can be considered valid in the case of aged people, so that the results of our studies cannot be read from the literature but from our series alone.

We did not learn from Drs Jowsey and Riggs's letter whether their studies—which in general are based on a very small number of patients—included any control series. If there was one, were the studies done blind and did the plausible control series also receive calcium and vitamin D, which are indeed very interesting and potent drugs even used separately? If not we cannot be very impressed with their results regarding the effect of fluoride but rather horrified because they observed three fractures in a series of eight patients during the first year and still continued the administration of fluoride. Drs Jowsey and Riggs claim that fluoride might have a beneficial effect on the bones beginning from the second year. It is only unfortunate that with each patient we cannot avoid the first year, during which according to their and our results fluoride might just do harm. As an end result of treatment changes in bone biopsy and in quantitative radiology might be of a certain value but from the point of view of the patient and of the practitioner the most interesting thing to know is whether the bones break or not and that must also be the main guide for treatment.

WALTER J BRAY

Abingdon

Measuring blood pressure

Sir,—Your leading article on measuring blood pressure (15 November, p 366) mentions preliminary assessment of the systolic blood pressure by palpation but fails to stress fully the importance of this procedure.

If blood pressure is actually being done alone one may miss the "silent gap," which can occur during phase I or phase II Korotkoff sounds. The true systolic blood pressure will be that detected by palpation and may be as much as 30 mm Hg greater than that measured by auscultation.

Furthermore, at any level of diastolic blood pressure cardiovascular mortality increases in proportion to the associated changes in blood pressure (15 November, p 714) reported abnormal systolic pressures. Thus accurate measurement of the systolic blood pressure is as important as also had elevated serum AFP levels (mean silent gap can be reduced by inflating the sphygmomanometer cuff quickly and by not having the arm hanging down."

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Nutritional protein needs

Sir,—I was astounded to read in the BMJ (30 August, p 547) what purported to be a review of a book by Francis Aylward and Mogens Jul on "Protein and Nutrition Policy in Low-income Countries" but which was not only a diatribe distorting the reviewer's one-sided approach to malnutrition.

In it Mr P R Payne dismisses the general need for protein by asserting that "there is no evidence to show that protein deficiency even exists outside the laboratory." To substantiate this sweeping statement he cites only a Ministry of Overseas Development report which he cowrote. As an American scientist working in Britain I can attest that his conclusion is totally incorrect, as evidenced by the current US National Science Foundation study of protein resources in which almost 100 of the country's food and nutrition experts are participating.

Mr Payne criticizes Aylward and Jul for claiming that protein alone is the answer to world nutrition problems. This is a view the mid-1960s textbook that payne implied in his book. He further goes on to say that malnutrition is merely "a symptom of poverty," a simplistic statement that offers little in the way of a solution to the extremely complex real problems. In fact, regarding nutrition there is only one acceptable position: all the elements which go to make up a nutritionally balanced diet for a population are equally important, and this must include protein.

WALTER J BRAY

Abingdon

Penicillamine therapy, antistriational antibody, and myasthenia gravis

Sir,—In view of recent reports of myasthenia gravis apparently induced by d-penicillamine1 and our own experience of a patient with Wilson's disease complicated by myasthenia gravis, thymic hyperplasia, and anti-acetylcholine receptor antibody while on penicillamine we have reviewed 34 patients treated with penicillamine for rheumatoid arthritis. In particular, we have examined sera for the antistriational antibody found in association with thymoma and myasthenia gravis.6 Six of these patients (18%) developed antistriatal antibody at some stage during the course of therapy. One further patient was found to have antistriatal antibody before and during therapy. The titre of the antibody was found to vary somewhat from time to time and in this respect the results are similar to those that we have found in the case of antineuronal factor apparently induced by penicillamine.

In the six patients who developed antistriatal antibody the latent period after starting penicillamine was 6-24 months. The period of follow-up after the development of the antibody ranges only from one to four months, but none of these patients has manifested overt myasthenia gravis.

PENICILLAMINE THERAPY, ANTISTRIATIONAL ANTIBODY, AND MYASTHENIA GRAVIS
These results are of special interest for a number of reasons. Firstly, although myasthenia gravis has been found after the introduction of penicillamine therapy, we are not aware of other reports of this disease which indicated that antistriatal antibody may occur in a similar situation. Secondly, antistriatal antibody is associated with myasthenia gravis complicating thymoma rather than with myasthenia gravis per se. For this reason alone patients on penicillamine should be followed for the development of a thymoma in addition to the development of myasthenia gravis. Thirdly, no previous examples of drug-induced antistriatal antibody have been recorded and hitherto it has been assumed that this autoantibody had far greater diagnostic specificity than other autoantibodies such as antinuclear factor and anti-smooth-muscle antibody, both of which may occur after drug therapy and viral infections and in the aged. Fourthly, it is now clear that penicillamine induces a variety of autoimmune diseases and in view of the present results perhaps a variety of autoantibodies in addition to the antinuclear factor. Finally, we have previously suggested a role for immunodeficiency in the pathogenesis of myasthenia gravis and thymoma. Since penicillamine can be considered immunosuppressive in some respects the present data provide a further argument for the immunodeficiency hypothesis.

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2 Blakley, G. et al., Scandinavian Journal of Rheuma-
tology, 1975, suppl 8, workshop 21, abstract 28.
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5 Czlonkowska, A., Annales de Medecine Interne, 1974, 125, 71.
6 Zilo, P. J. and Dawkins, R. L., Proceedings of Sentiemental Maladies of the Skeletal Disorders, Royal Perth Rehabilitation Hospital, Perth, April 1975, in press.

Low protein diets in chronic renal failure

Str.—Your leading article (29 November, p 486) states correctly, as many of us know, that the imposition of a low protein intake for patients in chronic renal failure introduces in the long term more troubles than it is really worth. Firstly, other than the fact that a low-protein diet was and still is a compromise to postpone the day of dialysis, one multiplies the whole rationale, since most people still think that it is the toxic products of gut bacteria that are absorbed into the circulation to account for uraemic symptoms. Secondly, when in compensation for the low protein intake a patient is obliged to eat supernormal amounts of carbohydrate and fat it is inevitable that there will be increased triglyceride synthesis by the liver to add to the other explanations of this lipidemia, all of which in the long term lead to premature vascular disease and further difficulties in haemodialysis and transplantation.

Is it really true that "measurement of nutritional status is infuriatingly imprecise"? We have shown that serum transferrin levels and even the blood haemoglobin concentra-
tion give a better guide to nutritional status than the serum albumin.1 Other groups have made similar observations.2 3

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2 Ooi, B. H., Polack, V. E., and Nephron, 1972, 9, 200.
3 Schaeffer, G. et al., Clinical Nephrology, 1975, 3, 228.

Immunisation against dental caries

Str.—We should like to comment on your thoughtful leading article (22 November, p 424) which discusses the possibility of im-
munising against dental caries. There are, of course, many problems to be solved before a clinical trial of Streptococcus mutans vaccine should be attempted. However, some of the questions you have posed can be answered directly.

The slow antibody response to Str mutans in some rhesus monkeys was found only when a laboratory strain of Str mutans (Ingbritt) was used.6 As soon as an animal-passaged strain or a strain isolated from man has been used all monkeys yielded a satisfactory antibody response within one month. Even if the response were to be delayed by a few months this should not cause much concern, as immunisation should be carried out before eruption of the deciduous dentition—
the same as in the case of Str mutans.6 Thus if the triple vaccine is usually administered.6 7

As to the bias towards a positive result in that the heavy load of implanted organisms in the mouth of the animal was the same as the organisms used for immunisation, this does not apply to our second series.6 Indeed, no organisms were deliberately implanted into the mouth of the rhesus monkey because a naturally occurring Str mutans (serotype c) develops if the animals are placed on a human type of carbohydrate-rich diet.8 9 Colonisation of a cariogenic flora occurs under conditions analogous to those found in man and artificial implantation of organisms, possibly disturbing the microbial ecology of dental bacterial plaques, is not required.Immunisation with Str mutans induces protection from caries by changes in the development of a naturally acquired and not artificially induced cariogenic flora.

We wish to correct a possible misunderstanding of our results in the abstract of our pronounce-
ment but also a decrease in the incidence of smooth-
surface caries in deciduous teeth. Some of these animals have now been followed for four years—
which is, at the time of shedding of most of the deciduous teeth—and the decrease in the incidence of smooth-surface caries in the effectively immunised compared with the sham-immunised monkeys was maintained at about 70%.10

The answer to the question why an attack of the disease does not produce natural immu-

nity is more complex. It is possible that the antigenic dose of Str mutans on the teeth is inadequate or inaccessible to the lyophilised tissue and does not result in effect-

ve immunisation. The immunogenicity of Str mutans is rather poor, and effective anti-

body titres, decrease in the number of colonising Str mutans, and protection from caries resulted only when an adjuvant was used with the whole organism.6 Alternatively, it is possible that the antigenic stimulation is not effective inasmuch as the bacteria, which occur, particularly with bacteria normally found adjacent to the gingival crevice,10 it is possible that a low dose tolerance11 might be induced in some subjects who might then be unable to respond to the relevant organism. However, there is some evidence from immunological studies in man that natural immunity may occur in a small number of subjects.10

We have noted the fears expressed in your article that inhibition of some strains of Str mutans by immunisation might lead to the development of other serotypes of this species or other cariogenic organisms. Our experience in immunisation of rhesus monkeys has so far not substantiated these fears. If a new cariogenic flora were to have emerged under the pressure of immunisa-
tion, then the incidence of caries should have increased. In fact, it is found that Str mutans resulted in a very significant protec-
tion from dental caries from the time the deciduous teeth were fully erupted to the time they were shed.

We think that an immunological approach to dental caries might well lead to a sig-

nificant prevention of dental caries, as the results of the experiments with Macaca fascicularis12 and our investigation with M mulatta suggest.

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4 Centers for Disease Control. Collected Recom-

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9 Mitchison, N. A., Immunology, 1968, 15, 509.
11 Challacombe, S. J., Caries Research, 1974, 8, 84.

Laparoscopy explosion hazards with nitrous oxide

Str.—In reply to our warning letter (27 September, p 764), J. M. Corral and his colleagues (1 November, p 288) report that over a three-year period more than 3000 laparoscopies have been performed at King's College Hospital and that "sterilisation by tubal diathermy has accounted for less than 30% of these, which they consider to be but a small proportion, even though it represents about 300 cases per year. If this use of nitrous oxide became common there would be likely to be many thousands of such cases per year. Even if the risk of an explosive mixture being ignited is small (for example, less than one in 10000) is it right to ignore that risk? Considerable amounts of monoxide are contained in the explosion hazards involved in using diethyl ether as an anaesthetic agent. Several ex-

plosions have been reported4 when diathermy has been used in electro surgical procedures on the prostate gland, and rectum, some of which have been fatal.

As intestinal gas generally contains only a very small percentage of oxygen (less than 1%), an explosive mixture can be formed