The bleeding time (Ivy method) was, however, normal in all 23 patients studied. None of the patients in this small series was thrombocytopenic.

It is unlikely that this acquired platelet function defect will be of clinical significance, but until further experience is gained with this agent it would seem advisable to measure the bleeding time and platelet count before major surgery in patients taking sodium valproate.

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SI units

SIR,—We wrote to you previously (17 May 1975, p 389) protesting against the introduction of the mole and pascal as units of measurement in clinical medicine. We therefore think it appropriate to inform you that the East Anglian Regional Medical (Advisory) Committee has reluctantly concluded that, despite the reservations expressed from many quarters in the medical journals and in correspondence with our committee, the pace of change has been so great that the East Anglian Region can no longer maintain its stand against the new units. Accordingly the committee has advised that the new units should be introduced in the hospitals in the region. Naturally we have stressed the dangers inherent in the changeover and have emphasised the need for adequate education of all concerned and for carefully phased and monitored implementation.

We wish to make known our belief that the professional organisations which advised the DHSS on this matter acted without adequate consultation with those who carry responsibility at the bedside and in the laboratory. We have accordingly written to these august bodies expressing our disapproval and venturing to suggest that in future such far-reaching decisions should be made only after wider consultation with appropriate members of the medical profession.

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Ischaemic necrosis of lesser curve of stomach

SIR,—We read with interest Dr P D Mohr's letter (13 December, p 650) concerning ischaemic necrosis of the lesser curvature of the stomach following highly selective vagotomy, but we cannot accept that interruption of the vasa nervorum accompanying the vagus could possibly jeopardise the viability of the lesser curvature. These vessels are branches of the left gastric artery, which is routinely ligated in many forms of gastric surgery. Indeed Appleby[1] has advocated ligation of the coeliac axis for gastric malignancy and reported 13 cases without loss of viability of the stomach. Forty years ago Wilson-Hey performed a "four-point gastric ligation" for duodenal ulceration in over 300 patients in which the four major arteries to the stomach were ligated without ischaemic necrosis ensuing.

Vagotomy will certainly reduce gastric mucosal blood flow, and patients with gastric ulcers on the lesser curvature have low mucosal flow rates,[2] but the mucosa of the lesser curvature in the dog is as well perfused as other areas of the stomach.[3] Autoradiographs of the rat stomach after administration of $^{86}RbCl$, using the indicator fractionation technique of Sapirstein,[4] have also failed to demonstrate a diminution in the perfusion of the lesser curvature.[5]

In-vivo study of the microvasculature of the gastric mucosa shows a rich syncytium of communicating vessels which is capable of shunting blood towards or away from any particular area provided suitable conditions of vessel control exist.[6 7]

It is well known that the stomach has an almost unrivalled resistance to ischaemic damage. We wonder whether either excessive use of diathermy along the lesser curvature might be responsible for perforation, oedema, and ensuing ischaemic necrosis or ligation of small areas of serosa, including submucosal vessels, might have similar consequences after highly selective vagotomy.

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Massive intoxication with metoprolol

SIR,—Beta-adrenergic-blocking agents are extensively used in Sweden as prophylactic therapy in angina pectoris and as basic treatment for hypertension in young adults. Despite the widespread use of these substances, poisoning is rare. It is therefore of interest to report a case of massive intoxication with the new β_1-receptor blocking drug metoprolol (Seloken, Betaloc, Lopresor). The drug is devoid of intrinsic activity and has very little membrane-stabilising activity.

The 19-year-old son of a hypertensive patient under treatment with metoprolol was admitted to this hospital after a reported intake of 200 50-mg tablets of metoprolol—that is, a total of 10 000 mg or 160 mg/kg body weight. On admission he was conscious and had peripheral cyanosis. The heart sounds were weak. The pulse was palpable in the femoral artery but not in the radial artery. The blood pressure was not registrable. The heart rate was 60-70/min. ECG showed sinus rhythm with normal AV conduction and normal S-T segment and T waves. Blood gas determination showed base excess —5 mmol (mEq)/l, pH 7·41, P_{CO_2} 3·9 kPa (29 mm Hg), and standard bicarbonate 20 mmol (mEq)/l. The patient was treated during the first few hours with 2 l of balanced electrolyte solution (Ringer's solution) and the acidosis was corrected with 150 mmol of sodium bicarbonate. Intravenous administration of 7 mg metaraminol and 6 mg of glucagon raised the blood pressure to 115 mm Hg systolic in 10 minutes. Another fall in blood pressure to 75 mm Hg systolic one hour later was successfully treated with a further dose of 3 mg metaraminol intravenously. The blood pressure then stabilised at a level slightly above 100 mm Hg, which was the patient's usual level.

The initial treatment included gastric lavage, which yielded a cloudy product containing food and tablet residues. During the first six hours there was some fluid retention, which was treated with frusemide. Twelve hours after admission the patient was quite comfortable and without any signs of cardiovascular depression

The plasma level of metoprolol two hours after admission was 12 200 ng/g plasma, at seven hours 9400 ng/g, and at 10 hours 5700 ng/g. After a single dose of 100 mg to healthy volunteers the maximum plasma concentration has been found to be about 100 ng/g plasma on average.[1] To judge from the plasma levels almost all of the ingested dose (10 000 mg) must have been absorbed.

In animal experiments the lethal dose has been found to be 2000-3000 mg/kg in the mouse and rat and at least 10 times lower in the dog.[2] This difference in oral toxicity between the species is explained by the difference in bioavailability, which is 10 times higher in the dog than in the rat.[3] The bioavailability of metoprolol in man is similar to that in the dog.[3 4] The dose of 160 mg/kg body weight ingested by the patient in this case must therefore be near the lethal dose. Plasma levels of metoprolol have been analysed in dogs after oral doses up to 10 mg/kg. The maximum plasma level was 1200 ng/g one hour after administration. The concentration found in the patient—12 200 ng/g—three to four hours after ingestion is therefore what would be expected from the dog data and dose taken.

Earlier reports on suicidal attempts have documented a relatively low toxicity of this type of drug. One patient survived 900 mg of practolol[5] and another 2000 mg of propranolol.[6] In both cases modest signs of cardiac depression were reported.

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Lactic acidosis after glucose infusion

SIR,—Dr A C Ames and others (13 December, p 611) report that after the infusion of glucose, sorbitol, or fructose to women with ketosis in labour there was an increase in blood lactate but an accompanying fall of acetoacetate and 3-hydroxybutyrate levels. The most marked increase in lactate followed the infusion of 30% glucose. In contrast, infusion of normal saline produced a fall in lactic acidosis with little significant change in the level of ketones. Dr Ames and his colleagues conclude, therefore, that while it is known that increased lactic acidosis may occur with fructose, the infusion of sorbitol or glucose should likewise be administered with caution to women in labour because of the hazard of a base deficit in the fetus.