Distribution of Haptoglobin Subtypes in Greeks

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Human haptoglobin, the serum haemoglobin-binding protein, can be differentiated into three common phenotypes (Hp 1–1, Hp 2–1, and Hp 2–2) by means of starch gel electrophoresis at pH 8·6 (Smithies, 1955). These differences were thought to be determined by a pair of allelic genes Hp1 and Hp2 (Smithies and Walker, 1955, 1956). However, chemical reduction of purified haptoglobin followed by electrophoresis in starch gels, prepared in formic acid buffer containing 8M urea, enabled Connell, Dixon, and Smithies (1962) and Smithies, Connell, and Dixon (1962a) to classify individuals of phenotype 1–1 into three subphenotypes, HpiF–IF, HpiF–IS, and HpiS–IS. These three subphenotypes are controlled by two alleles, Hp1F and Hp1S. People of haptoglobin phenotype 2–1 could also be subtyped in a similar fashion into Hp2–1IF or Hp2–1S. Thus, a series of six phenotypes in the haptoglobin system can now be recognized (Hp1F–1F, IF–1S, 1S–1S, 2–1IF, 2–1S, and 2–2).

Chemical reduction of purified haptoglobin separates the protein into two polypeptide chains. Only the α chain has been found to vary in the six phenotypes, and the allele designations are referred to the α chain. The β chain appears to be unaffected by the genotype of the Hp locus (Smithies, Connell, and Dixon, 1962b). Chemical studies on the α chains (Smithies et al., 1962b; Dixon, Smithies, and Connell, 1962) have disclosed a single amino acid difference between the α18 and the α19 chain. The α2 chain has characteristics of both α18 and α19 chains and appears to represent the unequal fusion of two α1 chains. However, two α2 chain variants were found in a population of Indians from Brazil (Nance and Smithies, 1963).

Although the distribution of the three common phenotypes in various populations is well known, very little information on the distribution of the subtypes of haptoglobin 1–1 is available. Two interesting surveys (Giblett and Brooks, 1963; Shim and Bearn, 1964) of the distribution of haptoglobin subtypes in various populations have shown that oriental populations are restricted to the Hp1S allele, whereas both Hp1S and Hp1F alleles are present in Caucasian and Negro populations. In Caucasians, in particular, about 30% of the Hp1S allele frequency consists of Hp1F alleles.

The purpose of this paper is to present data on the distribution of haptoglobin subtypes in Greek population.

Material and Methods

The common haptoglobin types were determined in 2026 healthy Greek adults. Sera were stored at −20°C. Of 2026 (172 of phenotype 1–1 and 430 of phenotype 2–1), 602 were examined for haptoglobin subtypes. Haptoglobin purification was performed according to the method of Smithies et al. (1962a), except that the electrodes were reversed and a formate-bridge solution (pH 3·7) was used in the two lower and front upper electrode chambers. A voltage gradient of approximately 5 volts/cm. was applied for 18–20 hours at 18°-20°C. Under these conditions, the resolution between the two types of α1 polypeptide chains was satisfactory (Fig.).

Results and Discussion

The number of samples examined, the distribution of phenotypes 1–1, 2–1, and 2–2, as well as the frequencies of genes Hp1 and Hp2 in Greek population are summarized in Table I (Angelopoulos, Karalis, and Danopoulos, 1966).

The distribution of haptoglobin subtypes and the gene frequencies of Hp1F and Hp1S are shown in Table II.

Smithies et al. (1962a) examined a random sample of 93 White American and Canadian blood donors and estimated the Hp1S and Hp1F frequency to be 0·24 and 0·16, respectively. Giblett and Brooks (1963), by testing the sera of 66 White Americans, gave a frequency of 0·25 for Hp1S.
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Fig. Results of subtyping procedure. No. 1 = (Hp 1F–2), No. 2 = (Hp 1F–1F), No. 3 = (Hp 1F–1F) No. 4 = (Hp 1F–1S) No. 5 = (Hp 1F–1S) No. 6 = (Hp 1S–1S) No. 7 = (Hp 1S–1S) No. 8 = (Hp 1S–2) No. 9 = (Hp 1S–2).

and 0.13 for Hp1F. Shim and Bearn (1964) examined a sample of 72 Italians and estimated the Hp1S and Hp1F frequency to be 0.25 and 0.11, respectively. The observations by Giblett and Brooks (1963), that Oriental populations have the Hp1S allele whereas Caucasian and Negro populations have both Hp1S and Hp1F alleles, were confirmed by the study of Shim and Bearn (1964) who extended their investigation to many Mongolian populations.

A comparison of the results obtained in the present study with those published by Giblett and Brooks (1963), Shim and Bearn (1964), and Smithies et al. (1262a) is illustrated in Table III.

Table III illustrates that the Hp1F gene frequency in the Greek population is a little higher.
than in the Italian and White American populations.

**Summary**

The haptoglobin subtypes after chemical purification of haptoglobin were studied in 602 healthy Greek adults. The \(Hp^{1F}\) and \(Hp^{1S}\) gene frequencies were found to be 0.137 and 0.202, respectively. Our results are compared with the results of other published investigations.

**REFERENCES**

Angelopoulos, B., Tsoukantas, and Danopoulos (1966). The distribution of serum haptoglobin types in Greek population and their correlation with blood groups. In the press.


**TABLE I**

**DISTRIBUTION OF HAPTOGLOBIN PHENOTYPES AND FREQUENCIES OF GENES Hp1 and Hp2 IN THE GREEK POPULATION**

<table>
<thead>
<tr>
<th>Phenotypes</th>
<th>Population Proportion (P)</th>
<th>Sample Proportion (P)</th>
<th>Gene Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Hp^{1F})</td>
<td>224</td>
<td>0.1096</td>
<td>0.439</td>
</tr>
<tr>
<td>(Hp^{1S})</td>
<td>928*</td>
<td>0.4586</td>
<td>0.561</td>
</tr>
<tr>
<td>(Hp^{2F})</td>
<td>874</td>
<td>0.4318</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2026</td>
<td>1.0000</td>
<td></td>
</tr>
</tbody>
</table>

* 9 were 2-1 modified.

**TABLE II**

**DISTRIBUTION OF HAPTOGLOBIN SUBTYPES AND FREQUENCIES OF GENES \(Hp^{1F}\) AND \(Hp^{1S}\) IN THE GREEK POPULATION**

<table>
<thead>
<tr>
<th>Total No. Tested</th>
<th>(Hp^{1F})</th>
<th>(Hp^{1S})</th>
<th>(Hp^{1F}:Hp^{1S})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-1</td>
<td>2-1</td>
<td>(1F-1S)</td>
</tr>
<tr>
<td>602</td>
<td>172</td>
<td>430</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>61</td>
<td>171</td>
<td>259</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gene Frequency</th>
<th>(Hp^{1F})</th>
<th>(Hp^{1S})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.137</td>
<td>0.202</td>
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</tbody>
</table>

**TABLE III**

**HAPTOGLOBIN GENE FREQUENCIES IN CAUCASIANS**

<table>
<thead>
<tr>
<th>Population</th>
<th>No. Tested</th>
<th>Gene Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>American</td>
<td>66</td>
<td>0.133</td>
</tr>
<tr>
<td>American</td>
<td>93</td>
<td>0.16</td>
</tr>
<tr>
<td>Italian</td>
<td>72</td>
<td>0.118</td>
</tr>
<tr>
<td>Greek</td>
<td>602</td>
<td>0.137</td>
</tr>
</tbody>
</table>

Gene Frequency | Reference
---------------|-------------
0.251          | Giblett and Brooks (1963)
0.346          | Smithies et al. (1962a)
0.24           | Shim and Bearn (1964)
0.319          | Present study