frequent some years ago from a well known bridge in Edinburgh which had a low parapet and might almost be said to invite suicide. The parapet was raised and crowned with sharp spikes, with the result that no suicide has occurred there since.

We have seen that carbon monoxide is a cumulative poison, and that fatal results will occur with even small amounts in the atmosphere provided the exposure continues for some time. Would a reduction in the amount of carbon monoxide in lighting gas, and thus a prolongation of the time necessary to produce a fatal result, be of any use? In a number of cases it would result in the person being found before it was too late. This is shown by the fact that of eighty-two admissions to the Royal Infirmary, Edinburgh, of lighting-gas poisoning in the last six years only six have died. On the other hand, a suicide frequently tries to make certain of a speedy result by covering his head with blankets, or putting his head inside the gas oven, etc., and so artificially raises the concentration in the atmosphere he breathes. In such circumstances, it must be admitted, reduction in the carbon monoxide content would not have much effect.

The question of limiting the amount of gas supplied by means of a penny-in-the-slot meter is likewise of little advantage, as I have seen fatal results in cases where such meters were in use. Approximately 25 cubic feet of gas are obtained for a penny, which, if it contained 20 per cent. carbon monoxide, would give 5 cubic feet of carbon monoxide—a quickly fatal concentration in an ordinary sized bedroom.

It seems a pity that the question of suicide should have been eliminated from the Government inquiries, especially in view of the statements of Yandell Henderson and Dr. Stevenson, and of the rapid increase in suicidal cases.

In considering the question of the limitation of suicide we must not confine ourselves to a discussion of the composition of gas, but must consider any other methods which are applicable. There is no doubt that a large number of cases of suicidal gas poisoning are due to the publicity given to this matter by newspapers. As I mentioned before, suicides are easily influenced by example and suggestion. A suicide occurs by some unusual means which is reported in the press, and is quickly followed by another in which the same means are employed. An example of this occurred recently in Edinburgh, where two men cut their throats, and then jumped from a viaduct into a river below, within a few days of each other.

Not infrequently the relatives state that the deceased had remarked on similar suicides which he had read about in newspapers. There can be no question that the publication of details and reports of inquests in cases of suicide does a great deal of harm. A few months ago these cases were broadcasted in the evening news bulletins, but fortunately the B.B.C. eliminated such items when their attention was directed to the grave results of such publicity.

Legislation has recently been proposed to suppress the publication of certain classes of divorce court proceedings. It is surely of greater importance to suppress reports of suicides, which constantly remind unfortunate individuals of the ease and certainty of death as a way out of their troubles. Whether the suppression of publication of suicides would have any beneficial effect on the number of cases of coal-gas poisoning cannot, of course, be definitely asserted, but that absence of such details would be an advantage to the community cannot well be doubted.

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BILHARZIA OVA AND THE TEST TUBE.

BY

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THE statement that antimony tartrate kills the ova deposited in the tissues during treatment for bilharzia disease has been assailed by Dr. Mohamed Khalil,* who states that the action of tartar emetic in curing bilharziasis is not due to its effects on the eggs, and that miracidia are not affected by tartar emetic in the dilution approximating to that used during treatment. Lately, Captain W. H. Dye¹ has said more specifically: "I cannot agree that the ova are killed by tartar emetic." In view of the fact that there is general agreement that antimony, both *in vitro* and *in vivo*, kills the parasite² which produces the ova—a fact contested for some time—the question of the effect of antimony on the ova might appear of no great importance; it is, however, important, for if the ova are not killed, they will leave the bladder or rectum and continue to infect the intermediate hosts, and the drug is not so great a prophylactic agent as is claimed; further, if antimony has no therapeutic effect on the ova we lose a reliable method of observing the results of the action of antimony during a course of treatment.

Certain facts with regard to the ova during the administration of antimony tartrate can be made out by anyone who has a microscope and a patient with bilharzia disease. They occur in rectal and in vesical infections; they are obviously more easily observed in the urine than in the faeces. A specimen of the urine of a moderately severe case of bilharzia disease is cloudy and contains blood—macroscopic or microscopic; if it be allowed to stand for half an hour in a conical glass the sediment at the bottom will be found to contain ova, most of which are more or less transparent, showing the miracidium usually with the anterior end at the extremity which is not spined. The outlines of primitive embryonic organs will be easily seen within the miracidia; these are live ova and comprise by far the greater portion.

There are a few which appear shrunken with double contour replaced by a single bounding membrane. The contents of such ova are granular, without shape or form, dead; some are calcified. If the urine containing the ova be diluted and the temperature of the solution raised to 110° or 120° F., most, but not all, of the living ova will hatch out within half an hour; none of the granular-looking ova will hatch. If fresh specimens of urine are examined day by day the same facts will be noticed with little change, the number of the ova varying, but always there will be dead and living, the living outnumbering the dead.

Now commence treating the same person with intravenous injections of antimony tartrate. After a few days the urine will clear perceptibly, the blood will diminish, and blood obvious before to the naked eye is now obvious only under the microscope. It will be noticed that the number of ova in the urine has sensibly diminished. A decisive action has taken place, which has affected the number of ova and has diminished the blood in the urine.

These facts can only be logically explained by assuming either that the antimony is acting on the ova, or that its action on the female worms causes them to lay fewer eggs.* Continuing the injections every other day, the improvement is maintained, the local symptoms are relieved, and there is less pain, less frequency, and less difficulty in micturition.

Still continuing the injections, the initial dose of half a grain is increased by half a grain each succeeding dose according to rule, to the maximum dose of 2 or 2½ grains, which is then continued. On the eighth or ninth day of regular treatment a definite and increasing change in the character of the ova can be observed. Many containing well formed miracidia hatch slowly or not at all on the addition of water, while increasing numbers of ova show granular and degenerated miracidia. In fact, from the

* Recently Fairley has revived the theory that the action is a specific one on the female worm (he admits a definite action on the ova). It is difficult to understand why the antimony should affect female rather than male parasites as Fairley suggests, or why, acting on the female, the latter should continue to lay dead or added eggs. One can understand the female being affected by the antimony and laying no eggs at all. This Christopherson has suggested as a reason why ova are scanty during treatment.

ninth day onwards ova appear in the urine, which, owing to the action of the antimony tartrate, have become granular and black. By the end of a fortnight's treatment about half the ova discharged are obviously dead; many are quite opaque.

On about the twentieth day of treatment all the ova coming away will be dead; none will now hatch out on diluting and warming the urine, and if the adult worms are killed, as is probable, live ova will not reappear in the urine. The injections commenced early to affect the ova. The first action of the antimony *in vivo* is observed by testing the physiological function of hatching; as more injections are given the ova are increasingly affected and fewer living ova are found; lastly, the parent worms are killed and living ova no longer appear in any circumstances but reinfection. I think it is impossible to maintain that this sterilization change in the ova is not the direct result of the antimony injections. Other drugs also kill the ova, but no drug deals with bilharziasis so completely as antimony tartrate, because none have so great parasitotropic action and so little organotropic in comparison.*

These are changes which must be observed *in vivo* with the parasites in their natural media; they cannot be adequately studied in the test tube, nor can test-tube observations, however accurate and in many respects valuable, take the place of clinical experience. In support of this, if support be needed, we might contrast Dale and Dobell's⁴ experience with *Entamoeba histolytica* and emetine *in vitro* with the clinical results obtained with the same drug.

H. B. Day⁵ investigated a series of 1,000 cases at the Kasr el Aini Hospital, Cairo, and published carefully drawn charts to show the effect of antimony on the ova. He found that the ova of bilharzia *in vivo* are very susceptible to antimony; a short course of four injections will kill them, the effect being seen after about nine days, and it is the same when the doses are continued; it is evident that it is the small dose acting over a prolonged period which kills when antimony is given in clinical practice. When only small doses are given for two or three days dead ova appear after the ninth day, and the effect reaches its maximum on the fifteenth day, after which living ova become more and more numerous. Thus a very little antimony given kills the ova, but the worms revive and recommence laying. We have actual proof that antimony in a short course does not kill the worms till later, since Day found living worms at a *post-mortem* examination of a patient who died of an intercurrent disease after a short course.

It has been said by way of objection that granular ova occur in bilharzia cases not undergoing treatment. This is true, but the sudden diminution in the number of living ova coming through after a few days of antimony administration, and the cessation of pain and blood, and the clearing of the urine can only be explained satisfactorily by supposing that antimony has already attacked the ova and paralysed them, or that the worm is under the influence of the drug and therefore is not laying. The ova no longer penetrating the mucous membranes of the bladder in such numbers there is less cause for haemorrhage, and the urine becomes more acid and natural in appearance.

Further, if the dead ova in a case undergoing treatment are counted and the number compared with the number of live ova, it will be found to be out of proportion to the number of dead ova coming through in a case not receiving treatment. This points to the fact that it is the ova which are killed by the antimony. These shrivelled ova whose double contour is replaced by a single outline, the miracidia within replaced by a shapeless granular mass, always opaque, generally appearing black by transmitted light, are not capable of hatching in any circumstances. The foregoing facts may be verified by anyone with a patient and a microscope.

* One could understand a parasite laying one dead egg or two, which would correspond to abortion in a human being, but is it a biological fact that tartar emetic makes the parasite continue to lay dead ova? In other words, is not the action of the tartar emetic a direct one on the ova as they lie in the tissues?

Both Day and I, however, obtained in addition results with watery solutions of tartar emetic which showed that there was a distinct, though retarded, action by the antimony on the ova *in vitro*. In order to imitate natural conditions more closely the former also experimented with saline solutions. Day pointed out that work *in vitro* has its limitations. A time limit is imposed, since the ova are not in natural surroundings; they are, in fact, in contact with infected liquids, the ova being recovered from urine which is more or less contaminated with bacteria, whilst when living in the tissues they are bathed in serum—a benign medium from which the ovum derives its nutrition. By using serum for the medium the results of experiments on the ova *in vitro* might possibly have been still more striking.*

I submit, therefore, that *in vitro* experiments also prove the direct toxic effect of antimony on the ova. They further suggest that the phenomenon of hatching of the bilharzia ova is a vital process, not governed exclusively by physical laws, for whereas antimony appears to have a profound effect on the live ovum, it apparently has no effect on the dead ovum.

The action of antimony on the living ova is real, an early manifestation, and only second in importance to the action of the antimony on the adult worms, which it kills later. The action on the ova and on the adult parasite makes antimony the most valuable therapeutic agent we have in bilharziasis, and probably one of the most complete remedies in our therapeutic armoury.¹⁰

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THE OSCILLOMETRIC EXAMINATION OF ARTERIAL PERMEABILITY.

BY

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It is often necessary in clinical work to determine the state of permeability of the arteries of the upper or lower limbs. In obliterating arteritis the need for determining the presence of an obliteration, its degree, its localization, and also the condition of the collateral circulation, is frequently felt. In arterial or arterio-venous aneurysms it is necessary to know if the limb is receiving a normal blood supply. In diabetes, in arterio-sclerosis, and in other morbid conditions the degree of permeability of the arteries of the limbs—especially of the lower limbs—is important from the points of view of diagnosis and prognosis. There are not many clinical methods which assist in answering these clinical problems. Digital examination of the radial or the femoral artery or the dorsalis pedis does not give very definite results. The Moschcowitz and Matas tests, which utilize the degree of the hyperaemic blush following artificial ischaemia caused by the application of an elastic bandage, also fail to give very definite results, and are not without danger in their application.

In 1912 I introduced the oscillometric method for the study of arterial permeability.¹ It is based on the use of Pachon's oscillogram, and has been developed in France by a great number of workers—principally by Heitz,²

* Tartar emetic was shown recently by Fairley⁷ to be relatively innocuous to bilharzia cercaria in aqueous solutions, but it developed marked lethal properties in the presence of human serums derived from both normal and bilharzia patients.