Distribution of Abnormal Hemoglobins in Puerto Rico and Survival Studies of Red Blood Cells Using Cr$^{51}$

By Ramon M. Suarez, Roberto Buso, Leo M. Meyer and S. T. Olavarrieta

The first study on sicklema in Puerto Rico was that of Pons and Oms (1934). They reported an incidence of sickling in 5.6 per cent of the subjects studied.

More recently (1957) Torregrosa, Rivera Trujillo and Ruiz Soler reported an incidence of sicklema of 4.2 per cent in a series of 618 Puerto Ricans. In a group made up exclusively of Negroes the incidence of sicklema was found to be 6.7 per cent.

Menéndez Corrada, using paper electrophoresis, reported on a hemoglobin survey among 500 unselected admissions to San Patricio Veterans Administration Hospital during the years 1955-56 and found abnormal hemoglobins in only 13 patients, which gave an incidence of 2.6 per cent. Eight of the 13 cases showed the combination AS, and there was one instance of pure S (sickle cell anemia). A single case of hemoglobin SC disease was found; this was the first case ever reported in Puerto Rico. Another subject also exhibited SC hemoglobins, but appeared healthy. Two cases of AC were found. The incidence of hemoglobin C in this series was only 0.8 per cent.

In Cuba, Chediack and collaborators (1939) reported an incidence of 5.3 per cent of sickle-cell trait. In Jamaica the incidence, according to Jellife et al. was 5.7 per cent. In Martinique, Montestrué and Cautet reported (1948) an incidence of 5.5 per cent and Languillon found the trait to be 8 per cent in Guadeloupe.

The association of sickle cell anemia with a hemoglobin molecule exhibiting an abnormal electrophoretic mobility when compared to the normal adult hemoglobin was demonstrated by Pauling, Itano and their associates in 1949. Rapid identification of other hemoglobin molecules with different mobilities and their relation to several hemolytic syndromes followed this original work.

The synthesis of these abnormal hemoglobins has been shown to be regu-
lated by inherited genes which, with the single exception of hemoglobin H, lead to no clinical symptomatology when heterozygous, or to clear-cut diseases when homozygous. The most outstanding reason for clinical manifestations is an increased rate of red cell destruction. Hemoglobinopathies are, therefore, classified as hemolytic disorders due to intracorpuscular defects. The inheritance of the governing genes in various combinations explains the existence of a variety of clinical syndromes, some of which are new clinical entities, others which were until recently confusing variants of known hemolytic anemias.

The recent technics of paper electrophoresis and radiochromium survival have facilitated a study of the incidence and ethnical distribution of abnormal hemoglobins in Puerto Rico and the life span of the red cells in the abnormal population. We hope that the data obtained in an island-wide survey may enrich the information on sources of morbidity already available.

METHODS

Electrophoretic mobility for hemoglobin classification was determined according to the filter paper technic. Alkali-resistant hemoglobin was measured by Singer's method. Red cell-labeling procedure and the radioactive assay of peripheral blood as a function of time after reinjection of the subject's own labeled blood were carried out following the technics standardized in our laboratory. The survival time of Cr\(^{51}\)-labeled whole blood by our method is reported as the "apparent" half-life because the plotted curves are not corrected for elution of radiochromium from the cells. This phenomenon has been shown to occur at the same rate in abnormal as well as in normal red blood cells, thus making the quantitative relationship between normal and abnormal "apparent" survival curves accurate. The normal mean value for our technic is 24.5 days.

MATERIALS

A total of 2,089 persons were studied. All were natives of Puerto Rico. There were 1,487 whites and 602 classified as Negroes. Women comprised one third of the entire group, 556 cases, and there were 1,533 men. The ages varied between 18 and 70, but the great majority belonged to the fourth decade of life. No children were studied.

The population of the island of Puerto Rico according to the 1950 census is 2,210,703. The island is divided into five geographical zones, and a proportional number of individuals from each area was examined through the centralized facilities of the state district hospitals. The blood of nearly all patients admitted to the Mimiy Hospital during the year 1956-57 was studied, and specimens of blood were also obtained from the blood bank of the School of Medicine of Puerto Rico.

The colored population included pure blooded Negroes and Negroids of African descent. The white population as determined by individual census workers possibly included some degree of Negro blood admixture. It is also possible that there is some Indian blood in our population, but this should be minimal, and there are also a few people of Mediterranean racial extraction, but no admixture with Oriental races is as yet evident.

The map of Puerto Rico shows the area and the population served by the different district hospitals of the island. The number of persons examined in each area appears in brackets.

*Information obtained from the Department of Health of the Commonwealth of Puerto Rico.
ABNORMAL HEMOGLOBINS IN PUERTO RICO

FIG. 1.—Map of the Island of Puerto Rico showing the population served by each of the district hospitals and, in brackets, the number of cases studied in each area.

Geographical Distribution of Abnormal Hemoglobins

Table 1 summarizes the data on the geographical distribution of abnormal hemoglobin patterns in Puerto Rico. The frequency of hemoglobin abnormalities follows closely the general racial distribution in the island, whereby the Negro population concentrates chiefly on the northeastern plains. We observe that the San Juan area has an incidence of hemoglobin anomalies of 3.5 per cent in its total population; the incidence in the Humacao section is 2.5 per cent. These values contrast with those observed in the zones covering the mountain belt, where the population is mainly of pure Spanish stock. Thus we find only 0.6 per cent in the district of Ponce-Guayama, 0.9 per cent in Mayaguez-Aguadilla and 0.3 per cent in Arecibo.

Racial Distribution

Table 2 reveals the incidence of abnormal hemoglobin molecules among the Negroes and whites. We can say that 6.8 per cent of Puerto Rican Negroes carry combinations of genetically abnormal hemoglobins.

TABLE 1.—Geographical Distribution of Abnormal Hemoglobins

<table>
<thead>
<tr>
<th>Geographical Zone</th>
<th>Population 1950 Census</th>
<th>Subjects Examined</th>
<th>Subjects with Abnormal Hgb</th>
<th>Negroes with Abnormal Hgb</th>
<th>Whites (f) with Abnormal Hgb</th>
<th>Ratio of Abnormal Hgb</th>
</tr>
</thead>
<tbody>
<tr>
<td>San Juan</td>
<td>357,500</td>
<td>757</td>
<td>28</td>
<td>28</td>
<td></td>
<td>3.5%</td>
</tr>
<tr>
<td>Humacao Fajardo</td>
<td>260,980</td>
<td>324</td>
<td>8</td>
<td>7</td>
<td>1</td>
<td>2.5%</td>
</tr>
<tr>
<td>Ponce Guayama</td>
<td>555,333</td>
<td>338</td>
<td>2</td>
<td>2</td>
<td></td>
<td>.6%</td>
</tr>
<tr>
<td>Mayaguez Aguadilla</td>
<td>549,378</td>
<td>334</td>
<td>3</td>
<td>3</td>
<td></td>
<td>.9%</td>
</tr>
<tr>
<td>Arecibo</td>
<td>267,512</td>
<td>336</td>
<td>1</td>
<td>1</td>
<td></td>
<td>.3%</td>
</tr>
<tr>
<td>Total</td>
<td>2,190,703</td>
<td>2,089</td>
<td>42</td>
<td>41</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>
In the group of 1,487 white subjects there was only one person from the Humacao area who showed a combination of hemoglobin A and S. This man had blue eyes, blond hair and typical Caucasian features. In spite of these we entertained serious doubts of the ethnical purity of his blood. If we include this man, as we have, in the group of white people, the incidence of abnormal hemoglobins among them would be only 0.06 per cent, but it would be zero if we discard him.

The percentage of abnormal hemoglobins among the 2,089 persons examined was only 2.01 per cent.

Table 3 shows the various types of hemoglobins found among 602 Puerto Rican Negroes. It is apparent that the only abnormal hemoglobins found were hemoglobin S and hemoglobin C, as well as various combinations with hemoglobin A. Fetal, or alkali-resistant hemoglobin, was present in very small quantities among these people. It varied from 0.45 per cent to 3.25 per cent, averaging only 1.12 per cent of the total red cell hemoglobin.

Hemoglobin S was found to be four times as frequent as hemoglobin C. Both abnormal hemoglobins appeared from 8 to 15 times more prevalent in the heterozygous (SA or CA traits) than in the homozygous (S or A diseases) state. Table 4 finally reveals that hemoglobin S, which accounts for the sickling phenomenon, is present in 5.2 per cent of the Negro population of Puerto Rico, and that 5.9 per cent of those exhibiting sickling are presumably homozygous and suffer from sickle cell anemia.

**Apparent Half-life of Erythrocytes**

Table 4 shows that the “apparent” half-life of the red blood cells in persons showing hemoglobinopathies S and SC is markedly shortened when measured by our technic of Cr⁵¹ survival. The “apparent” half-life of 10 days for S hemoglobins and of 7 days for the combination SC disease contrasts sharply with our normal mean of 24.5 days. The case of hemoglobin C disease had a shortened half-life of 18.5 days.

On the other hand, people with heterozygous states (SA and CA traits) showed either normal or slightly decreased “apparent” half-life as evidenced
by the finding of an average of 20.6 days for the combination SA and of 21.5 days for the combinations of hemoglobins CA.

These findings correlate well with those reported by Weinstein et al.\textsuperscript{15} from Chicago. They also corroborate the generally accepted concept that an increased destruction of red cells is the outstanding manifestation of disease due to hereditary hemoglobinopathies.

**SUMMARY**

1. A survey of the incidence of abnormal hemoglobins in different racial groups distributed over the island of Puerto Rico was performed. The relation of the rate of destruction of red cells to the presence of abnormal hemoglobin patterns in the affected population was also studied.

2. The abnormal hemoglobins were classified by the difference in paper electrophoretic mobility. Fetal hemoglobin was measured by its resistance to alkaline denaturation. The red cell life span was determined by measuring the survival of erythrocytes labelled with radioactive sodium chromate.

3. A total of 2,089 inhabitants were studied. There were 1,487 white subjects and 602 Negroes. Forty-two individuals were found to harbor abnormal hemoglobins. All but one were Negroes or Negroid of African descent, and their relative numbers agreed closely with the geographical distribution of ethnic groups in the island. Abnormal hemoglobins were found in 2.01 per cent of the entire series of 2,089 persons, but in those considered Negroes or Negroids the incidence of abnormal hemoglobins was 6.8 per cent.

   Of the 42 persons showing abnormal hemoglobins, thirty-four or 81 per cent, had hemoglobin S; only two of these had sickle cell anemia. The incidence of the sickle cell trait among the Puerto Rican Negro population was 5.2 per cent; and the incidence of hemoglobin S disease among those harboring the trait was 5.9 per cent.

   Eight, or 19 per cent of the abnormal cases had hemoglobin C; only one of these had hemoglobin C disease with clinical hemolytic anemia. The incidence of the hemoglobin C trait among the Puerto Rican Negro population is 1.3 per cent; and the incidence of hemoglobin C disease among those harboring the trait may reach 12.5 per cent.

4. All 42 cases harboring abnormal hemoglobins showed very small quantities of fetal or alkali-resistant hemoglobin ranging from 0.45 per cent to 3.25 per cent, averaging 1.12 per cent.

5. The “apparent” half-life of the red blood cells was found to be 10 days in sickle cell anemia, 7 days in SC disease, 20.6 days in cases of hemoglobin SA, 18.5 days in one case of hemoglobin C disease and 21.5 days in 2 cases of the combination CA. The normal “apparent” half-life in our laboratory is 24.5 days.

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**TABLE 4.—Apparent Cr' Half-Life of Red Cells in Puerto Ricans with Hemoglobinopathies**

<table>
<thead>
<tr>
<th>Subjects Studied</th>
<th>Hgb S</th>
<th>Hgb SA</th>
<th>Hgb C</th>
<th>Hgb CA</th>
<th>Hgb SC</th>
<th>Hgb A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Apparent Cr' Half Life</td>
<td>10 Days</td>
<td>20.6 Days</td>
<td>18.5 Days</td>
<td>21.5 Days</td>
<td>7 Days</td>
<td>24.5 Days</td>
</tr>
</tbody>
</table>
SUMMARIO IN INTERLINGUA

1. Le incidentia de hemoglobinas anormal in varie gruppos racial del insula Porto Rico esseva investigate. Le mesura del destruction de erythrocytos esseva ponite in relation con le presentia de hemoglobinas anormal in le population studiate.

2. Le hemoglobinas anormal esseva classificate secundo lor differentias de motilitate in le electrophorese a papiro. Hemoglobina fetal esseva mesurate per su resistentia al disnaturation alcalin. Le duration vital del erythrocytos esseva determinate per mesurar le superviventia de erythrocytos marcate con radio-active chromato de natrium.

3. Un total de 2.089 habitantes del insula esseva studiate, incluse 1.487 subjectos de racia blanc e 602 negros. Esseva trovate que 42 individuos albergava hemoglobinas anormal. Omnes—con un exception—esseva negros o negroides de ancestria african. Lor numeros relative in varie regiones se concordava ben con le distribution geographic del gruppos ethnic in le insula. Hemoglobinas anormal esseva trovate in 2,01 pro ceneto del serie total de 2.089 personas. Inter le individuos considerate como negre o negroide, le incidentia del hemoglobinas anormal esseva 6,8 pro cento.

Inter le 42 personas exhibiente hemoglobinas anormal, 34 (81 pro cento) habeva hemoglobina S. Solmente duo de istes habeva anemia a cellulas fal- ciforme. Le incidentia del tracto de cellulas falciforme in le population negre de Porto Rico esseva 5,2 pro cento. Le incidentia de morbo de hemoglobin S inter personas con ille tracto esseva 5,9 pro cento.

Octo del 42 casos anormal (i.e. 19 pro cento) mostrava hemoglobina C. Solmente un del individuos in iste gruppo habeva morbo de hemoglobin C con anemia hemolytic clinic. Le incidentia del tracto de hemoglobina C inter le population negre de Porto Rico esseva 1,3 pro cento. Le incidentia de morbo de hemoglobin C inter personas con ille tracto esseva 12,5 pro cento.

4. Omne le 42 individuos con hemoglobinas anormal monstrava micrissime quantitates de hemoglobina fetal (o de hemoglobina resistente a alcali). Iste quantitates variava inter 0,45 e 3,25 pro cento. Le valor medie esseva 1,12 pro cento.

5. Pro le “apparente” medie vita del erythrocytos in casos de anemia a cellulas falciforme, un valor de 10 dies esseva constatate. In casos de hemoglobin SC iste valor esseva 7 dies. In casos de hemoglobina SA illo esseva 20,6 dies. In un caso de morbo de hemoglobin C illo esseva 18,5 dies. In duo casos con le combination CA illo esseva 21,5 dies. Le valor normal del “apparente” medie vita de erythrocytos secundo le studios effectuate in nostre laboratorio es 24,5 dies.

REFERENCES


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