Hypothesis

A dental approach to carrier screening in X linked hypohidrotic ectodermal dysplasia

SUMMARY The frequency of carriers of X linked hypohidrotic ectodermal dysplasia among females with hypodontia of the permanent dentition (excluding third molars) could be as high as 1 in 500, and among females with deciduous hypodontia could be as high as 1 in 50. Since it may be possible to identify carriers from among female hypodontia cases in general by virtue of a reduced sweat pore count, the potential exists for a reasonably practical method of screening for carriers at the population level.

The X linked form of hypohidrotic (anhidrotic) ectodermal dysplasia (XHED) is a severe disorder characterised by hypodontia, hypotrichosis, and hypohidrosis, in which affected males can succumb to brain damage and even death through hypothermia. Expression in heterozygous females is variable but generally mild and the majority of carriers are likely to escape detection even rigorously. Clinical criteria are employed by experienced observers. The counting of sweat pores has been used as a means of identifying carriers within families, but is not a practical proposition on a much larger scale. On the other hand, the majority of schoolchildren undergo regular dental examinations and hypodontia, a lower than normal number of teeth caused by failure of development, is a simple objective criterion that could perhaps be of value in preliminary screening for carriers at the population level. The purpose of this short paper is simply to draw attention to the probable frequency of carriers of XHED among females with hypodontia.

Assuming equilibrium, normal fitness of carriers, and a mutation rate common to both sexes, the population incidence of carriers, c, can be estimated from the equation c/m = (4 + f)/3, where m and f are the incidence and fitness of affected males. Substituting f = 0.6 and a range for m of 1 in 100 000 to 1 in 10 000, the population incidence of XHED carriers can be calculated as 1.73 to 17.3 per 100 000 females. Average figures for the prevalence of hypodontia among females from the general population are 0.6% for the permanent dentition (excluding third molars) but only 0.5% for the deciduous dentition, that is, 6000 and 500 per 100 000, respectively. The prevalence of hypodontia among carriers of XHED, estimated from published reports of families, is 75% for the permanent dentition (excluding third molars) and 60% for the deciduous dentition. Given the calculated incidence of XHED carriers, this provides ranges of 1.3 to 13.0 and 1.04 to 10.4 per 100 000 females for the population frequency of carriers with hypodontia of the permanent and deciduous dentitions, respectively. The table shows that using these figures the frequency of carriers among females with hypodontia of the permanent dentition is in the range 2.17 x 10^-4 to 2.17 x 10^-3, or approximately 1 in 5000 to 1 in 500, and the frequency of carriers among females with hypodontia of the deciduous dentition is in the range 2.08 x 10^-3 to 2.08 x 10^-2, or approximately 1 in 500 to 1 in 50.

Preliminary screening for hypodontia therefore brings population screening for carriers by sweat pore counts were markedly reduced in all of six XHED carriers but in none of eight control female hypodontia cases, the level of hypodontia in the permanent dentition (excluding third molars) ranging from one to seven missing teeth for the carriers and one to eight missing teeth for the otherwise apparently normal females. Sweat pore counts can therefore be used to distinguish between carriers of XHED with hypodontia and females whose teeth have failed to develop for other reasons.

TABLE The frequency of carriers of XHED among female hypodontia cases

<table>
<thead>
<tr>
<th>Population frequency per 100 000 females</th>
<th>Carrier frequency among female hypodontia cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carriers</td>
<td>Carriers with hypodontia</td>
</tr>
<tr>
<td>Permanent dentition (excluding 3rd molars)</td>
<td>1.73-17.3</td>
</tr>
<tr>
<td>Deciduous dentition</td>
<td>1.04-10.4</td>
</tr>
</tbody>
</table>

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pore counting down to a reasonably practical level. However, the efficiency of such a screening method would depend not only on the proportion of carriers who have missing teeth, but also on the regularity with which carrier sweat pore counts fall below the normal range. The reported frequency of abnormally low sweat pore counts in small samples of carriers ranges from 20 to 25%\(^2\) to 80 to 100%\(^1\)\(^3\)\(^4\)\(^9\). Furthermore, a reliable diagnosis of carrier status depends on the lack, or relative rarity, of alternative causes of hypohidrosis that could occur in conjunction with hypodontia, either as part of the same syndrome or simply by chance. Perhaps the most important possible drawback of the proposed screening method concerns the autosomal recessive form of hypohidrotic ectodermal dysplasia, since carriers of this disorder have a negligible chance of producing affected offspring. However, the available evidence suggests that carriers of the recessive form have normal dentitions, and normal sweat pore counts.\(^10\)\(^11\) A summary of the clinical features (including sweat gland number and dental abnormalities) of several ectodermal dysplasia syndromes\(^12\) indicates that none of these conditions, nor other disorders characterised by hypohidrosis,\(^13\) is likely to jeopardise the potential of the proposed screening method.

Larger scale investigations than those already undertaken are required before the practicability and reliability of any such screening programme could be assessed, but it seems likely that a substantial proportion of carriers of XHED could be identified by sweat pore counting from among cases of hypodontia found at routine dental examinations.

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J A SOFAER

Department of Oral Medicine and Oral Pathology, University of Edinburgh, Old Surgeons Hall, High School Yards, Edinburgh EH1 INR, and University Department of Human Genetics, Western General Hospital, Edinburgh EH4 2XU.

References


Requests for reprints to Dr J A Sofaer, Department of Oral Medicine and Oral Pathology, University of Edinburgh, Old Surgeons Hall, High School Yards, Edinburgh EH1 INR.
A dental approach to carrier screening in X linked hypohidrotic ectodermal dysplasia.

J A Spfaer

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