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Dr. Margaret Chan
Director General of the World Health Organization (WHO)
WHO, CH-1211 Geneva 27, Switzerland

Dear Dr. Margaret Chan,

We, the International Coalition to Ban Uranium Weapons (ICBUW), are a global civil society network working towards a ban on the use of conventional uranium munitions; weapons that we consider to be both inhumane and indiscriminate. Worldwide public concern about the impact of uranium weapons on human health and the environment has been increasing in recent years as a more complete understanding of their hazards has developed.

As far back as 2002, the former UN Secretary General Kofi Annan expressed concern about the environmental threats posed by new technologies such as depleted uranium (DU) ammunition in a message delivered on 6th November 2002, which marked the first observance of The International Day for Preventing the Exploitation of the Environment in War and Armed Conflict [resolution 56/4].

In December 2008, the UN General Assembly considered: “the potential harmful effects of the use of armaments and ammunitions containing depleted uranium on human health and the environment,” and adopted its second resolution on the issue entitle: “*Effects of the use of armaments and ammunitions containing depleted uranium*” [A/RES/63/54]. And, in accordance with the resolution, the UN Secretary General has requested relevant international organizations, including the WHO, to update their research on the effects of the use of DU weapons on human health and the environment, in time for a discussion on this issue at the 65th UN General Assembly in 2010.

ICBUW strongly requests that the WHO seriously consider the issue of DU weapons from a humanitarian perspective – and accept that the need to protect civilian health in armed conflict is paramount. Because of the growing concerns over the indiscriminate nature of these weapons, both the European and Latin American Parliaments have called for immediate moratoriums on their use, correctly classifying them along with anti-personnel landmines and cluster munitions as inherently inhumane. It is now up to the UN and, by extension its agencies to facilitate further action on this issue.

It came as a great disappointment to many NGOs that DU weapons were used again in Iraq in 2003 after the publication of the WHO’s monograph on DU in 2001.

The WHO has not yet fully referenced current scientific papers on the issue since the publication of its monograph on DU in 2001, although your organization has come out with several short reports,

including one in 2003. The WHO also submitted a view to the UN Secretary General in June 2008, this was based on its previous reports and again failed to reflect the current state of our understanding of the issue.

Recent peer-reviewed papers have provided us with a more cogent understanding of the issue, grounded in data from animal and cellular studies; these studies suggest deleterious effects on human health from DU particles, through both radiological action and chemical toxicity, as well as possible synergistic effects. The data clearly indicate that internalized uranium can cause a broad spectrum of detrimental health effects, including cancer.

That DU is potentially carcinogenic was confirmed by the WHO agency, International Agency for Research on Cancer (IARC), which reaffirmed the carcinogenicity of internally deposited radionuclides that emit alpha particles in volume 100 of their monograph. In the monograph, IARC classifies all types of ionising radiation as “carcinogenic to humans” based on the mechanistic considerations: complex DNA damage caused by ionizing radiation and subsequent processing of this damage including many responses (eg, cell killing, chromosomal aberrations, mutations, genomic instability, cell transformation, and bystander effects) that contribute to carcinogenesis.

We still do not have scientifically reliable epidemiological data from areas affected by contamination from these weapons. This is partly because of the latency period between exposure and development of diseases such as cancers. It is also still difficult to conduct full-scale epidemiological studies in affected areas because of the social, economic and security problems typical of post-conflict environments. Furthermore, there has been little interest from the users of DU weapons in assessing their impact on civilian populations.

Under these circumstances, an approach based on the “precautionary principle” is necessary to assess the health effect of DU weapons.

We would like the WHO to consider the following in their update on DU:

1. To review scientifically all peer-reviewed papers published since 2001.

Please refer to the appendix where we have included a list of significant papers that we believe should be reviewed by the WHO.

2. To consider the probability that we are facing a novel form of uranium contamination as a result of the legacy of these weapons.

The ceramic particles in DU aerosols that are created at extremely high temperatures when a DU shell impacts a tank, may have no analogue in history. The very fine micron- and nano-sized particles that are created in the extreme heat generated from an impact can be easily inhaled and can travel throughout the body. Therefore, it is inaccurate to focus only on the radiological toxicity to the lungs and the chemical toxicity to the kidneys, which were the focus in epidemiologic studies of uranium miners and nuclear industry workers.

3. To assess fully the risk to children and pregnant women, who may be particularly sensitive to DU contamination.

4. To understand that the International Basic Safety Standards (BSS), which were derived from the “risk-benefit theory”, can never apply to the risk assessment of weapons.

In the case of DU weapons, the civilians living in affected areas will never enjoy any benefit from their use.

5. To consider the “precautionary principle” in making recommendations to avoid any further contamination and potential harm from DU, which may result from the continued use of these weapons.

ICBUW requests that the WHO approach this issue in a transparent and scientifically open manner and we invite your organization to launch a constructive dialogue with us in order to accurately define the risk to civilian populations posed by uranium weapons.

We look forward to your response.

Sincerely yours,

Katsumi Furitsu M.D. Ph. D.
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Appendix

List of Recent Research on Depleted Uranium

[Revised in Nov. 22, 2009]

LEUKEMIA, CANCER, CHROMOSOMAL ABERRATIONS

F.F. Hahn, et al., Implanted depleted uranium fragments cause soft tissue sarcomas in the muscles of rats, **Environ. Health Perspect.** **110**; 51-59, 2002.

Hahn and co-workers showed that implanted DU squares in the thigh muscle of rats could cause soft tissue sarcomas if the size of the squares were at least 2.5X2.5 mm or 5.0X5.0 mm in size. Results indicated that DU squares caused tumors in the vicinity of the squares, accompanied by fibrosis and inflammation. The researchers speculated that radiation might have been involved in the carcinogenic reaction of muscle tissues near the DU squares.

Alexandra C. Miller et al., Leukemic transformation of hematopoietic cells in mice internally exposed to depleted uranium, **Molecular and Cellular Biochemistry.** **279**(1-2); 97-104, 2005.

Mice implanted with DU pellets were injected with murine hematopoietic cells. Seventy-six percent of the DU-exposed mice developed leukemia.

Alexandra C. Miller et al., Observation of radiation-specific damage in human cells exposed to depleted uranium: dicentric frequency and neoplastic transformation as endpoints, **Radiat. Prot. Dosimetry**, **99**(1-4); 275-278, 2002.

This study demonstrated that the radiation component of depleted uranium can cause specific effects in human bone cells. DU produced a significantly higher number of dicentric chromosomal abnormalities than the heavy metals nickel and tungsten. Human bone cells were also exposed to DU and two other uranium compounds, all with differing isotopic concentrations and specific activities. The three uranium compounds caused different rates of neoplastic transformation in the bone cells, indicating a radiation effect for DU in as much as the three compounds were chemically similar in their effect.

Alexandra C. Miller, et al., Potential late health effects of the heavy metals, depleted uranium and tungsten, used in armor piercing munitions: comparison of neoplastic transformation and genotoxicity using the known carcinogen nickel. **Mil. Med.** **167**(2 suppl): 120-122, 2002.

This was the first study to demonstrate that DU exposure could cause dicentric chromosomal abnormalities (a radiation effect) in human cells. DU exposure yielded a 25-fold increase in transformed cells as opposed to controls. Exposure of cells to a nickel compound produced only a 9.5-fold increase over control cells. This study proved for the first time that DU is genotoxic in vitro.

Alexandra C. Miller et al, Transformation of Human Osteoblast Cells to the Tumorigenic Phenotype by Depleted Uranium – Uranyl Chloride, **Environ. Health Perspect.** **106** (8), 465-671, 1998.

Miller and colleagues showed in this experiment that depleted uranium (DU) in the form of uranyl chloride can transform human bone cells to a malignant type. The transformed cells were injected into athymic nude mice; the mice developed tumors within a month, showing that DU is potentially carcinogenic.

The human transformed cells exhibited heightened levels of a ras oncogene, stimulating cell growth and also suppressing the Rb tumor-suppressor gene. DU exposure in the human bone cells also elevated sister chromatid exchanges two-fold per cell. Sister chromatid exchanges are a form of mutation.

REPRODUCTIVE HEALTH, GESTATION PROCESS, FETUS

Emilie Arnault et al., Natural uranium disturbs mouse folliculogenesis *in vivo* and oocyte meiosis *in vitro*, **Toxicology** **247**(2-3); 80-87, 2008.

Arnault and co-workers found that chronic exposure of female mice to uranium nitrate through drinking water over 15 weeks slowed the process of folliculogenesis in mouse ovaries in vivo compared to controls. It also retarded the process of meiosis in vitro leading to a decrease in the number of Metaphase II oocytes. This could potentially result in a reduction in an unfertilizable oocyte or an oocyte culminating in an abnormal embryo. Another finding was that uranium accumulated significantly in mouse bone and kidney but not in mouse ovaries.

J.L. Domingo, Reproductive and developmental toxicity of natural and depleted uranium: a review, **Reproductive Toxicology** **15**: 603-609, 2001.

There are very few scientific papers on exposure to uranium or depleted uranium and reproductive and developmental effects. Domingo reviews 11 studies, over half of which do not have data regarding no observed adverse effect levels (NOAEL). All the studies demonstrate some adverse reproductive or developmental effects. Domingo found that chronic exposure to uranium by male mice caused decreased pregnancy rates in mated females. They also showed that pregnant mice given uranyl acetate dihydrate by gavage led to reduced weight gain and increased liver weight in the mice. Their fetuses showed increased rates of congenital malformation. More research in this area is needed.

Alexandre Feugier et al., Alteration of mouse oocyte quality after a subchronic exposure to depleted Uranium, **Reproductive Toxicology** **26**(3-4); 273-277, 2008.

This study demonstrated that DU ingested by female mice through drinking water at concentrations of 20 and 40 mgL⁻¹ caused absence of the first polar body and/or abnormal perivitelline space in oocytes. The authors linked one or other of these effects to an inhibition of the resumption of meiosis, and impaired oocyte maturation.

DU concentrations from 20 mgL⁻¹ also led to a reduction of healthy oocytes by 50 percent compared to controls. While DU accumulated in mouse bones and kidneys, it did not accumulate in the ovaries. The no observed adverse effect level (NOAEL) was set at 10 mgL⁻¹ of DU (1.9 mg/kg⁻¹ day⁻¹).

Victoria Linares et al., Combined action of uranium and stress in the rat II. Effects on male reproduction, **Toxicology Letters** **158**; 186-195, 2005.

This study showed that female rats mated with male rats that had ingested uranyl acetate dihydrate (UAD) at different concentrations (10, 20 and 40 mg/kg/day) for three months, had a significant reduction in pregnancy rate. The reduction was not dose-related. At the highest concentration of UAD ingested by male rats, their female partners' pregnancy rate was lowered due to restraint stress sustained by her male partner. UAD also caused a significant decrease in number of spermatid in UAD-exposed rats. UAD accumulated in a dose-dependent way in the testis and kidney of rats that ingested UAD. Restraint stress did not cause any significant differences between restrained or unrestrained rats. Histopathological examination of the testes found little basic difference between the testes of rats exposed to UAD and controls although changes in testes of UAD-exposed rats included progressive nonstatistically significant cellular loss.

Stefanie Raymond-Whish et al., Drinking Water with Uranium below the U.S. EPA Water Standard Causes Estrogen Receptor-Dependent Responses in Female Mice, **Environmental Health Perspectives** **115** (12); 1711-1716, Dec. 2007.

This study found that DU is an endocrine-disrupting chemical like diethylstilbestrol (DES) with various

adverse effects on the female mouse reproductive system in both adult and pup females. Exposure doses of uranium were at or below U.S. EPA Safe Water Standards for uranium in drinking water given adult female mice. Results suggest that higher uranium concentrations in drinking water might lead to adverse reproductive health problems over time in women drinking the water. In this study, uranium caused adverse effects similar to those caused by DES.

BRAIN

Wayne Briner and Jennifer Murray, Effects of short-term and long-term depleted uranium exposure on open-field behavior and brain lipid oxidation in rats, **Neurotoxicology and Teratology** **27**; 135-144, 2005.

In this experiment rats were exposed to DU in drinking water for 2 weeks or 6 months. At two weeks, males taking in 150 mg. DU per liter (the highest dose) showed significantly greater line crossing and rearing behavior as compared to controls. There was a statistically different amount of lipid oxidation for both experimental male and female rats compared to controls at two weeks. At six months, the same was true for male rats exposed to 150 mg. DU per liter as compared to controls, and both male and female experimental rats showed significant differences in bolus deposition as compared to controls. Lipid oxidation was also evident at six months but appeared to be influenced by a compensatory mechanism. Other behaviors were involved but these were particularly significant.

C. Bussy et al., Chronic ingestion of uranyl nitrate perturbs acetylcholinesterase activity and monoamine metabolism in male rat brain, **NeuroToxicology** **27**; 245-252, 2007.

Rats were given 40 mg uranium per liter in their drinking water for 1.5, 6 and 9 months. The experimental rats lost weight after 6 and 9 months. Acetylcholinesterase activity was “perturbed” transiently in the cerebellum after 6 months. There seemed to be chronic damage to monoamine metabolism, decreasing both dopamine and serotonin in several parts of the brain, including the cerebellum, after 9 months. Dopamine is important in locomotor activities. Duration of exposure was important.

P. Lestaevel et al., “The brain is a target organ after acute exposure to depleted uranium” **Toxicology** **212**(2-3); 219–226, 2005

Rats were implanted intraperitoneally with 144 ± 10 micrograms/kg⁻¹ or $70 \pm$ micrograms/kg⁻¹ of uranyl nitrate. Effects of the higher dose were evidenced in the kidneys and the brain. After 3 days, the kidneys of rats that had been given the higher dose, showed the equivalent of a subnephrotoxic dose of 2.6 micrograms DU g⁻¹. Rats in both exposure groups took in a significantly reduced quantity of food on the first two days as compared to controls. The higher dose rats suffered a decrease in paradoxical sleep on the third day as compared to controls. The rats in the lower dose group did not sustain any change in their sleep-wake pattern. Rats exposed to the higher dose had traces of DU (1.3 micrograms g⁻¹) but the rats given the lower dose had no traces of DU in their brains.

BONE

S. Fukuda et al., Clinical Diagnostic Indicators of Renal and Bone Damage in Rats Intramuscularly Injected with Depleted Uranium, **Radiation Protection Dosimetry** **118**(3); 307-314, 2006. *In this study, the highest dose (2 mg kg⁻¹) of DU injected into the femoral muscle of rats caused inhibition of bone formation and an increase in bone breakdown in the rats. DU-exposed rats also lost weight, which was related to level of dose.*

E. Tissandie et al., Effects of depleted uranium after short-term exposure on vitamin D metabolism in

rat, **Arch. Toxicol.** 80(8); 473-480, 2006.

This research showed that an acute short-term exposure to DU in rats altered vitamin D metabolism. An initial increase in plasma vitamin D was countered by a severe decrease several days later. Vitamin D is important in bone metabolism. It also promotes heart health and may protect breast cancer survivors from death or the spreading of the cancer.

E. Tissandie et al., *In vivo* effects of chronic contamination with depleted uranium on vitamin D₃ metabolism in rat, **Biochimica et Biophysica Acta** 1770; 266-272, 2007.

Rats took in 40 mg DU per liter in their drinking water for 9 months. This is twice the quantity of uranium found in Finnish drinking water in Kurttio's study. DU influenced the active form of vitamin D and vitamin D₃ (the active form of the vitamin) showed lower levels of the vitamin in brain and kidney.

KIDNEY

Hanaa Berradi et al., Renal Anemia Induced by Chronic Ingestion of Depleted Uranium in Rats, **Toxicological Sciences** 103(2); 397-408, 2008.

Rats were given 40 mg DU per liter in their drinking water for 9 months. Rats who took in the DU showed kidney deterioration and a 20 percent decrease in red blood cell (RBC) count. Renal dysfunction led to an alteration of iron transport and accumulation of iron in the kidney which in turn led to oxidative stress. There was a reduction in a factor protecting kidney cells from apoptosis or cell suicide, leading to kidney injury, including "irreversible tubulo-interstitial lesions". The researchers suggested that the consequent kidney dysfunction would solve the problem of why the RBC cell count had been reduced by 20 percent.

M. Goldman et al, Nephrotoxicity of uranyl acetate: effect on rat kidney brush border membrane vesicles, **Archives of Toxicology** 80(7); 387-393, 2006.

This study found that uranyl acetate caused a decrease in the transport of glucose across the brush border cells of the kidney. Glucose is an energy source for cells.

Bernard S. Jortner, Effect of stress at dosing on organophosphate and heavy metal toxicity, **Toxicology and Applied Pharmacology** 233(1); 162-167, 2008.

Jortner found that rats subjected to a single intramuscular injection of 0.1, 0.3 or 1.0 mg/kg uranium and were severely stressed for a week, did not demonstrate any toxic effects from the stress. However, the two higher dosage levels of DU caused significant elevations of serum creatinine and blood urea nitrogen at days 3 and 7 post-dosage, but returning to normal by day 30. By day 3, the proximal tubule epithelium of the kidney at the two higher doses showed definite signs of necrosis but these had lessened considerably by day 7 and were gone by day 30. The lowest dose of DU did however cause some necrotic cells in the proximal tubule epithelium. Stress did not produce any additional damage to the kidney.

Celine Thiebault et al., Uranium Induces Apoptosis and Is Genotoxic to Normal Rat Kidney (NRK-52^E) Proximal Cells, **Toxicological Sciences** 98 (2); 479-487, 2007.

This study showed that DU from 300uM to 800uM is genotoxic and can cause cell death (apoptosis) – apoptosis can even result from 200uM DU exposure although the DNA damage can be reversed at concentrations up to and including doses of 400uM. At low doses, this study indicates that DNA damage can be repaired. The study also showed that reactive oxygen species (oxidative stress) "is deeply implicated in U toxicity".

Guoying Zhu et al., Renal dysfunction induced by long-term exposure to depleted uranium in rats, **Arch. Toxicol.** **83**(1); 37-49, 2009.

Rats had varying weights (0.1, 0.2 and 0.3 grams) of DU fragments implanted in leg muscle. The rats were studied over 90, 180 and 360 days. Weight loss in the DU-implanted rats was dose-dependent and was statistically significant compared to controls. The major accumulation of DU was in kidney and bone. The aim of the study was to observe alterations in the structure and function of kidneys of rats receiving a chronic exposure to DU. The study showed a marked deterioration of the kidney tissue and changes in kidney function. The authors said, "Our results confirm the hypothesis that the excretion of uranium via kidneys and its accumulation in this organ may result in structural and functional damage to the whole kidney".

K.L. Zimmerman et al., Temporal clinical chemistry and microscopic renal effects following acute uranyl acetate exposure, **Toxicol. Pathol.** **35**(7); 1000-1009, 2007.

According to the abstract, male rats were given a single intramuscular injection of 0, 0.1, 0.3 or 1.0 mg DU per kg. Rats were either swim-stressed or not swimstressed. Rats sustained kidney damage, in some instances quite profound but by 30 days post-DU-exposure, much of it had been reversed. This was true for glomerular changes in all the DU-exposed groups. Swim-stressing the rats made no difference.

IMMUNE SYSTEM

Isabelle Dublineau et al., Modifications of Inflammatory Pathways in Rat Intestine Following Chronic Ingestion of Depleted Uranium, **Toxicological Sciences** **98**(2); 458-468, 2007.

This paper showed that DU in the intestine increased the neutrophil population and decreased the macrophage population. "The ultimate effects of DU chronic contamination could be pathogenic, by either suppression of defense mechanisms or induction of hypersensitivity" because of the effect of DU on the neutrophils and macrophages. Low doses of DU led to inflammation in the intestine and adversely affected the immune system as per the above.

Bin Wan et al, *In vitro* Immune Toxicity of Depleted Uranium: Effects on Murine Macrophages, CD4+T cells, and Gene Expression Profiles, **Environmental Health Perspectives** **114** (1); 85-91, 2006.

The findings of this study implicate DU as potentially leading to cancer, allergies and autoimmune diseases. The research demonstrates how DU can alter immune function and kill immune cells.

CHEMICAL TOXICITY, MUTATIONS AND DNA REPAIR

Virginia H. Coryell and D.M. Stearns, Molecular Analysis of *hprt* Mutations Generated in Chinese Hamster Ovary EM9 Cells by Uranyl Acetate, by Hydrogen Peroxide, and Spontaneously, **Molecular Carcinogenesis** **45**(1); 60-72, 2006.

The researchers found significant differences between mutations induced by UA (a stand-in for DU), hydrogen peroxide and spontaneous generation. UA caused a total of 59 mutations as opposed to 45 mutations induced by hydrogen peroxide and 38 spontaneously occurring mutations. This study indicated that DU through its chemical toxicity causes damage by a mechanism or mechanisms which differ from DU's radioactivity and DU's ability to generate free radical damage (which in this experiment was done by hydrogen peroxide).

Diane M. Stearns et al., Uranyl acetate induces *hprt* mutations and uranium-DNA adducts in Chinese hamster ovary EM9 cells, **Mutagenesis** **20** (6); 417-423, 2005.

DU when exposed to Chinese hamster ovary EM9 cells, formed uranium-DNA adducts which are

compounds. The uranium-DNA adducts produced mutations which could lead to cancer. UA also caused DNA strand breaks and was genotoxic as well.. DU acted as a heavy metal in forming uranium-DNA adducts.

Wendy J. Hartsock et al., Uranyl Acetate as a Direct Inhibitor of DNA-Binding Proteins, **Chem. Res. Toxicol.** **20**(5); 784-789, 2007.

This study shows that DU inhibits repair proteins which ordinarily repair DNA as for example when free radicals (from DU's chemical toxicity and radiation) damage DNA.

Sandra S. Wise et al., Particulate Depleted Uranium Is Cytotoxic and Clastogenic to Human Lung Cells, **Chem. Res. Toxicol.** **20**(5); 815-820, May 21, 2007.

This research showed that insoluble (particulate) DU is clastogenic, meaning that it can induce breakages in chromosomes. Here clastogenicity was determined by the development of chromosomal aberrations. The researchers found significant clastogenicity at high DU concentrations, such as 5 ug/cm² and 10 ug/cm² although at 24 hours, the percent of damaged metaphases in the cells exposed to insoluble DU was statistically significant even at a concentration of 1ug/cm² as compared to controls. Total number of chromosomal aberrations per metaphase were as follows: 6 for a DU concentration of 0.5ug/cm², 11 for a DU concentration of 1 ug/cm², 19 for a concentration of 5 ug/cm², and 32 for a concentration of 10ug/cm² – per 100 metaphases. Soluble DU was not clastogenic even at 72 hours of exposure. It should be noted that a metaphase is the second stage of cell division.

INHALATION AND GENOTOXICITY

Marjorie Monleau et al., Distribution and Genotoxic Effects After Successive Exposure to Different Uranium Oxide Particles Inhaled by Rats, **Inhalation Toxicology** **18**; 885-894, 2006.

The authors point out that “the effects of inhalation of U compounds after complex scenarios of exposure are poorly understood” (p. 892). They found that repeated pre-exposure with one DU oxide followed by exposure to a second DU oxide increased genotoxicity caused by the second compound (UO₄).

M. Monleau et al., Genotoxic and Inflammatory Effects of Depleted Uranium Particles Inhaled by Rats, **Toxicological Sciences** **89** (1); 287-295, 2006.

These researchers demonstrated that inhalation of DU by rats led to DNA strand breaks in broncho-alveolar lavage (lung) cells and the production of hydrogen peroxide as well as an inflammatory response. (Inflammation, like oxidative stress (in this case, hydrogen peroxide) , underlies chronic disease).

M. Monleau et al., The Effect of Repeated Inhalation on the Distribution of Uranium in Rats, **Journal of Toxicology and Environmental Health, Part A**, **69**; 1629-1649, 2006.

This paper's aim was to look at ICRP biokinetic models for workers who were repeatedly exposed to DU through inhalation. They found that ICRP models based on acute exposure might not be valid for certain organs. (They used the work “accurate”).

DNA HYPOMETHYLATION [epigenetic mechanism]

Alexandra C. Miller et al., DNA methylation during depleted uranium-induced leukemia, **Biochimie** (March 25, 2009), doi:10.1016/j.biochi.2009.03.010 (E pub ahead of print)

Using a mouse in vivo leukemogenesis model, the authors showed that aberrant DNA hypomethylation takes place during hemopoietic differentiation in spleen cells in DU-induced leukemia in mice. Other

studies have indicated that heavy metal exposure and also radiation can influence the condition of DNA methylation. The production of hypomethylated DNA in this study is likely evidence of an epigenetic mechanism.

OXIDATIVE STRESS, PRO-OXIDANT EFFECTS

P. Lestaevel et al., Different pattern of brain pro-/anti oxidant activity between depleted and enriched uranium in chronically exposed rats, **Toxicology** **258**(1); 1-9, 2009.

The chief finding of this study was that oxidative stress caused by an overproduction of ROS or free radicals, is highly correlated with the neurotoxicity caused by uranium. Male rats were exposed to DU or EU (4 percent enriched uranium) at a dosage of $2 \text{ mg}^{-1} \text{ kg}^{-1} \text{ day}^{-1}$ in their drinking water for 9 months. There was a direct correlation between uranium levels and lipid peroxidation. The major anti-oxidant systems, superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx), showed a significant increase due to DU exposure, to offset ROS. EU exposure however led to a reduction in anti-oxidant levels. The effect of DU and EU on nitric oxide (NO) metabolism in the brain is discussed; chronic exposure to DU increased the expression of the iNOS gene. NO can be protective or add to uranium's toxicity depending on its concentration in tissue. With regard to iron metabolism, chronic exposure to DU in the cerebral cortex was associated with a dramatic increase in mRNA levels of ceruloplasmin, a discovery of the researchers who hypothesized that ceruloplasmin was safeguarding the cerebral cortex from oxidative stress.

Victoria Linares et al., Pro-oxidant effects in the brain of rats concurrently exposed to uranium and stress, **Toxicology** **236**, 82-91, 2007.

Linares and co-workers demonstrated that rats that ingested drinking water with three different concentrations of uranyl acetate dihydrate (10, 20 and 40 mg/kg/day) over a three-month period, accumulated significant amounts of uranyl acetate dihydrate (UAD) in three regions of the brain. The most UAD accumulated in the hippocampus, followed by the cerebellum and the cortex; all accumulations were significant compared to controls. UAD caused an imbalance in oxidative stress (overproduction of free radicals) in the different areas of the brain leading to changes in the chief constituents of the endogenous system of anti-oxidants, superoxide dismutase (SOD), Glutathione peroxidase (GPx) and catalase (CAT) as they counteracted the free radicals. Free radical production caused lipid peroxidation which could damage cell membranes. Stress restraints on the rats did not basically increase adverse effects in the different regions of the brain but prolongation of the stress brought about oxidative stress in varying degrees in the areas of the brain under investigation.

Victoria Linares et al, Assessment of the pro-oxidant activity of uranium in kidney and testis of rats, **Toxicology Letters** **167**; 152-161, 2006.

In this study, male rats were exposed to 0, 10, 20 and 40 mg/kg/day of uranyl acetate dihydrate (UAD) through drinking water for three months. UAD accumulated in the kidney and testis of the rats in a dose-dependent manner. The amount of accumulation was proportional to changes in the antioxidant systems in the cells. The activity of the anti-oxidant superoxide dismutase (SOD) was significantly increased in both kidney and testis cells. Testis has a high quantity of polyunsaturated fatty acids, like the brain, which are a prime target for free radicals. UAD led to considerable lipid peroxidation in the kidney that was dose-dependent. Another finding in the kidney was a dose-dependent angiomatose transformation of blood vessels that became more severe in restraint-stressed rats. However, in both testis and kidney of rats that were restraint stressed, there were no significant differences in markers of oxidative stress between groups of the same exposure level, such as 40 mg/kg UAD per day.

Adaikkappan Periyakkappan Periyakaruppan et al., Uranium induces oxidative stress in lung epithelial cells, **Arch Toxicol.** **8**(16); 389-395, June 2007.

Rat lung epithelial cells were treated with 0, 0.5 and 1.0 mM concentrations of uranyl acetate (DU), causing oxidative stress (an excess of damaging free radicals compared to endogenous defensive anti-oxidant proteins which neutralize free radicals). One such anti-oxidant system was reduced by 50 percent at a UA concentration of 1 mM, indicating that the anti-oxidant protein (SOD-2) could not keep up with the neutralization of free radicals. When the UA-treated lung cells were supplied with individual anti-oxidants including vitamin E, oxidative stress was reduced. The researchers found that increased oxidative stress reduced cell proliferation and increased the oxidation of lipids, and potential damage to cell membranes. The authors conclude by saying that the increase in oxidative stress due to UA exposure may lead to mutations. (Free radicals like inflammation are found in chronic disease).

Jalal Pourahmad et al., A Search for Cellular and Molecular Mechanisms Involved in Depleted Uranium (DU) Toxicity, **Environmental Toxicity** **21**(4); 349-354, 2006.

Another paper dealing with DU here in the form of uranyl acetate. Isolated rat liver cells were exposed to UA. UA caused cytotoxicity and the production of reactive oxygen species (free radical generation) as well as collapse of the mitochondrial membrane (the mitochondria in cells is where energy (ATP) production takes place. UA “causes severe ATP depletion” among other types of injury such as lipid peroxidation. The research also focuses on how some of these problems can be mitigated.

DRUGS

Y. Gueguen et al., Effect of acetaminophen administration to rats chronically exposed to depleted uranium, **Toxicology** **229** (1-2); 62-72, 5 January 2007.

Rats received 40 mg DU per liter of drinking water for 9 months. Acetaminophen is a common drug which is safe but an overdose can adversely affect the liver and kidney of sensitive animals. Rats were given one dose of 400 mg/kg of the drug which is a slightly toxic dose. Chronic low doses of DU in sensitive animals led to toxicity especially in the kidney. The CYP2E1 gene (part of the CYP gene family), known to be involved in acetaminophen toxicity was increased three times over in the DU-exposed rats as compared to controls. DU reduced the activities of the CYP gene in both the liver and the kidney. This could explain increased levels of acetaminophen in the plasma and altered metabolism.

Y. Gueguen et al, Short-term hepatic effects of depleted uranium on xenobiotic and bile acid metabolizing cytochrome P450 enzymes in the rat, **Arch. Toxicol.** **80**; 187-195, 2006.

Bile acids are needed for the digestion and absorption of dietary fat. Rats were given a single subcutaneous shot of DU – a sublethal toxic dose. Rats were examined at 1 and 3 days after exposure to DU. Livers had reduced weight and liver lipid metabolism was altered by day 3. DU exposure even on day 1 showed “onset of a major renal dysfunction”. Plasma triglycerides levels were also reduced. Cholesterol is broken down to form bile acids and the findings of the study suggested that metabolism of cholesterol in the liver was affected by the DU exposure. The results also suggested that the disruption of xenobiotic metabolism in the liver could lead to dysfunction in the liver’s ability to detoxify xenobiotics, “particularly for medical drugs”. They also hypothesized that DU’s negative effect on certain types of liver metabolism over time could result in lipid diseases. (See Souidi et al. for a definition of “xenobiotic”).

M. Souidi et al., *In vivo* effects of chronic contamination with depleted uranium on CYP3A and associated nuclear receptors PXR and CAR in the rat, **Toxicology** **214** (1-2); 113-122, 15 October 2005. *Souidi and co-workers investigated the effect of DU through drinking water (40 mg DU per liter of water or 1 mg DU/rat/day) in rats over a 9-month period in order to study the ability of rats to*

metabolize xenobiotics – which include drugs, carcinogens and insecticides. Their results suggested that in this instance DU acts as a heavy metal and can interfere with the metabolism of drugs and other xenobiotics.

ACUTE TOXICITY

Satoshi Fukuda et al., Acute Toxicity of Subcutaneously Administered Depleted Uranium and the Effects of CBMIDA in the Simulated Wounds of Rats, **Health Physics** **96** (4); 483-492, April 2009. *Fukuda and co-workers demonstrated that DU subcutaneously injected into a wound in male rats caused damage at the site of the wound and accumulated in different organs, The rats received either of two doses, 4m/kg⁻¹ or 16mg/kg⁻¹ per day in a pH 1 solution or a pH 7 solution, the latter chosen to look at chemical toxicity. The 4 mg kg⁻¹ in the pH 1 solution retained 57-61 percent of the DU at the injected site 1-3 hours after injection. Fifty-three to 71 percent of the higher dose (also pH 1 solution) was retained at the injection site for the entire 24 hours. The percentages were lower for both pH 7 solutions. Urinary and fecal uranium excretion increased with time after injection. Histologic study using a light microscope showed structural damage in the kidney especially in the pH 7 group. Liver and femur also sustained damage as indicated by abnormal levels of BUN and other markers. DU-injected rats were exposed to the chelating agent, CBMIDA. CBMIDA significantly reduced DU accumulation at the wound site as well as decreasing DU concentrations in bone and kidney in the low dose pH 1 group. In addition, CBMIDA significantly increased excretion of DU in the urine and feces.*

HUMAN STUDIES

Rosalie Bertell, Depleted Uranium: All the Questions about DU and Gulf War Syndrome are not yet Answered, **International Journal of Health Services** **36**(3); 503-520, 2006. *This is a far-ranging paper on the many ills that may result from exposure to depleted uranium munitions. The author is concerned about the illnesses experienced by veterans and also residents of Oak Ridge. The paper deals with DU's radiation and high chemical toxicity as a heavy metal. The free radicals created by DU's radiation and chemical toxicity disrupt cellular metabolism and in a number of ways create the background for chronic disease as well as the symptoms of Gulf War Illness. Bertell also indicates the unique qualities of the DU aerosol which includes sublimated metal particles from the struck tank, all of which become harmful debris in the body. [There was an error on p. 505 and an error message was published in the next issue of the journal. The correction was that in one day, 1 milligram of pure U-238 would release 1,073.9 alpha particles rather than 1,071,000 alpha particles.]*

Paivi Kurttio et al., Bone as a Possible Target of Chemical Toxicity of Natural Uranium in Drinking Water, **Environmental Health Perspectives** **113** (1); 68-72, January 2005. *Kurttio and co-workers found that high concentrations of natural uranium in drinking water (median daily uranium ingested was 36ug) led to increased bone turnover in Finnish men. Over half of the men in the study drank water with higher concentrations of uranium than the WHO guidelines which are now 15ug per liter. Women were not affected. Prior research had determined that uranium in drinking water increased fractional excretion of calcium and phosphate through the kidneys.*

M.A. McDiarmid et al., Surveillance Results of Depleted Uranium-Exposed Gulf War I Veterans: Sixteen Years of Follow-Up, **Journal of Toxicology and Environmental Health, Part A**, **72**(1); 14-20, 2009.

This study showed that 35 Gulf War I veterans were still excreting uranium 16 years after exposure to DU in friendly fire incidents. At least 13 veterans had embedded DU shrapnel in their bodies. Isotope

analysis ($^{235}\text{U}/^{238}\text{U}$) revealed that 12 participants, 11 of whom had embedded shrapnel, tested positive to DU. 19 others had urine samples with total uranium that the researchers found too low to test for the presence of DU; lowest limit of detection was 0.001 microgram. The study, the 7th in a series of surveillance studies, included several new participants; the rest of the participants had not been in all the studies. The study consisted of two groups, the high urine uranium group (N=10) and the low urine uranium group (N=25) with a cut-off point between the groups of 0.1 micrograms per gram creatinine. With such a small sample size and the lack of a non-exposed control group, it is difficult to compare studies or extrapolate results to other veterans.

Snezana Milacic et al., Examination of the health status of populations from depleted-uranium-contaminated regions, **Environmental Research** 95; 2-10, 2004.

This study investigated blood cell parameters and chromosomal aberrations in subjects from 3 regions in the Balkans where DU munitions had been used during the Balkans' conflicts. Control groups consisted of subjects from a non-contaminated area and a group of occupational workers exposed to X-rays. The group from Vrange/Bujanovac, an area contaminated by DU, had the highest incidence of rogue cells (multidamaged cells) and chromosomal aberrations (cells with dicentrics, ring-centric or acentrics) in any of the DU-exposed groups. The X-ray occupational workers had the highest incidence of chromosomal aberrations, significantly higher than the Vrange-Bujanovac group but not a higher incidence of rogue cells than the Vrange-Bujanovac group. Nuclear and cytoplasmic changes (toxic granulations) were found in 85 percent of Kosovoan subjects and in 67 percent of subjects from Vrange-Bujanovac in contrast to 15 percent in the control unexposed group. DU contamination in the areas in this study was low for the most part and basically present in soil only.

Randall R. Parrish et al., Depleted uranium contamination by inhalation exposure and its detection after ~20 years: Implications for human health assessment, **Journal of the Science of the Total Environment** 390(1); 58-68, 2008.

Parrish and his team found that 5 former workers and up to 4 residents or former residents, had DU in their urine over 20 years after their last exposure to DU aerosols from the National Lead Industries factory in Colonie, New York which had produced DU weapons and was closed down in the early 1980's. DU contamination in the vicinity had been heavy during the time the factory was open and producing uranium products as well as DU weapons. Those tested were ill but this was not a health study. The researchers would like to do a health study of workers and former workers at factories producing DU munitions.

H. Schröder, et al., Chromosome aberration analysis in peripheral lymphocytes of Gulf War and Balkans War, **Radiation Protection Dosimetry**, 103 (3); 211-219, 2003.

A study of 16 ill Gulf and Balkans War veterans thought to have been exposed to DU through inhalation, demonstrated a 5.2 greater than expected rate of dicentric and ring centric chromosomal abnormalities in the peripheral lymphocytes of the veterans. Dicentric and ring centric chromosomal abnormalities are considered to be due to ionizing radiation.

TRANS-GENERATIONAL EFFECTS

D. P. Arfsten et al., Two-Generation Reproductive Toxicity Study of Implanted Depleted Uranium (DU) in CD Rats, **Journal of Toxicology and Environmental Health, Part A**, 72; 410-427, 2009.

This is a study of rats over three generations (F0, F1 and F2) to ascertain what the effect of DU exposure in the F0 generation was on the different generations. F0 rats were exposed to varying amounts of DU from DU pellets (1X2 mm) implanted in leg muscles. Some rats were unexposed but their mates had implanted DU pellets. Rats with implanted inert tantalum (Ta) pellets served as

controls or several groups of rats mated with rats with DU pellets, had Ta pellets. DU-exposed males were implanted with either 12 or 20 DU pellets. DU-exposed females were implanted with 4, 8, 12, or 20 DU pellets. In addition to tantalum controls there was a sham surgery control group of rats. Twenty DU pellets implanted in a rat was considered to be equivalent to the body burden of 0.22 Kg in a 70 Kg man.

This complicated study indicates that there is no difference between treatment groups (including Ta and sham surgery control groups) on most indices such as weight gain in pregnant females and in pups, sperm parameters (mostly) and neurobehavior. The researchers did not find any clinical signs suggestive of illness or toxicity (p. 410).

However, this study showed some suggestive evidence for trans-generational effects of DU. In the F1 generation, 7 rats from three DU groups – with at least one parent having 12 implanted DU pellets – or both – died before postnatal day 120. That is, 7 died out of 54 rats in the groups from which the 7 dead rats had died. Also in F1 female rats, mean relative liver and heart weights were significantly greater than those descended from sham surgery control rats. (The DU group this was true of was the group where both parents had each been implanted with 12 DU pellets).

Also in the F1 generation, mean pup weight per litter was significantly lower for young whose fathers had had 20 implanted DU pellets, than mean pup weight per litter for rats from Ta- implanted parents. However this difference was not significant compared to sham surgery controls.

F2 generation males descended from grandparents who both had had 20 implanted DU pellets, had significantly lower mean relative heart weights compared to F2 controls. F2 males from this same group had sperm VSL's (progressive straight line velocity) that were significantly different from Ta-control descended rats.

In their conclusion, the researchers note the deaths in the F1 generation as possibly being a DU-effect. They also mention "possible hyperactivity" in females with high numbers of implanted DU pellets and some F1 adult rats but this was not highlighted in the text.

NON-MAMMALS

Sabrina Barillet et al., Bioaccumulation, Oxidative Stress, and Neurotoxicity in *Danio Rerio* (Zebra Fish) Exposed to Different Isotopic Compositions of Uranium, **Environmental Toxicology and Chemistry** 26(3): 497-505, 2007.

DU and a DU-U²³³ mixture largely accumulated in the gills and liver of Zebra Fish, and additionally in bone, kidneys, gonads and brain. In liver, site of detoxification, DU and also uranium caused the decrease of endogenous anti-oxidant systems (3 in all) important in neutralizing free radicals. One of these anti-oxidants, Glutathione peroxidase, protects membranes from damaging membrane lipids (fats that add structure to membranes). The results of the experiments suggested that radiation effects from uranium and from DU separately, brought about a reduction in several anti-oxidants which took place prior to chemical toxicity effects. DU and uranium exposures also increased the level of the neurological biomarker acetylcholinesterase (AChE) activity by 30 percent. AChE is important in memory and other neurological operations. Research has shown that an increase in AChE could lead to a "continuous depletion of acetylcholine" (a neurotransmitter) which could result in impaired neural transmission and/or could indicate "increased axonal repair".

Stephanie Bourrachot et al., The effects of waterborne uranium on the hatching success, development, and survival of early life stages of zebrafish (*Danio rerio*), **Aquatic Toxicology** 90, 29-36, 2008. Bourrachot and coworkers studied the effects of different concentrations of DU and Uranium²³³ on the

embryo and pro-larvae stage of zebrafish (U^{233} has a higher specific activity than DU). Concentrations of DU ranged from 20 micrograms L^{-1} to 250 micrograms L^{-1} . Accumulation of DU in the chorion (egg envelope) occurred at all DU levels but DU was detected in the embryos of the fish only at the highest DU dosage. Embryonic development appeared to be normal for fish exposed to DU. Hatching rates of eggs from fish exposed to 20 micrograms L^{-1} of DU were statistically different from controls. Body lengths of DU-exposed pro-larvae were statistically significantly shorter than that of controls, at days 9 and 15. Mortality rate by day 15 was 100 percent for the fish in the 250 microgram L^{-1} DU group and was close to 95 percent in the other DU dosage groups. By comparison, 34 percent of control pro-larvae were dead by day 15. The embryos. (Pro-larvae of fish exposed to U^{233} were more severely affected by uranium exposure).

Sarah E. Mitchell et al., Effects of Depleted Uranium on Survival, Growth, and Metamorphosis in the African Clawed Frog (*xenopus laevis*), **Journal of Toxicology and Environmental Health, Part A**, **68**; 951-965, 2005.

This study investigated various levels, mostly high concentrations, of DU and its effect on the embryos and tadpoles of xenopus laevis. The acute exposure experiment in which embryos were immersed in from 4.8 to 77.7 mg/L, lasted 96 hours during which time the yolk sac provided all nourishment and the gills were not fully developed. Total cumulative mortality and malformations were put at under 2 percent although the lowest concentration group had a figure of 2 percent and the assay for teratogenesis (FETAX) registered 8 percent for mortality and 5 percent for malformations. Length was not statistically significant between experimental groups and controls.

In the chronic experiment lasting 64 days, tadpoles were attacked by an external parasite early on, killing all the tadpoles in the lowest DU group (6.26 mg U/L) and over 80 percent in well-water controls and reference controls.

A chief finding of the study was that time to metamorphosis was delayed in the DU-exposed frogs but the difference with the two control groups was not statistically significant.

The water used for these experiments were high in hardness and alkalinity. This leads to DU being potentially bound to carbonates and so less bioavailable. This may have decreased the degree of DU's toxicity, according to the researchers.

THE ISSUE OF MICRO- AND NANO-PARTICLES

C.W. Lam, et al., Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation, **Toxicological Science**, **77** (1); 126-134, 2004.

G. Oberdorster, et al., Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles, **Environ. Health Perspect.** **113** (7); 823-829, 2005.

J.M. Samet, et al., Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994, **The New England Journal of Medicine**, **343** (24); 1742-1749, 2000.

[NON-PEER-REVIEWED PAPER, Heath Effects]

Johnniye L. Lewis et al., "Inhalation of Uranium Oxide Aerosols: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness". October 2003.

Contacting Organization: University of New Mexico Health Sciences Center, Albuquerque, NM 87131-5041

Prepared for: U.S. Army Medical Research and Materiel Command, Fort Detrick, MD 21072.

The researchers investigated different uranium oxides (UO_2 , UO_3 , UO_2+UO_3 and $DUOx$) on the

brains of rats using an acute high dose of 300-660 mg/m³ lasting 15 minutes through nasal-only inhalation. Fifteen rats in the UO₃ treatment group that were to have been sacrificed at 30 days post exposure, died between days 0-12 after exposure. Fourteen rats died of acute renal tubular necrosis and uremic pneumonia from uranium toxicity (UO₃ is a soluble uranium oxide). A rat also from the UO₃ group was found to have detectable uranium in the mitral cell layer of the brain's olfactory bulb at 30 days post exposure. Two hours after exposure, neuroinflammation was found in glomeruli of rats in all uranium exposed groups and in tantalum controls. GFAP immunoreactivity, a marker for the inflammation, was significantly greater in these groups compared to control rats breathing air only. The UO₃ group had the highest level of the marker. No detectable levels of uranium were found in the kidneys of 15 rats sacrificed at 30 days after exposure.

Johnniye L. Lewis et al., "Inhalation of Uranium Oxide Aerosols: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness", October 2004.

Contacting Organization: University of New Mexico Health Sciences Center, Albuquerque, NM 87131-5041

Prepared for: U.S. Army Medical Research and Materiel Command, Fort Detrick, MD 21072.

This 2004 paper continues the research of the 2003 paper. The 12 female rats that died from the UO₃ group in the previous research, had uranium concentrations in their kidneys ranging from ~23 to ~34 mg/kg dry weight. At 30 days post-exposure from the high acute nasal inhalation dose described in the 2003 paper, a mild nephropathy was found in 61 percent of males and 22 percent of females in all the U groups that was greater than the incidence in the control groups. One hundred percent of the rats in the UO₃ and 67-100 percent of the rats in the DUOx treatment groups had pulmonary septal fibrosis. Only rats exposed to uranium compounds (excepting the rats that had inhaled insoluble UO₂) had septal fibrosis. Rats with septal fibrosis also had alveolar macrophage hyperplasia with particles in the macrophages. At 360 days post-exposure, a minimal to mild nephropathy existed in 25 of 37 male rats and in a few female rats, in the U-groups and most rats in the UO₃ and DUOx groups, a female in the UO₂+UO₃ group and a male in the UO₂ group had pulmonary septal fibrosis.

Johnniye L. Lewis et al., "Inhalation of Uranium Oxide Aerosols: CNS Deposition, Neurotoxicity, and Role in Gulf War Illness", October 2005.

Prepared for: U.S. Army Medical Research and Materiel Command, Fort Detrick, MD 21072.

A chronic moderate dose of 1mg Ug/m³ using the compound UO₂+UO₃ with or without endotoxin (a compound that irritates the nasal mucosa) was given by nasal inhalation only to these groups of rats. Of the animals sacrificed at 0 day, two females exposed to either UO₂+UO₃ or UO₂+UO₃+endotoxin, showed detectable uranium concentrations in the glomeruli (rat 1) or in the mitral cell layer (rat 2). (The mitral cell layer is adjacent to the glomeruli). In another experiment rats were re-exposed to 1.0 mg/m³ of UO₂+UO₃ and had weekly instillations of endotoxin. Control rats received air or air with endotoxin. Rats participating in the experiment had originally been exposed for either 30 days or 1 day. Two male rats were found to have detectable U in the olfactory glomeruli. One male had been exposed twice for 30 days and the other had originally been exposed for one day before re-exposure for 30 days. A female (1 of 7) that had been exposed twice for 30 days, had detectable U in both glomeruli and mitral cells. These were some of the findings of the paper.

ENVIRONMENTAL STUDIES, HUMAN CONTAMINATION

Wenming Dong et al., Sorption and bioreduction of hexavalent uranium at a military facility by the Chesapeake Bay, **Environmental Pollution** 142; 132-142, 2006.

The Aberdeen Proving Ground testing site is next to the highly polluted Chesapeake Bay. The researchers took a sample from the surface sediment (sandy) from a marsh near a creek and a sample

(chiefly silt) from the bottom of the creek, which flowed periodically into the bay. Both samples contained organic matter and were from an acid environment. Creek water was also collected, sterilized and used in the experiments. The researchers found that when soluble U(VI) was added to slurries of the sediments, that the U was sorpted to the organic matter quite rapidly. Indigenous bacteria in the sediments/organic matter acted to reduce U(VI) to the insoluble, immobile U(IV). The addition of acetate speeded up the process and brought Clostridiales bacteria to the fore leading to faster reduction of the U(VI) which however was a slow process compared to the sorption of U(VI). Re-oxidation of the U(IV) was a possibility, as was the transport of uranium of either oxidation state into the bay through heavy rainfall.

Guogang Jia et al., Concentration and characteristics of depleted uranium in biological and water samples collected in Bosnia and Herzegovina, **Journal of Environmental Radioactivity** **98**; 172-187, 2006.

The Italian Environmental Protection Agency collected samples of lichen, barks, mosses and mushrooms from at least 8 sites that had been potentially contaminated by DU munitions during the conflict in the mid-1990's. Water samples were also taken. DU was found to be present at very low levels in the majority of the biological samples. It was noted that DU can be taken up by insects and earthworms but no samples were obtained.

Water from two wells at the Hadzici Tank Repair Facility tested positive for DU. Overall, the activity ratios in the water samples were higher than those for drinking water and rivers in Central Italy, but lower than those for mineral water and under the 2004 WHO guidelines for drinking water. However, the researchers stated that DU corrosion products in the soil could migrate and could potentially lead to possible contamination of underground aquifers.

Guogang Jia et al., Concentration and characteristics of depleted uranium in water, air and biological samples collected in Serbia and Montenegro, **Applied Radiation and Isotopes** **63**; 381-399, 2005.

The Italian Environmental Protection Agency went to Serbia and Montenegro with the UNEP team in the fall of 2001, 2-3 years after use of DU munitions by NATO forces. The team's chief concern was the potential problem of groundwater contamination but in addition to water samples, they took biological samples (lichens, mosses, barks, mushrooms) and samples of air. Overall, they found widespread but very low levels of ground-surface contamination. Uranium isotopic concentrations in the biological samples were 0.67-704 Bqkg⁻¹ for ²³⁸U, 0.48-93.9 Bqkg⁻¹ for ²³⁴U and 0.02-12.2 Bqkg⁻¹ for ²³⁵U, values that were greater than control values. Eight air samples tested positive for DU. Uranium isotopic concentrations for water samples taken in Serbia and Montenegro were as follows: 0.40-21.9 mBqL⁻¹ for ²³⁸U, 0.27-28.1 mBqL⁻¹ for ²³⁴U and 0.01-0.88 mBqL⁻¹ for ²³⁵U. Two well water samples tested positive for DU. However, mineral water in central Italy had higher values and the results indicated that there was no significant radiological risk from DU at any of the sites. However, the researchers indicated that groundwater contamination might be a problem in the future.

Guogang Jia et al., Concentration, distribution and characteristics of depleted uranium (DU) in the Kosovo ecosystem: A comparison with the uranium behavior in the environment uncontaminated by DU, **Journal of Radioanalytical and Nuclear Chemistry** **260** (3); 481-494, 2004.

A team from the Italian National Environmental Protection Agency (ANPA) went to Kosovo with the UNEP mission in late 2000. They took samples from DU anti-tank shells lying on the surface soil, from biological specimens (lichen, bark, mosses) and from wells, reservoirs and streams. Analysis of smear samples taken from DU shells gave uranium isotope activity levels of 0.126±0.003 for ²³⁴U/²³⁸U, 0.0144±0.0006 for ²³⁵U/²³⁸U, and 0.0057±0.0004 for ²³⁶U/²³⁸U. Heavily contaminated soil samples gave similar activity ratios: 0.122±0.006 for ²³⁴U/²³⁸U, 0.142±0.0008 for ²³⁵U/²³⁸U and 0.0055±0.0006 for ²³⁶U/²³⁸U. In some soil samples, the uranium concentrations were 7,483 times greater than

background natural uranium levels. DU was detectable in all biological samples; as with the soil, there was wide variation in DU concentrations. DU was detected in water samples from two wells. Uranium concentrations in Kosovoan water samples were low compared to drinking water (mainly mineral water) in central Italy, and below WHO's guidelines for uranium in drinking water, However, the ANPA team was concerned about possible future groundwater contamination.

U. Oeh et al., Measurements of daily urinary uranium excretion in German peacekeeping personnel and residents of the Kosovo region to assess potential intakes of depleted uranium (DU), **Science of the Total Environment** **381**(1-3); 77-87, 2007.

Oeh and co-workers tested over 1,300 urine samples from German peacekeeping personnel all of whom had lived in areas of Kosovo and southern Serbia where DU munitions had been used. The researchers found no significant differences in urine uranium excretion between peacekeepers and controls. The researchers stated that none of the peacekeepers had taken in significant amounts of DU –significance being determined as a dose of 1mSv or more a year or the inhalation of 8.33 mg DU. Urine samples were also taken from residents of Kosovo and southern Serbia where DU munitions had been used. There was a wide variation in the amount of uranium in the samples, from ~3 ng/day to 266.817 ng/day but analysis showed that the samples contained natural uranium or were within +/- 0.3 percent of natural uranium.

Total uranium concentrations in water samples from various sites in Kosovo and Serbia contained no DU although some exceeded the WHO guidelines of 2 micrograms/l for uranium in drinking water. One water sample taken from tap water at a school in Kosovo tested positive to DU.

Ian W. Oliver et al., Distribution and partitioning of depleted uranium (DU) in soils at weapons test ranges – Investigations combining the BCR extraction scheme and isotope analysis, **Chemosphere** **72**(6); 932-939, 2008.

This study looked at DU in partitioned soil samples through the use of the BCR extraction scheme. Soil cores were taken from soil at two British Ministry of Defense firing ranges. Isotopic analysis of uranium in the different partitions in the core samples indicated that DU was present. DU was found to have penetrated to the depth of the soil core, in some instances as far down as 20 or more cm. In general, DU decreased in concentration as it descended the core. The study demonstrated the importance of organic soil material for the retention of DU, rather, that DU was found to be associated with it. The percent of the DU fraction was very highly associated with the exchangeable, reducible and oxidizable fractions in the soil for nearly all samples. This indicated that DU stays in an exchangeable form, can be transported by water and is potentially bioavailable.

Ian W. Oliver et al., Depleted Uranium Mobility Across a Weapons Testing Site: Isotopic Investigation of Porewater, Earthworms, and Soils, **Environ. Sci. Technol.** **42**(24); 9158-9164, 2008.

This paper found that DU present in soil, porewater and earthworms at the Dundrennan firing range in Scotland, was more bioavailable than the natural uranium in the soil. Soil and porewater was taken not only adjacent to the gun pad, but along a straight transect line ending near a stream. Calculation of the U^{235}/U^{238} ratio in all the earthworm tissue samples gave a low ratio, indicating that the earthworms had suffered more DU contamination than the soils they had been in. This showed that the DU was bioavailable. Isotopic analysis using this ratio on porewater also found that the ratio was low, much lower than that of the adjacent soil. This indicated that the DU was more soluble than the natural uranium in the soil and was mobile. The isotopic ratio increased with the increasing distance of porewater from the gun pad, to nearly natural uranium levels at about 185 meters from the gun pad. Except near the gun pad, peaks in uranium in the porewater, occurred with peaks in organic material, indicating that the U present in the porewater was associated with organic colloids.

Mirjana B. Radenkovic et al., Depleted Uranium Mobility and Fractionation in Contaminated Soil (Southern Serbia), **Env. Sci. Pollut. Res.** **15**(1); 61-67, 2008.

This is a highly technical description of DU distribution in 5 sequential extraction phases, in order to investigate DU mobility, contamination distribution and how DU accommodates itself to the soil constituents it interacts with.

The DU penetrator in question was found at a depth of half a meter below the ground surface in Bratoselce. The penetrator caused a hot spot. The specific activity of ^{238}U the site of penetration of the earth was 90 ± 14 Bq/kg and was 263 ± 25 Bq/kg in the soil next to the DU shell. Radiation at approximately 150 mm from the shell was reduced to one percent of the initial radiation or twice the background radiation. The profiles that unfolded during the 5-step extraction process were complex and indicate that the composition of the soil can lead to both the mobility and immobility of DU and U in the soil depending on the circumstances.

B. Salbu et al., Oxidation states of uranium in depleted uranium particles from Kuwait, **Journal of Environmental Radioactivity** **78**(2); 125-135, 2005.

Using SR-based X-Ray u-XANES techniques, Salbu and co-workers were able to determine the oxidation states of DU particles taken from penetrator holes in DU-destroyed tanks and from sand contaminated by DU at the time of the Doha Fire in July 1991, in which 600 pounds of DU were burned and destroyed. Samples taken from the penetrator holes and from sand below the tanks showed small DU particles ranging in size from 2-64 microns (median 13 microns) whose characteristics were similar to the DU found in Kosovo. DU particles from the Doha Fire however were larger (range 0.2-1,500 microns, with median, 44 microns) and had a crystalline structure unlike that seen in DU particles elsewhere. The oxidation states of the DU particles at the Doha site were slightly higher than those of the DU particles from the tank. Doha DU oxidation states were +5 or +6. In samples taken from the tank, the oxide U_3O_8 had an oxidation state of $+5.5\pm 0.5$. Higher oxidation states result in increased particle weathering rates, bioavailability and remobilization of uranium. These oxides will not act like natural uranium.

Umberto Sansone et al., Radioecological survey at selected sites hit by depleted uranium ammunitions during the 1999 Kosovo conflict, **The Science of the Total Environment** **281**; 23-35, 2001.

A team from the Italian National Environmental Protection Agency (ANPA) was responsible for collecting samples of water, soil, lichen and tree bark as well as smears from DU shells during the 2000 UNEP mission to Kosovo. Eighty-five percent of the water samples taken had the signature of natural uranium. Two water samples taken from a well at Rznic indicated $^{234}\text{U}/^{238}\text{U}$ ratios of approximated 0.5, evidence of possible DU contamination of the samples. Overall, ^{238}U activity in the water samples was quite low, lower than that in European waters. ^{238}U activity in soil samples ranged from that in natural uranium ($\sim 20\text{Bq/kg}^{-1}$) to $\sim 2.3 \times 10^5\text{Bqkg}^{-1}$ (or about $18,000\text{ mg/kg}^{-1}$). Soil samples had been taken from areas where A-10 jets had fired DU shells. ANPA took deep cores of soil and was surprised at the degree to which DU migration in the soil had occurred after just 18 months since the conflict. DU was detected in all lichen and tree bark samples, even in samples taken where no DU in the soil had been detected. ANPA was concerned about the possibility of DU contamination of groundwater in the future.

W. Schimmack et al., Leaching of depleted uranium in soil as determined by column experiments, **Radiat. Environ. Biophys.** **44**(3); 183-191, 2005.

The researchers investigated the extent to which DU from anti-tank shells leaches into the soil and to assess the long-term activity of DU in the environment. In the experiment, DU shells or fragments were placed in columns filled with two types of soils common in Europe and seepage water was collected weekly from below the columns over the period of a year. Leaching rates of 0.1 to 10 micrograms per

week were found for concentrations of U^{238} . Leaching variability was high and was especially pronounced in luvisol soil. Mean mass loss of the DU fragment was 3.8 g U^{238} or 1.6 percent of the initial DU mass, over the year. The researchers estimated that the leaching of U^{238} is a long-term process lasting thousands of years.

W. Schimmack et al., Long-term corrosion and leaching of depleted uranium (DU) in soil, **Radiat. Environ. Biophys.** 46(3); 221-237, 2007.

In an assessment of long-term leaching of U^{238} from DU anti-tank shells, Schimmack and co-workers looked at leaching rates in seepage water which collected at the bottoms of columns filled with either cambisol or luvisol soils over a period of 3 years. Each column contained a DU shell or a DU fragment. About 7.9 percent of the mean initial mass of the DU fragment was corroded during the 3 years, at a rate of about 2.7 percent a year.

Mean concentration of U^{238} in the seepage water increased to over 1 mgL⁻¹ in the second year and levels were also high during the third year. At the end of 3 years, mean accumulated leached U^{238} ranged from 0.04 mg to 60 mg. with an over-all mean of about 13 mg. Such variability made any prediction of future leaching rates not feasible. The researchers also found no correlation between the corroded DU mass and the accumulated leached U^{238} that had been collected in the seepage water.