TROPICAL MEDICINE AND HYGIENE.

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It has long been recognized that a number of diseases are peculiar to, if not confined to, warm climates. Many hypotheses in explanation of this circumstance have been advanced, but it is only of late years—only since we have been able to recognize the germ causes of many of these diseases, or the media by or in which they are conveyed—that it has become possible to arrive at the true explanation. Almost without exception, tropical diseases—that is to say, those diseases which require for their successful propagation a warm climate—are caused either by a protozoal organism or by a helminth, which, in their turn, in order to pass from one vertebrate host to another, demand either an animal vector peculiar to warm climates, or require a warm medium in which to qualify for such passage. Hence, although tropical disease once acquired can run its usual course even if the person remove to a cold or even frigid climate, that person cannot spread the disease there, nor, under natural conditions, can the disease be acquired there. On the other hand, bacterial diseases may be acquired and spread in any climate, as the germs in their passage from one human host to another do not necessarily demand any special animal intermediary, nor are they destroyed in their passage by ordinary temperatures. In the following summary relating to British contributions to tropical medicine bacterial diseases are therefore not considered. It is true such bacterial diseases as leprosy, cholera, and plague are often referred to as tropical diseases, but a little consideration—a little investigation into their history and geographical range—will show that they have no more claim to be considered tropical diseases than have tuberculosis or syphilis.

MALARIA.

Although a number of contributions of considerable importance in tropical pathology had been made by British as well as by other investigators prior to 1880 there can be no question that it was the discovery by Laveran of the malarial parasite, in the November of that year, that has led to the recent rapid and remarkable development in tropical medicine. It was some time before the value of Laveran's discovery was recognized, or the nature of the organism concerned and the significance of its various phases determined. Golgi made an important advance in these respects by working out the morphological features of the tertian and quartan parasites, and of what is now known as the schizogony or asexual phase. Further advances in our knowledge of this part of the life-cycle of the malarial parasites were also made by other Italian observers; but here, for the time being, progress ceased. It may therefore be said that, except as providing an invaluable guide in diagnosis and treatment, Laveran's discovery for more than a decade remained barren. It gave no clue to prevention; it did not tell us in what way malarial infection was acquired, nor did it explain its peculiar geographical and topical distribution and limitation.

As the development towards sexual maturity—a biological necessity for the malaria parasite as for all animal parasites—had never been traced in the human body, it follows that to effect this necessary development escape from the human body is essential. Neither Laveran nor Golgi's observations had filled in this important gap in the life-history of the parasite.

Golgi, it is true, had made out the significance of certain phases of the parasite as seen in the circulation; he showed in what way the invading organism multiplied after it had obtained entrance into the human body, but neither he, nor any of his co-workers, had grasped the significance of certain additional phases also represented in the blood, and more especially manifested on the microscope slip—that is to say, in blood after its removal from the human body.

Perhaps the most striking feature in connexion with the malarial parasite as observed under the microscope is the so-called "flagellated body." This squirming, wriggling, many-armed organism had long been a puzzle to the naturalist as well as to the pathologist. Some got over the

difficulties of its explanation by pronouncing it to be a moribund or effete form of the parasite in its death agony. It had been observed that this flagellated body shows itself only in blood that had been for some time on the microscope slip—that is to say, after the parasite had been removed from the human body. It had never been seen in quite newly-drawn blood. Its development had been witnessed over and over again from certain intra-corporeal forms of the parasite, but only after the blood containing these forms had been in the field of the microscope for a considerable period. This fact of the flagellated body coming into existence as such only when the parasite from which it was evolved had left the human body suggested to the writer that its function lay outside the human body, and, if so, that it was the early extra-corporeal phase of the parasite and, if we may use the expression, designed for its passage from one human host to another. But, assuming that such was the case, it remained to explain how an organism, which while still in the body was invariably included in a red blood cell, could spontaneously and by its own efforts escape from the human body. Such a feat on the part of a passive organism was inexplicable. I was driven to the conclusion that if this phase of the malarial parasite were really the first stage in its development outside the human body some extraneous agency must act as liberator. The question then came to be what this extraneous agency might be.

Many years before the writer had shown that in the case of another blood parasite—*Filaria bancrofti* (the *Filaria sanguinis hominis* of Lewis)—the mosquito acted as a liberating and also as a fostering agent. Impressed by the close parallelism, as regards their respective physical conditions and necessities, between the malaria parasite and the filaria—the one being imprisoned in a blood corpuscle and powerless to escape, the other, the sheath-included and equally helpless filaria—as well as their respective biological necessities, he thought that the same, or a similar liberating agency might be operative in both instances. An additional circumstance pointing to such a hypothesis was that both parasites are limited in geographical range to warm climates. On these considerations it was concluded that as the mosquito had been proved to be the liberating agent in the case of the filaria, it might be, and probably was, the liberating agent in the case of the malarial parasite, and therefore that the first phase of the malarial parasite outside the human body had to be passed in this insect. I formulated this hypothesis in the BRITISH MEDICAL JOURNAL of December 8th, 1894. Unfortunately, circumstances made it impossible for me to follow up the fate of the flagellated body in the mosquito, but Sir Ronald Ross, who was then in England, was so impressed with the probability of my hypothesis being correct, that on his return to India in 1895 he set to work to endeavour to establish it. After many years of intense application and in the face of many difficulties, he succeeded in tracing the malarial parasite into the stomach wall of certain "dapple-winged" (*Anopheles*) mosquitoes. In consequence of difficulties in procuring material and suitable human subjects for observation and experiment, he transferred his attention to a malaria-like parasite (proteosoma) of birds. In these he succeeded in tracing the development of the parasite in the stomach wall of *Culex* mosquitoes, and thence into the salivary glands and saliva of the insects, and by experiment showed that such insects were capable of conveying the infection to hitherto immune birds. Ross's observations were quickly confirmed by Daniels, Christophers and Stephens, Grassi, and many others. Grassi recognized Ross's "dapple-winged" mosquito as belonging to the anophelines, and showed conclusively that certain members of this family of mosquitoes were efficient transmitters of malaria. Ross had not ascertained what exactly happened to the malarial parasite immediately after ingestion by the mosquito, and while still in the lumen of the insect's stomach, which enabled it to pass into the tissues of the stomach wall. An American observer—Macallum—filled in this gap. He showed that the flagellated body of halteridium, another malaria-like parasite of birds, was the male parasite, that the flagella it produced functioned as spermatozoa, that when they broke away in the blood in the stomach of the mosquito they entered a female parasite, inducing therein a development that eventuated, while the female was still in the stomach

of the insect, in the formation of that "travelling vermicle," which penetrated the stomach wall and therein entered on the development Ross had so successfully traced. Thus was completed the history of the life-cycle of the malarial parasite outside the human body, confirming the mosquito-malaria hypothesis.

Although the work of Laveran and Ross was accepted by those best competent to judge, and although the direction in which its principal application should be made was evident to all well-informed tropical sanitarians, the public was by no means convinced of its reliability or of the importance of the mosquito as a diffusing agent of malaria. Experiments on human beings had succeeded in the hands of the Italians in demonstrating that a mosquito fed upon a malarial patient could, after an interval of ten to twelve days, convey malaria to hitherto immune individuals, but the public did not appreciate this, and moreover, as the experiments had been conducted in malarious countries there was always a possibility that some unsuspected fallacy associated with locality had crept in, seeing that other influences which might include the true malaria influence were possibly operative. Accordingly, the British Colonial Office, believing in and recognizing the importance of the discoveries as bearing on the health and prosperity of tropical countries, devised an experiment designed to convert the public to the mosquito-malaria theory and to facilitate in this way practical measures based on that theory. In 1900 it sent to the Roman Campagna an expedition consisting of Drs. Sambon and Low, of the London School of Tropical Medicine (who were subsequently joined by an artist), with instructions to live in a mosquito-protected hut located in a highly malarious district of that highly malarious region during the most malarious season of the year, protected at night only, and by wire gauze covering only, from mosquito attack. Although the people about them were heavily affected with malaria these observers, relying solely on mosquito protection, remained in perfect health. At the same time mosquitos infected in Rome with malarial parasites were sent to London by the same observers, and were there fed on two Englishmen who had never been exposed to malarial influences, or been in malarious countries, with the result that both these men contracted malarial fever and showed malarial parasites in abundance in their blood. This crucial experiment was accepted by the most sceptical as conclusive proof of the mosquito-malaria theory.

It was long before Laveran's discovery was appreciated in England, but it made way by degrees, and its significance and importance became thoroughly apprehended by a few. It may be said that it led more or less directly to the establishment, at the instance of the late Mr. Joseph Chamberlain, of our schools of tropical medicine, wherein large numbers of post-graduate students destined for service in tropical countries were taught haematology and the study of the blood parasites generally. These students, well taught in blood examination with high powers of the microscope, were, as a result of this training, not only more efficient practitioners but before long were instrumental in discovering other pathogenic organisms of importance in tropical pathology. Some of these discoveries may be referred to.

TRYPANOSOMIASIS.

Forde, a former student of the London School of Tropical Medicine, found in the blood of an Englishman living in the Gambia and suffering from an irregular fever an organism the nature of which he failed to recognize. He showed it to Dutton, an emissary of the Liverpool School of Tropical Medicine, who recognized it to be a trypanosome, and named it *Trypanosoma gambiense*. Later, Castellani, also a former student of the London School of Tropical Medicine and at the time a member of the Royal Society's Commission for the study of sleeping sickness in Uganda, found the same parasite in the cerebro-spinal fluid of patients suffering from sleeping sickness. Sir David Bruce, Nabarro, and many others confirmed Castellani's observation, and definitely linked up the trypanosome of Forde and Dutton with sleeping sickness as cause and effect. The parasite having been discovered and its association with sleeping sickness confirmed, it became a matter of importance to ascertain in what way the infection was conveyed. Just as happened in the case of the malarial parasite, some

antecedent observations led to the clearing up of this point. Many years before Forde and Dutton's discovery Lewis described a similar organism (*Trypanosoma lewisi*) as a frequent parasite in the blood of the rat. Apparently this parasite of the rat was non-pathogenic. Not long afterwards Evans found a similar parasite in the blood of equines, bovines, and other domestic animals, in association with, and as the undoubted cause of, the deadly disease known in India as "surra."

In 1894 Sir David Bruce investigated in Zululand the disease known in South Africa as "fly disease," an epizootic extensively prevalent among and fatal to domestic animals in South Africa and other parts of that continent, and therefore of great economic importance. He very soon found a trypanosome (*Trypanosoma brucei*) in the blood of the stricken animals and also in the wild game of the infected districts, and confirmed the popular belief that the disease was conveyed by the bite of the tsetse fly—*Glossina morsitans*—one of several species belonging to a genus of biting flies peculiar to Africa.

In the light of this antecedent knowledge it was not long before Bruce and his colleagues in Uganda were able definitely to link up sleeping sickness and its parasite with another species of tsetse fly, *Glossina palpalis*, very prevalent in the afflicted sleeping sickness areas. Observations on the topical distribution of the fly and of sleeping sickness confirmed the conclusions arrived at by experiment on the lower animals—some of which were found to be susceptible to the infection, and to be harbourers of the parasite even under natural conditions.

Bruce at first supposed that the fly transferred the trypanosome directly and in a mechanical way on its blood-fouled proboscis from the infected to the uninfected, just as the lancet inoculates the vaccine virus; but a German (Kleine) showed that although such might be the case in a small proportion of instances, and for a short time—twenty-four hours—after the fly had bitten, in the majority of cases the parasite was conveyed only after it had undergone developmental changes in the fly—changes which require some eighteen days to complete, and which eventuate in a proportion of flies becoming permanently infective. Miss Muriel Robertson, who had previously made important contributions in the morphology and life-history of the trypanosomes of some of the lower animals, confirmed Kleine's observations, and also considerably expanded them by showing that it was only during a particular period in the recurring cyclical multiplication of the trypanosome in the circulation of the vertebrate host that it could be efficiently conveyed to its intermediary the tsetse fly. Further, this talented protozoologist traced the development of the parasite in this insect through its various phases in its passage from the alimentary canal to the salivary glands and thence to the vertebrate. Concurrently with investigations into the life-history of the trypanosome others were directed to ascertaining the topical distribution and bionomics of *Glossina palpalis*, notably by Hodges and Bagshawe.

For some time it was believed that man was subject to only one of the considerable number of trypanosomes now known to affect the vertebrates, but recent discoveries have shown that he is subject to invasion by at least two other members of the group equally, if not more, dangerous—namely, *Trypanosoma cruzi*, an American species which so far has not been studied specially by British observers, and *Trypanosoma rhodesiense*. The discovery of this latter trypanosome we owe to Stephens and Fantham. It appears to be confined to Rhodesia, particularly, but not entirely, to the north of the Zambesi. Morphologically it resembles *Trypanosoma brucei*, if it be not identical with that trypanosome, and like *Trypanosoma brucei* is transmitted, as shown by Kinghorn and Yorke and others, by *Glossina morsitans*.

Much attention has been given by British workers to the symptomatology and morbid anatomy of sleeping sickness. As regards the latter, the most important observations are those of Mott, who has shown that the nervous symptoms of the disease are the result of an extensive small-cell infiltration of the perivascular connective tissue of the brain, very similar to that occurring in general paralysis of the insane.

TICK FEVER.

Vandyke Carter was the first to describe a spirochaete in association with the relapsing fever of India, a spiro-

chaete possibly identical with the *Spirochaeta recurrentis* of Obermeyer. According to Mackie, it is transmitted in India by the louse. Livingstone and Sir John Kirk had called attention many years ago to a fever prevalent in particular parts of Portuguese East Africa (notably Tete on the Zambesi) which was attributed locally to the bite of the carrapata, a tick having bug-like habits. It was reserved for Milne and Ross in Uganda and Dutton and Todd on the Congo to show that this African carrapata disease is a relapsing fever, and that it is caused by a spirochaete—*Spirochaeta duttoni*—which, in its turn, is transmitted from man to man by the bite of the tick *Ornithodoros moubata*; and, further, that it can be transmitted not only by the tick originally infected but also by the progeny of that particular tick. At first there was some doubt as to whether or not the new spirochaete was identical with that of Obermeyer, but well marked differences in their respective pathological and clinical effects on man, as well as the experimental work of Kinghorn and Breinl, showed that, although morphologically similar, they were specifically distinct. The life-history of the spirochaete in the vertebrate host has been worked out to some extent, particularly by Breinl, of the Liverpool School of Tropical Medicine, and in the tick by Sir William Leishman, R.A.M.C. According to Breinl, the parasites, when they disappear from the blood at the crisis of the characteristic recurring febrile paroxysms, are taken up and destroyed for the most part by the phagocytes; a proportion, however, enter certain cells wherein they coil up and, ultimately, after breaking up into a number of granules, escape as such from the cell and develop in the blood into the spirochaetes which, on maturing, give rise to the succeeding paroxysm of fever. As regards the spirochaetes in the tick, Leishman found that on entering the stomach they also break up into minute granules, which pass into the cells of the Malpighian tubes, and thence into the eggs of the tick, and also into its excreta. Thus the parasite has double opportunity of survival, either in the next generation of ticks or by passing out in the excreta of the tick and so obtaining access to a human or other vertebrate host through contamination of the wound it inflicts when the tick next proceeds to feed. Balfour has made some very interesting observations on the process of granule formation and discharge in the case of a similar spirochaete in Sudanese fowls, which tend to throw light on what occurs in *Spirochaeta duttoni*, both in the tick and in the human body.

YAWS.

Soon after the discovery of the spirochaete of syphilis by Schaudinn, Castellani, then of the Ceylon Medical Service, described a similar though different organism, *Spirochaeta pertenuis* (v. *pallidula*) as the germ cause of yaws. His observations have been confirmed and are now generally accepted. The same observer described another species of spirochaete, *Spirochaeta bronchialis*, as the cause of a form of chronic bronchitis occurring in Ceylon, and probably in Africa.

LEISHMANIASIS.

Medical men in India and elsewhere have long been familiar with a form of chronic irregular fever associated with great enlargement of the spleen and liver. It is a deadly disease. In parts of India—Assam, for example—where it is especially prevalent and is called kala-azar, it is a serious matter, having swept away a large part of the population of some districts, and is, or was, spreading steadily as an epidemic over a large part of the Brahmaputra valley. The disease was generally relegated to the malarial group, although some observers, being struck with the absence in this febrile splenomegaly of the three pathognomonic marks of malaria—namely, tertian or quartan periodicity, amenability to treatment with quinine, and the presence of the malarial parasite or its product, haemozoin, in the blood—refused to acknowledge its malarial nature. Several commissions sent by the Government in India to ascertain the exact nature of the disease completely failed to establish its etiology. Some of us thought that kala-azar might possibly be due to some parasite similar to the trypanosome, at that time recently discovered in association with a chronic irregular fever and sleeping sickness. Sir William Leishman in 1902, and again in 1903, almost simultaneously with Donovan, found in the spleen, in cases of Indian febrile splenomegaly, a minute

oval body possessing two nuclear masses, one spherical or oval and relatively of considerable size, the other linear or bacilliform and very minute. Extended investigations have shown that these oval bodies are present in the spleen, liver, bone marrow, and elsewhere in every case of kala-azar, and that they are characteristic and the cause of this deadly disease, which, as we now know, is by no means confined to India. Attempts at cultivation on bacteriological lines, that is to say in warm media, were unsuccessful. Later, however (in 1904), Sir Leonard Rogers ascertained that if these Leishman-Donovan bodies, as they came to be called, were kept at ordinary tropical atmospheric temperatures, about 22° Centigrade, in a sodium citrate solution, they underwent a remarkable development, first multiplying by division and later on developing into flagellated herpetomonas forms. This discovery indicated that the parasite is capable of living outside the human body, it may be in some cold-blooded animal, such as an insect or other intermediary. From the point of view of prevention, it is extremely important that the life-history of *Leishmania donovani* be completed. In endeavouring to attain this desirable end workers must not allow themselves to be too much obsessed by the fact that in the similar parasites of malaria, of trypanosomiasis, of spirochaetosis, as well as those of yellow fever and of dengue, an arthropod intermediary is essential in their life-history. Possibly *Leishmania* requires such a vector and intermediary; analogy certainly suggests this, but suggestion is not proof. The recent, and to my mind very important, observations of Laveran and Fantham and Porter have shown that similar flagellated organisms—proper to insects, etc.—can be transmitted both by inoculation and by the mouth to warm-blooded vertebrates and flourish in them, such transmission being by no means in every instance a biological necessity for these parasites. It is true that Patton has succeeded in tracing the development of *Leishmania donovani* up to a point in the bed-bug, but so far his observations have not been accepted as conclusive that the bug is the transmitter or a necessary agent in the life-history of *Leishmania*.

Not long after the discovery of the Leishman-Donovan body in kala-azar similar parasites were found by Wright in Oriental sore, of which troublesome form of ulceration they are undoubtedly the germ cause. Still more recently similar bodies have been found in a variety of other ulcerative affections in tropical America and, by Christopherson, in the Sudan, one of them, *Espundia*, being a very grave disease indeed.

YELLOW FEVER AND DENGUE.

There are two fevers peculiar to warm climates which, though differing very much as regards gravity, have in some respects, both etiologically and clinically, many features in common. I refer to yellow fever and dengue. (1) Their respective germs exist in the blood and are ultramicroscopic; (2) their germs are conveyed to man by the same species of mosquito, *Stegomyia calopus*; (3) one attack confers absolute or relative immunity; (4) in both there is a primary fever and generally a secondary fever; (5) in both there is marked flushing of the skin, violent headache, general aching, and a rapidly attained high temperature which is generally associated with a relatively slow pulse; the duration of the primary fever—three, four, or five days—is about the same in both. These etiological and clinical features held in common suggest some kind of relationship as regards the respective germs. Carlos Finlay of Havana was the first to endeavour to prove experimentally that yellow fever was conveyed by mosquito bite, and he distinctly indicated *Stegomyia calopus* as the species concerned. His experiments were neither numerous nor convincing, and the subject was dropped till the American commissioners—Reed, Carroll, Agramonte, and Lazear—took the matter up and definitely established the fact that yellow fever is transmitted by the bite of *Stegomyia calopus* and, in nature, by no other means. The practical application of this discovery, in Havana and on the Panama Canal by Gorgas and his colleagues, and by others elsewhere in tropical America, has led to what must be regarded as one of the greatest triumphs of preventive medicine, whether in the tropics or elsewhere. Any claim for a share in this important achievement that might be advanced for British workers can be at most only an indirect one.

Fortunately the deadly yellow fever has hitherto been confined to tropical America and West Africa, extending to Western Europe and parts of America only at long intervals and only during the hot months of the year, and even then only in circumscribed epidemics. Not so dengue; it occurs in extensive epidemics throughout the entire tropical and subtropical belts, where in certain places it is more or less endemic. Why yellow fever has not a similar distribution is hard to explain, seeing that both diseases are conveyed by the same *Stegomyia* mosquito. It is only quite recently (1916) that *Stegomyia* has been proved to be a vector of dengue. For this important piece of information we are indebted to three Australian physicians—Burton Cleland, Bradley, and McDonald. It is true that previous workers had blamed the mosquito as the vector of the germ of dengue—notably Graham in Syria in 1903, and, later, Ashburn and Craig in Manila, but in neither case were the experiments satisfactory, and it would appear now that the mosquito which they blamed—namely, *Culex fatigans*—is not the only transmitter, if it be a transmitter at all. The Australian physicians referred to, although they failed with *Culex fatigans*, succeeded in communicating dengue, under conditions which completely excluded every possible source of fallacy, by infected *Stegomyia calopus*.

PAPPATACI FEVER.

Pappataci fever—an ephemeral fever of approximately three days' duration and regarded sometimes in tropical countries as a fever of acclimatization—has long been known to tropical practitioners. Shortly before the part played as vector by *Phlebotomus papatasi* was known the clinical characters and specific nature of this fever were described and recognized by James in India and McCarrison in Chitral. Subsequently Birt confirmed the discoveries of Doerr, Franz, and Taussig as regards the part played by *Phlebotomus*, and British naturalists have worked out in a great measure the bionomics of that insect.

UNDIFFERENTIATED FEVERS OF THE TROPICS.

There can be little doubt that in addition to the foregoing there are other fevers of a specific nature peculiar to the tropics, whose germ causes and vectors have hitherto escaped detection. Many attempts have been made by British observers, particularly Crombie and Leonard Rogers, to classify these fevers on a clinical basis, but until the germs or their vectors have been recognized, any arrangement of this nature can be regarded only as a temporary one.

HELMINTHIASES.

Trematodes.

Of late years many additions have been made to the list of trematodes invading tropical mankind, as well as to our knowledge of the pathological effects and life-histories of the more important of them. For much of this we are indebted to British investigators.

I may cite the new West African fluke, *Watsonius watsoni*, discovered by Dr. Watson in 1904, and since found to be not uncommon in certain parts of Nigeria; *Gastrodiscus hominis*, discovered by Lewis and McConnell in India in 1876; *Echinostoma malayanum*, by Drs. Macaulay and Stanton in 1911 in the Malay States; *Clonorchis sinensis*, by McConnell, in 1874; *Opisthorchis novercæ*, by Lewis and Cunningham, in 1872; *Fasciolopsis buskii*, by Busk, in 1843; *Paragonimus westermanii*, for the first time in man, by Ringer in Formosa in 1880, its ova having been recognized previously and independently by Baelz and the writer as a characteristic feature in the sputum of patients suffering from a somewhat serious form of endemic haemoptysis occurring in Japan, Korea, Formosa, and the Philippines.

Schistosomiasis.

These discoveries, though interesting to the helminthologist, are of comparatively small importance to the pathologist, especially if compared with the most recent discoveries in connexion with that peculiar family of trematodes, the Schistosomidae, including *Schistosoma haematobium* (Bilharzia), *Schistosoma mansoni*, and *Schistosoma japonicum*.

Since Bilharz, in Egypt, in 1851, discovered the parasite which bears his name it has been ascertained that this trematode is widely distributed throughout the African

continent, the adjacent islands, and in parts of Asia; that in many districts it is very prevalent—for example, Lower Egypt, where it affects one-third and in some places even 90 per cent. of the fellaheen population; that it is the cause of grave and even fatal disease; and that it has a decidedly deteriorating influence on the general health and therefore on the economic condition of the seriously affected area. Its pathological effect has been fairly exhaustively studied of late years, especially by Madden, Milton, Sandwith, and others, and the morphology of the adult worm and its ova determined, but the important matter of its life-history and the channels by which it enters the human body were until quite recently (1916) either quite unknown or at most mere matters of speculation. Dr. Leiper of the London School of Tropical Medicine, by a series of brilliant observations and successful experiments, has now completely filled in this hiatus in our knowledge, and has thereby placed in the hands of the sanitarians a sure guide in developing methods for the prevention of a disease which hitherto has proved the despair of the therapist. The history of Leiper's discoveries is interesting, not only as regards the subject they concern more particularly, but also as once more showing how what at the time appears to be a discovery with relatively small bearings may, sooner or later, lead to others of vastly greater importance.

A chronic and very fatal disease characterized by enlargement of the liver and spleen, blood and slime in the stools, anaemia, and ultimately ascites, had been recognized for a considerable time as endemic in certain parts of Japan and China. Subsequently the ova of a trematode were found to be a feature in the stools and organs of such cases. Still more recently Katsurada found in the liver of cats from one of the endemic areas numerous schistosomes containing eggs identical to all appearances with those found in the faeces of the human subjects of this disease; and still later, 1905, Catto found the same parasite and eggs in the organs of a Chinaman who died in Singapore. The disease is now known as Katayama's disease. Japanese observers have found that its parasite, *Schistosoma japonicum*, can be communicated to cats simply by immersing them in the water of certain rice fields in the endemic area. It was not essential that the water should be swallowed; simple immersion of part of the body of the cat sufficed. Myari succeeded in infecting animals from a mollusc common in these rice fields. He traced the development of the trematode in the mollusc and concluded that man acquired infection by working in the rice field, a conclusion supported by the experience of Europeans in China, principally sportsmen devoted to snipe shooting, who, it is to be presumed, had acquired the disease in wading through rice fields or swamps. Leiper, impressed by these observations and recognizing their possible bearing on bilharzia disease of Egypt, applied for and obtained permission and facilities from the London School of Tropical Medicine to proceed to the Far East to familiarize himself with and to test Myari's conclusions. The latter, somewhat modified, he confirmed. Returning to England, he placed the matter before the War Office authorities, who, recognizing the importance of bilharzia disease to the large body of troops assembled in Egypt, and acting in concert with the Medical Research Committee, commissioned Leiper to proceed at once to that country to study locally the etiology of bilharziasis and to suggest measures for its prevention and for the protection of the troops. In a very short time Leiper, assisted by Drs. J. G. Thomson and Cockin, ascertained that on emerging from the terminal-spined egg, opportunity serving, the miracidium of *Schistosoma haematobium* enters the liver of a fresh-water mollusc, a species of *Bullinus* (*dybowskii*), very common in the irrigation canals of Egypt, and transforms into a sporocyst and daughter sporocysts, wherein vast numbers of cercariae develop. The cercariae ultimately escape into the water, penetrate—opportunity offering—the skin of man or other vertebrate, and, dropping their tails in the passage, find their way into the liver of the vertebrate host, wherein, after six to ten weeks, they attain sexual maturity, becoming adult trematodes, which, passing into the veins of the bladder, produce the characteristic terminal-spined eggs which escape in the urine.

During these investigations Leiper was able to settle another and much disputed point in connexion with bilharziasis. It had long been recognized that there are

two types of bilharzia ova, one terminal-spined and passed principally in the urine and only occasionally in the faeces; the other lateral-spined and, practically, found exclusively in the faeces. Both types of ovum were generally attributed to the same species of trematode, the difference in the position of the spine being variously explained. In 1903 the writer, in examining the faeces of an Englishman from the West Indies, encountered numerous lateral-spined ova. Seeing that the patient had never visited Africa or any other region where bilharziasis was known to be endemic, that the urine contained no terminal-spined ova, and that, although thousands of examinations of the urine must have been made in the West Indies, bilharzia ova had never been reported from that part of the world, he suggested that the schistosoma producing these lateral-spined ova must belong to a species other than that producing terminal-spined ova. Sambon, adding many additional reasons, concurred in this view and paid me the compliment of naming the new species *Schistosoma mansoni*. Lóoss, who considered that this trematode did not require an intermediary, refused to accept the species. Leiper, however, in the course of the investigations just referred to, found that the miracidium of the lateral-spined ova enters a species of snail, *Planorbis boissyi*, quite distinct from the *Bullinus* favoured by the terminal-spined ova, and that on reaching the vertebrate host developed into a sexually mature schistosoma anatomically quite distinct from that resulting from infection from the miracidium of the terminal-spined ovum. Thus *Schistosoma haematobium* produces only the terminal-spined ova, and *Schistosoma mansoni* only lateral-spined ova, and are distinct species. Quite recently many cases of lateral-spined bilharziasis have been reported from the West Indies and Brazil, but never a case of terminal-spined bilharziasis, so that now there can be no question as to the validity of the new species *Schistosoma mansoni*. In further confirmation of this conclusion Lutz has found that a *Planorbis* is its intermediary host also in Brazil.

Dracontiasis.

Although the anatomical features of the adult guinea-worm and of its larva had been ascertained, little was known of the life-history of this formidable parasite until Fedschenko discovered in 1870—a discovery subsequently confirmed by the writer—that the larva on being passed into water enters the body of a fresh-water cyclops, wherein it undergoes extensive developmental changes. In 1907 Leiper was sent by the London School of Tropical Medicine to West Africa to endeavour to ascertain in what way the parasite after leaving cyclops returns to man. He found that if the infected crustacean were immersed in a weak (0.22 per cent.) solution of hydrochloric acid (in imitation of gastric juice) the cyclops was immediately killed, whilst the included parasites, on the contrary, were stimulated to great activity, and bored their way through the integument of the cyclops. This experiment, he conjectured, indicated the route likely to be followed by the guinea-worm in nature. As confirmatory experiment on man was out of the question, Leiper administered infected cyclops to a monkey, and had the satisfaction, on the death of the monkey several months later in England, of finding three female and two male guinea-worms in an advanced state of development in its tissues. From this we may conclude that the infection is acquired by man from cyclops-infested drinking water fouled by guinea-worm carriers. Efficient preventive measures are clearly indicated by this new knowledge.

Ascaris lumbricoides.

It has been generally accepted that the experiments of Davaine, Grassi, and other Continental workers had proved that the larvae in the ripe eggs of ascaris were hatched out in the human intestinal canal, and therein immediately proceeded to sexual maturity. Quite recently, however, the experimental work of Stewart tends to show that the life-history of this very common parasite may be not quite so simple. Sambon already had pointed out that the papilla or beak, a conspicuous feature in the larval ascaris, indicated that the little organism at an early stage of its existence bores its way into the tissues. Stewart has now shown that if ripe ascaris eggs are fed to a mouse many of the larvae liberated in the intestinal canal pass to the lungs, and, if the dose of eggs is large, may even induce fatal pneumonia. The complete bearing

as regards man—the normal host of *Ascaris lumbricoides*—of this observation is not quite apparent, but it certainly goes a long way to prove Sambon's view that, before attaining sexual maturity, the parasite must enter the tissues of its human host.

Filariasis.

In 1872 Timothy Lewis, in India, ascertained that the larval filaria discovered by Demarquay and Wucherer in pathological fluids was normally a parasite of the circulation. He called it *Filaria sanguinis hominis*. In 1876 Bancroft, in Australia, discovered the parental worm, *Filaria bancrofti*. Subsequently, in 1878, the writer ascertained that a *Culex* mosquito served as its intermediary host, abstracting the microfilaria from the blood and providing it with an opportunity for undergoing important developmental changes, during which it increases in size from a microscopic object to one just visible to the naked eye, and possessing an alimentary canal as well as remarkable powers of locomotion. In 1900 Low at the London School of Tropical Medicine, and subsequently James in India, made the important discovery that at this stage of development the larval worm passes into the labium of the mosquito's proboscis, and gets back into man direct, the old idea of the mosquito dying on the water and the embryos escaping into this medium and so reaching man, being thereby, if not absolutely disproved, rendered improbable. Noë, Grassi, and Fülleborn in the case of the allied parasite (*Filaria immitis*) of the dog, and Bahr in the case of the human parasite, have shown the exact mechanism of how this takes place. Finally, the metamorphosed embryos arrive at the lymphatics, where development is completed and the new generation of embryo filariae born.

When working in China at the life-history of the filaria I stumbled on the phenomenon known as "filarial periodicity." The microfilariae, I found, under normal circumstances come into the general circulation in the evening, increase in number till midnight, and gradually disappear towards morning, being almost entirely absent from the peripheral circulation during the day, when, as I subsequently ascertained, they lie up in the lungs and greater blood vessels. Stephen Mackenzie showed that by inverting the habits of the human host as regards the times of sleep this periodicity was correspondingly inverted, the filariae then coming into the peripheral circulation during the day and disappearing from it at night. For many years it was believed that this type of periodicity was observed by *Filaria bancrofti* embryos in all countries and climates. It certainly applies in most instances to China, India, Africa, and America, but we now know that it does not hold good for the islands of the Pacific—lands in which filariasis is particularly prevalent. Thorpe was the first to notice this, and later Lynch and others, especially Bahr, confirmed his observation in Fiji and elsewhere.

A larval filaria described by Ashburn and Craig in the Philippines in 1906 under the name of *Filaria philippinensis* has recently been proved to be only an example of *F. bancrofti*, adults from such cases being indistinguishable from the latter. Further, Leiper, after careful study, has failed to find any anatomical differences between the adult worms from Fiji and those from Asia and elsewhere. It seems to the writer that Bahr may have supplied the explanation of the discrepancy as regards periodicity between the ordinary and the Pacific microfilaria. This observer has shown that although in Fiji, as elsewhere, the night-feeding *Culex fatigans* is an efficient intermediary for the filaria, it is not the usual or most efficient intermediary in that group of islands. In Fiji the day-feeding mosquito, *Stegomyia pseudo-scutellaris*, is not only a very common insect but in respect of efficiency as an intermediary for the filaria is ahead of *Culex fatigans*, and he concludes that the filaria has partially adapted its habits to those of its favourite intermediary in the Pacific, just as it has adapted itself to the habits of *Culex fatigans* and other nocturnal mosquitos, its favourite intermediaries in Asia, Africa, and America. It may be suggested that the explanation might lie in some peculiarity of climate or other circumstance peculiar to Fiji and the Pacific islands generally; but the same writer has shown that the microfilaria of coolies imported from India, who, presumably, had brought their parasites with them from their native country, retained the

nocturnal periodicity habit even after years of residence in Fiji, whilst Indians born in Fiji acquired the non-periodic filaria only. The point, however, is not settled, as *Culex fatigans* does exist and can carry the filaria in Fiji.

Although in many instances the filaria appears to be non-pathogenic, nevertheless, seeing that it is apt in a considerable proportion of instances to give rise to serious disease, especially elephantiasis, and that it occurs in a large proportion (5 to 75 per cent.) of the inhabitants of many tropical countries, it is a very important element in tropical pathology.

Many British workers have studied the pathological bearings of this parasite, and have definitely linked it up as the cause of lymphangitis, of chyluria, varicose groin and axillary glands, lymph scrotum, chylocele, various forms of lymphangiectasis and of tropical elephantiasis, and also of fatal septicaemia supervening on suppuration in abdominal and other seats of lymphatic varix. Of interest are the observations of Wise in Demarara, and Bahr in Fiji, on the cretified remains of effete filariae in the lymphatic glands and elsewhere.

Other Microfilariae.

As opportunity presented itself the writer made systematic examination of the blood of the natives of many different tropical countries, and in this way was enabled to discover the blood-haunting larval filariae of three additional and specifically distinct nematodes, namely, *Filaria loa*, *Filaria perstans*, and *Filaria demarquayi*.

The embryos of *Filaria (loa)*, the eye worm of tropical West Africa and its hinterland, and the cause of the peculiar condition known as "Calabar swellings," so common in Europeans in those regions, and so often mistaken for erythema nodosum, resemble very closely those of *Filaria bancrofti*. It differs, however, from the latter in minute anatomical details, and also in observing an exactly opposite periodicity, entering the general circulation during the day and disappearing from it at night. This circumstance led the writer to suggest that its liberating and intermediary host must be a biting fly of corresponding habit, and as the mangrove fly, *Chrysops dimidiata*, was very common and very active during the day in the endemic districts, he suggested that it might be the intermediary host, and therefore responsible for the spread of the parasite. This suggestion has been proved to be correct by Leiper, whose observations have been confirmed quite recently by Kleine in the Cameroons.

Acanthocheilonema perstans.

The larval form of this parasite was found in 1891 in the blood of a Congo negro suffering from sleeping sickness, and subsequently found in many cases of that disease. I concluded that it might be the cause of this condition, but Low and others have shown that this is not so. We now know that it is a very common parasite in West Africa, on the Congo, in Uganda, in British Guiana, and probably elsewhere in the tropics. Daniels was the first to find the adult worm in aboriginal Indians of British Guiana.

Filaria demarquayi.

The larvae of this species I found in the blood of the Caribs of St. Vincent, West Indies, and subsequently in aboriginals of British Guiana and possibly of New Guinea. Low has shown that it occurs also in others of the West Indian Islands—Dominica, Trinidad, and St. Kitts. He experimented with many insects to determine the intermediate host, but failed to find it. The adult form was discovered and described by Daniels in 1898. Whether the two last-mentioned nematodes produce any serious pathological effects has not been absolutely determined. It is unlikely that they do so.

SPRUE.

Sprue is one of the more important diseases of the tropics, particularly as regards Europeans, among whom, especially among the older residents, it is a very common, very intractable, and very deadly disease. It is only of late years that its characters, symptoms, and diagnosis have come to be generally recognized, mainly through the writings of Fayrer, Thin, myself, Carnegie Brown, Begg, Castellani, and Bahr. The histopathology of the disease has been well worked out by British pathologists. There has been much speculation about the assumed specific cause—bacteria, hyphomycetes, and even helminths having

been at different times incriminated; so far nothing definite in this respect has been arrived at. We are therefore still at a loss to indicate a scientific prophylaxis of a disease which amounts to a positive curse in such places as Ceylon, the Malay States, parts of India, of China, and of many other tropical countries.

THE DYSENTERIES.

It is only of late years that anything approaching to a scientific conception has been attained of what is indicated by the term "dysentery." Formerly the word was taken to indicate one definite and distinct disease, but nowadays we must regard it as indicating several forms of colitis brought about by a number of specifically distinct disease germs. Thus we have protozoal dysenteries attributable to such germs as the *Entamoeba histolytica*, the malarial parasite, leishmania, and *Balantidium coli*; helminthic dysenteries resulting from invasion of the walls of the colon by *Schistosoma japonicum* and *Schistosoma mansoni*; bacterial dysenteries produced by the several members of the *Bacillus dysenteriae* group, and probably of other bacteria. Although most of the original discoveries which have enabled us to arrive at this classification of the dysenteries are to be attributed to workers other than British, some of them may be fairly assigned to our fellow-countrymen, especially those having a bearing on the prevention of these diseases, such as the elucidation of the part played by dysentery carriers and their treatment.

BERI-BERI.

How many etiologically distinct forms of tropical multiple peripheral neuritis are included under the term "beri-beri" it is at present difficult to say; probably there are several. If we confine the term to that form of endemic multiple peripheral neuritis occurring in the Malay archipelago, China, and Japan, evidence is rapidly accumulating that, if it be not the only and sole cause of the disease, a dietary deficient in the vitamins essential for healthy nutrition has much to do with it. Although the initial observations which have led to this conclusion are to be credited to a Dutch physician—Eijkman—much has been done by British workers in narrowing the field for observation and in giving precision to conclusions. The observations of Eijkman on beri-beri in the Dutch East Indies distinctly indicated that in some way or other the disease was associated with a particular kind of prepared rice. Later Braddon insisted on this; and although his explanation of the *modus operandi* of the rice factor was not the right one, yet his insistence led to careful and fruitful investigation and experiment by Fraser and Stanton under Government auspices. The last named observers have distinctly shown that a leading element, if not the only element, in the causation of beri-beri, at all events in the Malay States, is absence (owing to excessive milling) of the pericarp and germ of the rice which constitutes the staple food of the Chinese, Indian, and Japanese coolie. And, further, they have shown that the administration of the millings of the decorticated and highly polished rice can arrest the development of a threatened attack of beri-beri, and, if it is not too far advanced, cure the disease. These observations on man are supported by experiment on the lower animals, especially on fowls, in which, as Eijkman and many others have shown, a diet exclusively of the incriminated forms of rice induces a polyneuritis closely resembling, if not identical with, that of beri-beri. The conclusions of Fraser and Stanton have been substantiated by many independent observers in the Philippines, in Japan, and elsewhere, and action based on these conclusions has had most happy results in prisons, asylums, hospitals, and other public institutions, as well as on native labour in plantation and mining camps. Mott, Halliburton, Durham, and Hamilton Wright have made important contributions to the pathology and anatomy of this disease.

SKIN DISEASES.

Mycetoma.—Since Vandyke Carter, in 1859, demonstrated the mycotic nature of the melanoid and ochroid forms of what is variously termed Madura foot, fungus disease of India, and mycetoma, considerable attention has been given to this and allied diseases by British and French pathologists, notably in Britain by H. J. Carter, Kanthack, Boyce, Hewlett, Adami, Kirkpatrick, and many others. Owing to the labour of these observers, it is now known

that mycetoma occurs in many tropical countries besides India, and in a variety of forms, and that the germs are introduced through wounds in the skin.

Ulcerating granuloma of the pudenda was first described in India by McLeod, and in 1896 by Conyers and Daniels in British Guiana, and subsequently by other British workers in Africa, Australia, and elsewhere. Donovan called attention to certain coccoid parasites included singly, or more usually in groups, in the large mononuclear cells obtained by scraping the surface of the characteristic ulcers. Intravenous injections of antimony have lately been used with good effect in the treatment of this disease by workers in Brazil, and Low and Newham have recently published the details of a case in England cured by this method.

The systematic study of the tropical dermatomycoses had been neglected until recent years, and until the adoption of Sabouraud's methods by Castellani and Chalmers had brought about a certain amount of order into this little understood department of tropical dermatology. Other British workers have from time to time contributed to the advancement of the subject, and I may mention Turner and Sir William MacGregor. The tropical practitioner is no longer satisfied with a comprehensive diagnosis of the mycotic skin diseases by the expression "dhotie itch." He now recognizes that there is a great variety of hyphomycetic skin disease both in the native and in Europeans; he distinguishes between erythrasma, tinea cruris, tinea imbricata, pityriasis versicolor, and so forth, and he knows now that these are only a few of the many forms of hyphomycetic skin disease fostered by the heat and moisture of tropical climates and contact with tropical animals.

Vomiting Sickness of Jamaica.—For many years it has been known that a peculiar disease, called "vomiting sickness," occurs from time to time in certain districts in the island of Jamaica. It is an extremely fatal disease, the mortality being anything from 80 to 90 per cent. It occurs particularly in children, although sucklings are exempt. Naturally its etiology has been the subject of much speculation and several commissions have attempted to clear this up. Some have regarded it as a manifestation of yellow fever, others of malaria, but it has been reserved to Dr. H. Harold Scott, Government bacteriologist, Jamaica, to solve the mystery. He has found that the so-called disease is produced by poison liberated in some mysterious way in immature or damaged ackees, the fruit of *Blighia sapida* (a tree very common in Jamaica) and much used by the negroes of that island. Shortly after the consumption of damaged fruit, especially of the soup prepared from the damaged fruit, vomiting sets in; presently this subsides, to be followed three or four hours later by a recurrence and a rapid supervention of convulsions, coma, and death. The average duration of the illness is little over twelve hours. Dr. Scott has proved that certain animals are susceptible to the poison and show *post mortem* a remarkable fatty degeneration of the liver and other tissues, a condition which is also a notable feature in fatal cases of vomiting sickness in man.

TREATMENT OF TROPICAL DISEASES.

Many recent advances in our knowledge of the germ causes of tropical diseases and in our diagnostic methods have led to a more accurate application of certain drugs long recognized as efficacious in particular types of dysentery, and to the introduction of new drugs and methods of treatment in other diseases. I can allude to a few only of these drugs, and such as are justly attributable to British workers. The value of atoxyl in the treatment of trypanosomiasis was first indicated by Thomas, then of the Liverpool School of Tropical Medicine, and the use of salts of antimony in the same disease by Plimmer and Thomson of the Lister Institute.

Sir Leonard Rogers, following up Vedder's work on emetine, introduced this drug to be given hypodermically as a substitute for ipecacuanha in the treatment of amoebic dysentery and amoebic hepatitis. It has recently been demonstrated that this method does not, in many instances, sterilize the individual of his amoebae, and that many of these cases become chronic carriers. Quite recently, Dale, Low, and Dobell have used a new compound, emetine bismuth iodide, by the mouth in such cases, and have found its sterilizing effect on the amoebae to be much greater than that of emetine given by hypo-

dermic injection. It is quite likely, therefore, that the oral administration will supplant the hypodermic method in the treatment of the disease in the future. Donovan and other British physicians have proposed radiotherapy in the treatment of granuloma of the pudenda, and many British practitioners in Africa and the West Indies have demonstrated the value of the intravenous injection of salvarsan and other arsenicals in tick fever and yaws.

INDIA AND MEDICAL PROGRESS.

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To what extent has India contributed to the advancement of medical science?

In providing an answer to this question it is necessary to indicate that Western medicine, even at the present day, is represented in India by only about 1,000 British medical men, the major part of whom form the Indian Medical Service. One thousand British doctors in a land of over 300 million people! In a land where plague, pestilence, and famine are the crude problems of everyday life. In a land where tropical heat and torrential rains sap the vitality of the strongest frame and the resolve of the strongest will. In a land where strange diseases lurk in unsuspected places and death comes in a moment to even the most watchful.

To the teeming millions of such a land this small service has, since the earliest days of the East India Company, brought the benefits of Western medical science, carried into its waste places and most desolate outposts the standard of medical progress, and evolved sanitary order out of pestilential chaos. It has established medical schools and training colleges, and has brought into being an army of Indian-born and Indian-taught medical men. It has provided the professorial staff for the medical colleges, and has taught as well as practised the science and art of medicine and surgery. It has instituted a sanitary service, and has laid the foundations on which the science of tropical sanitation is built. It has established hospitals and dispensaries in every city and town in every district from Ceylon to the Pamirs, and has made it possible for twenty-eight and a half millions of India's people to receive the benefits of Western medical and surgical treatment in a single year. It has organized medical research and established research institutions where problems peculiar to India are studied by competent experts recruited from its own ranks. It has founded Pasteur Institutes for the treatment of rabies and the manufacture on a large scale of prophylactic vaccines and serums. It has ministered to the needs of India's army in peace, and tended to the sick and wounded in her frequent campaigns. It has organized the jail system of India, and taught her convicts trades. It has established tropical schools of medicine in Calcutta and Bombay, which bid fair to hold premier rank amongst such institutions in the world. All this the Indian Medical Service has done in the ordinary discharge of its duty, and what more?

Our knowledge of the natural sciences—botany, zoology, and geology—has been enriched by its aid. It has sifted from amongst the mass of tropical fevers a number of definite disease entities, described their etiology and symptomatology, and elucidated their cause or their mode of spread. It has made important contributions to our knowledge of other diseases of more universal distribution, discovered the means of cure of some of the tropics' most deadly maladies; and, finally, it has made striking additions to forensic medicine and to the art of surgery. It is with these, since they represent additions to the sum total of medical knowledge, that it is necessary to deal, emphasizing the fact, however, that they have been made during the performance of a task which in itself was colossal.

Let us consider, then, these contributions of India to the medical knowledge of the world.

Malaria.

The discovery by Ross that the plasmodium of malaria is conveyed to man by anopheline mosquitos (Fig. 1) ranks