Similarly large mononuclear increase in malaria means tissue response to the malaria parasite. Absence of a large mononuclear increase is not a sign that malaria is not present; it is simply a sign that the patient is not reacting.

Both large mononuclear increase in malaria and eosinophilia in bilharzia are indications of the response of the tissues—both are signs of good omen, but neither is a specific sign. Absence is in neither case a reliable sign that either malaria in the one case or bilharzia in the other is absent.

The Complement Fixation Test.

The complement fixation test for bilharzia is diagnostic of bilharzia disease—it is not always present. It cannot be used as a test for the presence of live bilharzia during treatment—(1) because it is difficult to obtain antigen in many places; (2) like eosinophilia the test remains positive for some time after the elimination of the worms. In short, there is no method of deciding when the worms are all dead during the treatment with antimony tartrate. The worms* probably die during all stages of treatment, a small total number of grains killing the less resisting and a larger total amount the more resisting.

The curative dose is the amount which will kill the most resisting worm (this is approximately 30 grains, given in about twenty-eight days). Adult patients should therefore be given this dose, and the few who require more than this should have another modified course later, when the remaining worms become active again, as indicated by live ova in urine or faeces. The fact that the symptoms have cleared up and no ova (or no live ova) are found in the urine is in itself no indication to suspend injections until the full dose has been given.

Antimony tartrate commences to stop the ova appearing in the urine at about 5 grains. At 10 grains some of the ova which appear in the urine are dead. The antimony tartrate acts on the ovum (the motor mechanism) first, and also affects the worm so as to suspend its egg-producing activities; but the worm is not killed till later—if too little antimony is given it recovers and recommences egg laying, and hence a relapse takes place after an apparent cure.

Cases are sometimes reported in the medical periodicals (and these are more frequent now owing to more complete examinations of patients) of vesical bilharzia where there is also rectal bilharzia with papillomata, both due to *Schistosoma haematobium*, or it may be to *S. haematobium* and *S. mansoni* in the same patient. It would be interesting for those who have the opportunity to make examinations and take specimens of the rectal papillomata at intervals to watch the local effect of the injections of antimony tartrate.

KANGRI-BURN CANCER.†

BY

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SINCE the year 1881 operations for epithelioma performed in the Kashmir Mission Hospital have numbered 2,491; of these approximately 2,000, or 84 per cent., were for kangri cancer. The kangri is an earthenware bowl five or six inches in diameter, surrounded by basket-work and surmounted by a wicker handle. It is heated by means of wood-charcoal, and is worn, by the poorer class of Kashmiris, against the skin, under a single loose garment not unlike a smock-frock. The primary factor in the causation of kangri cancer is, doubtless, heat, but it is possible that the volatile substances resulting from the combustion of the wood play a secondary part. The seats of election of the growths are the inner sides of the thighs and the anterior surface of the abdomen above or below the umbilicus. The disease is considerably commoner in men than in women, probably owing to the less continuous use of the kangri by the latter in their mostly domestic occupations. The average age for the onset of the cancer is 55; in a few cases it occurred before the age of 40, and in 7 per cent. of the cases over the age of 70. Many elderly

Kashmiris show a great tendency to localized superficial overgrowth of the epithelium; small, slightly scaly, pigmented patches or papules may be found scattered over the entire surface of the body. Owing to the constant application of heat the skin of the thighs and abdomen often appears dry and horny, the course of the superficial veins is marked out by a brown discoloration, and every degree of chronic dermatitis may be met with, from a mere redness, with or without desquamation, to thickened patches, warty projections, or horny outgrowths from the surface. Scars, resulting from previous kangri burns, are frequent, and are apt to undergo a malignant change.

Kangri-burn cancer is never found on the back or on the extensor surface of the limbs. It may be single or multiple, and the skin around it usually shows scarring. In the early stages ulceration is absent, and the growth consists of a mere horny or warty thickening, beneath which an epithelial infiltration is demonstrable microscopically. The cancer is met with in three forms, the commonest of which consists of a circular or oval ulcer about an inch and a half in diameter, with deep crater-like centre and raised edges. In some cases part of the tumour is fungating and the rest deeply excavated. In a somewhat less common form the growth consists of a cauliflower excrescence, which may project one or two inches from the surface and measure three or four inches across. A less usual form, which occurs generally in the aged, consists of an excavation with very little evident sign of overgrowth. It presents small or large ulcerated areas with irregular steep edges, in places undermined, and a rugged floor rendered uneven by deep recesses.

These cancers are always very foul and the skin around is sodden with septic discharge, which dries and becomes adherent at the margin of the growth and to some extent on the surface. The glands are usually involved in cases in which the ulceration is advanced. In cancer of the thigh they are affected generally in the following order: those along the internal saphenous vein, deep in Scarpa's triangle, near the spine of the pubis, transversely below Poupart's ligament, and, in advanced cases, the deep femoral and external iliac glands. In cancer of the abdominal wall the inguinal and then the external iliac glands become involved if the growth is below the umbilicus, the anterior axillary glands if it is above that level. In more advanced cases the deep glands beside the axillary vessels may become infected. The subscapular glands are rarely involved, but occasionally small glands are found across the side of the chest from the epigastrium to the axilla. The glands frequently attain the size of a pigeon's egg and often soften early. When they break down diffuse infiltration results. The overlying skin becomes red and brawny, and finally gives way from suppuration. A secondary deposit in this condition presents an appearance similar to that of the primary growth, except that the ulcer is deeper and the subcutaneous tissues are infiltrated. There is an abundant foul discharge, and after months of suffering the patient dies of exhaustion, septic intoxication, or haemorrhage. In the case of such deposits in the groin or axilla, the femoral or axillary artery may be perforated by ulceration comparatively early in the course of the disease.

The average duration of life in kangri-burn cancer is about fifteen months; in about 10 per cent. of the cases, from one to five years; and, as an exceptional event, as long as twenty years. The malignancy varies. As a rule a small growth, if superficial, is slow to grow and still slower in infecting the glands. There are, however, striking exceptions, and at times a slowly growing tumour will suddenly show a rapid increase. More than 50 per cent. of the cases show secondary infection of the glands when first seen.

In operating on cases of kangri-burn cancer the glands should be dealt with in the first place, because the primary tumour is always septic. The glands also are likely to be septic and require careful handling during removal in order to avoid rupture. Small glands are apt to escape notice, especially the external pubic group and those in the axilla in cases of epigastric growths. In order to avoid septic contamination of the operation wound during removal of the primary tumour the surrounding skin should

* The fact that some cases of bilharzia disease are cured by quite a small dose of antimony tartrate, whilst others require a total of 20 to 30 grains, is explained by the fact that the power to resist antimony tartrate varies in different worms. This may be also the explanation of the varying opinions about the curative dose.

† In order to ensure the publication of Dr. Neve's clinical observations this paper has been curtailed by the omission of certain paragraphs discussing general questions.

be rendered aseptic and two or more volsellae applied outside the growth and clear of it, and the mass lifted as far as possible and removed with a rapid incision. Many cases occur in which, although the primary growth could be removed, the glandular infection has become extracapsular, and it is impossible to gauge the extent of the disease owing to the presence of the ill defined and more or less diffuse induration. Cases such as these, if operated upon, are mainly responsible for the mortality, due to rapid recurrence or early haemorrhage from some large vessel. Our records show sixteen deaths from operation, mostly resulting from haemorrhage; this, however, is far from representing the total mortality. Recurrence took place in probably about 20 per cent. of the operated cases.

THE TREATMENT OF GENERAL PARALYSIS OF THE INSANE BY MALARIAL INFECTION.

(Preliminary Note.)

BY

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As a result of the observation that had been made from time to time since 1816¹—namely, that cases of dementia paralytica (degenerative encephalitis or general paralysis of the insane) frequently showed prolonged remissions and even apparent cure following a febrile illness or protracted suppuration—Wagner-Jauregg,² in 1909, began a series of experiments in the treatment of certain degenerative diseases with intercurrent infections. After preliminary trials with tuberculin and various vaccines, in 1917, he inoculated with benign tertian malaria nine cases of general paralysis of the insane (six early and three advanced cases). Favourable results were reported in the early cases, three of them being still at work four years after the treatment. Wagner-Jauregg then treated further cases, allowing each patient to have eight to twelve malarial paroxysms followed by a course of six neo-salvarsan injections, until it now appears that definite cures are claimed. Gerstmann (quoted by Templeton³) states that of 296 cases treated, and in whom it was possible to make complete observations, remissions of varying degree occurred in 202, while 112 showed complete remission with the disappearance of mental disturbances and a return to former business capacity (that is, remission occurred in 68 per cent. and complete remission in 38 per cent. of cases treated). Weigandt⁴ reports that, of fifty cases treated, remissions were obtained in 88 per cent. and good remissions in 48 per cent.

So encouraging were these reports of the results of treatment by malaria that early this year (1923) we began to treat cases of general paralysis of the insane at the West End Hospital for Nervous Diseases by the same method. Apart from those reported by Wagner-Jauregg and Gerstmann⁵ in Vienna, the only cases in which the treatment appears to have been tried (for example, those recorded by A. R. Grant⁶ and W. McAlister⁷) are those who have become in-patients in mental hospitals—that is, cases who presumably have reached a stage sufficiently advanced as to render them certifiable under the Lunacy Act. It was considered, therefore, that if improvement is obtained in such cases, even more might be achieved in earlier cases. In the out-patient clinic of a hospital for nervous diseases general paralysis of the insane is frequently met with in its earliest stage, and if cures result from the treatment, as the originators of the method claim, one would naturally expect such early cases to show the maximum response.

At the time of writing fourteen cases have been treated: 11 of the cases were in a relatively early stage of the disease, 1 resulted from congenital syphilis, and 2 cases, treated for purposes of comparison, were advanced. Apart

from the physical signs of the disease, the diagnosis in our cases has rested upon the presence of an increased number of lymphocytes, positive globulin and Wassermann reactions, and a colloidal gold reaction curve of the "paretic" type in the cerebro-spinal fluid, as well as a positive Wassermann reaction in the blood serum. In only one case (of undoubted general paralysis of the insane) was the colloidal gold curve "leutic" in type. Those cases tested have also shown the characteristic speech inscription described by E. W. Scripture.⁸

Through the courtesy of Dr. G. C. Low and Dr. Gregg of the Hospital for Tropical Diseases, Endsleigh Gardens, the first sample of malarial blood was obtained from a man suffering from benign tertian malaria who had not been treated with quinine: 2 c.cm. of the malarial blood were injected into the subcutaneous tissue of the interscapular region of the first case. Subsequent inoculations were made from case to case of general paralysis of the insane as each developed malaria. Wagner-Jauregg recommends that the blood be removed from the malarial patient during the febrile stage, but we find that this is not really necessary as the inoculated subject becomes just as efficiently infected if the blood is taken at any stage (pyrexial or apyrexial) of the period over which the attacks are permitted—that is, before the administration of any quinine. All cases were easily infected, only one injection of malarial blood being necessary. The incubation period varied from nine to twenty-four days in different cases (average period fourteen days). In four cases after about the fourth attack, the tertian ague was replaced by one of quotidian type, a phenomenon also observed in some of Wagner-Jauregg's patients. As a rule twelve attacks of malaria were permitted, the infection then being terminated by one or two intramuscular injections of quinine bihydrochloride (gr. xv) followed by the oral administration of quinine sulphate (gr. v daily) for a week. This treatment has proved quite efficacious as regards the malaria, no relapses having occurred. In each case the earlier malarial manifestations were pronounced, the temperature rising to 103°-105° F. during the febrile stage; the last four or five attacks were usually not so severe, the maximum temperature becoming progressively lower. Although the malarial infection had passed through fourteen cases it was just as potent for the purpose of transmission after the fourteenth case as at first. Following the termination of the malarial period, novarsenobillon was given intravenously in full doses (0.9 gram) at weekly intervals for six weeks.

Of the twelve early cases of general paralysis of the insane treated, all but one exhibit varying degrees of improvement; in two cases the improvement has been remarkable, and both have returned to work. Another case only recently treated continues at work that he was unable to do for some weeks prior to treatment. Brief details of these cases are as follows:

CASE I.

F. B., aged 38; general paralysis of the insane, early. In March, 1921, the patient first began to have difficulty with regard to speech. When first seen (August 25th, 1922) he complained of headache and insomnia and difficulty in articulating certain words. Mentally, he was easily agitated, talkative, laughed inanely without adequate cause, and had a high opinion of his accomplishments, in spite of the fact that he was unable satisfactorily to carry out his duties as a school caretaker.

Physical Signs.—Pupils: right excentric and sluggish to light; left normal. Lingual and labial tremors. Knee-jerks and ankle-jerks brisk; plantars flexor. Wassermann reaction: blood positive; cerebro-spinal fluid, 21 cells per cubic millimetre. Globulin and Wassermann reactions positive. Colloidal gold test positive; paretic curve.

Present Condition (five months after malarial treatment).—His remarkable improvement is a matter of general comment in his locality. He has lost his exaltation, answers all questions rationally, and is able to carry out his work satisfactorily.

CASE II.

R. C., aged 30; tabo-paresis. All the patient's symptoms were said to date from the time he was wounded while serving with the army in 1918. He complained of headache and "fits" (which occurred every few weeks). Later, his memory began to fail and speech became difficult. Early in July, just prior to treatment, he was found "wandering" by the police and taken to the infirmary with a view to certification. Mentally he was somewhat exalted, excitable at times, alternating with fits of depression. He was also self-satisfied, suspicious, and occasionally experienced aural hallucinations. His speech was slurred and his memory poor.