Mediterranean Anemia in the Negro
A Re-evaluation of Four Patients and Their Families

By STEVEN O. SCHWARTZ AND WILSON H. HARTZ, JR.*

IN 1949, under the title of Mediterranean Anemia in the Negro, one of us (S. O. S., and Mason) reported the presence of Mediterranean anemia in four patients and their families. The diagnosis rested, among other things, on the presence of target cells, a feature at that time prominently associated with Mediterranean anemia. The report antedated the recognition in 1950 of C hemoglobin by Itano and his co-workers, and the clinical studies in which target cells were found to be an outstanding characteristic of red cells containing hemoglobin C.

In discussing the patients presumed to have Mediterranean anemia as reported by Schwartz and Mason, Kaplan and his colleagues suggested in 1951 that perhaps hemoglobin C disease might have resulted in the same clinical as well as hematologic manifestations previously diagnostic of Mediterranean anemia. A re-examination of our data was therefore in order.

In the course of re-evaluation and the extension of our studies on abnormal hemoglobins, it was established that Kaplan and his associates had indeed been correct in their surmise in that two of our patients proved to have hemoglobin C disease rather than Mediterranean anemia. In the other two patients, however, the diagnosis of Mediterranean anemia was confirmed and, provided eventual disclosures do not nullify our present criteria, the diagnosis has been further substantiated by new criteria presented herein.

METHODS

1. Hemoglobin analyses were performed with filter paper electrophoretic apparatus similar to that described by Kunkel and Tiselius. A veronal buffer of pH 8.6 was used.

2. Hemoglobin F was determined by the method of Singer. In our laboratory values to 1.8 per cent are considered normal. In most instances, determinations were in duplicate.

3. Serum iron levels were obtained by the method of Barkan and Walker. The normal range is from 50 to 150 micrograms per cent.

FOLLOW-UP INVESTIGATIONS

With the exception of three members in Family III, all members of the original families were available for study. D. N., a girl, died in 1950 at the age of 13 ap-
TABLE 1.—* Differential Diagnosis*

<table>
<thead>
<tr>
<th></th>
<th>Hemoglobin C Disease</th>
<th>Mediterranean Anemia (Adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Julius M. (Family I)</td>
<td>Frank F. (Family II)</td>
</tr>
<tr>
<td>RBC</td>
<td>5.60</td>
<td>5.80</td>
</tr>
<tr>
<td>Hgb</td>
<td>12 Gm.</td>
<td>13.7 Gm.</td>
</tr>
<tr>
<td>MCHC</td>
<td>35%</td>
<td>36%</td>
</tr>
<tr>
<td>Target Cells</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Poikilocytosis</td>
<td>+</td>
<td>±</td>
</tr>
<tr>
<td>Hypochromia</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Nucleated RBC</td>
<td>41*</td>
<td>0</td>
</tr>
<tr>
<td>F Hgb</td>
<td>1.8%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spleen below LCM.</td>
<td>25 cm.*</td>
<td>10 cm.</td>
</tr>
<tr>
<td>Abnormal bone growth</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Electrophoretic pattern</td>
<td>CC†</td>
<td>CC</td>
</tr>
</tbody>
</table>

* Post-splenectomy
** Prior to splenectomy
† Homozygous C hemoglobin
‡ Normal with large amount of fraction F

Table 2.—*Family I*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Relationship</th>
<th>Red Blood Cell Count</th>
<th>Hemoglobin, Grams</th>
<th>Hematocrit</th>
<th>White Blood Cell Count</th>
<th>Mean Corpuscular Volume</th>
<th>Mean Corpuscular Hemoglobin</th>
<th>Reticulocytes per cent</th>
<th>Serum Iron, mc. per cent</th>
<th>Hypochromia per cent</th>
<th>Hypochromia, %</th>
<th>Hemoglobin per cent</th>
<th>Electrophoretic Pattern</th>
<th>Blood Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>Julius M. 58 yrs.</td>
<td>Index case</td>
<td>5.6</td>
<td>12</td>
<td>34</td>
<td>61</td>
<td>21.3</td>
<td>33</td>
<td>2.6</td>
<td>130</td>
<td>33</td>
<td>Dist. HbO 41</td>
<td>1.8</td>
<td>CC</td>
<td></td>
</tr>
<tr>
<td>Julius Jr. *</td>
<td>Twin brother</td>
<td>6.29</td>
<td>17.7</td>
<td>43</td>
<td>72</td>
<td>27</td>
<td>41</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
<td>1.7</td>
<td>CA</td>
<td>Targeting +++</td>
<td></td>
</tr>
<tr>
<td>Alma M. *</td>
<td>Sister</td>
<td>5.59</td>
<td>14.0</td>
<td>40</td>
<td>68</td>
<td>25</td>
<td>35</td>
<td>0.4</td>
<td>—</td>
<td>—</td>
<td>1.6</td>
<td>CA</td>
<td>Targeting +</td>
<td></td>
</tr>
<tr>
<td>Hezekiah M *</td>
<td>Brother</td>
<td>5.43</td>
<td>14.7</td>
<td>42</td>
<td>77</td>
<td>27</td>
<td>35</td>
<td>0.5</td>
<td>—</td>
<td>—</td>
<td>1.4</td>
<td>CA</td>
<td>Targeting +</td>
<td></td>
</tr>
</tbody>
</table>

* 1949 Data (except for hemoglobin analyses).

Apparently as a result of chronic nephritis; postmortem examination was not made. Aside from signs and symptoms referable to kidney disease, findings had been typical of Mediterranean anemia and mirrored those of her surviving sister, L. N. A brother, G. N., serves in the Air Force, and the father, W. N., is separated from the family; thus the brother and father were not available for study.

The hematologic, physical and geneologic information gathered in 1949 concerning the four families will not be repeated in this publication except when specifically designated, because there have been no significant changes over a six-year period which is in itself diagnostically emphatic. (Tables 2 to 5 inclusive.)
TABLE 3.—Family II

<table>
<thead>
<tr>
<th>Patient</th>
<th>Relationship</th>
<th>Red Blood Cell Count</th>
<th>Hemoglobin, Grams</th>
<th>Hematocrit</th>
<th>White Blood Cell Count</th>
<th>Mean Corpuscular Volume</th>
<th>Mean Corpuscular Hemoglobin</th>
<th>Reticulocytes per cent</th>
<th>Serum Iron mg. per cent</th>
<th>Hemoglobin per cent</th>
<th>Electrophoretic Pattern</th>
<th>Blood Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frank F.</td>
<td>Index (father)</td>
<td>5.8</td>
<td>13.7</td>
<td>38</td>
<td>7000</td>
<td>68</td>
<td>23.5</td>
<td>36</td>
<td>5.2</td>
<td>143</td>
<td>.36 Dist. Hb</td>
<td>1.9 CC</td>
</tr>
<tr>
<td>Mary F.*</td>
<td>Daughter</td>
<td>4.96</td>
<td>11.4</td>
<td>36</td>
<td>6100</td>
<td>73</td>
<td>23</td>
<td>.01</td>
<td>106</td>
<td>36</td>
<td>to 21</td>
<td>1.3 CA</td>
</tr>
<tr>
<td>Frank Jr. *</td>
<td>Son</td>
<td>4.33</td>
<td>12.5</td>
<td>34</td>
<td>7000</td>
<td>78</td>
<td>29</td>
<td>.8</td>
<td>66</td>
<td>.36</td>
<td>to .24</td>
<td>1.6 CA</td>
</tr>
<tr>
<td>Dorothy F.*</td>
<td>Daughter</td>
<td>5.21</td>
<td>11.7</td>
<td>35</td>
<td>7600</td>
<td>67</td>
<td>23</td>
<td>1.0</td>
<td>107</td>
<td>.33</td>
<td>to .18</td>
<td>1.5 CA</td>
</tr>
<tr>
<td>Belah F.*</td>
<td>Daughter</td>
<td>4.56</td>
<td>11.2</td>
<td>34</td>
<td>7500</td>
<td>73</td>
<td>24</td>
<td>.6</td>
<td>.73</td>
<td>—</td>
<td>1.5 CA</td>
<td>Targeting +</td>
</tr>
<tr>
<td>Mrs. F.</td>
<td>Wife</td>
<td>4.42</td>
<td>12.5</td>
<td>40</td>
<td>5150</td>
<td>90</td>
<td>28</td>
<td>31</td>
<td>89</td>
<td>.42</td>
<td>to .30</td>
<td>1.7 AA</td>
</tr>
<tr>
<td>Joanne F.</td>
<td>Daughter</td>
<td>4.43</td>
<td>11.4</td>
<td>31</td>
<td>7600</td>
<td>69</td>
<td>26</td>
<td>.6</td>
<td>.76</td>
<td>—</td>
<td>1.1 CA</td>
<td>Targeting +</td>
</tr>
<tr>
<td>Joseph F.</td>
<td>Son</td>
<td>4.58</td>
<td>11.1</td>
<td>33</td>
<td>4700</td>
<td>71</td>
<td>24</td>
<td>.4</td>
<td>—</td>
<td>.36</td>
<td>to .24</td>
<td>1.0 CA</td>
</tr>
<tr>
<td>Olivia F.</td>
<td>Daughter</td>
<td>5.01</td>
<td>12.2</td>
<td>33</td>
<td>9000</td>
<td>70</td>
<td>24</td>
<td>.8</td>
<td>.58</td>
<td>.39</td>
<td>to .24</td>
<td>1.7 CA</td>
</tr>
<tr>
<td>Jasper F.</td>
<td>Son</td>
<td>5.00</td>
<td>11.4</td>
<td>34</td>
<td>9000</td>
<td>68</td>
<td>23</td>
<td>.8</td>
<td>—</td>
<td>—</td>
<td>1.4 CA</td>
<td>Targeting +</td>
</tr>
</tbody>
</table>

*Offspring first marriage.

Family I

J. M.* died in 1954 from uremia. He had been incapacitated by congestive heart failure since 1949. Except for 1.8 per cent F hemoglobin his hemoglobin exemplified hemoglobin C disease, i.e., exclusively C.

The brothers and sister have remained in good health and their hemoglobin patterns are CA, indicating only the hemoglobin C trait.

* Reported in a previous communication.
### Table 4—Family III

<table>
<thead>
<tr>
<th>Patient</th>
<th>Relationship</th>
<th>R. B. C. Count</th>
<th>Hemoglobin, Gm.</th>
<th>Hematocrit</th>
<th>MCV (Mean Corpuscular Volume)</th>
<th>MCH (Mean Corpuscular Hemoglobin)</th>
<th>MCHC (Mean Corpuscular Hemoglobin Concentration)</th>
<th>Reticulocytes %</th>
<th>Hemoglobin %</th>
<th>Hemoglobin F %</th>
<th>Epoetin Ficotic Polarity</th>
<th>Blood Film</th>
</tr>
</thead>
</table>
| Lillian N.    | Index Case        | 3.66           | 7.8             | 28         | 9000                          | 75                                 | 21                                     | 28             | 28           | 9.6           | --                         | AF
|               |                   |                |                 |            |                               |                                    |                                   | 112            | .42          | .42           | 15 to 17                 | Poikilocytosis +++
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting +++
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Microcytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Nucleated RBC 18
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Normal
| Henrietta B. 68 yrs. | Maternal Grandmother | 4.41           | 13.0           | 40         | 5350                          | 91                                 | 32                                     | 35             | 1.6          | 68            | .42 to .27               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Normal
| Mrs. N. 48 yrs.  | Mother            | 4.63           | 11.2           | 36         | 5050                          | 78                                 | 24                                     | 31             | 1.6          | 53            | .39 to .27               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Poikilocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Nucleated RBC 18
|               |                   |                |                 |            |                               |                                    |                                   | 1.6            | .68          | .68           | 1.6 to 1.7               | AA
| David N. 22 yrs. | Brother           | 5.31           | 11.6           | 41         | 5100                          | 77                                 | 22                                     | 28             | 3.0          | 100           | .39 to .24               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Poikilocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Stippling +
|               |                   |                |                 |            |                               |                                    |                                   | 2.2            | .22          | .22           | 2.2 to .30               | AA
| William N. 15 yrs. | Brother           | 4.84           | 14.5           | 43         | 4650                          | 89                                 | 39                                     | 34             | 1.9          | 122           | .42 to .30               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Normal
| Rochelle N. 11 yrs. | Sister           | 5.73           | 12.6           | 38         | 5700                          | 70                                 | 22                                     | 28             | 2.7          | 86            | .36 to .24               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis +
|               |                   |                |                 |            |                               |                                    |                                   | 2.5            | .25          | .25           | 2.5 to .30               | AA
| Robert 9 yrs.   | Brother           | 6.14           | 12.0           | 40         | 4650                          | 64                                 | 21                                     | 32             | 1.7          | 48            | .43 to .13               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Microcytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   | 2.8            | .28          | .28           | 2.8 to .32               | AA
| Joanne N. 8 yrs. | Sister            | 6.02           | 10.5           | 38         | 8050                          | 63                                 | 18                                     | 28             | 2.7          | 86            | .36 to .24               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Microcytosis +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis +
|               |                   |                |                 |            |                               |                                    |                                   | 3.3            | .33          | .33           | 3.3 to .44               | AA
| Carl N. 5 yrs.  | Half-brother      | 4.42           | 12.6           | 40         | 6600                          | 91                                 | 29                                     | 32             | 96           | .42 to .27               | AA
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Normal
| Dorothy* at 13 yrs. | Deceased sister  | 5.26           | 8.5            | 33         | 12900                         | 63                                 | 16                                     | 26             | 9.6          | --            | --                       | --
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Poikilocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Microcytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Nucleated RBC 12
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Normal
| Gary N.* 21 yrs. | Brother           | 6.50           | 12.8           | 40         | 5200                          | 89                                 | 19                                     | 19             | 1.6          | -             | --                       | --
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Poikilocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   | 1.6            | .44          | .44           | 1.6 to .20               | AA
| Mr. N.* 48 yrs  | Father            | 7.00           | 14.7           | 51         | 12100                         | 72                                 | 21                                     | 29             | 1.9          | --            | --                       | --
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Targeting + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Poikilocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Hypochromia + + +
|               |                   |                |                 |            |                               |                                    |                                   |                |              |               |                           | Anisocytosis + + +
|               |                   |                |                 |            |                               |                                    |                                   | 2.7            | .27          | .27           | 2.7 to .30               | AA

* 1949 data.
MEDITERRANEAN ANEMIA IN THE NEGRO

Table 5—Family IV

<table>
<thead>
<tr>
<th>Patient</th>
<th>Relationship</th>
<th>R. B. C. Count</th>
<th>Hemoglobin Em.</th>
<th>Hematocrit</th>
<th>W. B. C. Count</th>
<th>Volume Mean corpuscular</th>
<th>Mean corpuscular</th>
<th>Hypochromia</th>
<th>Reticulocytes</th>
<th>Serum Iron sat.</th>
<th>Hyposplenism</th>
<th>F Hemoglobin</th>
<th>Electrophoretic Pattern</th>
<th>Blood Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>George D. <strong>37</strong></td>
<td>Index Case</td>
<td>4.51</td>
<td>9.0</td>
<td>32</td>
<td>3000</td>
<td>71</td>
<td>20</td>
<td>29</td>
<td>5.0</td>
<td>58</td>
<td>39</td>
<td>40</td>
<td>AF</td>
<td></td>
</tr>
<tr>
<td>Felanthes D.</td>
<td>Brother</td>
<td>3.07</td>
<td>14.1</td>
<td>47</td>
<td>6700</td>
<td>93</td>
<td>29</td>
<td>30.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3.1 CA</td>
<td>Targeting +</td>
</tr>
</tbody>
</table>

* Errorously Frank D. in 1949.

Family II

All members of Family II are living and in good health. F. F.* is also an example of hemoglobin C disease, his children, of whom there are three more since 1949, have the hemoglobin C trait.

Family III

L. N., the most severely affected living member, continues to have suboptimal health. Fatigue is the dominant symptom and she is constantly jaundiced. Short stature, bosselation of the skull with a prominent forehead, moderate liver enlargement and extensive splenomegaly constitute the deformities of the disease. Leg ulcers are absent. These findings combined with a large proportion of F hemoglobin, 80 per cent, and a hemoglobin pattern of AF are those of severe Mediterranean anemia.

The remainder of the family have had good health. The maternal grandmother, H. N., half brother C. N., and brother W. N. presented normal data in the hematologic and electrophoretic studies and they had no increase in F hemoglobin. In the others, normal hemoglobin electrophoretic patterns were also seen; however, lowered hemoglobin values, abnormalities in the red blood cells, and increased values of F hemoglobin from 2.2 per cent to 3.3 per cent were noted. These deviations from the normal were interpreted to represent the presence in mild degree of the Mediterranean anemia hemoglobin anomaly.

Family IV

G. D. has no skeletal manifestations. Jaundice is intermittently present and hepatomegaly is absent. The spleen is moderately enlarged. Except within a small area, extensive leg ulcerations have healed. Hemoglobin analysis is AF in which F comprises 40 per cent. Although the findings are comparable to those of L. N. in family III, the constitutional effect appears to be less pronounced.

The brother F. D. is living and well. His hemoglobin pattern is CA with a normal F fraction. Other members still live outside Chicago. They, along with G. D. and F. D., were investigated hematologically and reported by Singer.* Admixtures of the Mediterranean anemia hemoglobin anomaly with hemoglobin C were found in the mother and a sister.

ADULT MEDITERRANEAN ANEMIA VS. HEMOGLOBIN C DISEASE

The facility with which one may differentiate between moderately severe adult Mediterranean anemia and hemoglobin C disease by hemoglobin analysis should

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* Reported in a previous communication.²
FIG. 1.—HEMOGLOBIN C DISEASE. The folding and cupping phenomena also observed in wet preparations of target cells, are especially prominent. The pseudospherocytosis is well demonstrated.

not discourage attempts to distinguish the two disorders clinically. Information from the index cases has been recorded and divided for ease of comparison (table 1). The more subtle alterations found in those less severely affected are magnified in these patients.
The main points of difference are distinct:

Significantly greater lowering of hemoglobin levels and reductions in the MCHC were noted in Mediterranean anemia. Although the findings of target cells, poikilocytes, and a hypochromic appearance of the red cells are common to the two conditions, greater numbers of target cells are present in hemoglobin C
Fig. 3.—Hemoglobin C Disease. Bony changes are absent.

Fig. 4.—Adult Mediterranean Anemia (Patient L. N.). Marked bony changes characteristic of severe long-standing hemolytic anemia.
MEDITERRANEAN ANEMIA IN THE NEGRO

Fig. 5.—Paper Electrophoresis. The pattern of L. N. exemplifies Mediterranean anemia hemoglobin with a substantial F fraction. Its migration lags behind that of normal hemoglobin thus resembling cord hemoglobin. This difference is not observed in minimal Mediterranean anemia with small F fractions.

Hemoglobin C is easily identified in the trait or pure state.

blood; on the other hand, a greater degree of poikilocytosis and hypochromia is observed in the blood of patients with Mediterranean anemia. (Figs. 1 and 2.)

Jaundice and roentgenologic evidence of bone changes occurred only in the Mediterranean anemia groups. (Figs. 3 and 4.)

Both groups manifested erythroblastosis and splenomegaly of similar magnitude; thus these factors lose differential diagnostic importance.

Evaluation of the aforementioned differential points is worthy of consideration, but hemoglobin analyses are essential to establish the exact hemoglobin defect. The filter paper electrophoretic patterns are distinctive (fig. 5). The F hemoglobin component reaches high levels in the severe forms of Mediterranean anemia. On the other hand, hemoglobin C disease shows no significant change in the F fraction.

MINIMAL MEDITERRANEAN ANEMIA VS. HEMOGLOBIN C TRAIT

The blood changes in the least affected members of the Mediterranean anemia and hemoglobin C families are similar; there were no consistent differences. An occasional stippled cell and ovalocyte were encountered in a few members of the family with Mediterranean anemia; whereas target cells existed without exception in all patients with hemoglobin C. Electrophoretic differentiation, however, is readily made inasmuch as C hemoglobin is easily identified. Although values
for F hemoglobin were normal in patients with the C trait, small increases were invariably noted in members of the family with Mediterranean anemia exhibiting red cell changes.

**Comment**

When in 1949 we reported the cases here re-evaluated, it was reasonable on the basis of blood changes and clinical findings to include the patients that are now known to possess hemoglobin C. In the light of newer knowledge, the presence of large numbers of target cells, microcytosis, hypochromia and relatively higher hemoglobin values are seen to be manifestations of the hemoglobin C abnormality.

This re-evaluation has allowed division of the families according to their respective hemoglobin defects as we now understand them. Until the fundamental reason for the variations within the Mediterranean anemia syndrome are comprehended, it is our intention to retain the term "Mediterranean" to designate the racial origin in most cases.

**Summary**

1. Four Negro patients and their families previously reported in 1949 as examples of Mediterranean anemia were re-evaluated with regard to hemoglobin composition. The data have been presented.
2. Mediterranean anemia was confirmed in one entire family and in the index case of another family.
3. Two entire families and one member of another family were found to possess hemoglobin C.
4. Differential diagnostic points of Mediterranean anemia and hemoglobin C disease are presented.

**Summario in Interlingua**

1. Quatro negros e lor familias, previamente reportate in 1949 como exemplos de anemia mediterranee, esseva re-evalutate con respecto al composition de hemoglobina. Le datos obtenite es presentate.
2. Le presentia de anemia mediterranee esseva confirmate in un familia complete e in le caso indiciat de un altere.
3. Il esseva constatate que duo familias complete e un membro de un altere habeva hemoglobina C.
4. Es presentate detalios de interesse differentio-diagmiostic pro anemia mediterranee e morbo a hemoglobina C.

**References**

MEDITERRANEAN ANEMIA IN THE NEGRO

Mediterranean Anemia in the Negro: A Re-evaluation of Four Patients and Their Families

STEVEN O. SCHWARTZ and WILSON H. HARTZ, JR.

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