THE CONNECTION BETWEEN LIPID PEROXIDATION AND THROMBIN-FIBRINOGEN INTERACTION
(message I)

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While modeling experimental conditions with accelerated or inhibited process of lipid peroxidation in thrombocytes (rat tests), it was shown that acceleration of continuous intravascular blood curtailing is supervened upon hyperoxidation, thrombin-fibrinogen interaction plasma markers' value being controlled. The same was seen among patients with insulin-dependent diabetes, basedowians, prostate gland adenoma, persons with atherosclerosis of lower limbs arteries, women with physiological pregnancy and the pregnancy complicated with eclampsia and the pregnant after cesarean section.
Between lipid peroxidation intensity in thrombocytes and the rate of intravascular blood curtailing, a very close to linear direct dependence was detected. Using a complex antioxidant, selmevit, alongside usual therapy, restricts lipid peroxidation and continuous intravascular blood curtailing acceleration, and thus, a thrombotic complication hazard.

Taking into account the dependence of many life-support systems from lipid peroxidation (LPO), its changes at some physiological and pathological conditions [1, 2, 3], the data about the connection between hemostasis and LPO [4], the supposition according to which this connection is realized by blood platelets [5], we have studied the dependence between the intensity of thrombin-fibrinogen (ITF) and lipid peroxidation (LPO) interaction in blood in various experimental and clinical situations, hoping, that it will allow to estimate the role of lipid peroxidation in hemostatic potential maintenance and the possibility of the direct influence on intravascular clotting (inopexia) (IVC) – the process going on continuously in physiological conditions [6, 7, 8].

In experiences on rats changes of ITF products value (soluble fibrin monomeric complexes - SFMC, products of fibrin degradation - PFD, D-dimers, P_3 and P_4 factors, general blood coagulability, platelet value, their general coagulant activity, spontaneous and ADP-induced aggregation) when introducing LPO inhibiting compounds (mercasolil , 6-methyluracil, a complex of oxidation preventive vitamins - selmevit, a synthetic antioxidant dimephosphon), and also the LPO activating compounds, (lead, thyroxin, sex steroids) were studied. Alongside with it, the LPO and ITF changes when being affected by primarily accelerating or slowing down the ITF factors (heparin and adrenaline injections, blood loss, seasonal factors) were evaluated. For the estimation of the ITF markers level, platelet aggregation and the LPO rate displays, well known methods were used [9, 10, 11]. In some experiments the tests were selected with small intervals to estimate the sequence of hemostasis and lipid peroxidation shift occurrences.

The data about positive influence of oxidation preventive vitamins on hemostasis having been obtained, the ITF rate among patients suffering from the diseases which are usually accompanied with

hyperoxidation, was clinically studied, the LPO being preliminary activated; applying usual therapy or the same therapy added by a complex of antioxidants - selmevit. Patients with insulin-dependent diabetes, basedowians, prostate gland adenoma before and after the operation (strumectomy or adenomectomy accordingly), persons with atherosclerosis of lower limbs arteries, women with physiological pregnancy and the pregnant with eclampsia before and after easy delivery or after cesarean section were examined.

Analyzing the results of experimental observations continued more than 15 years, we have received the bases for ascertaining of some positions:

1.The introduction of various biologically active compounds accelerating LPO (ethinylestradiol, levonorgestrel, thyroxin, lead) to experimental animals (white rats), increases the value of direct and indirect ITF markers in blood. The introduction of LPO inhibiting compounds (selmevit, complivit, dimephosphon, arachidonic acid paralyzers – mepacrin, aspirin and dasoxiben) causes the opposite effect.

2.When the hemostasis activating compounds or those leading to its activating (adrenaline, blood loss, low temperature of the environment, seasonal factors) introduced, alongside with the growth of ITF markers value, the LPO rate is increased. The ITF slowing down influences (the introduction of heparin, pelentan) weakens the LPO process intensity.

3.The introduction of LPO accelerating compounds (lead, sex steroids, thyroxin), simultaneously with antioxidants (selmevit, dimephosphon) inhibits or excludes the LPO activation and the ITF markers' value growth.

4.By physiological and pathological conditions (texis, puerperal period, the pregnancy complicated with eclampsia, cesarean section, atherosclerosis of lower limbs vessels with ischemia, toxic goiter, prostate gland adenoma), which are characterized with hyperoxidation and shifts in hemostasis (general high coagulability of blood and platelet coagulation activity), the ITF markers' value in plasma of blood increases.

5.The addition with antioxidants of the usual therapy used at these diseases, inhibits the LPO intensification and antioxidant thrombocyte potential decrease, and reduces the hemostasis condition showers' restoration period up to the amounts peculiar to healthy donors.

6.The LPO acceleration in thrombocytes precedes the platelet coagulant activity shifts and the ITF markers level, different by nature and properties compounds capable to cause hyperoxidation, affecting; confirming the role of thrombocytes in realization of the connection LPO-HEMOSTASIS.

The connection between LPO and ITF, hence, and the connection of LPO with continuous intravascular blood curtailing, is carried out through thrombocytes: LPO changes in these cells precede their coagulant activity shifts, and this, in its turn, precedes ITF acceleration. The proof of close connection between lipid peroxidation and intravascular blood curtailing is close to linear character of dependency between lipid peroxides value in thrombocytes and the ITF markers value in blood plasma (at the graphic analysis of LPO and ITF dynamics, the dependence between them is close to linear one and excels with a high approximation coefficient, approached to one - from 0.9867 up to 0.9987). In particular, lipid peroxide growth level and antioxidant potential decrease in thrombocytes, the release reaction acceleration of P_3 and P_4 factors and spontaneous platelet aggregation, their general coagulant activity growth, ITF acceleration attributes (SFMC, PFD and D-dimers value growth), are supervened upon a thyroxin injection. Thus, the factors changing LPO intensity, realize the influence on ITF through thrombocytes activation.

Taking into consideration the existence of bilateral dependence between thrombinemia and platelet activity [12], and also the data, indicating the bilateral dependence LPO ↔ hemostasis [13], it is possible to express the idea in the form of a closed cycle:

hyperthrombinemia ® LPO activation in thrombocytes ® hyperthrombinemia (the cycle is closed)

The data about the sequence of changes in time allow to detail this scheme, having included in it also the results of ITF intensity supervision, estimated upon the markers of the process:

LPO activation (or inhibition) in thrombocytes being affected by prooxidants (antioxidants)

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Platelet coagulant activity increase (or decrease)

E

Acceleration (or limitation) of thrombin and fibrinogen interaction

Such representation testifies the expediency of the research continuation aimed at profound studying of shifts' dynamics at pathological conditions, proceeding with the hyperoxidation phenomena.

We document the generalizations resulted here in messages II-VI with decoding of experimental schemes and the fact sheet.

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