

to the wound, a portion often dusting the floor. We thought that if the powder could be made more adherent—for example, by using it in a paste—we could circumvent these problems. Saline and glycerol were suggested, but both of these liquids would initiate swelling of the polymer, reducing its ability to absorb wound exudate and prematurely releasing iodine. We decided to try using macrogol 400 (polyethylene glycol 400), which is one of a series of condensation polymers of ethylene oxide and water, the number indicating the average molecular weight.¹ The molecules of macrogol 400 are too large to enter the Iodosorb matrix, and the compound is a hydrophilic, stable, and non-irritant liquid.² Iodosorb powder (3 g) is mixed with a small amount (about 0.5 ml) of macrogol 400, the paste is applied quite thickly to the surface of the wound, and a dry gauze dressing and support bandage are applied as usual.

The advantages from the nurses' point of view are easier application and removal of the paste compared with plain Iodosorb while efficacy is maintained. Stinging on application of the paste seems less than with Iodosorb, and, in general, patient acceptability has been good. We have had no sensitivity reactions to the paste. It is well documented that reactions to iodine occur in about 1% of patients when iodine is widely used in the population,³ and to macrogol 400 in 0.3% of eczematous patients⁴; to date, however, we have had no reactions to either ingredient or their combination.

We feel that our method of application of Iodosorb has distinct advantages over the manufacturer's current recommendations and justifies further consideration.

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Fatal immune haemolysis associated with nomifensine

SIR,—Dr R J Sokol and colleagues describe a fatal case of immune haemolysis induced by nomifensine (3 August, p 311). In their case, and in other reported cases,¹⁻⁶ there was acute intravascular haemolysis with haemoglobinuria. As in most of the other reported cases there was acute renal failure. The antibody in their case produced its effect by the "innocent bystander" mechanism—that is, the drug and antibody combined together and then bound to red cells. Activation of complement followed, producing acute intravascular haemolysis.

I report a case of chronic autoimmune haemolytic anaemia associated with nomifensine. A 56 year old woman had been taking nomifensine for three months when mild congestive cardiac failure developed. Haemoglobin concentration was 85 g/l; the reticulocyte count was 8%. Spherocytes were seen in the blood film. Results from a direct antiglobulin test were strongly positive for IgG. Serum bilirubin concentration was raised (24 µmol/l (1.4 mg/100 ml)), and serum urea concentration was normal. Haemoglobinuria was not seen.

Two weeks later the haemoglobin concentration was 83 g/l. Treatment with nomifensine was then stopped. During the next six weeks haemoglobin

concentration rose steadily to 135 g/l. Results from the direct antiglobulin test were still strongly positive five months after stopping nomifensine treatment.

The mechanism of haemolysis in this case is similar to that seen in patients taking methyldopa.⁷ The antibody is directed against a red cell antigen, not the drug. Haemolysis is not intravascular. Results from the Coombs test may remain positive for months after the drug has been stopped.

Thus nomifensine can produce immune haemolytic anaemia by two different mechanisms with different clinical features. Acute intravascular haemolysis is soon obvious, but mild chronic haemolysis may be undetected in a patient taking nomifensine as symptoms of anaemia may be ascribed to depression.

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What about the bleeding time?

SIR,—Dr T J Hamblin's leading article (13 July, p 91) is admirable for its brevity. It is unfortunate, however, that the take home message for the general reader is misleading with regard to the advice given on the normal range.

It is our experience, and that of others, that an upper normal limit for the Simplate device of 8.5-10.5 minutes is too high. In a controlled study of 21 female and 19 male normal volunteers we established an upper limit of 6.25 minutes (mean+2 SD) and a range of 2.25-5.5 minutes (men) or 1.75-6.5 minutes (women).¹ This confirmed our uncontrolled clinical experience that patients with significant qualitative platelet defects or von Willebrand's disease could be missed using the range quoted by Dr Hamblin, which I believe is extracted from the notes provided by the manufacturer of the device. It is the policy in our laboratory to consider a bleeding time of less than 6.5 minutes as definitely normal; greater than 9.5 minutes as definitely abnormal; and between 6.5 and 9.5 minutes as more or less important, depending on other available information, particularly a personal or family history suggestive of a bleeding diathesis. I should emphasise, however, that these data are applicable only to adults.

I am not aware of any good paediatric data. Our uncontrolled experience is that many prepubertal children may have Simplate bleeding times of up to 12 minutes without a haemostatic abnormality detectable by further investigation. This probably relates to technical difficulties related to skin thickness, etc. Consequently, it is our policy not to pursue aggressively further investigation of children with bleeding times of 12 minutes or less in the absence of a significant clinical history or prolongation of the remaining coagulation screening tests performed in our laboratory—that is,

activated partial thromboplastin time, prothrombin time, thrombin clotting time, and full blood count.

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Diabetes, driving, and the general practitioner

SIR,—The recent paper by Drs B M Fisher and others (20 July, p 181) prompts me, a non-member of the medical fraternity, to draw attention to what appears to be an ignored aspect of gastric surgery—namely, the dumping syndrome, hypoglycaemia, and driving.

As a result of gastric surgery I suffer from the dumping syndrome and have found from experience that my concentration while driving is severely affected for at least an hour after meals. As a careful driver I find that my inability to react normally to stimuli such as pedestrian crossings, children, other vehicles, etc., and my total lack of judgment during these periods, is frightening in the extreme. Consequently, I now do not drive within one and a half hours after a meal.

I have never been warned about the dangers of driving while hypoglycaemic and thus felt duty bound on reading the paper by Dr Fisher and others to point out that all subjects with hypoglycaemia (however acquired) should be counselled on the risks of driving while in that condition, the advice not being restricted to diabetics alone.

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Comparison of barium swallow and ultrasound in diagnosis of gastro-oesophageal reflux in children

SIR,—In recent years several investigatory procedures have been used to detect gastro-oesophageal reflux in children in addition to conventional radiology—acid reflux tests, 24 hour intraluminal oesophageal pH probe monitoring, isotope scintigraphy, and, as advocated by Dr D R Naik and his colleagues (29 June, p 1943), ultrasound. The use of these techniques has confirmed the frequent occurrence of gastro-oesophageal reflux, especially in infants. It is now generally accepted that this finding usually constitutes a normal physiological event. Recognition of reflux per se does not therefore necessarily establish a causal relation with the clinical disorder under investigation. In most instances it is more likely to be a coincidental finding. Nevertheless, some investigators have tended to consider all gastro-oesophageal reflux as being actually or potentially harmful—a particularly regrettable interpretation when taken to the point of surgical intervention.

A major problem confronting the clinician is therefore one of having to decide whether gastro-oesophageal reflux is physiological or pathological—that is, clinically important. The need for some objective distinguishing criteria is thus of major clinical importance. Objective criteria aimed at distinguishing between physiological and pathological reflux can be accurately defined only by reference to detailed clinical assessment of the natural history and response to treatment of a large series of infants with reflux. In my 35 years' experience of this problem I have found that in