Studies of postoperative DVT should take account of anaesthetic technique and management should be standardised whenever possible.

The study was funded by the Canterbury Medical Research Foundation. We are grateful for help and advice from the medical and nursing staff of the anaesthetic and orthopaedic departments, Christchurch Hospital, Joanna Stewart, biostatistician, and Helen Johnson, technician, Christchurch Clinical School.

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(Accepted 8 October 1980)

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Haemolysis after granulocyte transfusions

Granulocyte transfusions are being used increasingly to treat patients with neutropenia and infection whose fever continues despite use of broad-spectrum antibiotics.¹ Granulocyte transfusions may, however, cause complications, including febrile reactions that may be related to the presence of leucoagglutinins in the recipient's serum, the transmission of infection, and the development of graft-versus-host disease attributable to leucocytes collected either from normal donors or from patients with chronic granulocytic leukaemia.² We report here a further complication of granulocyte transfusions.

Case report

A 45-year-old woman with preleukaemia was admitted to the hospital in September 1978 with a febrile illness. She was severely neutropenic. Her blood group was A positive. No focus of infection was identified and no causative organism isolated.

She was treated initially with intravenous antibiotics but gained little benefit. She was then treated with daily granulocyte transfusions from different donors with chronic granulocytic leukaemia; she improved considerably and left the hospital. Three weeks later she was readmitted with recurrent fever. Intravenous antibiotics were restarted but with no benefit. On 27 October she was transfused with 200 ml buffy-coat cells collected from a group O+ donor with chronic granulocytic leukaemia. On 28 October she received a second transfusion of leucocytes collected from the same donor. During this transfusion she complained of nausea and experienced a rigor. Her next urine sample was red and when tested on the ward showed evidence of blood. Subsequently the presence of haemoglobin in the urine was confirmed. A direct antiglobulin test on her cells was strongly positive for IgG and complement. The table shows haematological changes over this period. On 29 October she received a blood transfusion. Spherocytes persisted in the blood film for a further seven days; reticulocytopenia was present throughout, reflecting lack of marrow reserve. Further investigations of her red cells showed the presence of an anti-A alloagglutinin. The donor's

Haematological changes

	Haemoglobin (g/dl)	Reticulocyte count (%)	White cell count ($\times 10^9/l$)	Blood film
26 October	9.0	0.2	1.9	Anisocytosis
28 October (10 am)	7.9		2.8	Spherocytosis +
28 October (8 pm)	6.3		3.2	Spherocytosis + +
29 October	5.8	1.0	3.2	Spherocytosis + + +

serum was found to contain an IgG anti-A alloagglutinin at a titre of over 1:512.

We believe that this patient had a haemolytic transfusion reaction owing to transfusion of plasma containing high-titre IgG anti-A. Thereafter she was transfused with O positive packed cells and had no further immediate haematological problems.

Comment

The ability of IgG "immune" antibodies present in type O plasma to cause red-cell destruction when transfused to patients with type A, B, or AB blood is well recognised.³ Haemolysis due to immune anti-A antibody after infusion of factor VIII concentrates has also been reported.⁴ We are not aware that immune anti-A alloagglutinin has previously been implicated in haemolysis after transfusions of granulocytes.

Subsequently we screened the serum of 13 patients with blood group O in chronic-phase chronic granulocytic leukaemia for the presence of high-titre IgG anti-A and anti-B alloagglutinins. We identified three patients with an IgG anti-A titre of over 1:128, in one of whom the IgG anti-B titre was also over 1:128. These three patients were therefore potentially dangerous as plasma donors to recipients with blood groups other than O. We suggest that if it is necessary to give group O granulocytes to patients with group A, B, or AB blood the O plasma should first be removed (as for red-cell transfusion) and the cells should be resuspended in AB plasma. This should prevent haemolytic episodes such as the one reported here.

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(Accepted 16 October 1980)

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Acute renal failure and interstitial nephritis after clofibrate treatment

Clofibrate has been associated with a variety of adverse reactions including acute myalgia,¹ gall stones,² a lupus-like syndrome,³ and deterioration of renal function in patients with chronic renal failure.⁴ The first case is reported here of acute reversible renal failure due to interstitial nephritis after treatment with clofibrate.

Case report

A 51-year-old miner, an insulin-dependent diabetic for 16 years, was started on clofibrate 500 mg 6 hourly because of exudative retinopathy. Three weeks later he developed nausea, a rash, and severe backache. He had noted similar symptoms 12 years earlier when given phenindione after a myocardial infarction. He was admitted four weeks after first taking clofibrate. The results of examination were normal apart from retinopathy and a generalised erythematous rash. His blood pressure was 150/90 mm Hg. Blood concentrations were as follows: urea 29 mmol/l (175 mg/100 ml), plasma sodium 123 mmol(mEq)/l, potassium 5.0 mmol(mEq)/l, bicarbonate 22 mmol(mEq)/l, glucose 36 mmol/l (649 mg/100 ml), and creatinine 395 μ mol/l (4.5 mg/100 ml). Plasma total protein and albumin concentrations, and creatine phosphokinase activity were normal. Creatinine clearance was 4 ml/min, urinary protein 0.8 g/24 h, and urinary myoglobin absent. The erythrocyte sedimentation rate was 58 mm in 1 h, antinuclear factor negative, platelet count $200 \times 10^9/l$ ($200\,000/mm^3$), and complement, immunoglobulins, and coagulation studies were normal. An intravenous pyelogram was normal. A renal biopsy specimen showed a heavy cortical and medullary infiltrate of

lymphocytes, polymorphonuclear leucocytes, plasma cells, and occasional eosinophils. The cortical infiltrations were often around the glomerular vascular pole and one or two aggregations of macrophages were noted in the adventitia of small interlobular arteries. Early diffuse diabetic glomerulosclerosis was present. Immunofluorescence to IgG, IgA, fibrin, and C3 was found in glomerular capillary walls and mesangial regions. The appearances suggested that a granulomatous arteritis was developing in addition to interstitial nephritis.

Clofibrate was discontinued and the rash faded over two days. The urine output was always greater than 800 ml/24 h, but despite appropriate fluid, electrolyte, and insulin treatment the blood urea concentration rose over five days to 56 mmol/l (337 mg/100 ml). It then fell, without dialysis, to 6.5 mmol/l (39 mg/100 ml) nine days later, with a daily diuresis of 5-7 l. Three weeks after admission creatinine clearance was 85 ml/min and the urine was protein free.

Comment

All described cases of an adverse effect of clofibrate on renal function⁴ had pre-existing chronic renal failure and were associated either with myalgia and muscle damage¹ or with severe vomiting causing salt and water depletion.⁴ In none of them were renal biopsy findings reported. In the present case renal function returned almost to normal on withdrawal of clofibrate and there was no evidence of muscle damage or of vomiting and hypovolaemia. The principal feature of the renal biopsy specimen was interstitial nephritis although there was also evidence of granulomatous arteritis, presumably reflecting a general hypersensitivity to the drug. There is an association between adverse reactions to clofibrate and renal disease^{4,5} and the drug should be avoided in patients with renal impairment.

I thank Professor J S Robson, Dr Anne T Lambie, and Dr L F Prescott for permission to report this case, and Dr Mary K MacDonald, Department of Pathology, University of Edinburgh, for the histological description.

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(Accepted 17 October 1980)

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Liver damage induced by oxyphenisatin

Oxyphenisatin, a constituent of laxatives, has been associated with hepatocellular damage.¹⁻⁴ We describe a patient who developed prolonged hepatitis after continual ingestion of a laxative (Silklax) containing oxyphenisatin.

Case report

The patient, a 21-year-old woman, had been unwell during December 1979 with anorexia, tiredness, nausea, and an inability to drink alcohol. During January 1980 she developed jaundice. Infective hepatitis was diagnosed, although no investigations were done, and she was advised to rest. The jaundice began to disappear after three weeks but had worsened again by late April. She was admitted to hospital in June 1980 with increasing jaundice and nausea. There was no history of contact, infection, or blood transfusion, and no abdominal pain or pruritus. A detailed drug history disclosed that she had taken Silklax, purchased from a health food shop, in a dose of four tablets a day for five days each week for the past year. Silklax contains oxyphenisatin acetate 5 mg, methylcellulose 100 mg, extract of cascara 50 mg, and extract of prunes 25 mg.

On examination she was jaundiced with no signs of chronic liver disease

although the liver was enlarged. Haematology was normal (erythrocyte sedimentation rate 44 mm in the first hour). Liver function tests showed gross abnormalities (table). Tests for hepatitis-associated surface antigen and lupus erythematosus cells were negative, and for antinuclear factor and smooth-muscle antibody strongly positive; non-organ-specific mitochondrial antibody and other organ-specific antibodies were not detected. Liver biopsy showed a prominent chronic inflammatory infiltrate in the portal areas, some destruction of lobular architecture, and mild patchy, piecemeal necrosis. The chronic inflammatory cells were mainly lymphocytes with a few plasma cells and eosinophils. Reticulin staining showed increased fibrosis. The picture was consistent with chronic active hepatitis.

Repeat liver function tests 10 days later (table) showed a definite improvement. Although withdrawing the drug caused some improvement, in view of the severity of changes shown by liver biopsy she was started on prednisolone 10 mg by mouth three times daily on day 11 before being discharged home. One month after admission she was feeling well, the jaundice had disappeared, and no other abnormality was detected. Liver function tests showed continuing improvement, and the prednisolone dosage was gradually reduced.

Results of liver function tests

	On admission	After 10 days	After 1 month
Serum glutamate oxaloacetate transaminase (IU/l) (normal 0-30) ..	1325	895	103
Serum glutamate pyruvate transaminase (IU/l) (normal 0-24) ..	1220	780	Not done
Bilirubin (μmol/l) (normal 3-17) ..	132	111	19
Alkaline phosphatase (IU/l) (normal 25-100) ..	204	154	93
Total proteins (g/l) (normal 62-80) ..	80	89	71
Albumin (g/l) (normal 35-50) ..	38	45	40
γ-Glutamyl transaminase (IU/l) (normal 10-55) ..	136	137	Not done
Immunoglobulin G (g/l) (normal 8-18) ..	20.0		11.91
Immunoglobulin A (g/l) (normal 0.8-4.5) ..	2.27		1.77
Immunoglobulin M (g/l) (normal 0.6-2.8 l) ..	2.52		2.27

Conversion: SI to traditional units—Bilirubin: 1 μmol/l ≈ 58 μg/100 ml.

Comment

Oxyphenisatin-induced liver damage usually occurs when the drug has been taken for at least six months and usually two years.⁵ Patients may present with an acute episode of jaundice, fatigue, or abdominal discomfort, or with a more chronic course,² and recovery usually follows withdrawal of the drug.³ In severe or prolonged reactions benefit has been shown with corticosteroids.

Contrary to the widely held belief that oxyphenisatin is not available in Britain, the case reported here shows that oxyphenisatin is still available over the counter in so-called health food shops. This case emphasises the importance of taking a particularly careful drug history, noting any laxatives, however benign they may appear. A wide variety of proprietary laxative preparations are available over the counter, and reluctance by the public to consider them to be drugs suggests that increased diligence is required and particular attention should be paid to their formula.

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(Accepted 9 October 1980)

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Correction

Effects of oral propranolol on parathyroid hormone secretion in chronic renal failure

An error occurred in this paper by Dr K Farrington and others (15 November, p 1320). The top curve in the figure (▲) should have been labelled phosphate and the middle curve (■) calcium.