Military medical aspects of depleted uranium munitions

Alex Bordujenko, MB BS, MPH, FAFPHM

DEPLETED URANIUM MUNITIONS have been developed and trialled over the past 40 years, but it was only in the Gulf War that these heavy-armour penetrators were first used in combat. Subsequently, they were also used by NATO forces in Kosovo and Bosnia. While depleted uranium has many long-established commercial uses, its military use has led to considerable discussion regarding the potential for adverse health effects on military personnel and civilians.

In January 2001, news media in many parts of the world carried reports suggesting links between NATO's use of depleted uranium ammunition in Kosovo and Bosnia and allegedly higher rates of leukaemia, other cancers, and other ill-health among NATO (KFOR/SFOR) troops and the local civilian population. These followed earlier media reports of concerns that ill-health among veterans of the Gulf War and Iraqi citizens may be linked to exposure to depleted uranium. This hypothesised association has not been established in the primary literature or authoritative reviews of the subject.[1,2]

Several contemporary reviews of the available literature concerning uranium and depleted uranium exposure and risks are available, including those from the US Agency for Toxic Substances and Disease Registry (ATSDR), the RAND review and the US Institute of Medicine.[1-3] The United Nations Environmental Program (UNEP) published assessments in 1999 and 2001.[4,5] As well, reports from the European Union and World Health Organization on the risk from depleted uranium exposure were published in 2001.[6-8] These international organisations have conducted environmental surveys in Bosnia-Herzegovina and Kosovo and have consistently reported no widespread depleted uranium contamination and no current impact on the health of the general population or deployed personnel.

Specific assessments by the Office of the Special Assistant for Gulf War Illnesses (OSAGWI) considered depleted uranium exposure and modelled dose and risk estimates.[9,10] The US Department of Defense is undertaking further experimental assessments of depleted uranium exposure models. The UK Royal Society (2001) also undertook mathematical modelling of depleted uranium exposures and resultant dose estimates.[11]

Additionally, individual NATO countries have sought to re-evaluate the available literature and undertake further research into the potential risks experienced by military personnel and exposed populations. At least 13 countries have sent teams to the Balkans to collect and analyse soil, air, water, vegetation, and food samples. A number of the nations that deployed peacekeeping personnel to the Balkans have undertaken medical monitoring and epidemiological assessments. The objective of the assessments is to determine whether there is any increase in medical problems in personnel who served in the region compared with those who did not. To date, none have found a connection between depleted uranium exposure and leukaemia or any other disease process.

Repatriation Medical Authority, Brisbane, QLD.
Alex Bordujenko, MB BS, MPH, FAFPHM, Principal Medical Officer.
Correspondence: Dr Alex Bordujenko, Repatriation Medical Authority, PO Box 1014, Brisbane, QLD 4001.

Background

Depleted uranium is chemically identical to and less radioactive than natural uranium. Uranium is a natural element found in all soils, rocks, rivers, lakes and oceans, plants and animals. The ATSDR estimates that there are typically four tons of uranium in one square mile of soil, one foot deep (comparable to 1.4 t/km²).[3] Small amounts of uranium are consumed and inhaled by all people on the planet. The human body contains about 100 μg of uranium, with about 66% in the skeleton, 16% in the liver, 8% in the kidneys and 10% in other body tissues.[3]

Uranium is a heavy metal (a metal with a specific gravity of 5.0 or greater) with a very high density (18.95 g/cm^3, 1.7 times higher than lead's density of 11.35 g/cm^3). Metallic uranium has a high melting point (1132 °C) and boiling point (4131 °C), has a tensile strength similar to most steels and is chemically very reactive.[12,13] In powdered form it has pyrophoric properties (ie, it has a tendency to spontaneously ignite in air when in the form of fine particles).

Natural uranium consists of three isotopes. Their concentrations by mass are U^{238} 99.276%, U^{235} 0.718% and U^{234} 0.0056%. The uranium used in nuclear power production and nuclear weapons requires a greater concentration of U^{235}, ranging from 2%–90%.[3] To achieve this increased concentration, naturally occurring uranium is subjected to an enrichment process. Enriched uranium contains an increased percentage of the fissionable isotope U^{235} and is then suitable for nuclear reactor fuel and nuclear weapons. Depleted uranium (uranium with decreased concentrations of U^{235}) is a byproduct of the enrichment process. It may also be obtained by reprocessing spent nuclear fuel. Naturally occurring uranium, enriched uranium and depleted uranium all have the same number of protons and have identical physical and chemical properties.[1,2]

The three isotopes of uranium decay by alpha particle emission. The isotopes possess very long half-lives, the shortest being 250 000 years for U^{234}. U^{238} decays by emission of alpha particles into two short-lived "progeny": thorium-234 (Th^{234}; half-life, 24.1 days) and protactinium-234m (Pa^{234m}; half-life, 1.17 minutes) which emit beta particles and (weakly) gamma particles. Because of this constant nuclear decay process, very small amounts of these progeny are always present in both natural and depleted uranium. U^{235} decays into

protactinium-231 (Pa^{231}; half-life, 32 500 years), which emits alpha, beta, and gamma particles.

Natural uranium in ore emits 7–8 times as many alpha particles as pure uranium. When uranium is separated from ore, the decay products, being different elements, are removed. After separation, the uranium isotopes continue to decay. The first members of the decay chains have short half-lives, and soon return to their equilibrium values. However, Th^{230} (formed from decayed U^{234}) and Pa^{231} (formed from decay of Th^{231}) have long half-lives, and so "grow" in processed uranium very slowly. Hence, in processed uranium, the activities of Th^{230} and Pa^{231} and subsequent members of the chains are negligible.[1]

The primary radiation emitted from uranium is in the form of alpha particles. These particles have an extremely short range and are unable to penetrate a sheet of paper or human skin. Radiation from the decay of depleted uranium is predominantly alpha particles and, in alpha decay, the nucleus of the atom emits a particle consisting of two protons and two neutrons (a helium nucleus). The alpha particles released by depleted uranium can travel only about 30 μm in biological tissue,[11] and so are not considered to be an external hazard. Inhalation and retention of uranium dusts or vapours may expose immediately adjacent tissue to ionising radiation from alpha particles.

Uranium also emits very small amounts of the more penetrating beta and gamma forms of radiation. Levels of these emissions are low in comparison to levels arising from natural sources such as cosmic rays and other naturally occurring radioactive minerals.

The unit of measurement for radioactivity is the Becquerel (Bq). An activity of one Bq means that one decay takes place per second. U^{238}, U^{235} and U^{234} predominantly emit alpha particles (> 95%). The alpha activity of natural uranium amounts to about 25 kBq/g. The progeny from the alpha decay of uranium themselves continue to decay, mostly by emitting beta particles. The activity of these progeny is added to that of uranium. The beta radiation of the progeny of natural uranium and depleted uranium have practically the same intensity, amounting to about 25 kBq/g. Uranium, together with its progeny, has an activity of 50 kBq/g (ie, 50 000 decays take place per gram per second).

The very long half-life of U^{238} (4.5 billion years) yields a low decay rate per unit mass of uranium. Naturally occurring uranium, which mostly consists of U^{238}, is one of the least radioactive substances containing unstable isotopes on the planet (Box 2). It is classified by the International Atomic Energy Agency in the lowest hazard class for radioactive materials.[2,3]

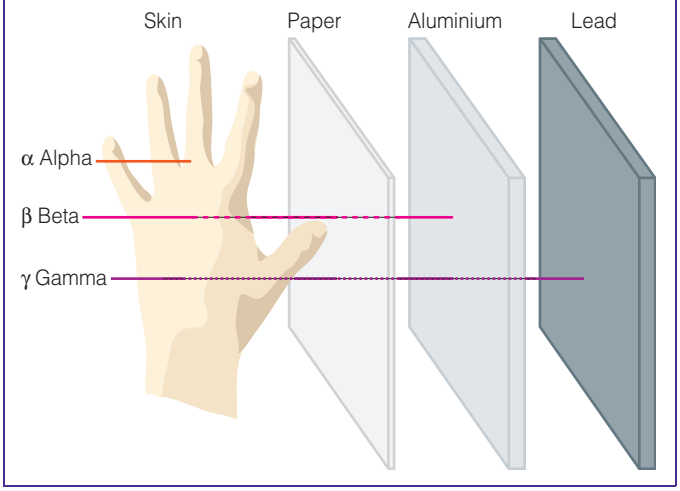
Exposure to the radiation emitted from uranium can occur if it is outside the body or if it is ingested, inhaled or taken in by other means. It is useful to consider the exposure pathways with regard to average radiation exposure in the normal environment. The Sievert (Sv) is the international measure of radiation expressed as a dose-equivalent. In the general population ingestion of uranium and its decay series in food and drink gives a committed effective dose of 0.11 mSv per year for adults, as compared to 0.0058 mSv through inhalation, excluding inhalation of radon (1.2 mSv). This dose corresponds to 5% of the average annual dose due to internal and external exposure to natural sources of radiation (2.4 mSv). It relates essentially to progeny, Pb^{210} and Po^{210}. U^{238} accounts only for 0.00025 mSv total dose and 0.000021 mSv for inhalation. External exposure from all natural U^{238} in soil is also negligible. U^{238} series, together with other primordial radionuclides, Th^{232} and K^{40}, cause a world-average annual external exposure of about 1 mSv per year.[14]

Uranium is but one of many sources of ionising radiation. The earth is bathed with low levels of radiation all the time. The sources of radiation include radon (55% of the total annual average dose of 2.4 mSv), cosmic rays (8%), and human-made sources, such as x-rays, medical radioisotopes, consumer products such as smoke detectors and colour television.

Uses

Depleted uranium has a wide range of civilian applications. For example, it is used in health care (radiation shielding in equipment used for radiation therapy and containers for radioisotopes), aviation (passenger aircraft counterweights),

1: Relative penetration of alpha, beta and gamma emissions



2: A comparison of the activities of selected radioactive materials[6]

Radioactive material	Specific activity (kBq/g)
Iodine^{131}	4,598,000,000,000
Cesium^{137}	3,206,000,000
Plutonium^{239}	2,298,000
Natural uranium together with its progeny	50
Depleted uranium together with its progeny	40
Natural uranium	25
Depleted uranium	15

boat building (counterweights in racing sailboat keels), satellite ballast, and petroleum exploration (drilling equipment). It may also be used as a chemical catalyst (eg, in the production of synthetic ammonia).[9]

Due to its high density, high melting point, tensile strength, pyrophoric properties in particle form and availability, depleted uranium metal has military applications in heavy tank armour and munitions, including armour-piercing antitank shells. The heavy-armour variant of the Abrams M1A1 tank uses sheets of depleted uranium enclosed in steel plate to protect against penetration by projectiles made of less dense metals, such as tungsten carbide.[10] Depleted uranium is used in cartridges and munition rounds (penetrators) to pierce armoured targets. For this purpose the depleted uranium is alloyed with 2% molybdenum or 0.75% titanium. These munitions carry no explosive charge but do have a considerable energy of motion (kinetic energy). Large calibre (120 mm) depleted uranium rounds can be fired from tanks at a muzzle velocity of 1.5 km/s; at this velocity, the kinetic energy of a 5 kg depleted uranium penetrator is equivalent to 1.4 kg of TNT.[15] The kinetic energy of a 30 mm Gatling-gun penetrator (with about 275 g of depleted uranium) is equivalent to about 50 grams of TNT.[15] Additionally, conventional explosive munitions may also be fired with the depleted uranium munitions to take advantage of the greater penetrance offered by these weapons.

Upon impact with a hard target such as an armoured tank, depleted uranium munitions maintain their form better than those of tungsten or steel; additionally, the penetrator "sharpens" itself on impact, in contrast to tungsten projectiles, which tend to blunt.[10] On impact, a proportion of the kinetic energy of a depleted uranium penetrator is converted into heat. The rapid release of energy converts some of the depleted uranium into small, hot fragments and particles. The particles and smaller fragments burn, increasing the destructive effect of these munitions and generating depleted uranium oxide aerosol.

Military use of depleted uranium to date

About 320 tons of depleted uranium munitions were expended during the Gulf War. The US Army used about 9500 large calibre (120 mm) antitank rounds containing depleted uranium, many as training and practice rounds. About 3000 large calibre rounds were destroyed, many in a fire at Camp Doha, Kuwait.[1] An estimated 783 500 small calibre (30 mm) depleted uranium rounds were fired by A-10 aircraft in that conflict. Use of depleted uranium munitions by the US Marines, US Navy and British forces was relatively minor.[2,9]

During the Gulf War some Allied military personnel were exposed to depleted uranium oxides in aerosols, dusts and retained fragments. The US Department of Defense has reported that depleted uranium munitions struck about 30 of its own armoured vehicles.[16] In addition, personnel recovering, repairing or decommissioning vehicles damaged by depleted uranium penetrators may have inhaled or ingested residual depleted uranium fragments and particles. There were also several accidental tank fires and an ammunition explosion and fire at Camp Doha, Kuwait, which burned, oxidised and fragmented many depleted uranium rounds. Other personnel entered Iraqi vehicles destroyed or damaged by depleted uranium.

Only small calibre depleted uranium munitions are known to have been used in the Balkans conflict. About 10 000 30 mm rounds (2750 kg) were fired by NATO forces from US A-10 "Warthog" tankbuster aircraft in Bosnia in 1994–1995. About 31 000 30 mm depleted uranium rounds were fired from A-10 aircraft in the Kosovo conflict in 112 attacks on 84 geographically separate sites in Kosovo and environs from 6 April to 11 June 1999.[4]

Exposure pathways

On impact, a fraction of the depleted uranium in munitions undergoes spontaneous ignition and small, relatively insoluble particles, mainly uranium oxides, as well as fragments of metallic depleted uranium, are formed. When a hard target such as an armoured tank or a rocky outcrop is hit, 10%–35% (with a maximum of 70%) of the original depleted uranium metal forms into an aerosol of the metal and its combustion products, which are predominantly uranium oxides.[1,10] Aerosols and dusts containing depleted uranium and its oxides may be inhaled into the lungs. It has been estimated, based on particle size, that about 60%–69% of the aerosolized fraction of this depleted uranium is respirable.[1,10] When a penetrator strikes a soft target, such as a personnel carrier, truck or soil, much less aerosol is generated and much of the metal remains intact.

The routes for entry into the body following exposure to depleted uranium that has been used in military operations are:

- inhalation in smoke and dust
- contamination of wounds
- skin contact
- hand-to-mouth contamination and ingestion of dusts;
- ingestion via the food chain (eating contaminated crops or animals)
- accumulation in drinking water.

Health effects of uranium exposure

Available evidence relating to the health effects of depleted uranium has been obtained from data on human exposure to uranium, studies of miners and workers in the uranium industry, animal experiments, and some studies of Gulf War veterans. A detailed analysis of this literature is to be found in the Review of Scientific Literature on the Health Effects of Exposure to Depleted Uranium.[17]

There are relatively few specific studies of the health effects of depleted uranium in animal or human models, partly because interest in the effects of this specific agent has only arisen relatively recently and partly because there is a considerable research base available on the health effects of natural uranium. The toxicology of uranium has been comprehensively

3: Epidemiological studies of uranium (U) exposed workers used by Beral and Darby, 2001[25]

Study	Plant and location	Population studied	Exposure data	Total workers	Total deaths	Earlier studies with same or overlapping population
McGeoghegan and Binks, 2000[26]	Springfields Lancashire	Radiation workers at plant fabricating U fuel and UF6	External monitored radiation dose	13 960	3 476	None relevant
McGeoghegan and Binks, 2000[27]	Capenhurst, Cheshire	Radiation workers at U enrichment plant	External monitored radiation dose	3 244	585	None relevant
Dupree-Ellis et al, 2000[28]	Mallinckrodt, Missouri	Workers at a U processing plant	External monitored radiation dose	2 514	1 013	Dupree et al, 1995[29]
Ritz et al, 2000[30]	Rocketdyne/ Atomics Int, California	Workers involved in nuclear fuel assembly and disassembly	Internal radiation dose to lung	2 297	433	None relevant
Ritz, 1999[31]	Fernald Feed, Ohio	U processing workers	External monitored radiation dose and internal radiation dose to lung	4 014	1 064	Dupree et al, 1995[29]; Ritz 1999[31]
Frome et al, 1997[32]	Four Federal nuclear plants, Oak Ridge, Tennessee	Workers involved in U enrichment or nuclear fuel fabrication	External monitored radiation dose and internal monitoring status	~67 600	22 724	Dupree et al, 1995[29]; Loomis and Wolf, 1996[34]; Wing et al 1991[35]; Frome et al 1990[36]; Checkoway et al, 1988[37]; Checkoway et al, 1985[38]; Polednak and Frome, 1981[39]; Cookfair et al, 1983[40]
Teta and Ott, 1988[41]	Linde, NY	Workers at a site previously contaminated with U and other radionuclides	Not available	8 146	1 160	None relevant
Cragle et al, 1988[42]	Savannah River, South Carolina	Workers at a nuclear fuel production plant	Not available	9 860	1 091	None relevant
Beral et al, 1988[43]	Atomic Weapons Est., Berkshire, UK	Workers at a weapons production plant	External radiation dose and U monitoring status	3 044	137	None relevant
Dupree et al, 1987[44]	Linde, NY	Workers at a U processing facility monitored for U exposure	Estimated internal lung dose	995	429	None relevant
Brown and Bloom, 1987[45]	Portsmouth, Ohio	Workers at a U enrichment facility	Not available	5 244	483	None relevant
Stayner et al, 1985[46]	Polk, Florida	Workers at a phosphate fertiliser production facility	Not available	3 160	155	None relevant
Waxweiler et al, 1983[47]	Seven mills, Rocky Mountains region	U mills and mines	Not available	2 002	533	Archer et al, 1973[48]; Wagoner et al 1964[49]
Hadjimichael et al, 1983[50]	United Nuclear, Connecticut	Workers at a nuclear fuels fabrication plant	Not available	3 512	219	None relevant

reviewed.[2,3,18] Studies of its toxicity have assessed both radiological and chemical effects.

Animal studies

Research in animal models has shown that the more soluble compounds (uranyl nitrate hexahydrate, uranium hexafluoride, uranyl fluoride, uranium tetrachloride, and uranium pentachloride), which most readily enter the systemic circulation, produce the greatest chemical toxicity. Depleted uranium exposure may contribute to internal and external radiation dose. Internal radiation effects, if any, are theoretically more likely to be associated with the insoluble compounds, such as uranium dioxide particles, which, if inhaled, may be deposited in the lungs and retained for long periods.

The chemical toxicity of uranium varies according to dose, chemical form and route of exposure. Animal experiments have found uranium to have a low order of metallotoxicity in mammals. It is less toxic than other heavy metals, such as lead, arsenic and mercury, at the same dose level.[3]

The 1999 ATSDR review summarised the findings of 119 inhalation, 84 ingestion and 37 skin exposure assessments in a range of animal species.[3] The review examined minimal effect levels for a variety of systemic effects, including death. Animal experiments use exposures which produce doses orders of magnitude greater than those of most documented human exposures, which may limit the relevance of these studies to levels of human risk. It has been calculated, for example, that a man would have to inhale nearly 2000 mg of uranium per day to achieve the same blood levels as the lowest exposure (0.15 mg) in animal (mouse) feeding studies.

Studies in several species confirm that the kidney is the major target organ associated with exposure to uranium compounds. The effects, when present, are of acute onset, occurring within days of exposure, and range from microscopic lesions to severe necrosis in the proximal renal tubules and death.[3,18]

The more water-soluble uranium compounds (uranyl nitrate hexahydrate, uranium hexafluoride, uranyl fluoride, uranium tetrachloride, and uranium pentachloride) have been shown to enter the systemic circulation, and are the most potent renal toxins. The less soluble compounds (sodium diuranate, ammonium diuranate) are of moderate to low renal toxicity, and the insoluble compounds (uranium tetrafluoride, uranium peroxide, and the uranium oxides uranium trioxide, uranium dioxide and triuranium octaoxide) have little potential to cause renal toxicity.[3]

Animal experiments of inhalation, ingestion and skin contact have demonstrated that some uranium compounds at high dose levels can cause a range of systemic effects. Acute respiratory effects have been described after inhalation studies using soluble uranium compounds.[19]

Non-malignant respiratory, neurological and haematological effects have been reported after high doses of uranium. Cardiovascular, gastrointestinal and hepatic effects are not prominent in animal experiments by any route of exposure.[3,18] Uranium has low-order metallotoxicity in mammals. An increase in lung cancer has been reported in beagles, but not monkeys, in one long-term, high-dose inhalation study.[20] Most animal studies considering the potential for carcinogenic effects have not found an association with uranium exposure. Rats implanted with depleted uranium pellets showed elevated serum uranium levels, with uranium deposition in bone, kidney, brain, lymph nodes, testes and spleen. No physiological or histological evidence of organ damage was evident.[21-24]

Most animal studies employ very high dose regimens to explore maximum tolerable and toxic dose levels, and so are of questionable usefulness in interpreting human exposures at levels orders of magnitude below those of experimental exposures.

Occupational studies

There have been a few human reports of acute exposure to high levels of uranium. Long-term exposure to uranium, largely through inhaled and ingested dust, has been examined in occupational cohort studies involving uranium miners and uranium industry workers. Uranium exposure in mining arises from uraninite (uranium oxide). Studies of uranium miners are of limited relevance to the health effects of depleted uranium, as miners work underground for prolonged periods in an environment with high concentrations of radon gas, a known carcinogen. Uranium industry workers are involved in the processing of uranium and may inhale and ingest uranium dust and aerosols. Studies of uranium industry workers are not confounded by exposure to radon gas, but these workers may be exposed to other radionuclides (these vary with workplace, but include enriched uranium, thorium, tritium, plutonium, americium, curium and californium, as well as other agents, including beryllium, mercury, solvents and other industrial chemicals).

A number of cohort studies have examined the causes of mortality in uranium industry workers and assessed the potential for kidney toxicity and for radiation-related carcinogenesis. Uranium dusts may be deposited in the lungs and associated lymphatic tissues, and after systemic absorption some is stored in the bone, kidneys and liver.

Several authoritative reviews have summarised the epidemiological studies. The latest, by the UK Royal Society, focused on 14 major studies (11 US and three UK) of the health of uranium industry workers who were followed for many years (Box 3).[11] In total about 120 000 workers were studied and 33 000 deaths from all causes were reported from this cohort. The causes of death for these study participants were analysed against the expected death rates in the general population.

There are some acknowledged problems in interpreting the data from such occupational cohort studies, including the lack of reliable exposure data for workers, a lack of reliable smoking information, limited ability to detect very small risks, and a potential "healthy worker" effect.

The combined analysis found no evidence of any increase in deaths from any cause, nor from all cancers, individual types of cancer or genitourinary disease. Mortality from lung cancer, osteosarcoma, lymphatic cancer and leukaemia was not found to be increased (Box 4).[25] The summary epidemiological data

do not support exposure to uranium or depleted uranium as a significant risk factor with respect to death, mortality from cancer or kidney disease in humans.

While no overall increase in lung cancer was observed, several studies described a dose–response relationship between external radiation exposure and deaths from lung cancer.[31,33] Fulco et al, after a detailed assessment of the available literature, concluded that there was limited/suggestive evidence of no association between exposure to uranium and lung cancer for cumulative internal doses below 200 mSv.[2] They also found that there was inadequate/insufficient evidence to determine if any association existed at higher doses.

There is no established increase in respiratory disease, neurological disease or immunological disease mortality or morbidity in cohorts exposed to uranium in uranium processing. However, the available epidemiological data are limited by uncertainty in assessment of exposure, low statistical power for studying rare events and a lack of data on exposures to other potentially confounding agents.

Depleted uranium exposure

Studies of Gulf War veterans have found that, in the absence of retained depleted uranium metal fragments, elevation of urinary uranium is unlikely, as are any uranium-related health effects.[51] A cohort of US Gulf War veterans who have retained fragments of depleted uranium and with elevated urinary uranium concentrations has shown no kidney toxicity or other adverse health effects related to depleted uranium after a decade of follow-up.[52,53]

Retained depleted uranium fragments

This form of exposure has drawn interest following "friendly fire" incidents during the Gulf War, when depleted uranium munitions struck about 30 US Bradley infantry fighting vehicles and Abrams tanks.[9,16] More than 10% of the men in these tank crews were killed instantly. Among the survivors, many had serious physical injuries and some had retained depleted uranium shrapnel.[15]

While the risk associated with depleted uranium fragments is very small in comparison to the incidents which produced them, there is a desire to assess and quantify this risk.

Urinary analyses were undertaken in 1993–1994 of 33 veterans exposed to depleted uranium, many by retained munitions fragments. Increased urinary uranium was detected in those with retained fragments (mean urinary uranium excretion, 4.47 μg/g creatinine v 0.03 μg/g creatinine in those without confirmed retention of fragments).

In 1997, 29 of the initially assessed group and 38 non-exposed Gulf veterans were evaluated extensively.[53] Seventy-six percent of those with retained depleted uranium fragments continue to have active medical problems due to the injuries received during the Gulf conflict, compared with 14% of the veterans in the control group.[53] How these injuries and resultant medical conditions impact on the study of depleted uranium itself remains to be determined. Currently, there are no clinical conditions (other than injury) which have been found to be more prevalent in the exposed cohort. In 1999, 21 original participants and 29 newly identified participants who had been exposed to friendly fire incidents were assessed in the exposed cohort (M A McDiarmid, presentation, January 2001 GWI conference, Washington, DC).

4: Mortality in uranium workers compared with the general population[25]

Cause of death	Deaths	Ratio of observed to expected deaths (95% confidence interval)
All causes	33502	0.86 (0.79-0.93)
All cancer	7442	0.91 (0.85-0.97)
Stomach cancer	365	0.76 (0.62-0.89)
Colorectal cancer	728	0.91 (0.78-1.04)
Liver cancer	123	0.84 (0.62-1.07)
Lung cancer	2846	0.94 (0.83-1.05)
Bone cancer	30	0.93 (0.53-1.33)
Prostate cancer	490	0.98 (0.89-1.07)
Bladder cancer	196	0.83 (0.71-0.96)
Kidney cancer	151	0.78 (0.59-0.96)
Brain cancer	223	0.91 (0.65-1.17)
Thyroid cancer	7	0.38 (0.00-0.81)
Non-Hodgkin's lymphoma	266	0.82 (0.71-0.92)
Hodgkin's disease	68	0.83 (0.61-1.06)
Leukaemia	295	0.90 (0.67-1.14)
All genitourinary disorders	318	0.70 (0.54-0.87)

The published analysis of the 1997 assessment compared urinary uranium levels, clinical laboratory values, and psychiatric and neurocognitive test results for 29 Gulf War veterans with retained fragments of depleted uranium shrapnel, and 38 non-exposed Gulf War veterans. History-taking and follow-up medical examinations were performed.[53]

Urinary uranium levels in these Gulf War veterans with retained depleted uranium shrapnel have been shown to be greater than those from Gulf War veterans without such exposure when measured at two, four and seven years after the conflict.[52,53] The level of increase in urinary uranium has been as much as 150 times that of the controls. Veterans with retained depleted uranium shrapnel had urinary uranium levels of 0.01–30.74 μg/g of creatinine, while in control veterans urinary uranium ranged from 0.01–0.047 μg/g of creatinine. Hooper et al report excretion levels between 10–20 μg/L.[52] Despite higher levels of urinary uranium in those with retained depleted uranium shrapnel, renal injury has not been described and renal function, as measured by serum creatinine, β_2-microglobulin, retinol-binding and urine proteins, is the same for both exposed and control veterans. These findings suggest that chronic exposure has not caused renal damage.[53]

McDiarmid et al reported that results of standard neurocognitive function tests were similar in those with depleted uranium

shrapnel and controls.[53] However, results from computer-based neurocognitive tests performed in 1997 showed an association between the level of urinary uranium and "problematic performance on automated tests assessing performance efficiency and accuracy". This association was not evident at the reassessment in 2000 (MA McDiarmid, presentation, January 2001, GWI Conference, Washington, DC).

Reproductive function has been assessed by a number of means. Semen has been shown to contain uranium, but the semen volume, sperm concentration, morphology and motility are the same in both those with high and low uranium excretion. Additionally, measures of follicle-stimulating hormone, luteinising hormone, testosterone and prolactin were similar in those with high and low urinary uranium excretion. As of January 2001, 38 children have been born to the exposed cohort and no birth defects have been reported in these offspring (M A McDiarmid, presentation, January 2001, GWI Conference, Washington, DC).

One post hoc subgroup analysis from the 1997 assessment revealed higher urinary uranium excretion in men with prolactin levels greater than the median compared with those with prolactin levels below the median.[53] This finding was assessed by the National Academy of Sciences, which considered this an unconventional analysis of questionable validity in a small sample; also, no measures of cortisol (a mediator of prolactin plasma levels) or account of moment-to-moment daily variation in prolactin levels were available, and it was suggested that the findings were hypothesis-generating, not evidential.[2] The association with prolactin levels had disappeared by the 2000 reassessment (M A McDiarmid, presentation, January 2001, GWI Conference, Washington, DC).

Haematological measures were reported to be similar in those with retained depleted uranium fragments and the control group of Gulf War veterans. As well, no differences existed in subanalyses between those with shrapnel who had high or low urinary uranium excretion. Retained depleted uranium was found to have no association with haematocrit or levels of haemoglobin, platelets, lymphocytes, neutrophils, basophils, eosinophils, or monocytes. Additionally these groups demonstrated the same background frequency of chromosomal aberrations and sister chromatid exchanges in peripheral blood lymphocytes.[53]

No dermal, ocular or musculoskeletal effects of depleted uranium have been reported in human studies.

Other studies of soldiers potentially exposed to depleted uranium

The total number of US military personnel deployed at one time or another during the Gulf War was about 700 000.[54] Despite the arduous conditions, morbidity rates among US troops were lower than in previous wars.[55] Mortality was also much lower than expected. Altogether 372 deployed US troops died in 1990–1991: 40% from combat, 52% from accidents (primarily related to training and motor vehicles), and 8% from illness.[56] About 53 000 UK troops saw service in the Gulf. Australia's involvement was small, with some 1800 (predominantly naval) personnel seeing service. No Australian deaths were recorded.

McDiarmid et al have examined exposure scenarios and 24-hour urinary uranium concentrations in Gulf War veterans outside those assessed in the "heavy exposure" studies outlined in the previous section.[51] In 1998–1999, 169 US Gulf War veterans submitted 24-hour urine samples for determination of urinary uranium levels and completed questionnaires describing their potential exposures to depleted uranium while in the war zone. Depleted uranium exposure was assessed by the questionnaire for 19 exposure scenarios. Results of urinary uranium analysis were stratified into high and low uranium groups, with 0.05 μg uranium per gram creatinine being the cut point and approximate upper limit of the normal population distribution. Twelve individuals (7.1%) exhibited urinary uranium values above this level, while the remaining 157 had urine uranium values in the low range. Six of these 12 individuals had a repeat urine test, which produced uranium levels in the low range for three. The presence of retained shrapnel was the only scenario predictive of a high urinary uranium levels. The authors suggest that elevated urinary uranium is unlikely, as are any uranium-related health effects, in the absence of retained depleted uranium metal fragments.

Studies of the health of Australian, US and UK veterans of the Gulf War are in progress and depleted uranium exposure is one of many exposures being considered. US and UK studies demonstrate a small excess mortality among veterans of the Gulf War from external causes in the years after the war.[57,58] This is a finding which has been described in several cohorts of returned soldiers during the 20th century.[59,60] No study of veterans of the Gulf or Balkans wars has so far described any excess mortality which could be attributed to the chemical or radiobiological effects of depleted uranium, although the follow-up period is relatively short.

Conclusion

Uranium is chemically classified as a heavy metal and is weakly radioactive. Any health effects would potentially arise from chemical toxicity or radiation emissions. Available evidence on the health effects of depleted uranium has been obtained from animal experiments, studies of miners and workers in the uranium industry, and studies of Gulf War veterans.

Current knowledge reveals that there has been no established increase in mortality or morbidity in workers exposed to uranium in uranium processing industries. The available epidemiological data are, however, limited by uncertainty in assessing exposure levels, low statistical power for studying rare events and a lack of data on exposures to other potentially toxic workplace and environmental exposures.

Studies of Gulf War veterans show that, in those who have retained fragments of depleted uranium following combat-related injury, it has been possible to detect elevated urinary uranium levels, but no kidney toxicity or other adverse health effects related to depleted uranium after a decade of follow-up.

References

1. Harley N, Foulkes CE, Hilborne L, et al. A review of the scientific literature as it pertains to Gulf War illnesses. Vol.7. Depleted uranium. [MR-1018/7-OSD.] Santa Monica, CA: RAND, 1999.
2. Fulco CE, Liverman CT, Sox HC, editors. Gulf War and health. Vol 1. Depleted uranium, pyridostigmine bromide, sarin, vaccines. Washington DC: Institute of Medicine, National Academy Press, 2000.
3. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for uranium. Prepared by RTI under contract no 205-93-0606 for USDHHS, Sept 1999.
4. United Nations Environmental Program. The Kosovo Conflict. Consequences for the environment and human settlements. UNEP, UNHS, 1999.
5. United Nations Environmental Program. Depleted uranium in Kosovo—post-conflict environmental assessment. 2001. <http://balkans.unep.ch/du/reports/report.html>
6. European Commission: Directorate-General Environment. Opinion of the Group of Experts Established According to Article 31 of the Euratom Treaty — depleted uranium. 2001.
7. World Health Organization (WHO). Report of the World Health Organization: depleted uranium mission to Kosovo. 22 to 31 January 2001.
8. World Health Organization (WHO). Depleted Uranium: Sources, Exposure and Health Effects. WHO, Department of Protection of the Human Environment, Geneva, 2001. [WHO/SDE/PHE/01.1.]
9. Office of the Special Assistant for Gulf War Illnesses. Environmental Exposure Report: depleted uranium in the Gulf (I). 1998. <http://www.gulflink.osd.mil/du/>
10. Office of the Special Assistant for Gulf War Illnesses. Environmental exposure report: depleted uranium in the Gulf (II) and health risk assessment consultation. No. 26MF-7555-00D. Depleted uranium — human exposure assessment and health risk. Characterization in support of the environmental exposure report "depleted uranium in the Gulf" of the Office of the Special Assistant to the Secretary of Defense for Gulf War Illnesses, Medical Readiness and Military Deployments. 2000. <http://www.gulflink.osd.mil/du/>
11. The Royal Society. The health hazards of depleted uranium munitions — Part 1. May 2001.
12. Kirk W. Depleted uranium. In: Kirk W, editor. Mineral facts and problems. Washington, DC: Department of Interior, Bureau of Mines, 1981: 997-1003.
13. Lide DR, editor. The elements. CRC Handbook of Chemistry and Physics, 76th Edition, 1995: ch4, 31-32.
14. UN Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. Report to the General Assembly, with Scientific Annex. Vol I and II. New York. UN Publications, 2000.
15. Fetter S, von Hippel F. The hazard posed by depleted-uranium munitions. *Science and Global Security* 1999; 8(2).
16. Livengood DR. Introduction to the problem. AFRRI Special Publication 98-3, 1998: 3-5. <http://www.afrri.usuhs.mil/www/news/news.htm>.
17. Australian Expert Committee to Examine Balkan Veteran Exposure to Depleted Uranium. Review of scientific literature on the health effects of exposure to depleted uranium. 2001.
18. Voegtlin C, Hodge H, editors. Pharmacology and toxicology of uranium compounds. Vols I-IV. New York: McGraw Hill: 1949-1953.
19. Leach LJ, Gelien RM, Panner BJ. The acute toxicity of the hydrolysis products of uranium hexafluoride (UF6) when inhaled by the rat and the guinea pig. Final report. ISS K?SUB-81-9039-3. NTIS DE84011539 in Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for uranium. Prepared by RTI under contract no 205-93-0606 for USDHHS, Sept 1999. ATSDR, 1984.
20. Leach LJ, Yuile CL, Hodge HC, et al. A five-year inhalation study with natural uranium dioxide (UO2) dust. II. Postexposure retention and biologic effects in the monkey, dog and rat. *Health Phys* 1973; 25: 239-258.
21. Pellmar TC, Fuciarelli AF, Ejnik JW, et al. Distribution of uranium in rats implanted with depleted uranium pellets. *Toxicol Sci* 1999; 49(l): 29-38.
22. Pellmar TC, Hogan JB, Benson KA, Landauer MR. Depleted uranium distribution and toxicology in a rodent model. Armed Forces Radiobiology Research Institute (AFRRI) Special Publication 98-3 pp7-9, 1998. <http://www.afrri.usuhs.mil/www/news/news.htm>
23. Pellmar TC, Hogan JB, Benson KA, Landauer MR. Toxicological evaluation of depleted uranium in rats: six-months evaluation report. Armed Forces Radiobiology Research Institute (AFRRI) Special Publication 98-1, 1998. <http://www.afrri.usuhs.mil/www/news/news.htm>
24. Pellmar TC, Keyser DO, Emery Q, Hogan JB. Electrophysiological changes in hippocampal slices isolated from rats embedded with depleted uranium fragments. *Neurotoxicology* 1998; 20: 785-792.
25. Beral V, Darby S. Appendix 3. In: The Royal Society. The health hazards of depleted uranium munitions — Part 1. May 2001.
26. McGeoghegan D, Binks K. The mortality and cancer morbidity experience of workers at the Springfields uranium production facility, 1946-95. *J Radiol Prot* 2000; 20: 111-137.
27. McGeoghegan D, Binks K. The mortality and cancer morbidity experience of workers at the Capenhurst uranium enrichment facility, 1946-95. *J Radiol Prot* 2000; 20: 381-401.
28. Dupree-Ellis E, Watkins J, Ingle JN, Phillips J. External radiation exposure and mortality in a cohort of uranium processing workers. *Am J Epidemiol* 2000; 152: 91-95.
29. Dupree EA, Watkins JP, Ingle JN, et al. Uranium dust exposure and lung cancer risk in four uranium processing operations. *Epidemiology* 1995; 6: 370-375.
30. Ritz B, Morgenstern H, Crawford-Brown D, Young B. The effects of internal radiation exposure on cancer mortality in nuclear workers at Rocketdyne/Atomics International. *Environ Health Perspect* 2000; 108: 743-751.
31. Ritz B. Radiation exposure and cancer mortality in uranium processing workers. *Epidemiology* 1999; 10: 531-538.
32. Ritz B. Cancer mortality among workers exposed to chemicals during uranium processing. *J Occup Environ Med* 1999; 41: 556-566.
33. Frome EL, Cragle DL, Watkins JP, et al. A mortality study of employees of the nuclear industry in Oak Ridge, Tennessee. *Radiation Res* 1997; 148: 64-80.
34. Loomis DP, Wolf SH. Mortality of workers at a nuclear materials production plant at Oak Ridge, Tennessee, 1947-1990. *Am J Indust Med* 1996; 29: 131-141
35. Wing S, Shy CM, Wood JL, et al. Mortality among workers at Oak Ridge national laboratory: evidence of radiation effects in follow-up through 1984. *JAMA* 1991; 265: 1397-1402.
36. Frome EL, Cragle DL, McLain RW. Poisson regression analysis of the mortality among a cohort of World War II nuclear industry workers. *Radiation Res* 1990; 123: 138-152.
37. Checkoway H, Pearce N, Crawford-Brown DJ, Cragle DL. Radiation doses and cause-specific mortality among workers at a nuclear materials fabrication plant. *Am J Epidemiol* 1988; 127: 255-266.
38. Checkoway H, Mathew RM, Shy CM, et al. Radiation, work experience, and cause specific mortality among workers at an energy research labo-ratory. *Br J Ind Med* 1985; 42: 525-533.
39. Polednak AP, Frome EL. Mortality among men employed between 1943 and 1947 at a uranium-processing plant. *J Occup Med* 1981; 23: 169-178.
40. Cookfair DL, Beck WL, Shy C, et al. Lung cancer among workers at a uranium processing plant. In: Proceedings of the Health Physics Society 398-406. In: Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for uranium. Prepared by RTI under contract no 205-93-0606 for USDHHS, Sept 1999. ATSDR, 1983.
41. Teta MJ, Ott MG. A mortality study of a research engineering, and metal fabrication facility in Western New York State. *Am J Epidemiol* 1988; 127: 540-541.
42. Cragle DL, McLain RW, Qualters J, et al. Mortality among workers at a nuclear fuels production facility. *Am J Indust Med* 1998; 14: 379-401.
43. Beral V, Fraser P, Carpenter L, et al. Mortality of employees of the atomic weapons establishment, 1951-82. *BMJ* 1988; 297: 757-770.
44. Dupree EA, Cragle DL, McLain RW, et al. Mortality among workers at a uranium processing facility, the Linde Air Products Company Ceramics Plant, 1943-1949. *Scand J Work Environ Health* 1987; 13: 100-107.
45. Brown DP, Bloom T. Mortality among uranium enrichment workers. Report to NIOSH, Cinncinati OH. NTIS PB87-188991 In: Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for uranium. Prepared by RTI under contract no 205-93-0606 for USDHHS, Sept 1999. ATSDR, 1987.
46. Stayner LT, Meinhardt T, Lemen R, et al. A retrospective cohort mortality study of a phosphate fertilizer production facility. *Arch Environ Health* 1985; 40: 133-138.
47. Waxweiler RJ, Archer VE, Roscoe RJ, et al. Mortality patterns among a retrospective cohort of uranium mill workers. In: Epidemiology applied to health physics. Proceedings of the Health Physics Society, 1983: 428-435.
48. Archer VE, Wagoner JK, Lundin FE Jr. Cancer mortality among uranium mill workers. *J Occup Med* 1973; 15: 11-14.
49. Wagoner JK, Archer VE, Carroll BE, et al. Cancer mortality patterns among U.S. uranium miners and millers, 1950 through 1962. *J Natl Cancer Inst* 1964; 32: 787-801.
50. Hadjimichael OC, Ostfeld AM, D'Atri DA, Brubaker RE. Mortality and cancer incidence experience of employees in nuclear fuels fabrication plant. *J Occup Med* 1983; 25: 48-61.
51. McDiarmid MA, Engelhardt SM, Oliver M. Urinary uranium concentrations in an enlarged Gulf War veteran cohort. *Health Phys* 2001; 80: 270-273.
52. Hooper FJ, Squibb KS, Siegel EL, et al. Elevated urine uranium excretion by soldiers with retained uranium shrapnel. *Health Phys* 1999; 77: 512-519.
53. McDiarmid MA, Keogh JP, Hooper FJ, et al. Health effects of depleted uranium on exposed Gulf War veterans. *Environ Res* 2000; 82: 168-180.
54. Institute of Medicine Committee on the Evaluation of the Department of Defense Comprehensive Clinical Evaluation Program. Adequacy of the comprehensive clinical evaluation program: a focused assessment. Institute of Medicine. National Academy Press, Washington DC: 1997.
55. Hyams KC, Hanson K, Wignall FS, et al. The impact of infectious diseases on the health of U.S. troops deployed to the Persian Gulf during operation Desert Shield/Desert Storm. *Clin Infect Dis* 1995; 20: 1497-1504.
56. Writer JV, DeFraties RF, Brundage JF. Comparative mortality among military personnel in the Persian Gulf region and worldwide during operations Desert Shield and Desert Storm. *JAMA* 1996; 275: 118-121.
57. Kang HK, Bullman TA. Mortality among U.S. veterans of the Persian Gulf War. *N Engl J Med* 1996: 335: 1498-1504.
58. Macfarlane GJ, Thomas E, Cherry N. Mortality among UK Gulf War veterans. *Lancet* 2000; 356: 17-21.
59. Freed G, Stringer PB. Comparative mortality experiences 1946–1963 among former Australian POW (J). *Australian Repatriation Department Research Bulletin* 1965; 2: 1-28.
60. Centers for Disease Control, Vietnam Experience Study. Postservice mortality among Vietnam veterans. The Centers for Disease Control Vietnam Experience Study. *JAMA* 1987; 257: 790-795.

(Received 8 Feb 2002, accepted 6 Jun 2002) ❑