due to biliary obstruction from enlarged portal glands.

Confirmation of the diagnosis during life has been made by histological examination of material from an infected mastoid, a cervical lymph node, or tibial bone-marrow (Amick, Alden, and Sweet, 1950). To the best of our knowledge, our patient is the first case of congenital tuberculosis diagnosed by liver biopsy.

Summary

A case of congenital tuberculosis presented with hepatosplenomegaly during the first month of life is reported. Diagnosis was confirmed by liver biopsy. The baby was treated with streptomycin, isoniazid, PAS, and prednisone, and survived without sequelae.

REFERENCES

- Amick, F. E., Alden, M. W., and Sweet, L. K. (1950). Congenital tuberculosis. *Pediatrics*, **6**, 384.
 Beitzke, H. (1935). Über die angeborene tuberkulöse Infektion. *Ergebnisse der gesamten Tuberkulose- und Lungenforschung*, **7**, 1.
 Choremis, C., Vlachos, J., Anastassia-Vlachou, C., and Matsaniotis, N. (1963). Needle biopsy of the liver in various forms of childhood tuberculosis. *Journal of Pediatrics*, **62**, 203.
 Corner, B. D., and Brown, N. J. (1955). Congenital tuberculosis. Report of a case with necropsy findings in mother and child. *Thorax*, **10**, 99.
 Hudson, F. P. (1956). Clinical aspects of congenital tuberculosis. *Archives of Disease in Childhood*, **31**, 136.
 Miller, F. J. W., Seal, R. M. E., and Taylor, M. D. (1963). *Tuberculosis in Children*, p. 470. Churchill, London.

E. KOUTSOULIERIS and E. KASLARIS
Paediatric Unit, 'Aghia Sophia' Children's Hospital, Athens, Greece.

Hypoprothrombinaemic Bleeding in Infants Associated with Diarrhoea and Antibiotics

Report of Two Cases

Hypoprothrombinaemic bleeding in infants associated with diarrhoea and antibiotics is an interesting and little-known clinical condition. The purpose of this paper is to draw attention to the disorder and to the extremely good response of bleeding to vitamin K administration.

Case Reports

Case 1. A female infant, 6½ months old, was admitted to the hospital with a history of fever, vomiting, and diarrhoea for 7 days. She had been treated at home with chloramphenicol by mouth for 6 days and was given only fluids and diluted milk until the day of her admission. She was breast-fed during the first 4 months, when

solids, meat, and vegetables were added. On examination severe dehydration was detected. Every attempt to withdraw blood resulted in huge haematomata and prolonged bleeding.

Escherichia coli type O₂₆B₆ and proteus were recovered from the stool.

Prothrombin time was 90 seconds (control 12 seconds). Factor II 3·5% (control 100%), factor VII 1% (control 100%), factor IX 2% (control 100%), factor VIII (antihaemophilic globulin) 100% (control 100%), clot retraction normal, fibrinogen 185 mg./100 ml. (normal values 200–400 mg./100 ml.), platelets 300,000/cu. mm.

The patient was given 4 mg. vitamin K intramuscularly and 6 hours later she stopped bleeding from the skin punctures. On the following day prothrombin time was 14 seconds (control 13 seconds), and the patient was discharged 10 days later in excellent condition.

Case 2. A male infant, 4½ months old, was admitted to the hospital because of fever, diarrhoea, and cough for 12 days. He had been treated at home with penicillin intramuscularly and chloramphenicol by mouth for 10 days, and was given oral fluids and diluted milk. He was exclusively breast fed until the day of his illness. He bled for hours from various skin punctures. When femoral vein puncture was attempted a huge haematoma developed within a few seconds. The patient became suddenly very pale, the haemoglobin dropped to 4·5 g./100 ml., and he was urgently transfused.

Escherichia coli type O₁₁₁B₄ was cultured from the stool.

Prothrombin time was 100 seconds (control 13 seconds). Factor II 4·5% (control 100%), factor VII less than 1% (control 100%), factor IX 1% (control 100%), factor VIII 100% (control 100%), clot retraction normal, fibrinogen 195 mg./100 ml., platelets 350,000/cu. mm.

The patient was given 4 mg. vitamin K intramuscularly and on the following day prothrombin time was 20 seconds (control 13 seconds) and the patient had stopped bleeding. Another 2 mg. vitamin K was given daily for 2 days. Two weeks later his prothrombin time was 15 seconds (control 12 seconds).

Discussion

The bleeding episodes in our two cases probably resulted from the simultaneous occurrence of destruction of normal intestinal flora by chloramphenicol and interference with absorption of vitamin K as a result of diarrhoea. Low vitamin K in the diet may have played another important role in the second patient who had been exclusively breast-fed. Though this condition is evidently rare, there have been similar reports (Rapoport and Dodd, 1946; Burgio and Vaccaro, 1966; Goldman and Deposito, 1966). Vitamin K supplements should be given to patients with long-lasting diarrhoea treated with antibiotics.

Summary

Two infants suffering from protracted diarrhoea and treated with chloramphenicol by mouth developed bleeding episodes. There was hypoprothrombinaemia which was corrected by vitamin K.

Addendum

Since this paper was submitted, Goldman and Amadio (1969) have reviewed 12 cases from the literature and added 3 new ones. 60 infants aged 1 to 18 months with diarrhoea were treated with skimmed milk diet and succinylsulphathiazole. Hypoprothrombinaemia occurred in those infants who had not received supplemental vitamin K.

REFERENCES

- Burgio, G. R., and Vaccaro, R. (1966). Porpora nodulare del lattante. *Gazzetta Sanitaria*, **37**, 275.
 Goldman, H. I., and Amadio, P. (1969). Vitamin K deficiency after the newborn period. *Pediatrics*, **44**, 745.
 — and Deposito, F. (1966). Hypoprothrombinemic bleeding in young infants. *American Journal of Diseases of Children*, **111**, 430.
 Rapoport, S., and Dodd, K. (1946). Hypoprothrombinemia in infants with diarrhea. *American Journal of Diseases of Children*, **71**, 611.

N. MATSANIOTIS, J. MESSARITAKIS, and C. VLACHOU
St. Sophie's Children's Hospital, Paediatric Clinic of Athens University, Athens, Greece.

Serum Levels of Fibrin/Fibrinogen Degradation Products in the Haemolytic-Uraemic Syndrome

The phenomenon of intravascular coagulation is becoming increasingly recognized as having an important part, primarily or secondarily, in the pathogenesis of a wide variety of disease states. Abildgaard (1969) has recently reviewed such conditions, and of the instances he gave, the haemolytic-uraemic syndrome of Gasser appears to provide a classic example of intravascular coagulation, as suggested by Piel and Phibbs (1966).

One of the most useful methods of detecting the existence of even low-grade intravascular coagulation is the quantitative estimation of degradation products of fibrin/fibrinogen (FDP) which may also be used as an index of progress and response to treatment. Normal values of serum FDP are already known both for children (Uttley, Allan, and Cash, 1969) and for adults (Das *et al.*, 1967), as measured by the tanned red cell haemagglutination inhibition immunoassay. We have been able to study serum FDP from an early stage in the presentation of a case of the

haemolytic-uraemic syndrome and subsequently to follow progress during treatment with heparin.

Case Report

A child aged 21 months presented after the sudden onset of pallor in association with irritability and listlessness. For 2 weeks previously he had had mild diarrhoea. Shortly before his admission his mother had noticed transient jaundice, easy bruising, and a haemorrhagic rash. After a normal birth, this child had continued to develop satisfactorily and suffered no significant illnesses. There was no history of hereditary disease nor of renal disease in his family.

Examination confirmed the pallor and petechial rash with a positive Hess test. Jaundice was no longer detectable but several large bruises persisted. His blood pressure was 130/90 mm. Hg. No further clinical abnormalities were noted.

Laboratory results. Renal involvement was confirmed by the finding of protein + + +, red blood cells, and casts in the urine, the 24-hour volume of which was only 300 ml. on the first day. Blood urea nitrogen was 51 mg./100 ml. and serum K 4.1 mEq/l. Initial creatinine clearance gave a value of 17.7 ml./min. (62.0 ml./min. per 1.73 sq. m.). Urine culture was negative throughout. Hb was 6.4 g./100 ml., PCV 20%, WBC 7200, reticulocytes 10%, ESR 25 mm./hr., and platelets 81,000/cu. mm. The film showed the marked fragmentation of red blood cells and the burr cell formation typical of this syndrome.

While clotting and bleeding times were normal and the thrombin clotting time 13.5 sec. (control 12.0), serum FDP was 512 µg./ml. (normal 10.9 ± 4.7) (Uttley *et al.*, 1969). Plasma fibrinogen was normal. Factor VIII activity was 160%. Plasma haemoglobin was 48.5 mg./100 ml., and haptoglobins were absent. Urinary haemosiderin was present as was urobilinogen.

Treatment and progress. Heparin therapy was initiated with a dose of 500 I.U., and continued with the constant intravenous infusion of 1500 I.U. daily. A transfusion of 250 ml. whole blood was given on the second day. Pertinent data are shown in Fig. Over-all clotting status was monitored by daily thrombin clotting times, with and without protamine titration but never became abnormal.

Dietary salt intake was initially restricted until diuresis occurred on the eighth day. Heparin therapy was continued until all the clinical and laboratory findings had returned to normal. The most persistent abnormality was fragmentation of the red cells on the blood film.

Percutaneous renal biopsy was performed on the 23rd day, the features being essentially those of a progressive proliferative glomerulonephritis, with focal but significant glomerular hyalinization. No definite glomerular necrosis, no arteriolonecrosis and no thrombosis were seen, but the features were compatible with the clinical diagnosis. There was in addition evidence of fibrin deposition within the glomerular capillaries.