safety in dentistry. As an additional safety factor may I make the plea for adequate oxygenation from the outset monitored as described? I feel certain that virtually all anaesthetic deaths would then be avoidable. I should add that I have acted as operator anaesthetist for many years, after 1500 cases originally carried out with a consultant anaesthetist (1961-3). Any prolonged or difficult case assessed as being out of my scope as an operator-anaesthetist has always been referred for a consultant's help.—I am, etc.,

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### Epanutin and Isoniazid Interaction

SIR,—The hazards of interactions between different groups of drugs are becoming increasingly recognized.[1] Interaction between antiepileptic drugs and antituberculosis drugs, particularly isoniazid, has been well documented in the American literature[2] but does not seem to be widely recognized in this country. A recent death associated with this interaction reported in the press prompts me to report the following case where the interaction was fortunately recognized.

A 30-year-old chronic epileptic woman had been treated with epanutin 100 mg three times a day and phenobarbitone 60 mg three times a day for 12 years. She had episodic postictal confusional states and had been admitted to a psychiatric hospital on five occasions. During the last admission she was found to have apical tuberculosis. Isoniazid 300 mg, rifampicin 600 mg, and ethambutol 1200 mg were given daily in addition to antiepileptic drugs. After three days her consciousness became clouded, she was unable to stand, and she exhibited bizarre postural and semi-purposive movements of her limbs. Over the next seven days her level of consciousness deteriorated further and she became hypertensive, hyperglycaemic, and showed evidence of hepatotoxicity. All medication was stopped as the patient was thought to be suffering from rifampicin toxicity. She then began to improve, the level of consciousness lightened, she was able to walk, and liver function tests returned to normal. Antituberculous drugs were again given, substituting streptomycin for rifampicin. The E.E.G. by this time showed continuous "spike and wave" activity and in view of the possibility of status epilepticus anticonvulsants were restarted. After three days consciousness again became clouded, the patient became ataxic with slurred speech, and was unable to stand. (serum epanutin 4·9 mg/100 ml). The possibility of an epanutin toxic encephalopathy due to interaction between epanutin and isoniazid was now recognized. Antituberculous drugs were stopped and the anticonvulsant regimen changed to carbamazepine 200 mg daily and ethosuximide 250 mg three times a day. The E.E.G. became normal and serum epanutin levels fell to zero over the next 12 days, paralleling her continuous improvement. Since then she has been admitted to a tuberculosis hospital where antitubercular drugs have been restarted with no complications.

The development of epanutin toxic encephalophy from doses within the normal therapeutic range was in this case thought to be due to interference in the biotransformation of epanutin in the liver by the simultaneous administration of isoniazid. While hepatotoxicity due to rifampicin may have been partly responsible for the first episode of epanutin toxicity isoniazid was clearly responsible for the second. Antituberculous drugs, particularly isoniazid, should be avoided in epileptics who are taking hydantoinates unless epanutin levels can be measured daily. A rise of serum epanutin to toxic levels indicates that an alternative anticonvulsant regimen is necessary. Wider recognition of this dangerous interaction between hydantoinates and isoniazid is clearly necessary.—I am, etc.,

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1 Hansten, P. D., *Drug Interactions*, 2nd edn. Philadelphia, Lea and Febiger, 1973.
2 Woodbury, D. M., Penry, J. K., and Schmidt, R. P., *Antiepileptic Drugs*. New York, Raven Press, 1972.

### Oats and Coeliac Disease

SIR,—The letters from Dr. P. G. Baker and Mrs. Elizabeth Segall (7 December, p. 588) both betray a lack of appreciation of the fact that gluten intolerance is no more a standard disease than is diabetes. Some people with gluten intolerance are able to ingest all cereals other than wheat and rye with perfect comfort; those more sensitive have to exclude oats and barley as otherwise they are ill.

As it is possible that gluten intolerance is in fact an intolerance to one or more of the polypeptides of glutamine, and as these are widespread throughout the vegetable world, it is easily understandable that some coeliacs have to exclude a much wider range of foodstuffs than those normally accepted. Maize and its derivatives liquid glucose and corn oil, onions, green and red peppers, peanuts and groundnut oil, the bean group, including coffee and cocoa beans, and tea are some of the more exotic intolerances.

The essential factor in dealing with a coeliac (of whom I am one) is that he or she should be totally well. If there is flatulent dispepsia, heartburn, steatorrhoea, abdominal or chest pain, or skin lesions (embracing dermatitis herpetiformis and particularly including perianal soreness or eczema), if there is poor bladder control with frequency, urgency, precipitancy, or stress incontinence, or if there is headache, irritability, bad temper, bloody-mindedness, depression, or insomnia, then the dietary exclusions for that particular person are inadequate.

The failure to respond to treatment noted in some cases by Dr. Baker is a clear indication that dietary control is not adequately strict. It must also be borne in mind that a coeliac suffering from stress will have a poorer tolerance than normal. A coeliac on holiday with no worries and no stresses will have a better tolerance than he normally does. In conclusion, if your coeliac is well, his diet is adequate. If he is unwell his diet, however official, is not adequate for him.—I am, etc.,

DUNCAN MILNE

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### Cardiovascular Disease and Peptic Ulcer

SIR,—In your leading article on the association between cardiovascular disease and peptic ulcer (28 September, p. 760) you cite the article by Brooks *et al.*[1] in support of your statement that "patients with coronary artery disease have a somewhat greater than average frequency of peptic ulcer, particularly duodenal ulcer." In fact, these authors stated that there was a "relatively small but statistically significant increase in incidence of coronary occlusion at necropsy in patients with duodenal ulcer." They accepted that there might be common aetiological factors, but were mainly concerned that diets high in fat content used in the treatment of peptic ulcer might be contributory to the increased incidence of coronary occlusion. This possibility was not considered in your leading article.

Sandweiss *et al.*[2] had earlier reported that the incidence of coronary occlusion was higher in ulcer patients treated with a Sippy diet than in those not so treated. Even more convincing was the investigation carried out at 10 hospitals in the U.S.A. and five in Britain reported by Briggs *et al.*,[3] who found that ulcer patients treated with milk diets had double the frequency of myocardial infarcts compared with those not so treated and with non-ulcer patients.

Other published findings also suggest that milk may be a factor in causing ischaemic heart disease.[4-7] In my practice, of the last 14 patients who sustained an acute myocardial infarct, nine admitted to a daily intake of milk of one pint (0·6 l) or more.—I am, etc.,

J. J. SEGALL

London N.W.2

1 Brooks, F. P., Sandweiss, D. J., and Long, J. F., *American Journal of Medical Sciences*, 1963, **245**, 277.
2 Sandweiss, D. J., *et al.*, *Sinai Hospital of Detroit Bulletin*, 1961, **9**. 188.
3 Briggs, R. D., *et al.*, *Circulation*, 1960, **21**, 538.
4 Annard, J. C., *Journal of Atherosclerosis Research*, 1967, **7**. 797.
5 Annard, J. C., *Atherosclerosis*, 1972, **15**, 129.
6 Davies, D. F., *American Heart Journal*, 1971, **81**, 289.
7 Davies, D. F., *et al.*, *Lancet*, 1974, **1**, 1012.

### Thrombolytic Therapy in Haemolytic-uraemic Syndrome

SIR,—Dr. E. Ekert (30 November, p. 533) states that children with renal failure caused by the haemolytic-uraemic syndrome should not be assessed for prolonged periods while receiving conservative treatment before they are selected for anticoagulant or thrombolytic therapy. No one would disagree with this and we are not aware of any publication which suggests it. Dr. Ekert also restates the point made in our paper (27 July, p. 217) that the efficacy of thrombolytic therapy should not be evaluated on mortality during the acute phase but on its ability to prevent long-term residual renal abnormality.

One difficulty is that in many parts of the world, including the United Kingdom, children are not referred as soon as they might be to specialist centres with facilities for dialysis. Until this situation is corrected anticoagulant and thrombolytic therapy will continue to be given at a relatively late stage of the disease. Secondly, in children not given streptokinase the high incidence of residual renal abnormality found in the Argentine (52%)[1] and in Australia (41%)[2] was not observed in California (9·5%).[3] Differences such as these render the comparison of treatments used in different centres virtually meaningless.

The relative merits of anticoagulant and thrombolytic agents cannot be assessed in uncontrolled series employing retrospective comparison with the results of previous years but should be studied under randomized trial conditions. It will be the responsibility of participants in these trials