Observations on Erythrocyte and Plasma Cholinesterase Activity in Dyscrasias of the Blood

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The purpose of this investigation was (1) to establish erythrocyte cholinesterase activity levels in healthy individuals, using a new technic, (2) to determine erythrocyte and plasma cholinesterase activities in patients suffering with various blood dyscrasias and (3) to study the changes in cholinesterase activity of the blood during therapy of patients ill with hypoplastic anemia, pernicious anemia or macrocytic anemia of nontropical sprue. Even though some data have been reported on these subjects, additional information is required to establish and to explain the relationship of erythrocyte and plasma cholinesterase activity to normal or disturbed hematopoiesis.

Low erythrocyte or whole blood cholinesterase activity has been observed previously in patients ill with pernicious anemia in relapse, acute leukemia, aplastic anemia or myelophthisic anemia; high enzyme activity, in pernicious anemia during early remission, sickle cell anemia or hypochromic, normocytic anemia; and normal activity, or variations in results, in other blood dyscrasias. Serum or plasma cholinesterase activity has been reported as low in patients ill with various types of severe anemia, hypochromic anemia and hemolytic anemia, acute myeloid leukemia, or pernicious anemia in relapse.

In patients suffering with pernicious anemia, the erythrocyte cholinesterase activity increased from low to abnormally high levels with adequate therapy and then returned to normal. The plasma cholinesterase activity gradually changed from initial low to normal levels, during therapy, but never increased above normal. Several theories have been advanced to account for the relationship of erythrocyte cholinesterase activity to erythropoiesis, especially in pernicious anemia, but each one has certain limitations.

Methods

Patient material. Plasma and erythrocyte cholinesterase activities were determined on blood samples obtained from 20 healthy men and women, varying in age from 20 to 60 years, and from 20 patients ill with various blood dyscrasias. Blood specimens were obtained before therapeutic measures were instituted, except as noted in the text. Determinations of liver function tests and of serum total protein and albumin were made on blood from most patients.
of the patients, using the methods outlined elsewhere.\textsuperscript{26} Serial hematologic and blood cholinesterase studies were made before and during therapy in 1 patient ill with hypoplastic anemia, in 4 with pernicious anemia and in 1 with a macrocytic anemia associated with nontropical sprue. Body weights were recorded each day and frequent observations were made of the clinical status of the patients.

Hematologic observations. Venous blood was collected in heparinized tubes. The hematocrit, total hemoglobin, erythrocyte and reticulocyte counts were determined on each specimen. In addition, white blood cell, differential and platelet counts were made on most specimens of blood obtained from the patient ill with hypoplastic anemia. Examinations of sternal marrow were made before and one or more times during therapy. The mean corpuscular volume (M.C.V.) and the mean corpuscular hemoglobin (M.C.H.) were calculated by the usual formulas.

Cholinesterase activity. The cholinesterase activity of the erythrocytes and plasma was determined by the electrometric method of Michel\textsuperscript{17} and recorded as the change of pH with time ($\Delta$ pH/hr.). A red cell solution was prepared from the heparinized blood sample by separating the plasma and then washing the red cells with 0.9 per cent sodium chloride solution and diluting as described by Michel.\textsuperscript{17} Both the plasma and the washed red cell mixture were placed in a deep-freeze cabinet (\(-16\) C.) to hemolyze the red corpuscles and to preserve the cholinesterase until the measurement of the enzyme activity was made.

The capacity of a buffer solution used in the erythrocyte determinations is more than three times that used for plasma, which explains why the erythrocyte cholinesterase activity appears to be less than that of the plasma by this method. With other methods the red cell cholinesterase activity is much greater than that of the plasma per unit volume.\textsuperscript{13, 14, 20, 22, 25} Since acetylcholine bromide or chloride is used as a substrate, Michel's method measures only the ability of enzyme(s) in the erythrocytes or plasma to hydrolyze the acetyl radical. No attempt was made to characterize the enzymes or to differentiate the various types of cholinesterase by using different substrates as suggested by Zeller and his associates.\textsuperscript{27}

The mean corpuscular cholinesterase activity (M.C.E.) was calculated by multiplying the erythrocyte cholinesterase activity in 0.1 ml. of packed red cells by the mean corpuscular volume with appropriate corrections as suggested by Sabine\textsuperscript{26} and Sawitsky et al.\textsuperscript{23} and expressed as ($\Delta$ pH/hr.) $\times 10^{-8}$. As we shall show, the relative M.C.E. value, in most instances, varies in about the same manner as the red cell cholinesterase activity.

RESULTS

Blood Cholinesterase Activity in Healthy Individuals

The mean erythrocyte cholinesterase activity of the blood from 20 healthy men and women was $0.71 \pm 0.11 \Delta$ pH/hr.\textsuperscript{*} with an actual range from 0.55 to 0.99 $\Delta$ pH/hr. The normal range\textsuperscript{†} was from 0.49 to 0.93 $\Delta$ pH/hr. The mean value compares favorably with that reported by Michel.\textsuperscript{17} The average M.C.E. was $(0.68 \pm 0.11) \times 10^{-9} \Delta$ pH/hr. Hematologic data from the healthy subjects were within the normal range. No correlation was found between the erythrocyte cholinesterase activity and the red cell count, hemoglobin, M.C.V., M.C.H., age or sex. The mean plasma cholinesterase activity was $0.98 \pm 0.17 \Delta$ pH/hr. with a normal range of 0.62 to 1.30 $\Delta$ pH/hr., which is in close agreement with the values reported previously.\textsuperscript{25}

Blood Cholinesterase Activity in Various Blood Dyscrasias

\textit{Erythrocyte cholinesterase activity}. Blood cholinesterase studies of 6 patients with macrocytic anemia are shown in table 1. The 4 patients ill with pernicious

\textsuperscript{*} Mean plus or minus the standard deviation.
\textsuperscript{†} Normal range is represented by the mean plus or minus two standard deviations.
anemia in relapse and 1 patient ill with nontropical sprue had low erythrocyte cholinesterase activity and will be reported in greater detail later in the text. Normal erythrocyte cholinesterase activity was observed in blood from the patient in hematologic remission.

**TABLE 1.—Erythrocyte and Plasma Cholinesterase Activity in Blood from Patients Ill with Macrocytic Anemia**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Hematologic Data</th>
<th>Cholinesterase Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>J. E.</td>
<td>73</td>
<td>M</td>
<td>Pernicious anemia in relapse; subacute combined degeneration of cord.</td>
<td>1.20</td>
<td>0.35 0.17 0.21</td>
</tr>
<tr>
<td>L. W.</td>
<td>68</td>
<td>F</td>
<td>Pernicious anemia in relapse; subacute combined degeneration of cord.*</td>
<td>2.00</td>
<td>0.36 0.65 0.65</td>
</tr>
<tr>
<td>G. P.</td>
<td>54</td>
<td>F</td>
<td>Pernicious anemia in relapse.</td>
<td>1.42</td>
<td>0.59 0.48 0.61</td>
</tr>
<tr>
<td>M. R.</td>
<td>69</td>
<td>F</td>
<td>Pernicious anemia in relapse.*</td>
<td>1.74</td>
<td>0.69 0.63 0.79</td>
</tr>
<tr>
<td>T. S.</td>
<td>56</td>
<td>M</td>
<td>Pernicious anemia in remission.</td>
<td>4.32</td>
<td>0.82 0.86 0.87</td>
</tr>
<tr>
<td>J. M.</td>
<td>66</td>
<td>M</td>
<td>Nontropical sprue.</td>
<td>1.66</td>
<td>0.32 0.60 0.65</td>
</tr>
</tbody>
</table>

* Therapy started a few days before these determinations were made.

**TABLE 2.—Erythrocyte and Plasma Cholinesterase Activity in Blood from Patients Ill Due to Blood Loss Anemias**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Hematologic Data</th>
<th>Cholinesterase Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. S.</td>
<td>44</td>
<td>F</td>
<td>Duodenal ulcer; chronic bleeding.</td>
<td>2.13</td>
<td>0.54 0.75 0.75</td>
</tr>
<tr>
<td>F. H.</td>
<td>47</td>
<td>M</td>
<td>Acute gastritis. Diverticulitis; acute bleeding.</td>
<td>2.50</td>
<td>0.48 0.96 0.95</td>
</tr>
<tr>
<td>M. W.</td>
<td>62</td>
<td>F</td>
<td>Duodenal ulcer; acute bleeding.</td>
<td>2.55</td>
<td>0.34 0.68 0.68</td>
</tr>
<tr>
<td>G. W.</td>
<td>36</td>
<td>M</td>
<td>Carcinoma transverse colon; recent bleeding.</td>
<td>2.82</td>
<td>0.82 1.08 0.99</td>
</tr>
<tr>
<td>J. D.</td>
<td>65</td>
<td>M</td>
<td>Adenocarcinoma jejunum.</td>
<td>2.96</td>
<td>0.71 0.67 0.68</td>
</tr>
<tr>
<td>J. B.</td>
<td>68</td>
<td>M</td>
<td>Carcinoma prostate.</td>
<td>2.97</td>
<td>0.72 0.67 0.68</td>
</tr>
<tr>
<td>J. M.</td>
<td>44</td>
<td>M</td>
<td>Hepatic cirrhosis.</td>
<td>3.24</td>
<td>0.24 0.58 0.58</td>
</tr>
<tr>
<td>P. K.</td>
<td>50</td>
<td>M</td>
<td>Atrophic gastritis; acute bleeding.</td>
<td>3.50</td>
<td>0.46 1.01 1.01</td>
</tr>
</tbody>
</table>

Mean ........................................ 0.54 0.80 0.79
The hematologic data and cholinesterase studies on the blood from 8 patients ill with anemia as a result of hemorrhage are listed in table 2. The average erythrocyte cholinesterase activity was 0.80 Δ pH/hr. The M.C.E. was 0.80 × 10⁻⁴ Δ pH/hr. In 3 of 4 patients in whom anemia was due to acute hemorrhage, the erythrocyte cholinesterase activities were above the normal range and higher than in the 4 who were suffering from chronic blood loss.

Observations on blood from 6 patients ill with other dyscrasias are recorded in table 3. Low erythrocyte cholinesterase activity was found in 1 patient ill with Hodgkin's disease and another ill with hypoplastic anemia. In the remainder of these patients the erythrocyte cholinesterase activity was normal.

**PLasma cholinesterase activity.** The values for plasma cholinesterase activity in patients suffering with various blood dyscrasias are indicated in tables 1, 2 and 3. In patients ill with nontropical sprue or pernicious anemia in relapse,

<table>
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<tr>
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<th>Cholinesterase Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. C.</td>
<td>30</td>
<td>M</td>
<td>Hypoplastic anemia: &quot;Methan&quot; toxicity. Epilepsy.</td>
<td>R.B.C. (M. ca. /mm³) 1.16</td>
<td>Plasma (Gph/hr) 0.66</td>
</tr>
<tr>
<td>L. D.</td>
<td>43</td>
<td>M</td>
<td>Chronic lymphocytic leukemia.</td>
<td>Hgb. (Gm./100 ml) 5.0</td>
<td>0.13</td>
</tr>
<tr>
<td>G. D.</td>
<td>31</td>
<td>M</td>
<td>Cooley's anemia.</td>
<td>M.C.V. (μ) 1.4</td>
<td>0.15</td>
</tr>
<tr>
<td>D. H.</td>
<td>26</td>
<td>F</td>
<td>Hodgkin's disease mild.</td>
<td>M.C.H. (g/) 26</td>
<td>0.13</td>
</tr>
<tr>
<td>R. S.</td>
<td>18</td>
<td>F</td>
<td>Polycythemia. Pulmonary stenosis; patent foramen ovale.</td>
<td>Plasma (Gph/hr) 0.71</td>
<td></td>
</tr>
<tr>
<td>K. L.</td>
<td>56</td>
<td>F</td>
<td>Polycythemia vera.</td>
<td>Plasma (Gph/hr) 0.50</td>
<td></td>
</tr>
</tbody>
</table>

the plasma cholinesterase activity was definitely below the normal range. The average plasma cholinesterase activity of 8 patients suffering with anemias resulting from hemorrhage was only 0.54 Δ pH/hr., considerably below normal. However, in 3 of these patients (G. W., J. D. and J. B.), the plasma cholinesterase activity was within the limits of normal. Of all the other patients studied only 1 (G. D.), ill with Cooley's anemia was found to have low plasma cholinesterase activity.

Usually plasma cholinesterase activity reflected the general clinical condition or state of debility of the patients. There was no definite correlation between a variety of liver function tests and cholinesterase activity in the patients in whom these tests were done. A comparison between the plasma cholinesterase activity and the serum albumin in healthy individuals, in patients suffering with various blood dyscrasias and in patients ill with cirrhosis of the liver is shown in figure 1. Low albumin concentrations of the serum were, in most instances, associated with low plasma cholinesterase activities.
Changes in Hypoplastic Anemia During Therapy

Case history.* D. C., a 30 year old white male, had been suffering from epilepsy since the age of 14. Since June 13, 1947, he had been treated with “Dilantin” (diphenyl-hydantoin sodium), Phenobarbital (phenylethyl-barbituric acid), “Mesantoin” (3-methyl-5,5-phenylethyl-hydantoin) and “Thyphenytoin” (5,5-phenylthienyl-hydantoin). On August 31, 1948 a diagnosis of hypoplastic anemia as a result of “Mesantoin” therapy was established. All anticonvulsant medication was withheld for several days, but later “Dilantin” and Phenobarbital were given to control his convulsive disorder. Between August 31 and September 7, 1948, 4,600 ml. of whole blood were given in multiple transfusions. He was given

2 units of crude liver extract intramuscularly every other day from September 3, 1948 until he was discharged on November 9. Thiamine hydrochloride 50 mg. was injected intramuscularly each day and later given by mouth; “Hykinone” (Menadione sodium bisulfite) 2.4 mg. daily, intramuscularly; and vitamin C, at first 500 mg. intramuscularly each day and later 200 mg. daily by mouth.

Hematologic and cholinesterase changes. The details of the hematologic response and cholinesterase changes during therapy are illustrated in figure 2. The eryth-
erythrocyte count and hemoglobin increased rapidly following the blood transfusions, then relapsed slightly until a mild reticulocyte response occurred (maximum 6.9 per cent), when a more permanent rise was noted. During the period of observation the platelets remained low, but there was a gradual increase in leukocytes and improvement in clinical status. The bone marrow changed from extremely hypocellular with lymphocytic infiltration to normocellular with normoblastic reaction.

The plasma cholinesterase activity was at a low normal level of 0.66 $\Delta$ pH/hr. on admission and only varied between 0.65 and 0.71 $\Delta$ pH/hr. during the entire seven month period of observation.

Initially, the erythrocyte cholinesterase activity was extremely low (0.13 and 0.12 $\Delta$ pH hr.) but, after the whole blood transfusions, it increased abruptly to 0.67 $\Delta$ pH hr. Later there was a slight drop to 0.59 $\Delta$ pH hr. but, shortly after the onset of the reticulocyte response, the erythrocyte cholinesterase activity increased to 0.80 $\Delta$ pH hr. The calculated M.C.E. values paralleled the curve of erythrocyte cholinesterase activity. The M.C.V. remained constant except for a small increase at the time of the final peak in erythrocyte cholinesterase activity.
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Changes in Pernicious Anemia and Nontropical Sprue During Therapy

Case 1. J. E., a 73 year old white man known to have pernicious anemia for eighteen years, was now suffering from pernicious anemia in relapse complicated with subacute combined degeneration of the cord and a peripheral blood picture as shown in table 1. He was treated with an oral liver fraction daily for the first twenty-seven days of study, 15 units of liver extract injected intramuscularly each day, for the next nineteen days, and then three times a week thereafter. His general condition began to improve on about the sixteenth day of study, and progressed slowly thereafter with gradual improvement of function in his extremities. The bone marrow smears on the thirty-third day of therapy revealed moderate normoblastic hyperplasia, but on the one hundred and eighth day were normal.

Before treatment the cholinesterase activity of the blood was very low as shown in table 1 and figure 3. The erythrocyte cholinesterase activity began to increase on the sixth day, reached a plateau in the normal range on the thirty-eighth day and dropped to a low normal level by the sixty-fifth day. The M.C.E. followed this same pattern. The number of reticulocytes also began to increase on the sixth day, reached a maximum of 17 per cent on the sixteenth day and returned to basal levels by the twenty-fourth day. Changes in M.C.V. and M.C.H. did not coincide with any of the enzyme changes. The plasma cholinesterase activity started to increase on the twentieth day and slowly reached a low normal level. The erythrocyte count, hemoglobin and body weight increased slowly, parallel with the changes in plasma cholinesterase activity.
Case 2. G. P., a 54 year old white woman, had a seven month history of a severe anemia, which had not responded to iron therapy. A diagnosis of pernicious anemia was established with a peripheral blood picture as listed in table 1. She was treated with an oral liver fraction daily for twenty-eight days and 15 units of a purified liver extract injected intramuscularly three times a week thereafter. Four intramuscular injections of di-isopropyl fluorophosphate (DFP), 1 mg. each, were given between the twenty-fourth and thirty-sixth days. The patient's general condition began to improve after one week of treatment and continued thereafter. The bone marrow smears were normal on the fifty-fifth day.

![Graph showing changes in erythrocyte and plasma cholinesterase activity and hematologic response to treatment.]

Before therapy the cholinesterase activity of the blood was markedly reduced as shown in table 1 and figure 4. The erythrocyte cholinesterase activity began to increase on the fifth day, reached a maximum of 0.96 Δ pH/hr. on the nineteenth day, declined abruptly when DFP was administered and then returned to a low normal level. The M.C.E. followed a similar pattern. A good reticulocyte response was observed, beginning on the second day, reaching 27 percent by the tenth day and then returning to normal. The red cell count and the hemoglobin increased rapidly at first and then slowly. When DFP was given, the number of erythrocytes continued to rise despite the suppression of cholinesterase activity. The M.C.V. and M.C.H. slowly decreased to normal. The plasma cholinesterase activity did
not change until it was diminished by the administration of DFP. Thereafter it regenerated
to original levels in twenty-one days and then gradually increased to normal. The body
weight began to increase slowly after the twenty-second day.

Case 3. M. R., a 69 year old white woman, known to have pernicious anemia for fifteen
years, was admitted to the hospital because of a hematologic relapse (table 1). She was
treated with 15 units of parenteral liver extract and 15 µg of vitamin B₁₂ periodically as
indicated in figure 5. This patient improved gradually during her stay in the hospital.

This patient had received 15 units of liver extract one week before admission and a reticulocyte response was in progress. During her stay in the hospital three separate reticulocyte responses of 21, 11 and 17 per cent respectively were observed (fig. 5). The erythrocyte

![Graph of erythrocyte and plasma cholinesterase activity.](image)

**Fig. 5.**—The changes in erythrocyte and plasma cholinesterase activity and the hema-
tologic response of a patient (M. R.), suffering with pernicious anemia in relapse, during
treatment with parenteral liver extract and vitamin B₁₂.

Cholinesterase activity was at a low normal level (0.63 Δ pH/hr.) when first measured, after
the first reticulocyte response had started, but increased to a peak about ten days after the
first reticulocyte response and then declined slightly. There was a suggestion of a second
rise ten days after the second reticulocyte response, but the cholinesterase activity was
still increasing when the third prolonged reticulocyte response started. This increase was
followed by a slight decrease in erythrocyte cholinesterase activity to a high normal value.
The M.C.E. reflected these same changes but the M.C.V. and M.C.H. did not. The hemoglo-
in, erythrocyte count and plasma cholinesterase activity increased slowly to normal
levels during therapy. The body weight remained constant.

Case 4. L. W., a 68 year old white woman, was suffering from pernicious anemia and sub-
acute combined degeneration of the cord with a peripheral blood picture as listed in table
She was given a 500 ml. whole blood transfusion on admission and then 15 units of a purified liver extract intramuscularly each day. The patient's general condition improved slowly but the vibratory and position sensations were still absent from her toes when she was discharged on the twenty-sixth day of therapy.

The erythrocyte cholinesterase activity was at a low normal level (0.65 Δ pH/hr.), when first measured on the fourth day, but gradually increased to 0.92 Δ pH/hr. by the twenty-sixth day of therapy (fig. 6). The M.C.E. varied in essentially the same manner. There was a mild reticulocyte response of 13 per cent by the ninth day. The M.C.V. and M.C.H. did not vary significantly. The erythrocyte count, hemoglobin and plasma cholinesterase activity improved slowly.

Case 5. Nontropical sprue. J. M., a 66 year old white man, was admitted to the hospital with a history of intermittent diarrhea. Laboratory studies revealed a fecal steatorrhea; histamine achlorhydria; deficiency pattern on small intestine roentgenograms; normoblasts, megaloblasts and myeloid left shift in sternal marrow smears; and a peripheral blood picture as shown in table 1. A diagnosis of a macrocytic anemia associated with nontropical sprue was established. Vitamin B₁₂ in 15 μg. doses was injected intramuscularly on the first and nineteenth days of study and at more frequent intervals from the thirty-first to forty-second days. The number of bowel movements gradually decreased until the pa-
The patient was having only one to three fairly well-formed stools a day and his general physical condition improved considerably.

The erythrocyte cholinesterase activity (fig. 7) was at a low normal level (0.60 and 0.52 Δ pH/hr.). Two days after the peak reticulocyte count of 41 per cent and seven days after the injection of 15 μg. of vitamin B₁₂ the erythrocyte cholinesterase activity had increased to 0.77 Δ pH/hr. then dropped slightly, but gradually increased to 0.95 Δ pH/hr. two days after the peak of a second reticulocyte response of 14 per cent. There was a third and final increase in erythrocyte cholinesterase activity to 1.01 Δ pH/hr. which followed a third series of vitamin B₁₂ injections. It is possible that a third reticulocyte response oc-

curred at this time but reticulocyte counts were not done during this period. The M.C.E. varied in a similar pattern. The M.C.V. and M.C.H. revealed marked variations, in part related to the number of reticulocyte or young cells. The erythrocyte count, the total hemoglobin and the plasma cholinesterase activity, which was very low initially (0.32 Δ pH/hr.), began increasing on about the seventh day and gradually reached normal values. The body weight fluctuated considerably.

DISCUSSION

In patients suffering with blood dyscrasias the plasma cholinesterase activity seems to be related to their general clinical status and, in most instances low
plasma cholinesterase activity is associated with low albumin concentrations in the serum. The low enzyme activity may be related to minimal liver damage, which is not reflected by less sensitive tests of liver function, or to the state of nutrition. The slow rate of improvement in plasma cholinesterase activity during therapy for hypoplastic anemia, pernicious anemia or nontropical sprue seemed to parallel changes in erythrocyte count, total hemoglobin and body weight and to reflect clinical improvement. The rate of regeneration of plasma cholinesterase in pernicious anemia following suppression with D.F.P. is similar to that observed in healthy individuals or patients ill with liver disease.

The low erythrocyte cholinesterase activity observed in the patient severely ill with hypoplastic anemia probably was associated in some manner with the depression of bone marrow activity. The initial rise in erythrocyte cholinesterase activity noted in this patient evidently was the result of the whole blood transfusions, either by simple addition of or by stimulation of enzyme formation. Discontinuation of “Mesantoin,” which apparently was toxic may have played a role in this early response. Barnard and Mentha found that multiple blood transfusions produced an increase in the blood cholinesterase activity. However, Barnard later wrote that the erythrocyte cholinesterase activity is quickly lost from transfused blood and Michelson found that blood stored in a blood bank lost up to 50 per cent of the erythrocyte cholinesterase activity after a week at 2 to 4 C. The final rise in erythrocyte cholinesterase activity in this patient to high normal values closely followed a reticulocyte response and preceded a rise in total number of erythrocytes to normal.

The erythrocyte cholinesterase activity was low in the patients suffering with pernicious anemia or macrocytic anemia of nontropical sprue, but it increased rapidly during adequate therapy to high values and later returned to normal levels. The onset of this increase in erythrocyte cholinesterase activity began at the same time as, or within six days after, the onset of the reticulocyte response. The maximum enzyme activity was attained from two to twenty-two days after the peak of the reticulocyte response. In 2 patients, in whom two or more reticulocyte responses developed there were corresponding fluctuations in cholinesterase activity. The return to normal levels occurred when the rate of erythropoiesis began to decline and the erythrocyte count approached normal levels. There was no close correlation between the changes in erythrocyte cholinesterase activity and those observed in the number of erythrocytes, total hemoglobin, M.C.V. or M.C.H.

The findings of low erythrocyte cholinesterase activity in the blood of patients ill with anemias where there is bone marrow depression and of high enzyme activity in patients showing a reticulocytyosis, suggest that the erythrocyte cholinesterase activity may be related to erythropoiesis and reticulocytyosis. In support of this concept it has been shown that erythrocyte cholinesterase activity can be suppressed by DFP without altering the erythrocyte count, but the enzyme regenerates at a rate which approximates the calculated rate of red cell replacement and which is proportional to the number of circulating reticulocytes. Furthermore, Pritchard and Sabine have shown quite conclusively that significantly greater cholinesterase is present in reticulocytes or young red cells than in the older or mature erythrocytes. Sabine also has indicated that cholin-
Estherase activity can be used as a test of bone marrow function in severe anemias. The normal values for erythrocyte cholinesterase activity in some chronic leukemias and the paucity of data on enzyme activity in hemolytic anemia are the main weaknesses in this hypothesis.

The changes in erythrocyte cholinesterase activity evidently are the resultant of alterations in erythropoiesis and reticulocytosis. The low erythrocyte cholinesterase activities are associated with decreased erythropoiesis due to bone marrow depression and fewer young red cells rich in cholinesterase being released into the circulation. The high erythrocyte cholinesterase activity is produced by the release of reticulocytes rich in enzyme during increased erythropoietic activity. The continuation of the increase in erythrocyte cholinesterase activity, after the reticulocyte response in pernicious anemia is complete, may be explained by the maturation of reticulocytes to young cells, which still contain large amounts of enzyme. Normal erythrocyte cholinesterase activity is present when there is a balance between the numbers of young and mature red cells in the peripheral blood. It is possible that the erythrocyte cholinesterase activity may be a more accurate index of hematopoiesis than the reticulocyte count.

**Summary**

1. Erythrocyte and plasma cholinesterase activities of the blood were determined by Michel’s potentiometric method in 20 healthy individuals and in 20 patients ill with various blood dyscrasias.

2. The mean erythrocyte cholinesterase activity in the blood of healthy individuals was 0.71 ± 0.11 Δ pH/hr. and the mean plasma cholinesterase activity was 0.98 ± 0.17 Δ pH/hr.

3. Low erythrocyte cholinesterase activity was found in the blood of patients ill with pernicious anemia or ill with hypoplastic anemia.

4. High erythrocyte cholinesterase activity was found in the blood of patients suffering with anemia secondary to hemorrhage and of patients ill with pernicious anemia or macrocytic anemia of nontropical sprue in early remission.

5. The plasma cholinesterase activity of blood from patients ill with blood dyscrasias usually reflected the general clinical status of the patients and, in general, was related to the albumin concentration in the serum.

6. The low erythrocyte cholinesterase activity increased following multiple blood transfusions and during a reticulocyte response in a case of hypoplastic anemia, whereas the plasma cholinesterase activity remained unchanged.

7. The erythrocyte cholinesterase activity in patients ill with pernicious anemia or macrocytic anemia of nontropical sprue increased rapidly during therapy beginning with the reticulocyte response and continuing during the period of increased erythropoietic activity. The plasma cholinesterase activity increased slowly parallel to improvement in hematologic and clinical status.

8. The possible relationships between alterations in erythrocyte cholinesterase activity in blood dyscrasias and reticulocytosis and erythropoiesis are discussed.

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H. H. SCUDAMORE, L. J. VORHAUS AND R. M. KARK


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