



## Markers of thrombophilia and endothelial dysfunction under the technogenic influence of the dust factor

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### ABSTRACT

Thrombophilia markers (rising of activity of the VIII coagulation factor, decrease of the activity of protein C) and endothelial dysfunction (rising of activity of von Willebrand factor, contents of glycosaminoglycans in blood, and microalbuminuria) are revealed at the prolonged technogenic impact of the dust factor in workers of the dust hazardous jobs. The revealed markers of thrombophilia and endothelial dysfunction correlate with degree of fibrogenity of dust aerosols in the workers contacting with highly fibrogenic and mild fibrogenic dust aerosols.

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## Introduction

At the present stage one of the priorities of preventive medicine is identification of the general and specific body response to action of harmful production factors for the purpose of development of the criteria allowing to objectively diagnosing early implications of professional and production related diseases. At long-term exposure of adverse production factor, including dust, there is attrition of protective systems in the organism that triggers a series of universal mechanisms of damage of cells with accumulation of toxic metabolites and development of a toxic membranopathy. This causes development of chronic multisystemic pathology.

The endotheliocyte is one of "cells targets" for dust influence that defines disturbance of its functions, in particular, rising of prothrombotic potential [1]. Proteoglycans of glycocalyx on a surface of phospholipid membranes, first of all endothelial cells, are blasted, changing properties of biological membranes, at long-term contact with exotoxin and endotoxins. A number of studies proved that fibrosis of vascular wall is followed by high-quality changes of glycosaminoglycans: concentration of hyaluronic acid decreases and considerably level of sulfated glycosaminoglycans increases [2]. Nowadays in scientific works the high level of egestion of albumin is regarded as the indicator reflecting development of systemic endothelial dysfunction in response to accumulation of exopathogens and endopathogens in an organism [3].

Thus, identification of markers of thrombophilia and endothelial dysfunction remains topical issue while studying technogenic influence of the dust aerosols (DA) on workers of the dust hazardous jobs [4, 5].

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## Aim of the Research

Estimation of the importance of definition of indicators of activity of the VIII coagulation factor, protein C, von Willebrand factor, microalbuminuria (MAU) and contents at bloods of glycosaminoglycans as the markers of thrombophilia and endothelial dysfunction in workers of the dust hazardous jobs.

## Materials and Methods

57 workers of the dust hazardous jobs are examined (middle age  $48.0 \pm 7.3$  years). The first group (16 people) consisted of patients with chronic professional dust pathology of lungs (CDPL) (pneumoconiosis caused by influence of highly fibrogenic dust aerosols and mild fibrogenic dust aerosols); the second group (13 people) consisted of patients CDPL (mechanic non-obstructive chronic bronchitis (MNCB) caused by the influence of low fibrogenic dust aerosols). The workers contacting highly fibrogenic dust and mild fibrogenic dust aerosols composed the third group (14 people); the fourth (14 people) – the workers with low fibrogenic dust (LFD) aerosols more than 10 years.

Men (donors, 30 people) who does not have contact to dust aerosols on production entered into the control group (CG). Activity of von Willebrand factor (WF) in blood plasma (“Tekhnologiya-Standart”, Russia), activity of the VIII coagulation factor and protein C (“Instrumentation Laboratory”, the USA), egestion albumin urine (“BioSystems”, Spain) were estimated in all patients. Extraction of glycosaminoglycans from blood serum was carried out after proteolysis by papain with additional cleaning of the received glycosaminoglycans. Their quantity was determined by the content of the uronic acids (UA) and the sulphated glycosaminoglycans. Statistical processing of the obtained data was carried out by the standard techniques.

## Results and Discussion

Indicators of activity of the VIII coagulation factor and protein C in blood plasma were defined at patients of all clinical groups. Thrombophilic state develops at workers of the dust hazardous jobs at long-term influence of industrial dust aerosols that is expressed at the workers contacting to highly fibrogenic dust and mild fibrogenic dust aerosols in reliable augmentation – in 1.76 times ( $p < 0.001$ ) concerning indicators of control group of activity of the VIII coagulation factor and depression by 1.4 times ( $p < 0.001$ ) of protein C activity, and at patients of control group – in rising of activity of the VIII factor (by 2.8 times;  $p < 0.001$ ) and depression ( $r = 0.504$ ;  $p < 0.001$ ) activity of protein C (by 1.9 times;  $p < 0.001$ ) concerning control group.

Only reliable rising of activity of the VIII coagulation factor by 1.2 times ( $p < 0.001$ ) concerning indicators in control group was revealed in patients with mechanic non-obstructive chronic bronchitis. Indicators of activity of WF authentically differed and exceeded control values only in group of patients with pneumoconiosis in 1.65 times ( $p < 0.001$ ) and in group of the workers contacting to highly fibrogenic dust and mild fibrogenic dust aerosols in 1.37 times ( $p < 0.001$ ). It is established that the activity of WF reflecting extent of activation/disturbance of endothelium of vascular bed increased at influence of highly fibrogenic dust and mild fibrogenic dust aerosols and low fibrogenic dust aerosols.

The urinary egestion of albumin in the examined groups was the highest in patients with pneumoconiosis and exceeded values of control group by 3.9 times ( $p < 0.001$ ). The indicators of urinary egestion of albumin were authentically exceeded by control values by 2.2 times ( $p < 0.001$ ) in patients with mechanic non-obstructive chronic bronchitis. Values of urinary egestion of albumin authentically exceeded control group values in 2.72 times ( $p < 0.001$ ) among workers of the dust hazardous jobs only at the workers contacting to highly fibrogenic dust and mild fibrogenic dust aerosols.

Glycosaminoglycans’ content in blood serum in all groups of the examined patients was estimated on presence of uronic acids and sulphated glycosaminoglycans. The study of the state of proteoglycan metabolism revealed the most expressed rising of glycosaminoglycans level among the patients with CDPL in patients with pneumoconiosis (the uronic acids level exceeded control values by 22.6 times ( $p < 0.001$ ), sulphated glycosaminoglycans by 8.9 times ( $p < 0.001$ )). These indicators were the highest at the workers contacting to highly fibrogenic dust and mild fibrogenic dust aerosols (the uronic acids level exceeded control values by 13.2 times ( $p < 0.001$ ), sulphated glycosaminoglycans by 3.6 times ( $p < 0.001$ )) among workers of the dust hazardous jobs, at the same time the first and third clinical groups authentically differed from each other ( $p < 0.001$ ), and reliable differences isn’t revealed between the second and fourth ones ( $p < 0.05$ ). Feature of response to influence of a dust factor is rising of contents in a blood mainly to sulphated glycosaminoglycans.

Direct correlation dependence between influence both highly fibrogenic and the mild fibrogenic dust aerosols and rising of activity of the VIII coagulation factor ( $r = 0.603$ ;  $p < 0.001$ ), decrease of the activity of protein C ( $r = 0.52$ ;  $p < 0.001$ ), glycosaminoglycans level in blood plasma ( $r = 0.745$ ;  $p < 0.001$ ), urinary egestion of albumin ( $r = 0.513$ ;  $p < 0.001$ ), WF ( $r = 0.501$ ;  $p < 0.001$ ) is established. The study of the ratio between WF activity in blood plasma and

the level of urinary albumin excretion revealed the direct correlation link confirming the data that microalbuminuria is a marker of endothelial dysfunction ( $r = 0.617$ ;  $p < 0.05$ ).

## Conclusion

The obtained data confirm the importance to determine activity level of the VIII coagulation factor, protein C, von Willebrand factor, glycosaminoglycans level in blood plasma and urinary egestion of albumin as the markers of thrombophilia and endothelial dysfunction at the prolonged technogenic influence of the dust factor at workers of the dust hazardous jobs.

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