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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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, angiopathy, 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