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Drs Kimpen, Embrechts, Callaert, and Bosmans comment:

We thank Drs Tseng, Lam, and Davies for their interesting remarks concerning our article in the Archives. The difference in contamination rate (2.9% ν 3.9%) is small and may not be significant when both groups are compared. The number of serum samples examined (5838 ν 153) may be partially responsible for it.

The cord blood samples were taken directly from the umbilical stump immediately after it was cut.

Of the 157 cord blood samples with a IgA value higher than 32.3 ug/ml, 79 samples had a IgE concentration higher than 1 IU/ml (50%). In general the absolute IgE concentration tended also to be higher in the group with a high IgA. Only 30 samples had a concentration below 0.4 IU/ml (19% ν 90% in the group with an IgA concentration below 32.3 ug/ml) and 14 samples had an IgE concentration below 0.2 IU/ml (8% ν 72% in the group with a low IgA concentration). From this study it can be concluded that IgA concentration in the cord blood is a good marker for contamination with maternal blood.

We do not have an exclusive answer on the last question. Methodological change in screening technique is most probably not responsible for the difference in incidence because the values that would make the difference lie near the cut off point.

Figures 1 and 2 of our paper show that the normal values are clustered around the lower limit of the interval between 0.01 and 1 IU/ml. We do not think that a difference in detection methods could possibly make such a remarkable difference as 50%. Ethnic and environmental differences cannot be ruled out as causative mechanisms and could indeed be responsible for the lower incidence of raised cord blood IgE in Belgium.

Loose hair on toys

Sir,

Loose hair on toys is considered to pose a potential asphyxiation hazard to children. There has been a single tragic death where loose fibrous hairs from a toy were present in the child's trachea. However, there is a dearth of evidence of other problems associated with hair or with pile fabric. For example, a detailed breakdown of the Department of Trade and Industry's Home Accident Surveillance System 1984 data on accidents concerning toys contains no reports of ingestion or inhalation of hair or fur from pile, and no other deaths have been reported from this cause. Nevertheless, some concern is being expressed in various quarters about this matter.

There are many other forms of childhood accident which occur frequently and whose cause is well proven. The Child Accident Prevention Trust is concerned that energy and resources are being diverted from these problems into consideration of the possible problems of hair on toys. Accordingly, we are asking other medical practitioners to report any experience they have of real difficulties caused by inhalation or ingestion of hair or fur pile, so that we may develop an informed opinion as to whether this is a genuine hazard.

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Sex ratio and heterozygote advantage in cystic fibrosis: hypothesis and research proposal

Sir,

Cystic fibrosis is a serious disease probably caused by autosomal recessive transmission. In some white populations it is relatively common, and in such populations the gene frequency has been estimated at around 0.02. Such a value would seem too common to be maintained by mutation, so workers have proposed that some form of heterozygote advantage may be responsible for keeping the gene frequency so high. No disease has been identified to which heterozygotes are resistant, but it has been shown that sibships containing affected cases are larger than control sibships.¹ This line of argument is not conclusive, however, because in such studies parents at risk are discovered only if they have an affected child, and the larger the sibship the more likely this is to happen. This objection does not apply so forcibly to those studies showing that grandparents of affected children produced more offspring than grandparents of normal controls.² Moreover it has been found that uncles of affected children sire larger sibships than normal controls.³ Thus it seems that heterozygotes for cystic fibrosis, particularly males, are more fertile than controls. Why should this be so? I wish to suggest an answer.

There is an excess of male offspring in sibships with cystic fibrosis both among the affected and the unaffected. Moreover this male excess extends to the children of the uncles of patients (table), so it seems that men heterozygous for cystic fibrosis sire large families with an excess of male offspring.

I have offered evidence that the sexes of human offspring are partially determined by parental hormone concentrations at the time of conception, high concentrations of testosterone being associated with the subsequent births of sons.⁴ High androgen concentrations may be assumed to be associated with fertility either through behavioural or physiological mechanisms. Accordingly I hypothesise that men heterozygous for cystic fibrosis have high androgen concentrations. If this were true, it might explain, firstly, the high sex ratios in cystic fibrosis sibships

Table Sexes of cases of cystic fibrosis and their relatives

Source		Males	Females	Males per 100 females	χ^2	p Value
Danks <i>et al</i> ²	Cases of cystic fibrosis	190	155	122.6	1.87	NS
Todd ⁶	Cases of cystic fibrosis	37	21	176.2	3.6	NS
Danks <i>et al</i> ² plus Todd ⁶	All cases of cystic fibrosis	227	176	129.0	3.9	0.05
Danks <i>et al</i> ²	Unaffected siblings of cases	256	200	128.0	4.1	0.05
Pritchard <i>et al</i> ³	Offspring of uncles of cases	41	23	178.3	4.1	0.05
Pritchard <i>et al</i> ³	Offspring of aunts of cases	38	32	118.7	0.2	NS

In order to estimate the significance of the sex ratios in the table, one has to choose an expected value. Sex ratios for white people are generally higher than those for black people; 105.8 males per 100 females is reasonable for a white value.⁵ All the χ^2 values in the table have been calculated on the basis of this expected value. The total number of cases and their unaffected siblings and cousins comprise 562 males and 431 females, giving a sex ratio of 130.4 (with $\chi^2=10.7$, $p=0.001$, tested against this expected sex ratio).

(both affected and unaffected); secondly, the high sex ratio in the sibships sired by uncles of cases and thirdly, the high relative fertility of male heterozygotes, thus accounting for the high gene frequency.

To test the hypothesis, I suggest that the androgen concentrations of men heterozygous for cystic fibrosis should be contrasted with the androgen concentrations of controls.

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