

Europeans is low; overt diabetes is seen in 3-12% and glucose intolerance in up to 35% of offspring.¹ In a large series of offspring of conjugal diabetic parents in India we found that 50% had overt diabetes and 12% impaired glucose tolerance.² Thus 62% of offspring have abnormal carbohydrate tolerance and this figure exceeds by far those reported in any European series.

Reports from India³ and South Africa⁴ have shown that the form of diabetes referred to as maturity onset diabetes of the young is common in Indians but uncommon among Europeans.⁵ This type of diabetes is associated with autosomal dominant inheritance. One of us (VM) had the opportunity of working at Ealing Hospital and seeing some of Dr Mather's patients. Vertical transmission of diabetes and diabetes in parents were both more common in Asian patients, suggesting that dominantly inherited diabetes is more frequent in Asians than in Europeans.

We do not agree with Dr Hugh Trowell (30 November, p 1572) that the high prevalence of diabetes in Indians could be due to their eating rice and consequent low fibre intake. Firstly, Southall Asians are mostly Punjabis and Gujaratis and both communities eat wheat chapatis more commonly than rice. Secondly, there is no evidence to suggest that the prevalence of diabetes is higher in south India, where rice is the staple food, than in north India, where wheat is the staple diet. Thirdly, a recent analysis of the diabetic diet taken by patients at our diabetes centre at Madras in south India showed that it contained 52 g of dietary fibre, which is about double that of the standard American diabetic diet.⁶ Along with rice or wheat Indians usually eat pulses and legumes, which are rich sources of natural fibre.

The high prevalence of diabetes in migrant Indians probably results from multiple factors rather than a single one. In a background of stronger genetic influence a combination of factors consequent on changes in lifestyle and prosperity probably act together. These factors could include overnutrition, overweight (sometimes even marginal), and decreased physical activity. The problem faced by epidemiologists is to study the influence of these environmental factors separately as there is often overlap between some or all of them.

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Water intoxication

SIR,—In reply to Dr M E Dodson's criticisms (30 November, p 1577) we wish to point out that our comments were principally directed towards water intoxication occurring during percutaneous nephrolithotomy, this (absorption secondary to extravasation) being a more insidious problem than the acute intravenous infusion of irrigant through open prostatic veins during transurethral resection. As the mortality of water intoxication is directly related to the rapidity with which it occurs,¹ treatment should be adjusted accordingly.

In his leading article on water intoxication in patients with psychiatric illness (7 December, p 1594) Dr I N Ferrier writes, "Infusion of hypertonic saline has been advocated, though serious complications may result from this treatment." Under these circumstances fluid restriction remains the mainstay of treatment, which, under surgical conditions, amounts to recognition of the problem and abandonment of the procedure.

With respect to Dr Dodson's subject—water intoxication occurring during transurethral resection of the prostate—we are still wary of advocating the use of hypertonic saline except when neurological manifestations of the syndrome ensue. Our scepticism is shared by others: Pierce considered hypertonic saline potentially lethal since it may readily precipitate pulmonary oedema²; Rhymer *et al* advocated using a diuretic alone³; Bird *et al* suggested that the only effective treatment was to discontinue all fluids and await the spontaneous diuresis⁴; and Berg *et al* considered the routine use of hypertonic saline to be illogical except in the treatment of serious (central nervous system) effects of water intoxication.⁵ The use of hypertonic saline is made more controversial as a result of impaired renal handling of sodium in these patients, secondary to expansion of the extracellular fluid and suppression of aldosterone, which results in the prompt excretion of any sodium load in the urine.⁶ Furthermore, this effect is increased after spinal anaesthetic (the commonest form of anaesthesia in transurethral surgery), as a result of both the pre-load intravenous infusion and impaired postoperative sodium retention—that is, indicating a further source of aldosterone suppression.⁷ Synchronous administration of a loop diuretic will further exacerbate the kidney's inability to conserve sodium. Equally there are those authors whose experience is such that they admonish any criticism of hypertonic therapy, although in the case reported by Charlton the improvement in cardiac function was just as likely to be a response to calcium gluconate administration (dilutional hypocalcaemia) as to hypertonic saline.⁸

We therefore feel that it is difficult to be dogmatic about either form of therapy and that given the choice we would use that which is effective and least hazardous to the patient. Once again we are drawn to the same conclusion: the fundamental of treatment is abandoning the procedure once it is determined that water intoxication is occurring.

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Children in cars

SIR,—We are always pleased to find colleagues interested in preventing children's accidents, but there are some points in the paper of Ms Ruth Eatough and others (19 October, p 1092) that puzzle us.

Firstly, they state, "If the rear anchorage point is too near the back of the seat in an estate or hatchback car the wearer can move within the restraint" and readers are referred to the figure. The figure does not show this but only anchorage points. Surely what they mean is that the straps will be more effective in restraining the car seat itself if the upper anchorage point is "ideal" rather than incorrect.

Secondly, we do not understand the figures on the fitting of the anchorage points. They say, "Full information was obtained for 95 of the 108 back seat restraints fitted, of which 34 were incorrectly anchored." They then state that 29 out of 55 fitted by owners were correctly fitted—that is, 26 were incorrectly fitted—and 9 out of 24 fitted professionally were correctly fitted—that is, 15 were incorrectly fitted. This gives a total of 41 incorrectly fitted out of 79 and not 34 out of 95.

Thirdly, they say, "In 1983 577 car and van occupants under the age of 14 were killed or seriously injured." Table 38 of *Road Accidents Great Britain 1983* indicates that there were 70 deaths and 1008 seriously injured casualties among children under 14 years in cars and light vans.¹

In 1980 the Child Accident Prevention Trust published the report of a working party which included members from the Department of Transport and the Transport and Road Research Laboratory.² Its recommendations were used by the department as the basis of the current regulations relating to children. We agree that these are less than ideal, and this was recognised by the working party. However, regulations have to be understandable, acceptable, and enforceable and there was no possibility of the recommendations of the British Standards Institution and Department of Transport, which are ideal from the safety viewpoint, being introduced by regulation in 1980, when public understanding and acceptance of seat belt legislation was less than it is now.

Nevertheless, change and improvements will come, and in view of the proposed introduction of the compulsory fitting (not wearing, be it noted) of rear seat belts our working party is being recalled to review the situation and possibly advise about further regulations.

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- 1 Department of Transport, Scottish Development, Welsh Office. *Road accidents Great Britain 1983*. London: HMSO, 1984.
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Handling cytotoxic drugs

SIR,—The use of cytotoxic drugs is increasing both within hospitals and in the community. The potential hazards to those handling and especially those reconstituting these drugs has been recognised and was highlighted in his leading article by Dr C J Williams (9 November, p 1299). Many regional health authorities along with the Health and Safety Executive have formulated policy documents on the handling of cytotoxic agents. The problems now probably lie with the occasional user of cytotoxic drugs, especially those in smaller hospitals and in some general practices. The question is how best to inform staff of the potential hazards and correct procedures to use when handling cytotoxic agents.

The Committee on the Review of Medicines (CRM) has considered this subject and agrees with Professor B M Colls's observation that there is considerable variation in both the quality and the quantity of information carried in the current data sheets. The CRM has drawn up the following guidelines which it would like to see included in both data sheets and package inserts: (a) trained personnel should reconstitute the drugs, (b) reconstitution should be carried out in designated areas, (c) protective clothing (including gloves) should be worn, (d) the eyes should be protected and means of first aid should be specified, (e) pregnant staff should not handle cytotoxic drugs, and (f) adequate care should be taken in the disposal of waste material, including syringes, containers, and absorbent material.

Whereas the data sheet may be read by only the medical practitioner, the package inserts are more likely to be read by those actually handling the drugs (nurses and pharmacists). These proposals have already been discussed constructively at a recent meeting between the CRM and the Association of British Pharmaceutical Industries.

The CRM recommends that its guidelines should be incorporated into data sheets and package inserts along with any additional warnings the individual companies may feel to be appropriate. This approach should answer the deficiencies in the existing information and help to limit potential hazards to those handling these useful drugs.

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Infiltrating lobular carcinoma of the breast

SIR,—The leading article by Drs Anthony Howell and Martin Harris (16 November, p 1371) failed to make two important points about this disease. Firstly, it did not make it clear that a definite histological diagnosis of lobular carcinoma is not always possible. None of the individual features mentioned are in themselves diagnostic, including the so called characteristic "Indian file" pattern, and even using them in combination one is left with a small but significant number of carcinomas that cannot definitely be categorised as either lobular or ductal.

Secondly, the fact that infiltrating lobular carcinoma is often accompanied by lobular carcinoma in situ was not discussed. This is clinically important because lobular carcinoma in situ is usually multicentric and may be bilateral. Because of this most would advocate more extensive treatment than "lumpectomy" alone for this type of carcinoma: either mastectomy or lumpectomy plus irradiation of remaining breast tissue. Careful follow up for detection of carcinoma in the contralateral breast is essential and a case can be made for contralateral breast irradiation or even mastectomy when this histological type of breast carcinoma is diagnosed.¹

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SIR,—Drs Anthony Howell and Martin Harris ask what a diagnosis of infiltrating lobular carcinoma means to the clinician and then fail to provide a complete answer.

The major importance of recognising infiltrating lobular carcinoma of the breast lies not in its pattern of recurrence, or in its increased incidence of oestrogen receptors, but in the high reported incidence of synchronous and metachronous involvement of the second breast by carcinoma.¹ This incidence varies from 17%² to 36%³ in reported series and has led to the proposal that patients with infiltrating lobular carcinoma should have contralateral mastectomy⁴ or an elective contralateral breast biopsy⁵ in addition to appropriate treatment for the homolateral lesion.

Our recent work confirms that women with infiltrating lobular carcinoma of the breast are almost twice as likely as women with other types of breast carcinoma to develop a second breast cancer. It also shows that a second carcinoma detected by careful follow up and treated appropriately does not reduce the subsequent survival in

these patients. As there is no effective treatment for metastatic disease, the main purpose of follow up is to detect disease when it is potentially curable.⁶ A second carcinoma is potentially curable and it should be clearly understood that a diagnosis of infiltrating lobular carcinoma of the breast means that the contralateral breast should be regularly screened for the rest of the patient's life.

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- 1 Dixon JM, Anderson TJ, Page DL, Lee D, Duffy SW, Stewart HJ. Infiltrating lobular carcinoma of the breast: an evaluation of the incidence and consequence of bilateral disease. *Br J Surg* 1983;70:513-6.
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SIR,—In response to the points raised by Dr Cary and Mr Dixon we would like to make the following comments.

Firstly, it is correct to say that a definite histological diagnosis of infiltrating lobular carcinoma is not always possible. The usual difficulty is provided by a carcinoma which displays a subtle blend of lobular and ductal features, making a clear cut categorisation impossible; in our experience such tumours are infrequent. A further occasional problem arises when a carcinoma has a genuinely mixed pattern of typical lobular and typical ductal features in different areas. For example, we have recently seen a carcinoma which combined both invasive and in situ elements of typical ductal and lobular types. Such tumours should be reported as "mixed pattern" with the components specified.

Secondly, we agree that the published evidence indicates that lobular carcinoma is associated with a higher rate of multicentricity and bilaterality than in ductal carcinoma, although, as Mr Dixon indicates, the estimates of bilaterality vary widely. Mr Dixon suggests that the importance of a diagnosis of lobular carcinoma is that the contralateral breast "should be regularly screened for the rest of the patient's life" because of the high risk of development of a later (or metachronous) second primary carcinoma. In his own series¹ (so far as we can judge) 10 out of 103 patients (9.7%) with infiltrating lobular carcinomas and 17 out of 250 patients (6.8%) with infiltrating duct carcinomas developed a metachronous second primary tumour when criteria for the diagnosis of a second primary cancer were applied rigorously. Similar small differences were reported by Fisher *et al* for 1578 women enrolled in protocol 4 of the National Adjuvant Surgical Breast Project.² While these authors identified a statistically significant increased risk of a second cancer associated with lobular carcinoma it should be noted that in 39 of the 66 cases the first tumour was of infiltrating duct type (including those with a tubular element), whereas 18.2% were invasive lobular.

Thus, it is important to appreciate that ductal carcinoma is also associated with a risk of bilateral disease and we feel that the implication that the follow up and management of the "other breast" should be different in lobular as opposed to ductal carcinoma is fallacious. In both types careful screening is indicated because both are subject to similar risks, albeit at a somewhat different prevalence. We do not agree that contralateral biopsy or mastectomy is indicated as a routine in any form of

breast cancer and nor have these procedures gained widespread support; indeed a recent study³ argues against them and Mr Dixon himself has argued that they are unlikely to improve survival.¹

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- 1 Dixon JM, Anderson TJ, Page DL, Lee D, Duffy SW, Stewart HJ. Infiltrating lobular carcinoma of the breast: an evaluation of the incidence and consequence of bilateral disease. *Br J Surg* 1983;70:513-6.
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Early neurological complications of coronary artery bypass surgery

SIR,—I congratulate Dr Pamela J Shaw and her colleagues on their comprehensive list of neurological complications after coronary artery bypass surgery (16 November, p 1384) and would like to add one further example encountered in a recent clinic.

The day after a coronary artery bypass operation a 40 year old man complained that everything smelt very strong and unpleasant (parosmia) and that room sprays, soap, petrol, and body odour were especially abhorrent (cacosmia). The complaint distressed the patient so much that he developed paranoid ideas and had to be prematurely discharged home. At the same time he developed mild nominal dysphasia for a few days. The symptoms gradually subsided over eight weeks. When tested with the usual test bottles his sense of smell was reduced (but not absent) in both nostrils and he said that all the test bottles smelt of disinfectant.

Parosmia and cacosmia are usually attributed to damage to the peripheral part of the olfactory tract,¹ but in view of the nominal dysphasia damage was probably central in this case and affected the temporal lobes. This would be in keeping with the type of cerebral hypoxia described by Dr Shaw and colleagues.

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SIR,—We were surprised that Dr Pamela J Shaw and others (16 November, p 1384) did not include carotid artery disease as a cause of stroke in their review of early neurological complications of coronary artery bypass grafting.

Kartchner and McRae reported a 17% rate of ischaemic stroke among 41 patients with abnormal findings on oculosplenocephalography (OPG) before cardiovascular surgery compared with a 1% rate among 192 patients with normal OPG findings.¹

We studied carotid artery disease by duplex ultrasound scanning in 103 patients before cardiopulmonary bypass.² Severe atherosclerosis (>50% carotid stenosis) was identified in 11 internal carotid arteries in 6 out of 56 patients (11%) before coronary artery bypass grafting and none of 47 patients before mitral and aortic valve replacement. Carotid endarterectomy was undertaken without perioperative stroke or mortality in five patients undergoing coronary artery bypass grafting.

It is premature to draw firm conclusions on the role of carotid endarterectomy in combined