

The regimen being evaluated in our study is based on the two-day cyclical treatment shown to be effective in late breast cancer.¹ A dose reduction of one-third has been made as a further safeguard and this modified regimen is being evaluated on a multicentre basis in histologically established stage 2 breast cancer.

Recruitment of cases began in the summer of 1975, and although we have had over 80 registrations so far it is hoped that more clinicians will participate in the trial in the near future. Detailed information is available on request.

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¹ Edelstyn, G A, *et al*, *Lancet*, 1975, 2, 209.

Early diagnosis of cancer in the head and neck

SIR,—May I take this opportunity of supporting Mr H J Shaw (14 February, p 379) in his plea for centralisation in the management of head and neck tumours. Such a philosophy is never popular of course since it implies that not every ear, nose, and throat surgeon is competent to care for these patients; nor for acoustic tumours, the more sophisticated middle ear techniques, or many other problems. Since we all remain limited by personal preference, past experience, and present facilities it is sensible to accept our limitations with a brave face and ensure our patients' welfare by referral to those with particular interests and opportunities. This particularly applies to cancers affecting the head and neck region, where, as Mr Shaw has so ably shown, treatment requires a plethora of skills and experience. Let us ensure that those that should be cured have their chance, although I still adhere to my belief that every team must have a clinically experienced leader—and in this field it is usually a surgeon. "Surgery by committee" leads to confusion.

With regard to Mr Shaw's slightly optimistic figures for cure rates in these cancers—40-45%—it must be appreciated that all-embracing figures mean little in this region unless they are broken down to reveal the numbers at different sites and stages of disease. Early tumours in some sites such as the maxillary antrum remain extremely rare and overall cure rates consequently remain low. Alternatively, the larynx is a relatively good site. If a centre's experience is biased towards the larynx, oral cavity, or paranasal sinuses obviously a generalised figure could be unusually good or bad. Such a comment of course in no way contradicts the author's plea for early diagnosis and early referral. Only a few experienced specialised units exist for the care of such patients, and there is as yet little evidence that trained personnel exist for more. Many patients are still unwilling to travel and it therefore remains the responsibility of general practitioners to ensure that their patients do find themselves under the care of skilled and experienced individuals in adequately equipped units.

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Shortage of organs for transplantation

SIR,—Shortage of cadaver kidneys constitutes the main bottle-neck in renal transplantation, as pointed out repeatedly and again recently by Professor R Y Calne and others on behalf of the British Transplantation Society (20 December, p 704).

However helpful the Department of Health may be in launching surveys and registers and whatever legal changes are made, close liaison between each renal transplant unit and the medical and nursing staffs of its own and adjacent groups of hospitals will always remain of critical importance. This relationship cannot be built up overnight and will be achieved only by painstaking and continued contact, essentially on a personal basis. Members of the renal transplant unit, and particularly its director, should attend seminars to present cases and give talks on transplantation, not only to members of the medical and nursing and ancillary staffs but also to clergy and to lay societies, which are always delighted to have speakers on this subject. All these activities would generate an interest in transplantation and would allow people outside the unit to assess at first hand the type of persons responsible for this relatively new, possibly still somewhat mysterious, and even "suspect" surgery.

A specially appointed "liaison officer" does not possess the necessary knowledge or authority to fulfil these tasks adequately. They are essentially the duty of the director of the unit and of his trained staff, whose time, however, is fully committed to routine work and to emergency calls to remove and to transplant kidneys. How can all this be carried out in the centres without increase in staff? The transplant activities of a major centre such as the one in Sheffield were, on opening six years ago, added to the duties of existing fully committed urology and nephrology staff, and no amount of representation has made any difference to central policy on regional attitudes to organisation and treatment which has now become no less successful, and in some cases more so, than that of accepted major cancer surgery.

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Reticuloendothelial phagocytosis in patients with nephritis

SIR,—I read with interest the short report by Dr G Drivas and others (7 February, p 321) on the use of ¹²⁵I-labelled aggregated albumin as a test of reticuloendothelial system function in patients with nephritis. They suggest that rapid clearance of this substance from the blood of patients with certain types of nephritis could reflect the presence of circulating immune complexes in these patients.

One obvious drawback in the interpretation of in-vivo tests of macrophage function such as the one that they describe is the fact that it is difficult to be very sure what one is measuring. Uptake by Kupffer cells is markedly influenced by hepatic blood flow, while metabolism of the injected substance with consequent release of the radioactive label can give false results. This is particularly true of albumin, except where appropriate corrections are made. In this context the recently described polyvinyl pyrrolidone (PVP) test¹ may be

considered an advantage. Besides, uptake of aggregated albumin, unlike that of immune complexes, is essentially a non-specific process. It is therefore not surprising that colloidal carbon has been shown to inhibit clearance of intravenously injected ¹²⁵I-labelled aggregated albumin.² In contrast, we were unable to demonstrate inhibition by this substance, in vitro, of uptake by guinea-pig macrophages of ¹²⁵I-labelled HSA/anti-HSA complexes which are phagocytosed through specific receptors. It is possible that specific phagocytosis of some immune complexes could lead to stimulation of the non-specific process.

The finding by Dr Drivas and his colleagues of increased clearance of ¹²⁵I-labelled aggregated albumin in patients with proliferative and membranous glomerulonephritis, as well as in Henoch-Schönlein nephritis, is therefore of interest because it suggests the possibility of a "switch-on" effect on macrophage function produced by certain soluble complexes. This is in keeping with our observed in-vitro enhancing action on uptake of radio-labelled aggregated human IgG by guinea-pig macrophages in the presence of sera from rheumatoid patients with cutaneous vasculitis.³ We showed that such enhancing action was related to the presence of IgM rheumatoid factor complexes. Their results may well represent the in-vivo expression of our enhancing phenomenon. It will thus be interesting if they can show that sera from patients in whom the clearance half time of injected ¹²⁵I-labelled aggregated albumin was significantly reduced also contained soluble immune complexes, presumably of the IgM type.

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¹ Morgan, A G, and Soothill, J F, *Clinical and Experimental Immunology*, 1975, 20, 489.

² Iio, M, and Wagner, H, *Journal of Clinical Investigation*, 1963, 42, 417.

³ Onyewotu, I I, *et al*, *Clinical and Experimental Immunology*, 1975, 19, 267.

Rebound effect of hyoscine butylbromide on postoperative bowel contractions

SIR,—Atropine antagonises the muscarine actions of neostigmine except for intestinal contractions,¹ which have been known to tear open recent bowel suture lines.² It seemed that the addition of hyoscine butylbromide to the neostigmine and atropine given to reverse the residual muscular paralysis after operation under muscle relaxant drugs might reduce the strength of consequent bowel contractions.

One hundred consecutive patients anaesthetised for laparotomy with the addition of muscle relaxant drugs were placed randomly by an electronically derived numerical series into two groups. To reverse muscle paralysis the patients in group A (13 male, average age 57.7, and 37 female, average age 41.6) were given neostigmine 2.5 mg and atropine 0.6 mg intravenously while those in group B (17 male, average age 46, and 33 female, average age 45.9) also received hyoscine butylbromide 40 mg intravenously a few minutes before the other two drugs. As soon as a dressing had been applied to the wound the abdomen was auscultated for 20 seconds by a doctor who did not know which drugs had been injected and the presence or absence of bowel sounds noted.

Bowel sounds were heard in 42 cases from group A compared with 13 from group B (χ^2 test, $P < 0.001$). When it became likely that an effect was present (after 50 cases) the scope of the investigation was widened to include observations of the bowel sounds 30 and 60 minutes later by trained recovery room staff who did not know which drugs had been injected. Of 31 patients from group A, 24 had audible bowel sounds at the end of the operation and 25 half an hour and 29 an hour later; for 19 patients from group B the figures were 5, 19, and 17 respectively. The first pair of figures show a significant difference ($P < 0.001$), but the remaining pairs do not. Moreover, in 11 cases, all from group B, the bowel sounds 30-60 minutes after operation were loud enough to be heard without a stethoscope.

Hyoscine butylbromide evidently has too short an action to be useful in this context and the rebound contractions that follow its use can be more powerful than those caused by neostigmine and atropine alone. The use of hyoscine butylbromide should therefore be avoided during the immediate recovery period following anastomosis of bowel.

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- ¹ Doughty, A G, and Wylie, W D, *British Journal of Anaesthesia*, 1952, 24, 66.
² Bell, C M A, and Lewis, C B, *British Medical Journal*, 1968, 3, 587.

Bran content of wholemeal bread

SIR,—In a recent reply to a query (24 January, p 203) it was erroneously stated that 900 g of wholemeal bread was equivalent to 150-200 g of bran. The correct value is of the order of 90 g bran (at 14% moisture content), assuming 40% moisture content in the bread and making due allowance for the yeast, salt, and fat used in bread-making. The calculation is based on a bran content of wheat of 15%.

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* * * Our expert agrees that the corrected figure is right but does not think it alters the point he was trying to make—Ed, *BMJ*.

High-pressure medicine

SIR,—The statement in your leading article (6 December, p 541) that most surgeons operating at 20 atmospheres would prefer to rely on local anaesthetics with heavy doses of morphine if necessary is a facile and inadequate solution. This not only ignores the dangers of vomiting and respiratory depression associated with morphine but also ignores the ability of anaesthetists to cope with unfamiliar situations—an ability demonstrated throughout the development of modern anaesthesia at one atmosphere.

As Dr I C F Wisely (7 February, p 340) says, the problem is not simple. Even an invited paper in an anaesthetic journal on "The treatment of the diving casualty"¹ failed to give any guidance, though on reading the article it became obvious that the author's

remit was treatment of the patient once he had reached a casualty department. Ketamine alone is unsatisfactory in adults at normal pressure because of its hallucinogenic effects,² but combined with diazepam it has been used very effectively in emergency situations.³ Althesin (alphaxolone/alphadolone) alone does not guarantee sufficient anaesthesia.⁴ Nevertheless, a combination of Althesin or propanidid with neuroleptanalgesia may be satisfactory. There are therefore at least two potentially satisfactory techniques that would permit endotracheal intubation to protect the airway or the use of muscle relaxants if these were indicated.

As well as the academic projects mentioned by Dr Wisely, basic scientific research is continuing into the mode of action of inhalational anaesthetics utilising high atmospheric pressure as a research tool with potential spin-off information for deep-diving gas mixtures. However, there appears to be no research into the suitability of different intravenous anaesthetic agents for use at 20 atmospheres.

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- ¹ Elliott, D H, and Hanson, R de G, *Anaesthesia*, 1976, 31, 81.
² Hunter, A R, in *Recent Advances in Anaesthesia and Analgesia*, ed C L Hewer, 11th edn, chap 1. Edinburgh, Churchill Livingstone, 1972.
³ Carmichael M, personal communication.
⁴ Savage, T M, et al, *Anaesthesia*, 1975, 30, 757.

SIR,—Dr I C F Wisely (7 February, p 340) finds that Government expenditure on bone necrosis research is a luxury we cannot afford. I deny this.

I have, at the second Dartford tunnel, 320 men working to establish a new road link between the north and south sides of the river Thames. Scattered about the British Isles are numerous similar tunnels and underneath all our major cities are telephone cable tunnels, sewers, water conduits, and similar structures on which our society depends. Many of these tunnels could not have been constructed without the use of compressed air. The number of men who have been involved in this work up and down the country is somewhat close to the 25 000 sport divers who dive off our summer coasts. Unlike these divers they are at considerable extra risk from dysbaric osteonecrosis, and it was because of these men that the Medical Research Council Decompression Sickness Panel and Registry was first created.

I am probably the biggest single spender of the MRC's money for joint radiographs of these men and of divers. What depresses me most is the very small amount of money that can be made available for this study. I am personally proud to be associated with the work, which has established the diagnostic criteria for this disease throughout the world and continues to evolve higher standards of diagnosis and reporting.

The very fact that long-bone x-rays are now standard in our medical fitness examination for divers is clear indication that it has passed beyond the academic and is now of utmost clinical and medicolegal importance. The medical profession of late has been too involved with sordid commercial interests rather than professional activity. I am happy to inform Dr Wisely that my professional activities know no national boundaries; but, holding a British passport, I am jealous to preserve our commercial interests. In his penultimate

paragraph Dr Wisely asks for a single clear assessment of the various problems and asks for positive action to be taken. It is unwise for anybody to ask for single clear assessments. There is no single answer to any of the problems that presently beset the world of underwater and underground medicine.

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Geriatric patients in acute medical wards

SIR,—I have been interested to see the very different interpretations of our paper on this subject (6 December, p 568). Several correspondents have questioned the economics of the study. In reply I would point out that the figure of £178.60 is the 1974 average weekly cost of an acute medical bed in this hospital. It represents the "opportunity cost"—that is, the availability of the acute medical bed. However few of the ward's resources patients use, this opportunity cost remains the same. In contrast to Dr P W Hutton (3 January, p 41) I believe that patient costs do in fact depend on the type of ward in which a patient is treated.

The fixed costs of being able to offer acute medical care are far higher than the variable costs of actually providing it. The facilities associated with acute medicine are expensive—for example, purchase, maintenance, and depreciation of machinery, provision of highly specialised medical, technical, and general hospital staff, who are paid for being available rather than on an item-of-service basis. By comparison the additional costs of actually treating a patient are small—for example, reagents, drugs, syringes, and x-ray films.

As Professor B Isaacs (p 40) says, had the study patients been transferred and those waiting taken their places the cost of the 160 bed-weeks might not have been saved in overall terms. However, the money and beds in the acute medical ward could have been used by those in need, while the study patients would have benefited from the specialised resources of a geriatric ward.

Dr Monnica C Stewart's (p 41) mind boggles to read that a patient died for whom medical treatment had been completed. Perhaps she is forgetting that the average age of these patients was over 79 years and that patients, no less than "ordinary people," die some time.

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Oxytocin and neonatal jaundice

SIR,—Professor E A Friedman and Mr M R Sachtleben's suggestion (24 January, p 198) that operative delivery and not oxytocin induction is responsible for an increased incidence of neonatal jaundice prompts comment.

An association between oxytocin use and neonatal jaundice was first described by Mast and his co-workers in two studies^{1,2} which are seldom mentioned by those discussing this field. An association with instrumental delivery was sought but not found. Most of the subsequent work has emanated from Britain, where there has apparently been an epidemic of