DEPLETED URANIUM INDUCED FETAL MALFORMATIONS - LITERATURE REVIEW

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Abstract

Depleted uranium is a byproduct of the enrichment process of uranium for its more radioactive isotopes to be used in nuclear energy .Because depleted uranium is pyrophoric and a dense metal with unique features when combined with alloys ,it is used by the military in armor and ammunition and frequently used in combat scenarios.
This review reports on uranium uses and its published health effects, with major focus on its effects on reproduction and fetal development.
Key words: uranium toxicity, fetal toxicity, congenital malformations

Depleted uranium (DU) is a man-made, radioactive, heavy metal derived from natural uranium (fig. 1). It reacts with most non-metallic elements; it has pyrophoric properties and may spontaneously ignite at room temperature in air, oxygen and water. These unique properties make it appealing for use in many civilian and military applications.

DU is used as X-ray radiation shielding in hospitals, as counter weights for rudders and flaps in commercial aircrafts, in keels of sailing yachts and as ballast in both military and non-military airplanes.[1]

It is used by the military for the production of distinctly powerful projectiles (e.g., bullets/ penetrators, missile nose cones) and also as a protective armor for tanks. As a projectile, a DU penetrator ignites on impact under high temperature; it has a low melting point.

Large quantities of DU and/or radioactive decay products and other radioactive impurities can lead to substantial external exposure. A Geiger counter measurement by a correspondent in the recent Iraq war show that radiation emitting from a DU bullet fragment registered nearly 1000 – 1900 times the normal background radiation level.

A three-foot long DU fragment from a 12 mm tank shell registered radiation 1300 times the background level. A DU tank found by the U.S Army radiological team emitted 260 – 270 millirads of radiation per hour compared to the safety limit of 100 millirads per year. A pile of jet-black dust registered a count of 9839 emissions in one minute, a level more than 300 times the average background level.[2]

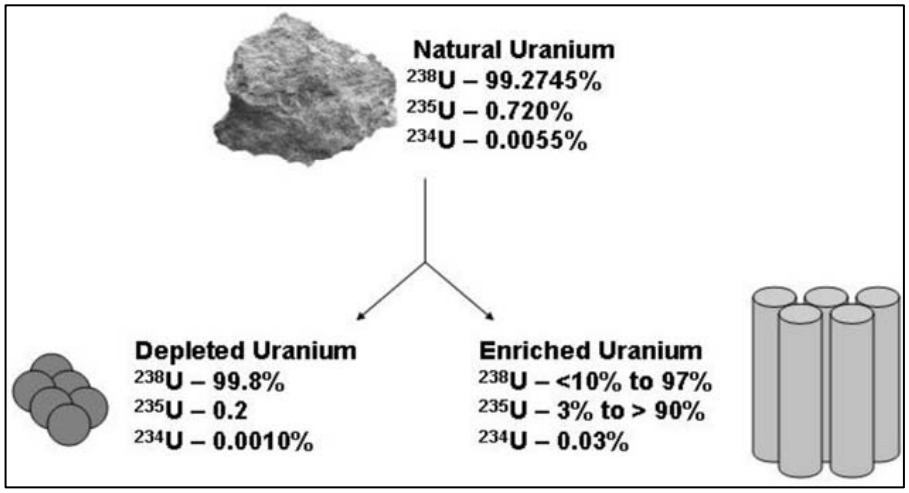

Fig. 1 Uranium forms and isotopes.[6]

The U.S. military deployed DU munitions for the first time during the 1991 Gulf War. DU weapons were also used in the 1994– 1995 war in Bosnia, the 2002 U.S. invasion of Afghanistan and in Iraq in 2003.[1]

However, until recent years little attention was paid to the potential toxic effects of uranium on reproduction and development. Moreover, most experimental studies on uranium-induced developmental toxicity have been performed in a sole species of mammals, mice.[4]

Until recent years, the potential adverse effects of uranium exposure during pregnancy had been scantly investigated, with an evident lack of published observations.[4]

Potential mechanisms of toxic action of DU alloy include mutagenicity and genotoxicity, disturbances in cell division, changes or inhibition of protein or steroid synthesis, disturbance or inhibition of enzyme systems, and disruption of behavioral patterns involved in normal reproduction.

The end product of these mechanisms may be:

1) increased or decreased cell death;
2) disturbed cell-to-cell contact;
3) reduced biosynthesis;
4) increased morphogenetic pattern formation;
5) disruption of tissue structure that may lead to abnormal pathogenesis in the reproductive system or developing fetus. If the repair processes inherent to fetal tissue become overwhelmed, dysmorphogenesis of the developing fetus may occur resulting in too few cells or cell products being formed to affect structure and functional maturation of the developing individual.

Depleted uranium exposure routes

The three traditional exposure pathways are inhalation, ingestion, and dermal contact (fig. 2). In nonmilitary situations, the main routes of uranium uptake are by inhalation and ingestion. Recently, internalization of DU fragments resulting from embedding of projectile fragments has increased because of the military's use of DU in ammunition and must now be considered as a potentially significant route of exposure for DU.[6]

The risk of uranium inhalation increases during or following the use of DU munitions. This is because the impact of the ammunition will cause DU to become aerosolized, forming oxides and small particles that become suspended in the air by the wind, or settle into the environment for later resuspension.

The ingestion route of entry becomes important if food and drinking water are contaminated by DU. Additionally, ingestion of soil by children is considered a potentially important exposure pathway. The daily intake of uranium in food is estimated to be between 1 and 2 μg/d.[7]

Typically, dermal contact is a relatively unimportant route of exposure because DU does not pass through the skin into the blood unless there are open wound.

Animal studies of developmental toxicity from exposure to depleted uranium

Maynard and Hodge, identified uranium as a possible reproductive toxicant in rats. Fifty male/female pairs were fed diets of Purina Fox Chow containing 2% uranyl nitrate hexahydrate [UO2(NO3)2] for seven months and were then placed on control diets of Purina Fox Chow for an additional five months.[9]

A satellite control group of 50 male/female pairs was fed stock rations of Purina Fox Chow for the duration of the 12-month experiment. Both groups were allowed to breed continuously and the number of litters and average number of pups per litter were recorded. After the first seven months, average body weights of both male and female breeders were depressed as compared with those of the satellite control group.

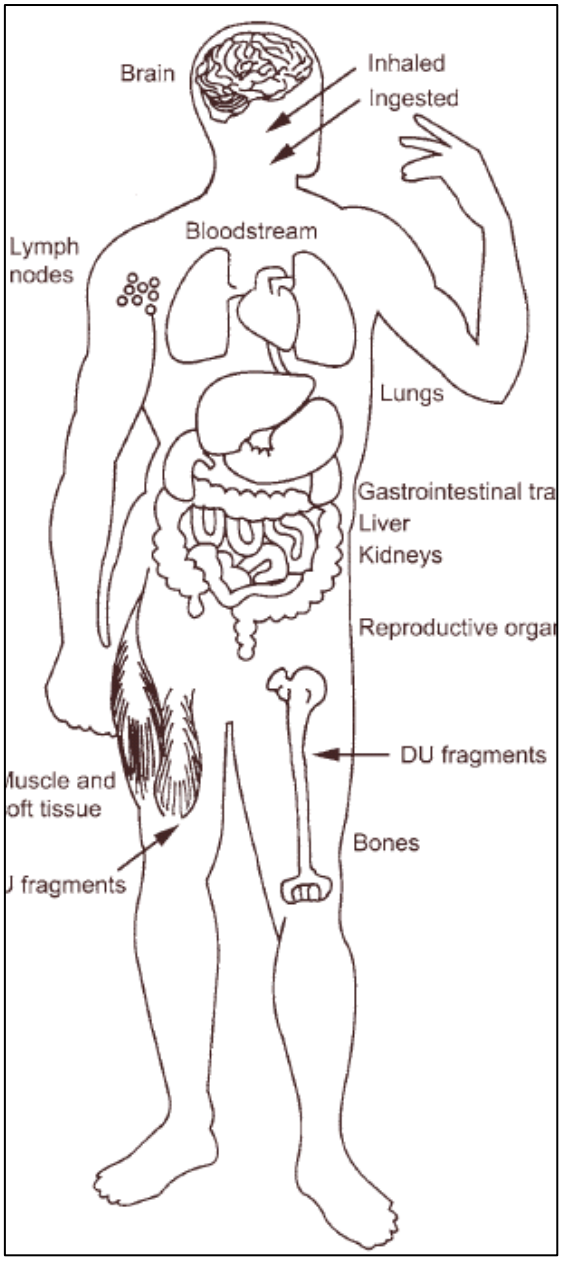

Fig. 2: The three traditional exposure pathways; inhalation, ingestion, dermal contact and the main routes of uranium uptake.[6]

At the end of seven months, the control breeder pairs had given birth to 249 litters as compared to 135 litters for uranium exposed breeding pairs. The average number of young per litter was also lower with uranium-exposed pairs giving birth to 7.8, 7.8, and 7.5 pups per litter for the first, second, and third litters as compared to 7.9, 9.9, and 9.7 for these same litters born to control breeders. The average body weight of uranium-exposed breeders increased noticeably after their diets were shifted to the diet of satellite controls.[9]

However, body weights of uranium-exposed animals were still below those of controls at the end of the

12-month experiment with average female body weights of uranium exposed breeders 25–40 g below those of satellite control females.

Females in the uranium-exposed group that did not have litters over the first seven months of the experiment did not have any litters over the last five months of the experiment. It was concluded that the decrease in reproductive success in uranium-exposed animals may have been an indirect effect resulting from decreased food intake as evidenced by depressed body weights and irregular estrous cycles.[9]

Benson, implanted adult female Sprague–Dawley rats with up to 12 DU alloy or tantalum steel pellets and mated them with male rats with no exposure to DU. All pregnant females were euthanized on gestation day 20 and the pups were delivered by cesarean section.[8]

There was no effect of DU implantation on maternal weight gain, food and water intake, time-to-pregnancy, or the percentage of litters carried to term as compared with controls implanted with steel only. Similarly, total number of pups per litter, litter sex ratio, and fetal weight were not affected by DU implantation in the mother. No signs of overt teratology were found in any of the litters. However, a trend for increasing uranium concentration in maternal kidney tissue, placenta, and whole fetus tissue was found in relation to increasing number of implanted DU pellets.[8]

According to Bosque et al., 1992, Domingo et al., 1989; and Paternain et al., 1989 exposure of the pregnant rodent dam to uranium either by oral gavage or subcutaneous injection produces maternal toxicity, as well as fetotoxicity and developmental defects.

Exposure of both male and female adult Swiss mice to uranyl acetate dihydrate by oral gavage at 5–25 mg/kg per day before mating and through gestation did not have an apparent affect on the ability to reproduce, according to Paternain. However, the total number of absorptions and dead fetuses were increased and the number of live-born fetuses was decreased among litters from parents exposed to a dose level of 25 mg U/kg per day.[10]

Pup body weight and length were also significantly reduced as compared with controls when measured at birth and on postnatal days 4 or 21 indicating that uranium retarded growth in uranium-exposed litters.

Domingo et al. observed in their study that fetal growth was reduced and a higher incidence of cleft palate and dorsal and facial hematomas was found among litters from pregnant Swiss–Webster mice dosed with uranyl acetate dihydrate at 5–50 mg/kg per day by gavage on gestational days 6–15 .A dose-related increase in liver weight was found among pups with increasing maternal dose levels of uranyl acetate dehydrate.

Brain, heart, lung, kidney, and spleen weights of pups with exposure to uranium during gestation and lactation were not significantly different from the weights of these organs from control animals.

Bosques et al. (1992), noticed that after administration of 1/40, 1/20, and 1/10 of uranyl acetate dihydrate by subcutaneous injection on gestational days 6–15 resulted in both maternal toxicity and embryotoxicity at all dose levels (0.5, 1.0, and 2.0 mg/kg per day).

Fetotoxicity characterized by significant decreases in fetal weight and incomplete bone ossification at several sites was observed in offspring born to dams exposed to 1 or 2 mg/kg per day. He found that the number of dead and reabsorbed fetuses and percentage of postimplantation loss was greatest on day 10 of gestation following single subcutaneous injections of uranyl acetate dihydrate (4 mg/kg) on gestation days 9 – 12. Also, fetal weight was significantly reduced and a higher incidence of skeletal variations occurred among surviving offspring as compared with negative controls.[11]

Human fetal malformations due to exposure to depleted uranium

There are only a few human studies so far that looked at the relationship between depleted uranium and congenital malformations (fig. 3). The present studies were a result of the observations made in military combat area in the postwar period.

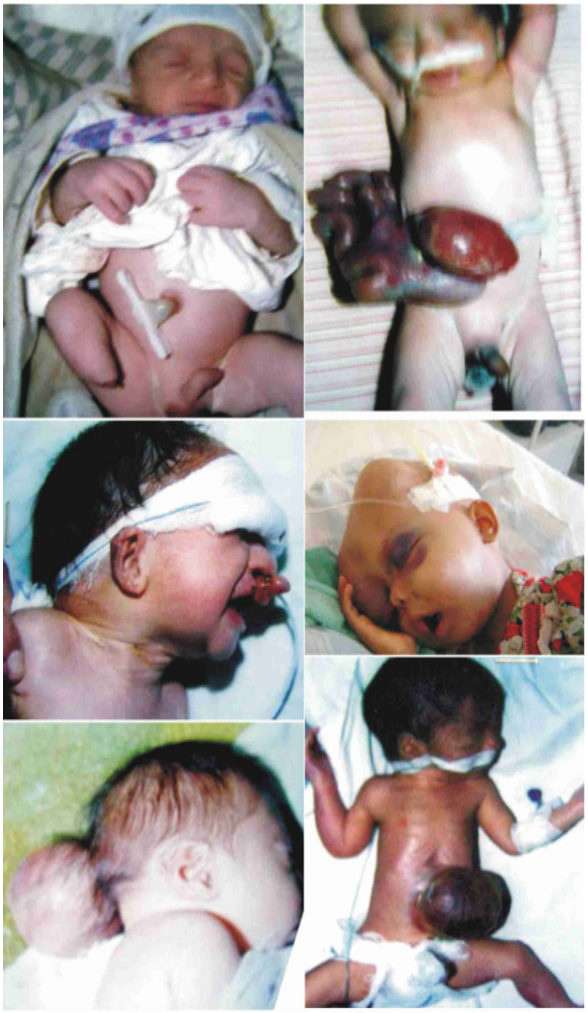

Fig. 3: Photos of Babies Deformed at Birth as a Result of Depleted Uranium (DU) 2003 (Dr. Jenan Hassan).

The Nuclear Policy Research Institute, USA reports that as early as 1995-96, Iraqi doctors suspected a rise in leukemia and birth defects among children born or treated at the Women and Children's Hospital in central Basra, Iraq's second largest city.

The hospital diagnoses all children less than 15 years of age in the whole government of Basra with a malignancy or suspected malignancy.

The Iraqi studies, the only population-based studies available, have their limitations including a lack of independent measures of exposure such as tissue and urine samples, no control city for comparison, mobile population so that some exposed individuals moved from the area while unexposed people moved into the area and, as a retrospective study, a question of assessment bias.

The findings can be summarized as following:

• 1990 - 2001 rate of malignancies per 100,000 children < 5 years of age has tripled.

• 1993-2000 rate of malignant diseases in children compared to 1990 has quadrupled.

• Children under 5 with leukemia:

o 2 cases reported in 1990

o 41 cases reported in 2000

• Congenital Malformations: Incidence per 1000 births

o 3.04 cases reported in 1990

o 17.6 cases reported in 2000

Additional information comes from, Imad Al-Sadoon et al., who performed an analysis of registered congenital malformation among births in Basrah, Iraq for the period from 1990 to 2000.[12]

In general there was an apparent increase in the incidence rate from 1995 upwards. In 2000 such incidence was almost six folds higher than in 1991. To improve statistical efficiency of the data collected and overcome small numbers of cases recorded, the pattern and incidence of congenital malformations are grouped into three periods, 1991 to 1994, 1995 to 1998 and 1999 to 2000.[12]

The incidence rate for the first period was 2.5 congenital malformations per 1000 births while the respective figure for the second period is 4.57 and for the third period were 13.49.

Congenital heart diseases and chromosomal aberrations were reported at a higher frequency during the latter years. Such unusual malformations as phocomelia and icthyosis, which were not reported in 1990 have been recorded later though in small numbers. The frequency of cleft lip and palate followed a similar trend. No apparent trends were observed in the remaining malformations.[12]

Sumanovic-Glamuzina et al., investigated the prevalence of major congenital malformations in West Herzegovina, a part of Bosnia and Herzegovina, immediately and five years after 1991-1995 military activities, which allegedly included the use of weapons with depleted uranium.[13]

The study included all live-born and stillborn neonates and excluded all aborted fetuses in two one-year cohorts (1995 and 2000) of neonates in the Maternity Ward of the Mostar University Hospital.

Major malformations were found in 40 (2.16%) out of 1,853 neonates in 1995 (95% confidence interval [CI], 1.49-2.82%) and in 33 (2.26%) out of 1,463 neonates five years later (95% CI, 1.50-3.01%), ie, at comparable prevalence.[13]

Anomalies of the musculoskeletal system were the most common, followed by anomalies of the digestive system (in 1995) and the cardiovascular system (in 2000).

Authors of this study concluded that against all the current studies that show the teratological influence of depleted uranium, the alleged environmental pollution in some regions of the former Yugoslavia, which was attributed to military activities and the presence of depleted uranium (the "Balkan syndrome"), there was no significant postwar increase in the prevalence of congenital malformations.[13]

In a review on the chemical toxicity of uranium, Stopps and Todd mentioned that during World War II two studies were carried out, one of which featured exposure to high levels of the metal and another involved only a brief 24-hr exposure. Although it was reported that in both studies significant effects on reproduction were observed, the results were not repeated or extended by other investigators.[4]

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