A high prevalence of hypodontia was detected among 820 first degree relatives of 305 probands and there was an increased risk if a second family member was affected. Hypodontia is a common trait in the population, and a deviation from normal sex ratio was observed in those affected. These results suggest a polygenic mode of inheritance.

Family studies have indicated that hypodontia is genetically determined, although the mode of transmission is unclear. Dahlberg suggested that a dominant, possibly X-linked gene is responsible. Grahnen concluded from an investigation of 171 families that hypodontia is probably transmitted by an autosomal dominant gene, with incomplete penetrance and variable expressivity. Gravely and Johnson and Boruchov and Green concluded from studies on twins that hypodontia is genetically determined and that environmental factors also play a role in the etiology.

Mandeville and Alvesalo and Portin in family studies of hypodontia of maxillary lateral incisors suggested autosomal dominant inheritance. Woolf concluded that although an autosomal dominant gene probably was responsible for hypodontia of maxillary lateral incisors, it also was plausible that a recessive or polygenic mode of inheritance existed in some families.

The prevalence of hypodontia in the population has been investigated. The purpose of this study was to investigate the heredity of hypodontia among Israeli Jews.

Materials and Methods

The families of 305 probands randomly selected from a prevalence study in Israeli schoolchildren were examined. As in the prevalence study, children having hypodontia as part of a general syndrome were not included.

The clinical diagnosis of hypodontia of permanent teeth had been confirmed by radiographs in all probands. Family members, all first degree relatives—mothers, fathers, and siblings—were examined in their homes. The examinations were performed by the same dentists who participated in the prevalence study. At the time of the examination a case history was taken in every instance of suspected hypodontia in order to exclude the possibility of extractions, known impactions, or loss resulting from trauma. Whenever a definite diagnosis was impossible because of early loss of teeth, the fact also was recorded. The analysis was of missing teeth only and although peg-shaped maxillary lateral incisors have been described as being related to hypodontia of this tooth, they were not included in this study and will form part of a separate report. The country of birth of the parents and consanguinity between the parents were recorded.

Only siblings aged 12 and older were included in the analysis. This was done because during the prevalence study it was found that in children under age 12 the ability to diagnose hypodontia clinically was limited. It also was found that in children aged 12 and older a clinical diagnosis of hypodontia of maxillary lateral incisors was confirmed radiographically in 90% of the cases; hypodontia of the mandibular incisors was confirmed in 95% of the cases and that of premolars in 70% of the cases. The family members were not examined radiographically.

For the analysis of the data, the parents and siblings were classified for hypodontia of
the same groups of teeth that were missing in the proband, as described in the prevalence study.\(^8\) The distribution of the families studied, according to the groups of teeth missing in the proband, is presented in Table 1. The families were further classified into two types: type \(A\), those families in which neither parent showed hypodontia of the same groups of teeth as the proband, and type \(B\), families in which at least one parent showed hypodontia of the same groups of teeth as the proband.

All those members not available for examination were treated as "unknown," as were those members in which a definite clinical diagnosis was impossible.

For statistical analysis of the data, the normal test for difference between means and the normal test between proportions were used at the 95% level of significance.

**Results**

The results are summarized in Table 2. Hypodontia of the same group of teeth as the probands was observed in 11.8% of 820 first degree relatives comprised of 449 parents and 371 siblings. Among the siblings of probands the prevalence was 14.8%, which is significantly higher \((P < 0.05)\) than that observed in the general population. If it is accepted that the prevalence of hypodontia found in the 12- to 18-year-old group holds for the adult population, then the 9.4% prevalence of hypodontia in parents of probands is also significantly higher. In the general population more females (4.80%) than males (4.38%) were affected.\(^8\) Among relatives more mothers and sisters than fathers and brothers were affected.

The prevalence among first degree relatives of 153 probands with missing maxillary lateral incisors and of 54 probands with missing mandibular incisors were analyzed separately. Those with missing second premolars were not analyzed separately because of the lower degree of accuracy in the diagnosis without radiographs as mentioned previously.

The overall prevalence of missing maxillary lateral incisors among 426 first degree relatives of probands was 10.3% as compared with 2.11% in the general population. The prevalence of 11.1% among siblings and of 9.7% among parents is significantly higher than that observed in the general population. In the prevalence study\(^8\) females had a significantly higher prevalence (2.32%) than males (1.89%). Similarly, mothers and sisters were more often affected than fathers and brothers.

The overall prevalence of missing mandibular incisors among 152 first degree relatives of probands was 9.2% as compared with 0.68% in the general population. The prevalence of 5.6% among parents and of 14.3% among siblings is significantly higher than that of the general population. In the prevalence study\(^9\) males had a significantly higher prevalence (0.89%) than females (0.48%). Similarly, fathers and brothers were more often affected than mothers and sisters.

The siblings of type \(B\) families were more often affected than siblings of type \(A\) families when (1) all hypodontia, and (2) hypodontia of maxillary lateral incisors or mandibular incisors were studied. The differences observed in all hypodontia and hypodontia of mandibular incisors were statistically significant.

Consanguineous marriages between first cousins or closer relatives were recorded in 8.9% of the 305 families examined. None of these were among parents of Ashkenazi origin.\(^8\)

**Discussion**

The higher rates of hypodontia observed in the parents and siblings of probands as compared with the rates of hypodontia in the general population, are in accord with the hypothesis that hypodontia is genetically con-

**TABLE 1**

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>DISTRIBUTION OF FAMILIES EXAMINED ACCORDING TO THE GROUP OF TEETH MISSING IN THE PROBAND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missing Teeth in Proband</td>
<td>Maxillary Lateral Incisors</td>
</tr>
<tr>
<td>No. of families</td>
<td>153</td>
</tr>
</tbody>
</table>
tioned. It is possible that different types of hypodontia are caused by different genetic factors. This is indicated by the differences in the male-to-female ratios observed: 0.82 in hypodontia of maxillary lateral incisors and 1.85 in hypodontia of mandibular incisors.8

If hypodontia resulted from an autosomal recessive gene one would expect about 25% of siblings to be affected. The percentage of affected siblings was 11.1% for maxillary lateral incisors and 14.3% for mandibular incisors. If hypodontia was an autosomal dominant trait with full penetrance, one would expect about 50% of siblings to be affected. The rates in parents are 9.7 and 5.6% for maxillary lateral incisors and mandibular incisors, respectively, which would represent a penetrance of about 19 and 11% only. Similarly, the penetrance of 22 and 28% in siblings is low if determined by a single autosomal dominant gene. Furthermore, if the condition was transmitted by such a gene with partial penetrance, no difference in penetrance would be expected in siblings of type A and B families. The deviation from the normal sex ratio is not in accordance with either autosomal recessive or autosomal dominant conditions. The high percentage of consanguineous marriages observed is similar to that reported previously in the non-Ashkenazi Israeli population.9

### Conclusions

Polygenic inheritance is a mode of inheritance caused by a number of genes each with a relatively small effect and is best known in continuous traits such as stature and intelligence. Some traits and congenital malformations that are discontinuous such as cleft lip and palate have the same type of inheritance.10 It is assumed that there is a biological threshold for the genetic predisposition below which individuals are unaffected and beyond which individuals are affected. It is proposed that polygenic inheritance with a threshold effect may be responsible for hypodontia among Israeli Jews. This conclusion is based on the following observations, all of which correspond to characteristics of conditions caused by polygenic inheritance10,11:

1. Hypodontia is common in the Israeli

<table>
<thead>
<tr>
<th>Population Examined</th>
<th>All Hypodontia</th>
<th>Hypodontia of Maxillary Lateral Incisors</th>
<th>Hypodontia of Mandibular Incisors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Examined</td>
<td>Affected</td>
<td>No. Examined</td>
</tr>
<tr>
<td>General population*</td>
<td>21,384</td>
<td>983</td>
<td>4.60</td>
</tr>
<tr>
<td>Male</td>
<td>10,371</td>
<td>454</td>
<td>4.58</td>
</tr>
<tr>
<td>Female</td>
<td>11,013</td>
<td>529</td>
<td>4.80</td>
</tr>
<tr>
<td>Parents of probands</td>
<td>449</td>
<td>42</td>
<td>9.4†</td>
</tr>
<tr>
<td>Fathers</td>
<td>212</td>
<td>16</td>
<td>7.6</td>
</tr>
<tr>
<td>Mothers</td>
<td>237</td>
<td>26</td>
<td>11.0</td>
</tr>
<tr>
<td>Siblings (age 12 and older)</td>
<td>371</td>
<td>55</td>
<td>14.8†</td>
</tr>
<tr>
<td>Brothers</td>
<td>186</td>
<td>25</td>
<td>13.4</td>
</tr>
<tr>
<td>Sisters</td>
<td>185</td>
<td>30</td>
<td>16.2</td>
</tr>
<tr>
<td>Siblings of type A families (negative parents)</td>
<td>168</td>
<td>18</td>
<td>10.7‡</td>
</tr>
<tr>
<td>Siblings of type B families (at least one positive parent)</td>
<td>47</td>
<td>16</td>
<td>30.0‡</td>
</tr>
</tbody>
</table>

* See reference 8.
† Significant difference from general population. (Normal test for difference between means, P < 0.05)
‡ Significantly different. (Normal test between proportions P < 0.05)
population; 2.1% have one or more missing maxillary lateral incisors and 0.7% missing mandibular incisors.\textsuperscript{8}

2. The risks in first degree relatives are greater than in the general population (10.3% and 9.2%, respectively), but less than expected by single gene (recessive or dominant) inheritance.

3. The risk to relatives for hypodontia of maxillary lateral incisors, the more common condition, is relatively less than that for hypodontia of mandibular incisors. These are 5 and 14 times, respectively, the risk to the general population.

4. A statistically significant deviation from normal sex ratio was observed in both subtypes of hypodontia.

5. There is an increased risk to relatives when more than one person in the family was affected as shown in type B vs type A families.

From the population studied by Grahn\textsuperscript{7} similar deductions may be made. He found 3 out of 16 (19\%) affected siblings when no parent was affected and 22 out of 56 (39\%) when at least one parent was affected with any kind of hypodontia.

In the present study, the risk to parents was found to be lower than that to siblings. This may be due to the method of investigation in which probably proportionally more affected than nonaffected parents were classified as unknown.

Some further methods of analysis important for the determination of polygenic inheritance were not investigated because of insufficient data. Among these are the comparison of the risk in first, second, and third degree relatives, and the comparison of risk to relatives of male and female probands.\textsuperscript{10}

The varying conclusions of different investigators concerning the mode of transmission can be explained by the fact that multifactorial inheritance may simulate dominant or recessive autosomal inheritance in certain families.\textsuperscript{11}

References


