SCHISTOSOMIASIS OF THE BRAIN*

FRANCIS A. CARMICHAEL, JR., M.D.,† AND HOWARD S. COWLEY, M.D.‡
Veterans Administration Center, Wadsworth, Kansas

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Although there is much to be found in the literature concerning intestinal and hepatic involvement by Schistosoma japonicum, the reports on cerebral involvement are infrequent. Because of the extreme gravity of complications from this disease, we feel that the members of American medical profession should be aware of it as a neurological differential diagnostic problem in anyone presenting a bizarre neurological picture who has been in an endemic area. That the disease may well assume the roles played by typhoid fever in the Civil War, by influenza in World War I and by malaria in World War II was suggested at a recent meeting of the Society of American Bacteriologists.

HISTORICAL REVIEW

Fujii35 first mentioned this disease entity in 1847, but it was 42 years later before any cerebral lesions were associated with the disease65 and not until 1904 was the etiological agent discovered and named by Katsurada.37 The first autopsy reports on cerebral findings were made in 1905.58 Presumptive evidence that abnormal neurological reactions in infected patients were attributable to lesions caused by eggs or worms in the central nervous system was initially presented by Houghton33 in 1910, but not until 1935 was the first report of surgical verification of a cerebral lesion made by Shimidzu,49 which was followed by similar reports by Edgar19 in 1936, and Greenfield and Pritchard29 in 1937. No further cerebral granulomas were verified surgically until Swanson55 reported the fourth case in 1946. Since that time, 11 instances of operative and microscopic verification of such lesions have appeared in the literature,14,19,29,31,47,48,49,51,55,65 although others may have been unreported, as Chang and his co-workers14 referred to 2 cases surgically verified by Sanders, and Watson and his co-workers62 mentioned 1 case verified by Maltby and Schmidt and 1 by Chasoff. Hunt and his co-workers34 reported 1 operative case which, however, was not verified microscopically. Faust32 mentioned 1 case verified by Palmer.

Many observers have reported on presumptive ectopic cerebral lesions.10,12,15,17,20,26,36,52,56,57

Eight authors3,4,5,23,56,61,65 reported 11 postmortem examinations on

* The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
† 411 Nichols Road, Kansas City 2, Missouri.
‡ Former senior neurosurgical resident, Wadsworth Veterans Administration Hospital, Wadsworth, Kansas.

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patients who had exhibited neurological manifestations of the disease and among these only 1 cerebellar and 4 cerebral granulomas were microscopically verified as containing Schistosoma japonicum ova. Perhaps significantly the number of surgical verifications since 1941 overshadows the number of autopsy verifications.

ENDEMIC AREAS

The disease is apparently limited to areas containing a certain species of amphibious fresh water snail known variously as Oncomelania, Katayama or Schistosomophora which presently is the only known intermediate host suitable for the larval development of Schistosoma japonicum in the field.

Known endemic areas include Japan (Honshu and Kyushu Islands), China (especially southern and central), Formosa, Korea, the Celebes and the Philippine Islands of Leyte, Samar, Mindoro and Mindanao.\textsuperscript{10,16,24,40,41,43,44,50,54,59,64}

Abbott,\textsuperscript{1,2} and Berry and Rue\textsuperscript{9} have reported a species of fresh water snail having a wide range of distribution in the United States which is capable of serving as the intermediate host under laboratory conditions. Their medical significance is presently unknown, but one must recall that after World War I Australia was faced with the previously unknown problem of endemic Schistosoma hematobium due to the adaptability of a certain species of one of their native fresh water snails.

ROUTE OF CEREBRAL INFECTION

The route of larval migration was reported by Miyagawa\textsuperscript{42} in 1912, and restudied by Faust and Meleney\textsuperscript{25} in 1924 whose description of the stage-by-stage development in mammals is classical. However, this deals only with the normal portocaval development and does not embrace the far distant sites of ectopic lesions.

The largest number of proven or presumptive sites of ectopic lesions in schistosomiasis japonica is in the cerebrum. However, the route of cerebral infestation is not clearly understood. Five routes have been theorized and include (a) the valveless vertebral veins or “Batson’s circulation”,\textsuperscript{7,8} (b) migration of the worms outside their normal habitat against the venous blood flow and into collateral vessels with egg deposition on reaching the end venules.\textsuperscript{23,29,45,51} It has been shown that worms do migrate out of their normal habitat and the nature of most of the verified cerebral lesions supports this hypothesis, but no worker has explained how the worms reach the cerebral venous sinuses; (c) normal development outside the hepatic-caval system,\textsuperscript{23,29} this has been disproven by the studies of Faust and Meleney\textsuperscript{25} and Waelsch,\textsuperscript{62} (d) the presence of a patent foramen ovale which, although a rational explanation, does not occur with enough frequency to serve as an explanation; none of the 9 autopsy reports on cerebral ectopic lesions mentions the presence of such an anomaly; (e) eggs deposited in the usual sites filtering through the capillary barriers of the liver and lungs into
the general circulation and hence to end arterioles. The objections to this are the facts that reaction is reported only around venules and never around arterioles, and that the cerebral foci are composed of nests of eggs rather than diffuse lesions, although 3 autopsy reports mention a diffuse process.

Pathology

On invading the central nervous system an intense reaction follows in both the cerebral vessels in which the organism lodges and in the surrounding parenchyma. This may be caused by blood-vessel occlusion and resultant passive congestive changes, foreign protein reaction, elaboration of a chemical toxin, or any combination thereof.

Shimidzu's description of the microscopic changes occurring in the involved area of the brain in the first case in which operation was performed is typical except that subsequent authors also report the presence of multinuclear foreign body giant cells. The picture is not radically different from the general reactive one that occurs in cerebral abscess or other granulomas, as previously described in detail by one of us (F. A. C.).

No investigators have mentioned any pathologic changes in the cerebral arteries, and none has reported finding an adult worm in the human cerebrum, but all have noted intense infiltration of nearby cerebral veins and degenerative changes in surrounding ganglion cells, as well as walled-off ova inside the low-grade inflammatory mass.

Later in the paper we shall describe surface features of the pia and arachnoid which we believe provide a rather accurate gross pathologic diagnosis at the operating table and which we have not found recorded heretofore.

Most of the reported gross pathological lesions have been unilateral granulomas in the parieto-occipital or parietotemporal areas. There is apparent predilection for the parietal lobe and questionable affinity for the left hemisphere.

Course and Symptomatology

The course of this disease may be divided into incubative, acute and chronic stages, although these are continuous and thus the clinical signs and symptoms ascribed to each stage may overlap. As the latent period is variable and of unknown duration, symptoms have been reported as long as 4 years after infection.

The symptomatology of lesions in the central nervous system caused by the presence of eggs and the unidentified substance given off by them has been recorded by many authors.

During the incubative stage symptomatology simulates many diseases of the regions endemic for Schistosoma japonicum.

In the acute stage neurologic signs and symptoms include headache, delirium, confusion, aphasias, amnesia, convulsions, hyperreflexia, visual disturbance, nuchal rigidity, loss of superficial reflexes and motor weakness
(especially sudden plegias). Usually these occur about 5 or 6 weeks after infection.

As in all diseases, the individual reaction to infection is variable and because the early signs and symptoms vary as to time of appearance and intensity, they may be entirely overlooked. Furthermore, the early symptoms as a rule subside spontaneously. They are never an index to the severity of the infection. It is noteworthy that many cases of cerebral involvement may give no history whatsoever suggestive of primary infection (including the 3 in this report).

In the chronic stage neurological symptoms and signs comprise headache, language dysfunction, sudden motor weakness or paralysis of one or more extremities or Jacksonian epilepsy (usually ushered in suddenly).

**DIAGNOSTIC AIDS**

During the incubative stage, only a presumptive diagnosis may be made and the history of exposure is the most important point. Leukocytes and marked eosinophilia without anemia may be found in the blood stream.

Important features noted in the acute stage include the history of exposure, eosinophilia in the absence of allergy or other helminth infestation and the presence of ova in the stools, which may be demonstrated by direct smear or other recommended methods. Proctoscopy as advocated by Johnson and Berry may yield valuable results, and these workers as well as others advise biopsy as it gave positive results before ova could be demonstrated in the stool. Because of possible complications such biopsy should be done with caution. The recognition of the eggs is excellently presented in a paper by Faust. Intradermal and complement fixation tests are valuable adjuncts. Gastroscopic studies are of no diagnostic value. Cerebrospinal fluid analysis is regarded as diagnostically valueless because the ova have become walled off in the granulomatous mass; however, later in this paper we shall report for the first time in medical literature our isolation of the ova from both the spinal and ventricular fluid.

The chronic stage is somewhat more difficult to diagnose because of the variable clinical pattern, the unknown latent period, and the difficulty in obtaining positive laboratory findings. Usually eosinophilia and fever are absent, and the finding of ova in the stools problematical—the biopsy methods may be superior to fecal examination in the chronic stage. Results of the formol-gel test are variable as are those of the complement fixation and skin tests.

The differentiation between a cerebral granuloma and a neoplasm is difficult and in fact probably only a surmise until operative biopsy is undertaken. Electroencephalography, ventriculography or pneumoencephalography in patients with focal neurologic signs and papilledema may not aid in the differentiation although the ectopic lesions of Schistosoma japonicum usually do not present such large defects in the ventricular system. We have
not encountered any description of the angiographic picture of these lesions although we presume the design would not be specific.

We should like to stress a point made by Tillman\(^7\) and others, that any patient presenting an obscure neurological pattern who has a history of having been in an endemic area should be thoroughly investigated for schistosomiasis.

**TREATMENT**

Ferguson and his co-workers,\(^7\) Sullivan and Ferguson,\(^54\) and others suggest that prevention of the disease is better than treatment and to this end they advocate the education of persons in and those going into known endemic areas, the application of cercaricidal preparations to the skin and clothing and the wearing of protective clothing by those who must work in suspected surface waters. They emphasize that the criteria of safety are neither the absence of snails nor the presence of clear or swiftly flowing water, pointing out that cercaria may be carried for miles on water surface films.

Because of the gravity of the disease and its complications, students of it\(^10,16,23,25,32,36,40,43,53,60\) advise institution of specific chemotherapy as soon as schistosomiasis has been diagnosed, not only to guard against further complications but also because it is the only efficacious method of removing the parasites. The commonly employed agents are antimony compounds, including stibophen (neoantimosan or fuadin) and antimony potassium tartrate (tartar emetic) which are toxic and dangerous but which should be given promptly unless contraindicated by the presence of another serious disease. They emphasize particularly close observation of the patient and mention that other heavy metal salts and cardiac depressants should not be administered concurrently. It is stressed that insufficient dosage of the drug usually is followed by therapeutic failure. Recent military experiences have demonstrated the superiority of tartar emetic for specific therapy; however, if this drug cannot be tolerated in its maximum recommended dosage, then fuadin should be employed.

Lippincott and his co-workers\(^58\) noted no harmful effect on the liver from antimony given to 2 infected patients who came to autopsy during the treatment of 481 cases.

The results of treatment should be carefully checked, especially by examination of the stools, and the patient should be re-examined frequently for at least 1 year for possible recurrence.

As antimony presumably affects only the adult parasites and has no effect upon the granulomatous lesions, the treatment for ectopic lesions is surgical excision. However, in our Case 3 the ova were identified by cerebral biopsy and in the cerebrospinal fluid, and yet at autopsy multiple lesions were found in the cerebrum but no ova could be microscopically verified although the ova were identified in the preservative solution. Surface lesions can usually be completely removed, intracranial pressure, which in some cases is not only dangerous to vision (50 per cent have papilledema) but also to
life, can be alleviated, and without surgical intervention neoplasm cannot be ruled out with certainty.

PROGNOSIS

Our conclusion on reviewing the literature is that prognosis for life is good. The early cases show much more favorable response to specific therapy than do the latent cases. Mild to severe neurologic residuals may be expected in most of the operated latent cases for at least 1 year.

CASE REPORTS

Herewith follows the report of 3 surgically verified cases, 2 with gratifying results and 1 terminating fatally. We shall describe certain gross pathological findings and laboratory phenomena which have not heretofore received notice.

Case 1. A 30-year-old white male, a packing house worker, was admitted to the hospital on June 28, 1948, complaining of periods of inability to speak and a recent convulsive seizure.

In December 1947 while at work he noted a burning sensation in the right buttock and involuntary movements of the right leg, following which he was unable to move the leg. This phenomenon lasted approximately 5 minutes, after which he felt perfectly normal. During the next 2 weeks, he had four similar attacks and was then symptom free until about 1 month prior to admission when he began to experience headaches and visual difficulty.

On June 23, 1948, he first noted inability to speak although he was able to understand what his fellow worker was saying. This lasted 20 minutes. The same afternoon he had a similar attack of motor aphasia which was accompanied by weakness and Jacksonian convulsive seizure, which began in the right hand and became generalized, with loss of consciousness. There was no tongue biting or incontinence. The unconscious period lasted 1 hour following which he was unable to speak for 15 minutes. He felt well except for a slight pressure behind the left ear. On June 26, another bout of motor aphasia occurred, lasting 20 minutes. On the day of admission, he experienced another attack of similar duration and character.

Past History. His past civilian medical history was not contributory. His military history from July 1942 until January 1946 consisted of 31 months of service in the Southwest Pacific, 6 months of which were spent on the Philippine Island of Leyte. He recalls no illness except mild diarrhea which he thought everyone had at one time or another during their Pacific tour. This caused him no loss of time from his duties.

Examination. The patient was fairly well developed and well nourished and did not appear ill. Positive neurological findings were lateral nystagmus, more pronounced on looking to the right; slight left central type facial weakness; generalized hyperreflexia, more marked in the deep reflexes on the right, especially in the upper extremity; slightly impaired stereognosis on the right and an associated weakness in the right grip. Tentative diagnosis: expanding intracranial lesion in the left parieto-occipital area.

Initial laboratory studies revealed an eosinophilia of 14 per cent, and a leukocytosis of 14,000/c.mm., with 60 per cent neutrophiles and 24 per cent lymphocytes. X-rays of the chest, skull sinuses and mastoid were reported as normal. EEG was reported as evidencing a disturbance in the left parieto-occipital region. CSF
pressure was 180 mm. on the conventional water-type manometer. Pneumo-
encephalography was done, with fractional displacement of 120 cc. CSF with air.
The films evidenced some flattening of the posterior horn of the left ventricle.

On July 9, 1948 the patient was seen for the first time by one of us (F.A.C.),
who, concerned by the diagnosis of an expanding intracranial lesion, suggested the
possibility of cerebral schistosomiasis and recommended further laboratory exami-
inations. The 15th stool specimen was reported as being positive for the presence of
the ova of Schistosoma japonicum.

Operation. On Aug. 6, 1948, a left osteoplastic parietal craniotomy was under-
taken. Immediately underlying the dura numerous fine, small, punctate granular
adhesions, yellowish-white in color and the size of millet seeds, were encountered
all through the pia. Such clusters were adherent to the overlying dura mater and
were separated with some difficulty by cotton pledget dissection. Remnants of these
clusters could be seen attached to the internal surface of the dura. Palpation of
the brain in the posterior parietal area gave a sense of density immediately under-
lying the cortex. Therefore, incision was made in one of the postparietal convolu-
tions; exploration revealed very dense granulomatous tissue, which was ill circum-
scribed and not clearly defined from the rest of the brain in this area. A block dissec-
tion was made, following which the cut surface of the granuloma could be readily
recognized. Several smaller granulomas were removed by blunt dissection and the
electric loop.

Pathological Report (Dr. Ferdinand C. Helwig). Granuloma of the brain contain-
ing ova of Schistosoma japonicum.

Course. Postoperatively transitory right-sided weakness, confusion and aphasia
were noted. All symptoms subsided by the 6th postoperative day.

On August 19, blood serum was submitted for complement fixation test, at which
time skin-testing antigen also was employed. It was subsequently reported negative
and the skin test read as positive. At this time specific tartar emetic therapy was
begun. Stool specimens continued positive for Schistosoma ova until August 31,
following which the stool specimen taken every 3rd day was reported negative for
parasites or ova. The specific therapy was completed on September 24 and the pa-
tient was subsequently discharged. Neurological and eye findings were normal.

Neurological and laboratory examinations every 3 months in 1948 and 1949,
and every 6 months since show him to be well and without evidence of further in-
fection. He was last examined in May 1952.

Case 2. A 27-year-old farmer was admitted on Sept. 8, 1948 complaining of
headache, failing vision, and clumsiness and weakness of all extremities.

He had been in good health until October 1947, when he first noted flashes of
light before his eyes, which he described as being like a neon sign flashing on and
off, and difficulty with close vision. This phenomenon would last for several minutes
and was followed by severe occipital headaches of variable duration. Usually, how-
ever, the headaches lasted for several days, with only partial relief on rest and pre-
scribed medications. They became progressively worse, and since May 1948 had
been constant. He no longer experienced visual phenomena but was unable to read
because of failing vision. During the last month, he had had progressive difficulty
in gait; he could not walk without staggering, preponderantly toward the left. For
4 months he had also noted progressive clumsiness of the upper extremities, espe-
cially marked in the last 6 weeks. For several months he had had difficulty in thinking
nausea and expressing himself. He would often say the wrong words, would be unable to complete sentences, and could not figure out small problems. There had been no nausea or vomiting, no diplopia, and no convulsions.

Past History. His past civilian medical history was not contributory. His military history from October 1942 to December 1945 included 13 months spent in the Southwest Pacific on Leyte, Mindoro, and Mindanao Islands. During his service on Mindoro, he was hospitalized for about 1 week with what was diagnosed as dengue fever. He also admitted to several episodes of diarrhea.

Examination. He was a fairly well developed and well nourished white male who was ambulant on a very wide base. All movements were accomplished very slowly and deliberately. He was completely oriented but had some difficulty in cerebration as well as speech and seemed to grope for words, his speech being slow and somewhat slurred.

There was tenderness to percussion over the calvarium in the left occipital area. Two plus nuchal rigidity was present. Lateral nystagmus was noted. There was bilateral papilledema of 1D. Confrontory visual fields suggested a right inferior quadrantanopsia. A flattening of the skin of the left forehead was noted on attempting to raise the eyebrows; however, both the patient and his wife believed this had been present for several years. There was difficulty in movements of the tongue and mild fibrillation was noted. The plantar response was equivocal. There was generalized hyperreflexia. All extremities were mildly spastic and voluntary movements were carried out very slowly, more difficulty being noted on the right. No sensory disturbances were elicited. There were dysmetria and dysdiadochokinesis of both upper extremities, more marked on the right. Ataxia was marked, especially in the right leg. The Romberg was very positive, with the patient falling to the left.

Routine laboratory findings were normal except for elevation of sedimentation rate to 31 mm./60 min., and 5 per cent eosinophils in the differential leukocyte count. The stool specimen was reported positive for the presence of hookworm and whipworm. Roentgenograms of chest and skull were normal. The EEG indicated a focal lesion in the left occipitotemporal area.

Operation. On Sept. 17, 1948 ventriculography was performed. The ventricular fluid showed a total protein of 95 mg. per cent; smear, culture, cell count and serology were normal. During the procedure a hard firm mass was encountered under the left occipital burr hole. A biopsy of this mass was reported as protoplasmic astrocytoma. Previous ventriculograms had shown definite asymmetry of the ventricular system, with the left lateral ventricle being depressed somewhat downward, especially in the posterior horn.

A left osteoplastic flap was reflected to expose the left occipital pole. Incision of the dura at the most superior exposure of the cortex showed the color of the tissue to be rather brown and greenish. As the dura was reflected from the pia, a multitude of small, yellow, glistening discrete millet seed-like dots in clusters were seen forming adhesions between the dura and the underlying arachnoid. (The operator remarked at once that these were identical to the clusters of ova of Schistosoma recently seen in a previous case.)

Exploration with the cannula revealed a very hard, tough tumor mass underlying all the occipital cortex at a depth of less than 1 cm. Incision was then made in the occipital cortex and piecemeal removal of the mass was begun. The tumor, except for its large nutrient and traversing arteries, was mainly avascular. It presented...
a tough, yellowish, avascular, granulated surface when cut with the Bovie or with the scalpel. Extensive dissection of the uncircumscribed tumor mass was done, at which time it was appreciated that tissue approximately 6 cm. in diameter had been removed and that an equally large portion seemed to extend forward toward the mid-parietal lobe and that it was intimately connected with the torcular angle. It was thought most advisable to close and give the patient a course of tartar emetic therapy before considering the advisability of re-exploration for total removal.

Pathological Report (Dr. Ferdinand C. Helwig). Granuloma of the brain, containing Schistosoma japonicum ova (Fig.1).

Course. On September 25, skin and complement fixation tests were done. The skin test evidenced a suspicious positive and the complement fixation test was positive for schistosomiasis.

On September 27, examination by the eye department disclosed blurring of the disk margins, which they assumed to be postpapilledemic, and a right homonymous hemianopsia.

Daily stool specimens continued to be negative for the presence of Schistosoma ova, and continued so throughout the period of hospitalization. However, specific tartar emetic therapy was begun. Sigmoidoscopic examination carried out in search for lesions proved negative.

Examination prior to discharge revealed visual defects as mentioned. Cranial
nerves were intact and there was no longer an ironing-out of the left forehead on raising the eyebrows. There was generalized hyperreflexia with no pathological reflexes or sensory disturbances. During his convalescence he had complained of two transitory bouts of flashing lights.

Subsequent physical and laboratory examinations every 3 to 6 months to May 1952 paralleled the discharge findings. He is able to continue his farming activities satisfactorily.

Comment. Ova were never demonstrated in this patient's stools despite the unquestioned finding of ova in the cerebral granuloma.

Case 3. A 30-year-old butcher was seen in consultation by one of us (F.A.C.) on Mar. 7, 1949, complaining of a feeling of numbness over the entire right side of the body including the face, slowing of all his muscular movements, staggering gait, and some slurring of speech. He gave a history of occasional spells of uncontrollable jerking or twitching in the right arm and leg, followed by severe headache over his right eye and tiredness, which began about November 1948. Examination revealed bilateral nystagmus, more marked on the right, dysarthria, dysmetria and adiado-kokinesis on the right, a positive Romberg, ataxic gait, sluggish abdominal reflexes, and a suggestion of increased reflexes in the right lower extremity. He exhibited a right hemiparesis including the face, and a subjective right hemihypesthesia. Diplopia was noted on lateral vision toward the right. Admission to the hospital was advised.

Past History. His service medical history from Dec. 14, 1942 to Feb. 18, 1946, included 2 years of overseas duty, 8 months of which were spent in Luzon and Korea. He recalled no bouts of illness except diarrhea, which he described as mild. The patient had been hospitalized elsewhere on Sept. 13, 1948 because of transitory, dull, aching pain in the lower right abdominal quadrant of 1 ½ years' duration, at which time stool examination revealed ova and parasites which were not positively identified but were thought to be ascariis lumbricoides. The onset of this pain was rather insidious and occurred while he was returning from duty in the South Pacific in 1946. These attacks of pain were unrelated to activity, rest or bowel movement. They were not associated with diarrhea or melana.

The patient returned to his work and remained symptom free until November 1948 when he began to experience intermittent attacks of jerking movements of the right extremities, dizziness and occasional fainting spells accompanied and followed by right frontal headache which was very severe but which would disappear about 1 hour after reclining. These attacks continued intermittently for several months and became so incapacitating that they seriously interfered with his working efficiency.

In February 1949 the attacks of headache and dizziness became more severe although they were no longer accompanied by the jerking movements of the right extremities. The patient consulted an ophthalmologist because in addition he had noted some double vision. No ocular pathology was found. Soon the patient began to notice more frequent bouts of diplopia, usually present with the attacks of dizziness and headache. In March 1949 he had convulsive movements of the right extremities followed by a feeling of right hemianesthesia. Daily vomiting had occurred for approximately 5 days and his frontal headache was much more severe.

His wife stated that for 18 months she had noted considerable personality change, especially marked in the last 6 months, in that he wished to withdraw from
was very irritable and depressed, and had predicted his own death.

**Examination.** On admission Mar. 11, 1949 examination revealed an acutely and critically ill, semicomatose patient with mucous rales in the throat, inability to swallow, dyspnea, cyanosis and profuse perspiration. There was bilateral papilledema of 1 D. One plus stiffness of the neck was noted. There was no tenderness nor rigidity of the abdomen nor were any masses palpable. The patient was completely aphasic and dysphagic and was aroused with some difficulty. There was a right central type facial weakness. The deep reflexes of the extremities were hyperactive, more marked on the left. The plantar response was flexor on the right and equivocal on the left. The Hoffmann sign was positive on the right. The patient was incontinent of urine and feces.

Lumbar puncture yielded a clear, colorless fluid under 140 mm. of water pressure. The cell count, chemistry and colloidal gold curve were normal. WBC was 19,150: 83 per cent neutrophiles, of which 55 per cent were segmented, 14 per cent lymphocytes, 1 per cent myelocytes and 2 per cent eosinophiles. The stool specimen was positive for ova of Schistosoma japonicum.

**Course.** Tartar emetic therapy was begun. The patient gradually improved and by March 21 could swallow liquids. However, he remained very depressed and cried considerably. He was able to speak several unrelated words. He exhibited left hemiparesis, right central type facial weakness, irregular pupils with the right being larger, bilateral papilledema, bilateral weakness of the 9th and questionable paralysis of the 12th cranial nerve. The left Hoffmann was positive and the plantar response was bilaterally extensor. Deep reflexes of the lower extremities were increased, being more marked on the left. X-rays of the chest and skull were normal. Stool examination on March 21 still revealed ova of Schistosoma japonicum, although all subsequent stool examinations were negative for the ova. Complement fixation test for Schistosoma japonicum was reported as negative. Skin testing was not done as the antigen was not available.

Subsequently it was found that the left side of the tongue was hypesthetic. Hyperesthesia over the 2nd branch of the right 5th cranial nerve was also noted. The patient was still unable to protrude his tongue or to phonate, and no movement of the palate was noted.

**Operation.** The patient continued to improve generally and on June 15, 1949 ventriculography was done. On entering the parenchyma of the brain through the right occipital burr hole some resistance was encountered and the right ventricle was entered with extreme difficulty. However, air passed freely from one ventricle to the other. The ventriculograms showed asymmetry of the bodies of the lateral ventricles with a slight depression in the roof of the body and occipital horn of the right lateral ventricle and a shift of the ventricular system to the left.

A right parieto-occipital osteoplastic craniotomy was then carried out. On elevation of the bone flap the dura was noted to pulsate normally and gave no evidence of increased intracranial pressure. On reflection of the dura, there was no evidence of the millet seed-like adhesions indicative of surface schistosomiasis, as described.

Exploration was made through the right posterior superior parietal gyrus and an area of resistant grayish, translucent, firm, tough tissue was encountered from which several biopsies were taken. Throughout the whole exposure of the parieto-occipital cortex, the shotty induration could be felt, giving the impression of disseminated granulomatous lesions throughout the subjacent areas of this hemisphere. It was deemed that such a lesion was not removable and therefore further manipulation following biopsy was not carried out.
Pathological Report (Dr. Ferdinand C. Helwig). Granuloma of the brain containing ova of Schistosoma japonicum. The ventricular fluid contains free floating ova of Schistosoma japonicum. (This finding, to our knowledge, has never previously been described in the literature.)

Course. Because of poor postoperative response lumbar puncture was done on June 17, the fluid being under pressure of 320 mm. of water. The laboratory reported that the fluid contained ova of Schistosoma japonicum. Specific tartar emetic therapy was reinstituted and was continued until time of death.

On June 18 the patient exhibited right facial twitchings which occurred during his sleeping hours as well as when he was responsive. At times twitchings would involve the left upper extremity as well. On June 20, left-sided Jacksonian seizures occurred, which were controlled by dilantin and phenobarbital. On June 21, his condition had improved although a left hemiplegia was still present as well as some twitching of the left face, most marked about the mouth. He continued to improve generally until July 1, when his temperature suddenly rose to 104°F. Cyanosis and rales in both lungs developed, and the patient expired on July 4, 1949.

Autopsy. Multiple sections taken from the brain, including the cerebellum and the meninges covering the cerebellum, the basal ganglia, floor of the lateral ventricle, and cerebral cortex, all show a similar lesion. In the areas of softening noticed grossly there is extensive encephalomalacia with loss of substance and large numbers of gliter cells. The capillaries are packed with red blood cells. The adjacent tissue generally shows vacuolization and a very few protoplasmatic astrocytes were noted in some instances. Glial cells were frequently noted alongside the blood vessels. In a single one of the many sections taken from the cortex, there was found one multinucleated giant cell similar in structure to those found in the lungs. A very careful search failed to reveal the presence of a single ovum. In some instances, however, dark blue-staining bodies are present, particularly in the meninges covering the cerebellum.

Following failure to identify the ova in any of the sections taken, the sediment from the solution in which the brain was stored was concentrated and examined. By that time the brain was in Kaiserling III, having been successively in formalin and Kaiserling I and II. In the wet preparation, structures resembling the ova of Schistosoma japonicum were found. Sections of cerebral vessels and the choroid plexuses were then macerated and examined. In this wet preparation many oval and round structures were present, some of them resembling Schistosoma japonicum and some of them corpora amylacea. In the stained preparations any distinction was very questionable.

Along with the routine material, the concentrated sediment from Kaiserling III was forwarded to the Army Institute of Pathology for further examination and evaluation.

SUMMARY

A review of the literature on Schistosoma japonicum is presented, with particular reference to ectopic lesions that involve cerebral tissue.

A report is made of 3 cases which came under the authors' personal observation and which were surgically verified. Certain heretofore unreported clinicopathological features of the lesion are described which may be of help in identifying this lesion at the operating table. For the first time also, it is believed, the isolation of the ova of Schistosoma japonicum from the cerebrospinal and ventricular fluid is reported.

Case 3 is of particular interest in that it was verified surgically by both the
biopsied tissue and ventricular fluid removed at the operating table but could not be verified at autopsy in a patient who had been under intensive antimony tartrate treatment following surgery.

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