SIR,—I must take exception to the study design, and therefore the conclusions, of the investigation by Dr Morley and colleagues. By failing to randomise infants they have biased their results. The treated infants were cared for differently from the controls in that one additional expert (Dr Morley) was present in the delivery room for the treated infants only; I find it very difficult to believe that his presence had no effect upon the care of the infant. In most circumstances more knowledge and more hands result in quicker action and more rapid stabilisation of the infant. If this results in the infants entering the special care baby unit in better condition than the controls (and it should), the treated infants would be expected to have a lower mortality rate, regardless of surfactant treatment.

Unfortunately, the dedication and patience lavished upon the basic biochemistry of such studies is often forgotten or exhausted when it comes to the clinical trial. It would have been possible to randomise all infants born when Morley was present, disregarding others. Even a single or double blind study would be possible by using an empty, opaque gelatin capsule for half of the infants. Even if the individual administering the medication became unblinded to the assignment, it would still be possible to avoid passing this information along to the physicians caring for the infant.

It is now necessary to do this study again, properly controlled this time. How much easier it would have been to do it correctly the first time. Now scientific and ethical issues will be more difficult for the research review committee and also for the Cambridge team for they have obviously convinced themselves of this surfactant's efficacy.

This study seems to have been approved by the maternity hospital's ethics committee without insistence on informed consent, presumably because it would have been impossible to obtain such consent in the circumstances. This is, in my opinion, an appropriate application of the authority of such committees. Unfortunately this particular study raises the issue of whether it is ethical to do a study (even a very low risk one) if the design is faulty. I think not. If a study design is such that it can not prove or disprove what it has set out to test, then the risks (however small) taken by the participants are unjustifiable.

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⁂These letters have been shown to Dr Morley, whose reply follows.—ED.L.

SIR,—I acknowledge the criticism of Dr James and Dr Phelps but would like to make the following points.

The trial was a preliminary study of the effects of pure artificial surfactant in premature babies. We do not claim that the results are definitive or that the two groups are accurately matched. However, we do show that one small dose of dry artificial surfactant powder given at birth may have some beneficial effects and that, in consequence, this important subject warrants other well conducted clinical trials.

I am flattered at the suggestion that my presence at the delivery of these babies was statistically more effective than that of my very competent neonatal colleagues. However, since I did not resuscitate the infants I do not feel I can accept this accolade.

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LAMBSWOOL IS SAFER FOR BABIES

SIR,—Dr Tyler and colleagues (24 Jan., p. 211) describe a preterm infant nursed on an artificial "sheepskin" mat who experienced respiratory difficulties, apparently due to ingestion of loose fibres. While it is important to be aware of this possibility, we believe that, provided some simple precautions are taken, natural lambswool is a safe bedding for babies which has advantages over traditional materials.[1,2]

Natural and artificial sheepskins are very different materials. As far as we know there have been no published evaluations of the use of artificial sheepskins for nursing babies. The ones we have seen are less resilient and more slippery than the wool products, and there is a greater tendency for the fibres to come free. For these reasons we do not think they make a suitable bedding material for the newborn.

We have been using three types of natural lambswool in our studies. Two have the original leather backing ('Babycare' and 'Winganna') and the other is made by weaving lambswool into an artificial backing ('Dermalex'). Before use, the washed mat should be brushed with a stiff wire brush which will remove any loose fibres. Occasionally, a baby seems to acquire the habit of sucking its lambswool. In such cases, as an additional precaution, a piece of cotton cloth can be placed beneath the baby's head.

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SOURCES OF ERROR IN FRAGILE-X DETERMINATION

SIR,—X-linked mental retardation displaying the fragile X chromosome seems to be a very common cause of mental defect and soon it will be necessary for every cytogenetic laboratory to use this investigation and to know the possible sources of error. The letter from Dr Leversha and her colleagues (Jan. 3, p. 49) prompts us to report our experience based on about fifty cases with fra(X). Leversha et al. reported other C group chromosomes (most of them no. 6) which can be misinterpreted as fragile X and referred to the dilemma—either to band the chromosomes, with resulting poor morphology of the fragile site, or not to band, and face the possibility of an error.

We solved this problem in a different way: the fragile sites are located using unbanded chromosomes. Then the slides are destained with acid alcohol, banded,[3] and then the fragile sites are re-checked. Using this method we identified all fragile-like chromosomes in six carriers and in twenty-five non-carriers of fragile X. The results were similar in both groups. In about 1·2% of cells chromosome no. 6 is involved, and 0·9% other C-group chromosomes simulate fra(X) morphology. It means that, for example, in patients with 10% of fra(X), out of ten positive cells two are possibly false positive. For patients with high level positivity this error does not change the diagnosis but in low level positive patients there is a definite possibility of diagnostic error. In a low level subject the exact identification of each fra(X) is essential.

We do not think that C group chromosomes (and very often no. 16 and other chromosomes) with satellite-like appendix on long arm should be always considered as "fragile sites" in the strictest sense.[4-7] In contrast with real fragile sites a proportion of these can be found in nearly every subject but their level is always very low. Probably they are common chromosomal gaps located at the end of long arms.

Leversha et al. mention cases where banding had shown fra(X)-like chromosomes which were actually no. 6 and state that "mental retardation might have been interpreted as X-linked".

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