for publication the following open letter to British psychiatrists:

Dear Fellow Psychiatrists,

I understand that it was your intervention that helped me so quickly (and comparatively painlessly) to leave the U.S.S.R., where the right to hold one's own beliefs is being constantly violated.

Life in the Soviet Union has taught me that the authorities in my country are extremely sensitive to the public opinion of the Western powers. I saw that help was especially effective where Western colleagues had interfered resolutely and uncompromisingly. That is why, on behalf of my colleagues in the Soviet Union, who have no possibility of expressing their opinions openly, I ask you to help those who have tried to defend the honour of psychiatry—Vladimir Bukovsky and Dr. Semyon Gluzman. By defending these honest and brave people you are also defending the integrity of our profession.

Whatever decision you choose to take, please keep in mind that while you are able to think and speak freely many sane people are forcibly detained in prison hospitals—with the connivance of our profession.

(Signed) Dr. Marina Voikhanskaya

—We are, etc.,

S. SHAFAR

Psychiatric Day Department,

A. THEODOSSIADIS

Psychiatric Department,
North Manchester General Hospital,
Crumpsall, Manchester

L. STEEN

Psychiatric Department,
St. Thomas's Hospital,
Stockport

Indomethacin, Prostaglandins, and Dysmenorrhoea

SIR,—The Danish general practitioner Dr. A. Christensen, whose serendipitous discovery of the beneficial effect of indomethacin in dysmenorrhoea is mentioned in your recent leading article (31 May, p. 461), perhaps reads *Nature* no more regularly than I read *Ugeskrift for Læger*. An article in the former journal¹ in 1972 stated: "One of the anti-inflammatory drugs could possibly prove of value in dysmenorrhoea, which may be associated with abnormal prostaglandin action; especially as aspirin has commonly been recommended for its simple treatment." The fact that anovulatory cycles (normally pain-free) in one young subject ended with menstrual losses having only one-fifth the usual content of prostaglandin-like material was reported briefly in 1967,² and a little evidence on the prostaglandin content of menstrual fluid from normal and dysmenorrhoeic subjects was given as long ago as 1965.³ Recently, as your article implies, these questions have been further investigated by more powerful methods and with better understanding of prostaglandin metabolism. The work of the Stockholm group is particularly notable. For example, Lundström *et al.*⁴ have recently found that the concentration of the prostaglandin metabolite 15-keto-13,14-dihydroprostaglandin $F_{2\alpha}$ in plasma is high in dysmenorrhoeics and is lowered by indomethacin treatment.—I am, etc.,

V. R. PICKLES

Physiology Department,
University College,
Cardiff

¹ Pickles, V. R., *Nature*, 1972, 239, 33.

² Pickles, V. R., *International Journal of Fertility*, 1967, 12, 335.

³ Pickles, V. R., *et al.*, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1965, 72, 185.

⁴ Lundström, V., Wiqvist, N., and Green, K., *International Conference on Prostaglandins*, Florence, May 1975. Abstracts, p. 222.

SIR,—It seems from your leading article on dysmenorrhoea (31 May, p. 461) that you are more familiar with the correspondence columns of Danish journals than with those of your own.

In 1973,¹ several months before Dr. Christensen's letter, you published a letter from me stating that for several years I had successfully treated most cases of dysmenorrhoea with indomethacin, usually in a dose of 25 mg four times daily. I had in fact mentioned this on more than one occasion to the representatives of the makers but without apparent interest on the firm's part. Subsequently in a letter² Professor V. R. Pickles suggested the possible role of prostaglandins in dysmenorrhoea and drew attention to his suggestion in 1972³ that non-steroidal anti-inflammatory drugs might be of value.—I am, etc.,

G. G. HILL

Hemel Hempstead,
Herts

¹ Hill, G. G., *British Medical Journal*, 1973, 3, 106.

² Pickles, V. R., *British Medical Journal*, 1973, 3, 349.

³ Pickles, V. R., *Nature*, 1972, 239, 33.

SIR,—For a number of years I have been prescribing phenylbutazone for patients with dysmenorrhoea and the results have been very satisfactory. The treatment is started the day before the onset of the period, if this can be calculated, or when the period starts and continues for 24-72 hours as necessary; side effects have been minimal.

Reports on the value of phenylbutazone in dysmenorrhoea first appeared over 20 years ago.¹ By a similar piece of serendipity to that used by Christensen² when he found that indomethacin prescribed for other reasons also relieved dysmenorrhoea (leading article, 31 May, p. 461) Fox—and later others³⁻⁵ found the identical happy result with phenylbutazone when they used it for rheumatic conditions. My memory is that it was the paper by MacQueen⁶ which led me to adopt this treatment.

If any credit is to be given for the earliest uses of prostaglandin synthetase inhibitors in dysmenorrhoea, it should surely go to those who discovered the value of phenylbutazone.—I am, etc.,

STUART CARNE

London W.12

¹ Fox, W. W., *Lancet*, 1953, 1, 195.

² Christensen, A., *Ugeskrift for Læger*, 1974, 136, 592.

³ Strazza, J. A., and Ressetar, M., *Journal of the Medical Society of New Jersey*, 1953, 50, 333.

⁴ Arden, G. P., *Rheumatism*, 1954, 10, 44.

⁵ Black, E., *Canadian Medical Association Journal*, 1958, 79, 752.

⁶ MacQueen, R. L., *Practitioner*, 1960, 184, 787.

Hormonal Pregnancy Tests and Congenital Malformations

SIR,—In 1967, before drawing attention to the teratological effect of the hormonal pregnancy test¹ I consulted the then Committee on Safety of Drugs. Though the committee found that my observation obviously had clinical importance a formal warning was not issued because other data were not available on the topic at that time. This precaution was taken to prevent alarming the public. In 1969, however, the manufacturers were advised by the committee to discourage the promotion of the hormonal

pregnancy test tablets and consequently manufacturers in Great Britain no longer recommend their products for testing pregnancy and have changed the indications for such preparations as Primodos, Amenorone-Forde, and Orasecron. These measures appear to be sufficient to safeguard the manufacturers, but they are less satisfactory from the public point of view as most of these preparations are available and recommended for the treatment of secondary amenorrhoea.

Following the publication of the detailed findings which indicated the teratogenic hazard of the pregnancy test² the problem has gained wide interest, and I am pleased that your recent leading article (30 November 1974, p. 485) and Dr. Gillian Greenberg and her colleagues (26 April, p. 191) have reiterated my view that "unnecessary risks are being taken by diagnosing pregnancy with an in vivo method when many other reliable in vitro methods are available."² Still, it is clear that some general practitioners have continued to use the tablets for pregnancy testing, probably because the changes introduced by the manufacturers were rather inconspicuous.

The warning notice which has now been issued by the Committee on Safety of Medicines (14 June, p. 625) is therefore to be welcomed. It would seem appropriate, however, to reinforce this warning by further measures such as: (1) changing the name of products which were formerly recommended for pregnancy testing and which are at present indicated for the treatment of secondary amenorrhoea not due to pregnancy; and (2) continuing to remind the medical profession of the unnecessary risks of using the tablets either for diagnostic or for abortifacient purposes.—I am, etc.,

ISABEL GAL

Department of Biological Sciences,
The Hatfield Polytechnic,
Hatfield, Herts

¹ Gal, I., Kirman, B., and Stern, I., *Nature*, 1967, 216, 83.

² Gal, I., *Nature*, 1972, 240, 241.

Safer Cigarettes

SIR,—In your leading article (17 May, p. 354) it was pointed out that anti-smoking campaigns had failed and that attention was now being turned to "safer cigarettes." Addiction is suggested as the reason for failure of the former. If this is so no substance with an absent or reduced nicotine content would be an acceptable substitute.

In 1963 I suggested¹ that "any means to reduce the temperature of combustion of cigarettes without lowering palatability would be advantageous to health because burning tobacco at a temperature significantly under 700°C should be successful as heterocyclic carcinogens were produced at combustion temperatures of 700°-900°C when burning skin, yeast, etc."² Pipe and cigar smokers are less subject to lung cancer than cigarette smokers—I believe both because of the lower temperature of combustion of these materials (550°-700°C)⁴ and because pipe tobacco is left to "cure" at ambient temperatures. It is also possible to use a coarser flake with pipe tobacco, producing a different ratio of air to tobacco in the smoke, which is probably significant. Beffinger (personal communication) has pointed out that since 1900 most cigarette

tobacco has been heated to "cure" it, immediately inactivating enzymes and thereby leaving more unchanged hydrocarbon, while pipe tobacco and Spanish and Polish cigarette tobaccos are treated by the old method.

Our experiments showed that pipe tobacco made loosely into a cigarette⁴ burned at a lower temperature than cigarette tobacco packed loosely into a cigarette. We also showed⁵ significant lung cancer production in Swiss white mice compared with controls when smoke from manufactured cigarettes was used. We showed no cancer production in Swiss white mice when loosely packed pipe tobacco was used in the cigarette and, more significantly, no deaths at all in the experimental period (equivalent to nine years' smoking in man); also negligible bronchitis and no cardiac failure. Fifty-five per cent of the mice succumbed to cardio-respiratory illness when commercial cigarettes burning at high temperatures were used for the same time.

We also noted that draw-back was associated with less lung cancer in man than simple puffing⁶ and pointed out a logical reason for this; simple puffing fills to the carina, while draw-back dilutes the advancing gas cloud quickly from the carina into the less susceptible alveoli. The nicotine content of the reduced-temperature-burning cigarette is similar to the nicotine content of the high-temperature commercial cigarette, so that smoking satisfaction on this level should be similar. Heterocyclic hydrocarbons producing satisfactory flavour may be reduced in the cigarettes with a lower temperature of combustion, but the smokers who smoked some 200 of these test cigarettes made the comment that the flavour was acceptable to a smoker.—I am, etc.,

E. R. TRETHEWIE

Department of Physiology,
University of Melbourne,
Parkville, Victoria,
Australia

1 Trethewie, E. R., *Medical Journal of Australia*, 1963, 1, 145.

2 Trethewie, E. R., *Lancet*, 1966, 2, 52.

3 Zanetti, J. E., *Journal of Industrial and Engineering Chemistry*, 1916, 8, 674.

4 Trethewie, E. R., *Medical Journal of Australia*, 1967, 1, 483.

5 Trethewie, E. R., *Medical Journal of Australia*, 1971, 1, 854.

6 Fisher, R. A., *Smoking: the cancer controversy*. London, Oliver and Boyd, 1959.

G.M.C. and Indian Doctors

SIR,—Dr. S. K. Roy (7 June, p. 562) appears to be very indignant about the new G.M.C. legislation whose aim is to prevent totally unsuitable doctors coming to this country from overseas and finding it difficult to obtain appointments. I find this indignation surprising as the new legislation can be nothing but advantageous to those overseas doctors, of whom Dr. Roy is obviously one, who have had an excellent training and are now well settled in this country.

Unfortunately the public, including, I fear, many of our own profession, do not seem to realize the vast difference that exists between the type of medical education that is given in the great centres such as Calcutta and Bombay and that which is given in the countless small medical schools which have neither the facilities nor the teachers to give a proper training. The whole economic situation in certain countries makes it

quite impossible for a universal standard to be maintained and many doctors have in the past been reaching this country with pre-graduate knowledge that is so scanty that all the postgraduate training in the world will never make them competent.

By preventing doctors of this sort coming over here a different perspective towards the overseas doctor will be built up and the present feeling against them will surely disappear entirely.—I am, etc.,

ROBIN BURKITT

Ashford Hospital,
Ashford, Middx

Immigrant Doctors

SIR,—As the wife of a Commonwealth immigrant doctor I would like to make a few observations in connexion with the recent militancy and bad manners shown by immigrant doctors towards the B.M.A. by threatening mass resignations on the grounds that the B.M.A. has not represented their case adequately to the E.E.C. Commission.

I feel that the B.M.A. has done a lot for the cause of immigrant doctors. I quote one of your leading articles (4 November 1972, p. 249) which adequately clarified the attitude by the B.M.A.: "Racial discrimination, whether under the cloak of political, religious, or biological doctrines, is peculiarly repugnant to doctors . . . because it flatly contradicts the tradition and guiding ethic of their profession, by which they treat all men alike irrespective of their colour, creed, or nationality."

Asian doctors should be grateful to their host country, which has given them an opportunity of advancing their medical knowledge and acquiring decent careers which probably they would not be able to obtain in their own countries of origin.

I, for one, and my husband are not prepared to show ingratitude.—I am, etc.,

F. ALI

Basingstoke

Alternatives to the Fluoridation of Water

SIR,—Will Professor D. Jackson (5 April, p. 35) be good enough to tell us what agent is responsible for the "very infrequent" attacks of dental caries "beyond the age of 40" if, as he also claims, "the benefits of fluoridation of drinking water tend to fade with increasing age"?—I am, etc.,

WINIFRED M. SYKES

Hon. Treasurer,
National Pure Water Association

Bardwell, near Bury St. Edmunds,
Suffolk

** We showed Mrs. Sykes's letter to Professor Jackson, whose reply is printed below.—ED., *B.M.J.*

SIR,—A brief description of the age-dependence of dental caries may help to answer the questions, both explicit and implicit, that are contained in Mrs. Sykes's letter.

In English non-fluoride communities the age-specific attack rate of caries in permanent teeth reaches its maximum between 12

and 15 years of age.¹ The attack rate then declines with advancing age, and beyond the age of 40 years relatively few attacks occur.¹ In Hartlepool, where the natural concentration of fluoride in drinking water is 1.5 to 2.0 p.p.m., the age-prevalence of dental caries is markedly lower than that in non-fluoride communities at all ages. However, the ratio of the age-prevalence of caries (Hartlepool: non-fluoride communities) is at its lowest in young people and it gradually rises to a plateau, or limiting value, of approximately 0.6 at around 40 years of age.¹ Thus, though substantial benefits from fluoridation are seen at all ages, they are most conspicuous in young people below the age of 15.

In my view the factors responsible for the infrequent attacks of dental caries beyond the age of 40 do not differ in kind from those that operate at lower ages. However, their rate diminishes with increasing age in adults. My collaborators and I have described in detail elsewhere¹⁻⁵ our interpretation of the somewhat complicated problem of the aetiology and pathogenesis of dental caries.—I am, etc.,

D. JACKSON

University Department of Child Dental Health,
School of Dentistry,
Leeds

1 Jackson, D., *British Dental Journal*, 1974, 137, 347.

2 Burch, P. R. J., and Jackson, D., *British Dental Journal*, 1966, 120, 127.

3 Jackson, D., *Proceedings of the Royal Society of Medicine*, 1968, 61, 127.

4 Jackson, D., and Burch, P. R. J., *Gerontologia*, 1969, 15, 203.

5 Jackson, D., Fairbro, C. G., and Burch, P. R. J., *Archives of Oral Biology*, 1972, 17, 445, and 1973, 18, 31.

Inhibition of Ristocetin-induced Platelet Aggregation by Haemacel

SIR,—Most patients with von Willebrand's disease have a deficiency of the plasma co-factor required for ristocetin-induced platelet aggregation, and diagnostic tests using this antibiotic are rapidly gaining acceptance. We wish to report that the gelatin plasma expander Haemacel (Behringwerke) inhibits ristocetin-induced platelet aggregation at concentrations that are achieved therapeutically. Thus an erroneous diagnosis of von Willebrand's disease could be made when bleeding patients have been treated with this agent.

We first discovered this effect in patients undergoing open heart surgery in the Academic Hospital Rotterdam-Dijkzigt. Ristocetin-induced platelet aggregation (platelet-rich plasma, ristocetin 1.5 mg/ml) was completely abolished or strongly diminished after the start of cardiopulmonary bypass. The cause was shown to reside in the plasma of the patient, since addition of platelet-poor plasma of the patient to normal platelet-rich plasma (1:1) abolished or diminished ristocetin-induced platelet aggregation. It is the normal procedure in this hospital to prime the heart-lung machine with a mixture of Haemacel and fresh heparinized blood. Addition of Haemacel to normal platelet-rich plasma (1:4 v/v), comparable to the intravenous administration of 500 ml of the plasma expander, abolished or strongly inhibited ristocetin-induced platelet aggregation.

Other experiments indicate that Haemacel inhibits ristocetin-induced platelet aggrega-