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## Depleted uranium: properties, military use and health risks

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*(Accepted 17 September 2008)*

This article describes uranium and depleted uranium (DU), their similar isotopic compositions, how DU arises, its use in munitions and armour-proofing, and its pathways for human exposures. Particular attention is paid to the evidence of DU's health effects from cell and animal experiments and from epidemiology studies. It is concluded that a precautionary approach should be adopted to DU and that there should be a moratorium on its use by military forces. International efforts to this end are described.

**Keywords:** carcinogenic; depleted uranium; endocrine disruptor; Gulf war; munitions; synergism; toxicity; United Nations; U-234, U-235, U-238

### Introduction

Depleted uranium (DU) is a matter of natural interest to *Medicine, Conflict and Survival*, as it lies at the intersection of several matters within the journal's remit, including nuclear weapons proliferation, the impact of warfare, adverse health effects, international politics, toxic agents, radiation and radioactivity. In addition, the continued use of DU in munitions and armour-proofing by the United States and United Kingdom is a matter of controversy – not unfamiliar territory for this journal.

DU is a waste product mainly from the production of enriched uranium for nuclear weapons. It has been, and continues to be, used by UK and US armed forces in recent conflicts in the Middle East<sup>1</sup> and the Balkan region<sup>2,3</sup>.

Many claims have been made of adverse health effects, including the Gulf war syndrome, putatively arising from DU contamination during these conflicts<sup>4</sup>. Uranium and its decay products have a unique combination of toxic chemical and radiation properties which merit close scrutiny. In the past, radiation protection authorities may have paid insufficient attention to the combination of DU's properties, to the possible synergisms between

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them which may result in multiplied adverse effects, and to the existence of DU's decay daughters.

DU use is a controversial matter and a subject of current debate among international organizations including several United Nations agencies, such as the General Assembly, United Nations Environment Programme, United Nations Human Settlements Programme and United Nations Institute for Disarmament Research<sup>5</sup>.

It is notable that most military forces do not use DU: it is thought that only the US and UK armed forces presently do so<sup>6</sup>. DU is obtained as a waste product of nuclear power and of nuclear weapons manufacturing. Uranium and DU are isotopically very similar and chemically identical and for most practical purposes they may be considered the same. Uranium is a radioactive heavy metal that is hazardous to humans in four ways:

- as a toxic heavy metal.
- as a chemical carcinogen.
- as an endocrine disruptor, and
- as a radiation carcinogen.

DU has about 75% of the radioactivity of natural uranium (U) (see below) and therefore a similar percentage of the radiation carcinogenicity of U. But it has the same chemical toxicity, endocrine disruptive property and chemical carcinogenicity as U.

Because of the controversy over DU, uranium is now one of the most studied radionuclides. In recent years, at least eight official reports<sup>7-14</sup> have been published on its toxicity and health effects, together with at least five sizeable reviews<sup>15-19</sup>. Until the recent United States National Research Council report<sup>7</sup>, perhaps the most authoritative review was published in the two reports of the Royal Society in the United Kingdom on DU's chemical risks and radiation risks, respectively. The Royal Society reports stated that there were legitimate concerns about the possible health consequences of using a radioactive and chemically toxic material for munitions but concluded that the risks of DU munitions to soldiers were very low<sup>8</sup>. In particular, the Royal Society stated 'Exposure to sufficiently high levels might be expected to increase the incidence of some cancers, notably lung cancer, and possibly leukemia, and may damage the kidneys'. Using a worst-case scenario, they estimated an extra 1.2 deaths per 1000 from lung cancer amongst those most highly exposed (e.g. surviving personnel in a vehicle struck by a DU penetrator) (Ref. 9: p. 21, Vol. 2). However, since the Royal Society's reports, much new evidence from radiation biology has emerged.

The two main sources of information on DU health risks are epidemiology studies, that is, studies of DU exposures and risks to human

populations, and radiation biology studies in cells and animals. Although lay persons often feel that the former are more relevant, in fact much more information on the health effects of DU is available from the latter source.

### **Uranium – properties**

U is a constituent of the earth's crust with an average concentration of about three parts per million. Some uranium ore regions of the world contain much higher concentrations of uranium – typically about 1000 parts per million.

In the nuclear power fuel cycle, uranium ore is mined, and uranium is leached from ore and refined to almost pure uranium dioxide (UO<sub>2</sub>) for use in nuclear fuel<sup>6</sup>. (In passing, it is mentioned that uranium mining is highly destructive of local environments and that uranium refining creates very large quantities of radioactive tailings, which continue to release large quantities of the radioactive gases radon and thoron for millennia.)

U consists of three main isotopes, U-238 (99.3%), U-235 (0.72%) and U-234 (0.0054%). The isotopes U-238 and U-235 are primordial – that is, they were created at the same time as the earth about 4.6 billion years ago. U-234 is a decay product of U-238.

The vital consideration is that U-235 is fissile, that is, it maintains nuclear fission in nuclear power reactors and is used in nuclear weapons. Most nuclear reactors are designed for uranium fuel that has been only slightly enriched in U-235, typically from 0.7% to between 2% and 4%. This is known as low enriched uranium. This concentration is achieved by the process of enrichment, whereby UO<sub>2</sub> is converted to a gas (uranium hexafluoride, UF<sub>6</sub>) and passed through gaseous diffusion or centrifuge facilities. U-235 is also a vital ingredient of many nuclear weapons but here the enrichment required is to about 90% U-235. This is termed highly-enriched uranium.

DU is a waste product mainly from the manufacture of nuclear weapons. (It is also a waste product from nuclear fuel reprocessing, but such DU is not thought to be reused in significant quantities.) The enrichment processes for nuclear weapons create about seven metric tons of DU waste for each metric ton of enriched uranium<sup>19</sup>. The result is that very large quantities of DU are produced as waste. In 1996, worldwide production of DU was estimated by the European Parliament's Science and Technology Options Assessment (STOA) panel at about 35,000 metric tons per year<sup>7</sup>. As a result, it is estimated that over 1.2 million<sup>81</sup> metric tons of DU are currently stockpiled worldwide, mostly in the United States, and mostly in the unstable form of uranium hexafluoride: this is a major environmental waste problem to which insufficient attention is given. Uranium and DU can exist in a number of chemical forms as described in Box 1.

## Box 1. Chemical forms of uranium and depleted uranium.

*Uranium oxides*

Uranium oxides include  $U_3O_8$ ,  $UO_2$ , and  $UO_3$ . Both  $U_3O_8$  and  $UO_2$  are solids that are relatively stable over a wide range of environmental conditions, with low solubility in water. DU is chemically more stable and suitable for long-term storage or disposal in these forms.  $U_3O_8$  is the most stable form and the form most commonly found in nature, and in 'yellow cake', a solid produced during mining and milling operations, named for its characteristic colour.  $UO_2$  is a solid ceramic material, and the form of uranium used in nuclear reactor fuel. At room temperatures,  $UO_2$  gradually converts to  $U_3O_8$ .

*Uranium hexafluoride*

Uranium hexafluoride ( $UF_6$ ) is an unstable form of uranium used during conversion and enrichment. It is a major chemical hazard.  $UF_6$  can be a solid, liquid or gas within a range of temperatures and pressures. Solid  $UF_6$  is a white, dense, crystalline material, resembling rock salt. While  $UF_6$  does not react with oxygen, nitrogen, carbon dioxide or dry air, it does react rapidly with water or water vapour to form highly corrosive hydrogen fluoride (HF) and uranyl fluoride ( $UO_2F_2$ ). Although very convenient for processing,  $UF_6$  is contraindicated as a chemical form for long-term storage or disposal because of its instability.

*Uranium metal*

Uranium metal is among the densest materials known, with a density of 19 g per cubic centimeter ( $g/cm^3$ ). The silvery white, malleable and ductile metal is not as stable as uranium oxide and will undergo surface oxidation. It tarnishes in air, with the oxide film preventing oxidation of the bulk material at room temperature. Uranium metal powder or chips will ignite spontaneously in air at ambient temperature.

Small amounts of DU are sometimes used in hospitals and laboratories as radiation shielding and, in the past, DU was used in counterweights in some aircraft wings; however these uses are small and declining in comparison with the large amounts generated each year. The largest users of DU are military services, but even they do not put much of a dent in DU stockpiles. For example, the STOA Panel<sup>19</sup> estimated that the total quantity of DU in ammunition used in Iraq and Kosovo corresponded to only 4 days' DU production worldwide, that is, about 2% of annual DU production. DU stockpiles worldwide pose serious disposal problems to the governments involved – mainly the US, UK and Russia.

**Military uses of depleted uranium**

The US and UK military services use DU in ammunition and projectile munitions, and in the armour-plating of vehicles for a number of reasons. One is that DU is inexpensive and plentiful supplies are available. Another is uranium’s properties, as the chemical and physical properties of U metal and DU metal are almost identical. Uranium is a very dense metal with a specific gravity approximately 70% greater than lead. This is useful in a military context because of the higher penetrative power and greater trajectories of DU projectiles compared with tungsten-tipped munitions. Also, DU alloys are very hard and pyrophoric, properties which make DU armour-piercing munitions superior to conventional (tungsten) munitions. DU armour-plating is also more resistant to penetration by conventional anti-tank munitions. Probably another reason for DU’s use by US and UK military forces is that it provides a partial solution to the mounting problem of DU wastes mentioned previously.

DU munitions were first used extensively in the 1991 Gulf war, in Bosnia in 1995 and Kosovo in 1999. It has continued to be used in Iraq since 2003 and perhaps in Afghanistan since 2002. Table 1 indicates the amounts of DU used in recent wars by the US armed forces who are by far the largest user of DU munitions.

Table 1. Depleted uranium used by United States armed forces in recent wars (metric tons).

Gulf war	Balkan wars	Iraq war
286	11	75

Source: Ref. 7 [Tables 1–4].

On impact, DU in projectiles may be dispersed as aerosols which can be inhaled or ingested, or imbedded in tissue as shrapnel. Frequent continuing reports of illnesses suffered by combatants<sup>4</sup> and civilians<sup>1</sup> in these wars have resulted in speculation that these may be because of DU exposures. See Box 2 for a discussion of the Gulf war syndrome.

**Box 2. Gulf war syndrome.**

Many soldiers and civilians from Gulf war areas have self-reported a variety of symptoms, usually collectively termed the Gulf war syndrome. The syndrome appears to be a complex, progressive, incapacitating, multi-organ, system disorder whose symptoms can include fatigue, musculoskeletal and joint pains, headaches, neuropsychiatric disorders, confusion,

*(Continues)*

## Box 2. (Continued)

visual problems, changes of gait, loss of memory, swollen or enlarged lymph nodes, respiratory impairment, impotence and urinary tract morphological and functional alterations.

Whatever the causes, it is clear that the suffering is widespread, measurable and real to those affected. Nearly 20% of all US personnel deployed to the 1991 Gulf war were receiving some form of disability compensation because of these effects by 2001<sup>75</sup>. A number of studies, summarized by Komaroff, have found that armed forces from a number of countries deployed to the Persian Gulf region were statistically significantly more likely to report chronic, debilitating symptoms than military personnel deployed to other areas<sup>76</sup>. Eisen et al. measured the prevalence of self-reported chronic illness among Gulf war combatants compared with a control group of not deployed veterans. They found that deployed veterans reported dyspepsia, a group of common skin conditions (fibromyalgia), and chronic fatigue syndrome much more often than the control group. The most striking association was with chronic fatigue syndrome<sup>77</sup>.

Some authors<sup>79,82</sup> have alleged these symptoms may be because of, at least in part, DU exposures. There is some chromosomal evidence of increased radiation exposures in soldiers in the Middle East<sup>80</sup>. In addition, the UN Environmental Programme<sup>3</sup> found over 300 DU-contaminated sites in Iraq. However, many soldiers and civilians reporting these symptoms were unexposed to DU or were exposed to low concentrations, so the single explanation of DU exposure for ill health outcomes is considered unlikely. [There is one aspect which could result in greater (and more widespread) exposures to DU aerosols than those received from munitions use on tanks and buildings, and these are fires and explosions at DU weapons dumps. Anecdotal reports indicate that there have been two such fires in Iraq, with one fire lasting 8 days. Clearly this is a matter which should be investigated, and consequent DU exposures estimated.]

Many Gulf war personnel were exposed to many substances that in theory could have produced chronic tissue damage: solvents, insecticides, smoke and other combustion products, agents of chemical warfare (irreversible anti-cholinesterase inhibitors, such as sarin), and pyridostigmine bromide (a reversible anti-cholinesterase inhibitor taken to prevent the effects of sarin). Also, they received an intensive battery of simultaneously administered immunizations, which some believe<sup>75</sup> could have produced chronic debility.

(Continues)

## Box 2. (Continued)

In conclusion, although our understanding of the etiologies of these symptoms remains poor to say the least, it is difficult to ascribe anything more than a minor role to DU exposures, given the present level of knowledge about DU exposures. More discussion on the Gulf war syndrome is at [http://en.wikipedia.org/wiki/Gulf\\_war\\_syndrome](http://en.wikipedia.org/wiki/Gulf_war_syndrome).

**Comparison of the radioactivity of DU and natural uranium**

Many reports state that DU has 60% of the radioactivity of U. However, the correct figure is closer to 75% for two reasons: enrichment facilities sometimes use reprocessed (as opposed to 100% mined) uranium, and the presence of U decay products.

***The presence of reprocessed uranium in DU***

The DU used by the US military contains the isotope U-236 (at a concentration of 0.0003%)<sup>8</sup> which is not present in natural (i.e. mined) uranium. This man-made isotope arises only in nuclear reactors and its presence indicates that the DU batch used contained some uranium from the waste streams of reprocessing spent nuclear fuel, carried out mainly by France, the Russian Federation, the United Kingdom and the United States. Thus there are two types of DU depending on its source; that is, from reprocessing or from mined uranium ore.

The important matter is that the former includes small amounts of reprocessed uranium from spent nuclear fuel. This is problematic because reprocessed uranium is contaminated with the fission and activation products found in spent nuclear fuel. In particular, the fission product Tc-99 and the activation products Np-237, Pu-238, Pu-239, Pu-240 and Am-241 are sometimes found in DU munitions<sup>20</sup>. DU made with some reprocessed uranium is therefore more radioactive than the DU derived solely from mined uranium ores<sup>20</sup>. Most reports state that the amounts of contaminants in DU munitions from spent nuclear fuel are low. According to the US Office of the Special Assistant for Gulf War Illnesses, the dose from these contaminants amounts to less than one 1% of the equivalent dose from DU exposures, and the authors have concluded that their risk impact was low<sup>12</sup>. The Royal Society also stated that the concentrations found in the DU batches it had examined were low, but it recommended continued vigilance on the matter<sup>9</sup>.

***Uranium decay products***

Once DU has been made into munitions and placed in a warehouse, the U-238 and U-235 isotopes slowly decay and create various daughter products.

The main daughter products of U-238 are Th-234, Pa-234m, Pa-234 and U-234; the main daughter products of U-235 are Th-231 and Pa-231. Within about 6 months, these daughters are in secular equilibrium with their parents: that is, the daughter amounts being created by the parent are equal to the daughter amounts disintegrating. Therefore the radiation from these decay products should be added when assessing the dangers of DU.

The key matter is that the decay products are mostly beta emitters, particularly Pa-234m, which emits very energetic beta particles. As explained by the Royal Society<sup>9</sup>, these beta radiations may constitute as much as 40% of the absorbed dose (that is, 2% of the equivalent dose) to tissues near embedded DU. It is important to realize that the additional risk from the beta particles of decay products is currently not taken into account by the International Commission on Radiological Protection in its dose coefficients (which estimate radiation doses from incorporated radioactive substances) for uranium isotopes. This should be corrected as soon as possible.

Bishop<sup>21</sup> has estimated the total alpha, beta and gamma emissions per year from 1 g samples of U and DU. He concluded that DU together with its decay products in equilibrium are 75% as radioactive as U plus its decay products. The STOA report<sup>19</sup> to the European Parliament using a cruder method estimated that DU has 80% of the radioactivity of U. This means that the adjective 'depleted' in DU may give a misleading impression: a more accurate description would be the phrase 'slightly less radioactive'. For almost all practical purposes, DU and U can be considered as the same.

## **Depleted uranium pathways**

### ***DU in the environment***

DU exposures can occur via several pathways. One is external radiation, whereby beta radiation (and, to a much lesser degree, gamma radiation) from the decay products of DU irradiate the body, but in most cases such exposures are very small. More important are the internal exposures resulting from inhalation of DU aerosols and dusts, from ingestion of DU contaminated water and food, and from wounds – in other words by inoculation of DU shrapnel.

When DU projectiles penetrate armoured vehicles, their occupants are often injured by DU shrapnel, which can remain in the body for lengthy periods. When tanks are struck by DU projectiles, depending on the material and thickness of their armour, about 10%<sup>13</sup> is volatilized into an aerosol that immediately burns to form poorly-soluble uranium oxides that may remain in high concentrations in enclosed spaces, such as tanks and bunkers. These aerosols can contain very small particles of uranium oxide of between 0.1 and 10 microns in diameter ( $1 \mu = 10^{-6}$  m or one millionth of a metre) which can be inhaled and deposit in the lungs. White blood cells scavenge these particles and transport them to tracheobronchial lymph nodes for lengthy periods. These particles are usually insoluble, and are unlikely to be detected in urine

samples. Therefore the routine practice of urine sampling of returning soldiers is likely to be ineffectual at detecting uranium oxide exposures.

***DU in soil***

Uranium’s transport in soil depends very much on its solubility in water, but this is highly complex and highly variable at different pH values. Uranium can exist in the +3, +4, +5 and +6 oxidation states, with the +4 and +6 states most common in the environment. These oxides are only sparingly soluble, but will gradually form hydrated uranium oxides in moist conditions. The hydrated uranium oxides will then slowly dissolve and be transported into surrounding soil, pore water and eventually groundwater. With metallic U particles, the oxidation rate depends on fragment size, pH, humidity, soil moisture content, soil chemistry, soil oxygen content and the presence of other metals in the soil. Soil pH and dissolved carbonate concentrations are the two most important factors influencing the adsorption behaviour of the common U<sup>6+</sup> in soil<sup>22</sup>. However recent studies of DU munitions buried in soils over for 3 years have shown accelerated corrosion and U leaching rates<sup>23</sup>.

***DU in drinking water***

Because of the increased awareness of the health hazards of uranium, there has been growing pressure to tighten drinking water standards for uranium in recent years. National standards vary considerably, partly because of different assumptions about the daily consumption of water. See Table 2.

Table 2. National and international standards for uranium in drinking water.

Country/agency	Uranium standard $\mu\text{g}$ (micrograms) per litre
WHO (1998)	2
US (1996)	20
Canada (2001)	10
Germany (2008)	10 (two for infants)
UK	No standard
EU	No standard

For example the US EPA’s maximum permissible concentration for U (i.e. and therefore for DU) in drinking water is 20  $\mu\text{g/l}$  (micrograms or millionths of a gram, per litre), but this is lax in comparison with the WHO guideline value (GV) of 2  $\mu\text{g/l}$ . In Canada, the Government’s Federal – Provincial – Territorial Committee on Drinking Water calculated the health-based GV of uranium in drinking water to be 10  $\mu\text{g/l}$ . In 1998, the World Health Organization proposed a ‘tolerable daily intake’ (TDI) of

0.6  $\mu\text{g}$  per kg bodyweight<sup>24</sup>. This was derived by dividing the lowest U concentration in rats at which effects were observed by an uncertainty factor of 100 ( $\times 10$  for interspecies variability and  $\times 10$  for intra-species variability). The TDI is an estimate of the amount that can be ingested daily over a lifetime without appreciable health risk. (See discussion at <http://www.dwi.gov.uk/regs/infolett/2001/info0101.htm>.) The WHO also derived a GV of 2  $\mu\text{g}/\text{l}$  for U drinking-water. According to the WHO report, the GV 'represents the U concentration ... that does not result in any significant risk to the health of the consumer over a lifetime of consumption' (the reasoning was as follows: for an adult weighing 60 kg, the TDI corresponds to a daily U intake of 36  $\mu\text{g}$ . Drinking-water is not the only source of U intake, so assume that up to 90% of the TDI comes from other sources (in practice, food). In other words, assume that food might provide as much as 32  $\mu\text{g}$  daily. Then upto 4  $\mu\text{g}$  may be allocated to the normal consumption of 2 litres of drinking-water per day – hence the GV of 2  $\mu\text{g}/\text{l}$ . See <http://www.dwi.gov.uk/regs/infolett/2001/info0101.htm#b7>).

Surprisingly there are currently no UK regulatory limits or official guidance for uranium in mineral water, bottled drinking water or tap water (see <http://www.food.gov.uk/multimedia/pdfs/tox200527uranium.pdf>). Similarly, the European Commission has not introduced a drinking water standard for uranium because of pressure from some member states, although one is expected within a few years. In September 2008, the German federal and state Ministers of consumer protection, responding to German consumer concerns about uranium in domestic water supplies, agreed to introduce a 10  $\mu\text{g}/\text{l}$  drinking water standard for uranium<sup>25</sup>. It remains unclear whether this value will be introduced in Germany before the European Union introduces its own value. Earlier in 2006, the German Parliament had approved regulations limiting the uranium concentration in bottled mineral waters to 2  $\mu\text{g}/\text{l}$  for water designated for infants<sup>26</sup>.

### ***DU in humans***

The initial distribution of uranium compounds in humans strongly depends on their solubility and absorption route. On average, 1–2% of ingested uranium is absorbed in the gastrointestinal tract in adults. The absorbed uranium rapidly enters the bloodstream and forms a diffusible ionic uranyl hydrogen carbonate complex ( $\text{UO}_2\text{HCO}_3^+$ ) in equilibrium with a non-diffusible uranyl albumin complex. In skeleton, the uranyl ion replaces calcium in the hydroxyapatite complex of the bone crystal. Once equilibrium is attained in the skeleton, uranium is excreted in urine and faeces. Under alkaline conditions, the uranyl hydrogen carbonate complex is stable and is excreted. In more acidic environments, the U complex dissociates and binds to the cellular proteins in the tubular wall. The half-life of uranium in the rat kidney is about 15 days, and considerably longer (300–5000 days) in the rat skeleton<sup>27</sup>.

Large fractions of administered soluble uranium compounds can be absorbed. For example, 20–30% was found in the bones of male rats within 2.5 hours of uranium administration, and 90% of the uranium remaining after 40 days was found in bone<sup>28</sup>. Uranium compounds are distributed to all tissues, preferentially bone, kidneys, liver and testes<sup>10,29</sup>. Rats implanted with DU pellets also show uranium concentrations in heart, lung tissue, ovaries and lymph nodes<sup>17</sup>. Like many heavy metals, uranium reacts with DNA, ions and blood proteins to form special compounds called complexes. Uranium can cross the placenta and the blood-brain barrier and accumulate in the brain. Soluble uranium compounds are cleared more rapidly than insoluble compounds: two-thirds of uranium in blood is excreted in urine over the first 24 hours. Elimination of soluble uranium is primarily by the kidneys and urine. The release of DU from embedded particles in shrapnel is slow: it takes 1.5 years for 80–90% of uranium in bone to be excreted<sup>17</sup>. A recent study has revealed that U excretion is very slow and that urinary excretion of DU can be detected in people more than 20 years after they inhaled U aerosols<sup>30</sup>.

### ***Health effects of DU***

Since at least the Second World War, it has been known that uranium, a radioactive heavy metal, was hazardous to humans. Like other heavy metals, such as chromium, lead, nickel and mercury, uranium is chemically toxic to kidneys, the cardiovascular system, liver, muscle and the nervous system. In kidneys, U is thought to interfere with proximal tubular function at very low levels apparently without a threshold concentration<sup>31</sup>.

As all uranium isotopes are radioactive, they all also emit radiation. This means that, in the United States (which perhaps has the most detailed regulations covering uranium) U exposures are regulated in two different ways – by radiation protection authorities and by chemical regulation authorities. The former stipulates maximum doses from uranium radiation exposures to the lung via insoluble uranium particles, as it was thought their long residence times in the lung could result in lung cancers. The latter stipulates maximum concentrations of soluble uranium chemicals, particularly in the kidney<sup>32</sup>. Uranium's chemical effects were previously thought to occur at lower uranium concentrations than its radiation effects<sup>33</sup>. However it is now known that this is incorrect, as both effects can be stochastic, that is they can occur down to the very lowest levels.

### **Chemical carcinogenicity of DU**

Scientists are increasingly aware that uranium and DU are hazardous to humans in a third way: they are chemically (as well as radiologically)

carcinogenic. This considerably increases our perception of DU and U hazards because low concentrations of soluble uranium throughout the body – previously considered to be harmless (and therefore neglected) – are now considered to be carcinogenic without threshold. In other words, no matter how low the DU or uranium concentration, a small risk of chemical carcinogenesis remains. However, Taylor and Taylor have estimated that the risks of chemical carcinogenicity are low<sup>15</sup>.

The Royal Society's 2001 report<sup>9</sup> discussed the then emerging evidence of DU's chemical carcinogenicity and it suggested that uranium's chemical and radiation effects may act synergistically, that is, their effects may need to be multiplied rather than added together. More recently, the US NRC report<sup>7</sup> also examined uranium's chemical carcinogenicity and expressed variable views on the matter. For example, its Chapter 7 called for research on 'whether' a chemical mechanism of uranium carcinogenesis existed. However, Chapter 8 recommended that studies be conducted to determine the relative contributions of 'the' chemical and radiological mechanisms of uranium carcinogenesis. Unfortunately, since 2004 the US government appears not to have granted further funds to research DU carcinogenicity: for example, the lead agency on this research, the US Armed Forces Radiobiology Research Institute, has significantly reduced its pioneering work on this research.

### **Uranium as endocrine disruptor**

Recent evidence<sup>34</sup> suggests that DU may be hazardous to humans in a fourth way. It may act as an endocrine disruptor, that is, a substance which interferes with hormones. A number of studies have indicated that heavy metals act as endocrine disruptors<sup>35</sup>. For example, cadmium stimulates the proliferation of human breast cancer cells<sup>36</sup>, interacts with estrogen receptors<sup>36</sup> and stimulates estrogenic responses *in vivo*<sup>37</sup>. Raymond-Whish et al.<sup>34</sup> tested whether DU added to drinking water caused responses in the female mouse reproductive tract like those caused by the estrogen diethylstilbestrol. They concluded that uranium is an endocrine-disrupting chemical and that populations exposed to environmental uranium (including indigenous populations in the United States living near uranium mine tailings) should be examined for increased risk of fertility problems and reproductive cancers.

### **Enhanced radiation from photoelectric effect?**

A very recent article<sup>38</sup> discussed a suggestion that DU and U atoms could have an enhanced radiation effect because of interactions with background gamma radiation. It is well known that such interactions occur because of the photoelectric effects of gamma rays interacting with atoms of high atomic number (high Z). Such interactions result in a shower of secondary emissions near the site of the relevant high Z atoms. However, the gamma

flux from background radiation is likely to be much too low for high exposures (that is, adverse health effects) to occur. This is because each U or DU particle would have to be 'hit' by many background gamma rays to achieve this. If such large background fluxes existed, background radiation doses would have to be increased considerably for other reasons and this seems very unlikely. If one were to switch a laboratory radiation detector to its highest sensitivity, one would get a few 'clicks' per second in a Geiger tube with an area of about 4 cm<sup>2</sup>. Each 'click' represents a gamma photon from background radiation. One would need to observe a much higher rate of 'clicks' for the gamma fluxes necessary for the above suggested effects.

There are other matters which argue against this suggestion (for example, the preponderance of high energy over low energy gammas in background radiation, and the existence of Compton scattering which will diminish the photoelectric effect) but low gamma flux is the main problem. Further calculations are understood<sup>38</sup> to be continuing to estimate the actual (very low) level of doses from the background photoelectric effect on U particles, and what background gamma fluxes would be needed to observe adverse effects.

## **Cell, animal, human and epidemiological studies**

### ***A) Human cell evidence (in vitro studies)***

A comprehensive body of research indicates that DU exposures to human cells *in vitro* results in genotoxic effects and induces cell phenomena closely associated with carcinogenesis. These cellular effects and phenomena were reviewed by Professor Baverstock<sup>39</sup> in 2006 for the Belgian Parliament.

The cell effects include the following:

- genomic instability – a process involved in carcinogenesis<sup>40</sup>.
- transformation to a tumorigenic state, whereby affected cells grow as cancers when injected into mice<sup>41–45</sup>.
- induction of mutations whose presence characterizes most cancers<sup>46</sup>.
- DNA oxidative damage<sup>47</sup>.
- activation of gene expression pathways<sup>48</sup>.
- formation of DNA-U adducts<sup>49</sup>.
- induction of dicentric in chromosomes – a radiation-specific change in human cells<sup>50–52</sup>.
- chromosomal damage<sup>53</sup>.

### ***B) Animal evidence (in vivo studies)***

Long-term studies of insoluble uranium oxide inhalation in monkeys indicate the carcinogenicity to lung of this kind of exposure and possibly its involvement in non-Hodgkin lymphoma<sup>54,55</sup>. Monleau et al. measured the induction of DNA double strand breaks by inhaled DU in rats<sup>56</sup>. Hahn et al.

found an elevated risk of cancer in rats implanted with small DU foils. They concluded that DU fragments embedded in muscle tissue were carcinogenic if large enough; however the mechanism was unclear<sup>57,58</sup>.

After mice were exposed to embedded DU for 3 months then injected with progenitor cells, Miller et al. found that 75% of mice developed leukemia compared with 10% in control mice<sup>42</sup>. In addition, mice showed changes in the musculoskeletal system, such as bone formation and remodelling, after oral, intra-peritoneal, intra-venous and implantation uranium exposure<sup>41</sup>.

*In vivo* studies with embedded DU pellets in animals showed aberrant expression of oncogenes and tumour suppressor genes associated with carcinogenesis<sup>52,59</sup>. Although these effects may be caused by DU radiation, there are many reasons suggesting that its chemical effects pre-dominate. In the *in vitro* transformation and sister chromatid exchange studies, induced effects were very much more frequent than expected from the very small number of cells hit by an alpha particle (1 in 100,000 cells from a 10  $\mu\text{m}$ -sized DU particle). In addition, similar transformation frequencies were observed with the non-radioactive heavy-metal carcinogens nickel and lead; it was speculated that genotoxicity of DU may be because of uranyl ions acting to produce free radicals, particularly if the ions are effectively chelated to DNA like other metal ions<sup>52,59</sup>.

### **C) Biological evidence in humans**

Uranium is a well-established nephrotoxin (that is, toxic to kidneys) in humans, the primary target being the proximal tubule. Damage occurs when uranium forms complexes with phosphate ligands and proteins in tubular walls which impair kidney function. Biomarkers of these tubular effects include enzymuria and increased excretion of small proteins, amino acids and glucose. Uranium is also a bone seeker and is incorporated into the bone matrix by displacing calcium to form complexes with phosphate groups<sup>60</sup>.

McDiarmid et al.<sup>61</sup> observed a statistically significant increase in mutations in peripheral lymphocytes in three US Gulf war veterans with embedded DU fragments (from 'friendly-fire' incidents) shown by uranium measurements in their urine. However, their continuing surveillance over 14 years has yielded no evidence of reproductive system dysfunction, abnormalities in sperm or alterations in neuroendocrine function. Nevertheless, it should be recalled that soldiers are a healthy subset of the wider population, and the numbers of exposed soldiers in these studies are very small. Monleau et al. found that repeated uranium inhalations tended to potentiate, that is increase uranium's genotoxic effects<sup>56</sup>. Zaire et al.<sup>62</sup> observed the induction of chromosome aberrations in uranium mineworkers in Namibia. Such rearrangements of genetic material in chromosomes are involved in the carcinogenic process.

#### ***D) Epidemiological studies***

Few, if any, epidemiology studies have shown convincing effects specifically from DU, as opposed to U, exposures. The Royal Society examined 14 epidemiological studies of occupational uranium exposures to workers engaged in the extraction, milling and machining of uranium<sup>9</sup>. These showed no sign of excess deaths because of cancer or kidney disease related to inhaling or ingesting uranium. However, the Royal Society report stressed these studies should be interpreted with care. First, there were few reliable data on uranium exposure levels to workers, particularly in the early years of uranium processing when exposures because of inhalation of uranium-containing dust were thought to be high.

In addition, smoking was a powerful confounder causing approximately 90% of lung cancers, and information on smoking habits was not available for any of the studies. Another problem was the healthy worker effect, which meant that risk comparisons should be made with other workers and not the general population. The report stressed that these types of epidemiological studies were not able to detect small increases in risk, although a twofold increase in cancer might have been detectable. A cardinal rule in epidemiology is that the absence of evidence in studies should not be used to allege evidence of absence<sup>63</sup>. In many cases, it may mean merely that the studies were not powerful enough to detect an increased risk.

A number of studies have examined health effects in small numbers of military personnel<sup>51</sup> exposed to DU in 'friendly-fire' incidents, but their exposures to uranium dusts and aerosols were much lower than those experienced during uranium mining and milling activities. Unfortunately, very few studies have been made of the many civilians exposed to DU in various conflicts<sup>52</sup>. The two main exceptions are by Al Sadoon et al.<sup>64</sup> in 2002, and Fasy in 2003<sup>65</sup>.

Those studies actually carried out raise as many questions as answers, particularly on the unusually low incidence rates of congenital malformations in Iraq pre-1990 compared with Western rates. Hindin et al.<sup>66</sup> carried out an extensive literature review of congenital malformations following DU exposures in US military personnel. They concluded that the human epidemiological evidence was consistent with increased risk of birth defects in offspring of persons exposed to DU.

Therefore, despite the existence of many reports on DU, it remains difficult to assess whether (and to what degree) DU exposures have caused increased ill health among exposed soldiers and others. This is because of the inconclusive findings of some of the reports; the large uncertainties in the assessed doses and risks from DU exposures; the possible presence of confounders; and the paucity of data from past battlefields. In other words, the available epidemiological evidence on DU exposures in Iraq and other battle grounds is unreliable for establishing risks.

### **Possible synergism between radiation effects and chemical effects**

As discussed above, many studies clearly indicate that DU has both chemically-induced and radiation-induced effects. An important question is whether synergism exists between these effects, that is, whether they potentiate one another. For example, synergistic responses occur when nickel exposure is combined with exposure to gamma radiation<sup>66</sup>. And bystander (that is, un-irradiated) cells are vulnerable to both radiation-induced and chemical-induced effects (Ref. 67:p. 277).

A significant number of scientists have theorized that such synergism may occur. For example, Miller et al. specifically proposed that the radiological and chemical effects of DU might play tumour-initiating and tumour-promoting roles (Ref. 48:p. 254). If this were the case, it would be a clear example of synergism. In addition, the Royal Society's report stated:

One could speculate ... that the potential for synergistic effects between the radiation and chemical actions of DU would be greatest in the vicinity of particles or fragments of DU, from which essentially all the surrounding cells are chemically exposed and may thereby be sensitized to the occasional radioactive decay particle<sup>9</sup>.

It concluded that further studies were required to examine the possibility of synergy between the chemical effects and radiation effects of DU<sup>9</sup>. The US NRC report<sup>7</sup> also recommended that studies be conducted to determine the relative contribution of chemical and radiological mechanisms of uranium carcinogenesis. It added that if the chemical contribution were found to be substantial, studies should then be undertaken to calculate cancer risks resulting from the combined chemical and radiological effects of DU.

### **Discussion**

Many articles in the scientific media have posed questions about the incidence of ill health and death in Iraq following alleged DU exposures in both wars. For example, see Ref. 1 and <http://www.newscientist.com/article.ns?id=dn3635>, <http://www.newscientist.com/article.ns?id=dn3627>.

In addition, many private or unofficial websites cite a great deal of anecdotal evidence of serious ill health among the Iraqi population. For example, among the many websites on this matter are the following:

<http://www.antenna.nl/wise/uranium>  
<http://www.bandepleteduranium.org>  
<http://www.cadu.org.uk>  
<http://www.ieer.org>

<http://www.idust.net>  
<http://www.miltoxproj.org>  
<http://www.nirs.org>  
<http://www.nuclearpolicy.org>  
<http://www.traprokpeace.org>  
<http://www.umrc.net/papers.aspx>  
<http://www.nukewatch.com/du/factsheet.html>  
<http://electronicdrum.wordpress.com/2004/07/13/more-articles-depleted-uranium-use-in-iraq-war/>  
<http://electronicdrum.wordpress.com/2004/07/13/us-forces-use-of-depleted-uranium-weapons-is-illegal/>  
<http://www.reachingcriticalwill.org/legal/du.html#five>

Although clearly much public concern exists, the problem as stated above is the palpable lack of credible epidemiological evidence. This is partly because of the many practical methodological<sup>83</sup> problems with conducting epidemiology studies in Iraq, as mentioned above and recently discussed by Hotopf and Wessely for example<sup>68</sup>.

But it is acknowledged that it is also partly because of political interference as well, particularly by the previous US administration. For example, in 2000, the UN General Assembly voted to recall a WHO team which had been sent to Iraq to investigate the many claims of ill health from DU exposures. Many observers considered the vote was because of pressures by the US on non-aligned governments re-withdrawals of US aid to their countries. This is similar to the previous US administration's reluctance to find evidence of ill health among US war veterans<sup>69</sup>. In addition, in 2001, a draft WHO report on the radiological toxicity of DU was suppressed and not published, allegedly on orders from the then US government<sup>70</sup>.

An aspect rarely discussed is the apparent inability or reluctance of some observers to accept the overwhelming preponderance of evidence of DU ill effects at low concentrations from biological research, i.e. from animal and cell studies. It is argued here that these are more useful sources of data for deriving uranium's risks than DU epidemiology studies. In fact, for safety regulation purposes, uranium's chemical risks are derived almost completely from animal studies. This is not unusual as the risks of most chemicals are based on the concentrations found not to be harmful in animals. These concentrations are further divided by safety factors of 10–1000 then applied to humans. That is, acceptable concentrations for humans are 10–1000 times safer than those in animals. This simple system works well and is clearly precautionary.

With radionuclides, the precautionary approach for chemicals is unfortunately not used. Instead, radiation scientists insist that human data (that is, from epidemiology studies) must be used to derive risks. Many may instinctively think that these are a better source because humans are

obviously different from animals, and this is correct, in theory. But in practice the matter is less clearcut, as many practical difficulties exist with epidemiology studies as indicated above. The greatest difficulty is that one needs very large, time-consuming and expensive studies involving thousands of cases to obtain statistically significant findings. Another difficulty is that to estimate risks per unit exposure, one needs estimates of these exposures and these are almost always lacking or highly uncertain. The result is that epidemiological studies are a blunt tool for investigating risks and the existing DU studies are highly unsatisfactory for deriving human risks. Insisting on using such studies alone rather than relying on cell and animal studies means that we might be underestimating DU's risks. Sole reliance on epidemiological studies (which so far are all too statistically weak to pick up effects) tends to downplay the substantial body of radiobiological evidence that overwhelmingly points to DU being a chemical carcinogen, a radiological carcinogen, a heavy metal nephrotoxin and an endocrine disruptor, all at relatively low levels of exposure<sup>71</sup>. Indeed, continued reluctance to act on the many research findings from radiobiology could be considered a breach of the precautionary principle in law<sup>72</sup>.

### **International and legal considerations**

There are other problems with continued DU use, apart from health concerns. For example, its use acts to blur the distinctions between conventional weapons, chemical weapons and (to a degree) nuclear weapons. In addition, DU use provides another indication of failed civilian control of the military. It appears there was no prior civilian discussion of DU development, and the first public knowledge of DU weapons apparently came via media reports from a soldier whistleblower. A moratorium on DU use could therefore be seen as politically as well as ethically desirable and health-wise sensible.

The legality of DU weapons use is a complex subject: a good review by Karen Parker is available at <http://130.94.183.89/parker.html#uranium>. It appears that no international laws directly govern the use of DU weapons. At present, two schools of thought exist among anti-DU campaigners on how to achieve a ban on DU use, one is via the anti-land mine legislation route; the other is via the 'DU is a humanitarian crime' path: both appear to have advantages and disadvantages which require a separate article to themselves.

As reported by the UN<sup>6</sup>, many countries voluntarily do not use DU weapons and are not seeking to do so: in fact, in March 2007, the Belgian Parliament voted unanimously to ban DU ammunition from June 2009. Therefore DU does not appear to be seen as militarily necessary or decisive by most countries.

International agencies have often debated whether DU should be banned from military weapons. In 2001, 2003 and 2005, the European Parliament

called for a moratorium on the use of DU munitions. The 2005 Resolution regarding DU was part of an 11-page document 'Texts adopted by European Parliament, on non-proliferation of weapons of mass destruction; A role for the European Parliament'. The Resolution reminded all European Union Member States that they had signed the 1968 Nuclear Non-proliferation Treaty, the 1972 Biological and Toxin Weapons Convention, the 1993 Chemical Weapons Convention and the 1996 Comprehensive Test Ban Treaty.

In December 2007, the UN General Assembly carried a Resolution (Number 62/30) by 136 votes to five, recognizing the health concerns over the use of uranium weapons and requesting that states report to the Secretary-General on the matter<sup>73</sup>. Finally, in May 2008, the European Parliament for the fourth time carried a DU motion that strongly reiterated its previous calls on all European Union Member States and North Atlantic Treaty Organization countries to impose a moratorium on the use of DU weapons with a view to the introduction of a total ban. The resolution was adopted with 491 votes in favour, 18 against and 12 abstentions<sup>74</sup>.

## **Conclusion**

With the preponderance of cell and animal studies indicating that DU is a very hazardous substance, it is concluded that the safest, and precautionary, approach would be to seek an immediate moratorium on its use. In addition, the above political reasons argue for the adoption of a moratorium on its use.

## **Notes on contributor**

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