between the liver damage and the length of anaesthesia could be detected, but it was pointed out, as in our case, that most of these patients had received two or more halothane anaesthetics within a short time.

It might be expected that since halothane is similar chemically to chloroform the liver would show centrilobular necrosis and not patchy damage. However, this latter picture is well known in other forms of drug damage—for example, iproniazid (Popper and Schaffner, 1959; Sherlock, 1960).

In all, our patient received butobarbitone, pethidine hydrochloride, hyoscine, papaveretum hydrochloride, methohexitone, suxamethonium hydrochloride, nitrous oxide, halothane, dichloralphenazone, and sulphadimidine before she showed any jaundice, and it might be contended that any one or combination of these may have caused the liver damage. Other factors to be considered are previous liver damage, anoxia or hypotension during or after the anaesthetic, and the possibility of coincident infectious hepatitis or homologous serum jaundice. This last group of factors was ruled out by the post-operative observations and history from the patient and her family. Which of these drugs caused this fatal toxic hepatitis it is impossible to be sure, but the main anaesthetic agent was halothane, and in view of the previous 11 deaths reported it would be wise for a proper evaluation to be carried out. This is impossible in retrospect, and a prospective study, with full investigations of every patient who is jaundiced after such an anaesthetic, may prove valuable.

ADDENDUM

Since the above patient died, a second, luckily non-fatal, case of jaundice following halothane anaesthesia has been brought to our attention.

A woman of 47, after menorrhagia, had a curettage under a general anaesthetic in January, 1963. Pethidine, hyoscine, and promethazine were given, and anaesthesia was induced with 70 mg. of methohexitone and continued with gallamine triethiodide, 60 mg., nitrous oxide, oxygen, and halothane. The operation lasted 20 minutes.

Curettings showed a non-secretory endometrium, and three weeks later a hysterectomy was performed. Premedication was similar to the above, and anaesthesia for the two-hour operation was induced with 60 mg. of methohexitone and continued with 25 mg. of tubocurarine chloride, nitrous oxide, oxygen, and halothane. Atropine 0.6 mg. and neostigmine 0.25 mg. were also given later. The operation was uneventful and the patient made a normal recovery, post-operative analgesia being with pethidine and dipipanone combined with cyclozine.

Five days after operation the patient became jaundiced, and two days later the blood showed bilirubin 3 mg./100 ml. (direct 2.4 mg.); plasma proteins 5.7 g./100 ml. (albumin 4 g., globulin 1.7 g.), serum alkaline phosphatase 13.5 units; thymol turbidity 1 unit; zinc sulphate 4 units; S.G.P.T. 560 units.

Treatment with high-carbohydrate, fluid diet was started, and the patient did not become ill. Ten days later the jaundice was at the same level, and the liver-function tests were almost identical except for a rise in the alkaline phosphatase to 20.8 units. Three weeks later she felt well, and beyond the continuing jaundice had no abnormal signs. She is still under surveillance, and undoubtedly this picture of liver damage fits into the picture of toxic hepatitis. It is of interest to note that she had halothane anaesthesia on two occasions.

SUMMARY

A case of death from toxic hepatitis is reported after halothane anaesthesia. The possibility of this being due

to the anaesthetic agent is discussed. A further case of non-fatal jaundice after similar anaesthesia is included.

My thanks are due to Mrs. C. L. Beynon, under whose care both patients were treated, for her help and permission to publish. I would also like to thank Dr. T. A. Copp, who anaesthetized both patients, for his co-operation and help in the preparation of this brief communication.

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Medical Memoranda

Acute Tuberculous Septicaemia

Acute tuberculous septicaemia is a rare condition. It is a definite entity, but few cases have been recorded. Ball *et al.* (1951) described three fatal cases and gave short accounts of eight others that had appeared in the literature. Brennan and Weaver (1956) reported four cases. It is an acute illness which without treatment is invariably fatal within three to twelve weeks. Since the disease runs a rapid course, an early diagnosis must be made if chemotherapy is to have a chance of success. This paper describes a pyrexial illness which presented considerable diagnostic problems and which eventually proved to be acute septicaemic tuberculosis. Recovery was rapid with appropriate treatment.

CASE REPORT

A Uganda African sub-inspector of police aged 24 was admitted to a small hospital near Kampala with a week's history of mental confusion and mild pyrexia. Prior to admission it had been noted that he was behaving strangely; he scribbled on report books and did odd things. In view of his mental confusion he was referred to a mental clinic. There it was decided that the abnormal mental picture was related to the fever, and so the patient was transferred to a general medical ward of Mulago Hospital.

On admission he gave a history of bouts of fever associated with profuse sweating and mental confusion for one week. The attack usually came on at night and lasted two to three hours. Examination showed him to be well nourished and intelligent. He looked febrile and toxic. His temperature was 100° F. (37.8° C.) and his pulse rate 92/min. The tongue was clean and moist. There was no lymphadenopathy. No signs were present in the chest; the abdomen was normal; and there was no evidence of meningitis. No past history of any serious illness or contact with tuberculosis was elicited.

In the evening of the day of admission his temperature suddenly rose to 103° F. (39.4° C.) and he began to sweat profusely. Blood slides were examined for malaria parasites but none were seen. Since typhoid fever was the most likely diagnosis he was treated with chloramphenicol 500 mg. 6-hourly pending further investigation.

The Hb was 17.2 g./100 ml. and the white cells numbered 5,100/c.mm., with a normal differential. The E.S.R. was 11 mm./hour (Wintrobe). The urine showed no abnormality and stool culture did not grow any of the *Salmonella* group of organisms. The blood urea was 33 mg./100 ml. Widal, Weil-Felix, and Paul-Bunnell tests were all negative, but the Heaf test was strongly positive. Sputa were examined serially for acid-fast bacilli but none were seen. A chest radiograph showed a bilateral homogeneous opacity in the hilar region consistent with enlarged hilar lymph nodes. The rest of the lung fields were quite clear even on an under-penetrated film. The first blood culture grew *Proteus* which was sensitive only to tetracycline and sulphafurazole.

By this time the patient had been on chloramphenicol for one week without improvement. He continued to have moderate pyrexia interrupted by bouts of high fever and profuse sweating. In view of the blood-culture and sensitivity reports, and no clinical response to chloramphenicol, he was put on tetracycline 500 mg. 6-hourly.

In spite of the change in antibiotics the patient's condition continued to deteriorate; he was losing weight and getting more toxic. After he had been on tetracycline for 10 days with not the slightest response in spite of the subsequent blood cultures being sterile, it was evident that *Proteus* must be a contaminant after all.

Temperature chart illustrating failure to respond to antibiotics but showing an excellent response when P.A.S. and isoniazid were given.

Another chest film and white blood count showed no significant changes. The sternal marrow showed slight hypocellularity with a normal distribution of cells. Unfortunately the marrow was not cultured for acid-fast bacilli.

After tetracycline was stopped a week passed without any chemotherapy. The patient remained febrile, continued to lose weight, and became more toxic. It was then decided to put him on antituberculous therapy as a therapeutic test. He was given P.A.S. 4 g. t.i.d. and isoniazid 100 mg. t.i.d. Streptomycin was deliberately not given in case a non-tuberculous organism sensitive to it was present, thus obscuring the diagnosis.

Response to this treatment was most dramatic. The temperature fell the very next day and remained normal. There were no further episodes of fever with sweating. The patient felt very much better and put on 10 lb. (4.5 kg.) in weight in three weeks.

In view of such a dramatic response to antituberculous therapy, there was no doubt of the diagnosis of acute tuberculous septicaemia. Needle biopsy of the liver was performed; the histology showed several small granulomata composed of histiocytes and lymphocytes consistent with septicaemic tuberculosis. The specimen was sectioned and stained for acid-fast bacilli, but none was found.

The patient has now been on antituberculous therapy for six months and he continues to remain symptom-free and has fully resumed his duties as a sub-inspector of police.

COMMENT

When this disease presents as a case of P.U.O. it is often diagnosed late or missed altogether because the presentation and the clinical picture may be unusual

and misleading. The most important factor in making a diagnosis is to consider the possibility of septicaemic tuberculosis in cases with a low white-cell count or frank leucopenia, and to be prepared to give antituberculous treatment when diagnosis has proved impossible and the case is early enough for such treatment to be effective.

An attempt should be made to confirm the diagnosis by sternal-marrow puncture, by needle biopsy of the liver, and by splenic puncture. The material should be examined histologically and cultured, animal inoculation being carried out if possible. The causal organism may be demonstrated in bone marrow and splenic-pulp smears or in the biopsy material. The liver-biopsy tissue may show multiple acute granulomata consistent with a diagnosis of tuberculosis. Bone marrow has confirmed the diagnosis in such cases in as high a proportion as 89% (Katz and Lifschutz, 1950). Chest radiography is usually of little help in making a diagnosis of tuberculous septicaemia. Böttiger *et al.* (1962) have recently described five fatal cases of disseminated tuberculosis which presented as P.U.O. and remained clinically undiagnosed. They suggest that the negative chest x-ray findings contributed to the missed diagnosis.

In cases of prolonged unexplained fever, especially when there are puzzling blood changes, it is advisable to give antituberculous drugs before it is too late. Wenderoth (1962) has suggested that in such cases it is worth while considering the administration of antituberculous drugs as a routine procedure.

I am indebted to Dr. P. P. Turner, under whose care this patient was admitted, for permission to publish this case and for his very helpful advice.

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"There are two short notes that I have read with special interest in the second volume of the *Concise Dictionary of National Biography*. They relate to persons who had entirely different backgrounds and experience, but who had, it seems to me, one great gift in common—the gift of true graciousness. The first note relates to Reginald Brabazon, twelfth Earl of Meath (1841–1929), who originated the idea of celebrating Empire Day and who founded the Hospital Saturday Fund Committee which did so much to help hospitals in the years before the State was interested. I met the Earl of Meath in London early in 1927, when he was 85, and he made an impression on me that thirty-six years have not effaced. . . . The second consists of only eighteen lines, which attempt to sum up the life of Sir William Osler (1849–1919). How little that is compared with the 1,372 pages in my copy of Harvey Cushing's biography of this great physician, teacher, and scholar. . . . I remember that I once asked one of the most distinguished London surgeons if he had known Osler and whether he was as great a man as Cushing showed him to be. The answer was, 'I knew him well; he was a much greater man than that.' At that time, our own Sir William Thomson (W.D.) was alive and I often used to think how much he resembled my image of Osler. Grace is high in the list of virtues I admire, even if I sadly lack it." ("A Clerke," in *Hospital News*, Northern Ireland Hospital Authority.)