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Original article

Assessment of purine catabolism and morbidity in miners depending on their work experience

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Abstract: *Objective* — The role of end products of purine metabolism as predictors of the development of pathological changes and diseases caused by the impact of dust on the human body in a professional environment vs. the work experience (duration of underground experience in the field).
Material and Methods — We analyzed the content of the end products of purine metabolism in the blood plasma of coal miners depending on the length of working in dusty conditions and evaluated the morbidity in the studied individuals via an analysis of the biomarkers.
Results — The median levels of xanthine and uric acid exhibited similar significant trends with a decrease in values with underground work experience under 3 years and an increase in values with 5 or more years of experience. When assessing outcomes 1-3 years after the selection of coal miners into the study, we revealed that both acute diseases (acute respiratory viral infection (ARVI), COVID-19, acute bronchitis, and community-acquired pneumonia) and chronic diseases were present in all groups. One coal miner (2.9%) from the group with 7-10 years of underground work experience was diagnosed with an occupational disease. The development of radiological changes in the chest organs (pulmonary fibrosis, symptoms of chronic bronchitis) was detected in the groups with an experience of up to 3 years, 3-5 years, 5-7 years, and 7-10 years in 6.4%, 9.4%, 11.1%, and 5.8% of miners, respectively.
Conclusion — According to logistic regression data, underground experience of 7-10 years has led to the reduction in the levels of xanthine and uric acid in the blood, which inflicted a statistically significant effect on the development of diseases in miners. Long-term underground work yielded 8.6-fold increase in the risk of developing diseases in miners.

Keywords: morbidity, purines, xanthine, uric acid, miners.

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Introduction

The issues of protecting and promoting the health of the working population constitute the most important health care problem. The development of occupational diseases has a social nature due to significant economic damage to the country and the increase in disability among people working in hazardous conditions. As for employees at mining enterprises in the Republic of Kazakhstan, 24.5-46.6% of them worked in hazardous working conditions during 2017-2022 [1-3]. Exposure to air pollution in the workplace (particulate matter, gases, and exhaust) resulted in 450 thousand deaths [4].

According to the annual reports of the freelance republican occupational pathologist, the number of patients with occupational respiratory diseases who were put on dispensary records in the entire Republic of Kazakhstan in 2018 was 65 per 10 thousand working population. The number of dispensary patients with occupational pathology in the Karaganda Oblast in 2018 was 2,966, of which 644 were with pneumoconiosis. An analysis of newly diagnosed occupational diseases during the period of 2017-2019 has revealed a trend towards an increase in the number of patients with occupational diseases in Karaganda Oblast from 66% to 85%.

The dust generated in the process of coal mining, when inhaled, accumulates in the lungs, damages the main macromolecules (DNA, proteins and lipids), thereby stimulating a cascade of pathological effects with the development of respiratory symptoms (cough, sputum, wheezing) and life-threatening diseases such as chronic bronchitis, occupational asthma, pneumoconiosis, emphysema and chronic obstructive pulmonary disease (COPD) [5]. Many authors reported that when dust enters the human body, oxidative stress occurs earlier than respiratory diseases caused by dust develop, and this stress is a central link in the development of dust pathology. Free radicals are generated either by the activity of dust particles or by the inflammatory effect caused by them, leading to oxidative stress, which contributes to the development of processes preceding pneumoconiosis [6, 7]. Lesions caused by mild pneumoconiosis become diagnosable approximately 10–20 years after exposure to hazardous dust, while severe pneumoconiosis may become clinically evident approximately 5–10 years after dust exposure [8, 9].

Currently, the search for metabolic components with noteworthy prognostic potential in the early diagnosis of diseases, including lung diseases caused by dust, is very relevant. Purines are a group of molecules utilized by all cells in the body for many important biochemical processes. Purine metabolism has a pronounced effect on the permeability of cell membranes, blood clotting, secretion of prostaglandins, along with participating in redox reactions, etc. [10, 11]. Since recently, the role of extracellular purines in chronic lung diseases was actively studied.

The release of purine nucleotides from airway epithelial cells is increased during acute inflammatory processes and plays an important role in the pathophysiology of chronic lung diseases. In the blood plasma of patients with COPD, an increase in the level of purine bases (adenine and guanine) and intermediate products of purine metabolism (hypoxanthine, xanthine and uric acid) was detected with a clear dependence on the severity of the disease [10]. In patients with idiopathic interstitial pneumonia, reduced concentrations of adenine, hypoxanthine and xanthine were detected with an increase in xanthine oxidase activity [12]. Uric acid is present in the fluid of the epithelial lining of the respiratory tract and, along with other endogenous antioxidants, it contributes to the protection against oxidative stress [13]. The respiratory system is exposed to high levels of reactive oxygen species (ROS) as a result of industrial air pollution, cigarette smoke, and repeated infections. Levels of serum antioxidants, such as uric acid, may play a particularly important role in susceptibility to respiratory disease. In a population-based cohort study, scientists from the UK determined that low uric acid levels in long-term smokers were associated with the risk of developing COPD and lung cancer [14].

The relationship between the levels of purine metabolism end products and pulmonary dysfunction may be explained by several phenomena. Hypoxia in patients with impaired pulmonary function causes the production of the end products of purine metabolism. The appearance of pulmonary hypertension in lung diseases also leads to an increase in uric acid levels. Oxidative stress and inflammation cause damage to lung tissue and lead to increased purine catabolism. Increased uric acid levels in turn cause systemic inflammation, which ultimately leads to impaired pulmonary function. Therefore, end products of purine metabolism can act both as antioxidants in the upper respiratory tract and proinflammatory components, which implies the need to control their levels.

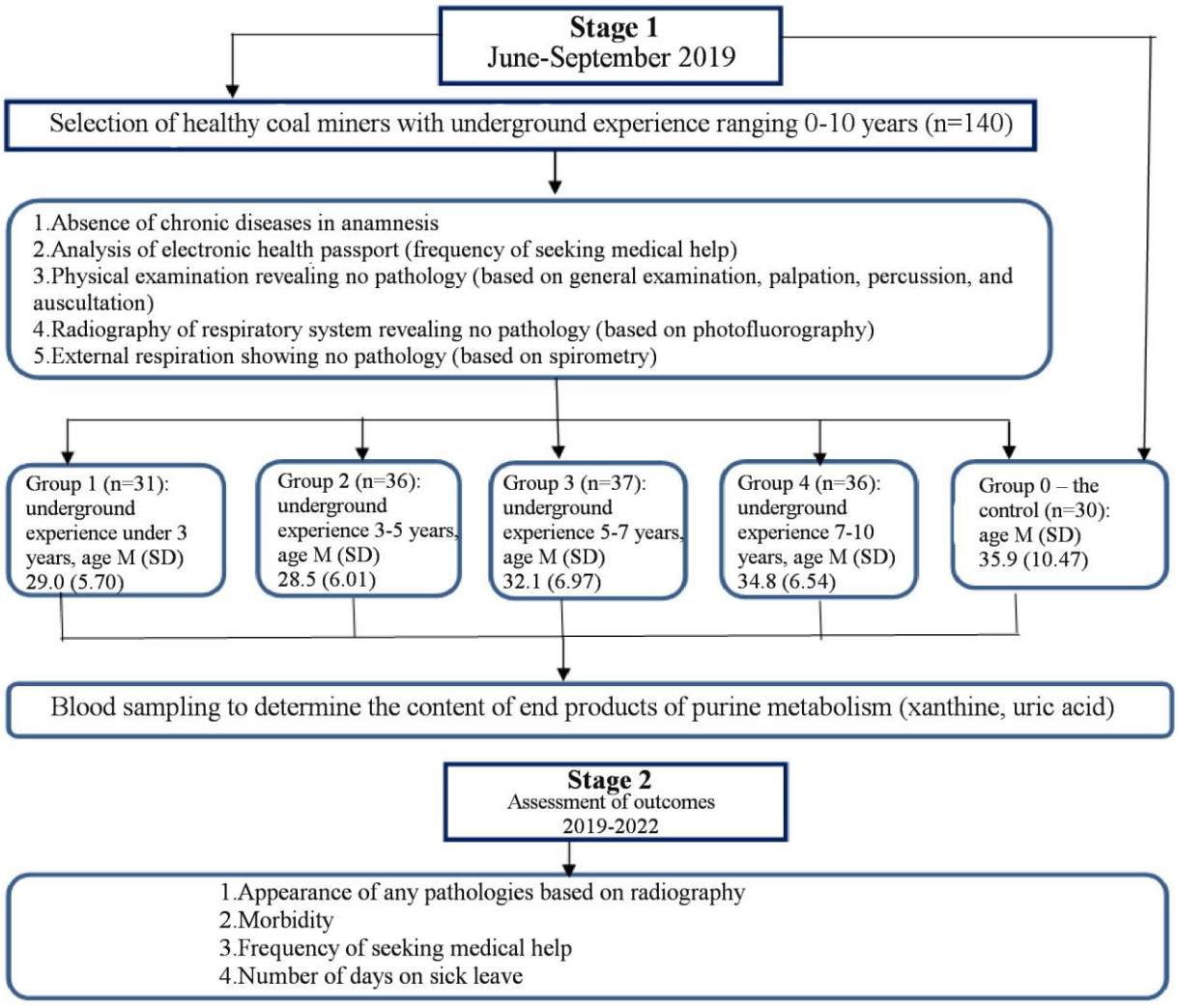

Figure 1. Study design.

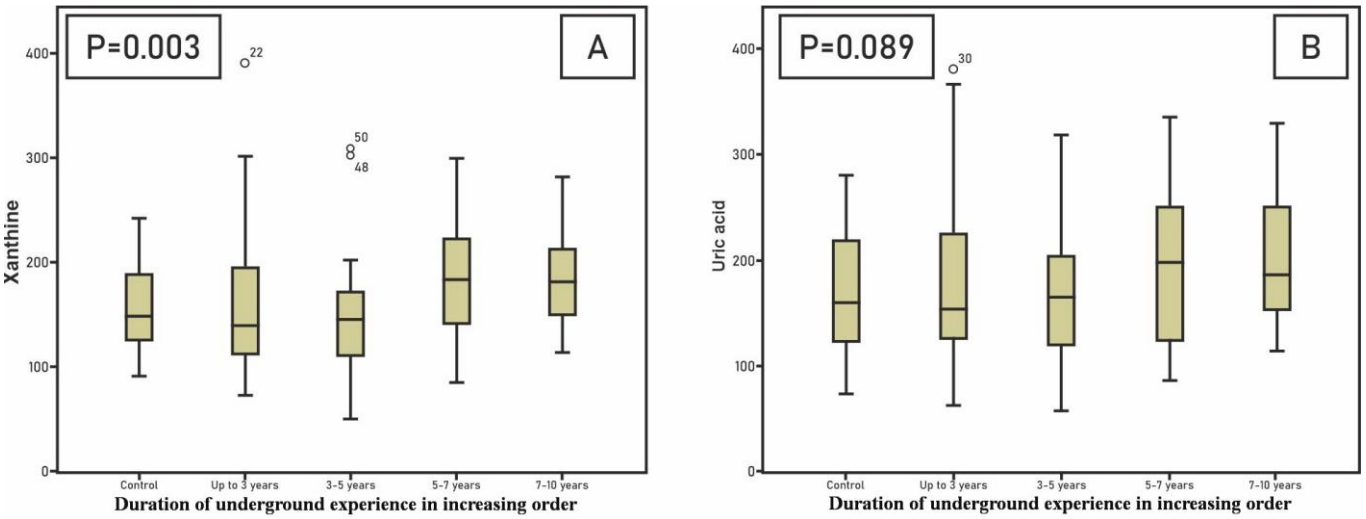

Figure 2. Comparative characteristics of end products of purine metabolism in the blood plasma of coal miners depending on the duration of underground work using the Kruskal-Wallis test (A – xanthine, B – uric acid). Xanthine and uric acid were measured in ext. units and mmol/L, respectively. Critical significance level p=0.0127.

Table 1. Pairwise comparative analysis of uric acid content between study groups based on the duration of underground experience, using the Mann-Whitney test

Group	*Indicator*	*Mean rank*	*U-statistic (Mann-Whitney)*	*Z*	*P**
Group 2	Uric acid	25.57	302	-1.738	0.082
Group 3		34.59			
Group 2	Uric acid	25.03	286.0	-2.343	0.019**
Group 4		36.77			
Group 1	Uric acid	26.98	344.5	-1.076	0.282
Group 3		33.12			
Group 1	Uric acid	26.23	322	-2.082	0.037**
Group 4		35.61			

* Critical significance level p=0.05; ** Statistically significant level (p) is achieved.

Studies of purine metabolites in miners depending on work experience with the risk of developing occupational pathology are not covered in the published sources. Therefore, the study of metabolic changes occurring in the body under the impact of various dust particles is of interest from the standpoint of the possibility of carrying out preventive procedures to prevent their development, which will help preserve the health of the working population. Hence, the *goal* of our study was to examine the role of the end products of purine metabolism as predictors of the development of pathological changes and diseases during the exposure of the human body to dust in a professional environment vs. work experience (i.e., duration of underground experience).

Material and Methods

Study design

We conducted an observational prospective cohort study (*Figure 1*). It involved 140 miners who experienced impact of dust on their body.

Inclusion criteria: apparently healthy coal miners (without internal diseases or chronic occupational pathology) as reported by an occupational pathologist, male gender, 18 years of age and older, work experience in dusty conditions up to 10 years, absence of any radiological changes in the respiratory system and changes in external respiration at the time of physical examination, and signing of written informed consent.

Exclusion criteria: age under 18 years old, female gender, internal diseases, and chronic occupational pathology.

The study was approved by the Bioethics Committee of Karaganda Medical University, protocol No. 18 of 05 May 2019.

Table 1 presents comparative characteristics of the study groups. All included miners were distributed among four groups depending on their professional experience: Group 1 with work experience up to 3 years (n=31), Group 2 with professional experience of 3-5 years (n=36), Group 3 with miners working 5-7 years (n=37), and Group 4 with work experience of 7-10 years (n=36). The control group (Group 0) consisted of 30 apparently healthy individuals who were not exposed to dust in the course of their professional activities.

The study was conducted in two stages. At the first stage (from June to September 2019), reasonably healthy coal miners with different lengths of underground experience were included in the study using a stratified sampling method. Health assessment was performed during annual occupational medical examination, and its results were recorded in an electronic health passport. At the time of selection for the study, all miners belonged to the *apparently healthy* category, did not have a history of any chronic diseases or frequent visits to medical institutions for help due to illness, and their physical examination data, radiography of the respiratory system, and external respiration function were normal. The clinical examination was carried out in accordance with the generally accepted methodology and was accompanied by filling out primary documentation, which included patient passport data, anamnesis data (presence of chronic diseases, frequency of visits to medical institutions for help due to illness, number of days on sick leave), and results of physical examination (general examination, palpation, percussion, auscultation), photofluorography and spirometry. All study subjects underwent blood sampling to determine the levels of purine metabolism indicators.

Table 2. Pairwise comparative analysis of uric acid/xanthine content between study groups based on the duration of underground experience, using the Mann-Whitney test

Group	*U-statistic (Mann-Whitney)*	*Z*	*P**
		Uric acid/Xanthine	
Group 0 Group 2	414.5	-1.805	0.071
Group 2 Group 3	457.5	-2.301	0.021**
Group 1 Group 2	597.5	-0.935	0.350
Group 0 Group 1	449.5	-1.683	0.920
Group 2 Group 4	486.0	-1.297	0.195

* Critical significance level p=0.05; ** Statistically significant level (p) is achieved.

Table 3. Results of logistic regression to assess the effects of independent factors on total outcomes in coal miners with different underground experience

Indicator	*B (SE)*	*P*	*95% CI for exp B*		
			Lower	Exp B	Upper
Constant	1.721 (0.209)	0.000		5.593	
Xanthine	-0.051 (0.025)	0.044*	0.904	0.950	0.999
Uric acid	0.020 (0.011)	0.072	0.998	1.020	1.043
Group 0	-	0.113			
Group 1	0.089 (0.791)	0.911	0.232	1.093	5.149
Group 2	0.712 (0.803)	0.376	0.422	2.037	9.835
Group 3	1.786 (0.952)	0.061	0.922	5.964	38.561
Group 4	2.159 (0.966)	0.025*	1.304	8.664	57.549

* Critical significance level p=0.05.

Table 4. Results of radiography of respiratory organs in 2020-2022 (%)

Detected signs of:	*Group*	*2020*	*2021*	*2022*
Pulmonary fibrosis	1	-	-	3.2
	2	-	6.3	3.1
	3	-	11.1	2.8
	4	-	2.9	-
	0	-	-	-
Chronic bronchitis	1	-	-	3.2
	2	-	3.1	-
	3	2.7	5.6	2.8
	4	2.9	2.9	2.9
	0	-	-	-
Emphysema	1	-	-	-
	2	-	-	-
	3	-	-	-
	4	2.9	2.9	2.9
	0	-	-	-
Minor residual changes (calcifications)	1	-	-	-
	2	-	-	-
	3	-	-	-
	4	2.9	2.9	2.9
	0	-	-	-

At the second stage (2019-2022), based on the electronic health passport, dynamic monitoring of the health status of coal miners was carried out, revealing emergence of any lesions according to radiography, morbidity, frequency of seeking medical help due to illness, and number of days on sick leave

Laboratory studies

Venous blood was sampled from June through September 2019 on an empty stomach in the morning and analyzed at the Department of Biochemistry at Karaganda Medical University. After centrifugation at 3,000 rpm, plasma was separated and used to determine the content of end products of purine metabolism (xanthine and uric acid) [15-17]. Purine bases were determined by direct spectrophotometry in an aqueous extract of venous blood serum after thermocoagulation. Blood plasma (0.3 mL) was injected into a standard glass tube followed by thermocoagulation in a boiling water bath for 5 minutes. A prerequisite was active boiling to avoid defragmentation of the coagulant. After cooling at room temperature for several minutes, 3 mL of double-distilled water were added to the test tube. After 30 minutes of incubation at 37 °C, the extinction of the extract against the pure extractant (double-distilled water) was measured in an optical cuvette with an optical path length of 10 nm using an SF Apel PD 303 spectrophotometer (Japan). In solutions, the studied purines have the property of maximum absorption of UV radiation at a specific wavelength for each metabolite (extinctions at 276 and 293 nm, respectively, for xanthine and uric acid), varying slightly depending on pH value. The content of purines in the aqueous extract of the blood serum subjected to thermocoagulation is directly proportional to their true concentration in whole blood serum. The concentrations of purine bases and uric acid were expressed in extinction units (ext. units) and in µmol/L, respectively, and calculated by the formula (1):

$$C=E\times 1{,}000, \quad (1)$$

where: C is the concentration of metabolites of purine metabolism, ext. units (µmol/L), 1,000 is the coefficient for converting extinction into concentration.

Statistical data processing

Statistical processing of the collected data was carried out using conventional software packages for applied statistical analysis (IBM SPSS Statistics 22, STATISTICA 13.2). The normality of the data distributions was assessed via the Shapiro-Wilk test. Given the non-normal distribution, comparisons of plasma content of purine metabolic intermediate products among miners of five independent groups were performed by the Kruskal–Wallis test with Bonferroni correction. Pairwise post hoc intergroup comparisons were conducted using the Mann-Whitney test.

Multivariate logistic regression was employed to assess the effects of end products of purine metabolism in blood plasma, duration of underground work, and duration of sick leave on the outcomes of patients in all five groups. The total group of outcomes included such medical conditions as COPD, bronchial asthma, bronchitis, sinusitis, polyarteritis nodosa, pneumoconiosis and were coded as follows: 0, presence of any outcome; 1, absence of any outcome. We used forced inclusion method with the simultaneous inclusion of independent predictors. Multivariate analysis included covariates with $p<0.05$ (or if they changed the main effect size by ≥10%). When testing the statistical hypotheses, we applied a critical significance level of p=0.05.

Table 5. Data from the electronic health passport on the number of sick study subjects and whether miners and individuals in the control group were on sick leave, annual number of instances of seeking medical help per 100 workers, depending on the frequency of instances (1-4 times a year) in 2019-2022.

Indicator	*Years*	*Group*				
		1, n=31	2, n=36	3, n=37	4, n=36	0, n=30
Number of sick people per 100 workers, median (Q1, Q3)	2019-2022	33.9 (32.3; 38.0)	40.3 (36.8; 41.7)	28.4 (25.0; 37.2)	30.6 (27.1; 33.3)	33.3 (28.3; 38.3)
Number of people on sick leave per 100 workers, median (Q1, Q3)	2019-2022	30.7 (28.2; 33.1)	32.0 (26.4; 36.8)	23.0 (20.3; 27.7)	25.0 24.3; 25.0)	11.7 (8.3; 17.5)
Total number of days on sick leave, abs. / median (Q1, Q3)	2019-2022	107.0 (83.04 133.8)	74.0 (62.5; 88.5)	76.5 (63.5; 110.3)	95.0 (86.3; 146.3)	46.5 (347.0; 62.0)
Total number of days on sick leave, abs. / mean per 100 workers	2019-2022	439 354.03	308 213.89	389 262.84	550 381.94	210 175
	Number of incidences of seeking medical help					
Annual number per 100 miners in 2019-2022, median (Q1, Q3)	1	60.0 (59.3; 63.2)	85.5 (79.7; 93.2)	78.7 (72.3; 82.7)	78.9 (72.9; 80.8)	80.0 (78.8; 83.4)
	2	32.9 (27.1; 36.8)	8.1 (5.3; 11.8)	14.6 (9.1; 22.2)	18.4 (15.3; 23.3)	10.0 (9.1; 13.8)
	3	3.6 (0.0; 7.6)	0.0 (0.0; 3.6)	6.8 (0.0; 13.7)	4.2 (0.0; 9.0)	0.0 (0.0; 2.5)
	4	0.0 (0.0; 2.5)	0	0	0	0.0 (0.0; 2.5)

Table 6. Morbidity by nosology based on electronic health passport in miners during 2019-2022, median (Q1, Q3)

Nosology	*2019-2022, per 100 miners*				
	Group 1	Group 2	Group 3	Group 4	Group 0
ARVI	30.7 (29.0; 33.1)	33.3 (31.2; 34.7)	18.9 (18.2; 24.3)	0.9 (0.8; 6.2)	18.4 (15; 24.1)
COVID-19	0 (0; 1.5)	2.8 (2.1; 2.8)	4.1 (2; 6.8)	1.4 (0; 3.5)	3.3 (2.5; 5.8)
Acute bronchitis	3.2 (2.4; 4)	4.2 (2.1; 6.2)	0 (0; 1.4)	1.4 (0; 3.5)	3.3 (3.3; 3.3)
Community-acquired pneumonia	0 (0; 0.8)	0	2.7 (2; 2.7)	0 (0; 1.4)	0 (0; 0.8)
COPD				2.8 (2.1; 2.8)	
Pneumoconiosis (anthracosilicosis)				2.8 (2.1; 2.8)	
Chronic sinusitis	0 (0; 0.8)	0	0 (0; 0.7)	0 (0; 0.7)	
CAD					3.3 (2.5; 4.2)
Arterial hypertension	1.6 (0; 3.2)	1.4 (0; 3.5)	1.35 (0; 4.1)	2.8 (2.1; 3.5)	10 (7.5; 11.7)
Arrhythmia			0(0; 0.7)		
Pituitary microadenoma	1.6 (0; 3.2)				
Polyarteritis nodosa	1.6 (0; 3.2)				
Internal hemorrhoids		0 (0; 0.7)	1.4 (0; 3.4)	0 (0; 0.7)	
Varicose veins				0 (0; 0.7)	

Results

The mean age of coal miners included in the study (Groups 1-4) was (31.2±6.78) years (ranging from 20 to 60 years) or 35.9±10.47 (ranging from 22 to 58 years) in control individuals (Group 0). The mean age of coal miners of Groups 1 and 2 with work experience of up to 3 and 3-5 years virtually did not differ from each other (29.0±5.70 years and 28.5±6.01 years, respectively). In Groups 3 and 4 (with work experience of 5-7 years and 7-10 years, respectively), it was 32.1±6.97 years and 34.8±6.54 years, correspondingly. In 2019, at the time of inclusion in the study, none of the study subjects had a history of any chronic diseases or frequent visits to medical institutions seeking help due to illness, and their physical examination data, radiography of the respiratory system, and external respiration function were normal. When analyzing the electronic health passport for 2017-2019, we observed mainly visits to medical institutions related to acute respiratory viral infection (ARVI) both in the control group and in all groups of coal miners just once a year.

The levels of end products of purine metabolism in the blood plasma, depending on the duration of underground experience of coal miners, are presented in *Figure 2*. There, we can observe a trend of a slight reduction in the median indicators with an experience of up to 3 years, then their increase with an experience of 3 to 5 years, and a maximum increase with an experience of 5 to 7 years.

A comparative analysis of the end product levels of purine metabolism in blood plasma vs. the duration of underground work of coal miners using the Kruskal-Wallis test showed statistically significant differences in xanthine levels between the groups (p=0.003). The content of uric acid did not differ significantly (p=0.089). However, the general trend remained: a decrease with experience of up to 3 years and a subsequent statistically significant increase with experience of more than 5 years. To search for statistically significant differences, we conducted pairwise comparisons of uric acid levels between Groups 1 and 3, 1 and 4, 2 and 3, and 2 and 4, using the Mann-Whitney U test (*Table 1*). The table shows statistically significant changes in uric acid ranks between Groups 2 and 4 (p=0.019), and 1 and 4 (p=0.037).

Considering that the activity of xanthin oxidase in terms of the uric acid/xanthine ratio in the studied groups did not reach statistical significance, pairwise comparisons were performed between the underground experience-based groups of coal miners using the Mann-Whitney U test (*Table 2*). Statistically significant differences were revealed in the uric acid/xanthine solely between Groups 2 and 3 (p=0.021), which implied an increase in the oxidative activity of xanthine oxidase during an underground experience of 3 to 5 years, catalyzing the oxidation of xanthine into uric acid with further reduction in its concentration.

The results of the logistic regression are presented in *Table 3*. As can be seen from the obtained logistic regression data,

underground experience of 7-10 years and xanthine have a statistically significant effect on the combined outcomes. That is, long-term underground experience yields an 8.6-fold increase in the risk of a miner developing a combined outcome. Uric acid and 5-7 years of underground experience approached statistically significant levels, but perhaps due to insufficient sample size and covariates, there was insufficient power. The predictive ability of this model was 85.4%.

In coal miners with underground experience, 1-3 years after their selection for the study (in 2020-2022), we revealed structural changes in the chest organs according to photofluorography, plain radiography, or computed tomography (*Table* 4). When analyzing the dynamics 1-3 years after the onset of the study (in 2020-2022), no radiological changes in the respiratory organs were detected in any individuals of the control group.

When conducting an analysis of the studied individuals over 2019-2022 to assess outcomes, the frequency of visits to medical institutions for help due to illness and the number of days on sick leave in dynamics after 1-3 years from the start of the study, we obtained the results presented in *Table* 5. As for the number of annual medical visits on the part of miners over 2019-2022, their majority, as well as subjects in the control group, sought medical help just once a year (*Table* 5).

Along with acute diseases (ARVI, COVID-19, acute bronchitis, community-acquired pneumonia), chronic diseases were diagnosed in all groups over time. The analysis of morbidity by nosology is presented in *Table* 6.

Discussion

The identified changes in the relative reduction in the content of end products of purine metabolism with work experience of up to 3 years may be associated with the adaptation of the body of coal miners to strenuous physical activity and dusty conditions of their workplace environment. It was experimentally proved that exposure to coal dust contributes to the triggering of the body's adaptive compensatory mechanisms via activating the metabolism of purine nucleotides in the liver, lymph nodes, adrenal glands, thymus and lympholysate, as well as through reducing it in the spleen [18]. Similar changes in the level of these indicators were detected by a group of authors [19] in patients with arterial hypertension, and two trends were identified: an increase in the level and a decrease in the values of end products of purine metabolism. However, that study did not evaluate the history of hypertension.

In coal miners of Ukraine, disorders were established that indicated the mechanism of pneumoconiosis development associated with changes in purine metabolism, with an increase of xanthine oxidase activity and the level of uric acid in the blood serum and subsequent incidence of autoimmune reactions against the background of the nonspecific resistance system disorders [20]. A study by Japanese scientists noted that men with hypouricemia and daily physical overload were at higher risk of cardiovascular morbidity and urinary system disorders [21].

Hypoxia in patients with impaired pulmonary function causes the production of the end product of purine metabolism and leads to increased purine catabolism. The emergence of extracellular end products of purine metabolism in the blood plasma can also occur due to cell lysis. The main sources of end products of purine metabolism are neutrophils, endothelial cells, and activated macrophages. An increase in the pool of extracellular purine metabolites is facilitated by ectoenzyme CD39, CD73, a complex of soluble enzymes (nucleotide pyrophosphatase, adenylate kinase and nucleotide diphosphate kinase) [22], purine-catabolizing enzymes (adenosine deaminase, alkaline phosphatase and 5'-nucleotidase) [23], and membrane purine transporters [24-27].

In healthy tissues, end products of purine metabolism are located intracellularly, the appearance of their extracellular pool is caused by an inflammatory response, and this process is controlled. In case of prolongation of inflammation and transition to pathology, the production of end products of purine metabolism becomes uncontrollable, which ultimately maintains aseptic inflammation. It was established that hyperuricemia negatively affects the endothelium, triggering its dysfunction; stimulates the growth of free radicals and superoxide anions, which increase oxidative stress and reduce the production of nitric oxide. This paralyzes the microvasculature, triggers the release of proinflammatory cytokines, promotes hypercoagulation and increased thrombus formation [28]. An increase in xanthine oxidase activity is considered as one of the mechanisms of damage to the epithelium of lung tissue. E.g., in patients with severe COPD, a decrease in xanthine oxidase activity was observed [10].

Purines, representing alarmins, signal the development of a pathological process leading to the activation of protective responses. At the same time, xanthine has a negative effect on the condition of the vascular wall resulting in disruption of its function, further damage to the endothelium and the release of purines from cells. Ultimately, a vicious circle develops in which one process aggravates the other and vice versa.

Study limitations

The incidence of COVID-19 among study participants could be one of the confounding factors affecting its results.

Conclusion

The duration of working in dusty conditions of up to 3 years is cumulative, i.e., contact and partial cleansing of coal particles occurs in the body of miners, which is accompanied by a decrease in the levels of xanthine and uric acid. Periods from 3 to 5 years, and especially from 5 to 7 years, are accompanied by an increase in the levels of xanthine and uric acid and higher activity of xanthine oxidase. The latter is aimed at the oxidation of xanthine into uric acid. These processes are progressively increasing and are aimed at the physiological elimination of solid particles from the body. The period from 5 to 7 years is accompanied by an increase in the number of diseases of the upper and lower respiratory tract, but organic lung lesions may not yet be detected during radiography. During this period, diseases of the cardiovascular system, primarily arterial hypertension, appear, which can probably be explained by the onset of endothelial dysfunction. Underground experience of over 7 years is associated with unfavorable outcomes on the part of respiratory and cardiovascular systems. As for laboratory indicators, there is a reduction in the levels of xanthine and uric acid, which is probably associated with the onset of endotheliosis accompanied by the formation of fibrosis in the pulmonary and vascular endothelial tissue. This physiological response is already pathological in its nature, implying a failure of adaptation. Hence, the time factor (from 5 to 7 years) and exposure to coal particles is important for the formation of pathological abnormalities in the lung tissue and cardiovascular system.

Conflict of interest

The authors state that they have no conflicts of interest.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Data availability

The data presented in this study are available on reasonable request from the corresponding author.

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