Two Rare Mixed Heterozygotes for the Fluoride Variant and Silent Cholinesterases

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Serum cholinesterase (acetylcholine acetylhydrolase, EC 3.1.1.8) breaks down the muscle relaxant, succinylcholine. The usual \(E_1\), dibucaine variant \(E_t\), fluoride variant \(E_f\), and silent \(E_s\) genes function as alleles at the \(E_1\) locus and control the type of cholinesterase present. Kalow and Staron\(^1\) have described the dibucaine variant gene; Harris and Whittaker\(^2\) the fluoride variant gene; Liddell \textit{et al.}\(^3\) the silent gene. Individuals with the \(E_t\), \(E_f\), and \(E_s\) genes are at risk when exposed to succinylcholine.

Whittaker\(^4\) made the first identification of the mixed heterozygote for the fluoride variant and the silent cholinesterases (genotype \(E_tE_s\)) in the course of a family study. Simpson\(^5\) made the second identification of this rare genotype in a 40-year-old Caucasian woman who had 20 minutes' apnea after 30 mg of succinylcholine. The present family study was made because the propositus was markedly sensitive to succinylcholine.

**METHODS**

The propositus was a 4-year-old Caucasian boy. He received 40 mg of succinylcholine intramuscularly at 9:35 AM and was apneic until 11:45 AM. Respiratory assistance was needed until 12:15 PM, at which time respiration reverted to normal. Sera were collected from the patient and members of his family and stored at \(-20\) °C until needed.


**RESULTS AND DISCUSSION**

Table 1 gives the results of the family study. Serum cholinesterase activities were expressed as \(\mu\)mol of benzoylcholine hydrolyzed per min per ml of serum. Dibucaine, fluoride, Ro 2-0683, and Sernylan numbers refer to percentage inhibition of benzoylcholine hydrolysis in the presence of the inhibitor.

On the basis of the inhibition studies, the mother was genotype \(E_tE_s\); the propositus could be \(E_tE_s\) or \(E_sE_s\); the paternal grand-

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†Sernylan and Ro 2-0683 were donated by their manufacturers.
### Table 1. Activities and Inhibition Numbers

<table>
<thead>
<tr>
<th>Family Member</th>
<th>Activity</th>
<th>Dibucaine Number</th>
<th>Fluoride Number</th>
<th>Ro 2-08S3 Number</th>
<th>Sermylan Number</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paternal grandfather</td>
<td>0.898</td>
<td>65</td>
<td>44</td>
<td>89</td>
<td>69</td>
<td>$E_1^<em>E_1^</em>$</td>
</tr>
<tr>
<td>Paternal grandmother</td>
<td>0.657</td>
<td>80</td>
<td>64</td>
<td>95</td>
<td>76</td>
<td>$E_1^<em>E_1^</em>$</td>
</tr>
<tr>
<td>Paternal uncle</td>
<td>0.939</td>
<td>75</td>
<td>61</td>
<td>94</td>
<td>76</td>
<td>$E_1^<em>E_1^</em>$</td>
</tr>
<tr>
<td>Father</td>
<td>0.737</td>
<td>64</td>
<td>40</td>
<td>90</td>
<td>68</td>
<td>$E_1^<em>E_1^</em>$</td>
</tr>
<tr>
<td>Mother</td>
<td>0.990</td>
<td>67</td>
<td>57</td>
<td>77</td>
<td>66</td>
<td>$E_1^<em>E_1^</em>$</td>
</tr>
<tr>
<td>Brother</td>
<td>1.000</td>
<td>80</td>
<td>64</td>
<td>96</td>
<td>79</td>
<td>$E_1^<em>E_1^</em>$</td>
</tr>
<tr>
<td>Propositus</td>
<td>0.364</td>
<td>28</td>
<td>27</td>
<td>18</td>
<td>22</td>
<td>$E_2^<em>E_2^</em>$</td>
</tr>
</tbody>
</table>

mother, paternal uncle, and brother could be $E_1^*E_1^*$ or $E_1^*E_2^*$.

Whittaker and Simpson found dibucaine numbers of 67 and 69 and fluoride numbers of 43 and 34, respectively, in genotype $E_1^*E_1^*$. Six fluoride variant homozygotes ($E_2^*E_2^*$) have been reported. Two of these homozygotes had dibucaine numbers of 67 and 64, fluoride numbers of 34 and 35, and Ro 2-08S3 numbers of 88 and 75, respectively (Liddell et al.). The other four homozygotes had dibucaine and fluoride numbers of 68 and 35 (Whittaker), 68 and 35 (Griffiths et al.); and 64 and 67 and 36 and 39, respectively (King et al.).

The inhibition numbers obtained in the present family study are not compatible with the presence of the cholinesterase allele $E_1^*$ in the paternal uncle, the brother, and the propositus or the presence of the allele $E_1^*$ in the father. Therefore, the paternal grandfather and father were classified as genotype $E_1^*E_2^*$; the propositus as $E_1^*E_1^*$; and the paternal grandmother, paternal uncle, and brother as $E_1^*E_1^*$.

The author thanks Dr. Alfred Golden for bringing the case to his attention and for providing sera of the family members.

### References


