

these places had become dry, and consequently the presence of cyclops could not be determined.

The village pond seems to me undoubtedly the most likely source of the vast majority of the infections. Attention must, therefore, be mainly directed, on the Gold Coast at least, to their protection. My negative results seem to show that the wells are relatively less important. The wells should be surrounded by a stone parapet of about 2 ft. in height and the village pools stoutly fenced around in order to prevent the natives from bathing there or from wading into the water when filling their storage vessels. Each pool would have to be provided with a sufficient number of "drawing" wells dug at a short distance from the pool and connected with it by underground pipes in such a way as to ensure a constant supply of water. The openings of these would be protected by a stone or cement wall. In this way by preventing water in contact with the legs of the drawers returning into the pool the chances of infection would be reduced nearly 90 per cent. The "drawing" wells would most likely be used freely by the natives, as less labour is involved in obtaining water by draw-bucket or pump than by collecting it with a calabash. Nor would the prevention of the use of the pools for washing prove as great a difficulty as might be supposed, for at several places the natives have already learnt to do this at a place apart from where the drinking water is drawn. At Accra, the filling of the large reservoir by a thunderstorm a few days before I left gave me the opportunity of observing that there those using the water for washing purposes carried it over the embankment to the lower ground. These precautions were, however, rendered unavailing, as far as dracontiasis was concerned, for those drawing the water for home use frequently entered it for some distance in order to secure a more copious supply than that obtainable at the margin.

If by these or other and more practical methods the infection of the open ponds in the villages could be prevented there is little doubt that a considerable diminution in the disease would soon result.

There still remain for careful investigation in relation to the prophylaxis of dracontiasis many details regarding the life of the intermediate host. We have still to determine more accurately the conditions under which it lives and multiplies in these tropical countries, what are its natural enemies, and upon what other forms of life it depends for its food supply; whether it can survive the drought of the summer, buried beneath the sun-caked mud, or if, when once a pool has dried, it must be restocked from another source; lastly, if, by the addition of chemicals, we can destroy the cyclops in suspected waters without rendering these useless or dangerous to man.

No account of my investigations on the Gold Coast would be complete were I to leave unacknowledged the kindly interest with which Sir John P. Rodger and Major Bryan encouraged my work, the generous way in which the Principal Medical Officer and his deputy aided me with every facility the medical department could have provided, and the daily help and forbearance of Dr. Buée, who had charge of the Government hospital, and Dr. C. H. D. Ralph, the Medical Officer of Health for Accra.

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THE MEDICAL PROFESSION IN AUSTRIA.—According to official sources, the total number of medical practitioners in Austria at the end of 1906 was 11,957, being an increase of 173 as compared with the previous years. These are distributed according to provinces as follows: Austria, 5,813; Lower Austria, 409; Salzburg, 136; Styria, 696; Carinthia, 147; Carniola, 106; Coastland, 582; Tyrol and Vorarlberg, 622; Bohemia, 2,845; Moravia, 958; Silesia, 249; Galicia, 1,480; Bukowina, 155; Dalmatia, 138. In Bosnia and Herzegovina there are 118 practitioners. The following are the figures for the larger cities: Vienna, 2,902; Prague, 447; Graz, 263; Trieste, 199; Innsbruck, 97; Lemberg, 347; and Czernowitz, 68.

## ATOXYL IN THE TREATMENT OF TRYPANOSOMIASIS.

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SINCE a number of statements concerning the use of atoxyl in human trypanosomiasis have recently appeared in various journals, lay and medical, it seems opportune briefly to recapitulate what is known concerning the action of this drug on trypanosomes and to indicate what seems to be the best method of administering it.

"Atoxyl," a preparation of arsenic (meta-arsenic-anilid;  $C_6H_5NH As O_2$ ) which contains about 37.6 per cent. of arsenic, was first used in the treatment of various skin diseases and of anaemia.<sup>1 2 3</sup> The beneficial action of arsenic in trypanosomiasis (nagana) was first reported by Livingstone. Succeeding experimenters (Bruce, Lingard, Laveran and Mesnil, Thomas and Breinl, and others) also noted the marked action of arsenic, administered in various forms, on the parasites in the blood stream of animals infected with trypanosomes, of several different species. All these observers recognized, however, that, as a rule, the protective effect of the usual forms of arsenic was only temporary, and that, in the end, the parasites reappeared in spite of steadily increasing doses of arsenic, until a point was reached at which the animal died, either of its disease or through poisoning by the arsenic given to cure it.

Thomas and Breinl<sup>4 5 6</sup> thought that it might be possible to find in some of the compounds of arsenic with organic bases a form of the drug which would still retain its deleterious effect on trypanosomes, but would be less toxic to the animal treated. A number of preparations were tried without result, until atoxyl was found to possess both of the desired qualities in a marked degree. A large series of experiments on animals infected by various trypanosomes was carried out at the Runcorn Laboratory,<sup>7</sup> and it was found that when very severely infected animals were thoroughly and persistently treated with atoxyl a very marked improvement immediately followed. The parasites obviously degenerated, and totally disappeared from the blood in a very few hours. The animals gained weight, lost their symptoms, and seemed in apparent health. In some of them the amelioration was permanent. In others, if the treatment were stopped, the parasites reappeared in the peripheral circulation after a varying period, or, if the drug were given continuously, the parasites eventually reappeared in spite of treatment, and increased in numbers until the animal died, as in the ordinary course of an untreated trypanosome infection. Laveran, Mesnil and Nicolle<sup>8</sup> have had a similar experience. Thomas and Breinl were much impressed with the effect of atoxyl, and advised that the drug should be given in as high doses and as continuously as possible in cases of human trypanosomiasis. They stated that, "at the same time, all aids in building up the physical condition of the individual should be used." In their opinion, "if such a régime be carried out and treatment be begun at an early period, the prognosis (based on the experience of animals treated) will be good." As a result of the work of these authors, the Liverpool School of Tropical Medicine has ever since consistently advised that this drug should be given a most careful trial in the treatment of sleeping sickness.<sup>9</sup>

Since October, 1905, the Liverpool School of Tropical Medicine has sent large quantities of atoxyl (2,600 grams), with careful instructions for use, to various medical men and missionaries in West Africa, who have signified their readiness to give the drug a careful trial. Reports have as yet been received from none of them.

In the meantime, atoxyl has been used in Europe in the treatment of several Europeans and negroes, from both the east and west coasts of Africa, who were infected with *Trypanosoma gambiense*. In some of them the results have, so far, been most encouraging; in others, unfortunately, the drug has had but little action.

Kopke is quoted<sup>10</sup> as having treated cases by atoxyl with results encouraging at first, but later followed by

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rélapses. These are to be explained, according to Magalhaes<sup>10</sup>, by the impermeability of the meninges, which prevents drugs (potassium iodide and methylene blue) from reaching the cerebro-spinal fluid, and so protect the trypanosomes there present from harm. We regret we have not been able to obtain Professor Kopke's publication.<sup>11</sup>

Broden and Rodhain,<sup>15 12</sup> have between them treated by atoxyl four Europeans infected with trypanosomiasis. In three cases their results were very encouraging, in the fourth the drug is not well supported, and it has had but little beneficial action. At the London School of Tropical Medicine Dr. Daniels informs us in a private communication that in two cases treated respectively for fourteen and ten months not only can parasites no longer be found, but there are now none of the symptoms of the disease. The patients appear to be in excellent health, and injection of their blood into monkeys and rats does not cause trypanosomiasis in these animals. Small doses, 10 minims or less, of a 10 per cent. solution were given intramuscularly, and the dose increased to the limit of tolerance without symptoms—that is, in these cases, 25 to 30 minims of the 10 per cent. solution on alternate days. The administration of these doses has been continued with short intervals throughout the whole period the cases have been observed.

Van Campenhout informs us in a private communication that he has employed, in conjunction with atoxyl, strychnine and cold baths—the latter for their tonic and stimulating effects. He has had three European cases in the third stage of the disease under his care. All have reacted immediately to the treatment, have gained weight, and are at present apparently well. As a precautionary measure, the treatment is being repeated in two of these cases. The third has not returned for further treatment. Dr. Van Campenhout has also had good results from atoxyl in the treatment of a European in the first stages of trypanosomiasis. He prefers solutions of 5 per cent. to 10 per cent. of atoxyl, and regulates his doses in the following manner. He commences with a dose of 0.2 to 0.25 gram of atoxyl, and increases it daily by 0.05 gram until a dose of 0.8 gram or more is reached. If there are then no signs of poisoning, the daily dose remains at this point during a fortnight or three weeks, according to the gravity of the case. The dosage is then gradually lessened by 0.05 gram daily until a dose of 0.2 gram is reached, and the treatment is then interrupted for one or two months. Three or more such courses of treatment are given as required.

Most of these observers have given the drug subcutaneously; some, however, have given it by the mouth. This is a mistake, since atoxyl is certainly broken up by the acid contents of the stomach, and the untoward effects of over-treatment by arsenic are thus more easily produced.<sup>13</sup> We believe that the intravenous injection of a solution of atoxyl in distilled water is the method to be preferred. Its difficulties are apparent, and in routine treatment it will probably be usually replaced by subcutaneous injections. As in the ordinary administration of arsenic, the organism should be gradually accustomed to the drug.<sup>14</sup> We believe that this can best be done by<sup>15</sup> making a 20 per cent. solution of atoxyl in sterile normal saline. The solution should be warmed to blood heat just before use. In this way the drug is completely dissolved, and the pain at the site of injection, which occasionally follows atoxyl, is obviated. Give subcutaneously daily for four days 0.6 c.cm. On each of the four succeeding days give 0.8 c.cm., then raise the dose for a week to 1 c.cm. of the solution each day.\* Now give 1 c.cm. every two days for a fortnight. Then reduce to 1 c.cm. twice a week until all symptoms have disappeared and the patient's blood is negative to sub-inoculation into susceptible animals. Afterwards 1 c.cm. should be given weekly for as long a period as possible. Should signs of poisoning arise, the same doses should be given, but less frequently. Although we have indicated a definite treatment it is impossible to give a general rule for every case, since idiosyncrasies are bound to occur; but, as a guide, it may be said that the dosage should be brought to the limit of the patient's tolerance (no signs of

\* This dosage is based on the personal experience of one of us (A. B.), who made fruitless attempts to influence the course of an infection by *Spirochaeta italoni* in him-self and a laboratory servant by injections of atoxyl.<sup>14</sup> Both patients remained under treatment for fifteen days.

poisoning) and continued at that point. It is at present impossible to say for how long the treatment should be kept up; it is well known that no symptoms may be present for several years in cases of human trypanosomiasis which ultimately end fatally. We are, therefore, in complete agreement with Broden and Rodhain,<sup>12</sup> who have likened the treatment of trypanosomiasis to that of syphilis.

Van Campenhout, in his directions to the medical officers of the Congo Free State,<sup>16</sup> points out that the syringes used for injecting atoxyl should be sterilized by heat, since acids (carbolic) decompose atoxyl. He also points out that solutions of atoxyl break down and become yellowish if exposed to the light. All solutions should therefore be kept in dark (brown) bottles and made up afresh each week. Dr. Nierenstein, working independently at this school, had also found it necessary to follow these rules, since he had found that pure aniline is present in solutions of atoxyl which have been exposed to diffuse daylight for five days.

The signs of poisoning by atoxyl do not seem to be those usually associated with arsenic, and its administration has never been followed by albuminuria.<sup>17</sup> Schild describes them as "chilly feelings, vertigo, headache, and ticklings in the throat." Broden and Rodhain<sup>12</sup> saw severe abdominal cramps radiating to the hypochondria, slowing of the heart, and cold extremities, in cases to whom comparatively large doses of atoxyl had been given (to 4.10 grams of atoxyl in one week at the beginning of treatment). In none of these cases was there intestinal pain or diarrhoea.

Daniels, in a private communication, states that "burning on micturition, general dryness of the mucous membranes and skin, with the formation of pruriginous vesicles," followed the administration of 0.2 gram of atoxyl twice weekly for fourteen months in one case. In another case, early in the course of treatment, there was vomiting and diarrhoea. When these symptoms occurred the dose was reduced and subsequently very gradually increased. Other patients have been able to stand twice the doses mentioned, but in one 25 minims of a 10 per cent. solution given on alternate days produced abdominal cramps.

Van Campenhout, in a private communication, states that untoward effects followed the administration of from 0.2 to 0.5 gram of atoxyl given by the mouth daily for several days. He also found in one case that they regularly followed the administration of 0.8 gram of atoxyl given hypodermically in one dose. He describes the signs of poisoning as slowing of the pulse, cold extremities, and pectoral cramps.

In conclusion, although we earnestly advise the use of atoxyl in human trypanosomiasis, we cannot forbear uttering a word of warning lest the immediate amelioration which usually follows the administration of this drug should be thought to be always permanent. In some cases a cure may be effected; in others, from the experiments made at this laboratory, we are forced to believe that the improvement will prove to be merely transitory. Atoxyl is a great advance on previous methods of treatment, but it is not an absolute specific. What its actual therapeutic value in human trypanosomiasis really is can only be determined by the systematic treatment and subsequent observation, over a period of several years, of a large number of cases. It is therefore absolutely necessary that those who have an opportunity of treating cases of sleeping sickness should use every effort to keep a careful record of the after-history of their patients.

In the meantime, at Liverpool as elsewhere, the search for a treatment more efficacious than atoxyl is still being continued.

Our thanks are due to Dr. Daniels and to Dr. Van Campenhout for permission to publish those of their observations mentioned in this communication.

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## THE TREATMENT OF PARALYTIC TALIPES BY VALGUS BY TENDON TRANSPLANTATION.

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A MODERATE degree of this deformity is very suitable for treatment by tendon transplantation. The very severe forms where, in addition to the tibials, the muscles of the calf are very weak or completely paralysed, are unsuitable for this procedure. Stability of the foot can in these only be obtained by producing ankylosis at the ankle-joint. The three following cases which recently came under my care at the Children's Hospital illustrate many points in the treatment:

1. E. C., aged 4½ years, was attacked by infantile paralysis three years previously. The loss of power was at first complete in both legs. Some recovery took place, and when first seen by me the condition was as follows:—In the left leg, the only healthy muscle present below the knee was the extensor longus hallucis. The others were not completely paralysed, and reacted feebly to the faradic current. The limb, though not strong, was distinctly useful, but an extra amount of work was thrown on the opposite member. Fortunately the ligaments about the ankle-joint were not unduly lax, and there was no indication for any operative interference on this side. On the right side there was a well-marked valgoid position. The following muscles were involved, and did not react to faradism—tibialis anticus, tibialis posticus and extensor longus hallucis. The flexor longus hallucis and communis digitorum were feeble. The internal lateral ligament of the ankle was stretched, and well-marked flat foot was present, partly due to the want of support of the tibialis posticus muscle.

Tendon transplantation was performed on May 16th, 1906. The skin incision extended from 3 in. above the outer malleolus across the front of the ankle, and more than half way up to the popliteal space along the middle of the calf behind. The peroneus longus was cut as long as possible and brought across the front of the joint and fixed to the inner and under surface of the navicular bone by silk sutures. About one-third of the tendo Achillis was split off the inner side, and the separation extended well up into the calf muscle, as suggested by Drobnik.<sup>1</sup> An additional muscle was thus formed, which was placed behind the inner malleolus in the sheath of the tibialis posticus. The sheath itself was accurately sutured over the new tendon. This separated piece was fixed to the under surface of the navicular bone. It was impossible to get it within an inch of the selected spot, so the interval was bridged over by four strands of silk, as recommended by Lange.<sup>2</sup> The displaced central part of the tibialis posticus was fixed on to the os calcis, beside the tendo Achillis. Possibly a few fibres of this muscle were spared and might assist the calf muscles which had been weakened. The limb was then put up in plaster for six weeks.

After this was removed massage was performed daily, and the child allowed to get about. The boot used had the side stiffened to prevent over-stretching of the relaxed internal lateral ligament. This will be worn until the muscles of the transplanted tendons have hypertrophied and the child has learned to use them in a co-ordinated fashion. Marked improvement in walking resulted, but as the limb had to bear most of the body weight, it was not quite satisfactory. It was decided to ankylose the mediotarsal joint to give greater stability to the foot, a plan which has been advocated by Whitman.<sup>3</sup> Three and a half months later the astragalo-navicular articulation was opened and the opposed cartilaginous surfaces shaved off. Had it been possible to foresee the necessity of this operation it would have been better to have done it before the tendon transplanting. On exposing this area it was interesting to note the firm attach-

ment of the peroneus longus and the split part of the tendo Achillis to their new position. A dense mass of firm fibrous tissue had formed round the silk sutures joining the latter tendon to the bone. Thus the satisfactory result obtained by bridging an interval by silk stands was demonstrated. The limb is still in plaster-of-paris, where it will have to remain for at least three months to allow of the ankylosis becoming firm.

2. C. D., aged 3½ years. The paralysis in this case was of two years' duration; it affected the right leg, which was ½ in. shorter than the left. The following was the "distribution" of the paralysis: The tibialis anticus and posticus were quite useless, the inner head of the gastrocnemius was feeble, but the outer head reacted vigorously to the faradic current. The inner part of the extensor communis digitorum reacted very weakly to the interrupted current though the extensor longus hallucis was unimpaired. Of the thigh muscles the inner hamstrings and adductors were weak. There was not the same flattening of the arch of the foot as in the last case.

Tendon transplantation was done on May 25th, 1906. The tendo Achillis was not made use of as the calf muscles were partly paralysed. The extensor longus hallucis was divided and fixed to the inner and under surface of the navicular bone. The peroneus longus was brought across the ankle and fixed to the peripheral end of the divided extensor of the great toe. If I had a similar case in future I should cause the peroneus longus to support the joint behind by passing it underneath the tendo Achillis to the navicular bone.

3. K. P., aged 4½ years. The paralysis was of three years' duration and affected the left leg, which was ¾ in. shorter than its fellow. A very marked valgoid deformity was present, the child walking on the inner border of the foot. The peronei on the outer side of the ankle were markedly contracted. The following muscles were found not to react to faradic stimulation: Tibialis anticus and posticus, flexor and extensor longus hallucis. The inner part of the extensor communis digitorum and the inner head of the gastrocnemius were very feeble. In the left hand the interossei, the third and fourth intercarpal spaces were paralysed, resulting in a characteristic deformity.

On May 16th, 1906, tendon transplantation was performed. The peroneus longus was displaced out of its sheath and cut as far as possible in the sole of the foot. The tendon was then brought across the front of the ankle superficial to the deep fascia, and was fixed to the inner and under surface of the navicular bone. Much improvement resulted, though the deformity was not altogether corrected. After recovery there was considerable eversion of the foot, owing to lack of any support behind the inner malleolus. Apparently it would have been preferable in this case, too, to have brought the peroneus longus behind the inner malleolus, passing it beneath the tendo Achillis. The main support necessary in talipes valgus seems to be one bracing up the inner side of the ankle from behind.

### Technique of the Operations.

1. A tourniquet applied above the knee makes the operation much shorter and easier. It prevents bleeding from a large number of small veins which are divided on the front of the ankle and foot.

2. The transplanted tendons, when possible, were fixed directly to the bone by silk sutures. A periosteal flap was raised from the navicular bone, and was sutured over the tendon when that structure had been fixed in position. No doubt the immediate result is better if the transposed tendons be fixed to the peripheral ends of the paralysed ones. The denervated structures, however, subsequently stretch and the operation is nullified.

3. When the split tendo Achillis was used the separated portion was given the sheath of the tibialis posticus. It afterwards moved in this very satisfactorily. The separation of the tendon was continued some distance into the muscle. Tubby<sup>4</sup> does not advise this plan, but it is probable that not many muscular nerves are destroyed by it, as they run on the whole vertically down in the gastrocnemius. If this be done, it may be possible to some extent to get independent movement in the separated tendo Achillis. If the splitting be not carried up beyond the tendon this is obviously impossible. It is important, also, to put the right amount of tension on the transplanted tendons when fixing them. If this be insufficient, the muscle uses some of its contraction in making the slack tendon taut. If the tension, on the contrary, be too great, the sutures fixing the tendon to its new insertion are likely to give way. As Tubby has pointed out, the tendons acting on the toes can be utilized to give stability to the ankle-joint. Loss of power in the toes is of small moment compared to weakness of the ankle or mediotarsal articulation. After the sheath of the peronei is opened up to allow of using of one of them, it is subsequently united by continuous fine silk suture. After the operation the leg and foot are put up in plaster-of-paris for six