tant about the last patient is that if he had died the coroner would almost certainly have had to bring in the death as being due to combined drugs, with both the mother and doctor denying that he had more than ordinary doses of sedatives. After recovery he was safely given the combined antidepressant drugs for a fortnight.—I am, etc.,

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Fatal Septicaemia due to *Yersinia Pseudotuberculosis*

SIR,—The usual presentation of *Yersinia pseudotuberculosis* (*Pasteurella*) infection in man is most frequently manifested as mesenteric lymphadenitis. It occurs in children and boys are mainly affected. The infection occurs in many European countries including Poland.¹⁵ The diagnosis of *Yersinia pseudotuberculosis* infection is made on isolating the causative agent from the blood or lymph nodes. Serological and histopathological examinations are also of great importance. It is usually a benign infection, but fatal cases have been reported rarely.^{4 5}

Our patient was a 12-month-old girl admitted to the hospital on 19 December 1969. She was febrile with a temperature of 39.8°C., and had a fine macular red rash and numerous petechiae on the skin of the face, trunk, and upper and lower limbs. The child was unconscious; she had irregular breathing with breaks of apnoea, a rapid arrhythmia of over 200/min with faint sounds; liver enlarged around 4 cm, and the spleen was palpable beneath the left costal margin. Investigations showed protein in the cerebrospinal fluid 24 mg/100 ml and W.B.C. 10,050/mm³.

On the basis of the clinical picture acute insufficiency of the suprarenal glands was diagnosed, due to septicaemia of unknown aetiology. Despite intensive care, including controlled respiration, circulation-stimulating drugs, cardiovascular stimulants, and high doses of hydrocortisone the patient died 45 minutes after admission, with symptoms of circulatory and respiratory failure. Only a few hours had elapsed between the onset of the first symptoms and death.

At necropsy blood and specimens of the intestine, lymph nodes, and spleen were delivered to the department of microbiology of the medical school in Bialystok for bacteriological examination. Gram-negative rods were isolated from the blood that we identified on the basis of their biochemical reactions as well as antigenic structure as being *Yersinia pseudotuberculosis* type I. The micro-organisms also in other features did not differ from the standard *Yersinia pseudotuberculosis* strains; the bacilli produced flagella and were motile only while incubated at 22°C.

Histopathological diagnoses were: acute haemorrhagic colitis; acute mesenteric lymphadenitis; haemorrhagic and necrotic foci in the suprarenals; degeneration of the renal parenchyma, of the liver, and of the myocardium. Definitive diagnosis: fulminating septicaemia.

On the basis of the data obtained, mainly on the isolation of *Yersinia pseudotuberculosis* from the blood taken at necropsy, the diagnosis of fatal septicaemia from this micro-organism can be made.

We have found that hens were probably the source of infection in this child. The girl lived in the country, and in the sera of hens belonging to her parents we found a high level of antibodies against *Yersinia pseudotuberculosis* type I.

This fatal case of septicaemia due to *Yersinia pseudotuberculosis* is the only one thus far described in Poland and is therefore of special interest. Few similar cases have been described in the literature so far.—We are, etc.,

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1 Borowski, J., Kupryanow-Wolfart, K., Kurasz, S., and Sokolewicz, E., *Polski Tygodnik Lekarski*, 1970, 25, 401.

2 Brown, G. W., Brown, J. M., and Leditschke, J. F. *Medical Journal of Australia*, 1966, 1, 585.

3 Daniëls, J. J. H. M., *British Medical Journal*, 1961, 2, 997.

4 Knapp, W., *New England Journal of Medicine*, 1958, 259, 776.

5 Mollaret, H. H., et al., *Presse Médicale*, 1964, 72, 2671.

Bacillaemia in Leprosy

SIR,—It was interesting to read the suggestion by Dr. A. B. A. Karat and others (6 February, p. 307) that bacillaemia occurs in all forms of leprosy. Rhodes-Jones¹ demonstrated bacillaemia in both tuberculoid and lepromatous leprosy, while John Lowe² and Iyengar³ have also reported bacillaemia. The fact that this occurs deserves wider recognition.—I am, etc.,

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1 Rhodes-Jones, R., *Leprosy Review*, 1963, 34, 26.

2 Lowe, J., *Indian Medical Gazette*, 1933, 68, 503.

3 Iyengar, K. R. K., *Indian Journal of Medical Research*, 1919, 7, 235.

Jaundice after Treatment of Leukaemia with Busulphan

SIR,—We wish to report the terminal occurrence of cholestatic jaundice in a patient with acute relapse of chronic granulocytic leukaemia who had been treated with busulphan for more than six years. We have failed to find a similar instance of cholestatic jaundice attributable to busulphan recorded in the literature.

An engineer aged 25 years presented on October 1963 having been "off colour" for two years. In the last six months he had gradually lost weight and noted occasional discomfort under the left ribs. Pallor of skin and mucosae and firm splenomegaly reaching 4 cm below the costal margin were found. Relevant laboratory results were: Hb 9.1 g/100 ml; total W.B.C. 205,000/mm³ (promyelocytes 6%, myelocytes 20%, band cells 44%, polymorphs 28%, eosinophils 2%); platelets 155,000/mm³, bone marrow smears consistent with chronic granulocytic leukaemia; leucocyte alkaline phosphatase score 12; Ph¹-chromosome positive.

He progressed satisfactorily on continuous treatment with busulphan, the dosage varying between 4 mg daily and 0.5 mg every third day, until 2 December 1969 when coryza had developed. Two weeks later the spleen was enlarging and the haemoglobin level had fallen to 10.3 g/100 ml from previously normal levels. The leucocyte count was 25,000/mm³ with no blast cells and the platelet count was 100,000/mm³. At this time nausea, occasional vomiting, mild intermittent fever, and backache developed, also icterus. The direct van den Bergh reaction was positive, serum bilirubin was 2.3 mg/100 ml and serum alkaline phosphatase level 38 K.A. units with normal thymol turbidity and flocculation. Examination of the urine showed a trace of bilirubin with slight excess of urobilin and moderate excess of urobilinogen. The stools were paler than normal. Progressive fall in haemoglobin level to 4.7 g/100 ml, rising total leucocyte count to 55,000/mm³ with 24% blast cells, falling platelet count to less than 10,000/mm³, a rising serum bilirubin up to 8 mg/100 ml, along with slightly increased levels of transaminases (SGOT 52 m I.U./ml, SGPT 32 mIU/ml) occurred during the next few days, together with rapid increase in splenomegaly. Despite supportive and "specific" therapy the patient died on 5 January 1970.

The total dose of busulphan was 4.075 g of which 0.7635 g was given in the 12 months preceding the onset of jaundice as compared with an annual average of 0.6623 g busulphan during the previous five years. The only other medicaments at the time of onset of icterus and for two years before this were ferrous fumarate and occasional sodium amylal at night. Necropsy revealed icterus and scattered petechiae. The enlarged and focally infarcted spleen showed diffuse infiltration by primitive granulocytic cells. The soft enlarged liver showed a very striking degree of centrilobular cholestasis while in other areas there was some swelling of liver cells. A portal tract infiltrate of variable intensity consisting of lymphocytes and plasma cells was noted and a few primitive granulocytic cells were seen scattered throughout the liver lobules. There was no evidence of extrahepatic biliary obstruction or gall bladder disease, and the degree of leukaemic infiltration of the liver was minimal. Vertebral bone marrow was cellular with aggregates of granulocytic precursors.

Toxic effects from busulphan are relatively rare. Pancytopenia is the main danger with excessive therapy, thrombocytopenia being the usual warning. Other toxic effects with prolonged therapy include melanotic pigmentation of the skin and, very rarely, interstitial pulmonary fibrosis, a syndrome resembling adrenocortical insufficiency but in which a specific endocrine defect has not been demonstrated, atrophic bronchitis, glossitis, anhydrosis, alopecia totalis, impotence, sterility, and cataracts along with nuclear abnormalities in many other cells.¹ Amenorrhoea and mild gynaecomastia² and renal failure due to hyperuricaemia³ have also been noted.

The histological appearances of the liver strongly favour drug-induced cholestasis of hypersensitive type. The absence of an eosinophilic infiltrate in the liver that frequently accompanies this form of liver toxicity can be accounted for by the lack of circulating eosinophils during the terminal illness. Cholestatic jaundice in severe bacterial infections, with histology similar to that seen in this case has been described.⁴ However, there was no evidence either clinically or at necropsy to suggest severe infection of any form. It could also be argued the cholestasis was related to acute relapse of the chronic leukaemia, but this view has no histological support.