it is an incipient form of the same sort of thing. These are obsessions—the patients are obsessed by a tendency to think or to act in a certain way.

Then there are phobias, or fears—pathologically intensified fears. A very common phobia is the fear of heights. A phobia seems sometimes to be an exaggerated fear of the ordinary type, but in other cases one may find people fearing things that no ordinary person would dream of fearing.

Before turning to explanations, one ought to describe in a little more detail the state of mind of these patients. Besides the actual obsession or phobia, one has to attack in these patients a constant feeling of anxiety. Constitutional anxiety seems to be intensified in them, to be continuous throughout their lives, and to become more acute under certain conditions. To anticipate what I shall say later, one usually finds that, if one succeeds for a time in curing a patient of his obsession or phobia, he will return to this mental tendency. One of my patients felt a constant anxiety lest he should return to an obsession of some kind or other—a feeling which could not be allayed. Freud has a very interesting theory as regards compulsion neurosis. He says that the patient is really obsessed about the wrong thing. What has happened is that in the past, at some time or other, something has gone wrong with the development of his psycho-sexual life. He has done something that he is ashamed of, and which was charged with an intense emotion of a painful nature which he has tried to repress and to drive out of his mind. He has only succeeded in dissociating the emotion from the memory. The memory thus becomes harmless and walks quietly into the unconscious, but the emotion has still to be dealt with, and finds its way along association channels to other less suspicious ideas and memories. The patient, who should be worried about some guilty thought or act of the past, is now worried about something which is obviously innocent and harmless. Thus the obsession is really disguised vice. In certain cases this does work out according to theory. You do sometimes find that you gradually bring up past experiences which are out of harmony with the patient's general character, and which have been repressed. When these memories are recalled, they and the obsessing emotion link up together again, and everything is all right once more—the patient is no longer obsessed. In the case I referred to just now, my patient, who was a bank clerk, had an obsession of infection. He used also to tear up circulars, and then worry as to whether he ought to have read them before tearing them up, etc., etc. He was a homo-sexual, and I discovered that, at the age of 15, he thought that he had led a younger boy astray. He described this incident to me with great emotion, with the result that the obsession disappeared, permanently as far as I know, but there remained a general feeling of anxiety. My further treatment naturally was to carry my analysis still more deeply into his past. This analysis definitely helped me to trace back his tendency to homo-sexuality, and to bring out many other emotional experiences of his past life, and, as far as I can make out, he recovered. Some Freudians hold that all such cases are homo-sexual, but this does not seem to be correct, though it is true that a great many of them are.

In other cases the results were not of a similar nature. A case occurs to my mind of a well-educated patient, also homo-sexual, who had obsessions about the technique of his own particular work. I traced this back to a feeling of intense respect for his teacher and worry as to whether his views were out of harmony with those of his teacher. We traced this back for many years to a moment in his past, at the age of 8, when his sister, who was two years older than himself, had told him that God would punish him for every single little act of wrong-doing he committed. She told him that God was everywhere, and that He could see all the wrong things that he did. He remembered very vividly that he had gone up to his bedroom and had wept bitterly. His imagination, which was very vivid, had helped him to realize what such a situation would mean, and, as far as I could make out, that was the most important of his memories. I took him back earlier still to memories of intense affection for his mother. He had also appreciated her great affection for him, and he was always on the look-out for a love which should be as intense and as spiritual as his mother's love for him had been. This particular case has recovered from his obsessions completely,

but the mechanism seems not to be quite the same as the Freudian one. There was no question of his ever having reproached himself for any specific sexual or psycho-sexual actions. The conflict was of another nature. Other mechanisms seem often to be at work. It seems to me that one cannot well lay down a single definite generalization about such cases, but one is certainly tempted to believe that a very important factor in compulsion neurosis is great exaggeration of the innate tendency towards anxiety which these patients possess. That is why analysis sometimes does not help the patient much—may even make him worse—and why suggestion treatment often does make the patient better. In the past people have often claimed to have hypnotized such cases and to have made them better by this method. Janet, however, says in his latest book that he does not understand these reports, and my experience bears him out. I do not think that these cases are hypnotizable, though one may temporarily increase their suggestibility by making them passive, and thus help them to fight down their fixed idea and also to get rid of this general tendency towards anxiety. One may keep them in this attitude whilst they regain their physical and mental health.

Nevertheless, in many cases a course of autognostic treatment, with little or no suggestion, is sufficient to produce a cure.

REFERENCE.

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Observations

ON

SUBACUTE INFECTIVE ENDOCARDITIS.

BY

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(A Report to the Medical Research Council.)

THERE are in the United Kingdom about 80,000 men receiving pensions for some cardio-vascular affection. In the London Area there are, roughly, 8,000 pensioners with some cardiac disability, and 1,200 to 1,500 of these have structural disease of the heart. All of them come before the Resurvey Boards for re-examination and assessment at intervals of nine to twelve months. They are called up on special days, and all those with signs of structural disease are seen by a heart specialist. During the past year and a half I have acted as heart specialist at two Resurvey Boards. Such cases as required treatment or further examination I have referred to the Cardiographic Department at University College Hospital. At this clinic they receive out-patient treatment or are admitted to the wards of the hospital. Here I have been able to observe during the past year and a half a large number of selected cases presenting signs of structural disease of the heart.

The most striking clinical feature of this clinic has been the large number of subacute infective endocarditis cases that have been under observation.

From September, 1919, to June 1st, 1920, there were admitted as out-patients 159 pensioners presenting signs of aortic regurgitation, 136 with signs of mitral stenosis, and 65 with mitral stenosis and aortic regurgitation. In 30 of these the diagnosis of subacute infective endocarditis was made, and 11 were suspected as having this disease—that is, 8 per cent., and possibly more, of 360 patients with gross valvular disease had subacute infective endocarditis.

The observations which follow are based on a clinical study of 15 of these cases, together with a larger group of 40 patients with subacute infective endocarditis, whom I had under my care while in charge of the clinical services at the Sobraon Military Hospital, Colchester. Both at Colchester and at University College Hospital the conditions have been most favourable for making a careful study of the symptoms and signs which these patients presented; and through the Medical Research Council I have been able to obtain full after-histories of nearly all who were discharged from hospital. I hope to show from a study of these cases that subacute infective endocarditis is not an uncommon disease; that infection plays a most important, if not the most important, part in a certain number of patients with chronic valvular disease; that the signs of

an active infection are easy to recognize; and that these signs enable one to prognose with indubitable accuracy the clinical course of structural heart disease.

At a meeting of the Association of Physicians in 1908 Sir William Osler reported 10 cases of chronic infective endocarditis. He emphasized the chronicity of the disease, the clinical course ranging from four to twelve months. He noted that the fever was remittent in type, not usually high, and that during the terminal stage of the disease there was often an afebrile period. He observed that there was slight change in the character of the heart murmurs, and he indicated the special significance of tender spots on the skin, lasting from a few hours to several days, usually on the tips of the fingers and balls of the toes; these are now known as Osler's nodes. At the next annual meeting of this Association Sir Thomas Horder presented an analysis of 150 cases of infective endocarditis, and dealt especially with the chronic form of the disease; 88 of these cases he recognized as subacute infective endocarditis, the commonest form of the disease, and 18 cases of chronic infective endocarditis, a form occurring less frequently in his experience. He looked upon the remaining cases as acute infective endocarditis. In the diagnosis of the disease he laid stress upon the following signs: chronic valvular disease, the occurrence of embolism, and the presence of micro-organisms in the blood stream. This valuable contribution drew the attention of the profession in this country to the importance of recognizing the subacute and chronic forms of this disease.

Libman in America in 1912 reported cases, and stated that there were two stages of the disease—an early stage, when the *Streptococcus viridans* could be nearly always isolated from the blood if the temperature was not high; and a later stage, when the bacteria disappeared from the blood stream, and also from the valvular lesions. The explanation which he offered for this bacteria-free stage, together with the tendency for the valvular lesion to heal, was that the pathological condition at the seat of the infecting agent—that is, the valve—becomes stationary, although the clinical course of the disease is a progressive one. He attached great importance to certain signs in recognizing the bacteria-free stage of the disease. These are: a progressive anaemia, brown pigmentation of the skin, red blood cells in the urine, and enlargement of the spleen.

For reasons which I shall give later I have not found it possible to distinguish between subacute and chronic infective endocarditis, and I have therefore considered the 55 cases on which this study is based as cases of subacute infective endocarditis. Nor have I been able to divide this disease into the bacteria and bacteria-free stage, as the bacteriological examination will show.

All of the patients on whom these observations are based were soldiers who had served in the war or pensioners invalided from the army with structural heart disease. Their average age was 30 years—the eldest 51 and the youngest 19. The average duration of symptoms in 40 was fourteen months; one had been unfit for four years, and one had had a long period of military service without a single complaint until two months before death; 22 gave a history of gradually increasing unfitness, and no cause could be found to explain the onset of their symptoms; in 23, or 46 per cent., the symptoms followed after an infection; this number includes 2 cases of gas poisoning. The infections associated with the onset of symptoms in 3 were rheumatic fever, in 4 influenza, in one trench fever, and P.U.O. (pyrexia of uncertain origin) in one, dysentery in 3, pneumonia, rheumatism, cerebro-spinal fever, I.C.T. (inflammation of connective tissue), and tonsillitis in one each; in one only did the symptoms arise after a severe effort. The onset was sudden in 4, but in these no history could be obtained of a preceding infection. In 16, or 29 per cent., there was a history of rheumatic fever; in 7 the Wassermann reaction was positive; in 28 it was negative; one only gave a history of syphilis. The low incidence of syphilis might be anticipated, for syphilitic disease of the heart is uncommon below the age of 30. One would have expected a higher incidence of rheumatic fever in valvular disease of the heart in men of this age. I found in 50 cases of aortic regurgitation¹ and 50 with mitral stenosis² a history of rheumatic fever in 27 per cent. and 44 per cent. respectively, or an average incidence in the two groups of 35.5 per cent.

The number of cases with symptoms dating from an infection is lower in this group with infective endocarditis than that recorded in fifty cases of mitral stenosis in soldiers. In the former group the onset of symptoms occurred after an infection in 46 per cent., in the latter in 52 per cent. I make this comparison for the reason that I do not wish it to be understood that the average period of fourteen months during which symptoms were present represents the course of the disease. There is no striking difference in the symptoms or the clinical course up to the time they come under observation between chronic valvular disease without signs of infection and subacute infective endocarditis. There are exceptions, I admit, when embolic symptoms develop early. I do not therefore feel justified in stating that the course of the disease dates from the

onset of symptoms, and for this reason I have not subdivided infective endocarditis into the subacute and chronic types.

Symptoms and Signs.

The symptoms complained of were breathlessness on exertion, palpitation after slight effort or when excited, pain in the region of the heart or left costal margin, sharp and stabbing or dull, and felt with slight effort, but rarely anginal in character or distribution. Many gave a history of giddiness after effort or with change of position; a few had fainting attacks. Exhaustion, lassitude, headaches, sweating, and loss of weight were common complaints. Tender finger-tips or painful swellings of the hands or feet were not often complained of. Chills were infrequent, although a sense of feeling hot and cold was noted in a large number. Symptoms of embolism were present in a third of the cases. The large majority had symptoms of heart failure while under observation. In a few the clinical picture was one of toxæmia, and the symptoms were more uraemic than cardiac.

I have treated briefly the symptomatology of these cases. The history of a large number is that of chronic valvular disease. During the early period of the disease the symptoms are those felt after effort; later, with the onset of heart failure, those of venous engorgement were added. Cerebral embolism is not an infrequent occurrence during the clinical course of mitral stenosis. Embolic symptoms are more often observed in infective endocarditis. Embolism may occur although an active infective process cannot be discovered, and infective endocarditis may be diagnosed in the absence of symptoms which we recognize as embolic in origin.

The symptoms may be a guide, but it is upon the signs that we must rely in diagnosing this disease. In all but nine of the fifty-five cases signs of venous engorgement were present at the time of the first physical examination. The degree of venous stasis varied from fullness of the veins of the neck with crepitations at the bases of the lungs and doubtful enlargement of the liver, to oedema of the extremities and general anasarca. It was the rule to see signs of heart failure gradually increase until death. In some the dropsy was more renal than cardiac in its distribution. In these the face was bloated, the breathing Cheyne-Stokes in character, and the cyanosis slight. Often the picture was that of cardiac failure with chronic parenchymatous nephritis added. In a few the venous engorgement was slight with marked signs of toxæmia, delirium, coma, muscular twitching not unlike chronic nephritis, with urea retention.

Of the nine cases without signs of cardiac failure two were patients who developed infective endocarditis while under observation, one died unexpectedly of acute heart failure, one a doubtful case, two died suddenly of cerebral haemorrhage, and three were discharged from hospital and died from some unknown cause. It is probable that the early cases will develop signs of cardiac failure as the disease progresses, and it is not at all unlikely that had the course of the disease in three not been interrupted by cerebral haemorrhage and acute heart failure they soon would have presented signs of venous engorgement. It was the rule, then, for these patients to have signs of heart failure at the first examination.

Enlargement of Heart.—In all but two the heart was enlarged at the first examination. One of these died three months after the onset of symptoms with increasing heart failure and signs of aortic regurgitation and mitral stenosis. The other had symptoms for six months at least and died after discharge from hospital from some unknown cause. In 12 the heart was much enlarged—that is, three fingerbreadths or more to the left of the nipple line. In 17 there was moderate enlargement—two fingerbreadths to the left of the nipple line; and with the remaining 17 the left border was definitely to the left of the nipple line, but not more than one fingerbreadth.

I have given the left border of the heart as the index of cardiac enlargement. Enlargement of the right ventricle is difficult to determine by palpation or percussion. In hearts with mitral stenosis or aortic regurgitation I have found, on weighing separately the ventricles, that general increase in weight is the rule, although hypertrophy may predominate in one or the other ventricle.³ It is safe, then, to consider the whole heart enlarged when the left

border is felt definitely one fingerbreadth or more to the left of the nipple line.

The most common type of valvular disease in these cases was aortic regurgitation. In thirty-three there were signs of aortic regurgitation only, in fourteen aortic regurgitation and mitral stenosis, in two there was aortic regurgitation and doubtful mitral stenosis, in two aortic stenosis, and in four signs of mitral stenosis alone were recorded. It is difficult to estimate the duration of this disease from the clinical signs of valvular disease alone. Mitral stenosis can develop rapidly, and aortic regurgitation may have existed for years. It does not take long for the infecting agent to damage an aortic valve sufficiently to cause regurgitation, and vegetations may in a short time obstruct the aortic or mitral orifices. It takes years for valvular stenosis to develop when the process is one of sclerosis; vegetations may obstruct a valvular orifice within a few months. Fibrous contraction leading to an aortic reflux is a slow process; weeks are sufficient to produce aortic insufficiency when the infecting agent leads to ulceration.

Hypertrophy develops slowly; dilatation may occur in a few hours. It is often difficult, sometimes impossible, to assess the degree of hypertrophy and dilatation, when the two are associated. It is probable that a heart two fingerbreadths or more to the left of the nipple line, and with little or no stasis, weighs 15 oz. or more. Such a heart may be dilated; it certainly is hypertrophied. Clinically there were in the majority of these patients signs of chronic heart disease. Enlargement of the heart in men under 40 years of age is usually associated with valvular disease. We have therefore strong clinical evidence that most of these patients had chronic valvular disease.

The exercise tolerance was poor in all; this is to be expected, since all but nine had venous engorgement. The average minimum and maximum pulse range at rest was 88 to 110. An exercise test was given in ten; this consisted of a brisk walk up and down twenty steps twice. The average pulse rate at rest in these was 135, immediately after the exercise 181, and 137 at the end of two minutes.

Fever was present in all but one. The average range of temperature was not high. A daily rise to 100° for several weeks or longer was the rule; less frequently to 101° or 102°. In a few the temperature was remittent, rising each day to 104°. In a large number afebrile periods of one to four weeks were recorded. One ran a subnormal course throughout the whole period of his stay in hospital. It was common to see a normal temperature for a long period interrupted by an occasional twenty-four hour rise to 100° or 101°. It was often observed that with increasing heart failure the patient became afebrile, or a subnormal temperature developed; rigors were recorded in a few; sweating was more profuse when the temperature range was high.

It was the rule for these patients to have a toxic appearance. The complexion was usually sallow; the face having often a muddy or café-au-lait colour; in some the pallor was sufficient to suggest a primary anaemia. Occasionally there was a ruddy complexion, giving a healthy look to the patient.

Blood counts were done in thirty-six cases. The average number of red blood cells in these was 4,407,000, the haemoglobin 70 per cent., and the leucocytes 1,080. The lowest blood count recorded was 2,000,000, with 20 per cent. haemoglobin and 16,000 leucocytes. The highest count was 5,790,000, with 87 per cent. haemoglobin. The highest white cell count was 22,000. The average number of polymorphonuclear leucocytes in twenty-four was 64, and of lymphocytes 33. With an average colour index of 0.83 the blood picture was that of a chlorotic type of anaemia of moderate degree.

The appearance of these patients often suggested a greater degree of anaemia than the actual blood examination revealed. The colour of the patient and the blood picture are important signs of an active infection of a subacute or chronic type.

The Spleen was enlarged and easily palpable in 48; in 5 no mention was made of its size; in 2 it could not be felt. In some it was hard and felt three or more fingerbreadths below the costal margin; in others it was soft and not so easily palpable. Hyperaesthesia in the left hypochondrium sometimes rendered difficult palpation of this organ. Enlargement of the spleen in chronic valvular disease with heart failure is often ascribed to

venous engorgement. In these patients it was palpable in some when signs of venous engorgement were absent, and in many with only a moderate degree of venous stasis. Without attempting to maintain or disprove this explanation, it is a fact that the spleen was known to be enlarged in 48 cases, and in my experience it is uncommon to find this organ increased in size in chronic valvular disease with venous engorgement when the diagnosis of subacute infective endocarditis has not been made. Infarction is another cause given for enlargement of the spleen in heart disease. It is true that infarcts were found at autopsy in many of these cases, but in not a few they were absent. Venous engorgement and infarction are not the only causes of enlargement of the spleen. It is common knowledge that the spleen enlarges during the course of many infectious diseases, as in typhoid and malaria. I prefer to consider splenic enlargement in this disease as often a sign of an active infective process.

Clubbed finger-tips was one of the most striking clinical features of the disease in these patients. In cardiac affections it has long been associated with congenital valvular disease, and it is often observed in chronic disease of the lungs, particularly in association with bronchiectasis. Many explanations have been given for this sign, but the cause is not known. It is usually ascribed to a toxæmia due to deficient aeration of the blood supplying the fingers. In 25 no mention was made of clubbed finger-tips. These were cases under observation at Colchester, at a time when our attention had not been drawn to the importance of this sign. All the remaining cases and 25 others not included in this series presented this sign. In some the degree of clubbing was slight; in others most marked, giving a striking appearance to the fingers. Whatever may be the cause the frequent occurrence of finger clubbing gives us a most important sign in the diagnosis of subacute infective endocarditis.

Petechiae were observed in 40; no mention was made in 6; in one it was doubtful whether any were present; and in 8 none were seen while in hospital. These small dark red spots were most commonly situated in the skin of the neck, upper part of the chest, and conjunctivae of the lower eyelids; they may, however, occur on the back, abdomen, or extremities. They are small haemorrhages with a yellowish pin-point centre, and are probably the result of an embolus obstructing a small arteriole. They often occurred in crops lasting a few days, and then gradually faded away. They are of a dull red colour at first and later become brown; they are not palpable, do not disappear on pressure, and are thus easily distinguished from small naevi.

Osler's nodes—small tender and painful spots of nodular erythema on the hands and feet, disappearing within a week—were observed in 7 cases. These, too, are embolic in origin; the pain and tenderness which is characteristic of them may be due to the small amount of subcutaneous tissue and highly developed tactile sensation of these parts.

Emboli obstructing larger vessels were noted in 7. The central artery of the retina in one caused temporary loss of vision; another was admitted to the wards with an embolus blocking the posterior tibial; in a third there was an obstruction in the lower third of the brachial; a mycotic aneurysm of the radial, with a large pulsating tumour of several months' duration, was observed in a fourth. The frequent occurrence of petechiae in these cases makes them a most important sign of an active progressive infection. When petechiae are observed in association with gross valvular disease, pallor, enlarged spleen, clubbing of the finger-tips, the diagnosis of infective endocarditis may be made with certainty.

The urine in 34 was albuminous—in many a trace; in others with much venous engorgement a larger quantity was found. It was the rule to find red blood cells and granular casts in the urine when albumin was present; in a few there was macroscopic blood. The urinary reports in 13 showed no abnormalities; in 8 no analysis of the urine was recorded.

Diagnosis and Pathological Findings.

A bacteriological examination of the blood was made in 24 cases. Micro-organisms were grown in 11, or less than half. Streptococci were found in 8; streptococci and staphylococci in one; staphylococci alone in one; and a

Gram-positive diplococcus in one. In every instance the diagnosis of infective endocarditis was made without the aid of the bacteriological report. It was based upon signs of gross valvular disease—*aortic regurgitation* or *mitral stenosis* associated with *pallor*, *enlargement of the spleen*, *petechiae*, and in many *clubbing of the finger-tips*. There may have been no fever at the time of the examination, *petechiae* may not have been found, and the bacteriological examination of the blood was often negative. The diagnosis was correct, as the *post-mortem* findings proved in 22 cases.

Of the 55 cases, 44 are known to have died with an average duration of symptoms of fourteen months; no information could be obtained from 8 after discharge from hospital; three of these had no signs of venous stasis and one was a doubtful case. The cause of death in 26 was gradually increasing heart failure, acute heart failure in 5, the sudden onset of auricular fibrillation and death in a few hours in one; 3 died following a hemiplegia, one from pulmonary embolism, and one from a streptococcus pneumonia.

The pathological changes revealed at autopsy were typical in every instance of subacute infective endocarditis. There were recent vegetations, and these were usually engrafted on an old valvular lesion with extension in many with mitral disease on to the posterior wall of the left auricle, and on to the septal wall of the left ventricle in those with aortic disease. Sometimes myocardial degeneration was easily recognized. The spleen was enlarged in all, with old or recent infarcts in many. In others they were absent, and the organ was congested and swollen as in typhoid fever. Nephritis was always noted when sections of the kidney were made; usually of the parenchymatous type, but in all the glomeruli were more or less replaced by fibrous tissue. Infarcts were found in the kidneys of many. The other pathological changes were those found after death from cardiac failure.

Conclusions.

Subacute infective endocarditis is not a rare disease. It is seen in 8 per cent. of patients with signs of gross valvular disease attending a special heart clinic.

The signs are easy to recognize. In the diagnosis chief reliance should be placed on the following signs: Gross valvular disease, pallor, enlarged spleen, and clubbing of the finger-tips.

Aortic regurgitation is the type of valvular disease usually seen in this disease; it is rare to find the mitral valve alone involved.

The course of the disease from the onset of symptoms is usually less than fourteen months; death may occur within two months of the onset of symptoms.

A bacteriological examination of the blood is useful in confirming the diagnosis. Without such an examination the diagnosis may be made with certainty.

The disease is always fatal.

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ON THE ACTION OF TARTRATE OF ANTIMONY IN INTRAVENOUS INJECTIONS:

THE "PERMEABILITY" OF *BILHARZIA OVA* AND
SOME PROTOZOAL ORGANISMS.

BY

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THERE is a fact to be borne in mind regarding intravenous injections of antimony tartrate—namely, that the drug appears in the blood stream as antimony tartrate and not as a complex derivative of antimony, produced by contact with gastric and other secretions and elaborated by digestive glands, as is possibly the case when tartar emetic is given by the mouth.

Whether antimony tartrate remains as such as it circulates in the blood or whether it combines with a constituent in the blood stream we do not know, but it would not be unreasonable to think that a stable and simple

compound such as antimony, potassium (or sodium) tartrate remains in solution in the blood until it is dealt with by the kidneys, liver, bowels, and skin for the purpose of storing or of eliminating it.

It does not seem to be necessary, therefore, on the face of it, in order to explain the action of antimony tartrate in bilharzia disease, to introduce the complicated picture of antibodies and indirect action on the parasite. For living bilharzia ova are certainly porous and permeable, pervious and foraminous, whether they be imbedded in the tissues or free in urine. The miracidium living inside the chitinous shell is aware of what is taking place in the atmosphere around the shell.

In the specimen glass, and we may assume, I think, in the bladder also, the concentrated urine would be as deadly to the miracidium without the protection of the shell as it is to other forms of animal life. The miracidium inside the shell, it is true, may, and often does, turn right round in its shell in the undiluted urine (the preliminary step to hatching),* but it does not often hatch. But if bilharzia urine be diluted ten or eleven times with water, and the temperature maintained at about 130° F. (which is not hotter than water exposed to the sun in Egypt), hatching takes place in four or five minutes.

The miracidium inside the shell, in other words, is in touch with the world outside the shell, and is ready to respond to favourable local conditions; this communication can only be explained by supposing the shell to be permeable and porous.

There are several other facts which prove the permeability of the bilharzia ovum. In hunting for helminths or ova in faeces at Khartoum Civil Hospital we are in the habit of using an ounce of 40 per cent. formalin to the specimen. This acts as a deodorant and facilitates the examination in various ways. Now we (Mr. Newlove and myself) found that this formalin sterilized the bilharzia ova when present, but that it left ankylostoma ova unharmed. This fact suggests that the ovum of bilharzia is permeable and allows the formalin to penetrate it and kill the miracidium inside; it also indicates that all ova are not permeable, and as an example of an impermeable shell we have the ankylostoma; there are biological reasons for permeability or otherwise, but we are only concerned in the fact at present.

There is, therefore, no *a priori* reason why the bilharzia shell should be impermeable—in fact, certain biological facts can only be explained on the supposition that it is permeable. By direct experiment *in vitro* we are able to show that bilharzia ova are permeable to antimony tartrate which kills the miracidium within the shell. Mr. Newlove and I found at Khartoum that, if $\frac{1}{10}$ c.cm. of urine laden with ova was diluted with 6 c.cm. of tap water at 130° F., ova hatched out in four or five minutes, and most of the ova in the specimen were hatched out within one hour. If one grain of antimony tartrate were added, before the hatching, only about half the ova would hatch, a good many were found dead, half in and half out of the shell, or, in other words, they appeared to have survived the hatching process only a short time as they were seen lying dead by the side of the evacuated shell, like corpse and coffin. The more resisting miracidia which survived and which were swimming about, did not swim nearly so long as miracidia hatched in plain water. The addition of about 2 grains of antimony tartrate to the 6 c.cm. just about stopped the hatching process altogether.

Now if to a solution of about 6 c.cm. wherein were hatched miracidia swimming about, $\frac{1}{2}$ grain of antimony tartrate be added the movements of the miracidia were markedly changed. Normally they dart about with a pulsating movement, the sharp non-ciliated end forwards, revolving all the time on their own axis. This characteristic movement no doubt assists in the process of penetrating the snail, though it is not the engine of penetration. On the addition of the antimony the miracidia slow down, they wriggle, they writhe: they have, seemingly, convulsions, and, assuming a thicker and shorter form, they

* A bilharzia miracidium is as a general rule found with its head end in the blunt end of the ovum—that is, away from the spike, normally in fresh urine. Before the hatching takes place it turns right round in the shell; it escapes eventually by smashing a way through the shoulder, the broadest and weakest part of the shell. It is a curious fact that sometimes bilharzia patients, in order to "flush out the kidneys," drink a glass or two of beer or two or three cups of tea. This dilutes the urine and sometimes causes some of the ova to hatch, inside or outside the bladder, without further dilution of the urine.