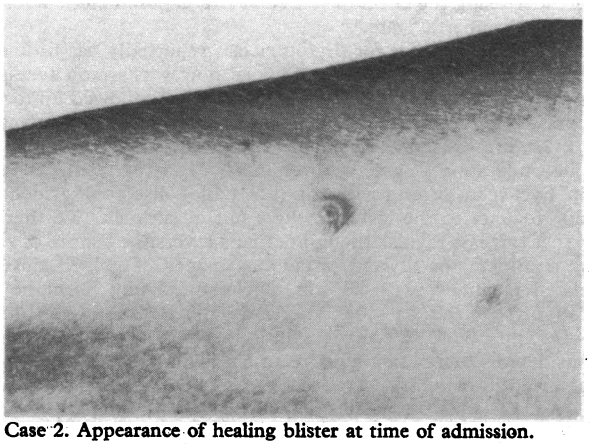
sent for virological examination. She described her illness, which had begun on 30 July with headache, fever, malaise, and tiredness followed by the appearance of mouth ulcers and several blisters on arms, legs, and trunk. This was clinically diagnosed as chickenpox. On admission she had several healing blisters on limbs and trunk (see figure). Her only child, a girl of



Case 2. Appearance of healing blister at time of admission.

16 months, had been unwell with a fever and papular rash on the buttocks the week before the patient's illness. Coxsackie virus A16 was isolated (in MRC_5 cells) from the products of conception and identified by neutralisation tests in suckling mice.

Case 3—A third patient reported that she had had a mild attack of hand-foot-and-mouth disease in the 14th week of pregnancy after contact with infected children. She described mouth ulcers and a few skin vesicles but no systemic upset. Her pregnancy was continuing normally to mid-term.

Pre-illness serum was available for these three patients, and convalescent samples obtained from each. Using an indirect immunofluorescence test for antibody to Coxsackie virus A16,[1] we showed a specific response in all three patients. Some IgG antibody was detectable in all pre-illness sera (titres 16, 8, 8), but there was a significant increase in each convalescent serum titre (128, 512, 512). The specificity of the pre-existing antibody remains to be determined.

Comment

Hand-foot-and-mouth disease caused by Coxsackie virus A16 was first described in Toronto in 1958.[2] Outbreaks of infection occur periodically in Britain, and there has been widespread activity this summer. The illness is generally mild and without complications.[3] Clinical confusion with chickenpox is understandable when numerous larger blisters are present. Differential diagnosis relies on the absence of cropping and failure to pustulate or scab in hand-foot-and-mouth lesions. In our second patient we detected pre-existing immunity to varicella.

Isolation of Coxsackie virus A16 from placental tissue confirms the causative role of this virus in abortion. It is not known whether there is any long-term effect of infection in pregnancy with any Coxsackie A viruses. A report of the Toronto A16 outbreak, localised in a particular housing area, mentioned that four babies born there six months after the epidemic had "minor congenital defects."[2] We hope to identify other patients infected during early pregnancy and study any effects in their babies.

We thank Dr D R Gamble and colleagues, of the Epsom Public Health Laboratory, for identifying the Coxsackie A16 viruses.

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Deep vein thrombosis and anaesthetic technique in emergency hip surgery

In investigations of postoperative deep vein thrombosis (DVT) little importance has been attached to the anaesthetic technique used. We have studied by means of ^{125}I-fibrinogen scanning the incidence of DVT in elderly patients undergoing emergency hip surgery under either spinal or general anaesthesia.

Patients, methods, and results

We studied 74 patients (10 men, 64 women) aged 63-95 years (mean 82 years) who had compression-screw-and-plate fixation of a femoral neck fracture within three days of injury. Preoperative assessment included a full history, physical examination, and laboratory investigations. Sixty-eight patients had significant concomitant medical problems. DVT prophylaxis is not given to patients in this unit with hip fractures as it is of uncertain efficacy. Each patient was randomly allocated to either spinal or general anaesthesia. Spinal anaesthesia was achieved in a routine sterile fashion with hyperbaric amethocaine 0·5% (mean dose 7 mg) with adrenaline. Diazepam (mean dose 9 mg) was given intravenously for sedation. General anaesthesia was induced with diazepam (mean dose 9 mg) and fentanyl (mean total dose 200 μg) followed by nitrous oxide-oxygen and pancuronium (mean total dose 6 mg). Fluid and blood were replaced according to clinical state and blood loss. Postoperative management and preoperative and postoperative haematocrit values were essentially the same in both groups. The thyroid gland was blocked with potassium iodide 120 mg by mouth continued daily for two weeks. Consent was obtained for the intravenous injection of 100 μCi ^{125}I-fibrinogen (Radiochemical Centre, Amersham), which was given immediately before anaesthesia. Leg scans were performed daily for seven days using a Pitman 235N Isotope Localisation Monitor. Details of the technique, computer analysis, and diagnostic criteria have been described elsewhere.[2] The scans were analysed sequentially according to Armitage.[3]

Scans showed DVT in 17/37 (46%) of patients given spinal anaesthesia and in 28/37 (76%) of patients given general anaesthesia (table). The difference was significant at the 5% probability level. The reduction in the former group was similar in both the operated and the non-operated limbs. Three patients given spinal anaesthesia and seven patients given general anaesthesia died in the first postoperative month. The difference in mortality was not significant (Fisher's exact test). Two patients given general anaesthesia were thought to have died from massive pulmonary embolism. Necropsy was performed on only one.

Results of ^{125}I-fibrinogen uptake scans in 74 patients undergoing hip surgery under spinal or general anaesthesia. Difference in incidence of positive scans significant at 5% level

	Positive scans				Negative scans
	Operated limb	Other limb	Bilateral	Total	
Spinal anaesthesia (N=37)	11	4	2	17	20
General anaesthesia (N=37)	13	5	10	28	9

Comment

Emergency hip surgery in the elderly places an ever-increasing load on hospital services in developed countries. The incidence of DVT in these patients exceeds 50%. Fatal pulmonary embolism occurs in 4-8% and the overall mortality is 10-30%.[4] The effectiveness of prophylactic measures in emergency hip surgery has been widely investigated[1 4] with considerably varying results. The anaesthetic techniques used in these studies have generally not been reported. ^{125}I-fibrinogen scan is an accurate way of detecting postoperative DVT originating in the calf[2] but it has some limitations in its application to hip surgery.[4] A lack of standardisation of technique and interpretation has been criticised previously.[2] Despite that it remains a useful screening method.[1]

Three major factors are thought to contribute to venous thrombosis —venous stasis, changes in blood constituents, and damage to the vessel wall. Spinal anaesthesia produces sympathetic blockade with vasodilatation and an increase in lower limb blood flow.[5] It is not known whether the coagulation and fibrinolytic responses to surgery are altered by the use of afferent neural blockade of the site of injury. Hip surgery causes blood vessel damage at the site of operation, but this cannot account for the occurrence of DVT in the non-operated limb. On the evidence of ^{125}I-fibrinogen scanning spinal anaesthesia for emergency hip surgery reduces the incidence of postoperative DVT.

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

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

Haematological changes

	Haemoglobin (g/dl)	Reticulocyte count (%)	White cell count (× 10⁹/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 + + +

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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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 μmol/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 200×10^9/l (200 000/mm³), 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