

Making allowances for the individual differences in the receptacles it is evident that no appreciable difference in time of survival can be observed corresponding to differences in acidity of the soil, although in so far as the figures are sufficient to indicate any difference, the difference is in favour of the more acid soils. A very striking difference in the soil nematode population of the different soils was observed, these becoming progressively more numerous in soil No. 1 until, on the last date of examination, an enormous number, certainly many thousands, were extracted. No progressive increase in soil nematodes was observed in the other samples.

It would appear, therefore, that the acidity likely to be present in ordinary agricultural soils, at least up to a hydrogen-ion concentration of 5.5, does not interfere with the survival of hookworm larvæ.

#### REFERENCE.

Hirst, L. F., 1924. Investigations on the Epidemiology of Hookworm Disease in Colombo. Part II, Observations on the Viability of Hookworm Larvæ. *Ceylon J. Sci.*, D, 1, Part I, 15-31.

### A NOTE ON THE TOXIC SYMPTOMS OF ORGANIC ARSENIC.

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THE treatment of syphilis has of late years tended more and more to resolve itself into a course of intravenous injections of one or other of the numerous preparations of organic arsenic, combined with mercurial medication or not as the case may be. So general has the treatment become and so dramatic the early results that the public has come to regard the giving of an intravenous injection as being far simpler and more convenient than taking a dose of medicine, and the practitioner, having acquired a certain manipulative dexterity, approaches it in much the same spirit. The following three cases, occurring in a series of 3,098 injections of organic arsenic extending over three years, shew that the procedure is not unattended with a definite risk of alarming sequelæ. It is a risk, moreover, of which we have no warning, for in the present state of our knowledge there is no method of estimating the tolerance of any particular individual to the drug.

*Case 1.*—A Hindu female, aged 24, was admitted into the Voluntary Venereal Hospital on 22nd March, 1925, suffering from a very generalised secondary syphilide. The eruption was of a maculo-papular character and

extended all over the trunk and limbs, involving both flexor and extensor surfaces and the palmar aspects of both hands. Her general health was good and her nutrition fair. There was no lesion on the genitalia and the urine contained no albumen.

The blood was examined on admission by both the Wassermann and Sachs-Georgi tests and in both a strongly positive result was obtained.

Hospital records showed that she had been admitted two years previously in an advanced state of pregnancy, suffering from hard chancre and gonorrhœa. The Wassermann reaction was at that time also strongly positive. She however then refused to have any injections and was therefore treated with mercury, etc. She was delivered of a male child in hospital which survived with the loss of one eye from ophthalmia.

She had the first injection consisting of 0.3 gm. novarsenobillon on 31st March, 1925; this was followed in half an hour by a rise of temperature to 100°F. and by a rigor accompanied by headache and nausea. These symptoms however passed off within 24 hours.

The second injection was given on 7th April, 1925. The same dose was given and was followed as before by a rise of temperature to 101°F. and a rigor; all symptoms passing off within 48 hours as on the previous occasion.

The following morning, i.e., the third day after injection, she again complained of headache, nausea and anorexia. The tongue was moist but furred; pupils slightly dilated; the urine was scanty but contained no albumen, and there was no rise of temperature. Adrenalin was administered at once. By the evening however she had become semi-conscious, though responding to stimulus and exhibiting irritability. The pulse was full and compressible, the tongue coated, the pupils dilated and the neck slightly rigid. Four ounces of urine were drawn off by catheter.

By the following morning coma had deepened, the pulse was full and irregular, the extremities and neck were rigid, and the jaws clenched. Well-marked epileptiform convulsions occurred during the day, but there was still a response to painful stimuli. Coma however continued to increase in spite of repeated injections of adrenalin, and muscular rigidity became still more marked. At this stage venesection was performed without any relief, and the patient died during the night, about 100 hours after the second injection.

*Case 2.*—A Hindu female, aged 22, was admitted into hospital on 9th December, 1922, with a mixed infection, having a hard chancre of two weeks' duration with a profuse gonorrhœal discharge. There were no cutaneous lesions and the Wassermann reaction was strongly positive.

The first injection, consisting of 0.45 gm. novarsenobillon, was given on 25th December, 1922, and was followed by headache and vomiting, but there was no rise of temperature or rigor.

On 5th January, 1923, i.e., 11 days after injection, she was seized with epileptiform fits following one another without any return to consciousness and remained in the "status epilepticus" throughout the day, making no response to stimuli. There was rigidity of the neck muscles and difficulty in swallowing; the pupils were normal. The "status epilepticus" persisted for nearly 24 hours with muscular twitchings, and there was no response to painful stimuli. The urine was drawn off but contained no albumen. Repeated doses of adrenalin were administered and by the evening of 7th January, 1923, she showed signs of returning consciousness. Convulsions had ceased but the dejecta were still passed in the bed. The next morning she could talk and sensation had returned. Improvement slowly continued throughout the next three days but prostration was marked. One week after the injection she had sufficiently recovered for her relatives to remove her from hospital and all trace of her has since been lost.

*Case 3.*—A Hindu female, aged 24, was admitted into hospital suffering from primary syphilis on 4th October, 1920. She at first underwent a short course of

mercurial treatment but later expressed her willingness to have a course of injections and accordingly started on 21st October, 1920, with 0.45 gm. novarsenobillon, followed on 1st November, 1920 by 0.6 gm. and on 18th November, 1920 by 0.9 gm., making a total of 1.95 gm. Her local lesions had by this time completely disappeared and her general health much improved. On 8th December, 1920, i.e., 20 days after the last injection, she developed jaundice which rapidly increased, accompanied by fever. Her condition became steadily worse till 18th December, 1920, when she commenced to have epileptiform convulsions which passed on to the "status epilepticus" and died on 20th December, 1920.

The treatment employed in this case, as in the other cases, consisted mainly in the injection of adrenalin.

The similarity of symptoms in Cases 1 and 2 is sufficiently marked to suggest a common cause coming into action at varying periods in the two cases, while the variation of jaundice in the third case differentiates it from the other two.

The train of symptoms exhibited by Cases 1 and 2 are spoken of by McDonagh as pseudotoxic, appearing on the third day after injection and are otherwise described as "reactionary inflammation" or the "Jarish-Herxheimer reaction." In every such case, the patient has, or has had, generalised syphilis and such symptoms never occur in the primary stage. The cases fall into two main classes, intracranial and visceral; the cases quoted being of the former variety. The lesion appears to be a hæmorrhagic encephalitis and is assumed to be due to the battle going on between the colloidal protein particles and the active phases of the organism. The remedy intensifies the engagement in which the host assists by a dilatation of the capillaries of the area involved, in order that more protein particles may be brought into the field. The dilatation results in a raising of the intracranial pressure with the sequence that certain nerves are pressed upon and the patient becomes comatose and dies.

As in Case 1 a post-mortem was not allowed we are unable to confirm the presence of hæmorrhagic encephalitis, but in other respects it conforms to McDonagh's description.

In the second case symptoms came on on the 11th day after injection, a delay that is not easy to reconcile with the theory put forward by McDonagh.

Case 3, which came under the observation of one of us (S. C. D.), appears to have been one of true arsenical hepatitis, passing into acute yellow atrophy with the fatal result that always attends this condition. In this case the probabilities are that the disease had not become generalised, and therefore the jaundice was not of syphilitic origin but was primarily toxic. Unfortunately there is no record in the notes as to whether leucin and

tyrosin were present in the urine neither was a post-mortem obtainable. The case, however, so nearly corresponds with the clinical picture of acute yellow atrophy that we think we are justified in attributing the death to that cause.

The undoubted benefits of adrenalin in the treatment of these so-called nitritoid crises has been dealt with by Ehrlich who expressed the belief that untoward symptoms are due to a deficiency in the secretion of adrenalin. Brown and Pearce have shown that arsenic has a selective action on the adrenals and Hirano has shown that there is a marked deficiency in the epinephric content of the blood and the gland itself after an injection of organic arsenic even in therapeutic doses.

Millian considers that the symptoms are due to a serous exudate following a vasodilatation in the cerebral vessels, causing cerebral manifestations varying in severity from headache to convulsions. He also concludes that there must be some intimate connection between arsenobenzol and the suprarenals. Experiments have shown that after the administration there is a sudden consumption of adrenalin in the circulating blood, and the glands may be unable to make up the supply. The following facts support this theory of the cause of these nitritoid crises:—

1. The symptoms may be averted by the use of adrenalin.
2. The blood serum of animals injected with novarsenobenzol contains a smaller quantity of vasi-contractile substance than does normal serum.
3. The adrenalin content of the suprarenals diminishes after the administration of arsenobenzol.

Of the various theories put forward to account for the occurrence of these nitritoid crises, it seems that the adrenalin theory has a certain clinical support in the benefit derived from the administration of adrenalin. One of us (A. D. W.) recently saw a case of syphilitic myocarditis occurring in an untreated case six months after infection. A minimum dose of sulfarsenol was given subcutaneously and was followed in 24 hours by a typical nitritoid crisis manifested by very severe convulsions, coma and peristaltic inhibition. Adrenalin 1 in 1000 in 10 minim doses was given subcutaneously every 4 hours with almost immediate relief and ultimate recovery in a case that appeared almost hopeless.

Our reason for the publication of these cases is, firstly, to remind our fellow practitioners that there is this ever-present risk in the use of organic arsenic, and, secondly, to draw attention to the remedy available in the use of adrenalin.