therapy, but she was left with an incomplete homonymous hemianopia. Her progress was otherwise satisfactory, and when discharged seven weeks after the operation she had no symptoms or other abnormal physical signs.

Biochemically, drainage of the ascitic fluid was followed by an immediate fall in the serum amylase and urinary amylase activities, both of which became normal. The bisalbuminaemia also gradually disappeared, the electrophoretic pattern four weeks after the operation being normal. The ascitic fluid itself showed an amylase activity of over 30,000 Somogyi units/100 ml., and on cellulose acetate electrophoresis the fast-type bisalbumin was clearly seen. The patient's only sister and her two nieces showed no plasma protein abnormality.

COMMENT

A gross increase in serum amylase activity without clinical evidence of acute or subacute pancreatitis has been described under the name of hyperamylasaemia by Berk, Kizu, Wilding, and Searcy (1967). This condition could be attributed to the binding of the amylase to a macromolecular immunoglobulin complex in plasma and its consequent retention by the kidneys (Levitt, Goetzl, and Cooperband, 1968). Amylase was not detected in the present abnormal albumin band, but there is no reason to think that amylase of so high a molecular weight and, relatively, in such a small quantity would be bound to albumin in this condition.

In the present case the high urinary amylase activity and the rapid fall of serum amylase and urinary amylase activities after drainage of the ascitic fluid suggest an alternative explanation. It would seem that ascitic fluid with a very high amylase activity had accumulated some time before the patient's admission, and that during a protracted period of simultaneous exudation and/or slow resorption it acted as an enzyme reservoir.

Three types of bisalbuminaemia have been described: a permanent slow type (Franglen, Martin, Hargreaves, Smith, and Williams, 1960; Cooke, Cleghorn, and Locky, 1961) (Figs. 1 A and 2 A), a permanent fast type (Wieme, 1960), and a transient fast type (Schleuren, 1955; Gabl and Huber, 1964) (Figs. 1 C and 2 C). The third type, transient bisalbuminaemia, to which the present case belongs, is less well

understood. It can be distinguished from the first two by immunoelectrophoresis (Clarke and Freeman, 1968). With this technique the abnormal "albumin" can be shown to be antigenically distinct from the patient's normal albumin and therefore appears as a separate peak (Fig. 2 C). In the first two types the abnormal albumin is antigenically similar to normal albumin and therefore appears on immunoelectrophoresis as a hump on the normal albumin peak (Fig. 2 A).

Schultze and Heremans (1966) suggested that the atypical transient fast "albumin" may reflect the temporary activation of a gene by some severe metabolic disturbance. An alternative, perhaps more likely, explanation is that during such acute episodes substances may be shed into the plasma and may be carried by part of the plasma albumin fraction. This may lead to a change in the electrophoretic mobility and, in some cases, in the antigenic properties of the binding fraction. Fatty acids, in particular, can accelerate the electrophoretic mobility of albumin, and the liberation of abnormal fatty acids (abnormal either in quality or in quantity) in pancreatic disease is not, perhaps, improbable.

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CASE REPORT

A 15-year-old schoolboy accidentally took 20 g. of sodium chlorate in mistake for sodium chloride and during the following 24 hours developed in sequence diarrhoea, abdominal pain, and vomiting. On the next day, after admission to the West Middlesex Hospital, he was found to be febrile and cyanosed, with some clouding of consciousness. He was anuric and his blood pressure was 95/70 mm. Hg.

The haematological and biochemical changes occurring during the course of his illness and subsequent recovery are shown in Fig. 1. At the time of admission (day 2) his plasma urea was 40 mg./100 ml. and his total haemoglobin was 13.6 g./100 ml., though his packed cell volume was only 36% and his plasma was very dark, containing large amounts of methaemoglobin. Platelets were present in normal numbers and his total leucocyte count was 23,000/cu. mm., with 86% neutrophils. No ghost cells were present in blood films at this time.

Peritoneal dialysis was begun immediately and methylene blue and ascorbic acid were given intravenously, without improvement in his clinical condition.

By the third day large numbers of ghost cells were present on blood films and there was striking erythrophagocytosis by large mononuclear cells. Platelets were still present in normal numbers. Most neutrophils had pale blue Döhle bodies and many of these cells had pyknotic nuclei. Free plasma haem pigments measured on three successive occasions within 24 hours gave values of 1.7, 1.25, and 1.6 g./100 ml. respectively, and methaemoglobin and methaemalbumin were detected spectroscopically.

A five-litre exchange transfusion was followed by pronounced

Haematological Complications of Chlorate Poisoning

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Ingestion of more than a few grammes of sodium or potassium chlorate results in acute intravascular haemolysis and anuric renal failure (Whitthaus, 1911). Before 1960 the renal complication of chlorate poisoning was almost invariably fatal though since then successful treatment of the renal failure by peritoneal dialysis or haemodialysis has been recorded on a number of occasions (Jackson *et al.*, 1961; Klendshoj *et al.*, 1962; Kennedy *et al.*, 1963; Knight *et al.*, 1967).

Chlorate has a direct toxic effect on the proximal tubule (Oliver *et al.*, 1951) and the resultant anuria blocks the main route of elimination of the drug, so prolonging exposure of red cells to its oxidant effects.

Dacie (1967) described a case in which large numbers of ghost cells (lysed red cells) containing Heinz bodies and phagocytosing macrophages were present in the peripheral blood. We report a case of severe chlorate poisoning which initially showed all the above haematological abnormalities and subsequently developed a microangiopathic haemolytic anaemia associated with subacute intravascular coagulation, a complication to which patients suffering from prolonged chemical haemolysis may be particularly susceptible.

clearance of ghost cells and the patient's condition transiently improved. On the fifth day, however, he again deteriorated. The haemoglobin concentration had fallen to 6.5 g./100 ml. and the platelet count to 19,000/cu. mm. His plasma urea was 206 mg./100 ml. Bilateral fundal and subhyaloid haemorrhages were present. He was transferred to the Hammersmith Hospital.

The appearance of the peripheral blood on the sixth day had changed remarkably. Ghost cells had virtually disappeared and the morphological appearances of the red cells suggested a microangiopathic haemolytic anaemia; there was pronounced fragmentation of red cells, many in form of schistocytes, microspherocytes, helmet cells, and burr cells (Brain *et al.*, 1962). The neutrophil count had risen to 40,000/cu. mm. and platelets had fallen to 12,000/cu. mm.

Coagulation studies at this time gave results which were consistent with a state of subacute intravascular coagulation.

Further studies on the seventh and eighth days confirmed the persistence of the abnormalities. The $t\frac{1}{2}$ survival of homologous ^{51}Cr -labelled platelets on the ninth day was only five hours (normal five days).

In view of these findings, on the ninth day treatment with intravenous heparin 40,000 units daily was begun. Three days after commencing heparin therapy (Fig. 1) the platelet count began to

Haematological and biochemical changes after chlorate ingestion.

rise and there was a good reticulocyte response. Within seven days red cell morphology was normal and a haemoglobin concentration of 12 g./100 ml. was maintained.

Despite continuous peritoneal dialysis since admission his blood urea continued to rise and by the 10th day was 330 mg./100 ml. In order to achieve more efficient exchange, dialysis fluid was run through a second catheter introduced subcostally into the peritoneal cavity, and simultaneous drainage was effected through the standard median infraumbilical catheter. On this regimen blood urea fell progressively. He began passing urine on the 15th day and a good diuresis was established by the 22nd day.

COMMENT

It is probable that the initial chlorate-induced haemolysis in this patient continued for at least four days and resulted in the destruction of almost half his circulating red cells. A very dark plasma was noticed within 24 hours of chlorate ingestion and this observation of the relatively rapid onset of intravascular haemolysis is consistent with older descriptions of chlorate poisoning (Witthaus, 1911), in which death as early as two-and-a-half hours after administration was attributed to this cause.

Apparently inconsistent with this pattern of early lysis was

the peak appearance in the peripheral blood of ghost cells, pyknotic neutrophils, and scavenging macrophages at 72 hours. Review of the peripheral blood appearances of Dacie's (1967) case and of a further case of chlorate poisoning seen at the Hammersmith Hospital showed a similar delay (72 to 96 hours) in the development of these morphological changes. The sudden appearance of ghost cells and also cells which are functionally part of the reticuloendothelial system at this late stage might well be due to saturation or blockade of reticuloendothelial function by the products of haemolysis.

The haematological abnormalities progressed in the present case from a chemical haemolysis to subacute intravascular coagulation at a time when there was a heavy load on the reticuloendothelial clearance mechanism, and the onset of coagulation abnormalities coincided with the appearance of microangiopathic haemolytic anaemia, a phenomenon which accompanies local or widespread intravascular coagulation in the presence of thrombocytopenia and defective fibrin polymerization (Rubenberg *et al.*, 1967b).

The rapid return of red cell morphology, platelet count, and clotting function to normal during or immediately subsequent to seven days of heparin therapy was consistent with the pathogenetic mechanism suggested above.

In view of the prolonged action of chlorate on circulating red cells it seems justifiable to start peritoneal dialysis or haemodialysis of these patients as soon as they are admitted to hospital and to administer heparin promptly if signs of intravascular coagulation occur.

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