picture of osteosclerosis with leucoerythroblastosis can occur in fluorosis. X rays have been known to produce fibrosis of the marrow; and Joan Ross (1932) describes the effects of gamma radiation over a period of three years. The marrow showed hyperactivity of the myeloid and erythroid cells with a marked increase in megakaryocytes. The nutrient vessels showed endothelial thickening and intravascular thrombi. It is not beyond possibility that repeated doses of deep x rays over many years may produce the picture of myelofibrosis in polycythaemia rubra vera.

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A CASE OF WEIL'S DISEASE, WITH TESTS FOR LIVER FUNCTION

BY

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Familiarity with Weil's disease during the war has resulted in several publications in the English and American literature. Although jaundice is usually a marked feature of this disease, there is no record of liver-function tests. The following case is therefore described, together with the result of tests for liver dysfunction and for other biochemical disturbances. These were of great help in excluding the diagnosis of acute hepatic necrosis, which was made on admission. It is hoped that this will stimulate physicians who have greater opportunities for studying this disease to investigate its chemical pathology, and to deduce from their findings evidence concerning the site of tissue damage.

Case Report

The patient, a plumber aged 58, was admitted on April 13, 1949. Up to a week previously he had been working on a boiler in a meat-pie factory in which fat was rendered down. Seven days before admission he had a rigor; this was followed by another two hours afterwards. Four days later he noticed he was yellow, and he began to vomit incessantly. There was no abdominal pain.

On examination he was a very ill man, dehydrated, with subsultus tendinum, deep jaundice, and a generalized purpuric eruption. The mucosae were pale. He was afebrile; the pulse rate was 90, the blood pressure was 130/80, the heart sounds were faint, and there were basal crepitations. The liver was not palpable. There was some free fluid in his abdomen, and his stools were pale. Three days later he developed a swinging temperature up to 102° F. (38.9° C.), which was maintained for five weeks and subsided by lysis, and which did not respond to penicillin, 250,000 units six-hourly intramuscularly for 10 days.

He was given 5 pints (2.34 litres) of fluid by mouth, 3 pints (1.7 litres) of "casydrol" by intravenous drip transfusion, 6 ml. of "campolon" intramuscularly, 500 mg. of ascorbic acid, and 15 mg. of vitamin K daily. Later he developed a urinary infection with *Pseudomonas pyocyanea*, for which he was given 4 g. of streptomycin daily by injection for five days.

Subsequent Course.—His rash cleared up in three days; the jaundice had faded by the first week in July, but he was pyrexial

for a month. However, he remained mentally in a state of stupor, with considerable clouding of consciousness, marked loss of memory for recent events, and disorientation in time and place. Some measure of recovery occurred, but when his wife took him on May 31 he was able to sit out in a chair, though he showed a good deal of mental deterioration, with lack of all initiative and poor memory. A letter from his wife on July 27 stated that his general condition had improved, but his legs were weak and useless and his mental state poor.

Investigations

Agglutinations.—*L. icterohaemorrhagiae*: April 20, 1:1,000; April 29, 1:1,000; May 5, 1:3,000. *L. canicola*, nil. *Salm. typhi*, *Salm. paratyphi A*, *Salm. paratyphi B*, and *Br. abortus*, nil.

Blood Counts.—Haemoglobin: April 14, 59%; May 9, 59%; May 23, 72%. Red cells: April 14, 3,750,000; May 9, 3,020,000; May 23, 3,500,000. White cells: April 14, 25,000 (P. 77%, L. 21%, M. 1%); May 9, 25,000 (P. 89%, L. 10%, M. 1%); May 23, 18,000 (P. 75%, L. 25%, M. 4%).

Serum Proteins.—April 24: total, 5.75 g.% (albumin 4.2, globulin 1.5; A/G ratio 2.7:1). May 5: total, 5.5 g.% (albumin 3.7, globulin 1.8; A/G ratio 2.05:1).

Liver-function Tests.—Alkaline phosphatase: April 24, 10.7 units; May 5, 16.3 units; May 23, 12.8 units. Thymol turbidity: April 24, 1.5 units; May 5 and 23, 1 unit. The Takata-Ara and colloidal gold tests were negative.

Urine.—April 19 and 25: specific gravity, 1010; albumin, sugar, and bile salts, nil; bilirubin was in excess on April 19 and urobilin was present on April 25. On April 25 there were 10 cells per field and *Ps. pyocyanea* was found. On May 30 there were many pus cells and *Ps. pyocyanea* was still present. There were no spirochaetes.

Haemolysins.—On May 30 no cold agglutinins were present, and Coombs's direct and indirect tests were negative.

On April 14 the serum diastase amounted to 320 mg. per 100 ml. (normal, 70–150 mg.). On April 22 the blood urea was 27 mg. per 100 ml., the alkali reserve 49 volumes, and the serum calcium 8.6 mg. per 100 ml. On May 10 the blood urea was 35 mg. per 100 ml. and the alkali reserve 43.9 volumes. On April 22 the blood sugar totalled 148 mg. per 100 ml., and the serum cholesterol 177 mg. per 100 ml. (free, 80 mg.; ester, 97 mg.).

The diagnosis was based on the presence of jaundice, the rash, the patient's occupation, and the rising titre of agglutinins.

Comment

The morbid pathology of the liver in Weil's disease is described by Hutchinson *et al.* (1946). They say that the liver in their cases was usually of normal size, with masses of bile pigment in the biliary canaliculi of the centrilobar part of the liver lobules, and emphasize the absence of necrosis. On the other hand, Heringman and Phillips (1947) mention considerable disorganization of the liver pattern with moderate vacuolization and swelling of cells and the formation of continuous cords of liver cells instead of normal groups of two or three cells.

In the case described by Jackson and Oleesky (1946) there was no macroscopic hepatic necrosis; there were scattered areas of fatty degeneration and areas of regeneration, with enlarged binucleated liver cells. They mention that Walch-Sorgdrager (1939) refers to the frequent misdiagnosis of acute yellow atrophy, as happened in our case.

Our case on admission, being afebrile at the time and extremely ill and toxic, closely resembled the picture of acute hepatic necrosis. The finding of normal plasma proteins and Takata-Ara, thymol turbidity, and colloidal gold tests was therefore of distinct value in excluding this diagnosis, and would seem to rule out any overwhelming degree of parenchymal damage.

The absence of urobilin in the urine in the early stages would seem to point to an obstructive element in the jaundice such as might be caused by the bile pigment masses in the small canaliculi that Hutchinson *et al.* described; however, the alkaline phosphatase was never above 16.3 units. Unfortunately the Coombs tests were done too late to exclude a haemolytic factor. Apart from the complicating *Ps. pyocyanea* infection there was no evidence of renal damage. The blood urea remained normal, and there were no casts or red cells in the urine. The serum diastase value of 320 mg. per 100 ml. would appear to suggest disturbance of pancreatic function.

The mental state of the patient is worthy of passing comment. There was never any sign of meningitis leptospiriosa. Three possible theories about causation are: first, that the condition was due to cerebral damage by the organism or its toxins; secondly, that it was due to the severe jaundice; and, thirdly, that the haemorrhagic state present at the onset in the skin was also present in the brain; this is, I think, the most likely.

Summary

A case of Weil's disease, with liver-function tests, is described.

An attempt is made to correlate these with previously described accounts of the pathology of this condition.

Other interesting features of the case are briefly dwelt on.

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PRIMARY LYMPHOSARCOMA OF APPENDIX OCCURRING IN CHILDHOOD

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Lymphosarcoma arising in the appendix is rare; only seven cases occurring in childhood have been published. In a majority of such cases the children have had symptoms suggestive of appendicular disease. In the following case the patient had no such symptoms, and the clinical picture which presented was therefore of special interest.

Case Report

A boy aged 6 years 9 months was admitted to hospital on October 1, 1948. The child had been well until four weeks before admission, when he was immunized against diphtheria. Since then he had been "off colour" but had attended school. Three days before admission he complained of pain in his chest and right thigh, and vomited once. His mother noticed a swelling on his left temple on the following day; but there had not been any loss of weight or other symptoms. There was nothing relevant in the family history or in the child's previous personal history.

On examination his temperature was 100° F. (37.8° C.), pulse 80, and respirations 20. The child's general condition was poor; he was very irritable and complained of pains in all his joints. A swelling on the left temple was noted and there were palpable glands in the left axillary and cervical regions. Abdominal examination revealed tenderness in both iliac fossae, but there were no palpable masses. Routine clinical examination did not show any further abnormal features.

For the first three days the temperature varied between 98.4 and 102° F. (36.9 and 38.9° C.). On the fourth day his temperature fell and remained normal until the eighth day, when it rose to 103° F. (39.4° C.). At this time the left knee-joint was slightly swollen. There was no cardiac enlargement, but a soft apical systolic murmur could be heard. The abdomen was rather large and doughy, with dullness in both flanks. The liver was enlarged one fingerbreadth below the costal margin and the tip of the spleen was felt. The kidneys were not palpable and no other abdominal masses were found. There were no abnormal signs in the central nervous system.

Radiographs of the chest, abdomen, and skull, a Mantoux test (1:10,000 dilution), blood culture, and Widal reactions

A = Gall Bladder; B = Liver; C = Kidney; D = Pancreas; E = Stomach; F = Ileal Mass; G = Appendix.

were all negative. The erythrocyte sedimentation rate was 50 mm. in one hour. The blood picture was: haemoglobin, 68%; red cells, 3,920,000; white cells 5,000 (polymorphs 54%, myelocytes 7%, metamyelocytes 14%, lymphocytes 20%, monocytes 3%, eosinophils 2%). An intravenous pyelogram, the blood Wassermann reaction, and a blood-urea estimation were all negative. No Bence-Jones proteose was present in the urine, and the stools did not contain either visible or occult blood.

The pyrexia was maintained despite penicillin and salicylate therapy. The liver increased in size to two fingerbreadths below the costal margin. The swelling over the left temple had increased in size and was now 1 in. (2.5 cm.) in diameter; it was tender and gave the impression of deep fluctuation. No further lymphatic gland enlargement developed. The child's appetite remained good, but despite this he was obviously becoming more wasted. His bowels were normal and he had no vomiting. An irregular soft mass, thought to be faeces, was felt in the right iliac fossa on the thirteenth day. The rectum was found to be loaded with soft brown faeces, but there was no palpable mass. Just below the ninth costal cartilage a small nodule was felt on the enlarged liver. There were no signs