

## Condition of Hemostasis System on Exposure to Dioxins

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### Introduction

Considerable recent attention has been focused on dioxin problems as well as on different aspects of their biological effects. These supertoxic agents are considered to exert a detrimental effect on the entire organism. We have carried out complex study of medico-biological aspects of dioxin effects on organism. Among many clinical and functional investigations indices of hemostasis system have drawn our special attention. Our searching in the scientific literature has not revealed any information about it. The distinctive characteristics of hemostasis system in people exposed to dioxin may be of considerable interest, since they could to a certain degree elucidate mechanism of cardiovascular desadaptation and cardiovascular system pathology formation under this toxic agent effect.

### Methods of investigations

We carried out clinical examination of people who in 1965-1967 had been engaged in production of butyl ether 2,4,5-T and had had chloracne. There were 73 people in the cohort group consisting in overwhelming majority (85%) of men whose average age was  $52 \pm 1,4$ . Alongside with abundant indices of functional condition of different systems and organs indices of plasma and thrombocytic hemostasis components were studied as well as number of thrombocytes, their aggregation power, prothrombin index, fibrinogen A,  $\beta$ -naphthol test (fibrinogen B), venous blood coagulation, hematocrit, plasma tolerance to heparin, spontaneous fibrinolysis.

When conducting the mentioned investigations we used methods suggested by Z.S.Barkagan (1), E.I.Ivanov (2), V.P.Balouda et all (3).

### Results and discussion

In morphological studies of peripheral blood smears from the examined people reliably increased mean values of monocyte number ( $8,7 \pm 0,3$  %) in comparison with normal data were detected. In 33,8% of the patients the amount of monocytes exceeded the upper limit of admissible variations ( $> 9\%$ ). The number of patients with moderate lymphocytosis was 18,6%.

Average amount of thrombocytes in the examined workers was within the normal range ( $240,0 \pm 2,3 \times 10^9/l$ ). Disturbances in their functional state about which we could judge by spontaneous agglomeration and ability to form pseudopodia were not revealed.

Unrolled coagulogram revealed shortening time of venous blood coagulation in 50% of the patients by mean values. Content of prothrombin complex factors was increased in 29,1% of cases. Amount of fibrinogen A in 33,4% of the patients exceeded the upper normal limits ( $4,0 \pm 0,13$ ).

The change data testified to tendency to hypocoagulation in 50% of the examined people on account of activation in all phases of blood coagulation and anticoagulation system suppression. Frequency of emerging positive samples in  $\beta$ -naphthol test (fibrinogen B) counts in favour of tendency to hypercoagulation in 33,4% of the patients.

Increase of plasma tolerance to heparin in 45,6% and decrease of spontaneous fibrinolysis in 83,4% of the patients exhibit suppression of anticoagulative system. Hematocrit indices are also increased as related to the norm in  $46,2 \pm 5,8\%$  of the patients.

Revealed disturbances of hemostasis manifested as hypercoagulation owing to activation of all blood coagulation phases and suppression of anticoagulative activity may promote the appearance of indications of intravascular blood coagulation. Positive  $\beta$ -naphthalan test (fibrinogen B) in each one of the three patients is sufficient proof of it.

It is significant that the first indications of blood hypercoagulation in these patients date back to the clinical course of chloracne as shortened time of venous blood coagulation. At that time the age of these patients with chloracne was about 23. Unfortunately then other tests which could characterize hemostasis were not carried out. But subsequent clinical examinations of the same people when they were about 40 gave more complete indices and showed that 42,7% of them had indications of hypercoagulation (Table 1).

Such increase of frequency and expressiveness of hemostasis system changes was observed during all the 30 years of the dynamic observation against the background of increasing cholesterol content in blood serum.

Diagnostic evaluation of clinical forms of the diseases shows that practically all the examined people have some or other deviations in the functional condition of cardiovascular and central nervous systems most often being a consequence of atherosclerotic processes or hypertension.

### **Conclusion**

Clinical manifestation of dioxin exposure is chloracne accompanied by disturbances in hemostasis system with the tendency to hypercoagulation on the part of hemostasis plasma components.

Changes in coagulative properties of blood are characterized by activation of all the phases of blood coagulation, anticoagulative system suppression and accompanied by hypercholesterinemia. They are gradually increasing in the dynamics of the postcontact period.

The revealed shifts in hemostasis system indices can be considered as one of the factors of cardiovascular disease pathogenesis on dioxin exposure.

### **Reference**

1. Barkagan Z.S. *Hemorrhagic Diseases and Syndromes*. M.; 1988.
2. Ivanov E.I. *Handbook on Hemostasiology*. Minsk, 1991.
3. Balouda V.P., Barkagan Z.S. *Laboratory investigations of hemostasis system*. Tomsk. 1980.

Table 1

Comparison between deviation frequency of some indices in hemostasis system  
of patients formerly having chloracne (in % to number of examined)

Indices of hemacoagulation	Deviation from norm	1984 age 40 ± 1,6	1994 age 50 ± 1,4	Control
Number of people with hypercoagulation indications		42,7	50,0	
Shortened time of venous blood coagulation		43,2	50,0	
Prothrombin index, %	> 100	27,0 ± 7,1	29,1 ± 5,3	8,7 ± 4,4
Fibrinogen A	> 4	32,4 ± 7,4	33,4 ± 5,5	11,1 ± 4,8
Fibrinogen B	positive	32,4 ± 7,4	33,4 ± 5,5	negative
Hematocrit, %	> 48	35,1 ± 7,5	46,2 ± 5,8	12,0 ± 5,0
Plasma tolerance to heparin, min	< 7	43,2 ± 7,9	45,6 ± 5,1	18,2 ± 6,0
Spontaneous fibrinolysis, %	* < 12	82,0 ± 6,1	83,4 ± 4,3	32,0 ± 7,2

