In the case under consideration I found that he was wearing a cylinder the axis of which was placed leaning 25 degrees from the vertical; this position made all vertical meridians correct when his eyes were directed straight ahead, when in fact no torsion of his visual axes was present. It is plain, then, from what has been said about the rotation which occurs when the eyes are turned in, that this position of the cylinder could not be the correct one when he was looking down and in, for rotation will have taken place behind the lens. This it was quite simple to prove. A plain sheet of paper was placed at the usual reading distance from his eyes; with his distant glasses on a double prism was put in front of his right eye. On the card was a single straight line, to which he directed his attention. He then saw three lines; the upper and lower belonged to his right eye, the centre to his left. If, then any rotation of his eye were present, it was plain that this central line would not be parallel with the other two. As I expected, he stated that this middle line sloped away down to the right. By simply moving the position of the cylinder 10 degrees nearer the horizontal, this line became at once parallel. However, on once more testing, with the cylinder in this new position, with the eyes directed straight ahead, he stated that his vertical meridians were out of truth. Their restoration was effected by putting the lens back to its original position.

It was evident, then, that he needed two pairs of glasses, one for distant use with the cylinder at its old situation and another with it at ten degrees nearer the horizontal for reading and close work. After using these for three weeks he wrote to say that there was already some improvement.

Here, then, was a cause which answered to the hypothesis that the error was trifling, yet constantly and easily overlooked. We have only, then, to explain briefly what caused it to give rise to such symptoms.

It was evident that his glasses for distant use were perfectly correct, but when he came to read with them the rotation of the eyes which then took place would lead to a want of parallelism of the lines of his book. These lines would, in fact, tend to cross when the images were fused, but as the brain will not tolerate double images it would make every effort to correct this want of alignment. This is overcome by a special effort on the part of the oblique muscles of the eyes, whose function it is to rotate the eyes.

Now, this torsional action of the obliques is directed and graduated by the will, and though this effort of the will may be easy and rapid it is none the less an independent action.

This characteristic feature explains how it was that this cause could persist so long before it produced any symptoms. At first the extra exertion would entail little strain on the nervous output of energy, but as time went on, and he approached the age when reading naturally became more difficult, its effects on the general nervous system would become more pronounced.

The phenomenon of the sloping of the ground, which was noticed after near work, is explained by the cramped position into which the oblique muscles had brought the eyes, causing them to become fixed in a position which made them incorrect for the gaze when directed straight ahead. This would also explain the trouble he experienced as he walked home through the "noisy streets of Manchester," as the lines of the buildings, etc., would all be out and his nerves in a highly sensitive condition to any external irritants.

This case is an example of the endless troubles to which such a condition can put both the patient and his medical advisers when it remains untreated and unrecognized.

Patient writes December 28th, 1909: "There can be no doubt that an improvement in my condition has taken place during the last few months . . . but though feeling my physical limitations I can safely say my condition is better than it was."

THE second International Congress on Cancer Research will be held this year in Paris from October 1st to 5th. The President is His Excellency Professor von Czerny; the General Secretary, Dr. G. Meyer. The office to which all communications should be addressed is at 13, Bendlerstrasse, Berlin, W.

ON A TRIAL OF NASTIN.

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THE treatment of leprosy is still the opprobrium of therapeutics, and promise of improvement in it has so much importance that the following account of a trial of Professor Deycke's nastin treatment will have interest for many in different parts of the world who have reported on, or who are still conducting, similar trials. It is confined to a summary statement for want of space. Here, for instance, charts of daily temperature extending over a whole year cannot be displayed, but it has been abstracted from my annual official records¹ for the years 1908 and 1909, in which such charts have been published, together with many other details not reproduced here. I would ask the reader to understand, therefore, that the statements made below do not represent general impressions, but result from clinical notes made from week to week. It is the more important to mention this in the case of leprosy, because the character of the disease is tenacity with long duration; even its untreated course is commonly remittent or fluctuating, is frequently interrupted by long terms of quiescence, and, not very rarely, is brought to a close, apparent or real, in a stage which may be accepted as recovery for all practical purposes. These features leprosy has naturally, but when patients are cared for other points have to be borne in mind. It must be generally known, I suppose, that lepers almost invariably improve considerably after having been removed from conditions of poverty, or even of irregular living, to those of a well-ordered hospital, and that often the improvement is not confined to their general state—as shown, for example, by increase of weight—but extends to the visible and tangible stigmata of the disease. Over and above that, I have noticed that the stigmata vary considerably from time to time, independently of all treatment; and, again, that lepers are usually very impressionable, and often benefit remarkably, for a time at least, when interest and hope are excited in them by any new treatment; and, therefore, it is hardly enough for writers to assert that whereas before treatment a patient exhibited such and such signs, these afterwards became favourably modified or disappeared. In order that the mere reader may be placed as far as possible in a position to judge whether the reporter's opinion has been well founded, all the conditions under which the patient lay must be mentioned at the same time.

After having studied Professor Deycke's earlier papers,² it seemed to me that his ingenious and interesting observations rested on foundations which were very largely speculative; but, further, that application of the result of his experiments to treatment was a widely different matter. In his opinion, formed after long experience, his clinical results testified that a step towards the scientific treatment of this ancient disease had been taken by him for the first time in its history. On that ground I took nastin into use at the beginning of 1908. My supplies, received from Biebrich, included nastin B1, nastin B2, and ketin; they were contained in original packages, and were in good order. The injections were actually administered by the medical superintendent of the hospital to which the lazarets are attached, Dr. R. J. Millard, M.B., D.P.H., who was formerly microbiologist in my department; the syringes were invariably dried by immersion in ether, which was allowed to evaporate before the nastin was drawn into them, and the remains of any partly emptied flask were thrown away. In no case did suppuration occur, but effects were produced at the site of injection—slight pain, which usually passed off in half an hour, with subsequent formation of hard and tender lumps. The latter resembled those caused by Haffkine's plague prophylactic, but were so much more persistent, that at the end of the course each patient had large areas of irregular subcutaneous induration on the outer sides of the arms used; and, in the cases of two patients at least, these areas still persist quite plainly, although a year has elapsed since the last injection was made. Nothing further happened in the third, fourth, and fifth of the cases described below, but in the second there was additionally quite severe pain on three occasions, which persisted for

twelve hours, while on one of those occasions there also occurred a transient oedema of the whole of the upper extremity used; and in the first of them, while prolonged pain was felt about the same number of times, on still two other occasions the injections caused eschars, which separated slowly, and which left indolent ulcers.

From among the patients whom from time to time I had admitted, and who thereafter had continued under my care and weekly observation, I selected the five described below. They were all whites. It will be observed that they were of both sexes, and of ages which varied between 7 years and 70. The duration of their illnesses was between six weeks and sixteen years. Two of them had been newly admitted when the treatment began; the other three had been under my care eleven, five, and four years. Three of them had the disease in its tuberculous form. One other was an old case of pure lepra nervorum, but in the midst of a marked remission. The fifth was originally a case of pure lepra nervorum of ten years' standing, but at the beginning of this treatment he was fifteen months advanced in the course of transition to the skin form, and, at the same time, was in about the third week of an exacerbation which was strictly confined to the nerves. Thus the series included three cases of special interest and value in the present connexion: Case I on general grounds—namely, the early stage of the patient's manifest disease, her tender age, the proportionately large doses of nastin she received, the long continuance of the treatment, and the ease and certainty with which accumulation of signs could be watched and distinguished; Cases III and V on grounds furnished by Dr. Deycke's impressive warnings against the exhibition of nastin in nerve leprosy.

It is difficult to ascertain from Professor Deycke's writings what measure of improvement may be reasonably expected from nastin treatment within a certain time, although it must be inferred from them, I believe, that restored sensation and dissipation of tuberosities may be looked for, as a rule, in the course of some months—more or less complete in different cases, and not without a few exceptions in which all response to it will be wanting. But what seems certain from them is this: While normal doses of nastin B 1 sometimes cause immediate reactions, namely, general (or febrile) and local in tuberosities, etc. (or necrotic), the same doses of the same form exhibited every second or third day may be relied upon to produce them. They may even be so violent as to endanger the patient's life. They are especially liable to occur in cases of nerve leprosy, and for that reason nastin B 1 must be exhibited in them with great caution, nastin B 2 not at all. In addition to these evidences of action, Professor Deycke finds that the bacilli become degenerated; he infers this from vacuolated, dotted or moniliform, and granular appearances which supervene. These results have their importance. For if nastin had no immediate effect, but its prolonged, silent exhibition were necessary before abatement of the disease could be looked for, the same doubt would be felt in forming a judgement on its efficacy as in the case of every other remedy for leprosy hitherto advocated, namely, whether the improvement ultimately distinguishable were due to it, or (not being uniformly observed in all cases) were merely attendant on the natural fluctuations of the disease, reinforced by careful general management and attention.

CASE I.—A. R., female, aged 7, came under treatment within six weeks of first appearance of the stigmata of tuberculous leprosy; her general health was not disturbed. Her treatment began on January 28th, 1908. After a preliminary injection of 0.5 c.cm. she had nastin B 1, 1 c.cm., every seventh day until June 3rd; from that date she received 1.5 c.cm. every seventh day; from August 23rd she had the same dose every fifth day; from September 25th the same every third day; but almost immediately afterwards it began to be repeated every second day, and was so continued to November 4th, when this medication ceased. On three separate days a single dose of nastin B 2 was substituted for B 1. Thus she had fifty-seven doses in all. There was not at any time any reaction to the injections, either local or general. Her case slowly got worse and worse during the year, in a way which I consider to have been usual.

CASE II.—G. M. S., female, aged 23, married; tuberculous form. The first signs had appeared in February, 1903, a few weeks after her confinement with her second child. She was admitted February, 1904. The signs of her disease were from the first marked and prominent, but at no time has her general health been affected; she was and continues to be lively, energetic, and industrious; only towards the end of 1907 did some disturbances of sensation, not recognized by her until pointed out,

begin to be observable. Between April 7th and 20th, 1908, she received three injections of 1 c.cm. of nastin B 1 every seventh day, and then ceased. On May 12th she resumed the same quantity at the same interval; on June 17th the dose was increased to 1.5 c.cm.; on August 12th the interval was reduced to five days; on September 12th nastin B 2 was substituted, same dose, same interval; on September 22nd she had nastin B 2, 2 c.cm., and on the 25th returned to nastin B 1, 1.5 c.cm., but repeated every second day, and on December 16th ceased. Thus she had sixty-five doses. Her case remained, and a year after cessation still remains, stationary. Neither local nor any general reaction occurred at any time.

CASE III.—H. W., male, aged 68, pure lepra nervorum. He set the first signs which could be ascribed to leprosy at 1892; admitted 1897. At the end of 1900 his disease appeared to have become quiescent, and so continued till 1907, when blisters began to appear spontaneously on his much-deformed fingers; and during the earlier months of 1908 he presented a number of very large maculae which had newly appeared. He was in the course, therefore, of an active remission, but his general health did not suffer. On March 16th, 1908, he began to receive nastin B 1, 1 c.cm., every seventh day; on August 18th the interval was diminished to five days; on September 12th he had nastin B 2, same dose, same interval; on November 2nd he resumed nastin B 1, 1 c.cm. every seventh day, and on December 28th ceased. His case was altogether unaffected; his temperature did not vary, and it is especially to be noted that there were no local reactions. His very marked and extensive anaesthesia remained, and still remains, exactly what it had been for many years; his maculae are now less brightly coloured, but are still perfectly plain.

CASE IV.—F. P., male, aged 70, tuberculous leprosy; had probably suffered for five or six years when he was admitted in January, 1908. From January 28th to August 5th he received 1 c.cm. of nastin B 1 every seventh day, then ceased. At the end of the year, after comparison of his then state with that recorded on admission, it was seen that no changes had taken place except those usually observed in old-standing cases as a result of the regularity of hospital life and feeding. Improvement was not to be expected in this case. The patient was senile on admission, and died of senile decay during 1909. But it is to be noted that there was no reaction at any time, either local or general.

CASE V.—F. E. B., male, aged 32. The first signs ascribable to leprosy were observed by the patient in 1898; he was admitted in 1903, and was then suffering from pure leprosy of the nerves. The disease continued active, as was shown in various ways (prolonged hypersensitiveness of, perhaps, all nerves; a general eruption of maculae, etc.), but mutilations, paralyses, and disturbances of sensation did not much advance, and his general health remained good. During September, 1908, a *léprome en nappe* appeared on the right buttock; from this bacilli were easily obtained in abundance for the first time in the case. He thus entered on the transition from nerve to skin leprosy, or, rather, the latter became added to the former manifestation. At beginning of April, 1909, when the signs of the skin form of his disease had slowly developed and progressed, he began to suffer from an acute exacerbation, which, however, was strictly confined to the nerves; they became greatly swollen, tender, and developed neuromas. On April 20th, that is to say, after the exacerbation had already lasted two or three weeks, he was given nastin B 1 every seventh day till May 21st, from May 28th to June 26th nastin B 2 every seventh day, thence to July 30th the same every fifth day; and from that date to the end of the year the same every fourteenth day. It produced no general reaction (his temperature remained unaltered till the middle of June; then he began to have some fever, which lasted, though with short intermissions, till the end of August only; but no connexion at all could be traced between this elevation of temperature and the injections, with which, it will be observed, it coincided only in small part). It did not cause any local reaction either. No effect on his disease was produced; the exacerbation followed a quite usual course. Disturbances of sensation and paralyses remain what they were before treatment.

Thus nastin showed itself in my hands an entirely inert body, save for some irritant effects limited to the seat of injection. My experience seems to have been identical with that of Dr. Lenz³ of Equatorial Africa. Both his and mine differ *in toto* from Professor Ziemann's⁴ account of his trial in the Cameroons, which was so favourable that he asked for a special appropriation of £400 for the purchase of supplies for the ensuing year. Both differ also from favourable accounts furnished by several independent observers⁵ in India. On the other hand, they would appear to resemble the result of trial in Manila;⁶ also in a single tuberculous case in London, and of a more general trial in Hamburg, as I have learnt from private communications. On the whole, the only suggestion that Dr. Lenz was able to make by way of explanation of the discrepancy—namely, that his supply for some reason had been at fault—seems unlikely to prove valid. The following experience bears upon it. Towards the end of 1908 I learnt that nastin had been administered to a single white patient, suffering from tuberculous leprosy, in the Dominion of New Zealand, and that an injection of

nastin B2 had been followed in him on one occasion by a reaction of such violence that the form was deemed to be unsafe and was definitively thrown out of use. I had no reason at all for doubting the soundness of my supply; but here, it seemed, was an opportunity of testing such a suspicion as Dr. Lenz has more recently mentioned, and at my request the Chief Health Officer of New Zealand was good enough to turn over to me the remainder of his stock of nastin B2. I applied it in the following way:

H. F., male, aged 40, lepra tuberosa, duration unascertained (but probably several years), received 1 c.cm. of nastin B2 (N.Z.) on three days with two intervals of two days each. His temperature remained unaffected and no other result ensued.

Cases I and II (above) each had 1 c.cm. of nastin B2 (N.Z.) on each of two days; Case III had one such dose; in Case V the nastin B2 continuously administered on and after May 28th to the end of the year was part of this New Zealand supply.

In none of the patients did it cause any reaction, either local or general. These discrepancies are puzzling. It is possible that they have their psychological aspect.

As regards the bacilli in the cases described above, they had their usual appearances, and no changes could be detected. Professor Deycke's description⁷ of the degenerative alterations observed after treatment do not (I think) indicate anything unusual. In cases of leprosy, in which bacilli can be easily obtained from the surface of the body, it is generally found that wholly-stained specimens lie among a larger number of others which are either vacuolated, or dotted, or reduced to mere acid-fast granules. In many situations none wholly stained are found; in some, which perhaps are generally more recent deposits, all may be wholly stained. The imperfect bacilli can take a differential stain.

REFERENCES.

- ¹ 1909-10. J. Ashburton Thompson: Eighteenth and Nineteenth Annual Reports of the Board of Health on Leprosy in New South Wales.
- ² 1904-7. Deycke: V Internationale Dermatologen-Kongress, Berlin; *Deut. med. Woch.*, 1905, SS. 480, 545; *Lepra*, vii, p. 174.
- ³ 1909. Lenz: *Lepra*, ix, p. 19.
- ⁴ 1909. Ziemann: *Ibid.*, p. 23.
- ⁵ 1909. Rodriguez: F. A. Smith and Bissett, Beauchamp Williams: *Trans. of Bombay Medical Congress*. F. Raschid: *BRITISH MEDICAL JOURNAL*, ii, p. 1343.
- ⁶ 1909. Heiser: *Amer. Journ. of Med. Sci.*, cxxxviii, September.
- ⁷ 1908. Deycke: *BRITISH MEDICAL JOURNAL*, i, April 4th.

THE SCIENCE COMMITTEE

OF THE

British Medical Association.

REPORT CXX.

PERITONEAL BLOOD TRANSFUSION.

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BLOOD injected into the peritoneal cavity is quickly absorbed into the circulation, with the exception of a small quantity which remains entangled in the omentum. The volume of the circulating blood is within a few days adjusted to its proper level, so that the concentration of red cells is increased and a condition of polycythaemia produced. The general phenomena are fully described by Hunter,¹ where an abstract of the older literature will be found.

In previous investigations Boycott and Douglas² determined the rate at which the red cells contained in the blood of normal rabbits transfused by direct intravenous injection into other normal rabbits are destroyed. They found that the mean daily amount of haemoglobin destroyed, expressed in terms of oxygen capacity, varied from -0.19 c.cm. to 0.44 c.cm., on an average 0.24 c.cm. It was the immediate object of the present research to see whether the rate of destruction of red cells passed into the circulation via the peritoneum was greater or less than this. In a series of twenty-two experiments a mean daily rate of 0.55 c.cm. was found. From a consideration of the nature of the stimulus which excites a rabbit to destroy the red cells of another rabbit which it may find in its

circulating blood, it appeared that the relatively foreign nature of the cells was an important factor. The degree of foreignness of the cells is presumably increased by passing them through an extravascular position (peritoneum) on their way to the circulation, and it is suggested that this is the reason why cells so transfused are destroyed more rapidly than when they are put straight into the blood of the recipient. With intravenous transfusions the rate of daily destruction increases as the process advances, while with intraperitoneal transfusions the rate is much quicker during the first than during the second week.

The red cells are not destroyed by a process of intravascular haemolysis, nor has it been found possible to induce the production of antolytic or isolytic substances in the blood serum of rabbits by repeated intraperitoneal injections of whole or laked blood, nor by destroying a rabbit's red cells inside the body by such a poison as phenylhydrazine. The initial phase of destruction seems to find its morphological expression in abundant phagocytosis of red cells by the endothelial (stroma) cells of the lymphatic glands and spleen pulp. Within these cells the red corpuscles are broken up, and pass gradually to a condition of amorphous pigmented debris, some of which gives the reaction for inorganic iron. This phagocytosis is very much more abundant with intraperitoneal than with intravenous transfusions—an observation in accordance with the view that the cells are made more foreign by passage through the peritoneum.

Apart from the various other reasons which point in the same direction,³ these observations suggest that intravenous transfusion is to be preferred to intraperitoneal transfusion, as giving a prospect of more lasting benefit to the recipient. This conclusion does not, however, necessarily follow, since experiments show that considerations of whether the red cells are needed in the body can outweigh those concerning the precise degree by which they are foreign to the economy.

REFERENCES.

- ¹ *Journal of Anatomy and Physiology*, vol. xxi, 1887. ² *Journal of Pathology and Bacteriology*, vols. xiii and xiv; *BRITISH MEDICAL JOURNAL*, May 22nd, 1909. ³ Crile, *Haemorrhage and Transfusion*, 1909.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

LYSSOPHOBIA OR HYDROPHOBIA?

In June, 1903, my orderly—a Mohammedan Sepoy of the Kapurthala Infantry—was bitten by a dog on the outer side of the left leg below the knee. The wounds (two) healed in eight days, and he had forgotten all about the incident until February 9th, 1905—one year and eight months later—when he felt unwell, irritable, and fretful; that evening he had some fear of water, and was evidently thinking about the bites. On the following day (February 10th), when sitting in the quarter guard, he told his comrades the story of the dog, mentioning his symptoms of the previous day and his fear of water. The native officer in charge did not think him really ill, but at 11 p.m. locked him up in an adjoining room, and at 6 a.m., when he opened the door, found that the man had developed symptoms of hydrophobia. His brothers were sent for, and they conveyed him to his house in the city. He was quite conscious, but, as he bit at the sight of water, his eyes were bandaged during the journey. When I saw him at 11 a.m. on February 11th he was sitting on his bed retching and spitting with a brass basin in front of him. His hands were kept down by a pillow placed in front of them. He was biting and snapping, with quiet intervals. His aged mother watched by his side and when he wanted to bite, a pillow was each time thrust toward him and he bit it. He occasionally raised his hand to his mouth as if to bite, but he never closed his teeth over it, nor did he leave any impression of teeth on the skin, although the pillow presented to him was torn to bits. His eyes were wild, ferrety, intensely congested, and the pupils dilated. In the intervals he spoke naturally, and asked his brother to give me a chair. He held up his leg and pointed out the scars of the bites, which had a blue congested look. With great vehemence he declared that he had felt pain in the