portion of what we catch goes to the home market.

Obviously we need much more research, but enough is known to prescribe the best British diet from available knowledge.

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¹ US Senate Select Committee on Nutrition and Human Needs, *Dietary Goals for the United States*, 2nd edn. Washington DC, US Government Printing Office, 1977.

² Ministry of Agriculture, Fisheries and Food, *Household Food Consumption and Expenditure: 1977*. London, HMSO, 1978.

SIR,—Your correspondent Dr Margaret Barker (10 March, p 681) raises a point which has intrigued me for a long time. Am I correct in assuming that ground-up wheat gives whole-wheat flour? If so, I presume that white flour is produced by picking out the brown bits (and what do they do with these anyway—an EEC brown bit mountain?). In which case, it should be dearer than brown flour. Since this is not so, do they pick out the brown bits to make white flour and then add them back to make brown flour again, thereby increasing the price?

I have also wondered whether some brown bread really does contain the necessary brown bits or whether some of it is not just ordinary brown white bread—and how can we tell?

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Labetalol and urinary metadrenalines

SIR,—Interference by the antihypertensive drug labetalol in the estimation of urinary catecholamines and their metabolites has been the subject of recent correspondence¹⁻³ and a report⁴ in this journal. Spuriously raised urinary values were evident²⁻⁴ after treatment both with a fluorimetric catecholamine assay^{5,6} and the standard spectrophotometric procedure⁷ for total (free plus conjugated) metadrenalines (metadrenaline and normetadrenaline).

Because our own modification⁸ of this spectrophotometric procedure gives substantially lower blank values than the present method, we were prompted to investigate whether the problem could be overcome with its aid. We compared total metadrenalines, as measured by our own modified Pisano technique,⁸ with values obtained when total normetadrenaline (NMA) plus total metadrenaline (MA) were determined by a highly specific and sensitive gas chromatographic procedure.⁹ Most of the specimens we examined were kindly supplied by Drs H J Dargie and C A Hamilton and were from the same patients on whom they had already reported.⁴

We agree with others²⁻⁴ that labetalol gives rise to factitiously raised values for urinary total metadrenalines when the classical Pisano method⁷ is employed. However, values yielded by our modified procedure⁸ correlated well with those obtained by gas chromatography, except in one patient out of eight studied. This patient had much the highest value of all when the original Pisano method was used, indicating that interference was great. Even here, however, the result obtained by our modified procedure was not markedly increased, although some interfering substance was obviously still present. It was found that maximum interference was not associated with maximum dose of labetalol.

Our simple improvement to Pisano's method, which involves three additional steps,

a pH adjustment of the column eluate, extraction into toluene, and back-extraction into potassium carbonate, seems to eliminate the interfering material in most cases. It has the advantage that it can be carried out where access to more specific gas chromatographic or radioenzymatic methods is not available. We therefore suggest its use for screening patients who are taking labetalol when a possible phaeochromocytoma is suspected. If occasional raised values are found, the sample might then be subjected to more careful scrutiny by one of the more specific procedures.

We are grateful to Mr M W Weg for helpful discussions.

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¹ Harris, D, and Richards, D A, *British Medical Journal*, 1977, **4**, 1673.

² Chapman, B P, Veitch, A G, and Shepherd, B, *British Medical Journal*, 1978, **1**, 364.

³ Kolloch, R, Miano, L, and de Quattro, V, *British Medical Journal*, 1979, **1**, 268.

⁴ Hamilton, C A, et al, *British Medical Journal*, 1978, **2**, 800.

⁵ Crout, J R, *Standard Methods of Clinical Chemistry*, ed D Seligson, vol 3, p 62. New York, Academic Press, 1961.

⁶ Von Euler, V S, and Lishajko, F, *Acta Physiologica Scandinavica*, 1961, **51**, 348.

⁷ Pisano, J J, *Clinica Chimica Acta*, 1960, **5**, 406.

⁸ Ruthven, C R J, and Sandler, M, *Clinica Chimica Acta*, 1965, **12**, 318.

⁹ Nelson, L M, et al, *Clinica Chimica Acta*, 1979, **92**, 235.

Difficulties in diagnosing meningococcal meningitis

SIR,—We read with great interest the findings of Drs Oliver C Smales and Nicholas Rutter in their review of bacterial meningitis in children (3 March, p 588). The difficulties encountered in the initial clinical evaluation of bacterial meningitis are well appreciated, especially in the setting of prior treatment with antibiotics.

In recent years the use of the counter-immunoelectrophoresis assay has been helpful in identifying some of the more common pathogens seen in the setting of meningitis¹; however, it is limited in terms of available antibody preparations, requires skilled technicians and strict quality control, and is not readily available in small hospitals.

The limulus endotoxin assay has proved to be a rapid (60-minute), reliable method in the initial evaluation of meningitis. On the basis of the findings of Levin and Bang² that minute amounts of endotoxin released by Gram-negative bacteria produced gelation of amoebocytes from *Limulus polyphemus* (the horseshoe crab), multiple studies have since confirmed the usefulness of the limulus assay as an aid in the diagnosis of Gram-negative meningitis.³⁻⁵ In comparing the sensitivities of limulus assays and Gram-stain smears on initial spinal fluid samples of patients with Gram-negative meningitis who did not receive prior antibiotic therapy, positive limulus assays were obtained in at least 97% of cases, whereas only 70% had organisms visible on smears.³⁻⁵ Moreover, when the results of the limulus assay were compared with the results of Gram stain and culture after 24-48 hours of antibiotic therapy in 25 cases of culture-proved meningitis with *Haemophilus influenzae* or *Neisseria meningitidis*, Gram-stains were positive in 4 (16%),

cultures in 6 (24%), and the limulus assay in 17 (68%).⁴ By contrast with the complexities involved with the counter-immunoelectrophoresis assay, the limulus assay could be used as a "bedside" test by house staff without sophisticated training.⁵

The chief drawback of the limulus assay is that a negative test does not rule out the possibility of meningitis due to organisms other than Gram-negative bacteria. However, with a thorough understanding of the advantages and limitations of the limulus assay it can serve as a valuable adjunct to other diagnostic modalities in the initial clinical management of meningitis.

We none the less strictly agree with the authors that a strong index of suspicion, aggressive repeated evaluation, and appropriate cultures are the mainstays in the clinical evaluation of suspected meningitis.

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¹ Edwards, E A, Muehl, P M, and Peckinpaugh, R O, *Journal of Laboratory and Clinical Medicine*, 1972, **80**, 449.

² Levin, J, and Bang, F B, *Bulletin of the Johns Hopkins Hospital*, 1964, **115**, 265.

³ Jorgensen, J H, and Lee, J C, *Journal of Clinical Microbiology*, 1978, **7**, 12.

⁴ Nachum, R, Lipsey, A, and Siegel, S E, *New England Journal of Medicine*, 1973, **289**, 931.

⁵ Ross, S, et al, *Journal of the American Medical Association*, 1975, **233**, 1366.

Benign presentation of tuberculous meningitis

SIR,—We were interested in the recent controversy about benign tuberculous meningitis in your journal (6 January, p 56) and would like to describe our experience with a similar case.

In October 1970 we saw a 23-year-old Dutch nurse for a routine physical examination. She had no symptoms, and the clinical examination was normal, as were the results of laboratory tests, including differential blood count. The Mantoux test was negative at a dilution of 1/10 000 but positive at 1/5000. Thirteen months later she returned complaining of malaise, dizziness, syncope, recurrent pulsatile headaches, insomnia, increased irritability, and clumsiness of her right hand. The physical examination was essentially unchanged, except for a highly labile blood pressure with frequently raised values (up to 160/115 mm Hg). There were no neurological signs of lateralisation or a focal lesion. The lumbar puncture showed a pressure of 13 cm H₂O, protein 0.20 g/l, glucose 3.39 mmol/l (0.61 g/l), a slightly positive Pandy reaction, and 1 × 10⁶ mononucleated cell/l. Surprisingly, the cerebrospinal fluid (CSF) culture was positive for *Mycobacterium tuberculosis, typus humanus*, which was subsequently shown to be sensitive to all antibiotics tested. We wondered whether this isolated CSF finding represented an actual infection or an extrinsic contamination. A second lumbar puncture was performed, and the CSF was sterile. Her Mantoux test was now positive at 1/10 000. Clinically, headache and blood pressure lability persisted for a few weeks, then progressively disappeared. Because of these facts the diagnosis of tuberculous meningitis was finally rejected and the patient discharged without specific treatment. A follow-up was not possible after six months, because the patient returned to Holland.

In view of the recent debate in your journal, this case might be another example of benign tuberculous meningitis, as described by Emond and McKendrick.¹ The symptoms, suggestive of raised intracranial pressure, and

the bacteriological findings correlate well with those in that condition. The normal cell count in the CSF is rare in tuberculosis of the central nervous system but may occur.¹⁻³ We think that a positive culture for *M. tuberculosis* might be a more common finding, were one to look for it, and that the possible tuberculous nature of meningitis should not be discarded because of benign presentation only.

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¹ Emond, R T D, and McKendrick, G D W, *Lancet*, 1973, 2, 234.

² Taylor, K B, Smith, H V, and Vollum, R L, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1955, 18, 165.

³ Kocen, R S, and Parsons, M, *Quarterly Journal of Medicine*, 1970, 39, 17.

Premenstrual tension

SIR,—Paraphrasing the opening sentence of the leading article, "Premenstrual tension" (27 January, p 212), I would say that there is nothing pleasant about inaccuracies, especially when they appear in such a well-written, well-documented, up-to-date article.

You cite two studies that "have failed to confirm any rise in prolactin concentrations in patients with premenstrual tension." This statement is incorrect, because Andersch *et al*¹ clearly report: "In patients with PMT prolactin levels were significantly higher premenstrually compared to levels during the follicular phase. In the control group no such increase was observed."

A careful examination of the second article cited² shows a very vague definition, selection, and mental evaluation of their sample group. According to table II in that article, the average severity of mental complaints among the group was 1.01—that is, slight—and they did not mention any control group for the drug-free cycle.

None the less, more than one variable seems to be implicated in the cause of the premenstrual tension syndrome, and, concerning the accumulating data, one may assume that we are dealing with a group of syndromes which may be caused by an imbalance between several factors affecting the central (and possibly CNS peripheral) nervous system.

A better understanding of the aetiology of these syndromes is unlikely before a precise definition is formulated.

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¹ Andersch, B, *et al*, *Acta Endocrinologica (Copenhagen)*, 1978, 88, Suppl No 216, p 165.

² Andersen, A N, *et al*, *British Journal of Obstetrics and Gynaecology*, 1977, 84, 370.

Treatment of orthopaedic tuberculosis

SIR,—Absence overseas has prevented my commenting earlier on the letters of Sir John Crofton (6 January, p 52) and Mr M Wilkinson (24 February, p 558) on the treatment of orthopaedic tuberculosis.

I was astounded to read of the practice attributed by Sir John to "some orthopaedic surgeons" of giving no more than one month's chemotherapy to patients with tuberculous sinuses. The absence of any letter questioning the frequency of such maltreatment leads me to fear that Sir John has no need to feel "ashamed" of his letter, but rather that he deserves every support for urging, as I have always urged myself, that any surgeon treating any case of tuberculosis should do so in consultation with an expert in chemotherapy, who will almost always be a chest physician. The simple fact is that tuberculosis of bone and joint, though done nothing but harm by inadequate or inappropriate chemotherapy, will be cured by adequate chemotherapy in almost every case. Mr Wilkinson is quite wrong in asserting that this does not apply to disease of the thoracic or thoracolumbar regions of the spine, even if large paravertebral abscesses are present. Reference to the last two reports^{1 2} of the Medical Research Council's working party on this subject makes this abundantly clear.

Radical anterior surgery of the "Hong Kong" type, performed by experienced experts and reinforced by adequate chemotherapy, hastens cure and lessens deformity, thus conferring great benefit on the patient with spinal tuberculosis. The high expectation of eventual cure, however, is not increased even by this operation and certainly not by any lesser surgical measure such as that suggested by Wilkinson. Our studies in Bulawayo and in Hong Kong indicate without question that even a full debridement of the focus confers no worthwhile benefit on the patient receiving adequate chemotherapy.

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¹ Medical Research Council, *Journal of Bone and Joint Surgery*, 1976, 58B, 399.

² Medical Research Council, *Journal of Bone and Joint Surgery*, 1978, 60B, 163.

Steroid treatment in giant cell arteritis

SIR,—In the reported discussion (17 March, p 727) on the first case in the clinicopathological conference held at the Royal College of Physicians questions were asked about steroid treatment, the sedimentation rate, and the age of patients affected by giant cell arteritis.

It might be helpful to recall observations made a quarter of a century ago and reported in the *British Medical Journal* (31 December 1955, p 1593). In case 1 of that report, the patient was aged 55 years at the time of onset of her symptoms and was first seen in medical outpatients in July 1954, when she was 56 years of age. The diagnosis of giant cell arteritis was confirmed by biopsy; her erythrocyte sedimentation rate (ESR) was 80 mm in the first hour. Oral cortisone was started, 200 mg being given daily during the first week. Thereafter the daily dose was 150 mg during the second, 100 mg during the third, 50 mg during the fourth, and 25 mg during the fifth week. After the first week of treatment the ESR fell to normal and remained so. A second biopsy performed five weeks after the first showed no inflammatory cellular infiltration.

In case 2 the initial ESR was 36 mm in the first hour. After 11 days' treatment with

ACTH gel by injection 25 mg three times a day a second biopsy specimen was totally free from cellular infiltration and treatment was stopped.

At that time we thought that these were the first cases reported in which serial biopsies had shown such histological changes. Our clinical and histological evidence suggested that cortisone and ACTH reduced the oedema and the inflammatory cellular reactions. This was probably the cause of the relief of symptoms. There was no evidence that the treatment had any effect on the scarring and intimal thickening that had already taken place; in fact in the first case thrombosis occurred despite treatment. It seems probable that it is thrombus that causes the arterial obstruction and symptoms after cortisone has been given, and it might be argued that there is an indication for using anticoagulants during and after cortisone therapy.

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Drugs and breast-feeding

SIR,—The British physician, at least, should not be ignorant about interference of drugs with breast-feeding, as you imply in your leading article (10 March, p 642). He may obtain for a mere 90p Dr Linda Beeley's marvellous booklet *Safer Prescribing*,¹ where, on page 37, most of the interfering drugs you mentioned and more are listed.

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¹ Beeley, L, *Safer Prescribing: a Guide to some Problems in the Safer Use of Drugs*. Oxford, Blackwell Scientific, 1976.

Cimetidine in acute upper gastrointestinal bleeding

SIR,—We write to report a trial of cimetidine in the treatment of upper gastrointestinal bleeding, and a negative result similar to that of Mr R G Pickard and others (10 March, p 661).

Patients admitted to the medical wards of a district general hospital with haematemesis or melaena were randomly allocated to a treatment or non-treatment group: the patients were stratified into two age groups, above and below 55 years. To those allotted to the treatment group cimetidine was given intravenously, 200 mg in 200 ml normal saline, over a period of two and a half hours, repeated six-hourly for 48 hours: this was followed by oral treatment, 200 mg three times a day and 400 mg at night, for five days. Except in a small number of cases, upper gastrointestinal endoscopy was performed within 16 hours of admission. Blood was transfused as necessary. Patients were referred for surgery if (a) there was no apparent improvement after transfusion of six units of blood or (b) deterioration continued during transfusion or (c) after an interval during which there was no sign of bleeding fresh blood was aspirated or there was evidence of hypovolaemic shock or rapidly progressive anaemia. The decision to refer a patient for surgery was made by a member of the team who did not know whether the patient was receiving cimetidine, but who had either performed endoscopy himself or was aware of the endoscopic findings.

Fifty-eight patients were allotted to the group treated with cimetidine and 55 to that without; in each group, eight patients were referred for surgery. In the group treated with cimetidine four