Brief Report

Hereditary Methemoglobinemia in Greece

By Athena V. Papaspyrou-Zona, Park S. Gerald and Edward M. Scott

The first reports of hereditary methemoglobinemia were made before the etiology of the condition was known; among these was a description of methemoglobinemia in four Greek families by Coudonis.1 More recently it has been possible to clearly distinguish two principle types of methemoglobinemia. The first is caused by any one of several kinds of abnormal hemoglobins which are collectively known as the hemoglobins M, each of which differs from normal hemoglobin by a single amino acid substitution.2 These abnormal hemoglobins can be detected by electrophoretic means and both the hemoglobin and the methemoglobinemia are inherited as a dominant character.3 The second principle variety of hereditary methemoglobinemia is caused by the lack of a red cell enzyme, DPNH diaphorase; this disorder can be distinguished by an enzymatic test and is inherited as an autosomal recessive.4

The four Greek families originally described by Coudonis1 were located once again, and one member of each family was tested to determine the type of methemoglobinemia present.

Methods

Two samples of blood from each subject were collected in ACD solution. One sample was tested for DPNH diaphorase.4 The other was tested for the presence of a Hb M by electrophoresis in starch gel at pH 8.6 (untreated hemolysate, vertical electrophoresis, TRIS-EDTA buffer) and at pH 7.0 (oxidized hemolysate, horizontal electrophoresis, sodium phosphate buffer).

Results and Discussion

The subjects selected were (as labeled by Coudonis) number VI in the Vaftochilari pedigree, number 10 in the Melaniarides pedigree and one member each of Zakopoulos' Tripolis pedigree and Ptolemais pedigree. The results of determinations of DPNH diaphorase activity are shown in table 1.

The presence of methemoglobin in these samples could easily be shown by electrophoresis of the untreated hemolysate at pH 8.6. The amount of methemoglobin far exceeded that found in specimens from noncyanotic patients. The persistence of the methemoglobin in the intact erythrocytes during transport is consistent with the diagnosis of methemoglobinemia due to an

From the Hippokrateion Hospital, Athens, Greece; the Children's Hospital Medical Center, Boston, Mass.; and the Arctic Health Research Center, Anchorage, Alaska.

This work was supported in part by a grant (HE-04706) from the U. S. Public Health Service.

The authors are indebted to Drs. H. Tseveris, K. S. Zakopoulos, A. Coudonis and E. Loutsides for their help in locating these families.

Submitted July 6, 1964; accepted for publication Aug. 1, 1964.

375

Blood, Vol. 25, No. 3 (March), 1965
Table 1.—Levels of DPNH Diaphorase in Greek Subjects with Methemoglobinemia

<table>
<thead>
<tr>
<th>Subject</th>
<th>Change in Absorbance x 10^4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vafortochilari</td>
<td>-1</td>
</tr>
<tr>
<td>Melaniarides</td>
<td>0</td>
</tr>
<tr>
<td>Tripolis</td>
<td>3</td>
</tr>
<tr>
<td>Ptolemais</td>
<td>5</td>
</tr>
<tr>
<td>Normal controls</td>
<td>30 to 80</td>
</tr>
<tr>
<td>Eskimos and Indians with</td>
<td>-3 to 5</td>
</tr>
<tr>
<td>methemoglobinemia</td>
<td></td>
</tr>
</tbody>
</table>

enzyme deficiency. On the other hand, electrophoresis at pH 7.0 failed to
demonstrate the presence of an abnormal hemoglobin. Since all specimens
of Hb M examined in this manner have shown an abnormal electrophoretic
pattern, this is sufficient to rule out the presence of this type of hemoglobin-
opathy.

It should be noted that one case of Hb M disease has been found in Greece.5
Subsequent study showed that the abnormal hemoglobin was Hb M_{maskatoon}.6

SUMMARY

The cause of the methemoglobinemia described by Coudonis in four Greek
families was found to be the absence of DPNH diaphorase in red cells.

SUMMARIO IN INTERLINGUA

Es monstrate que le causa del methemoglobinemia describite per Coudonis
in quatro familias grec es le absentia de diaphorase de reducite nucleotida
diphosphopyridinic in le erythrocytos.

REFERENCES

1952.
2. Gerald, P. S., and Efron, N. L.: Chemical studies of several varieties of Hb
3. —: The clinical implications of hemoglobin structure. Pediatrics 31:780,
1963.
6. Fellows, R. E.: Personal communication.

Athena V. Papaspyrou-Zona, M.D., Instructor in Medicine,
First Medical Clinic, Hippokrateion Hospital, Athens University
School of Medicine, Athens, Greece.

Park S. Gerald, M.D., Associate Hematologist, Children's Hos-
pital Medical Center, and Assistant Professor of Pediatrics,
Harvard Medical School, Boston, Mass.

Edward M. Scott, Ph.D., Biochemist, the Arctic Health Re-
search Center, U.S. Public Health Service, Anchorage, Alaska.
Brief Report: Hereditary Methemoglobinemia in Greece

ATHENA V. PAPASYROU-ZONA, PARK S. GERALD and EDWARD M. SCOTT