UDC 612.017:553.676

Characteristics of the immune system of the organism of workers in chrysotile-asbestos production

Хризотил-асбест өндірісіндегі жұмысшылардың иммундік жүйесінің сипаттамасы

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Өндірістік ортаның жағдайына бейімделу барысында адам денсаулығын қорғау үшін иммундық жүйе маңызды рөл атқарады. Авторлар хризотил-асбест шаңының әсер ету ортасында қызмет атқаратын қызметкерлердің иммундық жүйесінің жасушалық және гуморалдық тізбегін бағалаған. Жоғарғы тыныс алу жолдарының патологиясының қауіпті факторы болып иммунитеттің жасушалық және гуморалдық тізбектерінің тежелуімен жүретін қызметкерлердің ағзасындағы иммунореактивтің өзгеруі анықталды. Сонымен қатар хризотил-асбест шаңының әсерінен сілемейлі барьердің бұзылысына және жоғарғы тыныс алу жолдарының сілемейлі қабықшасының жергілікті иммунитетінің нашарлауына себепші болады.

В статье показана важная роль иммунной системы в сохранении здоровья человека при адаптации к условиям производственной среды, приведена оценка клеточного и гуморального звеньев иммунной системы организма работающих в условиях воздействия пыли хризотил-асбеста. Авторами выявлено, что фактором риска в развитии патологии верхних дыхательных путей является измененная иммунореактивность организма работающих, проявляющаяся угнетением клеточного и гуморального звеньев иммунитета. Установлено также, что воздействие пыли хризотил-асбеста приводит к нарушению слизистого барьера и снижению местного иммунитета слизистой оболочки верхних дыхательных путей.

Actuality

An estimate of the risk of respiratory pathology depends on experience exposure. With the increase of length of service in the «dusty» occupations mucosal defenses are gradually depleted, that confirmed by cytochemical and functional studies. Determination of the critical work experience in hazardous conditions can produce, according to some authors, to some extent alleviate prenosological diagnosis of occupational or professional work-related diseases [1, 2].

According to the concept of local immunity and mucous membranes and skin of both covers, addressed to the external environment, internal environment to protect and preserve its continuity through the close interaction of the complex evolution of produced non-specific and specific defense mechanisms [3].

Originally a local immunity implied complex cellular and secretory nonspecific and specific responses, including the barrier function of mucosal cells, the phagocytic activity of neutrophils and macrophages, T-cell immunity, antibody, anti-microbial proteins external secrets enzyme inhibitors. Local immunity is not identified with secretory immunity, but as it was considered a focal point of B-cell response to mucosal lymphoid tissue with glandular epithelium, which supplies the secretory component. Later, the concept of local immunity has expanded and now includes a set of responses of all cells of lymphoid series, occupying the mucous membranes, in cooperation with macrophages, neutrophilic and eosinophilic granulocytes, mast cells and other cells of connective tissue and epithelium [4].

Local immunity in otolaryngology — a barrier function of the mucous membranes, including limfo-epithelial bodies of the pharynx, located at the intersection of the respiratory tract and esophageal, first responding to another antigenic stimulation (infection) the inclusion of mechanisms of immune protection, and non-specific protective factors mucosa (mucociliary transport, production lysozyme, lactoferrin, interferon and others) [5, 6].

Change the immune status is one of the earliest and most sensitive signs of the impact of unfavorable factors of production in the body and can serve as a criterion for the risk of respiratory diseases among workers of chrysotile asbestos production.

The stability of the mucous membranes of microbial contamination is a «first wave immunity» and the state of the immune defense of the mucous membranes depends on the degree of exposure, a measure of pollutants from entering the air inhaled by man [7].

Indicators of the immune system of mucous membranes (the activity of lysozyme, secretory IgA, etc.) are highly informative in assessing the level of protection of mucous from harmful environmental factors [8].

Clinical manifestations and course of lung disease in asbestos workers in the production of defined immunological reactions in violation of immunoregulation and the development of secondary immunodeficiency, as well as relevant individual characteristics of the organism [9–11].

Thus, changes in immune reactivity play a leading role in the pathology of the respiratory system and study of the immune system in early stages of the disease process to predict the nature and degree of activity.

The aim of investigation

The aim of investigation is to study the cellular and humoral immune system in persons working under the impact of chrysotile asbestos dust on the JSC «Kostanai minerals.»

Materials and methods

The study was conducted according to the type of retrospective cohort clinical trial. The study was conducted at the National Center for Occupational Hygiene and Occupational Diseases, and was based on a survey of workers of JSC «Kostanai minerals». To study the influence of unfavorable factors of chrysotile asbestos production assessed the immune status of 106 male workers of JSC «Kostanai minerals» with industrial exposure to dust factor. The control group consisted of 20 males who do not have contact with asbestos dust. Analysis of the age structure of the surveyed showed that the vast majority of workers — those over 30 years of age 31–40 years, 29.4 % and 31.8 % were working 41 to 50 years. At the age of 50 years were 18, 6 % of men. All subjects depending on the duration of the production experience were divided into five groups in increments of 5 years, the largest number of workers have worked on this production of 6–10 years — 38.1 %, 16–20 years of experience have 21.9 % of people directly exposed to chrysotile asbestos dust.

To study the immune status of the surveyed population and determined the major subpopulations of lymphocytes: T cells, B cells, T helper, T suppressor cells and zero — 0-cells. Immunophenotyping of lymphocytes was performed using a «shortened» the panel of monoclonal antibodies (mAbs) to identify the following CD-markers: CD3 (T lymphocytes), CD4 (T helper), CD8 (T suppressor), CD20 (B lymphocytes), CD56 (natural killer cells). To assess humoral immunity held definition of serum immunoglobulins (IgA, IgM, IgG), secretory immunoglobulin A (SIgA) by ELISA according to the standard procedure [12, 13].

Statistical analysis of the results of the study was carried out using the software package Microsoft Office Excel 2003 and «Statistic 6,0» Windows'HR in the operating system, using the variational statistical analysis (mean values and their deviations — M ± m) with an estimate of the reliability of the results with respect to Student's t-test [14].

Results and discussion

Analysis of the cellular immunity system (Table 1) showed a significant difference in the content of CD3 (T lymphocytes) decrease in workers of the main group (59,1 ± 0,43 %) compared with controls (71,2 ± 0,52 %). There is also a significant gradual decrease in CD3 in workers with increasing length of service, so with 0–5 years experience — 70,1 ± 0,31 % ($p < 0.01$), and more than 20 years — 58,7 ± 0,41 % ($p < 0.01$).

Table 1

Indicators of T-managers the immune system surveyed in depending on the length (M ± m)

Indicators	Control=20	Experience				
		0–5 years (n=21)	6–10 years (n=19)	11–15 years (n=21)	16–20 years (n=23)	More than 20 years (n=22)
CD3, %	71,2±0,52	70,1±0,31	58,9±0,75	57,5±0,37*#	56,7±0,85*#	58,7±0,41*#
CD4, %	45,2±0,26	49,2±0,23*	44,9±0,45	42,8±0,25*	41,9±0,72*#	40,9±0,85*#
CD8, %	20,6±0,73	22,5±0,37	23,7±0,62*	24,1+0,57*	26,3±0,71*#	27,1±0,53*#
CD4/CD8	2,17±0,11	2,19±0,11	1,95±0,15	1,83±0,14	1,61±0,11*#	1,53±0,1*#

Notes: * — reliability of differences in indicators compared with the control, $p < 0.01$; # — reliability of differences in indicators compared to healthy workers with experience of 0–10 years, $p < 0.01$.

No significant differences in the content of CD-4 (T-helper cells) in the examined and control group is not found (43,8 ± 0,54 % and 45.2 0.26 %, respectively). Changing the contents of CD-4 from employees of chrysotile asbestos production, depending on the duration of exposure to industrial pollutants was complex: at the experience of 0–5 years, the relative abundance of CD 4 cells (49,2 ± 0,23 %, p <0.01) was significantly higher than controls, suggesting that activation of the immune system working under the impact of dust agent. Then have a CD4 workers with 6–10 years experience normalized 44,9 ± 0,45 %), which characterized the immune system to adapt to the conditions of the working environment.

Then there is a tendency to decrease their content in workers with experience of 16–20 years compared with not enough trained workers (41,9 ± 0,72 % and 49,2 ± 0,23 % (p <0.01), respectively). We work more than 20 years are set even lower rates as compared with the control group, and with short experienced workers — 40,9 ± 0,85 % (p < 0.01). This indicates a decompensation of the protective mechanisms of the immune system, manifested by a lack of activation of macrophages in the event that affected T-cells that perform the function of helper type 1, on the one hand, on the other hand, is the activation of humoral immunity (activation of specific B-lymphocytes to pro -induction of the anti-immunoglobulin) if affected by T-helper type 2.

No significant differences in the content of CD8 (T suppressor) in those basic and control groups could not be detected, but attention is drawn to increase their production levels with increasing seniority. So at the experience of 5 years CD8 figures were 22,5 ± 0,37 %, while at the experience of more than 20 years — 26,3 ± 0,71 % (p <0.01). Cytotoxic lymphocytes (CD 8) cells carry tumor immunity, therefore, takes place in the examined voltage killer lymphocyte function, which represents a risk in the development of cancer. The most efficient cells in the immune defense will probably be tested in B-lymphocytes, responsible for representation of allergens, peptides and other soluble antigens.

Comparative analysis of immunoregulatory index (CD4/CD8) showed a gradual decrease of this index (2,19 ± 0,11 — at the experience of 5 years, and 1,53 ± 0,1 — at the experience of more than 20 years, p < 0.01), which indicates an increase in cytotoxicity with increasing seniority in contact with chrysotile asbestos.

Significant reduction in the functional activity of T cells was observed in persons who have been working more than 20 years compared with short experienced workers, which confirms the hypothesis that the stage of decompensation, observed in the immune system in many years of contact with chrysotile asbestos.

Content analysis of CD20 (B lymphocytes) in the plasma revealed a decrease in performance with increasing seniority (Table 2). So in the group with experience of 5 years showed a trend toward lower CD20 (11,92 ± 1,7 % and 12,7 ± 1,09 %, respectively). Significant reduction in B-cells found at the experience of 11–15 years (8,89 ± 1,32 %, p <0.01) and lowest in comparison with the control group and not enough trained workers registered at the experience of more than 20 years (6.1 0.39 %, p <0.01).

Table 2

Indicators of B-lymphocytes and null cells of the immune system tested, depending on the length (M ± m)

Indicators (%)	Control (n=20)	Experience				
		0–5 years (n=21)	6–10 years (n=19)	11–15 years (n=21)	16–20 years(n=23)	More than 20 years (n=22)
CD20	12,7±1,09	11,92±1,7	10,51±1,1	8,89±1,32*#	8,4±0,47*#	6,1±0,39*#
CD56	18,97±0,45	34,25± 1,17*	37,3±1,67*	32,5±1,94*	32,7±0,96*	31,5±1,32*#

Notes: * — reliability of differences in indicators compared with the control, p <0.01; # — reliability of differences in indicators compared to healthy workers with experience of 0–10 years, p <0.01

In analyzing the parameters of CD56 (null cells) found a sharp increase in performance in the first years of contact with chrysotile asbestos, and there was an increase of 1.8 times (18,97 ± 0,45 % and 34,25 ± 1,17 % — respectively, p < 0.01). At the experience of 6–10 years of on-cell number increased to 37,3 ± 1,67 %, then tended to decrease. In highly trained workers (over 20 years experience) the number of zero cells decreased in comparison with the experience of 6–10 years.

The study revealed changes in the immune system, depending on length of service. In cellular immunity found significant reduction in CD3 rate in the intervention group (59,1 ± 0,43 %) compared with controls (71,2 ± 0,52 %). Depending on length of service options CD3 significantly decreased slowly, so at the experience of 0–5 years — 70,1 ± 0,31 % (p <0.01) and more than 20 years — 58.7 0.41 % (p < 0.01). CD4 count

in the subjects of the main group was not significantly different from controls. Changing the content of CD4 in chrysotile asbestos workers produce, depending on the duration of exposure to asbestos dust was complex: at the experience of 0–5 years, the relative content of CD4-cells (49,2 ± 0,23 %, p <0.01) significantly higher than controls. CD4 in workers with experience of 6–10 years to normal (44,9 ± 0,45 %), which characterized the immune system to adapt to the conditions of the working environment. Then there is a tendency to decrease their content in workers with experience of 16–20 years, compared with not enough trained workers (41.9 0.72 % and 49,2 ± 0,23 % (p <0.01), respectively). In workers with experience more than 20 years are set even lower rates — 40,9 ± 0,85 (p <0.01).

Analysis of the concentrations of different immunoglobulin classes revealed significant depending on the length of the study group (Table 3). Indicators of immunoglobulin A in the first years tend to increase (2,95 ± 0,54 g/l), the workers at the experience of more than 11 years was significantly reduced (1,85 ± 0,53 g/l), as compared to the control group (2,85 ± 0,27 g/l), and indicators of not enough trained workers (2,95 ± 0,54 g/l). The same trend is observed in the parameters of secretory IgA, where in the early years of contact with dust revealed an increase of almost 2-fold (0,64 ± 0,15 g / l, p <0.01), and a group of workers with experience of more than 20 years reduction target of 2 times (0,16 ± 0,03 g / l, p <0.01) compared with the control and 4-fold compared with not enough trained workers.

Table 3

Analysis of the concentrations of different immunoglobulin classes

Indicators	Control (n=20)	Experience				
		0–5 years (n=21)	6–10 years (n=19)	11–15 years (n=21)	16–20 years (n=23)	More than 20 years (n=22)
IgA, g/l	2,85 ± 0,27	2,95±0,54	2,21±0,72	1,85 ±0,53#	1,72±0,34*#	1,35±0,57*#
IgM, g/l	1,12 ± 0,56	1,98±0,61	1,91±0,53	1,28 ±0,24	1,45±0,78	1,17±0,81
IgG, g/l	11,27±0,14	15,35±0,86	13,27±0,54	17,25 + 0,12*	17,92±0,84*	19,27±0,57*
S IgA, g/l	0,34±0,07	0,64±0,15*	0,29±0,06#	0,23±0,06#	0,21±0,05*#	0,16±0,03*#

Notes: * — reliability of differences in indicators compared with the control, p <0.01; # — reliability of differences in indicators compared to healthy workers with experience of 0–10 years, p <0.01.

In the analysis revealed increased IgM parameters at the experience of 0–5 years (1,98 ± 0,61 g/l) and 6–10 years (1,91 ± 0,53 g/l) and nonsignificant reduction in the further work in contact with chrysotile asbestos in comparison with the indicators of short experienced workers.

Immunoglobulins IgG in all groups of workers increased in proportion to length of service. If the group were 0–5 years — 15,35 ± 0,86 g/l in the group over 20 years — 19,27 ± 0,57 g/l and had a significant difference only with the control group.

Thus, the characteristic feature of the humoral response of the body core working group was a significant decrease in the content of IgA and S IgA, increased IgM and IgG.

Correlation analysis of cellular immunity among workers with the experience of 0–5 years revealed a moderate negative relationship between the pH of the nasal cavity, and IgM (r = -0,51, p <0.05).

In conducting the correlation analysis within the established parameters of cellular immunity expected strong, medium level of communication. Moderate positive relationships found between experience and CD3 (r = 0,54, p <0.01), pH, and nasal sIgA (r = 0,58, p <0.01). Workers with 11–15 years experience of the main indicators of cellular immunity when correlations are determined: CD3, CD4, CD56, Ig G, sIg A.Moderate negative relation between age and identified IgG (r = -0,59, p <0.01), experience, and CD8 (r = -0,52, p <0.01).

Analysis of the correlation parameters in workers with 16–20 years experience within the set of the immune system strong ties between the average degree of relationship: age and CD20, CD56 (r = 0,6, p <0,01; r = -0,5, p < 0.01). The correlation parameters in the relationship highly trained workers with experience of more than 20 years, found an average degree of the relationship between age and IgA, IgM (r = 0,53, r = 0,57, p <0.01).

Conclusions

A risk factor in the development of pathology of the upper respiratory tract is altered immunoreactivity of the body work, manifesting by inhibition of cellular immunity: decrease in the content of CD3

(58,7 ± 0,41 %), CD4 cells (40,9 ± 0,85 %) and functional T-lymphocyte activity, decreased the content of CD20 cells (6,1 ± 0,39 %), humoral: a decrease in the concentration of IgA (1,35 ± 0,57 g/l), increased IgM, IgG.

Exposure to chrysotile asbestos dust leads to disruption of mucosal barrier and reduce the local immunity of the mucous membranes of the upper respiratory tract, in nasal secretions is a decrease in the concentration of secretory IgA (0,16 ± 0,03 g/l).

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