

AN ASSESSMENT OF THE EFFECTS OF URANIUM IN DRINKING WATER

(This note was prepared as a draft for development, to provide information to people with uranium concentrations, in private water supplies, lower than the World Health Organization 1998 provisional guideline value of 2 micrograms per litre. It is not a statement of Government policy).

Introduction

Uranium (U) is a naturally occurring material, present in soil, rocks, water, air and food. The concentration in water is measured in micrograms per litre (shortened to mcg/l). One microgram per litre (1mcg/l) is one part of U in a thousand million parts of water. Concentrations up to that level are very common, but in some places (such as Dartmoor) higher concentrations are found because U is present in the rocks and is dissolved by the water in the ground. In some parts of the world, such as Canada, this results in concentrations of several hundreds of micrograms per litre in people's drinking-water.

U is radioactive, but your exposure to radioactivity from the U in your drinking-water is hundreds of times smaller than your everyday overall exposure to radioactivity from natural sources in the environment.

We know that U can cause kidney damage at doses which, as far as we can tell, are too low to cause any other effects - and far too low to add significantly to exposure from radioactivity. The rest of this note, therefore, is about studies of kidney damage in laboratory animals given U, and in people whose drinking-water contains U.

Reviews of uranium toxicity

Two extensive reviews have been published recently.^{1,2} The chemical toxicity of U has not been evaluated by the expert scientific advisory committees which advise the Chief Medical Officer at the Department of Health. There is no official UK Government guidance or regulations on U in drinking-water.

Studies in laboratory animals

Recently published studies examined the effects of a U compound (uranyl nitrate hexahydrate) given in drinking-water to rats³ and rabbits⁴ for 91 days (13 weeks). The lowest concentration tested corresponded to a U concentration of 960mcg/l. To make comparisons easier, it is usual to express doses as micrograms of U per kilogram bodyweight (shortened to mcg/kg). The lowest daily U doses from drinking-water in these studies were about 50mcg/kg bodyweight in rabbits, and about 60mcg/kg bodyweight in rats. At these doses, the animals did not appear unwell, and there were no abnormalities in blood tests, urine tests, or on postmortem examination. On microscopy, however, there were changes in the kidney.⁵ These changes

were believed to have been caused by U and, it was thought, could progress and damage the way the kidneys worked.

The lowest doses tested were much greater than the highest human doses at the concentration in your drinking-water (over 100 times for a bottle-fed baby; over 200 times for a one-year-old; and over 400 times for an adult).⁶ This may suggest that the human doses are probably harmless, but it must be remembered that:

- the animal studies did not identify an apparently harmless dose (and perhaps there is no such thing);
- the animals were dosed for only a fraction of their normal lifespan;
- it may be the case that humans are generally more susceptible than rats or rabbits to the effects of U;
- laboratory colonies of animals are bred to be very similar to each other, but humans vary much more. There may perhaps be individuals who are more susceptible than most to the effects of U.

Acknowledging these uncertainties, experts advising the World Health Organization¹ (WHO) proposed a "Tolerable Daily Intake" (TDI) of 0.6mcg/kg bodyweight. This was derived by dividing the lowest dose in rats by an "uncertainty factor" of 100. The TDI is an estimate of the amount that can be ingested daily over a lifetime without appreciable health risk.

The WHO experts went on to derive a Guideline Value (GV) of 2mcg/l for drinking-water. The GV "represents the concentration of a constituent that does not result in any significant risk to the health of the consumer over a lifetime of consumption".⁷ *The reasoning was as follows: for an adult weighing 60kg, the TDI corresponds to a daily U intake of 36mcg. Drinking-water is not the only source of U intake, so assume that up to 90% of the TDI might come from other sources (in practice, food is the only other major source for most people). In other words assume that food might provide as much as 32mcg daily. Then up to 4mcg may be allocated to 2 litres of drinking-water per day - hence the GV of 2mcg/l.*

In fact, a daily dietary intake of 3mcg or below is usual. One could therefore argue that, for most adults, drinking-water could provide as much as 33mcg U daily without exceeding the TDI, and that therefore a GV of about 16mcg/l would be reasonable. In the United States, the regulatory limit for U in drinking-water is 20mcg/l.

Studies in human populations

Two recent studies looked for evidence of kidney problems in Canadian communities. The first⁸; examined 100 Saskatchewan residents with drinking-water containing U from less than 0.1mcg/l to 50mcg/l. The measure of kidney function (urine albumin) was not related to the U concentration in drinking-water, but it did tend to increase with what the authors described as "a crude index of the cumulative exposure to uranium".

The second study⁹ measured indicators of kidney function and kidney damage in the urine of residents of a village in Nova Scotia (where U concentrations in drinking-water from wells ranged from 2mcg/l to 780mcg/l) and in volunteers in Ottawa (where the U concentration in the municipal supply was below 1mcg/l). The authors measured individuals' daily intake of U from food and water over three days. Daily intakes ranged from 3 to 570mcg (and from 0.058 to 8.5mcg/kg bodyweight).

In this study, unlike the Saskatchewan study, urine albumin was not related to U intake. Three of the eight indicators were related to U intake, increasing as U intake increased. Of these three, two (β_2 -microglobulin, and alkaline phosphatase) were not evidently related to U intakes below 100mcg daily, but the third (urine glucose) still tended to increase with increasing U intakes in this range.

The second study, therefore, did not confirm the findings of the first, but instead found other indications that even such low levels of U intake perhaps affect kidney function. In this study, however, the group with the lowest U exposure comprised city-dwellers, while the group with the highest exposure was a rural community; it is therefore possible that some differences other than U exposure were behind the findings. Also, raised levels of the three indicators in urine do not necessarily mean that there has been kidney damage.

If U is indeed the explanation for the findings in the second study, then it is not possible to determine, from these results, whether there is a threshold - that is, an intake of U below which no harm occurs.

Conclusion

The doses of uranium which cause kidney damage in laboratory animals are much greater than the estimated intakes of uranium from your drinking-water - but the animal studies have not clearly identified a dose which seems to be harmless. The two studies in human populations hint that there may be effects on the kidney at even lower doses than those tested in laboratory animals, but are inconclusive. There is no evidence to suggest that intakes from your drinking-water are likely to be harmful - but, at the same time, there is no evidence that points clearly to a level of uranium intake that is harmless.

Michael Waring

Senior Medical Officer
Environmental and Chemicals Team
Department of Health
9 November 2000

REFERENCES AND NOTES

1. WHO (1998). *Guidelines for drinking-water quality. Second edition. Addendum to Volume 2. Health criteria and other supporting information.* Geneva, World Health Organization.
2. ATSDR (1999). *Toxicological profile for uranium.* U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.
3. Gilman AP, Villeneuve DC, Secours VE, Yagminas AP, Tracy BL, Quinn JM, Valli VE, Willes RJ, Moss MA (1998). Uranyl nitrate: 28-day and 91-day toxicity studies in the Sprague-Dawley rat. *Toxicol Sci* **41**, 117-128.
4. Gilman AP, Villeneuve DC, Secours VE, Yagminas AP, Tracy BL, Quinn JM, Valli VE, Moss MA (1998). Uranyl nitrate: 91-day toxicity studies in the New Zealand white rabbit. *Toxicol Sci* **41**, 129-137.
5. Glomerular (capsular sclerosis), tubular (anisokaryosis, nuclear vesiculation, nuclear pyknosis, apical displacement of nuclei, cytoplasmic vacuolation, cytoplasmic degranulation, tubular dilation) and interstitial (reticulin sclerosis, lymphoid cuffing).
6. Assuming that: an adult weighs 60kg, drinks 2 litres of water daily, and ingests 3 mcg of U daily from food; a one-year-old child weighs 10kg and drinks one litre of water daily; a bottle-fed baby drinks 0.2 litres of water per kg bodyweight daily.
7. WHO (1993). *Guidelines for drinking-water quality. Second edition. Volume 1. Recommendations.* Geneva, World Health Organization.
8. Mao Y, Desmeules M, Schaubel D, Berube D, Dyck R, Brule D, Thomas B (1995). Inorganic components of drinking water and microalbuminuria. *Environ Res* **71**, 135-40.
9. Zamora ML, Tracy BL, Zielinski JM, Meyerhof DP, Moss MA (1998). Chronic ingestion of uranium in drinking water: a study of kidney bioeffects in humans. *Toxicol Sci* **43**, 68-77.