

A Review of the Scientific Literature As It Pertains to Gulf War Illnesses

VOLUME 7

DEPLETED URANIUM

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SUMMARY

Uranium is a naturally occurring heavy metal that is both radioactive and ubiquitous. Small amounts are present in rocks, soil, and materials made from them. It is also present in air, water, and food, and thus people come into contact with or consume tiny amounts of it daily. Uranium is best known in its enriched form, which is used for nuclear power plants and nuclear weapons. Uranium is enriched by increasing the proportion of the more radioactive isotopes. The by-product of this process, which depletes uranium of its most radioactive isotopes, is called depleted uranium (DU). It is about 40 percent less radioactive than natural uranium and has a variety of commercial and military applications. The latter include improved armor and antiarmor rounds with increased penetrating power, both of which take advantage of the metal's density and metallurgical properties.

Very little literature directly addresses the health effects of DU. However, a wide body of literature deals with the health effects of natural and enriched uranium, and a review of that literature is relevant. The toxicological effects of natural uranium are identical to those of DU; while the radiological effects of DU are always less pronounced because DU is less radioactive than natural uranium. In general, heavy-metal toxicity is regarded as posing a more serious health risk than its radiation. This is because DU produces a low level of radiation per unit mass. The most abundant isotope in natural uranium, ^{238}U , has a very long half-life (4.5 billion years), which means that it decays slowly and thus produces fewer disintegrations per mass than an isotope that decays rapidly, such as ^{234}U (half-life of 245,000 years). As mentioned, DU is less radioactive than natural uranium and, indeed, is classified in the lowest hazard class of all radioactive materials.

In addition to being very dense (almost twice as dense as lead), DU, like any uranium, is pyrophoric, that is, in fine particles it can ignite easily. When a DU penetrator strikes armor or burns, it produces uranium dusts or aerosol particles, which can be inhaled. Once internalized, a fraction of the particles dissolve and enter the bloodstream, where most uranium is excreted from the

body through the kidneys. These inhaled fine particulates or dusts of oxidized uranium metal, uranium oxides, are presently thought in the published literature to be the primary compounds of interest.

REGULATION STANDARDS

Several different U.S. government agencies regulate and make recommendations about exposure to uranium. This report provides the present radiological standards for both occupational and population exposure. Both standards are important because military personnel are not classified as radiation workers unless their jobs specifically qualify as such. This report also provides the chemical toxicity guidelines and recommended kidney concentration standard of 3 $\mu\text{g/g}$ of kidney.

HEALTH EFFECTS

The health effects of DU depend on several factors. The first is whether the exposure is internal or external. Internal effects can be caused by either chemical or radiological toxicity. Health effects related to external exposure are limited to ionizing radiation emitted by uranium and its immediate decay products.

INTERNAL EXPOSURES

The main routes of natural uranium into the human body are by inhalation and ingestion. A very small percentage of the inhaled uranium is retained by the lymph nodes for a long time, and another small fraction is solubilized and goes to the blood, where most is subsequently excreted. A fraction of the blood content is deposited in the kidneys, liver, other organs, and the skeleton. In the military environment, additional routes of exposure exist. When a DU weapon impacts a target, the fragments can penetrate the body or any dusts produced can be inhaled, ingested, or be deposited on wounds.

Chemical Effects of Inhaled Uranium

Extensive information is available about the occupational exposure of workers in the uranium industry. No increase in overall deaths has been observed as a result of exposure to uranium in several epidemiological studies of workers exposed to uranium. One animal study designed to establish exposure end points induced mortality in rats when they were exposed to extraordinary concentrations of uranium oxides much higher than in occupational settings.

Evidence about hepatic effects from exposure to uranium oxides is more equivocal. Hematological effects have been observed in one study of miners exposed to uranium for up to 20 years. However, most animal studies found no hematological effects. Immune system effects have not been associated with inhaled uranium oxide exposure in uranium industry workers, and no evidence exists showing an association between uranium inhalation exposure and adverse effects on the nervous system.

The kidney is the target organ for uranium, and, as such, would be expected to experience the most dramatic health effects if sufficient uranium were present. A study of uranium mill workers occupationally exposed to "yellowcake," a soluble uranium compound, reported findings of reduced proximal renal tubular reabsorption of amino acids and of low molecular weight proteins. Another study of workers exposed to insoluble uranium dust reported no renal injury. Animal studies show that the solubility of the inhaled uranium compound dramatically affects renal outcomes. Although soluble uranium compounds have caused renal damage, insoluble uranium oxides appear to be far less toxic to kidneys. When exposure is less than American Conference of Governmental Industrial Hygienists (ACGIH) recommended amounts, the scientific literature does not indicate negative health effects.

Radiological Effects of Inhaled Uranium

Negative effects from the exposure to the ionizing radiation from depleted or natural uranium have not been observed in humans. Some epidemiological studies show evidence of lung cancer in miners, but this is associated with the exposure to airborne short-lived decay products of radon and cigarette smoking. Some animal studies have examined pulmonary damage from exposure to uranium oxides. Exposures over three years to $5.1 \text{ mg UO}_2/\text{m}^3$ in air did not result in lung damage but did cause minimal fibrosis, suggesting radiation injury, in the lymph nodes of dogs and monkeys and the lungs of monkeys.

Cancer rates in almost 19,000 highly exposed uranium industry workers who worked at Oak Ridge between 1943 and 1947 have been examined, and no excess cancers were observed through 1974. Other epidemiological studies of lung cancer in uranium mill and metal processing plant workers (environments without radon) have either found no excess cancers or attributed them to known carcinogens other than uranium, such as radon.

Human studies have examined bone cancers, and no associations between them and internal or external radiation exposure from natural uranium were reported. A variety of cancers developed when rats were exposed to enriched uranium; however, because DU is orders of magnitude less radioactive than enriched uranium, these data have little relevance to the possible health effects

of DU. High exposures may also be nephrotoxic; however, there is no evidence that either natural or depleted uranium can induce this effect. Gastrointestinal effects produced from inhalation of high levels of radioactive material have been reported in both human and animal studies. There is no conclusive evidence of reproductive effects.

In sum, cancer is the only radiation-associated disease that has been shown to be related to inhalation of radioactive particulates in humans, but there is no evidence documented in the literature of cancer or any other adverse health effect related to the radiation received from exposure even to natural uranium, which is more radioactive than DU.

Chemical Effects of Ingested Uranium

Chemical toxicity of ingested uranium is determined largely by the water solubility of the compound and, therefore, ease of uptake from the gastrointestinal (GI) tract. Compared with industrial compounds, uranium oxides are generally thought to be less soluble or insoluble and, therefore, of very low toxicity.

No studies report human deaths or other health effects from oral exposures to uranium oxides. Mortality, usually from renal failure, can be induced in animals at very high oral intake levels. No human studies were found in the peer-reviewed published literature that showed respiratory, cardiovascular, hematological, musculoskeletal, hepatic, endocrine, dermal, ocular, body weight, or other system effects in humans exposed to uranium compounds. No epidemiological studies were located that examined neurological effects following uranium ingestion.

While the possible toxic effects of uranium on other organ systems have not been rigorously excluded, extensive work points to the kidney as the major target organ. A recent study described analyses of renal function following a lifetime of drinking water with uranium levels in the range 2-781 $\mu\text{g}/\text{day}$. The exposed group excreted more glucose in urine than did the control group, but the only valid measure of glomerular dysfunction tested (proteinuria) remained unchanged.

Respiratory effects have not been observed in animals following ingestion of uranium oxides. Hepatic effects have been observed in animals dosed with very high levels of insoluble uranium. No harmful effects on body weight were seen in intermediate-duration oral studies of dogs given up to 10 g $\text{UO}_2/\text{kg}/\text{day}$ for a year.

Thus, only limited evidence suggests that even chronic exposure to natural uranium in food or water, except presumably at extraordinary concentrations,

is associated with morbidity in man or animals. This conclusion makes it unlikely that DU would have any such effects.

Radiological Effects of Ingested Uranium

No human or animal studies associate adverse health effects with ingested DU. No evidence has been found to associate human exposure to ingested uranium compounds and carcinogenesis. Likewise, no oral animal studies report evidence of cancer induction.

Chemical and Radiological Effects of Embedded Uranium

What is known about the health effects of embedded uranium results primarily from the clinical follow-up of the wounded veterans of the Gulf War. Thirty-three individuals are being followed by Department of Veterans Affairs (VA) researchers, and about half of these have been identified as having embedded DU fragments. To date, although these individuals have an array of health problems related to traumatic injuries, no manifestations of kidney disease attributable to the chemical toxicity of DU have been found. Neither do they appear to have any manifestations attributable to radiation effects. These patients continue to be followed. AFRRRI is also conducting important studies of the effect of embedded DU pellets on rats.

EXTERNAL EXPOSURES

Radiation rather than chemical toxicity poses the external health hazard.

DU exposes the skin to alpha, beta, and gamma radiation. In the case of short-term radiation from particulates deposited on skin, more than 95 percent of the radiation present is in the form of alpha radiation, which has a very short range and will not penetrate the dead outer layer of the skin and thus poses no documented health risk. Beta and gamma radiation from ^{238}U decay products can irradiate cells in the deeper skin layers. Sufficient mass of DU to create radiation sufficient to be of concern can occur with intact munitions and armor. However, DU munitions are shielded to limit emitted radiation, and thus people working with intact munitions or armor usually face little risk. The measured exposure to gamma and beta radiation from bare penetrator or armor is well below recommended occupational levels (CHPPM, 1998).

Studies of workers occupationally exposed to uranium show no skin cancers resulting from this exposure. No animal studies have found skin cancers with this cause. As a point of perspective, to reach the occupational radiation dose

limit for beta and gamma radiation, a soldier would have to hold an unshielded DU penetrator for more than 250 hours.

CLINICAL DISCUSSION

The clinical discussion section outlines possible health effects from a clinical perspective. After discussing common diagnostic procedures, including a 24-hour urine analysis, the section details symptoms and the relation, if any, of diseases of various body systems to exposure to DU. Areas discussed include lung cancer, kidney disease, liver disease, osteosarcoma, and reproductive and developmental conditions.

CONCLUSIONS

From the scientific literature, the review reaches the following insights and conclusions:

- Although any increase in radiation to the human body can be calculated to be harmful from extrapolation from higher levels, there are no peer-reviewed published reports of detectable increases of cancer or other negative health effects from radiation exposure to inhaled or ingested natural uranium at levels far exceeding those likely in the Gulf. This is mainly because the body is very effective at eliminating ingested and inhaled natural uranium and because the low radioactivity per unit mass of natural and depleted uranium means that the mass of uranium needed for significant internal exposure is virtually impossible to obtain.
- External radiation takes the primary form of alpha radiation, but amounts of beta and gamma radiation also exist. Alpha radiation is not capable of penetrating cloth or skin and would therefore have no negative health effect. Beta and gamma radiation, which can have negative health effects, have been measured at levels below those expected to be of concern.
- Large variations in exposure to natural uranium in the normal environment have not been associated with negative health effects.
- Radiation-related effects from embedded fragments will depend on the size of the fragment and its proximity to vital organs.
- Exposure to uranium and other heavy metals in large doses can cause changes in renal function and at very high levels result in renal failure.
- In spite of these findings, no increased morbidity or frequency of end-stage renal disease has been observed in relatively large occupational popula-

tions chronically exposed to natural uranium at concentrations above normal ambient ones.

- The cohort of individuals, about half of whom have embedded fragments, who are being followed at the Baltimore VA Medical Center as part of the DU Follow-Up Program, represents a group of Gulf War veterans who received the highest levels of exposure to DU during the Gulf War. Although many of these veterans have health problems related to their injuries in the Gulf War and those with embedded fragments have elevated urine uranium levels, researchers to date report neither adverse renal effects attributable to chemical toxicity of DU nor any adverse health effects they relate to DU radiation (McDiarmid, 1998b). They do, however, note several biochemical perturbations in neuroendocrine parameters related to urinary uranium concentrations and in some subtle neuropsychological test findings; the clinical significance of these is unclear.

Finally, the report encourages continued research because the use of DU is likely to expand in the future.