TICKS AND TICK-TRANSMITTED DISEASES.

By GEORGE H. F. NUTTALL, M.A., M.D., Ph.D., F.R.S.,
University Lecturer in Bacteriology and Preventive
Medicine, Cambridge.

(*Read: December 9th*, 1904.)

Ticks and tick-transmitted diseases promise to offer an increasing degree of interest to medical men, zoologists, and those economically concerned. Some of the diseases which ticks transmit, notably those due to the haematozoal parasites belonging to the genus Piroplasma, are amongst the most devastating which affect domesticated animals in many parts of the world. American investigators have, moreover, claimed that man is also subject to a similar disease, the so-called tick fever of the Rocky Mountains.

Before proceeding to consider some of the main points relating to tick-transmitted diseases, it appears in place to say something regarding ticks, more especially out of regard for those who have perhaps no special knowledge of these ectoparasites.

Ticks.

Ticks belong to the class Arachnoidea, in which are also included the spiders and mites; all the members of this class possessing eight legs when adults. Ticks constitute a well-defined group or family, the Ixodidae, in the Order Acarina. Neumann, in common with most zoologists, divides the Ixodidae into two sub-families, the Argasinae (including the genera Argas and Ornithodoros) and Ixodinae (including the genera Ixodes, Eschatocephalus, Aponomma, Amblyomma, Hyalomma, Haemaphysalis, Rhipicephalus, and Dermacentor). It would be out of place here to dwell upon the particular characters possessed by the different genera above-mentioned, especially as these can be found described in special works relating to the subject. (See Neumann, 1896-1901, and Salmon and Stiles, 1902.)

We are indebted to a long list of zoologists for what we know of ticks but our knowledge in the main refers

to the external features of tick anatomy. In the case of mosquitoes, the study of the diseases they transmit led to a more thorough investigation of their biology and internal structure, especially at the hands of medical men; and it is safe to say that the same impulse is leading us to turn our attention more closely to ticks.

Ticks, as far as known, derive their nourishment entirely by sucking the blood of their hosts. These hosts are almost exclusively terrestrial vertebrates, and include practically all classes of Mammalia, Aves, Reptilia (Chelonia, Sauria, Ophidia), and Amphibia (Bufo). Neumann records but two species as attacking insects (Coleoptera).

The geographical distribution of ticks is world-wide, but they are most numerous in warm countries, where they naturally find the conditions of temperature and moisture which are most favourable to their metamorphoses on or near the surface of the ground. The influence of low temperatures and desiccation in retarding, or completely checking, the developement of ticks from the egg to the larval and subsequent stages, has been already demonstrated in the laboratory. Ticks follow the lines of travel of their hosts. Some ticks attack a variety of hosts, whilst others appear to be more selective in this respect, and to be more limited in their geographical distribution.

The structure of ticks shows evidence of adaptation to a life of parasitism. The legs terminate in sharp claws and pads (the latter absent in Argasinae), with which they cling with wonderful tenacity to passing objects and animals. The pulvillum or pad permits even the ponderous gorged female tick to climb up vertical glass surfaces. The rostrum, with its beautiful structure, serves as a boring organ; the recurved teeth of the hypostome and the sharp denticles of the mandibles affording the tick a firm hold in the skin of its host, to which it may remain attached for a brief period (Argas), or for days.

Commencing with the egg, which is laid in recesses in the ground, the tick begins its chequered career, together with hundreds or, indeed, thousands of its fellows laid by its fertile mother. The period of metamorphosis, which ends in the hatching of the six-legged larva from the egg, is much influenced by temperature, being prolonged for months in cold weather. The larva creeps out, and, its chitin having hardened, it crawls upon the surrounding vegetation, there to play a wonderful game of patience, which may last for weeks or months, until it is disturbed into amazing activity by some passing animal, to which it promptly clings

as it brushes by through the tick-infested grass or shrubbery. The larva now seeks a suitable place upon the skin of its host, and in a few minutes may be seen boring its rostrum into the skin, and soon after it begins to suck the blood of its host. In some ticks, the larvæ having gorged, drop off upon the ground, there to undergo their metamorphosis into eight-legged nymphs, which in turn attack a fresh host in the manner described for the larvæ. This is the case, for instance, in *Haemaphysalis leachi*, which transmits canine piroplasmosis. In other ticks, the metamorphosis from larva to nymph may take place upon the host; this, for example, being the case with *Rhipicephalus annulatus*, which carries Texas fever. The nymph having gorged, may or may not drop off to undergo its metamorphosis upon the ground, emerging as a sexually mature tick. In the dog-tick just mentioned, then, the larva, nymph, and adult each drop off in turn when gorged, so that a single tick, to reach maturity, may be obliged to find and attack three different hosts. In view of the great loss of life this must entail in the ticks which fail to find a host, even after months of waiting, we can readily understand why a parent tick lays several thousand eggs. Starting with as many larvæ as there were eggs, it is certain in many cases that but few individuals survive to the adult stage, owing to the many vicissitudes to which they may be exposed.

The Effects of Tick Bites.

In a paper published in 1899, I described some of the effects of tick bites, and the accidents which may follow the attacks of various species of ticks on man and animals. Where an animal is attacked by large numbers of ticks, the cutaneous irritation and the loss of blood undoubtedly cause considerable injury. The seat of the bite is inflamed, and may serve as a point of entrance for infective agents. When ticks are forcibly removed, the rostrum may remain anchored in the skin and lead to serious consequences, which appear in some cases to depend upon infection from without; in others, possibly upon the toxic action of the embedded rostrum, with its attached soft structures. In other cases, toxic local or general effects have followed tick bites in a very brief period of time, suggesting the injection on the part of the tick of some poisonous substance into the wound. Some have attributed these effects to a toxic saliva, but it appears to me possibly due to disgorged

food residue. In any case, experimental investigation is needed to explain the cause of these effects. Cases are recorded in the literature of ticks boring themselves completely beneath the skin, and, in some instances, giving rise to the formation of abscesses, etc.; these seem to be exceptional occurrences.

Ticks as Disease Carriers.

There are several classes of diseases which are known at present to be transmitted by ticks. The diseases, which may be conveniently grouped under the class Piroplasmosis, being named according to the genus of parasites which cause them, affect a number of Mammalia, the protozoal parasites being apparently peculiar to each species of host. A disease of the domesticated fowl, analogous to relapsing fever in man, and likewise due to a spirochæte, has been proved to be transmitted through the agency of a tick. Heartwater, a disease affecting sheep and goats in South Africa, has also been communicated to these ungulates through the agency of infected ticks. In all these cases we have clear experimental evidence to go on.

The part played by the notorious *Argas persicus* in relation to a fever which occurs in Persia, and has long been attributed to the bite of this species of tick, also the grave effects attributed in Africa to the bites of *Ornithodoros savignyi* (Audouin), still require investigation. In both instances these ticks attack man. Further evidence is required with regard to the supposed part played by *Dermacentor andersoni* (Stiles, 1904) in the transmission of the disease known as Tick Fever of the Rocky Mountains. Reasoning by analogy, it is highly probable that species of tick will be found in the future to be the carriers of different species of Piroplasma. The discoveries in connection with the fowl disease above referred to are highly suggestive in their bearing upon the probable mode of transmission of relapsing fever to man. Although "louping ill" of sheep has been attributed to the consequences of the attacks of ticks, no positive evidence, worthy of serious consideration, has as yet been gathered in this respect.

In the Table on following page I have briefly summarised certain facts regarding tick-transmitted diseases.

When we come to consider the stage in its development at which a tick may transmit parasites, we find that this varies according to the species of parasite and species of tick concerned. In the diseases due to Piroplasmata, the

mother tick, having gorged on infected blood, drops to the ground in the usual manner, and in due course lays her eggs. These eggs are infected, and from them issue infected

Name of the Disease.	Animal Affected.	Geographical Distribution.	Tick Concerned.	Parasite Transmitted.
Texas Fever, or Redwater	Cattle ...	N. and S. America	Rhip. annulatus	Piroplasma bigeminum
		Africa, Queensland	Rhip. australis	,,
		Asia, Europe .	Ixodes reduvius ?	,,
Rhodesian Fever	Cattle ...	Africa ...	Rhip. appendiculatus	Piroplasma parvum
Carceag ...	Sheep ...	Europe ...	Rhip. bursa ...	Piroplasma ovis
Canine Piroplasmosis	Dog ...	S. Africa ...	Haemaphysalis leachi	Piroplasma canis
		Europe ...	Ixodes reduvius ? Dermacentor reticulatus	
Piroplasmosis .	Horse, Donkey, Mule	S. Africa ...	?	Piroplasma equi
		Madagascar ...	?	,,
		Venezuela ...	?	,,
		Germany, Italy	?	,,
Piroplasmosis .	Monkey ...	Uganda ...	?	Piroplasma nov. spec.*
Rocky Mountain Fever: Piroplasmosis ?	Man ...	Western U.S.A.	Dermacentor andersoni ?	—
Heartwater ...	Goat, Sheep	S. Africa ...	Amblyomma hebraeum (Koch)	Unknown
Spirochæte Disease of Marchoux & Salimbeni	Fowl ...	Brazil ...	Argas miniatus	Spirochæte Marchouxi

* Unpublished. See Paper by Philip Ross in forthcoming Number (January, 1905) of *Journal of Hygiene.*

larvæ ; but these do not necessarily convey the parasite in their larval stage of existence ; for instance, in the case of:—

Rhipicephalus annulatus (Say) and *Rhip. australis* (Fuller). The larval tick is able to transmit piroplasmosis to cattle.

Rhipicephalus bursa (Canestrini and Fanzago). Larva and nymph innocuous, adult infective to sheep, to which it communicates piroplasmosis.

Haemaphysalis leachi (Audouin). Larva and nymph innocuous, adult infective to dogs, to which it communicates piroplasmosis.

On the other hand, according to experiments cited by Theiler (1904), and work by Lounsbury:—

Rhipicephalus appendiculatus (Neumann). Fed as a nymph on cattle suffering from Rhodesian Fever, communicates the disease as an adult tick. If infected as a larva, it is infective as a nymph.

Again, in the case of *Amblyomma hebraeum* (Koch), which conveys the unknown parasite, which is the cause of Heartwater, Lounsbury (1900) states, that when the tick is fed upon an infected animal in the nymph stage, it communicates the disease as an adult. Or when fed in the larval stage, it proves infective as a nymph. In other words, as Mr. Lounsbury informs me, both in the case of Heartwater and Rhodesian Fever, the parasites are conveyed by the ticks—as he expresses it—"stage by stage." Nothing is known regarding the life-history of the parasites above mentioned within the bodies of the ticks.

On the other hand, in the case of the spirochætes of the fowl, these protozoa appear to multiply in *Argas miniatus*. When in Paris some months since, Dr. Borrel, of the Pasteur Institute, informed me that the spirochætes, after entering the stomach of the tick, together with the blood from the diseased bird, wander out through the stomach wall of the tick, and are found swimming about in the tick's blood; in a similar manner to what they do in the blood of the vertebrate host. The *Argas* does not become infected, and consequently infective, subsequent to feeding on spirochæte containing blood, unless it is maintained at a suitable temperature, say of 30 deg. C. As Dr. Borrel showed me in Paris, it is easy enough to demonstrate if a tick is infected or not. This is accomplished by snipping off the extremity of one of its legs, and examining the drop of blood which escapes for spirochætes.

Persistence of the Parasites in Ticks.

Once infected, *Argas miniatus* is capable of harbouring the parasite for a considerable length of time, and consequently of communicating the disease to a healthy fowl five or more months after it has ingested spirochæte containing blood. The mechanism whereby the spirochæte issues from these ticks into the vertebrate host is as yet unknown.

Observations on ticks harbouring Piroplasmata show that the latter may persist for months in the tick. For instance, in *Haemaphysalis leachi*, the *Piroplasma*

canis continues not only to live through all the stages of development of the tick from egg to adult, as Lounsbury showed—and this may be for many months—but it persists a long time in the adult tick. Working in Cambridge with adult ticks sent me by Mr. Lounsbury, I found them still capable of setting up a fatal infection in a dog, after they had been kept unfed, as adults for a period of seven months at room-temperature. As a number of these adult ticks died during these months, and the survivors proved infective, it is reasonable to conclude that the Piroplasma only died with the tick. Redwater can be communicated by larval ticks which have starved for months.

Incubative Period.

In all the above tick-transmitted diseases, the attack of the tick is succeeded by a period of incubation of several days. Experiments made in the laboratory with infected ticks have shown results comparable to those observed in nature. They are, however, necessarily more accurate.

Disease.	Incubation in Days.	Observer.
Texas Fever	10	Smith and Kilborne (1893).
Rhodesian Fever ...	8	Theiler (1904).
Tristeza	12 to 28	Lignières (1900).
Sheep piroplasmosis ...	5 to 6	Motas (1904), fever and parasites on tenth day.
Canine piroplasmosis ...	13 to 21	Lounsbury and Nuttall (1901 to 1904).
Heartwater	11 to 35	Lounsbury (1900).
Fowl Spirochæte Disease .	4 to 7	Marchoux and Salimbeni (1903).

The Piroplasmoses.

The diseases affecting cattle, sheep, deer, equines, dogs, and apparently monkeys, and possibly man, are grouped together as piroplasmoses, for the reason that they are caused by parasites, which at present are classed under the genus Piroplasma. The Piroplasmata are Protozoa, and, as their generic name implies, resemble each other morphologically in that they are pear-shaped, micro-organisms, occurring singly or in pairs, or more or less even-numbered groups of four to sixteen individuals within the infected animals' red blood corpuscles. Besides the typical pear-shaped organisms, spherical forms may be encountered, which resemble young forms of human malarial parasites. Working with *Piroplasma canis* in Cambridge, Dr. Graham-

Smith and I have observed large sausage-shaped extracellular parasites occasionally. These forms offer a certain resemblance to our malarial crescents, and it appears likely to me that they represent gametes. These forms have not as yet been described. The intracorpuscular piroplasmata, at certain stages of their development, apparently before they take the pear shape, may show active amœboid motion. Stained by modifications of the Romanowsky method, the protoplasm stains blue, the nucleus red. The protoplasm may show vacuolisation. In extravascular blood, Lignières described the occurrence of flagellate bodies in bovine piroplasmosis, "la Tristeza," of South America. Bowhill has since observed similar bodies in connection with other species of piroplasmata, and has been the first to photograph them. The significance of these bodies requires explanation, although from what we know of human malarial parasites, it seems tempting to make comparisons.

The parasites which occur in the horse and in Rhodesian fever appear to me possibly different to the others. Injection of large quantities of blood containing these parasites into susceptible animals appears, as a rule, to be without effect. The parasite of Rhodesian fever behaves differently with regard to ticks than do the others. The parasite is, moreover, different in its morphology, as we shall presently see. With the exception, then, of the equine and the Rhodesian-fever parasites, and the parasites affecting the deer, man, and monkey, about which we want more knowledge, we find that infection is readily set up by inoculation of blood containing the piroplasmata, affecting cattle, sheep, and dogs in different parts of the world.

If we, moreover, compare the last-named diseases with regard to their symptomatology and pathology, we are at once struck by their great similarity. In all we have the disease ushered in by fever, often preceded by the appearance of the piroplasmata in the blood. There is a great destruction usually of red-blood corpuscles, and the serum is tinged with hæmoglobin, which finds its way into the urine. Hæmoglobinuria is a usual, but not invariable, symptom. This also holds for the icterus. The animals show loss of appetite, prostration, accelerated breathing; the mucous membranes are pale; emaciation is especially marked in chronic cases. A fall of temperature far below normal precedes death. At autopsy the blood is found to be thin and watery, the serum tinged with hæmoglobin; the spleen and liver are often much enlarged and congested, etc. The gross pathological lesions in the organs may, how-

ever, be very slight. The blood count may show a reduction in the number of red-blood corpuscles to one-third, or less than the normal.

Immunity follows recovery; but the term immunity must be understood in a relative sense only, for the reason that the parasites, although not demonstrable microscopically, may persist for a long time in the blood of animals which have outwardly everyappearance of health. That the parasites are present in recovered animals can be demonstrated by inoculation of their blood into susceptible animals. In this manner, Schroeder, in the United States, was able to demonstrate that the parasites of Texas fever persisted in the blood of recovered animals, so-called immune animals, for six to eight years. In other words, the condition is one of latent infection. That this is the case has also been shown in Turkey, South Africa, and the Transcaucasus, where attacks of Rinderpest have been seen to lead to a recrudescence of the piroplasmosis in animals known to be "immune" to Redwater. Similarly, exposure to cold, fatigue, or other inimical conditions may lead to a recrudescence of the disease after long intervals of apparent health. Quite recently it has been observed in the Philippines, by Jobbling and Woolley (1904) that apparently healthy cattle, imported from China, harboured piroplasmata, for inoculations with their blood into healthy cattle imported from the northern United States resulted in the latter developing piroplasmosis. Similarly, in canine piroplasmosis, Robertson (1902) has found the blood of dogs infective up to four and a-half months after recovery. The significance of this persistence of the parasites will be the more appreciated when I add that the "recovered" animals may serve as fresh centres of infection of the ordinary carrying agent of the disease, the tick, and this for an indefinite time.

Epidemiology of the Piroplasmoses.

It has been observed in connection with Redwater, canine piroplasmosis, etc., that the disease is one of locality. Cattle are prone to acquire the disease in certain low-lying pasture lands, the dangerous area being at times quite clearly marked by the fence which limits a given field. Stabled cattle escape the disease. Dogs which are taken out hunting in certain districts acquire the disease, whilst those kept in town escape. The piroplasmoses occur especially in the spring and summer, this corresponding to the period when ticks are found upon their hosts. Animals indi-

genous to the soil are relatively resistant, this being doubtless due to their having grown up continuously infected from youth. The behaviour of the piroplasmoses in this respect reminds us of what has been observed in human malaria. Calves are more resistant than adult animals; in fact, as age advances, cattle appear to become more susceptible, for the disease is frequently observed in old cows living in endemic areas. In the case of the canine malady, on the other hand, the disease is more fatal to puppies than to adult dogs.

The influence of locality, season, etc., on the prevalence of these diseases is readily understood when we consider the biology of the ticks which carry the infectious agents.

Rhodesian Fever of Cattle.

The bovine piroplasmosis known as Rhodesian or East Coast Fever of South Africa is possibly identical with the "tropical piroplasmosis" of cattle observed in Transcaucasia this year by Dschunkowsky and Luhs. The parasites differ from those encountered in Texas fever or Redwater, and the pathology of the disease is not the same. Cattle immune to Texas fever are susceptible to Rhodesian fever. The parasites of Rhodesian fever are smaller than those described in Redwater, and Theiler (1904) considers them a different species, to which he gives the name of *Piroplasma parvum.* Whereas Redwater is readily communicated to healthy animals by inoculation with blood containing *P. bigeminum,* corresponding experiments with blood containing *P. parvum* have proved negative, even when injections of huge quantities of infected blood were practised (Theiler, Dschunkowsky and Luhs). These facts alone indicate that we are dealing with distinct diseases which are set up by different parasites. It is, moreover, highly probable that what we call *P. bigeminum* to-day is actually a collective term for several parasites belonging to different species. The determination of these species may not be possible on morphological grounds alone; we have to call in aid the species of tick which transmit them, as also the test of immunity in animals. It is not at all impossible, it appears to me, that a similar view will have to be held in the future with regard to human malarial parasites, which have hitherto been regarded as single species.

Returning to *P. parvum* (Theiler), I would state that it occurs in spherical, bacillary, and intermediate forms, and

that it reacts like the other species of Piroplasma to Romanowsky's stain. The disease is especially fatal; Koch (1904), for instance, stating that the loss in infected herds commonly amounts to 90 per cent.

Mixed Infections.

As Theiler points out, mixed infections with *P. bigeminum* and *P. parvum* may occur, a fact which has certainly led to both species having formerly been considered one by Koch and Laveran. There is further reason for such confusion in the statement made by Theiler that the inoculation of *P. bigeminum*, contained in the blood of recovered cattle, into calves, gives rise to the appearance in their blood of parasites resembling *P. parvum*, alongside of the typical *P. bigeminum*. Moreover, the latter parasites in the blood of salted cattle resemble *P. parvum*. This peculiar appearance of *P. bigeminum* would seem to depend upon inimical conditions operative in the bodies of salted animals.

I have already referred to the co-existence of Rinderpest and Piroplasmosis in cattle. Animals may harbour Trypanosomata and Piroplasmata, or the latter and Spirochætes. Similarly in horses, we may find mixed infections. Thus, in a specimen of blood recently photographed by Mr. T. Bowhill, at the Cape, a picture of which I shall project upon the screen, you will see *Piroplasma equi* present, together with embryo Filariæ, and this in a horse that died of horse-sickness! It will be readily understood how confusing such observations are, and how easily an investigator may fall into error regarding the actual cause of a disease.

Spirochæte Disease of Fowls.

The disease of fowls observed by Marchoux and Salimbeni (1903) in Brazil, and which they succeeded in transmitting by means of infected *Argas miniatus*, is one of considerable theoretical importance. The disease is usually very fatal and acute. The affected birds suffer from diarrhœa, anorexia, somnolence; the comb is pale, the birds lie down and die in convulsions. The disease may be subacute, lasting eight to fifteen days, during which the bird becomes emaciated, and paralysis appearing first in the legs, extends to the wings. Recovery is rare, either in the acute or chronic form. Fever appears at the onset, and lasts four to five days (42-43 deg. Cent.), then it falls to below normal before death. When recovery takes place, the temperature gradually returns to normal.

At autopsy, in acute cases, the liver is found greatly enlarged, fatty, and showing focal necroses. The other organs appear normal. The blood is claret-coloured and fluid. In chronic cases all the organs, even the liver and spleen, appear atrophied.

The spirochætes multiply up to the death of the animal, finally occurring in agglomerations and in great numbers in the blood. Corresponding with the crisis which ushers in the commencement of recovery the parasites disappear, owing to causes apparently similar to those which operate in relapsing fever in man. The spirochætes resemble *Sp. obermeieri*, and little is known about them. Their position amongst the Protozoa is as yet undetermined. Suggestive in this connection is the recent work of Schaudinn (1904), who has described a spirochæte-like stage developing out of a Trypanosoma, which represents in turn a stage in the life-history of an endoglobular parasite of birds, the Halteridium.

Contrary to what has been observed hitherto in the Piroplasmoses, the spirochætes appear to be less selective with regard to the species of host. For instance, human relapsing fever has been communicated to monkeys (Cercopithecidae); and the avian spirochætes here referred to possesses a fairly-wide range of pathogenicity amongst birds other than fowls. Thus, Marchoux and Salimbeni, and Levaditi (1904) more recently, have been able to infect the goose, duck, turtle-dove, pigeon, sparrow, lark, etc., with the new spirochæte; I say "new," for the reason that it appears to be different, in pathogenicity at any rate, from *Sp. anserini* of Sakharow. Nevertheless, this apparent wider range of pathogenicity amongst birds may receive a partial explanation in the fact that birds belong to a group of relatively closely-related vertebrates.

Contrary, again, to what has been observed in Piroplasmosis, there is no evidence that the spirochætes persist in the body after recovery; moreover, the immunity acquired after an attack is but of brief duration.

Immunisation.

The subject of artifically-induced immunity has naturally engaged the attention of many workers, more especially with regard to the piroplasmoses of cattle, dogs, and sheep. It was already observed by Smith and Kilborne (1893), with regard to Texas fever, that recovered animals remain protected in a large measure in succeeding years, and that

animals which have suffered from the disease when young appear to remain protected longest. They found that animals inoculated with Texas fever blood in winter acquired a milder form of the disease, and remained protected. Since then an extensive experience has been gained in different parts of the world, cattle receiving inoculations of blood from animals suffering from mild Redwater, or the blood of "salted" cattle (preferably calves), being used for preventive inoculation. The loss from these inoculations may vary from 3 to 25 per cent.; but this is small compared to, perhaps, the complete wiping-out of unprotected herds in which the disease may appear. Whereas this mode of preventive treatment seems justified in regions where the disease is endemic; it seems scarcely justified otherwise, in view of the fact that "salted" animals are a source of danger for years, wherever they go if accompanied by suitable ticks, which can convey the parasite to healthy animals.

In the case of Rhodesian fever, immunity has not been produced artificially with success of a practical character. Koch (1904) recommended repeated inoculations with recovered blood; but experiments conducted on a scale of 5000 animals have been deemed sufficient evidence of the method being a failure by the veterinary authorities in South Africa (Gray, VII., 1904; Theiler, XI., 1904).

Finally, treatment with the serum of immune animals cannot be said to have afforded results promising to have any practical value. Nevertheless, it may be noted that Nocard and Motas considered that inoculations with the serum of hyper-immunised animals afforded protection in canine piroplasmosis. More recently, Motas (1904) has carried out corresponding experiments with sheep piroplasmosis; but here again the results do not seem promising from a practical standpoint. It is impossible here to enter more fully into the problems relating to immunity in these diseases.

It would lead me too far afield to fully discuss the work that has been done on immunity in connection with spirochæte infections. Confining myself to the spirochæte disease of fowls referred to previously, I would state that Marchoux and Salimbeni report that infected serum heated five minutes at 55 deg. C., or infected serum kept two to four days at room-temperature, is not infective but protective. Fowls immunified therewith yield a protective serum. They also protected animals by inoculating them with a mixture of immune serum and blood containing

virulent spirochætes. Immune serum proved of no value therapeutically. Levaditi has, however, claimed since, that immune serum may hasten the crisis. Immune serum agglutinates and immobilises the spirochætes.

Prophylaxis.

Apart from necessary attempts to produce immunity in animals exposed to infection, there are several measures of prevention which have been recommended and actually resorted to in connection with piroplasmosis of cattle. Morgan (1898) advises that infected pastures shall not be used for grazing cattle on for a year. He gave this advice for the reason that cattle placed on such a field after it had been used for pasturing horses and mules for two years, did not develop the Texas fever. Lignières (1900), from his South American experience, recommends the sowing of clover on pastures. It appears possible that the changed vegetation may exert an influence, and the experiment is worthy of trial in suitable cases. The fencing-in and drainage of infected land has caused the disease to disappear in parts of Finland. Quarantine measures have been extensively adopted in the United States, in view of long experience proving that cattle driven northward from the endemic areas carried the infection with them. The disuse of fields, as recommended by Morgan, has an obvious scientific basis, for the ticks will die out in the absence of suitable hosts; or if they survive by attaching themselves to other hosts, they will, with time, cease to harbour the parasite they transmit. Destruction of ticks by burning of the grass on infected pastures in the autumn has also been advocated. Finally, dipping cattle has been resorted to on an extensive scale. In the latter case the cattle are driven through tanks, in which they may be obliged to swim in a bath containing constituents such as mineral oil, glycerine, sulphur, arsenic, etc. The process may have to be repeated several times. Unfortunately, the dip has its disadvantages; a certain number of animals are injured, and ticks adhering about the head are not affected. Nevertheless dips necessarily serve a useful purpose in lowering the number of ticks on animals.

Note Regarding the Geographical Distribution of the Piroplasmoses.

I have attempted, in the accompanying map, to give a general idea of the wide distribution of the piroplasmoses in different parts of the world. Most of the blackened areas

refer to bovine piroplasmoses. The distribution of the forms of piroplasmosis affecting different animals, exclusive of countries where diseases having similar symptoms occur, is about as follows :—

Bovine piroplasmosis (Redwater, Texas fever) occurs in the United States, West Indies, Southern Venezuela, Uruguay, Paraguay, Brazil, Queensland, various parts of Africa and Europe, India, China, the Philippines.

Rhodesian fever occurs in Rhodesia and the South-East Coast regions of Africa ; apparently also in Transcaucasus.

Ovine piroplasmosis occurs in Roumania, Italy, France, West Indies, the United States, South Africa.

Equine piroplasmosis occurs in South Africa, Madagascar, Germany, Venezuela.

Canine piroplasmosis occurs in Italy, France, North and South Africa, India.

Discussion on Dr. Nuttall's Paper.

Sir Patrick Manson : I have no doubt, gentlemen, that you will concur with me in expressing an appreciation of the exceedingly interesting, and, I might say, important paper which we have listened to, and the beautiful demonstration that Dr. Nuttall has given us.

Before I was invited to occupy the dignified position of presiding on this occasion, I was asked to open a discussion on Dr. Nuttall's paper. I suppose the fact of my promotion will not invalidate that arrangement: at any rate, I shall assume it does not.

There are many points in Dr. Nuttall's paper that suggest discussion, more particularly, to my mind, the bearing of the facts he has adduced on human pathology. I have noted a few points, and although I will not venture to discuss them all, there are one or two that I should like to mention. What struck me first was that the symptoms of piroplasmosis are exceedingly like those of that most important disease affecting man in hot climates, viz., blackwater fever. The occurrence of hæmoglobinuria and icterus, which are almost characteristic of piroplasmic diseases, are also the two most characteristic and important symptoms in blackwater fever. This is usually put down as a malarial disease, and there is a good deal of evidence in favour of such a supposition. But there is also a certain body of evidence tending to show that, even though it be malarial, this infection is not the only cause, or rather is not the entire cause of blackwater

fever: it may be a determining cause of the explosion and manifestation of the disease, but it is not the essential microbic cause of the malady.

Dr. Nuttall mentioned just now the fact (now generally recognised) that animals infected with piroplasma, yet apparently immune from symptoms, can be induced to manifest the characteristic pathological effects of piroplasma infection by inoculation with some other micro-organism, by exposure to cold, or by any other similar strain upon the physical powers. Exactly the same thing has been noticed in the case of blackwater fever, suggesting the hypothesis that this, too, is a tick infection which for a long time remains latent, until some intercurrent circumstance, such as a malarial attack, an overdose of quinine or exposure to cold, sets the latent parasite off, so to speak, on its pathogenic course. That idea has long been present to my mind, and Dr. Nuttall's remarks have accentuated it.

An excellent object of investigation, then, would be the hypothetical piroplasma of blackwater fever and the tick, or whatever intermediary it may be, that transmits the disease.

I was rather disappointed in one part of Dr. Nuttall's paper: I had hoped that he would give us some information about a curious disease that they get along the course of the Zambesi, and which is certainly produced by a tick, known as the Garrapato disease, and was first noticed by Dr. Livingstone; but it has since then been observed by many others —Sir John Kirk and Dr. Daniels, for example.

Looking over some papers, two or three days ago, I came across a letter from one of my old students, Dr. A. Park Ross, at the School of Tropical Medicine, who has recently gone out on a Boundary Commission to the Zambesi region. When I heard that he was going there, I requested him to make some enquiries on this particular subject—Garrapato disease. This is his letter; it is of so much importance that I take the liberty of reading it.

"River Loangwa, Lat. 15° 5′, 25th August, 1904."

"I ought to tell you that opportunities of doing medical or scientific work here have been few, and the following is as far as I have got with the Kufu disease (Kufu is the native name for Garrapato). The latter is not nearly so common as I was led to expect at Tete, and the reasons for the belief in its almost universal prevalence in this country are—first: that Kufu (that is, the tick) occurs in almost every dirty village (and these are many); and, secondly: that the natives ascribe almost every serious disease to it, in consequence of which I have had several wild-goose chases after it.

"The following clinical description of the disease, is taken from the statements of four exceptionally intelligent natives, each from a different part of the country, and each of whom has had the disease.

All their statements tallied. I required no interpreter, and took care to ask no leading questions.

"The disease extends from Angoni Land westwards, at least as far as the confines of North-western Rhodesia. It shows no preference for high or low ground, as it occurs in the Tanganyika Plateau, 5000 ft. above sea level, and on this river 1000 ft.: it occurs also at Tete, 340 ft. above sea level. It occurs during the rains, December to March; but is much more prevalent during the dry season. I could elicit no information as to its occurrence in epidemic form. Cases occur sometimes among the Kufu-infected villages, but the great majority occur in strangers sleeping in such villages, whose own villages are not infected. On the other hand, many of the villages infected with Kufu do not report the sickness, and the natives invariably say that sometimes bites produce sickness and sometimes not. It is impossible to get at the infant mortality in such a village, and the information as to whether Kufu is a factor would be unreliable if derived from any other source than a European doctor. Curiously, the idea was suggested by a native that a universal infection in childhood in such villages was the cause of the relative immunity of adults. Natives living always in infected villages do not consider themselves likely to acquire the disease, whereas natives whose own villages are not infected are very careful as to sleeping at huts in an infected village.

"The Kufu inhabits the dry earth in native huts, and can be found during the day about two inches below the ground, generally close to a hut-post or bed-post. It does not bite during the day, or where there is light (as I have proved myself).

"The following account was given by our interpreter, an intelligent man, who had had the disease, and it was corroborated by three of our personal servants, who also had had it. The bite produces irritation for two or three days, during which the patient otherwise feels well. On the third or fourth day fever begins: there may or may not be a rigor, but there is always violent headache and severe pain in the small of the back, and in the bones and joints generally. None of these boys admitted gastric pain, but one said he felt inclined to vomit. There is copious waterish diarrhœa, of a very dark colour, and the urine is also dark. (I would not like to pin my faith to the last statement, but three of the four were positive upon the point.) The pain in the back disappears when once the diarrhœa is established. This condition lasts for about two weeks, after which recovery is complete. I can elicit no history, and can see no signs of sequelæ. One attack confers immunity. A pregnant woman may, and generally does, abort during an attack. The disease is much more severe in children and in old people.

"Now, as to what I have seen myself. I first got on the track of it at Misah, when it was reported at Fort Young, 25 miles distant; but, on arriving there, I found the infected huts burned, and the natives could not, or would not, show me a case. At Fort Jameson, Dr. Cole showed me two cases sent in as Kufu, which were really suffering from another disease.

"I have twice tried to inoculate myself, but each time without result. I got three ticks in a house in Fort Jameson, which natives said was recently infected. I fed them on blood, but only one would bite: the other two refused to bite, and died. At Fundas village there were Kufu in every house. None of the people were ill, but a stranger coming there two weeks before had the disease, and had been carried away to his own village, where I could not follow him. I took four active ticks from this house, and put them on my arm in order that

they might bite. I found that when exposed to the sun they would not do so, but began at once when a cloth was put on them. The pain of the bites was not very perceptible, and I should have doubted their activity had not each tick swelled up like a balloon. When collectively they had withdrawn about half a c.c. of blood, I separated them with tobacco smoke: the bites were indicated by purple patches due to extravasated blood under the skin, and enough blood to make a film exuded from one of them. I covered the bites with a soft bandage: there never was the slightest irritation, and in three days the blotches disappeared. In seven days a little pink papule appeared over each bite; this lasted for several days and then disappeared. A fortnight has now passed, and I have never felt any symptoms of any kind.

"I was informed in Tete that, some years ago, tick fever was a serious deterrent to the slave trade. Dr. Livingstone's statement as to death occasionally occurring, I had corroborated by natives and in Tete; but the former allege that the disease is not so common as in the days of their forefathers. There are not so many villages burned for it. I have only seen two in some 4,500 square miles of country. An old man said it was not always in the country, and came from the north."

This Garrapato disease is certainly a subject well worthy of investigation, and I hope that anyone who has an opportunity of studying it will not fail to take advantage of it.

One word before I close these observations. What struck me about Dr. Nuttall's paper — and, indeed, about the entire subject of tick diseases and protozoa diseases of man and the lower animals—is the enormous extent of the subject and the rapid growth that it is undergoing. This fact we have recognised for some time at the London School of Tropical Medicine; and with the view both of giving instruction to our students and of advancing the study of the subject, we have determined to institute two Chairs, one dealing with protozoa and another dealing with Helminths. We hope to still further advance the subject in that way, and prepare men who may be of value as investigators. This, I think, is a step in the proper direction; but I think the subject is so extensive and important that the medical profession generally should recognise it more definitely than they do at present. I think Chairs of, say, Medical Zoology and Medical Haemology ought to be instituted in our great Universities, more particularly in the University of London. I think it would be a good thing if this Society could give expression to some idea of that sort.

Dr. Theodore Thomson: It is very kind of you to call upon me, but my sole acquaintance with ticks has been a strictly personal one, and I regret to state has not been so painless and so little disturbing as that of your friend in

Africa. I have practically no knowledge as to ticks, and therefore I can say nothing about the subject.

Dr. Bentley: I have had very little experience of tick-produced diseases. I have, however, met with two species of piroplasmosis in dogs in Assam, one of which showed a very small parasite, occurring sometimes in couples and sometimes in threes and fours in a corpuscle, apparently answering to the description usually given of the piroplasmon in cattle. Another kind was much larger, about three μ in diameter. The first variety I mentioned I saw in an acute attack that took place in a dog that had been brought from England the previous year. This dog was brought to my bungalow by the man who owned it, and who had noticed that it was suffering from severe anæmia, and, apparently, symptoms of syncope. I took its temperature, and found that it was suffering from fever at the time: on making blood-films I found an enormous number of small parasites, which occupied nearly every one of the corpuscles. The dog died in three days; it suffered a good deal, and showed signs of icterus and hæmoglobinuria. It struck me at the time that the symptoms of this case very much resembled those of blackwater fever which one sees described in text-books. That is all I can add to the discussion.

Professor W. J. Simpson: I am afraid I cannot make any remarks on this interesting question, further than to say that it seems to me rather alarming that the inoculation should spread the disease rather than prevent it, especially in the case of this Rhodesian fever. It is quite evident that some other kind of treatment will be required; and it would seem that it should rather be sought for in something similar to the quinine which is used for malarial fever rather than in inoculation, which is so effectual in other diseases.

I have listened with great pleasure and also with very great benefit to a most interesting lecture, and I thank Dr. Nuttall very much for it.

Dr. G. C. Low: I have listened with much pleasure to Dr. Nuttall's paper. This subject is now becoming of much more importance, both from the animal point of view and from the human point of view also. We have seen an enormous destruction of cattle and other animals brought about by tick diseases: and we know that much valuable

work has been done in America in connection with this subject in recent years.

I have heard recently from the principal medical officer of Natal, who tells me that tick diseases are killing off 90 per cent. of the cattle in some parts of the country: it is manifest, therefore, that these diseases will do an enormous amount of damage to colonising in that district. It is of great importance that we should know how the disease is spread, and, if possible, find some means to prevent it.

Some of the observations which Dr. Nuttall has made are of extreme importance and interest. One that struck me as very remarkable was that ticks kept for several months retain the parasite, and are able, on biting dogs, to produce disease. That shows how difficult it may be to stamp out the disease, if ticks retain their life so long.

With reference to Garrapato disease, I have recently had letters from a friend in Uganda, who has made some investigations as to that disease. He had six cases of it under observation; and after a very careful and prolonged examination, he was able to demonstrate the presence of a *spirillum* in all the cases. He has put forward the idea that this disease may be a *spirillum* one, and that on very good grounds: and it is by no means improbable that this tick disease is also spread by argas. My friend is going on with the work, and he will no doubt make further observations and experiments. The disease corresponds very closely to another disease, which comes after having slept in huts or houses in which ticks have been found. It is a fever, accompanied by intense pain and vomiting, and also by diarrhœa. After a few days the patient gets better, but there is often a relapse, with fresh attacks of fever. I think that is an exceedingly interesting observation, and one which will probably prove that the disease is really a *spirillum* disease.

Another point of interest one might mention is with respect to the question of blackwater fever, viz., the wonderful and peculiar local distribution of this disease in certain places. When I was in Uganda, there was a town at the end of the lake where everyone had blackwater fever. I have also known a special hill, and anyone living on this hill was almost certain to get blackwater fever, whilst the district all round was free from it. When I went there, there was no blackwater fever, but one day two cases occurred on this hill again. In the light of what we have heard, we may say that probably the ticks

always infect this hill: that they do not bite for some time, but that eventually they do bite and spread the disease.

There are plenty of ticks, of course, in Africa: it might even be this argas that has something to do with it, or some other tick. It is certainly a disease well worthy of further investigation, if one considers the vast mortality and loss of life due to this disease in Uganda and East Africa. It is spreading greatly, too, in Northern Nigeria.

There are many points in regard to the internal anatomy, and in regard to the development and spread of piroplasma through the tick, which still require working out. The anatomy is, as Dr. Nuttall has said, a very difficult subject, owing to the very strong integument which covers the insect. It is a subject that has apparently a large future before it, and we all look forward with great interest to future work on the tick question.

Dr. Nuttall: There is very little to say in response to what has been said. Sir Patrick Manson's suggestion with regard to blackwater fever is extremely interesting and very suggestive. It may be that we are dealing with parasites that are ultra microscopic—but it needs investigation.

With regard to Garrapato, I can only say that the question needs more investigation than has yet been given to it. I think that is where we stand at present with regard to all these things—they need more investigation. The subject of this disease is exceedingly suggestive, as also is this so-called disease due to argas, but we need more evidence—it is all very vague.

What Dr. Low has said brings out still more strongly the need of investigating these diseases. Dr. Philip Ross is now doing some work in this direction.

In answer to Professor Simpson, I may say that, unfortunately, quinine has no effect whatever, and at present nothing has been found that has any beneficial effect. A great many things have been tried, but nothing has been found to be of any use.

As to the remarks of Dr. Bentley, I would say that his description tallies exactly with what we have observed. Just as in cattle diseases, so in the tick, we have different forms of piroplasma.
