Original article

# Impact of atmospheric microparticles and heavy metals on external respiration function of urbanized territory population

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**Abstract:** *Aim* — This study was designed to determine the impact of the features of fractional composition of atmospheric suspensions and toxic heavy metals on external respiration function (ERF) of healthy people and patients with respiratory pathology living in Vladivostok, Russia.

*Methods* — The study of ERF of healthy people and patients with respiratory diseases was conducted by spirography and body plethysmography. Air pollution by suspended particulate matter (SPM; 0-700 µm and >700 µm) and toxic heavy metals was determined by collection of atmospheric precipitation (snow) in place of residence of patients. The effect of SPM on ERF was measured by discriminant analysis.

*Results* — We identified that small (0-1 µm) and medium (10-50 µm) dispersed fractions impact on total bronchial resistance in healthy people, SPM 50-100 µm influence on patency of small and medium-sized bronchi, expiration time; toxic metals (Mn, Cu, Zn) impact on bronchial patency. We revealed that the 0-50 µm fractions and metals (Cr, Mn, Co, Cu, Zn) impact on patency of large and medium-sized bronchi and bronchial resistance of patients with chronic catarrhal non-obstructive bronchitis. The impact of SPM and toxic metals on ERF of patients with controlled asthma has not been demonstrated. The maximal pathogenic impact of air pollution on ERF of patients with uncontrolled asthma has been found. We detected that SPM 0-1 µm and 50-100 µm have a negative effect on bronchial patency, hyperinflation of the lung and total bronchial resistance.

*Conclusions* — We determined that exposure intensity of SPM increase depending on severity of respiratory disease.

**Keywords:** air pollution, micro-sized particles of atmospheric air, external respiration function, respiratory diseases.

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## Introduction

Micro-sized particles of atmospheric suspensions, which act direct on the respiratory tract, have the most negatively impact on health in technogenic pollution in the urban environment.Such particles are a product of industrial, transport and other technogenic pollution. Micro-sized particles are characterized by a relatively long-term suspended state and make a very significant contribution to the background component, even if they are located at a considerable distance from sources of pollution, this due to slow (under certain climatic conditions) natural removal of microparticles from the atmosphere. Microparticles, unlike gas impurities, are a complex heterogeneous mixture of many components. Besides, the micro-sized suspended particles have a high specific surface area, which allows them to absorb a large number of substances from the environment, which can penetrate into the internal environment of the organism together with microparticles and exhibit toxic effect. The suspended particulate matters (SPM) with a diameter of less than 10 µm ($PM_{10}$) easily penetrate into the human body and settle in different parts of the respiratory tract. The suspended $PM_{10}$ are a complex of the thoracic particles that settle in the trachea and large bronchi. The respirableparticles with a diameter of 0.5-1.0 µm penetrate into the lower airways – bronchioles and alveoli. The prolonged exposure to elevated concentrations of suspended particles with a diameter of less than 2.5 µm ($PM_{2.5}$) in atmospheric air reduces the life expectancy in the population from several months to several years [1-5].

Currently in Europe, in the USA and in the countries of the Asian region the monitoring of $PM_{10}$, $PM_{2.5}$ is required. In Russia the monitoring is still conducted only by measuring of the total mass concentration of particle air pollutants. The air quality monitoring is carried out only in megapolises of the country or for scientific purposes. The processes of action of various fractions of microsuspensions on respiratory system have not been studied sufficiently in comparison with the effect of gas components of atmospheric air on the human body [6-8]. The precise mechanism as to how PM may influence health and lung function is unknown. Studies have suggested that PM may mediate adverse health effects via the generation of reactive oxygen species [9-11], activation of cell signaling pathways, and alterations of respiratory tract barrier function and antioxidant defenses, all of which may lead to airway inflammation and changes in pulmonary function [12]. Furthermore, activation of many cellular signaling pathways has been attributed to specific chemical and metal constituents of PM that have been isolated in vitro. This suggests that PM of various sources may lead to diverse responses, making compositional analysis of PM by region an important consideration for future research [13].

The aim of the study was to determine the features of the influence of various size fractions of microsuspensions and toxic heavy metals of the air environment on external respiration function (ERF) of healthy residents of Vladivostok (Russia) and people with broncho-pulmonary diseases.

### Material and Methods

Vladivostok located on the seacoast in the southern part of the Russian Far East with a population of about 607,000 residents was taken as an object of investigation. The main supplier of SPM to the city's atmosphere is road transport, seaports, thermal power stations and an incineration plant. The monsoon climate of the city in combination with a high technogenic effect causes increased physiological loads on ERF of people [14].

The methodology of the study was based on the principle of a spatio-temporal comparison of data of ERF of Vladivostok residents with parameters of air pollution by SPM. Air pollution was estimated by the content of dust and metals in a snow cover of the city, so patients were selected during winter period (2010-2015). We examined 131 residents of Vladivostok: the control group consisted of 27 practically healthy people; chronic catarrhal non-obstructive bronchitis (CCNOB) was diagnosed in 29 people; controlled bronchial asthma was diagnosed in 51 people; uncontrolled bronchial asthma was diagnosed in 24 people. Asthma and chronic bronchitis were diagnosed in accordance with the Global Strategy for Asthma Management and Prevention (GINA, updated 2015) and the International Classification of Diseases 10th revision (ICD-10). The survey was conducted in accordance with the standards of the Declaration of Helsinki «Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects» (2013). The study was approved by Institutional Ethics Committee. The voluntary informed consent was obtained from all patients. The patients have lived in areas with unfavorable ecological conditions associated with closed type of residential building, the proximity of highways, road junctions, thermal power stations, an incinerator plant, and other objects polluting the air for at least 5 years. The exclusion criteria were the presence of acute respiratory diseases, tobacco smoking and chronic diseases of internal organs during the phase of decompensation.

The complex study of the ERF was carried out using system Master Screen Body (Care Fusion, Germany). The study of ventilation capacity of the lungs was performed by spirography (VC – vital capacity; IC – Inspiratory capacity; FVC – forced expiratory vital capacity; FEV1 – forced expiratory volume after 1 second; FEV1/VC – FEV1 in % of vital capacity; FEV1/FVC – FEV1 in % of forced expiratory vital capacity; PEF – peak expiratory flow; MEF75 – forced expiratory flow at 25% of FVC; MEF50 – forced expiratory flow at 50% of FVC; MEF25 – forced expiratory flow at 75% of FVC; MMEF75/25 – mean maximal expiratory flow between 25% and 75% of FVC; FET – forced expiratory time) before and after using bronchodilator, that allowed to determine the type of pulmonary ventilation disorder, degree and reversibility of bronchial obstruction. The method of body pletismography ($R_{tot}$ – bronchial resistance total; $R_{in}$ – resistance inspiratory; $R_{ex}$ – resistance expiratory; FRC – functional residual capacity; RV – residual volume; TLC – total lung capacity; RV/TLC – RV in % of TLC) allowed to study of static lung volumes and bronchial resistance.

The state of the air was estimated by aerosol suspensions of solid particles, which were collected from precipitation (snow). Snow samples were collected during snowfall periods in districts with different levels of anthropogenic impact, where respondents are living. The melted snow was analyzed using a laser particle size analyzer Analysette 22 NanoTec (Fritsch, Germany), which determines the size distribution and shape of the particles [10]. SPM with various sizes were evaluated by size range and the adsorption of toxic heavy metals. We study distribution of air dust suspensions by size fraction (0-1, 1-10, 10-50, 50-100, 100-400, 400-700, and >700 µm) expressed as percent of total concentration of all fractions in the sample and the content of toxic heavy metals (Pb, Cr, Mn, Fe, Co, Ni, Cu, Zn) expressed in µg/l [15, 16].

The pathogenic impact of microsuspentions on ERF was determined by statistical discriminant function module (Statistica 8). Discriminant analysis is one of multivariate statistical methods that allowed us to identify independent variables (fractional composition and toxic metals) that discriminate emerging groups (ERF parameters). Pathogenic impact on the respiratory system was assessed by quantitative indicators of microsuspensions and toxic metals contained in the air. We supposed that the higher pollution level the more pathogenic impact on the respiratory system. As a result, each environmental factor was encoded by quantitative characteristics according to the median. The quantitative characteristics of pollution that were below the median were assessed as a weak pathogenic effect, characteristics that were within the median and above the median were done as moderate and strong negative effect on ERF, respectively. The successive determination of the discriminant functions for each encoded environmental factor, that best discriminate groups of dependent variables (ERF parameters), was conducted by «step-by-step analysis with exception». At each step dependent variables making a small contribution to the difference in the action of external factors were eliminated. Only discriminant functions had $p<0.05$ were selected. The optimality of discrimination of groups of ERF indicators according to the pathogenic impact of air pollution was assessed by Wilks' lambda (α) considering its statistical significance ($p<0.05$). The low discriminant index α indicated strong dependence of ERF on environment quality, conversely, the high value of α shown its insignificant effect.

### Results

Discriminant analysis in the group of healthy people (control group) has been carried out. The responsiveness of ERF parameters (32 parameters) has been found only for 8 environmental factors and 13 ERF parameters of 15 studying parameters of SPM and toxic heavy metals by iteration of calculations (*Table* 1). The discriminant functions according to the value of Wilks' lambda had quite high values ($\alpha$ = 0.6-0.78) that indicates a weak effect of air pollutants on ERF, therefore their influence can be attributed to the category of an adaptive-compensatory reaction (*Table* 1).

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**Table1. The impact (α) of fractional composition of suspended particulate matters and toxic metals on the parameters of external respiration function in healthy residents of Vladivostok**

| *Parameters of external respiration function* | | *Size fractions of suspended particulate matter, %* | | | | *Content of toxic heavy metal, µg/l* | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 0-1 µm | 1-10 µm | 10-50 µm | 50-100 µm | Cr | Mn | Cu | Zn |
| Body plethysmo-graphy | R tot, % | α=0.72, p=0.05 | | α=0.70, p=0.01 | | | | | |
| | FRCplet, % | | | | | | | | |
| | RV, % | | | | | | | | |
| | TLC, % | | | | | α=0.78, p=0.05 | | | |
| | RV/TLC, % | | | | | | | | |
| Spirography before bronchodilator test | FEV1/VC (or VCmax), % | | | | | | | α=0.64, p=0.02 | α=0.61, p=0.02 |
| | FEV1/FVC, % | | | | | | | | |
| | PEF, % | | | | | | | | |
| | MEF75, % | | | | | | | | |
| | MEF50, % | | α=0.65, p=0.04 | | α=0.66, p=0.05 | | | | |
| | MEF25, % | | | | | | α=0.64, p=0.02 | | |
| | MMEF75/25, % | | | | | | | | |
| | FET, s | | | | | | | | |

FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity; RV/TLC, RV in % of TLC; FEV1/VC, FEV1 in % of vital capacity; FEV1/FVC, FEV1 in % of forced expiratory vital capacity; PEF, peak expiratory flow; MEF75, forced expiratory flow at 25% of FVC; MEF50, forced expiratory flow at 50% of FVC; MEF25, forced expiratory flow at 75% of FVC; MMEF75/25, mean maximal expiratory flow between 25% and 75% of FVC; FET, forced expiratory time.

**Table 2. The impact (α) of fractional composition of suspended particulate matters and toxic metals on the parameters of external respiration function in patients with chronic catarrhal non-obstructive bronchitis living in Vladivostok**

| *Parameters of external respiration function* | | *Size fractions of suspended particulate matter, %* | | | *Content of toxic heavy metal, µg/l* | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 0-1 µm | 1-10 µm | 10-50 µm | Cr | Mn | Co | Cu | Zn |
| Body plethysmography | $R_{in}$, kPa/l/s | α=0.67, p=0.02 | | | α=0.67, p=0.02 | | α=0.70, p=0.04 | | α=0.70, p=0.02 |
| | $R_{ex}$, kPa/l/s | | | | | | | | |
| | $R_{tot}$, kPa/l/s | | | | | | | | |
| Spirography before bronchodilator test | FEV1/FVC, % | | α=0.60, p=0.01 | | | | α=0.60, p=0.01 | α=0.68, p=0.05 | |
| | PEF, % | | | | | | | | |
| | MEF75, % | | | | | | | | |
| | MEF50, % | | | | | | | | |
| Spirography after bronchodilator test | FEV1/VC (or VCmax), % | α=0.60, p=0.01 | | | α=0.60, p=0.01 | α=0.55, p=0.005 | α=0.60, p=0.01 | α=0.50, p=0.002 | α=0.60, p=0.01 |
| | FEV1/FVC, % | | | α=0.66, p=0.04 | | | | | |
| | PEF, % | | | | | | | | |
| | MEF75, % | | | | | | | | |
| | MEF50, % | | | | | | | | |

$R_{in}$, resistance inspiratory; $R_{ex}$, resistance expiratory; $R_{tot}$, bronchial resistance total; FEV1/FVC, FEV1 in % of forced expiratory vital capacity; PEF, peak expiratory flow; MEF75, forced expiratory flow at 25% of FVC; MEF50, forced expiratory flow at 50% of FVC; FEV1/VC, FEV1 in % of vital capacity.

**Table 3. The impact (α) of fractional composition of suspended particulate matters on the parameters of external respiration function in patients with controlled asthma living in Vladivostok**

| *Parameters of external respiration function* | | *Size fractions of suspended particulate matter, %* |
|---|---|---|
| | | 0-1 µm |
| Spirography before bronchodilator test | VCmax, % | α=0.77, p=0.03 |
| | IC, % | |
| | FVC, % | |
| | FEV1, % | |
| | FEV1/VC (or VCmax), % | |

VC, vital capacity; IC, inspiratory capacity; FVC, forced expiratory vital capacity; FEV1,forced expiratory volume after 1 second; FEV1/VC, FEV1 in % of vital capacity.

We have established that in healthy people fine (0-1 µm) and medium (10-50 µm) dispersed fractions of SPM impact on total bronchial resistance ($R_{tot}$) and parameters, which feature hyperinflation of the lung (FRC, RV, RV/TLC). We identified that fine SPM (1-10 µm) and the coarse fractions of SPM (50-100 µm) effect on indicators characterizing patency of small and medium-sized bronchi and expiration time (MEF50, MEF25, FET), and toxic metals (Mn, Cu, Zn) influence on ERF parameters describing bronchial patency. Besides, Zn impact on large-sized bronchi (MEF75), Mn act on small airways (MEF25) (*Table* 1).

The results of the study shown that fine SPM (0-50 µm) and toxic heavy metals (Cr, Mn, Co, Cu, Zn) effect on ERF parameters that characterize patency of large and medium-sized bronchi (FEV1/VCmax, FEV1/FVC, PEF, MEF75, MEF50) and bronchial resistance at inhale ($R_{in}$) and at exhale ($R_{ex}$) in patients with CCNOB. In this case, according to body plethysmography data, only micro-sized fractions of SPM (0-1 µm) and Cr, Co и Zn of heavy metals influence on bronchial resistance (*Table* 2).

SPM (except 0-1 µm fraction) and toxic heavy metals did not have a pathogenic effect on ERF parameters in patients with controlled asthma. SPM (0-1 µm) impact on parameters of bronchial patency weakly (α=0.77, p=0.03) (*Table* 3).

**Table 4. The impact (α) of fractional composition of suspended particulate matters and toxic metals on the parameters of external respiration function in patients with uncontrolled asthma living in Vladivostok**

| *Parameters of external respiration function* | | *Size fractions of suspended particulate matter, %* | | | | *Content of toxic heavy metal, μg/l* | |
|---|---|---|---|---|---|---|---|
| | | 0-1 μm | 50-100 μm | 400-700 μm | > 700 μm | Cr | Zn |
| Body plethysmography | R*tot*, %<br>FRC, %<br>RV, %<br>TLC, % | α=0.29, p=0.04 | α=0.29, p=0.05 | α=0.33, p=0.007 | α=0.33, p=0.02 | α=0.33, p=0.02 | α=0.3, p=0.02 |
| Spirography before bronchodilator test | FEV1, %<br>FEV1/ VC (or VCmax), %<br>FEV1/FVC, %<br>PEF, %<br>MEF75, % | α=0.29, p=0.04 | | | | | |
| Spirography after bronchodilator test | FEV1/FVC, %<br>PEF, %<br>MEF75, %<br>MEF50, %<br>MEF25, %<br>MFEF75/25, %<br>FET, s | | α=0.06, p=0.02 | | | | |

$R_{tot}$, bronchial resistance total; FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity; FEV1, forced expiratory volume after 1 second; FEV1/FVC, FEV1 in % of forced expiratory vital capacity; FEV1/VC, FEV1 in % of vital capacity; PEF, peak expiratory flow; MEF75, forced expiratory flow at 25% of FVC; MEF50, forced expiratory flow at 50% of FVC; MEF25, forced expiratory flow at 75% of FVC; MMEF75/25, mean maximal expiratory flow between 25% and 75% of FVC; FET, forced expiratory time.

Despite of the use of the basal therapy, in patients with uncontrolled asthma the maximum pathogenic effect of air pollution level on ERF (α=0.06-0.33) with a high significance level of the result (p=0.007-0.050) have been detected. Uncontrolled asthma is manifested by severe disorders of ERF, so the response to external influence by the number of factors increased to 8 in comparison with controlled asthma. Moreover, the dependence of both micro-sized particles (0-1 μm) and SPM of medium and coarse fractions (50-700 and >700 μm) increased. It is reflected in a significant decrease in Wilks' lambda (α=0.06-0.29, p=0.02-0.04). It have been shown that micro-sized particles (0-1 μm) and medium SPM (50-100 μm) have marked impact on indicators of ERF, which describe bronchial patency, hyperinflation of the lung and total bronchial resistance, coarse SPM (400-700 and >700 μm) and airborne toxic heavy metals (Cr, Zn) influence on the parameters that characterize hyperinflation of the lung and total bronchial resistance (*Table* 4).

In patients with uncontrolled asthma the external impact of coarse SPM (400-700 and >700 μm) and airborne toxic heavy metals (Cr, Zn) was manifested in functional changes in the lungs by the indices of body plethysmography. The influence of that micro-sized (0-1 μm) and medium (50-100 μm) SPM on ERF was revealed by both spirography and body pletizmography (*Table* 4).

## Discussion

According to statistics, the number of cars in Vladivostok is among the highest in Russia – more than 600 cars per 1000 citizens. The difficult terrain in the city, the lack of multi-level parking areas and the instability of road traffic worsen the atmospheric pollution by products of incomplete combustion of fuel. Besides road transport, the city's air is polluted by thermal power stations and a large number of boiler houses with a long service life (>25 years) of technological equipment. Energy facilities operate mainly on brown coal, hard coal, fuel oil, diesel fuel and only single facilities do on gas [6, 14, 17]. Therefore, the air environment of the city near highways and pollution sources has a high level of man-made pollution and causes an increased risk of development of respiratory pathology in the city's population.

High calculated values of Wilks' lambda (α=0.60-0.78) in healthy people of Vladivostok indicate that the response of parameters of ERF to the impact of SPM and toxic metals in them is an adaptive-compensatory reaction (*Table* 1). This group of people reacts predominantly to the presence of fine fractions of SPM, the most pathogenic components, in atmospheric air. The largest particles do not have a significant effect on healthy residents of the city. However, the findings suggest that violations of the ventilation capacity of the lungs develop in healthy people living in an urbanized territory with high technogenic pollution. It may further contribute to the development of respiratory diseases.

Calculations of discriminant function for the group of patients with CCNOB showed a slight decrease in Wilks' lambda (α=0.5-0.7), that tell about the increased of impact of air pollutants (*Tables* 1 and 2). Besides that, the change in the nature of the response has been occurred. Thus, coarse fractions of SPM (>50 μm) did not among influential SPM, and Co was added to the spectrum of the influence of toxic metals (*Table* 2). In this way, the pathogenic effect of SPM and toxic heavy metals on ERF in the group of patients with CCNOB increased in comparison with the control group, and the nature of the impact of toxic metals and micro-sized fractions of SPM was changed.

Complete control over the disease in patients with controlled asthma could be achieved by the use basal therapy, as the result, there will be no clinical manifestations and functional changes in ERF. Basal therapy can minimize the adverse effect of microsuspentions and toxic heavy metals of the air environment on ERF (*Table* 3).

Uncontrolled asthma is manifested by severe disorders of ERF, so the observed dynamic of the response may be related to the development of more severe obstructive disorders of pulmonary ventilation and hyperinflation in this group of patients, which increases the sensitivity of patients to the negative effect of both fine and coarse fractions of SPM.

PM exposure can have important impacts on lung function in those with and without existing lung disease; however, whether individuals with pre-existing respiratory disease are more susceptible to the adverse effects of PM exposure is unclear. Few studies examine the variability in lung function response to PM exposure specifically by respiratory disease status. Toxicological studies suggest that the presence of allergic airway conditions may increase susceptibility to PM exposure; however, epidemiologic studies have been inconsistent in clarifying this relationship [18]. Identifying risk factors of those who will be more susceptible to the health effects of PM exposure is a research priority.

## Conclusion

The negative influence of different intensity of SPM and toxic heavy metals of the air environment on ERF of healthy residents and patients with broncho-pulmonary pathology of various severities living in Vladivostok was found. The study demonstrated that a tendency of disorder of ventilation capacity of the lungs is formed in a healthy urban population at the presence of an adaptive-compensatory reaction of the external respiration function to air pollutants. It can contribute to the development of respiratory diseases in the future.

It has been determined that a degree of external impact increase depending on severity of pulmonary ventilation disorders. There is impact of fine fraction of SPM (0-50 µm) and toxic heavy metals on ERF of patients with CCNOB. Basal therapy minimizes the adverse effect of microsuspensions and toxic heavy metals on ERF of patients with controlled asthma. In uncontrolled asthma wide range of SPM fractions have the most pathogenic effect on ERF.

### Conflict of interest

We declare that we have no conflict of interest.

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