A study on schizophrenia : On the erythroeytes

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A study on schizophrenia: On the erythrocytes

Mutsutoshi Kosaka

Abstract

Blood cells of schizophrenics differ in many points from those of normal subjects. First of all the shape of them is flat and thin. This tendency is more marked in old group than in new group; the volume is small; flat corpuscles are more numerous in them in the normal; and the blood resistance against diluted saline solution is stronger than that of the normal. It has long since been known that the rate of corpuscle sedimentation is being accelerated in schizophrenics. A simple physical cause that blood corpuscles are flat and numerous can explain this phenomenon. It is said that there is an antisphering substance among the factors controlling the thickness and roundness of blood corpuscles. Yet it has not been determined whether this substance on the surface of the blood of schizophrenics is large or small. Blood corpuscles are said to lose their peculiar disc-shape and to be completely destroyed at the pH of 9.2 when the antisphering substance is removed from the surface of blood corpuscles. The lower the pH is the better is the absorption of this substance on the surface of blood corpuscles; and it seems that the more this substance attaches itself to blood corpuscles the greater is the degree of flatness and in this connection it is interesting to note that the pH of schizophrenic blood is low in general. On the other hand, however, sphericity is increased at the time when the acidity of blood is increased due to a sudden movement of acidic substances immediately after ECT. Again in the case of coma of insulin treatment, blood tends to be alkaline and even then an increase in the sphericity of corpuscles is indicated. Consequently it seems that the roundness of blood corpuscles is not solely dependent upon antisphering substance and pH.
A STUDY ON SCHIZOPHRENIA: ON THE ERYTHROCYTES

By

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Anyone who designs to carry out biological studies on schizophrenic pathology would generally select blood as the material for the study first of all. The author previously performed analyses of gas-picture in the brain and physical blood. As the results it was found that there existed a brain type and a somatic type as the criteria of aggravated schizophrenia, and that the respiratory quotient in the brain blood for an example at the early stage of the disease was as low as 0.4—0.8, showing aggravation, but at the chronic stage it gradually approached the normal value 1.0 while somatic criteria in the arterial blood such as alkaline reserve (AR), CO₂-contents and pH on the contrary were found to remain continuously below the normal values in majority of cases (Fig. 1).

Fig. 1.
In view of these, two or three problems such as carbonic anhydrase in erythrocytes, the metabolism of blood cells themselves, and morphology and characteristics of erythrocytes were taken up in order to pursue somatic changes still further.

Methods

Carbonic anhydrase (CA) of blood cells was prepared by Meldrum Roughton's method \(^2\) (raw enzyme liquid not refined by crystallization) and by using Warburg's apparatus \(\text{CO}_2\) release from the substrate \(\text{NaHCO}_3\) was measured at \(15^\circ\text{C}\) and made it CA-activity. As for the determination of the metabolism of blood cells, Ringer suspension was prepared by adding glucose to erythrocytes and with Warburg's apparatus by current method the \(\text{O}_2\)-consumption (\(\text{XO}_2\)), \(\text{CO}_2\)-output (\(\text{XCO}_2\)), \(\text{R. Q.}\), aerobic glycolysis (\(\text{X}_{\text{O}}\)), anaerobic glycolysis (\(\text{X}_{\text{N}}\)), and Meyerhof Quotient (M. Q.) were measured \(^3\). The morphology of erythrocytes is mainly of the relationship between their diameter and thickness while their characteristics are of specific gravity, Ht., blood count, resistance and spheric index; and as for the resistance Ribiere's method involving diluted saline solution was used. Further, in connection with the resistance the rate of appearance of Heinz body upon the addition of \(\text{HCl-phenylhydroxylamine}\), a blood toxin, was studied \(^4\).

Results

The values, as shown in the table No. 1, of AC-activity in the erythrocytes of schizophrenics are the contents of \(\text{CO}_2\) produced 0.4 cc. of enzyme liquid, obtained from 2 cc. of blood paste and kept at \(15^\circ\text{C}\) for 5 minutes. The average for normal subjects was \(124.6\mu 1\) and none less than \(80\mu 1\) while the average for schizophrenics was \(65.8\mu 1\), and especially noteworthy were those for excitatory cases in that \(90\%\) of them showed the values under \(80\mu 1\) and the average of \(54.2\mu 1\), less than half the value of the normal. (For details refer to the work of Matsutani\(^5\), my collaborator).

Next, the results concerning the metabolism of erythrocytes, as shown in the table No. 2 (expressed as means)\(^7\), were measured by using Warburg's apparatus. \(\text{XO}_2\) (\(\text{O}_2\)-consumption),
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Table 1. C. A. in the erythrocytes of schizophrenics.

<table>
<thead>
<tr>
<th>Group measured</th>
<th>CO₂ Output (ul)</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>cases</th>
<th>%</th>
<th>total</th>
<th>average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects</td>
<td>39</td>
<td>7</td>
<td>50</td>
<td>40-79</td>
<td>15</td>
<td>80-119</td>
<td>36</td>
<td>120-159</td>
<td>1</td>
<td>160-199</td>
<td>1</td>
<td>over 200</td>
<td>1</td>
<td>7</td>
<td>14</td>
<td>126.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>excitatory case</td>
<td>3</td>
<td>30</td>
<td>60</td>
<td>60</td>
<td>1</td>
<td>10</td>
<td>1</td>
<td>40-79</td>
<td>15</td>
<td>80-119</td>
<td>15</td>
<td>120-159</td>
<td>1</td>
<td>160-199</td>
<td>1</td>
<td>over 200</td>
<td>1</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>acute progressive case</td>
<td>4</td>
<td>19</td>
<td>62</td>
<td>40-79</td>
<td>15</td>
<td>80-119</td>
<td>4</td>
<td>120-159</td>
<td>1</td>
<td>160-199</td>
<td>1</td>
<td>over 200</td>
<td>1</td>
<td>7</td>
<td>14</td>
<td>60.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chronic progressive case</td>
<td>3</td>
<td>10</td>
<td>45</td>
<td>40-79</td>
<td>15</td>
<td>80-119</td>
<td>8</td>
<td>120-159</td>
<td>4</td>
<td>160-199</td>
<td>1</td>
<td>over 200</td>
<td>1</td>
<td>7</td>
<td>14</td>
<td>82.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>average</td>
<td>10</td>
<td>16.7</td>
<td>32</td>
<td>8.2</td>
<td>1</td>
<td>64.3</td>
<td>1</td>
<td>8.2</td>
<td>1</td>
<td>64.3</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>14</td>
<td>126.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>remissionary improving case</td>
<td>7</td>
<td>70</td>
<td>1</td>
<td>10</td>
<td>2</td>
<td>20</td>
<td>1</td>
<td>10</td>
<td>2</td>
<td>10</td>
<td>2</td>
<td>85.5</td>
<td>1</td>
<td>72</td>
<td>126.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Respiration and Glycolysis of erythrocytes in Schizophrenia

<table>
<thead>
<tr>
<th>38°C 60 minutes</th>
<th>XO₂</th>
<th>XCO₂</th>
<th>R. Q</th>
<th>M. Q</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal subjects</td>
<td>(10)</td>
<td>56.2</td>
<td>101.0</td>
<td>1.1</td>
</tr>
<tr>
<td>excitatory cases</td>
<td>(10)</td>
<td>43.4</td>
<td>58.6</td>
<td>1.3</td>
</tr>
<tr>
<td>chronic progressive cases</td>
<td>(8)</td>
<td>62.5</td>
<td>99.1</td>
<td>1.6</td>
</tr>
<tr>
<td>chronic stationary cases</td>
<td>(6)</td>
<td>50.1</td>
<td>90.1</td>
<td>1.8</td>
</tr>
<tr>
<td>remissionary improving cases</td>
<td>(10)</td>
<td>50.0</td>
<td>91.5</td>
<td>1.9</td>
</tr>
</tbody>
</table>

**O₂ Consumption** = \(X_{O₂}^M\)

**CO₂ Output** = \(X_{CO₂}^M\)

**Aerobic glycolysis** = \(M. Q.\)

**Anaerobic glycolysis** = \(M. Q.\)

numbers in ( ) are the case measured

Excepting chronic progressive cases, was lower than that of the normal. \(X_{CO₂}(CO₂\text{-output})\) decreased in all schizophrenics, and R. Q. (Respiratory Quotient) in the excitatory and chronic progressive cases was less than that of the normal. In comparison with \(X_{O₂}^M\) (aerobic glycolysis) of the normal, which being 8.2μl, that of every schizophrenics showed an increase, and that of excitatory cases was marked in that it was 34.8μl. As for \(X_{CO₂}^N\)
(anaerobic glycolysis) both the excitatory and chronic progressive cases showed a decrease. M. Q. (Meyerhof Quotient) was found to be 1.1 in the normal while it was less in all aggravated cases; and excitatory cases gave 0.48, chronic progressive 0.68.

From these results taking up the marked acceleration of aerobic glycolysis in particular and surveying its relationship with vitamins, $B_1$, $B_2$, and $B_n$, panthothenic acid, and ATP, in the outstanding group showing clinical, symptomatic picture such as schizophrenics in acute stage, or in excitatory or stuporous state, or in active delusion or hallucination, aerobic glycolysis in pathologically progressive state was lessened to the normal value by vitamins $B_1$ and $B_2$, and panthothenic acid,

Table 3. Table of the Average Values of Normal

<table>
<thead>
<tr>
<th></th>
<th>C. D.</th>
<th>$\mu$</th>
<th>S. G.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MCD</td>
<td>Mn</td>
<td>Ma</td>
</tr>
<tr>
<td>normal subjects</td>
<td>7.68</td>
<td>6.3</td>
<td>9.6</td>
</tr>
<tr>
<td></td>
<td>±0.115</td>
<td>±0.42</td>
<td>±0.40</td>
</tr>
<tr>
<td>total cases</td>
<td>7.92</td>
<td>6.4</td>
<td>9.7</td>
</tr>
<tr>
<td>of schizophr</td>
<td>±0.082</td>
<td>±0.21</td>
<td>±0.21</td>
</tr>
<tr>
<td>acute type</td>
<td>7.89</td>
<td>6.3</td>
<td>9.7</td>
</tr>
<tr>
<td></td>
<td>±0.075</td>
<td>±0.22</td>
<td>±0.22</td>
</tr>
<tr>
<td>chronic type</td>
<td>7.98</td>
<td>6.5</td>
<td>9.6</td>
</tr>
<tr>
<td></td>
<td>±0.179</td>
<td>±0.36</td>
<td>±0.36</td>
</tr>
<tr>
<td>excitatory</td>
<td>7.99</td>
<td>6.6</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>±0.079</td>
<td>±0.32</td>
<td>0</td>
</tr>
<tr>
<td>stuporous</td>
<td>7.87</td>
<td>6.3</td>
<td>10.0</td>
</tr>
<tr>
<td></td>
<td>±0.098</td>
<td>±0.34</td>
<td>0</td>
</tr>
</tbody>
</table>

LEGENDS
MCD......Mean Red Blood Corpuscle Diameter
Mn.........Minimum Diam.
Ma.........Maximum Diam.
Vb.........Deviation
SGB........Specific Gravity
SGP........Specific Gravity of Whole Blood
SGR........Specific Gravity of Plasma
SGB........Specific Gravity of Red Blood Corpuscles
RBC........Red Blood Count
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while it was not decreased by these vitamins in the group of chronic type and in the group whose clinical pictures had not been so marked\(^6\). By vitamin B\(_6\) and ATP, on the other hand, aerobic glycolysis was seen increased in both groups while no decreasing action could be observed in either group.

Recognizing such irregularities in the metabolism of erythrocytes themselves, the author turned back to the beginning and attempted a fundamental investigation on the question whether there were any differences in their characteristics and morphology between the erythrocytes of schizophrenics and those of the normal\(^7\). The mean values of these findings are summarily presented in the table No. 3.

Subjects and Those of Various Types of Schizophrenia

<table>
<thead>
<tr>
<th>R. B. C.</th>
<th>Ht</th>
<th>MCV</th>
<th>MCT</th>
<th>SI</th>
<th>Rs</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>×104</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>488</td>
<td>45</td>
<td>92.6</td>
<td>2.00</td>
<td>0.26</td>
<td>0.38</td>
<td>0.47</td>
</tr>
<tr>
<td>± 22.7</td>
<td>± 1.81</td>
<td>± 1.70</td>
<td>± 0.032</td>
<td>± 0.006</td>
<td>± 0.007</td>
<td>± 0.006</td>
</tr>
<tr>
<td>50.7</td>
<td>44.5</td>
<td>88.2</td>
<td>1.79</td>
<td>0.22</td>
<td>0.36</td>
<td>0.47</td>
</tr>
<tr>
<td>± 25.5</td>
<td>± 2.28</td>
<td>± 2.23</td>
<td>± 0.784</td>
<td>± 0.006</td>
<td>± 0.009</td>
<td>± 0.010</td>
</tr>
<tr>
<td>517</td>
<td>45</td>
<td>88.2</td>
<td>1.80</td>
<td>0.23</td>
<td>0.36</td>
<td>0.47</td>
</tr>
<tr>
<td>± 25.3</td>
<td>± 2.1</td>
<td>± 2.12</td>
<td>± 0.040</td>
<td>± 0.006</td>
<td>± 0.009</td>
<td>± 0.011</td>
</tr>
<tr>
<td>484</td>
<td>42.5</td>
<td>88.0</td>
<td>1.76</td>
<td>0.22</td>
<td>0.37</td>
<td>0.47</td>
</tr>
<tr>
<td>± 44.2</td>
<td>± 4.5</td>
<td>± 4.48</td>
<td>± 0.074</td>
<td>± 0.012</td>
<td>± 0.015</td>
<td>± 0.016</td>
</tr>
<tr>
<td>494</td>
<td>44</td>
<td>88.7</td>
<td>1.76</td>
<td>0.22</td>
<td>0.36</td>
<td>0.46</td>
</tr>
<tr>
<td>± 33</td>
<td>± 3.1</td>
<td>± 2.11</td>
<td>± 0.043</td>
<td>± 0.007</td>
<td>± 0.001</td>
<td>± 0.016</td>
</tr>
<tr>
<td>532</td>
<td>45</td>
<td>85.2</td>
<td>1.75</td>
<td>0.22</td>
<td>0.36</td>
<td>0.47</td>
</tr>
<tr>
<td>± 41</td>
<td>± 3.3</td>
<td>± 1.03</td>
<td>± 0.076</td>
<td>± 0.012</td>
<td>± 0.009</td>
<td>± 0.001</td>
</tr>
</tbody>
</table>

Ht·········Haematoerit Value
MCV·········Volume of Red Blood Corpuscles
MCT·········Thickness Red Blood Corpuscles
SI·········Spheric Index
Rs·········Resistance
Rs Ma·····Maximum Resistance
Rs Mn·····Minimum Resistance
Rs W·····Resistance Width
According to these values, the diameter in the case of the normal is smallest; that of old group is bigger than new group; the thickness of the normal, on the other hand, is thickest and next comes the new group, then old group. The volume of all except the normal is small, and that of patients in stuporous state is smallest. As regards the spheric index obtained by dividing thickness by diameter, it is 0.26 in the normal whereas it is less than 0.23 in all schizophrenics. Specific gravity of erythrocytes of stuporous state is lighter, and that of old group next light. Excepting stationary old group, blood counts are all greater than those of the normal, and those of new group and stuporous state particularly large. Ht value of old group is markedly small, and the resistance (Ribiere's method) against diluted saline solution in general shows that that of schizophrenia is stronger than that of the normal.

Upon examining the rate of appearance of Heinz-body in blood by adding HCl-phenylhydroxylamine, a blood toxin, in connection with blood resistance, and setting the value of the normal at 100%, those of schizophrenia were greater in general; namely, they were 227% in chronic progressive group, 224% in excitatory deranged group, 324% in chronic desolated group and 155% in chronic stationary group; and it was found that the resistance of the blood cells in which Heinz-body had appeared was weakened.

What temporary influence will the characteristics of erythrocytes mentioned above receive from treatments such as electric convulsive therapy (ECT) and insulin shock (IST) daily used in the field of psychiatry? The figure No. 3 shows the changes in ECT treatment.

The values increasing immediately after ECT, of the averages of schizophrenia, are of diameter, specific gravity of whole blood and plasma, Ht, volume, thickness, spheric index, and resistance. Those decreasing immediately after ECT are of
A Study on Schizophrenia: on the Erythrocytes.

Fig. 3. The changes of erythrocytes by ECT.

<table>
<thead>
<tr>
<th></th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>a.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>immediately before ECT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. immediately after ECT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>c. after 90 minutes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- a. immediately before ECT
- b. immediately after ECT
- c. after 90 minutes

specific gravity of erythrocytes and blood count. Ninety minutes after ECT these values again return to the values immediately before ECT, but blood count alone keeps on decreasing. As regards the comparison between new and old schizophrenic groups, the changes in diameter and blood count differ but all other values are almost same. The diameter in the case of new group is increased by ECT and returns while that of old group gets smaller first and then returns. As regards the changes in blood count, the count decreases first and then returns to the original in the new group, while it increases first and then decreases in old group.

In the case of IST, as shown in the figure No. 4, the changes are measured during the period from the time immediately before the insulin injection to 90 minutes afterwards and those during coma. Diameter has grown smaller 90 minutes afterwards, and during coma it has become larger than that before the insulin injection. Specific gravity of all, blood, plasma, and red corpuscles, increases throughout at whole course, but the increase of blood count lessens somewhat at the later stage; Ht, volume, thickness and spheric index, all increase during the
Summary and Discussion

Blood cells of schizophrenics differ in many points from those of normal subjects. First of all the shape of them is flat and thin. This tendency is more marked in old group than in new group; the volume is small; flat corpuscles are more numerous in them in the normal; and the blood resistance against diluted saline solution is stronger than that of the normal. It has long since been known that the rate of corpuscle sedimentation is being accelerated in schizophrenics. A simple physical cause that blood corpuscles are flat and numerous can explain this phenomenon. It is said that there is an antisphering substance among the factors controlling the thickness and roundness of blood corpuscles. Yet it has not been determined whether this substance on the surface of the blood of schizophrenics is large or small. Blood corpuscles are said to lose their peculiar disc-shape and to be completely destroyed at the pH of 9.2 when the antisphering substance is removed from the surface of blood corpuscles. The lower the pH is the better is the absorption of this substance on the surface of blood corpuscles; and it seems
that the more this substance attaches itself to blood corpuscles, the greater is the degree of flatness and in this connection it is interesting to note that the pH of schizophrenic blood is low in general. On the other hand, however, sphericity is increased at the time when the acidity of blood is increased due to a sudden movement of acidic substances immediately after ECT. Again in the case of coma of insulin treatment, blood tends to be alkaline and even then an increase in the sphericity of corpuscles is indicated. Consequently it seems that the roundness of blood corpuscles is not solely dependent upon antisphering substance and pH.

The temporary lowering of $O_2$-partial tension in blood can be observed both in ECT and IST. Would it not be this fact that greatly influences the shape of blood corpuscles? Further, copper salts belonging to Cu and Zn are said to influence the diameter and thickness of blood corpuscles, and since Zn is contained in blood corpuscles as a constituent of CA and the contents of it in schizophrenics being decreased to 1/2 of that of the normal, this substance need also have a close relationship to the change of shape.

Numerousness of blood count has been so far frequently mentioned, and the decrease of $O_2$-partial tension in blood, one of causes of increase in the number of erythrocytes, is the phenomenon which can often be encountered in schizophrenia. Scarcity of $O_2$-contents in the arterial blood, low CA-activity, and insufficient exchange of $O_2$ and $CO_2$, too, have already been stated. Blood corpuscles of Schizophrenics have stronger resistance against diluted saline solution than that of the normal but that against blood toxin like HCl-phenylhydroxylamine is weaker. There is an opinion that hemolysis is apt to occur in the acute stage of schizophrenia following frequent weakening of blood resistance. In any event, it is possible to suppose that erythrocytes are destroyed by some kind of causes, and haemopoietic substances being produced thereby stimulate the bone marrow, leading to the increase of erythrocytes.

Now concerning carbonic anhydrase, this enzyme, as is wellknown, existing not only in blood corpuscles but also in the gastric mucous membrane, spleen, brains, kidneys, eye-balls, aorta as well as in salivary glands, helps to induce a chemical reaction given in the formula (1) and...
plays an important rôle in the acid base equilibrium.

\[ \text{H}_2\text{O} + \text{CO}_2 \rightleftharpoons \text{H}_2\text{CO}_3 \]  
\[ \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \]  

Lack of this enzyme disturbs the release of \( \text{CO}_2 \) from the lungs, the secretion of \( \text{HCl} \) from the gastric wall\(^{27}\) and \( \text{NaHCO}_3 \) from the spleen\(^{28}\), and the transfer of \( \text{Cl}^- \) in erythrocytes\(^{29}\). According to the experiments of J. Nadell\(^{30}\) et al. using Diamox, an inhibitor of this enzyme, it is reported that the secretion of \( \text{CO}_2 \) and \( \text{Na}^- \), \( \text{K} \) phosphate in urine increases and that of \( \text{NH}_3 \) decreases, and \( \text{pH} \) as well as \( \text{CO}_2 \)-contents in the arterial blood lessen. Further, in the sub-renal urinary tubules, the exchange of \( \text{H}^+ \) and \( \text{Na}^+ \) is inhibited and resorption \( \text{Na}^+ \) is disturbed, thus leading to a loss of A. R. in blood.

The lowering of CA-activity in blood corpuscles not only interferes the gas-exchange in the tissues but it also interferes \( \text{Cl}^- \) and \( \text{HCO}_3^- \)-exchange; consequently it influences the exchange of \( \text{K}^+ \) and \( \text{Na}^+ \), and abnormally increases stimulating effect of \( \text{K}^+ \) on nervous systems, particularly on the central nervous system and will raise the excitation of nerves. Ashby\(^{41}\) has stated that CA-contents are great in the parts of the brains where \( \text{O}_2 \)-consumption is great; but supposing there should be a decrease in CA-activity in the area where it is needed, mental excitation of schizophrenics along with abnormal distribution of \( \text{K}^+ \) could necessarily occur in such an area.

It is quite natural to consider that the metabolism in blood corpuscles should differ from that occurring in other tissues (matured erythrocytes have no nuclei, and it is thought that there are already no cytochrome and no cytochrome-oxydase) but the reasons generally advanced today for the acceleration of aerobic glycolysis during the process of the aerobic and anaerobic glycolysis are for one, that because \( \text{CoA} \) receives acetyl-base from pyruvic acid and produces acetyl-\( \text{CoA} \)\(^{31}\) (the formula 3), which in turn reacting with oxalo-acetic acid produces citric\(^{22}\) acid; and instead of DPNH, possessing conjugating relation in the part where \( \text{CoA} \) receives acetyl base from pyruvic acid, being re-oxidized to DPN\(^+ \) through a series of conjugating relation including flavin and cytochrome, it acts as an agent to reduce pyruvic acid to lactic acid; and as for the other, that because pyruvic acid is not sufficiently oxidized even in the presence of \( \text{O}_2 \). The increase is thought to occur under these
two conditions.

\[
\begin{align*}
\text{CH}_3\text{COCOOH} & \quad \text{DPN} \\
\text{R. S. CoCH}_3 & \quad \text{laetic acid}
\end{align*}
\]

The reason for the acceleration of aerobic glycolysis observed in erythrocytes might be found in the above explanations, since among the ones in which aerobic glycolysis is being increased, a marked decrease of glycolysis by vitamins, B\textsubscript{1}, B\textsubscript{2}, pantothenic acid etc., is observable\textsuperscript{6}. This tendency is marked in schizophrenia of early stage, whose symptoms are active, while it is not common among old stationary Schizophrenics. Vitamin B\textsubscript{1} as pyro-phosphatic ester is the one that forms cocarboxylase acting as an agent in decarboxylation or oxydative decarboxylation of pyruvic acid, and vitamin B\textsubscript{2} either as flavinmononucleotid or flavin-adenin-dinucleotid, taking up hydrogen from substrate or co-enzyme of dehydroxylase, becomes itself a reducing type or by oxygen or cytochrome an oxidizing type; but by these processes DPNH is oxidized to DPN. And pantothenic acid is also known to be one of constituents of CoA. The effectiveness of these substances gives a ground to suppose that obstacles may lie around the reaction-formula as graphically shown above.

Now as regards the decrease of anaerobic glycolysis in the acute stage, Fujiwara\textsuperscript{33} once mentioned of increased contents of ester phosphoric acid in blood, pyruvic acid, and of lactic acid, in acute schizophrenics, and he further stated that majority of old chronic cases had shown values less than the normal value; but the part below ester phosphoric acid worthy of discussion is the point where the question came up at the time of aerobic glycolysis when DPNH was produced by oxidization of glycclin aldehyd-3-phosphate, and considering this DPNH carrying on the conjugation with di-phospho-glycelic acid, it can safely be assumed that the obstacles of anaerobic glycolysis might lie around this point. The erythrocytes of schizophrenics, themselves undergoing such changes, are also taking part in the somatic metabolism.
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