diarrhoea that are often provoked and by increased elimination of potassium by the normal kidney,⁴ though of course if the kidney is diseased, dangerous hyperkalaemia may ensue. Though this child vomited and apparently had normal kidneys he evidently absorbed enough potassium to overwhelm the excretory mechanism. The final serum level was probably inflated by the effects of anoxia and acidosis. The electrocardiogram shows an advanced stage of hyperkalaemia⁵ where atrial activity has stopped and there is an irregular ventricular rhythm with grossly elongated complexes. Asystole or fibrillation is imminent.

This sad case again illustrates how dangerous pills that look like sweets can be for children,^{6,7} and re-emphasizes that all medicaments, even those as apparently innocuous as Slow-K, should be kept securely out of reach.—I am, etc.,

CHRISTOPHER BACON

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- 1 Ciba Laboratories, personal communication, 1973.
- 2 Committee on Safety of Medicines, personal communication, 1973.
- 3 Black, D. A. K., *Essentials of Fluid Balance*, 4th edn., p. 99. Oxford, Blackwell, 1967.
- 4 Keith, N. M., and Osterberg, A. E., *Annals of Internal Medicine*, 1942, 16, 879.
- 5 Friedberg, C. K., *Diseases of the Heart*, 3rd edn., vol. 2, p. 165. Philadelphia, Saunders, 1966.
- 6 Jolly, H., and Forrest, T. R. W., *Lancet*, 1958, 1, 1308.
- 7 *Lancet*, 1956, 1, 898.

Breast Cancer Regression under Oestrogen Therapy

SIR,—We read with great interest the provocative article by Dr. B. A. Stoll (25 August, p. 446) as well as the letter from Drs. P. Garcia-Webb and M. H. Briggs (17 November, p. 419) raising several points in debate. One major issue in the discussion was the question whether high doses of oestrogens increase blood prolactin levels in postmenopausal breast cancer patients, as stated by Dr. Stoll quoting our unpublished data. We wish to report these data, as well as others which are pertinent to the discussion.

The effect on blood prolactin levels of two oestrogen-related compounds, ethinyloestradiol and nafoxidine (U11, 100A) which are both active in the therapy of advanced breast cancer^{1,2} was studied. Ethinyloestradiol 1 mg thrice daily by mouth, and nafoxidine 60 mg thrice daily by

mouth, were given respectively to four and six postmenopausal women with advanced breast cancer. None was receiving any other drug known to alter prolactin secretion. Blood samples were collected between 8 and 9 a.m. after an overnight fast for several days before and during treatment. All samples from the same individual were run in the same assay for prolactin as previously described.^{3,4} Since the distribution of prolactin values appeared to be log-normal, calculations and statistical analysis were made after logarithmic transformation.

Ethinyloestradiol in doses therapeutically active in advanced breast cancer significantly increased basal prolactin secretion (see table). This observed increase seems thus to refute the generally held theory explaining the therapeutic effect of high-dosage oestrogens in breast cancer by an alleged inhibition of prolactin secretion.^{5,7} On the other hand nafoxidine failed to stimulate prolactin secretion and even had an inhibitory effect in one case.

Nafoxidine is an oestrogen antagonist⁸ that binds to tissue-specific "oestrogen receptors," acting at this level as a competitive inhibitor of oestrogens.⁹ Nevertheless, this compound also behaves as a weak oestrogen in castrated animals¹⁰ and in postmenopausal women.² It inhibits growth of the dimethylbenzanthracene (DMBA)-induced rat mammary carcinoma^{11,12} yet it counteracts to a limited but definite extent the ovariectomy-induced regression of this tumour, possibly by its weak oestrogenic properties.¹³ In postmenopausal women with advanced breast cancer nafoxidine has been found to induce objective remissions in approximately 35% of the patients treated.² The question, however, is not entirely settled whether the therapeutic effect of nafoxidine in postmenopausal breast cancer patients is caused by oestrogen antagonism or by oestrogen action. The latter hypothesis finds some support in the observation that both ethinyloestradiol and nafoxidine seem active in the same category of patients—namely, those in whom cancer tissue contains "oestrogen receptors."¹⁴

If nafoxidine and ethinyloestradiol produce tumour regression in breast cancer through their oestrogenic properties, it is necessary to postulate that they do so independently of their divergent effects on prolactin secretion. In the DMBA-induced mammary cancer of the rat, in the development and growth of which prolactin plays a crucial part,¹⁵ it has been suggested by Meites¹⁶ that the inhibitory effect of large doses of oestrogens is exerted by inter-

ference with the peripheral action of prolactin on tumour cells. If this were also the case in human breast cancer, then greater antitumour efficacy may theoretically be expected from oestrogenic-type compounds, such as nafoxidine, which are devoid of stimulating effect on pituitary prolactin secretion.

Part of the research reported here was supported by grants from the Fonds de la Recherche Scientifique Medicale (Belgium) and the Ford Foundation (U.S.A.) and by a grant from the Fonds Cancérologique de la Caisse Generale d'Epargne et de Retraite.

—We are, etc.,

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- 1 Stoll, B. A., *British Medical Journal*, 1973, 3, 446.
- 2 E.O.R.T.C. Breast Cancer Group, *European Journal of Cancer*, 1972, 8, 387.
- 3 L'Hermite, M., Delvoe, P., Nokin, J., Vekemans, M., and Robyn, C., in *Prolactin and Carcinogenesis*, ed. A. R. Boyns and K. Griffiths, p. 81. Cardiff, Alpha Omega Alpha, 1972.
- 4 Nokin, J., Vekemans, M., L'Hermite, M., and Robyn, C., *British Medical Journal*, 1972, 3, 561.
- 5 Segaloff, A., et al., *Cancer*, 1962, 7, 758.
- 6 Kennedy, B. J., *Cancer*, 1962, 15, 641.
- 7 Kim, U., *Cancer Research*, 1965, 25, 1146.
- 8 Terenius, L., *Acta Endocrinologica*, 1970, 64, 47.
- 9 Rochefort, H., and Capony, F., *Febs Letters*, 1972, 20, 11.
- 10 Duncan, G. W., Lyster, S. C., Clark, J. J., and Lednicer, D., *Proceedings of the Society for Experimental Biology and Medicine*, 1963, 112, 439.
- 11 Terenius, L., *European Journal of Cancer*, 1971, 7, 57.
- 12 Heuson, J. C., et al., *Gynecologic Investigation*, 1971/72, 2, 130.
- 13 Gallez, G., Heuson, J. C., and Waelbroeck, C., *European Journal of Cancer*, 1973, 9, in the press.
- 14 Engelsman, E., Persijn, J. P., Korsten, C. B., and Cleton, F. J., *British Medical Journal*, 1973, 2, 750.
- 15 Pearson, O. H., Llerena, O., Molina, A., and Butler, T., *Transactions of the Association of American Physicians*, 1969, 82, 225.
- 16 Meites, J., *Journal of the National Cancer Institute*, 1972, 48, 1217.

Geriatric Orthopaedics

SIR,—In the section on hip fractures in his otherwise admirable article (2 February, p. 190) Mr. M. B. Devas states that "there is no contraindication to a geriatric patient receiving either general anaesthesia or hypotension, each of which materially benefits both patient and surgeon."

We have over 25 years' experience of anaesthesia for these cases and only occasionally have either we or the surgeon considered it desirable to induce hypotension. We make extensive use of induced hypotension in suitable patients of all ages for all types of surgery. In our view, however, it is undesirable and possibly dangerous to advocate the unrestricted use of this technique in a group of patients many of whom, perhaps the majority, are in such poor physical and mental shape that hypotension would be an unjustifiable risk. Further, these patients are not always operated on by surgeons of sufficient experience to make use of hypotension safely.

We believe that these patients should be investigated in the manner described by Mr. Devas and operated on at the earliest convenient moment without hypotensive

Blood Prolactin Levels before, after and during Treatment

Case	Age (years)	Type of treatment	Control prolactin*		Treatment prolactin*		P (Student's t test)
			Mean (± 1 S.E.M.)	n	Mean (± 1 S.E.M.)	n	
1	51	Ethinyloestradiol	357 (308-746)	2	673 (603-746)	3	<0.05
2	54	Ethinyloestradiol	89 (87-93)	5	202 (180-227)	7	<0.001
3	72	Ethinyloestradiol	542 (499-510)	9	893 (766-1042)	6	<0.02
4	89	Ethinyloestradiol	423 (399-449)	6	1302 (900-1157)	5	<0.001
5	61	Nafoxidine	74 (40-138)	3	50 (37-67)	5	N.S.
6	69	Nafoxidine	642 (630-654)	2	720 (667-777)	6	N.S.
7	72	Nafoxidine	552 (500-610)	9	484 (429-545)	2	N.S.
8	74	Nafoxidine	166 (134-205)	5	160 (113-226)	4	N.S.
9	75	Nafoxidine	47 (38-58)	4	64 (52-77)	4	N.S.
10	80	Nafoxidine	480 (469-490)	6	318 (297-341)	5	<0.001

*Expressed as mU/ml by reference to the laboratory standard. Calculations and statistical analysis after logarithmic transformation. n = number of determinations.
N.S. = not significant.

anaesthesia and with liberal replacement of blood.—We are, etc.,

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Death during Dental Anaesthesia

SIR,—With reference to your medicolegal report (2 February, p. 207) entitled "Death during Dental Anaesthesia" I wish to make the following comments.

In evidence Mr. Alan Williams said regarding intravenous methohexitone, that "he had been instructed in its use at a course run by the Society for the Advancement of Anaesthesia in Dentistry." From this it might be inferred that the S.A.A.D. claimed to turn out trained anaesthetists after three days' tuition. This is far from the case, and I quote from my own lecture on the course: "If you expect to go away after three days, fully trained and fit to launch yourselves on your unsuspecting patients, think again please. In this short time, we can only give you the rudiments of the subject for you to build on by further study. We lay great stress on the complications that can occur, and tell you how to treat them, and more importantly, we try to show how to conduct your practice so that you prevent complications occurring. We lay down strict basic rules of safe anaesthetic practice and insist that these are followed completely in every case."

Regarding Mr. Williams's "six breaths of nitrous oxide"; during the course, in lectures and demonstrations, he was repeatedly warned of the dangers of anoxia. This point receives frequent mention in the *S.A.A.D. Manual*, 3rd edition, which he was advised to study. The following extracts are appropriate to the case. P. 2, para. 1.—"The rules of safety are clearly defined. Until they can be adhered to, the method must not be attempted." P. 9, Recommendations, no. 2—"Oxygen restriction below 20% is never needed and should never be tolerated. Any technique . . . in which there may be a temptation to restrict oxygen . . . should be carefully avoided." P. 16, Criteria, para. 2—"Oxygen restriction neither follows the administration of methohexitone nor is it necessary in any of the techniques employing it." P. 31, para. 3—"Many complications can occur from abuse of the method. At all times the fundamental principles of safety must be strictly followed." P. 38, Care and Control, para. 4—"The dangers of anoxia must be avoided by *never reducing the oxygen below 20%*. P. 40, Causes of Anoxia, no. 2—"Oxygen restriction during inhalation anaesthesia." P. 39, Causes of Hypotension, (b)—"Anoxia."—I am, etc.,

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Society for the Advancement of
Anaesthesia in Dentistry

London W.1

Vaginal Cytology

SIR,—In reply to Mr. S. A. Way's letter (2 February, p. 201) it should be made clear that the Department of Health and Social Security has at no time stated that cervical cytological examination is unnecessary below

the age of 35. On the other hand, as the Registrar General's figures show, it is in those women aged 45 and over that the incidence of invasive cervical carcinoma is highest, and in situ carcinoma tends to precede the invasive lesion by 10 years.

The most urgent matter therefore has been to aim at comprehensive screening of women aged 35 and over, and to encourage this a fee for service is paid to general practitioners screening such women. This priority group has recently been extended to include selected higher-risk women below the age of 35. That general practitioners and others realize that younger women may be at risk is clear from the national figures, which show that about one-half of the two million smears taken annually in England and Wales come from women *below* the age of 35.—I am, etc.,

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D.H.S.S. Committee on Gynaecological Cytology

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Gamekeeper's Thumb on the Ski Slopes

SIR,—With reference to your leading article on this subject (9 February, p. 213), in addition to the mechanism described this injury appears to be more common on artificial training ski slopes, where the run is made of nylon mesh. In the event of a fall the thumb gets caught in the nylon mesh, and with the momentum of the body forced abduction ruptures the ulnar collateral ligament of the metacarpophalangeal joint of the thumb.—I am, etc.,

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British Academy of Psychopharmacology

SIR,—For many years the United Kingdom has lagged behind other countries in having no specific organization dedicated to psychopharmacology. Thus a number of other countries have established their own national organizations that are affiliated to the Collegium Internationale Neuro-Psychopharmacologicum (C.I.N.P.), one of the best known of these being the American College of Neuro-Psychopharmacology.

In view of the considerable contributions made by our country to psychopharmacology it appears to us that the present situation is anomalous and that the time has come to establish a national organization in Britain. To avoid confusion with the royal colleges we propose that this organization be called "The British Academy of Psychopharmacology."

We believe that there is a particular need to focus attention on the importance of drug treatment in psychiatry in the eyes of both the young clinician and the research scientist. Therefore the objects of the academy will be to further research in psychopharmacology, both clinical and experimental, and to improve the quality and standards of psychotropic drug evaluation. This can be accomplished by means of the spoken and written word through the media of meetings, study groups, and publications.

We propose to call a meeting in the near future of all those members of the profession who may have an active interest in psychopharmacology for the purpose of determining the constitution of the academy, to elect officers, and to consider the academy's policy, particularly in relation to the pharmaceutical industry. To this end we have drafted some suggestions and would be pleased to forward these to any interested member of the profession. We would also like to receive suggestions and comments concerning the establishment of the academy, and invite those interested to communicate with any one of the undersigned.—We are, etc.,

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ALEC COPPEN
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General Practitioner Research Group,
Twickenham

Home Graduates Only

SIR,—I heartily agree with Dr. T. K. Ghosh (16 February, p. 290).

I am a British subject now, but I am an Indian. I came to England in 1956 and have enjoyed every moment of my stay in this wonderful country. I was well aware of various attitudes in my medical colleagues but found that all these attitudes stemmed from a lack of communication by both parties concerned. When one appreciates British humour and their in-built sense of justice one soon realizes that the English as taught to us is vastly different from regional spoken English. When one masters this, one is no longer an outsider, no more so than a British missionary in, say, India can master the local vernacular and the local humour and still be an outsider. We are all colleagues, and if we would only "specialize" in the local English at the "local" (if you will pardon the pun), would not things be easier?—I am, etc.,

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London N.2

Vitamin A, Pregnancy, and Oral Contraceptives

SIR,—Mrs. Jennifer Wild and her colleagues (12 January, p. 57) sought to show that oral contraceptives increase serum vitamin A levels and investigated the hypothesis that there is an increased teratogenic risk for mothers who become pregnant at such a time. However, their conclusions were