

## CORRESPONDENCE

**Diet-induced polyuria**

SIR — We have observed a trait of C3H/He mice which makes them unsuitable for some experiments but which is of intrinsic interest. While testing a highly purified, minimal-antigen diet for acceptability by mice of this strain, we noticed that they produced vast quantities of urine, many excreting their body weights in urine daily.

Female C3H/He mice, weighing 15g, drank 7 ml water and excreted 2 ml urine daily when fed BP Nutrition Diet 3 (a typical breeding diet). After 3 days on the test diet the same mice drank 20 ml water and excreted 15 ml urine daily. When returned to the stock diet, they reverted to normal.

We have successfully maintained without polyuria strains NMRI and BALB/c on this test diet, so it seems likely that C3H/He mice have a genetically determined lesion in their regulatory mechanism for water balance. Although the composition of the diet is complex (49 ingredients) it is based on the National Research Council requirements for rats<sup>1</sup> and contains 13 per cent amino acid mixture, 3.6 per cent corn oil, 78 per cent glucose, 3.9 per cent mineral mixture and 1.1 per cent vitamin mixture.

As we ourselves are not studying water balance, we hope that this report will stimulate further investigation of this phenomenon by others with whom we would be pleased to cooperate.

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1. National Research Council, *Nutrient Requirements of Laboratory Animals* (National Academy of Sciences, Washington DC, 1978).

**A correction**

SIR — An article by Jasper Becker (*Nature* 20 August, p.665) describes the German Cancer Research Institute in Heidelberg and the politics at that institution. The third paragraph states, "The attack soon broadened to Neurath's qualifications and it turned out that he had in fact previously only been scientific advisor to the University of Seattle". I would like to set the record straight regarding this inaccurate reporting.

Dr Neurath was professor and chairman of the Department of Biochemistry at the University of Washington for 25 years. He has authored or co-authored over 350 manuscripts published in major scientific journals. Furthermore, he has been editor of *Biochemistry* during the past 20 years and editor or co-editor of a number of scientific books. Since 1961, he has been a member of the National Academy of Sciences in the United States. He was also the associate director for research at the Fred Hutchinson Cancer Research Center here in Seattle. Thus, for your article to state that he had in fact previously only been scientific advisor to the University of Seattle is totally erroneous. A simple phone call to any biochemist in the world could have clarified this poor reporting.

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We apologize to Dr Neurath and the University of Washington for this error — Editor, *Nature*.

**Resistant cattle**

SIR — I read with interest your comments on the plans for a new research institute in the Gambia to investigate why N'Dama cattle in Africa seem to be more resistant to trypanosome infection than Zebu cattle (*Nature* 9 July, p.102).

At least two new institutions have set up with the same objectives and are now operational. One is the Centre d'Élevage et de Recherche sur la Trypanosomiase et la Trypanotolérance located in Avetonou, Togo, which is sponsored by the German Agency for Technical Cooperation (GTZ) and the Togolese government. Several thousands of pedigree N'Dama, as well as Baoulé, Zebu and "local breed" cattle are available and the emphasis is on breeding cattle resistant to trypanosomiasis and making them available to local farmers. The other is the Centre de Recherches sur les Trypanosomoses Animales in Bobo-Dioulasso, Haute-Volta, sponsored by GTZ and the Institut d'Élevage et de Médecine Vétérinaire des Pays Tropicaux (Maisons-Alfort, France). Here the emphasis is on more basic research in immunology, biochemistry and genetics. There are also excellent tsetse fly raising facilities.

Research on some genetic markers of trypanotolerance, including erythrocyte groups, glucose-6-phosphate dehydrogenase, haemoglobins and transferrins, is near completion. Characterization of genetic markers for the identification of resistant cattle using monoclonal antibody technology is under way.

The two centres are working in close cooperation and have access to further material through a network of institutions and field stations in Togo, Ivory Coast, Upper Volta and Mali, hopefully to be extended to other geographical areas.

We would gladly provide technical information to anyone interested.

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**Random diets**

SIR — Dr Yudkin<sup>1,2</sup> agrees with the recent report of the Royal College of Physicians<sup>3</sup> that, while there is some evidence that dietary fibre may reduce the risk of colon cancer, it falls far short of proof beyond reasonable doubt. Drs Weisburger and Reddy<sup>4</sup>, on the other hand, believe that the present data base is adequate to conclude that fibre-rich bread and cereal "have every chance of reducing the risk of colon cancer". That correspondence<sup>2,4</sup> illustrates yet again how difficult it is to gain reliable information about the health effects of dietary factors. Our recent review<sup>5</sup> of the causes of cancer, while concluding that on present evidence it was very reasonable to hope that certain (though perhaps not all) types of dietary fibre were importantly protective, emphasized that it was also reasonable to remain unconvinced, and recommended that the practicability of randomly controlled interventions be investigated.

One of the currently favoured hypotheses is that certain types of fibre affect the *later*

stages of the process of carcinogenesis, in which case (to judge by the rapidity with which measurable effects of cessation of smoking are evident) there should be a substantial reduction in risk during a period only 5–9 years after switching to a high-fibre diet, so it might just be possible to obtain reliable evidence, acceptable to all parties, by means of a really large randomized trial lasting for about 10 years. However, even among people aged about 70, only about 1 per cent will develop cancer of the large intestine during a given five-year period. So, to observe a few hundred disease onsets between years 5 and 9 in such a study, a few tens of thousands of people would have to be randomized. The practical problems of such an enterprise are formidable, though they may not be insurmountable as long as the people to be randomized are selected appropriately (to judge by the degree of continuing collaboration among some thousands of members of the British medical profession in a randomized evaluation of treatment of the doctors with prophylactic aspirin). The feasibility of a randomized evaluation of particular types of dietary fibre (and of various other dietary hypotheses) is a matter that can be resolved not by assertion but by pilot studies, in carefully selected populations, of the number of subjects that can be recruited, the cost per subject (which must, by simplicity of design, be kept low), and the degree of compliance that can be attained in a large randomized trial.

If some such randomized studies are practicable then they could lead to an unequivocal resolution of many dietary hypotheses, relating to both neoplastic and vascular disease, that would otherwise be subjected to indefinite dispute. Although randomized evaluation of the top ten dietary hypotheses (including, hopefully, the role of various types of dietary fibre) may yield only one or two findings that are clearly positive, the public health implications of having a few pieces of *reliable* dietary information to communicate would easily justify the costs of several such trials, even if most found no differences.

Observational epidemiology does strongly suggest that some unidentified dietary factors are important determinants of cancer risks<sup>5</sup>, but although observational epidemiology alone has yielded proof beyond reasonable doubt of the main effects of tobacco, alcohol, radiation and certain occupational and reproductive factors<sup>5</sup>, the complexity of diet and the strong correlations that commonly exist between different dietary factors mean that equally reliable evidence about diet may be difficult to attain without large, simple, long-term randomized studies.

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1. Yudkin, J. *Nature* 291, 173–174 (1981).
2. Yudkin, J. *Nature* 292, 666 (1981).
3. *Medical Aspects of Dietary Fibre: a Report of the Royal College of Physicians* (Pitman Medical, Tunbridge Wells, 1980).
4. Weisburger, J.H. & Reddy, B.S. *Nature* 292, 666 (1981).
5. Doll, R. & Peto, R. *J. natn. Cancer Inst.* 66, 1191–1308 (1981).