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 pheochromocytoma 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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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