Correspondence

13·1% with a gradual decrease in fertility over the two ensuing decades. We conclude that it is this trend which has accounted for the fall in incidence of Down’s syndrome which we describe.

(2) The overall contribution of Down’s syndrome babies born to mothers aged 35 years and over is small, being only 20% of Down’s syndrome livebirths in British Columbia. Again, our fig 3 shows that the proportion of Down’s syndrome livebirths born to this maternal age group has fallen over the two decades. Despite this, the proportion is not as small as in British Columbia, being 57·1% for 1961 to 1969 and 40·9% for 1970 to 1979.

(3) Ascertainment for the latter years of the study may have been incomplete. While not claiming total ascertainment we do not feel that many cases have been missed for several reasons. Firstly, since our paper was drafted 2 years ago we have only picked up two extra cases for the years 1975 to 1979. Secondly, nearly all Liverpool and Bootle births occur in hospital in a health area where the neonatal services are excellent. Thus, we do not find that there are many cases of Down’s syndrome which are not recognised in the neonatal period. Finally, assuming that Lindso’s figures for the maternal age specific incidence of Down’s syndrome apply universally, and knowing the annual total births for quinquennal maternal age groups for Liverpool over the period of study, an estimate of the number of cases of Down’s syndrome which should have been born can be made. One finds that the estimated incidence falls gradually from 1·69 per 1000 livebirths in 1963 to a trough of 1·16 in 1977. This compares with an observed incidence of 1·62 per 1000 for 1961 to 1963 (using 3-year moving averages) to 1·09 for 1977 to 1979. Using the same calculated figures the degree of ascertainment can be estimated (observed cases of Down’s syndrome ÷ estimated cases × 100%). This is 98·8% for 1963 to 1969 and 83·1% for 1970 to 1979. Thus, while we acknowledge that the lower ascertainment may have contributed slightly to the fall in incidence of Down’s syndrome, we still believe that by far the major factor has been the decrease in mean maternal age in Liverpool and Bootle over the last two decades.

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Neural tube defects in sibs of children with tracheo-oesophageal dysraphism

Sir,

David and O’Callaghan1 and Warren et al2 reported an increased frequency of neural tube defects (NTD) in sibs of children with oesophageal atresia with or without tracheo-oesophageal fistula. They found NTD in nine of 495 sibs (1·8 ± 0·60%). At the same time, in the series by Chen et al3 only one of 358 sibs had NTD and Fraser and Nussbaum4 found NTD in one of 141 sibs. Baird and MacDonald5 found no cases of NTD among sibs of 167 infants with tracheo-oesophageal dysraphism. Unfortunately, they gave no total number of sibs in their series. As the mean ratio affected: sibs is 1:1·8 in most American series,6 7 we can approximately evaluate the total number of sibs in the series of Baird and MacDonald3 as 300.

In our series, 105 cases (64 males and 41 females) with tracheo-oesophageal dysraphism were analysed. Additional anomalies were found in 56 cases, of which two had anencephaly and spina bifida. There were 81 sibs, none of whom had NTD, though in one case hydrocephalus was present. Other congenital malformations and genetic disorders were observed in eight sibs, including two with adrenogenital syndrome (in one family), two with inguinal hernia, and one each with thoracopagus, duodenal atresia, cleft lip/palate, and rib malformations.

It is well known that the frequency of NTD varies significantly in different populations. In England, and especially in Ireland and Wales, it reaches 5:1000, whereas in Canada or the USA it is nearer to 1:1500.6 7 In the USSR it is slightly lower than 1:1000.8 Therefore we divided the data on NTD frequency in sibs into two groups, according to the incidence of NTD in the population (table).

This shows that there is no evidence for an increased risk of NTD for the sibs of patients with

<table>
<thead>
<tr>
<th>Population</th>
<th>No of sibs</th>
<th>NTD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. High incidence of NTD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>David and O’Callaghan (England)</td>
<td>365</td>
<td>6</td>
</tr>
<tr>
<td>Warren et al (England)</td>
<td>130</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>495</td>
<td>9 (1·8 ± 0·60%)</td>
</tr>
<tr>
<td>B. Low incidence of NTD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chen et al (USA)</td>
<td>358</td>
<td>1</td>
</tr>
<tr>
<td>Fraser and Nussbaum (Canada)</td>
<td>141</td>
<td>1</td>
</tr>
<tr>
<td>Baird and MacDonald (Canada)</td>
<td>300</td>
<td>0</td>
</tr>
<tr>
<td>Our data (USSR)</td>
<td>81</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>880</td>
<td>2 (0·23 ± 0·16%)</td>
</tr>
</tbody>
</table>

TABLE NTD in sibs of patients with tracheo-oesophageal dysraphism.
tracheo-oesophageal dysraphism, at least in populations with a low frequency of NTD.

HELENE G ILYINA AND
I W LURIE
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References

This letter was shown to Dr David, who replies as follows.

Ilyina and Lurie’s letter is most welcome, though I would like to get my hands on whoever first used the awful term ‘tracheo-oesophageal dysraphism’. Oesophageal atresia is a most neglected defect, and it is sad that current interest mainly centres not on the defect itself, but either with the probably spurious increase of neural tube defects in sibs, or with the VATER or VACTERL association, which embodies the statistical and teratological misconception of a non-random association of defects.

Ilyina and Lurie’s hypothesis that there may be a relationship between the risk of neural tube defect for sibs of patients with oesophageal atresia and the population frequency of neural tube defects may be right. It is perhaps akin to the suggestion that the recurrence risk of neural tube defects is to some extent a function of the background population risk. However, the general notion of an increased frequency of neural tube defects in the sibs of children with other malformations1 is most likely to be attributable to sampling errors or bias.

The cases of Fraser and Nussbaum2 were a highly selected group and in no way representative of the general population of patients with oesophageal atresia, and the same applies to the data of Warren et al.3 It is not clear how the cases of Ilyina and Lurie were ascertained, but it is likely that they were selected in some way. Our own study4 was happily free from this defect, only to fall victim to the entirely fair criticism5 that we did not seek to identify all sibs but just used available medical records. Probably the only suitable data come from Sweden6 and Canada,8 and from these studies it does seem that there is no increase in neural tube defects in the sibs of patients with oesophageal atresia.

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References

Routine diagnostic detection of the fragile X

SIR,
I enjoyed reading the recent report by Dr McDermott and his colleagues (J Med Genet 1983;20:169–78) on the fragile X chromosome. I would, however, like to take issue with their assertion that busy diagnostic cytogenetics laboratories cannot routinely screen unselected cases for the fragile X chromosome. Furthermore, their request that referring practitioners alert the laboratory to the possibility of this finding on clinical grounds is one which simply cannot work. While some males have the full ‘fragile X syndrome’, so well described by McDermott et al, and a family history suggesting the presence of the fragile X many, particularly children, have neither. About one-third of females...
Neural tube defects in sibs of children with tracheo-oesophageal dysraphism.

H G Ilyina and I W Lurie

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