ture to be used without providing nuclear medicine facilities. The simplicity of the technique enables it to be performed at the bedside at any time by anyone with a minimum of training in the use of radioisotopes and with the least inconvenience to the patient.

Since ^{131}I -MAA was initially described as a lung scintiscanning agent, it is ideal for extension into a formal lung scan, permitting evaluation of perfusion deficiencies in cases of suspected pulmonary emboli.

Nuclear medicine is an expensive pastime, but the procedure, as we have described it, demands little in expertise, special skills, or manpower. In comparison with other nuclear medicine investigations it is inexpensive. It could become widely available but has the disadvantage of requiring pretest blockade of thyroidal uptake by sodium iodide. Sensitivity (88%) and specificity (91%) are comparable to those of similar techniques for detecting deep-vein thrombosis. Even with this technique, however, the information yielded cannot be considered on a par with that of conventional α -ray phlebography. Although we have not undertaken any clinical studies, there would appear to be no objection to using ^{125}I -labelled MAA, with the consequent lowering of radiation dose to the patient. At the time of the original work ^{125}I -MAA had not become available.

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¹ D'Auria, D, *et al*, *British Journal of Surgery*, 1973, **60**, 908.

² Webber, M M, Webb, R, jun, and Craggin, M, *Medical Radioisotope Scintigraphy*, 2, p 773, Vienna, IAEA, 1969.

Driving after anaesthetics

SIR,—As an anaesthetist who has volunteered many times for brief experimental nitrous oxide and oxygen anaesthetics, and who has followed up 81 outpatients anaesthetised for orthopaedic procedures,¹ I would like to add a few observations to the discussion about residual effects of general anaesthetics (10 and 31 March, pp 686 and 891).

Subjective and objective changes in mood and behaviour induced by nitrous oxide may outlast retention of appreciable quantities of this gas. For example, a tendency to hypoxaemia induced by nitrous oxide in the lunch hour may be commented on by one's spouse in the evening, without knowledge of the precipitating circumstances. When nausea has resulted malaise has persisted. A lunch-time inhalation of 80% nitrous oxide with oxygen only up to the point of no response to repeated auditory stimuli may leave the volunteer subjectively aware of slight difficulty in assessing traffic speed while waiting at a T junction in the evening. Although residual effects were not noticed 24 hours after anaesthesia, the fact that they appeared to outlast the presence of the causative agent should warn against simplistic predictions of recovery.

Nine of the 81 patients felt nauseated or actually vomited after outpatient anaesthesia and it is noteworthy that this was often precipitated by the journey home. Two patients felt nauseated or "sickly" for about two to three days. Two patients felt very tired for 24 hours.

If anyone takes up Dr Ogg's suggestion of a

study of volunteers or patients subjected to driving tests at 24 and 48 hours after anaesthesia it might help to design driving tests to deliberately stimulate the semicircular canals, and to seek subjects who have a low threshold to general anaesthetics and who are easily nauseated. Duration of the driving test may also be relevant.

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¹ Smith, W D A, *Outpatient anaesthesia with particular reference to nitrous oxide*, appendix E. MD thesis, University of London, 1969.

Sex determination and the H-Y antigen

SIR,—Your lucid and comprehensive leading article (17 March, p 704) on H-Y antigen nevertheless omits certain evidence from one crucial abnormality of sexual development. As you mention, H-Y antigen is expressed in true hermaphrodites, yet by definition such patients have ovarian as well as testicular tissue. Moreover, the two types of gonads exhibit lateralisation, testes being preferentially situated on the right and ovaries on the left side.^{1 2} This asymmetry is strong evidence in favour of the involvement of an epigenetic factor in the gonadal differentiation of these patients. Clearly, if this epigenetic factor could be pinpointed, this might be expected to throw light on the general problem of gonadal differentiation.

A useful pointer comes from an observed asymmetry in the development of normal gonads. In human fetuses the two gonads differ in size and cell number, those on the right being on average somewhat larger, and containing more cells, than left-hand gonads.³ Furthermore, testes are markedly larger than ovaries in fetuses of similar crown-rump-length.³ If we make the assumption that fast growth is a prerequisite for testicular differentiation, the asymmetrical distribution of testes and ovaries in hermaphrodites is simply explained: testes tend to develop on the right because the gonad on this side is naturally faster growing than its partner on the left, and vice versa for the preferential location of ovaries on the left.

If we make the further assumption that the expression of H-Y antigen is normally confined to the sex whose gonads grow faster than those of the other sex, another puzzling finding is explained. As mentioned in your editorial, H-Y antigen is expressed in the males of mammals and is associated with testicular development, but in birds the antigen is expressed in females and is likely to be associated with ovarian development. What, then, is the underlying similarity between testicular development in mammals and ovarian development in birds? When we compare the relative growth rates of testes and ovaries, it becomes apparent that whereas mammalian testes grow faster than ovaries, in chick embryos aged 8 days onwards the ovaries grow faster than the testes.^{4 5} This difference in relative growth rates finds a parallel in the fact that in mammals the testis is the dominant embryonic gonad in contrast to birds, in which the ovary is the dominant embryonic gonad.⁶

The association of H-Y antigen with the fast growing, dominant embryonic gonad provides a simple explanation for the finding that the antigen is expressed by the heterogametic sex regardless of whether this is the

male, as in mammals, or the female, as in birds. It does not provide an answer to the chicken-and-egg question, whether the antigen causes gonadal differentiation or vice versa. Whatever the precise relationship it is clear, however, that the antigen is associated not with any particular type of gonadal differentiation but with a common denominator underlying the development of mammalian testes and avian ovaries.⁷ There appears to be strong evidence that this common denominator is a relative effect which becomes apparent in a measurable difference in growth rate.

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¹ Polani, P E, *Philosophical Transactions of The Royal Society of London B*, 1970, **259**, 187.

² van Niekerk, W A, *True Hermaphroditism*. Maryland, Harper and Row, 1974.

³ Mittwoch, U, *Annals of Human Genetics*, 1976, **40**, 133.

⁴ Mittwoch, U, *et al*, *Nature New Biology*, 1971, **231**, 197.

⁵ Gasc, J-M, *Journal of Embryology and Experimental Morphology*, 1978, **44**, 1.

⁶ Jost, A, in *Organogenesis*, ed R L de Haan and H Ursprung, p 611. New York, Holt, Rinehart and Winston, 1965.

⁷ Mittwoch, U, *Journal of Medical Genetics*, 1977, **14**, 335.

Polyunsaturated fatty acids in multiple sclerosis

SIR,—Dr D Bates and others (10 March, p 683) have had the misfortune to invest much time and effort in a clinical trial (18 November, p 1390) which, so far as α -linolenate is concerned, is entirely nugatory. They did, however, from time to time receive verbal warnings that the prostaglandin E_2 (PGE_2) reaction produced by prolonged exhibition of (tartrazine-coated) Naudicelle capsules was puzzlingly out of step with those given by linoleic and arachidonic acids (LA and AA).¹

The circumscribed use of the drug advocated in my letter (10 February, p 411) and the tentative suggestion made earlier with respect to children² surely do not merit the epithets "avowed propagandist for the use of Naudicelle" and "advocate of its administration to children." I plead guilty only to putting forward a new idea.

The electrophoretic tests used^{1 2} have been validated against widely accepted indicators of lymphocyte sensitisation.^{3 4} Failure to "catch on" in "other laboratories in Britain" is immaterial since the method currently receives scholarly and unprejudiced study in the United States, West and East Germany, Italy, France, and other countries. Three international meetings are scheduled over the next six months to discuss the fully automatic and advanced laser-Doppler machines developed recently for simplified objective measurements.

Bates *et al* write in their paper that "the frequency of attacks was not significantly different between the four groups (table II)" (a difference from the original findings of Miller *et al*), though when the "attack score" is used (a statistic of their own, inadequately explained) a "significant difference" emerges between columns C and D. The deterioration of Naudicelle patients faster than controls ($P < 0.05$) is rejected by the authors as not biologically significant. I agree. But what is the P value of the difference between C and D—not given in the statistical analysis?

A retest with pure α -linolenate and adequate laboratory control throughout is needed. We know that some of the patients of Bates *et al*

either did not take the material they were supposed to be taking or did not respond. Actually we already have evidence that patients who have been on tartrazine-Ponceau-R-free capsules for nine months or so do show the expected and not the anomalous PGE₂ reaction.

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¹ Field, E J, and Joyce, G, *European Neurology*, 1978, 17, 67.

² Field, E J, *Lancet*, 1978, 1, 780.

³ Mertin, J, et al, *Klinische Wochenschrift*, 1974, 52, 248.

⁴ Caspary, E A, in *Immunological Techniques for Detection of Cancer*, ed B Bjorklund, p 74. Stockholm, Bonniers, 1973.

⁵ Millar, J H D, et al, *British Medical Journal*, 1973, 1, 765.

"Trench foot" caused by the cold

SIR,—With reference to the letter (3 March, p 622) from Dr Paul Marcus, we have read it with interest and he does make some valid points, particularly in respect of the wind chill factor, which was without doubt of significance in the injury we described in our letter (10 February, p 414).

It was difficult to decide, when our case presented some six days after the initial injury, whether it was or was not one of frostbite; but on balance, because of the rather diffuse and ill-defined area of circulatory disturbance and the lack of tissue necrosis other than the two small blisters referred to, we considered that it was a case of "exposure foot," which might be a better title than trench or immersion foot.

Interestingly, some four months after the initial injury, there is still a sluggish capillary response of the upper surface of the affected foot from 2.5 cm proximal to the digital webs, and a reduction in the dorsalis pedis pulse on that foot. There is no evidence of any sensory loss or other neurological involvement. The patient himself is unaware of any difference in the two feet, other than that the affected foot still gets a little "puffy" by evening. On balance we think our original diagnosis was correct, although we cannot be certain.

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Unnecessary skiing injuries

SIR,—We have to report the disturbing fact that school skiing parties do not always take precautions which would reduce the number of serious leg injuries.

Several days ago we admitted to our orthopaedic department two 16-year-old girls who had been taking part in the same skiing holiday in the Italian Dolomites. The skiing experience of both of them was limited to six hours of training on a fibre-glass slope, arranged by the PE department of their school. While in Italy they had professional coaching supervision and used equipment hired locally. Not once, however, was the efficacy of the ski bindings checked, nor did the instructor make sure that the boots were capable of disengaging from the skis in prescribed conditions.

In consequence, while suffering minor falls when skiing both girls sustained injuries to the knee; significantly, the boot failed to disengage from the bindings on the affected side. The first of the girls was subsequently tobogganed to the local hospital, her knee was x-rayed, and a diagnosis of minor sprain was made. She was advised to walk on the

affected leg in protective knee dressing, which she did for almost a week. The second girl, who had a similar experience, would not be bothered to follow the first girl's example and walked on the affected leg for four days.

Both of them presented in our hospital with locked knee. The x-rays revealed in both cases avulsion of the anterior tibial spine from the intercondylar tibial eminence. Both girls underwent emergency explorative surgery. The avulsed bone was reduced and fixed with a lag screw; the cruciate ligament attached to it was found to be intact.

We consider that school teachers in charge of skiing groups should be appropriately trained in safety checks, including checks of ski bindings, in order to eliminate the risk of such injuries.

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Alopecia areata

SIR,—Your leading article (24 February, p 505) refers to dinitrochlorobenzene (DNCB) as a new form of therapy for alopecia areata, and doctors who are confronted by patients with this distressing condition will be tempted to try any new treatment which might promote hair growth. I would, however, like to present my experience with this agent and suggest a cautious approach to its use. Seventeen patients were successfully sensitised to 2% DNCB in acetone. They then applied a 0.1% solution to the right side of the scalp for two months and to both sides for three months. After five months regrowth of hair had occurred in eight patients, but could only be definitely attributed to DNCB in five. In those five patients growth started on the right side and then followed on the left. In the other three growth was simultaneous on both sides and eyelashes reappeared in two. While this may reflect a general immunological stimulation by DNCB, it could have been a chance occurrence.

It is essential to induce an allergic contact dermatitis to promote hair growth and all 17 patients complained of irritation. Five patients experienced marked vesiculation and four of these developed postauricular and occipital lymphadenopathy. Two developed oedema of the eyelids, one requiring admission to hospital. Two patients, in spite of wearing PVC gloves for application, developed dermatitis of the hands. One patient was unable to go to work on two occasions on the day following application. The spouses of two patients developed a rash on the face.

This high incidence of side effects, the possibility of cross-sensitisation of DNCB with other nitrobenzene compounds and chloramphenicol, and the unknown sequelae of such potent antigenic stimulation calls for reservation in the use of DNCB in alopecia areata.

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Differences between Leeds fractures and London fractures?

SIR,—The short report by Dr M R Baker and others of a study of the 25-hydroxy vitamin D (25-OHD) concentrations in elderly women with fractured neck of femur in Leeds (3

March, p 589) reveals a lower mean plasma concentration in the fracture group than in age-matched controls. This contrasts with our own findings, which have already been reported to the Medical Research Society¹ and which are shortly to be published in full.² It would be reassuring to know that the apparent difference in 25-OHD concentration in these women remains statistically significant after suitable steps have been taken to allow for the grossly non-normal distribution of the concentrations.

In a cohort of 70- to 80-year-old patients with fractured neck of femur drawn from the catchment area of this hospital we found a mean 25-OHD concentration of 17.7 nmol/l (708 ng/100 ml) in comparison with 20.3 nmol/l (812 ng/100 ml) for age-matched patients admitted for routine orthopaedic surgery. This difference was not significant, the 95% ranges being 4.2-73.8 (168-2952) and 10.0-84.7 nmol/l (400-3388 ng/100 ml) respectively (a logarithmic transformation was necessary to correct the skewed distribution of the data). The interview-assessed dietary intakes of vitamin D were not different (mean values of 78 and 71 IU), nor were the histories of exposure to sunlight (6.5 and 6.7 arbitrary units in patients with fractures and controls respectively). We agree, however, that the vitamin D status of these elderly people is more strongly correlated with sunlight exposure than with dietary vitamin D intake.³

The Leeds data appear to be compatible with the hypothesis that vitamin D deficiency may contribute to fractured neck of femur in the elderly in Leeds. But we have found no evidence to implicate vitamin D deficiency in the aetiology of this fracture in outer London.

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¹ Wootton, R, et al, *Clinical Science and Molecular Medicine*, 1978, 54, 28P.

² Wootton, R, et al, *Clinical Science*. In press.

³ Hodkinson, H M, et al, *Journal of Clinical and Experimental Gerontology*. In press.

Hypnosis

SIR,—I would like to take issue with Dr H G Kinnell on his remarks on hypnosis (17 March, p 751).

He says that hypnosis may on occasion be harmful and quotes Dr David Waxman in support of this statement. Dr Waxman is, in fact, one of the leading exponents of hypnotherapy in this country and the fact that he recognises the dangers of the technique simply means that he uses it responsibly, as may be said of any other method of treatment.

Dr Kinnell disparages what he calls clinical anecdotal accounts in support of hypnosis and seems to imply that without controlled trials it is impossible to come to hard-and-fast conclusions about the usefulness of any method of treatment. I submit that if I see a patient, as I have done recently, who has been smoking 50 cigarettes a day for 30 years and who has severe chronic bronchitis and emphysema and if this patient has only consulted me in desperation after all other attempts to give up smoking have failed and if, further, after three short sessions of hypnosis he neither smokes nor wants to smoke, nor suffers any withdrawal symptoms, substitution symptoms, or other ill effect from the treatment, I do not