study showed a significant reduction in lower oesophageal sphincter pressure after intramuscular administration of emepronium bromide. In the nine patients who completed the study no significant change in sphincter pressure was found after four weeks' treatment with a standard oral dose of emepronium bromide. This may have been due to the much lower serum concentrations seen after oral medication than after intramuscular injection, confirming the findings of Ritch *et al.*⁵

A local irritative effect of the tablets is probably the most common cause of oesophageal injury after oral medication, as no decrease in sphincter pressure was shown during oral treatment with emepronium bromide. Since, however, higher plasma concentrations of emepronium bromide decrease the sphincter pressure and the absorption of the drug from the gastrointestinal tract varies considerably, occasional high serum concentrations may be seen. This, combined with an individual variability in parasympathetic receptor sensitivity, might cause the lower oesophageal sphincter to relax, causing more severe cases of reflux oesophagitis in the lower oesophagus.

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Acute severe intravascular haemolysis: an unrecognised cause of pancreatitis

Pancreatitis or histologically proved pancreatic damage is common in chronic renal failure¹ and complicates 3-7% of renal transplant operations.² Hypercalcaemia as a result of hyperparathyroidism, hyperlipidaemia, and viral infections may be contributing factors in uraemic patients.³ Occasionally drugs—corticosteroids, cytotoxic agents, or thiazides—may be a factor.

We describe two patients receiving haemodialysis in whom acute pancreatitis developed in association with acute intravascular haemolysis owing to the use of hypotonic dialysate.

Case reports

CASE 1

A 42-year-old woman who had been receiving regular hospital haemodialysis for three months owing to end-stage renal failure secondary to reflux nephropathy complained of being unwell with central chest pain and diaphoresis 100 minutes into a dialysis session. Dark red blood was evident in the dialysis lines. She had no history of any viral illness or excessive ethanol ingestion. Her only medication was aluminium hydroxide gel 950 mg thrice daily. Physical examination was unremarkable except for moderate epigastric tenderness. Laboratory investigations showed packed cell volume 21%, serum sodium 109 mmol(mEq)/l, dialysate sodium 35 mmol/l, serum amylase activity 2000 U/l, and serum calcium 2.5 mmol/l (10 mg/100 ml). The plasma in a centrifuged specimen was pink. Dialysis was stopped immediately.

She was initially treated with 3% sodium chloride solution and dialysate containing 145 mmol sodium/l. She complained of increasing epigastric pain radiating into her back over the ensuing 24 hours. Physical examination

showed increasing epigastric tenderness with paralytic ileus. Dilated loops of small bowel were seen on an abdominal x-ray film; serum amylase activity had increased to 10 000 U/l. Clinical and biochemical variables gradually resolved over the next five days, treatment comprising nasogastric aspiration, intravenous fluids, and cimetidine. She remained well over the next six months and resumed hospital dialysis.

CASE 2

A 30-year-old man who had received home haemodialysis for four years was admitted because of failing vascular access. He complained of feeling hot, chest tightness, and dyspnoea 210 minutes into a dialysis session. Dark red blood was noted in the dialysis lines. A history of recent viral infection or ethanol ingestion was absent. His only medication was aluminium hydroxide tablets 375 mg thrice daily. Physical examination showed epigastric tenderness. Laboratory investigations showed serum sodium 115 mmol/l, serum chloride 83 mmol(mEq)/l, dialysate sodium 30 mmol/l, serum amylase 6600 U/l, and serum calcium 2.25 mmol/l (9 mg/100 ml). Centrifugation of a blood sample yielded pink plasma. Dialysis was immediately stopped. He was treated with 3% hypertonic sodium chloride solution, and dialysis was restarted with dialysate containing 145 mmol sodium/l.

He complained of increasing epigastric pain over the next 24 hours, developing paralytic ileus. Serum amylase activity was 17 600 U/l. His symptoms resolved over the next eight days with nasogastric aspiration, intravenous fluids, cimetidine, and analgesia. He remained well four months later, having resumed home haemodialysis. Barium-meal examination was normal.

Comment

Pancreatitis may be hard to diagnose in uraemic patients as serum amylase activity is commonly increased, usually less than threefold. Confirmation may be achieved by using the amylase to creatinine clearance ratio.⁴ The absence of a history of recent viral infection and ethanol ingestion, with normocalcaemia and satisfactory clearance on dialysis, exclude these as aetiological factors. The pathophysiology of haemolysis-induced pancreatitis is due to local release of intracellular lysosomal enzymes, especially cathepsin B, resulting in activation of trypsinogen and other zymogens with the sequelae of autodigestion and inflammation. Nevertheless, a further underlying risk factor may also be necessary, which in our cases was the uraemic state.

Although the intravascular haemolysis in our patients was due to human error in a recirculating single-pass positive-pressure system, its association with pancreatitis has not to our knowledge been reported before. We emphasise the importance of this complication, which may be prevented by strict attention to proper dialysis procedures and adequate treatment of water.⁵

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Comparative risks of rhesus autoimmunisation in two different methods of mid-trimester abortion

The introduction of anti-D immunoglobulin has greatly reduced the incidence of rhesus haemolytic disease, though cases still occur.¹ Autoimmunisation after spontaneous or induced abortion is an important factor and can probably be prevented: anti-D immunoglobulin is not always given to Rh-negative women.² Autoimmunisa-

tion may also occur if the dose given is inadequate. The DHSS recommends a 50- μ g dose if abortion takes place at less than 20 weeks' gestation and a 100- μ g dose if it takes place at more than 20 weeks' gestation.³ The recommended dose in the USA after full-term delivery is 300 μ g, but smaller doses are used in Europe.⁴ The risk of sensitisation seems to be related at least partly to the volume of fetal blood entering the maternal circulation. Thus a standard dose of anti-D immunoglobulin may be inadequate if there are a high number of fetal cells. While examining Kleihauer counts after mid-trimester abortions using amniocentesis and intra-amniotic prostaglandin and urea one of us (RB) found some counts of more than 100. All Rh-negative patients who had had an abortion by amniocentesis had received a routine dose of 100 μ g of anti-D immunoglobulin; this may not be enough, especially as patients who have had an abortion leave hospital soon afterwards and are not always followed up. High Kleihauer counts may be caused by amniocentesis if the needle passes through placental tissue, and even diagnostic amniocentesis may cause Rh immunisation.

We carried out a prospective controlled study to investigate the incidence and cause of high Kleihauer counts.

Methods and results

Venous blood was collected after mid-trimester abortion from 100 patients who had undergone amniocentesis at Wistons Nursing Home, Brighton and from 100 patients who had not undergone amniocentesis at the Robert Nursing Home. All the patients at Wistons Nursing Home had had abortions by intra-amniotic urea and prostaglandin while patients at the Robert Nursing Home had had extra-amniotic prostaglandin introduced by a transcervical catheter. Samples were collected shortly after abortion during the day and at 9 am from patients who had aborted during the night. All specimens were examined in the laboratory at Selly Oak Hospital alongside routine specimens from normal full-term deliveries. Fetal cells were counted using Shepard's modification of the Kleihauer technique, and one film was examined from the blood of each patient. Fifty low-power fields were scanned using $\times 8$ eye pieces and a $\times 10$ objective lens.

Most of the films showed no fetal cells (table). In patients with a positive

Number of fetal cells in maternal blood after mid-trimester abortion

Fetal cells in 50 low-power fields	No of patients	
	Extra-amniotic (no amniocentesis) (n = 100)	Intra-amniotic (amniocentesis) (n = 100)
0	81	81
1	12	7
2	3	2
3	2	3
4		1
5		1
6	1	
7	1	
16		3
160		1
237		1

result the counts were significantly higher in the amniocentesis group ($p=0.028$ using a one-tailed Mann-Whitney t -test); this group contained five patients with unusually high counts, including two with very high counts. None of the patients who had had extra-amniotic prostaglandin had counts of more than seven.

Comment

It appears that differences in abortion technique may be reflected in the amount of fetal blood entering the maternal circulation. Results in this study suggest that in most cases the differences have no practical importance, but it is interesting that high Kleihauer counts were found only in the patients who had had abortions by amniocentesis. Experience at this laboratory shows that two out of every 100 specimens taken after full-term delivery would be expected to have counts of more than 100. A larger study would be needed to confirm the hypothesis that the absence of high counts in patients who had had extra-amniotic abortions is related to the method of abortion.

High Kleihauer counts clearly occur after abortion, and in some cases the normal doses of anti-D immunoglobulin may be inadequate. Since follow-up is uncertain it is important that patients with unusually high Kleihauer counts are detected and treated within 24 hours of termination. This may be achieved either by doing Kleihauer counts routinely after mid-trimester abortions and giving patients with unusually high counts an extra 100 or 200 μ g of anti-D immunoglobulin or by giving a

larger-than-normal dose to patients with high counts and also testing them before discharge for free anti-D. The presence of free anti-D would show that any fetal cells had been saturated with antibody, while its absence would show that a further dose was needed.

Smaller doses of anti-D immunoglobulin are probably adequate for patients who have first trimester abortions, and attention may be concentrated on the relatively few patients who have later abortions.

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Pancreatitis caused by methyldopa

Methyldopa is a widely used antihypertensive but has a high incidence of adverse effects.¹ We report on two patients in whom pancreatitis was associated with methyldopa.

Case reports

CASE 1

A 61-year-old previously healthy woman was admitted because of high fever and pain in the back, arms, and legs, present for one week. She had no abdominal complaints. For three weeks preceding admission she had taken chlorthalidone 50 mg thrice weekly and methyldopa 250 mg thrice daily for hypertension. She had no evidence of biliary tract disease or alcohol abuse. Routine physical examination was normal. Temperature was 40.6°C, pulse regular at 90/min, and blood pressure 110/50 mm Hg.

Laboratory results included: normal urine analysis; erythrocyte sedimentation rate 68 mm in first hour; haemoglobin 12.4 g/dl; leucocytes $8.3 \times 10^9/l$ (96% neutrophils); potassium 3.0 mmol(mEq)/l (normal 3.5-4.8 mmol/l); calcium 2.09 mmol/l (8.4 mg/100 ml) (normal 2.25-2.60 mmol/l; 9.0-10.4 mg/100 ml); aspartate transaminase 25 U/l (normal <25 U/l); alanine transaminase 51 U/l (normal <30 U/l); alkaline phosphatase 92 U/l (normal <100 U/l); serum amylase 829 U/l (normal 70-300 U/l); protein 62 g/l; albumin 32 g/l (normal 36.5-51.0 g/l); direct Coombs negative. Blood and urinary cultures were negative. X-ray examination of the thorax, oral cholecystography, and ultrasonography of the upper abdomen were normal. All drugs were stopped and the temperature normalised within 24 hours. Serum amylase activity remained slightly raised.

She was rechallenged, with informed consent, with 250 mg methyldopa; in four hours she became feverish (39°C) and experienced the same pain as before admission. Physical examination was normal. Next day serum and urinary amylase activities were increased to 8190 U/l and 18 370 U/l (normal <2000 U/l) respectively; serum lipase activity was 4900 U/l (normal <80 U/l); erythrocyte sedimentation rate had increased to 104 mm in first hour. During the following weeks serum and urinary amylase and serum lipase activities gradually became normal.

CASE 2

A 69-year-old woman with cystic lung disease was admitted with increasing dyspnoea, fever, and abdominal pain over the preceding five days. For 24 hours she had been confused. She had been taking methyldopa 500 mg/day and frusemide 40 mg/day for two weeks; ampicillin had been started five days before admission because of the fever. On examination she was tachypnoeic, restless, and stuporous. Temperature was 39.2°C, pulse regular at 120/min, and blood pressure 100/60 mm Hg. Examination of the lungs showed no new abnormalities. The abdomen exhibited decreased bowel