do not do them. Some women would also be expected to entertain their husband's business colleagues.

My annual expenditure on costs incurred only because of my professional work amounts to £1980, made up as follows: car (£500 less mileage allowance), £300; domestic help (five hours daily at £1 an hour), £1250; extra help in school holidays (student help at £8 a week), £80; extra clothes (jeans and jumpers are unsuitable, even today, for consultants), £150; subscriptions to professional associations and journals and cost of books and conferences, £200.

Except for the B.M.A., most professional associations do not have earnings-related subscription rates at consultant level. Conference fees are paid pro rata to sessions worked, leaving a substantial sum to come from my pocket. My list of items of expenditure takes no account of hidden extras—for example, more easily prepared and therefore more expensive food; inability to shop round for bargains; no time to make clothes; hire of car or taxi when car out of action; and so on. My total annual take-home pay for 53 hours professional work a week and eventually a pension is £3600, leaving a net income of £1620.

If one-third or so of British-trained women doctors have to face these expenses in order to pursue their chosen career is it surprising that they drop out? This problem has not been adequately considered publicly. Of all hospital registrars 56% were born overseas. As you say, Sir, "international trends may cut off the supply." Can a solution be found to the problems of women doctors that would enable a large work force, eager to use their skills provided they are adequately paid, to return to work?—I am, etc.,

DORA BLACK

Fainting and Anaesthesia

SIR,—When a simple uncomplicated local dental anaesthetic is followed by "fainting" hypoxaemia may be the cause. This is due to the nervous and apprehensive patient involuntarily overbreathing in the interval before treatment and this being increased because of the sights and sensations related to the actual injection. When this type of faint occurs the lowering of the ionic calcium fraction consequent upon the hypoxaemia causes a tetanic contraction, particularly of the hands, followed by generalized clonic contractions. On recovery the patient complains of muscle pains, again particularly in the arms.

The use of a general anaesthetic for such a dental patient may be indicated because of the nervousness and apprehension. Thus even in the absence of an overt faint the respiratory drive of carbon dioxide may be greatly reduced and to this is added the respiratory depression of the particular drug used.

An effective premedication, as is given to the general hospital population prior to surgery, prevents overbreathing and its omission may be the reason why a general anaesthetic, as currently given for dental procedures, poses unique difficulties with, rarely, tragic results.—I am, etc.,

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Unexplained Fever

SIR,—In his article on unexplained fever (16 November, p. 397) Dr. A. M. Geddes states: "Benign tertian malaria can usually be treated successfully by a standard course of chloroquine. . . ." However, it should be noted that most patients with a *Plasmodium vivax* infection will relapse if treated with chloroquine alone, owing to the maturation of secondary exoerythrocytic schizonts in the liver and the subsequent invasion of erythrocytes. The 4-aminoquinoline group of drugs such as chloroquine acts only on the blood stages of *P. vivax*, having a potent schizonticidal effect on the asexual parasites and a lesser effect on gametocytes.

Eradication of tissue schizonts and the prevention of relapse are best achieved by a course of an 8-aminoquinoline drug such as primaquine. Usually, the standard course of primaquine (7.5 mg base twice daily for 14 days in an adult) will deal effectively with most strains of *P. vivax* imported into Britain, but people infected in some south-east Asian and western Pacific countries may require 7.5 mg primaquine base three or four times a day to clear all tissue schizonts. Since April 1973 11 such patients out of 367 with fully documented histories of treatment have come to the attention of the Malaria Reference Laboratory. These remarks on the need for primaquine treatment of *P. vivax* tissue stages apply equally to infections with *P. malariae* and *P. ovale*.

Dr. Geddes advises: "If there is any possibility of chloroquine resistance the patients must be treated with quinine." This needs qualification. Certain south-east Asian and central American strains of chloroquine-resistant *P. falciparum* have been shown to exhibit grade R-1 resistance to quinine, and we feel that such patients should be treated in hospital by a physician experienced in tropical diseases who has the facilities available for regular monitoring of parasitaemia together with experience of the other agents available for the treatment of multidrug-resistant *P. falciparum* infections. Further, there have been several proved cases of transplacental transmission of malaria in the U.K., and febrile illnesses in young children who have never left Britain may require careful history-taking of the mother's movements as well as blood-film examinations on mother and child.

It is also necessary to emphasize that, contrary to the implication of the last paragraph on malaria in Dr. L. Roodyn's article on immunization and other prophylactic measures against imported infections (14 December, p. 648), chloroquine resistance is not yet known from Africa.—We are, etc.,

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Erythema Infectiosum

SIR,—The B.M.J. of 23 November contained a leading article called "Fourth, Fifth, and Sixth" (p. 429) and also a letter from Dr. C. A. H. Watts (p. 466) reporting two cases of fifth disease, or erythema in-

fectiosum, occurring in close friends. I was interested at the time since, because I qualified fairly recently (1965) and despite having worked for three years in a fever hospital, I had never heard of the condition at all.

I am writing now because it may be of interest that over the past few weeks I have observed the same clinical picture, exactly as described in your leading article, in my own three children, aged 9, 6, and 2 years. They have had only minor constitutional upset but a brilliant red rash confined to their cheeks and a duller rash, variable and pleomorphic, on their limbs and trunks, lasting on and off for just over one week. Moreover, since being alerted to the condition I have so far seen at least three other children in High Wycombe with an identical illness, so presumably we are in the middle of a small local epidemic of this supposedly rare disease. I have so far been unable to find whether any definite viral cause for the illness has been established, or whether an increased incidence is being noted elsewhere in the country.—I am, etc.,

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Alpha-adrenoceptor-blocking Drugs in Asthma

SIR,—We have read with interest the paper by Professor S. Bianco and others on the prevention of exercise-induced asthma by indoramin (5 October, p. 18) and the letter from Dr. K. N. V. Palmer and others (16 November, p. 409) on the increased effect of salbutamol after intravenous administration of indoramin and thymoxamine.

We have drawn similar conclusions about the role of alpha-receptors from our studies with guinea-pig trachea and human bronchus in vitro. The tracheal chains of normal and egg-protein-sensitized guinea-pigs or spirals of human bronchus obtained during pulmonary operations were used in Krebs' bathing fluid perfused with carbogen. Several combinations of alpha-blockers and beta-mimetics were studied. The alpha-blockers dihydroergocristine, Hydergine (a combination of dihydroergotoxines), phenoxylbenzamine, phentolamine, and thymoxamine and the beta-mimetics salbutamol, terbutaline, isoprenaline, and ephedrine were used.

Small concentrations (10 $\mu\text{mol/l}$) of each of the alpha-blockers potentiated (to about double) the effects of beta-mimetics, though these doses of alpha-blockers alone did not show any effect. Concentrations over 10 $\mu\text{mol/l}$ were less effective. Egg-protein sensitization and the use of egg protein in the bathing fluid did not significantly change the potentiation. The degree of potentiation in human bronchus preparations was of the same order as in guinea-pig tracheal preparations. On the other hand, when alpha-blockers were combined with the same beta-mimetics in preparations of rat atria no potentiation of the beta-mimetics was observed.

Though the tracheobronchial alpha-receptors seem to be almost "silent," they seem to decrease the therapeutic effects of beta-mimetics to a considerable degree. The fact that the same is not true of the heart is additionally favourable for the combination of an alpha-blocker with a beta-

mimetic in the treatment of asthma.—We are, etc.,

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HBsAg in Papular Acrodermatitis of Childhood

SIR,—Your leading article on Australia antigen in papular acrodermatitis of childhood (9 March, p. 407), criticizing Gianotti's¹ hypothesis that serum hepatitis and papular acrodermatitis of childhood (P.A.C.) are the same disease or are closely related, prompts us to report our own experience in the matter. We have recently seen three children with the characteristic picture of P.A.C. as described by Gianotti. Their serum bilirubin was normal and transaminases were at the upper end of the normal range. Using radioimmunoassay as described by Ling and Overby² we found that all three children were HBsAg positive. None were living in any institution. Their parents were HBsAg negative.

We agree that the presence of HBsAg in cases of P.A.C. needs further investigation, and the most sensitive method available for this is radioimmunoassay. If such studies confirm previous reports they will provide strong support for Gianotti's theory of a close relationship between serum hepatitis and P.A.C. P.A.C. would then be the only disease other than serum hepatitis to be consistently associated with HBsAg. Considering the prevalence of anicteric hepatitis in children P.A.C. might be a peculiar form of hepatitis in childhood due to a particular reactivity of the reticuloendothelial system to the viral infection.—We are, etc.,

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- 1 Gianotti, F., *Archives of Disease in Childhood*, 1973, **48**, 794.
- 2 Ling, C. M., and Overby, L. R., *Journal of Immunology*, 1972, **109**, 834.

Single-dose Tinidazole Therapy for Giardiasis

SIR,—Because of increased travel *Giardia lamblia* infestation has become more common. Giardiasis may cause no symptoms but it may also cause long-lasting diarrhoea and bowel troubles.¹ Tinidazole 300 mg daily for seven days has proved to be an excellent treatment regimen with a cure rate higher than 90%.²⁻⁴ Treatment with a single 2-g dose of tinidazole has given excellent results in cases of trichomoniasis, and this encouraged me to try the effect of single-dose tinidazole treatment in giardiasis.

Fifty-three adults (18 women and 35 men) aged from 18 to 47 years and nine children aged from 3 to 10 years were selected for study. All had contracted giardiasis when abroad, and in each case the diagnosis was

confirmed by finding *G. lamblia* cysts in two formalin-preserved stool specimens. Salmonella and shigella infections were excluded by negative culture. The adults were given 2 g and the children 1 g of tinidazole in a single dose. Two stool specimens from each patient were examined by the formalin-ether concentration method of Allen and Ridley⁵ at follow-up examinations one, four to six, and 12 to 16 weeks after the drug was given.

All 53 patients came to the first follow-up examination after one week. Cysts were found in the stools of two, both of whom complained of diarrhoea and periodic stomach pains. The second follow-up examination 4-6 weeks after treatment was attended by 49 of the 53 patients. Cysts were found in the stools of four, all of whom complained of bowel dysfunction. One had been to eastern Europe in the interval since the first follow-up, had had a relapse of symptoms, and had probably been reinfected. Thirty patients attended all three follow-up examinations and at the third were free from cysts and had no symptoms. Seven of the nine children attended for all three follow-up examinations. They were all symptom-free and had no cysts in their stools. Two of these seven had been given a second dose of tinidazole 1 g after an interval of three days. Stool examinations were negative at two follow-up examinations in two children but they were lost to further follow-up.

The overall cure rate was 90%. Generally, the bowel symptoms disappeared one to three days after treatment. In a few cases some bowel discomfort lasted for about a week. A second single-dose treatment was given to the six patients in whom the first treatment failed. Two of them were cured, one of them being the patient who had probably been reinfected. The other four were finally cured with mepacrine hydrochloride after metronidazole had failed.

The single dose of tinidazole was generally well tolerated. Only minor side effects, including slight nausea and worsened diarrhoea during the day of treatment, were noted in 15% of cases. The efficacy of the treatment seems to be equal to the conventional one-week regimen. A single dose is much easier for the patient. So far as can be concluded from the small numbers 1 g of the drug is adequate for children.—I am, etc.,

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- 1 *British Medical Journal*, 1974, **2**, 347.
- 2 Andersson, T., Forsell, J., and Sterner, G., *British Medical Journal*, 1972, **2**, 449.
- 3 Howes, H. L., jun., Lynch, J. E., and Kivlin, J. L., *Anti-microbial Agents and Chemotherapy*, p. 261. Proceedings of the 9th Conference, Bethesda, American Society of Microbiology, 1969.
- 4 Pettersson, T. (1973). In *8th International Congress of Chemotherapy*, Athens, Abstract A-453.
- 5 Allen, A. V. H., and Ridley, D. S., *Journal of Clinical Pathology*, 1970, **23**, 545.

Drugs for Rheumatoid Arthritis

SIR,—We are indeed perplexed by the comments about our paper (28 September, p. 763) made by Dr. P. J. Rooney and his colleagues (28 December, p. 771). Having tried to repeat the χ^2 on our table III severally and together on a number of occasions, we find that our computing

apparatus obstinately produces the answer which we originally published and refuses to disgorge theirs. We did in fact use Yates's correction, though they seem unable to believe this.

Perhaps we were open to criticism for other reasons. It might have been better to analyse table III as a 2×3 table and partition it after the manner of Kimball.¹ This approach in fact reinforces the significance of our findings, as does Fisher's exact test. Contrary to your correspondents' charitable suggestion, the expected frequencies in table III do not quite meet Cochran's revised criteria.² However, it is probably wiser to accept that any wrangle about significance levels where the numbers are rather small is fraught with risk. Our result lies just over the significance boundary; readers should draw their own conclusions about the biological significance of it from a study of the paper. In fact we believe that the weighting method which we described was sufficient to compensate for the inhomogeneity of the initial joint scores which was noted by your correspondents, and by ourselves. Differences between those given prednisone and others were in fact tested and found not to be significant.

The rest of the comments seem to boil down to the assertion that if one could foresee the outcome of a clinical trial one might stratify the proposition in a manner different from that selected when the trial was designed. This is undoubtedly true and we congratulate any of our readers who may have that prophetic insight which we admit we do not possess and thank them for their interesting discussions of a well-known problem in clinical trial design.—We are, etc.,

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- 1 Kimball, A. W., *Biometrics*, 1954, **10**, 452.
- 2 Maxwell, A. E., *Analysing Qualitative Data*, p. 38. London, Methuen, 1961.

Diagnosis of "Reflux Oesophagitis"

SIR,—The problem of orientation of endoscopic oesophageal biopsy specimens was mentioned in the paper by Dr. G. E. Sladen and others (11 January, p. 71). A recent paper from Japan offers some help to pathologists who have to cope with these small specimens. Conventional histological assessment of oesophagitis may not be possible with tangential cuts, but Kobayashi and Kasugai¹ have described an appearance of overlapping of capillaries on tangential sections due to the proliferation of vessels into the epithelial layer with the ingrowth of lamina propria. In 31 of 32 patients with such capillary overlapping the lamina propria extended more than half way across the epithelial layer on cross-section. This sign has been helpful in some of my own cases and it may not be widely known.

It is a pity that the acid barium swallow² was not mentioned. This test involves the swallowing of barium sulphate at a pH of 1-6. The normal oesophagus responds with normal peristalsis, while if oesophagitis is present a variety of abnormal contractions may be seen which can be recorded on videotape. In 1973 McCall *et al.*³ described