nuclei, which presumably remains a constant number. The relative proportion of nuclear size to quantity of cytoplasm will not have any significant effect upon the total thickness of a vessel wall.

It seems that one major area of disagreement is with regard to an interpretation of the term 'chronic hypoxia' and the term must be defined separately for each study. In our cases we considered that children who were the subject of acute respiratory illness of less than seven days' duration were not chronically hypoxic. Using this as our basis, we have clearly shown that with regard to the amount of muscle tissue in pulmonary vessels of less than 200 microns, SIDS, sudden deaths from trauma, and children dying with acute respiratory infections of less than one week's duration all are statistically comparable, and the amount of muscle present is significantly less than that in neonatal deaths and congenital heart disease. We chose our cases after careful clinical and postmortem studies, which led to the exclusion of about two out of three possible control cases.

Our findings do not exclude the possibility that cases of SIDS are subjected to repeated episodes of hypoxia, as suggested by Steinschneider (*Pediatrics*, 1972, 50: 646), but simply that by using pulmonary vessel muscle thickness as an indicator, SIDS cannot be readily distinguished from most other rapid infant deaths of whatever cause and that they are significantly different from neonates and children with chronic respiratory embarrassment.

We think that the evidence for hypoxia being an essential part of the sudden infant death syndrome is overwhelming, and we have reported elsewhere that repeated episodes of hypoxia could account for a significant difference in the amount of fibrous remoulding of the conducting tissue in such cases (*Journal of Pathology*, 1975, 117:123). However, it is our unrepentant view that a study of the amount of muscle in pulmonary vessels of less than 200 microns in SIDS as a means of determining evidence of chronic hypoxia will be unrewarding.

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Alpha-1-antitrypsin globules in the liver and PiM phenotype

The case of α_1-antitrypsin phenotype PiM with intrahepatocytic globules recorded recently in the journal (Bradfield and Blenkinsopp, 1977) is almost certainly a carrier of the variant allele M_{Duarte}, described by Lieberman *et al.* (1976), which has PiM electrophoretic mobility, intrahepatocytic inclusions, and a serum α_1-antitrypsin level approximately the same as the Z allele. The $Pi^{M\,Malton}$ (Cox, 1976) and the 'M-like' phenotype (Kueppers *et al.*, 1977) may also be identical with the $Pi_{M}{}^{Duarte}$ phenotype. The serum level of 2·3 g/l at 24 hours after major surgery is perfectly consistent with heterozygosity for the deficiency allele M_{Duarte}. The case of Bradfield and Blenkinsopp (1977) would therefore be more aptly said to have an 'apparent M phenotype' or an 'M-like phenotype'. Their conclusion that the identification of characteristic globules can no longer be regarded as conclusive evidence of an abnormal α_1-antitrypsin phenotype is ill-founded when based on their evidence.

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The authors have asked Dr Cook to comment on their behalf.

Dr Kelly points out that the patient described as Pi type M by Bradfield and Blenkinsopp (1977) is 'almost certainly' a carrier of the variant allele $Pi^{M\,Malton}$ (sometimes known as M_{Duarte}). We must admit that anyone of the apparent phenotype M might be a carrier of this variant allele unless it could be excluded by family studies (which were not possible in this case). We considered the possibility of the genotype $Pi^{M}Pi^{M\,Malton}$ but thought it most unlikely for two reasons. The intensity of the Pi M bands was greater than we have ever seen in any Pi M heterozygote, even after surgery. Secondly, the $Pi^{M\,Malton}$ gene must be rare in the United Kingdom. We have studied 177 unrelated Pi Z individuals but have seen no examples of $Pi^{M\,Malton}Pi^{Z}$ or $Pi^{M\,Malton}$ homozygotes. Moreover, we have typed samples from 812 other unrelated individuals of various variant phenotypes such as Pi MS, where we would expect to detect the product of the $Pi^{M\,Malton}$ gene, yet have noticed it only once. We suspect that our patient was *almost certainly not* a carrier of the $Pi^{M\,Malton}$ gene.

Our case would have been stronger if the patient had been of a Pi phenotype such as S or MS, when a more positive exclusion could have been made. By chance, Fisher *et al.* (1976) have now described a Pi MS patient with globules in the liver. We admit that if our patient was of the common Pi phenotype M, he could not easily be explained on the current established genetic hypotheses about the Pi system. But this was one motive for publication.

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