district management team for all medical laboratory investigations performed in the district."

The IMLS document on "Future Staffing in the Medical Laboratory Service" further states that "senior members of the profession decide the priority of work to be done and play a part in deciding on further and consequent tests." I assume that "profession" referred to in this paragraph means members of the IMLS.

This advice and the submission to the Royal Commission are contrary to the recommendations of HSC (IS) 16 on the "organisation of scientific and technical services" and the submission of the BMA to the Royal Commission (paragraph 3.10. 29 January, p 303).

T HARGREAVES

Area Department of Pathology,
Heavitree, Exeter

Shortage of dialysis facilities

SIR,—Your report of an interview with Dr J M Forsythe, area medical officer, Kent Area Health Authority (12 March, p 698), states that he alleges that "there would probably be enough dialysis places if more kidneys were made available; in fact the nephrologists did not think they needed more dialysis machines." I would be grateful to know which nephrologists.

The majority of patients suffering from chronic renal failure are beyond the age when transplantation is justifiable and the cadaveric kidneys of half the patients whom it is justifiable to transplant will fail within one year. If Dr Forsythe, on the other hand, had in mind transplantation from live related donors, then the position is slightly different, but only for that minority of patients who can find a related living donor. Until there is a considerable advance in the methods used to prevent graft failure of cadaveric kidneys, particularly in patients over 50 years of age, the present shortage of dialysis facilities in this country will continue.

HUGH DE WARDENER

Department of Medicine,
Charing Cross Hospital Medical School
London W6

Immunotherapy trials

SIR,—The report by Dr M B McIlmurray and others (26 February, p 540) of an apparently unfavourable effect of adjuvant immunotherapy for stage IIB malignant melanoma ends with the warning that previous reports of benefit from immunotherapy for melanoma "should not be readily accepted." However, their experience is not unique¹ and their warning will not be heeded: 69 clinical trials of immunotherapy for melanoma are currently planned or in progress, 11 using the same technique as that used by Dr McIlmurray and his colleagues (BCG + lethally irradiated autologous tumour cells) and 35 using BCG (or a derivative) alone (*Compendium of Immunotherapy Protocols*, 1976).

With an overall total of 330 immunotherapy trials now in progress it is evident that the long, inglorious history of clinical immunotherapy² is to be indefinitely prolonged. This persistent verification of uncertainty is largely due to the enormous promotion of the topic and to the irresponsible claims for the clinical

relevance of certain animal tumour studies. Approximately one-third of the contents of current cancer journals is devoted to aspects of tumour immunity. Of the animal tumour studies contributing to this enormous literature, which provide the chief stimulus to clinical trials, practically all are done using tumours which are allogeneically transplanted or which were induced by powerful chemical carcinogens or by oncogenic viruses; whole volumes of leading cancer journals contain not a single instance of the use of any other type of tumour for experiments purported to be relevant to immunotherapy. Yet it has been known for over 20 years that the immunogenicity displayed by such tumours is *artefactual* and is rarely, if ever, displayed by naturally occurring tumours suitable as models of clinical cancer.³ This information has not been emphasised to clinical workers—rather, intimations of clinical relevance very commonly enter the discussion of papers reporting successful immunotherapy using the artefactual systems. Your leading article on adjuvant therapy for lung cancer (22 January, p 187) attributes to the distinguished tumour immunologist, Professor R W Baldwin, a recent statement that "the original concept that human tumours are antigenic and that immunotherapy may aid their elimination by an immune reaction is no longer tenable." This informed judgment is courageous because it is certain to be unpopular; but it is difficult to understand what new information has been acquired to sustain it and why it was not delivered earlier.

It is our view that retrenchments about the prospects of immunotherapy for cancer are about to become fashionable among its former proponents. If this proves to be so the basis of this expensive promotion and *volte face* deserves inquiry. We believe that research funding bodies have assisted this imbalance by too ready acceptance of the customer/contractor principle of assessing projects and programmes whereby generous facilities and encouragement are extended to those who rashly promise the early clinical application of investigations not yet done. There have been periods when no young cancer researcher could afford to deny his "belief" in immunotherapy or to supply interpretations of his data which were discouraging to it. This is an unhealthy influence, immensely dispiriting to uncommitted endeavour and unduly helpful to politic careerism. New ideas are outrageous and tend to come from sceptics and iconoclasts. Funding agencies could assist the inquiring spirit of youth by marking down those whose pioneering is to be done from the security of the bandwagon of the moment. Tumour immunology may well have important long-term implications for cancer biology and should be relieved of any need to promote premature and iterative clinical trials.

H A S VAN DEN BRENK

Dimbleby Department of
Cancer Research,
St Thomas's Hospital Medical
School,
London SE1

H B HEWITT

Cancer Research Council
Gray Laboratory,
Mount Vernon Hospital,
Northwood, Middx

¹ van den Brenk, H A S, *British Medical Journal*, 1969, 4, 171.

² Currie, G A, *British Journal of Cancer*, 1972, 26, 141.

³ Hewitt, H B, et al, *British Journal of Cancer*, 1976, 33, 241.

Toxic effects of depot tranquillisers in mental handicap

SIR,—Through your columns may I ask any doctors with experience of severe toxic reactions with the above to communicate with me?

Following reports of fatal hyperthermia with mentally handicapped inpatients on fluphenazine enanthate during an Australian heat wave the two UK drug companies marketing fluphenazine decanoate (Modectate) and flupenthixol decanoate (Depixol) advise doctors not to use these with the mentally handicapped. A check of original reports shows that most fatalities occurred among those also on anti-Parkinsonian agents, which decrease sweating, apart from other drugs such as for epilepsy. Under the auspices of the Royal College of Psychiatrists a small working party of consultants in mental handicap met on 15 February to review UK experience. From a background of up to seven years' practice among 4910 UK inpatients and 213 currently on depot medication no fatalities and only five severe toxic reactions were reported, each responding rapidly to anti-Parkinsonian drugs. The doses used were in general up to 100 mg of fluphenazine decanoate and 400 mg of flupenthixol monthly.

The rationale of not using depot preparations among the mentally handicapped was that it was believed that some brain-damaged patients were particularly sensitive to phenothiazines and there is evidence that this may well be so. The working party believed that, used with caution, depot preparations were both effective and valuable, but before attempting to set the record straight we would be grateful to hear from other doctors in community and hospital practice who work with child and adult mentally handicapped patients.

M J CRAFT

Bryn y Neuadd Hospital,
Llanfairfechan, Gwynedd

Use of depot tranquillisers in disturbed adolescent girls

SIR,—We have been treating girls in a secure home for disturbed adolescents with the intramuscular depot preparations fluphenazine decanoate and flupenthixol decanoate. Most of the girls admitted to this home have already been in care, all come from broken or severely disrupted homes, and all the girls have been uncontrollable in their previous situations. Many have been in conflict with the law. The environment of the home is extremely caring but with firmly defined limits of what is acceptable and what is not. The effect of maternal deprivation on many of these children is clearly observable and understood by the staff, and as far as possible the staff try to compensate for this. Oral medication is used with some of these girls, but tablet-taking default often occurs.

Over the past year 10 of these girls who were extremely disturbed, violent, and aggressive and who were not influenced by tender, loving care or by psychological strategies were started on depot tranquillisers. Five girls were treated with fluphenazine decanoate, the dose range being from 12.5 to 25 mg at weekly to monthly intervals, while five girls were treated with flupenthixol decanoate, the dose range being from 20 to 40 mg at weekly to monthly intervals. The ages of the girls ranged from

12 to 16 years. Two of the girls were suffering from a schizophrenic illness (one of these suffered from grand mal epilepsy) and one other girl, who was homicidal at the age of 9 years, suffered from temporal lobe abnormalities. Concomitant intramuscular and oral anti-Parkinsonian drugs were also given to these 10 girls. The girls on this regimen benefited, their disturbed behaviour subsided, they became approachable in a psychotherapeutic framework, and were alert, co-operative, and psychologically more stable. Five of them have remained on the treatment for nine months to one year and others for shorter periods of time. Three girls have improved sufficiently to stop the treatment altogether. The ultimate aim in all cases is to try to stop the treatment and help them to adjust to life. It was recognised that in these girls acting-out aggression and emotional outbursts were an important part of maturation and these episodes were used therapeutically as far as possible.

The following blood tests were performed on the 10 girls, initially weekly, then fortnightly, and then at monthly intervals: urine testing, haemoglobin level, white blood count, erythrocyte sedimentation rate, blood urea concentration, and liver function tests. The only abnormality detected in four cases was a raised serum alkaline phosphatase level (up to 30 U, the normal range being 4-15 U); this is being further investigated but is probably caused by active growth of bone. Plasma bilirubin, blood urea, and other blood and urine tests were consistently normal. In three of the girls there was a raised serum aspartate aminotransferase (SGOT) level, which was explained by the pathologist as due to muscle tissue breakdown.

We would be interested to hear of any other doctors' experience in this field.

M S PERINPANAYAGAM
ROBIN A HAIG

Stone House Hospital,
nr Dartford, Kent

Child health and environmental lead

SIR,—Your leading article on this subject (29 January, p 255) presents a literate but selective and incomplete review of a complex topic.

You take careful note of three retrospective studies¹⁻³ which found no relation between low-level lead exposure and neuropsychological functioning. You point out that two of those negative studies^{2,3} were characterised by precise matching for age, sex, and social variables of the children exposed to lead and of those not so exposed. You fail to note, however, that the findings in each of these negative studies are blurred by the inclusion in the "lead-exposed" group of children with normal blood lead levels. Thus 30 (64%) of 47 preschool children in the "lead-exposed" group described by Lansdown *et al*¹ and 37 (27%) of 138 children in the "lead-exposed" group of McNeil and Ptasnik² had blood lead levels below 2 $\mu\text{mol/l}$ (40 $\mu\text{g}/100\text{ ml}$). In the study of "eleven-plus" examination results and lead exposure described by Hebel *et al*³ lead exposure was defined only in terms of residence near a battery factory, a risk factor that we have found to produce elevated blood lead levels in no more than 50-60% of exposed children.^{4,5} The net effect of including normal children in the "lead-exposed" group is dilution of the

data. That factor could well account for the negative results obtained.

On the opposite side of the issue you fail to take note of several recent positive studies. Most important of these are the reports by de la Burd⁶ *et al*,⁷ which present evidence for psychological dysfunction in children now aged 8 years who (from 1 to 3 years of age) had asymptomatic increased absorption of lead. These investigations were carefully matched prospective studies of precisely the type which you suggest should be performed. In addition, several studies have found slowed nerve conduction velocity in children⁸ and adults⁹ with asymptomatic increased absorption of lead.

Further work is still required to refine these observations, but in our opinion the data indicate that low-level increased lead adsorption is capable of producing neurological change in children. In July 1976 the Committee on Toxicology of the National Academy of Sciences in the United States completed a lengthy review of subclinical lead exposure in children.¹⁰ The committee concluded that "although no single study cited represents a perfect model . . . the general trends seen in these studies indicate a relationship between asymptomatic lead poisoning and neurologic and behavioral handicaps." You should have broadened the perspective of your leading article and included these developments.

PHILIP J LANDRIGAN
EDWARD L BAKER

Environmental Hazards Activity,
Cancer and Birth Defects Division,
Bureau of Epidemiology,
Center for Disease Control,
Atlanta, Georgia

¹ Lansdown, R G, *et al*, *Lancet*, 1974, **1**, 538.

² McNeil, J L, and Ptasnik, J A, *International Symposium on Recent Advances in the Assessment of Health Effects of Environmental Pollution*, p 24. Luxemburg, Commission of the European Community, 1974.

³ Hebel, J R, *British Journal of Preventive and Social Medicine*, 1976, **30**, 170.

⁴ Landrigan, P J, *et al*, *New England Journal of Medicine*, 1975, **292**, 123.

⁵ Center for Disease Control, *Morbidity and Mortality Weekly Report*, 1976, **25**, 85.

⁶ de la Burd⁶, B, *et al*, *Journal of Pediatrics*, 1975, **87**, 638.

⁷ de la Burd⁶, B, *et al*, *Journal of Pediatrics*, 1972, **81**, 1088.

⁸ Landrigan, P J, *et al*, *Journal of Pediatrics*, 1976, **89**, 904.

⁹ Seppäläinen, T M, *et al*, *Archives of Environmental Health*, 1975, **30**, 180.

¹⁰ Committee on Toxicology, Assembly of Life Sciences, National Research Council, National Academy of Sciences, *Recommendation for the Prevention of Lead Poisoning in Children*. Washington, National Academy of Sciences of the USA, 1976.

*.*Drs Landrigan and Baker raise several interesting points in their letter. Unfortunately a leading article cannot have the scope of a review article and must of necessity be selective, particularly when commenting on a complex subject.

While it is true that Lansdown *et al*, McNeil and Ptasnik, and Hebel included children with normal lead levels in their "lead-exposed" groups, this is, of course, desirable in population studies. Selection of a "lead-exposed" group on the basis of blood lead levels is likely to lead to bias since there are well-known associations between elevated blood lead levels and pica and between pica and behaviour disturbance and mental handicap. The carefully matched prospective study of de la Burd⁶ *et al* was undertaken on a group of children, most of whom should properly be considered as having been lead poisoned, rather than exposed (all had positive tests for urinary coproporphyrins, mean blood

lead level of 2.8 $\mu\text{mol/l}$ (58 $\mu\text{g}/100\text{ ml}$) with a range of 1.5-4.8 $\mu\text{mol/l}$ (30-100 $\mu\text{g}/100\text{ ml}$), and many had lead lines on x-ray). Indeed, 20% of the "lead-exposed" group were treated with calcium versenate. All had pica of paint or plaster; the incidence of pica in the control group was not stated. Thus their findings of psychological dysfunction were hardly surprising in view of earlier studies referred to in the leading article. Landrigan *et al* have provided "modest evidence for an association between lead intake and subclinical motor neuropathy" (ref 8 above), but no frankly pathological conduction velocities were found in 32 children with blood lead levels between 3.0 and 4.8 $\mu\text{mol/l}$ (60 and 100 $\mu\text{g}/100\text{ ml}$) in that study.

The concern of Drs Landrigan and Baker is understandable in the light of their findings of elevated blood lead levels in 98.8% of children living within a 1.6-km radius of a lead smelter in Idaho, 22.1% of whom had levels of 3.9 $\mu\text{mol/l}$ (80 $\mu\text{g}/100\text{ ml}$) or more. Clearly such levels of exposure are intolerable, but they hardly constitute low-level increased lead absorption. Likewise, water lead levels in excess of WHO requirements must be eradicated, although the evidence for an aetiological relationship between water lead content and mental handicap is at present tenuous.

The conclusions of the leading article stand.—Ed, *BMJ*.

Chemoprophylaxis of malaria

SIR,—Your leading article (20 November, p 1215), your answer to Professor W Peters's letter (1 January, p 49), and Dr Victor Bergson of Roche Products Ltd (12 February, p 447) all recommend the fixed combination of pyrimethamine 25 mg with sulfadoxine 500 mg marketed as Fansidar for the chemoprophylaxis of malaria in areas of known chloroquine-resistant falciparum malaria.

However, Fansidar is not available in many countries, including the UK and the USA. If Fansidar were available in Britain people could take a supply with them before travelling to endemic areas in Asia and South America. Will Roche Products Ltd be marketing Fansidar in Britain?

ANTHONY HALL

Hospital for Tropical Diseases,
London NW1

*.*We are informed by Roche Products Ltd that there are no plans for marketing Fansidar in Britain at present, but it is available to doctors on request.—Ed, *BMJ*.

Future of child health services

SIR,—Dr J McLuskie (12 March, p 711) suggests that the recommendations of the Court Report¹ with which he and his colleagues disagree were engendered by the membership of the committee being weighted with "big-city paediatricians talking big-city paediatrics." Since many of your readers may not have access to the whole report and as the report does not identify the membership of the committee by profession or appointment it might be helpful to remind them of its composition.

Only 10 of the 23 members of the Court Committee were medically qualified and of these, three are consultant paediatricians,