Correspondence

possible that separate entities, caused by single gene disturbances, exist.

We thank Dr B Hamel (Nijmegen, The Netherlands) for making the x rays of family 4 of Majewski et al available for us.

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References


Fryns syndrome

SIR,
The review of Fryns syndrome (J Med Genet 1987;24:271-4) prompts me to point out that this review omitted the first case of this syndrome which was described by Fitch et al (J Med Genet 1978;15:399-401), one year before Fryns' original report was published. Our infant had the coarse face with the broad, flat nasal bridge, large nasal tip with antverted nostrils, thin upper lip, macrostomia, missing nails on the fifth fingers and hypoplastic nails on all other digits, hypoplasia of the terminal phalanges, absent left hemidiaphragm, and cerebral malformations. The parents were second cousins.

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Alpha, antitrypsin deficiency

SIR,
In their paper in Journal of Medical Genetics (1987;24:52-9), Cox and Mansfield attempt to estimate the risk of severe liver disease in a fetus of genotype PI ZZ given the severity of liver disease in the proband. The estimates are derived from pooling data from several studies in the United States, Canada, Norway, and Great Britain. The authors give point estimates of the risk, which appear to be different in the two groups, with the suggestion that this information will be useful for families seeking counselling.

The difficulty with the presentation is that the conclusion is based upon a very small sample, with 15 sibs of probands having resolved or no liver disease and 20 with severely affected probands, as shown in tables 4 and 5. Although the estimates are 13% and 40% respectively, it is doubtful that these represent different rates. I constructed a 2×2 table and used the SAS procedure FREQ which produces a number of statistics to accommodate different analytical viewpoints. None of the hypothesis testing probabilities suggests rejecting the null hypothesis of equal rates in the two groups, whether one considers χ² with or without continuity correction, a Fisher exact test, or a Mantel-Haenszel χ². If one prefers to use an epidemiological approach, the odds ratio is 4.33 for a severe proband to have a severely affected sib; however, the 95% confidence interval runs from 0.80 to 23.4. This interval clearly includes 1, so that the conclusion of a difference in risk cannot be supported. For the time being, the mean risk of severe liver disease appears to be 29%, with a 95% confidence interval between 14-6 and 46-3. This appears to be different from the 7% risk estimate of the Swedish study. Clearly, more data

FIG 3 Hypoplastic right hallux of sister of case 2.
and a proper segregation analysis are essential to answer the original question. A model involving more than one locus might also be necessary.

**Possible evidence for genetic predisposition to nondisjunction in man**

**SIR,**

Preliminary data from a community genetic survey at two district hospitals showed a high prevalence of chromosomal aneuploidy, particularly Down's syndrome, with marked temporal variation between the two districts.

In Jahra hospital serving an Arab population of 300,000, mostly (80%) Bedouins, 31 babies with autosomal trisomies were ascertained among 6874 consecutive live births (4.5/1000). Twenty-nine cases (93.5%) were Bedouins or Kuwaitis with Bedouin ancestors and two were other Arabs. The mean maternal age was 31.1 years. Parental consanguinity was observed in 29 cases with an average coefficient of inbreeding (\(\delta F\)) of 0.044, which is similar to that of parents with the traditional 'Bedouin' practice of consanguineous marriages. Among this group, two sibs, one with trisomy 21 and the other trisomy 18, had young first cousin parents. Another family had two sibs with trisomy 21.

In Farwania hospital serving a mixed Arab and non-Arab population of 400,000 with only 15% Bedouin, 14 babies with autosomal trisomies were ascertained among 8045 consecutive births (1.7/1000). Of these, six cases (42.9%) were Bedouins or Kuwaiti-Bedouins, six cases were other Arabs, and two cases were Asian. The mean maternal age was 32.7 years. Parental consanguinity was observed in eight cases with an average coefficient of inbreeding (\(\delta F\)) of 0.0225.

The overall prevalence of Down's syndrome in the two districts was 2.5/1000 which was more than double that of 1.1/1000 reported from Kuwaiti maternity hospital\(^1\) (table). The usual prevalence of Down's syndrome is 1 to 2/1000 live births but higher prevalence rates have been reported from West Jerusalem\(^2\) and among Negev Bedouins\(^3\) (2.4% for Bedouins).

**TABLE** Autosomal aneuploidies in Jahra and Farwania hospitals in 1986.

<table>
<thead>
<tr>
<th></th>
<th>Jahra</th>
<th>Farwania</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of live births</td>
<td>6874</td>
<td>8045</td>
<td>14919</td>
</tr>
<tr>
<td>Down's syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>25(21*)</td>
<td>12(10*)</td>
<td>37(31)</td>
</tr>
<tr>
<td>Prevalence rate</td>
<td>3.6</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Edward's syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>4(4)</td>
<td>1(0)</td>
<td>5(4)</td>
</tr>
<tr>
<td>Prevalence rate</td>
<td>0.6</td>
<td>0.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Patau's syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>2(1)</td>
<td>1(1)</td>
<td>3(2)</td>
</tr>
<tr>
<td>Prevalence rate</td>
<td>0.3</td>
<td>0.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

*One case de novo 14,21 translocation.

\(^{1}\)Two cases de novo translocations (14.21, 21.21).