Kammerer, I think that "Not proven" is the fairest verdict.

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¹ Fisher RA. *Ann Sci* 1936;1:115-37.

² Sturtevant AH. *A history of genetics*. New York: Harper and Row, 1966:13-6.

³ Wright S. In: Stern C, Sherwood S, eds. *The origin of genetics*. San Francisco: Freeman, 1966:173-5.

⁴ Koestler A. *The case of the midwife toad*. London: Hutchinson, 1971.

Postneonatal mortality and child abuse

SIR,—Jacqueline Roberts and others (12 July, p 102) demonstrated a threefold-raised post-neonatal death rate among siblings of abused infants. This finding fits in with our own observations in Cardiff infants.

We have been studying the feasibility of the use of scoring systems to assess groups of infants at high risk of non-accidental injury and sudden infant death syndrome, based on the data of the Cardiff births survey. Eight factors were found predictive of both these outcomes: low maternal age, low social class, residence in the poorer wards of the city, maternal smoking, lack of or late onset of antenatal care, lack of employment of the mother during pregnancy, admission to the special care baby unit, and artificial feeding. Three further factors were related to abuse: mother unmarried, low maternal weight, and low birth weight (which in our own data was, surprisingly, only weakly related to cot death). In addition, cot death was more common in male infants and twins and in deliveries occurring from August to January; when pregnancy had been complicated by antepartum haemorrhage, rupture of membranes 24 hours before onset of labour, venereal disease, or thromboembolism; after spontaneous deliveries and those in which the second stage of labour was short; when an episiotomy had not been judged necessary; when the mother had had two or more previous deliveries; and when the partner was unemployed. Many of the factors predictive of both abuse and cot death are likely to remain unchanged for the women concerned from one delivery to the next; most of the additional factors favouring cot death are specific to the index pregnancy. In view of this, the Oxford findings are not surprising.

We have quantified the predictive power of a scoring system in terms of the estimated probability that when an abnormal and a normal baby are chosen independently at random the abnormal one will have received the more adverse score (1-3). $P=1.0$ denotes perfect prediction while in the absence of discriminatory power p takes the values 0.5. The abuse predictor can predict abuse with a power of $p=0.858$ and cot death with a power of $p=0.768$. The cot death score predicts cot death and abuse with $p=0.818$ and 0.773 respectively. Thus the two predictors do not select quite the same infants as being at high risk, but they are in quite close agreement. On epidemiological and social grounds, much the same group of infants is at high risk of both non-accidental injury and cot death.

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Recurrent abdominal pain in a patient on haemodialysis

SIR,—I was interested to read the report by Dr Martin Feinroth and others (27 September, p 838). A patient attending this hospital suffered from dialysis-induced abdominal pain which I believe was a further example of the syndrome they describe.

A 54-year-old woman had prior to her recent death been attending this hospital thrice weekly for the past 10 years for maintenance haemodialysis, chronic renal failure having been diagnosed in 1968. Her condition was complicated by hypertension, gross cardiomegaly, angina pectoris, and episodes of congestive heart failure. Her medication included digoxin; latterly the dosage required was 0.0625 mg twice daily (a typical random serum digoxin being reported as 1.5 nmol/l (1.17 ng/ml)). An attempted renal transplant in 1975 had been a failure. She unfortunately died in June. For the past few years she had complained of severe central abdominal pain about 10 or 15 minutes after dialysis was commenced. She always maintained that this pain was quite distinct from the angina she suffered on exertion and numerous electrocardiograms recorded during these episodes showed no evidence of new myocardial damage. Once dialysis was finished she became pain free until the next dialysis. Abdominal x-ray examination was reported on several occasions as showing "no evidence of intestinal obstruction." Her gall bladder was removed in 1977 following several attacks of typical cholecystitis.

We had always suspected that this patient's recurrent abdominal pain was due to intestinal ischaemia precipitated by (a) fluid removal during dialysis and (b) relative hypotension, her blood pressure typically falling from her normal 160/110 mm Hg to 100/60 mm Hg during dialysis. We considered the patient's general condition to be so poor that treatment was confined to analgesics. The most satisfactory method of treatment we found was the self-administration of 50% nitrous oxide and 50% oxygen from an Entonox apparatus.

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"Benign" monoclonal IgE gammopathy

SIR,—H Ludwig and W Vormittag (23 August, p 539) presented the case history of a rather remarkable patient who has apparently been identified as suffering from a benign monoclonal IgE gammopathy. It would appear from the data presented in this paper that it is very likely that this patient's IgE gammopathy is a benign one. My particular interest in the paper arises from some general remarks and claims made in the introduction to the paper.

The authors state that "benign" monoclonal proteins can be found in about 1% of the population at 25 years of age and that with increasing age the incidence of paraprotein rises to more than 2.5% in individuals over 70. This statement is not attributed to anyone, but it would appear likely that they are quoting the results published by Axelsson *et al* in 1966.¹ I would like to point out that there are other studies which do not show such a high incidence. Hobbs in 1967² found an incidence of such paraproteins in 0.8% of 7200 hospitalised patients and my own group,³ in a population study in New Zealand, found an overall incidence of 0.5% paraproteinaemia in a population study of adults over the age of 21 years. We also found that the incidence of paraproteinaemia seemed to increase with age and by the eighth decade the percentage had risen to 1.5%.

The other contentious point in the introduction

is the statement that "benign paraproteinaemia of the IgG, IgA, IgM class or of light chain type is relatively common and only rarely followed by multiple myeloma or Waldenström's macroglobulinaemia." This comment is not attributed and is presumably the opinion of the authors, and I would dispute it. In the population study previously alluded to, my co-workers and I found that we had detected 11 cases of paraproteinaemia in a population of 2670 people. Nine of these 11 people were studied clinically, the other two having died between the population study and the clinical study. One of these was aged 74 years and died of a gastric ulcer and the second was 89 years and died of myocardial infarction. Necropsy had not been carried out on these patients. A third patient died while under clinical study as a result of an accident and her necropsy, although inadequately done for our purpose, did not demonstrate any haematological disorder. Two of the remaining patients were shown to have myeloma and two Waldenström's macroglobulinaemia, and another was shown to have lymphosarcoma and acute myelomonocytic leukaemia. The remaining three patients from this population study remain well 13 years after the initial discovery of their paraprotein. Their gammopathies remain, and in each case there is some suspicion of a lymphoproliferative malignancy. Thus, in five out of the nine evaluable patients in this study a haematological malignancy has developed. This greater than 50% incidence could not be regarded as an only rarely occurring phenomenon.

I appreciate that Drs Ludwig and Vormittag have not defined their use of the term "benign" monoclonal paraproteins, which makes it rather difficult to refute entirely their proposition that benign paraproteinaemia is seldom important. Most workers involved in the evaluation of such subjects do recognise that the stable non-progressing peak which is unassociated with immunosuppression of the other immunoglobulins or other biochemical abnormalities may be labelled benign. On the other hand, I would like to submit that such patients should have serious consideration given to exclusion of haematological malignancies. In my own experience, a considerable proportion of such cases do have an associated immunocytoma. After the initial studies the matter may need to be reconsidered at a later date.

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¹ Axelsson U, Bachmann R, Hallen J. *Acta Med Scand* 1966;179:235-47.

² Hobbs JR. *Br Med J* 1967;iii:699-704.

³ Carrell RW, Colls BM, Murray JT. *Aust NZ J Med* 1971;iv:398-401.

Protein synthesis and breakdown after vaccination

SIR,—Dr Kirstine Adam and Professor I Oswald (20 September, p 809) have criticised our methods for measuring protein turnover in the whole body (26 July, p 263) because we suggest that protein synthesis exceeds protein breakdown during feeding. They say that direct measurements of incorporation of isotope into protein of a number of individual tissues show the opposite—that protein synthesis is highest while food intake is least. They also point out that in order to calculate the rate of protein synthesis it is necessary to know not only the rate of incorporation of isotope into protein but also the specific radioactivity of the free amino-acid at the site of protein synthesis. It is extremely unfortunate, therefore, that not one of the studies quoted by Dr Adam and Professor Oswald involved measurements of the specific

radioactivity of the free amino-acid. At best this omission leaves the interpretation of the results in doubt; at worst it can lead to severely misleading conclusions. Our own studies, and those of others, have shown that protein synthesis in skeletal muscle, which contributes 25-50% of total body synthesis in man,¹ is acutely sensitive to food absorption² and to the concentration of amino-acids and insulin.³

We do not dispute that the available methods for measuring whole-body protein turnover may not be ideal. Indeed, we have spent considerable time and effort in analysing possible sources of error and in comparing different approaches with ¹⁵N and ¹⁴C.^{4,5} The conclusion that amino-acids are retained in the body during food absorption can be made from simple nitrogen balance experiments and also from more sophisticated studies with L-¹⁴C-leucine.⁶ The latter technique has also been used to show that rates of protein metabolism do not alter during the day and night if the food intake is maintained constant throughout.⁷ Dr Adam and Professor Oswald may argue that stored amino-acids are retained in the free amino-acid pool of the tissues, rather than as protein, but this appears to us to be highly unlikely. The total body pool of free leucine is quite small compared with the daily intake from dietary sources,⁸ and the period of measurement (12 hours) allows plenty of time for re-equilibration after a change of intake.

In concluding that protein turnover is sensitive to food intake we have been particularly concerned with validating methods and with verifying results by using several different techniques both in man and in animals.^{4,5} From the studies cited by Dr Adam and Professor Oswald we wonder whether they have applied similar rigorous criteria.

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¹ Garlick PJ, In: Florkin M, Stotz EH, eds. *Comprehensive biochemistry*. Amsterdam: Elsevier, 1980: 77-152.

² Garlick PJ, Millward DJ, James WPT. *Biochem J* 1973;136:935-45.

³ Fuls RM, Li JB, Goldberg AL. *J Biol Chem* 1975; 250:290-8.

⁴ Waterlow JC, Garlick PJ, Millward DJ. *Protein turnover in mammalian tissues and in the whole body*. Amsterdam: North Holland, 1978.

⁵ Garlick PJ, Clugston GA, Waterlow JC. *Am J Physiol* 1980;238:E235-44.

⁶ Garlick PJ, Clugston GA, Swick RW, Waterlow JC. *Am J Clin Nutr* 1980;33:1983.

⁷ Golden MHN, Waterlow JC. *Clin Sci Mol Med* 1977;53:277-88.

⁸ Moller P, Bergstrom J, Eriksson S, Furst P, Hellstrom K. *Clin Sci* 1979;56:427-32.

Impotence in diabetic and non-diabetic hospital outpatients

SIR,—We were interested to read the article by Dr Eva Lester and others (2 August, p 354) but agree with Dr Peter d'A Semple and others (20 September, p 808) that the non-diabetic outpatient group which they use is an unsatisfactory control population. Apart from chronic obstructive airways disease, many conditions, such as ischaemic heart disease, uraemia, and multiple sclerosis, are known to be associated with sexual dysfunction. A much

larger control group would be necessary with detailed information of other medical illnesses documented.

Furthermore, in their comments on the lack of a known association of diabetic impotence with severity of diabetes, angio-pathy, and autonomic neuropathy Dr Lester and her colleagues seem unaware of more recent work on this subject. In our own study¹ we interviewed 541 diabetic males aged 20-59 years. Before starting the study we obtained expert statistical advice on selection of patients, who included over 100 patients selected randomly from the clinic population. In this way we ensured that our sample represented an unbiased 65% of the total clinic population of men aged 20-59 years. The prevalence of erectile impotence ranged from 5.7% in those aged 20-24 years to 52.4% in those aged 55-59 years (with an overall prevalence of 35%). Impotence in these men was clearly associated with severity of diabetes, and autonomic neuropathy ($p < 0.001$ in each case).

They imply that because widespread evidence of autonomic neuropathy (as demonstrated by postural hypotension and impaired cardiovascular reflexes) is not present in all impotent diabetic men the impotence may well be psychological. This has not been our finding after careful psychiatric evaluation of impotent diabetics (C Fairbairn *et al*, report in preparation). Some current research from our unit suggests that impotence may be the earliest manifestation of diabetic autonomic neuropathy and that cardiovascular reflexes become damaged only at a later stage.

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¹ McCulloch DK, Campbell IW, Wu FC, *et al*. *Diabetologia* 1980;18:279-83.

Sjögren's syndrome treated with bromhexine: a reassessment

SIR,—Some heavy arguments against the clinical trial performed by Dr L M Tapper-Jones and others (7 June, p 1356) can be put forward. On the basis of a trial comprising 14 patients, they claim that bromhexine 64 mg/day is no better than placebo in the treatment of patients suffering from Sjögren's syndrome, in contrast with the results of a previous and more extensive randomised clinical trial as well as of open studies.

We want to emphasise that bromhexine has no effect on salivary and lacrimal secretion in persons not suffering from Sjögren's syndrome. Most of the patients participating in the trial of Dr Tapper-Jones and others who were claimed to have Sjögren's syndrome do not seem to fulfil the criteria for that disease. We agree that Sjögren's syndrome is defined by the presence of at least two of the following criteria: (1) keratoconjunctivitis sicca; (2) xerostomia; and (3) a well-defined chronic inflammatory connective tissue disorder (for example, rheumatoid arthritis, systemic lupus erythematosus). If only the first two criteria are met the term primary Sjögren's syndrome

is used, whereas secondary Sjögren's syndrome denotes the presence of (3).

Patients may well suffer from a feeling of dry eyes or dry mouth without any objective, measurably abnormal parameters, which unfortunately is rather common. Our criteria for keratoconjunctivitis sicca and xerostomia are the demonstration of at least two abnormal results out of three tests performed for both organs. For the eye (lacrimal gland) we perform the Schirmer test, break-up time, and quantitative Rose-Bengal staining (Bijsterveld score). For the salivary gland we perform sialometry, lower lip biopsy, and salivary gland scintigraphy.

Dr Tapper-Jones and others seem to have performed only one of these tests (Schirmer test and sialometry) for each organ. According to their fig 1 the mean unstimulated salivary secretion for "SS patients" seems to be slightly more than 2 ml/15 min—a value within normal range.¹ That may explain why their patients get an increase in salivary flow after stimulation, as this does not usually happen in patients with true Sjögren's syndrome.

Thus our conclusion from their clinical trial is that bromhexine and placebo do not differ in their action on lacrimal and salivary glands in controls and in patients probably not suffering from Sjögren's syndrome. We have, however, performed a new trial including 32 patients with Sjögren's syndrome, and once more demonstrated that bromhexine may improve some of the abnormalities mentioned.² If mistakes are to be avoided, it is our hope that future clinical trials will include only patients that fulfil the criteria mentioned above.

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¹ Bertram U. *Acta Odont Scand* 1967;25, suppl 49: 1-126.

² Manthorpe R, Frost-Larsen K, Isager H, *et al*. *Scand J Rheumatol* (in press).

*.*We sent this letter to the authors, who reply below.—ED, BMJ.

SIR,—We thank Dr R Manthorpe and his colleagues for their interest in our paper (7 June, p 1356). Regarding their comments on our group of patients, we repeat that all fulfilled the criteria of Bloch *et al*¹ for the diagnosis of Sjögren's syndrome—that is, they had at least two of the following three features: xerostomia, keratoconjunctivitis sicca, and a connective tissue disorder. Obviously, if patients are initially selected on the basis of one of the sicca components, special groups will result with mean indices of lacrimal or salivary function lower than those generally obtained for patients with Sjögren's syndrome as a whole. However, even in the subgroup with sicca syndrome in our series, bromhexine was not more beneficial than placebo in any respect.

Dr Manthorpe and his colleagues assume that the Schirmer test and sialometry, which were used to measure the possible effect of drug and placebo, represented the only diagnostic investigations performed. Our report also referred to lacrimal lysozyme concentrations,² which are a more accurate index of lacrimal function than the Schirmer