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.

S G N RICHARDSON
D J FLETCHER
P M JEAONS
J STUART

Children's Hospital,
Birmingham

1 Jeaons, P. M., and Clark, J. E., *British Medical Journal*, 1974, 2, 584.

2 Sutor, A. H., and Jesdinsky-Buscher, C., *Medizinische Welt*, 1974, 25, 447.

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.

J T ROBERTS
Honorary Secretary,
East Anglian Regional Medical
(Advisory) Committee

Addenbrooke's Hospital,
Cambridge

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 Appleby¹ 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 ⁸⁶Rb Cl, 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.

T V TAYLOR
BRUCE TORRANCE

Department of Gastroenterology,
Manchester Royal Infirmary,
Manchester

1 Appleby, L. H., *Cancer*, 1953, 6, 704.

2 Taylor, T. V., et al., *British Journal of Surgery*, 1975, 62, 788.

3 Delaney, J. P., *American Journal of Digestive Diseases*, 1965, 10, 201.

4 Sapirstein, L. A., *American Journal of Physiology*, 1958, 193, 161.

5 Taylor, T. V., MD Thesis, University of Manchester, 1975.

6 Barlow, T. E., Bentley, F. H., and Walder, D. N., *Surgery, Gynecology and Obstetrics*, 1951, 93, 657.

7 Taylor, T. E., and Torrance, H. B., *Gut*, 1975, 16, 781.

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 prazosin⁵ and another 2000 mg of propranolol.⁶ In both cases modest signs of cardiac depression were reported.

BENGT HJ MÖLLER

Department of Medicine,
Sundsvall Hospital,
Sundsvall, Sweden

1 Johnsson, G., et al., *Acta Pharmacologica et Toxicologica*, 1975, 36, suppl V, p 31.

2 Bodin, N.-O., et al., *Acta Pharmacologica et Toxicologica*, 1975, 36, suppl V, p 96.

3 Borg, K. O., et al., *Acta Pharmacologica et Toxicologica*, 1975, 36, suppl V, p 104.

4 Regardh, C.-G., et al., *Acta Pharmacologica et Toxicologica*, 1975, 36, suppl V, p 45.

5 Karhunen, P., and Hartel, G., *British Medical Journal*, 1973, 2, 178.

6 Wermut, W., and Wojcicki, M., *British Medical Journal*, 1973, 3, 591.

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.

I note from their table II that there was a marked rise in blood glucose level after the infusion of glucose which was not seen when sorbitol, fructose, or saline was given. The advantage of glucose over fructose or sorbitol is that it demonstrates by such a rise in blood sugar the presence of the "diabetic-like state," similarly encountered in some patients after acute stress by the inhibition of insulin secretion by adrenaline and sympathetic overactivity.¹ It would seem likely that had Dr Ames and his colleagues included a further group of women to whom he had given with the glucose sufficient exogenous insulin to prevent hyperglycaemia this group would also have shown a reduction in ketones but with no rise in blood lactate. Froesch² has pointed out that during muscular work (for example, during labour) glucose is taken up by muscle cells even in the absence of insulin. Its fate, however, is then different, in that it is almost entirely converted to lactate. Under normal conditions the lactate will be metabolised in the liver, but this is prevented when sufficient sorbitol or fructose is infused and also metabolised to lactate in the liver. In the "diabetic-like state" lactate will then accumulate in the blood.³

It has been my experience in treating cases of acute or chronic renal failure complicated by a diabetic response that infusions of glucose accompanied by sufficient insulin to maintain the blood sugar strictly within the normal range prevent both ketosis and lactic acidosis. The advantage of glucose is that its blood level is readily monitored, whereas, as shown by Dr Ames and his colleagues, sorbitol or fructose can produce lactic acidosis without any concomitant rise in the blood sugar. I would suggest, therefore, that glucose with added insulin would fulfil their requirements for a substrate to infuse to women in labour for the treatment of ketonaemia without raising the blood lactic acid level. When insulin is infused at a rate of about one unit per 3 g of glucose hyperglycaemia is unlikely to occur, and none of our cases has become complicated by hypoglycaemia.

STUART J TOVEY

Department of Nephrology,
Southmead Hospital, Bristol

¹ Porte, D. Jr, et al, *Journal of Clinical Investigation*, 1966, 45, 228.

² Froesch, E R, and Keller, U, in *Parenteral Nutrition*, ed A W Wilkinson. Edinburgh and London, Churchill Livingstone, 1972.

³ Woods, H F, and Alberti, K G M M, *Lancet*, 1972, 2, 1354.

Cancer statistics

SIR,—Dr R F Mould's criticisms of cancer statistics (10 January, p 86) referred to the registration procedure and the Department of Health and Social Security statistical return SH3. The former is a matter for the Office of Population Censuses and Surveys; my immediate concern is to point out the inaccuracies and misunderstandings present in the criticism of the SH3 return.

There is evident confusion in Dr Mould's interpretation of the data collected in part 2 and part 3 of the form. The former records patients attending for consultation with medical staff whereas the latter is concerned with attendances for treatment not necessarily in the presence of medical staff. Patients attending for consultation do not necessarily attend a

treatment department and vice versa. In general the counts in parts 2 and 3 will not correspond and the relative sizes of the consultation and treatment counts at department level will depend on specific characteristics such as the type of service provided and referral patterns.

Dr Mould appears to have been misled by the identical figures for new outpatient consultation and treatments for two of the hospitals in his sample. Far from being the typical situation, these events are due to particular features of the radiology departments concerned. In one case, for example, it is known that all patients attending the radiotherapy department for the first time do so for treatment, the need having been confirmed elsewhere.

In the absence of specific instances the allegation of general ambiguity in the instructions for completing the form can be answered only in broad terms in a letter such as this. The treatment and care of patients are the responsibility of consultants; practice varies widely and it is very difficult to reflect this in a summarised statistical report such as SH3, which offers only a broad framework for measurement of hospital activity. Detailed notes are issued annually and the inevitable compromise has to be struck between excessive detail and insufficient guidance for consistent recording. These notes are reviewed every year both in response to known changes in the provision of care and as a result of queries received, generally from hospital medical records officers. I do not, of course, claim complete accuracy for every figure on each of the 3000 returns received annually. There are problems of misinterpretation of instructions, and recording errors do occur. Each return is subject to reasonable validation centrally, consistent with the accuracy required for the uses of the return.

For hospital statistics in general a single definition of new outpatient is in use and this relates to the first consultation or the commencement of treatment for a particular complaint. In radiotherapy post-treatment monitoring may continue for years following formal discharge to the care of a general practitioner. There may be a tendency to view recommencement of treatment as a continuation of a previous episode and to fail to record this as a new episode. This will affect both consultations and treatments and hence the balance between the two will remain unchanged. However, total workload as measured by attendances will be counted correctly.

F E WHITEHEAD

Chief Statistician,
Statistics and Research Division,
Department of Health and Social Security
London WC1

Modern obstetrics and the general practitioner

SIR,—I was surprised to find no mention in the article by Professor E Wilkes and others (20 December, p 687) of the need for GP obstetricians to become competent in the care of the newborn infant.

Now that maternal mortality has reached near rock-bottom perinatal mortality and morbidity have become a major concern to obstetricians; and if domiciliary midwifery is to survive, as I hope it will, and 24-48-hour admission to become the mode in maternity units it is the more important that those

responsible for mother and baby should be able to undertake the resuscitation of either than to act as a midwife or subconsultant and also that they should be familiar with the medical management of neonatal problems, including feeding, infection, jaundice, and congenital anomalies.

It is to be hoped that in future neonatology will once more become a mandatory part of obstetric training for GPs and consultants. Otherwise, for the baby, birth will be safe only in large units with a 24-hour paediatric service.

J A DAVIS

University Department of Child Health,
St Mary's Hospital,
Manchester

Surgical policy after Cyclone Tracy

SIR,—In his "Letter from South Australia" (16 August, p 419) Professor P Rhodes states: "the surgical policy was to excise wounds and primarily suture the skin, prior to evacuation." All surgeons of the armed Services will know full well the hazards involved in dealing with traumatic wounds by primary suture, and they will not be surprised to hear that there were a number of infective complications in the patients whose wounds were so treated at Darwin. These included some cases of gas gangrene.

As consultant surgeon to the Royal Australian Army Medical Corps it is my duty to point out that it remains our policy to deal with all traumatic wounds by delayed primary closure. This means that after proper excision of the damaged tissue the wound is left open for three or four days, after which it is closed either by direct suture or by the application of split skin grafts. Only by this method are such wounds rendered safe—safe against the hazards of anaerobic infection, safe against the hazards of primitive conditions and lack of supervision during evacuation. I am sure that all military surgeons will agree that no antibiotic cover is adequate to allow the treatment of these wounds by primary suture.

The surgeons of Darwin who worked under such adverse conditions a year ago now admit freely that their policy of primary suture for such wounds should not be taken as a precedent for the future. The only safe way to manage traumatic wounds is by delayed primary closure.

DOUGLAS LESLIE

East Melbourne,
Victoria, Australia

Hypothermia associated with nitrazepam administration

SIR,—We wish to report a case of hypothermia which occurred in an elderly patient following the administration of 5 mg of nitrazepam.

A woman aged 86 was admitted to the geriatric unit of this hospital in March 1975 with a one-year history of senile dementia, malnutrition, and iron deficiency anaemia. She was transferred to our long-stay wards on 16 July after successful treatment of her anaemia but an unsuccessful attempt at rehabilitation, being disorientated in time and space, incontinent of urine, and chair/bed-bound. She was then receiving no medication. At 10 pm on 27 July she was given 5 mg of nitrazepam, having been restless and sleepless the night before. At 10 am on the following morning she was drowsy, her pulse was 56/min, her blood pressure was 105/55 mm Hg, and the skin on her abdomen, felt cold. Her rectal temperature was 33.9°C