CHRONIC IDIOPATHIC AGRANULOCYTOSIS
Report of a Fatal Case Treated with Corticoterophin (ACTH)

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In 1922 Schultz described the clinical picture of a fatal necrotizing throat infection usually occurring in elderly females. Since then many cases of agranulocytosis (as it was named) have been described, the majority due to secondary marrow intoxication with chemical agents containing a benzene grouping. The primary or idiopathic variety still remains a mysterious malady, occurring at all ages, especially in females, and about whose causation little is understood.

Since 1934 only 30 cases or so have been recorded in the United Kingdom. There has been no survey of the whole subject in this country for the past 10 years, apart from the contribution of Adams and Witts in 1949, when five cases were described and discussed.

Treatment remains problematical. Many forms have been tried and are well known. They include splenectomy, irradiation, nucleotides, glutathione, liver extract, the various components of the B complex of vitamins, especially pyrodoxine, folic acid and cyanocobalamin, transfusion of whole blood or its constituents, especially leucocyte cream, bone marrow and leukaemic extracts. The greatest advance so far has been the use of antibiotics and in particular penicillin, which helps to prevent those infections previously proving fatal.

Due to the paucity of suitable cases, reports of the effect of ACTH have been few in number, especially in regard to the idiopathic variety. Its use in the following case, which was observed over three years, is therefore described.

Case Report

K.M.C., a housewife aged 53 years, was first admitted on 30.9.52 as a case of pneumonia. She had complained of pain in the right side of the chest for two days.

Shortly after the death of her son in 1943 she developed pains in the hands, knees, ankles and feet, which were ascribed to rheumatoid arthritis and treated as such. She had taken various proprietary brands of aspirin up to nine tablets daily to relieve these pains without much success.

In 1951 she was treated for septic feet.

On Examination


Investigations

X-ray chest 2.10.52. Patchy consolidation right lung field. Sputum: no predominant organism isolated. No acid-fast bacilli present.

On admission: white cells 1,600. No granulocytes, only a few premature cells.

Blood group 'O' Rh positive.

Sternal marrow film 11.10.52: no granulocytes. Only a few myelocytes. 42 per cent. lymphs. Normoblasts +.

Treatment

Benzy1 penicillin, 1,000,000 units intramuscularly six-hourly for 38 mega units. Chlortetraycline, 500 mg. six-hourly for five days. Sodium pentose nucleotide, 5 ml. twice daily for four days I.M. Aq. gentian violet, 1 per cent. to mouth. One pint compatible and cross-matched blood. Heparin, 10,000 units I.M. six-hourly for 2,800,000 units. Pyrodoxine, 100 mg. I.V. for four days. Ascorbic acid, 1,000 mg. daily.

Progress

Initial improvement occurred, apart from a herpetic eruption of the lip. The chest cleared by 8.10.52, but numerous small shallow ulcers of tonsillar fossae and palate developed. She was frail and weak. By 27.10.52 the ulceration was worse. On 3.11.52 a blood transfusion of one pint whole blood was given. Four days later pitting oedema of left leg developed with tenderness in Scarpa's triangle. By 11.11.52 both the leg and
mouth had improved. Progress, if any, was still very slow, but by 10.12.52 she had recovered sufficiently well to go home. The leg was still swollen and an elastic stocking was ordered.

**Follow-up**

1.1.53 to 6.6.53. Has felt well, apart from occasional headaches and hot flushes. No ulceration present. B.P. 150/90. Weight 11 st. 5 lb. Oral oestrogens prescribed.


28.11.53 to 27.2.54. Vague aches, headaches, hot flushes, but looks and feels well. Weight 13 st. Meibomian cyst of eyelid present. W.C.C. 1,400. Polys 10 per cent.


She died 17 days after admission and three years, 2/12 after originally seen. No post-mortem performed, but cause ascribed to bronchopneumonia despite negative X-ray findings.

**Investigations**


4.11.55. W.C.C. 600/cu. mm. No granulocytes.

25.10.55. Hb 99 per cent. R.B.C. 4,800,000/cu. mm.

4.11.55. Hb 75 per cent. R.B.C. 3,880,000/cu. mm. Group 'O' Rh positive.
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711.55: Sternal marrow puncture: the marrow is erythropoietic and shows red cell precursors.

No plasmocyte deficiency. The predominant cell is a small lymphocyte: cells of the granulocyte series are almost completely absent, a rare promyelocyte and a few myeloblasts are seen. The picture suggests an aplasia of granulocytes and slight megaloblastic change. The production of red cells is normal, and the leucocytes are small and immature. 

The present case as mentioned probably lived for 12 years. The present case as mentioned probably lived for 12 years.
they were unable to be stimulated. What the effect of agranulocytosis is on these glands, I do not know. However, it might seem in retrospect more rational to use cortisone rather than corticotrophin in this and similar states.

Martennson and Vikbladh (1954) discussed the serum protein findings in a woman of 49 years who had thyrotoxicosis in 1948 followed by granulopenia for six years. Studies showed a pathological protein fraction constituting 30 per cent. of total proteins which immigrated at the same rate as gamma globulin and which agglutinated normal leucocytes, especially neutrophils. They therefore postulated that neutropenia is the result of auto-immunization, causing intravascular destruction of leucocytes. Two other cases, however, did not show the same phenomenon. Whether the thyrotoxicosis, too, was a factor also remains disputable. If an allergic basis were postulated, the use of cortisone and ACTH might be rationalized still further. However, one swallow does not make a summer and no firm conclusions can be drawn from a single case. Its use, therefore, remains sub judice.

Summary
I am indebted to Dr. J. Spencer, consulting pathologist to this hospital, for the marrow films and to Mr. L. Whittaker, A.I.M.L.T., for the laboratory investigations. I must also thank the Librarian of the Royal Society of Medicine for help with the references and Dr. R. W. Tannahill (consultant to the N.E. Met. R.H.B.) for his encouragement.

BIBLIOGRAPHY
BRUCK, E. (1957), Amer. J. Dis. Child., 73, 156.
MARTENNSON, J., and VIKBLADH, I. (1954), Blood, 6, 632.

Manufacturers' Notes

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