a significant relation between the severity of the disease, as measured by its duration ($p < 0.005$) and the severity of the cough ($p < 0.25$), with the vaccination state of the child but not with age or social class. This relation showed that 37% of vaccinated children had a short illness (less than 31 days) compared with only 20% of non-vaccinated children. Similarly, a mild cough (0-8 coughing spasms per 24 hours) was experienced by 48% of the vaccinated group and 32% of the non-vaccinated group.

In the contact cases the severity of the illness was influenced not only by the vaccination state but also by the severity of the illness in the index case. We could not distinguish from the data whether this latter influence was due to a genetic predisposition toward the disease or to associated environmental or social influences.

It has been suggested that the most valuable test of the effectiveness of a vaccine is how well it protects those children exposed to the disease in their normal environment. In this study we found that whooping cough vaccination conferred a significant degree of protection to children exposed to the disease ($p < 0.001$). In practical terms this means that about two out of 10 vaccinated children, when exposed in the family to whooping cough, developed the disease compared with seven out of 10 non-vaccinated children with a similar exposure. We found that the incidence of bacterial isolation of *B pertussis* was higher among non-vaccinated children throughout their illness, which may indicate an increased infectivity in this group.

This study shows, therefore, that whooping cough vaccination modifies the clinical illness and offers a worthwhile degree of protection to children exposed to the disease.

We are deeply indebted to the participating general practitioners and their staff for their continuing enthusiasm, care, and energy throughout this project. We are grateful for the expert technical help given by Dr R Y Cartwright, Dr D G Fleck, Dr D R Gamble, and Dr E I Tanner, of the Public Health Laboratory Service. Especial thanks are due to the project co-ordinator, Ruth Lanzer, and all the staff of the epidemic observation unit of the Royal College of General Practitioners at the University of Surrey, together with those scientists who helped substantially in planning and interpreting the research project. Our grateful thanks are due to Professor J Knowelden for the very considerable advice he so generously provided. Finally, we express our thanks to the DHSS for its encouragement and financial support.

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(*Accepted 22 April 1981*)

SHORT REPORTS

Effect of emepronium bromide on lower oesophageal sphincter

Medical treatment of detrusor hyperreflexia and instability is often based on the use of parasympatholytics,[1] among which is emepronium bromide (Cetiprin). Side effects of emepronium bromide on the alimentary tract have been reported—namely, localised oesophageal injury and sporadic reports of ulceration of the oral mucosa. Recently 15 cases of oesophagitis during treatment with emepronium bromide were reviewed by Collins *et al*,[2] who added one case of changes in the oesophageal mucosal potential difference, suggesting gastro-oesophageal reflux as the cause of ulcerative oesophagitis.

Our investigation was aimed at assessing the effect of emepronium bromide on lower oesophageal sphincter pressure after parenteral and oral administration by using oesophageal manometry with a rapid pull-through technique.

Patients, methods, and results

Eleven patients (nine women and two men) with urinary incontinence due to detrusor instability entered the study. The median age was 54 (range 32-72) years. Treatment with emepronium bromide was indicated in all patients, none of whom had symptoms of oesophageal dysfunction. All gave their informed consent.

Oesophageal pressures were recorded with an Esophagus Motility Probe model 31™ (Kulite Semiconductor Products Inc).[3] Respiratory movements were measured by impedance recording. Swallowing was recorded as the registration of impedance across the neck. Lower oesophageal sphincter pressure was recorded using a rapid pull-through technique.[4] The pressure was calculated as the average of peak values given by the three transducers from three pull-throughs in the supine position during apnoea at sustained maximal expiration. The patients were fasting.

The trial was open, each patient being used as his own control. After the lower oesophageal sphincter pressure had been noted initially 50 mg emepronium bromide was administered intramuscularly. The pressure was noted 15 minutes after the injection, and a blood sample was obtained for determination of the serum concentration of emepronium bromide by gas chromatography. Thereafter, the patients were started on emepronium bromide 200 mg four times daily by mouth. Lower oesophageal sphincter pressure and serum emepronium bromide concentration were recorded after four weeks of treatment.

Only nine patients completed the four weeks of oral medication, as two suffered heartburn and dysphagia. Intramuscular administration of 50 mg emepronium bromide caused a significant reduction in lower oesophageal sphincter pressure ($p < 0.01$). After four weeks of oral medication the pressure was not significantly different from the pretreatment values ($p > 0.1$) (table). Higher serum concentrations of emepronium bromide were found after intramuscular than oral treatment ($p < 0.01$).

Effect of emepronium bromide on lower oesophageal sphincter pressure and plasma drug concentrations. (Figures in parentheses are pressures after treatment expressed as percentages of pressures before treatment)

Case No	Lower oesophageal sphincter pressure (mm Hg)			Plasma emepronium bromide concentration (μg/l)	
	Before treatment	15 minutes after 50 mg intra-muscularly	After 200 mg four times daily for four weeks	15 minutes after 50 mg intra-muscularly	After four weeks' oral treatment
1	43	34 (79)	35 (81)	963	112
2	48	30 (63)	53 (110)	705	0
3	46	23 (50)	*	727	*
4	36	19 (53)	40 (111)	1272	12
5	42	15 (36)	31 (74)	765	50
6	27	19 (70)	24 (89)	1370	106
7	19	17 (89)	14 (74)	913	52
8	60	40 (67)	*	2153	*
9	23	18 (78)	25 (109)	1089	99
10	27	19 (70)	28 (104)	925	108
11	21	19 (90)	25 (119)	729	46
Median	36	19 (70)	28 (104)	925	52
		$p < 0.01$†		$p < 0.01$†	

*Patient stopped treatment because of dysphagia and heartburn.
†Significance assessed using Wilcoxon's test.

Comment

The peak serum concentration of emepronium occurs about 15 minutes after intramuscular administration of the drug, a dose of 50 mg being sufficient to elicit relaxation of the bladder.[5] The present

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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(*Accepted 3 March 1981*)

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Acute severe intravascular haemolysis: an unrecognised cause of pancreatitis

Pancreatitis or histologically proved pancreatic damage is common in chronic renal failure[1] 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 lysozomal 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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(*Accepted 13 March 1981*)

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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-