

dissented from the view that the *possibility* of a direct relationship between multiple exposure to halothane and postoperative liver damage existed. They asked why the committee had not sought "expert opinion," presumably from anaesthetists, before publishing their circular letter.

It is apparent that the two groups who were working contemporaneously have now come to the same conclusion. As a general practitioner who is also a very part-time worker for the CSM I hope I am not out of order in expressing the view that it is a pity that some degree of effective communication, co-operation, and co-ordination between the two groups was not effected at an early stage and the hope that a lesson has been learnt for the future.

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¹ Inman, W H W, and Mushin, W W, *British Medical Journal*, 1974, **1**, 5.

² Simpson, B R, and Strunin, L, *British Medical Journal*, 1974, **1**, 288.

³ Coplans, M P, and Lewis, E B, *British Medical Journal*, 1974, **1**, 387.

⁴ Simpson, B R, Walton, B, and Strunin, L, *British Medical Journal*, 1974, **4**, 590.

Prophylactic chemotherapy for breast cancer

SIR,—The report on an international multicentre trial of the management of early breast cancer (1 May, p 1035) must surely convince the medical profession that no combinations of local treatment by surgery and/or radiotherapy will improve the survival statistics from this disease because, in the majority of cases, occult metastases are already present by the time of diagnosis. Breast cancer will be treated successfully only when it is recognised to be a systemic disease from the start, and I fully concur with the view expressed in the summary of the report that "conservative primary treatment and subsequent adjuvant chemotherapy may be the treatment of choice in future."

Unfortunately, the word "chemotherapy" seems to conjure up, in the minds of some consultants I have encountered, treatment with large doses of cytotoxic drugs having nasty side effects which no kind therapist would dream of inflicting on mastectomised patients merely for prophylactic reasons. Nevertheless, recent reports¹⁻³ have indicated the beneficial results of their prophylactic use and it is possible that doses which are a fraction of those used for curative purposes would suffice to deal with occult metastases without inconvenient side effects.

Before adjuvant therapy with particular cytotoxic drugs becomes entrenched as the accepted treatment for primary disease I feel that other possibilities for systemic prophylaxis should be thoroughly explored, keeping cytotoxic drugs as a last-line resort if all else fails. The lethality of breast cancer is due to its ability to metastasise quickly and widely. This might be countered by treatment with one of the antimetastatic drugs ICRF 159, warfarin, or tytoxapol (Triton WR 1399).⁴

If a woman is destined to develop cancer, in many ways she could be fortunate to have it in the breast. Here her primary cancer is accessible, making early detection possible, while her diseased organ is dispensable and can be replaced by a very acceptable external prosthesis. Her cancer is very often dependent on hormonal support in its early stages and it

may soon be possible to identify the individual hormones concerned by reliable in-vitro tests done on the malignant tissue removed at the time of surgery to eradicate the primary tumour mass. Drugs to counter specific hormones are available which could render ablation of endocrine organs, with their associated complications, unnecessary. Until such tests are generally available oestrogen and prolactin must be considered to be the most likely tumour-supportive hormones. Action against them can be taken by radiation sterilisation, administration of an antioestrogen (such as tamoxifen) and an antiprolactin (such as levodopa). Both drugs have been shown to bring about remissions in a proportion of cases of advanced breast cancer.

During my 25 years of interest in the cancer field I consider the real breakthrough in cancer treatment was that made by Mathé. In the 1960s he showed how that terribly rapid killer acute lymphatic leukaemia (which can be regarded as occult metastases all over the body) may often be cured—largely by combined chemotherapy, with a touch of radiotherapy and immune stimulation added. Choriocarcinoma is another case in which a highly malignant systemic disease has yielded to similar measures. Breast cancer is far more common than these rare malignant conditions, but it could be the next to be conquered if it is regarded as yet another systemic disease and treated more rationally from the start with "chemotherapy"—in the widest sense of the word.

My own experience (20 March, p 712) shows the benefit of adjuvant chemotherapy for both primary and secondary breast cancer but also shows that much work remains to be done to find the necessary dosages and duration of treatment required to cure the disease.

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¹ Fisher, B, *et al*, *New England Journal of Medicine*, 1975, **292**, 117.

² Bonadonna, G, *et al*, *New England Journal of Medicine*, 1976, **294**, 405.

³ Donovan, I A, *et al*, *Lancet*, 1976, **1**, 42.

⁴ Hoover, H C, and Ketcham, A S, *Cancer*, 1975, **35**, 5.

A rational approach to parenteral nutrition

SIR,—The excellent article by Mr B W Ellis and others (5 June, p 1388) fully justifies its title. However, at the risk of being labelled a "parenteral nutrition technocrat," I have one doubt concerning the otherwise highly attractive notion of "locking off" the cannula. "We do not eat continuously," but parenteral nutrition bypasses the intestines and portal system with important consequences for nutritional homeostasis. Although we eat a hypertonic diet, fluctuations in plasma osmolarity due to eating are minimal. Presumably the intestines and liver act as an osmotic buffer, allowing solute to enter the systemic circulation only at a rate commensurate with the metabolic production of water, the renal excretion of solute, and the pulmonary excretion of carbon dioxide. The portal system is well supplied with osmoreceptors.¹ Although, like the authors I use varying quantities of isotonic fat emulsions in intravenous feeding regimens, amino-acid and carbohydrate solutions for intravenous feeding are usually hypertonic. Consequently any intravenous feeding regimen providing

even the minimum requirements of protein and energy will have a mean osmolarity in excess of 600 mmol/l (and often much greater than this). In order to reduce to a minimum the homeostatic effects of infusing hypertonic solutions directly into the systemic circulation I have always infused intravenous nutrients at a regular rate over the whole day, particularly when using regimens containing large quantities of hypertonic carbohydrate solutions, as hyperosmolar coma, osmotic diuresis, and rebound hypoglycaemia may occur during or after infusion. A controlled trial to assess any differences in metabolic homeostasis induced by continuous or intermittent infusion of mixed intravenous regimens would appear to be indicated.

Mr Ellis and his colleagues emphasise the importance of electrolyte and trace mineral content in intravenous feeding. Although one recent study² did provide much needed information, there is a paucity of scientific data concerning this problem. "Data farming" is viewed with disapprobation in some medical circles, but the creation of a national data bank to collect information concerning patients fed intravenously might provide much useful information about this problem. It would take many years of study to accumulate sufficient data in one centre.

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¹ Haberich, F J, *Triangle*, 1971, **10**, 123.

² Rudman, D, *et al*, *Journal of Clinical Investigation*, 1975, **55**, 94.

SIR,—Mr B W Ellis and others (5 June, p 1388) suggest that a rational approach to parenteral nutrition should include the use of preoperative supplemental feeding in any patient who has lost 5 kg weight before admission and the use of postoperative parenteral nutrition in patients who cannot take oral nutrition 72 hours after surgery. The authors suggest that these patients are at risk of developing sepsis or complications of wound healing as a consequence of malnutrition, and it is their belief that appropriate nutritional therapy may reduce postoperative morbidity and mortality.

If one considers the practical implication of these recommendations then one will quickly realise that many surgical patients will become candidates for some form of nutritional therapy. However, it is less easy to see that any measurable improvement in the management of these patients will result. For example, in the past 18 months 21 patients in my care have undergone oesophagogastrectomy (11) or distal gastrectomy (10) for carcinoma. Seventeen patients had a history of weight loss exceeding 5 kg, and in some cases weight loss exceeded 10 kg. No patient received pre- or post-operative nutritional supplements (apart from postoperative dextrose-saline), but oral dietary intake was not resumed until 5-12 days after surgery. Two patients died of bronchopneumonia (confirmed at necropsy), but there was no clinical or radiological evidence of anastomotic dehiscence in any patient. Wound sepsis occurred in seven cases, but no other wound complications were encountered.

Could these results be improved on by the routine use of nutritional supplements before and after surgery? The absence of data from controlled clinical studies is not a particularly persuasive basis for changing the present regimen, but Mr Ellis and his colleagues are