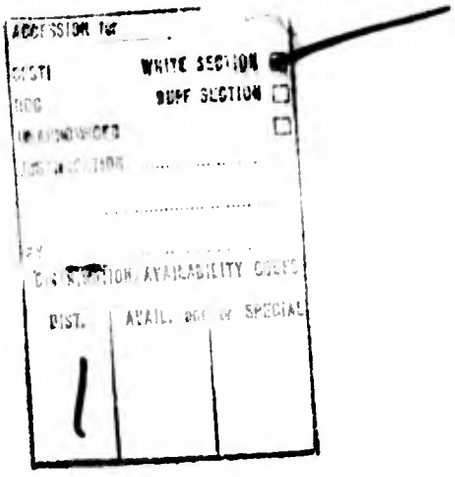
FTD-MT-24-452-68

FOREIGN TECHNOLOGY DIVISION

BLASTOMOGENIC PROPERTIES OF INDUSTRIAL METALS AND THEIR COMPOUNDS

by

P. P. Dvizhkov



This document is a machine translation of Russian text which has been processed by the AN/GSQ-16(XW-2) Machine Translator, owned and operated by the United States Air Force. The machine output has been post-edited to correct for major ambiguities of meaning, words missing from the machine's dictionary, and words out of the context of meaning. The sentence word order has been partially rearranged for readability. The content of this translation does not indicate editorial accuracy, nor does it indicate USAF approval or disapproval of the material translated.

EDITED MACHINE TRANSLATION

BLASTOMOGENIC PROPERTIES OF INDUSTRIAL METALS AND THEIR COMPOUNDS

By: P. P. Dvizhkov

English pages: 18

SOURCE: Arkhiv Patologii (Archives of Pathology), No. 3, 1967, pp. 3-11.

UR/9056-67-000-003

DATA HANDLING PAGE

01-ACCESSION NO. 98-DOCUMENT LOC	39-TOPIC TAGS
TP9500253	industrial hygiene, industrial institute, lung injurant, chromium, nickel, cobalt, beryllium, zinc, iron, aluminum, mercury, blastomycosis
09-TITLE: BLASTOMOGENIC PROPERTIES OF INDUSTRIAL METALS AND THEIR COMPOUNDS	
47-SUBJECT AREA: 06, 11, 13	

42-AUTHOR/CO-AUTHORS: DVIZHKOV, P. P.	10-DATE OF INFO: -----67
43-SOURCE: ARKHIV PATOLOGII (RUSSIAN) FTD-	68-DOCUMENT NO.: MT-24-452-68
	69-PROJECT NO.: 72302-78

63-SECURITY AND DOWNGRADING INFORMATION	64-CONTROL MARKINGS	97-HEADER CLASN
UNCL, 0	NONE	UNCL

76-REEL/FRAME NO.	77-SUPERSEDES	78-CHANGES	40-GEOGRAPHICAL AREA	NO OF PAGES
1888 0447			UR	18
CONTRACT NO.	**X REF ACC. NO.**	**PUBLISHING DATE**	**TYPE PRODUCT**	**REVISION FREQ**
	65-BJ7020901	94-00	TRANSLATION	NONE

STEP NO.	ACCESSION NO.
02-UR/9056/67/000/003/0003/0011	

ABSTRACT

A review of the literature on some important industrial metals and their compounds (chromium, nickel, cobalt, beryllium, zinc, iron, aluminum, and metallic mercury) with special reference to their effects on the lungs indicated that some of the metals (nickel and chromium) are definitely blastomogenic, while others (beryllium and cobalt) are potentially so. Iron, zinc, and aluminum have not been clearly implicated. The author notes the spareness of studies on morphological changes in humans and animals after exposure to the metals. Little attention has been paid to the pre-tumor, initial, and subsequent stages of the disease. There is also need for cytological studies.

U. S. BOARD ON GEOGRAPHIC NAMES TRANSLITERATION SYSTEM

Block	Italic	Transliteration	Block	Italic	Transliteration
А а	*А а*	A, a	Р р	*Р р*	R, r
Б б	*Б б*	B, b	С с	*С с*	S, s
В в	*В в*	V, v	Т т	*Т т*	T, t
Г г	*Г г*	G, g	У у	*У у*	U, u
Д д	*Д д*	D, d	Ф ф	*Ф ф*	F, f
Е е	*Е е*	Ye, ye; E, e*	Х х	*Х х*	Kh, kh
Ж ж	*Ж ж*	Zh, zh	Ц ц	*Ц ц*	Ts, ts
З з	*З з*	Z, z	Ч ч	*Ч ч*	Ch, ch
И и	*И и*	I, i	Ш ш	*Ш ш*	Sh, sh
Й й	*Й й*	Y, y	Щ щ	*Щ щ*	Shch, shch
К к	*К к*	K, k	Ъ ъ	*Ъ ъ*	"
Л л	*Л л*	L, l	Ы ы	*Ы ы*	Y, y
М м	*М м*	M, m	Ь ь	*Ь ь*	'
Н н	*Н н*	N, n	Э э	*Э э*	E, e
О о	*О о*	O, o	Ю ю	*Ю ю*	Yu, yu
П п	*П п*	P, p	Я я	*Я я*	Ya, ya

* ye initially, after vowels, and after ъ, ь; e elsewhere. When written as ё in Russian, transliterate as yё or ё. The use of diacritical marks is preferred, but such marks may be omitted when expediency dictates.

BLASTOMOGENIC PROPERTIES OF INDUSTRIAL METALS AND THEIR COMPOUNDS

(Contemporary State of the Problem)

Prof. P. P. Dvizhkov (Moscow)

Institute of Labor Hygiene and Occupational Diseases
(Dir. — Active Member of the Academy of
Medical Sciences, USSR Prof.
A. A. Letavet), Academy
of Medical Sciences,
USSR

(Received in Editorial Office 8 Aug 1966)

As a result of clinical, epidemiological, and experimental investigations, conducted during the last decade, our knowledge on the etiology of tumors has expanded so much that in the 1963 WHO commission of experts on the prophylaxis of cancer the opinion was expressed that no less than 75% of all tumors of man can be considered dependent on known causal factors, and this places on the agenda the problem of prophylaxis of cancer (quoted from L. M. Shabad, 1965).

The stated position pertains to a considerable degree also to tumors which develop due to the chronic influence of a number of already well-known occupational factors. The number of the latter which possess blastomogenic properties has gradually increased, and they include certain industrial metals and their compounds.

Tumors of respiratory organs, which develop under conditions of industrial contact with metals and their compounds in workers from different branches of industry, are a little studied division of oncology and occupational pathology.

In the twenties and thirties of our century substantiated statistical data has appeared on the great frequency of cancer of respiratory organs among workers, who in certain industries come in prolonged contact with various compounds of metals. Some researchers are carefully approaching the solution to the problem of the blastomogenic action of a number of metals and their compounds, and others are more positively and extensively dealing with the possibility of such action by a number of compounds. An account of these investigations is presented in our survey.

Chromium and Its Compounds

For the first time in 1890 Newman in England described cancer of the nasal cavity in a worker engaged in the production of chromates. Subsequently the number of reports from various countries (Germany, the United States, England, and others) about cancer of the lungs among workers having contact with chromates increased, and by the fifties of the present century the etiological role of compounds of chromium in the development of cancer of lungs did not cause any doubts (Spannagel). Various indices are cited for morbidity and mortality from cancer of the lungs among workers having contact with compounds of chromium, but all of them are considerably higher than corresponding indices for workers in other branches of industry and among the surrounding population (L. N. Belyayev; Ya. M. Grushko; E. Ye. Khachatryan; Machle and Gregorius; Mancuso and Heuper; Morgan; see also Doll, 1957, and others). The impression is created that the high rate of cancer of the lungs is observed in industries producing chromates without improved hygienic methods for obtaining them (Machle and Gregorius; Bidstrup and Case). Furthermore, judging by observations of different groups of workers, not all compounds of chromium are carcinogenic.

It is pointed out that dust, forming during the extraction and milling of ore, and the dust of chromates and bichromates as such apparently do not possess carcinogenic properties. But these data contradict experimental investigations (see below).

Representatives of the public health service of the United States, who were studying morbidity and mortality among insured workers in the United States who were engaged in the production of chromates (quoted by Doll), propose that carcinogenic properties may be possessed by a small quantity of 3-valence chromium which is insoluble in water but soluble in acid. It is contained in the deposit of end products from treatment of the ore. In English plants this deposit with compounds of 3-valence chromium is not subjected to repeated treatment after leaching, but is removed to a dumping ground. Therefore, in the opinion of these representatives, the workers in English plants are subjected less to the influence of 3-valence chromium and they have fewer cases of lung cancer. Six-valence chromium is not viewed as an etiological factor of cancer, but the possibility is not excluded of its transformation into 3-valence chromium in the organism during the process of metabolism.

During galvanic chrome plating the harmful factor is 6-valence chromium, but lung cancer is not characteristic for workers of this industry.

Controversial is the question of the significance of the degree of solubility of chromium compounds in different liquid media for the development of tumors, especially in respect to 3- and 6-valence compounds. Compounds of 3-valence chromium, in particular its oxide, due to poor solubility and weak toxicity ("biological inertness") up until recently were viewed as substances which did not cause the development of blastomogenic growth.

However, a group of research workers (Mancuso and Hueper; Kahlau) notes that a high percentage of workers with cancer of the respiratory organs was subjected primarily to the influence of

insoluble compounds of chromium, and in their lungs were found accumulations of dust of chromite ore, which in the opinion of authors, as a result of its prolonged influence, is possibly a carcinogenic factor.

Due to their high acute toxicity hexavalent compounds of chromium have long been accused by German and American researchers of possessing blastomogenic properties. Visek, Mackenzie, and associates apparently indicated the same theory. They demonstrated that tissues of rats which had received intravenously 6-valence chromium contain 9 times more of it than the tissue of rats which had received 3-valence chromium intravenously, and therefore it should be considered potentially more dangerous than 3-valence. During a one-year period of feeding with 6- and 3-valence chromium no toxic symptoms were observed in rats of either group, but the content of chromium in the tissues was approximately 9 times greater when 6-valence chromium was given.

Hueper and Pain, and Grogan, on the basis of experimental investigations, consider that the valence of chromium compounds apparently does not play a considerable role in their carcinogenic properties. The latter are caused mainly by their degree of solubility in water and biological liquids. It is even possible to compose a scale of chromium compounds based on the degree of their carcinogenic properties, the upper part of which is occupied by chromium salts, which are moderately or insignificantly soluble in water, and the lower part by compounds which are easily dissolved in water. The clinical aspects of cancer which develops from compounds of chromium are no different from the clinical aspects of ordinary lung cancer. The content of chromium in the lungs during the cancerous process comprises 0.25-4 mg % (normal is 0.085 mg %); during a spectrographic investigation of the organs of a victim who had died, E. A. Khachatryan detected the greatest amount of chromium (3-6 mg %) in region of the portal of the lungs. In pensioners chromium was frequently detected in the urine and especially frequently in sputum. In the tissue of a cancerous tumor there was little chromium or none at all. Frequently metastasis is

encountered in the kidneys, which supposedly is connected with the prolonged separation of chromium by these organs.

Hueper also considers the stomach and larynx as organs in which cancer can develop due to compounds of chromium.

In the list of occupational diseases of Ministry of Public Health of the USSR, lung cancer which develops in workers who come in contact with compounds of chromium is regarded as an occupational disease.

Experiments on animals (chiefly on rats) showed that blastomogenic properties of various degree are possessed by chromite ore (dust of calcined chrome iron ore – Cr_2FeO_4), 3- and 6-valence chromium, and synthetically produced slag calcium-chromate. However, depending on the method of introduction chiefly sarcomas of various nature developed at the site of injection. Lung cancer was observed only in individual animals.

Hueper, Steffee, and Baetjer, following the administration of dust of chromium compounds by different methods to rabbits, guinea pigs, rats, and mice, did not cause cancer of the lungs in any of the animals. During the simultaneous intratracheal introduction of influenza virus and dust of chromates tumors also did not develop.

The last 2 series of experiments are far from the conditions in the production of chromates. First one should consider the numerous years of prolonged inhaling of dust of chromates by the workers. Secondly, it is doubtful whether the influenza virus as such should be considered a factor promoting the development of lung cancer during the influence of chromium compounds. There are no data in favor of this.

Analysis of results of experimental research in this division does not give bases, however, to dismiss the idea of blastomogenic properties of chromium compounds, since if they do not condition

the development of lung cancer in animals then they cause a high percentage of cases of sarcoma. Differences in the nature of the blastomogenic reaction in comparison with man are possibly caused by species distinction and also unequal conditions of contact.

Nickel and Its Compounds

In comparison with the surrounding population, the detection of cancer of the nasal cavity and lungs was noted more frequently in persons engaged in the production of nickel in England during the periods 1923-1948 and 1948-1956 (Doll).

Attention is attracted to the carcinogenic properties of a gaseous compound of nickel – nickel carbonyl – $Ni(CO_4)$, which is formed during the refining of nickel. For 1923-1950 among the workers of one plant in England with a length of service in the refining of nickel of 23-35 years cancer of the nasal cavity was observed in 52, and cancer of the lungs in 93 persons.

During the separation of nickel carbonyl a specially active highly-dispersed nickel is formed which has chemical properties which are not inherent to ordinary metallic nickel.

In England nickel is recognized as an industrial carcinogenic substance. Cancer of the nasal cavity and sinuses, and primary cancer of the bronchi and lungs in workers of the nickel industry are included in the official list of occupational diseases (Miruedzer).

Loken described a case in Norway of squamous cell bronchogenic carcinoma in the removed lungs of 3 workers who were engaged in the refining of nickel in which there was no formation of nickel carbonyl. For one 46 year old worker, who had worked 10 years at the plant and left work 8 years prior to removal of the lung, during chemical investigation of dry remains of lung tissue 2.8 mg of nickel were determined, and during spectrographic analysis – 1 mg, i.e., nickel was preserved in the lungs of worker 8 years after leaving the enterprise.

The tumor from nickel compounds originates from the lungs, nasal passages and cells of ethmoid bones, and spreads to the eye sockets and nasal and frontal bones; rare metastases are observed in the cervical lymph nodes.

Development of tumors from the influence of nickel is explained not by its direct action, but by a change of ferment processes, changing the aerobic type of cell metabolism into anaerobic, and also by the formation in the cells of products of metabolism which possess carcinogenic properties (Williams). Under the influence of certain compounds of nickel ($NiO_4 \cdot 7H_2O$) severe disturbances occur in the process of cell division (Levan).

The "arsenic theory" of tumors from nickel, ascribing the etiological role to arsenic, does not have general acceptance. The prolonged (for many years) use of sulfuric acid which is contaminated arsenic oxides in a number of branches of industry with considerable dust and smoke formation never caused tumors of the nose or lungs; even the severe influence of arsenic dust with the development of perforation of the nasal septum does not cause cancer of the nose or sinuses.

Carcinogenic properties of dust of metallic nickel and a number of its compounds have been confirmed experimentally on rats and hamsters following their introduction in muscles, pleural fissure, lungs and bones. At the site of introduction of a suspension of nickel compounds sarcomas with metastases develop (V. I. Fedorov; Gilman). Tumors developed more frequently from the influence of nickel sulfide than from its oxide.

Cobalt and Its Compounds

Up until relatively recent time cobalt has been considered an etiological factor in the development of cancer of the lungs in workers in the mines and in a number of factories (for example, in the interpretation of the etiology of Schneeberg cancer). But reliable statistical, clinical, and other data in confirmation of

this view are still lacking. Development of lung cancer in workers is now connected with the radioactivity of these ores and the presence of arsenic in them. However, experiments showed that a number of compounds of cobalt as such possess high blastomogenic properties (Schinz; Heatu; Gilman).

At the site of introduction fibro- or rhabdomyosarcomas developed.

In cultures of tissues Heath studied the influence of different metals, including cobalt, on mitosis of chick fibroblasts. In 72 hours numerous mononuclear and gigantic multinuclear cells were formed. In the latter large accumulations of ribonucleic acid were detected.

Beryllium and Its Compounds

Following chronic berylliosis hyperplasia and metaplasia of the epithelium of air-passage was observed in the lungs of persons who had died (P. P. Dvizhkov; Hazard; Vorwald and Reeves). Regarding malignant tumors, including cancer of lungs, then up to recent time there have been no clear indications of a connection between the influence of beryllium and its compounds and the development of tumors in workers who come in contact with them. Also the corresponding sectional cases have not been described. Barnes considers that the appearance of experimental osteogenic sarcomas from compounds of beryllium indicates the possible occupational danger of these compounds. Dutra and associates, in describing experimental investigations with beryllium oxide, note that during the last 20 years in the United States a considerable number of persons have been subjected to the influence of dust from weakly soluble compounds of beryllium, however, no cases of cancer were recalled. Only during the last few years isolated reports have appeared concerning cancer of the lungs in persons, who in industry had comparatively brief contact (3-4 years) with compounds of beryllium. Cancer of the lungs developed from subpleural sections of scarred pulmonary

pulmonary tissue in which simultaneously there was extensive fibrosis, chronic bronchitis, and bronchiectasis. During spectral analysis of lung tissue for beryllium a sharply positive result was obtained (Riemann and Jungbluth). Out of 191 cases of chronic berylliosis Hall and associates indicate only one case of primary cancer of the lungs. But a number of authors in experiments with insoluble compounds revealed the evident blastomogenic properties of these nonradioactive compounds.

For the first time in 1946 Gardner and Heslington detected the blastomogenic properties of compounds of beryllium. Following the intravenous introduction of a suspension of zinc-beryllium silicate and beryllium oxide to rabbits osteosarcomas developed in these animals. In guinea pigs and rats tumors did not develop. Following the prolonged introduction of beryllium oxide and calcined fluorescing powder from beryllium oxide, zinc oxide, and silica with an average particle dimension of each powder of less than 1 μm in the aural vein of rabbits, Dutra and Largent observed the development of osteogenic sarcomas. Tumors developed in animals which lived for no less than a year after the first introduction. In some animals the primary tumors were single, and in others they were multiple and with metastases in the lungs, pericardium, liver, and spleen. During chemical investigation in the primary nodes of a tumor the content of beryllium turned out to be insignificant, and in the metastases there was a relatively large amount of it, which is obviously connected with the functional activity of the reticuloendothelial cells of these organs. The kidneys and heart contained relatively little beryllium.

The experiments of Gardner and Heslington were repeated by Barnes in 1947. In some of the rabbits which received zinc-beryllium and beryllium silicate intravenously bone sarcomas developed which were hystologically similar to bone sarcomas in humans and similar to bone tumors in rabbits which had been exposed to radium. The same Barnes in 1949 reports that following intravenous introduction of 40 mg of finely dispersed <u>metallic beryllium</u> to 5 young rabbits in 2 the characteristic bone sarcomas

developed. Osteogenic sarcoma in a rabbit which was subjected to the prolonged influence of beryllium oxide dust is described by Dutra and associates.

Vorwald and Reeves, stemming from their experiments on the influence of beryllium oxide (BeO) and sulfate ($BeSO_4$) on rats, point out that these compounds cause inflammatory and neoplastic changes in the lungs of animals. At first the changes are characterized by proliferation of the epithelium of air passages. With an increase of duration and intensity of the influence, in the small bronchi, respiratory bronchioles, and alveolar passages changes appear in the epithelium: polymorphism of cells and metaplasia. In these sectors the first tumors were revealed 8 months after introduction of the stated substances in the trachea and in 9-18 months after daily inhalation. They were sometimes single and sometimes multiple nodes of adinocarcinoma, and less often there was squamous cell (keratinizing and nonkeratinizing) carcinoma with metastases in the lymph nodes and along the pleura.

Zinc and Its Compounds

As a metal it plays an important role in fermentative processes of cellular respiration and intermediate metabolism, since it is a component of a number of respiratory enzymes. Metabolism of zinc in the organism has been studied in detail during the last few years thanks to the use of the radioactive isotope Zn^{65}. Zinc which has been introduced into an organism turns up quite rapidly in the gastrointestinal tract and in a month 50% of it is passed out with the feces; it is also excreted by the kidneys, pancreas, and liver or is deposited in hairs, bones, lungs, kidneys, and liver.

The blastomogenic (teratogenic) properties of zinc compounds were pointed out for the first time by Michalowsky, who introduced a solution of zinc chloride in physiological solution into the testicles of young roosters and observed in them, starting with the

4th month, the development of teratoma of the testicles. The author considered that the most important factor influencing the development of teratoma was the season – spring (February-May), when the most active spermatogenesis occurs. Furthermore, depth and rate of introduction of the substance, and breed and age of the birds played a role. In such a way Michalowsky produced teratoma in 10 birds.

These experiments of I. O. Michalowsky were confirmed by Bagg. However, they were not supported by Ljvaga and Kahlau. The last author explained the difference in data by the different predisposition of separate breeds of roosters to the development of teratoma in the testicles. Doubts concerning the teratogenic action of zinc chloride arose also because Mashar revealed spontaneous intraabdominal teratomas in roosters. However, subsequently L. I. Falin and associates (1938-1940) observed in a series of experiments the development of structurally different teratomas of the testicles in 30 roosters following the administration of zinc chloride, sulfate, and nitrate, and also of copper sulfate. Willis conducted analogous experiments on rats with the introduction of zinc chloride, and also in combination with potassium permanganate, hydrogen peroxide, pyrogallol, alcohol, ether, and silicon dioxide and obtained negative results.

Several authors determined the content of zinc in tumors of various organs, including in carcinoids, and compared the data obtained with the contents of it in normal tissues of the same organs. The results obtained are different, indicating both a considerable increase in the content of zinc and its decrease in tumors of different organs (see L. I. Falin; Ya. A. Lazaris, and others). Till now there are no data about a frequent appearance of tumors in workers who come in contact with its compounds.

Compounds of Iron

Several reports about lung cancer in workers who inhale dust with iron oxide and who have siderosis of the lungs, and also

the observations of McLaughlin and Harding and Faulds and Stewart about the high frequency of lung cancer among English workers in the steel-casting industry and miners in the iron pits who have occupational siderosis of the lungs, as if testified that certain compounds of iron can possess blastomogenic properties. The first two authors, in 149 autopsies of corpses of workers revealed primary cancer of the lungs in 16 (10.8%) cases. This index was considerably higher than the index of mortality from lung cancer among the population. However, workers in these industries not only inhaled dust with iron oxide, but also soot, and came in contact with mineral lubricating oils and other organic compounds, therefore the data are not fully convincing.

Faulds and Stewart reported that based on sectional materials from 172 miners who were engaged in the exploitation of red hematite, for 1932-1953 primary lung cancer was found in 17 (9.4%), and for 1948-1953 – in 13 out of 89 (14.6%), while for 1932-1947 – only in 4 out of 91 (4.4%).

Most frequently cancer was revealed in miners who were over 50 years old. Its localization always coincided with region of the most profound siderosilicotic changes in the lungs. Inasmuch as based on the analyses of changed lung tissue there were no indications of the presence of carcinogenic or radioactive substances in them, the authors consider that the decisive role in the development of lung cancer belongs to siderosilicosis as the predisposing factor.

Experiments in which animals received highly-dispersed powder of metallic iron, its oxide, and iron sulfide turned out to be negative, i.e., around the suspension of iron powder which was introduced into the muscles or in the pleural fissure no blastomogenic reaction developed (Hueper; Gilman; Muller and Erhardt).

Consequently, the question of blastomogenic properties of iron compounds remains unclarified and little developed.

Mercury Metallic

Cases of the development of tumors in humans which could possibly be connected with the influence of mercury are not known. In the experiment of Druckrey and associates the development of sarcoma was observed in 5 out of 12 rats following the introduction of metallic mercury into their abdominal cavity.

Aluminum Compounds

In the twenties and thirties of the present century rather numerous prolonged experiments were conducted on different animals, including rabbits and dogs, which had received aluminum compounds with their feed for establishing the possible connection between the chronic influence of aluminum and the development of cancer of the gastrointestinal tract. Results of all the experiments turned out to be negative. Bertrand and Serbescu (1934) greased the ears of rabbits with coal tar and simultaneously every day introduced aluminum sulfate [$Al_2(SO)_4 \cdot 18H_2O$] into their stomachs. On ears of the rabbits cancerous changes were observed, but in the internal organs, including in the gastro-intestinal tract, tumors did not develop. There are also no indications that during pneumoconiosis — aluminosis — primary cancer of the lungs is encountered more frequently.

Conclusion

It is clear from what has been said that the question of the blastomogenic action of industrial metals and their compounds in various physical states, including dust, has been studied little and in many directions is not developed. Epidemiological-clinical and hygienic investigations and observation are not numerous enough to introduce final clarity in assumptions on the blastomogenic action of a number of metals and their compounds although certain clinico-epidemiological data clearly indicate these properties for a number of them (for example, nickel and some of its compounds).

At present different aspects of the question of blastomogenic properties of compounds of chromium have not been clarified: the role of valence, solubility, and what compounds as such or the products which develop during their processing possess these properties. It has not been clarified if the high indices of morbidity with lung cancer pertain only to workers in old factories for the production of chromates or can this pertain also to newly opened plants. In any case the question concerning blastomogenic properties of chromium compounds still requires comprehensive study.

The study of blastomogenic properties of beryllium compounds is in the initial stage. While experimental investigations do not create any doubts about their blastomogenic properties, the frequency of cases of cancer in people coming in contact with them still has not been established. Consequently, at present beryllium and its compounds should be considered as potentially dangerous for people and the study of the rate of cancer, lung cancer primarily, should be one of the assignments for occupational pathologists.

The same vague presentation exists concerning the blastomogenic properties of cobalt, zinc, and their compounds. Poorly developed is the question of possible blastomogenic properties of iron and its compounds.

Thus, it is necessary to expand the scale of clinical and hygienic inspections, which would make it possible to develop a true presentation about the cancer rate among the corresponding groups of workers. This is also dictated by the circumstance that cancer for the most part does not develop soon after beginning work at this or that enterprise and not after brief contact with the substance suspected of having blastomogenic properties, but after a prolonged period, for the most part in elderly people who frequently have quit work. Consequently, these investigations are also important from the point of view of prophylaxis of cancer.

Great scope has been obtained by experimental investigations of blastomogenic properties of the same metals, exposing of these properties for a number of metals and their compounds (nickel, chromium, beryllium, cobalt), and showing the various degree of blastomogenic properties of their different compounds. Here the same peculiarities are revealed which have been established, for example, for carcinogenic hydrocarbons: 1) significance of changes (transformations) in the chemical structure of a substance for the development of blastomogenic properties; 2) significance of species of animal and dose of substance during experimental investigations.

It is necessary to note that up to the present time clinical and hygienic data about cancer morbidity of workers who have contact with a given substance and the results of experimental investigations on a number of metals and their compounds do not agree. For example, in respect to cobalt investigations of the first kind do not give a clear answer to the question on its blastomogenic properties, but experiment indicates high blastomogenic properties for a number of compounds of cobalt. To a certain degree this also pertains to compounds of beryllium. Obviously these metals and their compounds should be considered potentially dangerous in the sense of blastomogenic influence on the organism of man and primarily on the lungs.

During the study of tumors which have developed in man and the various stages of their development in experimental animals at present the following has been well established.

1. There is considerable precipitation (depot) of this or that metal or its compounds in tissues, the lungs for example, which occurring in man over a prolonged time and which undoubtedly is rendering a chronic mechanical and chemical influence on the tissue.

2. Severe chronic changes are observed in the lungs and partly in other organs of persons who have contact with the compounds named here (especially from compounds of beryllium,

nickel, and zinc). They indicate deep reactive changes, such as: atypism of the epithelium small bronchi, the bronchioles, and profound changes in the large bronchi, accompanied by the development of progressive diffuse pneumosclerosis and creating the ground for subsequent development of a tumor. On the part of the lymphoid tissue there are hyperplastic processes which are frequently initial for the development of reticulosarcoma of the lungs in experimental animals.

However, corresponding morphological changes in man and experimental animals have still not been investigated sufficiently, for example, pretumorous, initial, and subsequent stages of development of the blastomogenic process have not been studied and a sufficient number of cytological investigations have not been made. All of this requires the realization of extensive and detailed morphological investigations in this region.

Literature

Belyayeva L. N. In the book: Promyshlennaya toksikologiya i klinika professional'nykh zabolevaniy khimicheskoy etiologii (Industrial toxicology and clinical aspects of occupational diseases of chemical etiology). M., 1962, s. 245.

Grushko Ya. M. Soyedineniya khroma i profilaktika otravleniy imi (Compounds of chromium and prophylaxis of poisoning by them). M., 1964.

Dvizhkov P. P. Pnevmokoniozy (Pneumoconiosis). M., 1965.

Konoplev V. P., Prigozhina Ye. L. In the book: Modeli i metody eksperimental'noy onkologii (Models and methods of experimental oncology). M., 1960, s. 106.

Lazarev N. V., Napalkov N. P. Gig. truda, 1962, No. 6, s. 5.

Lazaris Ya. A. Pat. fiziol. i eksperiment. terapiya (Pathological physiology and experimental therapy), 1960, No. 5, s. 75.

Malyugina L. L. In the book: Trudy Leningradsk in-ta onkologii AMN SSSR, 1958 (Transactions of the Leningrad Inst. of Oncology, AMN USSR, 1958), v. 2, s. 57.

Neyman I. M. Osnovy teoreticheskoy onkologii (Bases of theoretical oncology). M., 1961.

Pliss G. B. In the book: Mekhanizmy kantserogeneza (Mechanisms of carcinogenesis). M., 1965, s. 92.

On zhe (Idem), Vopr. onkol., 1959, t. 5, s. 524.

Pylev L. N. Vopr. onkol., 1962, No. 10, s. 35.

Falin L. I. Morfologiya i patogenez eksperimental'nykh teratoidnykh opukholey polovykh zhelez (Morphology and pathogenesis of experimental teratoid tumors of the sex glands). M., 1946.

Fedorova V. I. Tezisy dokl. 4-go Vsesoyuzn. s"yezda patologo-anatomov (Theses of reports of the 4th All-Union Congress of pathologo-anatomists). Kishinev, 1965, s. 165.

Khachatryan E. A. O kantserogennykh svoystvakh khromovykh soyedineniy. Diss. kand. (Carcinogenic properties of chromium compounds. Candidates dissertation). Erevan, 1965.

Shabad L. M. In the book: Mekhanizmy kantserogeneza (Mechanisms of carcinogenesis). M., 1965, s. 3.

Bagg H. J. Am. J. Cancer, 1936, v. 26, p. 69.

Barnes J. M., Lancet, 1950, v. 1, p. 463.

Bertramd G., Serbescu P., C. R. Acad. Sci., 1934, v. 198, p. 1100. Bull. Soc. chim. biol. Paris, 1934, v. 16, p. 917.

Bidstrup P. L., Case R. A., Brit. J. industr. Med., 1956, v. 13, p. 260.

Bischoff F., Long M. L., Am. J. Cancer, 1939, v. 37, p. 531.

Bischoff F., Long M. L., Rupp J. J., Ibid., 1940, v. 38, p. 404.

Kaydri Ye. (Cowdry). Rakovyye kletki (Cancerous cells). M., 1958, s. 665.

Doll R. In the book: Uspekhi v izuchenii raka (Successes in the study of cancer). M., 1957, t. 3, s. 11.

Doll R.,
Brit. J. industr. Hlth, 1958, v. 15, p. 217.—Druckrey H., Hamperl H., Schmähl D., Ratten. Z. Krebsforsch., 1957, Bd 161, S. 511.—Dutra F. R., Largent E., Am. J. Path., 1950, v. 26, p. 197.—Dutra F. R., Largent E. J., Roth J. L., Arch. Path., 1951, v. 51, p. 473.—Faulds J. S., Stewart M. J., J. Path. Bact., 1956, v. 72, p. 353.—Gardner L. U., Heslington H. F., Fed. Proc., 1946, v. 5, p. 221.—Gilman J. P. W., Ruckerbauer G. M., Cancer Res., 1962, v. 22, p. 152.—Gilman J. P. W., Ibid., 1962, p. 158.—Gregorius F., Arch. industr. Hyg., 1952, v. 5, p. 196.—Grogan C. H., Cancer, 1957, v. 10, p. 625.—Hall T. C., Wood C. H., Stoeckle J. D. a. Tepper L. B., Case data from the Beryllium Registry. Arch. industr. Hlth, 1959, v. 19, p. 100.—Hazard J. B., Ibid., p. 179.—Heath J. C. Nature, 1954, v. 173, p. 822.—Idem. Brit. J. Cancer, 1956, v. 10, p. 668.—Hueper W. C., Occupational Tumors and Allied Diseases. Baltimore, 1942.—Hueper W. C., J. nat. Cancer Inst., 1955, v. 16, p. 55.—Hueper W. C., Arch. industr. Hlth, 1958, v. 18, p. 284.—Hueper W. C., Pain W. W., Arch. environm. Hlth, 1962, v. 5, p. 445.—Kahlau G., Frankfurt. Z. Path., 1937, Bd 50, S. 281.—Körbler J. u. Frank P., Z. Krebsforsch., 1952, Bd 58, S. 589.—Levan A., Nature, 1945, v. 156, p. 751.—Livraga P., Pathologica, 1934, v. 26, p. 726.—Loken A. C. T.

norske Laegeforen, 1950, v. 70, p. 376. — Machle W., Gregorius F., Publ. Hlth. Rep. (Wash.), 1948, v. 63, p. 1114. — MacKenzie R. D., Byerrum R. U., Decker C. F. et al., Chronic toxicity studies. II. Hexavalent and trivalent Chromium administreted in drinking water to rats. Arch. industr. Hlth, 1958, v. 18, p. 232 — McLaughlin A. I. G., Harding H. E., Ibid., 1956, v. 14, p. 350. — Mancuso T. F. a. Hueper W. C., Industr. Med. Surg., 1951, v. 20, p. 358. — Mashar U., Arch. path. Anat., 1932, Bd. 285, S. 155.

Miruedzer E. A. (Merewether E. R. A.). Nekotoryye problemy gigiyeny truda i professional'noy patologii (Some problems of work hygiene and occupational pathology). M., 1960, s. 220.

— Мируэдзер Э. А. (Merewether E. R. A.) Некоторые проблемы гигиены труда и профессиональной патологии. М., 1960, с. 220. — Michalowsky I., Zbl. allg. Path. path. Anat., 1926, Bd 38, S. 585. — Michalowsky I., Arch. path. Anat., 1929, Bd 274, S. 319. — Morgan J. G., Brit. J industr. Med., 1958, v. 15, p. 224. — Müller E., Erhardt W., Z. Krebsforsch., 1956, Bd 61, S. 65. — Neubauer O., Bibliography of Cancer Produced by Pure Chemical Compounds. A Survey of Literature up to and Including 1947. Oxford, 1959. — Newman D., Glasg. med. J., 1890, v. 33, p. 469. — Richmond H. G., Brit. med. J., 1957, v. I, p. 997 — Riemann H., Jungbluth H., Radiologe, 1962, Bd 2, S. 261. — Schinz H. R., Schweiz. med. Wschr., 1942, Bd 72, S. 1070. — Schinz H. R., Uehlinger E., Z. Krebsforsch., 1942, Bd 52, S. 425. — Siering H., Aderhold K., Leitfaden der Nativcytomorphologie malignen Tumoren. Spezielle phasen- und fluoreszenzoptische Cytodiagnostik. Jena, 1956. — Spannagel H., Lungenkrebs und andere Organschäden durch Chromverbindungen. Leipzig, 1953. — Steffee C. H., Baetjer A. M., Arch. environm. Hlth, 1965, v. 11, p. 66. — Sundermann F. W., Donnelly A. J., West B. et al., Arch. industr. Hlth, 1959, v. 20, p. 36. — Vallee B. L., Physiol. Rev., 1959, v. 39, p. 443. — Visek W. J., Whitney I. B., Kuhn U. S. et al., Proc. Soc. exp. Biol. (N. Y.), 1953, v. 84, p. 610. — Vorwald A. J. a. Reeves A. L. Arch. industr. Hlth, 1959, v. 19, p. 190. — Williams W. J., Brit. J. industr. Med., 1958, v. 15, p. 235. — Willis R. A., Brit. J. exp. Path., 1934, v. 15, p. 234. — Wingler A., Arzneimittel-Forsch., 1957, Bd 7, S. 391. — Zlataroff A., Wien. med. Wschr., 1933, Bd 83, S. 46.