FUNCTIONAL INSUFFICIENCY OF ERYTHROCYTE THROMBOPLASTIN FACTOR*

I. Ya. Ashkinazi

The study of the thromboplastin activity of whole erythrocytes of healthy and sick persons revealed disturbances of the procoagulant properties of the erythrocytes, manifested as a decrease in the thromboplastin activity of the whole cell, despite an adequate content of the procoagulant factor in it. To describe these disturbances, which are similar to changes in the procoagulant properties of platelets in one form of thrombopathy, the term "functional insufficiency of erythrocyte thromboplastin factor" shortened to "erythrocytic thrombopathy" is suggested.

KEY WORDS: erythrocyte; thromboplastin factor; disturbance of mobilization.

The writer suggested previously that the process of mobilization of erythrocyte thromboplastin factor (ETF) is coupled with changes in the dynamic properties of the cell membrane [1].

In this investigation the degree of incorporation of ETF into the blood clotting process was compared in different states of the body, a problem not previously specially investigated. It was hoped that such an analysis would assist the understanding of the physiological mechanisms controlling ETF mobilization and would also answer the question whether, under natural conditions, changes in the procoagulant properties of erythrocytes which were previously observed in vitro after certain procedures directed against the cell membrane [1, 2] are also possible under natural conditions.

These comparative studies are also interesting from the clinical standpoint. Only a few studies, yielding conflicting results, have been devoted to the coagulant activity of erythrocytes, the major constituent of the blood cells [6, 7]. In diffuse diseases of the kidneys the procoagulant activity of whole erythrocytes, unlike that of the platelets, has not been studied at all, although it is known that in chronic renal failure the activity of platelet factor 3 is reduced and that whole erythrocytes can partly compensate for its deficiency.

EXPERIMENTAL METHOD

Since the thromboplastin activity exhibited by the whole cell is only a fraction of the activity contained in it, in order to assess the degree of mobilization of ETF not only the absolute thromboplastin activity of the erythrocytes (in seconds) was taken into consideration, but also the relative ETF — as a ratio of optimal (potential) activity of the cell; this was taken to be the activity of hemolyzed erythrocytes (the osmolysate), taken in the same dilution as the whole erythrocytes, namely 1/50 (the concentration of the original suspension of washed erythrocytes was $4 \cdot 10^6$ mm$^3$). The relative index of erythrocyte activity (IEA) was determined as the ratio between the absolute value of the index (in seconds) in the substrate plasma after addition of erythrocytes to it and the analogous index (in seconds) in plasma containing hemolyzed erythrocytes. Platelet-deficient plasma from healthy donors of blood group AB (IV), kept at 25-30°C in silicone-treated flasks, was used as the substrate plasma. The thawed plasma, activated by diatomite, was used once only. Thromboplastin activity was estimated from the recalcification time, prothrombin consumption, and thrombin generation [2].

* Paper read at the Fourth All-Union Conference on Problems in Blood Clotting and Fibrinolysis, Saratov, 1975.

Fig. 1. Effect of whole erythrocytes from healthy persons and patients on thrombin generation in platelet-deficient substrate plasma: 1) before addition; 2, 3, 4) after addition of erythrocytes from healthy persons, patients with atherosclerosis, and patients with kidney diseases, respectively. Abscissa, duration of incubation of clotting mixture (in min); ordinate, thrombin activity (in sec).

Fig. 2. Effect of disintegrated erythrocytes of healthy persons and patients on thrombin generation in platelet-deficient substrate plasma. Hemolyzed erythrocytes from the following sources were added to the substrate plasma: 1) healthy persons; 2) patients with atherosclerosis; 3) patients with kidney diseases. Remainder of legend as in Fig. 1.

TABLE 1. Index of Erythrocyte Activity for Healthy Subjects and Patients (M ± m)

<table>
<thead>
<tr>
<th>Subjects tested (n)</th>
<th>Recalcification time, sec</th>
<th>Maximal thrombin activity, sec</th>
<th>Prothrombin consumption time, sec</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>plasma with erythrocytes</td>
<td>plasma with hemolysate</td>
<td>IEA</td>
</tr>
<tr>
<td>Healthy (22)</td>
<td>143.5 ± 3.52</td>
<td>98.3 ± 2.56</td>
<td>1.48 ± 0.04</td>
</tr>
<tr>
<td>Patients with atherosclerosis (33)</td>
<td>145.9 ± 3.7</td>
<td>99.3 ± 3.3</td>
<td>1.49 ± 0.03</td>
</tr>
<tr>
<td>Patients with kidney diseases (29)</td>
<td>148.5 ± 2.3</td>
<td>92.4 ± 1.3</td>
<td>1.61 ± 0.024*</td>
</tr>
</tbody>
</table>

* P < 0.05 compared with healthy subjects.

The 84 persons investigated were divided into groups: 1) 22 healthy persons aged 19–46 years (mean age 33.7 ± 1.98 years); 2) 33 patients with atherosclerosis aged 46–78 years (mean age 62.5 ± 1.4 years); 3) 29 patients with diseases of the kidneys aged 18–59 years (mean age 36.9 ± 2.4 years), most of whom (22) had chronic diffuse glomerulonephritis, 12 had a disturbance of the nitrogen-excreting function of the kidneys, and 16 had impairment of filtration.

**EXPERIMENTAL RESULTS**

Under the influence of intact healthy human erythrocytes a characteristic increase in the thromboplastin activity of substrate plasma was observed: The thrombin generation time was shortened and its maximal activity increased, and the prothrombin consumption was increased. Under the influence of erythrocytes from patients with atherosclerosis the same changes were observed. The thromboplastin activity of the whole