be the first step on a slide to unacceptable inaccuracy and clinically useless results.

At least Dr Walker does not deny that some kits in the past have failed; if he does disbelieve this he can call on our laboratory and I'll show him my files of kits we could not use for one reason or another. If this is accepted as a fact, how do these kits get stopped when there is a blank acceptance of manufacturers' statements by the scientifically and technically naive? These "side room" kits will not be tested for amount of bias, interference, imprecision, or run in parallel with a referee technique by actual users. Even if they are, how about continuing control?

And so to return to my original letter and the major question in it. Manufacturing companies are leading us down a path of testing outside main laboratories to bring profit to them (Dr Walker said so). Do we tread this path? Sometimes we may have to if the clinician decides that the product offers real benefit to patients; and in these circumstances I say "Involve the hospital biochemist even if he has to be dragged screaming from his ivory tower." Without manufacturing companies we would presumably still be at the wattle and daub stage so obviously I accept advance—but not when that advance brings detriment to established order, as in the selling of milk feeds to primitive societies. In my mind the state of play for tests performed outside laboratories is just that.

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The incidence of biochemical emergencies

SIR,—As a result of the "industrial dispute" over emergency duty payments involving medical laboratory scientific officers (MLSO), the Torbay District Management Team asked that requests for emergency biochemical investigations outside normal working hours should be generated at consultant level. Thus instead of the request being generated by a junior doctor and passed to an MLSO the route became junior doctor to clinical consultant to laboratory consultant to MLSO. Throughout the preceding year, the average number of requests for out-of-hours emergency biochemical investigations had been 66 per week. During the month of consultant monitoring the average number of such requests was two a week.

Is this the true incidence of biochemical emergencies? As Professor Joad would have said, it all depends what you mean by "emergency."

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Berkson's fallacy in case-control studies

SIR,—In the review by Dr Charles du V Florey (17 November, p 1283) of an epidemiological textbook designed for "the uninitiated" I was very glad to see a reference to Berkson's fallacy in case-control studies. The demonstration of this potential bias was first published¹ with probability symbols in a journal known to very few clinical investigators, but a simple arithmetical demonstration, submitted

to Dr Berkson before publication,² was easily grasped by my students and clinical colleagues. During the subsequent quarter century statisticians and epidemiologists have paid curiously little attention to the possible risk. The frequent defence has been that it is theoretical, never shown on real data. Apparently it was not until 1978³ that there was published a search for confirmation, by comparison of frequencies of diseases in a hospital with the frequencies in the parent community; but now that this report has revealed the effect of Berkson-type biases there is no excuse for ignoring the risk. Some technical details in the report would be difficult for "the uninitiated," but any of us when trying to evaluate the report of a case-control study can ask whether the author has ignored Berkson's fallacy or has dismissed it casually as of no consequence.

In order to ask that question, however, we must know what we are looking for, and simple arithmetic still gives me the clearest picture. In a certain community are three features, A, B, and X, that cause some of their possessors to be admitted to a certain hospital (or clinic). The features may be diseases, injuries, signs, symptoms, or disabilities such as ocular refractive errors in the control group in Berkson's original paper. In a study conducted in the hospital the *As found there* will be the "cases," the *Bs found there* will be the "controls," and the *Xs* possess some feature that we are considering as possibly associated with A (perhaps as a clue to cause). In the community the respective populations are 1000 *As*, 1000 *Bs*, 300 *Xs* in the *As*, and 300 *Xs* in the *Bs*—that is, there is no closer association of X with A than with B. (For simplicity we omit the *As* that are also *Bs*.)

Ten per cent of the *As* are admitted to the hospital because they are *As*—that is their "inherent" admission rate. The inherent admission rate for B is 50% and for X is 20%. Of course, in the study we shall be ignorant of these admission rates; we postulate them here to see the effect. Thus, of the 700 *Anot-Xs* we put 10% (=70) into the hospital and of the 300 *AXs* 10% (=30), leaving 270 *AXs*; but 20% of these (=54) come in because they are *Xs*. Total *AXs* in hospital=84. After doing likewise with the *Bs* we have the following:

	X	Not-X	Total	% Xs
A	30+54= 84	70	154	54.5
B	150+30=180	350	530	34.0

The A-B difference in *Xs* is 20.5 percentage points, although in the community there was no difference whatever. It appears as if the greater admission rate of the *Bs* had pushed the *Xs* into the *As* (the "cases" under study). Under the postulated conditions the demonstration is as cogent as, say, the theorem of Pythagoras; and in the real world the crucial condition, a difference in the admission rates of *As* and *Bs*, is probably much commoner than identity of the two rates.

Using the same procedure we can⁴ ring the changes on the numbers of cases and admission rates, even showing how a real association between X and A could be masked by the interplay of admission rates. We can demonstrate fictitiously and facetiously a greater prevalence of bunions among bronchitics than among coronary disease patients. More plausibly, we can call X a sex difference in admission rates, and we can show that the admission rate bias could distort the results of a prospective study of health care that is dependent on voluntary attendance.

The Berkson admission rates bias is, of course, only one of many biases that can affect case-control studies—your leading article (13 October 1979, p 884) alluded to 35 of them. The production of methods of coping with them is an enormous task, but the producers (epidemiologists and statisticians) can be guided and helped by consumers (clinicians), who are not easily hoodwinked by

"significance" tests and "confidence" limits but are very sensitive to the multifarious pitfalls in the collection of data.

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¹ Berkson J. *Biometrics Bull* 1946;2:47-53.

² Mainland D. *Am Heart J* 1953;45:644-54.

³ Roberts RS, Spitzer WO, Delmore T, Sackett DL. *J Chron Dis* 1978;31:119-28.

⁴ Mainland D. *Elementary medical statistics*. Philadelphia: W B Saunders, 1963/4:117-25.

Whooping-cough immunisation

SIR,—Even though some of the reasons given for not having children immunised against whooping cough are manifestly absurd (19 January, p 179), it does not mean that the real reasons were absurd, still less that all misgivings about the value and safety of immunisation are thereby irrational. Absurdities are to be found on both sides of the controversy which has grown out of what should have been treated as a serious, necessary, and difficult scientific inquiry. The truth lies in what is actually known, and where people agree rather than where they differ.

The contraindications to pertussis vaccination first proposed by Köng in 1953, after he had surveyed 82 cases with cerebral complications following the use of the vaccine reported in the world literature, were: a family history of nervous disease, a history of convulsions in the child, allergic diseases, poor general condition, and evidence of acute infectious diseases.¹ He also advised that injections should be discontinued after a severe reaction to the first or second injection. Almost immediately, the need to exclude children with a record of allergy, nervous disease, or convulsions was strongly challenged^{2,3}; and indeed if Köng's criteria were strictly applied it would be difficult to attain the proportion of immune people in the population demanded by the theory of herd immunity. Despite being scientifically questioned, however, his list of contraindications has been retained, with emphasis on convulsions, to reassure the public that the risks of immunisation can be avoided by not vaccinating individuals who can be identified as vulnerable—but with little attention to the importance of reactions to previous injections.

Agreement does exist, however, on the need to withhold immunisation during periods of high poliomyelitis prevalence. Not many people doubt that pertussis vaccine can provoke clinical poliomyelitis in infections that might otherwise have remained latent. But what about its effect on other viruses? Can a vaccine which provokes activity in latent poliomyelitis not also provoke activity in other latent virus infections? *Bordetella pertussis* is known for its unexplained properties, useful and otherwise—enhancing antibody response to diphtheria and tetanus toxoids, being the only micro-organism that approaches mycobacteria as an adjuvant for inducing experimental allergic encephalitis.⁴ With such a repertoire is it not time to reflect on what else it might do?

Ten years ago Pittman wrote: "It is likely that in certain cases encephalopathy following pertussis vaccination is actually a viral infection which was in the incubation stage at the time of vaccination or was latent and provoked by the vaccine." After referring to Baird and Borofsky's work implicating pertussis vaccine with viral and bacterial encephalopathy as possible causes of infantile myoclonic seizures,⁵ and to Feldman and Schwartz's report of a possible association between such seizures and cytomegalovirus,⁶ she added: "Had these infants with latent virus been vaccinated, there would have been a chance of provoking a severe or fatal reaction."⁷ This association between myoclonic seizures and cytomegalovirus has not been confirmed but the infection is now "the commonest known viral cause of mental retardation in infancy"⁸ and is linked with school failure, behaviour

problems, and deafness,^{9,10} as well as sudden infant death.^{11,12}

The task of clearing the population of potentially dangerous viruses before immunisation may well prove impossible; but does that justify our setting up ill-founded contraindications, rather than real ones, and then shooting them down in order to prove that our vaccines are safe?

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- ¹⁰ Melish M, Hanshaw JB. *Am J Dis Child* 1973;126: 190-4.
- ¹¹ Potencz H, Diosi P. *J Paediatr* 1974;85:281-3.
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SIR,—In answer to Professor R S Illingworth's letter (19 January, p 179) about the multitude of curious reasons given for not allowing children to be immunised against whooping cough, I would suggest the following.

Mothers have just undergone nine months of bodily change of varying discomfort followed by a less comfortable, and perhaps dangerous, process at the end of it, in most cases to produce (one hopes) a wanted child. Not only are they then asked to submit that child to a possibly damaging procedure (the risks of which have been quantified differently by different authorities) but they are asked at a time when they may be suffering from mild postnatal depression; and, as anyone who has ever felt depressed knows, this is not a time when one can confidently and rationally take a decision.

Sometimes fathers can help by giving a firm lead, but often the mother looks to the health visitor or doctor to decide for her—something which is debatably not justifiable in the circumstances. She is frequently happier if the immuniser misses out the whooping-cough vaccine and afterwards she may present as reason for this any unusual fact in the child's family or medical history. The medical adviser may consciously or unconsciously have considered this, but in fact he or she is attempting to respond correctly to the mother's doubts and fears, while also acting in the interests of the child to protect it by immunisation against other diseases—at the very least polio only, which involves no "jab."

I sometimes consider postnatal depression sufficient of an argument to start immunisation at six months, not earlier. This is consistent with immunology, although other factors may sway policy towards an earlier start.

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Mortality of male doctors and reductions in cigarette smoking

SIR,—We disagree with Mr P N Lee's analysis of the mortality of male doctors (15 December, p 1538) and his provocative conclusion that the

benefits of giving up smoking may not be so great as has commonly been assumed. His calculations, which are obtained by a complex manipulation of standardised mortality ratios, showed "savings" in deaths from three major cigarette related diseases: coronary heart disease (83 deaths saved), stroke (16), and lung cancer (8). These savings are compared with "losses" from three stress-related conditions: accidents, poisonings, etc (30), suicide (26), and cirrhosis of liver (4). The implication is made that the doctors have become more prone to these stressful conditions partly owing to a possible adverse effect of giving up smoking. The analysis is based on the Registrar General's occupational mortality tables for England and Wales, which restrict attention to men under 65 years of age.

Life certainly does not end at 65 years; in England and Wales the expectation of life for men at 65 is 12 years and the doctors can expect to live even longer. It is therefore of vital interest to have an overall analysis of "savings" and "losses" in deaths over the whole life span of the doctors. Unfortunately national data are not available for this task; the answers on the extent of benefits arising from giving up smoking for the particular group of British doctors lie with the follow-up study of Doll *et al.*^{1,2}

The national figures for male deaths attributed to these cigarette-related diseases (table) show that a large majority of deaths occur in the postretirement age group.³ In contrast, the number of deaths from the stress-related conditions thought to be partly attributable to giving up smoking largely occur in the working age group. These opposing trends clearly demonstrate that the "savings" would rise and the "losses" diminish in the postretirement age. In this context we cannot understand why Mr Lee believes that the effect of giving up smoking might be seen most clearly in the younger age groups. It is most unlikely that these trends observed in the general population would be markedly different in the doctors. Ninety per cent of lung cancer deaths occur among smokers.⁴ It is estimated that in England and Wales the number of lung cancer deaths that could be saved by giving up smoking (22 000 lives) far outnumber the total number of stress-related conditions (12 383) that could partly be attributable to giving up smoking. These estimates are based on the assumption that 50% of adult males smoke cigarettes.⁵

Sixty-three per cent of ischaemic heart disease deaths occur among smokers; the number of lives saved annually is expected to be over 23 000. We firmly believe that the number of lives saved by giving up smoking will far outweigh the lives lost by the adverse effect of stress-related conditions arising

from giving up if all age groups are included in the analysis of male doctors.

Mr Lee's restricted analysis up to retiring age showing a small gain of 5% in lives saved by the reduction of smoking in doctors is misleading and can seriously affect the preventive programmes on smoking. There might be a small percentage of smokers who would be better off smoking than giving up but it is for the smoker himself to weigh up the relative advantages and disadvantages. For the large majority of smokers, however, it is prudent to give up rather than to continue. We believe that this overall conclusion is true for every subgroup of the population, including the doctors.

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SIR,—The conclusion by Mr P N Lee (15 December, p 1584) that the tar reduction in cigarettes occurred before publication of the first tar table in 1973 and that the table was "on the industry's own initiative" deserves comment.

The first publication of tar and nicotine retrieval from cigarettes identified by brand was in 1967.¹ This article was published despite the opposition of tobacco interests, some governmental groups, and even several fellow scientists who deplored its practical message. Shortly after this publication and the subsequent listings by the Federal Trade Commission industry began to publish tar and nicotine levels as part of their advertisements.

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- ¹ Moore GE, Bross I, Shamberger R, Bock FG. *Cancer* 1967;20:323-32.

Prophylaxis against postoperative pulmonary embolism

SIR,—The comprehensive study by Dr U F Gruber and others (12 January, p 69) on the prevention of fatal pulmonary embolus will interest all pelvic surgeons. Two deaths followed 414 gynaecological operations (all in women over 40 years and lasting more than 30 minutes). One was after dextran and the

Number of deaths in smoking-related and stress-related conditions in two broad age groups for men (England and Wales 1977)

		Number of deaths	Age		Ratio of deaths ≥65 y to <65 y
			<65 y	≥65 y	<65 y
Cigarette-related conditions	Ischaemic heart disease	89 411	28 613	60 798	2.12
	Lung cancer	26 679	9 193	17 486	1.90
	Cerebrovascular disease	27 831	4 896	22 935	4.68
	Subtotal	143 921	42 702	101 219	2.37
Stress-related conditions	Accidents, poisonings, etc	9 029	6 691	2 338	0.35
	Suicide	2 363	1 851	512	0.28
	Cirrhosis of liver	991	640	351	0.55
	Subtotal	12 383	9 182	3 201	0.35