control was unsatisfactory; she had occasional hypoglycaemic episodes and results of tests on the urine were poor. She generally resisted attempts to be restrained when being injected and developed a predilection for having injections in the lateral aspects of both thighs. Her dose of insulin was increased progressively to 20 units daily and after 8 months of treatment she was noted to have moderately severe lipoatrophy of injection sites. Because of this and her unsatisfactory control, she was changed to monocomponent porcine insulin with a mixture of Monotard MC and Actrapid MC (Novo Laboratories) once daily, and her mother was instructed to inject her in the periphery of the atrophic sites. During the next few weeks her dose of insulin stabilised to Actrapid MC 4 units and Monotard MC 8 units daily. Four months later her injection sites no longer showed lipoatrophy and her diabetic control was much improved, but she continued to co-operate poorly when being injected.

Reeves *et al.*[3] studied 14 patients with lipoatrophy at conventional insulin injection sites with a mean duration of treatment of 10 years (range 4 months to 10 years) and produced convincing evidence that lipoatrophy is the result of local immunological reaction to impurities in the insulin. The excellent response to monocomponent porcine insulin in these patients, together with the rarity of local reactions in patients treated exclusively with these insulins, lends strong support to this hypothesis. However, Jones *et al.*[4] recently reported the development of lipoatrophy in a patient treated exclusively with monocomponent porcine insulin (Monotard MC) which resolved on injecting a mixture of Actrapid MC and Monotard MC into atrophic sites. In their case there was no evidence of a local immunological reaction so that the cause of lipoatrophy in every patient is not known.

This report describes lipoatrophy developing in a diabetic girl treated with one of the new generation of highly purified beef insulins over a period of 8 months. I have subsequently treated another young girl with an almost identical presentation and outcome. Because of their purity, these insulins are thought to be unlikely to produce immunologically mediated reactions, but this case suggests that doctors will need to remain vigilant for the development of local injection site reactions in patients treated with highly purified beef insulin.

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Resuscitation of preterm babies at birth reduces the risk of death from hyaline membrane disease

Sir,

We were disturbed by the title of the paper by Robson and Hey.[1] Details of any method that reduces the risk of death from hyaline membrane disease should be published, but we do not think that the authors demonstrated the effect claimed.

Testing a hypothesis using two populations from different time periods is fraught with difficulties[2] and interpretation of significant results has often been challenged. In their study errors were made worse by interpreting a non-significant result as showing a cause-effect relationship. They reported that of infants of 1000–2000 g born between 1960 and 1967 there were 50 (10·7%) deaths out of 465 such births, whereas between 1971 and 1976 there were 23 (8·7%) deaths out of 264 low birthweight births. The authors stated that this represented a significant reduction, and we would like to know on what statistical test this conclusion is based. In fact, chi-squared with Yates's correction $= 0{\cdot}6$, df $= 1$, $P > 0{\cdot}5$.

We think that the following points should also be made: (a) Death from hyaline membrane disease bears a very strong relationship with gestation, but given gestation, birthweight has little part to play.[3 4] Preterm babies should *not* be defined by birthweight. (b) Comparison of risks pertaining in two groups should have ensured that in the two groups there were similar distributions of a number of background factors incontravertibly shown to be associated with death from hyaline membrane disease, particularly gestational maturity and whether delivered by caesarean section.[5] (c) The proposition that asphyxia is related to deaths from hyaline membrane disease rests largely on twin studies; the second twin is more likely than the first twin to suffer this fate, [6–8] especially if the interval between delivery of the two is longer than 30 minutes.[6] It seems possible that if this is important then obstetric management of labour, with increased use of oxytocics and shorter first and second stages, may have a more beneficial effect than the resuscitative methods employed after delivery.

Robson and Hey's claim may be correct but their data do not support it.

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Sister Robson and Dr Hey comment:

We knew that the observed 20% reduction in mortality from hyaline membrane disease in babies of 1–2 kg was not significant when assessed using a simple χ^2 test; it would have taken a very much larger study to confirm such a modest, but potentially important reduction using this approach. Nevertheless, mortality was constant throughout the 1960s and the immediate decrease in annual mortality after the deliberate introduction of a different treatment policy in 1971 *was* significant. We reported the difference in mean annual mortality for 1971–76 and 1960–67 (Figure), but it might have been more correct to undertake a logit transformation of proportional mortality before comparing the two means; such a transformation reduces, but does not abolish, the significance of the fall.

Such arguments about the most appropriate statistical 'treatment' of the data are insignficant when compared with the insoluble hazards inherent in using historic controls in the first place. We were aware of such dangers and did not doubt that readers would be equally conscious. We looked for changes in the mean length of labour but found none: labour was as often retarded by β-adrenergic agonists as accelerated by syntocinon in the latter years of the study, and it was often difficult to define the onset of labour or the timing of full cervical dilatation accurately when labour occurred prematurely. Golding and Butler seem to imply that speed and safety are always synonymous when delivering twins but this is not so.[1 2] We would agree that obstetric management may influence outcome at least as much as immediate care after birth and we made this point in our article, but we were unable to document any change in the incidence of toxaemia, abruption, multiple pregnancy, or caesarean delivery among babies of 1–2 kg between 1960 and 1976.

The relative merits of gestation and birthweight were not lost on the original authors:[3] indeed Farr *et al.*[4] led the world in the introduction of routine methods for estimating gestational age from an assessment of the baby's physical appearance at birth between 1966 and 1968. However, we could not be sure of the gestation of the babies born between 1960 and 1967 to mothers with uncertain menstrual dates and this was why we used weight rather than gestation. Nevertheless, we are confident that the observed change in mortality in these babies was not due to a shift in gestational age.

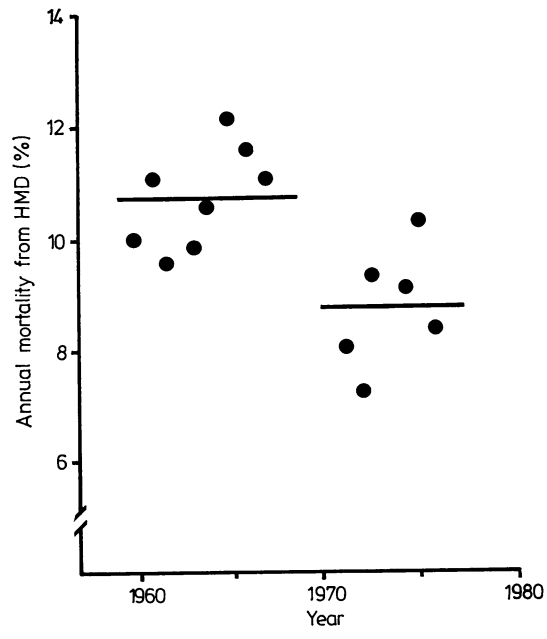

Figure *Mean annual mortality from hyaline membrane disease in babies of 1-2 kg af birth before and after the introduction of elective resuscitation at delivery in 1971*

Others will have to confirm the validity of our observation because we had to use an historic control group, but immediate elective intubation from birth halved mortality in babies of 0·5–1·5 kg in a recent control trial,[5] and Professor Milner and his colleagues are now looking for evidence that brief elective intubation at birth can produce prolonged improvement in pulmonary compliance as we first documented more anecdotally 10 years ago.[6]

We did not encounter one case of pneumonia, pneumothorax, symptomatic laryngeal trauma, or cicatricial retrolental fibroplasia in any of the 800 small babies in this study and conclude that elective resuscitation of the very preterm baby and endotracheal intubation for 20–60 minutes during early transfer and stabilisation after birth is at least reasonably free of hazard and worthy of further evaluation. Its introduction in our nursery appeared to be associated with as large a reduction in annual mortality in 1971 (Figure) as the introduction, in 1977, of prolonged ventilatory support for ill babies without waiting for evidence of terminal respiratory failure (mean annual mortality for babies of 1-2 kg in 1977–81:7·0%).

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