It will be seen that rodent ulcers may be multiple on the two areas of the fifth nerves at the same time; and that they may be multiple on the area of one fifth nerve; and no lesion elsewhere. Mr. McAdam Eccles had a case of two rodents on one fifth, and many others on the body and legs.

[I have omitted any reference to multiple epithelioma on the areas of the fifth, because the question of secondary deposits may be a factor in their appearance.]

I can quite appreciate the criticism that, singly or otherwise, infective processes can be shown occupying the same regions; but the incidence of cancer may not be due to the mere influence of infection as claimed by several observers.

Cancer, belonging essentially to the period of bodily degeneration, is a point which seems to me of some importance in considering the following facts. Lugaro has proved that peripheral irritation causes central changes of degeneration in the posterior root ganglia of the spinal nerves. In these the ganglia cells are seen swollen and rounded. The Nissl bodies break up; the nucleus is eccentric, and often quite at the periphery. Apart from senile degeneration there is, then, the fact that peripheral irritation can induce visible changes in the ganglion controlling the irritated area. At the same time I fully realize the importance of recognizing that central nerve impulses may

be abnormal, although nothing abnormal can be seen in the central nerve ganglia.

Before I knew of Lugaro's experiments I examined the posterior ganglion of the fifth dorsal spinal nerve of the right side, which I took away from a woman for the relief of agonizing pain in an inoperable cancer in the right breast, and Dr. Purves Stewart, who kindly stained the ganglion for me, found the same changes as described by Lugaro occurring in some of the ganglion cells.

I do not wish to infer that a degeneration of the ganglion preceded the carcinoma in this case, because I know not if this really occurred.

At the same time I cannot help alluding to the clinical fact that irritation is a great precursor of cancer, and added to this it causes degeneration in the particular ganglia whose peripheral ramifications are irritated.

Carcinoma often appears in tissues which are associated with disorders of growth such as moles, and these moles are themselves associated with definite nerve areas and the incidence of cancer. (See Fig. 18.)

Dr. Whitfield has pointed out to me that Foldau has shown that nerve fibres can be traced into these moles.

I wish it to be understood that I do not claim to have enunciated a new theory of cancer, but to have shown that there is reason to justify us in taking into consideration the possibility that the genesis and spread of cancer, even when considered apart, may be connected directly or indirectly with the nerve influences which preside over the areas affected. In conclusion, I thank Dr. Sequeira for the unreserved manner in which he placed his large clinic and wide experience at my disposal. My thanks are also due to Dr. Scott, from whose thesis upon rodent ulcer I gleaned a few cases. Major Pinch kindly gave me permission in Mr. Hutchinson's absence to copy many of Mr. Hutchinson's pictures in the Polyclinic. Dr. Andrews and Dr. Broadbent allowed me to reproduce some specimens from the respective museums over which they preside.

Fig. 17.—A tongue from the museum of St. Bartholomew's Hospital. The squamous epithelioma began in a wart which was situated in the centre of the tongue and occurred at a point on which the end of a clay pipe habitually impinged.

Fig. 18.—Dr. Sequeira's case, showing the distribution of moles and on the left side of the man's face was a squamous epithelioma.

ON THE ETIOLOGY OF SLEEPING SICKNESS.*

BY

ANNIBAL BETTENCOURT, AYRES KOPKE,
GOMES DE RESENDE AND CORREIA MENDES,
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THE bacteriological researches which we have prosecuted in investigating the etiology of sleeping sickness were principally on the organic tissues and liquids, for being guided by the knowledge of former pathological observations, and by the result obtained in the first necropsies made by us, we were aware that the principal lesions of this African disease were anatomically those of a meningo-encephalo-myelitis.

In our first report of June 9th, 1901, regarding the 6 cases observed in Principe, we said that the preliminary and restricted investigations up to that time accomplished seemed to "guide us in the sense of the infectious nature of the sleeping sickness."

Two months later, on August 10th, in Loanda, we first discovered the existence of a diplo-streptococcus in the cerebro-spinal fluid *intra vitam* (6 results positive in 9 cases) and in the subarachnoid exudate (in 13 necropsies), and we described the principal characters of the germ in an incomplete and summary way. These results were published in September, 1901.¹

In Lisbon on August 7th, 1902, we finally brought forward the results of our researches in a public conference, illustrating our communication by projections and by the demonstration of pathological specimens, cultures, and microscopical preparations which were collected from a great number of examinations, both of the cerebro-spinal fluid obtained by lumbar puncture *intra vitam*, of the exudate in the ventricles obtained at the necropsy, of the blood, ganglia, and spleen, and demonstrating also in numerous microscopical sections, especially of the nervous tissues, the existence of the micro-organism both inside and outside the vessels.

We were particular in pointing out, in order to avoid error, that the micro-organism in question ought to be included in the streptococcus group, and we proposed therefore to call it the hypnococcus.²

We wrote as follows: "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."

In our first report we were rather disposed to consider it as a type transitional between the streptococcus and Fraenkel's diplococcus. We can, however, now affirm that it is easy to distinguish it from the latter.

It will be sufficient to say that it grows on gelatine and in other media at a temperature below 24° C. in order to clearly separate it from Fraenkel's diplococcus.

But in order to go further, we followed the method proposed by His to establish the differential diagnosis between the pneumococcus and the bacteria of the streptococcus group. To water and ox's serum in equal portions, conveniently alkalized and sterilized, we added 1 per cent. of inuline. This sugar is fermented by the pneumococcus, giving a change in reaction from alkaline to acid, and producing the coagulation of the medium. Our diplococcus grew well in this fluid, the reaction was not modified, nor did the fluid coagulate even after a month's stay in the incubating oven.

We read recently in the *BRITISH MEDICAL JOURNAL*, March 14th, a preliminary report of the bacteriologist Castellani, a member of the English Commission sent to Uganda to study the sleeping sickness, in which he states that he had found, as we had already done, a streptococcus both in the cerebro-spinal fluid of living patients and *post mortem*, which he considers is different from ours.

This idea may probably be due to the fact that Dr. Castellani only knew of our first reports, which were erroneously translated before they came out in the *Journal of Tropical Medicine* in May and June, 1902, from which the description of our bacterium might reasonably give rise to some doubts in regard to its bacteriological classification.³ However, after this work we described it more precisely, and considered it as belonging to the large streptococcus group (August, 7th, 1902). It is necessary to say that though some divergences exist between what we said in our first report

* This note belongs to the first part of the chapter, *Recherches Factiologiques*, of our report now in the press.

regarding the bacteria and the one Castellani found in Uganda, they are not vital, and we think are not sufficient to allow Dr. Castellani to establish such a radical distinction.

It might be considered that the difference might proceed from the diversity of the two bacteria or from the working conditions of the observer. Castellani only speaks of the first and completely forgets the second, which was in reality the principal. The proof of the small value of the facts advanced by Castellani to establish this difference is obvious from the way he ends his report, being apparently exactly of the opinion we were in August, 1901, as written in our report.

We then said: "As to the bacteriological classification of the diplo-streptococcus, only investigations of greater number and with more time can establish. Its analogies with Fraenkel's diplococcus on the one hand and with the streptococcus on the other are not yet sufficient to constitute it a distinct species, or merely a variety of the same species; they do not allow any one to classify it as belonging to either of these groups, though there is close relation between the two, as all bacteriologists know. What we have said so far of our diplococcus is that it seems to be a transition between Fraenkel's diplococcus and the streptococcus."

Castellani makes the following statement about the bacteria found:

From the description first given I think 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.

Further on he says:

I think 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 came to precisely the same conclusion, and expressed ourselves in practically identical terms. We cannot understand how this could happen if in reality distinct species were in question, the investigations being made quite independent one from the other. With the considerable difference of time and place, the same impression being made on the investigators, 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, what reasons Castellani has to offer for considering his bacteria different from ours. We are sorry he did not see the Portuguese journal in which we published our second work, which was of much earlier date than his, after reading which all doubts would cease as to priority.

Castellani says, as regards the diplo-streptococcus of the Portuguese: I do not think any confusion can arise. The Portuguese state that the culture of their germ generally failed every time on the usual media like agar, gelatine-agar, etc., and with gelatine they never succeeded in obtaining cultures. The only differences then are merely—our cultures failing nearly always in the usual media and our not obtaining them on gelatine. We said conformably in our report (Portuguese): The diplo-streptococcus found by us is badly cultivated in nearly all the nutritive media usually employed. The bouillon, agar-agar, simple or glycerinized, fail nearly always. The liquid proposed by Martin for the cultivation of Loeffler'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 agar addition.

What must follow from reading our text is that the bacteria grows badly, but this does not mean that it does not grow at all. We subsequently added that it grows much better in Martin's media, and even one of our photomicrographs represents some of the colonies grown on the surface of the agar of this author. These facts might have been expected to have made Castellani suppose that the absence of constant growths in these media proceeded rather from some defects of these than from the biological peculiarities of the bacteria. In fact in our first report we referred to the direct inoculation as well as to the bacteria isolated from the body.

We may say that for the manufacture 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 are some others. Nicolle and Remlinger especially point out this fact in their excellent book *Traité de Technique Microbiologique* lately published, and we verified this recently on different bacterial species, including the hypnococcus. This last fact is not less important, and may have greatly influenced our results, especially in the inoculations made with the products gathered *post mortem*, because in these

circumstances, as is known, the bacteria are more easily influenced by the unfavourable conditions of the media.

In Martin's media, which have for bases a good 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, fortified with Chapoteau's peptone, cultures not being obtained when Witte's peptone was used, as it is usually employed in Germany.

All this is set aside because it is long since we managed to obtain, as Castellani did, growth in all these media. Months before the publication of his work we published a description of our cultures on agar, bouillon, and potato, with which we made identically the same observations as Castellani.

We similarly point out the absence of milk coagulation and the absence of gas production in the media containing glucose, and both these the author speaks of, thus agreeing perfectly with us.

Finally, even the question of its growth on gelatine does not subsist, for the simple reason that we have already obtained in Lisbon cultures in this medium (both on the flesh-peptone-gelatine and on Martin's gelatine), any one could have seen these cultures at the time of our conference, 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 cultures 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 had recourse to all the media he speaks of for the original cultures, or if some of them were only employed in subculture. This makes a great difference in regard to the results, as is well known to obtain for various species, amongst which we may mention the diplococcus intracellularis meningitidis of Weichselbaum-Jaeger. In short, all the characters which Castellani says distinguish the two germs do not exist, and consequently the difference between them does not exist either; on the contrary, what is indeed remarkable is our agreement in so many points of the description. Some have already been cited; among others is, for example, the identical morphology, according to our various reports, as to form and size, and the existence of groups, from the isolated diplococcus to chains, which may be shorter or longer, either in the body or in cultures, and to these Castellani also refers.

The characters of the cultures on bouillon which he describes, and the form in which the hypnococcus grows are in complete agreement with our observations.

We accentuate, in conclusion, that our investigations were not limited to culture and microscopical examinations of the pathological fluids of the organisms. We also studied numerous microscopical sections, above all those of the nervous tissues, and were the first to find and describe the presence of the hypnococcus. Such sections were seen by Dr. Patrick Manson some time ago in London; by Marmorek, of the Institut Pasteur in Paris; and were presented by Mense to the last Colonial Congress assembled in Berlin.

How is it to be understood that the bacterium 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 region of the body from which we obtained it during life, and *post mortem* fail to be the same we saw in our microscopical sections?

It is convenient to correct here a mistake of the English translation of our first report. It was said that we isolated constantly the diplococcus from the blood. This is absolutely false. What we clearly asserted was that in 4 cases examined from this point of view we found it only once. Now we can add that we have had 2 positive results in 7 cases. Castellani isolated it once only; we have here another point in which Castellani's researches agree with ours.

There cannot be the slightest doubt that Castellani's bacterium is the one we described, and that his investigations are in complete confirmation of ours. This is the essential and important fact. The priority in the matter is relatively a secondary one, as no one can honestly contest that it does not belong to us; but the researches of the member of the English Commission, made quite independently of ours, in quite different and distant regions, do not in the least lose their merit nor the important signification they bear in the clearing up of the etiology of sleeping sickness. It is, in fact, the first time that etiological researches on

African lethargy have had important verification and confirmation, coming, indeed, to identical results.

NOTES AND REFERENCES.

¹ Doença do Sono. Relatórios enviados ao Ministério da Marinha pela Missão Científica Nomeada por Portaria de 21 de Janeiro de 1901. Lisboa, 1901. ² Doença do Sono. 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, Avres Kopke, José Gomes de Resende Junior, Annibal Correia Mendes. *Revista Portuguesa de Medicina e Cirurgia*, Nos. 139 a 144, Agosto a Outubro, 1902. ³ Immediately after this translation was published we sent the editor a note pointing out the numerous mistakes in it. This unfortunately, however, was not published. ⁴ We never spoke of this medium because we never employed it. ⁵ August 7th, 1902. ⁶ *Archiv f. Schiffs- und Tropen Hygiene*, vii. 2.

NOTE OF SOME FURTHER EXPERIMENTS REGARDING THE NATURE AND SPECIFIC TREATMENT OF HAY FEVER.

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THE results of some of the experiments reported recently in the *BRITISH MEDICAL JOURNAL*¹ made it desirable that the special influence of Professor Dunbar's toxin upon some persons not actually suffering from hay fever, but showing a greater liability than the ordinary run of people, should be further tested. With this object Dr. Tilley and I experimented upon ourselves on April 3rd, whilst my son and a lady who suffers from typical hay fever also were subjected to experiments similar to those described in my last communication.

1. In the case of my son two drops of a toxic solution (1 in 500) were instilled into the right nostril, but remained without any effect.

2. Miss R. has been suffering from hay fever for twenty-one years, the symptoms occurring at the typical time, and consisting of violent sneezing, obstruction of, and considerable running from, the nose, great irritation of the eyes, and, towards the end, slight asthma. The results obtained in her case were much more marked than in any of the cases I have hitherto experimented upon, and were as follows:

A drop of toxin (1 in 1,000) plus an equal quantity of serum was instilled into the right eye at 2.53 p.m.

No symptoms, either objective or subjective, having occurred at

2.58 p.m.—One drop of 1 in 500 toxin, plus serum, was placed into the right eye.

3.0 p.m.—Itching complained of.

3.1 p.m.—Caruncle obviously swollen, itching increases, and becomes a burning feeling.

3.3 p.m.—Objective symptoms still increasing.

3.4 p.m.—Distinct reddening of both upper and lower lid.

3.5 p.m.—One drop of toxin (1 in 500), plus serum, rubbed into right nostril.

3.7 p.m.—Itching and burning begin.* No swelling as yet of turbinal bodies or septal mucous membrane.

3.10 p.m.—Mucous membrane of right nostril shows very obvious congestion at anterior end of inferior turbinal bone. Caruncle of right eye still markedly congested.

3.10 p.m.—Some degree of chemosis in right eye.

3.20 p.m.—Irritation felt in right eye almost disappeared; objective symptoms still apparent.

3.21 p.m.—One drop of antitoxin instilled into right nostril.

3.24 p.m.—Feeling of itching and burning in nostril also allayed.

3.23 p.m.—Two drops of 1 in 500 toxin rubbed into left nostril.

3.24 p.m.—Itching sensation becomes apparent.

3.28 p.m.—Mucous membrane between middle turbinate bone and septum very much swollen. Itching, etc., constantly increases.

3.35 p.m.—Septum and lower turbinate bone completely touch one another, and are bathed in watery fluid, which constantly runs from that nostril. The patient is quite unable to breathe through the nostril on left side. Voice is nasal in tone.

3.37 p.m.—In the right eye the symptoms have completely disappeared. A drop of antitoxin was rubbed into the left nostril.

3.40 p.m.—Nostril very slightly less occluded, although running of watery fluid still continues.

5 p.m.—Left nostril quite free. In the course of the evening patient suffered from dull headache, such as she generally experiences whilst suffering from hay fever. Next morning quite free.

3. In my own case the mopping of the interior of my right nostril with a swab of absorbent cotton-wool soaked with one to two drops of the 1 in 500 toxin solution produced in a moment a feeling of slight itching and burning in the right nostril, followed by swelling and congestion of the right turbinate body which was repeatedly examined during the next hour by Dr. Tilley, when this swelling remained permanent. The sensation of itching persisted for some length of time, although at about one hour after the

application it had become materially diminished. No sneezing fits as on previous occasion.

4. The following are the notes of Dr. Tilley's case:

2.59 p.m.—1 in 500 toxin mixture with serum.

3.3 p.m.—Itching first noticed.

From 3.2 p.m. to 3.20 p.m.—Itching constantly increasing. Swelling of mucous membrane of inferior turbinate bone, and septum becomes marked. The contrast between the mucous membrane of the left and right nostrils is very noticeable.

3.20 p.m.—A drop of antitoxin was applied.

3.29 p.m.—No change or amelioration of symptoms.

In the course of the afternoon the symptoms gradually wore off.

REMARKS.—Whilst the experiments in my son's and Miss R.'s cases fully accords with the results stated in my first paper, the phenomena appearing in Dr. Tilley's and my own cases tend to further justify the belief that there is a class of persons, who although not actually suffering from hay fever, yet are more susceptible to the influence of the pollen toxin than those of the great majority of persons experimented upon. It remains to be seen whether this fact establishes a connexion between genuine hay fever and paroxysmal sneezing or vasomotor coryza.

REFERENCE.

¹ March 28th, p. 713.

MEMORANDA: MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

BULLET WOUND OF BRAIN: RECOVERY.

THE following interesting case came before me on December 12th, 1902:

An Ashantee named Osey Cudjoe fought in the Ashanti rising of 1872 to 1874. At the battle of Fantiyan, Kumassi, fought about January, 1873, he received a bullet wound of the head. He and his friends gave the following account: He was unconscious for about a week. During this period the bullet was removed by native surgery and the wound dressed (most likely with leaf mould and leaves, as this is the native way of dressing all wounds). He was four months in recovering.

On examination there was found a hole on the left side of the head over the angle formed by the junction of the anterior inferior angle of the parietal bone with the frontal and temporal bones, the hole being a circular inverted cone, the base being external. It was $\frac{1}{2}$ in. in diameter at the apex and $\frac{3}{4}$ in. in diameter at the base. Skin, devoid of hair, lined the cavity, except for the area of the apex where the dura mater was seen uncovered by anything, and through it the brain substance showed clearly. There were a few melanotic spots and veins to be seen. There was some thickening of the periosteum for about an inch round the opening. The man was quite healthy and did not suffer from the sun, though his head was clean shaved. He stated he had never suffered ill-health or from fits of any kind. All the movements were perfect, as were sight, speech, and hearing. There were no signs of induration of the exposed dura mater, which looked healthy and clean. He did not suffer from headache.

The wound was caused by a Snider bullet at long range. The man was about 20 years old at the time.

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ACUTE DILATATION OF THE STOMACH WITHOUT APPARENT CAUSE.

SOME years ago I received an urgent call to a child 11 months old supposed to be dying. In a few minutes I was at the house and found the child dead; the heart had stopped, and all efforts at resuscitation were unavailing. The history was that the child had a short time before partaken of its bottle, and was laughing and playing on its mother's knee, when suddenly it seemed to stop breathing, "made a noise in its throat," and became insensible. There was no convulsion or struggle, and the child had apparently died immediately. There had been no previous illness or digestive troubles, and the child was well nourished and presented no evidence of rickets or congenital syphilis. The parents were both healthy.

I suspected "cardiac failure," but could find no clue to its causation. *Post mortem*, however, I found the stomach greatly dilated, containing 19 oz. of food—like fairly thick Mellin's