Circulating Siderocytes in Human Subjects

By Doris Kurth, A. Deiss and C. E. Cartwright

The occurrence of siderocytes in the blood of splenectomized patients, in the blood of some patients with hemolytic anemia, and particularly in splenectomized patients with persistent hemolytic anemia is well known. More recently, as a result of experimental studies in swine, it has been recognized that the physiologic significance and metabolic behavior of siderotic granules contained within reticulocytes (reticulated-siderocytes or R-S cells) is quite different from such granules contained within non-reticulated, mature erythrocytes (S cells).

Reticulated-siderocytes (R-S cells) were observed in the circulation of iron replete animals during rapid blood regeneration induced by vigorous phlebotomy. The granules in such cells consisted of cytoplasmic aggregates of ferritin. The granules were metabolized by or removed from the cells during maturation in the circulation. The disappearance of the granules was independent of the spleen.

Non-reticulated siderocytes (S cells) were observed in the circulation of animals with a defect in heme synthesis (pyridoxine-deficiency). The granules consisted of non-ferritin iron located within mitochondria. The removal of granules from these cells was dependent upon the spleen.

In view of these differences between the two types of siderocytes in animals, it seemed appropriate to examine the occurrence of iron-containing granules in circulating erythrocytes of human subjects with reference to the type of siderocyte present. Such a study has not been performed heretofore in man.

In this study the cells in the circulation of 80 normal subjects, 7 newborn infants, and 486 patients with a variety of hematologic disorders have been classified into those containing reticulum and no siderotic granules (R cells), those containing reticulum and siderotic granules (R-S cells), and those containing siderotic granules but no reticulum (S cells).
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METHODS

The methods for staining and counting siderocytes and both reticulocytes and siderocytes on the same preparation (double stain) have been published in detail. In all preparations, 1000 cells were examined.

The Prussian blue stain, as described by Rath and Finch,9 was used for staining siderotic granules. Siderocytes counted by this method will be referred to in this paper as “direct-total S cells.” With this stain, the granules stain a vivid blue or blue-green. Reticulum does not stain.

To differentiate reticulum from siderotic granules, the smears were first stained with new methylene blue, then stained for iron with Prussian blue, and finally counterstained with Safranin O.8 This method will be referred to as the “double stain” in this paper. Under these conditions, reticulum stains red and siderotic granules stain blue. Erythrocytes can be differentiated into those which contain reticulum and no siderotic granules (reticulocytes or R cells), those which contain siderotic granules but no reticulum (siderocytes or S cells), and those which contain both reticulum and siderotic granules (reticulated-siderocytes or R-S cells).

In this paper, the total reticulocyte count was obtained from the sum of the R and R-S cells in the double stain. New methylene blue alone cannot be used to determine reticulocytes in the presence of siderocytes because siderotic granules as well as reticulum stain blue and the granules cannot be distinguished from reticulum.8 In individuals without circulating siderocytes, the double stain method usually resulted in somewhat lower values than the direct new methylene blue method.8

The limitations of the methods are considerable and they can be considered to be semiquantitative only. The ability to visualize small granules varies considerably from one observer to the next. In general, the ability of the examiner in detecting small granules increased with experience. In this study, all of the counts were done by a single experienced individual (D.K.).

Siderocytes counted by the direct-total method should be equal to the sum of the R-S and S cells (total S cells) as determined with the double stain. The direct-total S cell method usually resulted in higher values than the total S cell determined on the double stain. Small granules, visible in the direct stain, are less readily visible in the double stain.

The normal subjects were medical students, nurses, laboratory personnel and physicians in the 20 to 40 year age range. Patients presenting to the hematology division were studied in a random fashion. No systematic effort was made to evaluate iron stores. The development of siderocytes is dependent upon the availability of iron5-6 and since the availability of iron was frequently the limiting factor, the data do not distribute in a normal fashion and could not be presented and evaluated by standard methods.

RESULTS

Normal Values

R, R-S and S cell counts and direct-total siderocyte counts were performed on 80 normal subjects and 7 newborn infants. The mean values and the observed ranges are presented in Table 1.

Few R-S or S cells were observed in the blood of normal adult subjects and there was no difference between males and females. The greatest value observed for R-S cells was 0.3 per cent and for S cells, 0.2 per cent. The direct-total S cells did not exceed 0.7 per cent. As shown in Figure 1, the values for the R-S and S cells did not distribute in a normal fashion. In a large proportion of the population, no R-S or S cells were observed.

The blood of newborn infants contained appreciably more R-S and S cells than the blood of normal adult subjects (Table 1).
Eight patients with hemolytic anemia were included in both categories. Therefore the number of patients studied was 486.

### Table 1—Reticulocytes (R Cells), Reticulated-Siderocytes (R-S Cells), and Siderocytes (S Cells) in the Blood of Normal Adults and Normal Newborns

<table>
<thead>
<tr>
<th>Group</th>
<th>No. (%)</th>
<th>Double Stain</th>
<th>Direct Stain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>R Cells</td>
<td>R-S Cells</td>
<td>S Cells</td>
</tr>
<tr>
<td>Adult</td>
<td>1.25</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Males</td>
<td>49</td>
<td>(0.2–3.0)</td>
<td>(0.0–0.2)</td>
</tr>
<tr>
<td>Adult</td>
<td>1.45</td>
<td>0.05</td>
<td>0.01</td>
</tr>
<tr>
<td>Females</td>
<td>31</td>
<td>(0.9–2.5)</td>
<td>(0.0–0.3)</td>
</tr>
<tr>
<td>Combined</td>
<td>1.33</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Adults</td>
<td>80</td>
<td>(0.2–3.0)</td>
<td>(0.0–0.3)</td>
</tr>
<tr>
<td>Newborns</td>
<td>5.39</td>
<td>2.06</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>(3.4–7.1)</td>
<td>(1.2–3.1)</td>
<td>(0.0–0.4)</td>
</tr>
</tbody>
</table>

Figures refer to mean and observed range. Total R cells equals sum of R and R-S cells. Total S cells equals sum of R-S and S cells. Direct-total S cells refers to siderocytes determined by the direct Prussian blue method. For details see Methods.

### Values in Disease

R, R-S and S cells and direct-total siderocyte counts were performed on 486 patients with hematologic disorders (Table 2). Values for total R cells greater than 3.0 per cent, for R cells greater than 3.0 per cent, for R-S cells greater than 1.0 per cent, for S cells greater than 1.0 per cent, and for direct-total S cells greater than 2.0 per cent were arbitrarily chosen as abnormal for the

### Table 2—Frequency of Increased Numbers of Reticulocytes (R Cells), Reticulated-Siderocytes (R-S Cells), and Siderocytes (S Cells) in the Blood of Patients with Various Hematologic Diseases

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Patients</th>
<th>Total R Cells &gt; 3%</th>
<th>R Cells &gt; 3%</th>
<th>R-S Cells &gt; 1%</th>
<th>S Cells &gt; 1%</th>
<th>Direct Total S Cells &gt; 2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolytic Anemia</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Sideroblastic Anemia</td>
<td>11</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>69</td>
<td>19</td>
<td>11</td>
<td>22</td>
<td>49</td>
<td>63</td>
</tr>
<tr>
<td>Splenic Atrophy and Hemolytic Anemia</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Iron Deficiency</td>
<td>12</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Leukemia</td>
<td>71</td>
<td>18</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myelofibrosis</td>
<td>16</td>
<td>12</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Polycythemia</td>
<td>41</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>21</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hodgkin's Disease</td>
<td>29</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>28</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Aplastic Anemia</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Thalassemia (minor)</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Idiopathic Thrombocytopenic Purpura</td>
<td>16</td>
<td>7</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>128</td>
<td>29</td>
<td>29</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Total * | 494 | 144 | 133 | 33 | 58 | 73 |

* Eight patients with hemolytic anemia were studied before and after splenectomy and are included in both categories. Therefore the number of patients studied was 486.
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Fig. 1.—Frequency of occurrence of R cells, R-S cells, S cells, and direct-total S cells in 80 normal adults. Direct-total S cells refers to siderocytes determined by the Prussian blue stain. R cells refers to cells containing reticulum but no siderotic granule; R-S cells refers to cells containing both reticulum and siderotic granules; S cells refers to cells containing siderotic granules but no reticulum.

purposes of analysis of the large amount of data. The selected values are greater than the upper limit of normal for these cells (Table 1) but by this means the conditions associated with definitely increased values could be separated more clearly from the conditions associated with values which were not distinctly increased. In only 36 patients were one or more of the values between the observed upper limit of normal and the arbitrarily selected values.

By the above criteria, increased values for R-S, S, and direct-total S cells were observed only in the following conditions: 1) hemolytic anemia, 2) sideroblastic anemia, 3) post-splenectomy and 4) hemolytic anemia in the presence of splenic atrophy. In all other conditions studied, the values for R-S cells and S cells were less than 1.0 per cent and values for direct-total S cells were less than 2.0 per cent. The data obtained in the above-mentioned four conditions will be presented and analyzed in the sections which follow.

Hemolytic anemia. Studies were performed on 24 patients with a variety
Table 3.—Frequency of Increased Numbers of Reticulocytes (R Cells), Reticulated-Siderocytes (R-S Cells), and Siderocytes (S Cells) in the Blood of Patients with Hemolytic Anemia or Acquired Sideroblastic Anemia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Patients</th>
<th>Total R Cells %, Observed Range</th>
<th>Number of Patients With</th>
<th>R Cells &gt; 3%</th>
<th>R-S Cells &gt; 1%</th>
<th>S Cells &gt; 1%</th>
<th>Direct Total S Cells &gt; 2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolytic Anemia</td>
<td>18</td>
<td>3.2–16.7</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>20.1–46.7</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Sideroblastic Anemia</td>
<td>5</td>
<td>0.1–2.3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>4.0–13.1</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

of hemolytic anemias (Table 3). These anemias included idiopathic acquired hemolytic anemia (12 patients), hereditary spherocytosis (7 patients), paroxysmal nocturnal hemoglobinuria (2 patients), symptomatic acquired hemolytic anemia (2 patients), and hereditary nonspherocytic hemolytic anemia (1 patient).

In the patients with a reticulocytosis (total R cells) of less than 20 per cent, the values for R-S and S cells were all less than 1.0 per cent and less than 2.0 per cent for direct-total S cells. In the 6 patients with severe hemolytic anemia and reticulocyte counts greater than 20 per cent, increased R-S cells were observed in four and increased S cells were observed in three. The maximum value for R-S cells was 31.9 per cent and for S cells, 7.0 per cent. The maximum value for direct-total S cells was 42.2 per cent.

No correlation was observed between the etiology of the hemolytic anemia and the values for the R-S, S and direct-total S cells.

Sideroblastic anemias. Eleven patients with idiopathic acquired sideroblastic anemia were studied (Table 3).

In the five patients with total R cells of 3.0 per cent or less, the R-S cells were less than 1.0 per cent in all five, the S cells were less than 1.0 per cent in four, and the direct-total S cells were less than 2.0 per cent in all five.

In the six patients with a reticulocytosis (total R cells greater than 3.0 per cent), the R-S cells were greater than 1.0 per cent in four, the S cells were greater than 1.0 per cent in two, and the direct-total S cells were greater than 2.0 per cent in four. The maximum value for R-S cells was 4.2 per cent and for S cells, 3.9 per cent. The maximum value for direct-total S cells was 9.6 per cent.

Post-splenectomy. Studies were performed on a total of 69 splenectomized patients (Table 4).

The values for direct-total S cells ranged from 0.2 to 83.9 per cent with an average value of 17.3 per cent. An increase in direct-total S cells was observed in 63 of the 69 splenectomized patients.

The values for S cells ranged from 0.0 to 70.0 per cent with an average value of 8.4 per cent. An increase in S cells was observed in 49 of the 69 splenectomized patients.

In the group of 42 patients splenectomized for traumatic rupture of the spleen, idiopathic thrombocytopenic purpura and hematologic disorders other than hemolytic anemia, the total R cells were more than 3.0 per cent in only
two patients. The R-S cells were greater than 1.0 per cent in only six patients and in these six the values for R-S cells were between 1.3 and 1.9 per cent. The average value for R-S cells in the group of 42 patients was 0.6 per cent.

Twenty-seven patients with hemolytic anemia were splenectomized. In the 10 patients with total R values of 3.0 per cent or less post-splenectomy, the R-S cells were greater than 1.0 per cent in two patients (1.0 and 1.4 per cent). In the 17 patients with total R cell values greater than 3.0 per cent, the R-S cells were greater than 1.0 per cent (1.8 to 45.3 per cent) in 14. In the three patients with R-S values of less than 1.0 per cent, the total R cells were 3.4 to 3.6 per cent. In general, a correlation was observed between the severity of the hemolytic process, as judged by the reticulocyte count, and the increase
in R-S cells. Similarly S cells were more numerous in the 17 patients with persisting hemolysis (mean 16.9 per cent) than in the 10 patients in whom hemolysis did not persist following splenectomy (mean 6.9 per cent).

The rate at which S cells appeared post-splenectomy in subjects with no increase in S cells presplenectomy was studied in 18 patients. In general an increase in siderocytes was observed on the first postoperative day and reached a peak during the first week. In seven patients the direct-total S cells subsequently decreased temporarily following this early maximum. Illustrative examples are presented in Figure 2.

In 38 patients splenectomized more than one week previously for indications other than hemolytic anemia, no correlation was found between the direct-total S cell values and the duration of time after splenectomy (Fig. 3). A tendency for the S cells to decrease over a period of years was not detected.

Hemolytic anemia and splenic atrophy or replacement. Three patients were studied, each of whom had a decreased amount of functional splenic tissue. Patient C.H., with alcoholic cirrhosis of the liver and a malabsorption syndrome, died shortly after the study, and the spleen weighed 30 Gm. Patient E.M. died with disseminated carcinomatosis and the spleen was nearly completely replaced by carcinoma. Patient R.P. had sickle cell anemia with splenic atrophy secondary to splenic infarction.

In each of these patients reticulocytosis was present and in all three increased numbers of R-S and S cells were observed (Table 5). In addition,
Table 6.—Summary of Abnormal Data

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Patients</th>
<th>R-S Cells &gt; 1%</th>
<th>S Cells &gt; 1%</th>
<th>Direct Total S Cells &gt; 2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolytic Anemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retics &lt; 20%</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Retics &gt; 20%</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Sideroblastic Anemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retics &lt; 3%</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Retics &gt; 3%</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Postsplenectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retics &lt; 3%</td>
<td>50</td>
<td>7</td>
<td>34</td>
<td>45</td>
</tr>
<tr>
<td>Retics &gt; 3%</td>
<td>19</td>
<td>15</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Hemolytic Anemia and Splenic Atrophy</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>58</td>
<td>73</td>
<td></td>
</tr>
</tbody>
</table>

The results of this survey indicate that an increase in siderocytes, either R-S cells or S cells, is a relatively infrequent event. An increase in siderocytes was observed only in the following conditions: a) severe hemolytic anemia (total R cells greater than 20 per cent), b) patients with mild hemolysis (total R cells 4.0 to 13.1 per cent) and sideroblastic anemia, c) splenectomized subjects and d) patients with hemolysis and splenic atrophy (Table 6). Siderocytosis in groups (a) and (b) was due primarily to an increase in R-S cells. Siderocytosis in splenectomized patients in the absence of evidence of increased red cell production was due to an increase in S cells. An increase in both R-S and S cells was observed in patients with splenic atrophy or post-splenectomy in the presence of increased red cell production (reticulocytosis).

The studies in the human subjects reported here are similar to those in the pig in that rapid blood regeneration, in the presence of adequate iron stores and in the presence of the spleen, was associated with an increase in R-S cells and little or no increase in S cells. However, a striking difference between the two species has been noted in another respect. A significant increase in S cells was observed in hematologically normal splenectomized human subjects in typical post-splenectomy changes, such as target cells and Howell-Jolly bodies, were observed on the blood smear of each.
this study, whereas a significant increase in S cells was not observed to follow splenectomy of hematologically normal pigs. A possible explanation for the difference between the two species is given in Figure 4. It must be understood that it is only one of several possible explanations and it contains a number of unproved assumptions.

Most R-S cells in the bone marrow mature to R cells (pathway a) under normal circumstances. R cells are delivered to the circulation (pathway b). Once in the blood reticulocytes mature to normal adult erythrocytes (pathway c). Normally, only a few R-S cells are found in the blood of either the pig or man (Table 1). Most of the siderocytes in the blood of either species, under normal conditions, are contained within reticulocytes (R-S cells). Therefore, it seems unlikely that S cells are delivered from the marrow to the blood in appreciable numbers.

When the rate of erythropoiesis is greatly accelerated, R-S cells are delivered to the circulation in increased numbers (pathway d) in both pigs and man.

Pig R-S cells contain an intrinsic mechanism for the metabolism of the siderotic granule (pathway e) and the rate of metabolism of the granule exceeds the rate of loss of reticulum. Hence an R-S cell is converted to an R cell. This process is entirely unrelated to the spleen in the pig. It has been shown that when R-S cells from the pig are incubated in vitro, the granules disappear rapidly from the reticulocyte. Furthermore, following transfusion of blood containing large numbers of R-S cells, the granules in the R-S cells disappear from the circulation of splenectomized recipients at the same rate as from the circulation of spleen-intact recipients.

Fig. 4.—Possible pathways of R cell, R-S cell, and S cell origin and maturation.
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Apparently in man, the intrinsic mechanism for metabolizing siderotic granules (pathway e) is not as active as in the pig since S cells accumulate following splenectomy of otherwise normal individuals. The reticulum matures first leaving an S-cell (pathway f). The granules in the S-cells are then removed from the cells by the spleen (pathway g), as shown by Crosby. Whether or not the human spleen can remove granules from R-S cells is unknown (pathway h). The studies contained in this paper do not provide an answer to this question.

The above hypothesis provides an explanation for the observation that S cells increase in the circulation of normal man but not normal pigs following splenectomy and is in harmony with our other observations concerning circulating siderocytes in both man and pigs.6

SUMMARY

The number of circulating erythrocytes containing reticulum and no siderotic granules (R cells), both reticulum and siderotic granules (R-S cells), and siderotic granules and no reticulum (S cells) was determined in 80 normal adults, 7 normal newborns and 486 patients with hematologic disorders.

Few R-S cells (maximum 0.3 per cent) or S cells (maximum 0.2 per cent) were observed in the blood of normal adults. The number of siderocytes as observed in the direct Prussian blue method (direct-total siderocytes) did not exceed 0.7 per cent. R-S cells greater than 1.0 per cent and direct-total siderocytes greater than 2.0 per cent were observed in each of 7 normal newborns.

Among the 486 patients, R-S cells more numerous than 1.0 per cent, S cells greater than 1.0 per cent, or direct-total siderocytes greater than 2.0 per cent were observed only in four conditions. Increases in R-S cells were seen in patients with severe hemolytic anemia and in patients with sideroblastic anemia associated with mild hemolysis. Increases in S cells were seen in splenectomy patients in the absence of hemolysis. Increases both in R-S cells and S cells were seen in patients with splenic atrophy or replacement and in splenectomized patients in the presence of hemolysis.

SUMMARIO IN INTERLINGUA

Le numero de erythrocytos circulante que contine reticulo sed nulle granulos siderotic (cellulas R), reticulo e granulos siderotic (cellulas R-S), e granulos siderotic e nulle reticulo (cellulas S) esseva determinate in 80 adultos normal, 7 neonatos normal, e 486 patientes con disordines hematologic.

Pauc cellulas R-S e S (al plus 0,3 e 0,2 pro cento, respectivemente) esseva observate in le sanguine de adultos normal. Le numero de siderocytos observate per medio del direkt metodio a blau prusse (total direkt de siderocytos) non exceedeva 0,7 pro cento. Cellulas R-S in excesso de 1,0 pro cento e totals direkt de siderocytos in excesso de 2,0 pro cento esseva observate in cata-un de 7 neonatos normal.

Inter le 486 patientes, cellulas R-S amontante a plus que 1,0 pro cento, cellulas S amontante a plus que 1,0 pro cento, o totals direkt de siderocytos amontante a plus que 2,0 pro cento esseva observate solo in quatro conditiones. Augmentos in cellulas R-S esseva vidite in patientes con sever anemia hemolytic e in
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patientes con anemia sideroblastic associate con leve hemolyse. Augmentos in cellulas S esseva vidite in patientes splenectomisate quando hemolyse non esseva presente. Augmentos in cellulas R-S e cellulas S esseva vidite in patientes con atrophia o reimplacamento splenic e in patientes splenectomisate quando hemolyse esseva presente.

REFERENCES

Circulating Siderocytes in Human Subjects

DORIS KURTH, A. DEISS and G. E. CARTWRIGHT

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