A case of paraproteinaemia associated with leucocytoclastic vasculitis and pyoderma gangrenosum has also been described.³ In that case the authors suggested that because of the histological findings the pyoderma gangrenosum could be regarded as a type of leucocytoclastic vasculitis. We may therefore reasonably assume in our case that the EED was associated from the beginning with paraproteinaemia. It is further consistent that the paraproteinaemia was of the IgA type. Most cases of pyoderma gangrenosum with paraproteinaemia are of the IgA type. EED associated with frank or possible myeloma was described some years ago,^{4,5} the myeloma being diagnosed four to six years after the EED. The evolution of "benign paraproteinaemia" to malignant gammopathy, if it occurs, could take some years. This was the sequence of events in our case since the myeloma was diagnosed nine years after the appearance of the erythema and five years after the discovery of the paraproteinaemia.

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² Pruzanski, W, and Ogryzlo, M A, *Medical Clinics of North America*, 1972, **56**, 371.

³ Thompson, D M, *et al*, *British Journal of Dermatology*, 1973, **88**, 117.

⁴ Duperrat, B, and Rappaport, M M, *Bulletin de la Société Française de Dermatologie et de Syphiligraphie*, 1959, **66**, 6.

⁵ Sams, M J R, *et al*, *British Journal of Dermatology*, 1968, **80**, 55.

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Fatal chlormethiazole poisoning in chronic alcoholics

Chlormethiazole edisylate (Heminevrin) is a sedative, hypnotic, and anticonvulsant drug widely used in the treatment of depression. It is stated to be of low toxicity, but its action is enhanced by alcohol.¹ I describe four fatal cases of self-poisoning in chronic alcoholics, all of whom were being treated for depression with chlormethiazole edisylate in tablet form.

Case reports

Case 1—The patient was a single man aged 45 who was a known chronic alcoholic. He was depressed and had made two previous suicide attempts. He had been implicated in a minor traffic accident and charged with driving while under the influence of drugs. Analysis of a blood sample showed it to contain 51 $\mu\text{mol/l}$ chlormethiazole (2.6 mg/100 ml). No alcohol was detected. Four days later he was found dead in his flat. Postmortem examination showed adherent pinkish-white powder in the upper third of the oesophagus and 10 whole white tablets in the stomach. The lungs were oedematous. No appreciable natural disease was found.

Case 2—The patient, a 60-year-old single man, was a known chronic alcoholic who had had psychiatric treatment for depression. He was found dead in a wood with a bottle nearby that contained chlormethiazole tablets. Postmortem examination showed adherent white powder in the lower third of the oesophagus and 20 whole white tablets with a sickly sweet smell in the stomach. Recent thrombus had occluded the right coronary artery and a large area of fibrosis was present in the interventricular septum.

Case 3—The patient was a man of 47 years. He had been an alcoholic for 20 years with fits of depression and attempts at suicide. He was found dead at home with a nearby bottle of chlormethiazole tablets. Necropsy findings showed 65 whole white tablets and much white granular material with a

sickly sweet smell in the stomach. There was no appreciable natural disease.

Case 4—This patient, a known alcoholic, was a single man aged 52 years. Shortly before his death he had become depressed and had been admitted to a psychiatric unit. The day after his discharge he was found dead on a river embankment. White sludge and 18 whole white tablets with a sickly sweet smell were found in the stomach at necropsy. There was adherent white powder in the lower oesophagus, and severe coronary atherosclerosis.

A toxicological analysis was performed in each of the four cases (see table).

Chlormethiazole concentrations in blood and urine ($\mu\text{mol/l}$), and liver (mg/100 g) from five alcoholic patients who died after self-poisoning with chlormethiazole edisylate tablets

Patient No	Blood		Urine		Liver	
	Chlormethiazole	Alcohol	Chlormethiazole	Alcohol	Chlormethiazole	Alcohol
1	78		127		6.2	
2	117		156		19.0	
3	35	48.6	19	48.8	6.2	NE
4	19	19.1	55	28.9	10.0	NE

NE = not estimated.

Conversion: SI to traditional units—Chlormethiazole 1 $\mu\text{mol/l}$ $\approx$ 0.051 mg/100 ml; alcohol (ethanol) 1 mmol/l $\approx$ 4.6 mg/100 ml.

Comment

The plasma concentration of chlormethiazole for a given dose varies with the pharmaceutical preparation. For example—ingestion of two 500-mg tablets of chlormethiazole edisylate produces a maximum concentration of about 19 $\mu\text{mol/l}$ (1.0 mg/100 ml) plasma after 70 minutes.² This concentration induces a hypnotic effect.

In a series of nine cases of death from chlormethiazole poisoning, Jakobsson and Möller reported the lowest recorded fatal plasma concentration of the drug—49 $\mu\text{mol/l}$ (2.5 mg/100 ml) (range 49–156 $\mu\text{mol/l}$ (2.5–8.0 mg/100 ml)).³ Nevertheless, the patient described in case 1 was driving a car, albeit unsuccessfully, with a plasma concentration of 51 $\mu\text{mol/l}$ (2.6 mg/100 ml) chlormethiazole. Clearly there must be individual variation in reaction to the drug or the development of tolerance. Fatal concentrations of the drug when taken with alcohol are very much lower. In cases 3 and 4 death occurred at, or close to, normal therapeutic concentrations. Similar concentrations were found in a series in which the mean plasma concentration of chlormethiazole was 41 $\mu\text{mol/l}$ (2.1 mg/100 ml) (range 10–92 $\mu\text{mol/l}$ (0.5–4.7 mg/100 ml)).³

These findings question the statement that the drug is of low toxicity. There is clearly a real danger of accidental death occurring, not only in alcoholics but also in others who ingest alcohol while taking the drug. The hazards of drinking alcohol while receiving treatment with chlormethiazole should be stressed. In the depressed alcoholic it would seem wiser to avoid the drug altogether.

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¹ *Data Sheet Compendium*. The Association of the British Pharmaceutical Industry, London, 1976.

² Fischler, E, Frisch, P, and Ortengren, B, *Acta Pharmacologica Suecica*, 1973, **10**, 483.

³ Jakobsson, S, and Möller, M, in *Abstracts of the Sixth International Meeting of Forensic Sciences*, Edinburgh, 1972, p 150. The Association of the British Pharmaceutical Industry.

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