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 previous studies which have indicated that antistriational antibody may occur in a similar situation. Secondly, antistriational 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 antistriational antibody have been recorded and hitherto it has been assumed that this auto-antibody 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.⁵ Finally, we have previously suggested a role for immunodeficiency in the pathogenesis of myasthenia gravis and thymoma.⁴ Since penicillamine can be considered immunosuppressive in some respects⁶ the present data provide a further argument for the immunodeficiency hypothesis.

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Low protein diets in chronic renal failure

SIR,—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 might question 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 a 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 for hyperlipidaemia, 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 concentration give a better guide to nutritional status than the serum albumin.¹ Other groups have made similar observations.^{2,3}

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Immunisation against dental caries

SIR,—We should like to comment on your thoughtful leading article (22 November, p 424) which discusses the possibility of immunisation against dental caries in man. 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.¹ As soon as an animal-passaged strain² or a freshly isolated strain of *Str mutans* (wild strain) was 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—that is, at three to six months, when the triple vaccine is usually administered.^{3,4}

As to the bias towards a positive result in that the heavy load of implanted organisms in the mouth is the same as the organisms used for immunisation, this does not apply to our second series.² 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.^{1,2,5} 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 plaque, 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 that there is not only a postponement 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—that is, up to 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%.

The answer to the question why an attack of the disease does not produce natural immunity is more complex. It is possible that the antigenic dose of *Str mutans* on the teeth is inadequate or inaccessible to the lymphoid tissue and does not result in effective immunisation. The immunogenicity of *Str mutans* is rather poor, and effective antibody 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, in view of the frequent transient bacteraemias that occur, particularly with bacteria normally found adjacent to the gingival crevice,^{7,8} it is possible that a low dose tolerance⁹ 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.^{10,11}

We have shared 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 immunisation, then the incidence of caries should have increased. In fact, immunization with *Str mutans* resulted in a very significant protection 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 significant prevention of dental caries, as the results of the experiments with *Macaca fascicularis*¹² and our investigation with *M mulatta* suggest.

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Laparoscopy explosion hazards with nitrous oxide

SIR,—In reply to our warning letter (27 September, p 764) Dr I 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 10 000) is it right to ignore that risk? Considerable amounts of money were spent on the reduction of the explosion hazards involved in using diethyl ether as an anaesthetic agent. Several explosions have been reported¹⁻⁴ when diathermy has been used in electrosurgical procedures on the colon, caecum, and rectum, some of which have been fatal.

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