

were also raised. The only other drug given in this period was cotrimoxazole, which was administered before, during, and after the reinstatement of cimetidine and thus seems unlikely to have been responsible for the abnormalities observed.

Initial animal studies and clinical trials of cimetidine failed to show any appreciable haematological abnormalities, although rises in serum transaminase concentrations were occasionally seen.<sup>3</sup> In particular, the agranulocytosis noted with the earlier H<sub>2</sub>-receptor antagonist metiamide<sup>4</sup> was not seen. Since then, agranulocytosis has been reported in one patient four months after stopping cimetidine.<sup>1</sup> More recently transient neutropenia has been noted in a patient with chronic renal failure associated with a bone marrow picture consistent with peripheral granulocyte destruction.<sup>2</sup> In our patient the leucopenia seems to have been part of a more generalised drug reaction that has not been described with cimetidine.

<sup>1</sup> Craven, E R, and Whittington, J M, *Lancet*, 1977, **2**, 294.

<sup>2</sup> Ufberg, M H, et al, *Gastroenterology*, 1977, **73**, 635.

<sup>3</sup> Sharpe, P C, and Hawkins, B W, *Proceedings of Second International Symposium on Histamine H<sub>2</sub> Receptor Antagonists*. Amsterdam, Excerpta Medica, 1977.

<sup>4</sup> Forrest, J A H, et al, *Lancet*, 1975, **1**, 392.

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## Bleeding gastric erosion after oral zinc sulphate

The use of oral zinc sulphate for chronic skin ulcers<sup>1,2</sup> and acne<sup>3</sup> has aroused interest recently. A case of gastrointestinal bleeding is described, which emphasises a potentially serious side effect of this treatment and seems to support the warnings of Glover and White.<sup>4</sup>

### Case report

One week before admission a 15-year-old English schoolgirl (weight 68 kg) with no history of dyspepsia had started taking zinc sulphate capsules

(Zincomed), 220 mg twice daily, for acne, the treatment having been prescribed by her general practitioner. She was receiving no other medication. After each capsule she experienced epigastric discomfort, and on the day before admission she had fainted after getting up from a chair. She subsequently twice passed melaenic stools.

On admission she was anaemic with a pulse rate of 110/min and a blood pressure of 120/60 mm Hg. Epigastric tenderness was present, and rectal examination confirmed the presence of melaena. Haemoglobin was 5.4 g/dl, platelet count was normal, and no abnormalities were found on clotting screen. Blood urea concentration was initially raised, but results of subsequent renal function tests were normal. Upper intestinal panendoscopy 15 hours after admission showed a normal oesophagus and duodenal cap, but patchy areas of gastritis were seen on the greater curve with a resolving haemorrhagic erosion.

Zinc treatment was discontinued and she was transfused 8 units of whole blood. After endoscopy she was started on a four-week course of cimetidine (1 g/day in divided doses) and made an uneventful recovery. At follow-up one month later she was asymptomatic and had maintained a haemoglobin concentration of 13.3 g/dl.

### Comment

Side effects from oral zinc sulphate in patients with normal renal function are rare,<sup>1,5</sup> though the capsule preparation gives rise to nausea, vomiting, and diarrhoea more commonly than the effervescent form.<sup>2</sup> Nevertheless, this is the first report of gastrointestinal bleeding. The patient had no history of dyspepsia, so the epigastric discomfort after taking each capsule and subsequent endoscopic finding of a bleeding gastric erosion are highly suggestive of a direct irritant effect on the stomach. Though the effervescent zinc sulphate preparations are probably preferable to the more readily available capsules for oral treatment, they are at present marketed only in Sweden.

I thank Professor Ivor H Mills for permission to report this case and Dr Richard Machell for performing the endoscopy.

<sup>1</sup> Hallböök, T, and Lanner, E, *Lancet*, 1972, **2**, 780.

<sup>2</sup> Haeger, K, Lanner, E, and Magnusson, P O, *Zeitschrift für Gefäßkrankheiten*, 1972, **1**, 62.

<sup>3</sup> Michaëlsson, G, Juhlin, L, and Vahlquist, A, *Archives of Dermatology*, 1977, **113**, 31.

<sup>4</sup> Glover, S C, and White, M, *British Medical Journal*, 1977, **2**, 640.

<sup>5</sup> Henzel, J H, et al, in *Proceedings of Congress of Clinical Applications of Zinc Metabolism*. Cleveland, C C Thomas, 1971.

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## SHORT REPORTS

### Clostridium welchii septicaemia after intrauterine caesium insertion

Two patients with adenocarcinoma of the body of the uterus were treated in the same operating session with intrauterine radiocaesium (<sup>137</sup>Cs). Both developed *Clostridium welchii* septicaemia.

#### Case 1

A 57-year-old woman had had a foul-smelling vaginal discharge before operation. She was anaesthetised and the cervix dilated. A rubber-covered tube, 67 mm long and 12.6 mm in diameter containing <sup>137</sup>Cs equivalent to 45 mg of radium, was inserted into the uterine cavity. Her obesity (she weighed 112 kg) and a fixed-flexion deformity of the right hip made insertion difficult. At one stage the tube was replaced in the lead-shielded well with other radioactive sources for the treatment session.

Twenty-four hours after the insertion the patient was febrile and slightly jaundiced. Twelve hours later she was bronze coloured and had passed only a little urine, which was black and contained free haemoglobin. Microspherocytes and staining by free haemoglobin were seen in the peripheral

blood film. The haemoglobin had fallen from 13.9 g/dl to 6.4 g/dl. The free plasma haemoglobin was 2.15 g/dl, the intracellular haemoglobin 4.5 g/dl, the white cell count  $26.3 \times 10^9/l$  ( $26\,300/mm^3$ ), and platelets  $60 \times 10^9/l$  ( $60\,000/mm^3$ ). *Cl. welchii* septicaemia was suspected. Bacteriological specimens were taken and the patient was started on benzylpenicillin, 4 megaunits intravenously every six hours, and gentamicin. An arteriovenous shunt was constructed in preparation for renal dialysis but before the shunt could be used the patient began to bleed from venepuncture sites, nose, and gut. She died 52 hours after the caesium insertion. Blood cultures and vaginal swabs grew *Cl. welchii*.

#### Case 2

The second patient (aged 49) was treated immediately after the first. A caesium tube was inserted into the uterine cavity without difficulty. Thirty-six hours after operation her temperature was 37.5°C. Blood cultures and high vaginal swabs were sent for bacteriological examination. When the tube was removed 55 hours after insertion her temperature had dropped to 36.5°C but she was slightly jaundiced (bilirubin 45 mmol/l (3 mg/100 ml)). Treatment with benzylpenicillin, 4 megaunits every six hours, was started immediately. Blood cultures gave negative results but *Cl. welchii* was isolated from the vagina. Over the next five days the jaundice disappeared but the blood urea concentration rose from 6 to 30 mmol/l (36-180 mg/100 ml).

With conservative treatment the patient's renal function returned to normal. Although the blood cultures gave negative results, the most likely cause for the patient's fever, jaundice, and renal failure was a transient *Cl welchii* septicaemia.

The *Cl welchii* organisms from both patients were serotyped. The bacteria isolated from the blood and vagina of the first patient were identified as  $\alpha\beta$ -haemolytic *Cl welchii* type 58. An identical type was isolated from the vagina of the second patient.

**Discussion**

Most *Cl welchii* septicaemias are endogenous.<sup>1</sup> We believe that *Cl welchii* was present in the vagina and the uterine tumour of the first patient and was carried into the blood stream after insertion of the caesium tube. Her infection seems to have been transferred to the second patient. After the first, unsuccessful attempt to insert the tube into the first patient the source was returned to the shielded "well" in the theatre. The tube must have been contaminated by vaginal organisms. Possibly it came in contact with the tube for the second patient, which was stored in the well.

*Cl welchii* septicaemias are usually fatal unless treatment begins within 24 hours of the onset of symptoms. In a recent review only two out of 14 patients survived.<sup>2</sup> High-dose penicillin should be given as soon as the condition is suspected.

*Cl welchii* may be isolated from the vagina of 5% of healthy women.<sup>3</sup> The hypoxic necrotic areas of tumours provide an ideal culture medium. It is therefore remarkable that *Cl Welchii* septicaemia is a rare complication of treating gynaecological tumours by intracavity radiation.

We thank Drs G E Flatman and M A C Cowell for permission to report on their patients and Drs E H Porter and J D Sleight for help in preparing this report. We are very grateful to Mr M F Stringer of the Central Public Health Laboratory, Colindale, for serologically typing the *Cl welchii* cultures.

<sup>1</sup> Bittner, J, et al, *Journal of Medical Microbiology*, 1970, **3**, 325.  
<sup>2</sup> Wynn, J W, and Armstrong, D, *Cancer*, 1972, **29**, 215.  
<sup>3</sup> Davis, D B, et al, *Microbiology*, 2nd edn, p 838. London, Harpers and Row, 1973.

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**Magnesium-saving property of an aldosterone antagonist in the treatment of oedema of liver cirrhosis**

Urinary magnesium loss during diuretic treatment with agents such as chlorothiazide, the mercurials, frusemide, and ethacrynic acid is well

documented and could lead to a state of magnesium deficiency with important clinical implications.<sup>1</sup> We investigated the effect of an aldosterone antagonist on urinary magnesium excretion in patients with oedema due to liver cirrhosis.

**Patients, methods, and results**

Twelve men with liver cirrhosis (aged 36-52 years) were studied. All were oedematous and hypoalbuminaemic; serum albumin ranged from 12 to 22 g/l. Results of other liver function tests for the whole group were: serum aspartate aminotransferase (SGPT) 28-64 IU/l; serum alkaline phosphatase 78-155 IU/l; serum bilirubin 13.7-46.2  $\mu$ mol/l (0.8-2.7 mg/100 ml). Creatinine clearance ranged from 75 to 98 ml/min. None of the patients had previously received diuretic treatment.

Throughout the study each patient was given a constant diet that closely reflected his normal dietary intake. For the whole group the daily dietary content of the principal cations was as follows: sodium 50-60 mmol, potassium 30-60 mmol, calcium 3.8-10 mmol, magnesium 5-10 mmol. At least two days of equilibration on the diet preceded control urinary collection. Two-hourly urine was collected every two hours from 6 am to 8 pm, and all urine passed from 8 pm to 6 am (next morning) was pooled. On the test day 200 mg canrenoate potassium, a soluble derivative of spironolactone, was infused over five minutes at 10 am. Twenty-four-hour urine collections were also made on the day after the test while the patients continued with the same diet and water intake.

Magnesium was estimated with the atomic absorption spectrophotometer (Unicam SP 90); SGPT with an LKB automatic reaction rate analyser; and sodium, potassium, creatinine, albumin, alkaline phosphatase, and bilirubin by a Technicon SMA 6 Plus autoanalyser.

Statistical analysis was performed by means of the Wilcoxon test for paired differences.

The table compares the excretion rates for magnesium, sodium, and potassium. Each patient served as his own control. Urinary excretion of magnesium decreased significantly ( $P < 0.05$ ) in the first six hours after administration of the drug. The cumulative reduction became highly significant ( $P < 0.01$ ) at 24 hours. Over the next 24 hours the residual effect of the drug was still discernible. Urinary excretion of sodium was significantly increased throughout the periods of observation, the increase remaining clearly significant ( $P < 0.05$ ) even on the next day. Urinary potassium excretion was significantly reduced ( $P < 0.05$ ) on the day of administration of the drug.

**Comment**

Canrenoate potassium has the unique property of saving magnesium by decreasing urinary excretion of this cation, while simultaneously producing significant natriuresis. This action of the drug is particularly useful in liver cirrhosis, in which there is often magnesium deficiency.<sup>2</sup> Treatment of oedema of liver cirrhosis with other more potent diuretics which are generally magnesuric may aggravate magnesium depletion. The introduction of an aldosterone antagonist to the diuretic regimen of such patients, as well as augmenting natriuresis, seems to be important from the point of view of magnesium economy. It has also been shown that long-term use of oral spironolactone is not associated with magnesium depletion.<sup>3</sup>

This aldosterone antagonist probably owes its magnesium-saving property to its anti-aldosterone activity,<sup>4</sup> which is also the basis of its natriuretic action. Its magnesium-saving effect and its natriuretic action are therefore valuable in oedematous conditions associated with aldosteronism, such as are found in liver cirrhosis, congestive heart failure, and the nephrotic syndrome. Furthermore, since the use of other diuretic agents is expected to exacerbate aldosteronism by virtue of natriuresis, canrenoate potassium would be especially

Comparison of excretion rates of cations before and after infusion of 200 mg of potassium canrenoate in patients with cirrhosis of the liver

Hours*	Magnesium ( $\mu$ mol/min)			Sodium ( $\mu$ mol/min)			Potassium ( $\mu$ mol/min)		
	Mean	Range	Significance of difference (P)	Mean	Range	Significance of difference (P)	Mean	Range	Significance of difference (P)
0-6									
Control ..	0.82	0.34-1.23	} <0.05	10.91	0.7-30.6	} 0.05	10.17	4.8-33.3	} <0.05
Test ..	0.66	0.35-1.14		16.61	2.5-29.7		7.63	3.8-10.1	
0-24									
Control ..	2.97	1.85-4.14	} <0.01	42.26	3.4-148.9	} <0.01	30.87	16.3-55.3	} <0.05
Test ..	2.55	1.88-4.35		79.73	24.1-131.7		22.76	11.4-28.0	
24-48									
Control ..	2.96	1.85-4.14	} 0.05	42.11	3.4-148.9	} <0.05	30.94	16.3-55.3	} Not significant
Test ..	2.47	1.57-4.31		65.78	30.3-134.7		28.15	20.4-35.9	

\*Hours from time of infusion of canrenoate potassium; control values were obtained on day before test.