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¹ *Lancet*, 1976, **1**, 730.

² *Alternative Approaches to Meeting Basic Health Needs in Developing Countries*, ed V Djukanovic and E P Mach. Geneva, World Health Organisation, 1975.

³ Gish, O, *World Development*, 1973, **1**, No 12, p 37.

⁴ Department of Employment, Statistics Division.

⁵ The British Volunteer Programme comprises the Catholic Institute of International Relations, International Voluntary Service, United Nations Association, and Voluntary Service Overseas.

Adjuvant therapy of lung cancer

SIR,—We read with interest your leading article on adjuvant therapy of lung cancer (22 January, p 187) and in particular the statement attributed to Professor R Baldwin that "the original concept that human tumours are antigenic and that immunotherapy may aid their elimination by an immune reaction was no longer tenable." We feel that this quotation without further comment is misleading and disappointing. Misleading because it appears to deny firstly the antigenicity of human tumours, secondly the therapeutic possibilities of manipulating host immunity, and thirdly, by implication, the possibility that immune reactions may be involved in the host responses to tumour cells. Disappointing because, as elsewhere in the article, it represents a note of pessimism which is based, presumably, on the failure of clinical trials to demonstrate specific immunological responses to active immunotherapy.

There is considerable evidence that human lung tumours express neoantigens.¹ By immunising a goat with cultured cells derived from a human oat cell carcinoma we have demonstrated both anti-normal and anti-tumour antibodies. This antiserum contained high titres of lymphocytotoxic, haemolytic, and haemagglutinating antibodies. Removal of the anti-normal antibodies by absorption with human spleen preparations did not affect the anti-tumour antibody titre in an indirect immunofluorescence test. The absorbed antiserum contained extremely high titres of antibodies to the onco-fetal antigen CEA. These findings of lung tumour antigenicity are similar to those of others.^{2,3}

The evidence that such tumours are immunogenic in the host is less convincing, although several authors have described, in vitro or in vivo, specific sensitisation to lung tumour antigens.⁷ At presentation cancer patients are immunosuppressed and have already proved themselves incapable of responding effectively to tumour antigens. They are therefore unlikely to respond to further stimulation with tumour antigens—for example, irradiated tumour cells. It is not

easy to believe that human tumours are completely different from those investigated in animal models, especially in spontaneous tumour systems. If they are is the enormous expenditure of resources and effort on research in such models justified? If they are not should we dismiss the possibility that human tumour elimination may involve an immune reaction? Combination of active and passive specific immunotherapy either alone or together with chemotherapy would probably be the ideal immunological treatment for cancer. The assessment of claims made for antibody drug synergism (ADS)⁸⁻¹⁰ and immune RNA^{11,12} may eventually enable us to reinforce the ineffective immune system of cancer patients.

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¹ Baldwin, R W, and Price, M R, *Annual Review of Medicine*, 1976, **27**, 151.

² Frost, M J, Rogers, G T, and Bagshawe, K D, *British Journal of Cancer*, 1975, **31**, 379.

³ Bell, C E, jun, and Seetharam, S, *International Journal of Cancer*, 1976, **18**, 605.

⁴ Hollingshead, A C, Stewart, T H M, and Herberman, R B, *Journal of the National Cancer Institute*, 1974, **52**, 327.

⁵ Wells, S A, et al, *Journal of Thoracic and Cardiovascular Surgery*, 1973, **66**, 557.

⁶ Boddie, A W, jun, et al, *International Journal of Cancer*, 1975, **15**, 823.

⁷ Roth, J A, et al, *Journal of Thoracic and Cardiovascular Surgery*, 1975, **70**, 613.

⁸ Davies, D A L, and O'Neill, G J, *British Journal of Cancer*, 1973, **28**, suppl 1, p 285.

⁹ Davies, D A L, Manstone, A J, and Buckham, S, *British Journal of Cancer*, 1974, **30**, 297.

¹⁰ Davies, D A L, Buckham, S, and Manstone, A J, *British Journal of Cancer*, 1974, **30**, 305.

¹¹ Pilch, Y H, Veltman, L L, and Kern, D H, *Archives of Surgery*, 1974, **109**, 30.

¹² Schlager, S I, Pague, R E, and Dray, S, *Cancer Research*, 1975, **35**, 1907.

SIR,—Your leading article on this subject (22 January, p 187) reminded me of the well-known phenomenon that new acquisitions need a considerable lapse of time before they reach the medical news media; their appearance in medical textbooks even takes several years. Therefore I should perhaps not have been surprised to read that "the enthusiasts [whoever they may be] for levamisole are now promoting a new image for this drug . . . as an 'immune-restorant,' whatever that may be, having failed to make the grade as an immune stimulant" and that "the initial disappointing results . . . in cancer may now, it seems, be explained as the consequence of getting the dose wrong" (my italics). I would like to make the following comments in that regard:

(1) More than a year ago it was concluded¹ that "levamisole is an antianergic chemotherapeutic agent. It restores to normal the function of phagocytes and lymphocytes when this is depressed. Cell functions are not stimulated above normal. The effect seems to be confined to cells involved in the cell-mediated immune reactions." This, at the same time, gives a reply to your question of what an immune-restorant may be. Finally, I, too, may wonder how much better immune stimulants may be as opposed to immune-restorants which have failed to make the grade as immune stimulants.

(2) As early as July 1975 it was realised² that the dosage used in our lung cancer study was probably too low for patients with a higher body weight. This observation for the first time clearly suggested that animal data pointing to an undeniable dose-

dependency of the levamisole effect have their clinical counterpart. I may add that the initial clinical results^{3,4} with levamisole as an adjuvant therapy of cancer were not disappointing at all, except, perhaps, for those people who expected levamisole to be a miracle drug. For the latter people I would like to make clear that we do not know about any miraculous effect of levamisole on top of its anthelmintic and antianergic properties.

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¹ Symoens, J, Paper presented at the 2nd Conference on Modulation of Host Immune Resistance in the Prevention or Treatment of Induced Neoplasias, Bethesda, Maryland, 1-3 December, 1975.

² Amery, W K, in *Chemotherapy*, vol 8, Cancer Chemotherapy II, ed K Hellmann and T A Connors. New York and London, Plenum Press, 1976.

³ Rojas, A F, et al, *Lancet*, 1976, **1**, 211.

⁴ Study Group for Bronchogenic Carcinoma, *British Medical Journal*, 1975, **3**, 461.

Whooping cough vaccination

SIR,—A survey of encephalitis among patients discharged from hospitals in Scotland in the two-year period 1968-9 revealed not a single case of brain damage due to whooping cough vaccination.¹ No such cases have been encountered in the Glasgow area by our two senior infectious diseases physicians with a combined experience of 60 years² or by the staff of the city's immunisation clinics.³ No such case has been confirmed at the regional assessment unit for paediatric neurology⁴ and none has been found in the register of handicapped children of the Greater Glasgow Health Board, although one child was noted to have suffered brain damage as a consequence of having contracted whooping cough itself.⁵ Is this experience shared by other parts of Britain?

Prensky's remark of 1974 is highly pertinent: "This 25-year old controversy, punctuated by limited clinical studies and testimonials, will remain a monument to the ineffectual nature of anecdotal reports and retrospective studies."⁶ It is high time that properly detailed evidence concerning the allegedly vaccine-damaged children was put on record for critical scrutiny by those able to evaluate it.

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¹ *Communicable Diseases, Scotland, Special Report 77/6*, Edinburgh, Scottish Home and Health Department, 1977.

² Lawson, J H, and McKenzie, P, personal communication.

³ Wilson, T S, personal communication.

⁴ Stephenson, J B P, *Lancet*, 1977, **1**, 357.

⁵ Forwell, G D, Note to Community Health Staff, Greater Glasgow Health Board, 10 February 1977.

⁶ Prensky, A L, *Developmental Medicine and Child Neurology*, 1974, **16**, 539.

Increased incidence of poliomyelitis

SIR,—We would like to draw attention to the recent increase in the number of notifications of paralytic poliomyelitis in Britain.

For the period 1972-5 there were 3-6 cases on average per year. During 1976 eight cases were notified, of which five occurred in October. In Addenbrooke's Hospital there are at the moment two further cases and there have also been two in London.