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Evaluation of the effect of implanted depleted uranium on male reproductive success, sperm concentration, and sperm velocity ☆

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Abstract

Depleted uranium (DU) projectiles have been used in battle in Iraq and the Balkans and will continue to be a significant armor-penetrating munition for the US military. As demonstrated in the Persian Gulf War, battle injury from DU projectiles and shrapnel is a possibility, and removal of embedded DU fragments from the body is not always practical because of their location in the body or their small size. Previous studies in rodents have demonstrated that implanted DU mobilizes and translocates to the gonads, and natural uranium may be toxic to spermatazoa and the male reproductive tract. In this study, the effects of implanted DU pellets on sperm concentration, motility, and male reproductive success were evaluated in adult (P1) Sprague–Dawley rats implanted with 0, 12, or 20, DU pellets of 1×2 mm or 12 or 20 tantalum (Ta) steel pellets of 1×2 mm. Twenty DU pellets of 1×2 mm (760 mg) implanted in a 500-g rat are equal to approximately 0.2 pound of DU in a 154-lb (70-kg) person. Urinary analysis found that male rats implanted with DU were excreting uranium at postimplantation days 27 and 117 with the amount dependent on dose. No deaths or evidence of toxicity occurred in P1 males over the 150-day postimplantation study period. When assessed at postimplantation day 150, the concentration, motion, and velocity of sperm isolated from DU-implanted animals were not significantly different from those of sham surgery controls. Velocity and motion of sperm isolated from rats treated with the positive control compound α-chlorohydrin were significantly reduced compared with sham surgery controls. There was no evidence of a detrimental effect of DU implantation on mating success at 30–45 days and 120–145 days postimplantation. The results of this study suggest that implantation of up to 20 DU pellets of 1×2 mm in rats for approximately 21% of their adult lifespan does not have an adverse impact on male reproductive success, sperm concentration, or sperm velocity.

Keywords: Depleted uranium; Reproductive toxicity; Rats; Sperm concentration; Sperm motion

1. Introduction

The impact of embedded depleted uranium (DU) alloy fragments on human health has been an ongoing subject of study since the first use of DU projectiles in combat in the 1991 Persian Gulf War. Exposure to DU has been blamed for reproductive problems and increased cancer rates in military personnel (Drozdiak, 2001; Durakovic, 2001; Ross, 2001; Schoettler, 2001). The potential health hazards associated with exposure to DU alloy are both radiological and chemical

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(Sztajnkrycer and Otten, 2004; Arfsten et al., 2001; McClain et al., 2001; Miller et al., 1998b) and both modes of toxicity would be expected to occur in cases where DU projectiles or fragments become internally deposited (e.g., embedded) in tissue (Arfsten et al., 2001; McClain et al., 2001). DU predominately emits alpha radiation along with small amounts of beta and gamma radiation (Sztajnkrycer and Otten, 2004; AEPI, 1995) and has a radioactivity that is approximately 60% of the radioactivity of natural uranium (0.4 μCi/g versus 0.7 μCi/g, respectively). DU is likely to be chemically toxic based on the findings of toxicity in animals exposed to natural uranium with the kidney being the likely target organ of DU chemical toxicity (Domingo, 2001). Implantation of DU alloy into rat muscle has been shown to increase the frequency of implantation site soft tissue sarcomas (Hahn et al., 2002) while in vitro studies have shown DU to be mutagenic (Miller et al., 1998a, b) and clastogenic (Miller et al., 1998b) suggesting that embedded DU could be carcinogenic in humans.

An ongoing study of Persian Gulf War (1991) veterans involved in DU friendly fire incidents has found evidence to suggest that DU exposure may be associated with changes in reproductive (McDiarmid et al., 2002) and neurocognitive function (McDiarmid et al., 2000) parameters. Several of these veterans were found to be excreting uranium in their urine at levels greater than background when assessed 9–11 years after the end of the Persian Gulf War (McDiarmid et al., 2004), suggesting that these veterans may be exposed to significant levels of uranium in part or wholly as a result of their exposure to DU in the 1991 Persian Gulf War. Hypoxanthine–guanine phosphoribosyl transferase (HPRT) mutation frequency was found to be correlated with high urine uranium levels in this friendly fire cohort (McDiarmid et al., 2004) and suggests that the veteran's continued uranium exposure could be hazardous. However, further follow-up and research is needed to evaluate the impact of increased HPRT mutation frequency on human health.

There are several possible mechanisms by which embedded DU fragments could possibly affect adult reproduction (Arfsten et al., 2001). DU exposure may cause reproductive toxicity by (1) interacting with germ and other cells of the reproductive system, (2) directly interacting with the central nervous system (CNS), resulting in abnormal reproductive behavior or function, and (3) modifying the CNS, leading to alterations in the secretion of hormones or gonadotropins. There have been no animal studies that have examined the effects of DU exposure on the male reproductive system, but studies in rats implanted with DU pellets have found that DU mobilizes and translocates to the reproductive organs (McClain et al., 2001; Pellmar et al., 1999; Benson, 1998; Benson and McBride, 1997). Administration of high doses of uranium has been shown to cause male reproductive toxicity in rodents. Chronic administration of uranium in the diet to male rats for 2 years at concentrations of 0.01–0.25% was found to be associated with aspermia and degenerative changes in the testes and epididymis (Maynard et al., 1953). The number of female mice impregnated successfully was significantly reduced following mating with male Swiss mice administered 10, 20, 40, or 80 mg/kg/day of uranium in their drinking water for 64 days as compared with negative controls (Llobet et al., 1991). Exposure to 80 mg/kg/day of uranium was associated with interstitial alterations and vacuolization of the Leydig cells, and the number of spermatozoa present in the epididymis was consistently lower for uranium exposed animals as compared with negative controls (Llobet et al., 1991). Injection of male rats with uranium compounds was shown to result in significant decreases in average testes weight (Malenchenko et al., 1978). Testicular injection of male mice with uranyl fluoride containing enriched uranium resulted in a dose-dependent increase in chromosomal aberrations in spermatogenia, primary spermatocytes, and mature sperm possibly as a result of both chemical and radiological toxicity (Hu and Zhu, 1990; Zhu et al., 1994).

In 2002 the Naval Health Research Center Detachment Environmental Health Effects Laboratory, formally Detachment Toxicology, applied for and was granted funding by the US Army Medical Research Acquisition Activity (USAMRAA) through the Peer-Reviewed Medical Research Program (PRMRP) to conduct a two-generation reproductive toxicology study of implanted DU pellets in rats. This paper describes the reproductive studies conducted on adult male rats implanted with DU pellets at 30–45 and 120–145 days postimplantation. Each animal was surgically implanted with 0, 12, or 20 DU pellets of 1 × 2 mm. Tantalum (Ta) steel pellets were used as inert control materials to account for potential physical effects of the pellets on reproductive health and behavior. Reproductive endpoints measured in this study included sperm motility and concentration, mating success, and average time to insemination used as an indirect measurement of reproductive behavior relative to that of untreated controls animals.

2. Materials and methods

2.1. Metal pellets

Cylindrical depleted uranium alloy (99.2% DU, 0.8% titanium) pellets, 1 × 2-mm diameter, were obtained from the United States Department of Energy (Y-12 National Security Complex (BWXT Y-12), Oak Ridge, TN) under DOE Project No. 2348-S535-A1. The