INSECTS AND DISEASE.

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A Paper read before the Royal Society of Queensland, on January 27th, 1908.

Casting about for some topic on which to address you, it has occurred to me to chose for my subject the relationship between insects and disease, or insects as disease carriers. I must, however, disclaim any attempt to treat this subject in an exhaustive fashion. Of recent years, this department of science has grown too large to be adequately dealt with in my time-limit. Instead of attempting a bare summary of the whole ground, I think it will be more interesting and instructive to select two or three of the better-known instances and to consider them more thoroughly.

Insects may convey disease in two ways. Firstly, they may act as occasional bearers of disease-organisms, which may happen to adhere to the outside of their bodies. In this way they may become fortuitous carriers of diseases, which are by no means entirely dependent upon them for propagation, but whose spread may under favourable conditions, be greatly increased by insect agency. There is no doubt, for example, that the common housefly may be, and is, a disease carrier.

When the late Mr. Darwin was investigating the methods by which plants might be conveyed to oceanic islands, apart from human agency, it occurred to him to examine the legs of birds. He found that it was not uncommon for small particles of earth to be found adhering to their legs and feet, and that this earth sometimes contained seeds, which could germinate and produce plants.

So that birds migrating or blown from a continent and alighting on an oceanic island might carry with them the germs of plants. The case of the house-fly is analogous. Its tastes are unfortunately diverse. It appears equally fond of filth and fæcal matter on the one hand, and of food prepared for mankind on the other. That a fly alighting on any substance containing bacteria, and subsequently alighting on a suitable culture medium, will inoculate the latter with bacteria is easily understood, and has been frequently verified by experiment. The disease-organisms most likely to be conveyed by flies are those of typhoid fever, and of dysentery and other diarrhœal disorders. If a fly, which has visited material containing these organisms subsequently alights on some food material, such as milk, which is a suitable culture medium for the disease organism, this food will within a few hours, in warm weather, teem with the organism, and any susceptible person who imbibes it will probably contract the disease. Though this is not of course the only way in which typhoid and dysentery bacilli may reach food material, it is, I think, one of the commonest and most dangerous. Again, a fly alighting on an inflamed eye, will carry away with it pus organisms, which are implanted on the next eye which the fly visits, and so the fly may convey ophthalmia. This disease may, of course, be conveyed in other ways, but the fly is a most persistent and dangerous carrier.

What practical lessons may we draw from these facts in the way of prevention ? The house-fly, we are informed by the entomologist, " runs through its life-history in a very short time. It lays about 150 very small eggs on dung, or any kind of soft damp filth ; the larvae hatch in a day or two, and feed on the refuse ; they may be full-grown in five or six days, and then pupating may in another week emerge as perfect flies." Consider what this means. Assume that $\frac{2}{3}$ of the progeny of a female fly survive. In two weeks the solitary fly has become 100, of which we will suppose half are of each sex. In four weeks they are 5,000. In six weeks 250,000. In eight weeks, 12,500,000. We need not carry our calculation any further. Evidently a plague of flies is no miracle, and any direct assault on the insect by flypapers or otherwise in a very feeble palliative.

If we want to keep down the numbers of the fly, we must keep down the food material of its larva. We must do our own sanitation, and not let the fly larvæ do it for us. This is the root of the matter. There are certain palliatives, which are, however, not to be neglected, for I am not so sanguine as to expect to see the domestic fly banished from our midst ; we must expect to see some, even though in reduced numbers. It is possible to exclude flies from dwellings by fly-proof doors and windows but at the expense of diminished light and air. We should at least exclude them from our food, and more particularly keep them out of the milk-jug. A small piece of mosquito-net, weighted round the edge with glass beads is sufficient for the purpose. All fæcal matters should be well-covered from flies, and the further addition of some disinfectant whose odour is disagreeable to the fly is a precaution not to be despised. In country districts where cowdung and horsedung are abundant, and inhabitants are few, palliative measures are, I fear, all that can be adopted.

While this method of conveyance of disease-germs by flies and other insects is probably more common than is generally suspected, there is a second class of instances in which the insect plays a more important role. In these the disease-germ is conveyed, not by accidental contact with the outer surface of the insect, but in its interior, and is inoculated into the body of the affected animal by the bite of the insect. Of these many examples are now known, from which I will select a few of those which have been most thoroughly investigated in connection with the human subject.

MOSQUITOS AND FILARIA.

Considerations of time will prevent me from more than a passing reference to the propagation of filarial disease by the mosquito. It is of interest, as being the first disease in man, which was proved to be conveyed exclusively by the bite of an insect, in this instance the common House Mosquito, *Culex fatigans*. The adult worm, which was first discovered by a member of this Society, the late Dr. Joseph Bancroft, inhabits the lymph vessels of man. Its embryos are discharged in myriads and through the

lymphatics, enter the blood stream, where they may be discovered in the blood of the superficial vessels during evening or night, as minute lively motile worms, disappearing in the daytime. *Culex fatigans* is a nocturnal insect, and bites during the hours when the filariæ are near the surface. Sir Patrick Manson, many years ago, discovered that the embryo filariæ escape from the stomach of the mosquito and develop in its thoracic muscles, increasing largely in size. This discovery has been confirmed by many later observers, among whom I may name Dr. Thomas Bancroft. More recently it has been shown that the larvae, when sufficiently grown, penetrate from the thorax of the mosquito into the proboscis, and from thence enter the blood stream of the human subject during the act of biting.

MOSQUITOS AND MALARIA.

Since the earliest beginnings of medical science it has been known that the inhabitants of certain districts, and visitors to those districts, are peculiarly liable to attacks of fever, characterised by their intermittent or remittent course. To these many different names have been given, such as ague, splenic fever, intermittent or remittent fever, paludism, malaria, besides a large number of local names derived from the districts in which fevers are prevalent. Though largely confused with other fevers, they had certain peculiarities, such as a frequent tendency for the attacks to recur at daily intervals, or on alternate days, or every third day, the so-called quotidian, tertian, and quartan agues. As a rule these attacks recurred at the same hour of the day, and often ran through three stages, more or less defined, the cold, hot, and sweating stages. It was also well-known that those who had suffered from such attacks were very apt to suffer from them again, even after long intervals of time, and removal to healthy districts, where the disease was not known to occur. Again, those who had suffered much from these attacks were known to develop an enlargement of the spleen, and, when microscopical examination became a method of research, deposits of minute particles of a blackish pigment were found in the spleen and other organs after death. In the seventeenth

century it was discovered that the attacks were preventable by the administration of large doses of quinine, and that the disease could be in most cases cured by the use of this drug. This discovery was valuable, not only for its therapeutic effect, but in differentiating malarial from other fevers, which were not influenced in the same way by quinine. But it threw no light on the causation of malaria, as to which the only thing really known was that it was a *place disease*. As to what peculiar feature of the locality was responsible there were various theories. One ascribed it to something in the drinking water, and this seemed to be supported by the fact that many fever districts were marshy, and that some had been freed from fever by drainage. But the most prevalent opinion was that malaria—as its name implied—was propagated through the atmosphere, and that the air was contaminated by exhalations from the soil of certain districts. But these exhalations were mere suppositions, and the various theories were gropings in the dark without a real clue.

The first ray of light came in 1880, from M. Laveran, a French physician working in Algiers. Laveran discovered peculiar bodies inside the red-blood corpuscles of patients suffering from malarial fevers, and recognised them to be the parasites that caused the disease. This discovery was at first received with considerable scepticism. The parasites were inconspicious and hard to find. Though many diseases were known to be due to various bacteria, these parasites were protozoa, belonging to the animal kingdom, very different to bacteria, and incapable of cultivation outside the human body. Nevertheless, by the labours of many observers, the life-history of the parasites inside the human body was thoroughly worked out, and their causal relationship to the disease sufficiently established. The earliest stage of the parasite is a minute colourless protoplasmic speck inside the corpuscle. It shows active amoeboid movements, and gradually increases in size at the expense of the corpuscle, at the same time developing blackish specks of pigment in its interior. After reaching full size it begins to show signs of segmentation, and assumes the rosette form. Finally the rosette separates into a number of minute spherules or spores, the corpuscle breaks down,

and the spores are liberated. Many of them are swallowed by the phagocytes of their host, but some escape and contrive to enter fresh red cells, in which the cycle of development is renewed. It is a very significant fact that the parasites may be present abundantly in the blood during the period in which the patient is free from fever, but the febrile paroxysm follows immediately on the stage in which the spores are liberated from the broken-down corpuscles. The intervals between the paroxysms and the frequency of their recurrence depend on the life-history of the parasites. Of these, there are several varieties differing slightly in their morphology, and considerably in the symptoms of the disease, which they cause. Into these differences we need not enter ; in the main points the various parasites are closely similar.

Though the discovery of these facts was a notable step in advance, we were nearly as far as ever from understanding the causation of malaria. In what way, and under what conditions do the parasites enter the human body ? For the answer to these questions we are mainly indebted to two British observers, Sir Patrick Manson and Sir Ronald Ross. Manson, starting from the proposition, that every parasite has some way of getting out of the body of its host, drew special attention to a remarkable form of the parasite, which had been previously discovered by other observers, without its true significance having been recognised. This is the so-called flagellate body. It is never found in blood freshly drawn, but appears only when the blood has been exposed to examination for some time after withdrawal. In such a preparation some of the parasites may be observed to slip out of their containing corpuscles, assume a rounded form, and suddenly project a half-dozen long whip-like arms, which perform rapid lashing movements, and finally break away and swim freely in the serum.

This striking phase in the history of the malaria organism was rightly regarded by Manson as the first phase in its extra-corporeal life-cycle, and he suggested that this stage of its life was passed in the tissues of the mosquito, and that from the mosquito the parasite in some way again entered man. A young Indian army surgeon, Ronald

Ross, was so much impressed with Manson's theory that he determined to verify the transmission of the malaria parasite by the mosquito if possible. His first observations were encouraging. He found that the process of exflagelation occurred in blood taken into the stomach of a mosquito much more freely than under other conditions. But here his progress stopped. He was not able to trace any development of the separated flagella, nor could he find in the tissues of mosquitos which had bitten malarious patients, any parasites that could be identified with the malaria organism. The research was an arduous and difficult one. He could not know what the organism he was looking for would be like, that is to say what form the malaria organism would assume in the mosquito. Again he could not know what species of mosquito, if any, were concerned in the matter, and at that time very little was known of the genera and species of mosquitos.

For two years, with admirable zeal and perseverance, Ross devoted his spare time to this quest, and dissected and microscoped many hundreds of mosquitos without success. Then having by chance obtained a few specimens of a mosquito hitherto unknown to him, and having fed them on malarious blood, he found on dissection, several days later, some round pigmented cells in the stomach of the mosquito. Such cells he knew were not normally present in the stomachs of mosquitos, and at last he had found his clue. Unfortunately, at this stage, official duties prevented his carrying the research further, and the next ray of light came from an American observer, MacCullum. MacCullum observing a parasite in the blood of birds, the halteridium, which is allied to that of human malaria, found that after exflagellation, the separate flagellæ swam about until they encountered and fused with certain rounded forms of the parasite, and that these thereupon assumed a vermicular form and exhibited active movements. That in fact the process was one of sexual conjugation, followed by a fresh stage of development.

At this stage, the Indian Government took a very enlightened step. They relieved Ross of his military duties, and sent him to a well-equipped laboratory in Calcutta to investigate the mosquito-malaria theory. It happened

to be the wrong season of the year for malaria, but nothing daunted, Ross commenced to investigate a closely allied organism, the *proteosoma*, found in sparrows. He had no difficulty in proving that round pigmented cells appeared in the stomachs of mosquitos that had fed on infected birds, just as he had formerly observed in malaria. He followed the development of the parasitic cells and found they gave rise, by internal sporulation to a number of fine rod-like spores which escaped into the tissues of the insect. And now came his crowning discovery. Dissecting an infected mosquito, he came upon two small glands connected by a duct with the proboscis. To his astonishment, he found the cells of these glands packed with enormous numbers of these parasitic rods. The inference that these rods were intended to pass with the secretion of the salivary or poison gland into the next bird bitten by the mosquito was obvious. He subjected it to the test of experiment, and found that birds whose blood was free of proteosoma, could be certainly infected by the bite of such mosquitos. That the malaria organism had a similar life-history appeared almost certain, and an Italian observer, Grassi, soon after confirmed Ross's conclusions with regard to this parasite.

The study of mosquitos was until recent years a much neglected province of entomology. But since Ross's discovery, so much attention has been given to the subject, that they are now among the most completely known families of insects. We now understand the reason of Ross's early failures in his investigation. Mosquitos may be divided into two groups—the *Culex* group, which comprises the great majority of forms, both in individuals and species, and the *Anopheles* group, which are far less noticeable by the casual observer, and yet are exclusively concerned in the propagation of malaria. Without entering into technical details, it is easy to enable anyone to recognise the difference between members of these two groups, both in the larval and mature stages. Mosquitos of the *Culex* group have the larval form which is so familiar to us in our domestic water. These little wrigglers are, of course, air breathers, and ascend to the surface of the water to breathe through a conical projection, called the

siphon, situated towards the tail, while the head hangs nearly vertically downwards. *Anopheles* larvae have no projecting siphon, and rest nearly horizontally on the surface while breathing. The mature *Culex*, when it alights, rests with the body horizontal, and the head well elevated. *Anopheles* rests with the body steeply inclined, and the head depressed, as though the proboscis was pinned into the surface rested on. The species are more quiet and retired in their habits than those of the *Culex* group, and need to be searched for, while the latter make their presence evident, whether we wish it or no.

We are now able, thanks to the work of later observers, to give the complete life-cycles of the malaria organism both in man and the mosquito. First we have the asexual circle as already described, occurring in the blood of the human host. It is now known that sexual forms also occur in human blood. They are most easily distinguished in the pernicious variety of malaria, where they are sausage-shaped, distorting the containing corpuscle to form the familiar "crescent bodies." The male and female forms can be distinguished by slight differences in the size and staining of the nuclei and cell granules. Confined to the human body, the male forms undergo no further development and die out. The female forms are more resistant, and indeed are capable of surviving when all the remaining forms of the parasite are killed off by quinine, or by the natural resistance of the host. When, however, this resistance is lowered by some external cause, such as a chill, they undergo a parthenogenetic development. The nucleus divides into two parts, the darkly staining portion divides into spores as in the asexual cycle, the paler portion which represents the sexual element is abandoned as useless to the organism. Meanwhile the unfortunate host experiences a relapse of his ague.

But when the blood is imbibed by a mosquito, the course of development is altogether different. The digestive juices of the insect destroy all but the mature sexual stages of the parasite. The crescents slip out of their corpuscles, and assume a rounded form, and undergo development. The nucleus of the male is transformed into the threads commonly known as flagella, but more accurately termed

microgametes. These, four to six in number, are rapidly shot out from the surface. They contain the nuclear chromatin, that is the portion concerned in reproduction, and lash wildly about, finally breaking away and swimming in a serpentine fashion, until they find and conjugate by fusion with one of the female cells. The fertilised cell develops into a rather elongate motile worm-like individual, which pushes its way through the epithelial lining of the mosquito's stomach. There it becomes a spherical, motionless rapidly-growing cell in a cyst-like envelope. The nucleus divides as it increases in size, and each daughter-nucleus again divides until the cell becomes filled with a crowd of spores, from some hundreds to over ten thousand, which are set free by the bursting of the cyst. The spores are minute spindle-shaped actively motile bodies. They are carried in the body-fluid of the mosquito until they reach its salivary or poison glands, which are filled with them. When the mosquito next takes a feed they pass down its proboscis into the blood-vessels of the man bitten. In his circulation, they develop according to the sexual cycle from which we started.

Now that this really marvellous life-history has been fully elucidated, there can be no doubt in the mind of any biologist that malaria is propagated by the mosquito; and we have no evidence that it can be propagated in any other way. This conclusion has been confirmed by rigorous experiment. Mosquito-proof huts have been erected in the most malarious parts of the Roman Campagna, and observers living in them throughout the fever season, have remained free from malaria. On the other hand, mosquitos which have been allowed to bite a malarious patient in Rome have been sent by post to London, and have there successfully infected an Englishman, who had never visited a malarious district. Already the knowledge acquired has borne practical fruit. We may free a district from malaria (1) by treating *all* the inhabitants of a district, including especially all the children, by quinine in sufficient doses to exterminate the malaria parasites in their human cycle. This method has been pursued with some success by Professor Koch, but the difficulties in pursuing it with thoroughness are immense, and unless thorough it is useless.

(2) By isolation of all infected by mosquito netting. This is impracticable. To some extent the healthy may be protected by netting, but the isolation from mosquitos is difficult to sustain. (3) By exterminating the Anopheles in its larval stage (*a*) by drainage (*b*) by screening all domestic water, and (*c*) by periodical spraying of all exposed feeding places with some form of petroleum. In this way various places have already been freed from malaria, if not entirely at least for the greater part. No doubt the task before the sanitarian is immense, but malaria is no longer inevitable. If we continue to suffer, it will not be for lack of scientific knowledge, but because of the ignorance, indifference and indolence of mankind.

MOSQUITOS AND YELLOW FEVER.

As Yellow Fever is fortunately unknown in this part of the world, it is necessary to give you some idea of what the disease is. This can be best done by comparing it to a disease with which most of us are familiar—Dengue. Like that disease, it has a sudden onset with fever, shivering, headache, pains in back and limbs, nausea, vomiting, and other symptoms. This stage lasts from a few hours to a few days, and is followed by a remission, known as the stage of calm, in which the symptoms subside. In favourable cases, this is succeeded by convalescence, but in others the temperature again rises, jaundice develops rapidly, and in bad cases altered blood is ejected from the stomach—the "black vomit"—bleeding occurs into the skin or other organs, or from the kidneys, and the patient dies. Like Dengue, it attacks a large proportion of the population, but unlike that disease it is fatal in a large proportion of cases, from 15 to 85 per cent. The towns of the Southern United States have been frequently the seat of epidemics. In New Orleans, in 1853, there were 29,020 cases, with 8101 deaths. In 1793, the town of Philadelphia contained 40,144 inhabitants, of whom 4,041 died of yellow fever—just one-tenth. I will not harrow you with details of these epidemics, I mention these facts merely that you may realise the importance of the question, that for over a century puzzled the medical profession of the United States, the question as to how yellow fever was spread. At first it

was held by the great majority to be a contagious disease, communicated directly from the sick to the healthy. This was of course the belief of the general public, and a general dread of infection and fear of approaching the sick added much to the horrors of the epidemics. But many facts appeared to controvert this theory of direct contagion, and gradually the opinion that yellow fever was a non-contagious and non-communicable disease became prevalent among the profession. This theory, however, failed to explain all the facts, and after much controversy, a middle position became generally held—that while not directly communicable from the sick to the healthy, yellow fever was spread by emanations from the sick which required a suitable nidus in which to germinate and develop before they attacked the healthy, and that this nidus was furnished by clothing, furniture and various articles of merchandise to which collectively was applied the term *fomites*.

This was the received theory in the year 1900. Many investigations had been made to discover the causal organism of the disease, but none had succeeded, though several observers had isolated organisms which were at first supposed to be those sought for. Meanwhile, the disinfection of fomites was the official weapon with which epidemics were combated. Dense ignorance prevailed as to the real mode of spread of the disease, and on this ignorance was based an official routine which was of small value for the purpose for which it was intended.

In this year, 1900, yellow fever appeared among the American troups in the island of Cuba, and a commission of medical officers of the United States Army was appointed to investigate the etiology of the disease. The head of this commission was the late Walter Reed, a U.S. Army surgeon, and to him we owe our present knowledge of the propagation of yellow fever. He was to some extent anticipated. Dr. Carlos Finlay, a physician of Havana, had promulgated the theory that yellow fever was spread by mosquitos, without, however, producing any cogent evidence in its favour, and he had few if any adherents. Nevertheless, some observations made by Reed on an epidemic in some barracks near Havana disposed him to believe that Finlay's theory had much to commend it, and was at least worth

investigating. The true nature of this outbreak had not been recognised until 35 cases had occurred, with 11 deaths. No precautions had therefore been taken with regard to the disinfection of bedding and clothing ; but the disease had not been contracted by the nurses nor by the men who washed the clothes. Indeed a little inquiry showed the presence of contaminated clothing in all of the eight barrack-rooms without apparent detriment to the occupants. This threw grave doubt on the accepted theory of propagation by infected *fomites*. Yet at the same time, a prisoner who had been in strict confinement in a cell of the guardroom for seven weeks contracted the yellow fever. Eight other prisoners in the same room escaped infection, though one of them continued to occupy the bunk vacated by the sick man. It was exceedingly difficult to explain this isolated case, but it was conjectured that some insect capable of conveying infection, perhaps a mosquito, had entered through the cell window, and bitten this particular prisoner. This was of course, merely a supposition, but it was not apparently possible to explain the case in any other way.

It seemed therefore advisable to Dr. Reed that the scheme of work planned out by the commission should be altered, so that its chief endeavour should be turned to the proving, or disproving the agency of the mosquito as an intermediate host in the spread of yellow fever. Fortunately, the mosquito selected for experiment, the *Stegomyia fasciata*, proved to be the right one. As the experiments proposed involved grave danger to life, it was considered that the members of the commission should run the risk themselves, before subjecting anyone else to it. The first successful experiment was performed on Dr. Carroll. The insect, which had been hatched and reared in the laboratory had been caused to feed on four cases of yellow fever, twelve, six, four and two days previously. Carroll duly contracted a severe attack of the disease from which his life was in the balance for several days, but eventually he recovered. Another member of the commission, Dr. Lazear, subsequently succumbed to a fatal attack after being bitten by a mosquito in the fever ward, but in his case the infection was an accidental one, and not having

been made under rigorous scientific conditions, it could not be proved that the mosquito had actually conveyed the disease. Eleven other experiments similar to that on Carroll were made; of these nine were negative, two positive. The negative experiments might be explained in several ways. The cases of yellow fever through which the mosquitos were infected were very mild, and the infection might not have been sufficiently virulent; or the interval between the two bites might not have been the right one. The positive experiments could not be explained away. A *prima facie* case for the mosquito as the intermediate host for yellow fever had been made out.

It remained now to subject the mosquito theory to a fresh trial on a larger scale and under rigorous conditions. Forunately for the commission, the then military Governor of Cuba, Major-General Leonard Wood, was an officer formerly in the medical service, and his scientific training enabled him to comprehend the nature of the experiments proposed, and to appreciate their importance. It is the common fate of scientific investigators to be misunderstood, and to find their work starved by the false economy, or thwarted by the interference of high government officials. In this instance, however, every assistance required was liberally furnished. An isolated camp was established, volunteers from the U.S. Army were called for, and offered themselves freely, though fully informed of the risks that they would run. One cannot refrain from noting the very high courage shown by those who thus voluntarily risked their lives in a campaign more calculated to inspire fear than many military operations. Those in the camp were subjected to strict quarantine, so that the possibility of accidental introduction of infection might be excluded. The pulse and temperature were taken thrice daily, so that any that might be incubating the disease should be at once detected, and this was continued until they had passed the full period of incubation of yellow fever, without developing any symptoms. Two buildings were erected in the camp, of similar size and construction, except that one known as the "Infected Mosquito Building," was divided in the middle by a permanent wire screen partition, and was well ventilated. The other known as the "Infected

Clothing Building" was purposely so built as to exclude efficient ventilation. Both were provided with wire screen windows, and double wire screen doors, so that mosquitos could be kept within or without the buildings, as the experimenters might desire.

The results of the experiments may be very briefly summarised. Non-immune subjects exposed to the bites of mosquitos that had previously bitten yellow fever patients were readily infected, provided the interval between the bites were at least twelve days. Before that interval the mosquitos were harmless, but they maintained their virulence for as long as eight weeks. Control subjects separated from the mosquitos in the same room by a wire partition remained uninfected. Meanwhile, in the "Infected Clothing Building," non-immune subjects lived and slept among clothing soiled by the discharges of yellow fever patients, and even wore the very shirts in which these patients had been clothed, for so long as twenty days without a single instance of infection. This experiment disproved the virulence of "fomites" in yellow fever. The problem of the method of transmission of yellow fever had been solved in the most conclusive way.

The practical importance of this discovery is immense. Yellow fever epidemics can now be stamped out. The method is simple. As soon as a case of the disease is notified, the patient is promptly isolated by wire screens, so as to prevent the possibility of mosquitos becoming infected from him. At the same time, the whole house is fumigated so as to destroy any mosquitos that may have already become infected. In addition, a "mosquito brigade" is organised to destroy the larvae of *Stegomyia fasciata* in their breeding places throughout the town. This mosquito is, I may observe, very abundant in Brisbane. We breed it in our water tanks, and if ever a case of yellow fever is imported here, which in these days of rapid travelling is not impossible, every condition is present to favour the occurrence of a considerable epidemic. We may then realise more fully the value of Dr. Reed's experimental work.

All the evidence at our disposal fails to indicate that yellow fever is spread naturally in any other way than

that I have described. But it may be communicated artificially by the direct inoculation of the blood of a patient suffering from the disease. Nevertheless, the most refined microscopical and cultural methods have not been successful in revealing in this blood the living organism that causes the fever. The germ of yellow fever still remains undiscovered. There is indeed good evidence that it is ultramicroscopic, for, unlike the smallest living organisms discovered by the microscope, it passes through the pores of a Berkefeld filter. The discovery of its method of propagation depends entirely on experiment, and is indeed one of the best instances of the application of the experimental method in medicine. As such, it is one of the greatest triumphs achieved in modern times in the prevention of one of the most deadly epidemics known to afflict mankind.

RATS, FLEAS, AND PLAGUE.

Early in 1900, Australia was invaded by the plague. Human nature is so constituted as to tolerate with indifference and apathy those epidemic diseases which are familiar, but to fly into a panic at the mere report of those which are novel. In the present instance, panic was doubly inevitable, for the plague had been practically unknown for centuries among European peoples, and the very name was charged with the vague terrors of old epidemics ; and particularly with recollections of the great plague of London in the seventeenth century, described by De Foe, an author distinguished for his talent in writing fiction so realistic in style, as to be indistinguishable from the facts, which are no doubt imbedded in his narrative.

At this juncture, I was appointed a special medical officer by the Government to advise and report regarding the epidemic in Northern and Central Queensland, some cases of plague having been reported in Rockhampton and Townsville. My first duty was to visit Sydney, where plague had been rife for several months, to acquire information. The situation, as I found it in that city, was certainly remarkable. On the one hand were a populace and a Government treating plague as a virulently infectious disease to be stamped out at any cost, regardless of expense,

private interests, and public convenience. In pursuance of this policy, every occurrence of plague was notified to the police, and not only the patient, but every one on the premises, and in the case of an hotel, their number might be considerable, was conveyed to the Quarantine Station, on the other side of the harbour. These proceedings certainly made a great stir, and had an appearance of energy. But I found to my surprise that the highest authorities in the Department of Health held views as to the epidemiology of plague, which were, to put it mildly, hardly consistent with these administrative measures. To them the infectiousness of plague from patient to patient was very problematical, and played very little if any, part in spreading the epidemic. They regarded plague rather as a disease of the rat, occasionally communicated to mankind, probably by the bite of rat-fleas, and therefore requiring for its prophylaxis entirely different measures from those that I have described. While excellently devised to stamp out an epidemic of small-pox, isolation and segregation of contacts were, they considered, quite inoperative in the case of plague, except in so far as they facilitated the cleansing of affected dwellings and areas and the destruction of rats.

To understand how this position was arrived at, we must briefly recapitulate the position at that time of scientific knowledge regarding plague. The discovery of the bacillus of plague was made in Hongkong in 1894 by Kitasato and Yersin, and since then there has been no room for doubt that the *bacillus pestis* is the causal organism. But its method of spread from case to case long remained a matter for conjecture. One of the characteristics of the plague organism in artificial culture is its slight power of resistance to unfavourable conditions. It behaves in the laboratory rather like a frail exotic, and in mixed cultures is readily killed out by more vigorous saprophytes. It does not survive long when dried in the ordinary way, and the conjectures that plague may be due to food or soil contamination had never any solid foundation. Again on the assumption that the disease is infectious it is difficult to understand how the bacilli make their exit from the patient. Certainly, in the rare cases of pulmonary plague, the bacilli are con-

tained abundantly in the sputum, and these cases are extremely infectious, as was shown in the small outbreak in Maryborough, in 1905. But in bubonic plague, and even in the septicaemic form, there does not appear to be more than an occasional and trivial exit of the bacillus, and in these cases, which form the vast majority, plague has been found by experience to be non-infectious.

It has been known for a long time that true plague is not a disease limited to the human species. Not only can many, we might say most or all mammalia, be infected by artificial inoculation, but the disease has in many species occurred under natural conditions. Especially is this the case with rodents, and among them the species of *Mus* that are associated with mankind are affected above all others. It has been found in Australia that epizootics of rat-plague have accompanied and preceded outbreaks of human plague, and this has been so also in many other parts of the world. It has been the case so uniformly, wherever adequate research has been made, as to suggest a causal connection between the epizootic and the epidemic. That is to say that plague is primarily a disease of the rat, communicated from rat to rat, and incidentally communicated, when the conditions are favourable, from rat to man. Now it is obvious that the conditions under which plague spreads naturally from rat to rat are open to experimental investigation, and if these were satisfactorily established, much light might be expected to be thrown on the occurrence of the disease among mankind.

The first direct experimental evidence as to the natural method of rat infection was obtained in Bombay, in 1898, by Simond, who showed that plague could be conveyed from one rat to another, not allowed to come into contact with it, provided fleas were allowed to pass from the infected to the healthy rat. He observed that on rats suffering from natural plague fleas were usually abundant, and that the fleas that left a rat which had died of plague contained virulent plague bacilli. Plague in man, he attributed to the infected persons having been bitten by fleas which had left a plague rat. This conclusion was strongly supported by an epidemiological study of the epidemic in Bombay, by Hankin, published in the same year. This rat-flea

theory of plague formed the working hypothesis adopted in Sydney in 1900 by Ashburton Thompson and Tidswell, and considerably strengthened by their observations.

In other parts of the world, however, this theory was received with less favour. Some observers flatly denied that rat-fleas would bite human beings. An Indian Plague Commission came to the conclusion "that Simond's proposition that suctorial insects play an important part in the transmission of plague from sick to healthy animals is so weak as to be hardly deserving of discussion." The more recent investigations of Gauthier and Rayband in Marseilles, of Liston in India, and especially of an Indian Plague Commission at present working in Bombay, whose preliminary reports were published in 1906 and 1907 have placed the rat-flea theory in an absolutely incontestable position as the natural method of plague infection. Let me briefly summarise the present state of our knowledge.

The species of *Mus* concerned are three :—

(1) *Mus rattus*, the Black or Old English Rat now almost exterminated in Great Britain by the Brown rat, but still abundant in countries in which plague has become endemic. This rat is a nimble climber, and lives in houses, preferring the space under the roof. It is also the common rat on ships. It has a reddish variety, known as the Alexandrine Rat—*Mus alexandrinus rufus*.

(2) *Mus decumanus*, the Grey, Brown, or Norway rat, which is a heavier, but clumsier animal, and lives especially in sewers and drains, from which it invades the basements and cellars of houses.

(3) *Mus musculus*, the Mouse. Of these, the last appears least susceptible to plague, and the number found to be infected is comparatively small. The two former are both extensively infected during the epizootic, but as Dr. Ham shows in his recent admirable report on the Plague in Queensland, *Mus rattus* and its variety *alexandrinus* is most concerned in the spread of plague in man, owing to its predeliction for human habitations.

So much for the rats. Special attention has been devoted of late to the study of rat-fleas, and the flea which has been proved to be the carrier of plague has been discovered to be a species almost unknown in temperate

Europe, but common in warm climates, which was till recently undescribed, but is now known as *Pulex cheopis*, Rothschild. Several species of flea are found on rats. The human flea, *Pulex irritans*, and the dog-flea, *Pulex serraticeps*, are occasionally found, but merely as stragglers. There are three species specially attached to the rat, known as *Ceratophyllus fasciatus*, *Ctenopsyllus musculi*, and *Pulex cheopis*. Much experimental work has been vitiated by neglecting to identify the species of flea concerned.

Pulex cheopis is nearly allied to the human flea. That it will readily bite man has been ascertained repeatedly. The statement that rat-fleas will not bite man are derived from experiments with the other species. It can indeed be kept alive for weeks by being allowed to suck human blood. Furthermore, it has been found on man. For instance, Liston writes, " About the 6th or 7th of April, rats began to die in large numbers in a chawl, or block of tenement houses. Suddenly the deaths among rats ceased, and on April 11th, the people became troubled with fleas. The fleas became so numerous that they had to quit their rooms and sleep out on the verandah. While living on the verandah on April 17th, one of the inhabitants of the particular room in which the fleas were taken became infected with plague. Another case occurred on the same day in a room adjoining. The people who inhabited the room where the above case occurred, were induced to collect some of the fleas. An examination of this collection was most instructive. Now I must tell you that on previous occasions, of 246 fleas that were caught on man under normal conditions, 1 had found only one rat flea, *Pulex cheopis*. But of the collection of 30 fleas caught on man under the circumstances above recorded, no less than 14 were rat fleas."

Though the geographical distribution of the rat-flea has not yet been worked out, there are indications that the freedom of certain ports from plague infection are due, not to any unusual vigilance in their port authorities, nor to any superior excellence in their sanitary conditions, but merely to the scarcity or absence of this particular flea on the local rats.

Let me now give a summary of the experimental

evidence from which we know that plague is propagated by *Pulex cheopis* :—

(1) Two wire cages are placed in a glass box. The cages rise above the level of the box, and both box and upper portion of cases are covered with fine muslin impervious to fleas. In case A. is placed a rat inoculated with plague, together with 10 to 20 living *Pulex cheopis*. As soon as the rat is dead, a healthy rat is placed in cage B. There is no direct contact between this and the first rat, nor with its excretions. The rat in cage B. develops plague. Some of the fleas are to be found on rat B. on examination. This experiment has been repeated many times.

(2) A rat is inoculated with plague. After death, it is searched for fleas. These are caught and transferred to a flea-proof cage containing a healthy rat. The latter dies of plague. On it are found some of the fleas, and in the fleas are plague bacilli. This experiment has been repeated many times.

(4) Simond, Gauthier and Rayband, and Liston never succeeded in infecting animals from one another when healthy and plague-infected animals were confined together in the same cage if fleas were excluded, and if the animals were not allowed to devour the bodies of their dead comrades. The recent Indian Commission verified this on a large scale. Fifty healthy guinea-pigs were confined with ten inoculated with a plague culture under flea-proof conditions. The latter all developed plague, but none of the former. The same experiment was repeated. One of the uninoculated animals developed plague. The animals were examined, and one rat-flea was found. The other forty-nine uninoculated escaped. Forty-nine guinea-pigs were confined, with ten inoculated guinea-pigs, rat-fleas being known to be present. In seventeen days, every guinea-pig was dead of acute plague. From the last two animals four-hundred fleas were recovered. And so on with similar experiments. For instance, guinea-pigs placed in a cage in a compartment where a guinea-pig plague epizootic was in progress, frequently contracted plague if the cage was suspended two inches from the floor, and fleas were found on them ; but if suspended two feet from the floor, remained free from both plague and fleas. The rat-flea cannot jump two-feet

high. A similar experiment was performed with two monkeys placed in cages of similar pattern, one unprotected, the other surrounded by a layer of "tanglefoot," six-inches wide. After two nights they were removed. Two fleas were caught on the unprotected monkey, while five fleas were found stuck on the "tanglefoot." The first monkey developed bubonic plague, the other remained healthy.

(5) Guinea-pigs were let loose in houses in which cases of plague had occurred recently. Large numbers of *Pulex cheopis* were subsequently collected from these guinea-pigs, and they died of plague. If, however, the guinea-pigs were in cages protected by flea-proof gauze, they escaped plague. In similar cages not protected with gauze ten per cent. of the guinea-pigs contracted plague, and fleas were found on them, though in fewer numbers than on the guinea-pigs that were allowed to run about.

This evidence is conclusive. For further details, I must refer to the original report. But one point must be mentioned. Rats can be infected by feeding on plague-contaminated material, for instance, the bodies of their dead comrades. In these cases, there are well-marked pathological lesions in the intestines and mesenteric buboes. In naturally infected rats, intestinal lesions and mesenteric buboes were not found in 5,000 infected animals examined. The Commission conclude that transmission by feeding is not of common occurrence in nature, and is not the method by which the epizootic is propagated.

We find then that plague epizootics among rats are propagated by a particular flea, *Pulex cheopis*. This flea leaves the rat soon after death, with its stomach engorged with blood, swarming with plague bacilli. In default of its natural host, it will fasten on other animals, and biting them will infect them with plague. This is not true only of other rodents like the guinea-pig, but of an animal widely remote from the rat and akin to man, the monkey. *Pulex cheopis* will bite man freely. The inference that plague may be and is conveyed to man from the rat by this particular flea is inevitable. With the exception of plague pneumonia, there is no reason for supposing that plague is naturally acquired in any other way. How well this

conclusion agrees with the epidemiology of plague as observed in Australia, may be learnt from the able reports issued by Dr. Ashburton Thompson and Dr. Ham.

I have sufficiently transgressed on your patience, but did time permit I might give you details of yet other diseases of mankind spread by insects, for instance, the sleeping sickness, which is spread by a species of tsetse fly, and the spirillar fever of West Africa, which is spread by the bites of a species of tick. If diseases of domestic animals were included, we might study the tsetse-fly disease of cattle and horses in Africa, or the tick-fever of cattle, which is so unfortunately familiar in our own country. But this would be too large an undertaking for the present occasion.

It is probable that the list of human diseases spread by insects will be extended in the future. Among diseases which are probably so spread, I may mention Dengue and Leprosy. The organism of Dengue is unknown ; the reasons for connecting it with mosquitos are (1) its similarity to yellow fever, and (2) certain peculiarities in the spread of epidemic, which suggest that, in the beginning of an epidemic at all events, it is a *house disease*. The hypothesis that leprosy is spread by insect bites is a very old one. The leprosy bacillus has been long known, and can be easily demonstrated. But it cannot be cultivated outside the body, and unfortunately, it cannot be made to grow in any animal but man. The long period of latency renders it peculiarly difficult to trace the source of infection, and as the experimental method can hardly be applied, no speedy increase in our knowledge is to be expected. With regard to Dengue, the application of the experimental method used by Reed in yellow fever is much to be desired.* If the propagation by the mosquito were proved, we might stamp out such an epidemic as vexed us in 1904. Few things have struck me more this summer than the disgraceful number of mosquitos in the houses I visit in Brisbane. I say disgraceful, because by adequate screening of domestic water tanks (which is easy, but seldom done), or by the

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* Since writing this I learn that this has actually been carried out by American observers in the Phillipines, and the connection between dengue and a mosquito is now proved.

addition of a spoonful or two of kerosene to the surface of the water every two or three weeks (which has no effect on its potability), the mosquito nuisance might be readily prevented.