

eight weeks. In no case was there any fever nor were any parasites found. It is worth recording that throughout the period of these experiments in no case was there a fall in the hæmoglobin content. Two control cases infected at the same time by the same batch of mosquitoes developed fever and parasites within the normal incubation period. Our interpretation of the success of these experiments is that sporozoites themselves were destroyed soon after they were injected by the mosquito."

In view of our findings it would appear that a more probable interpretation of the Horton experiment is:—(a) That the sporozoites were not destroyed as a result of the premedication soon after they were injected, and that (b) the patients were cured of their infection whilst it was still at a sub-clinical level by the courses of treatment, four weeks and eight weeks respectively, which they received subsequent to infection.

SUMMARY.

(1) The purpose of an investigation on the prophylactic, suppressive, and curative properties of mepacrine (atebrin) by experimental infections and field observations is stated.

(2) Experimental infections of mental patients who had received premedication with mepacrine are described.

(3) Observations in the field on the value of mepacrine both as a suppressive and curative agent are recorded.

The following conclusions are reached:—

- (a) Mepacrine is not a true prophylactic.
- (b) Mepacrine is a useful suppressant.
- (c) Mepacrine, if continued for a sufficient period, cures infections at a sub-clinical level.
- (d) An interpretation of the Horton experiment is advanced.

LEPTOSPIROSIS ICTEROHÆMORRHAGICA: AN UNUSUAL CASE.

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THE occurrence of a typical form of this not uncommon disease is well recognized and the varied clinical picture makes a satisfactory classification somewhat difficult. Thus Martin and Pettit [1] recognize the following clinical varieties:—

- (1) Cases with grave icterus.
- (2) Cases of the true febrile jaundice type with febrile recrudescence: (a) benign catarrhal; (b) prolonged febrile; (c) meningeal; (d) with nervous syndrome; (e) pulmonary.

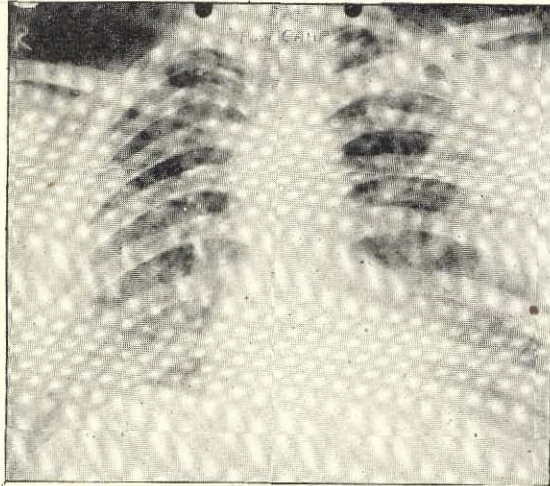
To these Willcox and Fairly [2] would add an *angular* and an *abdominal* variety.

The following case presents a most unusual combination in that there was clinical evidence of pulmonary, meningeal, hepatic and renal involvement at one and the same time and in one and the same patient. It serves to emphasize that infection with *Leptospira icterohæmorrhagica* is essentially a *septicæmia* in which one or more organs may be singled out for special attack or none at all. Clinical and pathological involvement do not necessarily run parallel—hepatitis is probably more common than the incidence of jaundice would suggest—nevertheless clinical evidence of hepatic and renal damage is common, of meningeal involvement distinctly less common, and of pulmonary involvement decidedly rare. As might be expected from pathological considerations the pulmonary lesion is a patchy hæmorrhagic consolidation. The radiological appearances in this case at the height of the infection are well seen in the accompanying photograph.

CASE HISTORY.

The patient, S.P., a male aged 22, a native of Voroshilovgrad in the Donetz, was admitted to hospital direct from a local P.O.W. cage late in the evening of September 11, 1944, with a provisional diagnosis of pulmonary tuberculosis. No clinical notes were available. In the absence of an interpreter it was impossible to obtain any history: it was learnt later that since his capture four days previously he had been complaining of headache, pain in the upper part of the left chest and blood spitting. His bowels had not been opened for four days prior to admission but had been opened that day. There was no complaint of urinary symptoms. There was a history of typhus in 1933 and of malaria in 1943.

Examination revealed a well-developed youth of distinctly Mongolian appearance. He looked ill and somewhat toxic. Temperature 101.4°F., Pulse 112, Respirations 28. His skin was hot and dry and his tongue was furred. Examination of the chest revealed no mediastinal displacement. The heart was not enlarged clinically, a short mitral systolic murmur being the only cardiac abnormality detected. Anteriorly chest movements were equal and good; the percussion note was unimpaired and breath sounds were vesicular. Posteriorly, there was diminished movement and impaired percussion note at the left base, and an area of bronchial breathing with superimposed fine crepitations, corresponding approximately to the left lower lobe. No pleural friction was felt and no rub was detected on auscultation. There was generalized abdominal tenderness but no rigidity. The liver,



spleen and kidneys were not felt and were not palpable at any stage of the illness. There was slight neck rigidity but no other evidence of any meningeal irritation. Knee-jerks and ankle-jerks were present and equal and plantar responses were flexor. Expectoration was free, the sputum consisting of a moderate amount of mucopurulent material together with small discrete blobs of bright red blood. A provisional diagnosis of left basal lobar pneumonia was made and a course of sulphathiazole was instituted—2.0 g. statim and 1.0 g. four-hourly.

The following morning the patient was re-examined and in the improved light was seen to be jaundiced. Re-examination of the chest no longer suggested lobar consolidation—the only positive findings were localized areas of harsh breath sounds at both bases. The patient's general condition was unchanged. A chest X-ray was ordered and a specimen of urine was sent to the laboratory with a request for chemical and microscopical examination.

The chest X-ray was reported on as follows: "Old healed T.B. right apex and first and second interspace right side. Both lung fields show extensive fluffy cotton-wool mottling especially in lower and middle zones. The hilar shadows are not markedly increased. *Conclusions*: Extensive patchy consolidation probably inflammatory. (1) Bronchopneumonia. (2) T.B. (3) Reticular type primary atypical pneumonia." The urine, in addition to bile, contained a small amount of albumen with hyaline and granular casts in considerable numbers.

The combination of pyrexia, jaundice, evidence of renal damage and hæmorrhages inevitably raised a suspicion that we might be dealing with a case of Weil's disease, and further investigations were undertaken with this in mind.

On September 13, two days after admission, there was still no appreciable change in the patient's general condition; the hæmoptyses were rather less, but on the other hand neck rigidity was a little more pronounced and Kernig's sign was now positive. A lumbar puncture was performed and was reported on as follows: "Faintly turbid fluid under increased pressure. Protein 20 mgm., Cells 205 per c.mm. and roughly 50 per cent Polymorphs and 50 per cent Lymphocytes, Chlorides 720 mgm. Culture: 'Air-borne contaminants only.'" Red and white cell counts performed the same day revealed a moderate anæmia—R.B.C. 3,850,000 per c.mm. Hb. 83 per cent, C.I. 1.04 and a relative and absolute polymorphonuclear leucocytosis, —W.B.C. 13,500 per c. mm., Polymorphs 82 per cent, Lymphocytes 10 per cent, Monocytes 6 per cent, Eosinophils 2 per cent. Blood-urea on 13th was 50 mgm. and a blood culture taken at the same time remained sterile. Sputum examination was repeatedly negative for tubercle bacilli.

There was considerable improvement in the patient's condition on the 14th. The temperature, which had fluctuated between 100° F. and 102° F., dropped to 98° F. on the morning of the 14th and there was a corresponding drop in the pulse-rate, and although there was an evening rise to 100.8° F. the temperature dropped to 99° F. the following morning and remained at that level for the following three days. At the same time the jaundice became fainter, the cough and expectoration diminished and all evidence of meningeal irritation disappeared.

Sulphathiazole was discontinued on the 18th after a total of 39.5 g. had been given. The patient's general condition was now excellent and his appetite unimpaired. Further chest X-rays were taken on the 14th and on the 22nd. The former showed a combination of confluence of the mottled opacities, previously seen combined with some resolution, whilst the latter showed the bronchopneumonic condition almost completely resolved. Urine examination on the 18th showed only faint traces of bile and albumin and absence of casts, whilst on the 20th all trace of albumen had disappeared.

Every attempt was made to confirm the diagnosis by demonstration of the causal organism. On the 13th a dark-ground examination of the blood was carried out but proved negative, and blood culture failed to grow any *Leptospira*. Following alkalization a centrifuged urinary deposit was examined on three occasions after the 10th day of illness with negative results on each occasion. No guinea-pigs were available for inoculation. The diagnosis remained unconfirmed until September 29, when the result of a sero-agglutination test on a specimen of blood taken a week earlier was returned as positive at a titre of 1:300. Ten days later the titre had risen to 1:10,000.

There was a brief but characteristic recrudescence of pyrexia beginning on the 22nd and reaching a peak of 102.8° F. on the evening of the 24th. The temperature returned to normal on the 26th and remained normal during the further fortnight he was under observation. This secondary pyrexia was accompanied by renewed malaise, increased cough and expectoration, and a slight increase of icterus which had never completely disappeared. These features rapidly disappeared when the temperature returned to normal and on discharge the patient was symptom-free apart from a slight cough, and the jaundice had completely cleared. During the latter part of his stay in hospital the patient was up and about and enjoyed a very healthy appetite.

DISCUSSION.

Leptospirosis icterohæmorrhagica must enter into the differential diagnosis of every case of jaundice associated with pyrexia, although in this case the added presence of pulmonary and meningeal symptoms presented a most bewildering clinical picture. In atypical cases the mode of onset with severe, often agonizing, muscular pains and the presence of conjunctival hyperæmia may suggest the correct diagnosis. Thus Witts [3], in a recent article describing two cases of *Leptospirosis icterohæmorrhagica sine icterus*, was enabled to reach a correct diagnosis as a result of observing these two characteristic features. That they may on occasion be absent is demonstrated by the above case in which there was at no time any complaint of pain in arms or legs nor the slightest suspicion of conjunctival infection.

A striking feature of the case was the complete absence of any hæmorrhages into the skin.

and visible mucous membranes; nor did the urine contain any red blood cells. It is most unusual for hæmoptysis to be the sole manifestation of the hæmorrhagic tendency which is such a marked feature of the disease.

Finally, it is worth while considering whether the administration of sulphathiazole modified the course of the disease in any way. In this case improvement followed exhibition of sulphathiazole and relapse occurred when the drug was discontinued. On the other hand the temperature settled and the clinical condition improved after the relapse in the absence of any form of specific therapy. Obviously it would be unwise to draw any conclusions from a single case, particularly as it is generally agreed that sulphonamides have little or no effect in infections due to *Leptospira icterohæmorrhagiae*, but in the absence of both anti-leptospiral serum and penicillin, sulphonamide therapy might be considered worthy of trial.

My thanks are due to Lieutenant-Colonel C. McComas, R.A.M.C., Officer i/c of a Medical Division, for permission to report this case; to Major D. P. King, R.A.M.C., for innumerable tedious pathological investigations; and to Captain H. C. Knox, R.C.A.M.C., for the photograph of the X-ray.

REFERENCES

- [1] MANSON. "Tropical Diseases." Eleventh Edition, 1942.
- [2] PRICE, ED., "Textbook of the Practice of Medicine," Sixth Edition, 1941.
- [3] *B.M.J.*, 1944.

Review.

CATALOGUE OF LEWIS'S MEDICAL, SCIENTIFIC AND TECHNICAL LENDING LIBRARY. New edition, revised to the end of 1943. PART I: Authors and Titles. Pp. 714. PART II: Classified Index of subjects with names of authors: Pp. 208. London: H. K. Lewis & Co., Ltd. 1944. Price to subscribers, 12s. 6d. net; to non-subscribers, 25s. net.

A copy of the above has been received and placed in the Library, Royal Army Medical College.

Notices.

ARMY MEDICAL DEPARTMENT BULLETIN.

A.M.D. Bulletin No. 44, February, 1945, has now been published by the War Office. Distribution scale: One copy to every Medical and Dental Officer.

SUMMARY OF CONTENTS.

Article No.

- 335 *Trench Foot*.—Trench foot has caused little trouble in the British Army during this war because methods of prevention have been understood and applied. General principles and details are discussed.
- 336 *Laboratory Diagnosis of Smallpox*.—A microscopic method can be used as an aid to clinical diagnosis, but it is emphasized that success demands practice; the technique has been fully described in an original article (*Brit. Med. J.*, 1944, October 21, 526) which should be consulted by any who mean to use this method.
- 337 *Varicose Veins*.—The indications for treatment in the Army have a functional and not a cosmetic basis. Simple injection without operation is not therefore recommended. Full details are given about when and how to operate.
- 338 *Mental Factors in Skin Disease*.—Can certain types of skin disease be related to definite psychological groups? A contributor has outlined his ideas.
- 339 *Peripheral Nerve Palsies from Intramuscular Injections*.—Badly given intramuscular injections can have disastrous results. The sites for intramuscular injections, in order of preference, are: (1) Outer side of the thigh; (2) upper and outer quadrant