

Uranium

Guideline

The maximum acceptable concentration (MAC) for uranium in drinking water is 0.1 mg/L (100 µg/L).

Identity, Use and Sources in the Environment

Uranium, which is a metal, has the highest atomic weight of the naturally occurring elements. It may exist in the +2, +3, +4, +5 or +6 valence states, the most prevalent being the hexavalent state. In nature, hexavalent uranium is commonly associated with oxygen as the uranyl ion, UO_2^{2+} . Naturally occurring uranium ($^{\text{nat}}\text{U}$) is a mixture of three radionuclides: ^{234}U , ^{235}U and ^{238}U , all of which decay by alpha emission.^{1,2} Uranium is widespread in nature, occurring in granites and various other mineral deposits.^{1,3}

The United States, Canada and South Africa account for about 80% of uranium production in the West.⁴ Canada produced more than 11 000 tonnes of uranium during 1984.⁵ The main use of uranium is as fuel in nuclear energy plants. It is chemically extracted from the ore and converted to gaseous uranium hexafluoride (UF_6). $^{235}\text{UF}_6$ is enriched and converted to uranium dioxide ($^{235}\text{UO}_2$), the final reactor fuel product.⁴

Exposure

Uranium may enter drinking water from naturally occurring deposits or as a result of human activity, such as mill tailings.^{2,6} Phosphate fertilizers may contain uranium at an average concentration of 150 µg/g and can also contribute uranium to groundwater.⁷ A mean uranium concentration of 32 ng/L in New York City tap water has been reported.⁸ Since 1975, the uranium concentration of the drinking water supplies of up to 17 Canadian cities has been monitored.⁹ Reported concentrations for monthly composite samples are usually less than 1 µg/L, but uranium concentrations in samples in some municipalities have been reported to exceed 8 µg/L. For the 18-month period of June 1975 to December 1976, about 50% of the uranium concentrations in monthly samples from 17 municipalities were below the detection limit of

0.05 µg/L. Private domestic supplies with uranium concentrations up to 700 µg/L have been identified in Canada.^{10,11} Reported estimates of daily uranium intake from water range from 0.035 µg for Reference Man in the United States to 2.1 µg in Finland.¹³ The estimated average daily uranium intake from water containing 0.05 µg/L is 0.075 µg (at 1.5 L/d) for an adult Canadian.

Vegetables and cereals normally contribute most heavily to the daily intake of uranium.⁴ Average per capita intake from food has been reported as 1.3 µg/d (United States)^{8,14} and 1.5 µg/d (Japan).¹⁵ Plant (vegetable) produce generally contains a 10-fold higher uranium concentration than animal produce, the highest concentrations being found in root and stem vegetables.

Coal and fuel combustion are major sources of uranium contamination in air. Average atmospheric uranium concentrations have been reported as follows: New York, 0.4 ng/m³;⁸ Upper New York State, 0.10 to 1.47 ng/m³;¹⁶ United Kingdom, 0.02 ng/m³.¹⁷ Tobacco smoke (from two packs per day) will contribute less than 0.05 µg uranium per day.¹⁸ If one assumes a daily respiratory volume of 20 m³ and an average uranium concentration in urban air of 0.1 ng/m³, then this would result in a daily uranium intake of about 2.0 ng.

Reasonable estimates of daily intake of uranium by adults may be summarized as follows: air, 0.002 µg; food, 1.5 µg; water, 0.075 µg. Based on the concentrations reported above, it is estimated that the average Canadian total daily intake is ~1.6 µg, 99.9% being derived through ingestion.

Analytical Methods and Treatment Technology

Uranium can be measured using fluorescence with either laser excitation or ultraviolet light after fusion with a pellet of sodium fluoride.¹⁹ The detection limit is at least as low as 0.1 µg/L and may be 0.005 µg/L.²⁰

Current municipal water treatment practices are not effective in removing uranium. Experimentation indicates, however, that uranium removal can be

accomplished by water treatment processes with modification of pH, chemical dosages (often with alum) or both.²¹

Health Effects

Data on chemical, not radiological, toxicity are considered here. Information pertinent to the derivation of a guideline based on radiological effects is discussed separately in the section on radioactivity.

Although ubiquitous in the environment, uranium has no known metabolic function in animals and is currently regarded as non-essential.⁴ Estimates of uptake from the gastrointestinal tract range from 0.01 to 30%.¹⁴ Absorption from the gastrointestinal tract varies with the solubility of the uranium compound⁴ and is markedly species-dependent. Absorption is consistently lower in the rat than in any other animal studied and should therefore not be used uncritically to imply human absorption.¹² From a recent review of six animal studies and four human studies, a “best” estimate of uranium uptake by humans exposed to environmental concentrations is 1.4%.¹² Absorption of water-soluble uranium compounds by the skin has been shown to be about 0.1%.²²

Animal studies indicate that the amount of soluble uranium accumulated internally is proportional to intake from ingestion or inhalation. Uranium predominates in the mammalian organism as the water-soluble hexavalent (uranyl) form. This forms soluble complexes with bicarbonate ions and proteins. A non-diffusible uranyl–albumin complex is formed in equilibrium with a diffusible ionic uranyl bicarbonate complex ($\text{UO}_2\text{HCO}_3^+$). The uranyl bicarbonate is stable but will dissociate under conditions of reduced pH, such as in bone, and in the kidney tubule.²³ The uranyl ion replaces calcium in the hydroxy-apatite complex of bone crystals.⁴ Hexavalent uranium is rapidly excreted by the kidney, the excretion rate being partly dependent upon the pH of the tubular urine.⁴ At high pH, most of the uranyl complex is stable and is excreted in the urine. If the pH is low, the complex dissociates to a variable degree, and the uranyl ion may then interact with cellular proteins in the tubular wall. This results in reduced uranyl excretion, and the protein binding can impair tubular function. The overall elimination half-life of uranium under conditions of normal daily intake has been estimated to be between 180 and 360 days.⁴

Uranium is a classic experimental nephrotoxin, and nephritis is the primary chemically induced effect of uranium in animals and humans.¹⁴ Lesions are seen in the kidney at both glomerular and tubular levels.²⁴ These effects have been seen down to a single dose level (intravenous) of ~0.1 mg/kg bw.^{14,25} In experimental animals, the most frequent renal injury caused by uranium is manifested by morphological changes in the

proximal convoluted tubules.⁴ At sublethal doses, regeneration of the injured tubular epithelium begins two to three days after exposure. The new epithelial lining differs morphologically from normal tubular epithelium.⁴ Biochemical and functional changes observed are consistent with damage to the distal two-thirds of the proximal tubule. There is evidence to suggest that tolerance may develop with repeated uranium exposure.^{26–29}

Comparative toxicological studies must be interpreted with particular attention to species, route of administration, formulation of uranium and frequency/duration of exposure. Rat models may be suitable for inferring human sensitivity to uranium when the route of administration is intravenous; however, the correspondence in sensitivity when uranium is administered orally should be considered carefully. The percent uptake of uranium by rats is less than the percent uptake by man when exposure is via the oral route. Furthermore, studies with rats must take into account age-dependent renal failures to which these animals are naturally prone. A 91-day study of rats and rabbits exposed *ad libitum* to 24 mg/L uranyl nitrate (~11.5 mg/L uranium) in drinking water indicated minor histopathological lesions in kidney tubules in male animals.³⁰ More extensive lesions and functional impairment of kidney (clearance time) occurred in male rabbits exposed to 120 and 600 mg/L uranyl nitrate (56.9 and 284.5 mg/L uranium, respectively).³⁰ Female rabbits showed no significant lesions at low doses; however, minor tubular lesions similar to those found in males appeared in animals exposed to 120 and 600 mg/L uranyl nitrate.³ A dose of 10 µg/kg bw (measured as uranium) delivered as uranyl salts by the intravenous route appears to be the threshold dose for renal injury to rabbits¹⁴ and dogs.³¹ However, intravenous doses of uranium below a threshold of 70 µg/kg bw have been administered to humans without detectable urinary abnormalities.¹⁴ The threshold concentration for renal injury in the dog is ~0.3 µg uranium per gram of renal tissue. Other recent work suggests a limiting uranium concentration above 0.5 µg/g renal tissue in the rat and rabbit.³⁰ The threshold concentration for renal injury in man remains uncertain but is likely to be above 0.6 µg/g renal tissue, and a value of 3 µg/g has been generally used in the past.¹² For metabolic modelling purposes, a reasonably conservative estimate at this time is 1.0 µg uranium per gram of renal tissue.¹²

The chronic health effects of natural environmental exposure to uranium have received little attention. In Nova Scotia, clinical studies were performed upon 324 persons exposed to variable amounts of ^{nat}U in their drinking water (up to 0.7 mg/L uranium) supplied from

private wells.^{10,11} There was no pattern of overt renal disease or any other symptomatic complaints that could be attributed to uranium exposure. A sensitive index of renal proximal tubular function might serve as an index of subclinical toxicity. Urinary β_2 -microglobulin excretion was reported in the Nova Scotia studies; a dose–response effect of increased excretion was observed with increasing uranium exposure, with evidence of reversibility for individuals who had stopped using the uranium-contaminated drinking water.^{10,11}

There are no data on the teratogenicity or mutagenicity of uranium.

Classification and Assessment

Although the potential exists for radiological toxicity of orally administered ^{nat}U , this has not been observed in man or animals, presumably because of the relatively low specific activity of this mixture of uranium radionuclides. Experimental evidence of the carcinogenicity of uranium is restricted to highly insoluble or enriched uranium compounds delivered by inhalation or injection. Although these observations do not seem relevant to ingestion of ^{nat}U in drinking water,¹² the associated risk for induction of bone cancer has been inferred from the known risk due to ^{226}Ra exposure. The estimated excess risk of induction of bone sarcoma is considered to be insignificant compared with the normal background lifetime risk.¹² The chemical toxicity of ^{nat}U has been observed in man and in animals. Because the chemical data reviewed to date suggest a more stringent recommendation than that based upon available radiological criteria, it is recommended that assessment of uranium toxicity in drinking water be based upon chemical criteria. Uranium has, therefore, been included in Group VA (inadequate data for evaluation).

For compounds classified in Group VA, the maximum acceptable concentration (MAC) is derived on the basis of division of the no-observed-adverse-effect level (NOAEL) for the critical response (i.e., nephrotoxicity for uranium) in an animal species by an uncertainty factor. For uranium, the acceptable daily intake (ADI) is derived as follows:

$$ADI = \frac{1.28 \text{ mg/kg bw per day}}{500} = 0.00256 \text{ mg/kg bw per day}$$

where:

- 1.28 mg/kg bw per day is the NOAEL for minor histopathological lesions in kidney tubules in the most sensitive sex (males) of the most appropriate species (rabbits) in the only available subchronic study (by ingestion);³⁰ the NOAEL was calculated assuming that the mean water consumption and body weight of rabbits are 0.45 L and 4 kg, respectively

- 500 is the uncertainty factor ($\times 10$ for interspecies variation; $\times 10$ for intraspecies variation; and $\times 5$ for less-than-chronic study offset by indications of reversibility of subclinical lesions).

Rationale

In general, drinking water is a minor source of uranium exposure, contributing 5% or less of the total daily intake. However, it should be noted that the total daily intake of uranium resulting from consumption of water and of diets containing typical levels of uranium would be considerably lower than the ADI (i.e., $\sim 10\%$ of ADI). Moreover, the uranium content of foodstuffs does not appear to be appreciably higher in areas where concentrations in water are high. The MAC has been derived, therefore, assuming that the estimated proportion of total uranium intake normally ingested in drinking water is 90%. This was based on the consideration that the total daily intake of uranium from food and from drinking water containing concentrations at the MAC (assuming 90% allocation to drinking water) is unlikely to exceed the ADI.

Therefore, the MAC is derived from the ADI as follows:

$$MAC = \frac{0.00256 \text{ mg/kg bw per day} \times 70 \text{ kg} \times 0.90}{1.5 \text{ L/d}} = 0.1 \text{ mg/L}$$

where:

- 0.00256 mg/kg bw per day is the ADI, as derived above
- 70 kg is the average body weight of an adult
- 0.90 is the estimated proportion of total uranium intake normally ingested in drinking water
- 1.5 L/d is the average daily consumption of drinking water for an adult.

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