die. Some appear to escape, but the period of activity is considerably diminished by the antimony in every case.

In making these observations with bilharzia the variation in resisting power of the different individual ova or embryos or miracidia was striking. Some ova hatched very much sooner than others under normal conditions, and some miracidia appeared to be more active than others, and some appeared to have a longer life, this quite apart from any accidental external circumstance such as becoming entangled in a wisp of mucus.

Therefore, judging from direct experiments *in vitro* with antimony tartrate, and from clinical results, one arrives at the conclusion that antimony tartrate has a profound and direct specific effect on bilharzia in all its stages. It kills the parent worm *in situ* in the portal tributaries. It penetrates the ova as they lie deposited in the tissue wall and kills the enclosed embryo. It has also the power of killing the free miracidium.

As no experiments have been made *in vitro* on the action of the antimony tartrate on the adult worms the matter cannot be considered settled. I have not had the opportunity of making them myself, but it would not be difficult to do the tests, obtaining the worms from animals experimentally infected.

We (Mr. Newlove and J. B. C.) concluded (speaking under correction and from clinical evidence only regarding the parent worms) that:

1. The parent worms are the most readily affected by antimony.
2. The ova next.
3. The miracidia are the most resisting of the three to antimony tartrate.

There are, therefore, ample grounds for believing that the action of the antimony tartrate introduced into the veins is a direct one on the ova, and probably on the adult worms also.

Continuing the doctrine of "permeability" and "direct action" further, it would appear likely that it also applied to the action of antimony tartrate on certain protozoal diseases; for instance, we know that it has a specific action on the Leishman-Donovan body in all its clinical manifestations, and that it has a decided curative effect in trypanosomiasis, though that disease is more resisting to antimony tartrate than either leishmaniasis or bilharzia. I am inclined to think that the enclosing membrane of the Leishman-Donovan body is also "permeable" (more permeable and less resisting than the enclosing membrane of trypanosome). If, in taking a specimen of splenic blood from a kala azar patient for the purpose of diagnosis, there be water in the syringe the bodies will not be found; they are hygroscopic. They take up water and disintegrate. The logical way of explaining this fact is, I think, that the shell or limiting membrane of the body is "permeable."

Permeability of the confining membrane may also be the explanation of the fact that in kala-azar it is extremely difficult to find the bodies in the peripheral blood. It may be that it is so delicate and sensitive to external conditions owing to the porosity of the "shell" that when it arrives in the peripheral blood exchange takes place between inside and outside "shell," and the body disintegrates. This is conjecture, but it is a fact which requires explanation that occasionally, though not often, the Leishman-Donovan body is found in the peripheral circulation. "Permeability" may also explain the difficulty in finding the body in tissues *post mortem*; so responsive is it inside its "shell" to external influences that it disintegrates and disappears as soon as the patient dies.

The four typical periodical rises of temperature in a twenty-four-hour kala-azar chart may possibly be associated with the periodical destruction in the peripheral

blood stream of the Leishman-Donovan bodies as they escape from the tissues where they have their habitat (liver, spleen, bone marrow, etc.).

There is a clinical fact also both in kala-azar and in trypanosomiasis which suggests direct action, and the breaking-up of the Leishman-Donovan bodies and trypanosomes with the introduction of the cell contents thereby liberated into the blood stream. If antimony tartrate is given to a patient with kala-azar or sleeping sickness the initial effect of the first dose or two is great aggravation of constitutional symptoms, shown by a sudden rise of temperature, etc. This is possibly due to the direct action of the drug entering and breaking up the organism, thereby liberating the toxins, etc.

Advancing this argument of "permeability" a step further, we find that parasites of "so many and so varied a nature" (Low) respond to antimony tartrate. It might be thought: It is a specific for bilharzia; why not, therefore, for other flukes and parasites, such as filaria, guinea-worm, and intestinal worms? It is a specific for leishmaniasis and trypanosomiasis, therefore why not for the plasmodium of malaria and the amoeba of dysentery? The answer to this may be found in the issue as to the direct action of drugs on the organism, and the question whether or no the organism is "protected" by a covering or membrane which is "permeable" to the antimony.

The following is a short statement made by Mr. N. H. Johnson of the Tropical Diseases Clinical Laboratory, from observations made independently by him on ova obtained from patients attending the Ministry of Pensions Clinic for treatment:

In the course of my experience during the past six months, examining the specimens of urine of bilharzia patients under treatment, I have discovered that antimony tartrate not only kills the miracidium but completely disorganizes the ova, which become shrivelled, blackened, and granular; I have repeatedly tried to hatch the treated ova, but without success. I have found that by adding 1 grain of antimony tartrate to 20 c.cm. of diluted urine at 37° C., with abundant ova, after twelve hours' incubation the ova appeared to be alive, but only a sluggish movement was noticeable. On adding 2 grains of antimony tartrate to 20 c.cm. of diluted urine at 37° C., on twelve hours' incubation the ova were completely sterilized, blackened, and granular, and I found it absolutely impossible to hatch these out. Not only do the ova appear to be blackened, but the surrounding debris and crystals are blackened; this, however, does not affect the blood corpuscles. Each of the above experiments has, of course, been worked with controls. In hatching out the untreated ova the miracidium revolves inside the shell prior to hatching until it finds a weak part—generally the centre of the lateral part of the shell—which it ruptures and escapes.—N. H. J.

In conclusion, I have to thank Dr. Broughton-Alcock, who has kindly given me the necessary facilities for carrying out observations at the Laboratory of the Tropical Diseases Clinic, Ministry of Pensions, London.

ANTIMONY IN LEPROSY.

BY

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In view of the remarkable improvement that was shown in some leper patients whilst undergoing a series of intramuscular injections with Oppenheimer's colloidal preparation of antimony (oscol stibium) in March of this year, I decided to give the treatment a further trial.

A report of the treatment appeared in the BRITISH MEDICAL JOURNAL for July 17th, 1920, page 76, where it was stated that the course was brought to an untimely end because the Union Government was unprepared for these leper patients to remain under observation in Natal. Six months after treatment was discontinued a letter was received from Madras to say that one of the lepers, David, was enjoying the best of health, carrying on his ordinary occupation in India, and was complaining of no symptoms requiring medical attention.

Two more lepers were admitted to the dépôt hospital of the Indian Immigration Board on August 23rd.

Sital stated that he had suffered from the condition for four years, during which time he had lived at Weenen, in Natal. The fingers were stiff and the extremities covered with a blood-stained discharge. All the fingers and both thumbs were discharging, and he had lost the nail of one finger of the right and two fingers of the left hand. All the toes were discharging,

* In the only case verified by *post-mortem* examination, made on a man who before was heavily infected with bilharzia, and who died of influenza and pneumonia a short time after his injections had been completed (gr. 33), the man was apparently cured of his bilharzia, for no parent worms were found in the portal vein.—*Journ. of Trop. Med. and Hyg.*, April 1st, 1919 (Archibald and James).

† The miracidium needs more formidable protecting paraphernalia to enable it to survive the varied conditions of life it will experience in the Egyptian puddle where it should be hatched.

‡ Oriental sore, naso-oral leishmaniasis, kala-azar.

§ The spleen is, practically speaking, a large blood swamp; openly connected with the arteries and veins, it is impossible to think that the Leishman-Donovan body does not get very frequently into the general circulation, and it needs explanation why it is so seldom found there.—J. B. C.

and only the small stump of one of the toes remained on the right foot. The face was free from signs of leprosy.

Oscol stibium 2.5 c.cm. was injected into the right deltoid muscle on August 23rd, 4 c.cm. on the 24th, and 5 c.cm. on the 25th and 26th. As there was some diarrhoea on August 27th and 28th, the injections were discontinued until August 30th, when 4 c.cm. were given without ill effect.

On August 31st the patient was feeling very well, and all the ulcers were dry. No further treatment has been given. On September 20th the extremities were still free from discharge, and all the stiffness had gone from the patient's hands, which he is able to use freely.

I asked Dr. J. Mackay, who has had an extensive experience of leprosy, to see this case, and he was agreeably surprised to see how effective the treatment had been. In his opinion there was no doubt whatever that the departmental medical officers had diagnosed the condition correctly as advanced leprosy. The case has also been under observation by Dr. Kerr Cross and Dr. G. L. Bonnar, the Indian medical officers of Durban.

On October 18th a swab was taken from the nasal secretion, as no discharge was available, and submitted to Dr. W. A. Murray, the Government pathologist at Durban, who reported the entire absence of *Bacillus leprae*.

Naukaklia was admitted to the Indian Immigration Hospital on August 19th in a very advanced stage of the disease. She was very frail, and not expected to live long. The hair was badly infested with nits. She was very emaciated, and her fingers and hands badly ulcerated. She had lost one digit of the right thumb, two digits of the right index finger, and the top digit of the middle finger of the left hand. The toes were not affected. The whole of the back of the right hand was covered with an extensive discharging scab, possibly the result of a burn. The discharge on several of the fingers was bloodstained. In several places bare bone was showing on the extremity of the fingers.

Oscol stibium 2.5 c.cm. was injected intramuscularly on August 23rd, 3.5 c.cm. on August 24th, and 4 c.cm. on August 25th. This caused diarrhoea for two or three days, and the injections were discontinued.

On August 29th the ulcers were nearly all dry, and on September 2nd, when I asked Dr. Kerr Cross to see the case, the ulcer on the back of the right hand was covered with a fairly clean scab showing evidences of rapid healing. On September 6th, though bare bone was still protruding through the ulcers on the extremities, all the ulcers were dry, and the scab on the right hand had come away, leaving a healthy dry skin.

On September 20th the extremity of one finger showed slight discharge and another ulcer on the hand looked unhealthy, so oscol stibium 2 c.cm. was injected intramuscularly. All the other ulcers were remaining dry, the condition of the scalp was much better, and all trace of diarrhoea had gone, though the woman was remarkably frail, somewhat hysterical, and took little food.

On September 23rd, as one little finger-tip was again moist with discharge, oscol stibium 3 c.cm. was injected intramuscularly. Since then no further injections have been given, for all the ulcers have remained dry. The patient is still very weak, and not expected to live much longer; but all signs of active leprosy conditions have disappeared.

In commenting on these two leper patients Dr. G. L. Bonnar, the acting medical officer, Durban Indian Circle, states:

"On admission both were showing active signs of the disease, with numerous ulcers on the fingers and toes. Although no further treatment has now been given for over a month there has been no recurrence of the signs of leprosy, and the ulcers have completely dried up."

TWO CASES OF DOUBLE GLIOMA RETINAE.

BY

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The following two cases of double glioma retinae were admitted to the Royal Eye Hospital, Manchester, under the care of Dr. Horsman McNabb. Both cases came under treatment about the same time.

CASE I.

S. R., aged 12 months, was admitted on March 23rd, 1920. According to the mother's statement, the child seemed to notice things up to the age of six months, but since then had "been different." In November, 1919, about four months before admission, he had measles and chicken-pox. Thereafter the mother noticed he had a "glide," and about two weeks before bringing him to hospital she saw a white speck in each pupil. There was one other child in the family, a boy aged 5, said to be quite healthy.

Condition on Admission.—The child was well nourished. There was a concomitant convergent strabismus of the right eye. Both anterior chambers were shallow. The right pupil was dilated and inactive. The left was smaller than the right, and reacted sluggishly to light. In both eyes a whitish tumour was visible by oblique illumination, and blood vessels could be seen on the surface. The tension in the right eye was about + 1, and in the left normal.

Operation.—Under general anaesthesia the right eye was removed on March 24th, 1920, and the left eye on the following day. In both cases the optic nerve was cut as far back as possible. Recovery was uneventful, and on September 17th 1920, the child was still quite well.

CASE II.

Henry H., aged 3 months, was admitted on April 16th, 1920. The mother had noticed "both eyes glassy" for five days before she brought the child to hospital. There were six other children in the family alive and well. The fourth-born, however, had died at the age of 4½ years from "meningitis with fits."

Condition on Admission.—Both anterior chambers were shallow. The pupils were dilated and inactive. By oblique illumination a large whitish vascular tumour mass could be seen through the pupil in each eye. Tension *plus* in both eyes. The child's general condition was not very good, and he was fretful.

Operation.—Under general anaesthesia the eyes were removed successfully on April 17th and 18th.

On May 25th there was still a slight discharge from the sockets. The child was fairly well, his general condition being better than on admission. In September there was still no sign of any recurrence.

PATHOLOGICAL REPORTS.

S. R. A typical glioma retinae, with well-developed rosettes. The blood vessels are better developed than in the other case, and necrosis is much less in evidence. It seems a decidedly less rapidly growing type of tumour than the other.

Henry H. Both eyes show a similar condition. The tumour is glioma retinae, but showing a good deal of necrotic change, and in general a sarcomatous type of growth, with a perithelial arrangement of the special cells. The characteristic rosettes are present. On the whole, the tumour suggests rapid growth and malignancy.

These two tumours are of interest as examples of a comparatively uncommon condition—namely, glioma retinae involving both eyes simultaneously. Collins and Lawford found both eyes affected in 12 out of 60 cases of glioma, and Marshall in 12 out of 32.¹ In cases of this kind the involvement of the second eye occurs more commonly months or even years after the first, according to Parsons.¹ In both these cases not only were both eyes affected, but the disease was almost equally well developed in both eyes at the same time.

In regard to prognosis, early diagnosis is of great importance as leading to timely surgical treatment. There seems to be general agreement that if the affected eye be removed before perforation by the growth, the prognosis is fair, but that in the absence of operation or in the presence of recurrence the outlook is practically hopeless. Immediate enucleation of the affected eye is therefore essential.

In the cases described diagnosis was a comparatively simple matter. The appearance of the tumours and the shallowness of the anterior chambers were characteristic. The increased tension supported the diagnosis of tumour, and the ages of the patients were in favour of the tumour being glioma, which is an affection of early childhood.

There was no sign of extraocular extension of the growth, and six months after operation the children were still quite well.

My thanks are due to Dr. Horsman McNabb for permission to publish an account of the cases, and to Professor Dean and Dr. Dible of Manchester University for the pathological reports.

REFERENCE.

¹J. Herbert Parsons, *The Pathology of the Eye*, London, 1905.

THE late Dr. Paul Redard, director of the Furtado-Heine Dispensary at Paris and author of valuable works on orthopaedics, has bequeathed a sum to the Académie de Médecine for founding a prize of 5,000 francs to be awarded every five years for the best work on orthopaedic surgery that has appeared in the meantime. The competition is open to foreign medical men. Communications should be sent to the Secretary of the Académie de Médecine.

MR. HENRY KIMPTON announces for early publication new editions of Dr. Eric Pritchard's *Infant Education* and Dr. H. S. Crossen's *Operative Gynaecology*.