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CERTAIN DATA ON THE ACTION OF URANIUM AND ITS COMPOUNDS ON THE HUMAN ORGANISM

(Literature Review)

/Following is the translation of an article by Candidate of Medical Sciences O. S. Andreyeva entitled "Nekotoryye Dannyye O Bozdeystvii Urana i Yevo Soyedineniy Na Organizm Cheloveka" (English version above) in Gigiyena i Sanitariya (Hygiene and Sanitation), Vol. 25, No. 5, 1960, Moscow, pages 77-82./

A large number of papers has been devoted to studies on the toxic properties and limits of uranium, both by us and others (Ya. Voroshil'skiy, A. P. Novikova, D. I. Zakutinskiy, V. A. Sanotzkiy, E. B. Kurlyandskaya, A. A. Rubanovskaya, S. M. Mikhaylovich, S. R. Perepelkin, Voegtlin and Hodge, Tannenbaum, Neiman, etc.).

Most authors relate uranium to the group of highly toxic substances which may effect the entire organism. The most distinct changes have developed in the kidneys (V. D. Mel'nichenko, A. P. Novikova, Fahr, Feyel, etc.). liver (A. Ya. Shulyatikova, Traissak, Sata), nervous system (M. N. Livanov, V. A. Nazarov, Ye. N. Klimova, S. R. Perepelkin), hematologic system (Robers, Rotermel), gastrointestinal tract, etc.

The uranium compounds have the capacity to engender changes in the metabolism of albumen (Dounce and Tien Holan), carbohydrates (A. Ya. Shulyatikova), lipids (S. M. Mikhaylovich), water (A. M. Charnyy, S. E. Krasovitzkaya and N. N. Lapteva).

The first findings on the effect of uranium on the human organism were reported towards the end of the Nineteenth Century, when American homeopaths introduced uranium into pharmacology as a therapeutic agent for diabetes mellitus, since at that time it was known that, among a number of other changes, uranium therapy reduces glycosuria.

It wal also known that Kennedy (1874), West (1895), Walsh (1904), Tylecote (1904) and others had used hexohydrated uranyl nitrate for treating a large number of

diabetics. Several authors reported the presence of albuminuria in the patients. Trials with uranyl nitrate were performed privately in patients with other diseases such as eczema, psoriasis, senile atrophy, etc. Later, Pack and Stewart (1930) studied the effect of intravenous administration of colloidal uranium-thorium preparations to eight cancer patients. The results of the above treatment are questionable, but it is known that two of the patients showed signs of renal impairment.

The primary danger of uranium compounds under industrial conditions was pointed out by de Laet and Meurice in 1925. Their work described four cases of peripheral blood and bone marrow changes attributed to poisoning with uranium compounds in a Belgian ceramics factory. The disturbance was expressed by a blood picture of leukopenia (3,100-5,100 leukocytes/cmm), anemia, and lymphopenia (Table 1).

No albumen and sugar were found in the urine. The chloride concentration tended to be decreased. Uranium was found in the urine of all workers.

In two individuals who were working with soluble uranium salts, changes arose after seven to 14 months, while the health of those working with insoluble uranium salts was found to fail after one year eight months to two years.

D. I. Zakutinskiy et al. demonstrated /the existence of/ a more pronounced toxic effect from easily soluble uranium compounds than from poorly soluble ones. It must be noted that the size of the dust particles is of great importance in inhalatory intoxication with uranium compounds.

Experimental investigation has demonstrated (Wilson, Silwester /sic/, Laskin, La Belle, et al.) that as the size of the dust particles decreases the toxicity of the uranium compound increase. However, this is not always taken into account when investigating the influence of uranium compounds on the human organism.

In pilot studies performed by American authors on personnel in uranium processing plants and plants for uranium production, no changes in the condition of healthy individuals working one to one and a half years with UF_6 were recorded, except in occasional cases. Khouland reported that investigation of the condition of health of groups of workers, including three individuals subjected during a year to the influence of various uranium compounds (such as uranium trioxide or peroxide, UCl_4, in concentrations attaining 155 mg/m^3 of air)[1], no changes in their

[1] It is to be considered that workers were protected against the inhalation of powder while working.

Table 1

Changes in the peripheral blood due to working with uranium (According to data of de Laet and Meurice)[1]

Blood Picture	Soluble Compounds		Insoluble Compounds	
	Duration of service: 7 months	Duration of service: 1 year 2 months	Duration of service: 1 year 8 months	Duration of service: 2 years
Erythrocytes	2 600 000	3 100 000	4 300 000	3 900 000
Hemoglobin (%)	40	60	75	60
Leukocytes	5 100	3 100	4 900	4 700
Polymorphonuclears (%)	60	36	58	49
Eosinophils (%)	3	2	6	4
Basophils (%)	0	1	1	0
Monocytes (%)	13	20	17	31
Lymphocytes (%)	10	25	13	13

[1] Cited in: "Toxicology of uranium," ed. by A. Tannenbaum, M. D., 1951, page 57, New York, Toronto, and London.

health were demonstrated. Nevertheless, Khouland considered the possibility of their delayed onset.

Subsequent groups of investigators (Eisenbud, Quigley, 1955) gave detailed characterization of specific detrimental factors and conditions of health aspects during the production of uranium. The authors presented data on levels of external β-irradiation (25-50 mg/hr) from radon during storage of enriched uranium ore ($1 \cdot 10$ c/l), of γ-irradiation during vacuum casting of uranium (2r/week), etc. Here the same results are reported regarding the influence of both soluble and poorly soluble compounds in dust form.

Specific data on interesting findings are presented in Table 2.

Medical investigation of workers demonstrated that under the chronic influence of soluble uranium compounds seven out of 130 individuals manifested nephrosis contracted from the toxic effect of uranium compounds in dust. Albumen, erythrocytes, and cylinders were demonstrable in the urine. Urinary tests revealed up to 3.46 mg of uranium per litre.

Investigations of other workers frequently exposed to the action of poorly soluble uranium compounds revealed no such pathology. In particular, 100 individuals exposed during five years to doses of 0.5-2.5 mg/m^3 of these compounds, as well as another 50 exposed to doses of 2.5-10 mg/m^3, were kept under medical surveillance. Among them Eisenbud, Quigley and other investigators discovered no workers with signs of damage to the kidneys or the external aspect of the liver, nor any with blood changes. The authors, however, held the reservation that pathologic manifestations in the aspect of the liver requires a long time.

The work of Czech authors (Pétraček et al.) giving observations on groups of miners extracting uranium ore, who are undergoing chronic exposure to the action of uranium and its disintegration products, demonstrated that side by side with liver pathology and stones (length of service being approximately 10 years) there were renal abnormalities (urinary albumen in 17% of the observations). At the same time, changes in the blood picture as well as loss of weight were demonstrated.

As to deterioration of the peripheral blood picture, prolonged contact with uranium and its disintegration products was demonstrated by Borovanski who examined 247 workers in [Yakhimove] (Czechoslovakia) and obtained the following results: 31% were anemic, and 23% evidenced considerable decreases in total leukocyte numbers - less than

Table 2

Types of Influence of Specific Factors of Damage During Work With Uranium Compounds (According to Data of Eisenbud, Quigley, et al.)

Potential Danger	Radiation Source	Potential Exposure During Operation Under Normal Controlled Conditions	Remarks
γ-rays	Manual manipulation of ore	50 mg/hr near stacks of ore drums	Radium content of ore is 100 mg/ton.
	Fallout of radium content	100 mg/hr near drum stacks	Ra226, for example, contains 300 mg/ton.
β-rays	Conversion of UF_4 to UF_6	2-3 r/week is the permissible average for workers during loading and unloading of vessels; the manual dose may be higher.	Gaseous UF_6 can be kept from precipitating by high concentrations of UX_1 and UX_{11}.
	Vacuum casting of uranium in vessels	Workers with dust may be subjected to about 2 r/weeks; the manual dose may be somewhat higher.	Sources of β-rays are pure admixtures containing UX_1 and UX_{11} accumulating on the inner surface of the furnace.
	Working with metallic uranium	Dose for basal epithelium of the skin, for example, is 235 mg/hr in case of contact with metallic uranium found in equilibrium is UX_1 and UX_{11}.	90% of β-activity equilibrium is restored 90 days after vacuum casting.

/Table continued on next page/

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Potential Danger	Radiation Source	Potential Exposure During Operation Under Normal Controlled Conditions	Remarks
Radon Inhalation	Storage of ore in sealed areas	Concentration of radon due to utilization of ventilation may reach 10^{-8} c/l.	Conditions may even be ameliorated by minimal ventilation.
Inhalation of α-particles of dust and smoke	Breaking up and grinding of ore	In case of absence of ventilation, the average magnitude of irradiation attains 5 mg/m^3.	The usual method is utilized for controlling the dust during operation
	Working with dry powdery salts and oxides	Possible average unit concentration to 5 ml/m^3 during operation, without adjustment for the operational process and the absence of ventilation.	The usual method is utilized for controlling the dust during operation.

5,000/cmm (0.5% has less than 3,000/cmm, indicating leukopenia).

Several authors ascribe the tendency to changes developing in the blood picture to radon found in mine air, but the presence of kidney pathology, accompanying the appearance of albumen in the urine, testified to an apparent effect of uranium inside the organism subjected to inhalation of uranium dust.

Changes in the blood in the form of leukopenia were demonstrated by Henn (1954) who found a deficiency in the composition of the blood of 35 miners at the Austrian venture at Wessenstadt, Fichtelgebirge.

Control groups consisting of 29 individuals (nine local inhabitants and 20 miners of non-radioactive iron ores) were taken for comparison.

Changes in the aspect of leukocytes occurred in the form of leukopenia (less than 5,000/cmm were observed in seven miners, and less than 4,000/cmm in three) whereas only two of the 29 individuals in the control group were leukopenic. The blood picture of the miners showed neutrophil hypersegmentation and other aspects -- neutropenia and relative lymphocytosis.

A possible effect of chronic exposure to uranium on hematopoiesis is mentioned in the investigations of Khouland[1] who indicates that "since uranium like other heavy radioactive substances is segregated in bone in excessive amounts, it is possible that small quantities of radium to which the bone marrow may be subjected during a prolonged period of time will evoke a condition of reduced red and white bone marrow together with abnormal changes of the white cell series." The validity of such a supposition is corroborated by the findings of de Laet and Meurice who found changes in the white and red blood picture of uranium workers.

Among workers in enterprises manufacturing chemical reagents for uranium salts, we also found some indications of instability of peripheral blood with a tendency to leukopenia and lymphopenia. The aspect of the CNS demonstrated phenomena of vegetative dystrophy. Besides this, several workers had prolonged contact with reactive uranium during packing, cases of uranium dermatitis and cysts of the hands and exposed portions of the face and neck being

[1]Dzh. Khouland. Action of Uranium Compounds in Man. In: Pharmacology and Toxicology of Uranium Compounds. Issued in the foreign literature, Vol. 11, 1951, pages 224-270, English periodical.

found. In occasional cases, traces of albumen were found in the urine.

General literature data on experimental studies of the toxicity of uranium compounds and material, characterizing their relation to the human organism, reveals that uranium intoxication affects the entire organism. It is impossible to consider uranium sickness as a renal intoxication.

Since similar intoxication is evoked by both soluble and insoluble uranium compounds, one must stress the highly uniform character of the changes, although easily soluble uranium compounds show more manifest toxic activity than do poorly soluble compounds.

It should be noted that in recent years many investigators working on the effect of uranium have considered not only such toxic substances but also radioactive elements (D. I. Zakutinskiy; Eisenbud and Quigley; Vacca and Perreau; etc.).

Eisenbud and Quigley cite the fact that during work with uranium compounds there is a potential danger of inhaling insoluble α-ray emitting uranium dust, as deduced from the persistence of light dust which, over a prolonged period of time, may induce the development of cancer.

Hueper, Zuefle, Link and Johnson demonstrated the possibility of inducing uranium cancer and sarcoma experimentally in animals (rats) by prolonged administration of uranium.

Vacca and Perreau (1955) demonstrated that under certain conditions (fusion of metallic uranium) intensive β-ray emission may result from the redistribution of products of uranium fusion, UX_1 and UX_{11}, which may also effect the worker's organism.

The possibility of a radioactive effect from a β-irradiation of uranium on tissues is demonstrated by the experimental investigations of a group of French authors, in particular Lacassagne, Lattès and Tournier. They showed that irradiation of animal testicles with β-rays of UX evokes the gradual development of severe injury including sterility and complete necrosis. In conclusion, the authors express the view that the biologic effect evoked by β-rays of UX is similar to that of X-ray irradiation (roentgen and γ-rays).

Besides the above α- and β-irradiation of uranium and its immediate fusion products, there may be a combined effect of uranium and its distant fusion products -- e.g. due to working with uranium containing minerals and uranium ores, the workers may be subjected not only to uranium dust but also to the additional effect of uranium

fusion products in the form of aerosol radium, polonium, radon, etc.

Thus, to evaluate the biologic effect of uranium on the organism, one must stress the fact that it is not only a toxic chemical element but also may have a radiation effect.

Previously, intoxication was attributed to the chemical effect of metallic uranium, poisoning occurring in acute or subacute form. Intoxication may entail renal pathology (albumen and cylinders in the urine, microhematuria, etc.), with changes in the aspect of the kidneys, disturbances of filtration (of albumen and water), and other phenomena sufficiently well documented in the literature.

The type of intoxication following long after exposure as well as during chronic intoxication with poorly soluble uranium compounds is due to their prolonged deposition and is similar to the effect of ionizing radiations (dynamic reduction in leukocyte numbers, neutropenia, lymphopenia, qualitative morphologic changes in the blood, changes in the nervous and neuroendocrine systems). However, these may be manifested like the toxic effect of metallic uranium (nephropathy, chronic hepatitis, gastritis, etc.). Influences besides uranium and its disintegration products -- such as radon, etc. -- undoubtedly will tell upon the general picture of intoxication, bringing it closer to that evoked by the chronic effect of ionizing radiations.

Consequently, prophylactic measures -- organization of sanitary hygienic and dosimetric controls purporting the safeguarding of working conditions for uranium workers -- acquire widespread application.

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