set in the last three or four days, and with increasing delirium and weakness he died on the twenty-first day of the disease.

At the necropsy I found the following conditions on the right side: General fibrinous adhesions firm and fibrous along the posterior border; posterior part of all three lobes solid, of dull red colour, on section wet and glazed; no granulation of surface; interlobular markings distinct; no coarse fibrous bands; no dilated bronchi; anterior margins emphysematous; left lung emphysematous, congested, and oedematous at the base; heart muscle soft, fibres granular; liver large, soft, and pale; kidneys, cortex cloudy; other organs normal.

Microscopical examination of hepatised right lung: The alveoli contained granular and fibrinous plugs which were more or less completely enclosed in a delicate sheath of young connective tissue consisting of a hyaline substance interspersed with scanty fusiform and round nuclei. In a few places the fibrinous matter had been entirely replaced by a knot of young fibrocellular connective tissue. Here and there an alveolus contained nothing but a few large desquamated epithelial cells. The capillaries of the alveolar walls were gorged with blood, but there was no interstitial thickening.

In this case organisation of the alveolar exudation into connective tissue had already begun at the end of three weeks. A similar change in the lung has been noted in a fair number of recorded cases.

Cases of fibrosis of the lung following pneumonia may be roughly divided into two groups. In the first the disease is febrile and progressive, terminating fatally as a rule in a few months. In most cases ulcerative cavities in the lung develop, and the sputum may become foul. In the case just described there was no breaking down, possibly owing to the fact that the patient died so soon. In the second group fibrosis takes place very insidiously, arising out of what appears to be delayed resolution, without fever or constitutional disturbance, and the patient recovers with a fibroid lung.

In a paper on Subacute Indurative Pneumonia, published in THE LANCET in 1890 I described two cases of pulmonary fibrosis supervening directly on subacute forms of pneumonia. The anatomical changes in the first of these closely resembled those above mentioned—i.e., organising pneumonia. The history of this case was that the disease began with sudden chills, weakness, and cough, but the patient was only confined to bed for two days, though ailing from the first, and complaining of cough, expectoration, dyspnea, and night sweats. Death took place about four months after the onset. The history suggested that it was not an acute sthenic pneumonia, the constitutional disturbance being relatively slight and transitory.

The case seemed to lend support to the view put forward by Wagner, Heitler, Talma, Hanau, and Pal, that the pneumonia which leads to induration is a special form distinct from the acute classical variety. These authors ranged themselves on the side of Rokitsky, Wilks, and Buhl, who denied that acute lobar pneumonia ever passes into a chronic stage, in opposition to the statements of Stokes, Charcot, Marchand, and Ziegler. But cases like No. 19 described above, as well as others published by A. Fränkel and other authors, have convinced me that this statement is too exclusive, and that it must be admitted that in exceptional cases acute lobar pneumonia may lead to induration. Why in some cases resolution delayed for months may be followed by complete recovery, while in another like the case just referred to induration should have begun at the end of three weeks must at present remain unexplained.

Dr. A. G. Auld, in the *British Medical Journal* in 1905, reported a case of "fibroid pneumonia" occurring in a child. The disease began acutely with vomiting and fever, soon followed by signs of pneumonia of the whole right lung, with remittent fever lasting for ten weeks. Improvement then began and the temperature became normal. So far there was no cough or expectoration. The lung remained very dull, but repeated punctures failed to yield any fluid. Subsequently slight fever returned, and when she was next seen, seven months after the onset, cough and expectoration had developed and tubercle bacilli were found in the sputum. Gradual improvement followed and eight weeks later her temperature was normal and her general health was good. Dr. Auld regarded the case as one of acute pneumonia going on to fibrosis with subsequent tuberculous infection.

A somewhat similar case was admitted into the London Hospital under my care about the same time.

CASE 20.—A labourer, aged 25 years, was admitted on June 28th, 1904. The patient, who had never been ill previously, first felt ill on June 17th, when he had much shivering, a stabbing pain in the left side, and soon afterwards cough, expectoration, and shortness of breath. On admission, pulse, 100; respirations, 20; temperature, 100° F.; signs of pneumonia (dullness, tubular breathing, and subcrepitant râles) of the left lower lobe. No change in the general or local condition followed.

The temperature for the first three weeks ranged from 103° to 100° and was remittent in character. For the next three weeks it ranged from 101° to 99° and for the next fortnight from 100° to 98°. As the left side remained very dull, it was punctured, and 12 ounces of clear fluid were withdrawn on July 13th. A further puncture was made on July 22nd with a negative result. The sputum was repeatedly examined for tubercle bacilli, but none were found. The patient improved greatly and was sent to a convalescent home on August 24th, when his temperature had become normal. The day the patient was discharged his sputum was found to contain tubercle bacilli for the first time. He was subsequently admitted into the Brompton Hospital, but discharged himself in a few days. In September, 1906, two years after the acute attack, he was seen by Dr. A. I. Simey, the medical registrar, who found signs of "typical phthisis" with tubercle bacilli in the sputum.

The case was originally regarded as one of pneumonia with delayed resolution, but when tubercle bacilli were discovered the diagnosis had to be reconsidered. Was it a case of lobar pneumonic tuberculosis from the first, or was it a case of lobar pneumonia associated with tuberculosis? The latter seems far more likely, for the lobar pneumonia form of tuberculosis is almost always progressive and a fatal issue usually reached in a few months at the latest. Whether tuberculosis was grafted on the pneumonia or whether tuberculosis was present though latent at the time that pneumonia developed admits of discussion, though I myself am in favour of the second view.

An Address

ON

THE MECHANISM OF INFECTION IN TICK FEVER AND ON THE HEREDITARY TRANSMISSION OF SPIROCHÆTA DUTTONI IN THE TICK.¹

Delivered before the Society of Tropical Medicine and Hygiene on Dec. 17th, 1909,

BY SIR WILLIAM B. LEISHMAN,
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MR. PRESIDENT AND GENTLEMEN,—For some years past I have been greatly interested in spirochætæ, and have, among others, worked with pallida, vincenti, recurrentis and duttoni, both from the morphological and the biological sides, one of the principal objects of my investigations being the vexed question of their protozoal as against their bacterial nature. You are all aware of the opposing views which have been held on this point, and I must at once confess myself an advocate of the protozoal theory. I need hardly add that the solution of this point is of more than academic importance, and is intimately concerned with problems of immunity, and may possibly lead to successful prevention and treatment in the future.

The main facts in connexion with infection in tick fever are well established, and I will only say that I have confirmed, if further confirmation were needed, the fact of transmission of the disease to animals by the bite of ticks sent to me from Africa. The hereditary transmission of the disease to the second generation of ticks I have also confirmed, as nymphs which I have reared in the laboratory from the egg are infective for mice and monkeys. Moeller's observation of the further transmission of the virus to the third generation I am not yet in a position to confirm as my second generation has not attained sexual maturity. Hereditary transmission through the tick, then, being established beyond doubt, my first observations were directed towards the discovery of spirochætæ in the bodies of infected ticks, and long and carefully did I search those which I first received from Africa through the kindness of my friend Captain Hallam Hardy, R.A.M.C., whose sad death from sleeping sickness you may have heard of. My search was in vain, no trace of a spirochæta was found. As these ticks had failed to infect a monkey by their bites, I concluded that they themselves were not infected and asked for more, stipulating that on this occasion the ticks should, if possible, be collected from huts in which cases of tick fever had occurred. I need

¹ The expenses of this investigation were in part met by a grant from the Royal Society.

not trouble you with details of further failures, but I was in the end successful in infecting a monkey with tick fever by the bites of *ornithodoros*, collected in Nyassaland in infected huts. At the height of the fever, when the blood was rich in *Spirochæta duttoni*, I allowed a large number of my ticks to feed on the monkey, and was then in possession of material with which to carry out the researches I had in contemplation.

I mentioned just now that my first batches of ticks showed no *spirochætæ* in any portion of their anatomy; to my surprise I was equally unsuccessful in my search in the case of the batch which infected the monkey, and, I may add, in the case of other batches since received from different parts in Africa, which also proved infective. It is, of course, impossible to exclude the chance that some of the ticks which bit the monkeys in question did harbour *spirochætæ*. This fallacy is one which is always present in such work as that under consideration. For example, whatever conclusion one arrives at as to the condition of a given batch or brood of ticks must be founded on the examination of a sample of such batch. However large the sample, and there are obvious limits to this where it is desired to follow up the course of subsequent events in such a batch, any conclusion is open to the objection that a different condition existed in a member of the group which was allowed to survive. Conservative surgery in the case of a tick is unfortunately impossible. The number of my examinations, however, totalling many hundreds, of ticks in all stages of development enables me to say with a fair degree of certainty that no *spirochætæ* were present in the tissues or body fluids.

Turning now to the hereditary transmission of infectivity to the second generation of ticks, which, as I have mentioned, I have personally confirmed, this confirmation was made with the progeny of those ticks which, if infected, brought their infectivity with them from Africa and had only fed on normal blood since their arrival in England. Here, again, no *spirochætæ* could be found, either in the very youngest eggs which it was possible to dissect out of the ovary, in eggs at various stages of incubation, or in the larvæ and nymphs hatched from such eggs. I may at this point remind you that the persistence of *spirochætæ* in the tick, their presence in the ovaries, and their presence in the eggs and in young hatched from these eggs has been observed by Koch and, in part, confirmed by Carter, the former working in German East Africa and the latter at the Liverpool School of Tropical Medicine. The negative results which I obtained were very puzzling in view of these positive ones, but I think now that they are reconcilable in the light of the subsequent experiments and observations which I shall mention.

I next turned my attention to a study of the fate of *spirochætæ* ingested by ticks, dissecting a tick of each batch every day for a fortnight; in every instance the following were examined: the coelomic fluid, the gut contents, the walls of the intestinal sac and portions of its diverticula, the genital organs, the salivary glands, the coxal glands, Gené's organ, the Malpighian tubes and Malpighian secretion. The result may be stated briefly: no recognisable *spirochætæ* could be detected later than the tenth day. The changes which the *spirochætæ* underwent in the intestinal sac were found to be very interesting, but would take too long to describe in detail. Dutton and Todd have described many of these changes, as well as others which were not encountered in my specimens. The principal features were the extrusion of lateral, more rarely terminal, swellings, which contained one or more particles of chromatin, and the breaking up of the chromatin core of the *spirochæta* into numerous fragments of coccoid or bacillary shape. In a few instances these small chromatin particles have been observed free in great numbers in the gut contents. Long before this I had observed in the Malpighian tubes of almost every tick dissected aggregations of curious clumps of chromatin granules, often in such numbers as to mask the cellular structure of the tube. These granular clumps I subsequently encountered in all stages of the tick's life, from the microscopical ovum up to the adult. Dutton and Todd have also noted granules in the Malpighian tubes of ticks recently fed on *spirochæta* blood which they considered to be derived from the *spirochætæ*, but I am in some doubt as to their identity with those in question, since Dr. Todd, to whom I had the pleasure of showing some of my specimens, informed me that

he had not observed this condition in the tubes of young nymphs. I may say at once that I consider these chromatin granules to be derived from *spirochætæ*, and, further, to be connected with them biogenetically. The situations in which they are encountered are the following. First, the Malpighian tubes, in which their distribution may be very irregular, some portions being distended by them, while none may be found in a long tract of the same tube. This irregular distribution may possibly be explained by the granules having escaped from the thin-walled intestinal sac into the tubes only in those situations in which the two structures happen to be in close contact. Secondly, in the ovary, where they are often encountered in great numbers and where, at times, a few clumps may be detected lying within the immature ova. Thirdly, they are sometimes found in small numbers in the walls of the intestinal sac. Finally, as a very rare occurrence, similar clumps of granules have been seen in the cells of the salivary glands.

From the time I first observed these granules, more than three years ago, I was suspicious of their possible protozoal nature, as they failed in many points to fit what appeared to me to be the only alternative explanations as to their nature—viz., first, artefacts resulting from the staining method employed; secondly, granulations connected with the cellular cytoplasm; and thirdly, bacteria. They appear to consist almost entirely of chromatin, although at times a faint blue-staining fragment has been seen attached to the granules or rods of chromatin. The tendency to adhere loosely in the form of little clumps or aggregations of a number of granules is very marked, both in those stained in the unruptured tissues and in such as have been liberated by the laceration or division of such tissues.

During the prolonged search for *spirochætæ* in the eggs, larvæ, and nymphs of infected ticks the same clumps of chromatin granules were almost invariably detected. From the youngest eggs recognisable under a high power in the teased-out ovarian tissue, up to the young nymph hatched out from the egg of an infected mother, granules have been observed at all stages. Only a small proportion, however, of the microscopic eggs showed granule clumps, and, as a rule, only one or two clumps were observed, with one exception, where a large number of clumps were seen, filling up the egg case. In larger eggs, which it was possible to dissect out from the ovary with fine needles under the microscope, the clumps were more abundant, while in mature eggs laid under natural conditions they were rarely absent and often numerous. The subsequent fate of these granules was studied from day to day after the eggs had been laid, and it was seen that, very soon after the first recognisable embryonal cells made their appearance, the granular clumps were found in the protoplasm of some of these cells. At a still later stage small masses of cells were seen, obviously in rapid growth, in which the clumps were once more found. From this point all the granule clumps seen were intracellular, never free unless such cells had been ruptured. Subsequent close investigation showed that such cell aggregations were the primitive commencements of the Malpighian tubes of the young tick, every intermediate stage being seen up to such fully formed tubes as could be recognised without doubt, many of which, even at this early stage, showed the characteristic crystals of the Malpighian secretion in their lumen. From this point up to the formation of the larva and the final emergence of the octopod nymph from the egg the granules were only to be encountered in the Malpighian tubules and only free when such tubules had been torn in the act of making the slide preparations.

Assuming their *spirochæta* origin, it is obvious that these granules are not mere "resting forms," as they multiply in the egg and in the young tick, the few clumps seen in the most minute egg giving rise to the thousands found at a later stage in the Malpighian tubes. In all the subsequent stages of the growth of the nymph, at any rate up to the sixth moult, which is as far as I have followed the generation bred in the laboratory, they are constantly present in the tubes, though their numbers show great variations and the irregularity of their distribution in such tubes is sometimes very marked. Contrasting nymphs hatched from females which had been known to feed on *spirochæta* blood with others hatched from females fed in the laboratory only on normal blood there was no doubt that the granules were much more abundant in the case of the former; at the same time, the latter nymphs almost

always showed the same granules, though in smaller numbers, while in a few instances I have been unable to detect any in the pieces of tube which were examined.

I may now proceed to describe some experiments aiming at the determination of the nature of these granules. Cultivation under very varying conditions gave nothing but negative results. Inoculations of mice, however, proved more successful. For this purpose various organs of ticks were carefully dissected out, washed in many changes of sterile salt solution, and, finally, broken up as far as possible by grinding in salt solution, the resulting emulsion being injected hypodermically into white mice. The presence or absence of spirochætæ or granule clumps was noted by staining and prolonged microscopic search. In a certain number of cases positive results were obtained with emulsions of Malpighian tubules, of ovarian tissue, and of the white secretion of the Malpighian tubes, never, so far, with emulsions made from the salivary glands. The mice in these cases, after an incubation period of seven to ten days, corresponding with the usual incubation period after natural infection by tick bite, developed tick fever and showed abundant spirochætæ in their blood. In all cases in which infection occurred the granules were proved to have been plentiful in the fluid or tissue inoculated, while no spirochætæ could be found. As already mentioned, the failure to find spirochætæ does not definitely prove their absence, but my search has been so close that I feel fairly confident that they were absent in the cases mentioned. Positive results from the inoculation of emulsions containing such granules were not, however, obtained in all cases, and the material which produced spirochæte infection was, in the majority of instances, derived from ticks which had been kept at a temperature of from 34° to 37° C. for a day or two before dissection. (Except where otherwise noted all the ticks were kept at a temperature of 22° to 24° C.) Subsequent work leads me to think that the higher temperature has the effect of inducing changes in the granules which are an essential preliminary to their ultimate development into spirochæte form. This point will be mentioned again in discussing the effects of heat upon ticks recently infected with spirochæte blood.

A few words may now be said upon the method of natural infection by tick bite. It has, I think, been generally assumed, if not actually asserted, that this occurs by means of the injection of spirochætæ through the biting parts of the tick, such spirochætæ having previously harboured in the salivary glands. My persistent failure to find a single spirochæta in the salivary glands of a tick, even in such as I had infected by allowing them to feed on heavily infected blood, appeared to me to throw some doubt upon the correctness of this view. At the same time, the inoculation of granules through the medium of the salivary secretion also appeared improbable in view of the extreme rarity with which I have encountered them in the salivary glands. An alternative method appeared to me as possible and was submitted to experimental test in the following way. Nine ticks which I had infected some months before were allowed to bite a monkey. After they had fixed and commenced to feed they were gently removed and placed on another monkey, on whom they were allowed to gorge. The fact of their all having bitten the first monkey was verified by observing the punctures and small ecchymoses which surrounded the bites. As is well known, when these ticks commence to swell they pass a large quantity of clear fluid from the coxal glands (whose anti-coagulating properties I have been able to determine), and some, in addition, pass the white secretion of their Malpighian tubes. These fluids, therefore, bathe the skin of the monkey and almost certainly may penetrate into the subcutaneous tissues through the punctures left when the tick has loosened its hold on its host. The two monkeys, then, although bitten by the same ticks, differed in the following respect: on the first none of this fluid had been passed, while on the other the wounds were bathed in it. Some of the fluid passed on the second monkey was also collected and inoculated hypodermically into a mouse. Careful search of this fluid showed neither spirochætæ nor granules; the latter, however, are so minute that they might readily be missed. The result of this experiment was interesting and suggestive; the first monkey was not infected, while the second monkey and also the mouse developed tick fever, which ran a typical course.

It would appear, therefore, from this experiment, and others of similar nature, that a possible method of infection, perhaps the common one, is through the medium of the secretions voided by the tick in the act of gorging and not, as usually supposed, by the direct inoculation of spirochætæ in the veneno-salivary secretions. This problem of the method of infection, however, appears to me to be still far from clear. Those who are familiar with the recorded experiments on tick transmission will recall that, in almost every instance, a number of ticks have been employed and not a single individual. I, too, have found that one cannot be certain of infecting an animal by the bite of a single tick, even when such tick is known to be one which is heavily infected. It is obvious therefore that other factors must come into play. One of these factors, though in my opinion by no means the only one, is undoubtedly the temperature at which the ticks have been kept prior to their being allowed to feed. In Africa it has been shown that to secure the infection of animals it was necessary to bring the ticks down from the high and comparatively cool country and conduct the experiments in the warmer low ground. Again, most workers before allowing ticks to feed keep them for some hours, or for one or two days, at a temperature approximating blood heat, although the reason for this is usually held to be simply that it renders the ticks more active and more inclined to feed. To my mind this preliminary heating has a different significance—namely, that it has the effect of inducing certain changes in the granules which may be held as heralding their transformation into spirochæta form. It is hardly necessary to add that I do not make such a suggestion as a mere hypothesis, but as the result of many months' labour in the study of infected ticks kept under varying conditions of temperature. It would occupy far too much time to describe these experiments in detail, and I shall confine myself to a brief summary of the results of the more important.

1. In nymphs of various ages and adults, which have been kept for a week or ten days at a temperature of 34° C., spirochætæ have, in some instances, been seen to reappear in various situations, chiefly in the Malpighian tubes and in the walls, not the lumen, of the intestinal sac and diverticula. These spirochætæ, however, did not resemble *Spirochæta duttoni* as encountered in the blood; they were shorter, more homogeneous, and less regularly curved; they occurred, too, as far as could be observed, not in the fluids, but actually in the cytoplasm of the cells lining the tubules and the intestinal diverticula.

2. The above change is preceded or accompanied by an alteration in the character of the granules so constantly found in the Malpighian tubes; these become more coccoid or spherical in form, and many are enlarged beyond the usual limits of size.

3. Control material in the shape of ticks of the same batches, which had always been fed at the same time and on the same animal, but which had been kept at a temperature of 24° C., showed on dissection no trace of spirochætæ, but only granules of the usual types and in the usual situations.

4. Spirochætæ which have reappeared in ticks under the above conditions of temperature, &c., may persist in such ticks for some months after they have been replaced at the lower temperature and are found in the same situations, though in smaller numbers.

5. Young nymphs newly hatched from infected parents, when kept at a high temperature, show the same changes in characters of the granules as older ticks and adults, but spirochætæ have never been noticed. This would suggest that a feed of blood may be another factor in inducing the change into spirochæte form.

6. A comparative study has been made of newly hatched nymphs whose first meal consisted of spirochæte blood and which were subsequently divided into three lots and kept respectively at 24°, 34°, and 37° C. Several nymphs of each group were examined daily up to three or four weeks after feeding. (a) In nymphs kept at the lower temperature of 24° C. the ingested spirochætæ were found to undergo speedy segmentation of the chromatin, and, after a period of 10 or 12 days, were found to have disappeared completely from the stomach; later than this no spirochætæ could be detected in any situation in the nymph's body. An increase in the number of granules in the Malpighian tubes appeared

to coincide with the disappearance of the spirochætæ from the gut, but this point was difficult to verify in view of the constant presence of the granules in almost all ticks and the variable numbers encountered in different individuals. (b) Nymphs kept at a temperature of 34° C. showed similar changes in the ingested spirochætæ, but such changes and the disappearance of the spirochætæ from the gut occurred more rapidly than in those kept at 24° C. A few days after the spirochætæ had disappeared they reappeared in the tissues and fluids of the lymph, but in greatly altered form, most being very much shorter than any of the forms usually seen in the blood, while many were little larger than cholera vibrios. The smallest forms of *Duttoni* as seen in the blood are about 16 μ to 19 μ in length, Dutton and Todd mention one of 13 μ , but many of these "young" forms, as I may call them, are no more than 8 μ to 9 μ . These young spirochætæ persisted as long as the ticks were kept at this temperature, but rapidly disappeared when they were replaced at 24° C. In some situations it was apparently possible to trace the origin of the young spirochætæ out of the granules. (c) Nymphs kept at a temperature of 37° C. showed a similar condition as regards the spirochætæ to those kept at 34° C., the young spirochætæ appearing after the ingested ones had disappeared from the gut, but in this case they were not so abundant, doubtless on account of the impaired vitality of the ticks, which, at this temperature, will not moult, and eventually die in about three or four weeks.

7. Attempts made with a view to the detection of spirochætæ in the eggs laid by infected parents. Out of many hundred eggs examined it is only recently that spirochætæ have been encountered, and this in four eggs only. Two of these were eggs laid by a tick which had been heated for five days at 37° C. some months before, but which had subsequently been kept at 24° C. In this case the spirochætæ were scanty and of the usual adult form. The two remaining eggs were dissected out of the ovary of a tick which, after feeding on normal blood, had been placed at 34° C., and kept at this temperature for nearly four weeks before dissection. In this instance the spirochætæ were extraordinarily abundant; they occurred in great tangles, and many of them appeared to be in process of development out of the granules.

With regard now to the influence of previous heating of the ticks in connexion with some of the experiments to which I have alluded. It is, of course, possible in cases in which infection of the animal resulted, whether through the agency of the bite of tick or through the inoculation of portions of tissues or secretions of ticks, that spirochætæ may have been present although they escaped observation. As I have already mentioned, it does not appear practicable in such experiments to exclude this possibility. At the same time, the most arduous and prolonged research of the material inoculated, or of the tissues of these ticks dissected after they had fed, has in many instances resulted only in the demonstration of the granules. In some cases in which infection was successful the ticks employed had been heated for from one to four days at 37° C. As already recorded, prolonged heating at this temperature has, in some instances, resulted in the re-appearance of what I have called young spirochætæ. The question arises, therefore, whether infection in these cases may have been due to the inoculation of such spirochætæ, and not, as I have suggested, to the inoculation of the granules. I do not feel able at the present moment to speak with confidence on this point, and will only say that the general analysis of my results leaves me with the impression that inoculation of the granules alone may cause infection, but that it appears probable that previous heating of the tick is an essential preliminary, inasmuch as it induces changes in the granules which are the initial stage of their conversion once more into spirochætæ. I may add, in connexion with this question, that a considerable number of mice inoculated with material containing granules only, although not becoming infected, died in from 24 to 48 hours, although but a small dose was inoculated, and this subcutaneously. A bacterial septicæmia was excluded in these cases by the post-mortem examination.

Two further observations made in the course of these investigations appear worthy of record before I proceed to my concluding remarks. First, the development of immunity

in the case of the monkey. One of the monkeys infected by tick bite recovered, an exceptional experience, after the third relapse. Infected ticks were allowed to feed on this monkey four weeks after recovery and infection again resulted; but in this instance there was no relapse. Five months later the bites of another batch of infected ticks resulted in the appearance of very rare spirochætæ on the eighth and twelfth days only, while a fourth feeding, one month later, demonstrated at last an apparently substantial immunity since no spirochætæ were subsequently found. Secondly, on two occasions I have observed clumps of the granules in spermatozoa found in the oviduct of an infected female. It appeared to me in these cases that there was no doubt as to the actual inclusion of the granules in the spermatozoon, as opposed to possible superposition. If this was the case, and if my views as to the nature of these granules prove correct, this suggests an interesting possibility as to the method by which the young intra-ovarian egg becomes infected, while it would not be unreasonable, on grounds of analogy, to suspect that a similar procedure might occur in the case of the hereditary transmission of the *Treponema pallidum*.

I shall resist the temptation to theorise upon the manner in which this view of the life-history of *Spirochæta duttoni* fits in with the facts known as regards other spirochæte infections, and will only point out that such a cycle of development would, in my opinion, afford a more satisfactory explanation of the mechanism of the relapse than some of the others which have been put forward.

In conclusion, gentlemen, you will realise that experiments such as I have described are inevitably long-drawn-out, and from their nature exceptionally difficult of interpretation. It is also inevitable that the necessary confirmation, if such be forthcoming, cannot be rapid. I may mention, however, the few pieces of confirmatory evidence which have come to my knowledge since the publication of my preliminary note.

First, Professor G. H. F. Nuttall was good enough to confirm my observations as to the presence of these granules in the eggs and ticks which I sent to him, and also to inform me that he had failed to find them in similar situations in some other Argasine ticks.

Secondly, Dr. A. Balfour, on searching the *Argas persicus*, which transmits the extremely interesting fowl spirochætosis of the Soudan which he has described, encountered similar granules in infected ticks, and was also able to confirm some of my experiments by injecting emulsions of tissues containing these granules, but no spirochætæ, with the result that the chick injected contracted spirochætosis.

Thirdly, I have recently been informed by Dr. S. T. Darling that he has found granular forms in the tissues of animals infected with the spirochætæ of the relapsing fever which occurs in the Isthmus of Panama, which granules he, also, suspects to be biogenetically connected with the spirochætæ; and that inoculation of such tissue, apparently completely free from spirochætæ, was followed by infection.

These observations are naturally encouraging, but I should like it clearly to be understood that no one realises better than myself how far some of my results are removed from absolute proof and how much they stand in need of control and confirmation.

PRESENTATION TO A MEDICAL MAN.—At the Eversfield Chest Hospital, St. Leonards, on Dec. 16th last, Dr. Thomas Gambier was presented with an oil-painting of himself in his study, handsomely mounted and inscribed, as a token of the affectionate regard in which he is held by old friends and patients and as a testimonial to his indomitable zeal and persistent labours. Dr. Gambier founded the hospital 25 years ago at Friedenfels, St. Leonards, but the growth of the work necessitated the erection of more commodious premises. It is now proposed further to extend the hospital. The purchase of land opposite the existing building is nearly completed, and on that site it is hoped to erect a nurses' home, an out-patients' department, and a laboratory. Further, it is proposed to extend the verandahs in order to permit of more patients sleeping in the open air. Since its foundation some 5561 patients have passed through the hospital—268 during the year 1909—the majority of the cases coming from London and Birmingham.