of only 2 g. of fibrinogen the previously incoagulable blood formed a stable clot *in vitro* and the clotting-time was normal. Similar cases have been recorded by Weiner *et al.* (1950, 1953). There seems to be no doubt that the intravenous administration of fibrinogen is a very efficient treatment for this condition, and that 2 g. is probably the smallest useful amount. In cases with continuing bleeding, or in cases in which the tests show a subclinical fibrinogenopenia, the administration of fibrinogen can be repeated until the clotting mechanism is normal. It is clearly advisable that a supply of fibrinogen should be available in all obstetric hospitals.

It might reasonably be anticipated that adequate blood transfusion would be a satisfactory method of curing this fibrinogenopenia, since blood transfusion can restore normal coagulation in those non-pregnant cases suffering from congenital absence of fibrinogen (Biggs and Macfarlane, 1953). However, in the particular type of acquired fibrinogenopenia described here, blood transfusion is not a successful line of therapy. It is the practice in this hospital to give at least 3 pints (1,700 ml.) of blood to all patients with moderate or severe accidental haemorrhage as soon as they are admitted, but this treatment failed to control post-partum haemorrhage in the two patients mentioned in this paper. The same failure has been noted by other workers.

Summary

A case of severe post-partum haemorrhage following accidental haemorrhage showed incoagulability of the blood. This defect of the clotting mechanism is a not uncommon complication of accidental haemorrhage. It can and should be identified before delivery, so that specific treatment by the intravenous administration of fibrinogen can be given.

My thanks are due to Dr. E. W. L. Thompson, Master of the Rotunda Hospital, for his help with the case report; to Dr. W. E. R. Hackett, Director of the National Blood Transfusion Service, Dublin, for supplying the fibrinogen; and to Professor H. L. Sheehan, who read the script and made many valuable suggestions.

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A startling report on alcoholism among children was made last month by Dr. SUZANNE SERIN to the Academy of Medicine in Paris. Her suspicions were first aroused by the case of a boy, aged 7 years, who was referred on account of character difficulties and temper tantrums. Close questioning drew from him the admission, "J'ai peur, je vois le soir des ailes, non des mains, des choses blanches qui dansent sur la commode de ma chambre; c'est épouvantable," an answer that led to inquiries about his drinking habits. His parents told Dr. Serin that he drank about a litre of undiluted wine a day, and sometimes, "parce qu'on le trouve nerveux," a glass of port with two yolks of egg beaten into it. Since that case Dr. Serin has always inquired about the alcohol consumption of the children she sees, and in her paper she quotes three similar cases as examples of what she has found. One of the most interesting features of this infantile alcoholism is that it occurs among well-off, cultured families, not, as might be expected, in bad homes where the parents are drunkards.

CRYOGLOBULINAEMIA WITH CEREBRAL PURPURA

BY

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In 1947 Lerner and Watson proposed the term "cryoglobulin" for an abnormal blood protein which undergoes reversible precipitation on exposure of the serum to low temperatures. Barr *et al.* (1950) described the clinical and pathological features of a patient who suffered from recurrent attacks of Raynaud's phenomenon, and whose blood contained on various occasions 4.9 to 9.8 g. of cryoglobulin per 100 ml. In a review of the literature these authors found eight other instances of high-grade cryoglobulinaemia; since then further cases have been reported by Lucey *et al.* (1950), Rörvik (1950), Blades (1951), Luckey *et al.* (1951), Cugudda (1952), Muirhead *et al.* (1952), McFarlane and Dovey (1952), Griffiths and Gilchrist (1953), and Hutchinson and Howell (1953).

This paper records the occurrence of cerebral purpura in a patient with cryoglobulinaemia, an association, to our knowledge, not hitherto described.

Case Report

A man aged 56 was seen in the out-patient department complaining of pain in the lower part of the chest of two months' duration. Clinical examination was negative and blood counts were normal. Four months later he attended again and was admitted to a medical ward for investigation.

The patient was found to have moderate pallor of the skin and mucous membranes. The spine, thorax, and shoulder-girdles were extremely tender on pressure. X-ray examination showed collapse of the eleventh and twelfth dorsal vertebrae; in the remainder of the skeleton there were numerous round translucent areas typical of multiple myeloma. The urine contained 1+ albumin but no Bence Jones protein. Sternal puncture showed a cellular marrow, 79% being myeloma cells of varying degrees of maturity. It was difficult to obtain samples of venous blood owing to its greatly increased viscosity. When samples of venous blood were allowed to stand at room temperature (25° C.) clot retraction was slow and imperfect, and the serum settled into two layers of approximately equal volume; the upper was a straw-coloured fluid and the lower a firm pearly-white gel. On heating to 37° C. the gel liquefied, and on subsequent cooling it again became solid. Long needle-shaped crystals formed when a drop of warmed serum was allowed to cool on a slide. The formol-gel test, carried out on the fluid fraction of the serum, was strongly positive. Laboratory investigations showed: haemoglobin, 11.3 g. per 100 ml.; erythrocytes, 3,000,000 per c.mm.; E.S.R. (Westergren), 141 mm. in one hour; E.S.R. (Wintrobe), 14 mm. in one hour; cold agglutinin titre, 1:4; serum calcium, 17.2 mg. per 100 ml.; blood urea, 113 mg. per 100 ml.

The patient's condition rapidly deteriorated, and he sustained several pathological fractures of the ribs during a fit of coughing. Eight days after admission he was given 7 mg. of nitrogen mustard by intravenous injection. On the following day he lapsed into coma. Retinoscopy revealed papilloedema with engorged veins and extensive retinal haemorrhages. Death occurred 16 days after admission.

During the last week of life venepuncture was possible only with a warmed syringe and needle; on standing at room temperature the entire serum became a firm gel. Diluted blood in an erythrocyte pipette showed marked pseudo-agglutination, and blood films could not be made owing to excessive rouleau formation.

The serum protein levels were estimated on three occasions:

	(1)	(2)	(3)
Albumin (g. per 100 ml.)	3.6	4.2	3.4
Globulin	5.5	6.0	7.9
Total	9.1	10.2	11.3

On the third occasion electrophoresis showed that the high value for serum globulin was due to an increase, mainly in the γ fraction:

α_1 -globulin, 0.78 g.	β -globulin, 1.17 g.
α_2 -globulin, 1.68 g.	γ -globulin, 4.22 g.

At necropsy the heart and great vessels were intrinsically normal, but contained casts of firm opalescent material. There was extensive oedema of the lungs. The kidneys were pale and swollen, and were separated from their capsules by a fluid exudate. Many pathological fractures were noted in the ribs and vertebrae, and the marrow of these and of the other bones was replaced by reddish-brown gelatinous tumour tissue. The brain was swollen, and section following formalin fixation revealed scattered petechial haemorrhages, mainly affecting the white matter, especially in the internal capsules and cerebral peduncles.

Microscopically the bone marrow was largely replaced by myeloma cells, and infiltrations of these cells were also present in the spleen and renal cortex. The renal tubules showed epithelial damage; many contained casts of crystalline protein material with surrounding giant-cell reaction. A number of vessels in sections from various organs contained "thrombi" formed of a peculiar hyaline acidophilic material; this substance was histologically identical with the larger casts formed in the heart and great vessels, and had evidently precipitated during cooling of the body after death. The small cerebral vessels also contained hyaline material, and each had an associated perivascular haemorrhage. Frozen sections stained with scharlach R showed no evidence of fat embolism in the brain.

Discussion

The association of high-grade cryoglobulinaemia with multiple myeloma and other varieties of plasmocytosis has been increasingly recognized during recent years. Among the more common clinical features of the condition are acropurpura and Raynaud's phenomenon (Wintrobe and Buell, 1933; Flemberg and Lehmann, 1944; Lucey *et al.*, 1950). Cugudda (1952) described a case of multiple myeloma and cryoglobulinaemia in which, following radiotherapy, extensive gangrene of the right leg developed; at necropsy multiple arterial and venous thromboses were found. Hutchinson and Howell (1953) reported a case with extensive gangrene of the digits.

Raynaud's phenomenon and peripheral gangrene occur also in patients with high serum titres of cold agglutinins; this has led several authors to comment on a possible relationship between cryoglobulins and cold agglutinins. However, the common clinical features can be adequately explained on the basis of the mechanical obstruction of vessels in the extremities which occurs at suitably low environmental temperatures, in the one case by masses of agglutinated erythrocytes (Marshall *et al.*, 1953) and in the other by casts of precipitated cryoglobulin.

There is only one report in the literature of extensive precipitation in visceral blood vessels. Muirhead *et al.* (1952) described a case of plasmocytosis with cryoglobulinaemia in which at necropsy the pulmonary vessels contained masses of precipitated protein undergoing early organization. They suggested that conditions in the lungs might occasionally be such as to cause precipitation of the globulin.

In the present case the most remarkable feature was the widespread cerebral purpura, a finding which has not previously been described. Histological examination showed that the haemorrhages were secondary to occlusion of the small vessels by masses of eosinophilic protein precipitate, similar in appearance to that found by Barr *et al.* (1950) in the bone marrow and the lumina of blood vessels and by Muirhead *et al.* in the pulmonary vessels. It seems that these changes in the cerebral vessels were due to the terminal flooding of the circulation with cryoglobulin. We can, however, suggest no explanation for the restriction of the circulatory changes to the brain and retina.

The patient studied by Hutchinson and Howell was on one occasion admitted to hospital with sudden loss of consciousness, from which he made a gradual recovery with no neurological sequelae. These authors were uncertain whether the patient's severe, though reversible, disorder was related to the presence of cryoglobulins in the blood; it may well have been due to lesions similar to those found in our case, but less extensive.

Summary

The clinical and pathological aspects of multiple myeloma in a man aged 56 are described.

Unusual features of the case were the presence of large amounts of circulating cryoglobulin and the terminal occurrence of purpuric cerebral and retinal haemorrhage due to the precipitation of cryoglobulin in small blood vessels.

We are indebted to Dr. J. T. Lewis for permission to publish this case, and to Professor J. H. Biggart and Professor G. M. Bull for their advice.

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Besides giving abundant statistical information about war pensions, the *Report on War Pensions for the Period April 1, 1953, to December 31, 1953*, published this month, records the transfer of Ministerial responsibility made on August 31 last year. Before then everything to do with war pensions was handled by the Ministry of Pensions. On that date the Health Departments took over responsibility for the medical treatment of war pensioners, while the new Ministry of Pensions and National Service was given the task of administering the pensions. Seven former Ministry of Pensions hospitals and two war pensions hospital units, totalling 2,200 beds, were transferred to the Ministry of Health, as well as the interest of the Ministry of Pensions in the administration of the Spinal Injuries Centre at Stoke Mandeville Hospital, Aylesbury. During 1953 nearly 12,500 patients were admitted to these hospitals. In Scotland there was a similar transfer of artificial limb and appliances centres to the Department of Health for Scotland. The steady decline in the number of war pensions which has been taking place since 1947 has continued. At the end of 1953 a total of 931,023 war pensions were being paid, a decrease of more than 28,000 in the year.