

## The evaluation of carcinogenic risk when exposed to asbestos dust on the population

### Халыққа асбест тозаңның әсерінен туындайтын канцерогенді тәуекелді бағалау

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Мақалада асбесттің өндірістік және өндірістік емес әсеріне байланысты халық саны өкпе ауруы және мезотелиома қатерлі ісіктеріне шалдығуының көлемін анықтап, бағалау әрекеті жүзеге асырылған. Адам ағзасында асбесттің әсер етуінде қосымша фактор анықталып, ол биоперсистенция (биологиялық тұрақтылық) жұту бөлшектерінің патогендік әлеуетін анықтауда маңызды шарт деп белгіленген. Науқастыққа шалдығу тәуекелділігін бағалаудың әр түрлі әдіснамалары қолданылған.

В статье предпринята попытка оценить масштабы заболеваемости злокачественными мезотелиомами и раком легких, связанными с непрофессиональным и производственным воздействием асбеста на население. Определен дополнительный фактор влияния асбестов на организм человека и признан как важный параметр для патогенного потенциала вдыхаемых частиц — биоперсистенция (биологическая стойкость). Авторы отмечают, что для прогнозирования отсроченной частоты асбестообусловленной патологии все более активно используются различные методологии оценки риска.

The main source of asbestos in environmental air are, apparently, construction materials, and also those industrial sectors where professional contact to dust which contains asbestos is possible. It's, first of all, industries which product production and enrichment of asbestos, asbestos-containing materials (enterprises of asbestos and cement, asbestos technical and asbestos fiber materials). The main consumer of asbestos today is production of asbestos and cement products (wavy and flat plates, pipes, etc.) which are widely used in industrial and civil construction [1–3].

According to classification of the International agency by research of a cancer (IARC) the hrizotil-asbestos is a carcinogen of the 1st category [4]. Along with existence of unique physical and chemical, and mechanical properties, asbestos possesses carcinogenic activity. In this regard, in many countries the prohibition of production and using of all types of asbestos and asbestos-containing production introduced into practice [5–7].

In the International Labour Organization convention (ILO) № 162 «About labor protection when using asbestos» the concepts «asbestos», «an asbestos dust» and all kinds of activity connected to influence of asbestos on workers in production are defined. In the document are provided a measure of protection and prevention according to the prevention of influence of asbestos, methods of monitoring of harmful production factors and human health are regulated. It obliges to assist in distribution of information and education of workers about the unhealthy factors appearing in the course of a production activity, and also assistance in training of the people working with asbestos, and in the questions concerning environmental protection.

Recently the additional factor of influence of asbestos on a human body was defined and is recognized as important parameter for pathogenic potential of inhaled particles — a biopersistentiya (biological resistance). It is characterized by duration of fibers' finding (survivability) in a pulmonary tissue. The risk of negative impact increases by health at the expense of duration of fibers' finding in a temporary corridor of a pulmonary tissue (biological resistance of fibers). Inhaled particles with short biological resistance are quickly removed and characterized by decrease of risk. During research it is established that hrizotil-asbestos it is quickly dissolved in the sour environment and it is deduced from lungs quicker unlike amphiboles which are more acids resistant [8].

The researches which have been carried out in Switzerland, Germany and the USA prove that the half-cycle of cleaning of lungs from fibers of hrizotil-asbestos (number of the days necessary for removal of 50 % of fibers, remaining in lungs after the termination of the period of influence), makes 15 days, and for amphibolic asbestos (amosites) — it is more than a year. It is the main proof that amphiboles are more dangerous, than hrizotil. For this reason amphibolic asbestos is forbidden around the world [9–11].

Hrizotil-asbestos in modern industry of Russia in a format of hygienic researches takes over 70 years. An assessment of influence of asbestos on health working and the population became since 1939. The early hygienic studies are carried out in 1936 during which was established that dust's content levels at asbestos dressing plants reached hundred mg/m<sup>3</sup>. According to the recommendation of the International agency of cancer studying (France) professor F.M.Kogan in Russia carried out for the first time researches of epidemiology of malignant neoplasms at production and asbestos enrichment, in asbestos cement and asbestos technical sectors, and also in production of asbestos-containing heat insulating materials. In the middle of the XX century professor F.M.Kogan with the professor of the Ural state medical academy S.A.Berzin studied epidemiology of a malignant mesothelioma, among workers of Bazhensky minefield of hrizotil-asbestos. Now monitoring of mesothelioma in Sverdlovsk region is held under direction of S.V.Kashanskogo [12].

The last ten years the Ekaterinburg medical scientific center of prevention and health protection of industrial plants' workers of the Russian Agency for Health and Consumer Rights successfully develops scientific contacts and carries out integrated researches in various directions of the problem «Asbestos and health» with scientists of foreign countries (Great Britain, Italy, Kazakhstan, China, the USA, Ukraine, Finland, Japan, etc.).

According to Russian scientists, there is a concept «respirable fibers» which easily get into distal segments of bronchopulmonary system, hold there for the longest term, and, therefore, possess the expressed biological action, thus «respirable» fibers in length more or equal 5 microns and less or equal 3 microns are considered diameter at ratio of length by the diameter more than 3:1 which most well get into lungs. Fibers with diameter less than 0,25 micron and length more than 8 microns [13–18] best of all remain.

The Russian oncologic scientific center named after N.N.Blochin of the Russian Academy of Medical Science developed crystal-chemical model of hrizotil's fibers' calcinations in cement matrix, change of its some physical and chemical, and biological aggressive properties is shown. When an asbestos cement dust get into a human body, big carcinogenic danger, probably, have the bunches covered with a cement matrix (units of fibers) which can be source of invariable fibers of hrizotil, than separate fibers and fibrils [15].

Over a period about 40 years fibers which considerable part is identified as asbestos were found in lungs of citizens in the western countries [19, 20].

The measurements which have been carried out in the big cities of USA, showed that atmospheric concentration of asbestos fluctuate in range 0,09–70 ng/m<sup>3</sup>. In air of the small cities and in rural areas asbestos is present at much smaller concentration — about 0,1 ng/m<sup>3</sup>. Considering distribution of the population of USA, the average level of influence of asbestos out-of-doors can be estimated amount of 1,5 ng/m<sup>3</sup> [21, 22].

The assessment of carcinogenic effect of so low concentration of asbestos appears quite difficult task as attempts of direct definition of carcinogenic action of low doses didn't give result, and indirect data are irrefutable. There is no consensus even on such question, as a contribution of professional influence of asbestos to the general mortality from a cancer: the most of researchers estimate this contribution in the size equal of 1–3 %, and by the assessment given by the government of USA in 1978, it much higher and makes 13–18 % [23].

For the assessment of cases of lungs' cancer caused by influence of low concentration of asbestos, extrapolation of the dependences received for the highest doses (can be applied at professional influence). This reception was already applied in research of 1981 studying of a contribution of dryers for hair with asbestos thermal screens and mortality from lung cancer was which subject.

Estimates of carcinogenic effect of low doses in this research were based on linear extrapolation of the dependence established for mortality from lung cancer among pensioners which was exposed to professional influence. Use of the results which were received allowed to estimate risk of cases of lungs' carcinoma, connected with asbestos influence in air during the whole period of life. In the making calculations was accepted that 1 ng contains 40 asbestos fibers in length more than 5 microns, seen in an optical microscope. It was considered, in addition, that lung's carcinoma can arise in 20 years after the beginning of influence and that average life expectancy makes 70 years so the effective period of influence is equal 50 years. Calculations showed that at the accepted assumptions the risk of disease of lung's carcinoma as a result of influence of 1,5 kg of asbestos in air during life is equal 2,08 on 1 million people. For all population of the USA (225 million people) it gives 468 cases of death (during the whole period of life) from lung's carcinoma [24].

Linear extrapolation of the data reported in English research led to a bit different conclusions, about association of professional influence of asbestos with lung's carcinoma. Using of data of this research in association with the same assumptions gives for all population of the USA figure of 60 cases of death from carcinoma of lung (during the whole period of life). However, there are bases to consider that levels of profes-

sional influence of asbestos carried out in English research are underestimated by workers approximately in 3 times. If this assumption is truly, figure of 1960 death has to be reduced in 3 times that will quite well be coordinated with the first of the received estimates (468 cases of death from lung cancer) [23].

Carcinogenic effect of asbestos is shown also in diseases by malignant mesothelioma. The total of diseases of malignant mesothelioma makes 1000 cases in a year (about 750 men and 250 women). In accordance with estimates carried out in literature, the contribution of professional influence of asbestos to incidences of malignant mesothelioma makes about 410 cases (397 men and 13 women). For nonprofessional influence of asbestos in air ( $1,5 \text{ ng/m}^3$ ) various estimates, which given in literature, give figure about 333 diseases in a year. It means that the risk of a disease of malignant mesothelioma during life owing to nonprofessional influence of asbestos is equal 100 on one million people [12].

It is noted that influence of air pollution on human's health was established at the beginning of the twentieth century. Authors refer to increase of mortality from pulmonary diseases in Pittsburg (USA) in 1930–1948 toxic which reason were emissions of steelmaking and zinc enterprises; then the murrain was observed. The similar cases which were taking place in 1924–1927 in East Prussia, and also sharp increase of smog in London are mentioned on December 5–9, 1952 that led to increase of mortality from diseases of lungs in 4 times (in 2 weeks 4000 people died) [24].

Incidence and mortality questions from carcinoma of lung depending on character and extent of air pollution in some cities and industrial centers of Germany are considered. The special group created in 1955 at VDI (association of German engineers) developed recommendations about decrease of air pollution in industrial regions. In the sequel, at VDI the Committee on air protection was created, to which duties development of actions and acts on control of pollution and protection of atmospheric air in cities were assigned [19].

In the analysis of atmospheric air in Hamburg (1961–1962) it was identified 12 substances polluting air, including beryllium in concentration of  $0,6 \text{ mkg/1000 m}^3$  and asbestos —  $0,6 \text{ mkg/1000 m}^3$ . Among factors which can influence on decrease of pollution of city air, the main place is allocated for activity of government and its bodies. It is noted that during 1961–1968 mortality indicators from carcinoma of lung increased in separate cities for 20–40 %, meanwhile greatest number of cases was the share of persons of middle age. However some decrease in this indicator (for 15 %) was noted among the women living in cities with a small number of the industrial enterprises [20].

One of essential factors of uncertainty in the making calculations is the factor of transfer of asbestos from ng in number of fibers. According to some data, it is accepted figure (40 fibers in ng) can be overestimated. In that case received estimates also are overestimated. On the other hand, one of few undertaken and reflected in literature (made in 1981 on the instructions of government of Germany Schneiderman's report) attempts to estimate carcinogenic effect of nonprofessional influence of asbestos gave much higher figures. Observational consideration of the empirical data presented in the report of Schneiderman and соавт., shows, however, that they include too small number of cases for removal of reliable dependences between level of influence and effect [20].

The received estimates specify that the risk of a disease of malignant mesothelioma owing to nonprofessional influence of asbestos in 50 times exceeds risk of disease of lung's carcinoma. These results won't be coordinated with data on professional influence of asbestos for which the risk of disease of lung's carcinoma occurs risk of a disease of malignant mesothelioma in 2–3 times. One of possible explanations of such difference is that nonprofessional influence of asbestos begins at very early age, and it, possibly, considerably increases risk of a disease of malignant mesothelioma. According to some data, mesothelioma develop in many years after the beginning of influence of asbestos, while carcinoma of lung can develop quickly enough after beginning of influence of asbestos so even if this beginning is the share of age of 30–40 years, there is a big risk of emergence of carcinoma of lung during the remained term of life (before manifestation of other causes of death) [19, 20].

Probably, the received assessment of risk of disease of lung's carcinoma as a result of nonprofessional influence of asbestos is underestimated. This assessment depends on the accepted size of the relation of effect to influence level. If instead of accepted to enter into calculations the highest of sizes of this relation specified in literature, the assessment of risk makes 40 diseases of lung's carcinoma during life on 1 million people. The risk, however, still will be less, than risk of a disease of malignant mesothelioma.

Today the world scientific community is familiar with individual works of Kazakhstan authors on prevalence of mesothelioma in Republic of Kazakhstan. In the republic there are neither national, nor regional registers of mesotheliomas. The first finding of a malignant mesothelioma was fixed in Kazakhstan in 1948. From the first message Kazakhstan authors published 69 observations of mesotheliomas of various localiza-

tions, including 87 % — pleura's mesotheliomas, 11,6 % — mesotheliomas of peritoneum and 1,4 % — pericardium's mesotheliomas. The greatest number of findings is the share of age groups till 60 years. According to Kashansky S.V. and ctr. [25] during mesothelioma observation in Republic of Kazakhstan it is registered in the territory 5 of 14 areas.

Distinctive feature of geography of mesotheliomas is absence of data on majority of countries of the world. Authentic indicators of prevalence and mortality from a mesothelioma are available only for 15 % of the population of the globe. Morbidity of mesothelioma varies in a wide range from 0,2 morbid event on 1 million population a year in Ukraine, to 35 morbid event on 1 million population in Australia. According to World Health Organization, background incidence of a mesothelioma makes 1–2 cases on 1 million people a year [12].

In recent years for forecasting of delayed frequency of asbestos conditional pathology various methodologies of assessment of risk more and more actively are used. Often in a basis of these calculations influence levels, characteristic for the period of uncontrollable use of asbestos (the 80th years of the XIX century — the 70th years of the XX century), without modern levels of a dust content on workplaces and type of used asbestos, distorted (as a rule, overestimated) information on quantity of cases of diseases that causes overestimate of indicators of risk of development of asbestos-conditioned incidence are put. Despite an asbestos' prohibition, only in countries of European Union mortality from mesotheliomas will grow from 5000 cases in 1908 to 9000 cases in 2008 and within the next 35 years from mesotheliomas about 250 thousand people will die. The peak of morbidity in these countries is predicted for 2010–2040 [26].

At the present time for the solution of problems of asbestos conditioned diseases in Republic of Kazakhstan the need is ripe of development and carrying out fundamental hygienic, sanitary-engineering, clinical, epidemiological and experimental research programs with monitoring creation in format of carcinogenic risk of republican level.

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## **The morphofunctional state of the mucous membrane of the upper respiratory ways among workers of chrysotile-asbestine production of JSC «Kostanaisky minerals»**

### **«Қостанай минералдары» АҚ хризотил-асбест өндірісіндегі жұмысшылардың жоғарғы тыныс алу жолдарындағы шырышты қабықшасының морфофункционалдық жағдайы**

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«Қостанай минералдары» АҚ хризотил-асбест өндірісінің байыту цехындағы тексерілген жұмысшылардың мұрынының шырышты қабықшасы (МШҚ) мен ұртының буккальды эпителиі (ҰБЭ) жасушаларының цитоморфологиялық зерттеу нәтижелері берілген. Еңбек өтіліміне қарай хризотил-асбест шаңы әсерінен жұмысшыларда МШҚ мен ҰБЭ цитоморфологиялық өзгерістері анықталды. МШҚ мен ҰБЭ жасушаларының функционалдық жағдайының бұзылуы еңбек өтілімінің жоғарлауына байланысты клиникалық көріністермен жүреді, сондай-ақ оған жергілікті иммунитеттің төмендеуі ықпал жасап, ол өз кезегінде жоғары тыныс алу жолдарының кәсіби аурулары дамуының негізгі қауіп факторы болып табылады.

В статье представлены результаты цитоморфологических исследований клеток слизистой оболочки носа (СОПН) и буккального эпителия щек (БЭЩ) у обследованных рабочих хризотил-асбестового производства цеха обогащения АО «Костанайские минералы». Авторы отмечают, что в зависимости от стажа работы при контакте с хризотил-асбестовой пылью у рабочих достоверно изменялся цитоморфологический состав СОПН и БЭЩ. Нарушения функционального состояния клеток СОПН и БЭЩ с повышением стажа работы сопутствуют клиническим проявлениям, но им нередко предшествует снижение местного иммунитета, что является основным фактором риска в развитии производственных заболеваний верхних дыхательных путей.

#### *Introduction*

Industrial dust in the conditions of modern production influences on the respiratory tract and mostly on the upper respiratory ways. Taking into account that between the nasal mucosa, pharynx, larynx and bronchi exist close morphofunctional connection, we can assume the presence of a common pathogenesis of profes-