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Exposure limits and assessment of intake for inhaled soluble uranium compounds

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Abstract

This paper describes the impact of renal threshold concentrations for uranium; the latest biokinetic models recommended by the International Commission on Radiological Protection; and the pattern of exposure on intake limits and their assessment. It is concluded that the current daily limit on intake of 2 mg is acceptable, but considerable uncertainties exist in assessment from urine analysis. It is suggested that the role of biochemical indicators of exposure should be pursued. © 1998 NRPB. Published by Elsevier Science S.A.

Keywords: Uranium; Exposure limits; Intake assessment

1. Introduction

The present occupational exposure limits for soluble uranium compounds were derived in the late 1950s from judgements concerning nephrotoxicity and the use of a simplistic metabolic model described in ICRP Publication 2 [1,2]. Recently, the International Commission on Radiological Protection (ICRP) has published comprehensive biokinetic models of the human respiratory tract and the systemic behaviour of uranium after absorption into blood [3,4]. Moreover, during the past 40 years, substantially more information on the nephrotoxicity of uranium has become available [5,6]. The aim of this paper was to evaluate the appropriate limits on intake, and the uncertainties in the assessment of exposure as a consequence of these developments. The work is discussed in greater detail elsewhere [7].

For this paper, soluble uranium compounds are considered to be those whose absorption characteristics from lungs into blood are bounded by those for Type F (highly soluble) and M (moderately soluble) compounds as defined by ICRP [3], and for which nephrotoxicity cannot be discounted. Apart from uranium octoxide (U_3O_8) and dioxide (UO_2) this consideration is likely to apply to all other compounds formed during the fabrication and reprocessing of nuclear fuels.

2. Historical perspective

The limit on exposure to uranium due to chemical toxicity is based on the judgement that a renal concentration of 3 $\mu g\ g^{-1}$ could be safely tolerated by man [1]. This value can also be derived from values listed in ICRP Publication 2 [2]; namely the maximum permissible body content of uranium commensurate with a dose limit of 50 mSv $year^{-1}$, 5×10^{-3} μCi (185 Bq), the fraction of uranium in the kidneys relative to that in the body (0.065), the kidney mass (300 g) and the specific activity of uranium (0.33 $\mu Ci\ g^{-1}$ or 12.2 $kBq\ g^{-1}$). Hence the threshold kidney concentration was

$$\frac{5\times10^{-3}}{0.33}\cdot\frac{0.065}{300}=3.3\ \mu g\ g^{-1}$$

The exposure limit was then derived according to the procedure shown in Table 1. In retrospect this value may be 7 times too high, due to changes in the dose limit recommended by ICRP, currently 20 mSv $year^{-1}$ averaged over 5 years [3], changes to the definition of specific activity of uranium, now 0.68 $\mu Ci\ g^{-1}$ or 25 $kBq\ g^{-1}$, and assumptions concerning the breathing rate of workers, now 9.6 m^3 per 8 h working day [3].

Effectively the chemical limits on intake and threshold limit values (TLVs) have remained unchanged for the past 40 years; some of the most recent relevant publications are summarised in Table 2 [8–12]. More detailed information is given elsewhere [7]. Whilst a recent American National Standard [13] has endorsed the 3 $\mu g\ g^{-1}$ kidney concentration limit, others have suggested, on the basis of the

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Table 1
Derivation of exposure limit for soluble uranium [1,2]

Assumption	Source
Renal threshold, 3 μg g^{-1}	ICRP-NCRP judgement
Kidney mass, 300 g	ICRP Publication 2
Retention half-time, 15 days	Animal and human data
% inhaled in kidney, 2.8	ICRP Publication 2
Air intake, 8 h, 6.9 m^3	ICRP Publication 2

Maximum kidney input for equilibrium at renal threshold, 0.0462×900 μg day^{-1}=41.5 μg day^{-1}. Corresponding maximum lung input=41.5÷0.028 μg day^{-1}=1.5 mg day^{-1}. Minimum TLV=1.5÷6.9 mg m^{-3}=0.2 mg m^{-3}.

Table 2
Exposure limits to soluble uranium compounds [7]

Year	Source	TLV	Daily limit (mg)
1959	ICRP 2/NCRP 2 [1]	0.2	1.5[a]
1980	OJEC [8]		2.5[b]
1988	ICRP 54 [9]	0.2	2.0[c]
1989	OSHA [10]	0.05	0.5[c]
1997	HSE, UK [11]	0.2	2.0[c]
1997	ACGIH [12]	0.2	2.0[c]

The primary exposure standards are in bold; the other values are derived from them.
[a]Based on 6.9 m^3 air inhaled in 8 h.
[b]Based on short-term exposure rule (ICRP Publications 6 and 10).
[c]Based on 9.6 m^3 air inhaled in 8 h.

evidence available, that it should be reduced by up to an order of magnitude [5,6]. It is noteworthy that, since 1988 [9], ICRP publications have been concerned solely with intake limits based on radiation dose and also that chemical limits are not addressed in recent European legislation [14].

3. Limits on intake based on new ICRP biokinetic models

The latest ICRP biokinetic models have been used to calculate the annual limits on intake, as Bq, for natural, low and highly enriched forms of uranium, with a default particle size of 5 μm AMAD (Table 3). The corresponding masses of uranium are also included in the Table. It can be deduced from Table 3 that acute intakes of Type F and Type M compounds of any isotopic composition will always be limited by chemical toxicity, i.e. 2 mg day^{-1}; annual limits of natural and low enriched Type F compounds will always be limited by chemical toxicity whatever the intake pattern; annual limits of highly enriched Type F compounds and Type M compounds of any isotopic composition will be limited by radiotoxicity. However, on the basis of the TLV recommended by the US Department of Labor, 0.05 mg m^{-3} [10], equivalent to a daily intake of 0.5 mg based on a breathing rate of 9.6 m^3 per 8-h working day, annual intakes of low enriched Type M compounds would also be restricted by chemical toxicity.

Table 3
Annual limits on intake for uranium[a]

Composition	Type F		Type M	
	kBq[b]	mg[c]	kBq[b]	mg[c]
U-nat	32.8	1300	10.8	430
3.5% ^{235}U	32.3	780	10.3	250
93% ^{235}U	31.7	105	9.9	33

[a]Aerosol, 5 μm AMAD.
[b]Based on dose limit of 20 mSv $year^{-1}$.
[c]Calculated from isotopic content; chemical limit, 2 mg day^{-1}.

3.1. Acute intake

The predicted retention of uranium in the kidneys after an acute intake of 1 μg of either a Type F or M compound for aerosols of 1 and 5 μm AMAD is shown in Fig. 1. For a Type F compound the maximum retention, 0.03, occurs after 1 day; assuming a kidney mass of 300 g, the concentration is 10^{-4} μg g^{-1}. For a threshold concentration of 3 μg g^{-1}, the corresponding intake is 30 mg. For Type M compounds the intake is 230 mg. These calculations may explain why known acute intakes in excess of the exposure limit of 2 mg day^{-1} have not resulted in observable kidney damage [7]. An intake of 2 mg day^{-1} of a Type F or M compound would result in a kidney concentration below the most restricted value considered here, i.e. 0.3 μg g^{-1}.

3.2. Chronic intake

The predicted retention of uranium in the kidneys after a chronic intake of 1 μg day^{-1} of either a Type F or Type M compound of natural uranium is shown in Fig. 2. The data for a Type F compound show that the amounts retained in the kidneys after 10, 100 and 1000 days are 0.24, 0.44 and 0.60 μg, respectively, corresponding to concentrations of 8×10^{-4}, 1.5×10^{-3} and 2×10^{-3} μg g^{-1}. The corre-

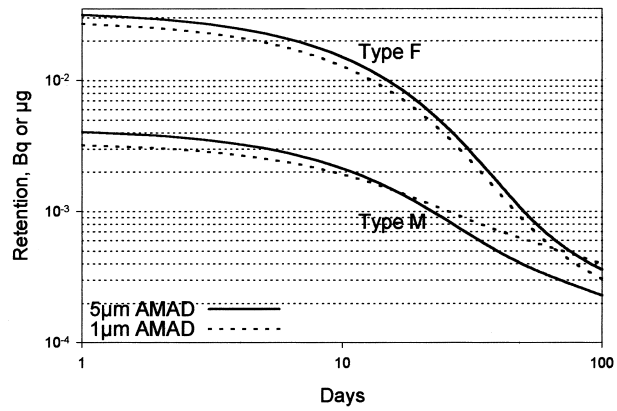

Fig. 1. Predicted retention of uranium in kidney after acute inhalation. Intake 1 Bq or 1 μg.

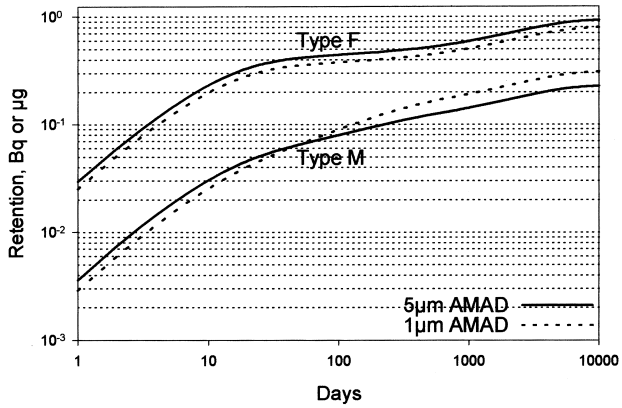

Fig. 2. Predicted retention of uranium in kidney after chronic inhalation. Intake 1 Bq day^{-1} or 1 μg day^{-1}.

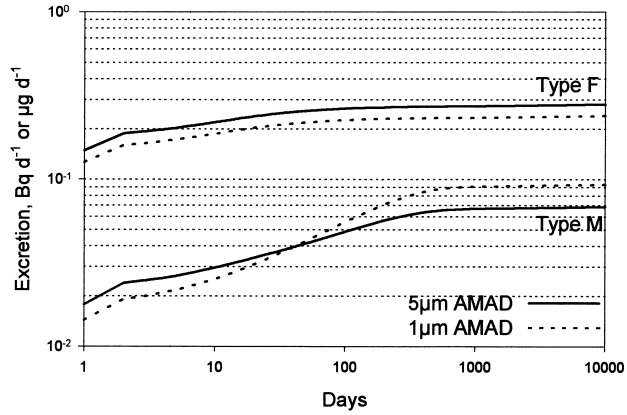

Fig. 4. Predicted urinary excretion of uranium after chronic inhalation. Intake 1 Bq day^{-1} or 1 μg day^{-1}.

sponding kidney concentrations for a chronic intake of 2 mg day^{-1} would be 1.6, 3 and 4 μg g^{-1}. Clearly, the importance of these values will depend upon what is considered to be the threshold concentration. The likelihood of kidney damage resulting from the inhalation of Type M compounds is appreciably less.

4. Interpretation of urine analysis data

4.1. Acute intake

The predicted urinary excretion of Type F and Type M uranium compounds based on the new ICRP biokinetic models after an acute intake of 1 μg are shown in Fig. 3. It can be deduced from the numerical data that the daily excretion of a Type F compound decreases by 30- and 50-fold between 1 and 2 days and 1 and 7 days, respectively. The difference between the daily excretion of a Type F compound at 1 day and a Type M compound at 7 days is 280-fold. The above calculations demonstrate the considerable uncertainty that can occur in the interpretation of urine analysis data unless the time of intake and the material specific absorption characteristics are known.

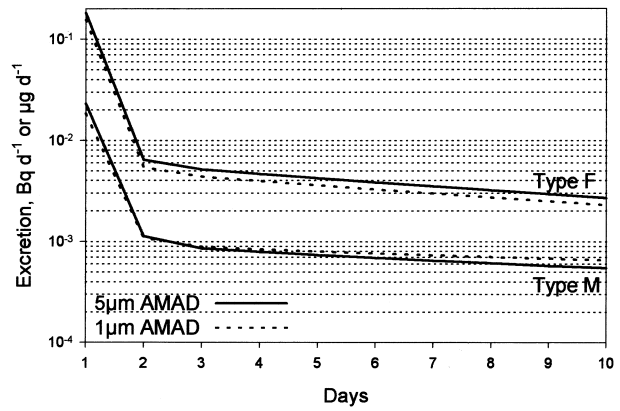

Fig. 3. Predicted urinary excretion of uranium after acute inhalation. Intake 1 Bq or 1 μg.

4.2. Chronic intake

The predicted urinary excretion for Type F and Type M uranium compounds based on a continuous intake of 1 μg day^{-1} is shown in Fig. 4. It can be deduced that a daily intake of 2 mg of a Type F compound will result in the daily excretion of 300 μg at 1 day and 560 μg at 10^4 days after the commencement of exposure. The corresponding values for a Type M compound are 40 and 140 μg day^{-1}. Thus, in principle, if bioassay is carried out at frequent intervals, continuous intakes in excess of 2 mg day^{-1} should soon become evident, particularly if the investigation level is based on the minimum value derived from Fig. 4, i.e. 40 μg day^{-1}.

However, in practice, chronic intakes can be considered continual or due to regularly repeated or frequent exposures, or more likely to random occasional exposures. Moreover, such intakes can vary appreciably in magnitude. For protection purposes these intake patterns can be represented by an acute intake at the mid-point of the sampling interval, but this methodology could have considerable uncertainty [7].

5. Relationship between kidney content and urinary excretion

The relationship between the contemporary kidney content and daily urinary excretion for a 100-day interval after acute and chronic intakes of Type F and M compounds are shown in Fig. 5. In the previous section it would be inappropriate to use these data for assessing intakes. However, they do suggest that the contemporary kidney content, and hence judgements on toxicity status, could be evaluated from urinary excretion data irrespective of the absorption characteristics or the pattern of intake.

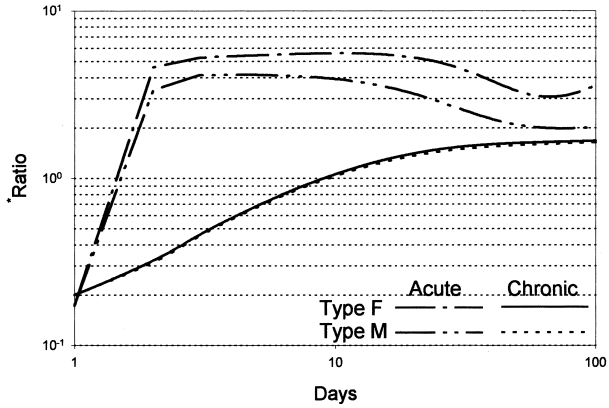

Fig. 5. Kidney to urine ratio after acute and constant chronic inhalations of uranium. *Kidney content at the end of the *n*th day divided by total excretion during the *n*th day. Points joined by continuous line for clarity.

Provided there is no overt kidney damage, an assumed ratio of 4:1 could be used for protection purposes.

6. Biochemical indicators of renal damage

Several biochemical indicators have been investigated for evaluating uranium-induced sub-clinical renal damage. These have included albumen, glucose, the cellular enzymes lactate dehydrogluase, *N*-acetyl-β-glucosaminidase and β-microglobulin [5,6]. However, doubts remain about the specificity of some of these compounds and their reliability over time. Their usefulness for detecting low level chronic exposures has also been questioned. Nevertheless, in view of the difficulties concerning the interpretation of urinary excretion data, further research on biochemical indicators of exposure appears to be warranted.

7. Summary

This paper has drawn attention to some of the uncertainties concerning the continued acceptance of a toxic threshold level of 3 $\mu g\ g^{-1}$ of uranium in the kidneys. The use of the most recent biokinetic models published by ICRP provides a more rational and robust basis for assessing exposure limits than the simplistic procedures used in the original derivation. Unless the exposure pattern and absorption characteristics of the uranium are well defined, considerable uncertainties will result from the interpretation of bioassay data. As a consequence it is suggested that further work on biochemical indicators of renal damage should be undertaken.

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