

This mechanism of diffusion explains how, at short distances, plague is propagated with a certain regularity, spreading from one house to the neighbouring ones, from one district to another, seldom following the great pathways of communication from the interior of the cities, or the most frequented roads between two neighbouring towns, but by mysterious routes, until the epidemic reaches the active period in which the number of those attacked is so enormous that it is impossible to establish the relation between the cases.*

The fact is also explained in this manner, that the lower stories of buildings suffer most severely; if the proportion in some statistics shows the contrary, that is because the number of those inhabiting the upper stories is relatively greater, the lower stories being generally used as warehouses for grain, cloth, etc., and not as dwelling-houses. The rats being the vehicles of contagion, it is understood how the first cases appear in grain and cloth warehouses, bakehouses, etc.—in fact, in buildings in which rats are numerous; and on the contrary, well-built new buildings, giving no shelter to the rodents, remain free from the disease.

Of the gang of dustmen appointed to carry out disinfection in Bombay, only those became infected who lived in houses, as the poor do, of bad sanitary conditions; those who slept in the huts built by the corporation, well-constructed and without rats, remained healthy, in spite of crowding.

* In contrast and confirmation of the facts indicated and conclusions arrived at in regard to plague, the translator may point to what occurs in a disease which is only conveyed from man to man, which, as shown by him many years ago, spreads along 'the great pathway of human intercourse' ('Leprosy,' p. 53).

In the houses in which the fugitives from infected towns have taken refuge the cases do not generally appear at once, but after the rats which have attacked the luggage of the fugitives die, and the fleas infect those living in the house; thus the first case may not affect the fugitives, but anyone among the inhabitants of the house. This complicated mechanism requires a certain time, during which new foci of contagion may arise in the same manner, or, indeed, people may become victims of the plague who have been *en route* while the disease was still in its period of incubation. The imported cases ought to precede on this last supposition, the indigenous ones, and this has actually happened on many occasions, especially when there has been a great rush of immigration into a previously healthy population.

The epidemic does not develop rapidly in any population, only during a period sometimes extending over ten to twelve months; it follows the insidious course actually observed at Oporto, which has caused it to be erroneously believed that it had no 'diffusive force.' This expression 'diffusive force' is one of many valueless words which circulate in intellectual intercourse like decoy partridges. It may signify either that the bacillus is meeting with considerable resistance, which is not to be supposed in a city like Oporto, or that it belongs to a species of slight virulence (p. 13), yet we know how easily the activity of these degenerated species can be revived (p. 14). It is more reasonable to suppose that it signifies nothing, or, what is more likely, that it conceals ignorance of the causes influencing the more or less rapid diffusion of the epidemic. To say of an epidemic that it does not spread because it is wanting in invading force is a play on words, but not an explanation.

I am not going to describe Oporto. I will not speak, then, of its hygienic conditions, which are sufficiently well known, but will limit myself to the discovery of the bacillus of the plague which has broken out in that city, though this has been frequently denied. Calmette took to Oporto very complete material for investigation, which had been used previously in making cultivations in Bombay, Hong Kong, and Nhatrang. I am able, therefore, to compare the biological characters of the Oporto bacillus with the others, and to assert its identity with them.

The form of the Portuguese bacillus, that of its colonies in the different media (p. 12), and finally the result of the inoculation of animals, make it clear that we have to deal with the microbe of plague. It was necessary to investigate its virulence, and this was experimented on by inoculating definite doses of the cultivation into white mice and guinea-pigs. It is known (p. 14) that the virulence is generally measured by the time in which a given dose of the cultivation kills the animal. Now, the duration of the illness in the mice and guinea-pigs was the same when the Portuguese bacillus was employed for inoculation as when the Indian bacillus was used. The virulence of the bacillus was equal from the cultivations preserved in the Pasteur Institute or those from the Asiatic epidemics.

An interesting fact was observed in these experiments. The transmission from one guinea-pig to another weakened the bacillus to such an extent that on inoculating animals with bacilli from one that had been infected with the Portuguese bacillus the sickness lasted a longer time, and in a third inoculation with the bacilli of the second it was still longer. I have said (p. 16) that this happens frequently; therefore it is not to be looked upon as strange. But it is believed that an analogous phenomenon has been

noticed in clinical experiences, and this is most interesting. It appears that the first cases in Oporto lasted from twenty to eighty or ninety hours, and that the duration of the disease in the persons whom it was thought were infected from them was much longer, reaching sometimes twenty to twenty-five days, and, finally, that a third series of cases infected by the last suffered from a very mild form of the disease.

It is not possible to form a judgment on these facts. In the first place, I consider that it is very doubtful whether it is possible to establish with certainty any connection between the three series of cases; and, on the other hand, there is no mention in India of this phenomenon of the exhaustion of the strength of the bacillus, which is not singular. Thus it is impossible to compare and appreciate definitely whether this is an ordinary effect produced in the transmission from man to man, as happens in animals (p. 16), or only an exception observed for the first time in Oporto.

There were during the month of June 17 attacks of plague and 6 deaths; in July, 14 attacks and 6 deaths; in August, 21 attacks and 12 deaths; and in the first ten days of September 12 attacks and 7 deaths. It has begun, therefore, as it does everywhere else, without showing either more or less 'diffusive force' than is usual.

In Hubli only eight cases occurred from November 4, 1897, to January 9, 1898. In the great epidemic in London in 1665 the first case occurred on December 20 of the previous year, the second on February 9, and the third and fourth on April 22. These epidemics show a 'diffusive force' much inferior to that which actually exists in Oporto, where in three months 64 cases have appeared. Notwithstanding that in the two first the mortality was consider-

able, that of London, though it began so quietly, was one of the most awful known to history.

As to the conveyance of infection by sea, where there is a great distance between the ports of embarkation and arrival, man does not carry it himself, since if anyone embarks who is already infected, the disease declares itself during the voyage; the disease is propagated by contaminated clothing or merchandise, or by rats, which are so numerous on board ship and so difficult to exterminate. A ship from an infected port may be the cause of an outbreak of the epidemic at a port visited by it without disembarking cargo, crew, or passengers; the infection should not in such a case be ascribed to the air, as the rats can reach the land by the cables or gangways. For the same reason a ship lashed to the side of another may infect it, and thus it sometimes happens that a vessel proceeding from a clean port carries the contagion to other ports, giving rise to a great deal of confusion in regard to the place of origin of the germ.

In the slow development of epidemics of plague the difficulties of adaptation of bacilli coming from one organic medium to another (p. 14) are sure to play some part. The frequency of the pneumonic forms at the beginning has been noticed; this may possibly indicate a nasal infection, caused by the hands, infected by impure contact, being raised to the nose. It is very possible that these cases are of great importance in the development of the epidemic, increasing the virulence of the bacillus (p. 9), adapting it to the human medium and fitting it for that medium, so that later on inoculation becomes possible even by the pricks of insects or other mechanisms already described.

The epidemic having developed, opportunities of infection

are multiplied by a number of mechanisms coming into play, some unknown, others easily understood by anyone who has read attentively the preceding chapters. It is generally admitted that the greater number of infections take place through the skin; and the frequency of the inguinal bubo would lead us to believe that the germ more frequently enters through the skin of the lower limbs than that of any other part of the body. This may be partly because the fleas, coming from the floors of the homes, reach the lower part of the body most readily. Some have also tried to explain it by ascribing it to many people going barefooted. But in the epidemic of London, in 1665, it attacked so many of the well-to-do classes, who wore well-made foot coverings, that it was called by some the epidemic of the middle classes.

In Mandvi the relative immunity of vagrants who go barefooted was noticed. Among thousands of individuals in Bombay employed in the work of disinfection, who went about all day barefooted, with their feet in the mud, there were very few cases. It has to be considered that in the soil the bacillus cannot always keep up the struggle with other species (p. 13), or loses its virulence. Finally, there are many questions in relation to the propagation of the plague which are not sufficiently cleared up.

The decline of the epidemic is generally slow, as was its beginning. That it takes several years for it to disappear was explained by some, by exhaustion of the receptivity *a priori*; a coefficient of population naturally immune, or on the contrary predisposed, is established. It appears to be the most prudent course to reject all such theories, which are undoubtedly most ingenious, but without scientific value, and to believe that the reason that anyone does not suffer from an infectious disease is, that he has not been exposed

to the contagion. Cornet believes that the whole human species is liable to suffer from tuberculosis; *cæteris paribus*, the same can be said of cholera, plague, and small-pox. The doctrine of predisposition only holds its place by the impossibility of showing that the person held to be immune has actually been reached by the infecting germ. Ten individuals go on an expedition, two return ill with pneumonia, and it may be said that the other eight had no predisposition to suffer from such illness. I do not consider that this is a really serious manner of reasoning. If the group in question had been fired on, and two men had been shot, nobody would say that the others were immune from the balls.

PROPHYLAXIS

Protection of the Individual.

Whatever else may be believed, the utility of disinfectants to the individual is very limited. Disinfection immediately after handling suspected substances is indispensable. Thus, medical men and nurses will do well to have recourse to it after visiting the sick, and more particularly after making post-mortems, the act of doing which has almost always been the cause of infection among medical men. The same precaution should also be taken after catching rats or any object of doubtful asepsis. In other cases the use of disinfectants is needless, and only tends to inspire unjustifiable confidence. These means are only efficacious when made use of by experts.

We frequently hear of ten or twelve articles recommended, each of which is held to guarantee the asepsis of a particular part of the body; what those forget who propose such complicated means is that in a few seconds after

disinfecting the hands, for example, they are infected *de novo*, since the least contact, and even the air itself, sows the surface immediately with the germs. Surgeons are to disinfect themselves just before commencing an operation, and if this is a long one, or even if an assistant has accidentally touched them with the towel, they disinfect themselves again, stopping the operation meanwhile. If we wished, then, to follow this rigorous antiseptic method, we would require to pass our lives during the epidemic in a barrel of corrosive sublimate, or surround ourselves with an enormous number of bottles of drugs, which would remind one of the collection of arms with which Tartarin prepared himself for the struggle with the lions, all of which is of course impracticable.

The celebrated Dr. Rubio has, very much *apropos*, made it known that soap and water form the best defence. This is indisputable; to meet the infinite variety of mechanisms of contagion hygiene demands the most simple means, and even for the moral effect it is well that it should be known to all that they may trust in cleanliness to preserve them from the plague.

Thus, then, I would venture to propose the adoption of the following rules, generally easy to carry out:

Personal cleanliness.—1. The greatest cleanliness of their persons and clothing is recommended to all persons. Those who cannot bathe daily ought to wash the whole body as frequently as possible.

2. The hands and face should be washed several times daily, the first especially before and after meals.

3. All scratching, punctures, wounds, contusions or pimples of the skin should be avoided; and if any of these lesions should be produced, it should be carefully washed and covered up with cotton-wool or taffeta.

4. Underclothing, working blouses, handkerchiefs, etc., should be washed frequently.

Food.—1. The use of food in a bad state of preservation is to be avoided.

2. Flesh and fish should be prepared immediately before being used, or exposed to very great heat if they are roasted in an oven.

3. Bread, fruit, and all food which is used without any previous preparation, are to be kept in perfectly clean baskets or bags; and besides this all those aliments that can be washed, such as fruit, should be so before being used.

4. The habit of rinsing the mouth before and after eating is very commendable.

Dwelling-houses.—1. The greatest cleanliness should be maintained in houses, damp cloths being used by preference for the soiled floors and walls.

2. The retention of soiled clothing in houses should be avoided; consequently all that is for use inside, as bedding, kitchen napery, blouses, etc., should be washed whenever they have been used.

3. All kinds of insects should be destroyed,* and the most scrupulous cleanliness of domestic animals, which so often harbour them, should be maintained.

Care of the sick.—1. The family should arrange for the patient being put to bed in a well-ventilated room with only one bed, and send at once for the doctor.

2. Only one person, or as few as possible, to have charge of the patient; and all others, especially children, must be forbidden to enter his room.

3. The person who has charge of the patient will avoid

* The translator may notice in this connection that *flies* die of the disease (Besson), to emphasize the rule, as applying to *all kinds* of insects.

contact with others, and will neither give nor receive any object from them without previously washing his or her hands in very hot soap and water.

4. All objects which have been in contact with the patient should be plunged for a quarter of an hour into boiling water before being touched by any other than the person in charge. The same precaution should be taken with clothing before it is given out to be washed, and with all discharges before they are thrown into the sewer.

The above includes all that need be recommended to the public. Other means of prevention fall to be adopted or prescribed by physicians or the authorities.

Whoever has read carefully the foregoing advice, will see that it contains nothing of a special nature. It is, however, sufficient, and represents the sole co-operation with which the public ought to assist the action of the authorities and the medical faculty. It is useless and even prejudicial for the public to take a more active part and attempt to play rôles for which they are not prepared. To the critical the simplicity of the counsel given above may appear strange; to meet this, I will mention only one consideration.

All the mechanism, apparently so complicated, brought into action by the Board of Health, with its inspections, disinfections, sanitary stations, warrants, etc., have for their principal object the confiscation of dirty clothing. It is possible that many of the public do not understand that this is the intention; for the sake of those I mention and explain it in precise terms. If the Spaniards resident in Portugal had found it convenient, as has been said by Señor Cavia, not to bring dirty clothing in their luggage, they would hardly have been interfered with on the frontier.

Since we know that the Government insists as a principal precaution that those who travel will do so with clean

clothing, it will appear less strange that we recommend to the people, as the sole preventative means, cleanliness of their persons and dwellings.

Local Defence.

The means of general hygiene (sanitation of houses, streets, quarters, etc.), are themselves excellent. At the same time it would be a great mistake and greater stupidity, when an epidemic is threatening, and much more so when it has broken out, for the authorities to give their attention to this subject in preference to other questions which demand it.

Every epidemic has its own *truc*, its special mechanism of diffusion, and we must decide in the first place to use means to destroy this mechanism. An example will make my idea more clear. Typhoid fever is spread by water; when an epidemic breaks out all the money and energy which is employed in the sanitation of districts, disinfecting houses, preventing overcrowding, etc., *will not check the spread of the disease as long as the water-pipes continue to distribute sickness and death to each house*. On the other hand, the stopping of the contaminated supply is sufficient at once to put a stop to the spread of the fever.

In the sanitary organization of a country it is necessary to make the same distinction as the military one between garrison service and that of war. The general rules of hygiene ought to be adopted as common law of civilized nations, regulating the normal and daily life of all. An epidemic, on the other hand, is, like war, an abnormal condition; and in it, without abandoning general hygiene, tactics must be adopted in the first place such as are required to meet the special mode of attack adopted by the enemy.

From February, 1897, 31,000 people (!) were engaged in Bombay in washing the streets, houses, drains, etc.; at the end of that year the mortality was frightful. In September it was decided to burn the bedding and clothing of the sick, to isolate them, and disinfect their dwellings; the epidemic continued indifferent to all. In disinfecting 180 houses the enormous quantity of 13,500 cubic yards of carbolic acid were used, quicklime was used in cartloads, and also lime with sublimate; liquid disinfectants were scattered about the houses by means of fire-bombs in such quantities that for some time afterwards, filtering through from one floor to another, they made necessary the use of umbrellas to those who repaired the houses—yet no effect was produced upon the course of the epidemic.

The attempt has been made to prevent overcrowding; nothing could be more correct, but on comparing the number of attacks in the different districts of an invaded city, it is seen that these are not in proportion to the number of inhabitants per square mile (Hankin), and it is a fact that not one case occurred on the steamers on which hundreds fled from Bombay, in spite of the enormous overcrowding. The trial has also been made to improve the hygiene of the houses and districts inhabited by the poor, a laudable determination; but in the great epidemic in London, though it began in the suburbs, it was not there that it raged most fiercely. And in Oporto the epidemic began in the Rua da Fonte Taurina, but starting from there, it continued to spread.

Finally, people are recommended to isolate themselves as much as possible (very excellent counsel); but in London and Bombay the prostitutes, tinkers, and beggars—people whose occupations force them to be sociable—were those least affected by the epidemic.

I repeat that I do not maintain that these means are useless, but I believe that as they do not attack directly the *truc* or special mechanism of the disease, they ought to take a secondary place in the attention of the authorities. The English Commission in India understood this when it qualified them from the first as *palliatives*. They are all convenient, yet the prodigality with which disinfectants were used in Oporto was of some utility. The streets were veritable pools of hypochlorite of lime and carbolic acid, the strong odour of which in some districts concealed that of misery and stinking fish, and raised at one and the same time the stomachs and spirits of the public. Generally speaking, the authorities prefer disinfectants with a strong odour, because they inspire public confidence; the people who stop half suffocated at some corner by a smell like a druggist's shop believe in good faith that millions of bacilli which would otherwise have attacked them are dead at their feet, and they go back praising the zeal of the authorities.

Our absolute ignorance of many circumstances which favour the diffusion of plague makes it imperative that the authorities should have perfect liberty to adopt every possible means of protection, so that by multiplying such means the probability of the enemy being hunted down may be increased. But in regard to the known or probable conditions, on the other hand, the use of the necessary means should be compulsory; and the actual data in regard to the propagation of plague by rats indicate the necessity for the destruction of these rodents in threatened towns before the epidemic breaks out.

The undertaking presents great difficulties, and to be successful it will be well to have recourse to all known mechanical and chemical means, and even to place a price on the heads of the rodents, as was done with deplorable

deliberation by the Municipality of Oporto (as referred to later on). Stopping up the entrances to the sewers in which they live, and suffocating them when possible with sulphurous acid, are means to be recommended.

The trial has been made to inoculate some of the animals with the *tinea favosa* of man, so that they may infect others; this is not a practicable proceeding, since it has been observed that only the weak ones succumbed, and that at the end of a long time.

S/ In Valencia it has been proposed to start an epidemic among the rats by inoculation with *Bacillus muri*~~septicum~~. S/ I do not dare to expect much success from the experiment. From various experiments of distinguished savants quoted by Loringa, it is shown that the disease is not very contagious among these animals; that several species among them are refractory to it, and that only those usually die from it that have ingested a great quantity of the cultivation, such a quantity as to bring the poison practically to the proportion of a chemical poison. Besides, several microbiologists have called attention to the surprising analogies which exist between this bacillus and that which is usually found in cases of puerperal septicæmia. This circumstance suggests the fear that the handling of the bacillus, and the diffusion of its cultivations, may not be so innocent as might have been believed.

When the epidemic has broken out in a town it is best that individual action should be limited to stopping up the holes in which the rats live, without attempting to organize battues, much less to collect the rats so obtained. Simond says that the dead body of a rat should not be touched until a large quantity of boiling water has been poured over it.

The hunting of rats may be a dangerous sport (p. 26), and for this reason the authorities should not encourage it

by premiums. On the other hand, the decision adopted in Oporto to place wire gratings in the channels of the drains to catch the bodies of rats, and burn them instead of allowing them to pass into the current of the rivers, is an excellent one.

The authorities count on fighting the rats by the personnel employed in disinfection; but strychnine should not be thrown into the drains, as in Oporto, but the places in which they abound should be put into a sanitary state, and the cellars, grain and cloth warehouses, bakehouses, etc., disinfected. When a case has occurred in a city the rats should not be persecuted, so to speak, foolishly and madly. Care need only be taken to prevent those of the infected district from passing to the uninfected ones, and so carrying the contagion; to accomplish this corrosive sublimate is used in the first place, and afterwards disinfectants of a strong and disagreeable order, with which to a certain extent they are surrounded and localized in the place first invaded. Perhaps these means are not always successful, but we have no others at our disposal.

SANITARY MEASURES

The old regimen of international sanitary policy in regard to epidemics has its foundation in *sequestration*; the modern one, as now established in Spain, depends almost entirely on *disinfection*. The former suited a period in which the natural history and mode of propagation of infectious diseases were unknown; the second is suitable for the present time, when the microscope and experimental inoculation of diseases in animals are clearing up the mystery. At first sight it would appear as if the traditional regimen

ought to protect the public safety more than the present one. The long quarantines, the lazarettos, the cordons, the closure of the frontier, the suspension of all kinds of traffic between the nation which is a victim to the epidemic and other countries, appear to be measures which render the extension of a disease quite impossible. 'There is no worse proof than that which proves too much,' or as the French say, 'Ce qu'est trop est insignifiant.' Hearing of the closing of the frontier, frightened public opinion goes to sleep confidingly. People have in their imaginations an enormous gate with ten or twelve padlocks, or rather an entirely impassable Wall of China. In practice the wall is reduced to a grille like that of 'La Gran Via,'* which has given so much pleasure to the partisans of the genus little boy.

To understand the inefficiency of the system it suffices to take into consideration that there are microbes which are transmitted by water, as those of cholera and typhoid fever, and that these microbes may not only be met with in the water of rivers below, but also on certain occasions above the infected point, in some cases at long distances, in spite of the autodepuration which goes on in running water.

The atmosphere is a vehicle for other micro-organisms which produce disease, and thus is probably transmitted the as yet not well-defined agent causing small-pox. Insects may be carriers of certain germs which they inoculate by their punctures; in this way certain species of mosquitoes propagate malaria, and fleas assist in the diffusion of plague. The little mammals carry with them other germs, and it thus appears that the rats flying from the plague take the devastating epidemic from one town to another, or in great cities from one district to another. It

* A Spanish play.

is easily understood that the closure of frontiers does not affect water, dust, insects, nor those small mammals; and that those possibilities of transmission more or less remote, but always effective, are so many other breaches in the Wall of China previously mentioned.

But besides this, with regard to persons and merchandise, the cordon, the 'closure of the frontiers,' is also illusory. The cordon is in plain terms a blockade, and in this war against infecting germs the maxim that a blockade must be effectual to be of value holds good. During the nominal blockade of Cuba all the ships reached the island whose captains had a little boldness and cunning. There is no cordon at which smugglers, for example, do not laugh; and besides them, everybody having any interest in doing so, or even those acting simply from caprice, cross over the established line.

At present the same holds good. When, on account of the lamentable deficiencies in the sanitary organization of our inland country districts, it was considered advisable to have recourse for some days to the famous 'closing of the frontier,' cases of this kind occurred. All the newspapers have published these facts, so there can be no indiscretion in registering and commenting upon them. It has happened that thirty-three people at one time crossed the line, reached a Spanish village, and amused themselves by relating everywhere the exploit they had performed. It will be said that the cordon was not yet complete at many points. It might have been; but the transgression of the regimen would still have happened. We are pleased to say that the failure will indeed discredit for ever the system of cordons. Among the people accustomed to travel in *wagon-lits*, the closure of the frontier is an efficacious measure; but it is exactly those persons, rich

and accustomed to the practice of hygienic measures, who are least to be feared in regard to the possibility that they may carry the contagion with them. On the other hand, the people of the *lower classes*, without means to live a hygienic life, without healthy clothing, every class of them enduring inconveniences and annoyances, if they cannot travel by railway, take the highway or the country roads, and if they find all these roads closed, go quietly across country, travelling by night, and contrive so that it is hardly possible to stop them—much less if the stimulus of smuggling, or the hope of any kind of gain, or the fear of becoming victims to the epidemic in the country they are leaving, spurs them on.

It results from this, then, that, exactly contrary to what is believed by the general public, it can be said that the defence of the territory has begun with the reopening of the frontier. If there had been any foresight in Spain, the sanitary stations would have commenced to act from the first day. The defence of the frontiers has been perfectly studied; the places in which inspections should be carried out were opportunely consigned to memorials accompanied by maps, which will be collected, I believe, as long as Señor Aguilera is a Government Minister. If all had been in order, a telegram from the Minister would have sufficed to set the mechanism to work.

The inspecting staff of railways ought constantly to be in readiness to enter on their functions, requiring only a telegram to the physician for that section of the line telling him to act, the necessary personnel being sent. The inspection of highways, country roads, etc., ought to be carried out under identical conditions, supervised by the Governors of frontier provinces. In this way the Government Minister, or the Director of Sanitation, would be able

by a word to cover the frontier in four to six hours, setting in action at once all the sanitary mechanism, which would move like clockwork with only a touch to the proper spring.

Apart from the trouble at the beginning for some days, now that the system of inspection is working, it may be said that it is being carried out according to the full modern regimen; and certainly in the defence of public health in Spain, the rapidity in obtaining information, and the efficiency of the methods of disinfection now in use, are taken advantage of.

The system of defence which has been adopted in Spain in consequence of the resolutions arrived at, and in the spirit of the last International Sanitary Conferences at Dresden and Venice, is worthy of these virile temperaments, which, without cringing before danger, arrange to check it, confident in scientific success. The first condition of its success is information—rapid information which makes known to the country, and immediately afterwards to the whole world, the appearance of a suspicious case, so that the means may at once be taken to smother the fire, and the countries threatened may prepare to defend themselves, if unfortunately the one first attacked is conquered in the struggle. Hence, it has been said with justice that the concealment to which the Portuguese Government appears to have had recourse constitutes a case of international responsibility.

The old system tended with all its rigour to form one line of defence only—the cordon—on the one side of which panic engendered frenzy, and on the other over-confidence prevented a rational plan of campaign being formed.

When the epidemic broke through the feeble barrier that had been raised, confusion, fear, and disorder acted together

and assisted in spreading it in the country, which found itself suddenly at the mercy of an absolutely irremediable danger; a cordon was drawn round the lodging, the house, the district, the village. The disease overleaped all obstacles, and the demoralization produced in the country by the successive failures reduced the people to despair, and robbed them of energy for the struggle.

On the other hand, the cordon, the uselessness of which applied to a frontier we have demonstrated, is still more difficult to keep up in the environs of a town, and totally impossible in a district or a house, besides being a cruel and immoral practice, dissolving the holy bonds of fraternity which ought to unite mankind. No city can live a life apart; to put a cordon round one is to add to the rigors of the epidemic that of famine.

To include in the cordon several surrounding villages so that they may support the town, and isolate those villages from the rest of the world, is one of the most barbarous abuses of power possible, reproducing at the end of the nineteenth century the ancient custom of binding a living slave to the corpse of an eminent man that he might accompany him to the other world.

The cordon of Oporto has caused much legitimate indignation in that unfortunate city. A severe sanitary inspection would have given results which will not follow, certainly, this inhuman order. After all, such a cordon amounts to vain talk. But, looking at the possibility, remote though it may be, that the epidemic will reach any part of Spain, it is necessary to act so that our Government may not fall into the temptation to have recourse to such ridiculous means.

In the modern regimen the sanitary inspections of the frontier would have formed the *third line of defence* for

Spain if the Portuguese Government had shown itself equal to the importance of its mission. The first would have been represented by the energetic means which the authorities of Oporto should have taken to destroy the first focus or foci of infection. That those means may be very efficacious is shown by the facility with which the plague was overcome in Vienna—such great facility that the population in the very neighbourhood was not alarmed. The second line was formed by the arrangements which the Portuguese Government agreed to adopt to localize the epidemic in the place where it found its first victims. Everything in this system is common to all, organic, demonstrating the solidarity of humanity. Thus the Alcalde of Oporto and the chief of the Portuguese Government, especially as they hold such official positions, ought to have consulted the first delegates of Europe at the infected spot as to how to smother the epidemic.

If the Portuguese Government had shown sincerity and diligence in making known the first cases, with energy and skill in the use of preventive measures, Spain would not have been suddenly called upon to fix a rigorous regimen, but would have been able to prepare herself for the struggle with the calm of a third reserve corps, which does not take part in the fight unless the two first have been conquered and the two corresponding lines of defence destroyed. She would also, above all, have been able to moderate or increase its rigor according to the success attained by the means used by the Portuguese Government, limiting her precautions during a great part of the time to what came from Oporto, and not extending them to everything coming from Portugal, until it was known that the first line of defence had broken down—in fact, would have followed the incidents of the struggle, waiting for the moment, if the

evil went so far, in which she would have to intervene in the fight.

The sanitary inspections instituted on the frontier hold, above all, the character of centres of information. They check the passage of goods, in regard to which there is very much suspicion, and of travellers who are *already sick*, and to this is now limited the application of the old cordon system. For the rest, all that is done is to disinfect the less suspected goods and luggage, and ascertain, both in regard to them and travellers, whence they came and their destination.* It will be said that under this regimen a person may pass the frontier who is already infected, but in whom the disease has not yet shown itself. This is true, but it is known where he goes; he is watched during the maximum number of days of the period of incubation of the disease, and hardly will the first symptoms appear when assistance will be given to destroy the infecting focus.

It is also to be remembered that, as regards the plague, travellers do not constitute the only medium of propagation, nor probably the most important; thus, it has been observed that the epidemic more readily follows the direction taken by the fugitive rats than that followed by the inhabitants of places who are victims of the panic. The addition of the cordon to sanitary inspections is useless, because in ordinary circumstances the frontier forms a natural cordon which keeps open through its own little gates the ways of communication so long as no one goes across country. The only people who pass the frontier anywhere are the inhabitants of villages scattered over both sides of the line

* In some inspections, according to the press, the dirty clothing of travellers is burned. This is an abuse, undoubtedly due to disinfecting stoves not being in use.

or neighbours in the hamlets near it; but this is not of great importance, even when the epidemic seizes its victims near the frontier, since the presence of a stranger is always noticed in these little centres, and the authorities can adopt at once the proper precautions.

It is true that in times of epidemic, as we have said, travellers may avoid the ordinary routes to escape inspection. If the inspections are limited to identifying the traveller and disinfecting the luggage in which there is any dirty clothing, the annoyance is so slight that no one will go through the fatigue of travelling by irregular ways to avoid it; but if clothing is burned, and the people subjected to annoying fumigations, they will prefer to break the cordon. In this case the inspections are useless, as all who wish to break the cordon can do so with comparative ease.

In the traditional regimen, as the cordon was the most important defence, the presence of a case beyond the frontier constituted a breakdown of it, which demoralized the country. Given the regimen as now established, there would be no failure of it, even if a traveller were taken ill in Badajos, Madrid, or Saragossa, since the inspection is not expected to prevent the passage of anyone except the sick, but only to ascertain the place to which each traveller is going, so that assistance may be given immediately to smother the infection if it is produced.

The appearance in Spain of a case, the origin of which could be attributed to contagion by objects, if it did constitute a breakdown of the regimen (because it would indicate that the merchandise and luggage had not been sufficiently examined and disinfected on the frontier), would not in any way produce a great effect on our opinion, nor have any frightful consequences, because the public attention

would be so fully alive that the case would be recognised immediately, and the infecting focus dealt with at the very first moment.

This first trial, which is being made in Spain on a great scale,* of a regimen founded on information, is of very great importance, because it will accustom the people to look quietly on the proximity of exotic infectious diseases without alarm. In this way they will be dealt with on the spot at which they appear, without the rest of the country taking the least notice, as in England, for example, in whose ports cases of cholera or other infectious diseases are sometimes registered without being considered of any importance to the country or to Europe, so great is the confidence in the action of the local authorities. On the day on which our ports are supplied with sufficient means of disinfection, and when the sanitary organization of the country is a fact, we shall be able to allow vessels coming from anywhere, save in very exceptional cases, to load and unload without interrupting commercial intercourse, in the confidence that either no case of exotic disease will be produced, or if, in spite of all precautions, it is produced, the focus will be extinguished at once without the disease being propagated in the same town.

To avoid the transmission of plague by sea, France has adopted means that are very much to be commended.

More recently Dr. Pulido has made public his opinion against cordons. This is worthy of notice, Dr. Pulido being a physician of superior intelligence and culture, and one who besides, in his position, is able to prove the irremediable deficiencies of the system.

* It was made on a more reduced scale in 1895, when the cholera appeared in Bilbao, and its success was complete, since only one case appeared beyond the place of inspection at Miranda.

THE DISEASE

Clinical Description.

Fulminant cases, in which the disease appears to have developed insidiously without visible symptoms, do not seem to be very frequent. Sometimes people are seen slightly indisposed, who die suddenly while still at work. Yersin mentions the two following cases in which the cause of death was proved by autopsies :

1. A fisherman, seventy years old, embarks as usual in the early morning. At nine o'clock he feels ill, and lies down in the bottom of the boat. An hour afterwards, when his comrades call him to breakfast with them, they discover that he is dead.

2. A woman, forty years of age, wife of a merchant, receives customers and supplies their wants, saying something about a mouse to them. A few seconds later she feels sick, and lies down to rest in bed. She dies immediately.

I pass over the fulminant cases in Oporto previous to September 10. However, I would not be so bold as to deny that they occurred, since the difficulty in obtaining information is extraordinary, even among medical men practising in that quarter. The most rapid case that I know of lasted twenty hours, and happened at the very beginning of the epidemic. In the press I have read that there were fulminant cases, but one of them was the very one referred to, and it is easily understood that a sickness which lasts twenty hours is too long continued to be classed as a 'fulminating' one. We ought not to call 'fulminating' any except such cases as those first cited, if we wish to avoid great confusion.

In typical cases, Yersin says, describing the cases which occurred last year at Nhatrang, the sickness begins by a shivering fit, after which the temperature rises rapidly to 39°, 40°, and even 41° (102·2° to 105·8° F.).

The patient is attacked by vertigo, and staggers like a drunken man; there is great lassitude and very severe headache; the pulse is frequent; respiration accelerated; the conjunctivæ are injected; he vomits repeatedly, and almost always suffers extremely.

The bubo appears within the first few hours, and develops rapidly; generally it is single, and the places in which it is most frequently found are the inguinal region, the axilla, and the neck. It is always very painful to the touch. It may remain limited to one group of glands, and may or may not be accompanied by diffuse tumefaction in the region in which it appears.

On examination of the patient on the following day there is found to be an increase in the frequency of the pulse and difficulty in breathing; the temperature continues high. There is often delirium. The bubo is larger, and reaches generally to the size of a hen's egg.

On the third day the frequency of the pulse is extraordinary, sometimes reaching over 120 in the minute. The patient is in the greatest anguish, and generally death is brought on rapidly by paralysis of respiration. The ganglionic swelling remains the size of a hen's egg.

A typical case of plague is exceptional. In reality there is such a variety in the manner in which the symptoms appear that in more than half the cases, diagnosis is only possible post-mortem, by discovering the presence of the bacillus.

The bubo is absent in about half of the cases. In such cases the disease develops like a simple pneumonia

or as a pernicious attack, without its being possible to diagnose it during life.

The most constant symptom is fever, which generally exceeds 39° (102.2° F.). Headache and vertigo are frequent, as well as vomiting and difficulty of breathing. In the pneumonic form there is often hæmoptysis. Diarrhœa is very unusual.

In the aged the plague generally advances insidiously, without decided symptoms. The temperature is sometimes high, sometimes normal. Death comes slowly (the fifth or sixth day), and diagnosis is not possible without a post-mortem examination.

In cases in which pneumonia is present, the illness frequently develops without cough or expectoration, perhaps on account of the profound adynamia. The disease can only be recognised by an examination of the chest—an examination which, naturally, does not reveal the specific character of the lesion, and only points to an ordinary broncho-pneumonia.

There is frequently meteorism, abdominal pain, hæmorrhagic spots, and other well-known signs of destruction of the blood, which it is usual to see in grave, acute or chronic intoxications (as by phosphorus or in cirrhosis, etc). Varioloid appearances also sometimes show themselves on the skin, due probably to microbic embolisms, which, if the illness is sufficiently prolonged, may give rise to pustules by secondary infection.

Albrecht, in twenty-four autopsies, found six of primary pneumonic plague, ten of inguinal bubo, four in the axilla and four in the neck. In some cases which develop without visible bubo this nevertheless exists, as has been proved by autopsies made by Calmette in Oporto, confirming former observations (Simpson).

The disease may be described as an infection which, in the greater number of cases, enters by the skin, and which is checked in the nearest glands when it is not very active, causing the known general effects by the absorption of toxic products. If the infection is more intense, the glands do not offer a sufficient barrier, and these reach the blood and internal organs (Koch). This phenomenon may be produced, especially if the infection is very active, almost without any struggle on the part of the glands; so that the bacillus rapidly reaches the deep lymphatic system, and even to the bronchial glands, causing broncho-pneumonia by a different mechanism to that of the direct infection already mentioned (Simond). Though from their nature none of these conjectures are capable of demonstration, the fact that the most benign forms of plague are those in which the bubo is found, while those that develop without, are grave, makes them probable. The gravest form is pneumonic plague; its termination is always fatal.

Lesions.

The subcutaneous injection of pulp of the buboes produces plague in animals in the laboratory. In the guinea-pig in a few hours there appear œdema round the situation of the punctures, and tumefaction of the nearest glands. In twenty-four or thirty-six hours the animal is attacked by convulsions, which continue until it succumbs.

In the autopsy œdema is found at the site of the inoculation and round the nearest glands, which are tumefied, and contain numerous bacilli. The abdominal organs, greatly congested, show numerous hæmorrhagic foci; there is sometimes on the spleen, which is very voluminous, as well as on the kidneys and liver, an eruption like miliary

tubercle. The pleura and the peritoneum usually contain serum, in which the microscope shows the bacillus, which is also found in the viscera and the blood.

These lesions make up what is generally seen in all autopsies. Besides this kind of groundwork, there are other special ones which depend chiefly on the position of the site through which infection has entered. In regard to the buboes it can only be said that they are absent in a great number of cases, or that at most there is an insignificant increase in the volume of certain glands, which, neither by their microscopic characters nor by the results of microscopic examination, can, strictly speaking, be spoken of as bubo (local action insufficient, p. 58).

The pneumonia of plague has been studied experimentally by Batzaroff, who distinguishes two varieties, which he calls primary and secondary.

In the primary the animal presents no phenomenon during the first twenty-four or thirty-six hours, except a slight fall in the temperature, which follows the injection, and which is to be explained as being caused by reflex action. An early diagnosis could be made, however, in those cases by a microscopic examination of the nasal mucus, which would show the bacillus in active proliferation. That such is the condition is proved by the abundance of *early* forms of the bacillus (p. 11). At the end of thirty hours fever begins, which rises very high; the animal appears to be miserable, depressed, breathes with difficulty, and coughs up a foamy liquid. From its nose there flows a serosity which irritates the mucous covering of the snout; the inflammation propagated by the lachrymal ducts reaches the conjunctiva, and causes serious mischief in the eye. Meanwhile the exhaustion of the animal increases, respiration becomes strident, there is distinct *wheezing*; paralysis

of the stomach and of the small intestine at least gives rise to distension of those organs, which, pushing the diaphragm upwards, increases enormously the dyspnœa; and, finally, in twenty-four or thirty-six hours the animal succumbs.

As specific lesions of this pneumonia of plague, apart from the general alterations of organs already described, and which are accentuated in this form, the pulmonary changes have to be taken into consideration. The lung appears dilated, congested, and wanting in elasticity; presents numerous swellings and foci of infiltration, sometimes separate, sometimes united. On pressure a liquid foam escapes. On the surface are numerous ecchymoses. The pleural and pericardial cavities contain abundance of serum. Microscopic examination shows that the intra-alveolar spaces are filled with cells from the parietes in distinct and recognisable stages of degeneration, with mono- and poly-nuclear leucocytes, red globules, and plague bacilli.

Pneumonococci, streptococci, etc., are also met with. Microbiological investigation shows the presence of the bacillus in the nasal mucus, in the sputa, in the pulmonary serum, in the fluid found in the pleura and pericardium, and in the blood retained in the heart.

In secondary pneumonia of plague the lesions resemble greatly those found in miliary tuberculosis. The lung is cribbled with those pseudo-tubercles, which are hard, and contain in their interior a liquid with numerous bacilli. At those spots where the tubercles are confluent the structure is so much altered that it can hardly be recognised, and the organ has an appearance analogous to that of great tubercular infiltration in caseous pneumonia.

I have described in full these lesions which post-mortem examination has disclosed in animals, because they agree essentially with those found in man.

Albrecht considers, as the result of clinical and necrological investigations, that there are two forms of the disease, the septicæmic and the pyæmic. In the first ecchymoses and hæmorrhages in the different organs dominate the scene, with mucous and serous discharge, and degeneration of the parenchyma; in the second there are numerous embolisms in the lung, liver, kidneys, etc. The spleen is enlarged in both forms.

When the disease has taken the pneumonic form there are to be found disseminated or confluent centres of inflammation, the description of which is useless, after I have described the results of the experiments of Batzaroff. In these cases the primary bubo generally affects the deep cervical glands. In cases in which the buboes have suppurated for several days the gland tissue disappears.

Treatment.

It is needless to reproduce here the long list of drugs mentioned in treatises on the subject. From the conception that we have formulated of the disease, we cannot hope for great results from any of them, and this is confirmed in practice.

In Oporto calomel is used as a purgative (40 to 60 centigrammes, in one or two doses), or as a diuretic (2 centigrammes three or four times daily), or finally to obtain general effects, an idea founded on old but now abandoned beliefs as to its action (6 to 8 milligrammes every two hours). The physicians of Oporto are also in the habit of prescribing a laxative as the ordinary drink of the patient, and use citrate of magnesia in lemonade. In cases of great adynamia they have used caffein and strychnine.

Certainly the medication chiefly indicated is that which,

by stimulating the secretions, favours the elimination of toxic material, and perhaps in the slight forms of infection this regimen may assist the organism to get rid of such. But in other cases this action will only be produced by the use of strong drugs, or insufficiently. It is easy to understand the reason of these failures, and equally comprehensible that so far as symptomatic medication fails in its modest attempts, we are unable to reduce the severity of the most painful symptoms.

For local treatment tincture of iodine and mercurial pomade is used in Oporto while the bubo remains hard, that is to say, the classic and little credited method of treatment of all kinds of ganglionic swellings. When the tumour softens, it is opened and treated antiseptically. Very much the same has been done as in India, so that in reference to treatment no progress has been made in the epidemic at Oporto. I have applied to a distinguished physician of that town, who is investigating the point as to whether any modification of the course of the complaint is produced by the *early* opening of the bubo and extirpation of the ganglia, as has sometimes been done with inguinal swellings of a venereal nature.

Simpson, in a remarkable article published in an English journal (*British Medical Journal*, September 16, 1899), says that opening the bubo, however early, gives no results. For the treatment of the swellings ice is indicated, which also naturally should be used for the headache. I consider that we should do our best to support the strength of the patient by every possible means, since experience has shown that when a patient has managed to survive to the sixth or seventh day, there is a great probability that he will recover.

To prevent cardiac failure digitalis, caffein, and hypo-

dermic injections of ether or camphorated oil may and ought to be used. Good nourishment ought to be given to the patient. Milk in sufficient quantity (four to six pints daily), a glassful being drunk every two hours, is very useful. Alcoholic stimulants ought also to be given.

It will be easily understood how the intensity of the infection influences the progress of the disease. There are cases of plague so benign that they only feel some malaise, with slight fever, some tumefaction of the glands and congestion of the conjunctiva. Between this slight form, in which the patient does not even stay in bed, and which it has been said is not infectious, and the pneumonic, there are many grades of infection which will influence the success of the treatment.

For the diagnosis during life of the pneumonia, Simpson recommends the examination of the sputum. On account of the great quantity of bacilli in the sputum, and the facility with which these infect handkerchiefs, bedclothes, the walls of houses, and even the air (Flügge), this form is more dangerously infectious than others.

SERO-THERAPEUTICS

Yersin's Serum.

All who have studied the plague, and have had occasion to try with their patients the various systems of treatment, agree in stating that the only agent capable of modifying the course of the disease is the serum, and that without it the physician finds himself disarmed. Even if it does not in all cases give such results as are to be desired, the serum is the one really useful means with which we can oppose the disease in private practice when once it has

broken out, or which we can use as a means of prevention in cases in which there is a possibility of contagion.

As to the Yersin serum, its use is limited to preventive inoculation, because the immunity which it confers does not last beyond three weeks. As the plague as an epidemic has a slow course lasting over a long period, with frequent recrudescences, it would not be practicable to resort to universal inoculation; and still further, it would not be possible. It is enough to say that to protect the population of Madrid it would be necessary to use about 250,000 flasks of serum, and even then the immunity would only last for the period mentioned. For this reason Yersin advises that only the inhabitants of the house in which the disease has appeared should be inoculated. As inexact accounts of the power of the serum are circulated which have their origin in natural ignorance of these questions, it is best to state the matter clearly, so that erroneous opinions may not prevail.

After studying the epidemic in Hong Kong in 1894, Yersin returned to Paris to devote himself at the Pasteur Institute to experiments relating to immunity. Calmette and Borell, under the direction of Roux, had indeed begun this work and succeeded in immunizing rabbits. Yersin inoculated the horse with a cultivation of the plague bacillus, first subcutaneously and afterwards directly into the veins, so as to avoid the tumours which in the first case were produced in the animal, and the suppuration to which they gave rise. These injections being repeated in increasing doses and at long intervals, to give time for the animal to recover, the serum obtained three weeks after the last injection was used with success to immunize mice. The tenth part of a cubic centimetre ($1\frac{1}{2}$ milligrammes) of this serum saved from death a mouse, into which twelve

hours later a quantity of bacillus cultivation which caused the death of another of the same species and equal weight was inoculated. A mouse which was inoculated by the plague, and twelve hours afterwards with a cubic centimetre of the serum, was also saved. The preventative and curative power of the serum is therefore indisputable.

Some time after these trials Yersin went back to Asia and founded the Pasteur Institute at Nhatrang, to obtain serum from the horse and try its efficacy on the human species; but before the installation of this centre was finished, the plague broke out at Hong Kong. The institute of Paris sent him eighty flasks, and with these he was able to experiment in Amoy, where there was a sudden recrudescence of plague imported from Hong Kong the previous year, and which had claimed some victims in the locality.

It is very dangerous to try to obtain the serum in great quantity, so much so, that Roux did not dare to inoculate twenty-five horses at one time (as was done by Yersin to obtain serum with which to fight the epidemic at Nhatrang), being afraid that, in spite of all precautions, some carelessness would give rise to the epidemic in France. It is also known that cases occurred in Vienna last winter through negligence in a laboratory, and, finally, the very epidemic at Nhatrang has been attributed by some, though apparently without foundation, to carelessness in Yersin's laboratory.*

The special conditions under which Yersin's serum has up to the present been handled, whether because only small quantities could be used, or that the quality of the product was not always equal—in fact, from the difficulties inherent

* *Translator's note.*—Bourges (p. 11) says emphatically as to this suggestion: 'Il a été démontré qu'il s'agit là de cas d'importation et non d'une épidémie de laboratoire, comme on l'avait prétendu d'abord.'

to these experiments—have made it impossible to formulate any useful statistics showing its action as a preservative against plague. In cases in which the trial has been made under favourable conditions the results have been highly satisfactory.

Preventive vaccination with anti-plague serum of the family of a patient *always* prevents the disease from spreading among them, while many are attacked who are not vaccinated. Among 500 vaccinated only five cases occurred, of whom three began twelve days after the inoculation, and two so rapidly that the disease was evidently at the time of the inoculation just about to appear. A similar result was arrived at in the trials at Cutch-Mandri in 400 vaccinations (the serum employed in those 900 cases was not strong). Yersin gives statistics of twenty-three cases treated in Amoy; of those only two were fatal, and in those the serum was used on the fifth day of the disease. Later statistics are not so favourable, giving generally an estimate of the success of the serum in rather over half of the cases, but those (in Amoy) are of interest as referring day by day to this, the only treatment of the plague.

The serum was used the first day of the sickness in six cases; the cure was effected in from twelve to twenty-four hours. The quantity of serum employed was 20 to 30 cubic centimetres. In six other cases it was used on the second day. The cure was slower; quantity used 30 to 50 cubic centimetres.

Third day.—Four cases. The fever resisted forty-eight hours. The buboes suppurated, which had not occurred in the former cases, but a cure was obtained. Convalescence was slow. The quantity of serum used was 40 to 60 cubic centimetres.

Fourth day.—Three cases. These required five to six

days before they recovered. Quantity of serum 20 to 50 cubic centimetres.

Fifth day.—Four cases. Two deaths.

In Oporto the serum has been used several times; the results are not yet known, the experiments having been made quite recently. In one case the treatment was begun on the fourth day of the illness. It was that of a woman who fell ill on September 1 with shiverings, fever, languor, etc. On the following day a bubo appeared in the left groin, forming a hard, painful, circumscribed swelling in that region. The case having been notified, she was taken to the hospital on the third day, where the temperature was found to be 40° (104° F.); on the fourth day in the afternoon she received an injection of 40 cubic centimetres, and two more on the two succeeding days.

In another case the serum was used on the second day. The victim was a girl of twelve, a servant, who fell ill on the night of September 3. On the following day, besides the ordinary general symptoms, there was pain in the right groin, which checked the movement of the corresponding leg. Her temperature on entering the hospital was 40.7° (105.2° F.). At night she received an injection of 40 cubic centimetres, the following day another of 20 cubic centimetres, and the day after that 20 more. The general condition of the patient improved.

In five or six other cases in which the serum was employed under favourable conditions the rapid success attained produced a profound impression on those who were watching the course of the disease. The opinion of the majority of the physicians of Oporto in regard to the curative action of the serum is now exceedingly favourable to Yersin's discovery.

Calmette, making inoculations and analyzing the blood

from the first days of the disease, has attained a triumph for the serum which is likely to be considered of great importance in the scientific world. In the first place, he concludes from his experiments that the bacillus is found in the blood *much sooner than is generally believed*. These results contradict the observations made up to the present time (p. 24). The reader therefore will do well to suspend his judgment on this point, and not underestimate the possibility of contagion during the first days of the illness (p. 28), and finally to accept with reserve the pathogenic theories emitted by some authors, and to which I have hardly referred, thinking them quite artificial and premature.

It appears that even while there is fever it is possible to demonstrate the presence of the bacillus in the blood, and that when that disappears under the action of the serum, the bacilli disappear also, not only from the blood, but also from the secretions and pathological products.

If this fact is proved in further experiments, it would be certain that the serum will act as a prophylactic of a local character, since, the bacilli in the patient being destroyed, he ceases to be a source of infection for others in the town, and thus the early application of the serum to patients would give one more means of checking the course of the epidemic. So far as concerns the patient, he might recover or not, according to the stage of intoxication with the plague poison reached by him, and the magnitude and reparability of the lesions which until then the disease might have produced; but he would cease to be a medium of contagion, which is most important.

How to use the Serum.—Yersin's flasks of serum are small. In each of them there are 20 cubic centimetres of serum, a liquid of a greenish yellow colour, similar in its appear-

ance to Chartreuse. The contents of a flask are sufficient to vaccinate two persons preventively. Used in cases in which the disease has already declared itself, for each injection 30 cubic centimetres are required, so that one patient needs at least two flasks; in some cases three or four flasks may be necessary. The liquid does not contain any antiseptic substance, so that it may be used in large doses without injury. It produces no inflammation whatever at the site of the injection, and, indeed, only slight pain.

The injection is made with a Roux syringe—the same as is used for antidiphtheritic serum—of 20 cubic centimetres capacity. Before being used the syringe should be put into cold water, the temperature of which is to be raised to boiling for a quarter of an hour. The syringe having been disinfected in this way, the part of the loins of the person to whom the serum has to be applied is to be disinfected by washing with corrosive solution, and this being done, the injection is to be made. If a preventive inoculation is being performed, 10 cubic centimetres are enough to use. In treating the sick, in place of using several small injections, it is best to begin with injections of 30 cubic centimetres. The injection should be made immediately the disease is diagnosed, if possible. The preventive injection should be repeated every fifteen or twenty days. Before injecting the physician should see that the liquid is transparent, understanding that a slight opacity or a little precipitate does not show that it has decomposed.

Lustig's Vaccine.

Lustig and Galeotti, treating the cultivation in agar with a solution of potash, and immediately afterwards with acids, succeeded in obtaining a substance free from bacteria,

which, inoculated in animals, proved to be exceedingly poisonous, and in small doses made them refractory to the gravest forms of the infection. This substance is employed after having been dissolved in an alkaline solution, then filtered, dried in vacuo, and redissolved in the solution mentioned.

The injection in animals produces no reaction, either local or general. The vaccination is done by injecting on three occasions, with two days' interval between each injection, the minimum mortal dose. The immunity it confers appears to last four weeks at the least. By bleeding the animal which has been vaccinated fourteen or fifteen days afterwards, a preventative and curative serum for animals is obtained.

Experiments have been made on man occasionally. Six cases treated in Bombay were cured. Of twenty-four treated at Poona three died, one of whom was probably not suffering from the plague, but from an ordinary pneumonia. With the matter obtained from the cultivations Lustig and Galeotti inoculated themselves and several other persons, using a dose of 5 milligrammes. A slight local œdema and a little febrile movement was produced, and they felt during thirty-six or forty-eight hours a sensation of depression and malaise.

Difficulties of all kinds have prevented those distinguished Italian experimentalists from carrying out experiments on a large scale with this serum.

Haffkine's Lymph.

Haffkine has prepared a lymph by killing, by the action of heat, the bacilli in a broth cultivation, and inoculating this in doses of 5 cubic centimetres. With this liquid it has

been possible to make numerous experiments, thanks to the ease with which it is obtained, and the decided support which the distinguished physician has received from the Indian authorities. The results from its use as a preventive agent are very favourable.

In 1897, 8,200 inoculations were performed in Bombay; only 18 inoculated persons suffered from the disease, in spite of being inoculated. Two died within twenty-four hours of the inoculation.

In Lanowlie, among 323 inoculated people there were 14 attacked and 7 deaths. Among 377 not inoculated, 78 were attacked, with 58 deaths.

Of the Mussulman population of Bombay, 5,184 were inoculated. Of these 7 died. Among 8,146 not inoculated, 177 died.

The medical body of Bombay held an important meeting in November to consider the value of these inoculations. Some physicians said that they considered it very dangerous to introduce into the organism a liquid containing the plague bacillus, and expressed their fears that those bacilli which had not been destroyed by the heat might produce the disease. Only four votes were given for this and similar propositions. The Congress by an overwhelming majority agreed that Haffkine's lymph confers immunity, and that this is prolonged *for six months* after the inoculation. The Congress also agreed that making a second inoculation ten days after the first considerably strengthened the activity of the lymph. The proof of this last fact can be seen in the statistics of the inoculations performed at Dharwar:

				ATTACKS.		DEATHS.
Inoculated once	...	5,712	...	69	...	31
Inoculated twice	...	3,349	...	9	...	5
Not inoculated	...	5,614	...	957	...	756

The inoculation causes a mild attack of plague. In six hours the patient suffers from malaise, headache, depression and fever, and this condition continues a couple of days, at the end of which there is usually vomiting and diarrhoea. The symptoms disappear slowly. The site of the inoculation is much congested, the skin desquamates, sometimes eruptions appear. These symptoms never appear to have been so intense that infants suckled by nurses who had been inoculated suffered any inconvenience; nor were any disagreeable consequences caused to the product of conception, or to the course of pregnancy in those cases in which the inoculation was practised on pregnant women.

The immunity does not begin till eight or ten days after the inoculation. It has been observed in malarious districts that those who have been inoculated with this lymph, do not suffer from intermittent fever. Haffkine's lymph is inoculated with a syringe of medium size, in the dose of 5 cubic centimetres for adults, and 1 to 2·5 for children.

THE PLAGUE IN OPORTO.

Dr. Jorge has exerted himself to establish a relation of dependence between the different cases who were first attacked. This work, of which we give a résumé, has vulnerable points, but shows a most estimable spirit. Some of the relations established will not entirely convince the reader; this of itself will show the difficulty of the subject.

The first case undoubtedly occurred in 88, Rua da Fonte Taurina. It was a man called Gregorio, a Spanish stevedore, who died of the disease. In the same house lived José Suarez (Case III.), José Soto (Case IV.), and José Paez (Case X.). All these men, who put their comrade in his shroud and watched the body, were attacked by the disease,

Suarez and Soto in the middle of the month, and Paez about the end of the same month. On the first floor of the house lived Alberto Tomé (Case V.), a small tradesman. Although confined to bed with a facial neuralgia, from which he was a constant sufferer, the disease also reached him in the middle of the following month. There were therefore five cases of plague in this house, two of them ending in death in three successive attacks, allowing for the period of incubation. The wife of Tomé and a servant-girl escaped out of the household.

José Lorenzo, living in the Bajada de la Verdad (Case II.), lived in intimate relationship with the inhabitants of the house No. 88, since he was a Spaniard like them and worked at the same employment. In spite of this intimate connection, it cannot be admitted that the case had any relation to Case I., since the sickness attacked him on the day following the burial of the latter. This case, therefore, must be considered a primary one, and parallel with that of Gregorio.

The house 84 is next door to No. 88, and on its second floor Domingo Loredó, Galician stevedore, also lived, with his wife, and was a friend and comrade of his compatriots in the other house. The wife (Case VI.) contracted a severe form of the plague, in which there was suppuration of buboes and eruption of carbuncles. The severity of the illness caused her to abort and die. Her husband only survived her a few days (Case VII.). With the death of a child of six months, their son, which happened a few days before those of his parents, this family became extinct.

These six cases occurred in the middle of the month, and developed simultaneously with a second series of invasions which took place next door. José Paez (Case X.), the last to suffer from the disease at No. 88, had shaved the corpse

of Domingo. On the first floor of the house No. 84 there lived a family, consisting of the parents and four sons. One of these suffered at the end of June from benign plague (Case XV.). The tenants of the third floor, a man and wife, were not attacked.

Between the houses numbered 84 and 70, which latter was the third visited by the contagion, there are two houses in which no case at all is known to have occurred. Domingo Loredó, terrified by the loss within a few days of his son and wife, changed his residence and went to live on the second floor of No. 70, which was occupied by four Galicians, his friends and comrades, as were those living at No. 88. Two of these Galicians escaped the disease. The two others are Roman Sanchez, who gave rise to Cases VIII. and IX., and Garcia (Case XVI.).

Roman Sanchez was very much in Gregorio's company, and visited him and other plague patients. During the week he lodged, after working hours, in the house mentioned, and he passed the Sundays with his wife and children, who reside in Argoncille, a few kilometres from Oporto. His own health was not at all affected, but he transmitted the disease to two of his daughters, who passed through a perfectly characteristic attack of plague in the middle of June.

These cases of indirect contagion are very significant, and the facts are very clearly in evidence, illustrating the manner in which plague is propagated. Garcia was attacked by the sickness during the first days of July, and came convalescent to the hospital.

On the first floor of the house No. 70 live Manuel Francisco de Silva, his wife and six children, the eldest of whom was the fourteenth case (XIV.), which appeared at the end of June. On the third floor of the same house lives

a family, 'a woman belonging to which appears to me to be affected with a suspicious illness, and a man affected with the slightest form of the disease.'

Case XVII. was that of an inhabitant of a house situated back to back to No. 84 of the Rua da Fonte Taurina. In the immediate vicinity there were several suspicious cases, of whom one was, and the others were not, in communication with those first attacked. From the barber of the Calle de Mercaderes (Case XI.) it was made quite certain that none of the Galician stevedores were his customers.

'This is the sequence of the cases,' says Dr. Jorge, 'so far as it has been possible for me to trace them. The disease had its first victims in one house, affecting nearly all, and spread to the next-door houses, then spreading to a distance.'

Those attacked have come, as it were, to seek the disease in its focus; and some, healthy themselves, have carried the disease to a distance.

APPENDIX

As the Spanish edition of my work was published at a time when medical men throughout Europe were watching the development of the plague in Oporto, I consider that I ought to write this chapter for the English translation, so that it may contain the results of the very latest scientific observations. I write in this way to respond to the honour done to my modest work in translating it into English, and to make that edition perfect, so that the reader of it may have before him notes and commentaries of all that has been done *up to the very date of publication of the work*. I desire that this book should be useful in conveying information.

The English edition is more fortunate than the Spanish, being published during a short period of rest in the investigations, when conclusions can be drawn with more care. These conclusions will not be in any way final. Scientific men of our day live in a constant state of mental instability as to their opinions, throwing aside ideas, and replacing them by others.

Bacteriology.

Bandi and Stagnitta say that the bacillus of Oporto is more virulent in the monkey and rat than that of Bombay, and on the other hand, less so in the guinea-pig. The morphological characters do not differ in the different animals used as media. These Italian experimentalists, however, believe that they have discovered a new variety, distinguishable by its virulence and the appearance of its cultivations. This new rare microbe which Bandi and

Stagnitta propose to study was isolated in the spleen and blood of the heart of a woman who died after six hours' illness.

Infection.

The most careful observations as to infection through the skin confirm the general opinion that this is the most frequent mode of entry of the bacillus, without there being necessarily any perceptible wound. Among the clinical histories published in the Portuguese reviews is one of infection by the conjunctiva, similar to that seen in Bombay (p. 19). It is not clear whether this was specific *ab initio*, or followed on existent catarrh. Calmette has seen several cases of this last condition.

The fact that disturbances of the digestive tube have occurred in numerous cases at the same time as the primary inguinal or axillary or other bubo has renewed the idea of the possibility of infection in this way. Wilm thinks that primary gastro-enteritis was the most frequent form of infection. Finally, the study of the lesions found at the post-mortem (ulceration of the mucous membrane and small intestine, and infiltration of the intestinal folds and follicles, etc.) increases the suspicion.

Studying attentively all the papers I have been able to collect, I have not succeeded in convincing myself that this mode of infection is as frequent as some suppose. Plague is in most cases a septicæmia; and it is to be expected that intestinal lesions will be found in the autopsies, such as are usual in all septicæmic states. The criterion by which the doubt can be removed is, in my opinion, the *primary* swelling of the mesenteric glands (p. 21). When this primary swelling exists, it can be held that the intestinal lesions show the first mischief caused by Yersin's bacillus, a kind of *plague chancre* to which the general infection succeeds. When the swelling of the mesenteric glands is not primary, I do not believe, however severe may be the intestinal lesions, that they suggest infection by the gastric

tract. On the contrary, a primary mesenteric swelling without intestinal lesions makes me inclined to believe in an infection in that way; for the same reasons that I consider that infection has entered by the lower limbs, though no wounds or scratches are found on them, when there is inguinal bubo. Intestinal lesions *per se* indicate nothing, since the mesenteric glands are always more or less affected, and it is natural that the difficulties of the lymphatic circulation should tend to infiltration and then ulceration of the intestinal mucous membrane. This distinction is of great importance, at a time when it has been denied that the intestinal lesions form the essence of typhoid fever (Sanarelli); and when it is asserted that in this disease, the most typical *medical* septicæmia, these lesions are not the *substratum* of the pathological process, but simply secondary phenomena.

Contagion.

In regard to the conveyance of the plague to man by means of fleas, Bandi and Stagnitta, observing how few medical men and nurses are attacked, cannot believe that the fleas play so important a rôle, since the very greatest care does not prevent fleas passing from the sick to the doctors or their assistants. This is the more worthy of notice as the patients in hospitals are of the poorer classes, and are infested by many insects.

The theory of transmission of plague from rats to man also suffers a blow from the results of the experiments of Galli-Valerio, from which he asserts that the fleas living on one species of animal do not attack other species. He describes several kinds of fleas, each of which lives on one definite species of animal, and neither lives on, nor attacks animals of, other species.

Nevertheless common daily experience shows that the fleas of domestic animals (dog, cat, horse, etc.) easily pass to man; such being the case, I do not think we should

attach too much value to his theory. And it appears to be probable that each of the varieties of fleas described by Galli-Valerio may live, not only on one species of animals, but on various similar species.

The real question then resolves itself into this: Can the fleas from rats pass to man like those of dogs or horses?

Galli-Valerio, experimenting on himself, did not find that the rat-flea (*Typhlopsylla musculi*) bit him; while the flea which infests man (*Pulex irritans*) attacked him. I can only say on this point that the *Typhlopsylla musculi* is not the only flea which infests rats; the *Pulex fasciatus*, with which he has not experimented, lives on them also.

Zabolotny, studying the plague in Mongolia, says that an epidemic was always preceded by one among some rodents of that region (*Arctomys bobac*), and that the natives, who eat those rodents without boiling them, suffer from a very severe disease, very contagious, with all the characteristics of plague.

Clinique.

The latest clinical descriptions add nothing to the masterpiece of Simpson, so that the medical practitioner will do well to carefully study the pages by this author in the *British Medical Journal*.

Calmette has recently called attention to the frequency of lung complications. These do not indicate primary plague pneumonia, but appear to be caused by a late localization of the bacilli. The patients cough and spit, and there are bacilli in the sputum. In the autopsies this complication is shown to consist of a lymphangitis pestis in the pulmonary lymphatic ganglia and spaces. The patients die with symptoms of pulmonary œdema. Calmette's observation is of great importance, because the sputum may be very frequently a means of propagation of the disease (p. 29); and now, when the transmission by fleas is much discussed, it is worthy of note that the frequency of lung complications favours the spread of the epidemic.

Sero-Therapeutics.

Bandi and Stagnitta do not agree with the French in their optimism in regard to the efficacy of the Yersin serum. It is indeed prudent not to allow ourselves to be led away by exaggerated and premature enthusiasm. The experiments in Oporto were very faulty.

I do not indeed consider that any conclusion can be drawn from a dozen trials in a laboratory. Sometimes, according to the press, the cats of the neighbourhood, having little respect for scientific investigations, breakfasted on the inoculated mice. This shows the by no means favourable circumstances in which the work was carried on, excusable in the state of the town. Finally, the careful perusal of the report of the Commission on serums does not make me consider it of any true scientific value, and indeed, I regret that any Spanish physicians should have weakly given the authority of their signatures to it.

As a means of treatment the Yersin serum has been used in 142 cases, with 21 deaths. Of 72 persons not treated by the serum, 46 died (Calmette and Salimbeni). These statistics have many weak points, one of these being the impossibility of knowing the number of those not treated by the serum, since those were attended at home; and it is known that in Oporto many cases were concealed. If, instead of 72, there were 100 or 200, which is probable, the statistics work out very differently. It is to be kept in mind that it is the general opinion that the epidemic at Oporto has been very benign and the rate of mortality low.

Of the 142 cases in which the serum was used it was employed in 31 from the beginning, and by intravenous injection—that is to say, under extraordinarily favourable conditions. The number of deaths was seven. In the 111 remaining cases in which the serum was used *under worse conditions*, the deaths were 14. This number appears to be too low, considering the results in the 31 cases under most favourable conditions. It is strange that there should be

7 deaths among 31 cases treated under the best conditions, while among 111 treated under less favourable only 14 died. There appears to be some error in this.

Apart from this question, it appears that the serum has a favourable influence on the disease, when used at the very beginning, in large doses, by intravenous injection. In all other cases the results are very doubtful. Lustig and Galeotti draw very similar conclusions in regard to their serum.

As a preservative agent the Yersin serum gives little immunity, and only for from 6 to 8 days. Calmette cites as an example of its preservative action the case of a physician who wounded himself at an autopsy a few days after being inoculated. The case is not a favourable one for the serum, as the professor in question suffered from a bubo in the axilla, prostration, fever, etc., and was compelled to inoculate himself again as a means of cure, which fortunately was successful. The unfortunate Dr. Pestona contracted the plague, as it appears, 26 days after inoculating himself with Yersin's serum.

On the contrary, scientific opinion has shown itself more favourable to Haffkine's lymph, and to that of Ferran, which was tried for the first time. Ferran proposed in 1889 to fight the cholera which was then raging in Spain by vaccinating with the broth cultivation of *Bacillus virgula* weakened by heat, and carried for the purpose to the Mediterranean coast, where many thousands of vaccinations were performed with it. I do not believe that the result was very favourable, since the special pathology of cholera is not suitable for this treatment; but the attenuation of cultivations by heat was a scientific method which might be useful in other diseases, and which has been used with success in plague by Ferran, as well as Haffkine.

Haffkine's and Ferran's liquids differ very little. Haffkine, in preparing his lymph, first attenuates the bacillus by depriving it of oxygen. It is known that Yersin's bacillus is aerobic. Haffkine covers the liquid in which the

bacillus is growing with grease, so that the cultivation takes place without being in contact with the air, and this to a certain extent weakens the bacillus. Ferran does not cover the cultivation with grease, so that the bacillus suffers no attenuation. When the cultivations have developed, both experimentalists kill the bacilli by heat.

None of these substances have been tried in Oporto in sufficient quantity for a proper judgment to be formed in regard to them. Haffkine's lymph has been tried in India in thousands of cases with highly satisfactory results, and I have no reason to suppose that it would have failed in Oporto if used to the same extent. It can be said of it that it has been well tried, and that the results are satisfactory. Ferran's lymph, from the mode of preparation, may claim to be more active; theoretically we may expect it to be so, as it is produced from normal cultivations of bacilli, not weakened by want of oxygen. On the whole it comes to the same thing, as has already been shown.

Haffkine's and Ferran's lymph do not produce immediate immunity; they take eight or ten days to do so, and their protection lasts for several months. This last circumstance recommends them for use in a town attacked by the disease, and among the inhabitants of the villages near it. On the other hand, the family of a patient and the inhabitants of houses in the immediate neighbourhood should be protected by Yersin's serum, which gives immediate immunity, to avoid immediate danger; then these should be vaccinated within a week with Haffkine's or Ferran's lymph, which alone can be confidently relied on.

MADRID,

February 1st, 1900.

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