very little improvement. A week after the transfusion a fragility curve (Creed's method) showed a definite increase in fragility, the haemolysis in 0.5% saline being still 8%. Patient died 11 days after admission to hospital.

Post-mortem findings were as follows: the liver was slightly larger than normal and showed cirrhosis. The colour was a green-brown and the surface was covered with small nodules. The spleen was congested and enlarged to twice the normal size. Section showed a portal cirrhosis with young fibrous tissue breaking up the lobules. There was infiltration of the fibrous tissue with lymphocytes. Quite a large proportion of the liver cells were distended by globules of fat. There were deposits of iron in the liver and spleen. The femoral marrow was red throughout its length and showed a normoblastic hyperplasia.

Discussion

In both cases a severe anaemia has to be explained. Haemorrhage can be discounted. Tests for occult blood in the stools were negative. In the first case there was no history of bleeding; in the second there had been a small vaginal haemorrhage and purpuric spots, but nothing which could account for a haemoglobin of 29%. The appearance of the blood films was quite unlike that of pernicious anaemia. Case 1 received an urgent blood transfusion on admission and a reticulocyte count was not done, but there is evidence of a haemolytic process in the remarkable behaviour of this case on transfusion. A total of 14 pints (8 litres) of blood was given to this patient over a period of 14 days and relatively little increase was obtained in the haemoglobin. This can be explained only by a rapid destruction of transfused cells, which is one of the features of haemolytic anaemia (Sharpe and Davis, 1938). In the second case there is clear evidence of a haemolytic anaemia: a high reticulocyte count, numerous nucleated red cells, increased fragility, and red marrow in the shaft of the femur.

The biochemical findings do not assist in the diagnosis of the anaemia. The positive direct van den Bergh reaction and the presence of bilirubin in the urine are not, of course, the findings of haemolytic jaundice, but can readily be explained on the basis of the coexistent liver damage. The large amounts of urobilinogen in the urine are more likely to be due to the cirrhosis than to the haemolysis.

My thanks are due to Dr. E. S. Gawne, medical superintendent, Townleys Hospital, for permission to publish these case reports, and to Drs. D. Mooney and R. Kearney for the opportunity to co-operate in the diagnosis and treatment.

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The village of Syrianokhorio in Cyprus has recently celebrated the eradication of malarial-carrying mosquitoes with religious services and a meeting at which the authorities were thanked, reports the Colonial Office. The offensive against mosquitoes was started by the Cyprus Government Medical Department in 1946, and is aimed at complete elimination of malaria from the island by 1952. The estimated cost is £300,000. The terrain is a difficult one to work in and covers about 3,500 square miles; the western half is mountainous, with steep precipices and rushing streams. *Anopheles superpictus* breeds in the streams and rock pools in almost inaccessible places. The country is divided into zones which are systematically sprayed with a solution of D.D.T. in oil.

TREATMENT OF ABORTUS FEVER WITH SULPHONAMIDES AND BLOOD TRANSFUSIONS

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The treatment of undulant fever has remained unsatisfactory in spite of recent advances in chemotherapy, although occasional successes have been reported from the use of sulphonamides, suramin, vaccines, and injections of brucellin. Recent reports of treatment with penicillin and streptomycin are also very disappointing. In an annotation in the *British Medical Journal* (1947, 2, 700) attention was called to a report by Huddleson, made to the Fourth International Congress for Microbiology at Copenhagen in July, 1947, of four cases of undulant fever which responded quickly to the administration of small doses of sulphonamides together with blood transfusions. No special care was given to the selection of donors; it was assumed that all human serum contains bactericidal brucella antibody, but it is difficult to understand why a weak antiserum in conjunction with a sulphonamide should have a bactericidal effect. Huddleson explains this on the basis of the Neisser-Wechsberg phenomenon—a serum may be bactericidal in high dilution yet not in low dilution.

This method of treatment was tried in two cases of undulant fever with the encouraging results indicated in the following reports.

Case 1

The patient, a woman aged 32, first complained of feeling ill about Dec. 16, 1947. A week later she was found to have an evening temperature rising to 102° F. (38.9° C.). She was seen by her doctor on Jan. 17, 1948, when she complained of tiredness, headaches, and pain in the back. On examination at this time her temperature was 100° F. (37.8° C.) and her pulse rate 86 per minute; she had lost a little weight and her spleen was much enlarged.

On Jan. 8 she was admitted to Clatterbridge (County) General Hospital, where re-examination confirmed the above findings. Her evening temperature ranged from 100.4° to 102.6° F. (38°–39.2° C.), but apart from the fever and the splenic enlargement no abnormality was found. On Jan. 19 the blood urea was 26 mg. per 100 ml. A blood count showed red cells, 5,000,000 per c.mm.; haemoglobin, 92%; white cells, 3,600 per c.mm. (polymorphs 52.5%, lymphocytes 45%, monocytes 2.5%). Agglutinations: positive in all dilutions up to 1:1,400 against *Br. abortus*; negative against *Salm. typhosus* and *paratyphosus*. The urine was free from sugar and albumin. Blood culture: contaminated by *Staph. albus* (coagulase-negative), no other organisms found. X-ray film of the chest was normal. Blood Wassermann reaction was negative.

The following treatment was given: penicillin, 9 mega units (Jan. 25 to Feb. 3), sulphadiazine, 75 g. (Feb. 7 to 19), and blood transfusions of 10 oz. (280 ml.) on Feb. 11, 13, 15, and 17. There was no clinical improvement with penicillin, but once the sulphadiazine and transfusions were begun the temperature rapidly subsided and the patient's condition improved. She was discharged from hospital on Feb. 26 and reported to the outpatient department on April 14. She had been afebrile since discharge, felt well in every way, and there was no splenic enlargement.

The following are the results of further investigations. Feb. 19:—Blood count: red cells, 4,380,000 per c.mm.; haemoglobin, 87%; white cells 5,200 per c.mm. Agglutinations: negative in dilutions of 1:25 and 1:50 against *Br. abortus*; positive in dilutions of 1:125, 1:250, and 1:1,250. April 16:—Blood count: haemoglobin, 95%; red cells, 4,680,000 per c.mm.; white cells, 6,600 per c.mm. (polymorphs 68%, lymphocytes 30%, monocytes 1%, basophils 1%). Agglutinations: negative in dilutions of 1:25, 1:50, 1:250, and 1:1,250 against *Br. abortus*; positive in dilution of 1:125.

Case 2

This patient, a woman aged 38, first complained of feeling ill on Jan. 24, 1948. She had shivering, sweating, headache, and pain in the right ear. On examination she was found to have an evening temperature swinging to 102° F. (38.9° C.), but no other abnormality was found. On Feb. 8 a blood count showed: haemoglobin, 84%; red cells, 4,690,000 per c.mm.; white cells, 4,000 per c.mm. (polymorphs 46%, lymphocytes 49%, monocytes 4%, basophils 1%). Agglutinations: positive in all dilutions up to 1:500 against *Br. abortus*.

The following chemotherapy was given: sulphamezathine, 48 g. (Feb. 2 to 5 and 9 to 11), penicillin, 1,200,000 units (Feb. 9 to 11), and sulphadiazine, 51 g. (Feb. 27 to March 3). Despite this treatment the patient's condition deteriorated; she had distressing rigors with profuse sweating and pyrexia rising to 105° F. (40.6° C.).

On March 4 she was admitted to the Staffordshire General Infirmary. She was still seriously ill, the temperature rising to 104° F. (40° C.), and the spleen was slightly enlarged. Treatment with sulphadiazine and blood transfusions was begun on March 5, as follows: sulphadiazine, 30 g. (March 5 to 9) and 6 g. (March 13); blood transfusions, 10 oz. (280 ml.) (March 5), 15 oz. (425 ml.) (March 8), and 4 oz. (110 ml.) (March 13). The patient felt much better after the first transfusion and there was an immediate lessening of the severe rigors and sweating. She was discharged from hospital afebrile on March 18.

She felt well and remained afebrile until April 6, when she developed pain under the right costal margin and a temperature of 102° F. (38.9° C.): a diagnosis of acute cholecystitis was made and she was readmitted to hospital on the following day. The condition showed no signs of settling despite 25 g. of sulphadiazine over a period of four days, and finally a cholecystectomy was performed by Mr. B. R. Sworn on April 19. The gall-bladder was acutely inflamed, and a pure culture of *Br. abortus* was obtained from the contents.

There was some increase in the pyrexia and malaise after the operation, so it was decided to try further treatment with sulphonamides and blood transfusions. Sulphadiazine, 12 g. (April 22 and 23) and 6 g. (April 27), and blood transfusions, 8 oz. (225 ml.) (April 23) and 6 oz. (170 ml.) (April 27), were given. There was a mild reaction to the second transfusion, a rigor, and transient rise of temperature, but immediately afterwards the pyrexia subsided completely and the patient said that she felt better than she had been throughout the whole illness. She was discharged from hospital on May 5 and has since remained well.

Comment

Both these cases of abortus fever had failed to respond to ordinary chemotherapy: Case 1 did not improve with penicillin and Case 2 was not affected by penicillin, sulphamezathine, or sulphadiazine. In each case there was rapid response to sulphadiazine and small blood transfusions. Case 2 returned three weeks later with acute cholecystitis due to *Br. abortus*; the temperature did not subside following cholecystectomy but responded to further sulphadiazine and blood transfusions.

While it is impossible to draw conclusions from only two cases, we feel that these results are encouraging and that this method of treatment should be given a more extended trial.

Our thanks are due to Dr. D. B. W. McKendrick, who called our attention to this method of treatment of abortus fever.

Medical Memoranda

Pneumococcal Meningitis in an Infant of 8 days: Recovery

The value of intrathecal penicillin in pneumococcal meningitis is now established, but the optimum dosage still seems to be a matter for controversy. Shalom (1945) reported eight cases of pneumococcal meningitis with three deaths, the patients having been given intrathecally 4,000 units of penicillin daily, together with penicillin intramuscularly and full doses of sulphadiazine orally. As purer preparations of penicillin have become available larger doses have been used. Smith, Duthie, and Cairns (1946) reported 18 cases (with only one death, due to fat embolism) treated with varying amounts of intrathecal penicillin, but they never gave more than 20,000 units in one injection, though 16,000 units 12-hourly were given in a few cases. They state that injections of 40,000 units or over may cause fits or gumming of the subarachnoid space. At that time they were using a preparation of penicillin containing 500 to 700 units per mg.

The following case is reported because of the extreme youth of the patient and because of the very large doses of penicillin which were given intrathecally without any ill effect.

CASE HISTORY

A male child aged 5 days was admitted on Jan. 16, 1947, with his mother, who had lobar pneumonia, for breast-feeding. He was fully examined on admission. The cord had separated and the stump was dry and clean. He was slightly jaundiced and apparently had been so since he was 2 days old. His heart and chest were normal and his spleen was not palpable. There was no neck rigidity and his mouth and throat were healthy. He weighed 6 lb. (2.7 kg.). According to the mother his weight at birth was 7 lb. 4 oz. (3.3 kg.).

In spite of adequate amounts of milk for a child of his size and age he had lost weight. On Jan. 19 he passed one green relaxed stool and his temperature was 100° F. (37.8° C.). No physical signs were found, and his jaundice had faded. On Jan. 20 the temperature was 102° F. (38.9° C.). He was not taking his feeds well, and there was slight neck rigidity, but no other signs. A lumbar puncture was performed, and a turbid yellowish cerebrospinal fluid was obtained. Penicillin, 30,000 units, was injected intrathecally. The report on the cerebrospinal fluid was as follows: Opalescent fluid; lymphocytes, 6 per c.mm.; polymorphs, 82 per c.mm.; total protein, insufficient fluid; globulin, ++; chlorides, 700 mg. per 100 ml.; film, Gram-positive diplococci ++++; culture, profuse growth of pneumococci, penicillin-sensitive.

He was also given 0.5 g. of sulphadiazine, followed by 0.25 g. four-hourly for seven days, then 0.125 g. six-hourly for seven days (total 14.6 g.); 30,000 units of penicillin daily intrathecally for eight days (total 240,000 units); 30,000 units of penicillin intramuscularly three-hourly for 16 days (total 2,880,000 units); and subcutaneous salines to combat dehydration when he was not taking feeds well.

After three days there was some clinical improvement—less neck rigidity—and he took his feeds better. At the end of eight days the pyrexia had almost settled and the cerebrospinal fluid was nearly normal. Intrathecal penicillin was discontinued. Further recovery was uneventful. Owing partly to the fact that she was ill herself, the mother's milk dwindled in amount, and the baby was gradually weaned on to a proprietary milk preparation. He was discharged on Feb. 7 when fit and gaining well, his weight being 7 lb. 2½ oz. (3.25 kg.).

DISCUSSION

It must be unusual for so young an infant to recover from pneumococcal meningitis. As the child was already in hospital, early diagnosis and treatment were possible.

A preparation of pure white crystalline penicillin, containing 1,650 units per mg., which is much less irritating than the older impure preparations is now available. Certain points are thought to be of importance in the avoidance of reactions to the injections and of the introduction of secondary invading organisms. The penicillin used was prepared in separate doses of 30,000 units in 3 ml., each in a sealed ampoule; this prevents contamination of the penicillin solution. The small volume of the dose is, I feel, important, as large quantities of fluid may raise the tension of the cerebrospinal fluid considerably, particularly in small infants. I always aim, however,