T H E S I S

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A STUDY ON THE ETIOLOGY

of

Certain Affections of Obscure Nature

which may follow upon

TICK-BITE

in

Man and Animals.

INTRODUCTORY.

Ticks: their association with Disease.

The Ixodoidea; Ticks; or Wood-lice as they are sometimes termed, although the last name is justified by their habits in but a limited number of species; constitute one of the divisions of the order Acari. They differ from all other members of this order, however, in being of much larger size, more especially when in the engorged state.

During the life of the individual tick several periods must be spent parasitically upon the body of a land host, by preference a bird or mammal. But they are by no means confined to such narrow choice, for they are not infrequently found on reptiles, and occasionally even upon invertebrates. The same species of ticks, in fact, may be found upon various hosts in different places.

With few exceptions the separate species have a very limited geographical distribution; yet some, as for example Argas persicus, have a widespread range of prevalence. This is

probably to be accounted for by the fact that many migratory birds are suitable hosts. The order as a whole, on the other hand, is distributed throughout all latitudes and on every continent; but it is chiefly in tropical and sub-tropical countries that its members are of pathological interest.

Ticks have been known from very early times as the cause of painful and occasionally dangerous bites in the human subject, and as a pest amongst domestic animals. They are mentioned as far back as the period of classical Greece by various authors. Aristotle referred to their being commonly found upon cattle, sheep, and goats; to the immunity of the ass; and to the infestation of dogs with the variety, called "Cynoraistae". Cato spoke of the treatment of sheep, with removal of the ticks, as producing more and better wool. Columella referred to the removal of ticks from cattle by the application of liquid tar, with a view to the prevention of ulceration: whilst Varro recommended inunction of the ears and toes of dogs, because flies, ticks, and fleas, were liable to cause sores on those parts.

Until the later years of the nineteenth century, however, the ticks remained without any greater significance than that of being objects of annoyance and trouble to graziers; and of disgust or semi-superstitious fear to others. Only then was it that their enormous economic importance to pastoralists, and to dwellers in certain countries of warm climate, became recognised.

Soon after the discovery by Laveran in 1880, of the blood parasite which is the effective cause of malarial fever, there arose a suspicion that the mosquito was responsible for the transmission of that disease, a view which was discussed and urged by King so early as 1883. (22)

Out of this belief there arose a new interest in, and there was lent an increased suggestiveness to, the question of the rôle of blood-sucking parasites in the causation of communicable disease.

Although it was not until nearly twenty years later that Ross and others demonstrated with certainty the part of the mosquito in relation to malaria, the activity consequent on this new interest had been bearing

fruits in the interval. One of the first of these was the discovery by Kilborne in 1889 of the agency of a tick - the Boöphilus annulatus - in the spreading of one variety of haemoglobinuric fever in cattle (Texas fever). (21) The way had been prepared for this success by the demonstration shortly before, by Theobald Smith, of the specific cause of the disease, namely, the Piroplasma bigeminum. (55)

The co-extensiveness in distribution of tick infestation and of this dread scourge of the cattle ranches of America and other countries had often been observed; but only now was the connexion shown as a scientific fact.

The next advance was the discovery by Marchoux and Salimbeni of the nature of spirillosis in fowls, and of its transmission by one of the Argasidae. (35) Our knowledge of the significance of ticks in relation to disease in man, in its turn, received great accession; and that, chiefly through the observations on African relapsing fever, by Ross and Milne in Uganda. (52)

In consequence of these discoveries, there has been of recent years, a great amount

of attention devoted to the acquirement of information regarding the ticks themselves, and to the devising of means for their systematic destruction. In spite of much labour, however, our knowledge of many problems associated with tick infestation is still vague, more especially in relation to a number of less frequent and very diverse minor affections attributable to them, which have been reported from time to time as occurring in man.

It is to such affections, and to certain closely related ones in animals, that I shall direct my attention in this paper.

My notice was first attracted to the subject by an unusual case of tick-bite in a little girl, that came under my observation; and later by the analogy of cases in some of the lower animals, which I have seen while practising in Queensland, a country where tick infestation is prevalent among cattle, sheep, and domestic animals generally.

This has induced me to make an enquiry into the history and state of existing knowledge of those members of the sub-order Ixodoidea which have been accredited with the production of pathological conditions in man

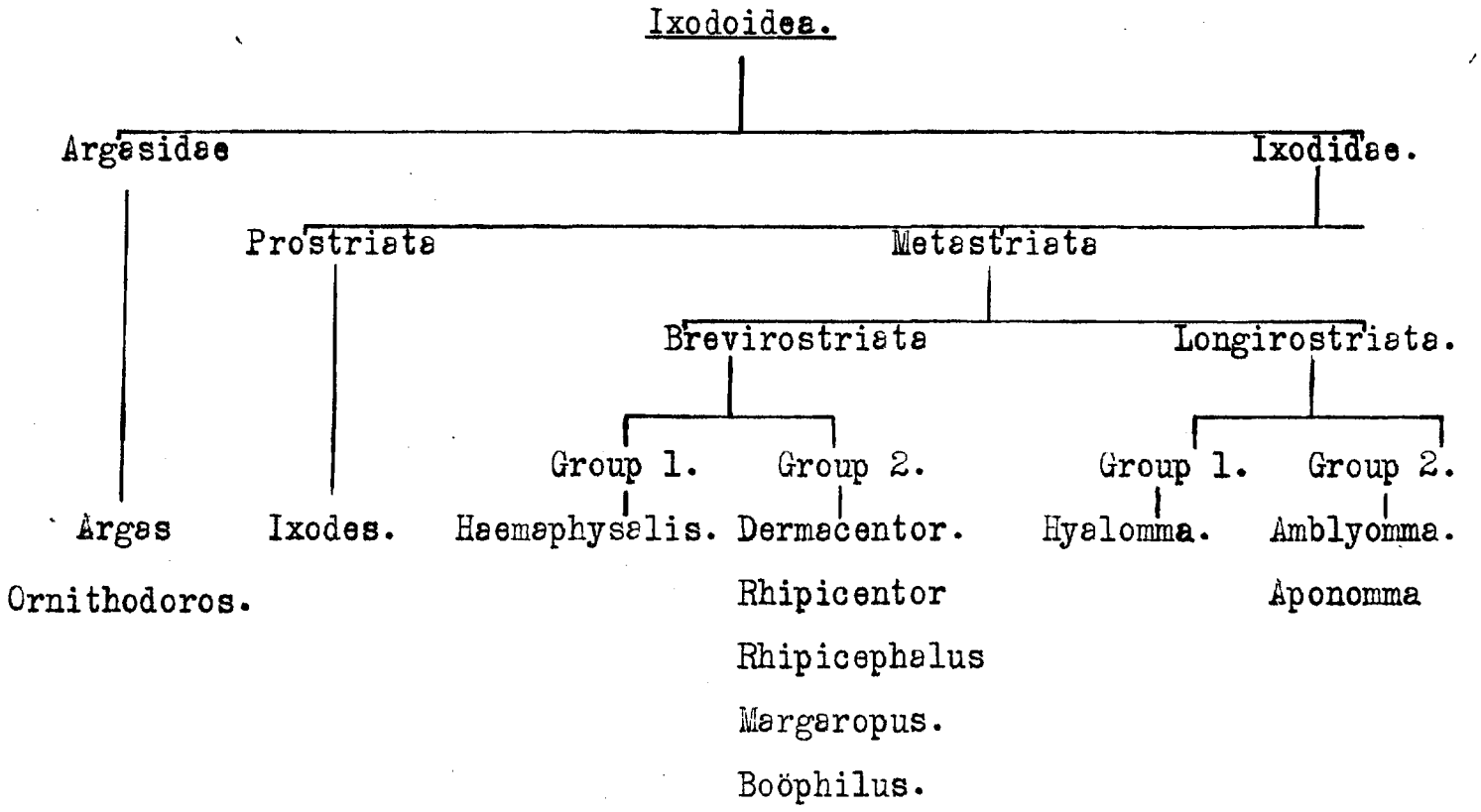
and other vertebrates.

The biological aspect of the subject has been studied extensively by members of the veterinary staffs of the various American and Colonial Government Agricultural Departments; and to them we owe the greater part of our knowledge of the ticks, and of the tick-borne infective diseases of animals. Two diseases in man have also attracted much attention, namely, South African Relapsing fever and Rocky Mountain Spotted fever; the former having been fully worked out, whilst the latter is, in respect of its ultimate cause, still obscure. Descriptions of the lesser affections, and more particularly of those of infrequent occurrence, are to be found, however, chiefly in disconnected reports of cases scattered throughout the periodical literature.

C L A S S I F I C A T I O N.

In 1795 the name "Tiques" was first used by Latreille in reference to the order Acari, two of the genera of which he named, respectively, Argas and Ixodes. In 1844 Von Koch withdrew the ticks from inclusion under the Acari, and constituted them a distinct order with name "Ricini", and within this he included three genera:- "Argasiden", "Ixodiden", and "Rhipistomiden". His classification, which was carried out with much detail was, in its main parts at any rate, in general use until 1896, when Neumann of Toulouse reverted to the older system and placed ticks as a family within the order Acari, specifying two sub-families:- "Argasinae", and "Ixodinae". (39) In 1907 Warburton introduced the classification which I give below in tabular form. (62) It is one of the most satisfactory that have been devised, but complete uniformity of custom has not yet been adopted. This is the system to which my references will be made throughout.

Warburton's Classification.



The difficulties of classification have had relation chiefly to the grouping of the Ixodidae, the genera of which form five-sixths of those differentiated, and are in several instances separated by featural differences which are relative rather than absolute.

The two principal divisions, the Argasidae and the Ixodidae, are readily distinguishable by the absence, in the case of the former, of a dorsal shield; and by the consequent concealment, from above, of the capitulum or head-piece, which is overhung by the soft and somewhat redundant covering of the upper surface of the body. In the latter division a well developed chitinous plate or shield obtains, which, in the male, almost wholly covers the dorsal aspect of the body; while in the female it is smaller, and extends over only a portion of this aspect anteriorly. To a forward extension of this plate the capitulum is articulated: it is thus exposed from above and forms a very striking and characteristic feature.

The sub-family Argasidae is the more important one from the point of view of relative frequency of pathogenic effects

in man; although, as we shall see, the belief hitherto commonly held, and expressed by Pocock*, that probably ticks of this division alone cause severe symptoms in the human subject, is not only inaccurate but is really much opposed to fact as viewed in light of records which, extending back for thirty years, have recently become considerably more numerous.

The Argasidae do not increase greatly in size from engorgement; and, with their flattened appearance in the un-gorged state, they are not unlike bed-bugs, and they have similar habits. For the most part they are nocturnal in their activity and retire to chinks in bed-steads, in wooden house-walls, et cetera, in the day time. In fact, they are often popularly mistaken for bugs. They inhabit warm climates and their hosts are most frequently birds; but they are often found on bats, and, when opportunity occurs, on man. They are divisible into two genera:- Argas and Ornithodoros.

Genus 1. Argas has the body of oval or somewhat rounded shape; it is flattened

* Article on Ticks; Allbutt and Rolleston's System of Medicine.

superiorly; and towards the margin the integument is differentiated in resistance from the general covering, in such a way that a sharp border is formed, which is not lost even at full distension. The members of this genus are without eyes.

Genus 2: Ornithodoros. The body is somewhat pointed anteriorly, giving more or less of a heart shape. It is more greatly distensible than that of Argas and is without the definite sharp margin. Eyes may or may not be present.

In the sub-family Ixodidae an important feature is a considerable degree of sexual dimorphism. This is due to the combined effects of two facts already mentioned; that they engorge very much; and that, while the males are almost entirely covered over by the hard scutum and are thus incapable of so great distension, the females have but a small shield which makes no interference with the often enormous enlargement of the body. Eyes are not found in any of the genera of the Ixodidae.

This sub-family is divided by Warburton (62) according to the disposition of the grooves on the ventral surface, relatively to the position of the anus, into Prostriata and Metastriata. There is but one genus of Prostriata:- Ixodes. The Metastriata are again subdivided according as they have short or long capitulum; and each of these subdivisions is arranged into two groups, in all ten genera of Ixodidae being recognized.

The number of differentiated species of ticks is very great, and is continually increasing; while the names of these are still more formidable in number than the species themselves, for in different places varying names are used. The following, however, are the chief varieties of pathologic importance:-

Argas persicus,
" reflexus,
" brumpti,
" savignyi,
Ornithodoros moubata,
" coriaceous,
" turicata,

Ornithodores talajae,
" tholozani,
" megnini,
Ixodes ricinus,
" holocyclus,
" pilosus,
Dermacentor venustus,
" reticulatus,
Haemaphysalis leachi,
Amblyomma hebraeum,
Rhipicephalus appendiculatus,
" decoloratus,
" bursa,
Boophilus annulatus,
" australis.

I have included some species which are pathogenic only to the extent of causing local affections of an incidental nature, and certain names have been omitted because the species denoted are but very questionably, if at all, to be differentiated respectively from one or other of those mentioned: Argas miniatus, for example, - the bane of Australian fowls - is but a variety of Argas persicus.

The list is, however, by no means exhaustive. To tabulate all the species which may indirectly cause symptoms of one kind or another, would be to enumerate all known ticks; for any parasite, which penetrates the skin, has that potentiality from the mere fact of its making an entrance wound for micro-organisms.

LIFE-HISTORY AND HABITS:

their bearing on pathogenic relationships.

The events of the life-history of any individual species have an intimate bearing upon the chances of its members conveying disease, quite apart from their specific fitness as infecting or toxic agents. In all varieties of ticks the life cycle consists of three phases:- those of the larva, the nymph, and the adult. But whereas in some cases one host suffices for all stages, in others two or more successive hosts are necessary; and in at least one the first period is completed before hatching of the egg occurs.

The habits also, have a restricting influence. Some species frequent places where access to a human host is easy - such as African natives' huts; while others are to be found only in the open, either on grass or upon shrubbery. The Argasidae alone, are commonly to be found in houses.

As typical life histories representing

two extremes in habits, those of Argas persicus and Rhipicephalus appendiculatus are good examples; and our knowledge of the details of both is well established.

Argas persicus, as has been mentioned, is widely distributed, owing probably to its preference for an avian host. It is found indifferently on birds whether in the wild state or in captivity; it is one of the worst pests of the domestic fowl in hot countries, both on account of direct injury and of the conveyance of disease (spirochaetosis); and it attacks and infects also geese (53) and turkeys.

These last I have seen rapidly killed when brought into a yard beside infested fowls, although the latter did not suffer unless attacked by great numbers of the ticks, for, having acquired immunity against the spirochaetal infection, they were injured only if the irritation or loss of blood became excessive. When opportunity avails the human subject is a readily accepted host.

Typically of its genus, this Argas is

nocturnal in habits; but the fact has often been observed, as was first mentioned by Oken, that it may occasionally attack man in the day time.

The tick after having fed freely upon its host retires to a crevice or chink, especially in wood such as the walls of a fowl house or of a hut, and there it digests its food. If it be of immature stage, it remains in its seclusion until metamorphosis occurs. It is in such a place as a rule that the eggs are laid although they may, rarely, be laid upon the body of the fowl. (6) The eggs are deposited in numbers averaging from twenty to a hundred and they take three weeks to hatch.

The larva is at first of a translucent, colourless appearance; but soon it acquires a chitinous covering, and with that the ability to attach itself to a host. This it does immediately an opportunity is available, and after four days to a week of feeding it drops off and rests for about another week, when partial metamorphosis takes place and the nymph stage is reached. It again feeds upon the host, but, in this instance only for a few hours, and, after a further

fortnight of inactivity, it moults and acquires a modified form, although not yet passing from the nymphal phase. For a third time the tick must now return to its host, and, after feeding, it once more retires for some weeks before achieving the adult form. The female engorges more than does the male, which remains of relatively smaller size. Feeding now takes place at intervals of five or six weeks, varying somewhat according to climate.

Throughout the period of its life the argas may never wander beyond the vicinity of the fowl-house in which it was hatched. If, however, its host should be a wild bird, it will be carried long distances; but such individual ticks as come into relation to the human subject are more likely to have been confined to the very narrow limits above mentioned, including probably the adjacent hut of the owner of the fowls.

Quite another kind of existence is that of Rhipicephalus appendiculatus which lives in the open, and out of the reach of human dwellings. When not upon its host it is to be found in a state of apparent inactivity

amongst the grass; or upon the branch of some small bush where it awaits the accidental opportunity of gaining attachment to a passing animal. In such circumstances the probability of its acquiring a human host is obviously small, and indeed the chance of its finding any host is precarious.

The eggs of this tick are laid in an unexposed situation amidst grass or other ground foliage, and at the end of seven or eight weeks the larvae are hatched.

After the integument has become sufficiently chitinized and the larva has acquired the power of locomotion, it climbs upon some convenient shrub and there awaits the chance approach of grazing cattle. Having found a host it feeds for about two days and then drops to the ground where it rests for approximately a month. At the end of this time metamorphosis takes place, and the larva gives way to the nymph, of which, in this case, there is but one form.

The process of seeking a host is repeated, and, if fortune favours and one is found, the nymph remains attached for eight or ten days and becomes engorged with blood. In its turn

it falls and rests amid the herbage for a period of about four weeks, when the second metamorphosis occurs and maturity is reached.

It is upon the body of the host that the sexes come together and soon thereafter the male dies. The female engorges in the same way as the immature forms and again drops on to the grass, where the eggs are laid. The number of those is several thousand; the vastly greater ratio compared with Argas persicus being in accordance with the circumstance that the developing young have to take so many more hazards, each individual having to procure successively three hosts, under conditions that make the finding of even one very doubtful.

This is a typical Ixodide life history, but there are many minor modifications found in other species: for example, one finds that in some, all three stages are passed on a single host; or two stages, larva and nymph, may be passed on one host and the third on another, as in the case of Rhipicephalus bursa. In Ornithodoros moubata the larval stage is passed completely before hatching occurs; and in Ornithodoros megnini no feeding is necessary during the

adult stage; that is, between the last metamorphosis and the commencement of egg-laying.

Speaking generally the life-cycle of ticks is much slowed by adverse circumstances, and where everything is favourable the cycle is at its shortest. As the male dies after coition and the female after egg-laying, it follows that the longevity of the individual will be increased by anything which will delay or prevent these incidents; in fact, the life may be several years instead of a few weeks or months, if only the conditions are made hard enough.

These life histories illustrate a point to which I wish particularly to call attention, namely, that the chances of an Ixodide carrying an infective disease in the human subject are, on the mere ground of mathematical improbability, greatly less than are those of an Argaside. Not only are the opportunities of the former for gaining attachment to man relatively few, but the probability of their gaining successive attachment to two human hosts, and so being able to acquire and again to transmit an infection, is further enormous-

ly reduced. In the case of an Argaside on the other hand, where it is but a matter of living by night upon the sleeper and by day in the nearest bed-post, probability is all in the other direction. The rarity of cases of Ixodides being concerned in the spreading of transmissible disease in the human subject is due, I have no doubt, to this cause.

Yet another factor which influences the pathogenic potentiality of particular species, is that of their differing capability to transmit infections relatively to their own stage of development. Thus the larvae hatched from the eggs of a female that has fed on blood infected with one of the pyroplasmoses may be capable of infecting, as in the case of Boöphilus australis and in that of Boöphilus annulatus; (55) or they and the nymph may be innocuous and the new adult will transmit, as is seen in Rhipicephalus bursa in relation to Carceag. (38) Haemaphysalis leachi if fed as nymph will infect as adult, and if fed as larva it will infect as nymph (49) The ticks which carry the cattle fever of Rhodesia and those that transmit "Heartwater" of sheep behave in the same way. (44)

The possible longevity of an infection

when harboured in the tick is also an element of importance and this, which must naturally be variable with the different infections, has been shown to be sometimes many months as in the case of spirochaetosis of fowls (35) This would allow of the reappearance of disease in a district that had been for a period entirely free from infected animals.

It will be seen then that these various factors in relation to the life history, habits, and characteristics, of the ticks, may account for many seeming anomalies. They may have a determining influence upon the occurrence of an affection, such as might readily incline one to an unfortunate preconception regarding etiology. In the case of general infective diseases they may lead to restriction of incidence to certain species of animals, although others might prove just as susceptible if given circumstances permitting of their becoming infected: and it will be observed also that such incidental features of life history may deprive a particular species of ticks of the opportunity of conveying an infection, which, in actuality, it may be as capable of transmitting as is the species which in fact does do so.

The Diseases consequent upon Tick-bite

Historical and General Statement.

The affections associated with tick-bite may readily be divided for purposes of discussion into two classes: those known to be due to a specific organismal infection, of which the tick is but the carrier and temporary host; and those of which the nature is obscure. The latter comprise a variety of conditions which range in severity from local itching of the skin to profound toxaemia which may have fatal results. Records of observations of such cases have been accumulating for many years; the first, of value, coming from Persia early in the last century; and others, from time to time since, from every part of the tropical belt and the regions adjacent.

Some of the Persian reports are interesting not alone in connexion with the present subject, but as examples of early observations of phenomena which have a bearing on such matters as immunity, longevity of infections, and other questions, which, although comparatively meaningless then, assume significance in light of modern knowledge.

Oken, who was probably the first to refer to the sickness caused by Argas persicus - the most notorious of the ticks that affect man, - wrote in 1818 of a death in the human subject within twenty four hours after the bite of a tick that had been kept in isolation for twelve months.

Dupré in 1819 wrote of tick-bite being followed by a "consumption" which it was necessary to treat by abstinence from meats and fermented drinks. Sugar was a specific. The ticks were not found in new and well lighted houses.

In the same year Kotzebue mentioned the habits of ticks - Argas persicus - to be like those of bed -bugs, the acari retiring to crevices in wood about the huts, and emerging only at night when their visits to the host were made. They avoided day-light but were not restrained by that of lamps or candles. He pointed out that natives suffered very little from the effects of the bite while foreigners were liable to be severely affected.

Heller in 1858, gave a systematic account of the anatomy of Argas persicus and

maintained that it did not possess poison glands.

It is to Africa that we must turn for the first observation of the relationship of ticks to the distribution of any of that series of diseases, since definitely known to be of a specific infective nature. In 1857 Livingstone reported that human Relapsing fever (African) was communicated by the bite of a tick, and his discovery has since been amply verified; but it was not until half a century later that the nature and details of the part played by this acarus - the Ornithodoros moubata - were demonstrated. (14, 24)

It is in connexion with such fevers that ticks assume their greatest importance, which may readily be conceived when one considers the ever increasing list of those affections that stand to their account, as the following table will illustrate.

29.

Disease.	Species affected.	Causative organism.	Tick transmitting	Geographical distribution.
South African Relapsing fever	Man	Spirochaeta duttoni	Ornithodoros moubata	South Africa
Rocky Mountain Spotted fever	Man	unknown (a)	Dermacentor venustus (=D. andersonii)	Montana, Idaho, and adjacent states.
British Redwater fever	Cattle	Piroplasma bovis	Ixodes ricinus (25)	Europe (North and Central)
Texas fever.	Cattle	Piroplasma bigeminum	Boöphilus annulatus, B. australis	America, Asia, Africa, Australia.
Rhodesian Redwater fever	Cattle	Piroplasma parvum	Rhipicephalus appendiculatus	South and Central Africa
Equine piroplasmosis	Horse, Ass, Mule, Zebra.	Piroplasma equi	Dermacentor reticulatus and others	Germany, Italy, South Africa, Madagascar, Venezuela.
Heartwater	Sheep, Goat.	unknown (b)	Amblyomma hebraeum	South Africa.
Carceag	Sheep	Piroplasma ovis	Rhipicephalus bursa	Lower Danube Valley (19) Italy, France.
Canine piroplasmosis	Dog	Piroplasma canis	Ixodes reduvius Dermacentor reticulatus, Haemaphysalis leachi	Europe, South Africa.
Spirochaetosis of fowls	Domestic fowl, Goose, Turkey.	Spirochaeta marchouxi	Argas persicus	Brazil, South Africa, Australia.

a. Formerly believed to be due to supposed "Piroplasma hominis". (63)

b. No organisms have been found in "Heartwater" but serous effusions which are infective become sterile after passing through a Chamberland filter. (56)

There remain beyond these, however, a number of affections in which no organisms have been found or very definitely suspected; cases commonly spoken of as being due to the "bite"; an attitude of complacent acceptance which I hold to be quite unjustified, and which I shall later discuss.

A Musculo-paralytic Case in the Human Subject.

Within the category last-mentioned falls a most interesting case in the human subject which came under my observation. The following description of it is taken, for the most part verbally, from my report communicated to the Queensland Branch of the British Medical Association in March 1913. (15)

A female child, aged four and a half years, was brought from a district on the upper part of the Brisbane River, with a statement by her father that she was paralysed from the bite of a tick.

The patient had been in good health until the preceding day, on the morning of which, however, she took an unusually small breakfast and declined food from then onward. In the early part of the afternoon of that day she became restless, and about four o'clock it was noticed that she was unsteady on her feet.

Having decided to put her to bed, the mother undressed her, and in the course of

doing so, discovered a tick on the back of the right shoulder. Its presence had evidently caused little or no discomfort, and was quite unsuspected. The body of the tick was cut off, leaving the penetrating parts embedded within the skin.

The child's father, who was an intelligent bushman, described the parasite as a "scrub tick" such as was commonly found on dogs. He said it was of a slate grey colour, and was flatter than the cattle tick (Boöphilus australis) and that the foremost pair of limbs were much longer than those of the latter species. The body was about three eighths of an inch long and a quarter of an inch in breadth, this being, he said, about the average size of this kind of tick at full development. I was unable to get more precise information than this.

After the parasite was cut off the child was given some infusion of senna, followed by a little water.

About seven o'clock in the evening the patient vomited, and for the next couple of hours seemed more comfortable; but during the

remainder of the night she was very restless, and slept, in short troubled spells, a total of only two hours. The bowels moved twice during that night, the motions being of a brown colour and semi-solid consistency.

Second day. In the morning the child vomited again three or four times. It was found now that she could not stand and she appeared to the parents very ill. About mid-day she was sent by sulky* to see me, the journey of twenty two miles taking three hours. Between two and three o'clock she drank a few spoonfuls of milk which was the first substance she had swallowed for thirty hours, excepting the senna and a wineglassful of water on the previous afternoon. This abstinence from fluids is the more remarkable in consideration that the weather was very hot, that the patient had made a long journey in an open vehicle, and that she had vomited half a dozen times in the period.

When I saw the child shortly after three o'clock she was in a state bordering on delirium, but was quite sufficiently conscious to be annoyed by examination. The

* A light gig.

temperature was 101.4 degrees in the axilla, and the pulse rate was 132. Systolic pressure, measured in the arm, was between ninety and ninety five millimetres, restlessness preventing greater exactitude of estimate; the tension was well preserved in the diastole, but this was not measured. The respirations numbered thirty six per minute; they were short, shallow, and jerky, and performed for the most part by the muscles of forced breathing. The skin was dry except for slight perspiration of the scalp. The eyes were somewhat glazed. The lids drooped but were not quite closed; the pupils were dilated and were inactive to the stimulus of light. In order to further investigate the inactivity of the iris a one per cent solution of pilocarpin was instilled into the conjunctival sac, but no reaction of the pupil was obtained. The ocular tension was slightly low, and the eyeballs were fixed in the position of rest. The tongue was covered with a thin white fur, and was only moderately dry. The muscles of the legs and thighs were quite flaccid, and the lower limbs were motionless save for such movements as were made from the hip joints.

The arm muscles could be moved with but very little force, and those of the forearms appeared to be incapable of action. Knee-jerks could not be obtained, nor could the wrist-jerks, or the normal or other plantar reflexes. Owing to delirium the sensations could not be estimated at this time, beyond that signs of annoyance were evident when stimuli of pain or of tickling were applied to any part of the trunk or limbs. Voice was not lost, but articulation was very defective. Over the lower part of the right scapula there was a bright pink patch of the size of a penny, neither raised nor indurated, and in the centre of this was a purplish-black spot about a quarter of an inch in diameter. In the middle of this spot was an aperture, somewhat less than a pinshead in size, through which one could see a greenish-grey body that was found to grate with a stony hardness against the point of a knife. A minute droplet of pus was expressed from the aperture. The object felt with the knife, evidently the head and chitinous mouth-parts of the tick, could not be removed without its being broken to

fragments. It was scraped out ultimately and the cavity, which was about the size of an average matchhead, was cleaned with a small curette, and cauterized with pure carbolic acid. A sixtieth of a grain of strychnine was given hypodermically.

Third day. During the next twenty four hours the bowels moved nine times, the motions being liquid and bile-stained, and containing a considerable quantity of mucus. There was no evidence of abdominal pain, however, and there had been no more vomiting. Sleep had been moderately good. By this time the temperature had fallen to normal, breathing was deeper and easier; the mental state had cleared, although there was still undue irritability; the appearance of the face was nearly normal,and the child now took drinks of milk freely. There was no sign of return of voluntary movement to the legs, but the muscles were not so limp. The strength of the arms had improved, and the fingers could be moved, but even such an object as a bunch of keys could not be held securely in the hands. The pupils were still enlarged, but now reacted feebly to pilocarpine, though not to light.

The eyes had fully recovered freedom of movement; and subjective examination, which could not be made on the previous day, revealed that vision was of normal acuteness but that accommodation was paralysed. A rough general test was made of the senses of contact, temperature, and pain, but no abnormality was found. There was no notable feature in the urine.

Fourth day. By the next day, the fourth since the onset of symptoms, the knee-jerks were both obtainable, but deficiently. The child could stand, and even walk a few steps with support. The pupils were still inactive to light but reacted well to pilocarpine. Diarrhoea continued, but was less severe.

Fifth day. On the fifth day the patient could walk without support, but the gait was knock-kneed, so that each leg was brought more directly under the weight of the body. In walking the heel and sole were placed upon the ground synchronously, and no attempt was made to rise on to the ball of the foot. The pupils now reacted to light but were still somewhat dilated. The blood pressure was

measured for the sake of comparison with the former reading. It was 105 millimetres (that is, systolic.) The pulse rate was ninety six, and the temperature still normal. The bowels had moved twice since the preceding day. The discolouration around the bite-mark had become reduced to about the size of a shilling, and had faded to a duller red shade. The cavity had not yet filled up, but was healing well. This was the last time I saw the patient, but I was informed that her progress to complete recovery within the next few days was uninterrupted.

As there was not an opportunity of examining the tick its identity must necessarily remain to some extent a matter of inference, but the evidence points to its probably having been a female specimen of Ixodes holocyclus. The ticks prevailing in the district are Argas persicus, Boöphilus australis, and Ixodes holocyclus. The differentiation of the first of these would be unmistakable even to a casual observer. The informant was familiar with the remaining two and was quite certain of the distinction of the tick he had removed, from that known there-

abouts as the cattle-tick (B. australis). Of the three species his description conforms only with the one mentioned. The man's own term "scrub tick" is the local popular name for Ixodes holocyclus which, as I shall have occasion to notice later, is known in New South Wales as the "bottle tick".

Tick-bite Affections in Medical Literature.

Regarding affections arising from tick-bite, other than those known to be due to general organismal infection, a representative work on Tropical Medicine - that of Castellani and Chalmers, (2nd ed.1913) - says that the Ixodoidea or Ticks are well known to cause severe symptoms by their "bite", apart from those due to the Babesiae or Spirochaetae which they may transmit. The following is a short summary of those symptoms from that source.

Argas persicus (in Persia) causes severe pain, fever, lassitude, delirium, convulsions, or even death in newcomers; while natives are immune.

Argas reflexus produces local pain and swelling with sometimes an erythematous eruption, and the site may be marked by a cicatrix for years.

Ornithodoros moubata is represented as causing severe itching and pain: while Ixodes ricinus is said occasionally to excite a severe

dermatitis which may be followed by the formation of pustules, by abscesses with oedema, and by lymphangitis, lymphadenitis, and fever.

The foregoing I quote as representing the types most commonly recognised: but there exist records of many others, some of which are, if less frequent, not less striking; yet it must be said that in the vast majority of instances the bites of ticks cause comparatively little disturbance.

Dugès writing from Mexico in 1876, of Ornithodoros turicata, of which he gives the earliest descriptions, says that it causes severe itching and the formation of an ulcer which may not heal for several months. Lymphangitis and dermatitis are common accompaniments; bullae may form, and even local gangrene may follow. On three occasions he observed symptoms of a more general type. Of two such cases, in which veins had been penetrated, one had difficulty in moving the tongue, in speaking and in swallowing; there was also a sensation of widespread swelling and numbness; and there was vomiting and diarrhoea; the intellectual

faculties were intact, but respiration was anxious in character. The other case showed the same symptoms but these disappeared within an hour, when they gave place to profuse perspiration with urticaria. Dugès observed that symptoms were much more severe if when the tick was removed the mouth parts were allowed to remain in the skin. He believed that the tick produced a specific venom but that there was also a personal idiosyncrasy on the part of the host.

Johanessen (Norway, 1885) describes the case of a boy from whom the tick's body (Ixodes ricinus) was removed but the capitulum remained imbedded in the skin at the back of the head. Swelling followed locally, with headache, stiffness and cramp in the muscles of one side of the body, partial loss of memory, and polyuria. The pupils became dilated. The boy made a slow recovery.

Dowson reports a case from Portuguese East Africa in which, when seen within twenty four hours after an alleged bite upon the great toe, there was much pain in that part, and also in the leg. The toe was slightly

swollen. The temperature was 104.2 and the patient had vomited twice. Pocock who examined specimens of the ticks from the hut in which this case occurred says that they were closely related to Argas savignyi. (50) Dowson mentions that the Portuguese say they have lost men from the bite of the carapato (tick). They recognize the comparative immunity of natives, and the great susceptibility of newcomes. Fever and acute dysentry are said by them to be the chief symptoms. I think it may not be justifiable, however, to assume definitely, as Dowson does, that this case is an example of the type prevalent in the district, to which the Portuguese residents referred. The latter is probably the affection from which Livingstone suffered (30) It is due to Ornithodoros moubata (the "tampan") and is endemic along the lower part of the Zambesi valley. The typical bite of Ornithodoros moubata has already been referred to, but there is in addition in these cases frequently a good deal of fever and also tingling which, Livingstone said, affects the legs and ascends as high as the abdomen when

it causes vomiting and purging. In his case the tingling remained for a week.

Bancroft describes a Queensland case, in which a woman aged forty was bitten on the external ear by a tick (not identified). She complained of weakness, and of a tendency to fall when stooping, or when rising from the stooping position. Her vision had so diminished that she could read half inch type only with difficulty. The pupil reactions and accommodation were normal, and there was no pain or other evidence of inflammation in the eye. The nervous symptoms cleared off within a fortnight; and gradually the sight returned to the normal standard, so that within a month she could read newspaper print.

Dr. J.B. Cleland (9) records two cases which were communicated to him from New South Wales. In one of these, an infant of thirteen months was bitten behind the left ear by a "bottle tick". The parasite was not discovered until a day after the illness had commenced and two days after the probable time of attachment. During the first night of the sickness there was merely restlessness but by morning the

child was too listless to stand. The condition became gradually worse and when seen by a doctor on the following day the state was as follows. The temperature was 101.6 and the pulse 140. The respirations were hurried and shallow, there was coughing, and the patient tried with difficulty to bring up mucus. He appeared to be partially paralysed, and the legs did not move during all the time of the examination. At the situation of the bite there was a circular patch of redness one inch in diameter, with a small purplish spot in the centre about one eighth of an inch in size. Four hours later the child got better; the temperature fell to 99, the pulse to 120, and the respiration improved. Six hours after that, however, the infant suddenly collapsed, and, failing to cough up mucus which had collected, died.

This case is particularly interesting in the considerable degree of resemblance which it shows to that which I have described. It is noteworthy that both cases were from the eastern coastal region of Australia, and that both were probably due to the same species of ticks.

The other case mentioned by Cleland is that of a man from whose body (trunk, arms, and legs) two hundred ticks, of unidentified species, were removed. There was faintness within one hour of attachment, and when, four hours later, the man was seen by a doctor, there was severe syncope with very feeble heart action. No local irritation of the skin ensued, despite so great an assault upon it; but the patient remained very ill with symptoms of cardiac failure during the next week, after which time the condition quickly passed off.

Todd has recently collected, in reply to enquiries, reports of thirteen cases in which paralytic or convulsive symptoms have followed upon tick-bite occurring in British Columbia. The records, which cover a period of many years, are from the routine notes or memory of Dr. Todd's correspondents, and give very little clinical detail. The following information, however, is available.

1. Two infants died of convulsions, and wood-ticks* were found upon the necks of

* Dermacentor venustus, the transmitter of Rocky Mountain Spotted fever.

both.

2. A child aged four years, from the back of whose neck a large wood-tick had been taken some hours before, developed almost complete paralysis of the legs. A purgative was administered, and after a few hours' rest there was complete recovery.

3. A girl of four years gradually lost the power of her legs during two or three days, until she was unable to stand: a tick was removed from the back of her neck and within three days she was again well.

4. A girl of five years was bitten on the back of the head by a tick. She died in convulsions which, it is said, were undoubtedly different from the ordinary infantile variety.

5. A child of four years old had complete paralysis of the legs, and, to a lesser degree, of the arms. A wood-tick was removed from the back of the neck and rapid recovery followed.

6. A child aged three and a half years, who was in perfect health until two hours before examination, was found to have both legs completely paralysed. The temperature and pulse were normal. She could not stand and

the reflexes were gone. A tick was found on the lower part of the neck, and within a day and a half the use of the limbs had returned.

7. An adult was known to have weakness in the legs after the bite of a tick.

8. (a) A child died suddenly "with symptoms of 'acute ascending paralysis'". After death a large tick was found on the neck.

(b) A child died after two days' illness with the same symptoms as "a"; and a tick was found on the right temple.

(c) A child was seen whose legs had become weaker for two days. A tick was found on the neck, and after its removal recovery proceeded to completeness in two days.

9. A girl aged three years became paralysed in the legs, with loss of reflexes. There was also marked paresis in the arms. Three ticks were found on the neck and after their removal complete recovery took place.

10. A child of three or four years had paralysis of the legs with absence of reflexes. A tick was found upon the neck and removed,

with resulting disappearance of symptoms.

These cases may be divided into two groups: those with convulsions, three in number, of which all were fatal; and the remaining ten which had muscular paralysis or paresis affecting the limbs. In none of the cases has the time from attachment of the tick until the onset of symptoms been observed. The temperature and pulse were recorded normal in one case; and the absence of any reference in the others would indicate the probability that there was no marked disturbance of that kind in them either. The period of invasion varied from an hour to two days, and recovery when it took place was in all cases rapid.

Manson (Tropical Medicine, 1914) speaks of the above cases and the one recorded by myself as being somewhat similar. Both, it is true exhibit paralysis of the limbs but they differ considerably in general type of illness, the former being apparently of an afebrile character and unaccompanied by respiratory difficulty, gastro-intestimal symptoms, et cetera. Still more recently, however, another series of cases from the almost adjacent state

of Oregon have come to notice through an article by Nuttall giving abstracts of a paper published in 1912 at Portland (Ore.) by Dr. I.U. Temple. Some of the latter cases more closely resemble my own than do the foregoing ones.

There are thirteen cases in Temple's records, four that he had observed personally and nine from correspondents. All of them occurred in the mountain region of the State of Oregon. The ticks were not identified but again the Dermacentor venustus is believed to be the most probable species. Some of the cases were in all respects like those from British Columbia, being without other symptoms than those of transient paralysis of the lower limbs with normal or even sub-normal temperature and no general disturbance. The chief divergences in other cases were that several had high temperatures - between 104 and 105 - some showed involvement of the larynx and the respiratory muscles, and others of the sphincters, while one took six weeks to recover from the paralytic condition and three cases were fatal.

Notes of the individual cases in this

series will be found in the article mentioned (41) but one case (number two) resembles my own in so many respects that I shall give a summary of it here. A female child aged six who had been in normal health on the previous evening was found one morning to be paralysed up to the knees. There was "slight" temperature, no pain, no interference with sensation, but motor paralysis with loss of reflexes. On the following day the arms were involved and by night the throat, thorax, and larynx, also. The patient was then unable to swallow liquids, breathing was laboured, phonation was lost and only guttural sounds could be made. Two ticks were found in the suboccipital region and removed. There was then gradual improvement and recovery within a week.

Dr. Temple regards the condition as an "ascending paralysis" but is satisfied that it does not produce any changes in the brain or cord, as in that case such rapid and complete recoveries - one day in two of the cases - could not take place.

Sickness in the Lower Animals due to Tick-bite.

The cases mentioned under the preceding headings comprise the chief types of tick-bite affections that have been recorded as occurring in the human subject, but before passing to a discussion of their causation I must refer to a number of conditions in the lower animals that come under the same category in respect of the obscurity of their etiology.

The first of those affects sheep. It occurs in the dry belt of British Columbia and the symptoms are said by Hadwen to be similar to those which are known to afflict man in the same district (that is, to the condition in the cases quoted from Todd). The illness is, like the latter, unaccompanied by fever and it is caused by the same species of ticks. Hadwen (16) experimented on its communicability making injections of mashed ticks, of cerebro-spinal substance and fluid, and of defibrinated blood, but all gave negative results. When communicated by the tick-bite under observation the "incubation" period was six to seven days.

Some of his experiments were confirmed in collaboration with Nuttall. They placed one of the ticks upon a healthy dog, which became paralysed in the limbs twelve days later, the hind limbs being affected first and more severely. Examination of the blood gave negative results. The animal ultimately made a full recovery. The observation was made that the disease is not communicable by innoculation, although it was produced experimentally through the agency of a tick (17)

Another interesting affection of sheep, which is described by Mally, occurs in the higher lying districts of the Transvaal, and is associated with the bite of the Ixodes pilosus. The affected sheep develops a paresis of the leg muscles, so that it has difficulty in rising to its feet; but if driven on it may run a few steps and then drop as if exhausted. Long grass and frosty weather are said to be essential conditions to the incidence of this disease. Ticks have been found upon sheep that remained in perfect health although located upon portions of the veldt known to be at the time

"dangerous". A sheep may be affected repeatedly, but only after the lapse of an interval between successive attacks. Young lambs that have had no food except milk may be affected, a fact which is noteworthy in relation to the possibility of the cause being that of ingestion of poisonous decomposing grass. "Dipping" the sheep- with destruction of the ticks - prevents spread in the flocks, while internal administration of the dip (as a control against any protective action it might have after absorption) does not protect.

Borthwick has since recorded the same condition in Cape Colony. Inoculation experiments were found by him to be negative. The number of ticks did not appear to influence the severity of the disease but their early removal led to more rapid recovery, this being often complete within twelve hours.

An affection of dogs which is not uncommon in Queensland, is also characterized by muscular paralysis or paresis, but there is in addition disturbance in other ways. It is caused by Ixodes holocyclus, and some of the cases appear to closely resemble that in the

human subject which I have described: it occurs in the same country and is due, so far as evidence is available, to the same parasite.

One of these cases came under my observation, the animal being a "sheep-dog" six years old. Symptoms commenced with loss of appetite, followed soon by unwillingness to take even milk or water, and by a disinclination to move from one spot. After three days from the first signs of illness there developed inability to use the hind legs, which rendered the dog unable to rise on to the feet. If disturbed he moved towards one or other side by effort of the fore legs only, but the hind ones were not dragged with the full relaxation of complete atonic paralysis. A tick (I. holocyclus) was found upon the skin in front of the left shoulder and was removed by the application of paraffin oil. The respirations had now (the fourth day) become more rapid and shallower, and the heart's action was also increased in frequency. The dog lay with the fore legs stretched forward and with the head resting upon the ground between them. The tongue was not protruded and the mouth retained its usual degree of

moisture. The eyes were open during waking, which, with the drooping of the head and motionless state, gave an expression of helpless appeal; but there was no effort to make any sound, or to solicit attention. After eight days the condition of the muscles began to improve; the appetite gradually returned; and within three weeks there was complete recovery. Throughout the whole period the fore-limbs had apparently not been affected. There was obstinate constipation during the first ten days, but after that time observation was not kept.

Bancroft who observed many such cases, both in dogs and cats, mentions that puppies affected have seldom been known to recover. Delirium is frequent, and on attempting to rise it is common for the animal to fall over insensible, and in a few minutes again to regain consciousness. In such attacks the lips are found to be pale and the heart beat almost impalpable, in short there is a state of syncope. In one of these attacks as a rule the animal dies. Muscular paralysis is usual and the muscles most remote from the heart suffer first and the heart itself last.

Retention of the detached mouth parts of the tick leads to greater severity of the affection. Animals in infected country become immune. Bancroft expresses the opinion that death is due chiefly to muscular paralysis.

Anderson-Stuart, who has heard of many cases from correspondents, says that the average course of symptoms is: at first, moping, with hot nose, and advancing muscular weakness affecting in order the hind limbs, fore limbs, and respiratory muscles. Constipation is usual and there is often trouble with retention. Death may result from epileptiform attacks, or from cardiac or respiratory failure. In the last case Cheyne-Stokes respiration may precede the end. Peripheral nerve paralysis sometimes occurs during convalescence. A single attack confers immunity.

Pastoralists in the coastal districts of Queensland inform me that it is not uncommon for foals and calves affected by tick-bite to have paralysis of the hind limbs, and that occasionally those animals are lost from this cause.

Repeated examinations of the blood of

dogs affected with this sickness have been made at the laboratories of the Queensland Agricultural Department but no organisms have been found.*

* Communicated by Mr. C.J. Pound, Director of Queensland Govt. Bacteriological Laboratories.

The Physiological Action of the Poison as exhibited in the Author's case in the Human Subject.

The principal questions which arise in connexion with the foregoing affections, all of which exhibit evidence of an intoxication of considerable severity, are: What is the nature of the poison? and What is its primary source?

These two questions are intimately correlated. An analysis of my case in a little girl will be instructive, especially in regard to the physiological action of the poison. Apart from that, however, both questions will be considered at greater advantage from a comparative study of the various groups.

The most outstanding feature in the case mentioned was a severe intoxication affecting in a selective way the activity of voluntary muscle, while the mental faculties were only moderately inhibited, and the perception of sensory impulses was probably not restricted at all.

It is of much importance to localize the site of the interference with muscular action. It will have been observed that there was sufficient consciousness for the exercise of voluntary movements; in fact the muscles of the neck, and many of those of the trunk, were still under control and were used quite freely. The disability must therefore have had its cause somewhere on the motor side.

Commencing with the highest of the motor functions, it is hardly necessary to adduce proof that a disturbance of the (frontal) centres for the conscious initiation of voluntary movements, is out of the question. For the sake of system, however, it may be said that the distribution was not restricted to the muscles concerned in individual purposive actions; and indeed there was included one involuntary muscle - the sphincter iridis: further, the condition was an actual paralysis; whereas in such cases the difficulty is not to produce movements but to direct them intelligently (apraxia). The lesion, then, must necessarily have been in the pre-Rolandic cortex, or in the muscles, or on the paths or secondary centres intermediately.

The manner of selection of the muscles involved, will afford the information required to differentiate between an affection of the nerve mechanism and one of the muscles themselves.

It is to be noted that those muscles which are not dependent for their activity upon cerebro-spinal nerve control, but upon their own inherent irritability and muscle continuity, or upon the sympathetic system, - in a word, the involuntary muscles - were not affected. One involuntary muscle, as has been mentioned, did however, lose its power, namely the sphincter of the pupil. It is a significant exception, for it is also an exception in being, unlike most involuntary muscles, dependent for its contraction on impulses received from a cerebro-spinal motor nerve, the third cranial. The intestinal muscle, far from being paralysed, was actually in a state of over-activity; the arterial muscle also must have been in good tone, for the blood pressure was within reasonable measure of its level after the passing of the acute state; the heart too, for the same reason, must have been little,

if at all, interfered with.

A depressant acting directly on muscle fibre would have affected all muscles indiscriminately, as, for example, drugs such as potassium in large doses, or antimony. The heart when first observed was running at the rate of 132, with a temperature of only 101.4°. That seems undue acceleration relatively to the temperature if there were no cardiac depression; but there is ample to account for this independently, if we remember that the respiration was greatly embarrassed, and that there would be a resulting excessive venosity of the blood.

The fact then that, consistently, the muscles affected, whether striped or unstriped (as in the iris), were innervated by cerebro-spinal nerves; and that, without exception, those not thus innervated escaped, is a sufficient evidence that the action was upon the nerve control and not upon the muscle fibre directly.

Turning now to the consideration of the motor nerve mechanism, we have seen that all the reflexes in the affected parts were abolished although the afferent tracts were intact. Also, there was complete loss of muscle tone.

These facts exclude an upper neurone site as a feasible explanation and point to the interference being situated in the lower neurone: that is, in the cerebro-spinal nerves with their cell-centres in the anterior horn of the cord or the cranial nerve nuclei, together with the nerve end-plates in the muscles. It is true that gross lesions of the motor cortex may be accompanied by more or less flaccid monoplegias when the inhibiting centres in the optic thalamus and their tracts in the internal capsule are not interfered with; but as a rule in such cases normal, or only somewhat diminished, reflexes remain. A toxic influence acting upon the cortical cells might very probably cause paralysis without spasticity in a similar way; but such an agent would not pick out the leg centres and, allowing the trunk to go free, catch up those of the arm, only toagain withhold its action from the lower part of the gyrus! Neither would it destroy the reflexes. This exception then forms no difficulty.

Suspension of activity of the lower neurones centrally would account for some of the phenomena; it would break the reflex arc,

and it would ensure the muscular flaccidity; but it would not afford an explanation compatible with the grouping of the muscles affected, nor would it account for the behaviour of the pupil. The intensity of the paralysis, and the lateness of regaining function, followed an order suggestive of ~~their~~ remoteness in the blood-stream and certainly not that of segmental level in the cerebro-spinal axis (although the invasion generally was of ascending type); thus the pupils were still affected when the arms had recovered, and, although these and some of the muscles of articulate speech suffered, those of the trunk such as the erectors of the spine were entirely missed; nor did the selection have relation to proximity of centres, for of muscles closely associated in the central nervous system some were deeply affected and others only lightly or not at all; as, for example, those of the hip on the one hand, which retained their function, and those below the knee, on the other, which completely lost theirs; although the centres for all these are close together in the lower lumbar

part of the cord.

The respiratory muscles which are certainly not remote in the circulation were considerably affected and are thus an exception. To this I shall refer later.

Further, if we take the case of the pupil, a central (nuclear) paralysis although interfering with the light-reflex would have left the mechanism intact for contraction by pilocarpine, whose action is local; and this would be equally true if the obstruction of the arc were in the axons.

A site in the lower centres or in the nerve trunks will therefore not satisfy the conditions, and interference with the activity of the end-plates in the muscles, remains as the actual cause of physiological discontinuity of the motor paths. This does not preclude the possibility of an accompanying effect upon nerve trunks, although it indicates that paralysis of the end organs was an essential element.

In general it may be said that the resemblance of the symptoms to those of conine poisoning is very close: there was an intense

paralysis of the motor nerve endings, with consequent muscular flaccidity, dilatation of the pupils and drooping of the eyelids; there was a particular picking out of the muscles of respiration, which in the case of conine is believed to be due to a separate action on the respiratory centre in the medulla; a late and relatively slight interference with mentality; gastro-intestinal irritation; et cetera. In fact the only marked point of difference from a typical hemlock case is that the onset of symptoms was more prolonged. The onset was not only prolonged in its development, but it was delayed in its commencement. The presence of fully formed pus on the occasion of my first examination would indicate that the tick had attached itself at least two days prior to that time, that is, not less than thirty hours before the commencement of severe symptoms: although it may have been longer. This point is of importance, as the fact of there being a latent period bears intimately upon the question of the source of the toxin.

The Possible Sources of Toxins in Tick-bite Affections.

In accounting for tick-bite "poisoning" the most generally accepted view is that a highly toxic saliva is introduced. Another suggestion is one made by Nuttall, who considers that there is some probability that it may be due to disgorged decomposing food-residue. (40) There are reasons, however, as I shall demonstrate, which show that only a minority of cases, and those chiefly of the local or milder types, can be accounted for on the foregoing hypotheses. Regarding the majority of cases, I believe that a proportion results from local elaboration of a toxin at the seat of the bite, with subsequent absorption; and the remainder from a general infection with micro-organisms. The last named causation, having been obviously inapplicable in certain cases where symptoms have followed very early, has been too lightly laid aside in regard to others.

At the outset, one might observe that there is no reason why one of these factors

may not avail in one group of cases, and another in a different group; and that while some of the local symptoms of tick-bite are beyond doubt due to salivary intoxication, the coincidence of symptoms from this cause does not contra-indicate the possibility of the more severe symptoms, present at the same time, being due to another agency.

Experiments made by Nuttall and Strickland have shown that the salivary secretion of ticks contains a substance that inhibits blood coagulation. (43) This of itself would, in sufficient quantity, cause general symptoms, and in any case would be liable to excite local disturbance, as in a case referred to by the above writers in which a large patch of ecchymosis was produced within a few minutes.

An interesting point in this connexion is the occurrence, soon after the attachment of a tick, of a peculiar tenderness by which those who have experienced it can recognise the identity of their assailant. (Bancroft) The incidence of this symptom without the lapse of an interval of time also points to the cause being the direct action of a pre-

formed poison.

On the other hand there is no doubt that certain affections, chiefly local, are due to the introduction of a bacterial infection; and to this cause must be attributed many cases, such as those where erysipelas, pustule formation, ulceration, or local gangrene - as has occurred in sheep, (51) and in man, (12) - have supervened.

A group of cases recorded by Tonnel is most instructive of this ability of ticks to transmit bacterial infections - a factor which I believe to have a much greater importance than is on the surface apparent, for non-pathogenic organisms may have an indirect yet essential rôle in the causation of tick-bite affections. The cases occurred in a house that had been for four years unoccupied and in which a previous tenant - a bird seller - had kept pigeons and fowls. A family, consisting of two parents and two children, of which one member (the father) had but recently recovered from a widespread furunculosis, came into residence. The man developed an eruption showing papules, of about five millimetres diameter, between the old

furunculous elements. A similar state shortly was exhibited in one of his children, accompanied in this case with oedema which developed into an actual phlegmonous condition with numerous abscesses. Soon the other child became affected in the same way. The family left the house, however, because it was infested with parasites resembling little spiders ("petites araignées"). Two days later a second family came into occupation, and the parents and one of their children developed the same affection as their predecessors, complicated in the case of the child with broncho-pneumonia. The place was now thoroughly disinfected and no further trouble arose. The house, it was found, had been infested, not with spiders, but with Argas reflexus.

Such cases, however, are of interest chiefly in their bearing upon others, for they are of a more or less obvious nature and are not specific results of tick-bite, but might probably be caused by many other biting creatures.

The cases under consideration are those where the tick is - or may be - a specific or necessary agent, but excluding of course

those cases due to known infections such as the various piroplasmoses. The latter, however, will afford some analogies that will be useful for comparison.

The former category is exemplified in the following groups of cases that have already been detailed, and which are now tabulated and numbered for more convenient reference.

	Condition	Subject affected	Prevalence
1.	Pain, fever, delirium, convulsions.	Man	frequent
2.	Swelling, numbness, vomiting, etc.	Man	several
3.	Itching, tingling, pain, fever.	Man	frequent
4.	Pain, swelling, vomiting, fever	Man	one case
5.	Cramp, loss of memory, polyuria	Man	one case
6.	Cardiac failure	Man	one case
7.	Amblyopia and vertigo	Man	one case
8.	Muscular paresis, fever, respiratory difficulty	Man	one case
9.	Muscular paralysis fever, abstinence from fluids etc.	Man	one case
10.	Muscular paralysis.	Man	several
11.	Muscular paralysis.	Sheep ..... Dog	frequent by experiment
12.	Muscular paresis, respiratory embarrassment.	Dog, Cat	frequent
13.	Muscular asthenia	Sheep	frequent

Species of ticks.	Geographical incidence	Writer recording
Argas persicus	Persia	Oken, Dupré and others.
Ornithodoros turicata	Mexico	Dugès
Ornithodoros moubata	S. & E. Africa	Livingstone and others
Ornithodoros savignyi?	East Africa	Dowson
Ixodes ricinus	Norway	Johannessen
unidentified	N.S.Wales	Cleland
unidentified	Queensland	Bancroft
Ixodes holocyclus?	N.S.Wales	Cleland
Ixodes holocyclus?	Queensland	Present writer
Dermacentor venustus?	British Columbia Oregon	Todd Temple
Dermacentor venustus	British Columbia	Hadwen
Ixodes holocyclus Others?	N.S.Wales Queensland	Bancroft, Anderson-Stuart, Present writer.
Ixodes pilosus	Transvaal	Mally

It is not to be assumed that this is a complete list of the class. Ornithodoros talajae, for example, may cause severe symptoms; and so may many others. But these contribute no interest, or data for enquiry, which is not comprehended in the above groups; and their inclusion would merely encumber discussion.

In regard to sicknesses of the types in question, the supposition of simple salivary intoxication has been, as I have mentioned, very generally accepted. But for the most part this has probably been on no better ground than that it was the readiest explanation to hand, and that it seemed to fit. It is an assumption which, for the reasons that follow, I consider wholly untenable in reference to most of the affections cited:-

Bites of ticks, and of the respective varieties known to cause the several affections, are much more common than are cases of resulting sickness. The bite is certainly often harmless. Loundsbury and Davidson who allowed themselves to be bitten by Argas persicus in South Africa, found in both cases that

there was no inconvenience beyond slight itching and a small sore which quickly healed. (32) This tick, in Persia, very frequently produces an affection which is well recognised and defined; but in Australia it is harmless, and apparently so it may be in South Africa also.

Mally, who experimented with sheep in South Africa, frequently found that animals subjected to the bite of Ixodes pilosus might fail to develop symptoms. (33).

Ixodes ricinus, abundant though it is over Europe, seldom is a source of more than slight annoyance; but as we have seen it may occasionally excite very severe symptoms. In short, there is no species of ticks, so far as is known, of which the bite is always poisonous.

The incidence of types of sickness among the cases is also very inconstant for any one species of ticks; I should say that it is really more nearly constant for any one district!

That such anomalies may be due to variation of the degree and type of toxicity of a physiological secretion produced by ticks of

one species is hardly credible. It is true that individual susceptibility and idiosyncrasy on the part of the host might account for some inconstancy, and so also might the condition of the tick in regard to stage of food digestion, but these factors could not account for the prevalence that is found in one region and for the complete absence of cases in another, although ticks of the same species should be equally abundant in both.

Lastly a latent period of from one to several days would not be found if the poison were pre-formed, and this obtains in most of the groups.

The second hypothesis, that of poisoning of the wound with disgorged food-residue, would afford a better explanation of the erratic incidence. It might also account for the variation of symptoms caused by an individual species of ticks in different districts, on the assumption that diverse types of hosts were available, and therefore that differences in the nature of the food-residue existed in consequence. But such variation of hosts is not actually found, at all events in most of the cases on which the question at present has

a bearing; for example, Argas persicus, which is very inconstant in its effects, has the same host in all countries, namely the domestic fowl - that is, the individual specimens which by circumstances have access to human dwellings and human hosts are almost always bred upon domestic fowls.

Another evidence which disfavours this suggestion in relation to certain cases is the fact of the occurrence of typical intoxications after prolonged periods of isolation and starvation of the tick as in the case mentioned by Oken.

Again, the fact of symptoms not supervening until the lapse of a latent period calls for some other explanation.

Both of these theories which may be classed together under the heading of <u>direct intoxication</u> leave essential points unexplained. As regards many cases they are not even compatible with the facts found.

One of the cases which I have cited may, however, be due to such a cause, but it is a very unusual case, namely that in which two hundred ticks were found upon the body. In that instance the symptoms commenced within

one hour, and quickly reached their maximum. After removal of the ticks improvement was regularly progressive until recovery had taken place, a course which would be expected if the cause were a toxic saliva. This case is exceptional, however, in that the number of bites was so great that a salivary intoxication, ordinarily too slight to cause marked symptoms, might here readily be of serious consequence.

As opposed to direct introduction of a toxin I suggest two other possibilities: that which I shall term local elaboration, and secondly general organismal infection. By local elaboration I mean that the formation of a poison, which is afterwards absorbed from the area, may result from the chemical interaction of the salivary secretions of the tick, the tissues of the host, the imbedded mouth-parts of the tick, and the products of micro-organisms which, having been introduced incidentally, propagate in the wound.

Such a means of intoxication would account for the considerable period that generally elapses between the time of attachment of a tick and the commencement of sickness; and it would permit of variability of types of illness,

and of a sporadic incidence in spite of great prevalence of the ticks. The same, however, might be true of a specific general infection; but this would not lead to the occurrence of the cases in such a peculiarly isolated way, and it would not account for the fact first noticed by Dugès and many times confirmed since, that the severity of certain of these affections is much increased, and the duration prolonged, by the retention of the mouth-parts within the skin after removal of the tick's body.

Regarding general organismal infection, we know that ticks do transmit a number of infective diseases of man and of the lower animals, of which the pathology is well understood; and it will be instructive to notice a number of facts pertaining to those, as follow, for their analogies afford useful suggestions:-

1. There is necessarily in all a latent period during incubation.
2. For the most part they affect only closely allied species; as, for example, the horse and the ass in the case of Equine piroplasmosis, or the sheep and the goat in that of "Heartwater". While this

limitation may be due to the specific micro-organism being infective only to certain species it is not necessarily so. We have seen that the ticks may be restricted in their agency, owing to their habits or to disability to infect during one or another phase of the life cycle. Such, in fact, is the position in the case of South African Relapsing fever which normally is found only in man, but which has been reproduced experimentally in rats, mice, and monkeys. (37) This point then is of value only if combined with evidence that under similar conditions the tick is parasitic on other species also.

3. The majority of such affections are of very limited geographical distribution, as, for example, Rhodesian fever of Cattle, or Piroplasmosis of Sheep (Carceag) which is almost confined to the low lying parts of the Danube Valley. (19)

4. Immunity, relative or absolute, after recovery is the rule; and in some cases animals reared in infected country are immune without having apparently con-

tracted the disease.

This last is seen in the case of Texas fever of Cattle.

5. None of those affections have a sporadic incidence.

6. As would be expected, removal of the ticks does not alter the course of the disease when once established, although as Nuttall and Hindle (42) have shown it will prevent its onset in the case of East Coast (Rhodesian) fever if the ticks are removed within two days of their attachment, which, however, is quite another matter.

7. These diseases although commonly carried by but one species of ticks may in unusual circumstances be conveyed by others; thus Schellack proved experimentally that the Spirochaeta marchouxi (of fowls) which is ordinarily disseminated only by Argas persicus can be transmitted also by Argas reflexus.

The phenomena of any particular affection viewed in relation to these features of known infective general diseases will afford a certain amount of presumptive evidence regarding its being of an analogous nature or otherwise.

The Case resembling Conine Poisoning.

as

an example of

Local formation of a Toxin:

Other Groups of Cases in relation to this Hypothesis.

The affection of the child whose symptoms have already been discussed in detail, was due, I believe, to a poison formed by "local elaboration"; and its further consideration may now be entered upon with advantage, as it will also serve the purpose of illustrating this principle.

It has been shown how closely the physiological action of the toxin resembled that of the alkaloid conine. Quite apart from the particular similiarity to the symptoms of poisoning by that substance, the condition was more typical of simple chemical poisoning than of general bacterial or protozoal infection.

The child was perfectly well immediately upon recovery from the paralytic symptoms: there was no period of convalescence: and while one system - or part of a system - was severely affected, there was relatively

slight disturbance of other organs or of the general state. Yet all the objections that I have raised against the acceptance of the introduction of a pre-formed poison as a sufficient explanation, hold in this instance: and apart from those there are other factors, special to this case, that are contra-indicative of such a causation; to them I shall refer later.

I do not recall any case of an infective disease, in which these features are found, at any rate in so marked a degree, with the one exception of tetanus.

In this malady the general or non-specific symptoms, except in so far as they are consequent on the special ones, are, even in acute cases, insignificant; and recovery when occasionally it does take place is rapidly completed. But tetanus differs from typical infective diseases in that the toxins are formed locally in the wound; not only so, but the principal and pathologically essential element of the product of the bacillus tetani, unlike those of most pathogenic bacteria, is a comparatively simple basic substance closely related to the ptomaines. The condition is

therefore almost analogous to a simple alkaloidal poisoning, and is in fact not unlike the means of intoxication of which I at present speak.

There is of course this difference, that tetanine is a constant and specific product of the bacillus tetani irrespective of its surroundings: whereas what I suggest here is a toxin which, although formed through chemical interchanges involving the presence of bacteria, may yet not be a specific or even a direct product of them, and which will therefore be variable according to the incidental circumstances of tissue environment: in a word, a ptomaine or other body formed in an analogous way.

More particularly, I think that the poison may have been a ptomaine closely related to conine itself. We know that conine is one of the easiest of the vegetable alkaloids to reproduce synthetically, and also that compounds very closely resembling it have been separated from decomposing animal matter. Pannum in 1856 found in septic fluids a toxic substance having an action resembling that of curare, a substance which was not destroyed by

boiling. (The wound in the case under consideration was a suppurating cavity.) Ten years later, Marquardt recovered from similar sources an alkaloidal body which has been named septicine, and which gave chemical reactions similar to those of conine. The constitution of septicine is still unknown, however, for it has never been obtained in a pure condition. (58)

The production of ptomaines requires a certain time, as a rule not less than two days; it requires suitable tissues; and it requires bacterial growth of a particular kind. It is a familiar fact that in circumstances so alike as to be apparently quite similar, differing ptomaines may be formed; and, indeed under the same actual conditions various ptomaines may be produced successively, each in its turn being reduced to one of a simpler form. (58)

There is here a probable explanation of the erratic incidence and variable type of affections of this sort, although tick-bites even by the same species should be very common, for the accessory bacterial factor would naturally be inconstant.

It will be remembered that in this case the tick's body was cut off and that the mouth-parts were left in situ. With this, the salivary flow must of necessity have ceased, and likewise any hypothetical disgorgement of food, yet the symptoms continued to increase in severity. On the other hand the cleaning out of the wound and removal of the retained structures led directly to recession of the symptoms. These phenomena are an additional evidence against direct intoxication, such as by saliva or food-residue, beyond those enumerated in the general discussion of poisoning by those means. Again, if the factor were an infection that had been introduced, that is a blood infection, the illness would not have been influenced in this marked way by local treatment of the wound after the disease had been established.

Most probably the continuing presence of the biting-parts has a chemical significance, for they form a source of readily accessible nitrogen through the breaking down of chitin.

No information upon the question of acquired immunity is available in the circumstance that the case is an isolated one, but

this important point will arise in regard to some of the other groups mentioned.

The cases quoted from British Columbia and from Oregon resemble the above case in having the same dominating symptom - muscular paralysis. Temple uses in regard to the condition the term "acute ascending paralysis". Clinically several of the cases certainly resembled that most characteristic of the diseases to which this title is applied, namely, Landry's paralysis. In my case, however, the order of muscles affected was not quite so systematically "ascending" as it is in typical examples of that disease.

Nuttall (17) considers that the evidence afforded by the production of the condition by experimental attachment of the tick proves it to be a "definite affection", although as yet of unknown nature. The records of a number, now considerable, of very similar cases from one region would also suggest that they constitute a separately definable affection - a pathological entity. But, as we have seen, very variable types of nervous symptoms occur

after tick-bites, such as cramps, amblyopia and vertigo, paraesthesiae, and convulsions; and in some other groups of cases symptoms referable to the nervous system are absent or subsidiary. Are these affections quite separate from the paralytic ones? and are they of different etiology? I do not think the available evidence points to that as being so. Yet, while it is sufficiently obvious that there must be a common cause for certain of the paretic cases, it would seem highly improbable, until one examines further, that such heterogeneous groups ought to be identified with them.

In an earlier chapter I said that tick-bite affections showed rather more constancy for districts than for tick species, but still there is throughout something curiously erratic in the types. This is to be accounted for, I believe, in our having to deal not with a definite disease or a number of definite diseases; but simply with an intoxication into which there enters an initial factor - the tick and its secretions - which is more or less constant, and a bacterial factor which is variable; thus accounting for local

similarity of cases, for the many varieties in differing circumstances and places, and for the commonest phenomenon of all - harmlessness of the bite. This would explain also the fairly frequent ability of suitably selected ticks to excite symptoms, although so very small a proportion of tick-bites are toxic on a general average of even reputed dangerous species. The tick with which Nuttall succeeded in producing paralysis in a dog was procured directly from one of the regions where that form of tick-bite affection is found. (17) In this connexion the probability of such a tick harbouring the appropriate bacteria has an important significance for it gives the conditions required for the mode of poisoning that I have suggested, and we have seen (Tonnel's cases) how good an agent for such harbouring the tick may be.

In regard to the question of poisons, that may not be chemically alike, causing paralysis of a more or less similar type to that under consideration it is interesting to note some of the varieties of circumstances in which this clinical picture may occur. "Many of the

common pathogenic organisms may, especially in patients debilitated by disease, give rise to symptoms of acute ascending paralysis. Thus, the typhoid bacillus may produce clinically an acute ascending paralysis". (Osler) It is one of the forms which acute anterior poliomyelitis may take. We know also that several vegetable poisons produce symptoms of the conine type; which are practically those of Landry's paralysis with hours substituted for days! It would seem therefore that poisons of a wide range are capable of setting up paralysis of this form.

To one or another poison formed within the wound under certain fortuitous conditions I attribute the occurrence of most of those groups of transient though severe tick-bite affections; and, if in this I am correct, the clinical differences even although so wide, are to be regarded as merely incidental.

The paralysis which may follow the bite of Ixodes pilosus in South African lambs requires the coincidence of long grass and frosty weather. (Mally) In British Columbia the affection of sheep occurs only in the early spring months (16), a fact which

I think indicates the necessity of some coincidental circumstance in this case also. Hadwen, who believes that the causation is probably direct poisoning (16) suggests as an explanation of the period of incubation, that the tick does not produce its poison until it approaches the end of its term of feeding - five or six days. This, it is said (17) would account also for the bites being often harmless, as the tick must in many cases be rubbed off at an earlier time. On the other hand such an hypothesis would not explain the restriction of incidence in accordance with the satisfaction or otherwise of certain required conditions, as has just been noted in regard to two of the affections; or the continuance of severity after removal of the tick's body for so long as the mouth parts should be left in situ, as has so often been observed (Dugès, Bancroft, etc.) and as was evident in my case in man.

The remaining alternative of an infective causation is also contra-indicated alike by Hadwen's experiments on communicability and by Borthwick's observation, of the Cape Colony affection, that early removal of the

ticks leads to more rapid recovery.

Analysis of Groups in relation to Etiology.

Having considered the characteristics and, consequent potentialities and restrictions of the various etiological theories that I have submitted, I shall now review in relation to them the several groups of cases described or quoted. This will be done most conveniently by applying in each case a series of questions embodying various differentiating factors as follow:-

1. Is there any considerable latent period?
2. Does early removal of the tick affect the course of the disease?
3. Does any prejudicial effect upon the course of the disease result from permitting the mouth-parts to remain in situ after removal of the tick's body?
4. Do ticks of the same species fail in other districts to cause the particular affection, although repeatedly causing it locally?
5. Is the affection which results from the bite of the individual species of ticks constant in incidence and type under similar conditions?

6. Is there any considerable degree of immunity conferred by a single attack?

7. Is the affection confined to the limits of a single or of a few closely allied species? and that although the same species of ticks, in the same place and circumstances, are parasitic also on other hosts?

8. May a tick that has been starved for a prolonged period cause the affection?

I shall comment upon the significance of these questions seriatim, and then exhibit their application to the various groups of cases in tabular form.

1. The existence of a considerable latent period, between the time of attachment of the tick and that of the appearance of symptoms, is essential if the cause be blood infection or the effect of a locally formed poison: immediate onset of symptoms, therefore, would preclude both of these, and would point to one of the two direct means of poisoning. The converse is not quite so definitely to be relied upon, for, even after absorption, a simple chemical substance may have a delayed action, as in the case of digitalin; but a latency of from one to several days after the

introduction of a toxin beneath the skin, particularly as the local circulation is in no sense diminished but rather increased, could hardly be explained in this way.

2. If early removal of the tick lessens the severity, or otherwise modifies the course of the illness, blood infection may be excluded; for in that case the disease would run its normal course, having once been established. A negative reply to this question while not necessarily excluding the other etiological agencies, points strongly against them. In each of these cases the source of intoxication would be removed, and a consequent arrestment of the sickness would probably follow. The last point must be qualified, however, to the extent of the possibility of continuing absorption from an imperfectly cleaned wound, or of retention within the body of a toxin that were only very slowly eliminated.

3. If the effect of removal of the tick's body and leaving the mouth-parts in situ differs from that of complete removal, the presence of these parts as dead material must have an influence in maintaining the supply of toxin. This it would not have in the case of blood infection or of salivary intoxication. It is

conceivable, however, that food-residue adhering to the parts might be left in place, which otherwise would be removed. As a factor in the production of a poison locally the presence of the mouth parts would have, as has been pointed out, an important rôle. An affirmative answer to this question would, then, contra-indicate salivary intoxication and general infection, but would be compatible with either of the other two causes.

4. If ticks of a particular species repeatedly cause an affection in one district, but never do so in another, there must be a local factor which has a bearing on the action. This would not be so in the case of salivary poisoning nor, as I have shown, would it occur in the case of poisoning by food residue; both of these would therefore be negatived.

5. If under similar conditions the results of the bite of any one species be markedly variable in type, or if the bite be as a rule harmless but occasionally highly dangerous, salivary intoxication may practically be excluded.

6. Should a single attack confer any considerable degree of immunity analogy would favour

general organismal infection. Toleration of certain alkaloids can be acquired to a remarkable extent, and the continuing presence in the blood of some chemical substances is known to lead to the production of "antibodies". We should expect therefore that repeated attacks of an affection caused by the introduction of a poison, whether formed in the wound or by the tick, might possibly confer partial or even full immunity; but it is not probable that a single attack would give complete protection as is the case with many infective diseases. The latter (so far as the extra-cellular toxins are concerned) may be compared to the frequently repeated administration of a chemical poison in doses, individually non-lethal, which are not discontinued until the protection has reached an effective degree or until the subject succumbs. It is this continuance until immunization is completed that renders full protection - permanent or otherwise - probable in the case of a general infection; whereas in that of transient chemical poisoning, or of absorption from a localized source, the process, even if commenced, is likely to remain unfinished. Thus, we do

not find that a person recovered from snake-bite has developed a protective quantity of antivenine; nor should we advise one who has survived an attack of tetanus to be any the less vigilant in the event of a subsequent wound.

7. The confinement of the incidence of an affection to the most closely related species, although the associated ticks should be prevalent also on other hosts, would disfavour direct intoxication; for, according to available analogies, a pre-formed poison would not show this limitation of range in its toxicity towards various animals. In the case of a locally elaborated poison such a restriction might take place; and in that of blood infection it would be even more surely expected.

8. If a tick that has been isolated and starved for a prolonged period may produce the affection typically, poisoning by decomposing food-residue may be ruled out. In these circumstances such a product would have disappeared from the anterior part of the alimentary tract of the tick: and even if not so, it would almost certainly have been reduced to a simpler and less toxic type.

In the table which follows the questions are applied to each of the groups of cases set out on page 72, the numbers on the left having the same reference. The numbers along the top refer to the test questions enumerated on pages 92 and 93. In the last column the conclusion deduced is entered. Where two letters appear both are compatible with the conditions, and if probability is against an entry, which cannot however be definitely excluded, the letter is enclosed in brackets.

A. represents poisoning by a toxic secretion of the tick.

B. represents poisoning by food-residue.

C. " " " local elaboration.

D. " " " general infection.

It will be observed that in each case only a minority of the questions are answered, owing either to the essential nature of the conditions or to the absence of records, making answer impossible in regard to the remainder. Affirmative and negative replies to the various questions are represented by the signs + and − respectively.

	Condition	Subject affected	Species of Ticks	Questions. 1	2	3	4	5	6	7	8	Conclusion
1.	Pain, fever, delirium, convulsions.	Man	Argas persicus				+	−	+	+	+	D.
2.	Swelling, numbness, vomiting, etc.	Man	Ornithodoros turicata			+		−		+		C.
3.	Itching, tingling pain, fever	Man	Ornithodoros moubata				+	−	+	+		(C),D.
4.	Pain, swelling, vomiting, fever	Man	Ornithodoros savignyi?				+	−				C,D.
5.	Cramp, loss of memory, polyuria	Man	Ixodes ricinus			+		−				B,C.
6.	Cardiac failure	Man	unidentified	−	+							A,B.
7.	Amblyopia and vertigo	Man	unidentified					−				B,C,D.
8.	Muscular paresis, fever, respiratory difficulty	Man	Ixodes holocyclus	+				−				C,D.
9.	Muscular paralysis, fever, abstinence from fluids, etc.	Man	Ixodes holocyclus	+		+		−				C.
10.	Muscular paralysis	Man	Dermacentor venustus		+		+	−				C.
11.	Muscular paralysis	Sheep, Dog	Dermacentor venustus	+			+	−		−		C. *
12.	Muscular paresis respiratory embarrassment.	Dog, Cat	Ixodes holocyclus; Others?	+	+	+		−	+?			C.
13.	Muscular asthenia	Sheep	Ixodes pilosus					−	+	+		C, D.

* Hadwen's experiments (16), as already referred to, contra-indicate "D" in this case.

Of the thirteen groups examined the analysis indicates the probability of the causation being:-

Salivary intoxication or food-residue poisoning	in 1	group(s)
Food-residue or locally produced poison	" 1	"
Food-residue, local production, or general infection	" 1	"
Local production or general infection	" 4	"
Local production	" 5	"
General infection	" 1	"

CONCLUSION.

The result of the analysis is surprising when it is remembered that such affections have been generally regarded as due to simple salivary poisoning. It is of course only by the demonstration of specific organisms on the one hand, or by the exact working out of the chemical processes involved on the other, that these conclusions may be actually established.

Where the cause is a specific infective one there is every probability that, sooner or later, such evidence will be obtained.

In the case of local elaboration of a toxin the difficulties are greater, at all events in the human subject. The cases are few and they occur at unexpected times and in out of the way places, so that facility for delicate and complex chemical investigations is not likely to be available at the moment when it is requisite. Organisms may be found in the wounds made by the ticks - they are probably present in all such lesions, a very important fact, but if, as my con-

tention is, the bacteria involved are non-specific in type, the mere demonstration of their presence can give, in ordinary cases, little assistance. The careful recording of cases clinically promises more in these circumstances; and although it is not easy to get affirmative evidence of a conclusive kind by this means alone, one can at all events often find proofs on the side of negation from which points of affirmation may be deduced.

As the affections of sheep occurring in British Columbia and in South Africa have been reproduced under control, the prospect of an exact etiology being worked out in regard to them is much enhanced. Many of the experiments prove ineffective, and bacteriological comparisons of the wounds of successful with those of unsuccessful experiments might be of much value.

It will be observed that of the groups of cases cited as many in man were due to Ixodides as to Argasides, although the former have customarily been supposed to be innocuous to the human subject. One

element that has contributed towards this mistake is the fact which I have pointed out, that the life habits of the Ixodidae enormously reduce their opportunities of affecting man, and thus the cases are extremely few - only one of each in many of the types recorded. The variety of the cases caused by them is on the other hand even greater, and the severity in some instances also greater, than that of the cases due to Argasides.

The fundamental error, however, that has made the foregoing misconception possible has been the assumption that toxic symptoms were due to simple salivary poisoning. The natural conclusion following from this has been, that if ticks of any one species were known commonly to bite and to cause no symptoms they were assumed to be consistently innocuous.

Another error arising from the same source is that of attributing to each particular species of ticks a definite and uniform set of symptoms. Because in one region a tick has been found to produce an affection of a certain type it has been

supposed that it would do so in all, while in fact the symptoms may vary with the locality and other coincident circumstances. That this should be so is but to be expected when a broader view of the possible etiological factors is taken. Such variations then become much more intelligible.

In the case in the human subject that came under my own care the conditions indicate that the cause was not direct intoxication, either by saliva, or by food or other residue; and was not general infection. The evidence is convincing that the toxin, of whatever chemical nature, was produced locally within the wound; and that the detached and embedded mouth-parts of the tick had some rôle in the reaction. That the poison may have been an animal alkaloid and a homologue of conine is an interesting possibility: the degree of similarity in physiological action was certainly remarkable, and the known fact that such a substance may be formed in septic products still further suggests it. Regarding the British Columbian and Oregon cases the information available is more limited, but

the conditions appear to be so similar as to point to a closely analogous means of causation. In some of the other groups examined the factor appears to have been probably blood infection: and in one case only, a case that stands apart from all the others in having an enormous number of ticks attached, does salivary poisoning prove a satisfactory explanation.

In tropical countries it is common to find that local popular opinion dreads the bite of some particular arthropod which may be known to have but feeble toxic power or perhaps no poison glands at all, and we are apt to be sceptical. In one district it is a "harmless" variety of tarantula, in another an equally innocent species of centipede, or again it may be a very ordinary type of spider: yet there is no doubt that these beliefs are often founded upon a real, if exceptional, case that has occurred in the vicinity.

I think that possibly in regard also to bites other than those of ticks, we might do well to look further than merely to the physiological secretions of the offender and the specific general infections it may convey, if

we would seek an explanation of some of those erratic and apparently anomalous cases.

B I B L I O G R A P H Y.

1. Anderson-Stuart, Sir T.P.: Anniversary address to Royal Soc. of New South Wales. Journal Roy. Soc. of N.S.W. vol. 28, 1894.

2. Aristotle (384-322 B.C.): History of Animals, Book V. Eng. trans. of R. Cresswell, Lond. 1862.

3. Bancroft, Jos. : "Queensland ticks and Tick blindness". Australasian Med. Gaz., 1884.

4. Borrel et Marchoux : "Argas et spirilles". Comptes Rend. Hebd. de la Soc. de Biol., Paris 1905.

5. Borthwick : "Tick paralysis affecting Sheep and Lambs". Veterinary Journal London, 1905. Abst. in Nuttall, G.H.F. (41)

6. Brown, A.A. : "Fowl tick (Argas miniatus)". Journal Dept. of Agric. of Victoria, Melbourne, 1902.

7. Castellani and Chalmers : Manual of Tropical Medicine 2nd. ed.; London, 1913.

8. Cato M. Porcius (234-149 B.C.): abst. in Pagenstecher, H.A. 1861. cit. Nuttall and Warburton.

9. Cleland, J.B.: "Injuries and Diseases of Man in Australia attributable to Animals; Phylum Arthropoda". Australasian Medical Gazette, 1912.

10. Columella, Jun. Mod. (cir. 60 B.C.); abst. in Pagenstecher, H.A. 1861. cit. Nuttall and Warburton.

11. Dowson, J.: "Poisonous tick" British Med. Journal; 1.1895 .

12. Dugès, Alf.: Repertorio de Guanajuato (Mexique); 1876. absts. in Mégnin, P. "Les Argas du Mexique". Journal de l' anatomie et de la physiologie norm. et path.; Paris, 1885.

13. Dupré : "Voyage en Perse fait dans les années 1807-1809"; Paris, 1819. cit. Laboulbène et Mégnin.

14. Dutton, J.E. and Todd, J.L.: "The nature of human tick-fever in the Eastern part of the Congo Free State". Liverpool School of Trop. med. Memoir XVII; 1905.

15. Eaton, E.M.: "A case of tick-bite followed by widespread transitory muscular paralysis". Australasian Med. Gaz.; IV, 1913.

16. Hadwen, S.: "On Tick paralysis in

Sheep and Man following bites of Dermacentor venustus". Parasitology Lond. vol. VI, 1913-1914.

17. Hadwen, S. and Nuttall, G.H.F.: "Experimental Tick Paralysis in the Dog". Parasitology VI Lond. 1913-1914.

18. Heller, Von Camil: "Zur Anatomie von Argas persicus". Sitzungsberichte der Kaiserlichen Akad. der Wiss.; Mathemat.-naturwiss. Classe; vol. 30; Wien, 1858.

19, Hutyra and Marek: Article "Ovine Piroplasmosis (Carceag)" in "Special Pathology and Therapeutics of the Diseases of Domestic Animals". Trans, by Mohler and Eichhorn; Lond., 1912.

20. Johanessen, A.: "Acute Polyurie bei einem Kinde nach dem Stiche eines Ixodes ricinus". Archiv fur Kinderheilkunde; Stuttgart, 1885. cit. Nuttall and Warburton, 1911.

21. Kilborne, F.L.: in Smith and Kilborne: "Investigations into the nature, causation, and prevention, of Texas or Southern Cattle fever". Bulletin 1, Bureau of Animal Industry, U.S. Dept. of Agriculture, Washington, 1893.

22. King, A.F.A.: "Insects and Disease; Mosquitoes and Malaria". The Popular Science Monthly; N.Y., 1883.

23. Koch, Von C.L.: "Systematische Übersicht über die Ordnung der Zecken". Archiv fur Naturgesichte; Berlin, 1844.

24. Koch, Robt.: "Ueber afrikanischen Recurrens". Berliner klinische Wochenschr., 1906.

25. Kossel and Weber : "Ueber die Hämoglobinurie der Rinder in Finland". Arbeiten aus dem Kaiserlichen Gesundheitsamte; Berlin, 1900.

26. Kotzebue, Maur. : Voyage en Perse a la suite de l'ambassade Russe en 1817; Paris, 1819. cit. Laboulbène et Mégnin.

27. Laboulbène, A. et Mégnin, P.: "Memoir sur les Argas de Perse". Journal de l'anatomie et de la physiologie norm. et path.; Paris, 1882.

28. Latreille, P.A.: Magazin encyclopedique, 1795. cit. Michael A.D.: British Oribatidae, vol. I, Lond. 1884.

29. Lignières: Sur la "Tristeza" (Piroplasma bigeminum). Compt. Rend. 13 me. Congr.

internat. Med., Sect. Bact. et Parasit.; Paris, 1901. cit. Pocock (49).

30. Livingstone, D.: Missionary travels and Researches in South Africa; 1857.

31. Loundsbury, C.P.: "The fowl tick (Argas persicus) Studies in its life-cycle and habits". Agricultural Journ. Cape of Good Hope, 1903.

32. Loundsbury, C.P.: "Insect bites and the effects thereof". Canadian Entomologist 1900, cit. Nuttall and Warburton.

33. Mally, C.W.: "Notes on the so called Paralysis tick, Ixodes pilosus". Agricultural Journ. Cape of Good Hope, 1904.

34. Manson, Sir Patrick.: Tropical Medicine, A Manual of the Diseases of Warm Climates, 5th ed.; Lond. 1914.

35. Marchoux, E. et Salimbeni, A.: "La Spirillose des Poules". Ann. de l'inst. Pasteur; Paris, 1903.

36. Marquardt.: ref. in art. Thomas, B. in Thorpe's Dict. of Applied Chem.; Lond., 1913, (vide 58)

37. Mollers, B.: "Experimentelle Studien über die Übertragung des Ruckfallfiebers durch Zecken". Zeitschr. fur Hyg. und In-

fectionskrank.; Leipsig, 1908.

38. Motas, M.: "Sur le rôle des Tiques dans le développement de la piroplasmose ovine (Carçeag)". Comptes Rendus Hebd. de la Soc. de Biologie; Paris, 1903.

39. Neumann, L.G.: "Révision de la famille des Ixodes". Mémoirs Soc. Zool de France; 1896.

40. Nuttall, G.H.F.:"Ticks and tick-transmitted diseases". Trans. Epidemiolog. Soc., Lond., 1905.

41. Nuttall, G.H.F.: "Tick paralysis in Man and Animals, further published records with comments". Parasitology, vol. 7 London, 1914.

42. Nuttall, G.H.F. and Hindle, Edw.: "Conditions influencing the transmission of East Coast fever". Parasitology vol. VI.; Lond., 1913-1914.

43. Nuttall, G.H.F. and Strickland, C.: "On the presence of an anticoagulin in the salivary glands and intestines of Argas persicus". Parasitology vol. I; Lond., 1908.

44. Nuttall and Warburton: "Ticks: A monograph of the Ixodoidea"; 1908-1911.

45. Oken, Von: "Sogenannte giftige Wanze in Persien"; Isis, oder Encyclopädische Zeitung; Jena, 1818.

46. Osler, Sir W.: "Principles and Practice of Medicine" (article on Landry's Paralysis) Eighth Ed. 1912.

47. Pagenstecher, H.A.: "Beitrage zur Anatomie der Milben". Leipsig 1861. absts. in Nuttall and Warburton, 1911.

48. Pannum: ref. in art. by Thomas, B. in Thorpe's Dict. of Applied Chem.: 1913. (vide 58)

49. Pocock, R.I.: Article "Ticks" in A System of Medicine by many Authors: Allbutt and Rolleston. 2nd. ed. vol.II.pt.2. 1907.

50. Pocock, R.I.: Note to Dowson's rep. on "Poisonous Tick". British Med.Journal; I, 1905.

51. Raillet, A.: Traité de Zoologie medicale et agricole, 2nd ed.,Paris, 1895.

52. Ross, P.H. and Milne A.D.: "Tick fever". British Med. Journal; II, 1904.

53. Sakharoff : ref. to by Marchoux and Salimbeni (vide 35)

54. Schellack, Von C.: "Versuche zur Über-

tragung von Spirochaeta gallinarum und Spirochaeta Obermeiri". Arbeiten aus dem Kaiserlichen Gesundheitsamte, vol. 30; Berlin, 1909.

55. Smith T. and Kilborne, F.L.: "Investigations into the nature, causation, and prevention, of Texas or Southern Cattle fever". Bull. number I, Bureau of Animal Industry, U.S. Dept. of Agriculture; Washington, 1893.

56. Spreull, J.: Article on "Heartwater". System of Veterinary Medicine ed. by E. Wallis Hoare; London, 1913.

57. Temple, I.U.: "Acute ascending paralysis or Tick paralysis". Medical Sentinel, Portland, Oregon, 1912. Abst. in Nuttall, G.H.F. (41).

58. Thomas, B.: Article on "Ptomaines" in Dictionary of Applied Chemistry, ed. by Sir Edward Thorpe, vol IV; 1913.

59. Todd, J.L.: "Tick-bite in British Columbia". Journal of Tropical Medicine; London, 1913.

60. Tonnel: "L'Argas reflexus parasite de l'homme". Abstract of, in La Semaine medicale, no. 46; XI, 1906.

61. Varro, M. Terrentius (116-27 B.C.):

abst. in Pagenstecher, H.A.; 1861, cit. Nuttall and Warburton.

62. Warburton, C.: "Notes on Ticks". Journal of Econ. Biol.; London, 1907.

63. Wilson, L.B. and Chowning, W.M.: "Studies in Piroplasmosis hominis (Spotted fever or Tick fever of the Rocky Mountains)". Journal of Infectious Diseases: Chicago, I, 1904.