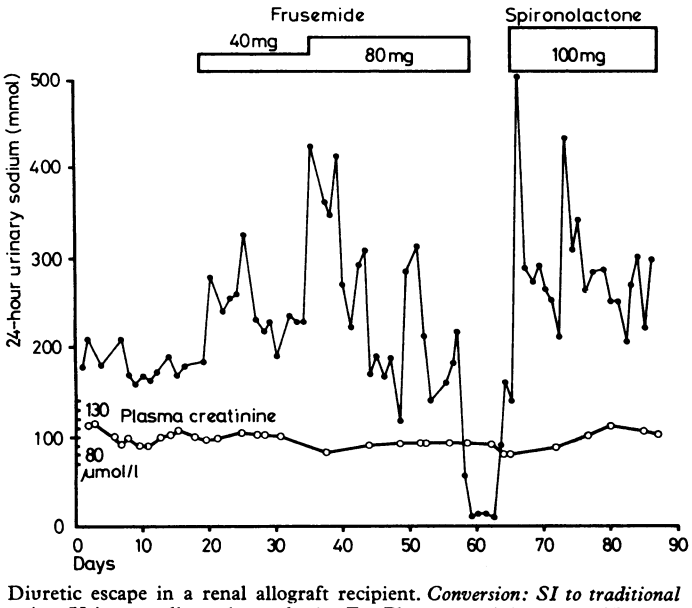

Diuretic escape in a renal allograft recipient. *Conversion: SI to traditional units*—Urinary sodium: 1 mmol = 1 mEq. Plasma creatinine: 1 μmol/l ≈ 11·3 mg/100 ml.

administering spironolactone. The excretion gradually fell but remained above baseline levels even after two weeks.

Comment

Oedema perpetuated by diuretics has been reported in patients with "idiopathic oedema."[1 2] Our results show that this phenomenon is commoner than generally realised. The pathogenesis of oedema during rejection episodes is multifactorial. The denervated kidney can secrete renin when stimulated.[3] A decreased filtration rate, increased renin secretion in response to renal ischaemia, and the mineralocorticoid activity of the increased dose of steroids will invariably produce oedema if the patient's fluid intake is not curtailed drastically. Frusemide, owing to its potent saliuretic effect, would further enhance secretion of renin, thereby producing the secondary hyperaldosteronism that probably caused the escape from the diuretic action of the drug. Sudden withdrawal of frusemide left the salt-retaining mechanism unopposed, resulting in rebound oedema. Thus patients become dependent on the diuretic and oedema is perpetuated. Prolonged diuretic treatment produces hyperuricaemia for which the unwary might prescribe allopurinol, which would cause severe marrow suppression because it potentiates the action of azathioprine. Furthermore, prolonged diuretic treatment depletes plasma volume and must increase blood viscosity, which may be specially relevant since some renal allograft recipients become erythraemic and risk thromboembolism.[4] Potent diuretics such as frusemide should be used sparingly. Since the maximal increase in urinary sodium excretion was in the first week, every effort must be made to discontinue the diuretic as soon as possible to avoid the counteracting secondary hyperaldosteronism. Frusemide should not be stopped abruptly in patients who have been taking it for some time. Spironolactone may reasonably be prescribed while the patient is being weaned off frusemide, thus avoiding the unpleasant rebound oedema.

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(*Accepted 2 May 1979*)

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Oral metronidazole in Clostridium difficile colitis

Diarrhoea after antibiotic treatment is common, and certain antibiotics, particularly clindamycin, may cause pseudomembranous colitis. Recent interest has focused on the cytopathic enterotoxin produced by *Clostridium difficile* as causing such conditions,[1] and treatment has therefore aimed at eradicating *Cl difficile*. Vancomycin has been used successfully[2] but is difficult to prepare in oral form. We describe success with oral metronidazole in two cases of clindamycin-induced colitis, in which *Cl difficile* and high titres of neutralisable cytopathic enterotoxin were found in the stool.

Case reports

Case 1—A 28-year-old woman with no past history of gastrointestinal disturbance was admitted for repair of a femoral hernia. Six days before operation she had completed a one-week course of oral clindamycin (250 mg six-hourly) for peridontal infection. Thirty-six hours after uncomplicated herniorrhaphy she became feverish and developed colicky, lower abdominal pain with watery, bloodstained diarrhoea. Sigmoidoscopy showed no obvious pseudomembrane, and histological examination showed patchy, non-specific acute proctitis with intervening normal mucosa. Stool taken at onset was cultured in reinforced clostridial medium with 0·2% paracresol[3] and grew *Cl difficile* (identified by morphological and biochemical criteria[3]) sensitive to metronidazole in vitro. Enterotoxin, measured by its cytopathic effect on HeLa cells in tissue culture and neutralisable by *Cl sordellii* antitoxin (Wellcome Foundation Research Laboratories), was found in the stool in high titre (table). Treatment was started with oral metronidazole 400 mg eight-hourly for five days, reducing to 200 mg eight-hourly for five days.

Effect of metronidazole given for Cl difficile-associated diarrhoea on stool culture and stool toxin titres

No of days of metronidazole treatment	Stool culture for *Cl difficile*	Neutralisable *Cl difficile* toxin titre in stool*
	Case 1	
Pretreatment	Positive	1/2000
Day treatment began	Positive	1/2000
3	Negative	1/500
4	Negative	1/50
10	Negative	Nil
	Case 2	
Pretreatment	Positive	1/1000
6	Negative	1/500
2 days after completion	Negative	Nil
19 days after completion	Negative	Nil

*1 g wet-weight stool extracted in 5 ml physiological saline.

Within 36 hours she had less abdominal pain and fewer bowel actions. After a further 36 hours there was no diarrhoea or abdominal pain, stool culture did not grow *Cl difficile*, and enterotoxin titre was reduced. Sigmoidoscopy showed slightly oedematous patches of mucosa to 18 cm. After completing treatment she remained symptom-free, with no toxin in her stool and negative cultures for *Cl difficile*. Subsequent barium-enema appearances were normal.

Case 2—A 57-year-old woman with no history of bowel disturbance received a five-day course of oral clindamycin (250 mg six-hourly) for paronychia. During treatment she noticed looser but formed stools which progressed over two weeks to watery diarrhoea without blood. She became weak and dehydrated and was admitted to hospital. Sigmoidoscopy showed slightly opaque rectal mucosa but no ulceration, bleeding, or obvious pseudomembrane. Stool culture grew *Cl difficile*, and cytopathic enterotoxin neutralisable with *Cl sordellii* antitoxin was found (table). She began treatment with oral metronidazole (400 mg eight-hourly for 10 days). Rapid symptomatic improvement was seen, and after six days stool culture for *Cl difficile* was negative with a falling titre of neutralisable toxin. After 10 days she was asymptomatic and stool culture remained negative for *Cl difficile* with no neutralisable toxin detectable.

Comment

Cl difficile is thought to be a common aetiological agent in antibiotic-associated diarrhoea[1 2 4] and that treatment should aim to eliminate the organism from the gut. This has been achieved with oral vancomycin,[2] but it is expensive, toxic, and available only in parenteral form, which is diluted for oral use. Successful use of metronidazole to treat diarrhoea after antibiotics has been reported,[5] but without specific bacteriological studies. Although *Cl difficile* is sensitive to metronidazole in vitro, it has been thought to be valueless in practice[2] owing to rapid absorption from the upper gut. Our findings, however,

suggest that oral metronidazole is useful in such cases, producing well-documented elimination of toxin and organism and symptomatic improvement. We therefore suggest that oral metronidazole is of value in treating *Cl difficile*-associated diarrhoea.

We thank Mr R N Baird and Dr C J Burns-Cox for permission to report cases under their care, Professor D C E Speller for advice, and Dr P D Walker, of the Wellcome Foundation Research Laboratories, for providing *Cl sordellii* antitoxin.

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(*Accepted 2 May 1979*)

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Mid-duodenal bleeding in chronic renal failure

We report on three patients with chronic renal failure who bled from the mid-duodenum. This has not been reported before.

Case reports

Case 1—A taxi driver aged 30 years underwent cadaveric renal transplantion on 10 February 1978 and was discharged on 3 March with a creatinine clearance of 27·8 ml/min. He was readmitted five days later with melaena and a haemaglobin concentration of 4 g/dl; barium-meal examination and gastroscopy were normal. He was given a transfusion and started on cimetidine but continued to have melaena, so on 11 March truncal vagotomy and pyloroplasty were performed. The melaena continued until 14 March, when mesenteric angiography was carried out showing bleeding in the mid-duodenum (fig (*a*)). At operation a bleeding point was found in the second part of the duodenum and underrun. No further bleeding occurred, but he died on 18 March 1978.

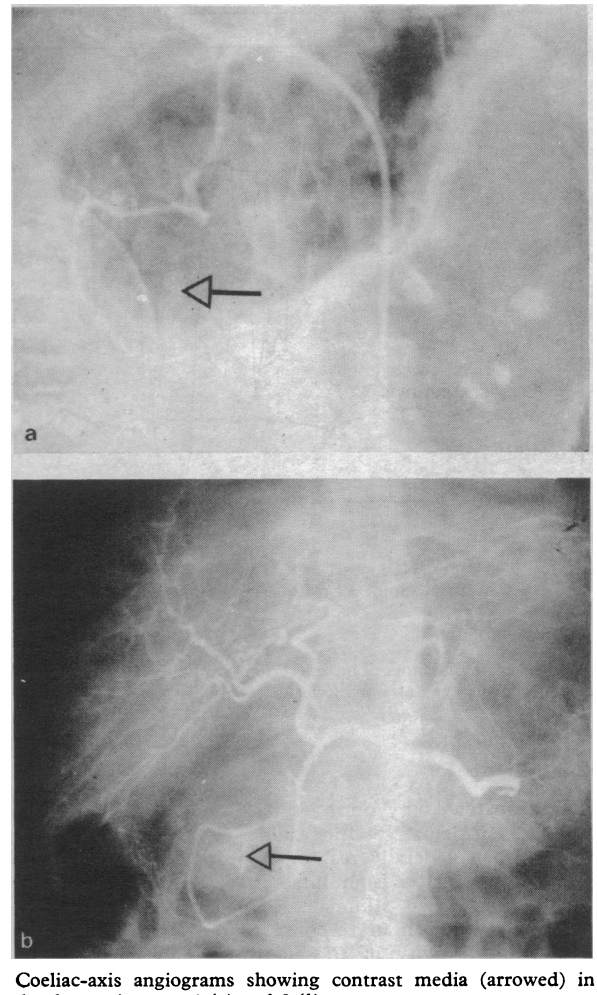
Case 2—A housewife aged 37 years presented in February 1978 with end-stage chronic glomerulonephritis and was accepted for haemodialysis. On 21 June she experienced epigastric discomfort and had melaena. Gastroscopy showed gastric erosions, and cimetidine treatment was begun. The melaena continued for two weeks. Repeat gastroscopy showed adherent clot in the first part of the duodenum so truncal vagotomy and pyloroplasty were performed on 8 July. As no blood was found in the stomach or upper duodenum the duodenum was opened. A bleeding point at the junction of the second and third parts was found, biopsied, and underrun. No further bleeding occurred, and she was discharged several weeks later.

Case 3—A 38-year-old housewife with chronic glomerulonephritis underwent cadaveric renal transplantation on 18 May 1978 and was discharged on 7 June with a creatinine clearance of 53·6 ml/min. She was readmitted one week later with a perforated duodenal ulcer, which was oversewn; she started cimetidine treatment and was discharged on 28 June. She was readmitted on 16 July, shocked and with haematemasis and melaena. Gastroscopy showed fresh blood in the first part of the duodenum. She underwent truncal vagotomy and pyloroplasty, and the previously perforated ulcer, the site of haemorrhage, was excised. After further haemorrhage and negative gastroscopy, coeliac-axis angiography was performed, which showed bleeding from the mid-duodenum (fig (*b*)). At operation a bleeding point at the junction of the second and third parts of the duodenum was biopsied and underrun. She made a slow recovery and was discharged on 1 September 1978.

The biopsies obtained in cases 2 and 3 were very similar. An inflammatory exudate was present with destruction of the normal mucosal pattern. Also apparent were abnormally dilated blood vessels with the appearance of an angiomatous malformation. Cytomegalovirus inclusion bodies were seen in case 3.

Comment

After renal transplantation the complications of peptic ulceration cause much morbidity and death.[1 2] Haemorrhage is the commonest complication, often coinciding with treatment of a rejection episode,[1] and mortality may reach 20-60%.[1 2] In our cases bleeding occurred in the mid-duodenum from a normal-looking mucosa, but microscopy showed inflammation and angiomatous malformations of unknown cause. Serological evidence of cytomegalovirus infections may be found in 73-91% of transplant patients.[3 4] It has not been definitely implicated as causing intestinal bleeding, although the virus has been seen in association with a duodenal ulcer in an immunosuppressed patient.[5] Although we think cytomegalovirus may have been an aetiological factor, it was not identified in case 2, and we therefore propose that some other pathogenic process must have been operating.



Coeliac-axis angiograms showing contrast media (arrowed) in duodenum in cases 1 (*a*) and 3 (*b*).

We thank Dr H J Whitely of the department of pathology, Cardiff Royal Infirmary for his help.

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(*Accepted 1 May 1979*)

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