

such reports as are published almost certainly underestimates the true probability, as the selective reporting and publishing bias is not taken into account.

It is certainly both wrong and misleading to present the probability ("less than one in a million") of obtaining specific kinds of unrelated abnormality (ependymoma, aqueduct stenosis, and kyphoscoliosis) *after* they have been observed when there was no *prior* hypothesis that such abnormalities would be seen. If the successive outcomes of tossing a coin 20 times are recorded the probability of obtaining the specific sequence observed is also less than one in a million; however, this does not necessarily allow us to infer that there is anything unusual about the coin.

That the five abnormal births in Birmingham were all female adds little weight to Dr Tomlin's findings, as there is a not unusually low probability (1 in 16) that five such births will involve children of the same sex by chance alone.

Finally, Dr Tomlin's statement that "since the only feature that is common to all the affected children was that the father was an anaesthetist this implies that there is an occupational hazard" is an extraordinary one. Since Dr Tomlin's study was limited to children born to anaesthetists it is hard to see how a different result could have been achieved.

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<sup>1</sup> Knill-Jones, R P, *et al*, *Lancet*, 1975, 2, 807.

SIR,—Sir Derrick Dunlop<sup>1</sup> commented that "the majority of our opinions are mere wish fulfilments, like dreams in Freudian theory, and the mind of the most rational can be compared to a stormy ocean of passionate conviction based upon desire, upon which floats perilously a few tiny boats carrying their cargo of scientifically vested beliefs." Dr P J Tomlin is a well-known crusader for the reduction of pollution in operating theatres, but I would suggest that his most recent evidence and conclusions (14 January, p 108) can only bring his cause into disrepute. The minute "cargo" on which Dr Tomlin's arguments are based would seem to have little scientific vestment. It is therefore all the more unfortunate that the local press and media appear to have accepted his views at their face value.

The assembly of a miscellaneous assortment of disorders identified in families in which the father is an anaesthetist, including an acquired lesion (hydrocephalus subsequent to meningitis), a tumour, and a possible degenerative or metabolic disorder (case 5 in the table), under the title of congenital deformities is not only terminologically incorrect but is also clearly misleading. I am not a statistician, but I doubt that the method of collection of the data and the arguments which follow are valid. Furthermore, it would seem remarkable that the *only* feature the five children had in common was their fathers' occupation, particularly as this was their reason for inclusion in the report.

If the irrelevant and equivocal disorders are excluded there are two cases of congenital dislocation of the hip (one associated with scoliosis), one of talipes (which may be related

to the central nervous system disorder), and one of hydrocephalus. All these malformations, with the possible exception of the last, are classified among the commoner abnormalities<sup>2</sup>; thus the absence of cleft palate and congenital heart disease in a series of four cannot be considered remarkable. Furthermore, four cases of differing anomalies can hardly be said to demonstrate a "pattern" of malformations either on statistical or embryological criteria.

I have criticised the data on abortion elsewhere<sup>3</sup> and I do not find that official recognition in any way influences my views. Abortions alone,<sup>4</sup> let alone abortions and underweight fetuses, do not form a homogeneous population on either morphological or aetiological criteria.

While there may be an argument for reducing theatre pollution on general environmental principles, the case against anaesthetic gases remains far from proved. The presentation of terminologically inaccurate data of, at the best, equivocal statistical significance can do little to enhance it, though it clearly attracted the attention of the media. The acceptance of malformations in children of exposed theatre staff as an "industrial" disease, which appears to be what Dr Tomlin is advocating when he asks the Department of Health and Social Security to accept responsibility for the affected offspring, would, on present evidence, seem to be opening the floodgates of teratological litigation far beyond the confines of the Health Service.

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<sup>1</sup> Doll, R, *Journal of the Irish Medical Association*, 1973, 66, 117.

<sup>2</sup> Polani, P E, *Guy's Hospital Reports*, 1973, 122, 53.

<sup>3</sup> Rushton, D I, *Lancet*, 1976, 2, 141.

<sup>4</sup> Rushton, D I, *Journal of Medical Genetics*. In press.

\* \* \* We sent copies of these two letters to Dr Tomlin, whose reply is printed below.—Ed, *BMJ*.

SIR,—The purpose of my letter expressing concern about the teratogenic effects of waste anaesthetic gases was to give an example of what information could be obtained on inquiry in one city in which the inquirer knows the local situation and the people involved, so as to encourage others to do the same. Surveys such as the Knill-Jones<sup>1</sup> survey do suffer from the problem of incomplete returns plus the resentment of the intrusion into the personal privacy of any affected family of an anonymous inquirer who requests a form of some sort to be completed. Since the defects observed were not the type to be observed at birth necessarily, inquiries into birth defects in the perinatal period, or thought to be confined to the perinatal period by those completing the survey, will inevitably lead to bias against any positive finding.

Dr Rushton and Dr McPherson and his colleagues appear to discount the case of ependymoma occurring in a child as being of congenital origin. In this they are in disagreement with experts in that field, but this assumption has coloured all their subsequent calculations.

The assumption by Dr McPherson and his colleagues that major congenital abnormalities occur in 1% of all births is a generous one and includes all types of major abnormality. A better appraisal would have been to give the percentage probability of observing by chance

a major defect in the central nervous or neuromuscular system in an apparently random sample of 135 children. I do not understand their statistical reasoning that the probability of a sequence of five female births is 1 in 16. The probability of a female birth is very nearly 1/2, for two females it is 1/2<sup>2</sup>, the alternative combinations being MF, FM, and MM, and for five females it is 1/2<sup>5</sup> or 1 in 32. Their remark that it is hard to see how a different result could have been achieved is naive—if all the children had been born in Birmingham it would be very easy to postulate a local environmental factor, but they were not; if there had been any common infection (an analogy is rubella) it would be very easy to postulate this, but there was no such infection.

Dr Rushton's letter raises two important moral arguments which I hope will not become widespread. These are (a) that one should not publish one's views in case they are socially inconvenient or disturbing medicolegally or otherwise; and (b) that if one finds an unusual set of circumstances which are similar to other reports in humans and similar to congenital abnormalities induced by anaesthetic agents in experimental animals one should take no action until all the scientific niceties of statistical exactitude have been satisfied, and never mind how many children suffer in the process of achieving this exactitude. One of the important aspects of the thalidomide disaster was that early warnings indicating a potentially dangerous situation were ignored in the interest of statistical exactitude until the evidence was overwhelming, and today many children bear the scars of that particular argument.

The protagonists for the no-action camp must prove beyond all reasonable doubt that constant breathing of anaesthetic waste gases is totally harmless. This they have signally failed to do. It is important that young children should not be put at risk just to suit their ivory-towered intellectual purity, for if they are wrong the price in terms of human suffering is a very heavy one.

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### Maternal pethidine and neonatal depression

SIR,—Dr P W Barritt and others (14 January, p 106) criticise our trial (23 July, p 229) because we did not compare naloxone with nalorphine or levallorphan as well as with placebo. However, we had already shown in adult volunteers<sup>1</sup> that levallorphan 1 mg intravenously caused as much respiratory depression as morphine 20 mg intravenously. (Nalorphine is even more depressant.) We were hardly likely therefore to include such drugs in a trial in neonates. Besides, neither nalorphine nor levallorphan had been used in our obstetric units for years. We cannot therefore accept their view that a comparison should now be made between naloxone and the older antagonists. If they are still unconvinced, let one of them personally try a dose of either drug. We have done so!

A previous study<sup>2</sup> from this department had shown that naloxone 40 µg intravenously reversed respiratory depression for up to 30 min. Subsequently we extended the period of observation to 48 h and demonstrated that at