known supraventricular arrhythmia prior to cardioversion. Eight patients had rheumatic disease of the mitral valve, with dominant stenosis in five cases, and dominant incompetence in three. Four patients had ischaemic heart disease, ten patients had arterial fibrillation, and two had arterial flutter. All patients received premedication for cardiac catheterization, and it was reported that in most cases the behaviour of the mean systemic arterial pressure paralleled that of cardiac output, and no consistent change in peripheral resistance was observed. Such a comparison with healthy ambulatory patients undergoing routine conservation appears irregular, while the complete absence of controls during the investigation is open to criticism.

Interpretation of Figs. 1 and 5 may depend on all or any of the following: timing, dose, solution strength of increment related to transient obstructions, operative stimuli, manual pressure on the tissues, and ineffective packing. The omission on a graph of one or more known synchronized variables, resulting in possible interpolation, can be misleading for future investigators. The inhalation of radiopaque materials may be irrelevant, as lung aspiration can occur in non-anaesthetized patients during sleep.³ The observations on salivation conflict with the findings of Shafto,⁴ who expressed no trouble from this in 500 young patients anaesthetized with methohexitone.

The data would suggest an incremental methohexitone technique pushed to the limit. Most experienced operators would have treatment planned to avoid it. With no reported morbidity following this investigation, there may be a compensatory factor at present obscure which may even highlight the inherent safety of methohexitone.—I am, etc.,

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Vitamin A and the Skin

SIR,—Your somewhat obtuse leading article "Vitamin A and the Skin" (24 May, p. 464) cannot be allowed to pass without comment. Contrary to the view expressed by your contributor, there is nothing mysterious about the action of vitamin A on the skin. It has a number of well-established effects which are:

(a) Stimulation of mitosis resulting in an increase in epidermal thickness.^{7, 8, 14} It has been shown that the degree of hyperplasia is directly related to the local concentration of the vitamin and is associated with parakeratosis.^{1, 7}

(b) Vitamin A destabilizes cytomembranes and acts as a liberator of lysosomal enzymes.⁴ These enzymes are involved in the cytolytic processes occurring in the granular layer,⁷ and it has been shown that there is a release of these hydrolases after the local application of vitamin A.¹²

(c) The normal granular layer is increased in depth and, moreover, a granular layer can be induced in areas previously without a granular layer.⁸ In sites without a granular layer there is an optimum concentration of vitamin A which produces this effect.^{5, 7, 8} At high local concentrations of the vitamin the mitotic stimulation results in parakeratosis, even in the presence of an induced granular layer.^{1, 7} This is why Puccinelli and Bellone¹¹ and Burgoon *et al.*³ were unsuccessful in their treatment of psoriasis with vitamin A despite the induction of a granular layer.

(d) High local concentrations of vitamin A have an irritant action and cause erythema in both human and animal skin.^{5, 7, 12}

(e) Vitamin A induces the synthesis of alkaline phosphatase by epidermal cells.¹³

Factors (a) and (d) are likely to make psoriasis worse, while (b) and (c) would tend to be beneficial. In ichthyosis vulgaris, in which the epidermis is not already hyperactive, the effect (a) is less likely to be detrimental. Glucocorticoids reduce epidermal mitosis² and the tendency for vitamin A to increase mitosis is reduced by the administration of corticosteroids.¹⁴ Fluorinated steroids are particularly effective in depressing this epidermal mitosis,⁷ and they also reduce erythema owing to their vasoconstrictive action.⁹ In successful combined treatment of psoriasis by Jarrett and Spearman^{6, 7} and Whittle *et al.*¹⁵ with balanced concentrations of vitamin A and triamcinolone, the steroid depresses the undesirable effects of vitamin A without affecting the induction of a granular layer, and this is associated with a change to the normal type of keratinization.

With oral vitamin A it is difficult to produce a sufficiently high local concentration in the skin without producing general toxicity when treatment is to be continued over a long period. The effect of topically applied vitamin A is different for the acid, alcohol, and the various esters. The solubility of the vitamin is also important, and oil-soluble preparations, owing to their poorer penetration of the epidermis, are less effective than artificially water-solubilized preparations.

Any mystery regarding the action of vitamin A on the skin lies in speculations about its supposed "antikeratinizing" effect in the face of a total lack of evidence that mucous metaplasia occurs in adult mammalian skin even when high local concentrations are involved.^{7, 8, 10}—I am, etc.,

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Metabolism in Parkinsonian Patients

SIR,—We were interested in the preliminary communication by Dr. J. Braham and others (31 May, p. 552). One part of their paper referred to a comparison of the D-xylose test in five Parkinsonian patients and five normal controls.

We have studied patients suffering from post-encephalitic Parkinsonism and arteriosclerotic Parkinsonism at Ruchill Hospital, Glasgow. We performed (25 g.) D-xylose tests on 28 patients with Parkinsonism and in five age-matched controls. The five-hour urine excretion in the patients with Parkinsonism was 3.3 g. $\pm$ 1.9 g. (mean $\pm$ S.D.), while that for the controls was 4.5 g. $\pm$ 1.2 g. The difference was not statistically significant. The blood xylose level at one hour was also measured. The level in the patients was 29.0 $\pm$ 11.8 mg./100 ml. (mean $\pm$ S.D.). The control group had values of 38.4 $\pm$ 8.3 mg./100 ml. The difference between the means was not statistically significant.

Although the Parkinsonism population as a whole did not show a statistically significant reduction in the blood and urinary xylose, there was a group of such patients in our population who had consistently low values. These patients with low five-hour excretion of xylose had normal blood levels of haemoglobin, calcium, phosphate and alkaline phosphatase, vitamin B₁₂, and folate; their Figlu tests were normal—as were their faecal fat collections. Analysis of the weight loss of these patients over the last three years showed that an abnormal D-xylose test did not select those who were losing weight. The general conclusion derived from these studies was that there was no evidence of malabsorption in these patients apart from the abnormal xylose tests. When the abnormal D-xylose tests were repeated and a 5–24-hour collection, as well as the 0–5-hour collection, undertaken blood xylose levels were estimated for up to four hours after the oral dose of 25 g. D-xylose. The mean ratio of xylose excreted in the 5–24-hour period to that in the first five hours in the patients was 3.72:1. The same ratio in the controls was 0.42:1. The difference just fails to reach statistical significance ($t=2.18$). The peak of the xylose absorption curve was delayed (mean 2.44 hours) when compared with the controls (mean 1.96 hours). This, together with the increased excretion of D-xylose in the 5–24-hour period in the patients with Parkinsonism, suggests delay in the absorption of the xylose.

The absence of malabsorptive disease in our patients agrees with this hypothesis. This delay in absorption could be due to autonomic nervous system disturbance in Parkinsonism or to the drug therapy of Parkinsonism. Delay in the absorption would also render invalid the oral L-phenylalanine and L-tyrosine loading tests used by Dr. Braham and colleagues, as these are based on the assumption that the time course of the absorption of L-phenylalanine and L-tyrosine are the same in patients and controls.

It is therefore suggested that these tests are not acceptable as indicators of abnormal metabolism of L-phenylalanine and L-tyrosine.—We are, etc.,

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Prevention of Prolonged Labour

SIR,—I read with great interest and enjoyment the article under the above title by Mr. K. O'Driscoll and his colleagues in your issue of 24 May (p. 477).

Those of us familiar with the National Maternity Hospital will be aware that the practice of this institution reflects modern obstetrics at its best, and the authors are to be congratulated upon their results.

For some years I have been a firm advocate of stimulation of labour both in private and hospital practice, and when proper supervision is exercised can confirm absolutely the desirability of this mode of management. However, may I beg to add a warning note from points made in the opening preamble under the heading, "Three Popular Fallacies"? In my opinion prolonged labour, if allowed to occur, is still on occasion a reflection of at least relative cephalo-pelvic disproportion, and if in the course of a stimulated labour cervical stasis persists for four hours at most the case must be very carefully reviewed with a strong bias towards abdominal delivery. I have found that this policy has revealed a number of unexpectedly large babies whose future might well have been compromised by a difficult vaginal delivery had this been permitted to take place.—I am, etc.,

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Abortion Act in Practice

SIR,—Dr. R. W. Penny (26 April, p. 248) and Drs. D. C. Sturdy and R. J. D. Browne (17 May, p. 447) raised the question of the ethical dilemma a second doctor may encounter when consulted by a woman whose regular general practitioner has refused to recommend her request for abortion.

Few if any doctors would claim that in considering a request for therapeutic abortion they are able completely to divorce themselves from their religious, moral, and ethical beliefs and attain an objective and detached viewpoint. Inevitably the woman refused abortion by her general practitioner is likely to believe, even if mistakenly, that the refusal was based on such grounds. She is quite likely to feel a sense of aggrievement and resentment, and when, as is her undoubted right, she seeks a second opinion, she may state that she is unwilling to allow the second doctor to contact the first.

When a doctor is consulted in such a way he has three possible courses of action. Firstly, he may refuse to consider the case unless and until he has permission from the original general practitioner; an action which may be harsh and neglectful in the face of

obvious and genuine distress. Secondly, he may insist on the patient writing and signing a declaration to him and to her original general practitioner that she wishes to change practices forthwith, thus withdrawing from the list of her original general practitioner. Or, thirdly, he may agree to consider the problem but insist upon notifying the general practitioner of any decision he reaches. It is this last course of action which has offended Drs. Penny, Sturdy, and Browne, but the motive may well have included a desire not to deprive a colleague of a patient.

The whole dilemma can be avoided if all doctors who refused to recommend an abortion would make it perfectly clear to their patient that she is at liberty to seek a second opinion with his full approval.—I am, etc.,

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G. J. DAVIES.

Treatment of the Phobic Anxiety State

SIR,—I hope I can reassure Dr. G. C. Wilson (14 June, p. 694) about the safety of combining the monoamine-oxidase inhibitor antidepressant drugs, in suitable dosage and given only during the day, with the tricyclics, especially tryptizol and trimipramine, 50–150 mg., best given in the evenings. By separating the giving of the two drugs in this way one can also better cope with any side-effects. For instance, if the patient is sleeping too deeply on the tricyclic drug the dose can be reduced; likewise if the patient is showing postural hypotensive symptoms on the monoamine-oxidase inhibitor drug during the day the dose is also lowered; but one need not stop using either drug. We have used combined antidepressant drugs now on literally thousands of in- and outpatients, and have repeatedly written about it over the past few years.¹ Dr. D. R. Gander, from this department, has also published a special symptomatic study of patients treated with combined antidepressants.² There were very few side-effects, and none of them dangerous.

In their article (1 March, p. 559) on the treatment of phobic anxiety states, I am fully aware that Professor Martin Roth and Dr. D. H. Myers said that it was dangerous to combine both groups of drugs in this way. This is partly why I wrote this letter. A warning is also still given in the drug pamphlets sent out with these drugs, and a warning to this effect was also issued by the Dunlop Committee. However, I feel that people have mostly repeated each other's fears and warnings without checking the actual facts at the bedside.

A possible explanation of some of the present quite unmerited fear of combining the antidepressant drugs may lie in the following facts. Only two or three deaths from supposedly combining antidepressant drugs in proper dosage have ever been actually reported in the literature. These were some time ago, and before the fatal results possible from the taking of cheese with the monoamine-oxidase inhibitor drugs were known about. Some months ago a patient of mine, who had had combined antidepressant drugs for over three months, died suddenly while taking Parstelin (tranylcypromine and trifluoperazine) during the day and trimipramine at night. Of course this was immediately blamed by others on the use of combined

drugs and a coroner's inquest ordered. This gave me time to set about looking for the real cause of death. This I was able to find out on careful inquiry. A large meal of macaroni cheese had in fact been eaten by him an hour before his fatal symptoms started.

This finding had not been known to my registrar treating the patient, who reached me by phone only after his death. I then also asked the pathologist to examine the stomach contents, especially for cheese. This, too, was found in large amounts. The coroner's verdict was death due to a cheese reaction. If I had not bothered to make these inquiries it would almost certainly have been wrongly attributed to combining the antidepressant drugs.—I am, etc.,

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Potassium Supplementation

SIR,—I am rather puzzled by the reference to "resin-based tablets" in the paragraph discussing potassium supplementation in the "Today's Drugs" article on hypotensive drugs (17 May, p. 430).

The statement is made that "resin-based tablets may pass through the gut unchanged." As a very large proportion of potassium chloride tablets being used at present are the wax-based Ciba tablets known as Slow-K, and few, if any, resin-based tablets are in use, many readers might wrongly assume that Slow-K is in fact resin-based and, as such, liable to the problem referred to. Certainly there is no evidence of Slow-K tablets passing through the gut unchanged, although "ghost" cores consisting of the wax matrix have occasionally been reported in the faeces. It has, however, been clearly shown that the potassium in Slow-K is completely absorbed.¹ Analysis of "ghost" tablets has also shown that they have yielded up their potassium content in passing through the gut.—I am, etc.,

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REFERENCE

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*We regret that the use of the term "resin-based" was inaccurate.—Ed., *B.M.J.*

Points from Letters

Tetracosactrin

Dr. A. F. TAYLOR (Director, Medical Development, Organon Laboratories Ltd., Surrey) writes: May I draw attention to an omission from your useful article "Corticotrophin and its Synthetic Analogues" (28 June, p. 809). Tetracosactrin is available in the United Kingdom as Cortrosyn and as a long-acting zinc hydroxide complex, Cortrosyn Depot. Cortrosyn is available in sterile ampoules each containing 0.25 mg. freeze-dried tetracosactrin. Cortrosyn Depot is presented in 2 ml. vials containing concentrations of 0.5 mg./ml. or 1 mg./ml.