bacilli of intestinal types have been isolated in pure culture.

(b) Injection of these cultures and subcultures into animals provokes an acute nephritis.

(c) From the kidneys of these animals in the earlier stages of nephritis the bacilli injected have been recovered in pure culture.

(d) Injections of cultures obtained from animals infected with these bacilli have reproduced the disease in other animals.

(e) The nephritis induced runs a somewhat prolonged course, and is accompanied by acute degeneration of liver cells and an enlargement of the spleen in the early stage.

(f) In human cases of nephritis treatment with appropriate vaccines has caused rapid amelioration.

(g) In some cases of nephritis a secondary or an independent infection of the urinary system may be present and obscure the original cause. This complication is probably more common in Egypt than elsewhere owing to the prevalence of bilharziasis.

In conclusion, it is my pleasant duty to record the valued help of my friend Dr. Clarke, who is responsible for the bacteriological classification and has done much to help the research. My thanks are similarly due to Dr. Yussef Barrada, who secured so many cases of nephritis for my section, and to my house physicians for their care of the patients, collection of urine, and injection of vaccine.

References.—1. Scheidemann: Münch. med. Woch., 1913, Nos. 60 and 61. 2. Hort: Brit. Med. Jour., October, 1914, p. 713. 3. Opie: Jour. Exper. Med., 1912, vol. xvi. 4. Oertel: THE LANCET, May, 1914, p. 1450. 5. Day: THE LANCET, May, 1920, p. 1009.

THE USELESSNESS OF ANTIMONY IN THE TREATMENT OF FILARIASIS.

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Sir Leonard Rogers¹ has recently reported some observations upon antimony injections given intravenously for the treatment of filariasis, and has pointed out that very careful and prolonged counts are necessary before coming to a conclusion as to the efficacy of this treatment. His results, on the whole, appear to indicate that these injections have a definite effect in greatly reducing the filarial embryos or causing them to disappear from the peripheral blood, presumably as a result of the destruction of the adult worms.

Recital of a Case.

One of us (G. C. L.) has recently pointed out that for all filarial work, such as estimating embryos, it is essential that measured quantities of blood should be taken, and that before any treatment is commenced the number of embryos occurring regularly in the blood should be known accurately. Variations are not uncommon, and may give rise to false impressions. The drug may act either by killing the embryos or by killing the adults or by killing both. Having had the opportunity of studying a case of filariasis (*F. bancrofti* infection), with plenty of embryos present in the night blood, we gave the patient a series of tartar emetic injections intravenously, and controlled these by nightly examinations of the blood, both before, during, and after the injections, the same measured quantity of blood (20 c.mm.) being taken at the same hour nightly. Dried films were made, the hæmoglobin then being washed out and the film stained with fuchsin. For the determination of death of the embryos wet cover-glass preparations were also employed.

History of the case.—Mr. V., a native of India, had lived there all his life till he came to England in July, 1919.

Previous illnesses.—No dysentery, no malaria, no venereal disease.

Present illness.—This began with an abscess on the inner side of the left thigh over the adductor tubercle ten years ago. *F. bancrofti* embryos were found in his night blood then. Six years ago he had another abscess, this time in the left groin; it was deep and was operated on and drained. In 1914 an abscess developed in the scrotum. After that the scrotum began to enlarge, the enlargement being of an intermittent nature and sometimes disappearing entirely. The attacks of enlargement were accompanied by pain, fever, and general malaise. Finally, the condition passed into a permanent one and definite elephantiasis supervened. The patient saw Sir James Cantlie on coming to London in 1919. The latter operated upon him, removing the elephantoid scrotum with successful results. Since then the patient has been living in England and has suffered from no further febrile attacks.

Examination.—Teeth had all been taken out for pyorrhoea.

Heart and lungs normal. Urine: No albumin, blood, or sugar.

Filarial condition.—Has had an elephantiasis of scrotum, successfully operated on. Penis also slightly affected. Deep scar in left groin, also another on inner side of left thigh. Glands enlarged just below Poupart's ligament on left side. Elsewhere no enlargement.

Blood.—A fair number of *Filaria bancrofti* embryos in night blood; definite nocturnal periodicity.

Injections and Filarial Counts.

Tartar emetic injections were given intravenously in the usual manner, commencing with $\frac{1}{2}$ gr. and increasing by a $\frac{1}{2}$ gr. each time till $2\frac{1}{2}$ gr. was reached, a total of $17\frac{1}{2}$ gr. in all being given. The patient bore these very well without ill-effects.

The following table gives the details of the filarial counts and the injections:—

(A) Number of filarial embryos in 20 c.mm. blood.

(B) Number of grains of A.T. injected.

Date. 1920.	Hour P.M.	(A)	(B)	Date. 1920.	Hour P.M.	(A)	(B)	Date. 1920.	Hour P.M.	(A)	(B)
June 21	11.55	15	—	July 10	11.55	15	—	July 27	—	20	—
" 22	"	17	—	" 11	"	18	—	" 28	—	17	—
" 23	"	15	—	" 12	4	—	1½	" 29	4	—	2½
" 24	3	0	—	" 11.55	6	—	—	" 11.55	22	—	—
" 25	11.55	13	—	" 13	"	18	—	" 30	"	20	—
" 26	"	16	—	" 14	"	16	—	" 31	"	18	—
" 27	"	14	—	" 15	4	—	2	Aug. 1	"	20	—
" 28	3	0	—	" 16	11.55	9	—	" 2	4	—	2½
" 29	11.55	21	—	" 17	"	18	—	" 11.55	23	—	—
" 30	"	16	—	" 18	"	22	—	" 3	"	19	—
July 1	"	12	—	" 19	4	—	2½	" 4	"	17	—
" 2	"	14	—	" 20	11.55	10	—	" 5	"	7	—
" 3	"	20	—	" 21	"	22	—	" 6	"	10	—
" 4	"	15	—	" 22	"	24	—	" 7	"	14	—
" 5	4	25	—	" 23	4	—	2½	" 8	"	19	—
" 6	11.55	15	—	" 24	11.55	10	—	" 9	"	16	—
" 7	"	15	—	" 25	"	18	—	" 10	"	10	—
" 8	4	32	—	" 26	"	20	—	" 11	"	17	—
" 9	11.55	4	—	" 27	4	—	2½	" 12	"	10	—
" 10	"	12	—	" 28	11.55	15	—	" 13	"	14	—
				" 29	"	—	—	" 14	"	15	—
				" 30	"	—	—	" 15	"	22	—

* It was decided at this date to stop the injections as they were doing no good.

Discussion of Results.

A perusal of the above table shows that the injections, consisting of a total of $17\frac{1}{2}$ gr. of tartar emetic, had no effect upon the infection at all, the adult worms not being killed and going on pouring embryos into the blood as before. The embryos were not all killed either as, even though reduced in numbers as on the night after the injections, those present were alive and healthy.

The only feature worthy of note is, that at first there were fewer embryos in the sample of blood taken on the night of the injections which were given at 4 P.M. This is not surprising when one considers that they would be in the lungs at that time and that the antimony would come in direct contact with them in a concentrated solution. That there was no effect upon the adults is shown by the numbers being up to normal the next evening and afterwards. Further, towards the end of the injections, even although the large dose of $2\frac{1}{2}$ gr. was being given, this temporary disappearance was no longer noticeable, the number found on the same evening as the injections being up to the average, or even a little above. The table illustrates also the considerable constancy, in this individual case, of the number of embryos in the blood every evening. If the female worms constantly pour young into the blood, then there must be a corresponding destruction going on, to keep the numbers at this mean rate. Possibly on the days when over 20

¹ THE LANCET, 1919, ii., 604; Brit. Med. Jour., May 1st, 1920.

embryos per slide were found there may have been an increased out-pouring from the female; or, of course, there may have been several females present giving birth to embryos intermittently.

It would appear, therefore, that antimony is not to prove a specific for filariasis as it is for bilharzial infections, but the only way finally to decide this point is to follow up cases, as has been done above, all results being checked by careful enumerations of the embryos. We have to thank Sir James Cantlie for letting us test the efficacy of the injections in this case.

NOTES ON THE TREATMENT OF RECURRENT MALARIA BY NOVARSENO BENZOL.

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So much has already been written as to the nature of malaria, the clinical and other characters of the disease, and the lines of treatment found to be most successful, that I propose here only to touch on a series of cases of recurrent malaria treated by me at the 3rd London General Hospital, Wandsworth, by intramuscular injections of novarsenobenzol (neokharsivan). Having seen during the last three years at least 500 cases of recurrent malaria from all parts of the world, I was struck by the fact that in all these cases the usual varieties of routine quinine treatment (i.e., by the mouth, intramuscular and intravenous) had been tried, in many cases pushed so far as to produce temporary blindness and deafness, and yet upon arrival in England the patients were still suffering from the disease, as shown by blood smears and a differential count. I therefore decided to venture on another line of treatment.

Rationale of Treatment.

My reasons for using novarsenobenzol were:
1. Because it has been conclusively proved that the malarial fevers are protozoal infections, infecting the red corpuscles of mammals, reptiles, and birds.
2. Because the organic compounds of arsenic in its trivalent form are more potent in action upon protozoa.
3. Because it is known to destroy the *Spirochaeta pallida*, the balance of opinion now being distinctly in favour of the *Spirochaeta pallida* being a protozoon.¹

The reason why the spirochaetes vanish so quickly after salvarsan, or neokharsivan, is that they contain free OH groups, since in their colloidal lipid membrane an unsaturated fatty acid exists. It is to these OH groups that the metals become attached, with the result that the organisms perish. I therefore hoped the same result might take place with the malarial parasite.

The preparation used was novarsenobenzol (B. W. and Co.), which is easily soluble in water, yielding a neutral solution suitable for intramuscular or intravenous injection. The first two injections consisted of 0.3 g. in 5 c.cm. 0.5 per cent. sterile saline, and the last two injections of 0.4 g. in 7 c.cm. 0.5 per cent. sterile saline. These injections are given at intervals of one week. A line is drawn backwards from the anterior superior iliac spine to the top of the natal fold; this line is divided into three equal parts; the point of intersection of the upper and middle third is the site of injection. All the usual antiseptic precautions should be taken with regard to the sterilisation of needles and syringe. The night before treatment the patient is given a laxative, the following morning, three hours before the injection, he is given a light breakfast, and the food on that day should be light so as to throw as little strain as possible on the digestive organs during the elimination of arsenic. The patient should stay in bed for at least three hours after the injection, and in order to prevent any after-pains or reactive painful infiltration hydropathic measures such as moist compresses, hip-baths, or the application of a hot-water bottle may be employed.

If the pain is very severe I give the following powder, which I find efficacious: Pyramidon, 10 gr.; medinal, 3 gr.; heroin hydrochlor., 1/12 gr. In between the injections he is kept on mist. malaria (contains 2½ gr. quin.).

In all cases an examination of the blood is made before each injection with regard to the presence of the malarial parasite, and a differential blood count to ascertain especially any increase of the large mononuclears. This is a very important feature, as in cases where the parasite cannot be demonstrated in the blood the mononuclear reaction, along with the presence of pigment in the mononuclear cells (due to phagocytosis of pigment formed by the parasites), has been taken as evidence that the case is one of malaria. The mononuclear reaction is especially interesting from the fact that in other protozoal diseases an activity of the same elements has been observed.

Notes on Cases.

The following cases were all treated by intramuscular injections.

CASE 1.—Capt. E., R.A.M.C.(T.), the first patient of the series, was suffering from malignant malaria, contracted in Palestine, which produced pyrexial relapses every fortnight in spite of 14 intramuscular injections of quinine, and 45 gr. or more by the mouth daily for a month, followed by 30 gr. for three months. The cachexia, anaemia, and myocarditis served to emphasise the inadequacy of quinine. The effect of neokharsivan injections was to extend the fortnightly periodicity of relapses to an interval of two months in the first series, and to six months for the second series of injections.

Treatment started on May 19th, 1919. Patient left hospital on Sept. 19th, 1919; reported no lapse in December, 1919, and up to date (July, 1920) reports no recurrence. This patient had four intramuscular injections and one intravenous. He was hypersensitive to arsenic and developed a rash and acute asthmatic symptoms.

CASE 2.—Lieut. B., age 36. Type, M.T. Previous attacks 21. Five injections from July 24th to August 26th, 1919. Left hospital well. Reported Oct. 29th, 1919. No relapse.

CASE 3.—Lieut. P. Type B.T. Four injections. No malaria parasites present upon discharge. An acute attack of exfoliative dermatitis after last injection.

CASE 4.—Lieut. E. Type B.T. Sept. 18th, 1919, four injections. Left hospital Dec. 19th quite well.

CASE 5.—Capt. S. Type B.T. Four injections Sept. 18th, 1919. Left hospital Dec. 19th, 1919, quite well. Reported Feb. 7th, 1920. No relapse.

CASE 6.—Lieut. L. Type B.T. Five injections. Discharged quite well Oct. 5th, 1919.

CASE 7.—Lieut. A. Type M.T. Ten previous attacks occurring every two weeks. Four injections. Discharged quite well, December 1919. First injection Oct. 14th, 1919. Reported hospital Feb. 20th 1920. Very well. No relapse.

CASE 8.—Capt. M., R.A.M.C. Type M.T. Four injections. Discharged quite well Oct. 8th, 1919.

CASE 9.—Lieut. B. Oct. 31st. Type M.T., contracted in Macedonia. Fifty-four attacks. Spleen enlarged, tender. Four injections. Left quite free Dec. 20th, 1919.

CASE 10.—Lieut. B. Type B.T. First injection, Nov. 11th, 1919; fourth injection, Dec. 3rd, 1919. Left hospital free. Reported hospital March 25th, 1920. No attacks for over four months.

CASE 11.—Lieut. D., R.A.F. Type B.T. Four injections. Left hospital Feb. 25th, 1920, quite well. Seen in June, 1920. No recurrence.

CASE 12.—Lieut. W., R.A.F. Type B.T. First attack in Persia, 1916; since 14. Completed course, four injections. Discharged quite well Jan. 19th, 1920.

CASE 13.—Lieut. J., 31st Punjab. Type B.T. First attack India, 1916; since ten. Four injections December, 1919. Patho. logical laboratory report: No parasites present.

CASE 14.—Lieut. F., R.F.A. Type B.T. First attack Batoum, 1919; since 3. November, 1919, four injections. Discharged free Jan. 26th, 1920.

CASE 15.—Capt. P., 2nd Glosters. Type M.T. First attack, 1917; since 12. Four injections. Discharged free Feb. 18th, 1920.

CASE 16.—Lieut. B., R.F.A. Type B.T. First attack Baku, 1919. Four injections. Discharged free.

CASE 17.—Lieut. F., R.A.F. Type B.T. First attack India, 1919; since 4. December, 1919, four injections. Reported hospital Feb. 7th, 1920. Quite free.

CASE 18.—Lieut. W., aged 24. Type M.T. Dec. 17th, 1919. M.T. parasites present. No history of malaria. Symptoms very pronounced—malaria, cachexia, anaemia, jaundice, vomiting. Urine bile-stained. Faeces normal in colour. Constipated. Dec. 17th temp. 104° F. First injection 0.3 g. N.K. Dec. 18th temp. normal. Patient feels better; jaundice commenced to disappear; and patient made uninterrupted progress. Discharged Jan. 28th, 1920, free and well. March 30th, 1920, reported at hospital; no recurrence. Feels quite well; weighs 13 stone.

CASE 19.—Major D., aged 35. First attack September, 1919. Type M.T. This was the most difficult case of all to deal with. Had nine intramuscular injections, one intravenous. Left hospital on May, 1920. Pathological laboratory report: No M.T. present.

CASE 20.—Capt. P. Type B.T. Jan. 3rd, 1920, first injection completed. Course of four. Feb. 21st, 1920, reports no recurrence.

Conclusion.

It will be noticed that in the 20 cases here reported 12 were Type B.T. and 8 Type M.T., none of which have reported a recurrence. To the above-mentioned I can add another 18 cases, of which I have

¹ Muir and Ritchie: Manual of Bacteriology, edition 1919, p. 506.