

affairs the posterior wall of the uterus was closely applied to the left anterior surface of the tumour. The uterus was slightly enlarged. The tumour elsewhere was enveloped by, and adherent to, omentum and bowel. The right mesovarian and mesosalpinx were ligatured and severed from the tumour and the uterus thereafter sank down into the pelvis. The omental and bowel adhesions were then dealt with and after freeing these the tumour was found to have a broad and thick attachment to the posterior abdominal parietes. The sac containing the foetus and the placenta was drawn out of the abdominal cavity and pressed over towards the left flank. It was freely incised and the foetus and placenta were now extracted therefrom. The wall of the sac varied in thickness from a quarter to three-quarters of an inch except over a small area about $2\frac{1}{2}$ inches in diameter at its upper and right border where it was extremely thin. It was thickest towards its junction with the posterior abdominal parietes with which it appeared to be structurally continuous. On this account and because the placenta had been implanted over this situation I excised the anterior half of the sac and stitched the remaining portion to the anterior abdominal wall, leaving an opening of sufficient size to allow of free drainage. Eventually the inner lining of the sac was shed piecemeal and on Feb. 3rd granulation from the bottom had so progressed that the cavity was almost obliterated and convalescence was well advanced.

The above is the fifth case of full-time extra-uterine pregnancy which I have had to deal with and all have been operated upon successfully. In two out of my five cases the foetus arrived at maturity without one symptom different from those of a normal uterine pregnancy being experienced. In three there had been occasionally a hæmorrhagic discharge from the vagina during the life of the foetus. In these three pain more or less severe had been complained of from time to time during the evolution of the pregnancy but in none of the five cases were labour-like pains experienced, not even at or about the time when the foetus probably died. In two only was there extrusion of decidual membrane per vaginam. In one case only was there elevation of temperature and in this suppuration of the sac had occurred and the foetus floated in about six pints of creamy inodorous pus. In three the foetus and placenta were lodged in the substance of the broad ligaments: two were on the right side and one was on the left. In one only of these broad ligament cases was I able to extract the foetus from its nidus without opening the peritoneum; in the other two the reflection of this serous membrane from the broad ligament on to the anterior abdominal wall had not been sufficiently elevated to allow of this, consequently the upper portion of my incision opened the peritoneal cavity in both more or less extensively. In two of my five cases the peritoneum was incised co-extensively with the abdominal wall generally and the tumour containing the foetus and placenta was to all intents and purposes in both covered in its entirety with peritoneum of its own. One of these, which was published in THE LANCET of July 25th, 1896, p. 241, was undoubtedly an example of ovarian gestation; the other is the case which I now record and in this the foetus and placenta were lodged in a peritoneal sac—a sac similar to the so-called ovarian capsule found in some vertebrata. This sac, except at its right upper border where it was thin and appeared to be composed of adventitious membrane, was dense and thick. Originally it communicated more or less freely with the general peritoneal cavity but at an early stage of the gestation it became closed by new membrane and in this way the very thin portion just referred to may be accounted for. At first it was difficult to explain the attachment of the sac to the posterior abdominal parietes, but this became comprehensible when one recalled that in some cases the ovarian capsule is formed in a peculiar manner by division of the ovarian ligament and that in such the ovarian ligament may be traced in the posterior abdominal parietes up to the level of the lower border of the kidney. The ovarian capsule is a structure quite distinct from the ampulla of the tube and in some cases the tube traverses for a distance the parietes of this capsule. In operating upon cases of intraperitoneal hæmatomata resulting from ectopic gestation one occasionally finds the ovary more or less concealed in a peritoneal sacculus and I am inclined to think that this is an abnormality of not infrequent occurrence. In cases of full-time extra-uterine pregnancy and quite independently of any operative interference the menstrual function tends to reassert itself in from four to 12 weeks after the death of the foetus—i.e., at about the same time as after normal delivery

when the child is either born dead or is not suckled. It is noteworthy, however, that although the menstrual discharge is not, as a rule, more profuse it is apt to be more prolonged in the former group of cases.

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NOTE ON THE ETIOLOGY OF THE SLEEPING SICKNESS.¹

By ANNIBAL BETTENCOURT,

AYRES KOPKE,

JOSÉ GOMES DE REZENDE, JUN.

AND

ANNIBAL CORREIA MENDES,

MEMBERS OF THE PORTUGUESE COMMISSION.

THE bacteriological researches which we have undertaken in order to illustrate the etiology of sleeping sickness were systematically carried out principally on those organs and tissues of the body in which, guided by the knowledge of former pathological investigations and by the results obtained in the first necropsies which we made, we knew that the principal lesions of the African disease, which is anatomically a meningo-encephalo-myelitis, are found.

In our first report, dated June 9th, 1901, regarding the six cases observed in Principe, we said that the preliminary and restricted work which up to then had been accomplished seemed to "guide us in the sense of the infectious nature of the sleeping sickness." Two months afterwards (August 10th), in Loanda, we first proved the existence of a diplo-streptococcus in the cerebro-spinal fluid *intra vitam* (six positive results in nine cases) and in the subarachnoid exudate (13 times in several necropsies which were performed); the principal characters of the germ could only be demonstrated in an imperfect and summary way owing to the absolute impossibility of making a complete study of it up to that date. These results were published in September, 1901.² In Lisbon (August 7th, 1902) we finally gave a demonstration, illustrated by diagrams and by the exhibition of specimens, of cultures, and microscopical preparations which had been collected in the course of a great number of researches from the cerebro-spinal fluid obtained by lumbar puncture *intra vitam*, and from the exudate and fluid of the ventricles obtained after death, from the blood, ganglions, and spleen, demonstrating also in numerous microscopical sections, especially of nervous tissue, the existence of the parasite previously described lying within and outside the vessels. We therefore particularly pointed out, in order to admit of no doubt, that the micro-organism in question ought to be included in the streptococcus group and we proposed to give to it the name of "hypnococcus."³ The following were our words: "The general description of the principal characteristics of the hypnococcus being given, let us see if it is possible to determine its place in bacteriological classification. We rather considered it, in our first report, as a type of transition between the streptococcus and Fraenkel's diplococcus. We can, however, affirm to-day that it is easy to distinguish it from the latter. It is enough to say in order to separate it from Fraenkel's diplococcus that it grows on gelatin and in other media at a temperature lower than 24° C. But we wanted to go further and we followed the plan proposed by His to establish the differential diagnosis between the pneumococcus and the bacteria of the streptococcus group. Water is mixed in equal portions with the serum of oxen, properly alkalinised and sterilised, and we add 1 per cent. of inuline. This sugar is fermented by the pneumococcus and a change takes place in reaction, from alkaline it becomes acid and causes the coagulation of the medium. Our diplococcus grows well in His's fluid and the reaction is not modified nor does the

¹ This note belongs to the first part of the chapter, "Recherches Bactériologiques," of our report now in the press.

² Doença do Somno: Relatorios enviados ao Ministerio do Marinha pela Missão Scientifica nomeada por Portaria de 21 de Janeiro de 1901, Lisboa, 1901.

³ Doença do Somno. Trabalhos executados até 6 de Agosto de 1902, pela Missão enviada a Angola pelo Exmo. Ministro da Marinha, composta de Annibal Bettencourt, chefe da Missão, Ayres Kopke, José Gomes de Rezende, jun., e Annibal Correia Mendes. (Revista Portuguesa de Medicina e Cirurgia, Nos. 139 a 144, Agosto a Outubro, 1902.)

fluid coagulate even after a month's stay in the incubating oven."

We read lately in a medical journal⁴ a previous report of the bacteriologist Castellani, a member of the English Commission sent to Uganda to study the sleeping sickness, in which he found while making his investigations in the same manner as we had already done a streptococcus in the cerebro-spinal fluid of patients during life and after death, which the author thinks is a different one from ours. This idea probably must be due to the fact that Castellani only knew of our first reports, which were erroneously translated,⁵ in which the description of our bacteria might give place to some doubts in regard to its bacteriological classification.⁶ However, after this work we described it more precisely and considered it as belonging to the numerous streptococcic group (August 7th, 1902).

It is necessary to say that, though some divergencies exist between what we said in our first report regarding the bacteria and the one which Castellani found in Uganda, they are not important, and we think do not justify Castellani in establishing such a radical distinction. It might be considered that the difference either proceeds from the diversity of the two bacteria or from the conditions under which the observers worked. Castellani considers only the first proposition and he completely forgets the second, which was in reality the principal one. The proof of the small value of the facts put forward by Castellani to establish this difference is shown by himself in the way in which he concludes his report, being apparently exactly of the same opinion as we were in August, 1901. We then said: "As to the bacteriological classification of the diplo-streptococcus only further experience and time can decide. Its analogies with Fraenkel's diplococcus on the one side and with the streptococcus on the other are certain; but the organism cannot be with certainty relegated to either group, though there is close relation between the two, as all bacteriologists allow. What we have said until now of our diplococcus is that it seems to be a transition between Fraenkel's diplococcus and the streptococcus." Castellani says the following about the bacteria which he found: "From the description just given I think that this germ must be considered a new variety of streptococcus. Every bacteriologist knows how difficult it is to differentiate sharply the varieties of streptococci on account of the numerous transition forms that occur, even a sharp separation between the streptococcus pyogenes and the streptococcus lanceolatus (Fraenkel's diplococcus) seeming to many authors to be impossible." Lower down he says: "I think that this organism is a distinct variety of streptococcus, to be classed between the streptococcus pyogenes and the streptococcus lanceolatus (Fraenkel's diplococcus), and it might be called the streptococcus of the sleeping sickness." This means that Castellani and ourselves in our first reports both came precisely to the same conclusion and expressed ourselves in identical terms. We cannot understand how this could happen if in reality distinct species were in question, the studies being made quite independently one from the other. The same impression on the investigators having been left, although there was a considerable difference of time and place at which the investigations were made, can only signify that the result of the researches was the same, or, in other words, that the two micro-organisms isolated by us in the West of Africa and by Castellani in the East are the same.

Let us see, however, upon what basis Castellani considers his bacillus to be a different one from ours. We are sorry that he did not see the Portuguese journal in which we published our second work, which was of much earlier date than his, for on reading this all doubts should cease and everybody would think it superfluous to speak of a question of priority. Castellani says, as regards the diplo-streptococcus of the Portuguese, he does not think that any confusion can arise. "The Portuguese state that the culture of their germ generally failed every time on the usual media like agar, gelatin-agar,⁷ &c., and with gelatin they never succeeded in obtaining cultures." The only differences, then, are merely that our cultures nearly always failed in the usual media and that we did not obtain them on gelatin. We said, conformably

to the text of our report, "The diplo-streptococcus found by us grows badly in nearly all the nutritive media usually employed. The bouillon, agar-agar, simple or glycerinised, nearly always fail. The liquid proposed by Martin for the cultivation of Löffler's bacillus and obtained by the maceration of the pig's stomach gives a much better result, especially if we can make it solid by the addition of agar." What is concluded in our text is that the bacteria grows badly, but this does not mean that it does not grow at all. We add that it grows much better in Martin's media, for one of our micro-photographs represents some of the colonies grown on the surface of the agar of this author. These facts ought to have led Castellani to suppose that the absence of constant growths in the media referred to proceed more from their defects than from the biological peculiarities of the bacteria. In fact, in our first report we showed that the failure to obtain a growth was really owing to the short time occupied by our researches and to the methods we employed for isolating the organism.

We may say that for the preparation of our media we always employed Witte's peptone, which being very rich in albumoses is not so favourable for the germination of the bacteria as some others are. Nicolle and Remlinger especially point out this fact in their excellent book, "Traité de Technique Microbiologique" lately published; we verified this recently on different bacterial species including the hypnococcus. This last fact is no less important and may have greatly influenced our results, especially in the inoculations performed with the products procured from the human body because in these circumstances, as it is known, the bacteria are more easily influenced by the unfavourable conditions of the media. In Martin's media, which have for bases a peptone prepared *ad hoc* in the laboratory, the same thing does not happen and that explains the better development. Finally, Wassermann isolated in acute articular rheumatism a micro-organism belonging to the streptococcus group which only grows in strongly alkaline media, to which has been added Chapoteau's peptone, cultures not being obtained when Witte's peptone is used, as usually employed in Germany. All this is set aside because for a long time we have managed to obtain, as Castellani did, development in all these media. Months before the publication of his work we published a description of our cultures on agar, bouillon, and potato, in which we obtained identically the same results as Castellani. We also point out the absence of the coagulation of milk and the absence of gas production in the media containing glyucose, in respect of both of which Castellani agrees perfectly with us. Finally, there is now no question of its growth on gelatin, for the simple reason that we have already obtained cultures in this medium in Lisbon—flesh pepton-gelatin and Martin gelatin. These cultures were exhibited at the time of our conference (August 7th, 1902) and the description of them may be found in the *Revista Portuguesa de Medicina e Cirurgia Praticas*, where we state the reasons to which we attribute the negative result obtained in Loanda.

We never made direct inoculations of morbid products in this medium, so we cannot say if they would be successful, nor does Castellani say in describing the streptococcus if he made use of all the media which he speaks of for the primary cultures or if some of them were only employed in the subculture; this makes a great difference with regard to the results, as is known, in regard to various species, amongst which we may cite the diplococcus intracellularis meningitidis of Weichselbaum-Jaeger. Briefly we maintain that all the characters which Castellani says distinguish the two germs do not exist and consequently the difference between them does not exist also. On the contrary, what is indeed remarkable is our agreement in various points of the description. Some have already been mentioned. We have also shown various instances of form and size, and the existence of groups from the isolated diplococcus to the chains (which may be shorter or longer) and have obtained these from the human subject or from the cultures to which Castellani also refers. The characters of the cultures on bouillon and the aspect which the hypnococcus takes according to this author's description, all is in complete agreement with ours.

We further point out, before concluding, that our investigations were not limited to culture and microscopical examinations of the pathological fluids of the organism. We also studied numerous microscopical sections, especially those of the nervous tissue, and were the first to find and mark out the presence of the hypnococcus. Such sections were also

⁴ THE LANCET, March 14th, 1903, p. 723.

⁵ Journal of Tropical Medicine, May and June, 1902.

⁶ Immediately after our revised translation was published we sent to the editor a note pointing out the numerous mistakes. It is, however, most strange that this was never published.

⁷ We never spoke of this medium because we never employed it.

seen by Patrick Manson some time ago in London, by Marmorek of the Institut Pasteur in Paris, and were finally presented by Mense at the last Colonial Congress assembled in Berlin.⁸ How can it be suggested that the bacteria so often isolated by us in pure culture may not be the same as the one seen in the sections and exudates, the identical morphology being given? and how can the germ isolated by Castellani from the same regions of the body where we obtained it during life and post mortem, not be the same we saw in our microscopical sections?

After all this there is not the slightest doubt that Castellani's bacterium is the one which we described and that his investigations are a complete confirmation of ours. This is the original and important fact. The priority in the question is relatively a secondary one, as no one can honestly and *sine ira* contest that it does not belong to us; but the works of this member of the English Commission, done quite independently of ours and in quite different and distant regions, do not in the least lose their merit or the important signification they bear for the clearing up of the etiology of sleeping sickness. It is, in fact, the first time that etiological researches of the African lethargy have been thoroughly verified and identical results arrived at.⁹

ON A CASE OF ARTERIAL OCCLUSION AND GANGRENE.

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IN November, 1899, I was consulted by a retired officer of the army on account of pain in the left leg and foot. He was a spare, active man, in his fifty-third year, with a complexion ruddy from enlarged capillaries and with the skin of the hands also of a high colour. In India, when a young man, he suffered from malarial fever and dysentery and he also had dysentery while in Egypt in 1882. Of late years he had been liable to dyspepsia, and in 1898 he had tobacco amblyopia which afterwards improved. Some time in the summer of 1899, I think, I had attended him for painful redness and swelling affecting the ball of the left great toe and running up the dorsum of the foot between the first and second metatarsal bones. The pain which he complained of when I saw him in November was intermittent, occurring in paroxysms which often came on in the early hours of the morning. It ran down the front of the leg and along the dorsum of the foot and was felt in the ball of the big toe and the distal part of the foot. The foot was sometimes dark red and congested, when it felt hot, and sometimes it was pale and cold, conditions resembling the syncopal and asphyxial states of Raynaud's disease. Stiffness and some pain behind the knee-joint were also complained of. The heart, though perhaps a little weak, was perfectly normal and there were no indications of atheroma or arterio-sclerosis in any of the accessible arteries. The urine was free from albumin and sugar and in all respects normal. The lungs were healthy. The tongue was somewhat furred and there were some dyspeptic symptoms but the abdominal organs were otherwise healthy. The temperature was normal. Later, pulsation was observed to have ceased in the posterior tibial artery and the dorsal artery of the foot; the pains became more frequent and severe and the varying conditions of heat with dusky redness and coldness with pallor became more marked. Pains of a slighter degree were also felt in the right leg and down the arms, and the right foot also showed some signs of varying congestion and pallor, as also did the hands.

In the spring of 1900 he improved somewhat for a time, but about May he got worse again and a black spot formed on the under part of the distal phalanx of the great toe and another on the tip of the little toe. The extreme tip of the little toe gangrened and the process there made no further

advance but it slowly went on in the big toe till it was entirely black and mummified. A distinct line of demarcation, well beyond the joint, formed in, I think, the month of July, but it made one or two advances during the next month or two. In September there was a good deal of constitutional disturbance due, apparently, to septic absorption, the temperature rose, and he had a severe attack of aphthous stomatitis. At the beginning of October, as the line of demarcation was making no further advance, Mr. A. E. Hind removed the gangrened toe by cutting through the first phalanx where the separation had taken place down to the bone, just beyond the metatarso-phalangeal joint. After the operation the patient improved rapidly and in a month or two the wound had healed and he was able to move about again.

From the end of 1900 to the spring of 1902 the patient was in excellent health, though he had occasional pains in the legs. About the month of April he consulted me on account of occasional attacks of sudden and severe pain at the bottom of the sternum and over the præcordial region, seizures which had very much an anginal character. A little later he had pain running down the sciatic nerve on the right side, and some time in May he began to have sharp attacks of pain running down the front of the right leg, the paroxysms very frequently occurring in the early morning as they had done in the other leg. In June the right foot was frequently, indeed mostly, hot and congested, and sometimes cold and pale, and soon no pulsation could be felt in the posterior tibial or in the dorsalis artery. About the end of the month two black spots appeared on the sole of the foot, one on the heel and the other on the under surface of the little toe, just on the bend of the first joint. In July suppuration occurred at the seat of the black spot under the toe and some matter was let out by a small incision. In August unhealthy-looking ulceration began to extend from this point, gradually spreading two or three inches up the outer side of the foot, and the toe became purple and gangrene set in. By the middle of the month the toe and the ulcerated part of the foot were completely gangrened and a line of demarcation had begun to form; but the next toe was evidently becoming implicated. All this time the patient's condition remained good. The temperature was normal or only slightly raised sometimes. The pulse was good but occasionally quick and not very strong. The urine was normal.

About the middle of September the fourth toe was gangrenous and the line of demarcation was advancing onwards and upwards. The constitution was now showing the effects of the disease. The temperature was frequently raised, though not often above 100° F., and at the end of the month there was a rather sharp attack of aphthous inflammation of the mouth and throat, as during his last illness. There was also an aphthous ulcer on the conjunctiva of the left eye which gave rise to inflammation. During all this time the pain in the leg and foot was frequent, almost constant, and often very severe.

On Oct. 4th, as the line of demarcation seemed at last to be stationary, the gangrened parts were removed by Mr. Hind, who cut through the fourth metatarsal bone and disarticulated the fifth at its tarsal articulation. The raw surface left looked pale and bloodless. About three weeks later the second and third toes had become gangrenous and a line of demarcation had formed on the dorsum of the foot which included them, though it was not developed on the under surface. The great toe had also a dry gangrenous patch on the tip and the nail had been removed owing to suppuration in the matrix. It was then decided that the dead and dying parts should be removed, and Mr. Hind, assisted by Dr. J. R. Muir, R.N., separated them by disarticulating the remaining four metatarsal bones at their tarsal articulation and making a flap of the sound skin of the sole to cover the wound made at this operation and the still incompletely healed one left by the last.

For a day or two after the operation the temperature rose in the evening to 102° and there was some general constitutional disturbance, but great improvement of the general condition soon set in. The mouth, which was still sore, got better, the inflammation in the eye gradually subsided, and an ulcer on the back part of the heel which had given some trouble began to mend. A week or ten days after the operation a part of the flap which was stretched over the internal cuneiform bone sloughed and the bone protruded through the opening. The projecting part became necrosed and on Dec. 1st it was found to be loose and was easily

⁸ Archiv für Schiffs- und Tropen-Hygiene, Band vii., 1.

⁹ It is convenient to correct here a mistake in the English translation of our first report. It was said that we isolated constantly the diplococcus from the blood. This is absolutely incorrect. What we clearly confirmed was that in four cases examined in this point of view we only found it once. To-day we can add that we have had two positive results in seven cases. Castellani only isolated it once. We have here another point in which Castellani's researches agree with ours.