area. Men now in England with a heavy, persistent infection, even though no longer inconvenienced by diarrhoea, would be extremely likely to suffer from a return of the complaint on proceeding again to a warmer climate. Of the 22 cases in which *Lamblia* has been present in the faeces, at least 6 have been very heavy infections. One instance has been already given in our previous note. Another case has been in the hospital for more than four months, and during this period every examination of the stools has shown enormous numbers of cysts, with, now and again, when the stool was very loose, many unencysted (active or inactive) forms in addition. Several efforts have been made to get rid of these troublesome parasites, but up to the present, unfortunately, we cannot say that a specific mode of treatment has been found. To certain of the resident medical officers, especially Drs. G. Dawson and F. J. McCarthy, who have been in charge of most of the cases concerned, we are greatly indebted for their cordial co-operation in these attempts.

Treatment.

The varying success obtained with different drugs may be briefly indicated.

The first case in which the parasites were found was also a case of bacillary dysentery. *Lamblia* occurred in enormous numbers for a period of about a week. The patient was given beta-naphthol 15 grains, with bismuth salicylate 20 grains, thrice daily, for some days. By the end of three weeks from the time of the first observation not a single flagellate or cyst was any longer to be found. Owing to other causes, this patient has remained in the hospital for six months; during this time the stools have been examined on several occasions, the last examination having been made only a few days ago. No sign of a flagellate infection, whether of active forms or cysts, has been again found. We may regard this case, therefore, as having been probably cured by the mixture.

Two other cases were treated with turpentine (térébenthine), following the opinion of various French workers as to its value. The dose was 10 minims, three times a day, for four or five days. This was followed by guaiacol carbonate, recommended to us by Dr. Thomson, 5 grains thrice daily, for a day or two before the stools were examined, but probably not long enough to have much effect. When the examination was made, in one case no cysts were found; in the other, after much searching, a few dead-looking cysts were seen. Four days later both stools were again examined, and in neither case were any cysts found. The patients were then sent out of the hospital. We cannot say, of course, definitely that no recurrence has taken place, but from our experience in the first case we consider this unlikely.

On the other hand, in two other cases, none of the remedies tried up to the present has produced any effect. Turpentine, guaiacol, thymol have all failed.

Beta-naphthol, together with bismuth salicylate, then, appeared to effect a complete cure in the only case in which we have been able, so far, to give the former drug. "Térébenthine," in small doses, for some days, was also apparently successful in two cases, but has failed in two others. We have not yet tried giving this drug in a single large dose.

MALARIA.

Altogether, 14 cases of malaria have occurred in the hospital up to the present. Of these, only two have been due to the pernicious parasite (*Laverania malariae vel praecox*), in which cases both small rings and crescents (gametocytes) were found. All the other cases have been due to the benign tertian parasite (*Plasmodium vivax*). We have had no instance of a mixed infection.

Postscript.—Since sending the above paper to press we have been able to treat another case of heavy chronic *Lamblia* infection by the administration of beta-naphthol and bismuth salicylate. The case was that already referred to as having been in the hospital four months, and other drugs had not made any impression on the parasites. The stool was examined a few days ago, after three days' treatment as above. No *Lamblia* cysts were found in the faeces. If their disappearance proves to be permanent, as in the first case, a good trial with the combined beta-naphthol and bismuth salicylate appears indicated in cases of heavy *Lamblia* infections. We are inclined to think that the bismuth salicylate is at least as important a factor as the beta-naphthol.

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SPIROCHAETES AND THEIR GRANULE PHASE.

BY

H. B. FANTHAM, M.A.CANTAB., D.SC.LOND.,

LECTURER ON PARASITOLOGY, LIVERPOOL SCHOOL OF TROPICAL MEDICINE.

SPIROCHAETES are thin, delicate, undulatory organisms which are widely distributed in Nature. Some of them are free-living and occur in stagnant water or in sea-water. Others live in the digestive tracts of animals, both vertebrate and invertebrate. In man *Spirochaeta buccalis* and *S. dentium* may be found in the mouth and *S. bronchialis* in the respiratory tract, while *S. eurygyrata* and *S. stenogyrata* may occur in human faeces. Also, *S. balbianii* is a well-known species found in the intestinal caecum and crystalline style of oysters and allied Lamellibranchs. Other spirochaetes occur in the tissues of vertebrates, and are often pathogenic. The causal agents of relapsing fever, such as *S. recurrentis* and *S. duttoni*, occur in the blood during the pyrexial periods. Another of these organisms—*S. schaudinni*—is found in tropical ulcers. Yet other spirochaetes, often placed in a separate genus *Treponema*, are the causal agents of syphilis and of yaws, and are known respectively as *Treponema pallidum* and *T. pertenue.*

Probably the longest spirochaetes are among those found free-living. Such an one is *S. plicatilis*, which may reach 200 μ in length. On the other hand, *S. laverani*, found in the blood of mice, is a very short form, and may be only 3 μ long. Spirochaetes may vary from 0.25 μ to 2 μ in width. The outline of the body of one of these Protista is corkscrew-like, and varies in appearance owing to its great flexibility. Quickly moving spirochaetes show many waves of small amplitude, while slowly moving forms present fewer, larger waves of greater amplitude. Hence it will be seen that it is hardly accurate to take as specific characters the number of undulations or coils found in fixed and stained specimens of spirochaetes. The number of turns or waves is, then, more an index of rate of motion —as well as of thickness, which is also a factor—than one of differentiation between various species. Further, owing to the processes of growth and division, the latter occurring by binary fission, there is much morphological variation among spirochaetes. This polymorphism results in differences in length and breadth within the same species, variations which tend to be overlooked unless a large number of specimens from a series of cases is examined and measured.

Internally, spirochaetes possess chromatin bars, rodlets, or granules distributed evenly along their body length. These chromatin granules are seen only with great difficulty in the smaller forms.

Spirochaetes of vertebrates may be transmitted from host to host directly by the contaminative method, or by the intermediation of an arthropod vector. Examples of the former are the causal organisms of syphilis and of yaws, while examples of the latter are the parasites of relapsing and African tick fevers. A consideration of the life-cycles of spirochaetes leads to a discussion of their granule phase, or capacity for "granule shedding," as it has been termed, a most interesting phenomenon around which a certain amount of controversy has centred. There is no doubt that spirochaetes produce such granules; it is only their significance, whether cyclical or degenerative, that is in question.

One of the spirochaetes best investigated with respect to granule formation is *S. duttoni*, which is transmitted from man to man by the tick *Ornithodorus moubata*. The life-cycle of this spirochaete was first outlined by Dutton and Todd in 1907, and was studied in detail by Leishman in 1909–10. Leishman's results essentially were that spirochaetes gave rise by multiple fission to granules or coccoid bodies inside the invertebrate host, and that these granules or coccoid bodies found their way more especially to the Malpighian tubules, gonads, and other organs of the tick. The granules themselves multiplied. The eggs of the female tick became infected with granules, and the progeny of infected females might be born infected. The observations of Leishman have been confirmed and extended by Balfour (1911), Fantham (1911), and Hindle (1911). The organisms investigated were *S. duttoni*, *S. recurrentis*, and *S. gallinarum*, or varieties of the last. The formation of granules in *Treponema pallidum* and in *T. pertenue* has been recorded by Balfour, by Ranken, and by Hoffman. It has also been observed in *Spirochaeta bronchialis* by Fantham in 1914–15. Similar multiple transverse fission has been seen in the larger molluscan spirochaetes—for example, *S. balbianii* and *S. anodontae*, by Bosanquet (1911), Fantham (1911), and Gross (1912). It may be mentioned that, even as early as 1882, Zopf recorded and figured the formation of micrococcoid and bacillary forms from spirochaetes of stagnant water and of the teeth, and stated that these forms stand in genetic relationship to one another.

The formation of coccoid bodies, as observed by me in various spirochaetes in fresh preparations, with or without the use of dark-ground illumination, is as follows:

The cytoplasm at first is very finely granular, in fact, almost homogeneous. The chromatin bars appear as minute refractile masses. A concentration of some of the cytoplasm occurs around each chromatin rodlet. These small concentrations gradually become oval, the outer cytoplasmic layer differentiates as a thin coat, and ultimately a series of coccoid bodies or granules is formed, lying usually transversely or slightly obliquely within the periplast sheath. Sometimes the coccoid bodies are set at liberty by a rupture appearing at one end of the spirochaete; at other times, several ruptures, or disintegration of the sheath, can be observed. Stained specimens show a series of darker, lozenge-like coccoid bodies alternating with relatively clear, pale-staining areas. Within the Malpighian or genital cells of a transmitting tick, and in certain mononuclear sputal cells penetrated by *S. bronchialis*, the coccoid bodies often seem to be liberated by the disintegration of the periplast. Groups of coccoid bodies still retaining the outline of the spirochaete from which they originated are of fairly frequent occurrence. When the coccoid bodies are released by a terminal rupture of the parent they tend to form irregular clumps. The progressive elongation of the granules, the assumption of the sinuous form, and the emergence of very small spirochaetes from the groups of granules have been observed in life. It is very probable that there is a definite period in the life of a spirochaete at which there is a marked differentiation of coccoid bodies. It must also be borne in mind that coccoid bodies may be present when spirochaetes as such cannot be detected. At the same time, the finding of chromatinic granules alone is not sufficient to justify the inference that spirochaetosis is indicated, as all such granules are not necessarily spirochaetal in origin. It is essential that motile spirochaetes should be found at some period of the disease, and the developmental stages leading to granules or coccoid bodies observed *in vivo*.

The coccoid bodies have been otherwise interpreted by Marchoux and Couvy (1912–13), Blanc (1911), and Wolbach (1914), who seem to consider these bodies either to be degenerative or to be unconnected with the life-cycle of spirochaetes. According to the first-named investigators, who worked on *S. gallinarum* in *Argas persicus*, the spirochaetes within an infected tick retain their spirochaetal facies, becoming at times so attenuated that they may cease to be visible, some having been observed already on the limits of visibility. Naturally, the question forces itself as to how it is possible to determine the spirochaetal facies if the organism has become invisible. Further, they state that granules occur in the Malpighian tubules, ova, and genital ducts of normal ticks and other arachnids, and that these have been mistaken by Leishman and his supporters for spirochaetal granules. However, it has not been denied that granules may occur in normal tick cells, nor was it asserted that all intracellular granules in infected ticks were spirochaetal in origin, for the granules seen in arachnid cells are not all of the same nature.

Regarding the development of *S. recurrentis* or its varieties in the louse, *Pediculus vestimenti*, Sergent and Foley (1914) state that the spirochaete in the louse assumes a very small form which is as virulent as the spirochaetiform stage. During eight days following a meal of infected blood the body of the louse does not contain any spirochaetes as such, though the spiral organisms reappear later, as was first observed by Nicolle, Blaizot, and Conseil in 1912. Very probably this minute form will be found to be of the nature of a Leishman granule or coccoid body. Also, Nicolle and Blanc (1914) find that the causal agents of relapsing fever are virulent or infective in the louse just before they reappear as spirochaetes. They think that there is an invisible stage in the life-cycle, though they do not appear to have examined for a granule stage, which might easily be overlooked. Further, it should be noted that in experiments with the invertebrate transmitters of such spirochaetes as *S. duttoni*, *S. recurrentis*, and *S. gallinarum*, careful attention should be paid to the temperature, humidity, and other climatic conditions under which the investigations are conducted, since these factors undoubtedly influence the development of spirochaetes therein.

Granule stages have also been recorded from time to time in spirochaetes in the blood of vertebrates. Thus, Balfour, in 1908, found such bodies in the red blood corpuscles of Sudanese fowls suffering from spirochaetosis. Prowazek, in 1906, recorded intracorpuscular stages of *S. gallinarum*. Breinl (1907) and others have observed encysted forms of *S. duttoni* in the spleen, which forms broke into granular bodies that gave rise to new generations of spirochaetes. Sergent and Foley (1914) also found that a minute but infective form occurred in the blood of patients suffering from relapsing fever during apyretic intervals when spirochaetes were absent. Personally, I have seen a very few of these spirochaetes on rare occasions breaking up into coccoid bodies in the blood of the vertebrate host. These minute bodies may appear to occur in or on the red blood corpuscles. They may be found at the crisis and may possibly explain the "after-phase," and may be connected with relapses in the vertebrate host. It is also interesting to note that Sir Patrick Manson, in his well-known book on tropical diseases, writes as follows regarding the etiology of relapsing fever: "Obermeier and von Jaksch describe certain refractile bodies present in the blood during the fever intermissions. The latter author says that he has observed the development of these bodies into short rods, from which the typical spirochaetes are eventually evolved."

Again, the passage of *S. bronchialis* from man to man is most probably by means of the coccoid bodies that leave the human host in the spray with expired air and by way of nasal secretions, as was shown by the present writer in 1914 and 1915. Linen soiled by such secretions, and indiscriminately packed with other soiled clothing, may also aid. Owing to the fragility and short life of *S. bronchialis* extracorporeally, the resistant coccoid bodies in air, dried sputum and dust, and possibly also on the bodies of flies and other insects, are probably instrumental in inducing attacks of bronchial spirochaetosis in human beings, especially those having a lowered bodily resistance, such as after a chill.

A historical interest attaches to the *Cytoryctes luis* of Siegel. These structures are probably explained by the granules shed by *Treponema pallidum* (*Spirochaeta pallida*).

Further evidence for the transition and growth of granules or coccoid bodies into spirochaetiform organisms may be briefly mentioned. Thus, Noguchi (1911), in his paper on the cultivation of *Treponema pallidum*, records in the explanation of one of his figures that "it is not rare to find a round body connected with one or two young *pallida*, as though the latter were just sprouting from the former." Balfour (1913) thinks that he seems to have succeeded in growing spirochaetes *in vitro* from infected tick eggs in which granules only could be demonstrated. Sir William Leishman (1913) repeated many of his former experiments with altered technique, employing dark-ground illumination instead of fixation and staining. He finds that "the granule clumps are not all alike, but that some of them show a much higher degree of refractility than others. Continuous observation of these refractile granules, with the microscope in a thermostat, has further shown me, in the case of two ticks, the definite extrusion of small and actively motile spirochaetes from these granule clumps. . . . After about ten days at a temperature of 28° C. to 30° C., and with a relatively high humidity, some of these clumps give rise to young spirochaetes, which become free, are actively motile, multiply by fission, and may persist in the tissues of the tick for many months."

In conclusion, the value of the recognition of the granule phase in the Spirochaetacea has been strikingly set forth by Noguchi, who, in an address given before the Royal Society of Medicine in London on October 20th, 1913, stated that he "was able to demonstrate . . . granules in the pure cultures of *Treponema pallidum*. This phenomenon, however insignificant it may appear in itself, was destined to furnish a key to one of the most disputed problems of the past fifty years—namely, the problem of so-called parasyphilis, since it was this very idea that prompted me to undertake to search for *Treponema pallidum* in one form or another in the brains of general paralytics and in the spinal cord from cases of tabes dorsalis." And again, "I was led by the observation that *Treponema pallidum* sometimes assumes a granular form in cultures to re-study sections of paretic brains stained for the *pallidum*."

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ON THE RELATION BETWEEN THE TERMINAL-SPINED AND LATERAL-SPINED EGGS OF BILHARZIA.

BY LIEUT.-COL. R. T. LEIPER, D.SC., M.B., R.A.M.C.,

WANDSWORTH RESEARCH SCHOLAR, LONDON SCHOOL OF TROPICAL MEDICINE; READER IN HELMINTHOLOGY IN THE UNIVERSITY OF LONDON.

THE final chapters of my report on the investigation into the mode of spread of bilharziosis in Egypt may not be issued for some time yet owing to my continued absence abroad. I have the kind permission of the editor of the *Journal of the Royal Army Medical Corps* to publish now a short summary of the results obtained in so far as they bear upon the etiological relation of vesical and intestinal bilharziosis and the explanation of the position of the spine in the eggs which give rise to these two distinct clinical manifestations of bilharzia infection. This question has been for years the subject of widespread discussion, but hitherto no finality has been reached.

The controversialists have arranged their arguments and facts around two principal theories.

(*a*) Looss's theory maintains that the terminal-spined eggs are the normal product of impregnated females of *Schistosoma haematobium*, while the lateral-spined eggs are those produced parthenogenetically where males have not developed.

(*b*) Manson's theory, based upon the constant and peculiar shape of lateral-spined eggs, their peculiarly limited geographical incidence, and their special selection for the intestinal tract, hypothesizes a zoological distinction in the adult parasites.

An examination of the fresh-water molluscs at El Marg during the spring and summer of 1915 showed that three species, *Bullinus contortus*, *Bullinus dybowski* (that is, the "*Physa alexandrina*" of Looss), and *Planorbis boissyi*, were infected with certain cercariae, which developed in mice under experimental conditions into bilharzia worms. These worms produced eggs of two kinds—namely, some with typical terminal spines and others with typical lateral spines.

By submitting individual mice, each on one occasion only, for a limited period to infection with the cercariae from single infected molluscs it has been possible to demonstrate that those developing in the *Bullinus* molluscs always produce bilharzia worms which give rise solely to terminal-spined eggs, while those which have developed in *Planorbis boissyi* always become worms which produce solely lateral-spined eggs. In all the experiments males developed and were more numerous than the females.

The cercariae found in *Bullinus*, although very similar to those found in *Planorbis*, showed differences in the suckers, in the relative length of tail, and in other minute points detailed in my final report. The adult worms experimentally reared also showed constant morphological differences. In the worms derived from *Bullinus* spp. the males have four or five large testes and the two lateral gut branches are late in uniting, so that even when mature the worms have a short intestinal caecum. In the female the ovary lies in the latter half of the body. The uterus is very long, voluminous, and contains many terminal-spined eggs, some of which lie in pairs. The yolk glands have a limited range in the posterior fourth of the body. These worms belong to the species *Schistosoma haematobium* (*sensu stricto*). In the worms derived from *Planorbis boissyi* the males are small, and have eight small round testes. The two lateral gut branches unite very early. In some of the smallest specimens found this union had already taken place. The intestinal caecum is correspondingly very long. The female has the ovary in the anterior half of the body. The uterus is very short, and almost invariably there is one egg only at a time in each specimen even when a number have already been laid. The yolk glands are extensive, ranging through the posterior two-thirds of the body along the whole length of the caecum. The eggs always have a lateral spine, the first laid is usually smaller than those succeeding, and the spine is then set almost at right angles to the long axis. Pending a consideration of the claims of other names to priority the specific name *Schistosoma mansoni* may be adopted rightly for these worms. They differ in their adult structure from *Schistosoma haematobium* (*sensu stricto*) more markedly than does *Schistosoma bovis*.

Vesical bilharziosis and Manson's intestinal bilharziosis are therefore etiologically properly regarded as entirely distinct diseases.

IODINE IN TETANUS.

BY

A. T. MACCONKEY, M.B., D.P.H.,

AND

S. S. ZILVA, PH.D.

(FROM THE SERUM DEPARTMENT, LISTER INSTITUTE.)

WHILE the value of iodine as an antiseptic has recently been the subject of discussion, no reference has been made to the well-established facts that iodine possesses the power of rendering tetanus toxin non-toxic, and that such a modification of this toxin can produce active immunity.

An example of this effect is shown in the first table.

TABLE I.—*Results of Injecting Subcutaneously into Guinea-pigs a Mixture, consisting of Equal Parts of Gram's Solution of Iodine and of Tetanus Toxin, some of which had been kept at 36° C. and some at Room Temperature for Different Periods before Injection.*

Weight of Guinea-pig in Grams.	Quantity of Mixture Injected.	Time and Temperature.	Day after Inoculation.						
			1	2	3	4	6	10	14
340	1 c.cm.	2 hrs. at 36° C.	—	—	—	—	—	—	—
380	1 c.cm.	2 hrs. at R.T.	—	—	—	—	—	t	—
310	1 c.cm.	1 hr. at 36° C.	—	—	—	—	—	—	—
365	1 c.cm.	1 hr. at R.T.	—	—	—	—	t	tt	tt
310	1 c.cm.	$\frac{1}{2}$ hr. at 36° C.	—	—	—	—	t	—	—
380	1 c.cm.	$\frac{1}{2}$ hr. at R.T.	—	—	—	—	tt	tt	t
375	1 c.cm.	$\frac{1}{4}$ hr. at 36° C.	—	—	—	—	t	—	—
350	1 c.cm.	$\frac{1}{4}$ hr. at R.T.	—	—	—	—	tt	t	—
355	1 c.cm.	At once	—	—	tt	ttt	+		

R.T. = Room temperature.