SIR,—Dr Whittington and colleagues confirm that current safeguards against aspiration are not reliable. Cæsarean-section patients are vulnerable from the time anæsthesia has been induced until intubation has been accomplished. If protection of the lungs cannot be guaranteed throughout this phase, some other solution must be sought.

A slightly less pleasant but vastly safer alternative is afforded by the sequence: (1) passage of a stomach tube; (2) endotracheal intubation with the patient conscious and laryngeal reflexes intact; followed at once by (3) induction of anæsthesia.

In skilled hands, the momentary discomfort of intubation is a small price to pay for safety. Conversely, anæsthesia given before intubation, so as to eliminate its minor discomforts, carries a disproportionately grave and unfortunately well-proven risk.

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SIR,—The patients described by Dr Whittington and colleagues had been in labour many hours. Had they also received pethidine, which delays gastric empyting? Before the anæsthetic, they took mist magnesium trisilicate BPC which contains peppermint water, a drug which relaxes the lower œsophageal sphincter and is unpalatable; the first reaction on taking it is always to retch.

Since none of the alternatives to operating on a full stomach (long delay, apomorphine, or nasogastric intubation) is acceptable, perhaps obstetricians and anæsthetists should join forces to insist that more cæsarean sections are done with the patient awake and under epidural anæsthesia rather than potentially hazardous general anæsthesia with relaxation.

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IDENTIFYING THE MEDICAL CONSULTANTS OF PHARMACEUTICAL COMPANIES

SIR,—Dr Lunde and Dr Herxheimer (July 28, p. 197) are concerned that bias may affect the advice of consultants asked to furnish opinions on subjects related to drugs or medical equipment. They suggest that consultant involvement with pharmaceutical companies should be declared. But why stop there? Surely multiple factors may lead to conflict of interest (bias) in the formulation of opinions. A short list of such influences might be: a spouse (or mistress); religious conviction; political party affiliation; share or stock ownership; race or origin; educational environment; overreaction to the fear of being accused of bias.

Perhaps Lunde and Herxheimer might suggest that before we consider a consultant opinion on matters relating to drugs we should ask for a sort of *curriculum vitæ* based on the life history of the doctor? After all, we wouldn't want to miss anything responsible for "enhancing the value of the opinion" (their phrase).

Am I naive in thinking that consultants whose opinions are sought on any medical matters are those whose integrity and ability to sift evidence dispassionately has been demonstrated from past contacts? Certainly I always try to avoid people who have either an axe to grind or just trundle out views that they think I would like to hear.

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DEATHS OF INFANTS AFTER TRIPLE VACCINE

SIR,—The occurrence of eight cot deaths following routine vaccination of infants with diphtheria-tetanus-pertussis vaccine (DTP) between August, 1978, and March, 1979, in Tennessee[1] raises yet again serious questions about the safety of standard batches of DTP. Four infants died within 24 h, the other four within 7 days of receiving their first dose of DTP at 6–8 weeks of age. In all cases, deaths were diagnosed as being due to sudden infant death syndrome. The deaths occurred in August, 1978, (1), January, 1979, (1) and March, 1979, (6) during a period of expansion of the childhood immunisation programme in Tennessee. In each case, the DTP given belonged to a single batch (64201) manufactured for routine use by approved procedures by a well-known pharmaceutical firm and passed by the Bureau of Biologics of the Food and Drug Administration. After the deaths, in March, the U.S. Surgeon General intervened and the company concerned withdrew all unused doses of batch 64201 of the vaccine—of which, it was estimated, 320 000 doses had already been administered.

Total deaths of infants in Tennessee were higher in 1978–79 than in 1977–78. Comparison of the periods in question (August–March) during these years, showed that of 61 sudden infant deaths in 1978–79, 33 had received DTP—a significant excess over the 16/53 similar deaths in 1977–78. There was no record of batch 64201 being used in 1977–78. The vaccine status of 34 of the total of 114 deaths during the two periods is unknown.

These incidents do not establish that DTP killed infants but they do show beyond doubt a highly significant, non-random clustering of an excess of undiagnosed sudden infant deaths following vaccination. Some months ago, I reported a similar cot death of an infant within 27 h of vaccination with DTP to the Committee on Safety of Medicines, to whom other deaths of infants had been reported previously[2] and, I believe, have been reported subsequently. Excluding fatalities, I have also investigated some hundreds of severe reactions,[3] most of which are also known to the C.S.M. These reactions are mainly neurotoxic in nature and some are life-threatening. They cannot be explained by a random distribution or frequency and show a consistent symptomatology long associated with pertussis vaccine[4-6] but not with other vaccines administered in childhood. There is no obvious association in my data between reactions and any identifiable batch or manufacturer of vaccine. All vaccines used appear to have satisfied the criteria of the National Biological Standards Board and the D.H.S.S., just as batch 64201 is stated to have, on test and retest, fulfilled the standards laid down by the Bureau of Biologics of the United States F.D.A. and therefore to be acceptable for international use by W.H.O. and member Governments. This is to say that there is no detectable difference between batch 64201 and all other batches and between manufacturers, except for the occurrence of these infant deaths.

It is customary, in Britain as in the U.S.A., to accept a measure of risk when vaccines are given because of presumed protection against the allegedly higher risk of death or disability from the corresponding disease.[7] But deaths, or indeed any form of permanent disability from pertussis, are now very rare indeed in developed countries and are far from common in many underdeveloped countries. It is therefore essential to test this presumption by comparing deaths associated with the disease with sudden unexplained deaths occurring after vaccination. Surveillance on these lines is long overdue and is now a matter of some urgency because the Year of the Child is being

1. Follow-up on DTP vaccination and sudden infant deaths.—Tennessee. *Morb Mort Wkly Rep* 1979; **28**: 134–35.
2. Stewart GT. Infection and immunization. *Scot Med J* 1979; **24**: 47–52.
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4. Byers R, Mill FC. Eucephalopathics following prophylactic pertussis vaccine. *Pediatrics* 1948; **1**: 437–41.
5. Ehrengut W. Convulsive reactions after pertussis immunization. *Deutsch Med Wchschr* 1974; **99**: 2273–75.
6. Christie AB. Infectious diseases: epidemiology and clinical practice 2nd ed. Edinburgh; Churchill-Livingstone, 1975.
7. Whooping cough vaccination: review of evidence by the Joint Committee on Vaccination and Immunization. London; H.M. Stationery Office, 1979.

celebrated by a world-wide bonanza of vaccination sponsored by W.H.O. on the basis of prevalence statistics which are questionable,[8] and of international safety standards which exclude from consideration incidents such as those reported above.

I am indebted to colleagues in the U.S.A. who have brought these matters to my attention.

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IDIOPATHIC ŒDEMA

SIR,—In the correspondence which followed our paper[1] and among the many people who have contacted us directly, there seems to be general agreement that the syndrome of diuretic-induced œdema we described does exist and that it probably accounts for the majority of patients who complain of intermittent swelling without obvious cause. Nevertheless, there is the remarkable statement by Edwards and Dent[2] that in over 70 patients they have seen none in whom "idiopathic" œdema could be ascribed to diuretics.

The real controversy is whether, in addition to those in whom diuretics are the cause of the œdema, there is another group in whom diuretics are not the cause. A potentially important argument in favour of the existence of such a group is that put forward by Streeten[3] who recalls having seen patients with intermittent idiopathic œdema in 1952, about two years before the introduction of oral diuretics. This new, hitherto unpublished observation, however, does not necessarily prove that these patients' œdema was due to a mechanism unrelated to some form of self-induced intermittent sodium deficiency. We have clearly demonstrated that in four normal young women large sudden fluctuations in sodium and carbohydrate intake can cause acute sodium and water retention accompanied by symptoms identical to those in patients with idiopathic œdema.[1] And since 1952 it has been increasingly recognised that the same syndrome can be caused by laxatives and surreptitious vomiting. The description by Dunnigan and Lawrence[4]—which they claim as the first of idiopathic œdema in 1922[5]—is that of a 28-year-old man with retention of sodium and water who had clinical and radiological evidence of a pituitary fossa tumour with visual field defects, an interesting but irrelevant case.

The second main argument in favour of there being a group of patients in whom intermittent œdema is due to some cause other than diuretics, is the claim that in some patients the reduced blood volume, the raised renin and aldosterone, and the exaggerated salt and water retention, particularly on standing, is due to an increased permeability to albumin. The work that has been published on this topic is confusing and the claims made are unconvincing. An early paper, which Streeten considers demonstrates this phenomenon, is a case-report of a nurse with persistent, massive œdema, proteinuria, and histological evidence of vasculitis in a skin biopsy specimen.[6] The likely possibility of systemic lupus erythematosus was not investigated. Another much cited paper is that of Edwards and Bayliss[7] who claimed that "the rate of loss of isotopically labelled albumin from the intravascular compartment was greater in patients with idiopathic œdema than in control subjects". But, as we pointed out in our earlier reply (March 24), and is now admitted by Edwards and Dent,[2] no measurements with isotopically labelled albumin in control subjects were made by Edwards and Bayliss, so that they were in no position to comment on whether the rate of loss of isotopically labelled albumin in their patients was abnormal. The only groups who have attempted to measure the permeability of capillaries to albumin in patients with idiopathic œdema and in normal subjects directly are Lagrue et al.[8] and Behar et al.[9] who favour an intravenous injection of isotopically labelled albumin, after which the forearm is monitored for radioactivity before, during and after venous occlusion. Radioactivity rises and falls rapidly. A failure to return to baseline is considered to be an indication of an increased permeability to albumin. The published results are difficult to interpret. Behar et al. considered that the test revealed an increased capillary permeability to albumin in all ill patients, but that the permeability was normal in heart failure, hypertension, and renal failure. In 14 patients with cirrhosis of the liver, 10 were considered to have normal capillary permeability, whereas in four, with severe œdema, the permeability was considered to be abnormal. In 13 of 15 patients with "cyclical" œdema, capillary permeability was considered to be abnormal, but it was stressed that 2 patients who were on spironolactone had the least abnormality. In these patients the "cyclical" œdema and the apparent abnormal capillary permeability were both related to menstruation and rapidly resolved after each period. It was claimed that the apparent capillary defect was not improved by diuretics, but was improved by the diuretic spironolactone, and preparations of vitamin P and anthocyanosides.[8,10] As the prolonged retention of albumin in the forearm in the patients with cirrhosis and cyclical œdema was present only when the patients were œdematous, and rapidly returned to normal when the œdema resolved, it is not clear whether or not the abnormality was a consequence of the œdema, rather than its cause. In other words an increased volume of interstitial fluid may delay the removal of the radioactive albumin from the interstitial space.

We still maintain that in most patients in whom so-called "idiopathic" œdema is diagnosed, the œdema has some cause other than an abnormal capillary permeability. The commonest cause, in our experience, is the taking of diuretics and we would stress that the effect of diuretics may, in some patients, take at least a year to wear off. Other causes that must be excluded are fluctuations in sodium and carbohydrate intake, laxative abuse, and surreptitious vomiting.

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BROMOCRIPTINE-RESPONSIVE FORM OF IDIOPATHIC ŒDEMA

SIR,—We were very interested to read the report from Dr Edwards and his colleagues describing two cases of bromocriptine-responsive idiopathic œdema (July 14, p. 94). We have recently completed a study of bromocriptine in seven patients with this disorder.[1] In two patients there was definite symptomatic improvement and in these two and one other there was a significant decrease in the excessive diurnal weight gains. However, the changes were by no means as dramatic as those previously described, and the frequent side-effects, with even low doses of bromocriptine, limited the usefulness of the drug, even in those patients who had shown symptomatic improvement.

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