med. a. It has many finer subdivisions, which I have not as yet fully worked out.

3. *The lateral nucleus* (No. 3, Figs. 5 to 14).—It is situated for the greater part in the lateral zone, but it extends also into the subventricular zone. Its subventricular portion, No. 3 A, is bounded by the internal medullary lamina, No. 11, and corresponds to "the semilunar nucleus of Flechsig," which lies, therefore, mesially to the lateral portion of the lateral nucleus, No. 3 B, and in front of the pulvinar, No. 4. The lateral nucleus proper, No. 3 B (Figs. 5 to 16), is divisible into a lateral anterior, 3 B a, and a lateral middle, 3 B b, and a lateral posterior, 3 B c, part. It corresponds to Nissl's lateral anterior and lateral posterior portions and to v. Monakow's *lat. a* and *lat. b*. Anteriorly the lateral nucleus extends almost as far forwards as does the anterior nucleus; laterally it is separated from the reticular layer, No. 9, by the external medullary lamina, No. 30. The middle portion of the lateral nucleus shows usually a well-marked division into a lateral, No. 3 B b, z, and a subventricular region, 3 B b, x (see Figs. 11 to 13).

As far as it is possible to tell by histological methods, No. 3 B consists of a distinct dorsal and a distinct ventral portion; the former 3 B a is seen in Figs. 5 to 12, while the ventral division is seen in Figs. 13 to 14. These divisions, not being quite definitely established, have been numbered in the same way.

4. *The posterior nucleus* (No. 4 in Figs. 5 to 14).—It consists of a more mesial portion, No. 4 A, on the ventricular side and a lateral division, No. 4 B. The mesial portion abuts in the more ventral regions on the optic nerve, No. 15, which separates it from the anterior corpora quadrigemina, No. 16. The lateral division is the pulvinar proper and is much more developed in the monkey than in the rabbit.

5. *The ganglion habenulae* (No. 5 in Figs. 6 to 9).—This ganglion may be called, with Edinger, the epithalamus. It is not included in the schematic figure of the thalamus, Fig. 3. In all animals from the frog to man it runs parallel to the middle line from before backwards. It is composed of a small-celled ventricular, No. 5 a, and a large-celled lateral subventricular part, No. 5 b. It receives its impressions from the taenia thalami, No. 17, and sends its impulses by the fasciculus retroflexus of Meynert, No. 18, to the interpeduncular ganglion of v. Gudden. It is comparatively feebly developed in the monkey while it is large in the rabbit.

6. *The external geniculate body* (No. 6, Figs. 14 to 20).—It is composed of two very distinct subnuclei, namely, a dorsal, No. 6 a, and a ventral one, No. 6 b. It receives its impressions through the optic tract.

7. *The internal geniculate body* (No. 7, Figs. 15 to 17).—It may consist of two parts, namely, an anterior portion (No. 7 a, Fig. 15) and a posterior portion (No. 7 b, Figs. 16 and 17).

8. *The pineal body* (No. 8, Figs. 7 and 8).

9. *The retinae*, not represented in the figures.

10. *The reticular nuclei* (No. 9, A, B, C, Figs. 6 to 17).—These nuclei are but subnuclei; thus No. 9 a is developed in connexion with the external geniculate body subserving sight, while No. 9 b is developed in connexion with the internal geniculate body subserving hearing. No. 9 c is intimately related to the ventral nucleus No. 10, in which the fillet terminates, and in its more dorsal reaches it seems to be developed in connexion with the lateral nucleus, No. 3. The dorsal reticular nucleus of Nissl, lying between 1, b and 3 B, a in Fig. 10, possesses cells of a motor type and is probably the emitting nucleus of the mesial nucleus, with the exception of the centre of Lays, the emitting nucleus of which is the nucleus magnocellularis of Nissl. Till the exact function of these nuclei has been determined experimentally it is best to put them under a separate heading as I have done here.

All the nuclei enumerated above lie in the dorsal half of the thalamus, while the ventral half contains:

11. *The ventral nucleus* (No. 10, Figs. 14 to 17).—It shows a distinct division into three zones, a, b, c. It receives its stimuli from the fillet arising from the caudate and lenticular nuclei; from the homologous nuclei developed in connexion with the sensory cranial nuclei, and perhaps from the cord directly. Its exact extent was studied by me in the rabbit by Marchi's method, and is now being investigated by v. Gudden's method.

In the discussion a complete series of sixty accurate drawings of transverse sections of the thalamus of the rabbit were used for elucidating the various points mentioned above. Inasmuch as without these figures a description of the nuclei would be of little value to the reader, a full description of the nuclei will be published as soon as the wax models of the

thalamic nuclei have been completed. There were also shown the actual specimens of the rabbit series and of the monkey series, reproduced in Figs. 4 to 21, as well as stereoscopic slides of the rabbit's thalamus. The following experimental work bearing directly on the structure and function of the thalamus has been done in rabbits one to three days old: complete removal of the sacral, the lumbar, and the lumbosacral cords, the cerebellum, the eyes, the middle ear, and one olfactory bulb. These animals were killed after three months, and injected by my micro-corrosive method. The results of these experiments I hope to be able to publish soon.

A complete historical account, dealing with the literature, and particularly with the work of v. Monakow, Nissl, Probst, Prus, Edinger, and his pupils, will be given later.

REFERENCE.

1 S. Ramón y Cajal, *Textura del Sistema Nervioso*, Tomo II, fig. 604. 1904.

Sir VICTOR HORSLEY, speaking from the degeneration point of view, agreed very fully with the morphological conclusions of Dr. Mann—namely, as to the possibility of dividing the thalamus, according to the original view of Burdach, into dorsal and ventral portions. He also agreed that the ventral division of the external geniculate nucleus had different pallial relations from the dorsal division. Further, he discussed the minute structure of the ventral division of the thalamus, and showed that the extremely restricted termination of the fillet axones, as localized by the degeneration method was now amply confirmed by the most recent publication by Ramón y Cajal. Both methods tended to show that the "fillet nucleus" consisted of three parts, a central globular portion to the opposite (antero-posterior) halves of which semilunar nuclei were applied. Further, he proposed that morphologically the plexuses of fibres should not be dwelt upon for subdivision of the thalamus, but that the true morphological point was the cell, and that neurologists needed for the analysis of function, the most minute description of the nuclear collections of cells.

Professor GOTCH thought that the most important side off the thalamus was afferent, and that the efferent was superadded.

Dr. WARRINGTON first of all referred to Probst's work, and agreed that the fillet terminates in the thalamus. The thalamus was, he thought, a great relay centre receiving the terminations of the nerve fibres from the pallium and the cerebellum.

Dr. MAY said that as illustrating the results of lesions in the thalamus in monkeys, and the symptoms resulting therefrom, the following observations might be recorded: In a large number of cases there was hemianaesthesia and hemianopsia of the opposite side of the body, confirming the observations made by Hughlings Jackson in man in 1874. Moreover, there was, in about half the cases, a most interesting symptom, which consisted in a deviation of the face and head, so that the face was directed to the side of the lesion, and the opposite ear was drawn down to the shoulder. In 15 out of 16 monkeys there was paralysis of the opposite side, due to implication of the fibres of the pyramidal tract; in 9 there was definite hemianopsia; in 8 there was turning of the head, and in 4 the pupils were unequal. In many cases the contralateral pupil was larger than the pupil on the side off the lesion, and nystagmus was occasionally present.

ON THE PATHOLOGY AND TREATMENT OF LEPROSY.*

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THE PREPARATION OF LEPROLIN.

In January, 1903, I read a paper at a meeting of this Branch on the antagonism between micro-organisms, and showed a theory, which I now again place before you, which I called the periodic law of diseases. In August, 1903, while working at the antagonism between micro-organisms in the direction of the bacillus tuberculosis, I hit on the way of cultivating this bacillus rapidly. The bacillus tuberculosis grows very slowly on glycerinated media, and as this slow rate of growth was fatal to the experiments that were being performed, research was made into a way of cultivating it more

* Read before the Burmah Branch of the British Medical Association. First and second communications in the *Indian Medical Gazette* for May and June, 1904.

rapidly. Passing a current of sterile air over glycerinized media in shallow flasks was tried to no effect, and I then turned to this table of the periodic law of diseases, and noticed that as there was a column in which there were all the anaërobic bacilli, and this column was headed by the element oxygen, on the corresponding theory of Mendeleïff of the periodicity of the elements, so I thought that the corresponding element to the column of the acid-fast group of bacteria might be the element most interfering with the growth of these acid-fast organisms. This element is chlorine.

The thing was, then, to try to remove the salts of chlorine from nutrient media, and the universal distribution of these salts showed that the matter was not a simple one. Trying to remove them by chemical means failed, as the nutrient medium was always rendered useless in the process. I then tried distilling beef extract, and found that it was possible to obtain a fluid smelling strongly of beef, and containing only the volatile substances in beef; in this medium the bacillus tuberculosis grew with the greatest ease, and so did the bacillus leprae and the bacillus of Lustgarten. But the fluid was of low nutrient value, at any rate I was satisfied that it was owing to the absence of salts that these bacilli grew in this medium, as the addition of the slightest trace of salt (NaCl) prevented the growth altogether.

The nutrient medium was then improved by passing a current of superheated steam from the autoclave over boiling beef extract, and lately it had been further improved by passing superheated steam over the beef extract soaked in pumice stone in bottles inside the autoclave.

In this medium one can obtain a growth of the bacillus tuberculosis in from one to three days, and the bacillus leprae in from three to five days, as well as the other acid-fast organisms. The characteristic appearance is a curly white, stringy heavy deposit at the bottom of the tubes, which is hard to shake up, but when shaken up appears as a curly white, stringy shred in the tubes. Both the bacillus tuberculosis and the bacillus of leprosy are very much alike in this respect, except that the former is more easily shaken up.

Of these cultivations there were made hundreds of removes, and the bacillus of leprosy was obtained from a great many different cases, and each time showed the same characteristics.

The next thing to do was to grow the bacillus on solid media in order to obtain a pure culture, and in this we had great difficulty, as agar contains quite a large amount of salt; however, the difficulty was afterwards got over by dialysis. By dialyzing nutrient agar in frequently-changed warm distilled agar, a nutrient agar was obtained entirely free from sodium chloride, and on the surface of this medium the acid-fast group of bacteria grow with the greatest ease. The bacillus of leprosy grows at first as a white, and later as a yellow or brick red, curly, thick growth on the surface of the agar, very much like the bacillus tuberculosis grows on the surface of glycerinized nutrient agar.

Staining Reactions.

These are very important, not only as a means of diagnosing the disease, but also in the examination of cultures for the preparation of leprolin. The bacillus of leprosy, like all the other acid-fast bacteria, retains the stain of acid dyes after immersion in acids, and the bacillus of leprosy does this more than any of the other bacteria of this group.

The bacillus of leprosy when stained may be differentially diagnosed from other acid-fast bacteria as follows:

1. As already stated, it retains the stain of acid dyes much more than any of the other bacteria of this class. It retains the stain of carbol-fuchsin even after decolorization in 25 per cent. nitric acid.
2. It is more irregular than the tubercle bacillus, and not curved, and is somewhat smaller.
3. It contains small oval spores within itself, which are highly refractile, and the end of the bacillus may be open where some have presumably escaped.
4. It has a beady appearance due to the presence of these oval spores.
5. Like the bacillus tuberculosis it may grow out into cultures into long, branching filaments, but there are often oval spores separate in the cultures, and these may be alone visible at times.
6. In the body it is found in great numbers inside epithelial cells, generally in the middle of the cells, whereas the bacillus tuberculosis is found in small numbers inside giant cells at the polar ends.

Cultivation.

As already stated, the bar to the cultivation of this bacillus has been salt. The fresh granulations of the ulcers of a case of leprosy are scraped and examined for the bacilli by the method of staining for the bacilli, and if they are found a tube of the medium prepared as already stated is inoculated with a piece of tissue, and is incubated at 100° F. in the incubator, and is examined after from three to five days. There is then found a thick deposit, which on being shaken up in the tube, forms a curly white stringy fluff. This, on being examined in the usual way, shows the bacilli of leprosy, with usually some contamination. This tube is then plated into a warm Petri dish of the dialyzed medium prepared as stated above, and after from three to five days the Petri dish is examined, and the colonies of the bacillus leprae isolated in the usual way by means of stabbing with a platinum needle, and inoculating into other dishes of the medium. The Petri dishes present the same appearance as those of the bacillus tuberculosis, except that the colour of the colonies changes to yellow or to a brick red.

Pasteur flask cultivations become cloudy after from one to two weeks, and when the culture is getting near the time for it to be examined to see if it is ready for making into leprolin, it should present a milky appearance on being shaken up. Usually after six weeks the culture is ready to be made into leprolin.

I have lately been making stock cultures in the medium reduced over sulphuric acid in a vacuum to one quarter its bulk, as the nutrient value of the medium is thus increased.

Manufacture of Leprolin.

The toxin of the cultivation of the bacillus leprae I call leprolin, and this is prepared on similar lines to the preparation of tuberculin. There are a great many different ways of preparing tuberculin, but Koch's original method was to grow the bacillus tuberculosis for six weeks in Pasteur flasks, and to heat the flasks to 100° C., and then filter the culture through a Pasteur filter, and reduce the fluid to one-tenth the original bulk, and add glycerine. This is practically the method I employ, except that I do not sterilize the cultures at all; I merely filter the cultures through sterile Pasteur candles several times, and then reduce the fluid to one-tenth the original bulk, and then refilter the fluid through re-sterilized Pasteur filters, the filters being previously tested.

Such a leprolin will produce a powerful reaction in a case of leprosy, which may last for three days or more.

I have now manufactured over 500 doses of this leprolin and injected it into 120 cases of leprosy, and in each case there has been the same reaction. The leprolin is now being used in thirty different places in India, and in order to meet the demands it is now being manufactured in large quantities, but, owing to the difficulty of preparation, not more than twenty doses can be turned out a day with the present arrangements. I hope before long to increase this to double. One dose of the leprolin is equivalent to 50 c.cm. of culture.

Action and Uses of Leprolin.

A case of leprosy, after the first injection of leprolin, will get a severe reaction, which may come on very soon after the injection, the temperature running up to 104° F. or higher, the anaesthetic areas becoming red, hot, and swollen, and the pulse and respiration rate going up very soon after injection. The fever may come down a little on the second day, but usually rises again to 102° or 103°, and then gradually falls to normal on the third or fourth day, the redness and swelling gradually subsiding, and with this subsidence the sensation may return in some of the anaesthetic areas to a large or small extent according to the case.

There is a good deal of smarting at first at the site of injection, due to the glycerine with which the leprolin is preserved, but this soon goes away. When I first made this material I used to inject large amounts. That was before I had procured the necessary apparatus for concentration. Now the dose is 10 c.cm., injected into the muscles of the arms or buttock.

The most remarkable effect of leprolin on lepers is the suddenness with which the sensation returns in the anaesthetic patches. I know that it is hard sometimes to say that some low-class Indians have anaesthesia or not, but the majority of my patients have been intelligent Burmans, and some Eurasians, and only the minority jungle folk. I have made absolutely certain before injection that the patient could not feel the prick of a pin in certain areas, and I am glad to say

that in almost every case injected with this material there has at least been some obvious return of sensation in some anaesthetic area.

The next thing that leprolin does in alleviating the symptoms of this disease is: it relieves the shooting pains in the limbs and joints that these patients suffer so badly from, and causes the heavy sensation in the limbs to disappear. It changes slowly the white anaesthetic patches by commencing in the centre and edges of the patch to change the colour of the skin to normal. It causes the rough furfuraceous skin to become smooth. After injection the anaesthetic patches will show redness in their centres, which gradually assume the natural colour of the skin, and these patches, which may have been anaesthetic before, become tender to the touch. It causes the nodules in the subcutaneous tissue to subside, and this in some cases has been a very marked feature of the improvement. It causes the ulcers to heal up, and this it does rapidly; some cases had had ulceration for years, and after only one injection the ulcers healed up. Even parts that are gangrenous slough away and leave a healthy granulating sore. Such a case—a man who came to hospital with gangrenous feet and loss of sensation in the entire legs—after four injections of leprolin was so much improved and almost healed up, with return of sensation completely in the legs, that he was able to walk about.

I showed you last month a Burman who, after the short space of ten days, lost all signs of the disease after one injection of leprolin. He had had ulceration of the foot for four years, and loss of sensation in both legs and feet. The ulcer completely healed and all sensation returned, and he went out apparently cured; he turned up again to-day, and I therefore show him to you again.

The same leprolin and the same preparation of the same culture of the bacillus will not always produce the same effect in all cases of leprosy. In some it may cause a slight reaction, in some it may cause a very severe reaction. As a rule, the severity of the reaction may be taken as an index of the benefit that is likely to occur, and this in itself is a good sign of the beneficial action of this material in this disease. I have been injecting only once a fortnight, but in some bad cases I have injected at intervals of only a few days.

If the injection is given at the interval of only a few days, or before the temperature of the first injection has reached normal, then it generally occurs that the temperature of the second injection will be prolonged.

I have now injected this material over four hundred times, and in every case there have been no bad symptoms, and in every case the disease has ceased to advance.

The action of leprolin, then, appears to be very similar to that of tuberculin, when the latter is applied in cases of lupus. There is a marked reaction in the affected area, and cases of lupus have been reported which have greatly benefited by the injection of tuberculin. As is well known, however, its action is dangerous, as it is liable to loosen the bacilli from the deeper tissues and cause a general infection of the disease. There appears to be no such danger with regard to the action of leprolin.

Tuberculosis is a disease which affects the hypoblastic tissues, while leprosy is a disease which affects the epiblastic tissues.

Treatment of Leprosy.

Of the total cases of leprosy now treated by this method, four have been cured; at least there remains no sign of the original disease; two of these cases I showed at the last meeting and two I showed this time.

The number of cases now under treatment in Burmah is about one hundred, and in the great majority of these there has been very marked improvement, and it is now being tried in thirty different places in India, by I.M.S. men and others, and I have heard from two of these gentlemen that the leprolin is causing very good results, and they have wired for more of the material.

Some of these cases are well worth seeing as showing how the anaesthetic patches gradually assume the natural colour of the skin, commencing from the edges and the centres of the patches, which later become invisible. As already stated, the principal sign of improvement is the return of sensation and the rapidity with which it causes this is difficult to explain.

Rapid improvement cannot be expected in such a chronic disease, but one case has been apparently cured after one injection of leprolin, while some cases have had as many as eight injections.

The difficulty of manufacture of this material, has prevented

me from treating my cases as regularly as I should have liked, as most of my spare time has been spent in my laboratory, but I hope soon to be able to produce enough culture to make sufficient leprolin for the injection of 300 cases a month. Since publishing my reports in the *Indian Medical Gazette* for May and June, I have been inundated with applications for this material, only some of which I have been able to supply.

Theory.

As to how the organism enters the body and causes the disease, it would appear from the method of growth of this bacillus that the theory recently brought forward that the disease is caused by the consumption of badly-cured fish is erroneous.

I have examined several samples of badly-cured fish, some very bad, so much so that one did not care to go too close to them; I found in all a large amount of salt, and moreover salt in certain amounts is not a preventive of putrefaction. I tried to grow acid-fast bacteria from these bad samples of cured fish in my medium, but failed.

In all kinds of fish and meat the amount of salt is considerable, and is certainly sufficient to prevent the growth of a bacillus that has such a marked aversion to salt as the bacillus leprae.

There are two views that may be taken as to the manner in which this leprolin acts beneficially in cases of leprosy. One is the autotoxic view, and the other is the antautotoxic view; the former is, that all cultures of bacteria eventually die out by poisoning themselves by their own excreta, and that, therefore, if one injects the toxins from the cultivation of the leprosy bacillus and injects them in large amount into the body the bacillus leprae is killed off before it has time to progenerate its species, as it is very slow in growing in the body. The antautotoxic theory is that if a bacterial poison is injected into the body, the body reacts to it in such a way that an antitoxin is eventually formed in the body which acts as an antitoxin and kills off the bacilli, so that when leprolin is injected into the body an antitoxin is formed in the body and acts as an antidote to the bacilli and their poisons.

In support of the first theory we have the fact that the action of leprolin in causing the sensation in the anaesthetic patches to return is most sudden, and therefore it would not be likely to be due to an antitoxin, as it would not have time to be formed in the body, to cause this sudden return of sensation.

A SECOND CASE OF CUTANEOUS ANTHRAX SUCCESSFULLY TREATED BY SCLAVO'S SERUM WITHOUT EXCISION.

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A FEW weeks ago one of us, in conjunction with Mr. C. B. Lockwood, recorded in the *BRITISH MEDICAL JOURNAL* a case of anthrax of the face successfully treated at St. Bartholomew's Hospital without excision, by the use of Sclavo's serum. A second and equally successful case has now to be recorded.

On January 17th, 1905, a man, aged 30 years, a horsehair dresser, presented himself at St. Bartholomew's Hospital with a characteristic anthrax lesion on the forehead. He gave the following history: On January 9th he had fallen, striking his forehead against a fender, bruising it but not breaking the skin. Four days later he noticed some watery fluid exuding from the bruise, and on January 14th, a small black slough was present in the centre of the bruise, which was more defined and evidently inflamed. The neck became a little stiff, and on January 15th an enlarged gland was felt at the left angle of the jaw. His general health was scarcely impaired and there was little pain. On admission to the hospital, under the care of Mr. Bowlby, the patient showed on the left side of the forehead, near the roots of the hair, a black slough about the size of a sixpence with a ring of vesicles around it from which a clear fluid exuded. There was not much inflammation or oedema around, but a large hard gland could be felt at the angle of the jaw. The temperature was 99.6° F. and the pulse 100. The fluid from the vesicles showed numerous characteristic anthrax bacilli, and cultures yielded, next day, a profuse growth of the bacillus practically unmixd with any other organisms. The bacillus was fully virulent when tested upon a mouse. In view of the success which had attended the use of Sclavo's serum in the previous case above referred to, the sole treatment adopted was the injection beneath the skin of the abdomen of 40 c.c.m. of the serum, which was kindly furnished by Dr. Legge, of the Home Office. The slough was kept covered by a piece of lint, coated with boracic ointment. No rise of temperature followed the injection, which