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INDEXING OF CHINESE MEDICAL LITERATURE

Note on Authors' Names

Considerable confusion in authors' names seems to exist in the indexing of Chinese medical literature. For example, Chung Hwei-Lan (in which Chung is the surname and Hwei-Lan the given name) has been variously referred to as "Hwei Lan Chung," "Lan Chung Hwei" or "Chung Hwei Lan."

As from the first issue, 1956, of the CHINESE MEDICAL JOURNAL, the authors' names will appear with the surname first and the given name (usually in two words) with a hyphen between them. Thus Kuo Pang-Fu or Liu Yang, for example, will be found in the contents and headings of articles as well as in the index and references, Kuo and Liu being the surnames.

The above rule will be followed in the case of the few surnames with two syllables, such as Siatu, Ouyang and Sium. To avoid confusion, these names will not be hyphenated. Thus, with the names Ouyang Ming or Siatu Wen-Ping, Ouyang and Siatu are the surnames and Ming and Wen-Ping are the second names respectively.

If initials instead of the given name in full are used, then the above names, Chung Hwei-Lan, Kuo Pang-Fu, Liu Yang, Ouyang Ming and Siatu Wen-Ping should be indexed as follows: Chung, H. L., Kuo, P. F., Liu, Y., Ouyang, M. and Siatu, W. P.

It is hoped that the above explanations will facilitate the indexing of Chinese medical literature.

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NUMBER 1

RECENT ADVANCES IN DIAGNOSIS OF PARAGONIMIASIS*

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This paper deals briefly with the methods of diagnosing inapparent, obscure or atypical cases of paragonimiasis together with some illustrative cases in so far as they are of common interest to students of parasitology and tropical medicine. These methods are part of the fruitful results(1-8) of active investigation on paragonimiasis undertaken in recent years and reflect our growing interest in medical research. It is safe to say that research work in New China has definitely advanced our knowledge of paragonimiasis, its pathology, epidemiology, clinical manifestations, diagnosis, treatment and prevention. Readers interested in the various aspects of this disease will find valuable information in the numerous articles recently published in the *Chinese Journal of Internal Medicine*, the *National Medical Journal of China* and the *Chinese Medical*

*This article was originally written by the senior author at the invitation of the Editor of the *Revista Brasileira de Malariologia e Doenças Tropicais* for a special number of that journal in homage to Dr. Samuel B. Pessôa on his retirement as Professor of Parasitology at the University of São Paulo. Much of the material was taken from a paper in Chinese written by the senior author and his associates for a symposium on paragonimiasis published in the *National Medical Journal of China* in December 1955. The paper now includes, in addition, the autopsy findings of 2 cases by Professor C. H. Hu, whose invaluable help is here gratefully acknowledged.



Journal. Three symposia on paragonimiasis(9-11) have recently been published in the first two of these journals.

Paragonimiasis occurs in different clinical forms. The typical cases with chronic cough, hemoptysis and ova in the sputum are easy to recognize, but symptomless cases (including very mild cases, inapparent infection or latent cases, early cases, and spontaneously healed or therapeutically cured cases) and cases with most atypical or very obscure symptoms without expectoration or with slight expectoration but no ova in the sputum are usually either missed, wrongly diagnosed or confused with other conditions. The various clinical forms of paragonimiasis which present diagnostic difficulties include the following groups of cases: 1. Cases with central nervous system involvement (cases simulating tuberculous meningitis, encephalitis, brain tumors, cerebral abscess, cerebral cysticercosis, idiopathic epilepsy, spinal neoplasm, and tuberculosis of the spine); 2. Cases with involvement of intrathoracic structure simulating chronic bronchitis, bronchiectasis, pulmonary new growth, lung tuberculosis, acute or chronic pleurisy with or without pleural effusion, chronic adhesive pericarditis, spontaneous pneumothorax, pyothorax, polyserositis, etc.; 3. Cases with involvement of intra-abdominal structures simulating chronic tuberculous peritonitis, chronic enterocolitis, chronic appendicitis, intestinal adhesions with or without obstructive symptoms, hepatitis, liver abscess, subphrenic abscess, perisplenitis, and renal tuberculosis or neoplasm; 4. Cases with involvement of the superficial lymph nodes, cutaneous or subcutaneous structures simulating localized inflammatory swelling of the lymph glands, the skin, or subcutaneous tissues. To ensure correct diagnosis of such clinical forms of paragonimiasis, particularly those without expectoration or with sputa containing no ova, we propose the application of three important diagnostic procedures in the study of all suspected cases as follows: 1. Epidemiological considerations; 2. Intradermal test; 3. Complement fixation test.

1. **Diagnostic importance of epidemiological data and considerations.** Epidemiological data are of paramount importance in the diagnosis of all infectious diseases. This is especially true in the diagnosis of all parasitic or endemic diseases. Since human paragonimiasis is contracted through eating raw or under-cooked crabs or crayfish containing metacercariae of *Paragonimus westermani* and since such infected crabs and crayfish usually occur only in endemic areas, it is most important in diagnosis to ascertain whether patients suspected of the disease come from endemic regions and whether they have the habit of eating raw or inadequately cooked crabs or crayfish. With the rapid development of modern communications, clinicians in nonendemic areas have to be ever alert to the possibility of meeting cases from infected areas. We believe that any

patient with a positive history of having eaten raw crabs or raw crayfish, particularly when the crustacea consumed were from endemic regions, should be considered as a potential case of paragonimiasis until proved to the contrary.

2. **Diagnostic importance of intradermal test for paragonimiasis.** In our experience(7,8) cases of paragonimiasis have invariably shown a strongly positive reaction to an intradermal injection with paragonimus antigen. Recently the intradermal test was used by us for screening paragonimiasis cases during surveys in endemic as well as in suspected areas. In one locality where 2,309 individuals were examined, 398 (17.2 per cent) were found to have paragonimiasis as evidenced by the positive intradermal test. Of these 398 patients with positive reaction, however, only 117 revealed ova in the sputum upon the first examination. Complement fixation tests of the sera collected at random from a group of these patients with positive intradermal reaction but with no ova in the sputum were done and they all showed a clear-cut positive complement fixation reaction. The disparity between the number of skin-test positive cases and that of sputum-positive cases, however, dwindled very rapidly in direct proportion to the number of examinations of sputum specimens collected at different times from the same patients, because most of the cases with positive skin-test but with negative sputum on the first examination eventually showed ova in the sputum when repeated examinations were made. Some of the patients actually had no sputum, and the so-called sputum specimens examined were saliva mixed with mere pharyngeal secretions. In such cases it was only natural that no ova could be found. It seems very clear that intradermal test with paragonimus antigen is a most valuable procedure for the diagnosis of paragonimiasis in clinical practice as well as in epidemiological surveys. According to our recent experience in Kwangtung province skin tests done with antigens made from adult worms of *Schistosoma japonicum* and *Clonorchis sinensis* separately were quite specific and useful.

3. **Diagnostic importance of complement fixation test of serum and spinal fluid for paragonimiasis.** We found that out of 51 inpatients with proved paragonimiasis whose sera were subjected to the complement fixation test, 50 cases or 98 per cent showed a clear-cut positive reaction and only 1 case or 2 per cent gave a negative result. The cerebrospinal fluids of 24 inpatients with cerebral paragonimiasis were also subjected to the same test, and 20 cases or 83 per cent showed a positive reaction and 4 cases or 17 per cent reacted negatively. On the other hand, the cerebrospinal fluids of paragonimiasis patients without cerebral involvement all gave a negative complement fixation reaction. It should be pointed out here that although the sera of some of the patients with clonorchiasis or leprosy also showed a positive complement fixation reaction, cerebrospinal fluids of these cases never gave a cross positive or a false positive reaction

with the paragonimus antigen. Hence it appears that the test is more or less specific for the diagnosis of cerebral paragonimiasis.

Through the application of the three diagnostic procedures above outlined we were able to diagnose correctly many difficult cases of paragonimiasis which would have been missed otherwise. Six of these cases, two with summaries of autopsy findings, are especially instructive and are here reported.

REPORT OF CASES

CASE 1. Patient Chuan, a 9 year old Korean schoolboy was admitted to the Central People's Hospital on October 28, 1954 for fever, headache and vomiting for six months. In the spring of 1953 he had been sent to a convalescent home in the northeast for "infiltrated pulmonary tuberculosis." In January 1954 he developed fever, mild headache, and vomiting. The symptoms became worse in May and the patient was occasionally in a state of coma. He was treated in a large hospital at Shenyang, where lumbar puncture showed the cerebrospinal fluid slightly turbid, and once "tubercle bacilli" were also said to have been found. His case was diagnosed as one of tuberculosis of the meninges. He was treated with 48 gm of streptomycin and rimifon of unknown dosage.

Physical examination showed that the patient was well developed and well nourished. The head organs, the heart and the lungs were normal. The neck was slightly stiff. The spleen and the liver were not palpable. Neurological findings were normal.

Laboratory findings. Erythrocytes 4,040,000. Hemoglobin 12 gm. Leukocytes 20,950. Eosinophils 20 per cent. Stool contained eggs of ascaris. Findings of cerebrospinal fluid were: appearance of ground glass, sugar positive for all five tubes—quantitatively 60 mg per cent, Pandy's test 4 plus, leukocytes 238 per cu mm, polymorphonuclear neutrophils 81 per cent, and chloride 735 mg per cent. The erythrocytic sedimentation rate was 15 mm at the end of one hour. Electrocardiogram showed normal findings.

Roentgenograph of the chest taken after the patient's admission showed no significant findings, and he was treated as a case of tuberculous meningitis. Rimifon orally and streptomycin intramuscularly and intrathecally were given. On November 19, the cerebrospinal fluid showed a reduction of leukocytes to 10 whereas Pandy's test was still positive. He was twice subjected to the intradermal test for paragonimiasis during hospitalization, and the results were strongly positive. The complement fixation tests of the serum and cerebrospinal fluid for paragonimiasis were also strongly positive. Repeated examinations of the cerebrospinal fluid, sputum, and gastric juice showed no paragonimus ova. A clinical diagnosis of paragonimiasis with cerebral involvement was finally made, and the patient was treated with chloroquine on November 18 at 0.225 gm daily by mouth gradually increasing to 0.45 gm. Eyeground examination on November 5 showed a bilateral edema of optic nerve head. However, re-examination made on November 31 showed normal findings. Roentgen examination of the chest made again on January 17, 1955 revealed a round, dense mass behind the cardiac shadow. Laminography of the chest on January 28 showed cavity formation not unlike that seen in paragonimiasis. By January 30, a total of 17.74 gm of chloroquine had been administered.

Beginning on January 30, 1955 the patient had headache and vomiting as well as convulsion once. On the following day he went into coma. Neurological examination revealed enlargement of the pupils with the right larger than the left. Reaction

to light was weak. Babinski's sign of both sides were normal. Kernig's sign of the right side was positive. Reflex of upper and lower limbs of both sides decreased. Pressure of cerebrospinal fluid was 290 mm. Leukocytes 4. Pandy's test 4 plus. Cardiac rate 140 per minute and rhythm weak. Emergency treatment was given without effect. The patient finally died on February 1, 1955.

PATHOLOGICAL EXAMINATION. Chest cavity. There were extensive fibrous adhesions between the lungs, chest wall, diaphragm, and pericardium as well as between the lobes of the lungs themselves.

Lungs. On the surface of the posterolateral aspect of the right lower lobe about 2 cm from the lower costal margin there was a horizontal band of fibrous thickening, moderately firm, measuring about 6 by 0.8 cm. On section it was found to contain a dry yellowish granular substance which microscopically was composed of necrotic tissue surrounded by fibrous tissue with infiltration of lymphocytes and a small number of leukocytes and foreign body giant cells. However, neither paragonimus ova nor parasites were observed. In the medial aspect of the left lower lobe four scattered lesions similar to the above were seen, the largest being 1 by 0.7 cm.

Brain. The two frontal lobes were not symmetrical, the right being larger, softer, with flattened convolutions and shallow sulci. The brain tissue of the left frontal lobe near the anterior third of the central sulcus was slightly depressed, dull and yellowish-red. Near the inferior sulcus there was a small amount of fibrinous exudate.

The left temporal lobe was soft and larger than the right, its sulci were shallow. Sections of the brain revealed the following:

a. Scattered necrotic lesions near the lateral side of the left frontal lobe (the largest measuring 0.4 by 0.3 cm) pale-yellow, and surrounded by dense fibrous tissue.

b. Scattered irregular intercommunicating necrotic lesions were seen at the posterior one third of the superior frontal sulcus of the right frontal lobe. These lesions had greyish-yellow coagulated material in the center. The largest measured 1 cm in diameter. The left ventricle was dilated.

c. The necrotic lesions in the right temporal lobe were even more extensive, occupying one third of the area in the coronal sections of the hemisphere. The lateral ventricle was compressed and reduced in size.

d. In the central part of the right temporal lobe the necrotic lesions were extensive. The basal ganglia, globus pallidus and claustrum were largely destroyed. The necrotic parts were close to the margin of the anterior branch of the internal capsule, the largest area of necrosis measuring 2 cm in diameter.

e. The lateral ventricles of the occipital lobes were all dilated, including the fifth ventricle.

Microscopic examination. The central portion of the necrotic area was stained red and was surrounded by several layers with different types of cells. The innermost layer contained small numbers of broken nuclei, the next layer contained granulation tissue, further out was a layer of dense tissue composed of fibrocytes and glia cells, and the outermost layer was infiltrated by many inflammatory cells composed of neutrophils, eosinophils, plasma cells, lymphocytes and phagocytes. In this region could be seen various numbers of ova, some of which were already surrounded or invaded by foreign body giant cells.

The right parietal lobe contained organized lesions in addition to necrotic foci, also containing ova. The meninges of the right parietal lobe were intimately adherent to the necrotic foci and they showed lymphocytic infiltration and ova.

The wall of the lateral ventricle in the left occipital lobe was also damaged. A few ova were seen in the ventricular cavity. The brain tissue surrounding the necrotic areas showed evidence of degeneration.

Pathological diagnosis. Paragonimiasis of brain; extensive necrosis of both frontal lobes, left temporal lobe, right parietal lobe; moderate hydrocephalus; old paragonimiasis of lungs; acute splenic tumor; slight fatty change of liver. Cause of death: extensive damage to the brain due to paragonimiasis. (There was no evidence of either pulmonary tuberculosis or tuberculous meningitis.)

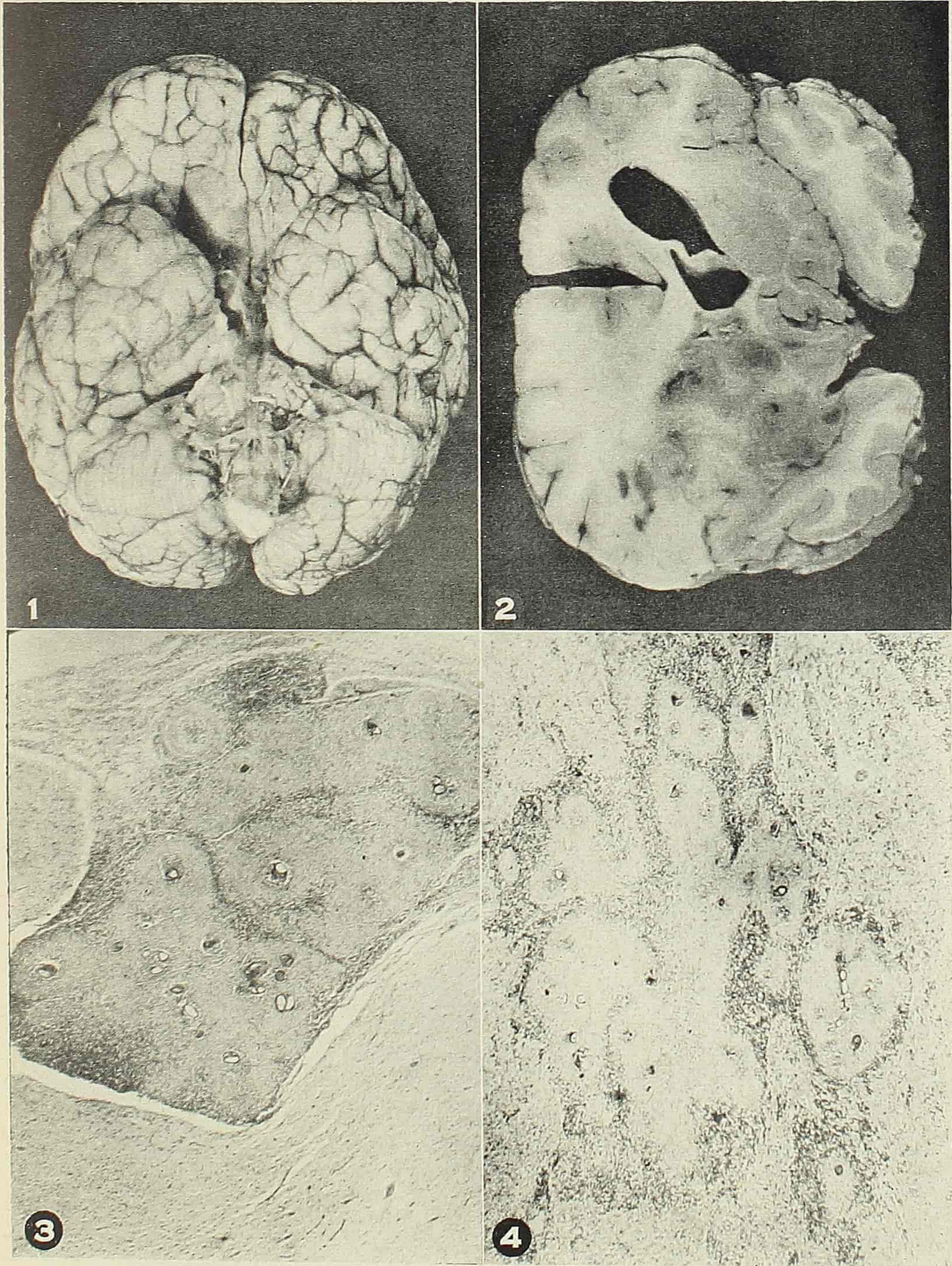
CASE 2. Patient Chin, a Korean boy, aged 12, was admitted to the Central People's Hospital on October 26, 1954 on account of fever, headache, vomiting, and attacks of convulsions for one month and a half. He was previously treated in a hospital at Yingkou. His cerebrospinal fluid showed: pressure 600 mm, cells 50-3,500 per cu mm, sugar 12.5 mg per cent, chloride 544.9 mg per cent, and pellicle formation twice. On October 13 tubercle bacilli were said to have been found in culture, and the patient was treated as a case of tuberculous meningitis with rimifon orally plus streptomycin intramuscularly and intrathecally but without any benefit. He was then sent to Peking for further investigation and treatment. The patient's past history was not known as he was a war orphan.

Examination on admission showed the following findings: moderately developed, and moderately nourished. Mentally clear. Neck slightly stiff. Heart and lungs normal. Liver and spleen were not palpable. Neurological examination revealed ptosis of left upper eyelid. Kernig's signs were positive on both sides. Eyeground examination showed slight edema of optic nerve head. Erythrocytes 3,700,000. Hemoglobin 12.5 gm. Leukocytes 8,800 with eosinophils 1-6 per cent. Urine and stool normal. Cerebrospinal fluid showed a pressure of 240 mm and 278 leukocytes of which 98 per cent were polymorphonuclear neutrophils, cerebrospinal fluid sugar was 37 mg per cent and chloride 684 mg per cent.

After admission the patient was treated with rimifon and streptomycin. On the fifth day of hospitalization, he suddenly developed high fever, lethargy, coma and incontinence of urine. Leukocytes in the blood were found increased to 27,000. The cerebrospinal fluid had a pressure of 330 mm, appeared cloudy, and contained 11,750 leukocytes per cu mm. Three days later the patient regained consciousness. By then the leukocytes in the spinal fluid were reduced to 175, but the spinal fluid sugar remained low at 25 mg per cent. Repeated examinations of the cerebrospinal fluid for tubercle bacilli including two animal inoculations were all negative. Roentgen examination showed no active lesions.

The patient after admission was subjected to paragonimus intradermal test and complement fixation tests of the serum and cerebrospinal fluid. The results were all positive. However, repeated examinations of the sputum, feces, and cerebrospinal fluid showed no parasite ova or tubercle bacilli. On November 12, the patient's left eyeball was found to show some limitation of movement. In the meantime the muscular tone of the upper and lower limbs of the right side was reduced and right-sided Babinski's sign and ankle clonus were demonstrated. Thereafter the patient often became lethargic and frequently vomited. The size of his pupils and their reaction to light varied from time to time. He was finally diagnosed as a case of paragonimiasis with cerebral involvement. He began to receive chloroquine treatment on December 4. Electrocardiogram done on December 27 revealed changes suggesting myocardial change. By December 31, 1954, the total dose of chloroquine given was 5.94 gm. The treatment was stopped as the patient showed signs of general muscular weakness. Exploratory craniectomy and a decompression operation to relieve intracranial pressure were considered, but the patient was too ill to be operated upon. His general condition became progressively worse and his visual power showed rapid deterioration. State of coma set in and eventually the patient died on January 12, 1955.

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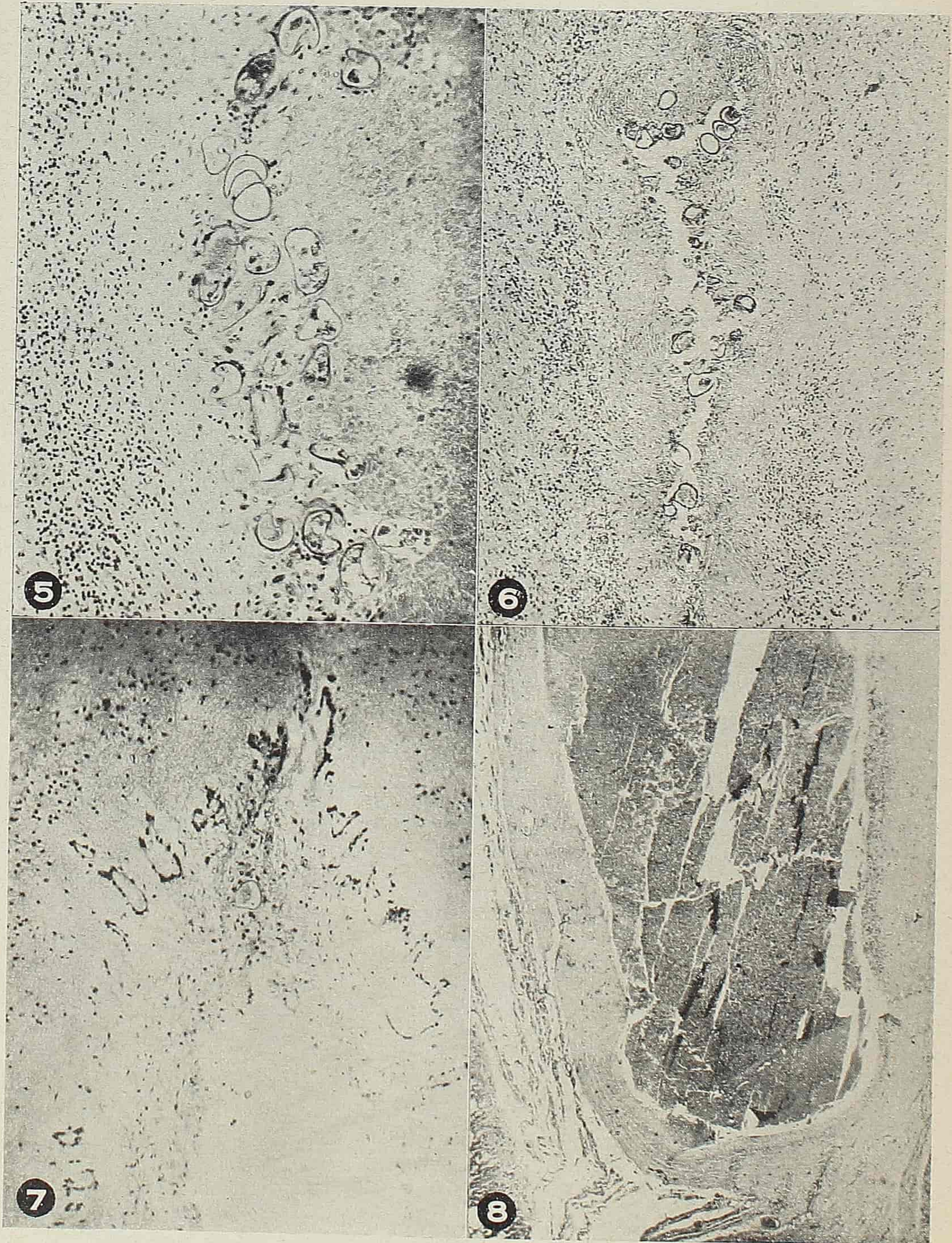
(Case 1)

Fig. 1. The right hemisphere is larger and its convolutions are flatter than those of the left. Fig. 2. The right temporal lobe showing fresh hemorrhages and old foci of necrosis. Fig. 3. Lesions in the meninges with ova. $\times 20$. Fig. 4. Lesions in the brain substance containing ova. $\times 20$.



RECENT ADVANCES IN DIAGNOSIS OF PARAGONIMIASIS

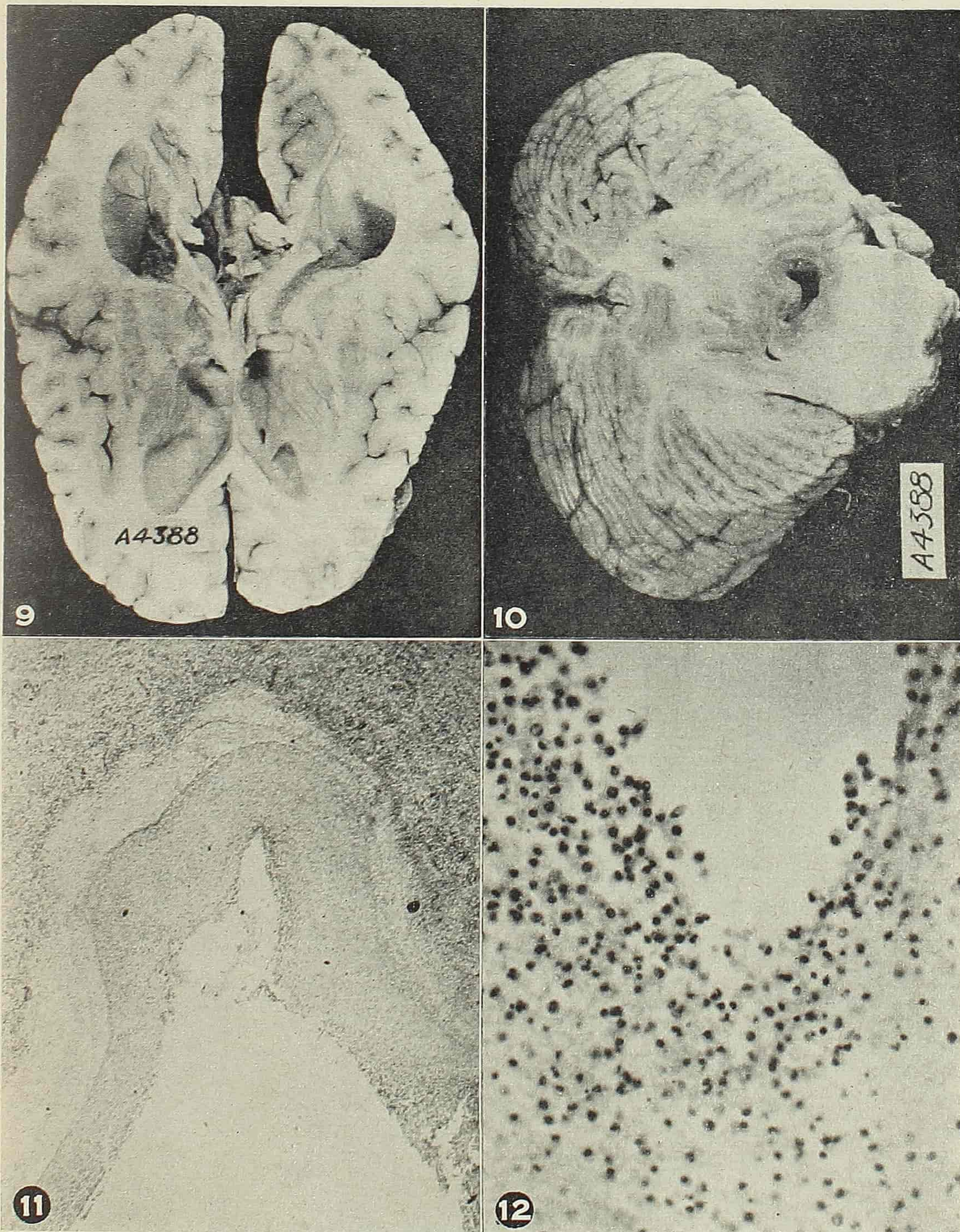
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(Case 1)

Fig. 5. Ova at the edge of the necrotic focus in the brain. $\times 125$. Fig. 6. An old focus in the brain, containing ova. $\times 55$. Fig. 7. The ependyma of the fourth ventricle of the pons, showing gliosis and regeneration of the ependyma cells underneath. One ovum present in the area of gliosis. $\times 100$. Fig. 8. An old lesion in the lung (produced by the worm). $\times 10$.

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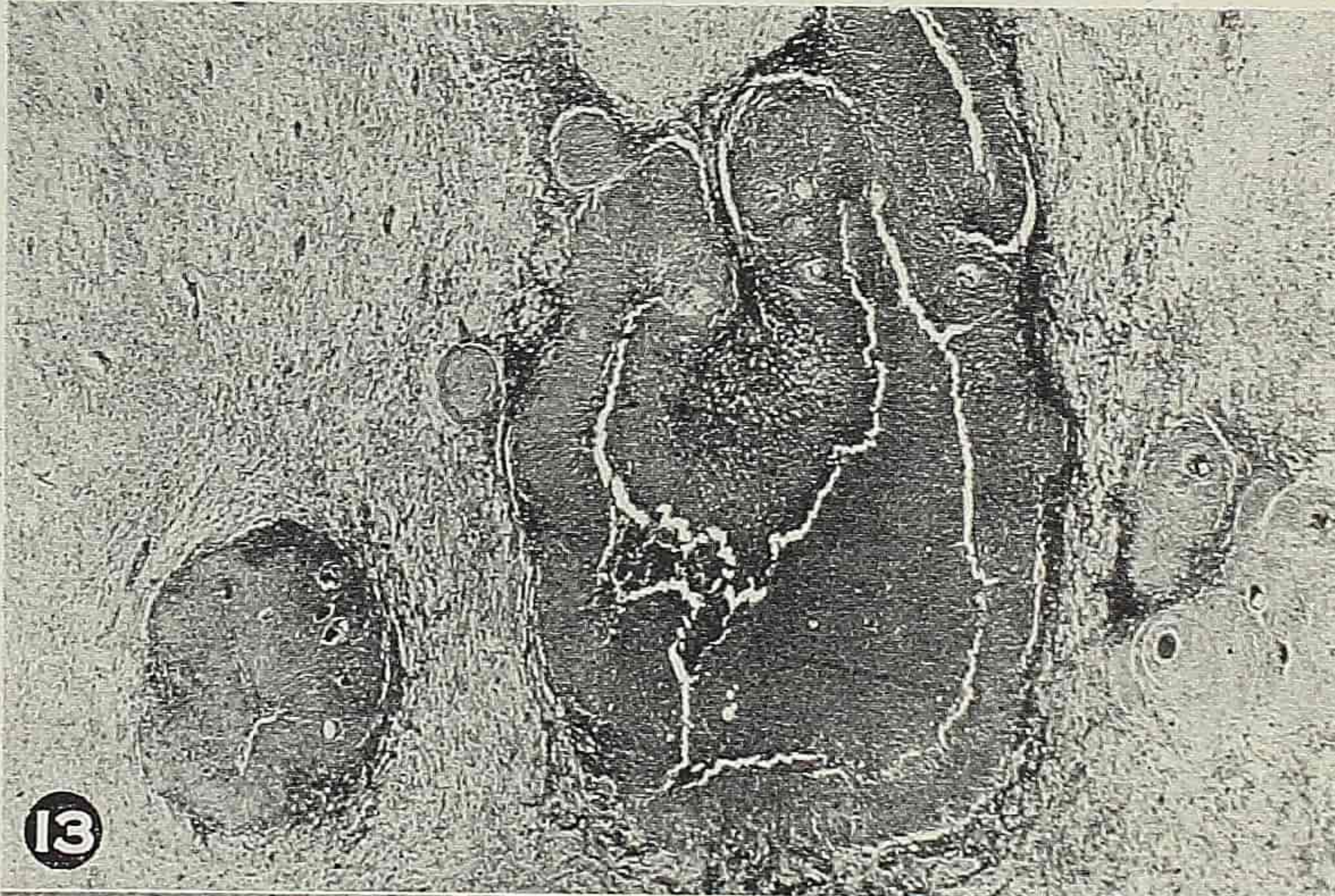


(Case 2)

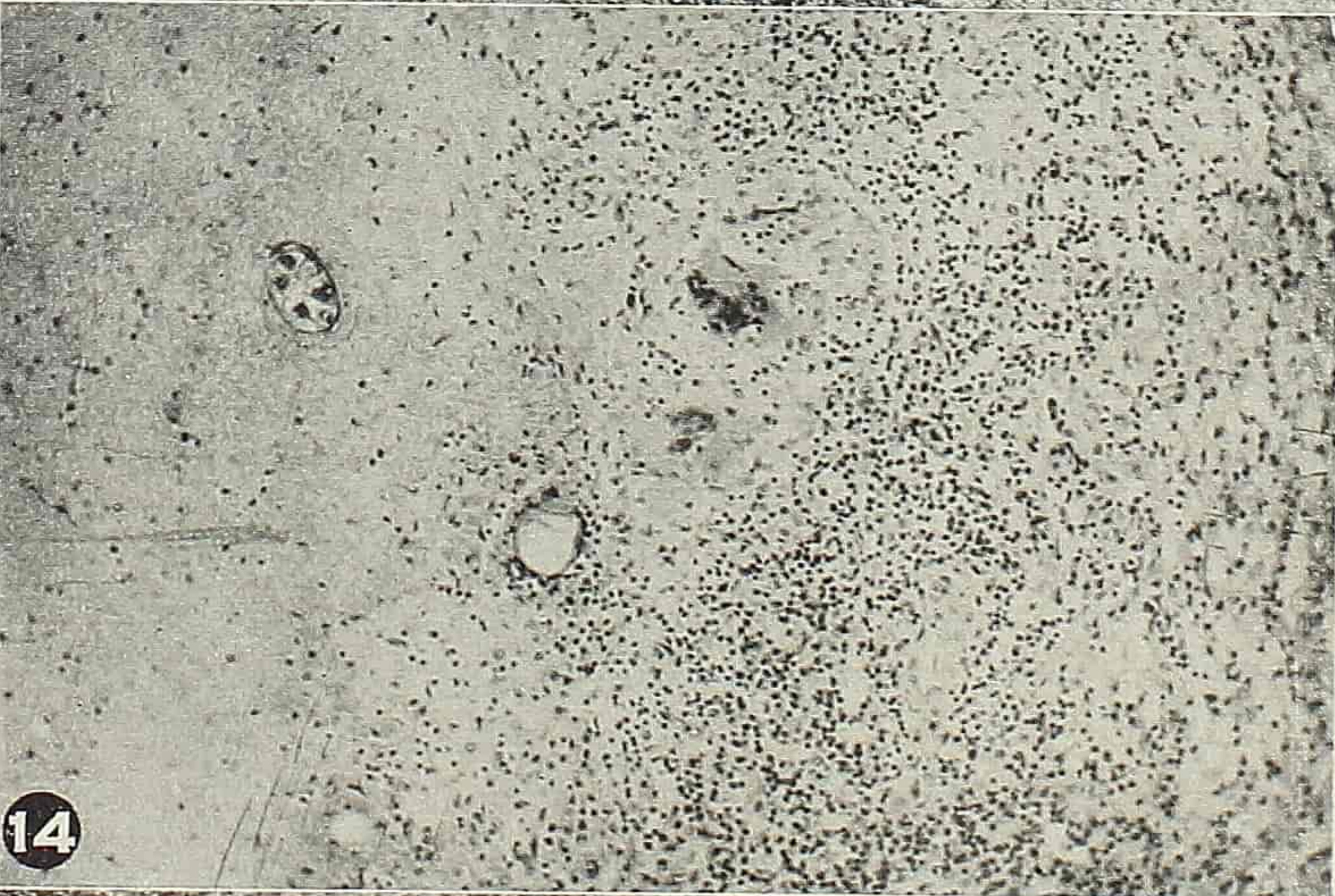
Fig. 9. Showing necrotic lesions in the left frontal lobe. Fig. 10. Abscess of the cerebellopontine region. Fig. 11. Wall of the abscess of the cerebellopontine region. $\times 22$. Fig. 12. Exudate on the surface of the abscess wall shown in Fig. 11. $\times 320$.

RECENT ADVANCES IN DIAGNOSIS OF PARAGONIMIASIS

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13



14



15

(Case 2)

Fig. 13. Old necrotic focus in the frontal lobe. $\times 5$. Fig. 14. Lymphocytic infiltration in the zone surrounding necrotic area. There are also a few ova and slight leukocytic infiltration and fibroblastic proliferation. Fig. 15. Small focal lesions with many ova in the brain. Marked lymphocytic infiltration at the periphery. $\times 20$.

PATHOLOGICAL EXAMINATION. Chest cavity. There were extensive fibrous adhesions between the right lung, chest wall, diaphragm and pericardium, and between the left upper lobe and the lingula.

Lungs. A triangular scar was present about 1 cm from the lower margin of the left upper lobe. On section it showed an old fibrous tubercle.

Brain. Fibrous adhesions were present in the meninges of the anterior portion of the left frontal lobe. The surface of the left frontal lobe was rather soft, and the sulcus shallow.

Sections of the brain showed dilatation of both lateral ventricles. The foramen of Monro was 1.3 cm in diameter. The inner surface of the ventricles was smooth and glistening.

There were five abscess-like lesions in the anterior end of the left frontal lobe, the largest measuring 1.2 by 0.8 cm.

In the calcarine fissure of the left occipital lobe were scattered smaller lesions of the same kind.

The left half of the midbrain was enlarged with loss of its normal structures. There was a tunnel-like cavity at the lateral margin of the central part of the midbrain, containing dark yellowish pus-like material. Near the medial end of the tunnel there was another tunnel, 1.7 by 0.3 cm, containing a degenerated grayish parasite. The aqueduct of Sylvius was compressed.

There was an abscess measuring 1.5 cm in the superior reticular formation of the pontine nucleus.

Microscopic examination. The microscopic changes of the above mentioned lesions were similar to those of Case 1. Ova were also found.

In the left cerebellum, in the region of the dentate nucleus, there was a soft lesion measuring 0.7 by 0.5 cm; 1.5 cm below this lesion there was an abscess, measuring 1.5 by 0.6 cm, which extended from the vicinity of the fourth ventricle below to the margin of tonsillar lobe above.

Pathological diagnosis. Extensive fibrous adhesions between the right visceral pleura, the entire right chest wall, the diaphragm and the outer surface of the pericardial sac. Abscess formation in the left frontal lobe, midbrain, pons, and cerebellum with moderate hydrocephalus. Some acute splenitis and fatty degeneration of liver. Cause of death was extensive necrosis of brain tissue due to paragonimiasis. (No evidence of tuberculous meningitis.)

CASE 3. Chiang, a Korean schoolboy of 14 was admitted on March 26, 1954 for intermittent pulsating pain of the forehead since April, 1953. Simultaneously he felt pain in both thighs and knee joints. After resting for three to four days he became better. However, about a month later he developed paroxysmal headache and illusion of seeing flying flies. He also frequently had abdominal pain with watery stools two to five times per day without blood or pus. In July 1953 he entered a hospital in Changchun for treatment on account of fever, cough and expectoration of yellowish-white sputum with blood streaks. By January 1954 the patient had developed numbness of the right upper extremity. The grip of the right hand was weak. A sudden attack of mental confusion accompanied by stiffness of the extremities appeared and lasted about five minutes. The same symptoms occurred several times later and were associated with incontinence of urination and white foam from the mouth. There was no convulsion or biting wound of the lips and tongue. The patient had severe headache after each attack. Prior to hospitalization, he had often had headaches but only occasional cough with



little sputum. He had not been treated previously with either antimony preparations or emetine hydrochloride.

Physical examination on admission. Body temperature 37.3 C. Body weight 64 pounds. Moderately developed and nourished. The patient was mentally clear but depressed. Skin normal. No general edema of lymph glands. Pupils were equal with normal reaction to light. Mild trachoma O.U. Ears, nose, and throat were all normal. Neck slightly stiff. No cardiac enlargement. No murmurs. Blood pressure 100/56 mm of mercury. Lungs clear. Abdomen flat without tenderness. Liver and spleen were not palpable. No fluid was found in the abdomen. The spine, the extremities, the rectum, the genitalia, and the tendon reflexes were all normal.

Neurological findings. Cranial nerves including visual field and eyeground examinations were normal. The deep and superficial sensations in general were also normal. The right upper and lower limbs showed a weakness of muscular tone without atrophy. Chaddock's and Babinski's signs were positive on both sides.

Laboratory findings. Hemoglobin 14 gm. Erythrocytes 4,410,000. Leukocytes 5,850. Neutrophils 40 per cent. Lymphocytes 38 per cent. Eosinophils 16 per cent. Monocytes 6 per cent. Urine normal. The thymol turbidity test showed a reading of 8 Maclagan units. Non-protein nitrogen 26 mg per cent. Cholesterol 218 mg per cent. Plasma albumin 4.62 gm per cent and plasma globulin 2.32 gm per cent. Blood sedimentation rate normal.

On the second day of admission roentgenography revealed a normal skull. A chest film showed a few nodular shadows with irregular calcified spots in the upper region of the right hilum. Cardio-diaphragmatic angle also showed irregular nodular shadows. Electrocardiogram showed normal findings. Cerebrospinal fluid was clear and colorless. Pandy's test negative. Sugar positive in all five tubes. Total cells 4. Leukocytes 2. Paragonimiasis complement fixation tests of the serum and the cerebrospinal fluid were negative. Repeated examinations of sputum and feces showed no paragonimus ova. Nor was tubercle bacillus found in the sputum. However, Charcot-Leyden crystals were found. On April 6 an intradermal test with paragonimus antigen (1:250) gave a strongly positive reaction. On April 22 and May 3 a few paragonimus ova were found in the sputum, and diagnosis of paragonimiasis was established.

The sputum of the patient had been repeatedly examined but no eggs of the parasite were found. Paragonimiasis complement fixation tests of the serum and the cerebrospinal fluid were both negative. The fact that the patient had lived in an endemic area of paragonimiasis, the positive intradermal test, the eosinophilia and the presence of Charcot-Leyden crystals in the sputum all confirmed the diagnosis of paragonimiasis.

The sputum was examined daily with the concentration method for paragonimus ova, and only on the twenty-eighth day and thirty-third day after admission were a few ova found. Thus it is clear that odd cases of paragonimiasis with a negative complement fixation test and absence of paragonimus ova can be diagnosed by means of epidemiological data and the intradermal test.

CASE 4. Patient Hsieh was a male of 28 and native of Hopei. He went to Korea in March 1951 and returned in March 1954. During his stay there he had eaten half-cooked crabs and drunk unboiled water. He began to have cough with dark red blood clot and occasionally blood streaks since March 1953. Half a month later the symptoms disappeared. He had no chest pain, fever or dyspnea. However, in August of the same year, he felt ill again with pain in the right upper chest

and afternoon fever. He recovered spontaneously after a week. In June 1954 he was fluoroscoped at the hospital where he worked and was found to have pleural fluid in the right chest cavity. He was admitted to the Central People's Hospital on October 29, 1954 for cough and hemoptysis.

Physical examination. Well developed and well nourished. Skin normal. No general glandular enlargement. Left submaxillary lymph glands were palpable and tonsils enlarged. Trachea was in the middle. Slight dullness was found in the right upper chest and dullness from the seventh thoracic vertebra downward. Respiratory sound was diminished. No rales. The heart was normal. The liver was found to be enlarged one finger breadth below the right costal margin. The spleen was just felt. Knee jerks normal. Body temperature 36 C. Blood pressure 118/70. Hemoglobin 14.8 gm. Leukocytes were 6,700 with 71 per cent of polymorphonuclear neutrophils and 4 per cent of eosinophils. Urine and stools were normal; the latter contained no ova. EKG showed suspicious evidence of incomplete right bundle-branch block and myocardial damage. X-ray of chest showed evidence of right-sided pleurisy with effusion. Tubercle bacilli were found in the sputum. Repeated examinations of the latter failed to show paragonimus ova. Clinical diagnosis: pulmonary tuberculosis and tuberculous pleurisy with pleural effusion. In view of the fact that the patient had been to endemic areas of paragonimiasis, the serum complement fixation test and the intradermal test for paragonimiasis were done. The results of both tests were strongly positive. Further examinations of the sediments of the pleural fluid showed presence of paragonimus ova. The patient was therefore suffering not only from pulmonary tuberculosis but also from paragonimiasis. The latter diagnosis would have been missed if the three diagnostic methods had not been used.

CASE 5. Patient Hsi, a male of 27 from Shansi province, began to have frequent dull pain around the umbilicus and severe attacks of hematemesis in the spring of 1951. The symptoms became worse in 1952 and he was unable to work. However, he had neither cough nor chest pain. In 1953 his stool was found to contain blood. He had been treated elsewhere in two different hospitals on many occasions as a case of peptic ulcer without any success. In the same year two small intra-abdominal masses were found on the left side of the umbilicus and the patient vomited blood. His lungs were normal. On January 17, 1955 he was admitted to the Chinese Union Medical College Hospital for severe abdominal pain.

Examination on admission. Development and nutrition normal. Chest not remarkable. Tenderness over right side of abdomen. An elongated mass was felt in the left umbilical area. Liver edge was just palpable. Other findings were normal.

During hospitalization, the patient was subjected to x-ray examination of the chest, bronchoscopy, biopsy of lymph nodules, examination of gastric juice and bile fluid, liver function test, cholecystography and rectal biopsy. The results were all normal. There was no sputum. Repeated examinations of the stools for paragonimus ova gave negative results. Except for an increase of eosinophils to 45 per cent, the blood picture was normal. Because of the unexplained eosinophilia the patient was subjected to the intradermal test and the complement fixation test of the serum for paragonimiasis. Unexpectedly, both results turned out to be strongly positive. Our attention was therefore focused on the diagnosis of paragonimiasis. On being further questioned, the patient admitted that on four different occasions from April to July 1950 he had eaten raw crabs caught from a brook in Wenkiang district some 20 miles from Chengtu in Szechuan province. Each time he ate 2 or 3

crabs. Seven or eight months later he developed abdominal pain and "hematemesis." Thus it appeared almost certain that the patient had paragonimiasis infection.* An additional epidemiological evidence in favor of the diagnosis of paragonimiasis was the fact that according to the medical literature (12), cats and dogs in Chengtu had been found to harbor lung flukes indistinguishable from *Paragonimus westermani*. The patient responded well to a subsequent course of chloroquine therapy which abolished all abdominal signs and symptoms and restored the blood picture to normal. This gratifying therapeutic result following specific treatment constitutes a further proof that the patient had paragonimiasis.

CASE 6. Patient P'eng, a girl of 18 from Kirin province, was transferred to the Central People's Hospital for further observation from another hospital in Peking in January 1955 for severe headache and vomiting. The results of our intradermal test and complement fixation test of the serum for paragonimiasis were both strongly positive. Complement fixation test of the cerebrospinal fluid was, however, negative. Earlier specimens of cerebrospinal fluid before the complement fixation test was made showed marked increase of eosinophils which gradually disappeared within two weeks. No sputum. Roentgenogram of the chest showed normal findings. (Detailed account of this case particularly in respect of the relationship between eosinophilia and paragonimiasis will be reported separately). Careful questioning showed that the patient had always lived at Yenpien in Kirin province, where the people have the habit of eating a kind of raw crayfish called Laku. In the past the patient herself had often eaten uncooked crayfish. It seems practically certain that all her symptoms were caused by paragonimiasis. Following the discovery of this case, a brief epidemiological survey was made at Yenpien, which confirmed that the locality is an endemic area of paragonimiasis hitherto unknown.

It is clear from the above cases, particularly Case 5 and Case 6 that we can determine, without our actual presence, new areas of paragonimiasis if full use of the three diagnostic methods are made. Szechuan and Kirin provinces from where no paragonimiasis cases have been reported before are now considered as endemic regions. Undoubtedly, these methods when extensively adopted will be very useful in investigating the epidemiology of paragonimiasis in all suspected or endemic areas.

SUMMARY AND CONCLUSION

1. Three procedures constituting an advance in the diagnosis of paragonimiasis particularly in cases with obscure, atypical, early, latent or inapparent infection without discharge of ova in excreta are presented.

2. Six very obscure cases are reported to illustrate the value of the new diagnostic triad.

* A recent survey made by us in Wenkiang district of Szechuan province has actually implicated that district as a paragonimiasis infected area. Details of this survey will be published later in the Chinese Medical Journal.

3. Summary of the main autopsy findings of 2 very instructive cases (Case 1 and Case 2) are given in some detail. The postmortem findings have fully proved the value of these diagnostic procedures and the un-wisdom of relying too much on the findings of certain highly specialized laboratory methods of diagnosis. In these 2 cases the roentgenological findings of the chest, the electrocardiographical changes, and the reported discovery of "tubercle bacilli" in the cerebrospinal fluid, obviously due to laboratory error, were disproved by the autopsy findings. Both the patients had no tuberculosis either of the lungs or the meninges but had paragonimiasis with fatal cerebral involvement and adhesions between the chest wall, the lungs, the pericardial sac and the diaphragm.

4. Two new endemic areas of paragonimiasis were discovered through the diagnosis of 2 exogenous cases (from Kirin and Szechuan provinces) seen in Peking. These cases would have been missed had it not been for the fact that the new diagnostic triad was carefully applied.

5. The proposed diagnostic triad constitutes a very useful weapon in surveys of and campaigns against paragonimiasis, as it facilitates early and accurate diagnosis. According to our recent experience in Kwangtung province the same principles, particularly the skin test, may be applied with advantage in surveys of and campaigns against parasitic diseases like schistosomiasis, clonorchiasis, etc.

6. The intradermal test is a very convenient and fairly reliable procedure for screening paragonimiasis cases in epidemiological surveys. Only skin-test positive cases need be subjected to sputum examination for paragonimus ova and serum complement fixation test.

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THE COMBINED USE OF PUMPKIN SEED AND ARECA NUT IN THE TREATMENT OF TAPEWORM INFECTIONS

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INTRODUCTION

Areca nut is found in anthelmintic prescriptions in old Chinese medical literature published more than twelve hundred years ago. For centuries it has been employed either in combination with other drugs or alone for the treatment of tapeworm infections. In 1936 Liu(1) first advocated the use of this remedy in the treatment of tapeworm infections in modern medicine in China. In 1949 Feng and his associates(2) first made investigations on the action of areca nut on tapeworms and found that areca nut had, in varying degrees, a paralytic effect on *Taenia solium*, *Taenia saginata* and *Hymenolepis nana*; the last named species being the most sensitive to the action of the drug, *T. solium* the next and *T. saginata* the least. In a 1-2 per cent extract of areca nut in normal saline, *H. nana* was found paralyzed almost instantaneously. In the same solution, the period from the time the head of *T. solium* lost its power of attachment to the time the head and immature segments became paralyzed was three to ten minutes; while with *T. saginata* the period was three to twelve minutes. The action of areca nut extract on the gravid segments of *T. solium* and *T. saginata* was less marked, as they became flaccid in ten minutes and twenty-five minutes respectively. Although the gravid segments of both species became flaccid under the influence of areca nut extract, they were never completely paralyzed, and the residual activity was more marked in *T. saginata* than in *T. solium*.

Beside the extract, Feng and his associates also prepared an areca bismuth compound which proved effective in the treatment of *Taenia taenaeformis* and *Dipylidium caninum* infection in a cat.

Feng(3) in 1950 further investigated the therapeutic effect of areca nut decoction, areca nut extract and areca bismuth compound in the treatment of human tapeworm infections. The results demonstrated clearly the difference in the therapeutic effect of areca nut preparations in *T. solium* and *T. saginata*. He treated 22 cases of *T. solium* infection with different areca nut preparations—decoction in 6 cases, extract in 10 cases,

and areca bismuth iodide compound in 6 cases—and all were completely cured, while among 16 cases of *T. saginata* infection only 5 cases were cured. It was concluded therefore that areca nut might be considered a specific for *T. solium*, while with *T. saginata* the therapeutic effect was only about 30 per cent effective. In recent years, through clinical application in this country, other authors have also proved that areca nut is more effective in the treatment of *T. solium* than *T. saginata* infections. In 1951 Chung and others(4) reported the cure of 32 out of 34 cases (94.1 per cent) of *T. solium* infection treated with areca nut, but in their 26 cases of *T. saginata* infection only 13 or 50 per cent were cured. In 1954 Wang(5) reported on 106 cases of *T. saginata* infection treated with the same remedy, among which 50 cases or 47.2 per cent were successful.

With regard to the therapeutic effect of areca nut on human cases of *Hymenolepis nana* infection, Feng(3), Hsü(6) and Wang(7) have all obtained good results.

Areca nut has also been found efficacious by Chang(8), Fu(9) and Chia(10) in the treatment of *Diphyllobothrium latum* infection and by Wu and Chen(11) in *Fasciolopsis buski* infection.

To sum up, areca nut is very effective for *T. solium*, *Hymenolepis nana*, *Diphyllobothrium latum* and *Fasciolopsis buski* infections. It is also useful in the treatment of *T. saginata* infection, but the rate of cure is only about 30-50 per cent. Although *T. saginata* is less dangerous than *T. solium*,* yet the infection with the former is more widely distributed. The population in some localities is heavily infected with *T. saginata*. For example, in one district in Sik'ang reported by Wang(5), among 150 Tibetans examined 106 were found to harbor the parasite. Furthermore, *T. saginata* infection lasts very long; many of our patients had a history of twenty or more years. Hence, further research is needed to increase the rate of cure in the treatment of *T. saginata* infection.

The use of pumpkin seeds in the treatment of tapeworm infections is found in the literature, but the effectiveness and pharmacological action of the remedy do not seem to have been carefully investigated. Krayer(12) appears to have given the most detailed account of this drug. According to him pumpkin seeds are widely used for the treatment of human tapeworm infections in the East, especially Lebanon. He pointed out that in most cases a greater part of the worm passed out but the scolex was seldom found. This happened with his treatment of 5 cases each with 30-35 gm extract of pumpkin seed that was equal to 600 gm of the seed.

* *T. solium* is more dangerous in that its larval stage, *Cysticercus cellulosae*, also occurs in man. A person harboring this tapeworm is not only a potential danger to himself but also to the community. The occurrence of *Cysticercus bovis*, the larval stage of *T. saginata*, in man has not yet been definitely established.

He stated that all the 5 patients were cured, because fecal examination two years later showed that no eggs and no more segments were passed out. The species of the worm was not mentioned. In recommending treatment with pumpkin seeds he emphasized the importance of using large doses of 200-400 gm for children and 400-700 gm for adults.

In the last three years we have investigated the mode of action of pumpkin seeds on tapeworms by making experimental and clinical investigations. Our results show that while pumpkin seeds have also a paralytic effect on tapeworms, their mode of action is quite different from that of areca nut. Pumpkin seeds act chiefly on the posterior part of the worm and areca nut on the anterior part. This being so, the combined use of pumpkin seeds and areca nut in the treatment of tapeworm infections (especially *T. saginata*) gives a high percentage of cure. The present paper is a report on the result of this investigation.

MATERIAL AND METHODS

The investigation consisted of two parts, namely: 1. to ascertain the action of pumpkin seeds on tapeworms by in vitro tests, 2. to use different preparations of pumpkin seeds and areca nut singly or in combination in the treatment of human cases.

The areca nut used was in slices purchased from traditional Chinese drugstores. Decoction with water was prepared. The decoction was sometimes titrated with a freshly prepared 2.5 per cent solution of gelatin to remove the tannin which has an irritative property. After filtration, the clear amber colored solution was reduced by evaporation to its original volume and used for in vitro tests or on clinical cases. About 15 gm of gelatin is required for each 500 gm of areca nut(2).

With regard to pumpkin seeds, the material usually recommended in the literature is raw seeds. We used, however, roasted seeds* which are easily obtainable from grocery shops. (Roasted pumpkin seeds are popularly served in tea shops along with water melon seeds.) The husks were removed and the kernels were used either as they were or after being ground up into a fine powder. Sometimes, pumpkin seed powder was boiled in water for about half an hour and filtered, and the filtrate was used for in vitro tests or clinical trials. Oil-free powder of pumpkin seeds was obtained by removing the oil through ether extraction. Decoction was prepared with the oil-free powder; it was filtrated and then used for in vitro tests or clinical trials.

In the treatment of clinical cases, whole kernels of pumpkin seeds, powdered whole kernels, oil-free powder, the filtrate of decoction, and

* Roasting of pumpkin seeds is done somewhat similarly as chestnuts are roasted in China. The seeds are mixed with sand and are heated in an open metal container.

pumpkin seed oil were used. In all in vitro experiments with either the decoction of pumpkin seed or areca nut, a proper amount of sodium chloride was added to make the solution isotonic.

During the whole course of the investigation, the results of the in vitro tests and of the treatment of the human cases were closely correlated from time to time, so that improvement in the procedures may be made in time. The results of treatment of human cases are given first.

THE TREATMENT OF HUMAN CASES

Pumpkin seed and areca nut either alone or in combination were used in the treatment of 185 cases, of which 165 were *T. saginata* and 20 were *T. solium* infections. As hospitalization was found unnecessary, all the cases were treated as outpatients. In order to find out the therapeutic effect of pumpkin seeds, the cases treated were arranged in several series. The aim being chiefly to improve the method of treating *T. saginata* infection, our cases were mostly patients infected with this parasite. However, we treated also a few cases of *T. solium* infection for comparison. Of the 185 cases, only a few required treatment more than once; those deserving special mention are recorded as illustrative cases.

In all the cases the administration of the anthelmintics was followed by a dose of saline purgative of 60 cc of 50 per cent magnesium sulphate.

The criteria for cure were: 1. the passing out of complete worms including the scolex, 2. no worm segments in the feces for at least three months after treatment.

1. **Cases with *T. saginata* infection.** The cases are divided into 8 series according to the method of treatment as follows:

a. *Pumpkin seeds alone.* Whole pumpkin seed kernels 120 gm taken by mastication, followed three hours later by magnesium sulphate given by mouth. Nine patients were treated and only 1 was completely cured. In some of them only gravid segments were passed out, in others parts of the worm broken by pulling were passed out, and in still others neither gravid segments nor parts of the worm were found. Subsequently, we learned through inquiry by mail that all the 8 patients had gravid segments in their stools as a result of their treatment.

b. *Areca nut and pumpkin seeds taken at the same time.* Areca nut 50-100 gm,* pumpkin seed kernel 50-120 gm.** The pumpkin seeds were

* The dosage of areca nut varied according to age and constitution of the patients treated. In general, the dosage was of 3 kinds, 50, 80 and 100 gm. For children under 10 years 30 gm or less were used. In all cases where decoction was used, it consisted of 150-200 cc.

** At the beginning of this investigation, 120 gm was used. Later it was reduced to 50 gm, as it was found that the results were about the same.

taken first by mastication, followed immediately by areca nut decoction. One hour later a dose of magnesium sulphate was given. Forty cases were treated in this series, among which 27 were completely cured.

c. *Areca nut and pumpkin seeds taken at intervals.* Areca nut 30-100 gm, pumpkin seed kernel 60-125 gm. First the seed kernels were taken by mastication, three hours later areca nut decoction was taken and still half an hour later a dose of magnesium sulphate. Thirty-eight cases were treated in this series, of which 35 cases resulted in complete cure.

d. *Areca nut and pumpkin seed powder taken at intervals.* Areca nut 80 gm, pumpkin seed kernel powder 50 gm. Pumpkin seed powder was taken first followed two hours later by areca nut decoction and another half an hour later by a dose of magnesium sulphate. In this series, 12 cases were treated and all resulted in complete cure.

e. *Oil-free pumpkin seed powder and areca nut.* Areca nut 80 gm, oil-free pumpkin seed powder 50 gm.* The oil-free pumpkin seed powder was taken first, then two hours later the areca nut decoction and after another half an hour a dose of magnesium sulphate. Of 46 cases treated in this series, 43 were completely cured.

f. *Areca nut and filtrate of decoction of oil-free pumpkin seed powder.* Areca nut 80 gm, filtrate of decoction of 50 gm oil-free pumpkin seed powder. The oil-free pumpkin seed was boiled in water for half an hour and filtered with filter paper. The filtrate amounted to about 50 cc. The areca nut decoction was taken first, then the pumpkin seed filtrate one hour later, and a dose of magnesium sulphate after another interval of half an hour. Nine cases were treated in this series and 8 were cured.

g. *Areca nut and pumpkin seed powder residue taken at intervals.* Areca nut 80 gm and the residue of boiled pumpkin seed powder left from filtration in series f, 40 gm. First the residue of pumpkin seed was given, then areca nut decoction two hours later, and a dose of magnesium sulphate after another interval of half an hour. Four cases were treated in this series and all of them were cured.

h. *Areca nut and pumpkin seed oil taken at intervals.* Areca nut 80 gm, pumpkin seed oil 30 cc. The oil was extracted in the course of obtaining oil-free powder used in series e. The oil was first given, areca nut decoction after two hours, and a dose of magnesium sulphate half an hour later. Seven cases were treated in this series and 3 were cured.

To facilitate comparison, the results of treatment of the above-mentioned 8 series of cases are summarized in Table 1. From this table

* The pumpkin seed contains about 30 per cent oil. The powder was extracted with ether, and the oil-free powder and oil were used separately in order to ascertain which portion contains the active principle.

it will be seen that pumpkin seeds when used alone have only little anthelmintic effect; in none of the cases treated was the entire worm expelled. Of the 9 patients treated with this drug, only 1 was completely cured; the remaining 8 patients passed gravid segments again later. Pumpkin seed oil is also not effective. In the series in which it was used

Table 1. Results of treatment of 165 cases of *T. saginata* infection

Series	Kind of preparation	Method of administration	Dosage (gm)	Interval between last drug and MgSO ₄ (hour)	No. of cases treated	No. of cases cured	No. of cases failed	Rate of cure (%)
a	Pumpkin seed kernels only	Whole kernels by mastication	Seed kernel 120	3	9	1	8	11.11
b	Pumpkin seed kernel and areca nut decoction	Whole kernel by mastication, areca nut decoction at same time	Seed kernel 50-120 Areca nut 50-100	1	40	27	13	67.50
c	" "	Seed kernel by mastication, 3 hours later areca nut decoction	Seed kernel 60-125 Areca nut 30-100	0.5	38	35	3	92.10
d	Pumpkin seed kernel powder and areca nut decoction	First take seed powder, 2 hours later areca nut decoction	Whole kernel powder 50 Areca nut 80	0.5	12	12	0	100.00
e	Oil-free pumpkin seed kernel powder and areca nut decoction	First take oil-free seed powder, 2 hours later areca nut decoction	Oil-free kernel powder 50 Areca nut 80	0.5	46	43	3	93.48
f	Decoction of oil-free pumpkin kernel powder and areca nut decoction	Areca nut decoction first, 1 hour later decoction of pumpkin seed powder	Areca nut 80 Oil-free kernel powder 50	0.5	9	8	1	88.88
g	Pumpkin seed powder residue and areca nut decoction	First take seed powder residue, 2 hours later areca nut decoction	Kernel powder residue 40 Areca nut 80	0.5	4	4	0	100.00
h	Pumpkin seed oil and areca nut decoction	First take oil, 2 hours later areca nut decoction	Seed oil 30 Areca nut 80	0.5	7	3	4	42.85

the rate of cure was only 42.85 per cent. This result was probably due to the effect of areca nut, because with its use alone a cure rate of 30-50 per cent is obtainable. It seems, therefore, that the active principle of anthelmintic property of pumpkin seed is contained in the oil-free portion, and that it is water-soluble. This is evidenced by the result of treatment

with the filtrate of boiled pumpkin seed powder as given in series f, which gave a rate of cure of 88.88 per cent. The 4 cases treated with the residue of boiled pumpkin seed also resulted in complete cure. Though the number of cases in this series was too small, it indicated nevertheless that the active principle was not completely removed by boiling in water.

Greater anthelmintic effect can only be obtained when pumpkin seeds and areca nut are used in combination. After pumpkin seeds are taken, time must be allowed for the anthelmintic to act inside the intestine; and when pumpkin seed powder is used the action is quicker. In series b, for example, when intact kernels of pumpkin seeds were taken by mastication and the decoction of areca nut was taken at the same time, the rate of cure was only 67.5 per cent, a result only slightly better than when areca nut was used alone. However, when pumpkin seeds were taken first (the intact kernel by mastication, the whole kernel powder or the oil-free powder), followed two to three hours later by a dose of areca nut decoction, the rate of cure (series c, d and e) was 92.1-100 per cent or an average of 95.19 per cent. Such a high rate of cure has never been obtained with the use of areca nut alone, the rate of cure with areca nut alone in the treatment of *T. saginata* infection being 30-50 per cent. The high rate of cure secured in the present work is, therefore, undoubtedly due to the combined use of pumpkin seed and areca nut.

2. Cases with *Taenia solium* infection. As mentioned before, the number of cases of *T. solium* infection treated in the present work is small. The results of treatment of 20 cases of this infection are given in Table 2. These results cannot be said to be entirely due to the combined use of pumpkin seeds and areca nut, since areca nut alone can also produce a high percentage of cure. On the other hand, the fact that the 2 cases treated with pumpkin seeds alone did not effect a cure shows that pumpkin seeds when

Table 2. Results of treatment of 20 cases of *T. solium* infection

Series	Kind of preparation	Method of administration	Dosage (gm)	Interval between last drug and MgSO ₄ (hour)	No. of cases treated	No. of cases cured	No. of cases failed	Rate of cure (%)
a	Pumpkin seed kernel only	Whole kernels by mastication	Whole kernel 120	3	2	0	2	0
b	Areca nut decoction only	Areca nut decoction	Areca nut 80-100	0.5	10	8	2	80
c	Pumpkin seed kernel and areca nut decoction	Whole kernels by mastication, areca nut decoction at the same time	Whole kernel Areca nut 75-120 45- 80	1	4	4	0	100
d	Pumpkin seed kernel and areca nut decoction	Whole kernels by mastication, 2.5-3 hours later areca nut decoction	Whole kernel Areca nut 60-120 80	0.5	4	4	0	100

used alone has little or no anthelmintic effect. It may be said therefore that the combined use of pumpkin seed and areca nut has greater curative effect.

3. **Repetition of treatment.** Some of the patients who were not cured returned for further treatment. Eleven cases of *T. saginata* infection were subjected to the combined use of pumpkin seeds and areca nuts in the re-treatment. Five of these cases were of the pumpkin seed series and, of these, 4 cases were cured after one treatment and 1 case after two treatments. Three cases were of the pumpkin seed oil and areca nut series and all were cured after one treatment. Of the remaining 3 cases which were not cured in the pumpkin seed and areca nut series, 2 cases were cured after one more treatment and 1 was cured after two more treatments.

None of the patients with *T. solium* infection who returned for further treatment were given the combination of pumpkin seeds and areca nuts. Two patients who were not cured with pumpkin seeds were treated with areca nuts; 1 was finally cured after two treatments and the other, who was not cured after one treatment, failed to return.

There were also 4 unsuccessful cases after one treatment with pumpkin seeds and areca nut (oil-free pumpkin seed powder in 3 cases, whole pumpkin seed powder in 1 case). The patients in 3 of these cases vomited soon after taking the areca nut, and naturally no therapeutic effect could be expected. The patient in the remaining case had not the slightest movement in the abdomen several hours after the anthelmintic and purgative, and he had also no purgation after returning home and no worm passed out. No re-treatment was given in these cases.

4. **Illustrative cases.** Among our cases of *T. saginata* infection about a half had been previously treated elsewhere. Some patients had taken areca nut decoction prepared by themselves, some had taken anthelmintic drugs purchased from worm specialists or drugstores, and some had been treated at outpatient clinics or hospitals. As regards the degree of infection, most of our patients had 1 worm, some had 2 or 3 worms, and there were 3 patients who had respectively 5, 6 and 14 worms. There was no relationship between the number of worms harbored and easiness or difficulty in the treatment of any case.

Brief histories of 4 cases treated with the combined use of areca nut and pumpkin seeds are here reported. Of these, 3 had been unsuccessfully treated several times elsewhere, and 1 had as many as 14 tapeworms.

CASE 1. Hsüeh, male, aged 36 years, a case of *T. saginata* infection. He had been infected for more than ten years and had taken anthelmintics purchased from a worm specialist in 1948 and 1949 without success. Between August and December 1954, he was treated three times, twice in a hospital with areca nut and once at home with areca nut and pomegranate fruit peels, all without avail. On February 25, 1955, he came to us for treatment. He received 50 gm of whole kernel pumpkin seed powder at 8:40 a.m., followed by a tannin-free decoction of

80 gm areca nut at 10:40 a.m. and 60 cc of 50 per cent magnesium sulphate at 11:10 a.m. At 12:30 a.m., during his second bowel movement, a complete tapeworm measuring 25 feet long passed out. The patient had no nausea or other untoward reaction after taking the anthelmintics.

CASE 2. Li, female, aged 39, a case of *T. saginata* infection. She had had the complaint for more than ten years and had been treated twice without success. The first time she had a decoction of 4 ounces each of areca nut and sour pomegranate fruit peels and the second time she was treated with an unknown amount of *lai wan* 雷丸, *Mytilitta latidensens* Hor. together with black sesame seeds and brown sugar. On October 21, 1954 she came to us for treatment. She was given a 50 cc decoction of 50 gm of oil-free pumpkin seed powder at 8 a.m., a decoction of 80 gm areca nut at 9 a.m. and a dose of magnesium sulphate at 9:30 a.m. At 10:50 a.m., during her first bowel movement about half of a worm was found hanging from the anus. She then had seven watery stools, and at 11:45 a.m. the major part of the worm was out, and helped by gentle pulling the whole worm with the scolex attached was passed out. Apart from feeling the urgency for bowel movement she had no other reaction after the anthelmintics.

CASE 3. Meng, male, aged 34, with *T. saginata* infection. His complaint had lasted for more than two years. He had once passed out about 20 feet of a worm after a dose of medicine from a worm specialist but was not cured and further segments were again found. In June 1953 he was treated three times at the Tungssu Federated Hospital with an interval of three to four days between each treatment but was not cured. On November 20, 1953 he came to us for treatment. He took 100 gm of pumpkin seed kernel by mastication at 2 p.m. immediately followed by a decoction of 80 gm of areca nut and then a dose of purgative at 3 p.m. He felt some peristaltic movement but otherwise no unpleasant feeling. At 5:30 p.m. he was asked to return home. He had no bowel movement until 7 a.m. the following day, when a tapeworm 20.5 feet long was passed out. The worm was found to be short of about 1 inch in length including the head. Inquiry made three months later showed that he was cured.

CASE 4. Tai, male, aged 43, with *T. saginata* infection. The patient had had the complaint for about eleven years. He had treated himself with decoctions of areca nut five or six times without success. He came to our clinic for treatment on May 14, 1954. He was given 100 gm of pumpkin seed kernel by mastication at 7 a.m., a decoction of 80 gm areca nut at 10 a.m. and 60 cc of 50 per cent magnesium sulphate at 10:30 a.m. At 12 noon, the first bowel movement took place and some parts of the worms passed out but were severed by pulling. At 12:30, during the second bowel movement, the remaining parts of all the worms came out. Careful examination showed that there were 14 tapeworms all with their heads attached. The total length of these 14 worms measured 259.6 feet. The patient had no untoward reaction from the anthelmintics.

In summarizing the results of treatment given in the foregoing pages, it may be concluded that one single treatment with the combination of pumpkin seed and areca nut can yield a high cure rate of about 95 per cent. Exceptionally stubborn cases may also be cured after one or two repetitions of the same treatment. The combined use of pumpkin seed and areca nut in the treatment is simple. It can be carried out in the outpatient clinic, hospitalization is unnecessary.

The taking of pumpkin seeds is simple. The kernels may be masticated or taken in the powder form. Fine pumpkin seed powder is

recommended, as it is more effective than the whole kernels taken by mastication.

Roasted pumpkin seeds known as "white seed" sold at the grocers are very suitable for the purpose. In country places seeds from the pumpkin fruit may be used raw or after roasting.

The results of treatment showed that pumpkin seed kernels taken by mastication together with decoction of areca nut at the same time are less effective. Better results are obtained when pumpkin seeds are taken first and allowed to act in the intestine for two to three hours, followed by an areca nut decoction.

Basing on the above results, we recommend that the treatment should be as follows:

1. **Pumpkin seeds.** In towns or cities, roasted pumpkin seeds may be easily purchased, while in the country seeds are obtained from the pumpkin fruit. The dosage should be whole seeds 2.5-4 *liang* or about 80-125 gm (equal to kernels 50-90 gm).* After the husks are removed the kernels are ground into fine powder. The powder is taken direct or after being boiled in a small amount of water. Pumpkin seeds are nontoxic and a larger amount may be taken without harm.

2. **Areca nut.** The dosage should be 30-100 gm, 30 gm or less for children under 10 years and 50-60 gm for adult patients of light build and 80 gm for patients of heavy build. A dosage of 100 gm used only in exceptionally heavy patients. A dosage over 100 gm does not always increase the rate of cure and is therefore unnecessary. Areca nut slices obtainable from Chinese drugstores are suitable for the purpose. They should be boiled in 500 cc water for about one hour when the decoction is reduced to 150-200 cc. After filtration, the decoction is ready for use. The decoction has a strong bitter and astringent taste and is to a certain extent irritant to the stomach. When desired, it may be titrated with a 2.5 per cent gelatin solution to remove the tannin. The solution is then filtered and the amber colored filtrate is reduced to its original volume of 150-200 cc by heating.

3. **The purgative.** A purgative with rapid action is preferred. Saline purgative such as magnesium sulphate is suitable. The normal dosage is 60 cc of a 50 per cent solution.

4. **Procedure of treatment.** Start the treatment in the morning on an empty stomach. First take the pumpkin seed powder, two hours later the areca nut decoction, and another half an hour later the purgative. Bowel movement usually takes place within three hours after the commencement of the treatment. The tapeworm may be passed out during the first, second or the third bowel movement. Therefore, if the treatment starts at 7 a.m., by 12 noon the treatment may be concluded. As soon as the worm is

* Sixteen *liang*=1 catty and 1 catty=500 gm, thus 1 *liang*=about 30 gm.

evacuated, the patient may take his meal. In some cases bowel movement may be delayed until the afternoon, but as a rule it does not exceed six hours from the commencement of the treatment. If after six hours no worm is passed out, the patient may be ordered to go home and take his food. In the same afternoon or the next morning, the worm may be evacuated.

THE PHARMACOLOGICAL ACTION OF PUMPKIN SEEDS ON TAPEWORMS*

As has been mentioned, in the course of treating the human cases, in vitro tests were made at the same time on the pharmacological action of pumpkin seeds on tapeworms. In our preliminary tests with pumpkin seed decoction it was found that with its use the segments of the middle and the posterior parts of *T. saginata* became thinner and broader, the central part of the segment became depressed, and at the same time there was a state of paralysis. The scolex and the anterior part of the worm on the other hand remained actively motile. These phenomena are quite different from those produced under the influence of areca nut. Based on this preliminary observation, the following tests, in vitro at the temperature of 37 C, were carried out with *T. saginata* and *T. solium*:

Experiment 1. *T. saginata*, test solution: 40 per cent decoction of oil-free pumpkin seed powder. When the worm was in normal saline, the scolex attached itself to the body segment of the worm. Six minutes after the worm was put into the test solution, the scolex detached itself from the place of attachment. The scolex and the immature segments moved actively. Segments of the middle part of the worm became thin and broad, with a depression at the middle of the segment. The gravid segments of the posterior part of the worm became paralyzed and showed only slight movement upon being touched. Another six minutes later, the scolex attached itself again to its body, but after two more minutes it loosened itself. Another six minutes later, i.e. twenty minutes after the worm was immersed in the test solution, the thinning and broadening of the segments of the middle and posterior parts became more marked. The depression at the center of the segments, especially those of the middle part of the worm, became more pronounced. The segments of the middle and posterior parts were now in a state of paralysis; they moved upon being touched but remained quiet when left alone. The scolex and the immature segments, however, kept on moving actively even when they were not touched.

*The tapeworms used for the experiments were from patients after treatment with either areca nut alone or areca nut and pumpkin seed. After they were washed in normal saline, they became active and motile.

Experiment 2. *T. saginata*, test solution: 30 per cent pumpkin seed extract.* The tapeworm was put into the extract saline solution. In five minutes the scolex attached itself to the body segments. The segments of the middle part of the worm became broader and thinner with a depression at the middle of each segment. Another seven minutes later the scolex was still attached to the body segments and the immature segments of the anterior part of the worm kept on moving actively. The segments of the middle part of the worm became still thinner and broader, and the depression in the center of the segments became more marked. The segments of the posterior part of the worm became paralyzed. Another eleven minutes later, i.e. twenty-three minutes after immersion, the scolex was still attached to the body segments and the immature segments of the anterior part of the worm were still actively motile, but the segments of the middle portion of the worm became even yet thinner and broader and these together with the segments of the posterior part became paralyzed, only showing movement upon being touched.

Experiment 3. *T. saginata*, test solutions: a. mixture of 30 per cent areca nut decoction plus 30 per cent pumpkin seed powder decoction in equal parts, b. pumpkin seed powder decoction 30 per cent. Ten minutes after the tapeworm was put into solution a the segments of the middle and posterior parts of the worm stopped moving and the scolex and the anterior part of the worm showed slight movement. Another ten minutes later the entire worm became paralyzed. The worm was then taken out of the solution and put into normal saline in which it resumed its activity in fifteen minutes.

The same worm after recovery was then put into solution b. Ten minutes later, while the scolex and the immature segments were still actively moving, the segments of the middle and posterior parts became thin and broad, with a depression at the center of each segment. Twenty minutes after the commencement of the experiment, the middle and posterior parts of the worm became paralyzed, while the scolex and the immature segments remained actively motile.

Experiment 4. *T. saginata*, test solutions same as in Experiment 3. Five minutes after the worm was put in solution a, the entire worm became paralyzed. The worm was then put into normal saline and it resumed activity in twenty minutes. The same worm after recovery was transferred to solution b. Twenty minutes later, the segments of the

* The extract was made from 35 gm pumpkin seed kernel. The extract consisted of two kinds, one in solid form and the other liquid form, but the effect on the tapeworm was the same. The experiment here recorded was made with a saline solution of the solid form. The extract was made by Mr. S. C. Kuoh of the Chemistry Department, Nan K'ai University, to whom the author wishes to express his thanks.

middle and posterior parts became thin and broad with a depression at the center of the segments and at the same time became paralyzed. The scolex and the anterior part of the worm remained actively motile.

Experiment 5. *T. solium*, test solutions: a. areca nut decoction 30 per cent plus pumpkin seed powder decoction 30 per cent in equal parts, b. pumpkin kernel powder decoction 30 per cent. Four minutes after it was put into solution a the whole worm became completely paralyzed. It was then taken out and put into normal saline to recover. After recovery it was put into solution b. Fifteen minutes later, while the scolex and the immature segments of the anterior part of the worm were still actively motile, the segments of the middle part of the worm became thin and broad with a depression at the center of each segment and these together with the posterior part of the worm became paralyzed.

In summarizing the results of the above experiments, it may be concluded that in a pumpkin seed decoction or in a solution of the extract *T. saginata* becomes paralyzed only in the middle and posterior parts but not in the scolex and anterior parts. At the same time, the segments of both the middle and posterior parts of the worm become thin and broad with a depression at the center, but that this is more marked in the middle portion of the worm.

In an areca nut decoction, on the other hand, as was pointed out by Feng and his associates(2), the same parasite becomes paralyzed completely only in the scolex and the immature segments, but not in the gravid segments.*

Experiments 3 and 4 above show that *T. saginata* in the mixed solution of the decoctions of areca nut and pumpkin seed becomes paralyzed completely from the scolex to the posterior end.

In regard to *T. solium*, although there was only one experiment performed, yet the result showed that the pumpkin seed decoction has the same kind of effect on this tapeworm as on *T. saginata* but somewhat stronger.

* With regard to the action of areca nut on *T. saginata*, we have made several experiments with the crude or the tannin-free decoction of the drug in various concentrations. The results show that the behaviors of the worm in the different concentrations (2-50 per cent) of the decoction are not uniform. However, one thing is certain, and that is the scolex and the immature segments of all the specimens of *T. saginata* always became paralyzed in all the concentrations of the decoction tested. The degree of paralysis of the gravid segments varied to some extent with different worms. This may serve to explain why areca nut is effective in some cases and not in others in the treatment of *T. saginata* infection. The present experiments in addition support the conclusion reached by Feng(2) that in a decoction of areca nut the paralyzed segments of the worm become long and slender, a phenomenon quite different from that observed in the decoction of pumpkin seeds.

DISCUSSION

As may be seen in the literature, although many drugs have been used for the treatment of tapeworm infections, very few have given reliable therapeutic results. Before the Second World War, the drugs used in most countries and considered most effective were preparations of *Filix mas*. However, owing to their high toxicity, they required thorough and complicated preparation of the patient to be treated. Also they were not always satisfactory. Atebrin which came into use later for the treatment of tapeworm infections cannot be considered as satisfactory⁽¹⁴⁾ since it is also toxic. In the Soviet Union Nazeroff and others⁽¹³⁾ found that akrihin, a preparation similar to atebrin, gives also unsatisfactory results.

In China, areca nut has been in use for centuries for tapeworm infections. Since its introduction in modern medicine, it has been found more effective than either *Filix mas* or atebrin as shown by the works of Chung and others⁽⁴⁾. Because it is simple to use, practically nontoxic and easy to get, it is now widely used throughout this country and many patients prepare decoctions from areca nut purchased from drugstores and treat themselves. However, as has been pointed out by Feng⁽³⁾ and proved by others^(4, 6-9) while the areca nut treatment is very effective in infections with *T. solium*, *Hymenolepis nana* and *Diphyllobothrium latum*, in *T. saginata* infection it is far from satisfactory. Hsü and Yang⁽¹⁵⁾ treated 8 cases of *T. saginata* infection with the combined use of atebrin and areca nut and obtained satisfactory results; but the number of cases is too small to give any definite indication as to the value of this method of treatment.

The result of the combined use of pumpkin seeds and areca nut in the treatment of *T. saginata* infection is entirely satisfactory. As shown in Table 1 (series c, d and e), of the 96 cases treated with pumpkin seeds (whole kernels by mastication, whole kernel powder and oil-free powder) taken at intervals with areca nut decoction, 92.1-100 per cent of the patients, or an average 95.19 per cent, were cured. This rate of cure has never been obtained by any method of treatment used before.

This combined method of treatment has a sound pharmacological basis. Our experiments with *T. saginata* show that while pumpkin seeds paralyze the middle and posterior parts of the worm, areca nut has a strong paralytic effect on the scolex and the immature segments. When used together the two drugs complement each other in their action and exert their combined anthelmintic effect on the worm. This has been proved in in vitro tests as well as clinically. The joint action of pumpkin seeds and areca nut in the treatment of *T. saginata* infection is a typical example of synergism in therapeutics.

Our result of treatment of *T. solium* infection is also very satisfactory. Although only 8 successful cases were treated with the combined method, its efficacy was clearly demonstrated in the in vitro tests.

Pumpkin seeds when used alone (Tables 1 and 2, series a), do not seem to give much effect. Krayner(12) stated that pumpkin seeds must be used in large doses of 200-400 gm for children and 400-700 gm for adults. He treated 5 patients with the extract of pumpkin seeds in this dosage, but in none of them were complete worms evacuated, although fecal examination later proved all the cases were cured. He likewise treated 6 dogs infected with *D. caninum*, *T. pisiformis* and *T. hydatigena* and in 5 of them tapeworms were evacuated. In the cases treated by us we did not use such large doses. Among 9 cases of *T. saginata* and 2 cases of *T. solium* infection in which 120 gm of pumpkin seed kernels were used only 1 was cured. However, from the results of our in vitro experiments it seems doubtful that any appreciable better result may be obtained by increasing the dosage.

The active principle of pumpkin seeds, as shown by Krayner, is located in the oil-free portion. It is water-soluble and thermostable.* Clinical trials and experiments have shown that the oil portion is of no value.

Crude areca nut decoction contains a large amount of tannin, which at first has an irritative effect on the tapeworm, but which is soon overcome by the paralytic action of the drug. Pumpkin seeds have no such irritative action on the worm. Under the influence of the paralytic action of the two drugs the whole worm becomes flaccid, and through the peristaltic movement of the small intestine, it is rolled up in a mass and is passed out in the feces. In most of our cases the whole worm was evacuated en masse, but in 22 cases the scolex and the very anterior portion of the worm measuring 0.5-3 inches were missing. However, all these 22 cases except 1 were later proved cured. The detachment of the scolex and the thin and delicate anterior part of the worm probably took place not in the small intestine but in the large intestine, or most likely in the rectum due to contraction of the anus, as has already been pointed out by Feng(3). The scolex remaining in the rectum or in the large intestine has practically no chance to survive, as these parts of the intestine are too far down, and it is hardly impossible for the scolex to crawl against the current to reach its normal habitat, the small intestine.

The dosage of areca nut employed by most people is 4 *liang* or 125 gm. We had one patient who had even used half a catty (250 gm) in one single dose without success. Unlimited increase of the dosage will not necessarily be followed by a cure. Although pumpkin seeds are nontoxic, some

* As stated before, in our investigation we used ready roasted pumpkin seeds. The roasting of pumpkin seeds requires a temperature of 140-170 C for about half an hour, a temperature which evidently does not destroy the active principle.

patients have a slight nausea after taking the drug. We are of the opinion that areca nut 2-3 *liang* (about 60-100 gm), pumpkin seeds 2.5-4 *liang* (about 80-125 gm) and magnesium sulphate 1 *liang* (30 gm) are quite sufficient. In the case of an inpatient, the physician, according to the state and constitution of the patient, may prescribe higher doses; but a dosage of over 100 gm of either areca nut or pumpkin seed seems unnecessary.

As stated before, areca nut contains a large amount of tannin; its crude decoction is not only unpleasant to taste but also irritative to the stomach and is unsuitable especially to patients with a "weak stomach". In clinics or hospitals where a pharmacy is available, the tannin may be removed by titration with gelatin solution to lessen the irritative property of the decoction.

With regard to pumpkin seeds, we recommend the use of powder prepared from the kernels, the powder as it is or after being boiled in water. A decoction of areca nut is taken two hours later and a dose of magnesium sulphate after another half an hour.

In conclusion, it may be said that the result of the combined use of pumpkin seed and areca nut in the treatment of tapeworm infections is entirely satisfactory. Traditional drugstores are found everywhere in the country and slices of areca nut can be purchased without difficulty. Pumpkin seeds can also easily be obtained in groceries in towns and cities, and in rural areas the plant is widely cultivated. Therefore, even in remote country villages there is no difficulty in obtaining the seeds. The combined use of pumpkin seed and areca nut could be popularized in the treatment of tapeworm infections.

SUMMARY

1. The results of investigations on the combined use of pumpkin seeds and areca nut in the treatment of tapeworm infections are reported.
2. In vitro experiments on *T. saginata* and *T. solium* show that the action of pumpkin seeds and areca nut on tapeworms is different. The paralytic effect of pumpkin seeds is on the middle and posterior parts of the worm and that of areca nuts is chiefly on the scolex and the immature segments of the anterior parts.
3. Both our in vitro tests and clinical cases prove that when pumpkin seeds and areca nuts are used in combination their actions are synergistic, and a high percentage of cure results.
4. We treated 165 cases of *T. saginata* and 20 cases of *T. solium* infections. Sixty-nine of the former cases were treated differently for ex-

perimental purposes. Of the 96 cases of *T. saginata* infection in which the combination of pumpkin seed kernels and areca nut decoction was used, an average cure rate of 95.19 per cent was obtained. Of the 20 cases of *T. solium* infection, 8 cases treated with the combined method were all cured.

5. The dosage of the drugs and the method of administration are discussed in detail.

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EXPLANATION OF FIGURES

The specific identification of the pumpkin seeds obtainable from groceries and used in this work was made by Prof. Ku'ang Ko-Zen (匡可任), Institute of Botany, Academia Sinica, Peking, to whom the author wishes to express his sincere thanks. Prof. Ku'ang states that in China the species earliest to be introduced and now most widely cultivated with the fruit used in the ripe state is *Cucurbita moschata*, known in Peking as *lao wo kua* 老窝瓜. The fruit is variable in shape and color (Figs. 1-5). The seeds obtainable in groceries (Fig. 6) chiefly belong to this species, though occasionally seeds of the other two species, *C. pepo* and *C. maxima*, may be found intermixed.

Areca nut, also called betel nut, and specifically known as *Areca catechu* (Figs. 8 and 9) needs no special comment.

Fig. 1. Longitudinal section of the long form of pumpkin. $\times 1/5$.

Figs. 2 and 3. The long form of pumpkin, side view. $\times 1/5$.

Fig. 4. The depressed form of pumpkin. $\times 1/5$.

Fig. 5. Longitudinal section of same. $\times 1/5$.

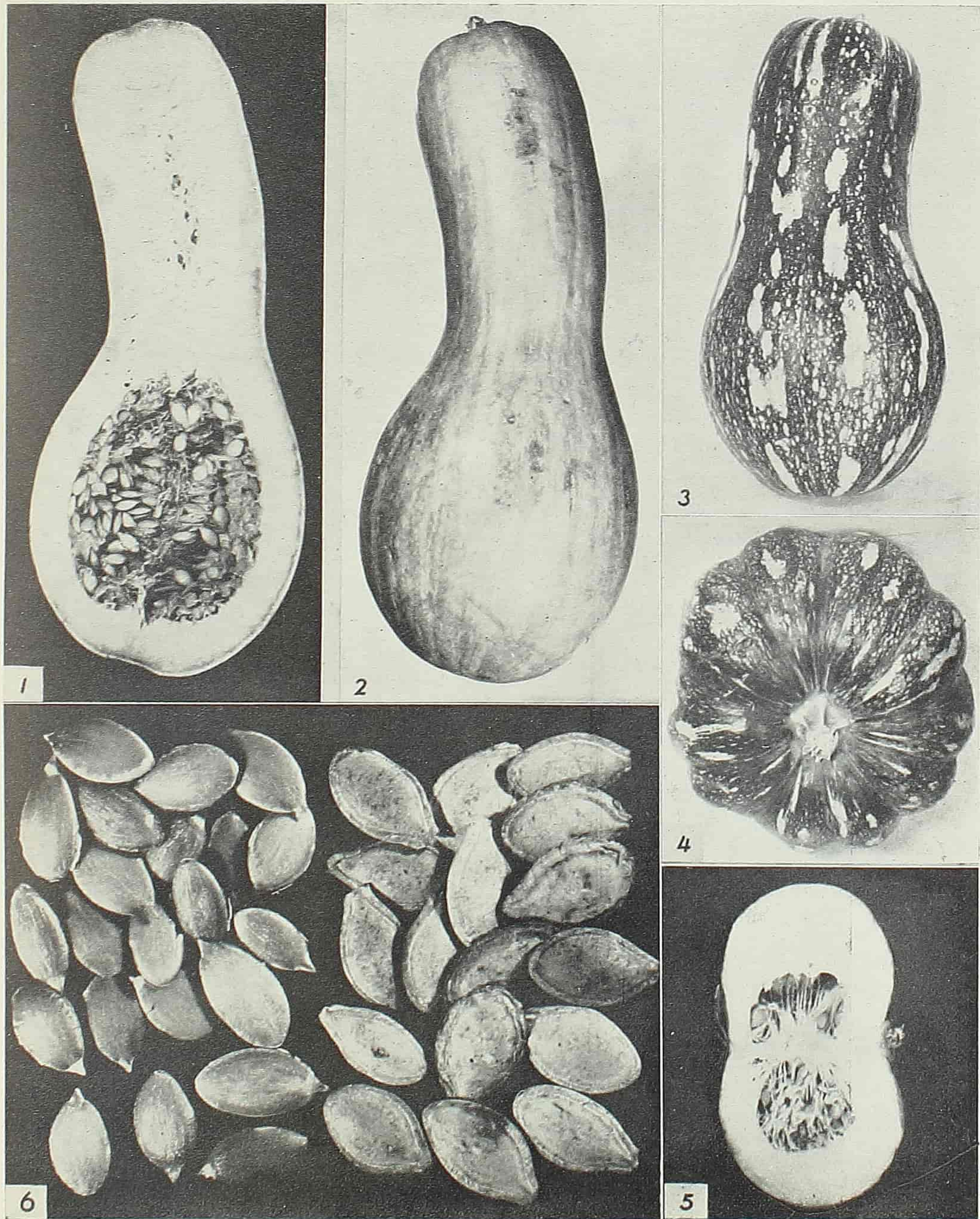
Fig. 6. Roasted pumpkin seeds, the kernel (left) and the intact seeds (right). \times natural size.

Fig. 7. Pumpkin plant growing in the field. $\times 1/8$.

Fig. 8. Intact areca nut top view (upper) and side view (lower). \times natural size.

Fig. 9. Slices of areca nut as are obtainable from Chinese drugstores. \times natural size.

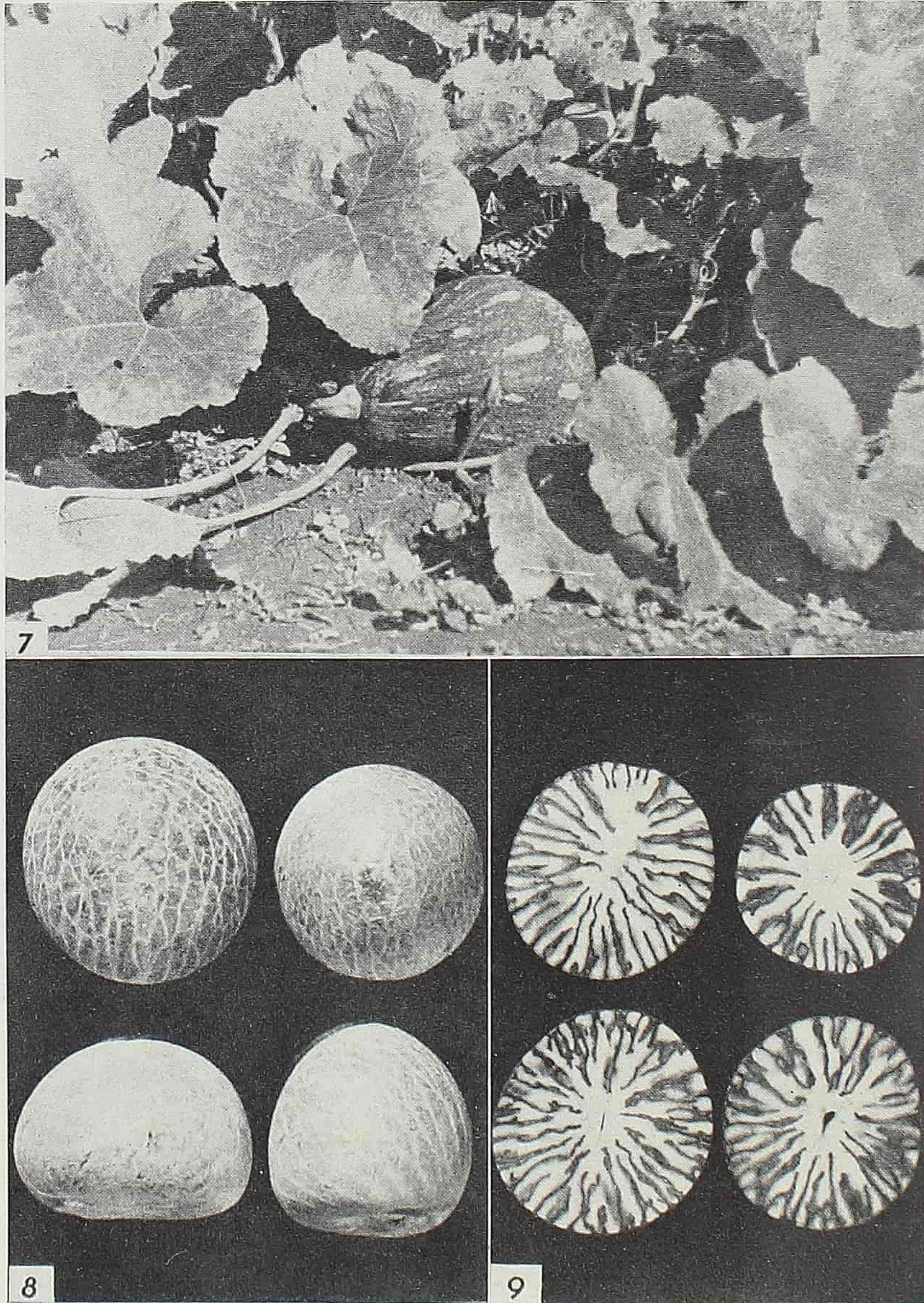
L. C. FENG



Figs. 1-6.

USE OF PUMPKIN SEED WITH ARECA NUT IN TAPEWORM INFECTIONS

L. C. FENG



Figs. 7-9.

PORTAL HYPERTENSION A CLINICAL STUDY OF SIXTY-FIVE CASES

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Portal hypertension, as now generally recognized, is a clinical syndrome caused by intrahepatic or extrahepatic obstruction of the portal system with manifestations of splenomegaly, pancytopenia, and tendency to ascites and repeated gastrointestinal hemorrhage, often accompanied by cirrhosis of the liver. The disease is not infrequently seen in China.

From March 1950 to February 1954, 78 patients with portal hypertension were admitted to the Central People's Hospital and 65 of them received various types of operative treatment. A clinical study of the 65 cases is presented in this paper, special emphasis being placed in comparing the differences between the intrahepatic and extrahepatic types of portal obstruction in regard to their symptoms, clinical findings and results of treatment.

ETIOLOGY

Any obstruction to the portal blood flow will cause portal hypertension. In our series of 65 cases the abdomen was explored and the diagnosis was confirmed by pathological section in 63 patients; in the remaining 2, mediastinotomy was done and the location of the obstruction was not ascertained. The obstruction was intrahepatic in 54 cases, or 85.7 per cent, and extrahepatic in 9 cases, or 14.3 per cent. In the extrahepatic group, the liver was found to be grossly and microscopically normal in all the cases but the exact site and cause of obstruction were not determined (Table 1). In a report by Lan and others⁽¹⁾ on 41 cases of portal hypertension seen in south China, the cause of obstruction in 80.5 per cent was schistosomiasis of the liver. In our group of patients, mainly inhabitants of north China, the cause of obstruction in 79.4 per cent of them was Laennec's cirrhosis of liver. These figures indicate that the pathogenesis of the condition in the two regions is quite different.

Table 1. *The etiology of portal obstruction in 63 cases*

Type of obstruction	Etiology	No. of cases	Percentage
Intrahepatic	Laennec's cirrhosis	50	79.4
	Schistosomiasis of liver	1	6.3
	Laennec's cirrhosis with concurrent primary carcinoma of liver	2	
	Cirrhosis following infectious hepatitis	1	
Extrahepatic	Undetermined	9	14.3
Total*		63	100.0

* The causes of obstruction in the 2 mediastinotomy cases were not determined and so they are excluded here.

SEX AND AGE

Among the 65 cases, 50 were males and 15 females with a ratio of 3.3 to 1. It is interesting to note that 8 were females and only 1 was male in the extrahepatic group, while there was a marked preponderance of males with a ratio of approximately 6.7 to 1 in the intrahepatic group. In a total of 4,523 cases admitted to our hospital from March 1950 to February 1954, the sex ratio of male to female was 2.3 to 1. It is evident that the incidence of liver cirrhosis is much higher in the male than the female while the reverse is true for the extrahepatic type of portal hypertension (Table 2).

Table 2. *Age and sex*

Age and sex	1-10		11-20		21-30		31-40		41-50		Total	Age in average	
	M	F	M	F	M	F	M	F	M	F			
Intrahepatic		1	4	1	28	3	14	2	1		47	7	27.0
Extrahepatic				2	1	2		2		2	1	8	28.1
Total*		1	4	3	29	5	14	4	1	2	48	15	

* The 2 mediastinotomy cases are excluded.

The youngest patient was 9 years of age and the oldest 45. Most of the patients (approximately 83 per cent) were between 21 and 40. There was not much difference in the average age incidence between our extrahepatic and intrahepatic group of cases (Table 2). In other words, the age of patients with portal hypertension does not give any diagnostic hint as to whether the site of obstruction is intrahepatic or extrahepatic.

SYMPTOMS

The patients usually complained of abdominal mass, gradual distension of the abdomen, general weakness or lassitude, anorexia and irregular feverishness. Epistaxis, hematemesis and melena are also frequently present. Among our 65 cases, the chief complaints were ab-

dominal mass in 54 cases, general malaise and epistaxis in 42 each, irregular feverishness in 39, melena in 19, and hematemesis in 17. Besides, edema of the legs and diarrhea were present in 8 cases each, and jaundice and epigastric pain in 4 cases each. The duration of symptoms dating from the discovery of an abdominal mass varied from one month to twenty-two years, and in most of the cases the history was longer than a year's duration (Table 3). No apparent difference in symptomatology can be seen between the intrahepatic and extrahepatic groups of cases.

Table 3. *Duration of the abdominal mass before admission*

Duration	Less than 1 year	1½-5 years	6-10 years	11-20 years	More than 20 years	Un- noticed	Not re- corded
Intrahepatic	16	20	8	2	1	6	1
Extrahepatic		5	1	1		1	1
Total	16	25	9	3	1	7	2

A history of hematemesis was present in 17 out of 60 cases, or an incidence of 28.3 per cent (5 cases in which the record was incomplete were excluded). Of these, 14 belonged to the intrahepatic group and 3 to the extrahepatic group. Their incidence of hematemesis was 27.5 per cent and 33.3 per cent respectively. The bleeding was either massive or recurrent in nature. In the 17 cases with hematemesis, it occurred once in 8 cases, twice in 4 cases and more than three times in 5 cases. All the 3 cases of extrahepatic portal bed block had more than three attacks of hemorrhage before admission.

CLINICAL FINDINGS

1. **Splenomegaly.** Fifty-four patients complained of an abdominal mass, but the spleen was found to be enlarged in all the 65 cases. We arbitrarily divided them into three groups: 1. where the lower pole was within 3 cm below the costal margin—3 cases; 2. within 8 cm from the costal margin—29 cases; and 3. beyond 8 cm from the costal margin—33 cases. In a few cases, the spleen was just palpable below the costal margin but actually its upper part was enlarged with the diaphragm pushing upward. Hence, in addition to palpation, percussion must be performed in order to determine the actual size of the spleen.

2. **Hepatomegaly.** The liver was not palpable in 28 cases. A slight enlargement of the liver with its edge extending within 3 cm below the costal margin was found in 21 cases, 3 being of the extrahepatic type. The liver was found moderately enlarged to within 8 cm below the costal margin in the remaining 16 cases, among which only 1 was of the extrahepatic type of portal obstruction. The incidence of hepatomegaly

was 61.1 per cent in the intrahepatic group and 44.4 per cent in the extrahepatic group.

3. *Ascites.* Ascites was present in 25 or 44.6 per cent of our cases. Nine cases were excluded because of insufficient data in the records. Excessive fluid of over 500 to 2,000 cc was found during operation in 4 cases. In an analysis of these cases, the following points in relation to the production of ascites were noted:

a. *The role of plasma protein.* It is well-known that protein plays an important part in maintaining osmotic pressure in the circulation. The serum albumin has a higher osmotic pressure than globulin because of its smaller molecules and higher concentration. Therefore, it is conceivable that a reduction of serum albumin might be the causative or a contributory factor in the production of ascites in cases of portal hypertension. We found in our present study that an abnormal albumin-globulin ratio was present in most of the patients with marked ascites and that, on the other hand, in those without ascites the plasma protein was usually normal (Fig. 1). It is apparent that abnormal variation of plasma protein may exert a great influence on the production of ascites.

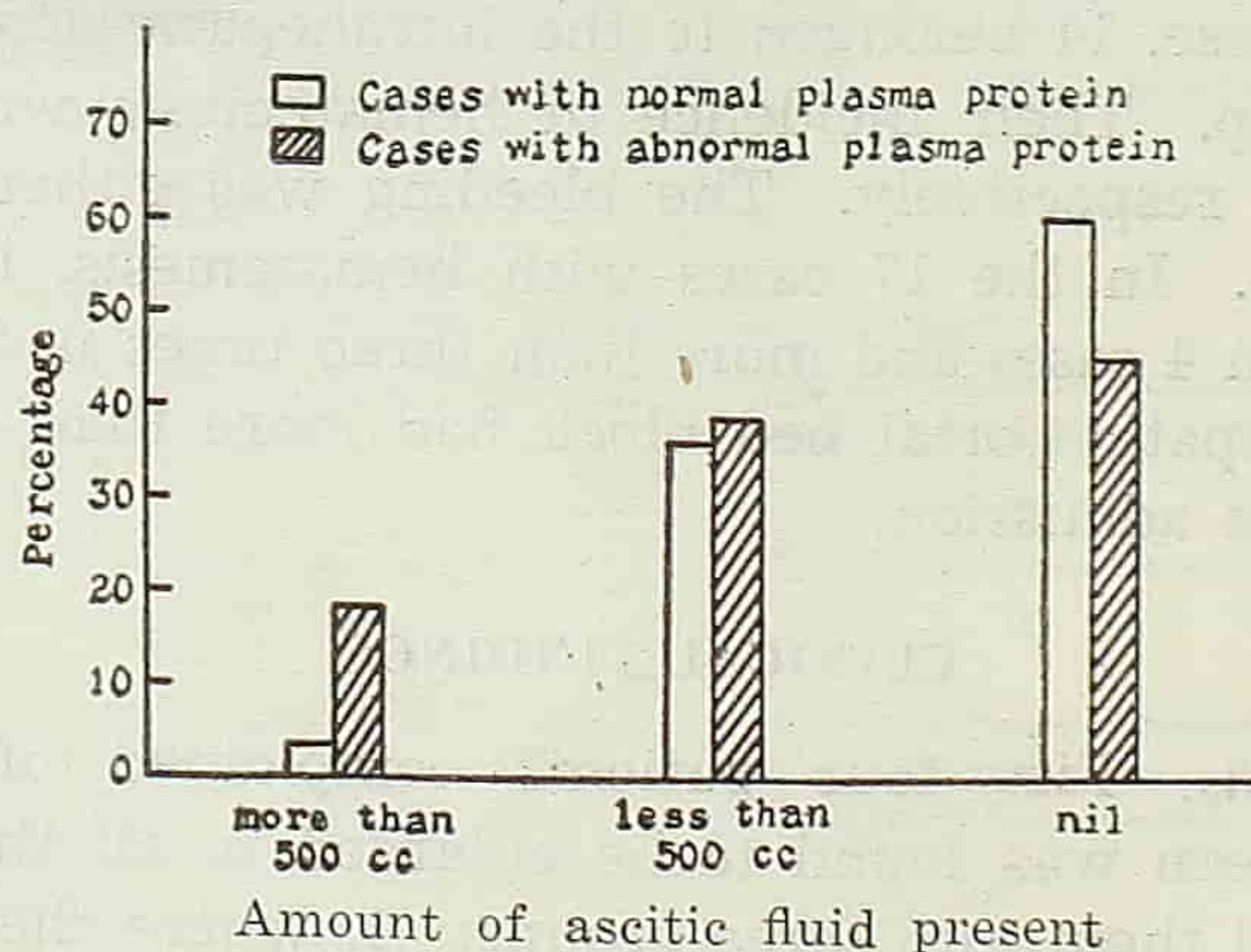


Fig. 1. The relationship between ascites and plasma protein.

b. *Portal pressure.* One would expect that ascites is likely to occur in cases of portal hypertension as a consequence of increased hydrostatic pressure within the visceral capillaries owing to portal obstruction. Analysis of our cases (see Fig. 2) shows that the incidence of ascites in general is in proportion to the increase of portal pressure.

c. *The type of portal obstruction.* In comparing the frequency of ascites occurring in the intrahepatic and extrahepatic groups, we found that ascites occurred in the former about twice as frequently as in the latter (Table 4) and that in none of the cases in the extrahepatic group

was ascites present in any marked degree. Liver damage evidently plays an important part in the production of ascites.

Table 4. *The relationship between ascites and types of portal obstruction*

Ascites	Nil	Under 500 cc	Over 500 cc
Intrahepatic	26	19	4
Extrahepatic	6	2	0

To summarize, it may be said that an alteration of the plasma protein level, the degree of portal hypertension and the presence of liver damage are all closely related to the pathogenesis of ascites, but no single factor can be considered as decisive. Recently, Hyatt and Smith(2) have reported that the ascitic fluid mainly originates from the liver, and they believe that sodium retention plays an important part; but other authors have emphasized also the importance of increase of permeability of the capillary wall, impedance to the lymphatic flow and excessive production of the antidiuretic hormone by the pituitary, etc. The fact is that the true mechanism in the production of ascites is not yet known. We believe that the cause of ascites is manifold and that alteration of the plasma protein level, elevation of the portal pressure and liver damage are important. Once ascites is formed, there is diminution in the excretion of sodium, and as a result ascites tends to persist or continue to progress in a vicious circle. Therefore, the treatment should be directed to the elimination of the above factors.

4. **Blood picture.** Another important finding is hypersplenism, which takes the form of anemia, leukopenia and thrombocytopenia accompanied with prolongation of both the bleeding and coagulation time. We studied the blood pictures of all the 65 cases before operation and observed varying degrees of pancytopenia and bleeding tendency (Table 5). Among these, leukopenia was the most constant and striking feature.

Table 5. *Blood picture*

Hgb gm per 100 cc	No. of cases	Percentage	RBC million per cu mm	No. of cases	Percentage	WBC thousand per cu mm	No. of cases	Percentage
Less than 5	8	12.3	Less than 2	6	9.2	Less than 2	10	15.4
5-10	27	41.5	2-3	17	26.1	2-4	42	64.6
10-12	18	27.7	3-4	34	52.3	4-5	8	12.3
Above 12	12	18.5	Above 4	8	12.3	5-6	5	7.7
						Above 6	0	0

Table 5. *Blood picture (Continued)*

Platelet count 10,000 per cu mm	No. of cases	Percent- age	Bleeding time	No. of cases	Percent- age	Coagulation time	No. of cases	Percent- age
Less than 5	3	4.6	< 4'	56	86.2	< 12'	24	38.7
5-10	26	40.0	> 4'	9	13.8	> 12'	38	61.3
10-15	18	27.7				Not recorded	3	
15-20	12	18.5						
Above 20	6	9.2						

5. Liver function test. Analysis of the results of the various liver function tests in 63 cases (2 cases of mediastinotomy were excluded) showed elevation of the serum bilirubin in 25 per cent of the cases (Table 6), alteration of the serum albumin-globulin ratio in 30.2 per cent (Table 7), increased thymol turbidity in 55.6 per cent (Table 8) and diminished excretion of hippuric acid in 26.7 per cent (Table 9). Difference between

Table 6. *Serum bilirubin*

Serum bilirubin	Normal	Abnormal			Not determined	No. of cases
		1-2 mg	2-3 mg	Percentage		
Intrahepatic	32	12	1	28.9	9	54
Extrahepatic	7	0	0	0	2	9
Total	39	12	1	25	11	63

Table 7. *Plasma protein*

Plasma protein	Normal	Abnormal			No. of cases
		Slightly*	Markedly**	Percentage	
Intrahepatic	37	7	10	31.5	54
Extrahepatic	7	2	0	22.2	9
Total	44	9	10	30.2	63

*The plasma albumin < 3 gm per 100 cc, A/G ratio > 1, or the plasma albumin > 3 gm but the A/G ratio < 1

**The plasma albumin < 3 gm per 100 cc, and the A/G ratio < 1

Table 8. *Thymol turbidity test*

Thymol turbidity	Normal	Abnormal			No. of cases
		6-9 units	10 units or more	Percentage	
Intrahepatic	21	17	16	61.1	54
Extrahepatic	7	2	0	22.2	9
Total	28	19	16	55.6	63

Table 9. *Hippuric acid test*

Amount of excretion	Normal	Abnormal		Percent- age	Not deter- mined	No. of cases
		3.0-3.3 gm (oral) 0.5-0.7 gm (I.V.)	Below 3.0 gm Below 0.5 gm			
Intrahepatic	38	12	3	28.3	1	54
Extrahepatic	6	1	0	14.3	2	9
Total	44	13	3	26.7	3	63

the intrahepatic and extrahepatic type of cases was distinctly shown. Impairment of liver function was more marked and more frequent in the intrahepatic group, and there was not a single case in the extrahepatic group that showed marked impairment of liver function. Hence it may be stated that if slight impairment of liver function is present, the case may be either an intrahepatic portal bed block or an extrahepatic one; but when marked impairment is present, it points to the diagnosis of intrahepatic type of portal obstruction.

6. *Urobilinurea*. Test for urobilin in the urine was carried out in 52 cases. It was positive in 16 cases with intrahepatic obstruction, or 36.4 per cent, and in only 1 case with extrahepatic obstruction, or 12.5 per cent (Table 10). The finding of urobilin in the urine favors the diagnosis of intrahepatic portal bed block.

Table 10. *Presence of urobilin in urine*

Urobilin	Negative	Positive		Not recorded	No. of cases
		No. of cases	Percentage		
Intrahepatic	28	16	36.4	10	54
Extrahepatic	7	1	12.5	1	9
Total	35	17	32.7	11	63

7. *Esophageal varices*. Barium meal examination of the esophagus was done in 61 cases. Definite varices were found in 37 cases, doubtful in 1 and negative in 23. The incidence of esophageal varices was 61.7 per cent. Correlation of the incidence of esophageal varices with that of hematemesis in the two groups showed (Table 11):

Table 11. *The relationship between esophageal varices and hematemesis*

Esophageal varices	With positive roentgenologic findings		With negative roentgenologic findings		Total	
	No. of cases	Cases with hematemesis	No. of cases	Cases with hematemesis	No. of cases	Cases with hematemesis
Intrahepatic	30 (58.8%)	10 (33.3%)	21 (41.2%)	4 (19.0%)	51	14 (27.5%)
Extrahepatic	7 (77.8%)	3 (42.9%)	2 (22.2%)	0	9	3 (33.3%)
Total	37 (61.7%)	13 (35.1%)	23 (38.3%)	4 (17.4%)	60	17 (28.3%)

a. In cases of demonstrable esophageal varices the incidence of hematemesis was 35.1 per cent and in those where x-ray examination failed to show any evidence of esophageal varices hematemesis occurred in 17.4 per cent of the cases. This might be due to the fact that the varices present were of a mild degree or they were located in the gastric wall below the cardiac end. Both these conditions were difficult to detect by the present methods of x-ray examination.

b. The incidence of esophageal varices, like that of hematemesis, was higher in the extrahepatic group. We consider that when the obstruction is in the extrahepatic portion of the portal bed, especially when it is in the splenic vein, the collateral channels are much fewer than when the obstruction occurs in the liver. The esophageal veins practically constitute the main diverting pathway of that part of the portal blood flow. Therefore, marked engorgement of these veins with varices formation is usually present.

8. Portal pressure. The portal pressure was determined through the epiploic branches during operation in 50 cases. The readings taken were based on the height of the blood column from the level of the cannulated vein. As only a relative rise or fall of the pressure is of importance, we usually did not take the level of the portal vein as the basal line. The results are shown in Table 12.

Table 12. Portal pressure as determined during operation

Portal pressure (mm in blood column)	Less than 150	150-200	201-300	301-400	Above 400	No. of cases
Intrahepatic	6	7	14	10	6	43
Extrahepatic		1	3	2	1	7
Total	6	8	17	12	7	50

No obvious difference in portal pressure was found between the intrahepatic and extrahepatic groups. In 6 cases, the pressure was below 150 mm but congestive splenomegaly was present in all of them and the diagnosis of portal hypertension was made before operation. The diagnosis of portal hypertension was established despite the low pressure for the following reasons: 1. The increased portal pressure might have been buffered by the enlarged spleen and the established collaterals, inasmuch as evident esophageal varices were found in 2 of them. 2. In measuring the portal pressure through the epiploic branches of 10 laparotomy cases without clinical manifestations of portal hypertension, we found that the average value was 99.4 mm blood column. The

portal pressure in all the above 6 cases was definitely higher than this normal average. 3. We measured the epiploic, splenic and portal vein pressures in 1 case during operation and found them 258, 290 and 310 mm blood column respectively. This showed that the pressure readings can be different when the basal line is put at different levels. Thus when the epiploic pressure is determined after the omentum is laid down over the abdominal wall, the pressure reading can be lower than the actual portal pressure.

In correlating the portal pressure with the clinical manifestations of esophageal varices, hematemesis and ascites we found that the incidence of esophageal varices was roughly in proportion to the height of the portal pressure (Fig. 2). Also, the curves for the incidences of esophageal varices and hematemesis were closely parallel, and the incidence of ascites had some relation to the height of portal pressure.

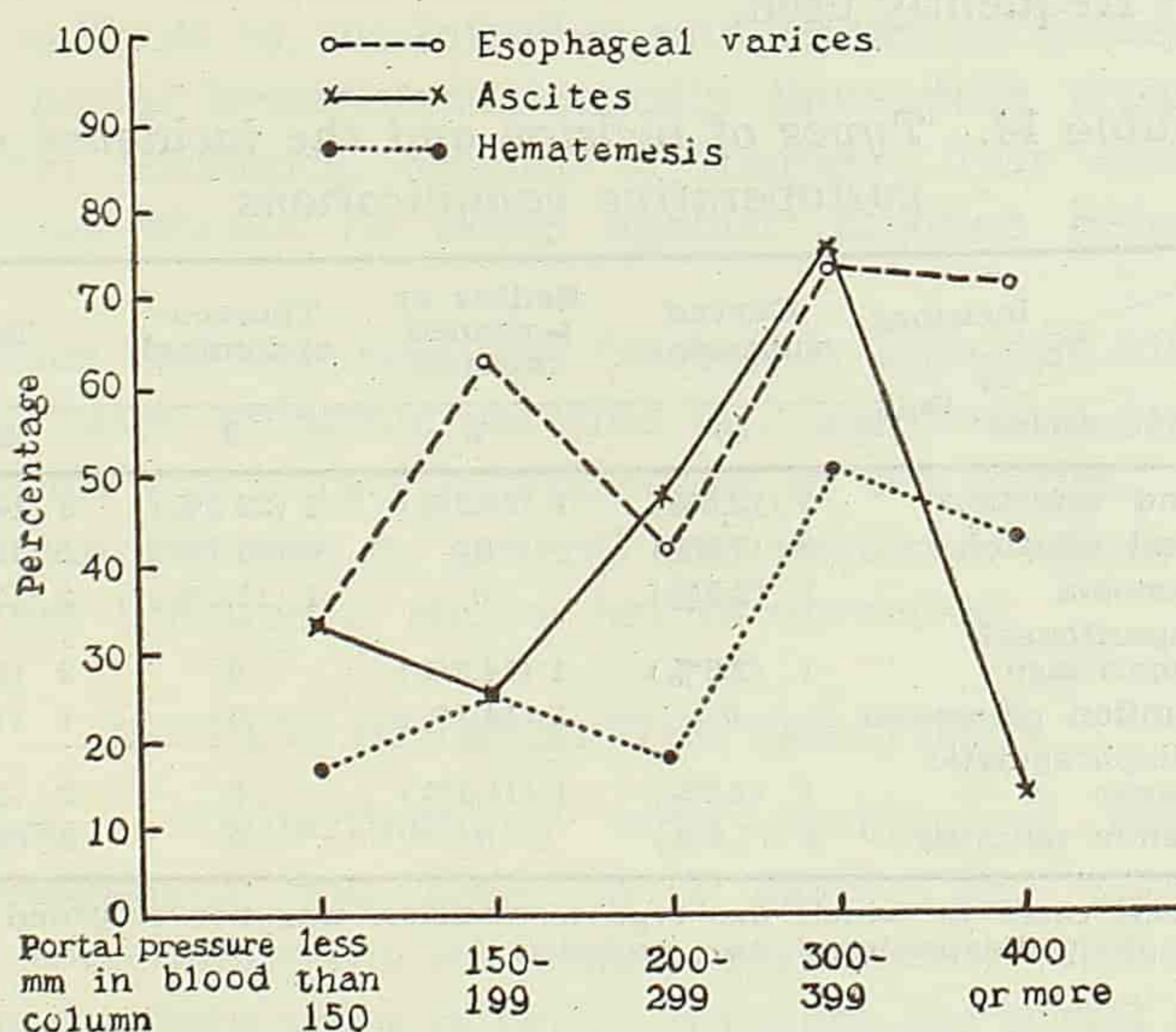


Fig. 2. The relationship between portal pressure and the occurrence of esophageal varices, hematemesis and ascites.

TREATMENT

The various types of operative treatment in our 65 cases are listed in Table 13. Splenectomy was carried out in most of the cases; spleno-renal shunt has been done in this hospital only since April 1953. Endotracheal ether or continuous spinal anesthesia (in the more recent cases) was employed.

Table 13. *Types of operation and anesthesia*

Types of operation	Ether	Continuous spinal anesthesia	Local	Total cases
Splenectomy	29	23		52
Mediastinotomy			2	2
Hepatic and splenic artery ligation	1			1
Splenectomy and hepatic artery ligation	1			1
Splenorenal anastomosis	1	7		8
Splenectomy and anastomosis of splenic and retroperitoneal collateral vein		1		1
Total	32	31	2	65

POSTOPERATIVE COMPLICATIONS

The approach was made through different types of incision (Table 14). The curved subcostal incision provides a relatively good exposure and has been most frequently used.

Table 14. *Types of incision and the incidence of postoperative complications*

Complications	Incisions				Total
	No. of cases	Curved subcostal	Rectus or T-shaped incision	Thoraco-abdominal	
		40	7	9	56*
Wound infection	5 (12.5%)	5 (12.5%)	1 (14.3%)	2 (22.2%)	8 (14.3%)
Pleural effusion	3 (7.5%)	3 (7.5%)	0	6 (66.7%)	9 (16.1%)
Pneumonia	1 (2.5%)	1 (2.5%)	0	1 (11.1%)	2 (3.6%)
Intraperitoneal hemorrhage	1 (2.5%)	1 (2.5%)	1 (14.3%)	0	2 (3.6%)
Disruption of wound	0	0	1 (14.3%)	0	1 (1.8%)
Subdiaphragmatic abscess	1 (2.5%)	1 (2.5%)	1 (14.3%)	0	2 (3.6%)
Epidemic parotitis	3 (7.5%)	3 (7.5%)	0	0	3 (5.4%)

* Seven cases in which the type of incision was not recorded and 2 cases of mediastinotomy are excluded.

In our cases, the thoraco-abdominal approach gave rise more frequently to chest complications than the curved subcostal incision. Also, when the latter was used, the patients usually had a more comfortable postoperative course. However, postoperative bleeding occurred in 2 cases in which splenectomy was done through an abdominal approach. In the first case, a T-shaped incision was used and the spleen was removed without difficulty, but capillary oozing immediately ensued from the splenic bed, omentum and muscles of the abdominal wall. The use of oxidized cellulose, packing with large pads, pressure with sand bags, and continuous blood transfusions failed to bring it under control, and the patient died of shock sixteen hours after the operation. Autopsy

revealed a large amount of non-coagulated blood accumulated in the peritoneal cavity, for which we could find no satisfactory explanation. In the second case a left curved subcostal incision was used and the spleen was removed without much difficulty; but signs of internal hemorrhage appeared about twenty-four hours later and the patient quickly went into shock. Exploration was carried out immediately and a spurting artery over the under surface of the diaphragm was found and controlled by transfixing ligatures. The postoperative course after the second operation was uneventful. While the bleeding in the first case seemed to be unrelated with the type of approach, the bleeding in the second case probably could have been avoided, if a thoraco-abdominal approach had been used. The thoraco-abdominal incision, we believe, gives the best exposure and facilitates the freeing of the spleen and control of bleeding. When the curved subcostal incision is used, a careful search for bleeders, especially under the diaphragm, should be made and the abdomen should only be closed after adequate control of bleeding has been achieved.

As shown in Table 14, the infection rate among our patients was high. Patients with portal hypertension usually have poor reparative power and low general resistance, because of frequent liver damage. Hence, special precaution should be taken against infection before and after operation.

Complications that occurred less frequently included subdiaphragmatic abscess in 2 cases, epidemic parotitis in 3 and wound disruption in 1. Wound disruption was a rare complication in this series. We consider that retention sutures are in general not required unless marked impairment of liver function is shown before operation.

RESULTS OF OPERATIVE TREATMENT

Mediastinotomy. Mediastinotomy with packing of iodoform gauze around the esophagus was done in 2 cases. The purpose of this operation was to promote the formation of abundant collaterals between the coronary and azygos veins in order to reduce the portal pressure. No distinct effect was observed in either case immediately after operation. In one of these cases, the patient after two attacks before operation had two more attacks about two months after operation and was admitted to another hospital where splenectomy was done. He returned to work soon afterwards and remained symptomless until six months later, when he died of hepatic coma following another attack of hemorrhage. Since no favorable results were observed with mediastinotomy, we made no more trials.

Ligation of hepatic artery. Ligation of the hepatic artery was done in 2 cases of portal cirrhosis. Both cases had a history of repeated attacks of profuse hematemesis before operation. In the first case, ligation

of the hepatic and splenic arteries was done. The patient vomited a small amount of blood following the operation and finally died of hepatic coma seven weeks later. The second case was a man of 44, who underwent splenectomy and hepatic artery ligation, and apart from occasional spitting of "bloody sputum" he has been enjoying fairly good general health and has resumed full duty. Now, over two years after the operation, there is striking improvement in his general condition. Examination shows no evidence of ascites and the liver function tests are all within normal limits. While opinions on the value of this operation are divergent and our limited experience can contribute little of value to the controversy, we feel that in relatively late cases of liver cirrhosis with a history of hematemesis, presence of ascites and marked impairment of liver function, where a shunt procedure is infeasible, this operation may lessen the occurrence of bleeding from the esophageal varices and also eliminate ascites. The point of ligation should be proximal to where it gives out the gastroduodenal branch so that some degree of arterial supply to the liver may be maintained.

Splenorenal anastomosis. The results following this type of operation have been reported by one of us⁽³⁾. In a case in which the splenic vein was anastomosed to a large retroperitoneal collateral, profuse bleeding from the esophageal varices occurred about six months after the operation. The patient was readmitted and trans-esophageal transfixion of the esophageal veins was done. For over eight months since the second operation the patient has been well apart from an attack of a small amount of bleeding. This case shows that the retroperitoneal collaterals may communicate with the esophageal veins, and therefore anastomosis may cause further engorgement of these veins, and should not be attempted.

Splenectomy. Splenectomy was done in 52 cases. Since the majority of our cases fall into this group, we shall deal with the operative results under this heading.

a. *Mortality.* There were two operative deaths within twenty-four hours after operation among the 52 cases of splenectomy. One patient died of bleeding because of non-coagulation of the blood; necropsy failed to show any apparent cause. The exact cause of the other death was not clear. In another case of splenectomy the postoperative course was smooth but the patient suddenly developed massive hematemesis on the twenty-fourth postoperative day and immediately died. Including the fourth death after ligation of the splenic and hepatic arteries, the hospital mortality of our 63 cases (2 cases of mediastinotomy excluded) was 6.3 per cent and the operative mortality was 3.2 per cent.

b. *Change in portal pressure.* In some of these cases, the portal pressure was determined through a gastroepiploic branch after ligation of the splenic artery, splenectomy and completion of the splenorenal shunt. A reduction of the portal pressure was observed in most of the

cases (Table 15). The reduction is most marked in the extrahepatic group. We believe that in cases of extrahepatic obstruction splenectomy alone can effect a satisfactory reduction of the portal pressure and that shunting is usually unnecessary.

Table 15. *The effect of operation on portal pressure*

	Procedure	Average reduction of portal pressure in mm
Intrahepatic	Ligation of the splenic artery	36.6
	Splenectomy	55.4
	Splenorenal shunt	77.4
Extrahepatic	Ligation of splenic artery	47.5
	Splenectomy	108.0

In 5 cases in which the portal pressure was not too high (all below 250 mm blood column) we found that after splenectomy there was a rise of the portal pressure instead of a fall. The possible explanations for this are: 1. The perisplenic collaterals were divided while the spleen was freed. 2. Since the spleen functions as a blood reservoir, its gradual enlargement tends to make it a buffer to the elevation of the portal pressure. This effect may be more marked in a soft spleen than a fibrotic one. The above cases presented low portal pressure either because of the existence of rich collaterals or a distensible spleen. Thus, although the arterial inflow to the portal system was reduced by approximately 40 per cent after splenectomy, the resultant portal pressure became higher than before operation.

c. *Changes in blood picture.* With the exception of 2 cases of mediastinotomy, 1 case in which only ligation of the splenic and hepatic arteries was done and 2 operative deaths, the blood picture in nearly all the other cases showed marked improvement immediately after splenectomy (Fig 3). In the case in which only ligation of the splenic and hepatic arteries was done, the white count increased from 4,300 to a maximum of 7,600 and platelets increased from 100,000 to 150,000, while there was no change in the red count or hemoglobin. It is apparent that this procedure is far less effective than splenectomy in relieving hypersplenism. In the majority of the cases there was moderate leukocytosis immediately after splenectomy. The white count usually returned to normal in one to two months. In 15 cases, followed up from one to two months, the white count was below 5,000 in 2 cases, between 5,000 and 10,000 in 11 cases, between 10,000 and 15,000 in 1 case and above 15,000 in 1 case.

d. *Changes in liver function.* Whether splenectomy or shunt operation has any influence on the course of liver cirrhosis is worth serious study. It is known that chronic passive congestion of the liver resulting

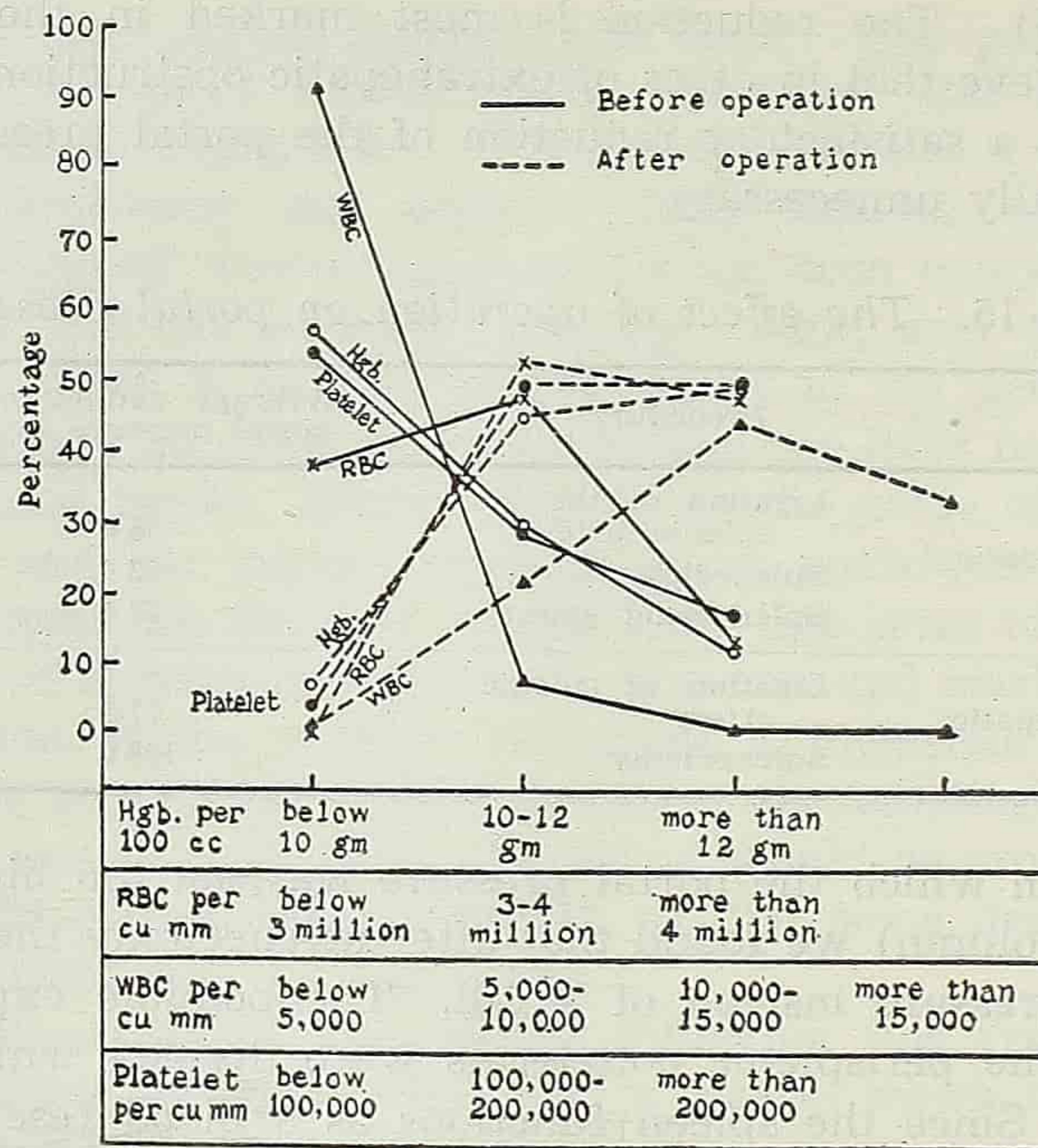


Fig. 3. Changes of blood picture before and after operation.

from heart failure may eventuate in cirrhosis, the so-called cardiac cirrhosis. In nodular cirrhosis of the liver, fibrosis and the irregular masses of regenerated liver cells may compress the portal radicles and result in venous stasis, which in turn stimulates fibrosis.

Theoretically speaking, an effective reduction of the elevated portal pressure should lessen the venous stasis in the liver, thus breaking the vicious circle, and a cessation or retardation of the progress in the clinical course of the disease might be expected.

In some of our cases, follow-up liver function studies including the plasma protein determination and thymol turbidity test were done at various periods after splenectomy. The results were compared with those before operation. If both these tests showed improvement or one of them showed improvement and the other no change, the case was considered as "improved"; if both showed poorer results or one of them gave a poorer result and the other no change, it was considered as "worsened"; if both gave the same results as before or one of them gave a better and the other a poorer result, it was considered as "not changed". The results are shown in Table 16.

There was often a depression of the liver function immediately after operation, probably as a result of operative trauma. But we found de-

Table 16. *The results of postoperative follow-up examination of liver function*

No. of cases Results	Duration of postoperative follow up						
	Within 1 month	1-3 months	3-6 months	6-12 months	1-2 years	2-3 years	More than 3 years
Improved	3	6	5	2	3	1	1
Worsened	15	3					
Not changed	7	3		1			
Normal	4	1	1	1	3		
Total	29	13	6	4	6	1	1

finite improvement of the liver function in most of the cases observed over a long period. The number of our cases is small and the results are certainly inconclusive. However, our observations suggest that splenectomy can reduce portal pressure on the one hand and correct anemia on the other, and that it provides beneficial effects to the liver by lessening its venous stasis and improving its nutrition, thus facilitating the regeneration of the liver cells.

e. *Effects on symptoms.* Twenty-one of the splenectomy cases were followed up from five months to three years. Among them, 11 cases were followed up from five months to one year and 10 cases from one year to three years (Table 17). Aside from the case in which the patient succumbed from hematemesis on the twenty-fourth postoperative day, there was only 1 case in which hematemesis recurred twice one and half years after operation and each time the bleeding stopped after conservative treatment. We feel that when abundant big collaterals are present in the abdominal wall or around the spleen, hematemesis is likely to recur after simple splenectomy without a shunt procedure.

Table 17. *The results of postoperative follow-up examination of patients*

Duration of postoperative follow up	Total no. of cases	Hematemesis		Ascites	
		Present before operation	Recurred after operation	Present before operation	Recurred after operation
5 months to 1 year	11	4	0	6	0
1 year to 3 years	10	3	1	4	0*

* In one case severe ascites developed after operation, but when the patient was examined one year and two months later ascites had entirely disappeared.

As to the effect on ascites, the results appear to be quite satisfactory (Table 17); but, except in 2 cases, the amount of fluid present before operation was small. It is hard to conclude that splenectomy alone can produce favorable result on ascites. In fact, we feel that if the liver dam-

age is marked and ascites is severe, one can hardly expect beneficial effects from splenectomy.

In regard to other symptoms, such as general weakness, fatigability, epistaxis and bleeding from gums, marked improvement was present in the majority of the cases after splenectomy. But some of the patients complained of insomnia, anorexia and postprandial epigastric discomfort. A prolonged period of convalescence with the aid of a diet rich in protein, carbohydrate and vitamins and a proper amount of sedatives (barbiturates should be avoided if possible) is often required.

f. *Prolonged fever after operation.* Patients after splenectomy (alone, or combined with some other procedure) often have a prolonged febrile course, irrespective of clinically detectable complications. In most of our cases the fever came down gradually to normal or nearly normal within two to three weeks, but in some it persisted for two to three months. Various antibiotics were used in the obstinate cases but without effect. The cause of the fever was not known. Culture of the blood from the splenic vein done in a few cases during operation showed no growth of organism. Such fever has been attributed by some authors to subphrenic accumulation of blood or thrombosis of the splenic vein, but the absence of prolonged febrile reaction in cases of splenectomy for other diseases invalidates this explanation. The problem awaits further study.

SUMMARY

1. A clinical analysis of 65 cases of portal hypertension is presented.
2. In this series, 85.7 per cent of the cases were of the intrahepatic type of portal bed block and 14.3 per cent were of the extrahepatic type. Laennec's cirrhosis was the most frequent cause, constituting 79.4 per cent of the cases. There was a preponderance of males over females in the intrahepatic group while the reverse was true in the extrahepatic group.
3. The incidence of hematemesis was 28.3 per cent. The longer the interval between the first attack of bleeding and the time of admission the more frequent were the attacks. In general, the incidence of hematemesis was directly proportional to the height of the portal pressure. It was higher in the extrahepatic group than in the intrahepatic group.
4. Ascites was present in 43.9 per cent of the cases. In most of the ascitic patients, there was a disturbance in the plasma protein level. There was also a close relationship between the incidence of ascites and the increase of portal pressure. Ascites occurred about twice as frequently in the intrahepatic group as in the extrahepatic group.
5. Esophageal varices were found in 61.7 per cent of the cases, more frequently in the extrahepatic group than in the intrahepatic group. This is also true with the incidence of hematemesis. Hematemesis may occur in cases without roentgenological evidence of esophageal varices, but its

incidence is only about one half of that in cases with demonstrable varices.

6. The operative treatment in this series included splenectomy in 52 cases, splenorenal anastomosis in 8, mediastinotomy in 2, ligation of hepatic artery in 2, anastomosis between the splenic vein and a retroperitoneal collateral in 1. The operative mortality was 3.2 per cent.

7. Mediastinotomy and anastomosis of the splenic vein to any collateral branch yielded no beneficial results and were abandoned.

8. Splenectomy relieved hypersplenism and reduced the portal pressure in most of the cases, especially those with the extrahepatic type of portal obstruction. Symptomatic relief and improvement in liver function were observed in the cases followed up postoperatively. The technic is simple, and it is suggested that in early cases of portal hypertension with marked clinical manifestations of hypersplenism and yet with no history of hematemesis, splenectomy should be the operation of choice, especially in the extrahepatic type of cases.

9. Ligation of the hepatic artery in addition to splenectomy may further reduce congestion in the portal system. Clinically, it may have the effect of lessening the occurrence of hematemesis and ascites. In late cases with a history of hematemesis and the presence of ascites in a large amount, ligation of the hepatic artery may be adopted.

10. Splenorenal anastomosis is a more effective procedure in reducing the portal pressure than simple splenectomy. In cases with a history of hematemesis, presence of a moderately enlarged spleen and absence of marked impairment of liver function, splenorenal anastomosis is indicated.

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RHEUMATIC HEART DISEASE WITH CUTANEOUS VASCULAR ENDOTHELIOSIS

REPORT OF A CASE

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Local cutaneous vascular endotheliosis associated with rheumatic heart disease is not commonly seen in clinical practice. A case similar to that reported by Yen(1) was encountered at the Southwestern Hospital, Chungking. The patient had a high leukocyte count. The blood taken from the ear lobe, finger tip, face and arm contained a large number of macrophages (also known as histiocytes or clasmatoocytes). During the period of observation, the macrophages gradually decreased in number and finally disappeared. The morphological characteristics of the macrophage also gradually changed to resemble the ordinary monocytes. The blood taken from the vein was normal and showed no macrophages. Our case is here reported.

CASE REPORT

The patient was a policeman, aged 28, native of Honan province. He had fever for two months in the summer of 1951 and later visited our outpatient clinic several times because of multiple migrating joint pain, frequent attacks of sore throat and dyspnea on exertion. Examination disclosed cardiac enlargement with a soft presystolic murmur over the apex, systolic murmur and diastolic murmur over the aortic area, and positive peripheral vascular signs of aortic insufficiency. The blood pressure was 104/? mm Hg. The blood Kahn test was positive; the patient admitted venereal exposure. The leukocyte count from the ear lobe was 7,050 per cu mm. The OPD diagnosis rested between syphilitic aortic disease and rheumatic heart with double valvular lesions. The patient received both sodium salicylate and anti-leptic treatment with penicillin injections, whereupon he felt better and the blood Kahn test turned to be negative.

He visited our clinic again on January 16, 1954, complaining of left upper abdominal pain that lasted nine days. Besides the positive cardiac findings he was found to have hepatosplenomegaly and tenderness over the spleen. The leukocyte count from the ear lobe was 150,000 per cu mm with 40 per cent macrophages. He was admitted on January 23, 1954 for further observation.

On admission the patient was found to be well developed and moderately well nourished, mentally clear and cooperative. Temperature 36.4 C. Pulse 92. Respiration 23. There was no general glandular enlargement. No edema or jaundice. The external aspect of the ear lobes appeared normal. The jugular veins were

prominent. The heart was enlarged mainly toward the left side. There was a systolic thrill over the sternal notch and the right first intercostal space. A blowing systolic and a diastolic murmur were heard over the right first intercostal space near the sternum. Over the apex there was also a diastolic murmur which was rough and rumbling in character. The pulmonary second sound was accentuated. The heart beat was regular. The blood pressure was 124/80-0 mm Hg. There were positive peripheral vascular signs of aortic insufficiency. The abdomen was slightly full. The liver was enlarged to 4.5 cm below the right costal margin, soft and non-tender. The spleen was enlarged to 7.5 cm below the left costal margin, with definite tenderness on palpation. No ascites or edema of the legs.

Laboratory findings. Hemoglobin 7 gm per cent, RBC 2,450,000 per cu mm. WBC and differential count were as shown in Table 1. Erythrocyte sedimentation rate 107 mm per hour. Hematocrit 29 per cent. Platelet count and reticulocyte count were normal. Blood Kahn and Wassermann tests were negative. Serum albumin 4.08 gm per cent, serum globulin 4.01 gm per cent. Venous pressure 200 mm of water column. Circulation time: arm to lung 10 seconds, arm to tongue 15 seconds. Blood culture negative. Thymol flocculation test 3 plus, cephalin-cholesterol flocculation test 3 plus. Urinalysis: albumin 1 plus, granular cast 0-3 per lower power field, RBC few. Stool examination revealed the presence of ascaris ova. EKG showed left ventricular preponderance.

Radiological examination of the chest revealed that the lungs were clear, the heart was enlarged mainly toward the left side, and the aorta was slightly widened with prominent pulsation. The esophagus was pushed backward by the enlarged left auricle as shown by barium meal examination.

After admission, the patient, in addition to the complaint of upper abdominal pain, developed edema of both legs, occasional petechiae over the skin and pain in the finger tips and toes. There were profuse sweating and cough with frothy sputum. He had shortness of breath while lying flat. No chills or fever. He was then diagnosed as a case of rheumatic double valvular disease with heart failure and subacute bacterial endocarditis. Besides the treatment for his heart failure, penicillin intramuscularly was started on February 2, 1954 with a dosage of 200,000 units every four hours for six weeks. The condition of the patient did not improve in the course of penicillin treatment. He still had profuse sweating and frequent attacks of pain over the spleen and the epigastric region as well as the tip of the fingers or toes. The spleen increased in size and reached at one time 12 cm below the costal margin.

On April 14, 1954 the bone marrow culture revealed the growth of streptococcus, D group, whereupon penicillin 200,000 units every four hours intramuscularly together with streptomycin 0.5 gm every twelve hours intramuscularly were given for another six weeks. Following this treatment, the symptoms began to improve: there was better appetite, less sweating, the liver and the spleen decreased in size and the tenderness of the spleen disappeared. But the patient still had occasional epigastric pain and loose bowel movements. The pain in the tip of the fingers or toes occurred less frequently.

The patient was discharged on July 6, 1954 with cardiac findings same as on admission. The liver and the spleen were just palpable and non-tender. He gained 10 pounds of body weight. The blood taken from the ear lobe and the finger tip revealed a normal leukocyte count and differential count. He came back for a follow-up examination on August 30, 1954 and was found in fairly good general condition.

He returned to duty after his discharge from the hospital although the symptoms of dyspnea and palpitation on exertion persisted. The blood taken from the ear lobe and the finger tip was normal.

Observations on the blood picture during hospitalization. On the day the patient was admitted, the interne on duty made a leukocyte count of the blood taken from the ear lobe and found it 11,500 per cu mm as compared with the count of 104,000 per cu mm taken at the OPD that very morning. On the second day the leukocyte counts were found to vary from 12,300 per cu mm to 58,750 per cu mm. Repeated examinations later showed that the white count fluctuated within a short period of time.

The blood smear taken from the ear lobe revealed the presence of macrophages (Figs. 1 and 2). They were numerous at the time of admission but became gradually decreased in number (Table 1 and Fig. 3).

Table 1. *The leukocyte count and differential count during the course of observation*

Date	WBC count		Differential count (%)							Large macrophage (%)	
	Ear lobe	Elsewhere	Neutrophil	Lymphocyte	Eosinophil	Basophil	Monocyte	Macrophage			
								Mature	Immature		
January	16	150,000		37	21	1		1	26.5	13.5	26.5
	21	104,000		44	20	1.5	0.5	2.5	23.5	8	17.5
	21	11,500									
	22	12,300									
	22	58,750		42	21			5		32	
	23	24,300									
	24	59,600		42	23.5	4.5	1	1	22.5	5.5	12
February	6	29,450		48	20	4		4		24	
	8	23,200		48	20	4		6		22	
	8		6,500 Vein	65	22	3		10		0	
	8		6,500 Vein	66	24	3		7		0	
	8		5,500 Finger tip	42	29	2		12	13	2	5
	12		5,500 Finger tip	42	31	4		16		7	
	23		— Face	44	29	2		12	10	3	5
23		— Arm	47	28	5		13	6	1	3	
27	10,500		54	30	5	1	10		0		
March	1	9,000								0	
April	17	8,500		63	28	6		3		0	
May	8	8,100								0	
June	5	7,300								0	
August	30	11,000		67	17	13		3		0	
	30		7,600 Finger tip	69	17	11		3		0	

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Fig. 1. The blood smear showing a small macrophage on the left and a large macrophage on the right. $\times 1,400$.

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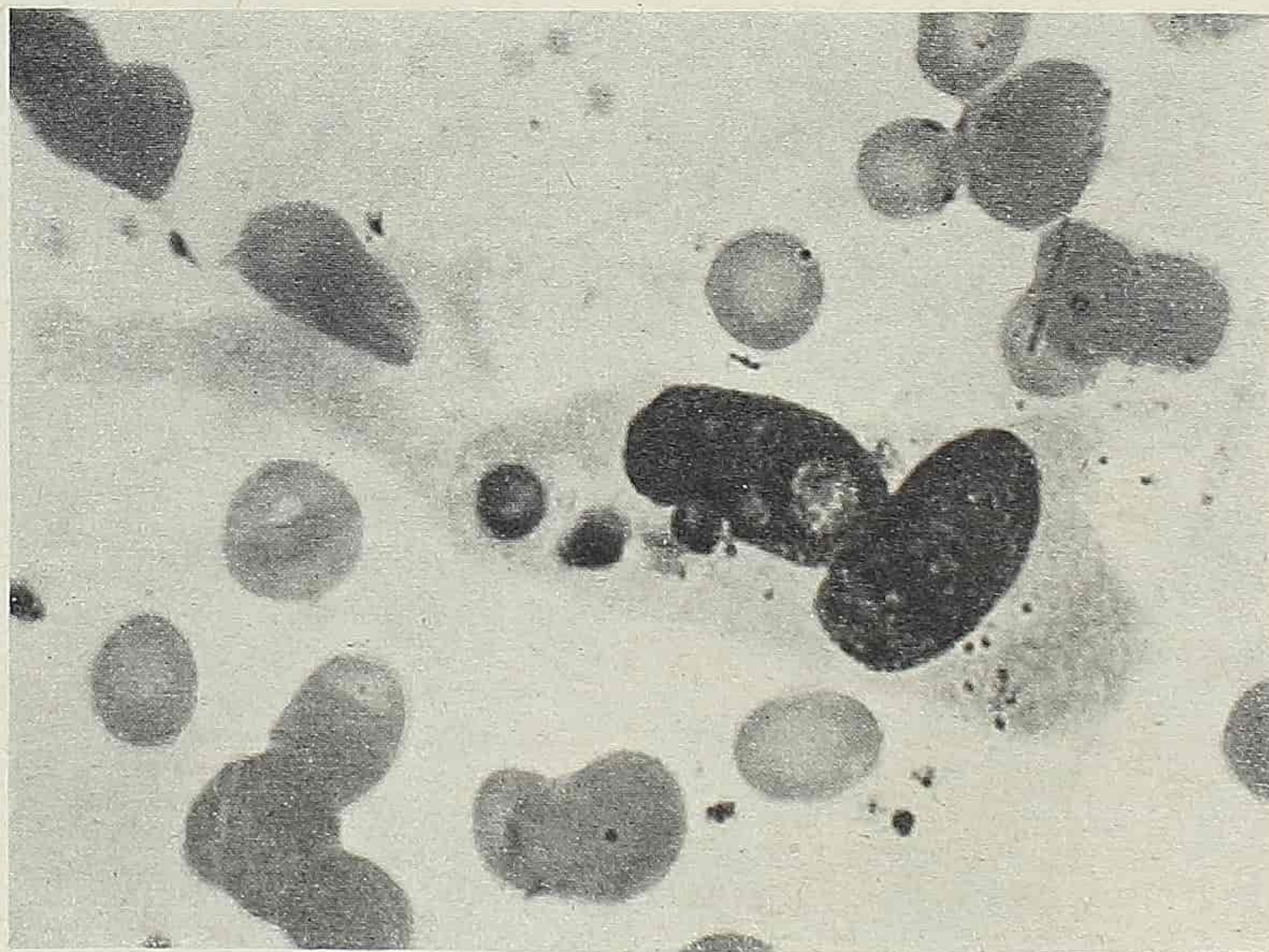


Fig. 2. The blood smear showing a large macrophage. $\times 1,400$.

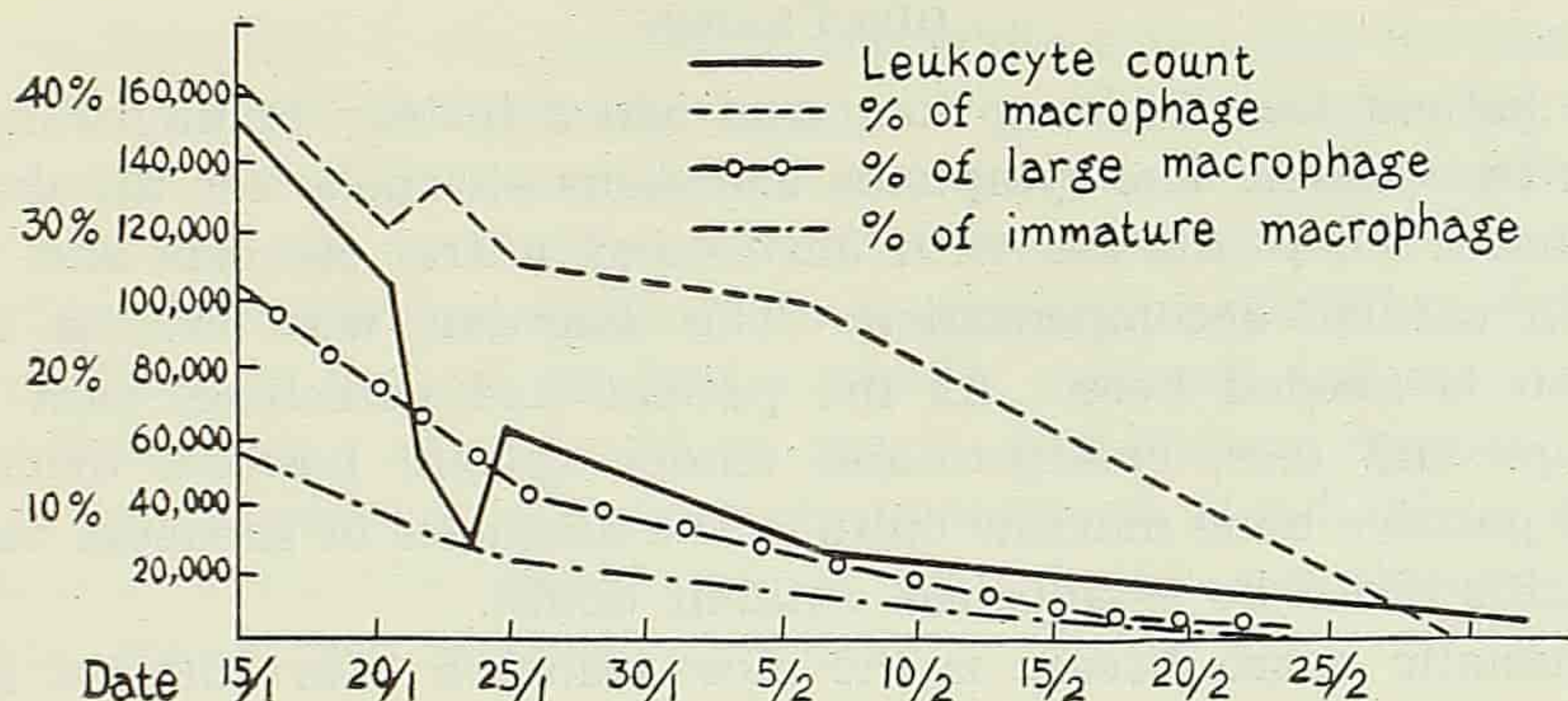


Fig. 3. Changes in leukocyte count and differential count (blood taken from the ear lobe) during the course of observation.

From these data, it was evident that:

1. Although the total number of white blood cells varied a great deal, in general it tended to decrease until it reached the normal value.
2. The number of macrophages was directly proportional to the total white cell count. Both of them showed the tendency of gradual reduction in number. The high leukocyte count of the blood taken from the ear lobe was not merely due to the presence of macrophages, but also to the absolute increase in the number of granulocytes and lymphocytes.
3. The greater the number of macrophages, the greater was the proportion of the immature type.
4. As the macrophages were reduced in number, they became smaller and smaller in size, and showed less phagocytic power and finally resembled the ordinary monocytes.

Observations on morphological characteristics of macrophages. Most of the large macrophages were 7-8 times the size of the neutrophils and appeared to have irregular contour with bleb-like or filiform pseudopodia. When stained with Wright's stain the cytoplasm was seen to be abundant, light blue in color, containing numerous red granules and ingested blood cells and debris. Often the cell appeared to be broken up with only one naked nucleus present. The nucleus was not uniform in shape and often appeared to be elongated, round or kidney-shaped, or twisted into several lobes. Occasionally there were 2-3 nuclei in one cell. The nuclear chromatin was spongy. The nucleus contained 1-3 nucleoli.

The small macrophage was only slightly larger than a neutrophil, its cytoplasm was scanty, stained sky-blue with Wright's stain and studded with a small amount of reddish granules.

The white blood cell count of the venous blood was normal. No macrophage was found in the smear. In order to determine whether the presence of macrophages was due to local changes of the ear lobe, blood smears were taken from the finger tips, face and arm at the same time, and examination of these smears showed that all of them were positive for macrophages.

Sternal puncture was done on January 25, 1954. The bone marrow was quite active. There were hyperplasia and a 'left shift' of the granular series, with 7 per cent myeloblasts and only 4 per cent segmented neutrophils. No macrophage was found in the bone marrow smear.

Skin tissue biopsies taken from the ear lobe, face and arm on April 17, 1954 showed nothing abnormal.

DISCUSSION

The patient was a young man who had a history of migrating joint pain for two years. The symptoms and signs all spoke for the diagnosis of rheumatic heart disease with aortic and mitral stenosis and insufficiency in cardiac decompensation. The diagnosis was obvious and no discussion is needed here. As the patient had petechiae, pain in the finger tips and toes, enlarged and tender spleen, positive urine findings and positive bone marrow culture, the diagnosis of subacute bacterial endocarditis could be established without doubt.

Rheumatic heart disease is the most common heart disease seen in southwest China and is often complicated with subacute bacterial endocarditis. But cases complicated with cutaneous endotheliosis, such as ours, are probably very rare.

Opinions differ as to the origin of macrophages. Some authors consider that they are derived from monocytes and others from reticulum cells(2). Soviet authors(3) have shown that in rheumatic or bacterial endocarditis the presence of macrophages results from the proliferation of endothelial cells of the blood vessels during the hypersensitive state. In rheumatic disease, this kind of endotheliosis may not be apparent as in bacterial endocarditis during routine blood examination but can be demonstrated by the 'cupping-glass' test. In Yen's case the biopsy from the skin of the ear lobe showed cutaneous endotheliosis of the blood vessel. Unfortunately this examination was not done in our patient during the early period of his hospitalization because his ear lobes were purplish red and swollen from too frequent punctures for blood examination.

Valedman(3) is of the opinion that endotheliosis is a generalized reaction in rheumatic heart disease and bacterial endocarditis, and the hyperplastic change of the endothelium of the blood vessels may vary in degree depending upon the location, the kind and the size as well as the degree of allergic reaction of the blood vessels. In this case, the variation of the white count from the blood of the ear lobe might be explained on the difference of the hyperplastic state of the blood vessels. However, the squeezing in the process of taking blood might also be an important factor. Its mechanism is similar to that which causes the appearance of macrophages in the blood smear when the cupping glass is applied.

In our patient, the white count and the percentage of the macrophages at first fluctuated a great deal, but soon after the middle of January they began to show a general tendency to decline and finally at the end of February they came down to the normal limits. It is believed that the improvement of the blood picture was not directly related to the subacute bacterial endocarditis, because when penicillin treatment was

started on February 2, the decline in the white count and the percentage of the macrophages had already begun. The blood picture had become normal at the end of February and yet the symptoms of endocarditis were still present and the bone marrow culture was still positive on April 10. The change of the blood picture could not possibly be related to the splenic infarction because the patient had a rapidly enlarged and tender spleen in early March, long after the blood picture had become normal. As the nature of endotheliosis is still not fully understood, it is hard to say whether or not it can be considered as one of the complicated clinical manifestations of the rheumatic disease.

SUMMARY

A case of rheumatic heart disease with subacute bacterial endocarditis is reported. During the course of observation the patient was found to have high leukocytosis and large numbers of macrophages in the blood smear taken from the ear lobe. Macrophages were also demonstrated in the blood taken from the finger tip, face and arm. The endotheliosis observed was apparently not related to the subacute bacterial endocarditis or to the splenic infarction. Whether it is one of the complicated clinical manifestations of the rheumatic disease is not certain.

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METASTATIC CARCINOMA OF THE HUMERUS FROM THE GASTROINTESTINAL TRACT

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While metastatic lesions in the skeleton from carcinomas of the prostate, kidney, thyroid, breast or lung are well-known, the incidence of bone metastasis from carcinomas of the gastrointestinal tract is relatively rare.

Table 1 summarizes the reports of various authors giving the number of cases of carcinomas of the stomach and the rectum and their percentages in relation to the total admission of cases of carcinomas of specific organs.

Table 1. *Incidence of bone metastasis from carcinoma of the stomach and the rectum reported by different authors*

Authors	Cases of bone metastasis from carcinoma of stomach	Percentage	Cases of bone metastasis from carcinoma of rectum	Percentage
Müller, 1892(1)	8	2.58	6	10.52
Sutherland, 1932(2)	20	1.9	5	—
Warren, 1933(3, 4)	4	5.9	2	2.2
Ghormley, 1939(5)	12	0.2	19	0.5
Geschickter and Copeland 1949(6)	7	1.3	3	0.6
Coley and Higinbotham, 1954(7)	3	3.15	2	0.88

The usual sites of metastasis are the spine, pelvis, skull and ribs. Metastasis to the humerus is uncommon in carcinomas of the gastrointestinal tract. Weston(8) in his review of the literature stated that Pitts in 1891, Aufses in 1930, Geschickter and Copeland in 1936, Hayden in 1936, and Brown and Warren in 1938 reported altogether 5 cases of metastasis to the humerus, and that his own case was the sixth.

We have encountered 3 cases of metastatic carcinoma of the humerus since 1952. Two of them were from carcinoma of the stomach and 1 from carcinoma of the rectum.

REPORT OF CASES

CASE 1. C. T. S., a male electrician, aged 54, came to the hospital on July 16, 1952 after a sudden onset of severe pain in his right arm two hours before admission. He was unable to move his right arm after attempting to throw an electric cable up a pole. In the summer of 1951 he fell from a bicycle. Since then he had occasionally experienced soreness in the right shoulder. He had constipation and tarry stool for five years.

Examination showed that the patient was well developed. The right humerus was found to be fractured. On rectal examination, a mass was found 1½ inches above the anal opening. Proctoscopic examination revealed a hard irregular mass involving the posterior wall and the right side of the rectum. Roentgenogram of the right humerus taken immediately after admission revealed a transverse fracture at the junction between the upper and the middle third without much displacement. There was bony destruction. Roentgenogram of the chest was negative.

The blood picture was within normal limit. The sedimentation rate was 25 mm at the end of one hour (Westergren method). The value of alkaline phosphatase was 2.6 Bodansky units. Findings of urinalysis and the Wassermann reaction were negative. Result of examination of stool for occult blood was strongly positive. Biopsy of the rectal lesion (Fig. 1A) revealed large groups of tumor cells of unequal sizes. Some of them were hyperchromatic while most of them were vacuolated with their nuclei pushed to one side forming signet ring cells. A smear (Fig. 1B) of the aspirated material from the site of fracture of the humerus consisted of a large number of round or polyhedral tumor cells with large hyperchromatic nuclei. These tumor cells were of unequal sizes and were scattered in groups among large numbers of red blood cells.

The patient returned to the hospital three months later. Further roentgenological examination of the right humerus showed generalized bony absorption with marked destruction. He died on May 18, 1953, ten months after the first visit. Our diagnosis was carcinoma of the rectum with metastasis to the right humerus.

CASE 2. S. M. Y., a male worker, aged 59, was admitted on October 13, 1952, complaining of intermittent soreness and pain in the right shoulder for one month. There was a history of gastric disturbance with tarry stool for four years and also venereal exposures.

The patient was well developed. There was severe tenderness at the middle third of the right arm, which presented no local swelling or reddening. Roentgenogram of the right humerus revealed an osteolytic lesion in the shaft with little periosteal reaction and that of the stomach showed a filling defect in the antrum. The chest film showed normal lungs.

The blood picture was normal. Alkaline phosphatase was 7.2 King-Armstrong units. The total cell count of the cerebrospinal fluid was 67 per cu mm with 12 per cent polymorphonuclear cells and 88 per cent lymphocytes. Pandy's test was 2 plus; the sugar was 80 mg per cent and the Wassermann reaction was negative. Gastric analysis showed high acidity, the free acid being 60 units and the total acid 112 units. Sections (Figs. 2A and 2B) prepared from the biopsy material of the lesion in the right humerus showed large sheets of cancer cells which were polyhedral with variation in size, shape and staining. The nucleoli of the tumor cells were prominent and mitosis was frequently observed. These cells were either in groups separated by a scanty amount of fibrous stroma or in cords surrounded by more abundant stroma.

On the night of the eighteenth day after admission, the patient woke up with an excruciating pain caused by a pathological fracture in the right humerus. Seven days later, he vomited about 75 cc coffee ground substance, which was acidic in reaction. On November 10, 1952, he died after another attack of massive hemorrhage. Our diagnosis was carcinoma of the stomach with metastasis to the right humerus.

CASE 3. W. A. T., a woman farmer of 33 years of age was admitted on March 5, 1955 complaining of soreness in the lumbar region for eight months and two movable masses in the lower abdomen for two months. Nine months prior to admission, the soreness became incapacitating although it was relieved after rest. Three months later, pain occurred in the cervical and the shoulder regions. The two movable masses in the lower abdomen had grown to the level of the umbilicus. Some four months prior to admission she had occasionally tarry stool but no other gastrointestinal symptoms.

The patient appeared healthy. Two oval-shaped movable masses with nodular surface were felt at the left upper and the right lower abdomen. The left mass was bigger than the right. Multiple skin nodules were noticed over the scalp, axilla, and the upper abdomen. The inguinal glands on both sides were palpable. Both pelvic and rectal examinations revealed that the masses occupied the pelvic cavity. Roentgenogram of the stomach showed a large filling defect at the pyloric antrum along the greater curvature. Filling of the duodenum cap was normal. Roentgenogram of the chest was negative, except for some obliteration of the left phrenic angle. Scouting films of bones revealed multiple circumscribed osteolytic lesions with moth-eaten appearance in the humeri, radii, ulnae, necks of scapulae, femora, ribs, vertebral bodies and the skull.

The red cell count was 2,020,000 per cu mm, hemoglobin was 6.5 gm per cent, and immature red cells were found. Blood Wassermann reaction was negative, Alkaline phosphatase was 82.8 King-Armstrong units and acid phosphatase was 4.95 King-Armstrong units. Urinalysis was negative. Stool for occult blood was 2 plus. Biopsy of the skin nodule revealed groups of cancer cells with presence of mitotic figures. The smear of the aspirated material from the right ilium revealed clusters of tumor cells of varying sizes and shapes. Signet ring cells could also be seen.

The patient was discharged on March 17, 1955 but did not return for follow up. Our diagnosis was carcinoma of the stomach with Krukenberg's tumor of both ovaries and wide-spread bone metastases.

DISCUSSION

Our 2 cases of carcinoma of the stomach and 1 case of carcinoma of the rectum with metastases to the humerus were diagnosed either by roentgenography or by biopsy. Though we were not able to perform necropsy, the clinical evidence was strong enough to determine the primary site of malignancy. Case 1 was proved by biopsy from the rectum and aspiration biopsy from the humerus. The metastatic lesion of Case 2 was also proved by biopsy from the humerus, while the clinical picture, gastric analysis and the roentgenogram of the stomach were consistent with our diagnosis of carcinoma of the stomach. Case 3 had multiple foci of metastases in the skeleton and the aspiration biopsy from the right ilium

showed the presence of tumor cells with clusters of signet ring cells. Though no surgical exploration was done, the roentgenogram of the stomach and the presence of Krukenberg's tumors of ovaries as diagnosed by our gynecologist strongly suggested that the primary lesion was in the stomach.

In all our cases, the site of metastases gave rise to early symptoms. The first 2 cases had pathological fractures of the humerus before the exact diagnosis was made. The third case gave the symptoms of pain and soreness over the back, shoulder and the cervical region instead of in the gastrointestinal tract. These facts show that metastatic lesions in bones might arise from concealed lesions in the gastrointestinal tract, whose investigation is of much importance.

Moreover, in some cases of carcinoma of the stomach with definite bone metastases, clinical evidence is often lacking, and even roentgenological examination may be negative. Lawton's(9) 10 cases of carcinoma of stomach which showed bone metastasis clinically were not seen in the x-ray film. Metastatic lesions were verified in 3 of them at necropsy. Thus, cases of bone metastases from carcinoma of the stomach and the rectum are probably more common than generally supposed.

The following four anatomical pathways(10) are possible routes of spread of carcinomas of the gastrointestinal tract: direct extension, the lymph vessels, the blood stream, and transplantation through the peritoneal cavity. Carnett and Howell(11) support the theory of lymphatic permeation in case of neoplastic extension within the abdomen. Mechling(12) asserts that the spread is either direct through the blood stream or secondarily through the embolus formation (e.g. in the lung with secondary growth and further spread therefrom) or the result of the passage of a single cancer cell through the lung capillaries into the general circulation. He believes that the tumor cell emboli entering the thoracic duct from the blood stream may produce the bizarre metastatic lesion. Batson(13) believes that metastasis may occur through the vertebral veins. The vertebral veins, according to him, form a separate system, having a rich, valveless ramification and connections, so that metastasis can occur without involvement of the heart and lungs. Geschickter and Copeland(6) state that, in view of cases with metastasis to the long bones as the humerus and the femur but without invasion of the intervening structures between the primary focus and the distant metastasis, one is forced to consider metastasis occurring by way of the blood stream. But it seems that each case should be considered individually. In our cases the hematogenous or lymphatic route appears to be the more likely channel of spread.

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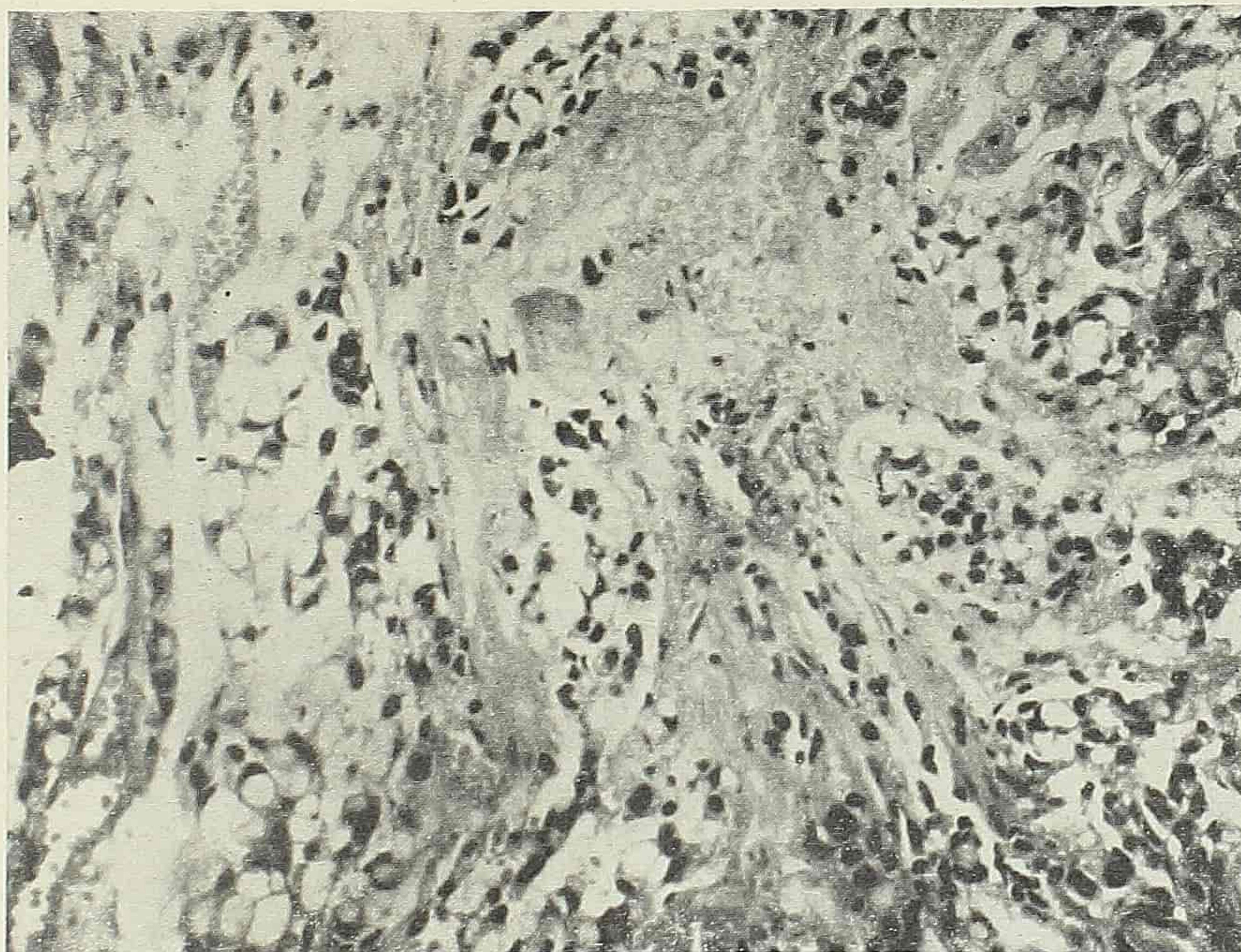


Fig. 1A. Photomicrogram ($\times 202$) of rectal biopsy showing typical signet ring cells, consistent with the picture of mucoid carcinoma of the rectum (hematoxylin and eosin stain).

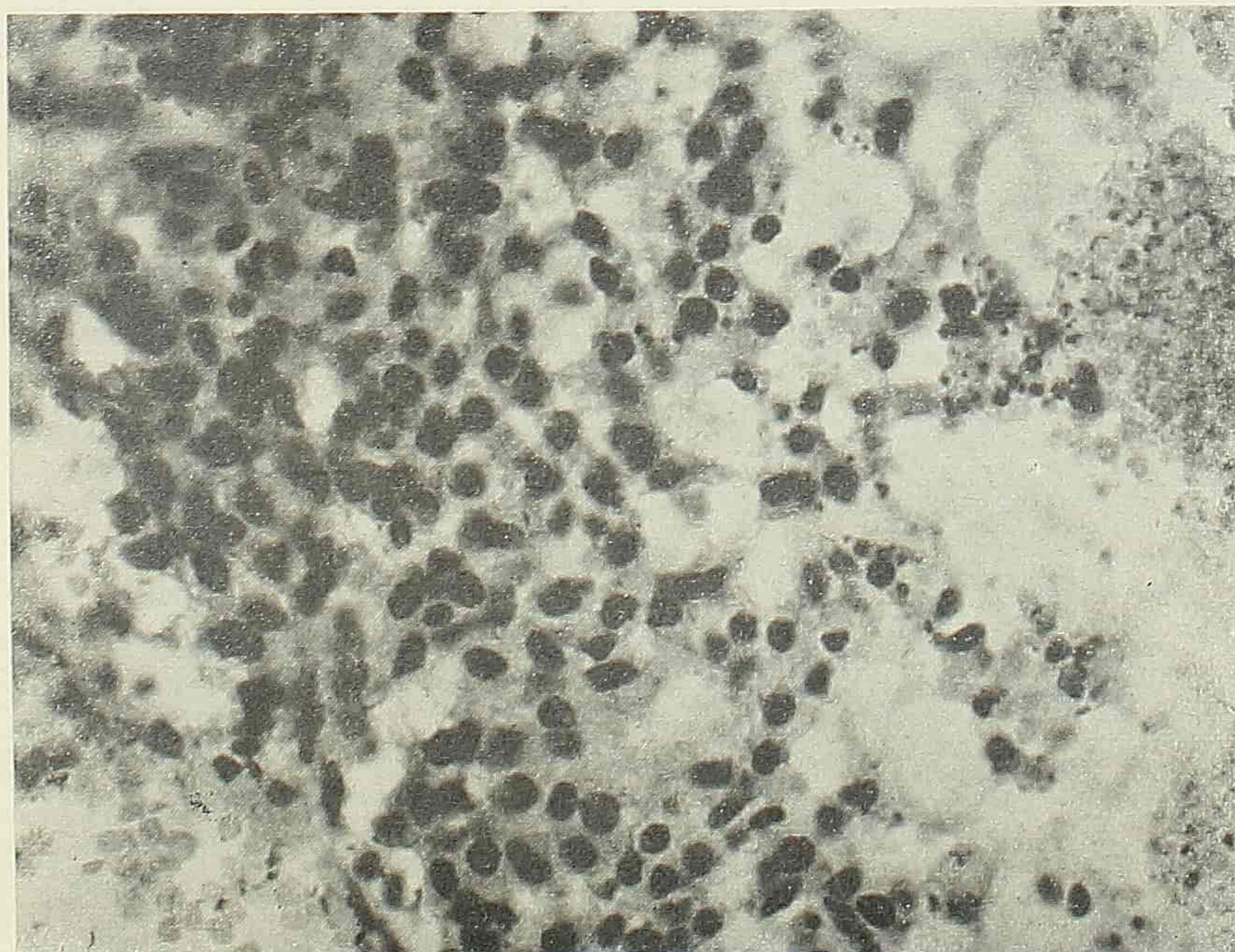


Fig. 1B. Photomicrogram ($\times 506$) of aspiration biopsy from the right humerus, revealing tumor cells of unequal size with hyperchromatic nuclei (hematoxylin and eosin stain).

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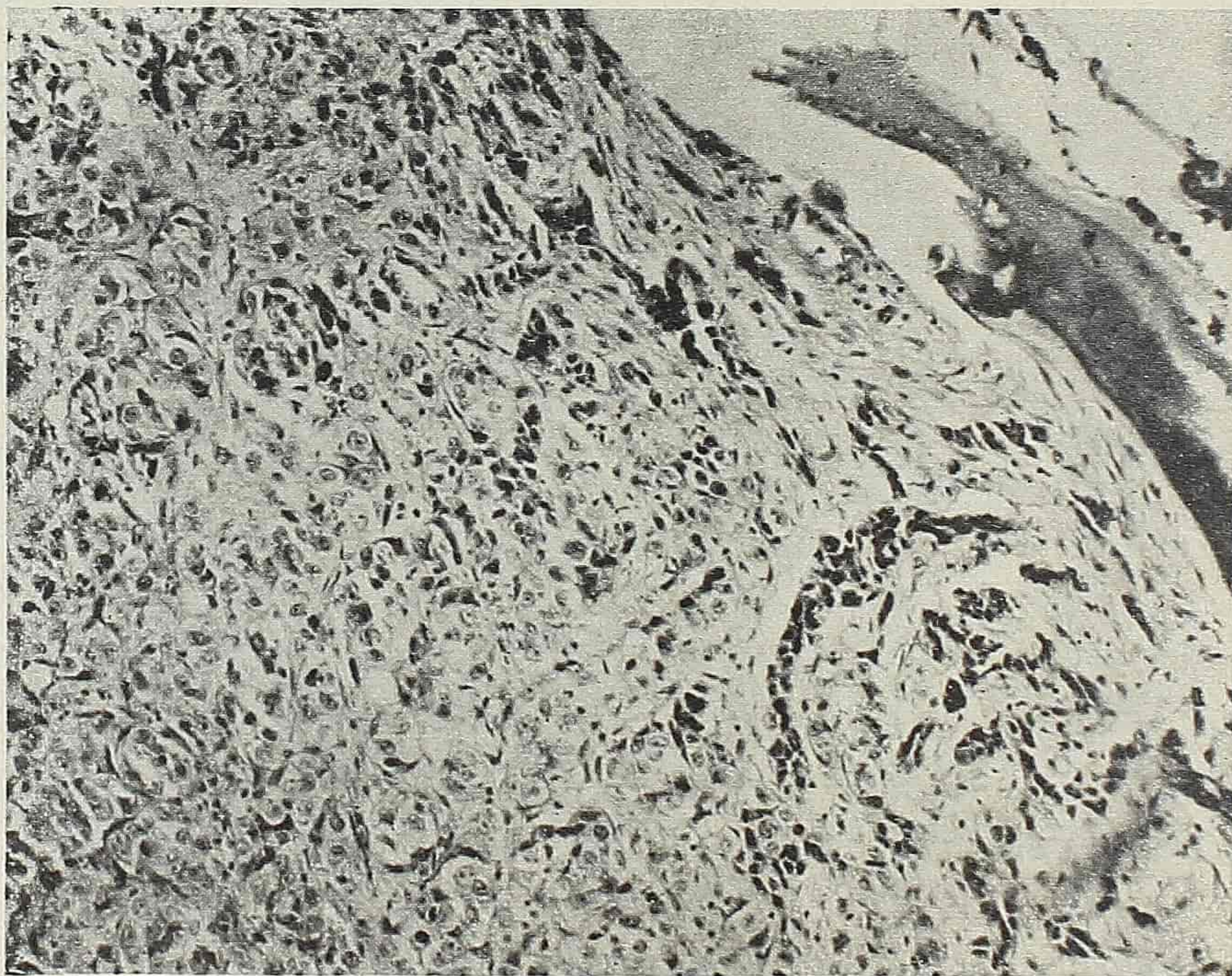


Fig. 2A. Photomicrogram ($\times 112$) of bone biopsy from the right humerus, revealing replacement of bony tissue by tumor cells from carcinoma of the stomach (hematoxylin and eosin stain).



Fig. 2B. Section of above under high magnification ($\times 506$).

INTESTINAL OBSTRUCTION DUE TO INTERNAL HERNIA FOLLOWING PARTIAL GASTRECTOMY

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Partial gastrectomy, a procedure widely used today, can be accomplished with a very low mortality. In seeking to further improve the safety of a dependable procedure one's attention is naturally directed towards the treatment and prevention of serious though rare complications that may arise. The present communication consists of a report of 2 cases of intestinal obstruction due to internal herniation of the proximal jejunal loop following partial gastrectomy and antecolic gastrojejunostomy. The report is made because due attention is not always paid to this rare but serious complication.

Between May 1951 and November 1954, 101 partial gastrectomies were done in this hospital, 98 for peptic ulcers (38 duodenal and 60 gastric ulcers) and 3 for gastric malignancies. All of them were resections of two thirds to three fourths of the stomach followed by gastrojejunal anastomoses of one type or another. In 97 instances the gastrojejunostomies were of the antecolic type with the proximal end of the jejunal loop sutured to the lesser curvature of the stomach and the entire cut end of the stomach used for the stoma (Balfour). In 1 instance, antecolic anastomosis was done by suturing the proximal end of the jejunal loop to the greater curvature of the stomach (Moynihan). In 3 instances, retrocolic gastrojejunostomies were done with the proximal end of the jejunal loop sutured to the lesser curvature of the stomach (Polya). The 2 cases of intestinal obstruction due to internal hernia occurred among the 97 cases of the Balfour type of antecolic gastrojejunostomies. Because of timely diagnosis and surgical intervention, the patients in both these cases recovered. They were found well and in good health three and a half and two and a half years later.

REPORT OF CASES

CASE 1. Chen, a 43 year old house wife, was first admitted to this hospital on November 15, 1951 for gastric ulcer of about ten years duration. The clinical diagnosis of gastric ulcer was substantiated by x-ray studies with barium meal. She was operated upon under ether anesthesia on November 28, 1951. A partial gastrectomy removing the pylorus and three fourths of the stomach was performed followed by an antecolic gastrojejunostomy, the proximal end of the jejunal loop being sutured to the lesser curvature of the stomach, and the entire cut end of the stomach

used for the stoma. The proximal jejunal loop measured about 14 cm from the ligament of Treitz. The postoperative course was uneventful and the patient was discharged sixteen days after the operation.

She was admitted for the second time on March 1, 1952, and for the third time on March 13, 1952. On both occasions she complained of upper abdominal distention and pain, and symptomatic treatment gave relief. The clinical diagnosis was partial intestinal obstruction due to postoperative adhesions.

She was admitted for the fourth time on April 21, 1952 (one hundred and forty-five days after her partial gastrectomy operation) for sudden onset of upper abdominal pain of twenty-four hours' duration accompanied by marked nausea and vomiting. The vomitus was scanty and without bile. On examination, she was found to be thin and acutely ill. The upper abdomen was moderately distended, tender and spastic on palpation. In the first twenty-four hours after admission, symptomatic treatment was instituted but failed to give any relief. The abdominal pain soon became colicky and unbearable. Her general condition also deteriorated as evidenced by weakened pulse and much sweating. A mass was then felt over the left upper abdomen, and distention, tenderness and spasm spread over the entire abdomen. A clinical diagnosis of intestinal obstruction was made and an immediate exploratory operation was decided upon.

Under ether anesthesia, the abdomen was reopened through a left rectus incision. About 400 cc of reddish-brown fluid were removed from the peritoneal cavity. Many adhesions were noted among the intestinal loops. A bluish cystic mass about the size of a fetal head with patches of necrosis was found in the left upper abdomen. In an attempt to identify the mass by minimal dissections, it was ruptured. About 800 cc of bilious and bloody fluid were aspirated from the cystic mass. It then became apparent that the cystic mass was actually the proximal jejunal loop, which had herniated through an opening made up by the distal jejunal loop of the gastrojejunostomy in front and the transverse colon behind. The herniated loop was distended with bile and intestinal secretions, and its wall gangrenous (Fig. 1). Resection of the gangrenous loop of jejunum was carried out, and after closing the cut end of the jejunum near the gastrojejunostomy, an end-to-side jejunojejunostomy was done (Fig. 2) to re-establish the intestinal continuity. She stood the opera-

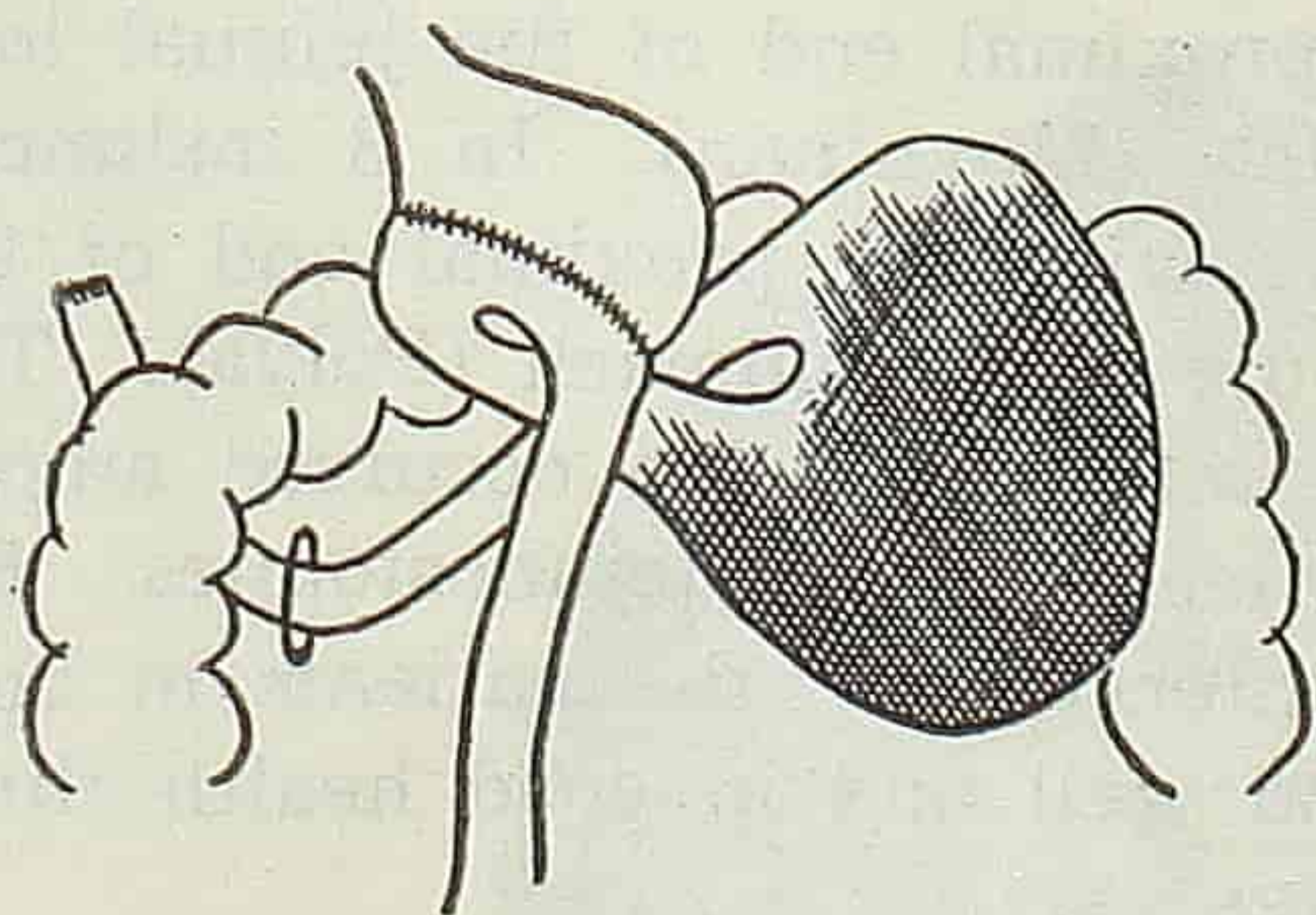


Fig. 1. Findings at second operation (Cases 1 and 2). Herniation of the afferent jejunal loop behind the anastomosis with gangrene of the bowel.

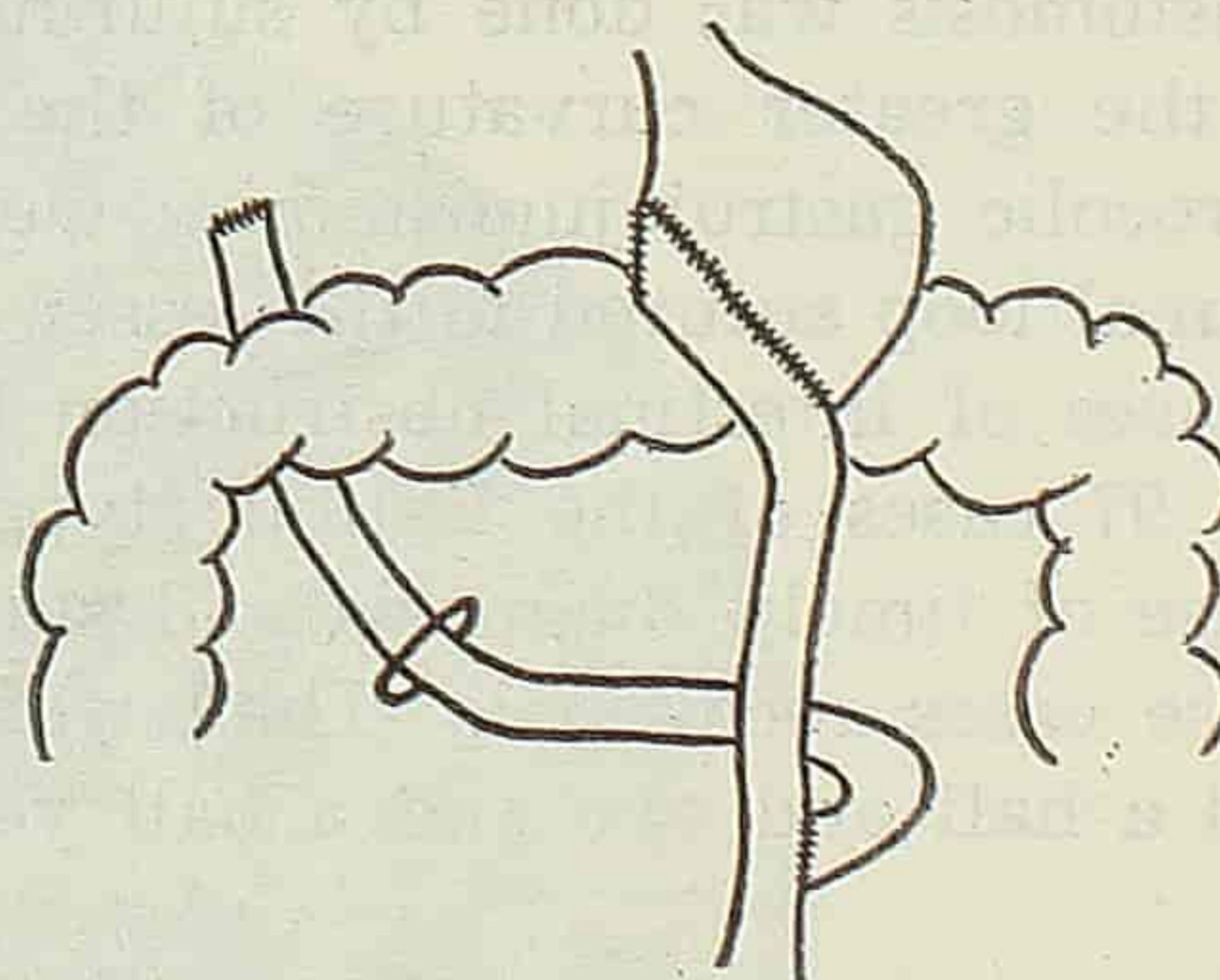


Fig. 2. After resection of the gangrenous jejunum, an end-to-side jejunojejunostomy was done.

tion well and was discharged on May 23, 1952, thirty-one days after the second operation. Two years later, upon follow up inquiry, the patient reported that she had gained 10 kg in body weight, ate with good appetite without any dietary

restrictions, and was free from all previous gastric symptoms. Second follow up one and a half years after the first showed that the patient remained well.

CASE 2. Shen, a 26 year old unmarried male, technician at this hospital, was admitted on October 27, 1952 for treatment of chronic duodenal ulcer proved by x-ray studies with barium meal. He was operated upon under ether anesthesia on November 1, 1952. A partial gastrectomy was done with the removal of the ulcer bearing duodenum near the pylorus and about three fourths of the stomach followed by an antecolic gastrojejunostomy of the Balfour type (same as in Case 1). The proximal jejunal loop measured about 14 cm from the ligament of Treitz. The patient was discharged on December 2, 1952, thirty days after the operation.

He was readmitted on December 8, 1952, six days after discharge or thirty-six days after operation for sudden onset of vomiting with chills and fever after a long pedicab ride on the previous day. Paroxysms of colicky pain with increasing severity were experienced in the upper abdomen after the onset. Examination showed that the patient was acutely ill and weak. The entire abdomen was distended, spastic and tender, particularly on the left side near the umbilicus where a mass about the size of a fist was felt. Increased peristalsis was detected on auscultation. Gastric decompression and colonic irrigations gave no relief. On account of our experience with the previous case, a clinical diagnosis of intestinal obstruction due to internal hernia was made and the patient was prepared for immediate exploration. Under ether anesthesia, the abdomen was reopened through a left rectus incision. About 200 cc of dark red and slightly turbid fluid were removed from the peritoneal cavity. The proximal jejunal loop was found to have herniated from right to left through the gap made up by the gastrojejunostomy. The herniated loop was markedly distended, measuring 10 cm in diameter, bluish, and with patches of necrosis, a condition similar to that found in Case 1. To reduce the intraluminal pressure the distended loop was aspirated and blood tinged brownish-green foul smelling fluid was removed. Reduction of the internal hernia was then made possible, but because of the patches of necrosis part of the proximal jejunal loop had to be resected. The cut end of the jejunum near the gastrojejunostomy was closed and the cut end near the ligament of Treitz was anastomosed end-to-side to the distal jejunal loop. A few interrupted stitches were placed between the mesentery of the jejunum used for the gastrojejunostomy and the transverse mesocolon. The patient stood the operation well and his postoperative course was smooth. He was discharged on February 9, 1953, or sixty-two days after the second operation.

On the first follow up two years after the second operation it was found that the patient had not gained much weight and that he had occasional gastric discomfort after meals; but six months later his body weight had increased by 4 kg and his appetite was good.

DISCUSSION

The type of anastomosis is not in itself the cause of internal hernia following partial gastrectomy. This is evidenced by the fact that such complication has arisen irrespective of the type of anastomosis, whether done anterior or posterior to the colon, or whether the jejunal loop is placed from right to left or from left to right. Each surgeon or clinic has a preference for a certain type of anastomosis, and this complication has been reported by different surgeons using the type of anastomosis they favor(1-5). Our 2 cases were internal hernias following antecolic

anastomoses, because in our hospital we prefer the antecolic anastomosis. The length of the proximal jejunal loop may have some bearing on the occurrence of the proximal loop hernias, as a long loop is more likely to herniate through an opening, and too short a proximal loop may twist under the pull of a short tense mesentery. But the length of the proximal loop has no influence whatsoever on the distal or efferent loop hernias.

The cause of these internal hernias is the opening or openings left unclosed after partial gastrectomy and gastrojejunostomy. After an antecolic gastrojejunostomy, an opening is created which is bounded in front by the gastric stump and the mesentery of the jejunal loop forming the anastomosis, behind by the transverse colon with its mesocolon and the posterior parietal peritoneum, superiorly by the reflection of the peritoneal attachments of the gastric stump, and inferiorly by the root of the mesentery of the jejunum at the ligament of Treitz (Fig. 3). After a retrocolic gastrojejunostomy, two openings are

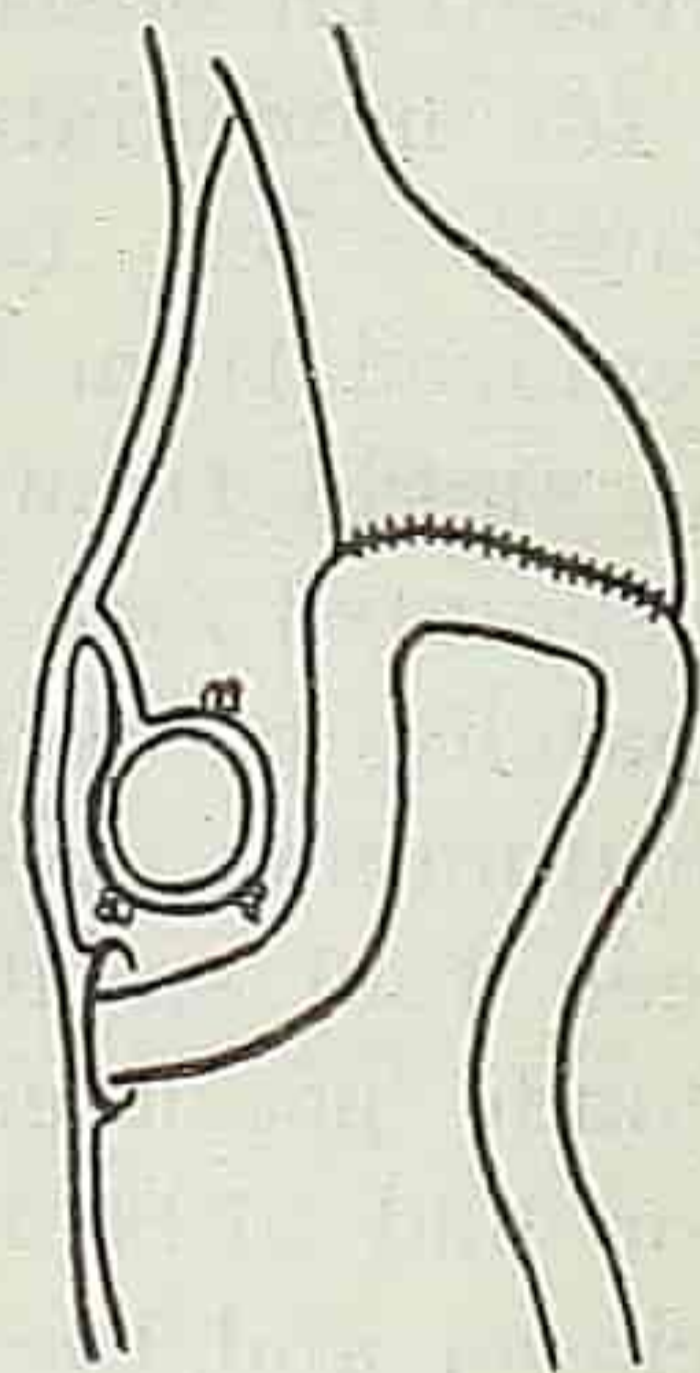


Fig. 3. Hernia ring resulting from antecolic gastrojejunostomy. Sketch also shows the appendices epiploicae of the transverse colon which may be utilized to close the ring.

created, an upper one formed by the gastric stump, the posterior parietal peritoneum and the transverse mesocolon, and a lower one beneath the transverse mesocolon formed by the posterior parietal peritoneum, the ligament of Treitz, and the mesentery of the jejunal loop used for the anastomosis (Fig. 4). These openings are potentially dangerous because

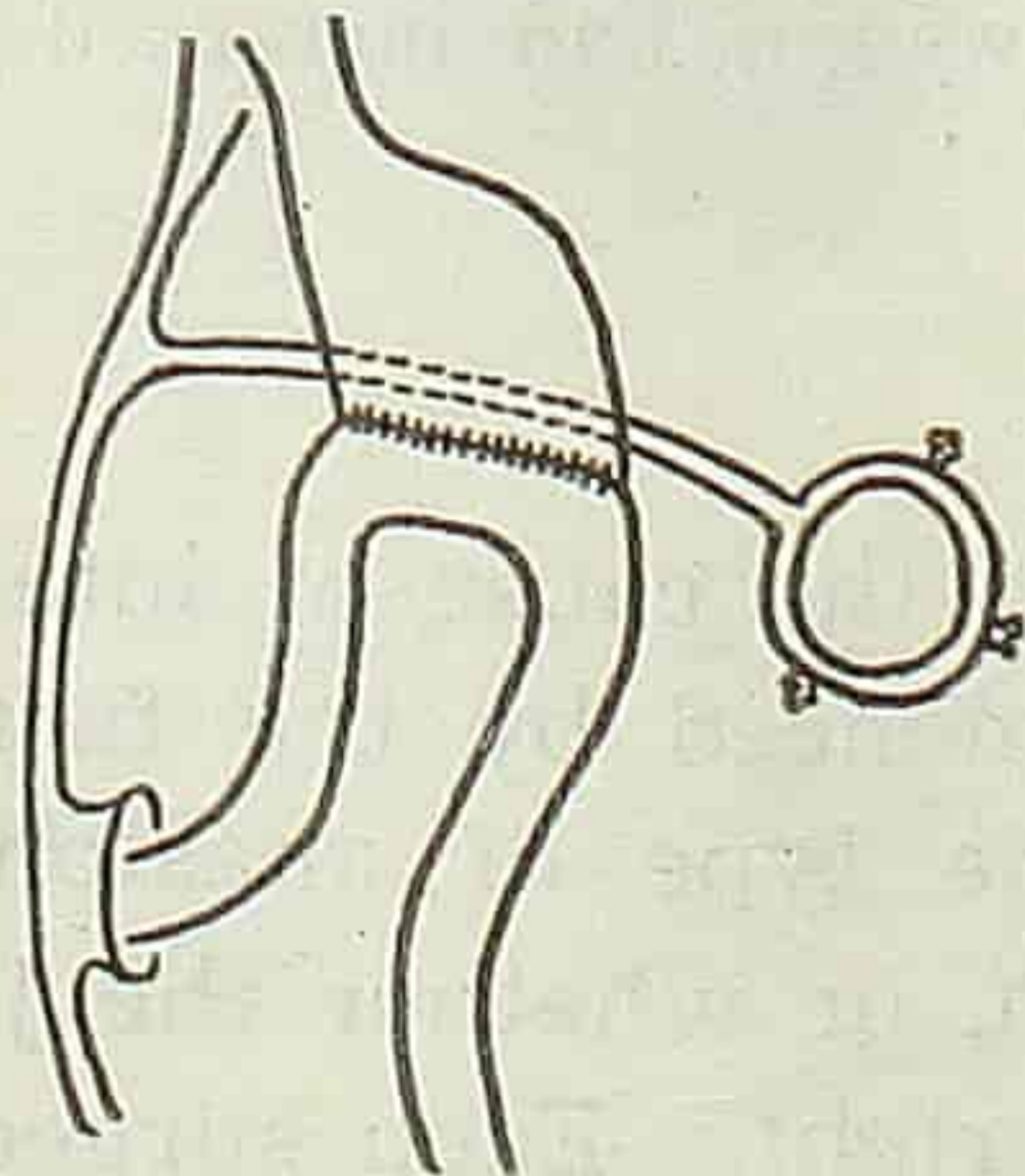


Fig. 4. Two hernia rings are created after a retrocolic gastrojejunostomy, one above and one below the transverse mesocolon.

they may give rise to internal hernias. In most clinics such openings are left unclosed routinely, hence it is surprising that internal hernias after gastrectomies are not reported more frequently. Recently, Morton

and his associates(5) surveyed the literature and found that since 1900 when internal hernia following gastroenterostomy was first reported by Peterson(6), approximately 70 cases had been reported beside their own 5 cases.

Such internal hernias, though infrequent, are serious conditions and usually end fatally unless diagnosed early and surgical intervention is carried out in time. Morton and others(5) gave the mortality among the reported cases as approaching 90 per cent. Herniation may occur a few days, a few months or years after gastrectomy and gastrojejunostomy. Its symptoms are characterized by sudden onset of severe upper abdominal pain and vomiting. The pain may be continuous or in paroxysms of increasing severity. Temporary relief may be obtained by gastric decompression but the symptoms will return with increased severity. When obstruction is due to a proximal jejunal loop hernia, the aspirated gastric content or vomitus contains no bile. Usually a mass can be felt in the left upper abdomen. When the strangulated bowel becomes gangrenous, signs of spreading peritonitis are evident. If a patient with a history of partial gastrectomy and gastrojejunostomy develops the above-mentioned symptoms, intestinal obstruction due to internal hernia should be considered.

The only treatment is early operation. If gangrene has not occurred, the herniated loop should be reduced followed by closure of the opening. In case of gangrene, resection of the gangrenous bowel and re-establishment of the intestinal continuity followed by closure of the opening should be done.

The only rational and sure way to prevent the occurrence of such intestinal obstruction following partial gastrectomy is to close the opening or openings created by the gastrojejunal anastomosis at the time of the primary operation. Although closure of the opening in an antecolic anastomosis is never complete because placing of stitches in the wall of the colon should be avoided, yet a few interrupted stitches judiciously made could cause enough local inflammatory reaction that might seal up the opening by adhesions. Closure of the openings in a retrocolic gastrojejunostomy can be accomplished in the following way: the upper opening is closed by stitching the gastric stump along its lesser curvature to the posterior parietal peritoneum; the lower opening is closed by stitching the mesentery of the proximal or afferent jejunal loop to the posterior parietal peritoneum at the base of the transverse mesocolon.

SUMMARY

1. Among 97 partial gastrectomies and antecolic gastrojejunostomies, 2 cases of intestinal obstruction due to internal herniation of the afferent

jejunal loop were encountered. Both cases recovered after operative treatment.

2. The salient points in the diagnosis, treatment and prevention of such internal hernias are briefly discussed.

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LAURENCE-MOON-BIEDL SYNDROME REPORT OF TWO CASES

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Laurence-Moon-Biedl syndrome is a combination of the following manifestations: pigmentary degeneration of the retina, mental retardation, obesity, hypogenitalism and polydactylism. It occurs in both sexes, but more frequently in males. Its incidence is markedly familial and is found chiefly among the white races although there have been Japanese and Egyptian cases. In 1942 Snell(1) reported 1 case in a 13 year old black girl. In China, no case hitherto has been reported. According to Radner(2) the number of cases reported in the literature up to 1940 was about 200. Sixty-eight cases were added between 1940 and 1951(3). In regard to cases of complete syndrome, Warkany and others(4) in 1937 analyzed 102 cases and found 24 with all the five symptoms.

REPORT OF CASES

CASE 1. The patient, a 15 year old boy, came to the clinic on December 10, 1951. As a child he was frequently ill. He had a fixed gaze and seemed always staring. His eyelashes were abnormally long. He had curly hair and was fat and short in stature. When 2 or 3 years old he could not see things placed at the lower part of the visual field. His eyesight became gradually worse and he saw poorly at night. In the daytime, he could see only things close to his eyes. Several physicians were consulted but they could do nothing for him. In the spring of 1951 he was given 100 subcutaneous injections of 1 cc placenta extract, after which there was some improvement of vision.

Family history. There was no history of consanguinity with the parents or among near relatives. One of the patient's younger brothers (Case 2) had the same trouble. Another younger brother aged 15 and a sister aged 13 were both normally developed.

Physical examination. Height 132 cm. Weight 37.5 kg. The patient was short and fat and showed prominence in the nipples and the pelvic region. The heart and lungs were normal, and the extremities showed no abnormalities except that the toes were somewhat flat. He had curly hair. His mentality was low. The genitalia was under-developed (Figs. 1 and 2) like that of a newborn child, the right testicle was absent.

Eye examination. Some of his eyebrows were 2 cm long, his eyelashes were 1.5 to 2 cm long. When he fixed with both eyes, there was deviation toward the right side. External ocular findings were normal. In both fundi bone-corpusele-like pigment patches could be seen scattered throughout the retina. There were no demonstrable changes in the retinal vessels and optic disk. In the macular region of both eyes there were well-defined and irregular-shaped whitish patches

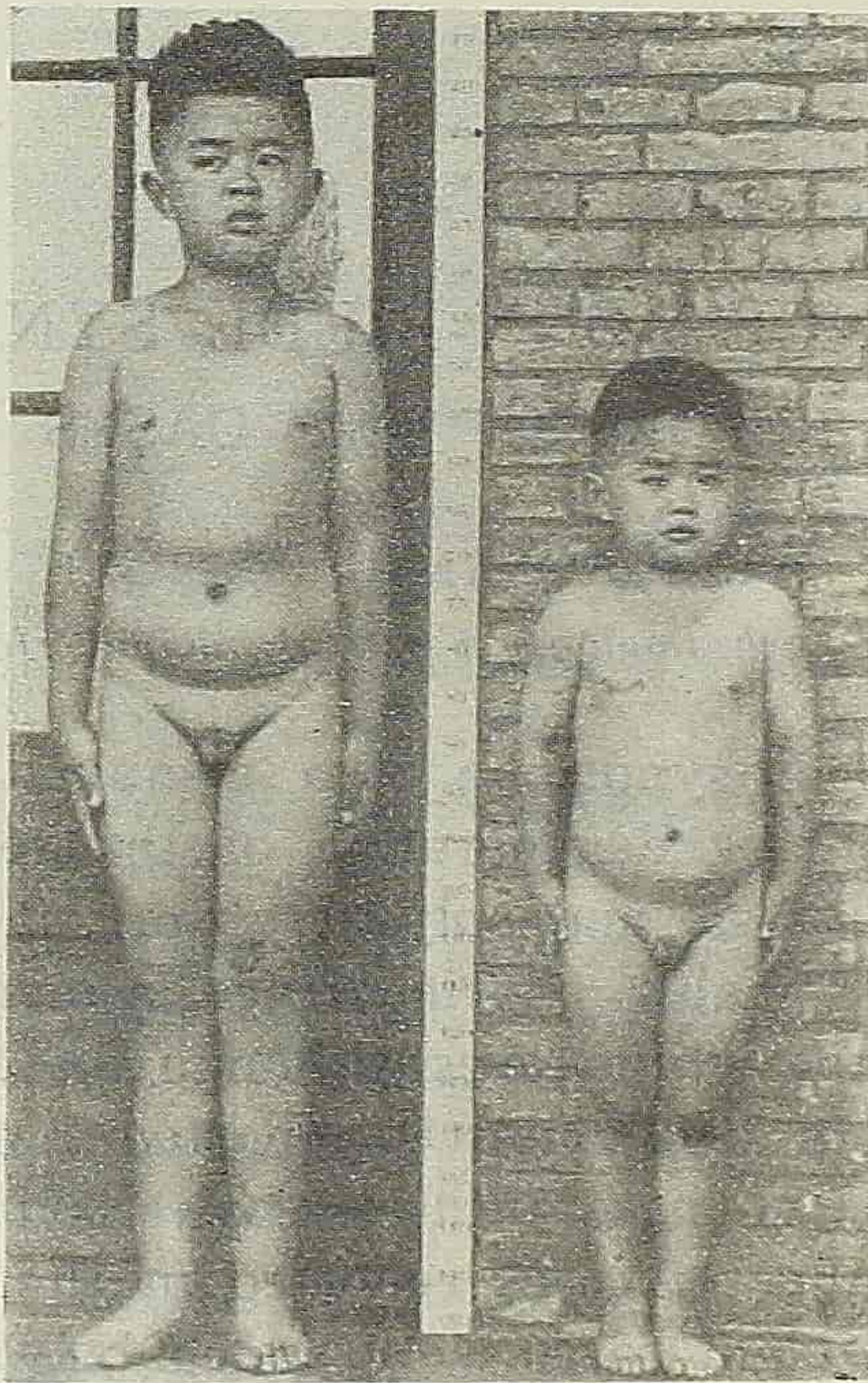


Fig. 1. Patients in Cases 1 and 2.

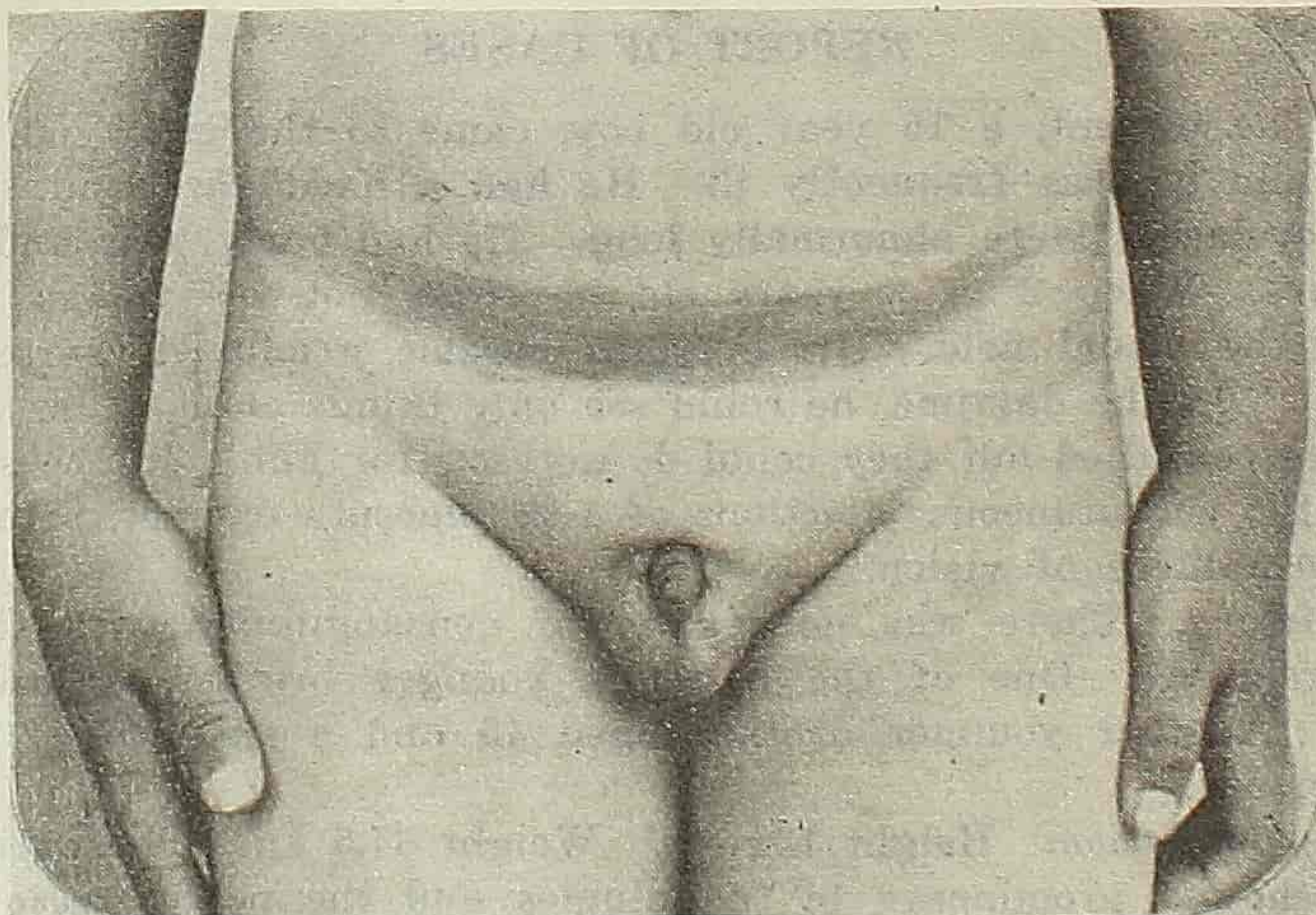


Fig. 2. Showing under-developed genitalia (Case 1).

(Figs. 3 and 4). The foveal reflex was invisible. Choroidal vessels could be distinctly seen. Vision: right eye 0.2 and Jaeger 4, left eye 0.2 and Jaeger 5. Visual field of both eyes was of the tubular type (Fig. 5).

Blood examination. RBC 4,560,000 per cu mm, Hgb. 86 per cent, WBC 7,800 per cu mm. Differential count: neutrophils 37 per cent, lymphocytes 63 per cent. Sedimentation rate of red blood corpuscles was 11 mm at the end of the first hour. Kahn and Wassermann reactions were negative. Blood grouping "A".

X-ray examination. Skull and sella turcica normal.

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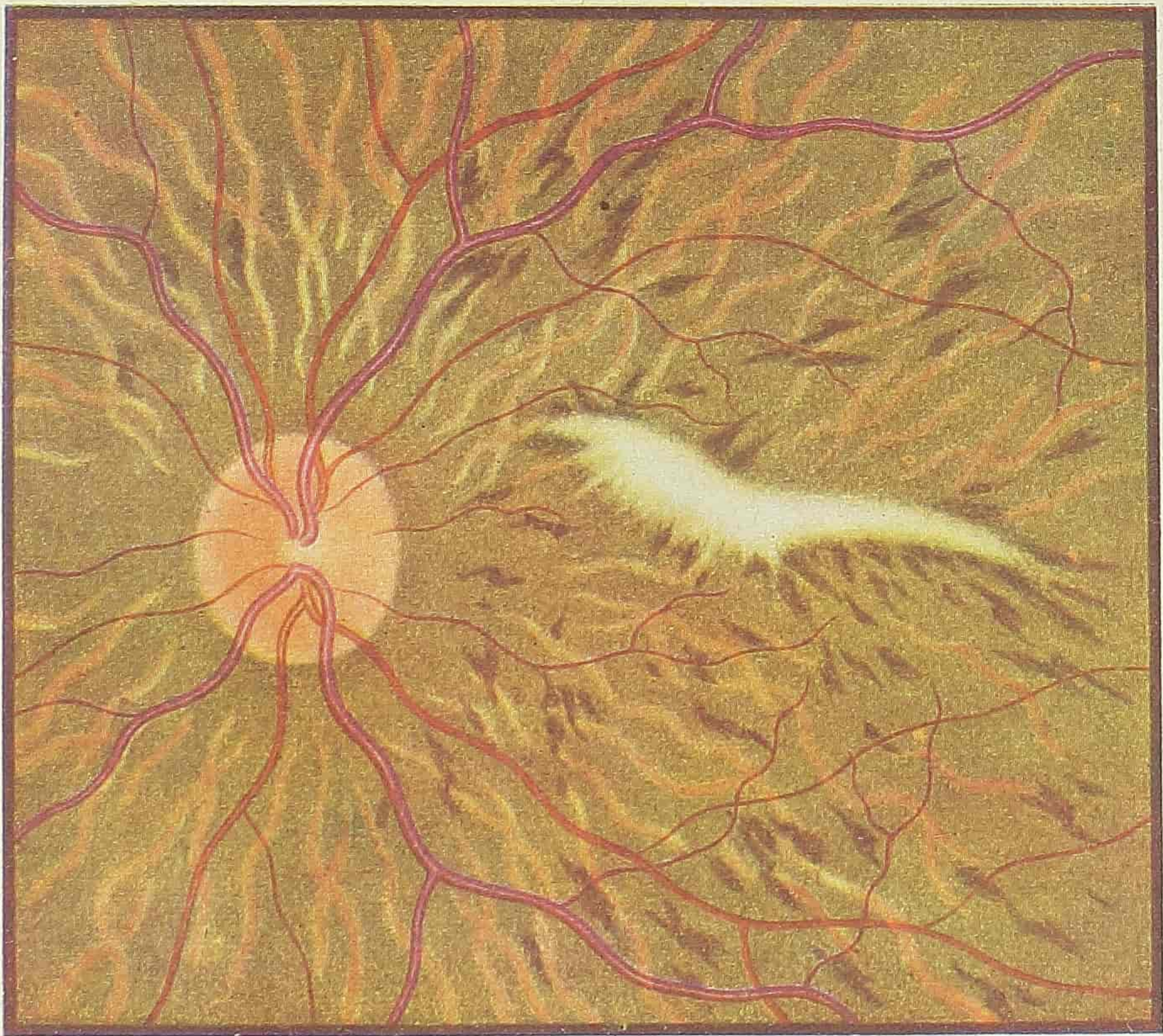


Fig. 3. Fundus O.S. (Case 1).

LAURENCE-MOON-BIEDL SYNDROME

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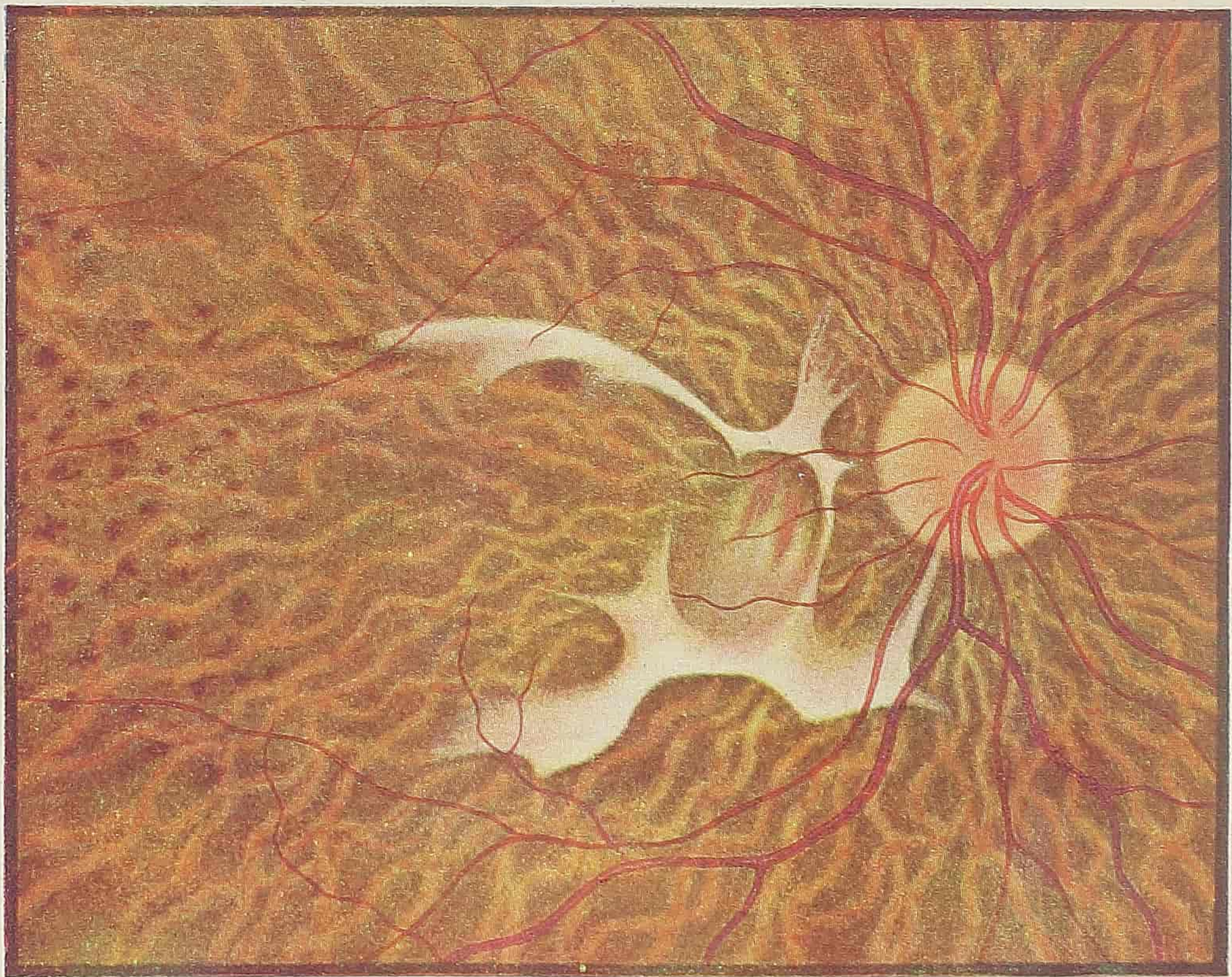


Fig. 4. Funds O.D. (Case 1).

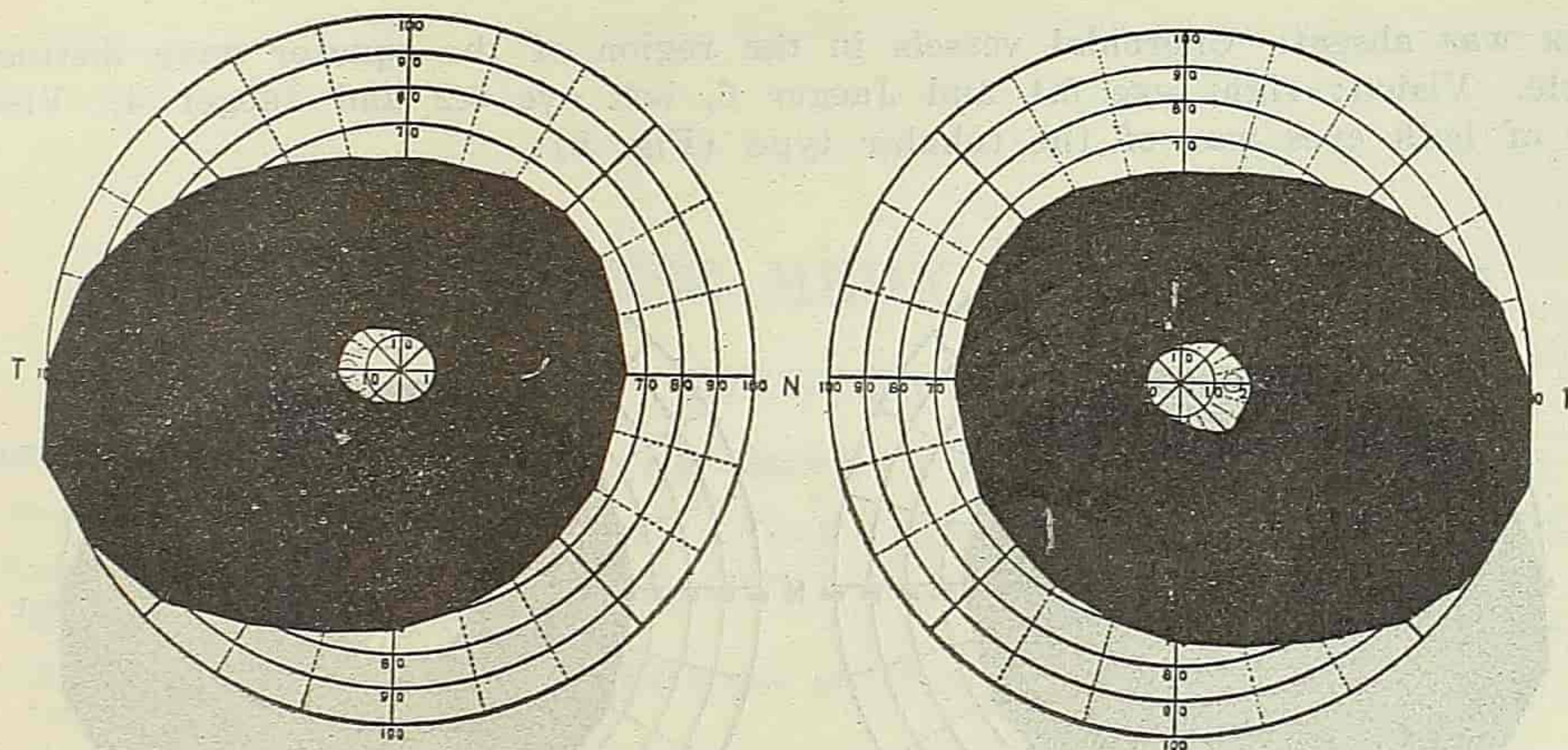
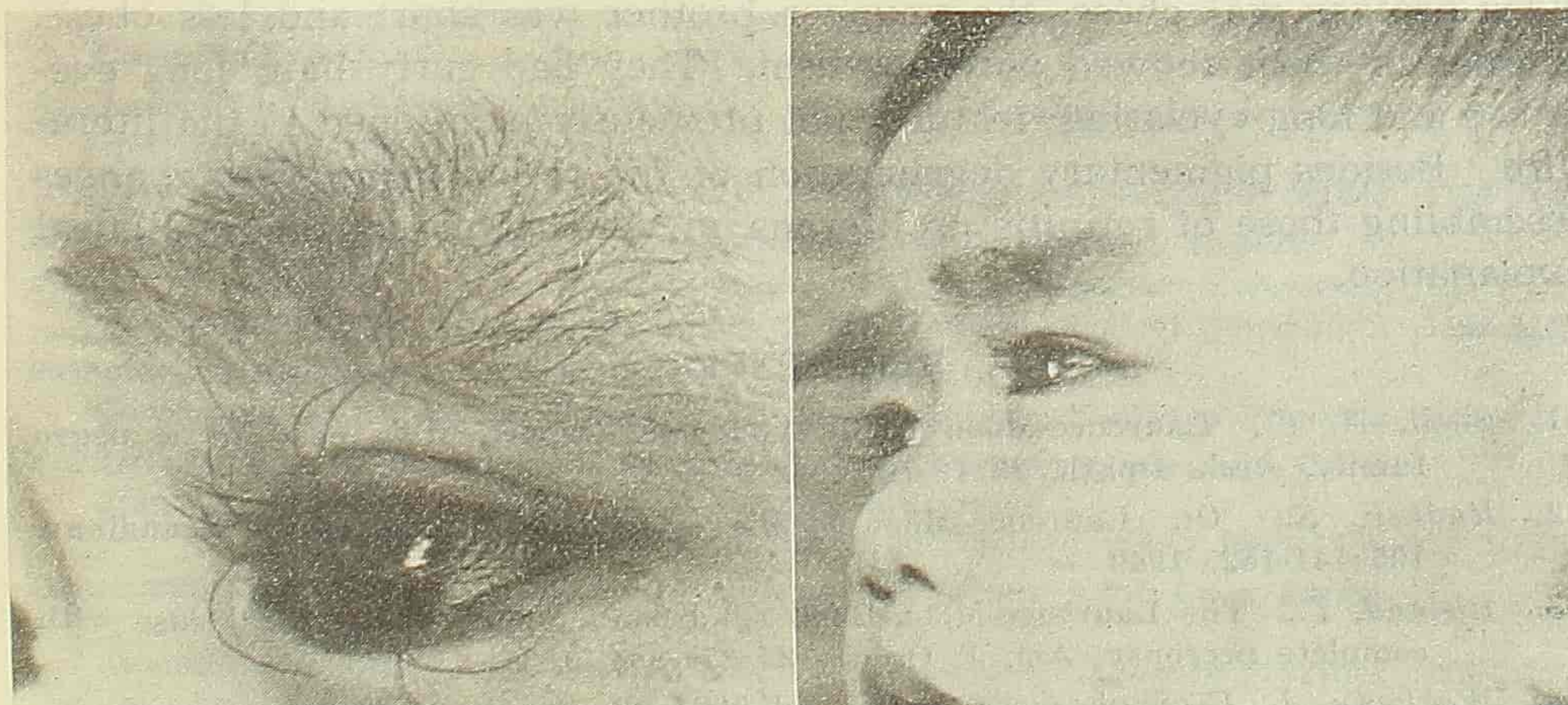


Fig. 5. Vision: O.S. 0.2 Jaeger 5, O.D. 0.2 Jaeger 4 (Case 1).

CASE 2. The patient, a boy, 9½ years of age, attended our clinic on December 10, 1951. He had impairment of vision and difficulty in seeing at night for the past three or four years. Like his brother he had also been given injections of placenta extract in 1951, totaling 100 cc. His vision remained unchanged.

Physical examination. Height 100 cm. Weight 20 kg. He was short in stature and fat. His heart and lungs were both normal. His extremities showed no abnormalities except flat toes. His hair was curly. His genitalia was underdeveloped but both testicles were present (Fig. 1). His mentality was also low, but he was comparatively more intelligent than his brother.

Eye examination. Some of his eyebrows reached 3.5 cm in length and some eyelashes were 3 cm long (Figs. 6 and 7). When he fixed with both eyes, there was deviation to the right side. The eyes showed no external abnormalities. The retina near the equatorial region of both eyes was sparsely studded with pigment patches like bone corpuscles. A short distance from the nasal side of both discs there were symmetrical crescent-like whitish patches concentric with the margin of the discs. The discs and the retinal vessels showed no demonstrable changes. The foveal



Figs. 6 and 7. Showing long eyebrows and eyelashes (Case 2).

reflex was absent. Choroidal vessels in the region of the equator were distinctly visible. Vision: right eye 0.1 and Jaeger 6, left eye 0.2 and Jaeger 4. Visual field of both eyes was of the tubular type (Fig. 8).

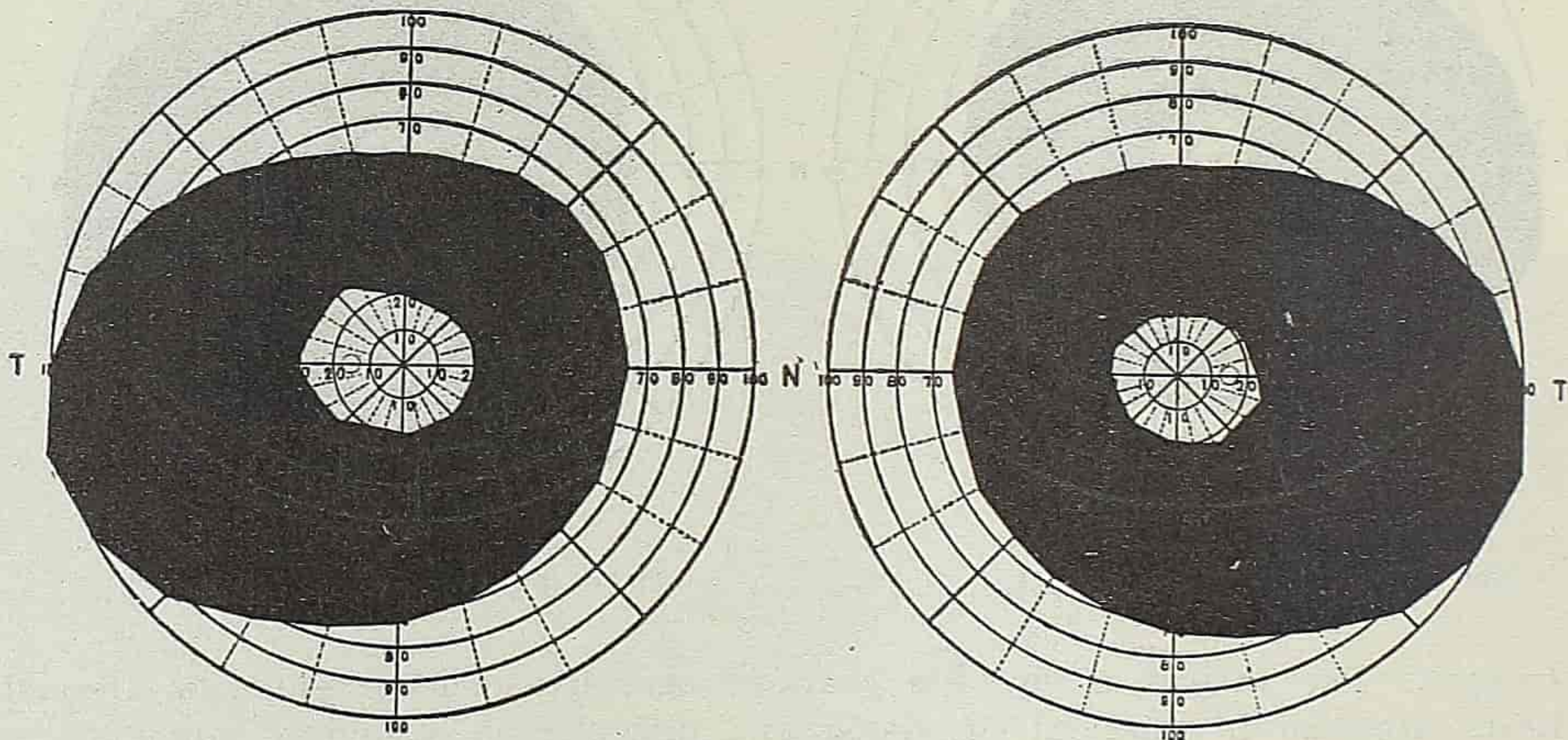


Fig. 8. Vision: O.S. 0.2 Jaeger 4, O.D. 0.1 Jaeger 6 (Case 2).

Blood examination. RBC 4,500,000 per cu mm, Hgb. 85 per cent, WBC 7,200 per cu mm. Differential count: neutrophils 50 per cent, lymphocytes 47 per cent, eosinophils 2 per cent, mononuclear 1 per cent. Sedimentation rate of red blood corpuscles was 11 mm at the end of the first hour. Kahn and Wassermann reactions were negative. Blood grouping "B".

X-ray examination. Skull and sella turcica normal.

SUMMARY

The 2 patients reported above were brothers. Of the five symptoms of Laurence-Moon-Biedl syndrome, pigmentary degeneration of the retina, obesity, hypogenitalism and mental deficiency were present. The elder brother was obese, the younger brother was short and less obese. Neither of them showed polydactylism. They had curly hair, long eyebrows and long eyelashes, features not previously mentioned in the literature. Besides pigmentary degeneration of the retina there were changes resembling those of retinitis proliferans, of which there is yet no clinical explanation.

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ABSTRACTS

Clinical Experience in the Use of *Coptis teeta* for Treatment of Bacillary Dysentery. Lo Lung-Chiang. Nat. Med. J. China 41(5):452-455, 1955.

Bacillary dysentery was described by traditional Chinese physicians about two thousand years ago, and effective prescriptions for this disease have been in use for about seventeen hundred years. One of the drugs is *Coptis teeta* 黄连. The Hangchow Isolation Hospital has made observations on the effect of *Coptis teeta* in the treatment of bacillary dysentery since 1951. The results in comparison with sulfonamides, streptomycin and bacteriophage are here presented.

The number of cases treated with *Coptis teeta* was 166. All the patients were adults except a 7 year old child. The duration of illness before treatment was from one to sixteen days. The clinical manifestations including stool examinations were typical for bacillary dysentery. Of the 166 cases, 87 gave positive stool cultures (mostly Flexner, a few Alcaligenes, Sonne and Schmitz). *Coptis teeta* was given by mouth (in a few cases it was changed to the intramuscular route during the course of treatment) in the form of extract (0.15 gm equivalent to 1 gm of the herb), 0.45-1.8 gm being given a day in three to six divided doses. The duration of administration was from five to seven days. The total amount of the extract given to each patient averaged about 6 gm. Retention enemas of 100-200 cc 2-3 per cent solution of *Coptis teeta* in addition to the extract were given once or twice a day to several patients with severe tenesmus or persistent mucoid stools. Other measures included symptomatic treatment of abdominal pain and replacement of fluid in dehydrated patients. One patient received streptomycin.

The results of treatment with *Coptis teeta* and other drugs are tabulated below:

Treatment	No. of cases	Normal frequency of bowel movement	Stool			Subsidence of abdominal pain	Subsidence of fever
			Normal color	Completely normal	Negative culture		
Sulfonamides	80	3.7+day	4.5-day	7.5-day	7 day	5.5 day	3+day
Streptomycin	41	3 ..	4.5 ..	7 ..	7.3 ..	4.5 ..	3.6 ..
Bacteriophage	30	3.5 ..	3.9 ..	7.2 ..	7 ..	5.2 ..	3.2 ..
<i>Coptis teeta</i>	116	3.9- ..	4.2- ..	6.7- ..	4.7 ..	5.8 ..	3.2 ..

All the patients treated with *Coptis teeta* were cured. None showed any toxic manifestation. As may be seen from the table, the stool cultures of the group of patients given *Coptis teeta* became negative more rapidly than the groups treated with sulfonamides, streptomycin or bacteriophage, while in other respects *Coptis teeta* was just as effective.

The results warrant the conclusion that *Coptis teeta* should be considered as a standard therapeutic agent for bacillary dysentery. H. P. Lei

Analysis of 4,269 Cases of Kala-Azar. Meng Hsien-Kao. Nat. Med. J. China 41(7):614-619, 1955.

An analysis of the clinical features of 4,269 kala-azar patients is here reported. In all the patients L.D. bodies were found by diagnostic punctures of either the bone marrow, the lymph glands, the liver or the spleen. In order to ascertain the relative merit of the different diagnostic punctures, two of the above mentioned organs were punctured at one sitting in every case. The results showed that the highest positive rate was obtained in bone marrow puncture, and the lowest in lymph gland puncture.

The ratio of male and female kala-azar patients was 11:9, and the highest age incidence was in the group under 10 years of age. Two per cent of the 4,269 patients had the disease over two years and 80 per cent had it less than one year. An overwhelming

majority of the patients (97.75 per cent) had splenomegaly. Only 96 patients (2.25 per cent) had no splenomegaly, probably because they were early cases. Enlargement of the liver occurred in only 40.2 per cent of all the patients. The white blood cell count was within normal limits in 26.1 per cent of the cases, and low in the remaining cases, among which 45.9 per cent had a count of between 2,100 and 4,000. Leukopenia was due chiefly to depression of polymorphonuclear cells. Although the relative percentage of lymphocytes showed an increase, the absolute number was less than normal. Anemia was common. Red blood cell counts between 2,010,000 and 4,000,000 occurred in 77.2 per cent and hemoglobin values between 41 and 60 per cent occurred in 51.36 per cent of the cases. Fever occurred in 95.99 per cent of the cases. Bleeding from the nose and gums was found in only 38.96 and 43.38 per cent of the cases respectively.

Free treatment of kala-azar patients since Liberation has greatly reduced serious complications. Agranulocytosis was very seldom seen. The incidence of noma also dropped; there was only 0.84 per cent in the present series, and no death was encountered following the institution of penicillin therapy for this condition.

Tumors of the Urinary Bladder. Shen Chia-Li, Hsiung Ju-Ch'eng, Ch'en Chia-Piao and Ho Tzu-Ming. *Chinese J. Surg.* 3(11):814-820, 1955.

Among 93 cases of tumors of the urinary bladder 82 (88 per cent) were primary and 11 (12 per cent) secondary, mostly metastatic growths from carcinomas of the cervix of the uterus. Of the primary tumors, 80 were of epithelial origin. There were 56 males and 24 females. The ages were between 41 and 60 years in 61.3 per cent. The main symptoms were gross hematuria, frequency and urgency of urination. The period from the onset of symptoms to the time of treatment varied from three months to over two years. No positive physical findings were elicited among most of the patients. Pathological examinations showed that most of the cases were carcinomas. Thirty-four cases or 45 per cent were of single growth, located mostly over the trigone region, lateral and posterior walls of the urinary bladder.

X-ray examination of the upper urinary tract was done in 44 cases and secondary lesion was seen in 23 cases. Of the 56 patients treated, 20 had local excision and electric cauterization, 14 had partial cystectomy, 13 had total cystectomy, 6 had palliative treatment in the form of anastomosis of ureters to sigmoid colon and 3 had deep x-ray therapy.

Thirty-eight patients were followed up for from half to five years. Of these, 15 had excellent results without recurrence, 7 had recurrence, and 16 died. These results are not satisfactory; the patients usually came for treatment too late. The authors believe that in tumors of the urinary bladder cystoscopic examination is the best method of early diagnosis and total cystectomy is the procedure of choice. P. H. Ch'en

Partial Nephrectomy. Ho Shang-Chih, Ts'ao Yü-Feng, Ch'en Pang-Tien and An Shih-Yuan. *Chinese J. Surg.* 3(11):837-841, 1955.

Partial nephrectomy was first introduced by Tuffier in 1891, but owing to the lack of adequate facilities and improper selection of cases, postoperative complications such as hemorrhage and urinary leakage were difficult to control, and the operation was soon discarded. Today, with the progress in surgical technic and the use of sulfonamides and antibiotics, partial nephrectomy has proved a safe and useful procedure. Criteria for this operation are: 1. the lesion is localized over a single pole of the kidney; 2. adequate renal tissue is left to maintain a normal excretory function of urine, if the opposite kidney is absent; 3. adequate blood supply and normal urinary drainage can be maintained for the remaining renal tissue. The authors used two types of operative procedures, one for partial hydronephrosis as described by Landes, and the other for non-hydronephrotic lesions as described by Lattimer. One case of bilateral double kidney, 4 cases with renal stone and 1 with renal tuberculosis were operated on with good results. P. H. Ch'en

Clinical Study of 35 Cases of Tuberculous Meningitis in Adults. Wei Pei-Hai and Kuo Hsien-Chien. Chinese J. Tuberc. 4(1):13-17, 1956.

From 1951 to September 1954 there were 35 adult cases of tuberculous meningitis in the authors' hospital, constituting 2.4 per cent of the total number of patients admitted and around 1 per cent of medical patients during the same period. The numbers of male and female patients were roughly equal. Fifteen of the 35 patients were from 15 to 24 years of age; 8 patients were older than 40 years.

Among the 35 patients, 16 (45.7 per cent) suffered from pulmonary tuberculosis at the same time, including 5 with military tuberculosis; 8 had extrapulmonary tuberculosis and 11 showed no evidence of tuberculosis elsewhere in the body.

All the patients had headache and fever, and in 17 of them headache was the earliest symptom. Nausea occurred in 80 per cent, vomiting in 60 per cent and mental cloudiness of varying degrees in 57 per cent. Stiffness of the neck occurred in 97 per cent and Kernig's reactions in 88.5 per cent. Increased white blood count occurred in 80 per cent of the patients, and polymorphocytosis in 60 per cent.

Spinal fluid findings. Except for 1 patient who had only 9 cells per cu mm all the rest had an increased count, 80 per cent showed chlorides of 700-600 mg per cent and 20 per cent showed below 600 mg per cent. Sugar: 22.8 per cent showed 40-50 mg per cent, 45.7 per cent 40-20 mg per cent, and 17.1 per cent showed 20 mg per cent or less. All were Pandy positive. Among 19 spinal fluid specimens examined, 63.1 per cent were positive for pellicle formation, and 37.9 per cent were positive for tubercle bacilli.

Treatment. Streptomycin 1 gm daily was first given intramuscularly; when the body temperature became normal it was reduced to 1 gm every three days. INH 300 mg daily orally and 30-50 mg per day intraspinally. PAS 12-15 gm daily. Treatment was divided into three stages of about three months each: streptomycin and INH in the first stage, streptomycin and PAS in the second and INH and PAS in the third.

Result. Seven patients died within ten days of treatment, 1 died during the first stage and another in the third stage of treatment: a total of 9 deaths (25.7 per cent) and, of these, 6 patients came to the hospital unconscious. T. Y. Ch'iu

Clinical Study of 80 Cases of Tuberculous Peritonitis in Adults. Ch'ien Yuan-Fu, Hsieh Yi-Jung, Ch'i Jen-An, Lin Hsüan and Ch'iu Shao-Chen. Chinese J. Tuberc. 4(1):29-33, 1956.

The material of this study was collected from the chest surgery and gynecological services of the authors' hospital from 1951 to 1954. The male and female cases were about equal in number. The cases were divided on a pathological basis into three groups: exudative or ascitic, 39 cases (48.7 per cent); adhesive or plastic, 38 cases (47.5 per cent); and caseous or ulcerative, 3 cases (3.8 per cent).

The diagnosis of tuberculous peritonitis is difficult. Except in a few cases where tubercle bacilli were demonstrated in the ascitic fluid or sputum, diagnosis of most of the cases in this series was made from general findings or the presence of tuberculosis in the lung or elsewhere in the body. Ascitic fluid, when obtainable, generally had specific gravity above 1.018, protein contents above 2.5 gm per cent and WBC above 5,000 per cu mm with preponderance of lymphocytes.

X-ray examination gave valuable information particularly with the adhesive type where adhesion and narrowing of the intestines could be seen. Of 62 cases of the present series thus examined, half of them showed positive findings.

Acute and chronic cases were particularly difficult to diagnose. With the former, differentiation from other forms of acute abdomen could only be made when the abdomen was surgically explored. There were 10 such cases in this series. With the chronic cases, there were a few patients who were mildly sick for one to two years before admission.

The most common complications were tuberculosis elsewhere in the body. There were in this series 32 cases (40 per cent) with tuberculosis of the lung, 20 cases (25 per cent) with tuberculosis of the pleura, and 13 cases (16 per cent) with tuberculosis of the intestine.

During the course of treatment intestinal obstruction developed in 2 cases, intestinal perforation in 2, and fecal fistula (through the abdomen) in 1.

In regard to treatment, 3 patients were light cases and were given general care, the rest were given antimicrobial treatment. Of the latter, 64 patients showed improvement, 6 no change, 7 died (3 cases of the caseous form, 3 of the adhesive form and 1 ascitic). Streptomycin was found to give the best result but the authors recommend the use of two antimicrobial drugs to prevent or delay the development of drug resistance.

T. Y. Ch'iu

Bronchoscopic Aspiration as Emergency Treatment for Massive, Asphyxiant Hemoptysis with Report of Two Cases. Shao Ch'ang-Jung. Chinese J. Tuberc. 4(1):38-40, 1956.

Massive hemoptysis is infrequent but often fatal. In most cases death is caused not by loss of blood but rather by asphyxia produced by blood clot in the air passage, and if the blood clot can be speedily removed the patient's life can be saved.

The author reported 2 cases of hemoptysis in which the patients had cyanosis, unconsciousness and incontinence of urine. With bronchoscopic removal of the blood clot (twice in each case) and the use of oxygen therapy and blood transfusion the patients were saved.

It is pointed out that speed, care and full co-operation between doctor, nurse and the blood bank are essential to successful treatment, and also good nursing after operation. The bronchoscope should not be left too long in the trachea. It should be removed as soon as the clot is taken out and no gross bleeding is evident in the lung, and replaced by a catheter which in turn should be removed when the patient becomes conscious. Preparation must be made to repeat the treatment if necessary.

T. Y. Ch'iu

The Treatment of Sore Throat by Internal Administration of "Liu Shen Wan 六神丸": A Preliminary Report. Wei Tsung-Wen. Chinese J. Otorhinolaryng. 3(4):255, 1955.

This report contains an analysis of 50 cases of sore throat treated by internal administration of *liu shen wan*, a drug used in traditional Chinese medicine, with good results.

In the first group of 27 patients with chronic pharyngitis, 6 were completely cured, 10 improved and 11 unknown. The second group consisted of 13 cases of chronic tonsillitis, among which 2 patients recovered, 6 improved, 3 were unknown and in 2 there was no effect. The third group of 5 patients with chronic laryngitis showed 3 improved and 2 unknown. In the last group of 5 cases of acute tonsillitis and peritonsillar abscesses, the drug showed no effect on the diseases.

The author emphasizes the excellent effect of the drug in cases of chronic pharyngitis where tonsillectomy has already been done and also in cases where drugs in western medicine give no relief.

The drug *liu shen wan* is composed of six ingredients having a combined weight of 0.014 Chinese ounce (一厘四毫). The ingredients consist of toad cake, cow bezoar, musk, pearl powder, chimney ash and cinnabarite. The dosage for adults is 10 pills to be taken internally twice a day or once at night before going to bed. For children the dosage is half to one third of the adult dose.

Liu shen wan has no ill effect but is said to be contraindicated in pregnancy.

J. H. Liu

Pneumogastric Sympathetic Block in Otorhinolaryngology: Report of 12 Cases. Sun Ch'i-Cheng. Chinese J. Otorhinolaryng. 3(4):256-260, 1955.

Based on the principle of conservative treatment, the author employed the method of pneumogastric sympathetic block on 12 E.N.T. cases with good results.

The procedure consisted of injecting 0.25-0.5-1 per cent novocain intradermally into the posterior border of the sternomastoid muscle below its attachment to the mastoid

process. After the injection the needle was carried vertically downwards to about 2-3 cm. If there was no blood upon withdrawal of the syringe, 30-50 cc of the solution was injected.

The cases treated were 1 patient with glossopharyngeal pain who was completely cured after two injection blocks; 1 patient with acute pharyngitis cured by one injection of novocain plus 300,000 units of oil penicillin intramuscularly, and 1 patient with periodontitis who was cured in two days after one injection and 300,000 units of penicillin. There were 3 cases of peritonsillar abscess, among which novocain alone was used in 1 and novocain with penicillin was used in 2. All these 3 patients were unable to open their mouth before treatment but recovered fifteen minutes afterwards. In 3 cases of chronic stomatitis, the effect upon the ulcers was not marked but the pain was greatly lessened. In the remaining 4 cases, the method was employed as a pre-tonsillectomy anesthesia. In 2 of these there was absolutely no pain, and in the third there was only slight pain on one side. No effect was found in the fourth due to nervousness on the part of the patient and the probability that he was inadequately prepared mentally before operation.

According to the author's observations the above procedure is indicated in acute pharyngitis and as a preoperative anesthesia in tonsillectomy.

J. H. Liu

Some Psychiatric Concepts in Traditional Chinese Medicine. Hsü Yu-Hsin. Chinese J. Neurol. & Psychiat. 1(3):167-174, 1955.

The author gives a brief review of the psychological and etiological concepts of mental diseases, clinical psychiatry and mental hygiene in the Ch'in and Han dynasties (221 B.C.-219 A.D.).

Of particular interest is the fact that Chinese physicians of this period realized the basic materialistic principle that mind reflects objective reality—the unity of the subjective with the objective—and that modifications in the conditions of life of the individual affected his physical and mental health.

Delirium, mania, depressive psychoses, epilepsy, hysteria and other neuroses as described in the early literature are explained. Psychotherapy and mental hygiene which had been stressed upon are also dealt with.

Y. K. Feng

A Study of the Carotid Reflex in 50 Psychiatric Patients. Feng Ying-K'un. Chinese J. Neurol. & Psychiat. 1(3):175-190, 1955.

The author gave a brief review of the present knowledge of the carotid sinus reflex. He pointed out that the reflex had been dealt with as an isolated phenomenon of a lower physiological order and its further study on the basis of Pavlovian principles would shed more light on the subject.

The carotid sinus reflex and oculocardiac reflex of 54 cooperative mental patients of various categories were studied by the author with the simultaneous use of an Offner's C-type encephalograph and a Keller's 302-model polygraph. This method was considered more objective and more convenient in the simultaneous registration of changes in the heart rate, respiration, blood pressure and cortical activity.

A positive carotid sinus response with syncope, convulsions, high-voltage and slow brain waves, slow, deep and irregular breathing, with or without changes in the heart rate or blood pressure was demonstrated in 7 of the 54 patients. The carotid sinus hypersensitivity was found to be unrelated to the age of the patient, the type of psychiatric condition, certain organic changes of the central nervous system (with the exception of neurosyphilis) and previous electric shock treatment, insulin shock therapy, and prefrontal lobotomy. There were indications that the type of the patient's nervous system (temperament) had something to do with the occurrence of a positive response.

The oculocardiac reflex was found to be associated with the usual attention phenomenon, irregular respiration and various changes in the heart rate. Two illustrative cases were reported. It was pointed out that with certain precautions the carotid sinus test (even bilateral compression) was a safe diagnostic procedure. The Author

Intracranial Meningioma. Chang Yuan-Ch'ang, Chiang Ta-Chieh, Ch'en Yu-Hsin and Tsou Huan-Wen. *Chinese J. Neurol. & Psychiat.* 1(3):191-208, 1955.

This contains an analysis of 30 cases of intracranial meningiomas with the following findings: The average age was 32.6 years. There were more female than male patients. The average duration of the illness was 21 months. The distributions were parasagittal, 8 cases; adjacent to the lateral sinus, 5 cases; cortical, 3 cases; cortical and subcortical, 3 cases; middle fossa, 5 cases; anterior fossa, 2 cases; sphenoid ridges, 2 cases; posterior fossa, 2 cases. Roentgenograms were taken in 29 cases and in 15 of them they were helpful in localizing the tumor. Ventriculograms were performed in 13 cases, 8 showing the site of the tumor. Angiography was done in 23 cases, 22 giving the location of the tumor. The authors claimed that angiography is safer and more helpful than ventriculography in supratentorial tumors. Pathologic study revealed 13 cases of endotheliomas, 6 cases of fibroblastomas, 6 cases of fibro-endotheliomas, 2 cases of psammomas, 2 cases of epitheliomas and 1 case of the muco-chondro-osteal type. Twenty-eight cases were operated on, 6 died soon after operation and 19 were discharged in an improved condition. Y. K. Feng

The Effect of Crude Soybean Lecithin on the Macrophages in the Subcutaneous Tissue of Rabbit's Ear. Ma Wen-Chao. *Acta Anatomia Sinica* 1(1):1-14, 1955.

Crude soybean lecithin was rubbed on the skin of the inner side of the right ear of the rabbit once every other day for a period of two months or longer. The other ear, for control, was also rubbed mechanically without lecithin. A conspicuous increase in size, number and activity of the macrophages in the subcutaneous tissue of the treated ear was demonstrated by means of vital staining through intravenous injection with Trypan blue.

The Striae Medullares of the Fourth Ventricle as Related to the Nucleus Arcuatus. Tsang Yü-Ch'üan. *Acta Anatomia Sinica* 1(1):15-24, 1955.

Three adult human brain stems which presented a unilateral hypertrophy of the striae medullares of the fourth ventricle were studied in serial Weigert sections with the following results:

The unilateral hypertrophy of the striae medullares is correlated with the hypertrophy of the contralateral nucleus arcuatus.

In the hypertrophied nucleus arcuatus the fibers collect themselves towards the bottom of the ventral median fissure. The large bundle thus formed courses dorsally along the raphé, crosses to the other side and emerges on the floor of the fourth ventricle. It then turns laterally in the subdymal layer, winding around the tuberculum acusticum to approach the cerebellum.

Besides the main nucleus arcuatus, the fibers of the accessory nuclei on the medioventral surface of the pyramid and of the ventral part of the nucleus raphes also participate apparently in the formation of the striae. The scattered gray patches on the lateral part of the ventricular floor are minor relay stations of the striae medullares.

The nucleus arcuatus and allied nuclear masses are the caudally displaced pontine nuclei. The striae medullares behave just like an aberrant bundle of the brachium points and, as such, they conduct towards the cerebellum.

Besides the striae medullares, the fibers of the nucleus arcuatus are also incorporated into the ventral external arcuate fibers on the same and opposite sides, which curve around the ventrolateral surface of the medulla oblongata towards the cerebellum.

Innervation of the Atrio-Ventricular Node of the Heart. K. T. Tcheng. *Acta Anatomia Sinica* 1(1):25-32, 1953.

The author's observations on the innervation of the atrio-ventricular node of the dog and the lamb by Weber's silver impregnation technic may be summarized as follows:

1. The atrio-ventricular node of the dog and the lamb receives a rich innervation, particularly the latter. With the aid of a reconstruction of the A-V node on the superposed glass plates, the topography of the nerves in the node in relation to the cardiac ganglia in the interauricular septum of the heart of the lamb is clearly demonstrated.

2. With Weber's silver impregnation technic, one can distinguish 3 kinds of nerve fibers in the A-V node: the coarse, deeply impregnated fibers as the sensory; the fine, black fibers as the parasympathetic postganglionic; and the finest, pale fibers as the sympathetic postganglionic fibers.

3. The sensory and parasympathetic preganglionic fibers degenerate after the vagotomy, while the sympathetic postganglionic ones degenerate after the removal of the middle cervical and stellate ganglia. The parasympathetic postganglionic fibers remain intact in spite of these operations.

4. The sensory endings in the A-V node are seen in one or more terminal grains, or in the form of "grappe de raisin". The majority of the sympathetic and parasympathetic postganglionic fibers terminate in the metaterminal apparatuses of Weber. The intraprotoplasmic ending in muscular fibers of the A-V node is also observed.

In Vivo Action of Ribonuclease on Mouse Liver Cells. Li Chao-T'eh. *Acta Anatomia Sinica* 1(1):33-44, 1953.

A solution of crystalline ribonuclease was injected intraperitoneally and intravenously into the blood stream of the mouse. A depletion of ribonucleic acid together with a decrease of calcium ash was observed in the cortical portion of the liver cell 12 minutes after the injection until recovery of normal distribution 122 hours later. The possible association of calcium with ribonucleic acid in the cytoplasm constituents of the liver cell is discussed.

Acid and Alkaline Phosphatases in the Early Development of Mouse Embryos. Chang Tso-Kan. *Acta Anatomia Sinica* 1(1):45-60, 1953.

Mouse embryos 1-9 days of vaginal plug age, ranging from fertilized ovum to 7-somite stages were used for the study of acid and alkaline phosphatases according to MacDonald's and Danielli's modified methods, respectively. We found that the distribution of the two kinds of phosphatases in the above mentioned stages to be similar in their general pattern. The phosphatases are weak in the fertilized ovum and morula but increase considerably during blastocyst formation and differentiation of ectoderm and endoderm. Subsequently, the reaction in the egg cylinder is weakened as a whole, the proamnion being relatively stronger than the extra-embryonic ectoderm, proximal endoderm and mesometrial side of trophoctoderm. The phosphatases begin to increase again during mesoderm formation and the amnionic folds and mesodermal cells get darker than the other structures of the embryo. During the primitive streak stage the intensity reaches the highest point in the primitive streak, neural plate and brain vesicles. The intensity of the mesoderm and endoderm decreases towards the anterior end of the embryo. After the appearance of 3 brain vesicles, the reaction in the mesencephalon is weaker than in the fore and hind brains and that in the evaginating part is weaker than in the adjacent regions between the vesicles of the two sides and between the general ectoderm and the vesicles. The above distribution indicates that actively proliferating and migrating structures have a higher content of phosphatases.

ASSOCIATION NEWS

DR. FU LIEN-CHANG AWARDED ORDER OF LIBERATION, FIRST CLASS

Chairman Mao Tse-Tung has conferred the Order of Liberation, First Class on Dr. Fu Lien-Chang, President of the Chinese Medical Association. We rejoice that Dr. Fu has been so honored. He has richly earned this recognition of his unceasing devotion for thirty years in the service of the People's Liberation Army and the people's health. He is indeed an example to all our members.

DR. WU YING-K'AI MADE HONORARY MEMBER OF THE U.S.S.R. SCIENTIFIC SOCIETY OF SURGEONS

Dr. Wu Ying-K'ai was elected honorary member of the U.S.S.R. Scientific Society of Surgeons at the Twenty-Sixth Congress of Surgeons of the U.S.S.R. for his outstanding contributions to the science of medicine. We heartily congratulate Dr. Wu on this well-merited honor.

THE TENTH GENERAL CONFERENCE OF THE CHINESE MEDICAL ASSOCIATION

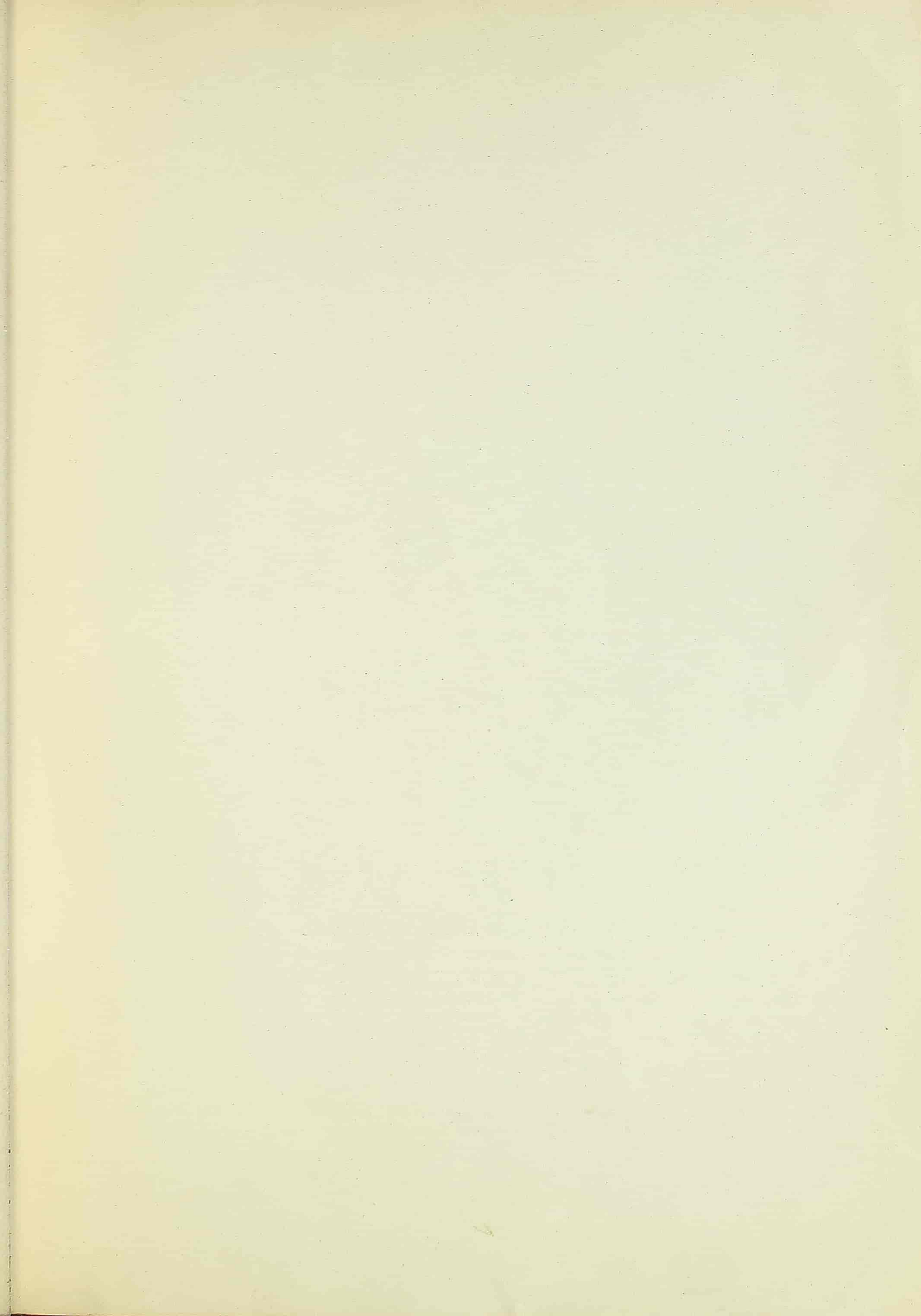
The Tenth General Conference of the Chinese Medical Association will be held in August this year. The main object of the meeting is to decide how we can best exert our efforts in socialist transformation and socialist construction. We shall have to consider, in the academic field, the problems of raising the standard of medical knowledge, learning from the advanced experience of Soviet medicine and the promotion of scientific research, and, politically, the implementation of the policy of further developing traditional Chinese medicine and advancing the unity and co-operation among physicians of traditional and western medicine.

The program of the conference in brief will be as follows:

1. Address by the President on the activities of the Association in recent years.
2. Adoption of resolutions on the future work and plans of the Association.
3. Papers on traditional Chinese medicine; tuberculous diseases; parasitic diseases, particularly schistosomiasis, kala-azar and paragonimiasis; and papers of the other scientific sections.
4. Revision of the Constitution.
5. Election of officers.
6. Scientific and technical exhibits.

As the business of the present meeting deals mainly with the work and plans of the Chinese Medical Association, guests from abroad will be invited not to this but to our next general conference.





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