and the diseased tissues being cut and scraped away. His leg healed up completely after some time, he put on flesh, and his general health improved considerably. On testing his eye again with the tuberculin at the end of last May it gave no reaction. This suggests that the test might be employed in consumptive sanatoriums to determine the length of time a patient should remain.

From these results I think it will appear that the test is a valuable, but, of course, not an infallible, aid in the diagnosis of tubercle.

ART. VI.—*Protozoal Diseases in Man.*^a By ARTHUR FRANCIS GEORGE KERR, B.A., M.D., Univ. Dub.; Senior Moderator and Gold Medallist in Natural Science; Government Medical Officer, Chiangmai, Siam.

IN recent years much work has been done on the protozoa causing disease in man. This work has chiefly been in connection with tropical diseases, but it is highly probable that many of the diseases of temperate climates, for which a bacterial origin has long and unavailingly been sought, will prove to be of a protozoal nature.

I propose to sketch briefly the general characteristics of protozoal diseases as far as they are known, leaving out of consideration purely local lesions, to note some of the difficulties met with in investigating these diseases, and finally to outline a provisional classification of the protozoa known to occur in man.

General Characteristics of Protozoal Diseases.—Most protozoal diseases are characterised by fever of a longer or shorter duration, which tends to be intermittent. Exacerbations of the fever are often connected with rapid multiplication of the parasite. This is well seen in malaria, the clinical varieties of which depend on the length of the life cycle of the parasite in the blood. In sleeping sickness also it has

^aA Thesis read for the Degree of Doctor of Medicine in the University of Dublin, July, 1908.

been observed that the trypanosomes are more easily found in the peripheral blood during the pyrexial periods. This is also markedly the case in tick fever. In the multiplication of various forms of protozoa a residual body remains after reproduction is complete, and it is probable that there is in this body a toxic substance which causes the pyrexia. If malarial fever be untreated there is, in addition to the regular periodicity, a longer and more irregular periodicity. The fever lasting for nine or ten days intermits for three or four days, and then returns with a shorter pyrexial period. But each succeeding pyrexial period becomes shorter and milder, and the apyrexial periods longer, till the fever disappears completely. In sleeping sickness and kala-azar the fever is of a very chronic nature, and may last for several years, but always with periods of apyrexia, which may last several weeks, the temperature usually being subnormal for some days before death. Even in the apyrexial periods the diurnal range of temperature is much greater than in a healthy person.

In other protozoal diseases, such as relapsing and tick fevers, as in malaria, the pyrexial periods tend to become shorter, and the apyrexial periods longer, until the fever is completely recovered from. In syphilis the fever is so slight as to be often not noticed.

The blood changes in protozoal diseases are, as a rule, characteristic. The red corpuscles are diminished in number, and show degenerative changes, such as poikilocytosis and polychromatic staining; normoblasts are not infrequently found. The white corpuscles usually show a marked relative increase of the mononuclear leucocytes in contradistinction to diseases of bacterial origin, where there is, as a rule, a polynuclear leucocytosis. In protozoal diseases these large mononuclear leucocytes act as phagocytes to a greater extent than the polynuclear leucocytes. The spirochæte infections, however, follow the bacterial diseases, and show a polynuclear leucocytosis, with the exception of the tertiary stage of syphilis, in which a mononuclear leucocytosis has been observed.

This mononuclear increase is most marked after the fever is over, and is thus a valuable aid to diagnosis in protozoal diseases at a time when no parasites may be found in the blood.

Several diseases in temperate climates have been reported to show a mononuclear leucocytosis during convalescence, such as measles, scarlatina, mumps, small-pox, and others. It is highly probable that these diseases will prove to have a protozoal origin.

This mononuclear leucocytosis of protozoal diseases is comparable with the polynuclear leucocytosis of bacterial diseases and the eosinophilia of worm infections. Unfortunately for diagnostic purposes there are a few exceptions in all three classes.

In many of the protozoal diseases there is, consequent on the destruction of the red blood corpuscles, a considerable deposit of hæmosiderin in the cells of the liver, spleen, and kidney. In malaria there is in addition a deposit of a darker pigment, melanin, in certain cells of the liver, spleen, and other organs. The later stages of sleeping sickness show a well-marked perivascular round-celled infiltration very similar to that seen in certain parasymphilides. This is interesting, as the trypanosome and the spirochæte are very closely allied.

In most of the protozoal diseases there is enlargement of the spleen and liver; it is in these organs that the parasites are usually found in greatest abundance.

Epidemiology.—The seasonal prevalence, geographical and topographical distribution of protozoal diseases, can be explained to a great extent by a reference to the habits of the intermediate hosts of the protozoal parasites. With the exception of dourine, a trypanosome disease of the horse, and syphilis, in both of which infection takes place by copulation, and yaws, all known general protozoal diseases of mammals have their infection transmitted by an intermediate invertebrate host which, in nearly all cases, belongs to the Phylum Arthropoda. It is extremely probable that in all cases some development of the parasite takes place

in this intermediate host, and that this host is not capable of transmitting the infection till this development has taken place. We know that the malarial parasite multiplies by asexual reproduction alone in man, but in the mosquito sexual reproduction takes place, and it is not until this is complete that infection can take place through the mosquito. In no other case has the development in the intermediate host been so well worked out as in malaria. In some cases, such as sleeping sickness and tick fever, no development in the intermediate host has yet been discovered.

It is interesting to note that, as a rule, a particular class of parasite is carried by a particular class of arthropod—for instance, the malarial *Plasmodium* is transmitted by the anopheline mosquitos, *Trypanosomes* in mammals by brachyurous or muscid diptera, *Spirochaetæ* by argas ticks, *Piroplasmata* by ixod ticks. These facts throw much light on the epidemiology of these diseases, as we know that conditions unfavourable to the intermediate hosts will be unfavourable to the disease, that great abundance of the intermediate host will favour increase of the disease, and so on. A knowledge of the habits and life history of the intermediate host enables us to combat the disease, and without this knowledge we practically work in the dark. This has been well demonstrated by the extinction of malaria in many places through measures directed against mosquitos.

Many of the problems of epidemiology are, however, more complicated. Malaria, as far as we know, is never now acquired in England, and yet *Anopheles maculipennis*, the chief carrier of malaria in European countries, is far from uncommon in that country. We know that at one time malaria was endemic in England. How, then, has it become extinct if the intermediate hosts of the parasite still exist there? Undoubtedly the *Anopheles* has been greatly reduced by drainage measures, and this, together with the introduction of cinchona, may account for the extinction of malaria; but this is improbable, as at that time cinchona was very expensive and not in general use. It has been shown that the bodies known as "Ross's black spores," which are sometimes found

in the stomach of the mosquito in company with the malarial zygotes are in reality a protozoan parasitic on the malarial zygote, and it is quite possible that it is to these "black spores" that we owe the extinction of malaria in England.

It is likely that the many problems of the epidemiology of temperate diseases will be elucidated by work on these lines. Many of these diseases may be transmitted by fleas, bugs, lice, ticks, and other biting arthropods. It has been shown that the infection of bacterial diseases may be carried by such agents, but in such cases the arthropod acts simply as a mechanical carrier. In protozoal diseases the parasite undergoes some development in the carrier, and so can be carried only by the one species in which such a development can take place.

Immunity.—With regard to immunity, a great deal of information is still required. In spirochæte infections—namely, syphilis, yaws, relapsing fever, and tick fever—one attack confers a considerable immunity. In malaria it is usually considered that after a number of attacks some immunity is acquired. In many of the protozoal diseases of cattle and other stock animals one attack renders the animal immune.

Difficulties in investigating Protozoal Diseases.—One great difficulty in investigating protozoal diseases is the frequent scantiness of the parasite in the peripheral blood. In some of the forms of malaria the parasite may be fairly plentiful in the peripheral circulation; in the malignant subtertian form, however, only the young parasites are found there, the older parasites being confined to the blood in the internal organs. In kala-azar the parasite is very scanty in the peripheral blood; at one time it was thought not to occur there, though it can be found in the spleen, liver, and bone marrow in enormous numbers. The trypanosome of sleeping sickness is never found in large numbers in the peripheral blood; the blood of the first case brought to London was steadily searched for one week before a single parasite was found. It will be understood how easily such parasites

may have been overlooked in diseases of temperate climates, which are, as a rule, investigated purely from a bacteriological point of view; if an organism is not readily found in cover slip preparations, cultures are made from larger quantities of blood. Most of these protozoal organisms have resisted all attempts at culture on artificial media. In the few cases in which they have been cultured, it has been done only after many failures. The Leishmann-Donovan body, for instance, was finally cultivated, but it was not actually on the medium that the growth was found, but in the condensation water at the bottom of the medium slope; such a growth would probably have been rejected by a bacteriologist as sterile.

But perhaps the greatest difficulty in investigation may be the size of the parasite. The spirochæte, or more properly the treponema, of syphilis, is difficult to see on account of its fineness, but that of yaws (*Treponema pertenue*) is still finer. Schaudinn has shown that trypanosomes and spirochætes may become, after rapid division, so fine that they are absolutely invisible under the highest powers of the microscope, their presence being ascertainable only when they are massed together and moving. In this condition of extreme fineness a trypanosome of the rat, *T. Lewisii*, has been passed through a Pasteur-Chamberland filter, the filtrate afterwards, on injection, infecting another rat.

It is highly probable that the organism of yellow fever is a trypanosome or allied protozoan which has an ultra-microscopic stage in man. The U. S. Commission of 1900 showed that the infective virus of yellow fever could be passed through a Pasteur-Chamberland filter, and that it is frequently transmitted by a mosquito, *Stegomyia fasciata*. This mosquito, however, is not capable of giving rise to infection till twelve or fourteen days after it has sucked the blood of a yellow fever case. This shows that the parasite must undergo some stage of development in the body of the mosquito, and almost proves it to be a protozoan.

If it is possible to find suitable media for cultivating

protozoal organisms, many of the difficulties in investigating protozoal diseases will be removed.

I append an outline for a provisional classification of the principal protozoa found parasitic in man and in the higher animals; some of the mammalian protozoa not yet found in man will probably be reported as causing human disease also within the next few years.

If Schaudinn's observations on the development of *Halteridium* and other forms be confirmed, and which has not been done up to the present, this classification will require revision.

PARASITIC PROTOZOA.

I. *Rhizopoda*.

(1) Amœbina.

Entamœba coli (not pathogenic).

Entamœba histolytica (dysentery).

II. *Mastigophora*.

(1) Protomastigina.

Spirochæta obermeieri (relapsing fever).

Spirochæta duttoni (tick fever).

Treponema pallidum (syphilis).

Treponema pertenue (yaws).

Trypanosoma gambiense (sleeping sickness).

Herpetomonas (not yet found in man).

Leishmania donovani (kala-azar).

Cercomonas hominis (not pathogenic).

(2) Polymastigina.

Trichomonas vaginalis (not pathogenic).

Lambliia intestinalis (not pathogenic).

III. *Infusoria*.

Balantidium coli (dysentery and diarrhœa).

IV. *Sporozoa*.

(1) Telosporidia.

(a) Gregarinidæ.

Hæmogregarina (not yet found in man).

(b) Coccididia.

Coccidium (several species occasionally found in man).

(c) Hæmosporidia.

Plasmodium immaculatum (subtertian).

Plasmodium vivax (tertian).

Plasmodium malaricæ (quartan).

Babesia hominis (Rocky Mountain fever).

Halteridium (not yet found in man).

(2) Neosporidia.

Sarcosporidia.

Sarcocystis (reported three to four times
in man, species not identified).

ART. VII.—*Clinical Reports of the Rotunda Hospital.*^a By
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operation of JOHN W. BELL, Senior Assistant Master; and
ARTHUR HOLMES, M.B., M.R.C.P.I., late Senior Assistant
Master.

THE public opening of our new wing by Her Excellency the Countess of Aberdeen and its full occupation is the most important event to chronicle in our present report.

The Hospital is now well equipped to meet the requirements of modern gynæcological and obstetrical practice. It contains 85 obstetrical and 36 gynæcological beds, together with 64 cots for infants. This accommodation has proved ample, and it has no longer become necessary to place patients on mattresses laid on the floor, a means formerly resorted to as the only alternative to refusing them admission. Should further accommodation be required in the future we have still space available to permit the number of our maternity beds to be increased to well over 100.

It is more than likely that this increase will be found necessary, for our patients are every year becoming more educated to the benefits derived from a prolonged stay in hospital. A few years ago numbers insisted on leaving the house as early as the fifth day; those who annually do so now could be counted on the fingers of one hand, whilst many at present

^a Read in the Section of Obstetrics of the Royal Academy of Medicine in Ireland on Friday, May 29, 1908.