Discussion

These six patients all had clinical histories and findings which were essentially similar, and which, furthermore, closely resembled previous descriptions of Bornholm disease. The condition was in fact suspected on the admission of Case 1 even before the occurrence of further cases in the family helped to establish the diagnosis. The first five patients, forming as they did a small group, could be fairly confidently diagnosed as suffering from Bornholm disease. In these cases the connexion previously described between Bornholm disease and Coxsackie-virus infection (Curnen, 1950) was confirmed by the isolation of virus in one case and by a rising agglutination titre in all four of the five patients who were available for testing; no such confirmation was obtained in Case 6, and the final diagnosis of this patient cannot be regarded as established.

Coxsackie virus was first isolated from two paralytic patients during an epidemic of poliomyelitis (Dalldorf and Sickles, 1948). During 1947 and 1948 there were reports from the United States of various outbreaks of febrile illness in which many cases resembled non-paralytic poliomyelitis. In some of these cases poliomyelitis virus was isolated, but in others faecal specimens and nasopharyngeal washings tested for poliomyelitis virus were non-infective for monkeys (Dalldorf, 1950). During these outbreaks Coxsackie virus was isolated from patients with various minor illnesses, with illness resembling epidemic myalgia (Bornholm disease), and with illness suggesting non-paralytic poliomyelitis. In some but not all of the last group poliomyelitis virus was also isolated (Curnen, 1950).

In some previously reported cases of Bornholm disease signs of meningeal irritation have been noted. DeRudder (1937) drew attention to the similarities between epidemic myalgia and poliomyelitis, although his views were to some extent disputed by Lindberg (1938). The similarities were also stressed more recently by Ronse (1949).

There is of course no reason why patients should not harbour both poliomyelitis and Coxsackie virus at the same time, and this association has in fact been recorded (Melnick, 1950).

The similarities and differences between these two groups of virus are summarized by Melnick (1950), who concludes that, though antigenically distinct, their biological behaviour is surprisingly similar. He points out, furthermore, that members of the Coxsackie group of viruses are now being repeatedly found where poliomyelitis is epidemic.

I am grateful to Drs. H. V. Morlock and E. W. Hart, under whose care these patients were treated, for their permission to publish this article, and to Dr. L. Cohen, who brought four of the patients to our notice. I am also very much indebted to Dr. G. M. Findlay, who carried out all the virological investigations, for his generous assistance.

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TUBERCULOSIS OF LIVER TREATED WITH STREPTOMYCIN

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The following case is of interest on account of its rarity and its clinical course.

Case Report

The patient, a student aged 20, was admitted to hospital on March 14, 1950. He enjoyed good health until June, 1949, and was living in a college pleasantly situated in the country. He noticed, however, that during the first two weeks of his summer vacation in 1949 he was becoming easily tired, could find little energy for his usual holiday activities, and had diarrhoea. Some few days later his stools became very pale and offensive, and he noticed that his eyes "were becoming yellow." A few weeks later he was drenched in a rain-storm, after which severe pain developed in the right loin accompanied by anorexia and malaise. He was confined to bed for seven days, and was seen to be slightly jaundiced. His condition improved with rest, and he resumed his usual activities. Before his return to college in September, however, two of his teeth were extracted; haemorrhage was profuse and persisted over four or five days in spite of plugging. His general condition as a result became very poor.

Lest any absence due to illness should mean the sudden end of his scholastic career, he returned to college, although he felt very weak. He had been advised to take iron, and with this therapy his pallor became less severe. His jaundice persisted, and during the last months of 1949 gradually became more intense. He began to have frequent sweats, often profuse, and especially at night. At the end of December he suffered a minor cut on one of his hands, and again the bleeding was prolonged. A vitamin-K analogue—self-prescribed—made no difference to this tendency to bleed. Bleeding from the gums occurred, becoming more and more frequent until it was a daily event. His appetite at this time was fairly good, and he was passing two or three loose pale motions each day. The urine was deep yellow in colour. He had no cough, and, so far as he could judge, had not lost weight.

His past history was of appendicitis at the age of 7 years and section of peritoneal adhesions at 15, when there was suspicion of mesenteric tuberculous adenitis. No proof of this was ever obtained. The family history shed no light on his illness.

Examination on admission showed him to be a tall lean youth, pale and slightly jaundiced. He was febrile and was sweating freely; his fingers were clubbed; enlarged lymph nodes were not detected. The left elbow-joint was painful and tender, its movements being limited to about a right-angle. The abdomen was distended and the liver slightly enlarged. The spleen and kidneys were not palpated. Examination of the chest disclosed no abnormality, and the cardiovascular and central nervous systems appeared to be normal.

Blood examination revealed an iron-deficiency anaemia: Hb, 76% Sahli (10.64 g.); red cells, 4,580,000 per c.mm.; colour index, 0.8; white cells, 8,000 per c.mm. The differential count gave average readings. The bleeding-time was 4½ minutes by Duke's method, and the coagulation time 8 minutes by the method of Lee and White. The red-cell-fragility test showed commencing haemolysis at a concentration of 0.5% NaCl, complete at 0.35%. The urine contained bile and urobilin. No blood or casts were seen on microscopical examination.

Diagnosis was at this point obscure, and many investigations were carried out. Radiological examination of the

chest showed no evidence of active pulmonary disease. On cholecystography the gall-bladder was considered to be non-functioning. X-ray examination of the left elbow-joint revealed no abnormality. The van den Bergh reaction gave a positive indirect result. No serum agglutinins were detected for *Leptospira icterohaemorrhagiae*.

By April, 1950, the left elbow-joint showed the signs of an infective arthritis, and was greatly swollen. Aspiration of the joint revealed pus, and a culture was set up. Epigastric pain was now becoming increasingly severe, and the possibility of impacted gall-stones was considered. The surgeon hesitated to operate on account of the possibility of severe haemorrhage. When the bleeding-time was found to be normal, laparotomy was carried out.

At operation, gall-stones were not found, but the liver was very congested and raw-looking, with numerous small yellow spots all over its surface. Around the liver there were many adhesions to the anterior abdominal wall and viscera. The gall-bladder was normal, but was fixed in adhesions. The head of the pancreas was slightly thickened, but was thought not to be the seat of malignant growth. A piece of the edge of the liver was removed for histological examination.

Three days after operation it became known that from the pus aspirated from the elbow-joint a culture of *Mycobacterium tuberculosis* had been grown. This finding reached startling significance when the pathologist's report on the liver specimen showed that tubercle follicles were present in the liver parenchyma deep to the capsule: tubercle bacilli were not demonstrated, but the lesions were histologically typical of tuberculosis. Also, there was an increase of connective tissue in and between the portal tracts, and the surrounding liver tissue showed irregular hyperplasia and atrophy. The connective tissue contained numerous plasma cells and lymphocytes, and there was pronounced bile-duct hyperplasia. The lesions were summarized as metastatic haematogenous tuberculous follicles, and early scarring resulting from prolonged, or recurrent, and still active infective hepatitis.

Streptomycin Treatment

The problem of diagnosis, of course, now included the possibility of a dual pathology. Nevertheless, it appeared that a case of tuberculosis of the liver had been diagnosed during life without evidence of generalized military infection, but with a distant focus which had become manifest long after the initial symptoms of hepatic disorder. Whatever the diagnostic difficulties, there seemed to be no similar therapeutic problem. Streptomycin, which is most successful in some of the rarer manifestations of tuberculous infection, seemed to be the most reasonable basis for treatment. It was first given on May 12, 2 g. daily being injected intramuscularly for the first five days, after which the daily dose was 1 g. This was continued until August 22, when a total of 107 g. had been given.

During the months of treatment the temperature, which previously had shown intermittent elevation, gradually settled and general clinical improvement began. Appetite improved steadily and there was a sustained increase in weight, though bile persisted in the urine, stools remained rather pale, and a tinge of jaundice was perceptible. The erythrocyte sedimentation rate was thought to be a useful index of progress, Westergren's method being used throughout. From the high first-hour reading of 95 mm. on April 18 a steadily continuous fall was observed. On August 27, five days after the cessation of streptomycin administration, the comparable reading was 15 mm.

The tuberculous arthritis of the left elbow-joint was treated by immobilization in plaster. During May the joint became unstable, and two months later was almost completely disorganized. A cold abscess pointed and discharged in the antecubital fossa, but by the end of August the resultant sinus had ceased to discharge and had filled with granulation tissue.

Further Progress

In September the patient became ambulant and seemed to be making steady progress. His appetite, however, was capricious, and injections of vitamin-B complex were given. These had the effect of making the appetite almost voracious, and a high-protein diet, rather unpalatable to an average person, was consumed with ease. Diarrhoea developed at this time, with the passage of loose, pale, unformed, and very offensive stools. They resembled closely the stool of steatorrhoea. Dietary adjustment—namely, lowering of the fat content and administration of an ox-bile preparation—was followed by immediate improvement. His general condition was now so satisfactory that he was allowed home to continue convalescence. There was no jaundice, pallor had been replaced by good colour, and his weight was 9 st. 4 lb. (59 kg.), an increase of over 14 lb. (6.4 kg.) since the beginning of streptomycin treatment. The elbow-joint was immobilized in plaster, in the position of flexion to just less than a right-angle, and he was quite capable of dressing and eating, etc., with only one efficient arm.

Since discharge he has been seen regularly at fortnightly intervals. The gain in weight has been maintained and his appetite has been enormous. The sedimentation rate (Westergren) on November 15 was: first hour 17 mm., second hour 47 mm.; and on November 29, first hour 20 mm., second hour 47 mm. Stools were still rather pale and loose, and there was slight tenderness in the right umbilical region. Examination of the chest still showed no abnormality. The elbow-joint was gradually becoming ankylosed.

At the time of writing the patient feels well, but, while the degree of recovery following streptomycin is as yet very satisfactory, the ultimate prognosis must remain doubtful, with the possibility of recurrence to be considered.

I wish to express my thanks to Dr. D. K. Adams for permission to describe this case, which was treated in his wards, and to Mr. G. Dalziel, who performed the laparotomy. My thanks are also extended to Dr. Adams and Dr. W. Kyles for their guidance, help, and criticism during the preparation of this paper.

Medical Memorandum

Special Visits by Medical Officers of a Public Health Department

The visits of medical officers on the staff of a public health department to suspected cases of infectious disease receive but scant publicity. During serious epidemics this work becomes more obvious, but the regular visits which take place throughout the year are but little appreciated until an epidemic such as one of poliomyelitis throws them into relief.

An analysis of a miscellaneous list of such visits covering the period 1935 to 1950 for the City of Manchester is most revealing in showing the diagnostic difficulties that are most common. A miscellaneous list has been chosen to show the range of clinical acumen necessary in this special field. An analysis of these visits is presented in the accompanying table.

The screening of cases by public health medical officers becomes increasingly important, for the available accommodation in infectious disease hospitals is limited by shortages of nursing staff and a standstill in building extensions to these hospitals. This work is essentially clinical, and requires that those undertaking it shall have