LETTERS TO THE EDITOR

Patent ductus arteriosus in four generations of a family

Several published articles have suggested a dominant form of persistent patent ductus arteriosus (PDA).\(^1,2\) We would like to report a four generation family affected with PDA (figure), which is only the second such family described. The proband (IV.1), his sister (IV.2), and their mother (III.1) presented to our genetics clinic because of a family history of isolated PDA. A medical history showed that all three subjects had been term newborns with PDA surgically repaired in infancy. Physical examination of the family showed no dysmorphic features or other anomalies. Further investigation disclosed other family members affected with PDA (I.1 and II.1). These subjects were reported to have no additional medical complications or abnormalities but were not available to us for examination.

McKusick's Mendelian inheritance in man suggests an autosomal dominant form of PDA.\(^3\) This family provides evidence for dominant inheritance; however, a lack of male to male transmission prevents us from distinguishing between an autosomal versus X linked pattern. Alternatively, the incidence of PDA in this family may simply indicate multifactorial inheritance. Regardless of the specific mode of transmission, this family was quoted a 50% recurrence risk for all those affected because of the multigenerational history. This case illustrates the importance of obtaining complete family and medical histories before discussing recurrence risks with affected families.

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Linkage disequilibrium between D16S94 and the locus for adult polycystic kidney disease (PKD1)

Pound et al\(^4\) have recently established evidence for linkage disequilibrium between the chromosome 16 marker D16S94 and PKD1, the major locus for adult polycystic kidney disease. In this laboratory 38 families have been examined for non-random allelic association with D16S125 and D16S94.

Stringent diagnostic criteria were used to choose this group. The families all include two or more subjects affected by bilateral polycystic kidneys.

Twenty of the kindreds were informative for a three point linkage analysis to determine the individual likelihood within a family of transmission of the disease at the PKD2 locus. One pedigree contained a subject who screened negative on several occasions by ultrasonography but who inherited a high risk flanking marker haplotype for chromosome 16. This family was excluded from the analysis. The remainder of the families are likely to bear the APKD gene at PKD1. From these data the upper limit for the presence of the PKD2 locus in the north west England population is unlikely to exceed 5%.

This set of kindreds is therefore suitable for assessing linkage disequilibrium around the PKD1 locus. Allele types for marker D16S125 were established for 29 APKD chromosomes and 77 normal controls drawn from unaffected spouses and normal chromosomes in affected subjects. For marker D16S94, the equivalent figures were 32 APKD chromosomes and 81 controls. The results of the study are presented in table 1a. These data indicate no statistically significant evidence of linkage disequilibrium between either D16S94 or D16S125 in this population.

The conflict between these results and those of Pound et al\(^4\) may be the result of a population cline between the north west of England and Scotland. It is possible that the latter population is relatively stable and homogeneous compared to the former.

This may be supported by the observation in this study of significantly different allele frequencies for D16S94 and D16S125 from those published for the Dutch and Scottish populations (table 2).

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Table 1 Linkage disequilibrium data.

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<thead>
<tr>
<th>Allele</th>
<th>Affected Control</th>
<th>Affected Control</th>
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<tbody>
<tr>
<td>D16S125</td>
<td>11 36 15 34</td>
<td>18 41 17 47</td>
</tr>
<tr>
<td>D16S94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allele 1</td>
<td>0.55 (NS)</td>
<td>0.79 (NS)</td>
</tr>
<tr>
<td>Allele 2</td>
<td></td>
<td></td>
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Table 2 Allele frequencies.

<table>
<thead>
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<th>Allele frequencies.</th>
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<tbody>
<tr>
<td>North west</td>
</tr>
<tr>
<td>D16S125</td>
</tr>
<tr>
<td>Allele 2</td>
</tr>
<tr>
<td>D16S94</td>
</tr>
<tr>
<td>Allele 2</td>
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</table>
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