Until unequivocal evidence is provided from well-conducted concurrently controlled trials the case for immunotherapy in malignant melanoma will remain unproved. No amount of optimistic speculation or vague assertion will convert a promising but nebulous idea into a realistic method of treatment.

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Chemotherapy in breast cancer

The term "breakthrough" applied to cancer therapy has become so commonplace that an intelligent lay person might be forgiven for expressing surprise that patients continue to die of this disease. A good example of the media over-reacting to an undoubted important contribution to cancer therapy has been the reception afforded two recent papers on the use of adjuvant chemotherapy for early breast cancer.[1 2] The muted acclaim with which these articles were received by the profession has been transformed into a triumphant fanfare by the popular media in the USA, and even the serious Sunday newspapers[3 4] and the radio in Britain.[5] A distinguished spokesman for the National Cancer Institute went so far as to state on a BBC 4 programme that 98% of women who had disseminated breast cancer at the time they had been put under treatment were being kept alive without recurrence of the disease.[5]

As a result of this kind of sensationalism clinicians in America are being placed in an impossible position. Patients and referring practitioners are now putting pressure on surgeons to give the new wonder cure, and in the climate of defensive medicine practised on the other side of the Atlantic such pressure may be difficult to resist. There are now early signs that this unfortunate state of affairs may have crossed to Europe. The statement by the British Breast Group (see p 861) on the current status of adjuvant chemotherapy in early breast cancer is, therefore, both timely and important. This authoritative report may go a long way towards checking the premature adoption of what must be considered still to be an experimental mode of treatment. Also relevant is the recent paper by Costanza[6] which gave four reasons for advocating extreme caution in the premature application of chemoprophylaxis in breast cancer. Firstly, the drugs used are immunosuppressive, and chronic immunosuppression is associated with the risk of the development of other cancers.[7] Secondly, the alkylating agents in these adjuvant programmes are also known to be carcinogenic, and there have now been reports of the development of second solid tumours[8] or leukaemia[9] in patients on long-term chemotherapy for malignant disease. Thirdly, the drugs have myelosuppressive properties, making them dangerous and potentially lethal in inexperienced hands. There are not enough medical oncologists in Britain to provide a chemotherapy service for every surgeon treating breast cancer. Finally, she reminds us that in as many as a third of patients with diseased lymph nodes chemoprophylaxis given on statistical grounds alone might be unnecessary—these patients would have escaped recurrent disease. While nodal status is the best prognostic indicator yet available, we still need to remember that the ideal index has yet to be described.

None the less, most workers on breast cancer believe that important improvements in survival after local removal of the diseased tissues are likely to be achieved only by some form of systemic therapy to attack the micrometastases present in so many women with apparently localised disease. There are, however, less toxic forms of treatment available that have not yet been adequately tested—a point emphasised by Stoll, who has argued[10] for well-designed trials of endocrine treatment at the time of mastectomy. The results of adjuvant chemotherapy from the NSABP[1] and the Milan group[2] have yet to show any significant improvement in survival in the group receiving additive therapy. So to anticipate the pressures that clinicians could face from an "informed general public," we can only echo Costanza's statement that "Until the ultimate value and risks are known, chemoprophylaxis should not be regarded as standard procedure." For the time being at least clinicians should stick to what they would consider conventional treatment, or alternatively enter their patients into one of the current trials evaluating adjuvant chemotherapy.

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[4] *Sunday Times*, 20 June 1976.
[5] BBC 4, 7 July 1976.
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Screening for breast cancer

In 1973 breast cancer killed almost 11 500 women in England and Wales and there is evidence that mortality from the disease is increasing, especially among those aged 45-64 years.[1] Despite this, recent reports from two areas of research provide grounds for cautious optimism.

Firstly, two groups of workers[2 3] have published results suggesting that systemic chemotherapy may be of value in the treatment of early breast cancer. Too much should not be made of their findings, which have been put into perspective by the statement by the British Breast Group (p 861) and the leading article on this page; but this new approach has lifted morale.

The second encouragement comes from the seven-year follow-up figures of the well-known Health Insurance Plan (HIP) trial in New York.[4] These showed a 35% reduction in the number of deaths from breast cancer in the group offered annual screening examinations when compared with the control group, which received only normal medical care. This benefit, however, was confined to those aged over 50 years.

While the HIP trial remains the only study capable of providing information about the effect of screening on mortality the results of a number of smaller uncontrolled investigations are also proving of value. When screening has been offered to clearly defined groups of women the acceptance rates have

varied[5 6] between 38% and 81%. Many of the women who present for "screening" already have symptoms, and no doubt factors such as these contribute to the wide variation in the cancer detection rates in different studies. Representative figures range from 2·7 per 1000 (aged 40-69 years) at the initial screening examination in the HIP trial,[7] to 7·6 per 1000 (aged 35-75 years, self-selected),[8] to 11·3 per 1000 (aged 35 years or more, "high risk")[9] and 12·0 per 1000 (aged 40 years or more, self-selected).[10] Even higher rates have been reported[8] (24·5 per 1000 "high risk, well women").

A number of different screening methods are under investigation, but most reports are based on the combination of clinical examination and mammography. The HIP data suggest that both these modalities are essential, since 44% of cancers would have been found only by the former and 34% only by the latter. Most other authors agree with the conclusions reached by the New York group. However, mammography is less effective in premenopausal women, in whom the breasts are homogeneously dense. Since it is this group of women that may be at risk of a radiation-induced breast malignancy, it is probably best to restrict mammography as far as possible to the over-40s.[11]

Another unresolved problem is the optimal frequency of screening. In the HIP trial 15% of all cancers diagnosed were detected within a year of a normal screening examination,[4] while in the Guttman Institute study[4] the corresponding figure was 9%. These data are difficult to interpret; some of the "interim" tumours must represent the result of "false-negative" screening, while others presumably arose de novo between examinations.

To co-ordinate British research the DHSS and the MRC have established working parties to study the service and biomedical aspects of a national screening programme. Four centres (Bath, Ealing, Edinburgh, and Manchester) are concerned at present, and some results from Ealing were published last year.[10] The paper at page 858 is a report from the screening clinic in the University Hospital of South Manchester. Using clinical examination and mammography the non-medical team of nurse and radiographer was as successful at detecting breast abnormalities as a team of surgeon and radiologist. The overall cancer pick-up rate was 8·4 per 1000, or 4·6 per 1000 in asymptomatic women. Four methods of mammography were used, and it was found possible to obtain satisfactory plates with a mean upper inner quadrant dose as low as 0·1-0·5 rad. The response rate of those invited for screening was 54% and was highest in the youngest women. Social class did not affect this response rate, but those who referred themselves were predominantly from the upper social classes. Among the women invited for tests the biopsy rate was 2·9% (other studies[4 10] have reported rates from 2·4% to 9·8%). Extrapolation of these findings to all women aged 40-65 years in Manchester would imply that a full screening programme would lead to surgeons carrying out an extra 20 biopsies per week.

Many people believe that eventually any screening programme should be universally available, so that careful consideration has to be given to economic factors. In 1971 it was calculated that the use of mammography to screen all women aged 40 years and over in the USA would cost $622 million annually.[12] Knox[13] estimates that at 1975 prices such a scheme would cost not more than £12 million annually in England and Wales. His simulation model indicated that the programme would produce a 12% reduction in mortality from breast cancer on the assumption of a 50% uptake and 30 successive annual screening examinations; thus the cost per "life saved" would be £8000. However, 95% of women will never develop breast cancer, so much discussion has centred on the definition of high risk groups for selective screening. Unfortunately the known correlates of the disease appear to have little predictive power,[14] but Knox has calculated that a selective programme aimed at a 10% reduction in mortality might be achieved at a cost of £2000-£3000 per "life saved."

There are other constraints on breast cancer screening. They include the availability of personnel and equipment, but the results of the Manchester study suggest that these problems are not insoluble.

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[13] Knox, E G, in *Probes for Health:* Essays from Health Services Research Centre, p 38. Oxford University Press, Birmingham, 1975.
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Safety for children

Accidents are the leading cause of death in childhood, and one in six of all admissions of children to hospital are the result of trauma. Yet recent attempts to evaluate the official returns of accidents in childhood have shown the information so inadequate and misleading that little reliance can be placed upon it. Nowhere is this more apparent than with the leading causes, road traffic and the home.

In the case of road accidents the returns (based on information collected by the police at the scene of the accident) of serious and slight injuries rely on definitions which bear little relation to clinical severity or to prospect of permanent disability. No distinction is made between a broken finger and paraplegia. There is considerable under-reporting and misreporting within this unsatisfactory classification, with an uneven distribution of errors between different categories of road user. The quality of the data is worst for cyclists and pedestrians, who are most exposed to serious injury. Only those child cyclists in collision with motor vehicles are officially reported as injured—but they represent only 11% of the total. Similarly, the Registrar General's returns of mortality show that over half of the fatal domestic accidents are among the over 65s, and this finding is generally assumed to reflect the age distribution of accidents. However, a recent survey[1] of one year's admissions to accident and emergency departments in six different areas of England showed that only 13% of home accidents were in the over 65s and that 30% were in children aged under 5.

It was against this background of inadequate information that last month an international conference, sponsored by the Medical Commission on Accident Prevention and the Department of Child Health of the University of Newcastle on Tyne, discussed the theme of "children, the environment, and accidents." To what extent should the environment be adapted to make it safer for children? Should children be protected