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# Uranium in urine as a bioindicator for detecting uranium accumulation in the human body

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## Abstract

This review presents data about the potential radiotoxic effects of uranium exposure on the human body and determination of uranium concentration in urine as a bioindicator of uranium accumulation in the human body. The paper discusses the potential applications and methods for determining uranium in urine. The article highlights epidemiological data related to uranium biomonitoring in urine among uranium workers, military personnel exposed to depleted uranium, and population living in contaminated areas. This article discusses the detected relationships between uranium concentration in urine and health outcomes, including nephrotoxicity. Additionally, the potential of alternative biosubstrates such as hair and nails for assessing chronic uranium exposure in environmental researches discussed. The review also presents our own studies of uranium content in the urine of Group A uranium workers of radiation-hazardous enterprises, for whom biomonitoring is a mandatory component of the annual medical examination, required by national legislation. Over 2,000 urine samples were analyzed using inductively coupled plasma mass spectrometry method. The average uranium concentration was 0.90 μg/l, and peak levels reaching up to 47.15 μg/L. The highest concentrations of uranium in urine were recorded among uranium workers involved in main technological processes. To assess the permissible level of uranium in the human body, the maximum allowable concentration in kidneys was calculated and compared with urinary excretion levels. It was determined that concentrations exceeding 15 μg/l indicate potential nephrotoxicity and necessitate improvements in working conditions for Category A uranium workers. The obtained biomonitoring data not only allow monitoring compliance with permissible dose loads, but also provide the necessary information for optimizing radiation protection measures and making decisions on intervention in cases where exposure levels are exceeded. Recognition of the risks associated with uranium mining and processing in Kazakhstan lead to policy changes aimed at protecting the health of workers and local populations.

**Key words:** uranium, mass spectrometry, uranium industry workers, uranium ore province, epidemiological studies, health status.

## 1. Introduction

Uranium is a critical resource for nuclear energy that has brought significant economic and social benefits to humanity. Intensive mining and processing of minerals, as well as nuclear energy complex enterprises' work, have now led, on the one hand, to a sharp increase in the number of people involved in production, and on the other, to the risk of environmental pollution with uranium compounds and its decay products, which poses a potential threat to human health [1-4]. The Republic of Kazakhstan is a unique uranium mining region, which contains about 30% of the world's uranium reserves [5-6]. The country's total uranium reserves are estimated at 802 thousand tons of uranium. In 2009, Kazakhstan took first place in the world in uranium production with an annual increase in this indicator [7].

There are 6 uranium provinces in Kazakhstan, located in the northern, southern, western and central regions of the Republic. The main method of uranium mining is the in-situ leaching method. The country also has uranium processing enterprises [8] and uranium fuel production enterprises. More than 20 thousand people work at uranium mining and processing enterprises in Kazakhstan, of which about 30% are Group A personnel who come into contact with sources of ionizing radiation [9]. In connection with the expansion of production, an increasing number of workers and the population will be involved in the zone of influence of the radiation factor, so the assessment of the influence of the ionizing factor becomes especially acute.

Uranium and its compounds can enter humans through the respiratory and digestive organs, as well as through the skin, wounds and burn surfaces [10].

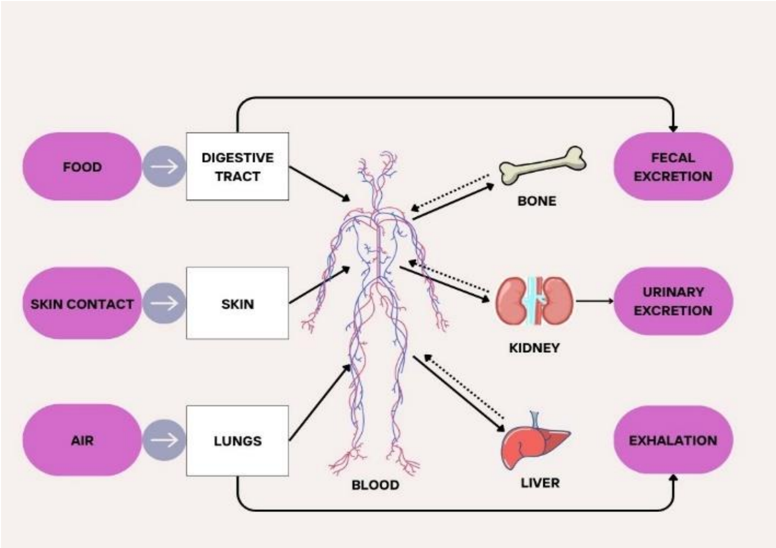


**Figure 1 - Receipt, distribution, accumulation and removal of uranium from the human body**

For workers involved in uranium industry enterprises, the inhalation route of uranium intake is of greatest importance [4], for the population - oral. The public may be exposed to natural background uranium on a daily basis through food, drinking water and air. However, of great concern is chronic exposure to higher levels of uranium from anthropogenic sources, as well as high dietary uranium intake through contaminated drinking water and food in industrial regions where uranium is mined [11]. Uranium can accumulate in the body, reaching levels in individual organs that may be unsafe for human health [12]. When ingested into the human body in large quantities, uranium can pose a serious danger, and its chemical toxicity exceeds its radiological toxicity. In this regard, regulatory documents provide the permissible value of uranium for chemical toxicity. In terms of its toxic effect, uranium belongs to the 1st hazard class - extremely dangerous chemical substances, and radioactive isotopes of uranium are included in the list of pollutants for which state regulatory measures in the field of environmental protection are applied [13,14]. A special feature of uranium is its dual toxicity due to its radiological effects as an alpha emitter and chemical effects due to its properties as a metal [15]. Assessing the potential adverse health effects of uranium is difficult without biological monitoring, which primarily involves measuring uranium concentrations in urine. Based on the fact that the amount of uranium entering the body can be approximately estimated by the uranium content in urine [16, 17], this article considers this indicator as a potential indicator of uranium concentration in the human body. Relevant studies regarding the content of uranium in the urine of workers and the population of uranium mining regions are described in the following sections of the article, including the own research of the Research Institute of Radiobiology and Radiation Protection of NJSC Astana Medical University.

*Aim:* to summarize data on the radiotoxicity of uranium and methods for its determination, with an emphasis on the using of mass spectrometry, and to evaluate the effectiveness of urine analysis as a biomonitoring of uranium in the human body of uranium industry workers.

## 2. Matreials and methods

*Methods for determining uranium in the human body*

Measuring the concentration of uranium in the human body can be carried out by two main methods: measurements in vivo and in measurements vitro. Methods in vivo measure the amount of uranium deposited within the body using a whole body radioactivity meter. Analyzes in vivo are the most direct method for quantifying radionuclides contained within the body. However, not all radionuclides emit radiation that can be detected with sufficient accuracy; these include 234 U and 238 U due to low-intensity gamma radiation [18]. Methods in vitro allow the assessment of deposited uranium by analyzing biological fluids, excreta, or tissue obtained through biopsy or post-mortem tissue sections [19].

Uranium analyzes in vitro is usually performed on urine samples, but other biomaterials such as blood or feces can also be used. Urine testing for uranium is usually the most preferred test because it is generally more sensitive and less expensive. Stool analysis does not provide information about uranium deposition, and also requires preliminary chemical preparation, and blood analysis is an invasive method [20,21].

Several methods are available for measuring uranium in urine that do not require chemical separation. These methods include spectrophotometric, fluorometric, kinetic phosphorescence analysis and measurement of total alpha activity. However, the listed methods do not allow determining the relative isotopic content of isotopes uranium, which may be important, for example, to distinguish between natural and depleted uranium [22].

Inductively coupled plasma mass spectrometry (ICP-MS), which has better detection limits for many elements, is becoming increasingly widespread as a method for measuring the activity of radionuclides in biosubstrates [23].

Mass spectrometry is a physical method for measuring the ratio of the mass of charged particles (ions) to their charge. Inductively coupled plasma mass spectrometry is based on the use of inductively coupled plasma as the ionization agent [24] and a mass spectrometer for ion separation and detection. The method also allows for isotopic analysis of a selected element; it sorts isotopes depending on their mass-to-charge ratio (m/z), i.e. activity is determined by the number of atoms in the sample, not by radioactivity [25-27].

Mass spectrometry is a more expensive method, but has a number of advantages: high sensitivity, accuracy of detection of uranium isotopes, low detection limit of radionuclides, small amount of material for research and economic benefits due to higher productivity, due to a significant reduction in the time of sample preparation and analysis [28]. In addition, the measurement of various elements, especially toxic metals, by this method is widespread due to the ability to simultaneously measure dozens of elements in a small amount of the test material [25].

It should be noted that methods for determining uranium in urine using inductively coupled plasma mass spectrometry differ and are constantly being improved. Thus, a rapid sample preparation method was developed for the determination of uranium isotopes in samples using a high-resolution ICP-MS sector instrument. This technique can analyze up to 24 urine samples in two hours with low detection limits, which may be useful in a radiation emergency [29].

## 3. Population outcomes of uranium content in urine

*Uranium content in urine of nuclear industry workers*

The safety of uranium industry workers requires careful and constant monitoring of their working conditions, therefore the concentration of uranium in urine is most often determined in this category of citizens [thirty]. The guide of the US Nuclear Regulatory Committee "Methods of direct and indirect bioanalysis for workers of uranium mines" shows the maximum permissible value of uranium in the urine of workers of uranium mining enterprises: with monthly analysis - 15 μg/l, with examination once a year - 0.90 μg/l and proposed corrective actions in production depending on the uranium content (Table 1) [31].

**Table 1 - Corrective Actions Based on Urine Uranium Test Results [31]**

| Concentration of uranium in urine | Interpretation | Actions (measures) |
|---|---|---|
| less than 15 μg/l | The uranium content in the air sample of the working area complies with regulatory requirements. | Does not require any action.<br>Conduct repeated laboratory tests to determine uranium in urine if the nature of the employee's work changes. |
| from 15 to 35 μg/l | The uranium content in the work area air sample does not meet the requirements | 1. Confirm the result (repeated urine test).<br>2. Determine the reason for the increase in uranium in the urine and, if the results are confirmed, take additional radiation monitoring measures.<br>3. Study the results of radiation monitoring to determine the radionuclide composition of air to determine the source and concentration of radionuclide entering the body. If values exceed, examine sampling procedures.<br>4. Have other workers been exposed to radiation and test their urine for uranium content.<br>5. Limit work until the concentration of uranium in the urine decreases to 15 μg/l.<br>6. According to the study, improve control over the intake of uranium through the respiratory tract |
| more than 35 μg/l | The content of uranium in an air sample is not acceptable | 1. Perform the above steps.<br>2. Continue further action only if another employee's urine concentration of uranium exceeds 35 μg/l.<br>3. Limit the work of employees,<br>of uranium content in urine when working with uranium dust and yellowcake.<br>4. Perform weekly laboratory tests for uranium levels in urine. |
| If the | When workers receive uranium above standard values | 1. Take all appropriate measures listed above.<br>2. Check the urine sample for albuminuria. |

| | | |
|---|---|---|
| concentration is confirmed to be above 35 µg/l for two sequential analyses; upon confirmation, values for any single analysis above 130 µg l or indication of air samples greater than a quarter of the annual limit on intake (that is ¼) | | 3. If the employee was exposed to a poorly soluble form of uranium or uranium dust, conduct a study of critical organs.<br>4. Assess the degree of exposure.<br>5. Establish additional measures to limit the intake of uranium into the body of workers.<br>6. Consider restriction of work until the concentration decreases to less than 15 µg/L and laboratory tests for albuminuria. |

Research at Egypt's uranium processing facilities included external radiation surveillance, monitoring of radioactive dust, and analysis of uranium concentrations in workers' urine. Urine samples collected from plant personnel at the ore crushing and separation site revealed elevated concentrations of uranium (up to 29.2 µg/L) and a strong correlation with serum creatinine levels. The average excretion of uranium in the urine of workers was more than 20 times higher than the permissible level [32]. The daily excretion of $U^{238}$ in urine is 1.4-4.7 times higher than the experimentally established values in the urine of uranium miners and has been shown in other studies [33,34]. Atomic weapons workers are also monitored for possible uranium exposure through urine uranium tests: their average excreted uranium concentration was 0.006 µg/g creatinine. Some urine samples exceeded uranium levels that had been established based on the likely contribution of environmental sources of the radionuclide. However, the health consequences of uranium enriched to <5-8 wt% U235 based on nephrotoxicity in this study were an order of magnitude lower than recommendations given in the literature [35].

## *Urinary uranium concentrations in individuals associated with military use of depleted anium*

Military weapons with depleted uranium have been used by the armed forces of developed countries for 20 years. The use of this type of weapon to solve combat missions in local conflicts (Iraq, 1991, 2003; Bosnia and Herzegovina, 1994; Kosovo and Metohija, 1999; Afghanistan, 2001; Libya, 2011) led to the emergence of a new dangerous factor of technogenic nature. Another object of study where urine tests for uranium content are used are military personnel and the population arriving in areas contaminated with depleted uranium [36-38].

American soldiers who participated in the 1991 Gulf War were injured by fragments containing depleted uranium, or may have been exposed to depleted uranium through other routes, such as inhalation, ingestion, and through wound contamination. Urinary uranium concentrations in soldiers injured by shrapnel were higher than in soldiers exposed to depleted uranium without shrapnel who were not involved in combat [39]. The UK has a biological monitoring program which includes uranium testing of personnel involved in the 2003 Iraq conflict. During The study analyzed urine samples for uranium and creatinine concentrations and for the uranium isotope ratio $U^{238}/U^{235}$. Uranium concentrations ranged up to 556 ng/g(-1) creatinine, slightly above reference values reported for the US population. Isotope ratio measurements showed that all samples contained a natural isotope and did not contain depleted uranium [40]. There is evidence of uranium concentrations in urine samples from Afghan civilians. From male civilians who developed symptoms of fatigue, fever, musculoskeletal and neurological changes, headaches and breathing problems after inhaling dust during the 2002 bombings, urine samples were collected and analyzed for the presence of $U^{234}$, $U^{235}$ and $U^{238}$. The average uranium concentration (275.04 ng/l) was significantly higher than the reference range (1-20 ng/l). The $U^{238}/U^{235}$ratio was 137.87 +/- 0.20, which corresponds to the ratio of natural uranium [41]. At the same time the population of eastern Croatia, who live in post-war areas affected by bombing and the potential use of depleted uranium weapons, have urinary uranium concentrations below values reported in the literature [42].

## *Uranium content in urine of the population*

There are a number of studies where uranium in urine was determined in populations not associated with the mining and processing of uranium and who did not participate in military conflicts, including people who live in areas contaminated with radionuclides. The concentration of uranium in the urine of the population is also being studied in order to create a database for comparing the uranium content in the urine of workers engaged in uranium mining and people who live in areas contaminated with radionuclides. There is information on uranium contamination resulting from coal mining activities in the Yi region of China, due to the mixed distribution of uranium and coal mines. This study collected water, soil, coal, and urine samples from the local population to assess the level of uranium intake and its effects on people. The results showed that uranium concentrations in groundwater were 8.71-10.91 μg/L, while lower levels of uranium were observed in river water. Coal ash contained high concentrations of uranium - 33.1 μg/g, due to enrichment during coal combustion. Uranium concentrations in urine samples were 8.44-761.6 ng/L, which is significantly higher than reference values for unexposed people [43]. An assessment of uranium excretion in urine was carried out among the population of the Czech Republic living near spent uranium ore mining and processing facilities. The average daily excretion was 0.15 mBq/day (12.4 ng/day). Despite the legacy of uranium mines and uranium ore processing plants in the Czech Republic, levels of uranium in urine were similar to those in other countries. It should be noted that this study found a significant difference in daily urinary uranium excretion between people using public water supplies and private wells as a source of drinking water [44]. A study was conducted in Japan to examine uranium concentrations in population urine samples to estimate daily uranium excretion. Concentrations ranged from 0.8 to 35.6 ng uranium per liter of urine (mean 4.5 ng/L(-1)). Urinary uranium was normalized to creatinine concentration to compensate for the degree of urine dilution. Normalized creatinine values ranged from 1.2 to 17.8 ng uranium per gram creatinine (mean 7.4 ng/g(-1) creatinine). These results were consistent with the lower limit of uranium uranium reported for the unexposed population of 0.04-0.40 μg/L. It should be noted that the upper limit of this range (0.4 μg/L) was found in an area with high concentrations of natural uranium in water [45].

The urinary concentrations of uranium during chronic exposure to drinking water were studied among households in southern Finland who consume drinking water from private wells. The population was selected to reflect a wide range of daily uranium intakes from drinking water (0.03-2775 μg/day). Urinary uranium was correlated with uranium intake in drinking water, especially at elevated levels of uranium in water (>or =10 μg/day) in wells [46]. A study was carried out to compare urinary uranium levels in the UK population with levels in British military personnel and ex-servicemen serving in areas where ammunition containing depleted uranium was used. Convalescent hospital patients were recruited as participants. The concentration of uranium in daily urine ranged from 1 to 10.6 ng/l( -1). Creatinine - standardized 24-hour urine concentrations ranged from approximately 100 to 800 ng mol (-1) creatinine. The uranium content was similar to that for US residents. All samples showed an isotope ratio of $U^{238}$ to $U^{235}$, corresponding to natural uranium [47]. Mass spectrometry for determination of $Th^{232}$ and $U^{238}$ in the urine of Jordanians not exposed to uranium showed a mean value of $U^{238}$ in all samples was 3955 μ/Bq/day (-1) (mean 1107 μ/Bq/day (-1)), which is higher than reported data from Germany and India, but consistent with ICRP publication number 23 [48]. The results of determining the activity concentrations of $U^{238}$ and $U^{234}$ in urine samples of Warsaw residents to estimate the background level of the rate of excretion of these radionuclides showed that the excretion rate of $U^{238}$ was in the range of 0.44-30.54 mBq/day (-1), and for $U^{234}$ – in the range of 0.33-28.61 mBq/day (-1). 70% of the results were below the upper limit of 6 mBq/day (-1) recommended by the ICRP for people not exposed to radionuclides (ICRP Publications No23) [49].

## *Relationship between uranium concentration in urine and human health status*

Studies on the concentration of uranium in the urine of uranium industry workers and the population living near uranium deposits in the available world literature. There is even less research regarding urinary uranium and its potential association with morbidity. However, a number of studies have attempted to trace the relationship between uranium concentrations in urine and various diseases. Thus, in the United States, epidemiological studies were conducted that examined the presence of metals in the urine and cognitive impairment in elderly people aged 60 years and older. High levels of urinary cadmium have been found to be potentially associated with impaired memory and mental performance. However, urinary uranium concentrations did not show any significant associations with cognitive impairment [50]. The association of environmental uranium exposure with changes in kidney function in residents of the United States was studied. Uranium was detected in the urine of 74.1% of subjects, and an association was demonstrated between detectable uranium concentrations in urine and microalbuminuria, but no association with clinical kidney disease was identified [51]. The association of urinary metals, including uranium, with the prevalence of diabetes was assessed. The odds ratio for developing diabetes associated with the highest metal concentration was 1.46 (1.09-1.96) for uranium, meaning uranium was positively associated with diabetes, even at relatively low levels observed in the US population [52].

## *Limitations and disadvantages of testing uranium concentration in urine*

The determination of uranium content in urine is carried out to assess its contribution to the dose load of internal irradiation of people, since the rate of excretion of a radionuclide in urine describes the dependence of its content in the body [53]. However, background levels of uranium must be known to assess potential human exposure. Natural background levels of uranium in the urine of unexposed individuals vary greatly depending on region and population, and due to varying intakes of uranium from food and water [54]. There are a number of disadvantages when determining uranium in urine, which can affect the final result. Thus, the amount of uranium in urine samples taken simultaneously (spot) is more variable than in samples taken over 24 hours (daily). Daily urine samples provide greater accuracy in estimating uranium concentrations, but are also more difficult to collect samples [47]. There are studies monitoring occupational exposure to uranium and other toxic heavy metals, including uranium, which show that variations in uranium concentrations in different urine samples from the same person can be quite significant. However, these differences usually correlate with creatinine levels in the same samples. In the studies of Karpas Z., Lorber A. are proposed that daily creatinine levels must be assessed taking into account weight, height and age; adjusted values can be used to determine the internal radiation dose from uranium [55].

In addition, the list of biomaterials for studying the concentration of uranium in the body is expanding. If we are not talking about uranium poisoning, but are studying the effects of uranium in small quantities, determining the concentration of uranium in hair and nails in population studies is especially relevant. Skin appendages are considered the end product of metabolism that absorbs microelements and their use is effective in environmental and toxicological studies [56]. Hair and nails are composed primarily of fibrous protein structures and grow relatively quickly [57, 58], and the hard outer keratin layer of hair prevents the release of internal components, including external contaminants [59]. In addition, hair and nail samples have several advantages over other types of biomaterials: painless removal, ease of collection and transportation, high stability at room temperature, and relatively high concentrations of elements compared to other body fluids and tissues [60–63].

Despite the above, determining the concentration of uranium in urine remains the most common method for monitoring the effects of uranium on uranium industry workers and the population of uranium mining regions.

## *Research of uranium content in urine at the Research Institute of Radiobiology and Radiation Protection*

The main directions of scientific activity at the Research Institute of Radiobiology and Radiation Protection of NJSC "Astana Medical University" are medical provision of radiation safety and the development of scientific foundations for regulating safe levels of technogenic radiation exposure on workers and the population. The objects of research of the research institute are uranium mining and processing enterprises, whose personnel come into contact with soluble and insoluble uranium compounds [64, 65], as well as the population living near uranium industry facilities [66-68].

According to the order of the acting Minister of Healthcare of the Republic of Kazakhstan No KR DSM-131/2020 dated October 15, it is mandatory to determine the concentration of uranium in urine of uranium mining enterprises (UME) personnel [69]. The main purpose of determining uranium in urine of UME personnel is to ensure radiation safety of workers within permissible dose values, obtain the necessary information to optimize protection, and make decisions on intervention in cases of increased radiation exposure.

Memorandum between the Ministry of Healthcare of the Republic of Kazakhstan and NAC Kazatomprom JSC on cooperation in matters of protecting the health of UME employees to enhancement the interaction between workers and local healthcare organizations was signed in 2018, with the organizational and methodological participation of the SRI of Radiobiology and Radiation Protection, NpJSC “AMU”. From 2015 to 2019, laboratory tests of 2,381 urine samples for uranium content in group A personnel were conducted at the Institute as part of the annual medical examination of UME employees. Laboratory tests of urine samples were carried out on an inductively coupled plasma mass spectrometer “Agilent 7800 ICP MS” (Japan), the error of this device in quantitative determinations is 1-5%.

The main results of measuring uranium in the urine of Kazakhstan UME workers are presented in Table 2.

**Table 2 - Uranium content in the urine of group A personnel uranium mining enterprise of Republic of Kazakhstan, μg/l**

| No | Research objects | Total number of samples | Number of samples with values less than <0.90 | Number of samples with values greater than >0.90 | Values (μg/l) |
|---|---|---|---|---|---|
| 1 | Uranium mining enterprise of Southern Kazakhstan 1 | 305 | 242(79,34%) | 63(20,66%) | average 0.74<br>max 13.68<br>min 0.029 |
| 2 | Uranium mining enterprises 1 | 146 | 95(65,06%) | 51(34,93%) | average 1.74<br>max 13.68<br>min 0.08 |
| 3 | Uranium mining enterprises 2 | 210 | 166(79,04%) | 44(20,95%) | average 0.59<br>max 2.91<br>min 0.001 |
| 4 | Uranium mining enterprise of Southern Kazakhstan 2 | 219 | 166(75,34%) | 54(24,65%) | average 1,49<br>max 33,48<br>min 0,12 |
| 5 | Uranium mining enterprise of Southern Kazakhstan 3 | 213 | 168(78,87%) | 45(21,12%) | average 0,59<br>max 2,91<br>min 0,001 |
| 6 | Uranium mining enterprise of Southern Kazakhstan 4 | 157 | 148(94,26%) | 9(5,73%) | average 0,58<br>max 16,97<br>min 0,10 |
| 7 | Uranium mining enterprise of Southern Kazakhstan 5 | 1131 | 1051(92,92%) | 80(7,07%) | average 0,43<br>max 47,15<br>min 0,001 |
| Overall average (2 381 samples): 0,90 μg/l | | | | | |

According to the results of the analysis presented in Table 2, the concentration of uranium in urine varied from 0.001 to 47.15 μg/l, with an average value of 0.90 μg/l. More than 65% of uranium concentrations in urine do not exceed the average meaning of 0.90 μg/l, only 35% and less of rates are above this value.

The presented data shows that in the workshops of the uranium enterprise, in which the main technological processes are carried out, is a significant increase in the average level of uranium concentration in urine compared to other divisions.

Earlier, in the studies of Aumalikova M. and others, studies were conducted to determine uranium in the urine of workers at the Saratov State Chemical Combine, where the concentration of uranium was determined to reach 26.7 μg/l in 4 workers. We reanalyzed urine samples at four workers who has high concentrations of uranium. Three of these workers had 3-5 times decreased uranium concentrations in the urine, while one worker still had urinary uranium concentrations above the maximum threshold (15 μg/L) [8].

To establish the reference value of uranium in the urine of UME personnel, the permissible concentration of uranium in the kidneys was calculated by the empirical formula used in the regulatory documents of the UK, Canada and the USA [70-73]:

$$C = \frac{(5{,}10 \cdot 10^{-34} \mu Bq) * (0{,}065)}{(300г) * (0{,}33 * 10^{-37} \mu Bqg^{-1})} = 3{,}3\ 10^{-6}\ g\ g^{-1} = 3{,}3\ \mu g/L\ g^{-1} \quad (1)$$

where:

C — the permissible concentration of uranium in the kidneys (in g/g),

- 5,10×10⁻³⁴ μBq – activity of uranium,

0,065 – coefficient for conversion in concrete unit of measurement,

- 300 gr – weight of organ (kidneys),

0,33 μBkg x $10^{-37}$ – a coefficient connecting the activity and concentration of a substance in tissue.

According to the above formula, the maximum uranium content in the kidneys is 3.3 μg/g.

It is necessary to analyze the uranium concentration of urine samples to reduce the impact of high level of uranium, the so-called "peak load" on kidneys. It has been established that this load on the kidneys ranges from 0.3 to 3 μg of uranium per gram of kidney tissue. If the uranium concentration in the renal tissue exceeds 3.3 μg/g (nephrotoxic limit) for a long time, it can lead to kidney damage, and determines the presence of retinol binding protein in the urine [70].

In this regard, the concentration of uranium in the body and the corresponding critical organs (lungs, bones, kidneys) is calculated from analyzes of urine samples taken after a break in work and from the corresponding conversion coefficient from urine activity to uranium content in the body. This method is based on the stabilized distribution of radionuclide in the body of a person working under conditions of chronic intake and achieving an equilibrium state.

According of reference, with a maximum concentration of uranium in the kidney of 3.3 μg/g, the excretion of uranium with urine during its continuous intake into the body after 30 days of exposure, taking into account the half-life of uranium from the body, will be equal to 15 μg/l [70].

Based on previously available data [70-72] and our own research data, to determine the permissible limit of uranium in the urine of UME workers, we constructed a graph compiling the concentration of uranium when yellowcake is ingested at low and high temperatures, as well as uranium ore dust (Figure 2). According to the graph, at the period of uranium exposure increases for UME workers, the concentration of uranium in urine decreases, because slightly soluble forms of uranium can settle in the kidneys, and rapidly soluble forms are excreted from the body in less than 5 days [73, 74].

Thus, the reference value of uranium in the urine of UME workers is 0.90-15 μg/l. If the uranium concentration in the urine of UME workers is exceeded, corrective actions used in world practice and presented in Table 1 are proposed.

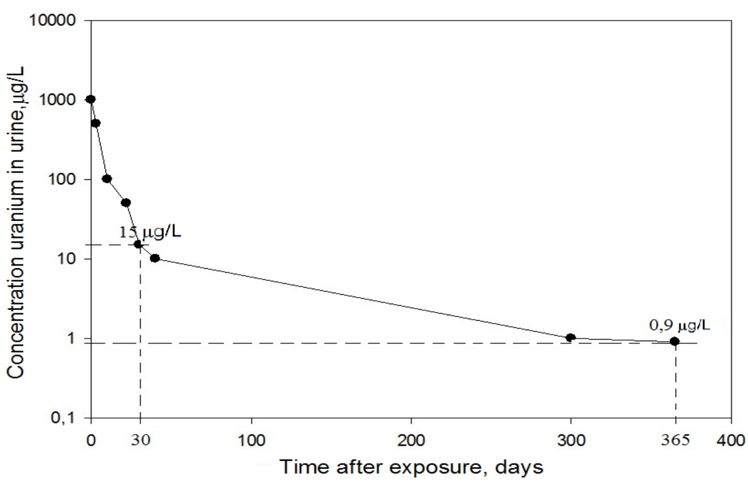


**Figure 2 - Uranium concentration in urine versus exposure time**

In general, conducting laboratory tests to determine the content of uranium in the urine of UME workers will allow us to identify "risk groups" at an early stage in order to timely predict the risk of developing work-related disorders and occupational diseases, and introduce treatment and preventive complexes aimed at protecting the health of the working population.

With the participation of the Research Institute of Radiobiology and Radiation Protection on the basis of the RSE at the Central Clinical Hospital for Disabled Persons of the Patriotic War and the Institute, the MORBUZ Consortium (Medical Radiation Safety and Morbidity Management) was created, where high-tech specialized clinical examination, treatment and medical rehabilitation of workers are carried out exposed to the negative effects of ionizing radiation.

Research into uranium concentrations in urine in uranium mining regions is ongoing. In the context of the rapidly developing uranium industry in our state, the Institute sets the goal of becoming a center in Kazakhstan for further improvement of comprehensive work to reduce radiation risk for personnel of radiation-hazardous enterprises and near the living population.

## 4. Conclusion

The use of biological samples to determine uranium levels in the body is important for monitoring the health of people who may be exposed to uranium at work or in the environment. In most cases, urine testing is used to detect uranium exposure through drinking water or inhalation of particles containing uranium. Urine monitoring is an effective method for determining a person's exposure to soluble uranium compounds because the daily urinary excretion of uranium depends on the total level of uranium in the body. The US Nuclear Regulatory Commission (NRC) has set urine uranium levels at 15 μg/L for persons occupationally exposed to uranium. For the population of different regions, the concentration of uranium in urine varies widely, usually in the range of 0.04-0.40 μg/l. Some studies show a relationship between uranium concentration and qualitative changes in the composition of urine, but there is insufficient scientific evidence regarding the existence of a connection between uranium content in urine and the occurrence of somatic diseases. The large body of knowledge obtained from studies of uranium in workers and the public at the Research Institute of Radiobiology and Radiation Protection should be included in the assessment of the health risks associated with uranium exposure. However, this biomonitoring approach has so far found only extremely limited application in the Republic of Kazakhstan; ultimately, we hope that the research conducted will contribute to improving the radiation protection system in our country.

**Conflicts of Interest.** The authors declare no conflict of interest.

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# Зәрдегі уран – адам ағзасындағы уранның жиналуын бағалаудың биоиндикаторы

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## Түйіндеме

Бұл шолуда уранның адам ағзасына әсер етуі нәтижесінде туындауы мүмкін радиоуытты салдарлар және ағзадағы уранның жиналуын биоиндикациялау құралы ретінде зәрдегі уран концентрациясын анықтау мәселелері қарастырылады. Зерттеу жұмысында зәрдегі уранды анықтау әдістері мен олардың қолданылу мүмкіндіктері талданады. Мақалада ластанған аумақтарда тұратын халықтың және кедейленген уранмен байланыста болған әскери қызметкерлер мен жұмысшылардың зәріндегі уранның биомониторингіне қатысты эпидемиологиялық зерттеулердің деректері көрсетілген. Зәрдегі уран концентрациясы мен денсаулық жағдайы, соның ішінде нефроуыттылық арасындағы анықталған байланыстар сипатталады. Сонымен қатар, уранның созылмалы әсерін бағалауда шаш пен тырнақ үлгілері сияқты перспективалық альтернативті биосубстраттар да қарастырылады. Шолуда радиациялық-қауіпті кәсіпорындарда жұмыс істейтін А тобының жұмысшыларының зәріндегі уран құрамына қатысты өзіндік зерттеулер нәтижелері ұсынылған. Бұл санаттағы жұмысшылар үшін биомониторинг заңды түрде бекітілген жыл сайынғы медициналық тексерудің міндетті бөлігі болып табылады. Индуктивті байланысқан плазмамен масс-спектрометрия әдісі арқылы 2000-нан астам зәр үлгілері талданды. Орташа уран концентрациясы 0,90 мкг/л құрап, кейбір жағдайларда 47,15 мкг/л-ге дейін жетті. Зәрдегі уранның ең жоғары мөлшері негізгі технологиялық үдерістерде қызмет атқаратын жұмысшыларда анықталды. Ағзадағы уранның рұқсат етілген деңгейін бағалау мақсатында бүйректегі шекті концентрация есептеліп, зәрмен

шығарылатын уран деңгейімен салыстырылды. 15 мкг/л-ден жоғары концентрациялар нефроуыттылықтың потенциалдық қаупін көрсетіп, А тобы жұмысшыларының еңбек жағдайларын түзетуді қажет ететіні анықталды. Алынған биомониторинг нәтижелері дозалық жүктемелердің рұқсат етілген деңгейлерін бақылауға ғана емес, сондай-ақ радиациялық қорғаныс шараларын оңтайландыруға және әсер ету деңгейі шектен асқан жағдайда араласу туралы шешім қабылдауға мүмкіндік береді. Қазақстанда уран өндіру және өңдеуге байланысты қауіп-қатерді мойындау – болашақта жұмысшылар мен халықтың денсаулығын қорғауға бағытталған саясатты жетілдіруге жол ашуы тиіс.

**Түйін сөздер:** уран, масс-спектрометрия, уран өнеркәсібі жұмысшылары, уран-кенді провинциясы, эпидемиологиялық зерттеулер, денсаулық жағдайы.

## Уран в моче как биоиндикатор для выявления накопления урана в организме человека

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### Резюме

В данном обзоре представлены данные о возможных радиотоксических последствиях воздействия урана организм человека и определения концентрации урана в моче в качестве биоиндикатора накопления урана в организме. В работе рассматривается потенциальное применение и методы определения урана в моче. В статье освещены данные эпидемиологических исследований, связанных с биомониторингом урана в моче у персонала, военнослужащих, контактирующих с обедненным ураном и у населения, проживающего на загрязненных территориях. В статье обсуждаются выявленные взаимосвязи между концентрацией урана в моче и состоянием здоровья, включая нефротоксичность. Кроме того, затрагиваются альтернативные биосубстраты, такие как волосы и ногти, как перспективные объекты для оценки хронического воздействия урана в условиях экологических исследований. В обзоре приведены и собственные исследования содержания урана в моче у персонала группы А радиационно-опасных предприятий, для которого биомониторинг является обязательной составляющей ежегодного медицинского осмотра, закрепленной на законодательном уровне. Было проанализировано более 2 тысяч образцов мочи методом масс-спектрометрии с индуктивно связанной плазмой. Средняя концентрация урана составила 0,90 мкг/л, при этом в отдельных случаях значения достигали 47,15 мкг/л. Наибольшие значения концентрации урана в моче были зафиксированы у работников, занятых в основных технологических процессах. Для оценки допустимого уровня урана в организме была рассчитана предельная концентрация в почках и сопоставлена с уровнями экскреции урана с мочой. Установлено, что концентрации свыше 15 мкг/л указывают на потенциальную нефротоксичность и необходимость коррекции условий труда персонала группы А. Полученные данные биомониторинга позволяют не только контролировать соблюдение допустимых дозовых нагрузок, но и обеспечивают необходимую информацию для оптимизации мер радиационной защиты и принятия решений о вмешательстве в случаях превышения уровней воздействия. Признание рисков, связанных с добычей и переработкой урана в Казахстане, должно способствовать изменению политики для защиты здоровья работников и населения в будущем.

**Ключевые слова**: уран, масс-спектрометрия, работники урановой промышленности, урановорудная провинция, эпидемиологические исследования, состояние здоровья.