

Britain this solution is called Synthamin. Recently minor elevations of serum bilirubin concentration and major elevations of serum alkaline phosphatase and aspartate aminotransferase activities have been observed in six patients receiving this solution following surgery of the head and neck. These patients did not have evidence of metastatic disease and no abnormalities have been observed in patients undergoing similar operations who did not receive nutritional support.

However, the same type of biochemical abnormalities have been seen in a patient receiving the intravenous amino-acid solution Vamin. Furthermore, 15 patients who received a nasogastric diet based on the beef protein derivatives Albumaid or Serameen and the glucose polymer Caloreen showed the same biochemical response. This latter observation would suggest that cholestasis occurring in patients receiving intravenous nutrients is unlikely to be due to a lack of stimulation of bile flow by food in the gut. Are these changes due to the absence of some dietary component or presence of some chemical agent that is common to artificial diets whether given intravenously or by the nasogastric route? These results will be reported in detail elsewhere.^{2 3}

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¹ Allardyce, D B, in *Advances in Parenteral Nutrition*, ed I D A Johnston. Lancaster, MTP, 1978.

² Skidmore, F D, *et al*, *Annals of the Royal College of Surgeons of England*. In press.

³ Tweedle, D E F, *et al*, *Research and Clinical Forums*. In press.

Primary autoimmune diabetes mellitus

SIR,—We were interested in the further evidence provided by Dr G F Bottazzo and his colleagues (4 November, p 1253) in support of a primary autoimmune type of diabetes mellitus (type 1a). Our own experience, including 61 (6 male, 55 female) insulin-dependent diabetics (IDDs) with coincident Graves's disease and 107 (16 male, 91 female) IDDs with primary thyroid failure confirms the characteristics of such a group of IDDs to include female preponderance, lack of seasonal variation in incidence, late age of onset, and a strong family history of organ specific autoimmune diseases including insulin-dependent diabetes.

Dr Bottazzo and his colleagues estimate that type 1a diabetics account for less than 10% of insulin-dependent patients but provide no evidence in support of this figure. We have considered the prevalence of the more common organ-specific autoimmune diseases in 445 IDDs attending the diabetic outpatient department of this hospital consecutively during the months April and May 1978. We found 23 (5.2%) to have had Graves's disease, 11 (2.4%) to have overt primary hypothyroidism, 14 (3.2%) to have pernicious anaemia, and one to have Addison's disease. Allowing for one patient who had both pernicious anaemia and Graves's disease, 48 patients (10.8%) had one or more organ-specific autoimmune disease, of whom 37 (77%) were female and 31 (65%) were first recognised to be diabetic over the age of 30 years.

These figures do not take account of the

prevalence of unrecognised thyroid failure in the diabetic population. Of 184 IDDs in whom a diagnosis of thyroid failure had not previously been suspected, 24 (13%) had a raised serum thyrotrophin concentration, of whom 8 (4.3%) had a low serum thyroxine concentration.

Thus we are confident that Dr Bottazzo and his colleagues have underestimated the proportion of IDDs who should be included in the category of type 1a diabetics.

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Tetracycline preparations for children

SIR,—Dr R J Rowlett's remarks (18 November, p 1436) on this subject prompt me to report the following information on the extent of prescription of these preparations.

I examined all prescriptions issued during February 1976 by a randomly selected sample of 12 general practitioners in the Grampian Area. A total of 328 prescriptions for tetracyclines had been issued, but only seven of these were for liquid tetracycline preparations. Four of the 12 doctors were responsible for these prescriptions and each had issued from one to three prescriptions for liquid tetracycline during the month in question, the mean quantity per prescription being 150 ml.

Not all of these prescriptions for liquid tetracycline would necessarily have been issued to children. The information therefore suggests that, in this area at least, the prescription of tetracyclines to children had been reduced to insignificant levels by 1976.

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Practical problems with insulin infusion pumps

SIR,—In their article on the use of intravenous insulin infusions in diabetic emergencies (11 November, p 1343) Drs R D G Leslie and J D Mackay mention that on two occasions the insulin infusion pump was accidentally switched off. We have encountered similar practical problems with the use of infusion pumps in the management of diabetic ketoacidosis. On two occasions the connection at the proximal end of the drip tubing has been slightly dislodged from the indwelling intravenous cannula by restless, uncooperative patients and the pump has subsequently infused the bedclothes rather than the patient. On two further occasions a three-way tap situated between the pump and the patient has been inadvertently closed, resulting in failure of insulin delivery. We have even seen failure to switch on the mains supply. Fortunately these slips have had no serious consequences, but they nevertheless illustrate the potential for human error in the use of these pumps, which we feel detracts seriously from their value in acute situations. Mishaps are more likely to occur and to remain undetected in restless, semicomatose patients, who may tug endlessly at the drip tubing.

The practical difficulties of supervising the insulin infusion in addition to the various other lines, catheters, and monitor leads while also

perhaps restraining the patient are obvious, and it is hardly surprising that mishaps occur, even with the best nursing care and adequate staffing. Since the benefits of low-dose intravenous over low-dose intramuscular insulin therapy are marginal it would seem sensible to use the latter, safer, route in diabetic ketoacidosis. These remarks do not apply to the use of insulin infusion pumps in less critical situations, such as in the postoperative management of diabetic patients, where they are much safer and undoubtedly effective.

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Data sheets and lactation

SIR,—As authors of the articles^{1 2} on drugs and breast-feeding described by Dr C D E Morris (18 November, p 1435) as "incomplete, inaccurate, and misleading" may we comment on his letter? Dr Morris complains that UK drug data sheets contain no reference to safety of the drug for use in lactating women. However, quantitative information on drug transfer in milk is available for very few drugs. Similarly the maximum "safe" dose of almost any drug taken by a suckling neonate in breast milk is unknown. For the majority of drugs, then, their safety in this context is still a matter of judgment, the exception being those drugs which we listed as contra-indicated, such as carbimazole and amantadine, where definite adverse effects have been reported. More research on drug transfer is desirable.

In this situation it is not possible for precise advice to be included in the majority of drug data sheets. In our articles we attempted to help doctors by pointing out that centrally acting drugs (anticonvulsants, sedatives, etc) have low plasma levels in relation to effective oral doses so that the concentration of drug in breast milk will generally be low also. The majority of these drugs will therefore be safe for lactating women to take, but no drug manufacturer could state this categorically in a document for which he has legal responsibility. If a statement in the data sheet is made compulsory, then most companies will play safe and recommend that the drug be withdrawn during breast-feeding.

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¹ Lewis, P, *Journal of Maternal and Child Health*, 1978, 3, 128.

² Harvey, D, *Modern Medicine (Great Britain)*, 1978, 23, 87.

Breakfast and Crohn's disease

SIR,—I venture to claim that the data of Dr J F Mayberry and others (18 November, p 1401) support my own¹ provided that equivalent figures are compared. In my study I took account of pre-illness habit. Their tabulated data record current habit, but they go on to tell us that 33 of the patients and 13 of the controls had stopped eating cornflakes, having previously taken them regularly. It follows that if pre-illness habit had been

recorded 62 of their 100 patients and 35 of their 100 controls would have been classified as regular cornflake eaters ($\chi^2=14.6$, $P<0.001$).

They have thus shown that 53% of regular eaters of cornflakes abandoned the habit when they developed Crohn's disease, bearing out my comments (9 September, p 767) on the findings of Drs L N J Archer and R E Harvey (19 August, p 540). I accept that recollection may be faulty, but the authors have recorded these data and the inference is there to be drawn.

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¹ James, A H, *British Medical Journal*, 1977, 1, 943.

Inadequacy of information on side effects

SIR,—At this hospital three patients have developed haemolytic anaemia due to phenazopyridine (Pyridium) in the past five years. They all showed exactly the same haematological features as the patient described by Drs H C Drysdale and M D Hellier (7 October, p 1021) and in all three the haemolysis ceased when the drug was stopped.

With this experience in one small health district, I find it difficult to believe that this particular complication of Pyridium therapy is as rare as the literature and Dr Witherspoon (p 1021) suggest. It should certainly not be classed as a "rather rare suspect event."

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Computer confidentiality

SIR,—The second of the three ethical principles which the Child Health Computing Committee has put forward to govern computing systems (11 November, p 1382) does not protect the right of the patient's parents to control the distribution of medical information about their child. I consider the following addition (in italics) to be essential:

(2) "Access to identifiable information held in medical records is to be confined to the author and to the person clinically responsible for the patient during the episode for which the data has been collected (or their successors) unless specifically authorised by the clinician in the clinical interest of the patient *and by the patient (or his or her parent or guardian).*"

I would have thought that this point was elementary and am very surprised by the apparently widespread British practice of sending copies of children's medical reports to school medical authorities without the knowledge and consent of the parents. Such behaviour, irrespective of its motives, should be made clearly illegal. It cannot be excused by saying that it is "well meant" or "for the ultimate good of the patient"; it is for the patient (or his parents) to decide what is for his ultimate good and it is for him to decide whether a copy of a medical report should be sent to the school medical authorities, Uncle Tom Cobley, or anyone else. As soon as patients learn that a "mailing list" (of which they have no knowledge) may be appended to any information which they divulge in the consulting room they will learn to be selective when talking to their doctors. And that, as you

probably realise, would be the beginning of the end of the doctor/patient relationship which people often enthuse about.

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Scombrototoxic fish poisoning?

SIR,—I recently observed a reaction which occurred 30 minutes after eating a Bombay duck, which is a type of dried fish. The patient developed headache and nausea concurrently with a flushing of the face, chest, and shoulders, and the lips became swollen. The redness of the face and upper trunk gave way to a blotchy urticarial pattern with weals after a further five minutes. An intramuscular injection of chlorpheniramine maleate 10 mg was followed by a dramatic improvement and one hour later the patient was completely recovered and had no further relapses.

I am not sure whether this reaction was due to scombrototoxic fish poisoning (9 September, p 739) or to simple allergy, but the patient has no allergic history and has eaten Bombay duck since with no ill effects.

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Intrauterine hiccup

SIR—Having just returned from five years of North American investigative medicine I find it delightful to read that the diagnosis of intrauterine hiccup is yet another use for real-time ultrasound scanning (Dr I Swann, 25 November, p 1497).

Most senior house officers who deal with postnatal patients would confirm our own clinical impression that intrauterine hiccups occur frequently (approximately one per 50 live births). They are noted by the end of the second or beginning of the third trimester and recur in subsequent pregnancies. They frequently occur at the same time of day for each patient and persist after birth. All the babies that we have seen have been normal. Most of our mothers correctly diagnosed themselves antenatally. This was usually confirmed by their midwife and so far there has been no need for a scan.

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Conservation surgery for laryngeal cancer

SIR,—Your leading article (11 November, p 1318) on this subject was timely, factual, and well informed. In the last paragraph you ask whether British laryngologists are perhaps unduly hesitant to use these techniques—presumably supraglottic partial laryngectomy—for irradiation failures. I therefore write to assure you that our unit at this hospital is devoting time and study to this problem.

Patients with suitable lesions are uncommon and assessment of the extent of disease after irradiation so difficult that a firm decision for a partial operation can be made only on the operating table. In my experience no more than a small minority prove to be treatable and curable in this way, the majority requiring total laryngectomy. Nevertheless, such efforts

are rewarding and further salvage may be possible by total resection if recurrence takes place. It must also be said, with emphasis, that all patients with laryngeal cancer at any site must be observed before and regularly throughout irradiation treatment by the radiotherapist and the surgeon, who will operate if treatment fails. Only in this way can the surgeon hope to gain an approximate idea of the extent of disease. It is also my belief that by ignoring the curative value of treatment by initial supraglottic laryngectomy as now demonstrated in many centres outside Britain we are condemning more patients to eventual total laryngectomy if irradiation fails.

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Nutrition and the cancer patient

SIR,—Mr A J Strain and his colleagues (4 November, p 1295) discuss the unavailability of appropriate animal models for the study of cancer-associated cachexia. I would certainly agree that the readily available rapidly growing transplantable tumours of laboratory rodents do not provide realistic models of cachexia in that significant loss of body weight does not usually ensue until tumours approach 40% of the body weight. Large tumours, especially when ulcerated, are commonly associated with extreme anaemia; the coincident weakness may itself discourage animals from eating and so give rise to a constitutional state indistinguishable from starvation.

In my experience of over 30 mouse tumours which have been maintained by serial transplantation for prolonged periods wasting is rarely seen in mice bearing tumours of up to 3 g ($\approx 10\%$ of body weight). The exceptions have been three squamous carcinomas (one arising in skin and two in the fore-stomach); all have been associated with extreme wasting at relatively small tumour sizes. In a comparative study of one of these tumours with a mouse mammary carcinoma (MMC) growing at about the same rate we observed that the squamous tumours when grown to a mean weight of only 1.1 ± 0.8 g were associated with a mean loss of body weight of 16% (range 0-30%). In contrast no loss of body weight was associated with growth of the MMCs to a mean weight of 4.6 ± 2.3 g. The wasted mice bearing squamous carcinomas rapidly became moribund and showed a depression of blood glucose concentration from the normal 8 mmol/l (145 mg/100 ml) to between 5.6 and 4.4 mmol/l (100 and 80 mg/100 ml) (as seen in mice starved for 24 h). Wasted mice did not appear to reduce their food intake (as measured by reduction in the weight of the food pellets to which they had access), but we did have some evidence that the food taken was not being masticated or swallowed. Since one of our squamous carcinomas has been shown to produce epidermal chalone¹ we entertained a hypothesis that such chalone inhibited mitoses in the normal squamous epithelia of tumour bearers and that this could reduce cell replacement in squamous mucosa and so give rise to painful mastication and swallowing. In support of this hypothesis was our finding that the mitotic rate in squamous epithelia (tongue, oesophagus, and fore-stomach) of wasting mice was reduced to between 50% and 20% of normal. However, we could not establish whether the mitotic inhibition preceded or followed the wasting.

It is of interest that the diet given to mice which exhibited cachexia was a standard formulation and fully supported weight output of weanlings. Wasting was not seen when the diet was changed to one with a higher fat content.

The point to be made here is that distinctive