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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¹ Knill-Jones, R P, *et al*, *Lancet*, 1975, 2, 807.

SIR,—Sir Derrick Dunlop¹ 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 abnormalities²; 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 elsewhere³ and I do not find that official recognition in any way influences my views. Abortions alone,⁴ 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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¹ Doll, R, *Journal of the Irish Medical Association*, 1973, 66, 117.

² Polani, P E, *Guy's Hospital Reports*, 1973, 122, 53.

³ Rushton, D I, *Lancet*, 1976, 2, 141.

⁴ 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-Jones¹ 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 1/2², the alternative combinations being MF, FM, and MM, and for five females it is 1/2⁵ 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 volunteers¹ 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 study² 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

the end of 4 h the reversal of pethidine depression had disappeared.⁴ It seemed logical to determine whether giving a larger dose of naloxone intramuscularly would be effective over a longer period. The degree and duration of reversal of pethidine-induced depression were surprising and it is possible that a smaller dose of intramuscular naloxone might prove equally effective. Naloxone 200 µg has been used frequently during the past year without ill effect, but we would agree that greater experience is necessary to give complete reassurance on safety. Very much larger doses, relatively, have been given to adult volunteers without detectable effects.

We chose to compare naloxone with placebo in healthy mature neonates so that drug effects could be clearly distinguished from any concurrent effects of prematurity, asphyxia, or birth trauma. The protocol was approved by the area ethical committee and the three divisions of anaesthetics, obstetrics, and paediatrics. A full explanation was given to each mother. We can assure Dr Barritt and his colleagues that no baby had umbilical venous cannulation; injection and sampling were done using a redundant section of umbilical cord. Indeed, the measurements were chosen because they were all non-invasive.

We have not administered naloxone to every neonate whose mother had pethidine during labour since treatment should be related to a clinical problem. However, naloxone is used whenever pethidine depression is suspected and this includes the need for differentiating pethidine depression from other perinatal insults.

A proper reading of our paper is inconsistent with their view that we have given any encouragement to "the over-prescribing of new 'wonder drugs,'" which we were especially careful to avoid.

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¹ Evans, J M, *et al*, *Anaesthesia*, 1974, **24**, 721.

² Evans, J M, *et al*, *British Medical Journal*, 1974, **2**, 589.

³ Evans, J M, *et al*, *British Medical Journal*, 1976, **2**, 1098.

⁴ Wiener, P C, *et al*, *British Medical Journal*, 1977, **2**, 238.

Regional variations in the incidence of urinary stones

SIR,—I read with interest the article by Dr D J P Barker and Mr S P B Donnan (14 January, p 67). The authors are very aware that they are not talking about "incidence" but rather "hospital discharge" figures.¹⁻³ It is always extremely difficult to find true prevalence figures in the literature, but these are essential, especially when a particular group in a population has to be studied. I would make a plea that because of the relative ease with which such a figure can be obtained greater effort should be made in several countries to establish true prevalence figures, which will provide the opportunity to define "incidence" of stone disease. It is lack of such basic figures which have, in my opinion, largely held back the realisation that certain work conditions are associated with a greater risk of stone disease, as in the case of cadmium-induced hypercalciuria and stone formation.⁴

By highlighting the problem the authors have certainly raised some interesting points,

but as they have suggested themselves the higher "incidence" in Leeds may simply reflect the work of the excellent mineral metabolism unit in that city. Hospital discharge rates in general can be interpreted as indicators of the standard and availability of radiodiagnostic facilities or even the willingness and geographical ability of general practitioners to send cases of ureteric colic to hospital for full radiological examination. In a multicausal disease such as stone disease, with its important socioeconomic implications, it is to the authors' credit that they have brought the problem to our notice and have attempted to speculate on possible aetiological causes which could be important. Might I add trace element contamination of the environment to their list?

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¹ R Scott, *et al*, *British Journal of Urology*, 1977, **49**, 589.

² Almy, B, *et al*, *Scandinavian Journal of Urology and Nephrology*, 1975, **9**, 249.

³ Ljunghall, S, *et al*, *Acta Medica Scandinavica*, 1975, **197**, 439.

⁴ Scott, R, *et al*, *Lancet*, 1976, **2**, 396.

SIR,—Based on analyses of hospital discharge rates Drs D J P Barker and S P B Donnan (14 January, p 67) claim that there are regional variations in the incidence of upper urinary tract stones. They also discuss several possible factors responsible for this pattern, among them the hardness of the drinking water.

It could be questioned, however, whether hospital statistics are suitable for this purpose since it is well known that patients with renal stone disease often do not seek medical care for each episode of stones. We have ourselves studied the incidence and natural history of renal stones in different unselected samples of the population outside the hospital, including altogether more than 17 000 individuals of both sexes aged between 20 and 67 years.¹ In these studies the annual incidence of stones was found to be between 1 and 2% of all males and around 0.5% of all females. Up to the age of 50 over 10% of all males and 3% of all females had experienced at least one renal stone. Further analysis disclosed that less than 25% of all stone-formers had ever been admitted for inpatient hospital care and only about 5% of all stones had been operatively removed. This incidence of renal stones is much higher than has generally been appreciated and the picture of stone disease in the population quite different from that seen in hospital statistics. It is therefore our definite opinion from this experience that evidence about true regional variations in the incidence of stones can be obtained only from studies of well-defined samples of the unselected population.

Naturally the identification of possible harmful factors for stone formation is important since stone disease is a rapidly increasing problem. Particular interest has been directed to the role of the composition of the drinking water, notably its hardness. Few if any studies, however, seem to have been concerned with this problem. In three Swedish cities located over 400 km apart and each with only one water supply the prevalence of renal stones among 50-year-old men ranged between 4.1% and 13.7% (see table). These apparent regional differences could not be explained by any differences in the hardness of the drinking water since the calcium content

Stone prevalence in health surveys of middle-aged men and results of analysis of drinking water in three Swedish towns

	Uppsala ¹	Gothenburg ²	Malmö ³
No. of participants	2322	853	707
Stone prevalence (%)	13.7	6.8	4.1
Water analysis (mg/l)			
Calcium	90	15	90
Magnesium	12	1.5	5.7
Sodium	12	10	8
Potassium	2.1	1.3	2.1
Chloride	31	12	24
Sulphate	50	30	74
Fluoride	1	0	0.2

was almost identical in the areas with the highest and lowest stone incidence. The importance of the fluoride content could be speculated about since it has been reported that fluoride is a common constituent of renal stones⁴ and also that artificial fluoridation is associated with an increased incidence of renal stones.⁵ For further analysis of this and other possible harmful environmental factors it is evident that further studies of unselected stone-formers are warranted.

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¹ Ljunghall, S, *Scandinavian Journal of Urology and Nephrology*, 1977, suppl 41.

² Tibblin, G, *Acta Medica Scandinavica*, 1967, suppl 470.

³ Isacson, S-O, *Acta Medica Scandinavica*, 1972, suppl 537.

⁴ Spira, L, *Experimental Medicine and Surgery*, 1956, **14**, 72.

⁵ Summers, J L, and Keitzen, W A, *Ohio State Medical Journal*, 1975, **71**, 25.

Help for parents after stillbirth

SIR,—I very much agree with Dr Ann Cartwright's and Mr Peter Diggory's comments (4 February, p 298) emphasising that it is relevant and useful but so hard to instruct doctors and nurses about the management of stillbirth. In preparing a leaflet designed as a hand-out for patients (21 January, p 172) we know this and hope that doctors would read it themselves and may be helped to think about their management of stillbirth. Bourne¹ describes stillbirth as a non-event in which there is guilt and shame with no tangible person to mourn. Studying stillbirth as a painful, empty tragedy which is difficult to talk and think about, I have described² how the utter emptiness in the clinical situation may sometimes be filled by making the most of what is available and can be remembered. Just as looking at and holding her dead baby gives the bereaved mother somebody tangible to remember and grieve about, so may the hand-out and other writings about stillbirth facilitate doctors' and nurses' thinking about the management of stillbirth.

Mr Diggory brings out a particular problem, the difficulty of showing a damaged or deformed baby to bereaved parents. What is imagined about the horror of a deformity is usually worse than the reality. The showing of a deformed baby can be carried out with sensitivity and imagination and then the experience is useful for parents, doctors, and nurses. The stillbirth can be partially or completely covered. The parents with gentle encouragement may gradually allow themselves to look at the bundle, feel through the sheet, and then partially or completely unwrap their baby. The wish to protect these bereaved