Compendium
of
Uranium
and
Depleted Uranium Research

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Preface

Since it became known that radioactive depleted uranium weapons were used in the 1991 Gulf War by the allied forces against Iraq, there has been considerable debate on the residual effects that these weapons have on the environment and on the health risks to soldiers and to the civilian population living in and around the battlefields where DU weapons are used. Governments and the militaries that use DU weapons insist that their effects are benign. Others, including many medical researchers and scientists, believe that the opposite is true and that these weapons should never be used.

This compendium was compiled in order to help shed light on the DU issue by collecting and organizing references, with summaries and abstracts, to the large amount of scientific research that has been done with uranium and depleted uranium. All citations within this document are to scientific research published in peer-reviewed scientific journals. It is the editor's wish ultimately to include every published peer-reviewed article that can be found, regardless of its results. Thus this publication is an on-going effort with periodic updates as new material is brought to the editor's attention.

Abstracts or summaries are provided with most references. Please note, however, that descriptive material relating to each article has been derived solely from that article's abstract. The editor has neither read nor analyzed the articles cited in this compendium. Any errors or misrepresentations as to the research covered are entirely those of the editor. Please take the time to pass along any comments or corrections to the editor at: dbishop@idust.net.

In each chapter, the citations are listed in chronological order with the most recent citations appearing toward the end of the chapter. Since this is an ongoing effort, citation numbers may include alphabetic letters (e.g. 18C) to allow citations to be inserted into their proper chronological sequence after the initial publication of this compendium.

Each reference has been given a key unique to that article. These keys are listed in the Author Index in Appendix A, and each entry is hyperlinked to that reference. Each key has the following format:

AuthorlastnameYYYYmmJournalAbbreviationVolumeNumberPage

For example: Yazzie200304CRTv16n4p524

Authorlastname is the last name of the primary author (the first author listed) for the paper. The Journal Abbreviation is the first letter of each significant word in the journal name (e.g. JACS for The Journal of the American Chemical Society). Since several different journals may have the same abbreviation, an alphabetical list of these journals is given in Appendix B. In some cases a month may be missing for the date, or a volume number may be missing. In these cases, the unknown numbers are replaced with 'x' or '0'.
By maintaining these keys in the author index, it is a simple matter to check this index to determine if a particular reference has been included in the compendium.

Each chapter covers a single major topic of interest. As might be expected, many articles contain material relevant to several chapter designations. It is therefore important to look through each chapter to find all of the references relating to a topic you might be researching. The choice as to which chapter a citation should belong is entirely the editor's.

Although not reflecting original research, review articles, if they are fair and unbiased, can be an excellent resource for further research, particularly if they are well referenced. Review articles have been included in the compendium. It may be that a specific reference in a review article is included in the compendium, along with its abstract or a summary statement. The Author Index will help you locate these references.

Of course, a review can be tailored to support a given set of conclusions by the choice of articles included and omitted, so the reader must use caution. Here again, this Compendium can be put to good use, in that it will become readily apparent when a review author has purposely omitted articles that provide research evidence contrary to the author's views and conclusions.

The introductory material for each chapter represents an effort to provide a brief but comprehensive overview of the conclusions reached in the articles cited within that chapter, with numbered references (hyperlinked) to the article in that chapter. In this way, the casual reader can be content to read just the chapter introductions, referring only occasionally to a specific citation of interest. The more interested reader and the researcher will find the abstracts or summaries filled with important and useful information and should find this volume to be an invaluable resource.

Since research is an on-going process, the material in this compendium is dated. However, our subject is of such vital importance that we hope to continue to make periodic updates so that this on-line compendium will provide a continuously comprehensive coverage of the state of scientific research in this arena. The title page lists the date of the most recent update and contains a link to a list of updates. Refer to this page periodically to keep abreast of the most recent additions to the compendium.

Introduction

At the outset, the reader must clearly understand that uranium and depleted uranium are radioactive heavy metals. Since the only chemical difference between the two is their isotopic composition, both have precisely identical chemical properties. Any research into the chemical behavior of one also applies to the other.

On the other hand, uranium and depleted uranium do exhibit different radiological properties, although that difference is slight. Both emit alpha, beta and gamma radiation. The alpha radiation results from radioactive decay of the various uranium isotopes present in the sample. The beta and gamma radiation comes from the further radioactive decay of the daughter products that are formed as a result of the uranium decay, primarily thorium and protactinium. The basic difference between depleted uranium and natural uranium is that 70% of the more radioactive U-235 isotope has been removed from natural uranium, leaving a product that is thus depleted in this isotope and therefore called 'depleted uranium'. In terms of alpha emissions only, depleted uranium has 60% of the specific activity (i.e. radiation output) of natural uranium. However, if all three types of radiation, alpha, beta and gamma, are taken into account, depleted uranium has 78% of natural uranium's specific activity. So even though depleted uranium is slightly less radioactive than natural uranium, the differences are small enough that any studies into the effects resulting from exposure to radiation from one can be expected to apply to the other as well.
For this reason the compendium includes citations of research for both uranium and depleted uranium.

The two conclusions above, however, assume that the depleted uranium is not contaminated with elements other than its naturally occurring decay products (thorium and protactinium). If the depleted uranium samples have been obtained from recovered or recycled nuclear reactor fuel, they will invariably be contaminated with other transuranic elements, such as plutonium, neptunium and americium. Since these components are not present in natural uranium, their presence in a sample of depleted uranium could seriously change the chemical and radiological behavior of that sample, both in laboratory tests and in epidemiological studies of health effects resulting from exposure to depleted uranium.

The reader should be alert to the following fact. Uranium and depleted uranium, as heavy metals, have long been recognized to exert toxic effects on exposed living tissues similar to those observed from exposure to chromium, nickel and lead, three non-radioactive heavy metals. It is also widely recognized that exposure to radiation can damage living tissues, particularly if the source of exposure is embedded within those tissues. Since uranium and depleted uranium exhibit both chemical and radiological effects, it is difficult (and perhaps impossible) in practice to separate the two effects in most experiments. One should evaluate with caution a researcher's claim that he/she has done so in a particular experiment. One should also keep in mind the possibility that having both factors present in a single source may lead to synergistic effects wherein the effects actually observed may be more profound than the mere sum of the two individual effects when taken alone.

Another assumption that pervades the scientific community's interpretation of effects resulting from radiation exposure is that exposure to alpha radiation is more harmful to living tissue than exposure to beta and gamma radiation. In fact, in establishing allowable dose levels, alpha radiation is assigned an enhancement factor of between 10 and 20 over a similar exposure to beta and gamma radiation. Although it is true that the much larger and heavier alpha particle creates severe destruction within the one or two cells it penetrates, it is often observed that this destruction results in cell death. The body deals with dead cells from a number of causes as a matter of course every day. However, a beta particle and the electrons generated by a gamma ray, are also ionizing radiation and, being much more penetrating than alpha particles, may in their course through living tissue merely ?maim? hundreds of cells, leaving them to continue their functions, albeit severely altered in some way. Some of these cells could provide the seeds for carcinogenesis.

Finally, the political and economic pressures that come into play in today's scientific community cannot be dismissed. The situation with studies based on uranium and depleted uranium are reminiscent of those done in the last half of the twentieth century on smoking and its relation to lung cancer. Long after most of the scientific community and the public at large recognized that a relationship exists, 'scientific' research from scientists employed by tobacco companies was still being published with conclusions? that smoking was not a proven causative factor for lung cancer. An example in the depleted uranium arena is the often cited commentary by N. D. Priest published in 2001 in Lancet that claims that there has been no evidence found for carcinogenic or cytogenic effects following exposure to depleted uranium. However, there were numerous studies published before 2001, cited in this compendium, that demonstrate exactly the opposite. The nuclear industries throughout the world, not to mention governments and their military establishments, have an enormous vested interest in continuing the mining and processing of uranium and depleted uranium and in the fabrication and use of products containing these materials.
Regulatory organizations at both the national and international levels are not immune to pressures from these entities when creating acceptable exposure levels and environmental safety standards. The reader therefore should pay particular attention to the source for each citation referenced in this document and weigh the validity of the experimental method used, the data obtained and the conclusions drawn in the light of the researcher's potential bias due to the influence of his/her employer, position, or source of funding.

Chapter I

Cellular and Molecular Response to Uranium and Depleted Uranium Exposure

Summary

The papers in this chapter show that uranium (in various forms) does cause chromosomal damage and genetic aberrations in cells, such as increases in sister chromatid exchanges and micronuclei formation, which are indicative of DNA strand breaks. These changes are often precursors to carcinogenesis. Increased strand breaks in germ cells (sperm and ova) can lead to greater risk of birth defects in offspring, a mutagenic effect, and direct effects on the developing fetus, a teratogenic effect. These combined effects are referred to as cytogenetic toxicity. Another common effect observed with radiation exposure is genomic instability. This occurs when the decendent cells from an irradiated cell are found to also exhibit functional abnormalities, even though they themselves were not directly exposed. Depleted uranium exposure has been shown to cause a significant genomic instability effect lasting through as many as 30 generations of progeny cells.
Finally, the bystander effect is observed when cells surrounding those that have been directly irradiated are also found to exhibit abnormalities.

Details

Cytotoxicity of uranium in rat lung tissue was reported as early as 1987 by Tasat (1). In 1993 Lin showed uranium compounds to possess cytogenetic toxicity and cause decreased cell viability in hamster ovary cells, explaining the teratogenic effects on developing fetal mice (2) observed and reported by Domingo in 1989.

Alexandria Miller's continuing work at the Armed Forces Radiobiology Institute in Bethesda has shown that uranium exposure transforms human osteoblast cells in vitro to a tumorigenic phenotype (3, 9), implying that internalized DU exposure would be biologically active and could lead to cancer, similar to exposure to other heavy metals such as nickel and tungsten (5), but more potent (7). She demonstrated that phenyl acetate, a chemotherapeutic agent, showed some tendancy to suppress these transformation effects of DU (6). In comparison with nickel and tungsten, neither of which are radioactive, she demonstrated that DU exposure resulted in significantly increased dicentric frequency, a radiation induced genotoxic effect, that was radiation-dose dependant (8). She also demonstrated that DU exposure produces a significant genomic instability effect that lasted three times longer (through 30 successive generations) than that for gamma radiation or for nickel exposure and that the affected progeny cells exhibited considerably more chromosomal damage than did progeny cells whose precurser cells were exposed to gamma radiation, while the nickel-exposed ancestor cells produced progeny with no elevated level of micronuclei formation (11). Her most recent work tested the ability of DU and metals in a typical tungsten alloy to induce stress genes in 13 different recombinant cell lines generated from human liver carcinoma cells, with the result that both DU and metal components of tungsten alloys activate gene expression through pathways that may be involved in the toxicity and tumorigenicity of these metals (14).

Prabhavathi has shown that smokers at a nuclear fuel manufacturing facility had considerably more signs of chromosomal damage than smokers and nonsmokers who were not exposed to radiation (4). Inhaled or embedded DU is known to become associated with macrophages. Kalinich reported finding that cell death (apoptosis) occurred in a line of mouse macrophages that were exposed to DU (10). He also noted other morphological changes and DNA fragmentation in the exposed cells. Yazze ran in-vitro studies on the effects of of uranyl acetate/ascorbic acid mixtures on cells and observed plasmid relaxation responses in pBluescript DNA leading to DNA strand cleavage, suggesting that uranium, like chromium, may be directly genotoxic (13). The effect observed increased as uranium concentration increased, and was inhibited in the presence of catalase. Free-radical scavangers showed no effect.

Schroder analyzed blood lymphocytes samples from 16 veterans of war theaters where DU was used and discovered in each sample a statistically significant increased frequency of dicentric chromosomes and centric ring chromosomes, compared to samples from unexposed controls (12). These chromosomal defects indicate a previous exposure of the veterans to ionising radiation.

1. Cytotoxic effect of uranium dioxide on rat alveolar macrophages, by DR Tasat, et al., Environmental Research Vol. 44, 1987 (pp. 71-81).
Tasat1987xxERv44nxp71].

2. Cytogenetic toxicity of uranyl nitrate in Chinese hamster ovary cells, by R.H. Lin, et al., Mutation Research Vol. 319, 1993 (pp. 197-203).
Uranyl nitrate decreased the viability of CHO cells in a dose-related fashion, with IC50 (conc for 50% inhibition) was 0.049 mM. At 0.01 to 0.3 mM uranyl nitrate decreased cell cycle kinetics, increased frequency of micronuclei and sister chromatid exchange and augmented chromosomal aberrations. Results indicates that uranyl nitrate causes genotoxicity and cytotoxicity in CHO cells and provides the biochemical basis for teratogenic effect of U on developing fetal mice (Domingo et al, Toxicology, 55, 143-152, 1989).
[Lin1993xxMRv319nxp197]

3. Transformation of human osteoblast cells to the tumorigenic phenotype by depleted uranium-uranyl chloride, by A. Miller, et al., Applied Cellular Radiobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20889-5603 USA. Environ Health Perspect. Vol. 106(8), Aug. 1998 (pp. 465-71).
Depleted uranium (DU) is a dense heavy metal used primarily in military applications. Although the health effects of occupational uranium exposure are well known, limited data exist regarding the long-term health effects of internalized DU in humans. We established an in vitro cellular model to study DU exposure. Microdosimetric assessment, determined using a Monte Carlo computer simulation based on measured intracellular and extracellular uranium levels, showed that few (0.0014%) cell nuclei were hit by alpha particles. We report the ability of DU-uranyl chloride to transform immortalized human osteoblastic cells (HOS) to the tumorigenic phenotype. DU-uranyl chloride-transformants are characterized by anchorage-independent growth, tumor formation in nude mice, expression of high levels of the k-ras oncogene, reduced production of the Rb tumor-suppressor protein, and elevated levels of sister chromatid exchanges per cell. DU-uranyl chloride treatment resulted in a 9.6 (+/- 2.8)-fold increase in transformation frequency compared to untreated cells. In comparison, nickel sulfate resulted in a 7.1 (+/- 2.1)-fold increase in transformation frequency. This is the first report showing that a DU compound caused human cell transformation to the neoplastic phenotype. Although additional studies are needed to determine if protracted DU exposure produces tumors in vivo, the implication from these in vitro results is that the risk of cancer induction from internalized DU exposure may be comparable to other biologically reactive and carcinogenic heavy-metal compounds (e.g., nickel).
[Miller199808EHPv106n8p465]. (PMID: 9681973 [PubMed - indexed for MEDLINE]).

4. Analysis of chromosomal aberration frequencies in the peripheral blood lymphocytes of smokers exposed to uranyl compounds, by P.A. Prabhavathi, et al., Mutation Research Vol. 466, 2000 (pp. 37-41).
Studied 115 workers at a nuclear fuel manufacturing facility (in India) for chromosomal aberrations and compared them with 94 smokers and 118 nonsmokers who were not exposed to uranium. U exposed smokers had signif. more chrom. aberrations than smokers not exposed and unexposed nonsmokers had the least aberrations.
[Prabhavathi2000xxMRv466nxp37].

5. Neoplastic transformation of human osteoblast cells to the tumorigenic phenotype by heavy metal-tungsten alloy particles: induction of genotoxic effects, by A. Miller, et al., Applied Cellular Radiobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20889-5603, USA. Carcinogenesis Vol. 22(1), Jan. 2001 (pp. 115-25). Heavy metal-tungsten alloys (HMTAs) are dense heavy metal composite materials used primarily in military applications. HMTAs are composed of a mixture of tungsten (91-93%), nickel (3-5%) and either cobalt (2-4%) or iron (2-4%) particles. Like the heavy metal depleted uranium (DU), the use of HMTAs in military munitions could result in their internalization in humans. Limited data exist, however, regarding the long-term health effects of internalized HMTAs in humans. We used an immortalized, non-tumorigenic, human osteoblast-like cell line (HOS) to study the tumorigenic transforming potential of reconstituted mixtures of tungsten, nickel and cobalt (rWNiCo) and tungsten, nickel and iron (rWNiFe). We report the ability of rWNiCo and rWNiFe to transform immortalized HOS cells to the tumorigenic phenotype. These HMTA transformants are characterized by anchorage-independent growth, tumor formation in nude mice and high level expression of the K-ras oncogene. Cellular exposure to rWNiCo and rWNiFe resulted in 8.90 +/- 0.93- and 9.50 +/- 0.91-fold increases in transformation frequency, respectively, compared with the frequency in untreated cells. In comparison, an equivalent dose of crystalline NiS resulted in a 7.7 +/- 0.73-fold increase in transformation frequency. The inert metal tantalum oxide did not enhance HOS transformation frequency above untreated levels. The mechanism by which rWNiCo and rWNiFe induce cell transformation in vitro appears to involve, at least partially, direct damage to the genetic material, manifested as increased DNA breakage or chromosomal aberrations (i.e. micronuclei). This is the first report showing that HMTA mixtures of W, Ni and Co or Fe cause human cell transformation to the neoplastic phenotype. While additional studies are needed to determine if protracted HMTA exposure produces tumors in vivo, the implication from these in vitro results is that the risk of cancer induction from internalized

HMTAs exposure may be comparable with the risk from other biologically reactive and insoluble carcinogenic heavy metal compounds (e.g. nickel subsulfide and nickel oxide).
[Miller200101Cv22n1p115]. (PMID: 11159749 [PubMed - indexed for MEDLINE]).

6. Suppression of depleted uranium-induced neoplastic transformation of human cells by the phenyl fatty acid, phenyl acetate: chemoprevention by targeting the p21RAS protein pathway, by A.C. Miller, et al., Radiation Research Vol. 155, 2001 (pp. 163-170).
This study was done as a follow up to a previous study [Miller et al., Envir. Health Persp.106, 465-471, 1998, above] that shows transformation of human cells to tumorigenic phenotype following exposure to U. This paper shows that phenyl acetate (a potential chemotherapeutic agent) could prevent transformation to the tumorigenic phenotype and decreased membrane associated p21RAS protein, an inducer of cell transformation. Phenyl acetate can interfere with p21 processing by blocking the mevalonate pathway and farnesol synthesis. Farnesylation of p21 results in its membrane association. The authors also speculate that uranyl ions may catalyze free radical that could be involved in transformation. They do not mention possible effects that phenyl acetate might have on the bystander effect (see following section).
[Miller2001xxRRv155nxp163].

7. Potential late health effects of depleted uranium and tungsten used in armor-piercing munitions: comparison of neoplastic transformation and genotoxicity with the known carcinogen nickel, by A. Miller, et al., Applied Cellular Radiobiology Department Armed Forces Radiobiology Research Institute, Bethesda, MD. Military Medicine Vol. 167 (2 suppl), Feb. 2002 (pp. 120-122).
Limited data exist to permit an accurate assessment of risks for carcinogenesis and mutagenesis from embedded fragments or inhaled particulates of depleted uranium (DU). Ongoing studies have been designed to provide information about the carcinogenic potential of DU using in-vitro and in-vivo assessments of morphological transformation as well as cytogenetic, mutagenic, and oncogenic effects. For comparison, we also examined tungsten alloys used in military projectiles and the known carcinogen nickel. Quantitative and qualitative in-vitro transformation studies were done to assess the carcinogenic potential of radiation and chemical hazards. Using a human cell osteosarcoma cell model, we demonstrated that soluble and insoluble DU compounds can transform cells to the tumorigenic phenotype, as characterized by morphological, biochemical and oncogenic changes consistent with tumor cell behavior. Tungsten alloys and nickel were also shown to be neoplastic transforming agents, although at a frequency less than that of DU. Sister chromatid exchange, micronuclei, and alkaline filter elution assays showed DU and tungsten alloys were genotoxic. Exposure to a non-toxic, nontransforming dose of DU induced a small but statistically significant increase in the number of dicentrics formed in cells. These results suggest that long term exposure to DU or tungsten alloys could be critical to the development of neoplastic disease in humans and that additional studies are needed.
[Miller200202MMv167n2p120]. (PMID: 11873492 [PubMed - indexed for MEDLINE]).

8. Observation of radiation-specific damage in human cells exposed to depleted uranium: dicentric frequency and neoplastic transformation as endpoints, by A Miller, et al., Applied Cellular Radiobiology Department Armed Forces Radiobiology Research Institute, Bethesda, MD. Radiat Prot Dosimetry Vol. 99(1-4), 2002 (pp. 275-278).
Depleted uranium (DU) is a dense heavy metal used primarily in military applications. Published data from our laboratory have demonstrated that DU exposure in-vitro to immortalsed human osteoblast cells (HOS) is both neoplastically transforming and genotoxic. DU possesses both a radiological (alpha particle) and chemical (metal) component. Since DU has a low specific activity in comparison to natural uranium, it is not considered to be a significant radiolgical hazard. The potential contribution of radiation to DU-induced biological effects is unknown and the involvement of radiation in DU-induced biological effects could have significant implications for current risk estimates for internalised DU exposure. Two approaches were used to address this question. The frequency of dicentrics was measured in HOS cells following DU exposure in vitro. Data demonstrated that DU exposure (50 micorM, 24h)induced a significant elevation in dicentric frequency in vitro in contrast to incubation with heavy metals, nickel and tungsten, which did not increase dicentric frequency above background levels. Using the same concentration (50 microM) of three uranyl nitrate compounds that have different uranium isotopic concentrations and therefore different specific activities, the effect on neoplastic transformation in-vitro was examined. HOS cells were exposed to one of three-uranyl nitrate compounds (238U-uranyl nitrate, specific activity 0.33 microCi.g-1; DU uranyl nitrate, specific activity 0.44 microCi.g-1; and 235U-uranyl nitrate, specific activity 2.2 microCi.g-1) delivered at a concentration of 50 microM for 24 h. Results showed, at equal uranium concentration, there was a specific activity dependent increase in neoplastic transformation frequency. Taken together, these data suggest that radiation can play a role in DU-induced biological effects in vitro."
[Miller200201RPDv99n1p275]. (PMID: 12194305 [PubMed - indexed for MEDLINE]).

9. Depleted Uranium-catalyzed oxidative DNA damage: absence of significant alpha particle decay, by Alexandra C. Miller, et al., Applied Cellular Radiobiology Department Armed Forces Radiobiology Research Institute, Bethesda, MD. Journal of Inorganic Biochemistry Vol. 91(1), July 25, 2002 (pp. 246-252).
Depleted uranium (DU) is a dense heavy metal used primarily in military applications. Published data from our laboratory have demonstrated that DU exposure in vitro to immortalized human osteoblast cells (HOS) is both neoplastically transforming and genotoxic. DU possesses both a radiological (alpha particle) and a chemical (metal) component. Since DU has a low-specific activity in comparison to natural uranium, it is not considered to be a significant radiological hazard. In the current study we demonstrate that DU can generate oxidative DNA damage and can also catalyze reactions that induce hydroxyl radicals in the absence of significant alpha particle decay. Experiments were conducted under conditions in which chemical generation of hydroxyl radicals

was calculated to exceed the radiolytic generation by 10(6)-fold. The data showed that markers of oxidative DNA base damage, thymine glycol and 8-deoxyguanosine could be induced from DU-catalyzed reactions of hydrogen peroxide and ascorbate similarly to those occurring in the presence of iron catalysts. DU was 6-fold more efficient than iron at catalyzing the oxidation of ascorbate at pH 7. These data not only demonstrate that DU at pH 7 can induce oxidative DNA damage in the absence of significant alpha particle decay, but also suggest that DU can induce carcinogenic lesions, e.g. oxidative DNA lesions, through interaction with a cellular oxygen species.
[Miller200207JIBv91n1p246] (PMID: 12121782 [PubMed - indexed for MEDLINE]).

10. Depleted Uranium-uranyl chloride induces apoptosis in mouse J774 macrophages, by J. F. Kalinich, et al., Applied Cellular Radiobiology Department Armed Forces Radiobiology Research Institute, Bethesda, MD. Toxicology Vol. 179 (1-2), Sept. 30, 2002 (pp. 105-114).
Depleted uranium entering the body as a result of inhalation or embedded fragments becomes associated to a great extent with macrophages. As part of our continuing studies on the health effects of internalized depleted uranium, we investigated the effect of soluble depleted uranium-uranyl chloride on the mouse macrophage cell line, J774. Using a cytochemical staining protocol specific for uranium, we found that uranium uptake by the macrophages increased in a time-dependent manner. Treatment with 1, 10, or 100 microM depleted uranium-uranyl chloride resulted in decreased viability of the J774 cells within 24 h. Flow cytometric analysis of the treated cells with annexin V showed the translocation of phosphatidylserine from the inner face of the plasma membrane to the outer surface indicating the loss of phospholipid symmetry and the beginning of the apoptotic process. Significant differences in annexin V labeling between control cells and cells treated with 100 microM depleted uranium-uranyl chloride were apparent within 2 h. Other events associated with apoptosis, including morphological changes and DNA fragmentation, were also apparent after depleted uranium-uranyl chloride treatment. These results suggest that the uptake and concentration of soluble depleted uranium by macrophages initiates events that results in the apoptotic death of these cells.
[Kalinich200209Tv179n1p105]. (PMID: 12204547 [PubMed - indexed for MEDLINE]).

11. Genomic instability in human osteoblast cells after exposure to depleted uranium: delayed lethality and micronuclei formation, by A. Miller, et al., Applied Cellular Radiobiology Department Armed Forces Radiobiology Research Institute, Bethesda, MD. Journal of Environmental Radioactivity Vol. 64(2-3), 2003 (pp. 247-259).
It is known that radiation can induce a transmissible persistent destabilization of the genome. We have established an in vitro cellular model using HOS cells to investigate whether genomic instability plays a role in depeleted uranium (DU)-induced effects. Transmissible genomic instability, manifested in the progeny of cells exposed to ionizing radiation, has been characterized by de novo chromosomal aberrations, gene mutations, and an enhanced death rate. Cell lethality and micronuclei formation were measured at various times after exposure to DU, Ni, or gamma radiation. Following a prompt, concentration dependent acute response for both endpoints, there was de novo genomic instability in progeny cells. Delayed reproductive death was observed for many generations (36 days, 30 population doublings) following exposure to DU, Ni, or gamma radiation. While DU stimulated delayed production of micronuclei up to 36 days after exposure, levels in cells exposed to gamma-radiation or Ni returned to normal after 12 days. There was also a persistent increase in micronuclei in all clones isolated from cells that had been exposed to nontoxic concentrations of DU. While clones isolated from gamma-irradiated cells (at doses equitoxic to metal exposure) generally demonstrated an increase in micronuclei, most clonal progeny of Ni-exposed cells did not. These studies demonstrate that DU exposure in vitro results in genomic instability manifested as delayed reproductive death and micronuclei formation.
[Miller200300JERv64n2p247]. (PMID: 12500809 [PubMed - indexed for MEDLINE]).

12. Chromosome aberration analysis in peripheral lymphocytes of Gulf War and Balkans War veterans, by H. Schroder, et al., Center of Environmental Research and Technology, University of Bremen, Bremen, Germany. Radiation Prot Dosimetry Vol. 103(3), 2003 (pp. 211-219).
Chromosome aberrations and sister chromatid exchanges (SCEs) were determined in standard peripheral lymphocyte metaphase preparations of 13 British Gulf War veterans, two veterans of the recent war in the Balkans and one veteran of both wars. All 16 volunteers suspect exposures to depleted uranium (DU) while deployed at the two different theatres of war in 1990 and later on. The Bremen laboratory control served as a reference in this study. Compared with this control there was a statistically significant increase in the frequency of dicentric chromosomes (dic) and centric ring chromosomes (cR) in the veterans' group indicating a previous exposure to ionising radiation. The statistically significant overdispersion of die and cR indicates non-uniform irradiation as would be expected after non-uniform exposure and/or exposure to radiation with a high linear energy transfer (LET). The frequency of SCEs was decreased when compared with the laboratory control.
[Schroder200303RPDv103n3p211]. (PMID: 12678382 [PubMed - in process]).
13. Uranyl acetate causes DNA single strand breaks in vitro in the presence of ascorbate (Vitamin C), by M. Yazzie, et al., Department of Chemistry, Northern Arizona University, Flagstaff, AZ. Chemical Research in Toxicology Vol. 16(4), April 2003 (pp. 524-530).
Uranium is a radioactive heavy metal with isotopes that decay on the geological time scale. People are exposed to uranium through uranium mining, processing, the resulting mine tailings, and the use of depleted uranium in the military. Acute exposures to uranium are chemically toxic to the kidney; however, little is known about chronic exposures, for example, if there is a direct chemical genotoxicity of uranium. The hypothesis that is being tested in the current work is that hexavalent uranium, as uranyl ion, may have a chemical genotoxicity similar to that of hexavelent chromium. In the current study, reactions of uranyl acetate (UA) and ascorbate

(vitamin C) were observed to produce plasmid relaxation in pBluescript DNA. DNA strand breaks increased with increasing concentrations of a 1:1 reaction of UA and ascorbate but were not affected by increasing the ration of ascorbate. Plasmid relaxation was inhibited by coincubation of reactions with catalase but not by coincubation with the radical scavengers mannitol, sodium azide, or 5,5-dimethyl-1-pyrroline-N-oxide. Reactions of UA and ascorbate monitored by (1)H NMR spectroscopy showed formation of a uranyl ascorbate complex, with no evidence of a dehyroascorbate product. A previous study inferred that hydroxyl radical formation was responsible for oxidative DNA damage in the presence of reactions of uranyl ion, hydrogen peroxide, and ascorbate [Miller et al. (2002) J. Bioinorg. Chem. 91, 246-252]. Current results, in the absence of added hydrogen peroxide, were not completely consistent with the interpretation that strand breaks were produced by a Fenton type generation of reactive oxygen species. Data were also consistent with the interpretation that a uranyl ascorbate complex was catalyzing hydrolysis of the DNA-phosphate backbone, in a manner similar to that known for the lanthanides. These data suggest that uranium may be directly genotoxic and may, like chromium, react with DNA by more than one pathway.
[Yazzie200304CRTv16n4p524]. (PMID: 12703969 [PubMed - in process]).

14. Effect of the militarily-relevant heavy metals, depleted uranium and heavy metal tungsten-alloy on gene expression in human liver carcinoma cells (HepG2), by Alexandra Miller, et al., Applied Cellular Radiobiology Department Armed Forces Radiobiology Research Institute, Bethesda, MD. 20889-5603, USA. millera@afrri.usuhs.mil. Mol Cell Biochem. Vol. 255(1-2), Jan. 2004 (pp. 247-56).
Depleted uranium (DU) and heavy-metal tungsten alloys (HMTAs) are dense heavy-metals used primarily in military applications. Chemically similar to natural uranium, but depleted of the higher activity 235U and 234U isotopes, DU is a low specific activity, high-density heavy metal. In contrast, the non-radioactive HMTAs are composed of a mixture of tungsten (91-93%), nickel (3-5%), and cobalt (2-4%) particles. The use of DU and HMTAs in military munitions could result in their internalization in humans. Limited data exist however, regarding the long-term health effects of internalized DU and HMTAs in humans. Both DU and HMTAs possess a tumorigenic transforming potential and are genotoxic and mutagenic in vitro. Using insoluble DU-UO2 and a reconstituted mixture of tungsten, nickel, cobalt (rWNiCo), we tested their ability to induce stress genes in thirteen different recombinant cell lines generated from human liver carcinoma cells (HepG2). The commercially available CAT-Tox (L) cellular assay consists of a panel of cell lines stably transfected with reporter genes consisting of a coding sequence for chloramphenicol acetyl transferase (CAT) under transcriptional control by mammalian stress gene regulatory sequences. DU, (5-50 microg/ml) produced a complex profile of activity demonstrating significant dose-dependent induction of the hMTIIA FOS, p53RE, Gadd153, Gadd45, NFkappaBRE, CRE, HSP70, RARE, and GRP78 promoters. The rWNiCo mixture (5-50 microg/ml) showed dose-related induction of the GSTYA, hMTIIA, p53RE, FOS, NFkappaBRE, HSP70, and CRE promoters. An examination of the pure metals, tungsten (W), nickel (Ni), and cobalt (Co), comprising the rWNiCo mixture, demonstrated that each metal exhibited a similar pattern of gene induction, but at a significantly decreased magnitude than that of the rWNiCo mixture. These data showed a synergistic activation of gene expression by the metals in the rWNiCo mixture. Our data show for the first time that DU and rWNiCo can activate gene expression through several signal transduction pathways that may be involved in the toxicity and tumorigenicity of both DU and HMTAs.
[Miller200401MCBv255n1to2p247]. (PMID: 14971665 [PubMed - in process]).

Chapter II

Organ and Organism Response to Uranium and Depleted Uranium Exposure (Including Reproductive Effects)

Summary

Uranium toxicity has been studied for many decades. The nephrotoxicity of uranium was recognized in the 19th century. Hodge (1) gives a good review of the history of uranium poisoning prior to the Manhattan Project. Other reviews of uranium toxicity in the decades following World War II, when the nuclear industry grew in those countries with nuclear capabilities, focus mostly on the kidney damage caused by uranium.

However, animal experiments have shown that inhaled uranium dioxide aerosols, such as those produced when DU is machined or when a DU weapon explodes and/or burns have a very long retention time in the lungs and slowly distribute DU throughout the body, coming to rest in bones, liver, kidney, heart, brain, spleen, lymph nodes and testicles. Tests on Gulf War veterans have shown measurable urinary DU even 10 years after their exposure, reinforcing the conclusions from the rat experiments. DU residing in the testicles may explain the observed teratogenic effects of DU exposure in which children of Gulf War veterans have a 50% greater risk of severe birth defects. DU-exposed rats have lower fertility, give rise to low birth weight offspring with a significantly higher rate of fetal skeletal malformations.The urine and blood tests of rats with embedded DU pellets or patches or injected DU solutions show dose and time-dependent mutagenic toxicity, and neurological disorders.

McClain, a researcher at the US Armed Forces Radiobiology Research Institute reports conclusions from his research that "DU is mutagenic and transforms human osteoblastic cells into a tumorigenic phenotype. It alters neurophysiological parameters in rat hippocampus, crosses the placental barrier, and enters fetal tissue."

Additional research specifically related to Gulf War veterans is presented in Chapters IV and V. Further studies into health effects of low level ionizing radiation is presented in Chapter III.

Details

Several reviews have been written dealing with the general body toxicity of uranium, including that by Hodge (6) in 1973. Durakovic (20) provides a 1999 review on the medical affects of contamination from depleted uranium. In 2000, Hartmann (26) reviews toxicity data with regard to risk assessment and evaluation of acceptable exposure levels. Bleise (42) provides a 2003 review on the properties, use and health effects of depleted uranium.

Uranium exposure to skin by Orcutt (1), and Ubios (17) and to sub-cutaneous implantation by Lopez (25) have been studied for over 50 years.

Inhalation of uranium and uranium oxide dust particles leads to internal exposure of bronchial, lung and lymph tissues to the chemical and radiological effects of uranium. Wilson (2), (3) and Walinder (4) first reported studies on these effects in the '50s and '60s. Leach's animal studies of inhaled uranium dioxide dust showed 90% retention in lungs and associated lymph nodes in monkeys, dogs and rats and found fibrotic changes suggestive of radiation damage after 3 years even though no sign of kidney damage had been observed (5). Butler (8) found the solubility of U_3O_8 in simulated lung fluid to be less than 12%. In 1988, Stradling (10) reported on the metabolism of uranium particles embedded in rat lung tissue. In the early '90s, Morris (15) and Eidsen (16) studied the long-term clearance of uranium particles embedded in pulmonary tissues. Katsaros (24) published a review with 15 references on effects of inhaled uranium in 1999 and Mould (32) addressed the issue of lung cancer and leukaemia resulting from exposure to inhaled depleted uranium in 2001. Dewit (32m) exposed rats to inhaled uranium dust in first half of life and followed bone and muscle accumulation of uranium in later life drawn from lung reserves of retained uranium. In 2002, Yang (38) conclusively showed that DU is carcinogenic in vitro by following gene expression characteristics in rat lung tissue cells exposed to DU. In 2003, Durakovic (45), using urinary analysis for DU and known biological half-life values of uranium clearance from lung tissue, was able to determine the time-zero lung burden of DU in veterans nine years after their initial exposure to DU aerosols. Results showed exposed veterans had inhaled 0.34 mg of DU, over 2200 times the time-zero estimated DU lung burden of non-exposed veterans. Mitchel (47) characterized DU-oxides formed from actual test firing of DU munitions and reported their retention rates in lung tissues (inhaled) and muscle tissues (implanted), finding both a soluble component and an insoluble component in the samples studied.

Ingestion of uranium, primarily through drinking water, has been found to affect primarily the kidneys and renal functions through its chemical toxicity. Wrenn (9) provides a 1985 review of the effects of ingested uranium, and Leggett (14), 1989, suggests a reassessment of uranium toxicity values. Zamora's 1998 report (18) indicates that the renal tubules are the primary site for renal uranium toxicity. Mirto (22) reports further on this issue and Kurttio (37) suggests appropriate uranium levels in drinking water based on well studies in Finland.

Studies have also shown that uranium and depleted uranium affect brain tissues and neurological behaviours in exposed individuals. Pellmar (23) discovered electrophysiological changes in hypocampal brain slices taken from rats with embedded DU fragments. Briner (35) reports in 2002 that elevated uranium levels in drinking water of mice lead to observable behavioural changes and increased lipid oxidation in the brain. Also in 2002, Abou-Donia (39) reports distinct sensorimotor deficits in rats injected with uranyl nitrate (inclined plane performance, grip time, beam walk score and beam walk time) and an increase in nitric oxide production in their central nervous systems.

Exposure to uranium and depleted uranium has been shown to have reproductive effects on the exposed animals. Domingo (13) in 1989 (BEFORE the 1991 Gulf War) reported on serious skeletal malformations such as cleft palate, bipartitie sternebrae, reduced ossification and ossified skeletal variations observed in offspring of mice exposed to uranyl nitrate while pregnant. Arfsten (30) and Domingo (33) have published 2001 reviews of the research into the mutagenic and teratogenic effects of uranium exposure.

Kathren reports in 1989 on the body distribution of uranium contamination from an autopsy of a chemical worker employed in a uranium processing plant for 26 years, finding a uranium deposition pattern of 63 to 2.8 to 1 in the worker's skeleton, liver and kidney (11).

Soluble uranium compounds such as uranyl nitrate have been injected into rats to study the metabolic pathways and distribution of uranium in animal bodies. Cooper (7) reports on these studies in 1982 as does Walinder (12) in 1989. Solid pellet implantation of uranium and depleted uranium metal have also been used. In 1998, Miller (19) reported the urine and serum mutagenicity from rats with embedded DU pellets, finding dose and time-dependent mutagenic toxicity in only the rats with embedded DU pellets. Pellmar (21) reported in 1999 on body distribution of DU from implanted pellets in rats. Autopsies on sacrificed rats throughout the 18-month study showed significant U levels in bone and kidney, with elevated U levels also found in the muscle, spleen, liver, heart, lung, brain, lymph nodes, and testicles, strongly suggesting unanticipated physiological consequences of U exposure from embedded fragments. Hahn (34), in 2002, reported soft tissue sarcomas resulting from embedded DU strips in rat muscle tissue, with sarcoma incidence dependent on strip size and no sarcomas developing in rats with embedded strips of tantalum. McClain (36) in 2002 summarizes studies at the US Army's own Armed Forces Radiobiology Research Institute in Bethesda, MD, (which includes the work of Pellmar and Miller) with the following: "Results indicate that uranium from implanted DU fragments distributes to tissues distant from implantation sites, including bone, kidney, muscle, and liver. Despite levels of uranium in kidney that would be nephrotoxic after acute exposure, no histological or functional kidney toxicity was observed with embedded DU, indicating that the kidney adapts when exposed chronically. Nonetheless, further studies of the long-term health impact are needed. DU is mutagenic and transforms human osteoblastic cells into a tumorigenic phenotype. It alters neurophysiological parameters in rat hippocampus, crosses the placental barrier, and enters fetal tissue. Preliminary data also indicate decreased rodent litter size when animals are bred 6 months or longer after DU implantation." Leggett (43) reports a biokinetic model to describe the migration of DU from embedded fragments to other tissues.

Nor is the plant world immune to the effects of exposure to DU. Panda found that uranyl nitrate inhibits plant growth and observed sister chromatid exchange, suggesting U inhibits DNA replication and/or repair processes (29). In 2002, Kuhne (40) reported an estimated 14-day LC50 for the Hyalella azteca assay was 1.52 mg/Liter of water.

General concerns on the overall health risks associated with exposure to depleted uranium has been the subject of several articles, including those by Kulev (27), Stadbauer (28), Durovic (31), and Murray (44), with particular emphasis given to the indiscriminate use of depleted uranium weapons and the resulting contamination of the environmment. Ushakov (41) showed that radiation and chemical damage to kidneys, lungs and other internal organs was observed in a study of over 600 humans exposed to DU. Craft's review (46) in 2004 covers the chemistry, pharmacokinetics, and toxicological effects of depleted and natural uranium on several systems in the mammalian body.

1. The toxicology of compounds of uranium following application to the skin, by JA Orcutt, in Pharmacology and Toxicology of Uranium Compounds Vol 1, C Voegtlin, HC Hodge, eds., McGraw-Hill, New York, 1949. Chapter 8 (pp 377-414). [Orcutt1949xxPTUCv1nxp377].

2. Relation of particle size of uranium dioxide dust to toxicity following inhalation by animals: II, by HB Wilson, et al., Archives of Industrial Hygiene and Occupational Medicine Vol. 6(2), 1952 (pp. 93-104). [Wilson1952xxAIHOMv6n2p93].

3. Relation of particle size of U3O8 dust to toxicity following inhalation by animals, by HB Wilson, et al., A.M.A. Archives of Industrial Health Vol. 11, 1955 (pp. 11-16).
[Wilson1955xxAMAAIHv11nxp11].

4. Incorporation of uranium: II. Distribution of uranium absorbed through the lungs and the skin, by G. Walinder, et al., British J. Industrial Medicine Vol. 24, 1967 (pp. 313-319).
[Walinder1967xxBJIMv24nxp313].

5. A five-year inhalation study with natural uranium dioxide (UO2) dust - I. retention and biologic effect in the monkey, dog and rat, by LJ Leach, et al., Health Physics Vol. 18, 1970 (pp. 599-612).
Found >90% of U retained in body in lungs and tracheobronchial lymph nodes. No evidence of U toxicity related to body weight or mortality. Kidney damage did not occur. Some fibrotic changes suggestive of radiation injury was observed in lymph of dogs and monkeys and in monkey lungs after more than 3 years. Implies minor risk from exposure to UO2 dust. [Leach1970xxHPv18nxp599].

6. A history of uranium poisoning (1824-1942), by H.C. Hodge, in Handbook of Experimental Pharmacology, New Series XXXVI, Uranium, Plutonium, Transplutonic Elements, H.C. Hodge, et al., eds., Springer-Verlag, New York,
1973 (pp. 5-69)
[Hodge1973Handbookp5]

7. The behaviour of uranium-233 oxide and uranyl-233 nitrate in rats, by JR Cooper, et al., Int. J. Radiat. Biol., Vol. 41(4), 1982 (pp. 421-433).
[Cooper1982xxIJRBv41n4p421].

8. A summary report on the solubility of depleted uranium oxide (U3O8) in simulated lung fluid, Ringers solution, and Ringers lactate, by WD Butler, et al., USAF Academy, CO. Gov. Rep. Announce. Index (US) Vol. 82(19), 1982 (p. 3780). Less than 12% solubility was shown in the biological fluids studied.
[Butler1982xxGRAIv82n19p3780].

9. Metabolism of ingested U and Ra, by M.E. Wrenn, et al., Health Physics Vol. 48, 1985 (pp. 601-633).
Reviews the literature and discusses absorption, distribution and elimination of consumed U. Recommends <100 ...g/L in drinking water to limit toxic effects of U to kidney.
[Wrenn1985xxHPv48nxp610]

10. The metabolism of ceramic and non-ceramic forms of uranium dioxide after deposition in the rat lung, by GN Stradling, et al., Human Toxicol. Vol. 7, 1988 (pp. 133-139).
[Stradling1988xxHTv7nxp133].

11. Uranium in the tissues of an occupationally exposed individual, by R.L. Kathren, et al., Health Physics Vol. 57, 1989 (pp. 17-21).
This group from Hanford and Los Alamos used radiochemical determination to analyze lung, kidney, liver and bone collected at autopsy of a 50 year old male employed from 1952 to 1978 as a chemical operator in a uranium processing plant and died of cardiac event at work. The Uranium deposition pattern was 63:2.8:1 in skeleton: liver: kidney. Numerous data are given in the paper over the life of this individual. Authors indicate that in vivo chest counts for this individual indicate long term U-deposition more than twice than estimated from postmortem analysis of lung and associated lymph, and argue that in vivo estimates may be high and therefore conservative from the standpoint of operational radiation protection. [ED.NOTE: They do not indicate any consideration of rib cage contribution to this comparison, suggesting there may be flaws in their model.] [Kathren1989xxHPv57nxp17]

12. Metabolism and sites of effects of uranium after incorporation along different routes in mice, rabbits and piglets, by G. Walinder, Radiation Protection Dosimetry Vol. 26(1/4), 1989 (pp. 89-95).
[Walinder198901RPDv26n1to4p89].

13. The developmental toxicity of uranium in mice, by J.L. Domingo, et al., Toxicology Vol. 56, 1989 (pp. 143-152). Treatment of pregnant mice with uranyl acetate resulted in decreased maternal weight gain and food consumption and increased liver weight. There was no change in the number of fetuses or fetal resorptions or dead fetuses, but there were dose related fetal effects, including reduced body weight and body length, and increased skeletal malformations, such as cleft palate, bipartitie sternebrae, reduced ossification and ossified skeletal variations. The lowest dosage of uranyl acetate dihydrate was 5 mg/kg, which produced a toxic effect.
[Domingo1989xxTv56nxp143].

14. The behavioral and chemical toxicity of U in the kidney: a reassessment, by RW Leggett, Health Physics Vol 57(3), 1989 (pp. 365-383).
[Leggett1989xxHPv57n3p365].

15. Long-trem clearance of inhaled UO2 particles from the pulmonary region of the rat, by KJ Morris, et al., Health Physics Vol. 58(4), 1990 (pp. 477-485).
[Morris1990xxHPv58n4p477].

16. The effect of solubility on inhaled uranium compound clearance: a review, by AF Eidson, Health Physics Vol. 67(1), 1994 (pp. 1-14).
[Eidson1994xxHPv67n1p1].

17. Skin alterations induced by long-term exposure to uranium and their effect on permeability, by AM Ubios, et al, Health Physics, Vol. 72(5), 1997 (pp. 713-715).
[Ubios1997xxHPv72n5p713].

18. Chronic ingestion of uranium in drinking water: a study of kidney bioeffects in humans, by M.L. Zamora, et al., Toxicological Sciences Vol. 43, 1998 (pp. 68-77).
This Canadian study compared low-exposure (<1 :g U/L) to high-exposure (2-781 :g U/L) levels in drinking water and found urinary glucose was significantly elevated in the high U intake group. Alkaline phosphatase and $-microglobulin correlated with U intake. Indicators for glomerular injury were not altered in the two groups, indicating the renal tubules are the primary site for renal uranium toxicity.
[Zamora1998xxTSv43nxp68].

19. Urinary and serum mutagenicity studies with rats implanted with depleted uranium or tantalum pellets, by Alexandra C. Miller, et al., Applied Cellular Radiobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20889-5603, USA. millera@mx.afrri.usuhs.mil. Mutagenesis. Vol. 13(6), Nov. 1998 (pp. 643-648).
During the 1991 Persian Gulf War several US military personnel were wounded by shrapnel fragments consisting of depleted uranium. These fragments were treated as conventional shrapnel and were not surgically removed to spare excessive tissue damage. Uranium bioassays conducted over a year after the initial uranium injury indicated a significant increase in urine uranium levels above natural background levels. The potential mutagenic effects of depleted uranium are unknown. To assess the potential mutagenic effects of long-term exposure to internalized depleted uranium, Sprague-Dawley rats were implanted with depleted uranium and their urine and serum were evaluated for mutagenic potential at various times after pellet implantation using the Ames Salmonella reversion assay. Tantalum, an inert metal widely used in prosthetic devices was used for comparison. Enhancement of mutagenic activity in Salmonella typhimurium strain TA98 and the Ames II mixed strains (TA7001-7006) was observed in urine samples from animals implanted with depleted uranium pellets. In contrast, urine samples from animals implanted with tantalum did not show a significant enhancement of mutagenic activity in these strains. In depleted uranium-implanted animals, urine mutagenicity increased in a dose- and time-dependent manner demonstrating a strong positive correlation with urine uranium levels ($r = 0.995$, $P < 0.001$).
There was no mutagenic enhancement of any bacterial strain detected in the sera of animals implanted with either depleted uranium or tantalum pellets. The results suggest that uranium content in the urine is correlated with urine mutagenicity and that urinary mutagenicity might be used as a biomarker to detect exposure to internalized uranium.
[Miller199811Mv13n6p643]. (PMID: 9862198 [PubMed - indexed for MEDLINE].

20. Medical effects of internal contamination with uranium, by A. Durakovic, Department of Radiology and Nuclear Medicine, Georgetown University School of Medicine, 3430 Connecticut Avenue, Washington, DC 20008, USA. ASAF@compuserve.com. Croat Med J. Vol. 40(1), Mar 1999 (pp. 49-66).
The purpose of this work is to present an outline of the metabolic pathways of uranium isotopes and compounds, medical consequences of uranium poisoning, and an evaluation of the therapeutic alternatives in uranium internal contamination. The chemical toxicity of uranium has been recognized for more than two centuries. Animal experiments and human studies are conclusive about metabolic adverse affects and nephro- toxicity of uranium compounds. Radiation toxicity of uranium isotopes has been recognized since the beginning of the nuclear era, with well documented evidence of reproductive and developmental toxicity, as well as mutagenic and carcinogenic consequences of uranium internal contamination. Natural uranium (238U), an alpha emitter with a half-life of 4.5x10(9) years, is one of the primordial substances of the universe. It is found in the earth's crust, combined with 235U and 234U, alpha, beta, and gamma emitters with respective half-lives of 7.1x10(8) and 2.5x10(5) years. A special emphasis of this paper concerns depleted uranium. The legacy of radioactive waste, environmental and health hazards in the nuclear industry, and, more recently, the military use of depleted uranium in the tactical battlefield necessitates further insight into the toxicology of depleted uranium. The present controversy over the radiological and chemical toxicity of depleted uranium used in the Gulf War warrants further experimental and clinical investigations of its effects on the biosphere and human organisms.
[Durakovic199903CMJv40n1p49]. (PMID: 9933897 [PubMed - indexed for MEDLINE])

21. Distribution of uranium in rats implanted with depleted uranium pellets, by TC Pellmar, et al., Radiation Pathophysiology and Toxicology Department, Armed Forces Radiobiology Research Institute, Bethesda, Maryland 20889-5603, USA. tpellmar@nas.edu . Toxicol Sci. Vol. 49(1), May 1999 (pp. 29-39).
During the Persian Gulf War, soldiers were injured with depleted uranium (DU) fragments. To assess the potential health risks associated with chronic exposure to DU, Sprague Dawley rats were surgically implanted with DU pellets at 3 dose levels (low, medium and high). Biologically inert tantalum (Ta) pellets were used as controls. At 1 day and 6, 12, and 18 months after implantation, the rats were euthanized and tissue samples collected. Using kinetic phosphorimetry, uranium levels were measured. As early as 1 day after pellet implantation and at all subsequent sample times, the greatest concentrations of uranium were in the kidney and tibia. At all time points, uranium concentrations in kidney and bone (tibia and skull) were significantly greater in the high-dose rats than in the Ta-control group. By 18 months post-implantation, the uranium concentration in kidney and bone of low-dose animals was significantly different from that in the Ta controls. Significant concentrations of uranium were excreted in the urine throughout the 18 months of the study (224 +/- 32 ng U/ml urine in low-dose rats and 1010 +/- 87 ng U/ml urine in high-dose rats at 12 months). Many other tissues (muscle, spleen, liver, heart, lung, brain, lymph nodes, and testicles) contained significant concentrations of uranium in the implanted animals. From these results, we conclude that kidney and bone are the primary reservoirs for uranium redistributed from intramuscularly embedded fragments. The accumulations in brain, lymph nodes, and testicles suggest the potential for unanticipated physiological consequences of exposure to uranium through this route.
[Pellmar199905TSv49n1p29]. (PMID: 10367339 [PubMed - indexed for MEDLINE]).

22. Intracellular behaviour of uranium(VI) on renal epithelial cell in culture (LLC-PK1): influence of uranium speciation, by H. Mirto, et al., Toxicology Letters Vol. 104, 1999 (pp. 249-256).
Used this kidney cell line in culture to study uranium toxicity to kidney tubule epithelium. Uranyl bicarbonate, but not uranyl citrate, was entered cells and precipitated in the cytoplasmic compartment as uranyl phosphate crystals. [Mirto1999xxTLv104nxp249]

23. Electrophysiological changes in hippocampal slices isolated from rats embedded with depleted uranium fragments, by TC Pellmar, et al., Radiation Pathophysiology and Toxicology Department, Armed Forces Radiobiology Research Institute, Bethesda, Maryland 20889-5603, USA. tpellmar@nas.edu . Neurotoxicology Vol. 20(5), Oct 1999 (pp. 785-792).
Although nephrotoxicity is considered to be the most serious consequence of uranium exposure, several studies have previously suggested the potential for neurotoxicity. In Operation Desert Storm, U.S. military personnel were wounded by fragments of depleted uranium (DU). This study was initiated to test the potential for DU fragments to cause electrophysiological changes in the central nervous system. Rats were surgically implanted with pellets of DU or tantalum (Ta) as a control metal. After 6, 12 and 18 months rats were euthanized, hippocampi removed and electrophysiological potentials analyzed by extracellular field potential recordings. Six months after implantation, synaptic potentials in DU-exposed tissue were less capable of eliciting spikes (E/S coupling). At 12 months, amplitudes of synaptic potentials were significantly increased in tissue from DU treated rats compared to Ta controls. E/S coupling was reduced.
The differences between the electrophysiological measurements in DU-treated and control tissue were no longer evident at the 18 month time point. An analysis of the changes in the synaptic potentials and E/S coupling over the three time points suggests that by 18 months, the effects of aging and DU exposure converge, thereby obscuring the effects of the metal. Since kidney toxicity was not evident in these animals, effects secondary to nephrotoxicity are unlikely. This study raises the possibility that physiological changes occur in the brain with chronic exposure to DU fragments, which could contribute to neurological deficits.
[Pellmar199910Nv20n5p785]. (PMID: 10591514 [PubMed - indexed for MEDLINE]).

24. Inhalation of depleted uranium and its effect on health, (in Greek), by N. Katsaros, Inst. Phys. Chem., EKEPhE, Dimokritos, Greece. Chemika Chronika, Genike Ekdose Vol. 61(7-8), 1999 (pp. 210-211).
A review with 15 references.
[Katsaros1999xxCCGEv61n7to8p210].

25. Percutaneous toxicity of uranyl nitrate: its effect in terms of exposure area and time, by R. López, et al, Health Physics, Vol. 78(4), 434-437, 2000.
[Lopez2000xxHPv78n4p434].

26. Overview of toxicity data and risk assessment methods for evaluating the chemical effects of depleted uranium compounds, by HM Hartmann, et al., Argonne Natl. Lab, Argonne, IL. Human and Ecological Risk Assessment Vol. 6(5), 2000 (pp. 851-874).
A heavily reference review discussing the chemical toxicity from DU exposure and using these data to determine reference values for risk assessments for both chronic and acute exposure.
[Hartmann2000xxHERAv6n5p851].

27. More about uranium and the danger from it, in Bulgarian, by I Kulev. Khimiya (Sofiya, Bulgaria) Vol. 10(2), 2001 (p. 115-124).
Covers background facts on DU and migration paths and toxicity of U to humans.
[Kulev2001xxKhv10n2p114].

28. Uranium Ammunition: heavy metal and radio-toxicity, in German, by EA Stadbauer, FH Giessen-Friedberg Labor fur Entsorgungstechnik, Giessen, Germany. Git Labor-Fachzeitschrift Vol. 45(4), 2001 (pp. 350-353). A review with 6 references. Concludes that tank crew radiation dose is less than 40 mSv and concentration of U in kidneys less than 4 ppm, less than the 50 mSv/year dose limit for occupationally radiation-exposed persons.
[Stadbauer200100GLFv45n4p350].

29. Evaluation of phytotoxicity and genotoxicity of uranyl nitrate in Allium assay system, by B.B. Panda, et al., Indian Journal of Experimental Biology Vol. 39, 2001 (pp. 57-62).
Uranyl nitrate inhibited growth of Allium cepa at >25 :M conc, with uranyl entry into root cells. U failed to induce micronuclei and was neither clastogenic nor aneugenic, but between 25 and 100 :M conc it increased significantly the frequency of sister chromatid exchange vs controls, that possibly interfered with DNA replication and/or repair processes. [Panda2001xxIJEBv39nxp57]

30. Review of the effects of uranium and depleted uranium exposure on reproduction and fetal development, by DP Arfsten, et al., Naval Health Research Center Detachment-Toxicology, Wright-Patterson Air Force Base (WPAFB), Ohio 45433-7903, USA. darryl.arfsten@wpafb.af.mil. Toxicol Ind Health. Vol. 17(5-10), Jun 2001 (pp. 180-191).
Depleted uranium (DU) is used in armor-penetrating munitions, military vehicle armor, and aircraft, ship and missile counterweighting/ballasting, as well as in a number of other military and commercial applications. Recent combat applications of DU alloy [i.e., Persian Gulf War (PGW) and Kosovo peacekeeping objective] resulted in human acute exposure to DU dust, vapor or aerosol, as well as chronic exposure from tissue embedding of DU shrapnel fragments. DU alloy is 99.8% 238Uranium, and emits approximately 60% of the alpha, beta, and gamma radiation found in natural uranium (4.05 x 10(-7) Ci/g DU alloy). DU is a heavy metal that is 160% more dense than lead and can remain within the body for many years and slowly solubilize. High levels of urinary uranium have been measured in PGW veterans 10 years after exposure to DU fragments and vapors. In rats, there is strong evidence of DU accumulation in tissues including testes, bone, kidneys, and brain. In vitro tests indicate that DU alloy may be both genotoxic and mutagenic, whereas a recent in vivo study suggests that tissue-embedded DU alloy may be carcinogenic in rats. There is limited available data for reproductive and teratological deficits from exposure to uranium per se, typically from oral, respiratory, or dermal exposure routes. Alternatively, there is no data available on the reproductive effects of DU embedded. This paper reviews published studies of reproductive toxicity in humans and animals from uranium or DU exposure, and discusses ongoing animal research to evaluate reproductive effects in male and female rats embedded with DU fragments, and possible consequences in F1 and F2 generations.
[Arfsten200106TIHv17n5to10p180]. (PMID: 12539863 [PubMed - indexed for MEDLINE]).

31. Biomedical aspects of using ammunition with depleted uranium, in Serbian, by AB Durovic. Hemijska Industrija Vol. 55(7-8), 2001 (pp. 325-329).
Aspects of DU poisoning and internal contamination, medical consequences, diagnostics, and therapeutic procedures are presented in this review.
[Durovic2001xxHIv55n7to8p325].

32. Depleted uranium and radiation-induced lung cancer and leukaemia, by RF Mould, richardfmould@hotmail.com. British Journal of Radiology, Vol. 74(884), Aug. 2001 (pp. 677-683).
[Mould200108BJRv74n884p677].

32m. Uranium and uranium decay series radionuclide dynamics in bone of rats following chronic uranium ore dust inhalation, by T Dewit, et al., Department of Biology, Laurentian University, Sudbury, ON, Canada.. Health Phys. Vol. 81(5), Nov. 2001 (pp. 502-13).
The accumulation and release of uranium and some uranium decay chain radionuclides were measured in the bones of rats that had been chronically exposed to inhaled uranium ore dust during the first half (approximately) of their natural adult lifespan. Endochondral bone (femur, tibia, humerus, radius, and ulna), membrane bone (skull roofing bones) and muscle of Sprague-Dawley rats (n = 55) that died at various times up to 65 weeks after the end of chronic inhalation of uranium ore dust aerosol (4.2 h d(-1) for 65 wk) and from age matched controls (n = 10), were analyzed for uranium, 230Th, 226Ra, 210Pb, and 210Po. Overall, during the period of dust inhalation, the nuclides accumulated in the above order of decreasing concentration in dry bone. However, the results demonstrate that there was some differential accumulation of uranium and uranium decay series radionuclides in muscle and two bone types of rats during the chronic inhalation period. The data also show that the bone levels of some, but not all, radionuclides decreased significantly with time after inhalation ceased. Lung uranium concentration at the time of death was a highly significant covariant for temporal changes in the levels of some radionuclides in both endochondral bone and membrane bone, indicating that lung remained a major source of these isotopes for accumulation in these bone types after ore dust inhalation had ceased. For some isotopes, the two bone types behaved differently during the dust inhalation period, and differently again after the dust inhalation ceased. The relative behavior of one bone type compared to the other for a particular isotope during the dust inhalation period did not predict the relative behavior after dust inhalation ceased. However, a faster accumulation of one bone type compared to the other for a particular isotope during the dust inhalation period predicted a faster decrease after dust inhalation ended. [Dewit200111HPv81n5p501].

33. Reproductive and developmental toxicity of natural and depleted uranium: a review, by JL Domingo, Laboratory of Toxicology and Environmental Health, School of Medicine, Rovira i Virgili University, Reus 43201, Spain. jlldr@fmcs.urv.es. Reprod Toxicol. Vol. 15(6), Nov-Dec 2001 (pp 603-609).
Although the biokinetics, metabolism, and chemical toxicity of uranium are well known, until recently little attention was paid to the potential toxic effects of uranium on reproduction and development in mammals. In recent years, it has been shown that uranium is a developmental toxicant when given orally or subcutaneously (SC) to mice. Decreased fertility, embryo/fetal toxicity including teratogenicity, and reduced growth of the offspring have been observed following uranium exposure at different gestation periods. The reproductive toxicity, maternal toxicity, embryo/fetal toxicity, and postnatal effects of uranium, as well as the prevention by chelating agents of uranium-induced maternal and developmental toxicity are reviewed here. Data on the toxic effects of depleted uranium on reproduction and development are also reviewed. [Domingo200111RTv15n6p603]. (PMID: 11738513 [PubMed - indexed for MEDLINE]).

34. Implanted depleted uranium fragments cause soft tissue sarcomas in the muscles of rats, by FF Hahn, et al., Lovelace Respiratory Research Institute, Albuquerque, New Mexico 87108, USA. fhahn@lrri.org. Environ Health Perspect. Vol. 110(1), Jan 2002 (pp 51-59).
In this study, we determined the carcinogenicity of depleted uranium (DU) metal fragments containing 0.75% titanium in muscle tissues of rats. The results have important implications for the medical management of Gulf War veterans who were wounded with DU fragments and who retain fragments in their soft tissues. We compared the tissue reactions in rats to the carcinogenicity of a tantalum metal (Ta), as a negative foreign-body control, and to a colloidal suspension of radioactive thorium dioxide ((232)Th), Thorotrast, as a positive radioactive control. DU was surgically implanted in the thigh muscles of male Wistar rats as four squares (2.5 x 2.5 x 1.5 mm or 5.0 x 5.0 x 1.5 mm) or four pellets (2.0 x 1.0 mm diameter) per rat. Ta was similarly implanted as four squares (5.0 x 5.0 x 1.1 mm) per rat. Thorotrast was injected at two sites in the thigh muscles of each rat. Control rats had only a surgical implantation procedure. Each treatment group included 50 rats. A connective tissue capsule formed around the metal implants, but not around the Thorotrast. Radiographs demonstrated corrosion of the DU implants shortly after implantation. At later times, rarifactions in the radiographic profiles correlated with proliferative tissue responses. After lifetime observation, the incidence of soft tissue sarcomas increased significantly around the 5.0 x 5.0 mm squares of DU and the positive control, Thorotrast. A slightly increased incidence occurred in rats implanted with the 2.5 x 2.5 mm DU squares and with 5.0 x 5.0 mm squares of Ta. No tumors were seen in rats with 2.0 x 1.0 mm diameter DU pellets or in the surgical controls. These results indicate that DU fragments of sufficient size cause localized proliferative reactions and soft tissue sarcomas that can be detected with radiography in the muscles of rats. [Hahn200201EHPv110n1p51]. (PMID: 11781165 [PubMed - indexed for MEDLINE]).

35. Lipid Oxidation and behavior are correlated in depleted uranium exposed mice, by W. Briner, et al., Department of Psychology, University of Nebraska at Kearney, Kearney, NB. Metal Ions in Biology and Medicine, Vol. 7, 2002 (pp. 59-63). “DU exposure via drinking water produces behavioural changes in mice. DU exposure also produces increased lipid oxidation in the brains of mice”
[Briner2002xxMIBMv7nxp59]

36. Health effects of embedded depleted uranium, by DE McClain, et al., Armed Forces Radiobiology Research Institute, 8901 Wisconsin Avenue, Bethesda, MD 20889-5603, USA. Mil Med. Vol. 167(2 Suppl), Feb. 2002 (pp. 117-119).
The health effects of embedded fragments of depleted uranium (DU) are being investigated to determine whether current surgical fragment-removal policies are appropriate for this metal. The authors studied rodents implanted with DU pellets as well as cultured human cells exposed to DU compounds. Results indicate that uranium from implanted DU fragments distributes to tissues distant from implantation sites, including bone, kidney, muscle, and liver. Despite levels of uranium in kidney that would be nephrotoxic after acute exposure, no histological or functional kidney toxicity was observed with embedded DU, indicating that the kidney adapts when exposed chronically. Nonetheless, further studies of the long-term health impact are needed. DU is mutagenic and transforms human osteoblastic cells into a tumorigenic phenotype. It alters neurophysiological parameters in rat hippocampus, crosses the placental barrier, and enters fetal tissue. Preliminary data also indicate decreased rodent litter size when animals are bred 6 months or longer after DU implantation. [McClain200201MMv167n2suppp117]. (PMID: 11873491 [PubMed - indexed for MEDLINE]).

37. Renal effects of uranium in drinking water, by P. Kurttio, et al., Environmental Health Perspectives Vol. 110, 2002 (pp. 337-342).
This Finish study showed U in drilled wells in this study had a median of 28 :g/L (max. 1920 :g/L). Median daily intake was 39 :g (7-224 :g/d). Found U excretion in urine associated with increased Ca and P excretion. U conc. in drinking water and daily U intake were associated with Ca fractional excretion, but not with P or glucose excretion. Results indicate U affects renal proximal tubules and not glomerulus. Authors indicate safe conc of U in drinking water may be within range of proposed (Finish) guidelines of 2-30 :g/L.
[Kurttio2002xxEHPv119bxp337].

38. Malignant transformation of human bronchial epithelial cell (BEAS-2B) induced with depleted uranium [Article in Chinese], by Yang Zhi-hua, et al., Institute of Radiation Medicine, Academy of Military Medicine Science, Beijing, China. Ai Zheng Vol. 21(9), Sept. 2002 (pp. 944-948).

BACKGROUND & OBJECTIVE: It is clear from works already reported that depleted uranium (DU) affect human health. However, the late effect, especially the carcinogenesis, was not clearly understood. This study was designed to investigate the malignant transformation of human bronchial epithelial cell induced by insoluble DU and lung cancer related gene expression pattern, through imitating the condition that human absorbs depleted uranium aerosol. METHODS: Adenovirus-12/SV40 virus immortalized human bronchial epithelial cells (BEAS-2B) were reacted with insoluble DU oxide (dUO2); the characteristics of malignant transformation of cells were identified through observing the multiplication time of different generation cells, serum resistance, colony formation rate of semi-solid agar, and tumorigenesis in nude mice. Gene expression pattern of transferred BEAS-2B cell induced by DU was determined using 213 lung cancer related gene arrays. RESULTS: The multiplication time of BEAS-2B cell treated with DU was obviously decreased and the serum reistance was significantly increased in 5th generation; the anchorage independent growth (semi-solid agar colony formation) was appeared in 10th generation cell. The 15th generation cell formed tumor in nude mice. DMSO showed overt protection effect on malignant transformation of BEAS-2B cell. The analyzing results of 213 lung cancer related gene arrays showed that the expression level changed in more than 70 genes of transferred cells, including the overt decrease of level of gene expression in more than 10 genes. CONCLUSION: DU has carcinogenesis in vitro.
[Yang200209AZv21n9p944]. (PMID: 12508538 [PubMed - indexed for MEDLINE]).

39. Uranyl acetate-induced sensorimotor deficit and increased nitric oxide generation in the central nervous system in rats, by MB Abou-Donia, et al., Pharmacology, Biochemistry and Behavior Vol. 72, 2002 (pp. 881-890).
The study was designed to follow effects of daily injections of 0.1, 1, 10 and 100 mg/kg in rats for 7 days, with an observation period up to 30 days. All rats in the 10 and 100 mg/kg group died before the 7th injection. Animals in the lower dose groups survived but showed neurological deficits wrt inclined plane performance, grip time, beam walk score and beam walk time. There were some specific changes in NO in cortex and midbrain of lowest dose group and increased AChE acty in cortex of the 1 mg/kg dose group. These results indicate subtle neurological deficits in relatively low dose U exposure as uranyl acetate.
[AbouDonia2002xxPBBv72nxp881]

40. Effects of depleted uranium on the health and survival of Ceriodaphnia dubia and Hyalella azteca, by WW Kuhne, et al., U.S. Geological Survey, New Mexico Cooperative Fish and Wildlife Research Unit, New Mexico State University, Las Cruces 88003-8001, USA. wkuhne@lamar.colostate.edu. Environ Toxicol Chem. Vol. 21(10), Oct 2002 (pp 2198-2203).
Depleted uranium (DU) has been used as a substitute for the fissionable enriched uranium component of atomic weapons tested at Los Alamos National Laboratory (LANL) (Los Alamos, NM, USA) since the early 1950s, resulting in considerable concentrations of DU in the soils within the test sites. Although the movement of DU into major aquatic systems has been shown to be minimal, there are many small-order ephemeral streams and areas of standing water in canyons throughout LANL that may be affected by inputs of DU via runoff, erosion, and leaching. Ninety-six-hour acute and 7-d chronic toxicity assays were conducted to measure the toxicity of DU on survival and reproduction of Ceriodaphnia dubia. A 14-d water-only assay was conducted to measure survival and growth of Hyalella azteca. The estimated median lethal concentration (LC50) to produce 50% mortality of the test population for the 96-h Ceriodaphnia dubia assay was 10.50 mg/L. Reproductive effects occurred at a lowest-observable-effect concentration > or = 3.91 mg/L with a no-observable-effect concentration of 1.97 mg/L. The estimated 14-d LC50 for the Hyalella azteca assay was 1.52 mg/L. No significant relationship was detected between growth and DU concentrations. Concentrations at which toxicity effects were observed in this study for both invertebrates exceeded concentrations of total uranium observed in runoff from LANL lands.
Thus, it is likely that current runoff levels of uranium do not pose a threat to these types of aquatic invertebrates.
[Kuhne200210ETCv21n10p2198]. (PMID: 12371498 [PubMed - indexed for MEDLINE]).

41. Depleted uranium: radiation and ecological safety aspects [Article in Russian], by I.B. Ushakov, et al., Voen Med Zh. Vol. 324(4), 2003 (pp. 56-58, 80).
The authors have analyzed the ecological, sanitary-and-hygienic and medicobiologic aspects of using the impoverished uranium in armaments and military equipment. The influence of impoverished uranium on human body (600 cases) was studied using medicobiologic investigation. It was shown that the particles of aerosol of mixed uranium oxide cause the radiation and chemical damage of kidneys, lungs and other internals. Uranium's alpha-radiation is very effective in induction of biologic effects during internal irradiation. Taking into account that bone tissue is the critical organ for uranium isotopes the medullar tissue is exposed to alpha-radiation. In the armed conflicts of the last decade wide use of armour-piercing means with elements consisted of impoverished uranium has led to the appearance of new technogenic risk factor for the environment and the man.
[Ushakov2003xxVMZv324n4p56]. (PMID: 12825370 [PubMed - indexed for MEDLINE]).

42. Properties, use and health effects of depleted uranium: a general overview, A Bleise, et.al., Journal of Environmental Radioactivity Vol. 64(2-3), 2003 (pp. 93-112). International Atomic Energy Agency (IAEA), Dept. of Nuclear Sciences and Applications.
Depleted uranium (DU), a waste product of uranium enrichment, has several civilian and military applications. It was used as armor-piercing ammunition in international military conflicts and was claimed to contribute to health problems, known as the Gulf War Syndrome and recently as the Balkan Syndrome. This led to renewed efforts to assess the environmental consequences and the health impact of the use of DU. The radiological and chemical properties of DU can be compared to those of natural uranium, which is ubiquitously present in soil at a typical concentration of 3 mg/kg. Natural uranium has the same chemotoxicity, but its radiotoxicity is 60% higher. Due to the low specific radioactivity and the dominance of alpha-radiation no acute risk is attributed to external

exposure to DU. The major risk is DU dust, generated when DU ammunition hits hard targets. Depending on aerosol speciation, inhalation may lead to a protracted exposure of the lung and other organs. After deposition on the ground, resuspension can take place if the DU containing particle size is sufficiently small. However, transfer to drinking water or locally produced food has little potential to lead to significant exposures to DU. Since poor solubility of uranium compounds and lack of information on speciation precludes the use of radioecological models for exposure assessment, biomonitoring has to be used for assessing exposed persons. Urine, feces, hair and nails record recent exposures to DU. With the exception of crews of military vehicles having been hit by DU penetrators, no body burdens above the range of values for natural uranium have been found. Therefore, observable health effects are not expected and residual cancer risk estimates have to be based on theoretical considerations. They appear to be very minor for all post-conflict situations, i.e. a fraction of those expected from natural radiation.
[Bleise2003xxJERv64n2to3p93]. (PMID: 12500797 [PubMed - indexed for MEDLINE]).

43. The biokinetics of uranium migrating from embedded DU fragments, by R.W. Leggett, et al., Life Sciences Division of Oak Ridge National Laboratory, Oak Ridge, TN, Journal of Environmental Radioactivity, Vol. 64(2-3), 2003 (pp. 205-225). Military uses of depleted uranium (DU) munitions have resulted in casualties with embedded DU fragments. Assessment of radiological or chemical health risks from these fragments requires a model relating urinary U to the rate of migration of U from the fragments, and its accumulation in systemic tissues. A detailed biokinetic model for U has been published by the International Commission on Radiological Protection (ICRP), but its applicability to U migrating from embedded DU fragments is uncertain. Recently, Pellmar and colleagues (1999) conducted a study at the Armed Forces Radiobiology Research Institute (AFRRI) on the redistribution and toxicology of U in rats with implanted DU pellets, simulating embedded fragments. This paper compares the biokinetic data from that study with the behavior of commonly studied forms of U in rats (e.g., intravenously injected U nitrate). The comparisons indicate that the biokinetics of U migrating from embedded DU is similar to that of commonly studied forms of U with regard to long-term accumulation in kidneys, bone and liver. The results provide limited support for the application of the ICRP's model to persons with embedded DU fragments. Additional information is needed with regard to the short term behavior of migrating U and its accumulation in lymph nodes, brain, testicles and other infrequently studied U repositories.
[Leggett200300JERv64n2p205]. (PMID: 12500806 [PubMed - indexed for MEDLINE]).

44. Depleted uranium: a new battlefield hazard, by VSG Murray, et al., Lancet (Supplement) Vol. 360, (pp. S31-S32).
The authors are members of the Royal Society Working Group on the Hazards of Depleted Uranium Munitions. They conclude that the radiation from DU is not sufficient to warrant concern about increases in lung cancer or other cancers such as leukemia. They go on to say that the critical organ for chemical toxicity effects is the renal proximal tubule epithelium, but with severe exposures could cause hepatic, haemological, respiratory and cardiac toxic effects. They mention that data regarding exposures are poor and there are problems with trying to predict long term effects. They suggest the health hazards of long-term DU are minimal compared to the inherent hazards of war.
[Murray200300Lv360nxpS31].

45. Estimate of the time zero lung burden of depleted uranium in Persian Gulf War veterans by the 24-hour urinary excretion and exponential decay analysis, by A. Durakovic, et al., Uranium Medical Research Centre, 3430 Connecticut Avenue/11854, Washington, DC 20008, USA, Mil Med. Vol. 168(8), Aug. 2003 (pp. 600-605).
The aim of this study was to estimate the amount of depleted uranium (DU) in the respiratory system of Allied Forces Gulf War Veterans. Mass spectrometry (thermal ionization mass spectrometry) analysis of 24-hour urinary excretion ofDU isotopes in five positive (238U/235U > 191.00) and six negative (238U/235U > 138.25) veterans was utilized in the mathematical estimation of the pulmonary burden at the time of exposure. A minimum value for the biological half-life of ceramic DU oxide in the lungs was derived from the Battelle report of the minimum dissolution half-time in simulated interstitial lung fluid corresponding to 3.85 years. The average DU concentration was 3.27 x 10(-5) mg per 24 hours in DU-positive veterans and 1.46 x 10(-8) mg in DU-negative veterans. The estimated lung burden was 0.34 mg in the DU-positive and 0.00015 mg in the DU-negative veterans. Our results provide evidence that the pulmonary concentration of DU at time zero can be quantitated as late as 9 years after inhalational exposure.
[Durakovic200308MMv168n8p600]. (PMID: 12943033 [PubMed - in process])

46. Depleted and natural uranium: chemistry and toxicological effects, by E. Craft, et al., Nicholas School of the Environment and Earth Sciences, Duke University, Durham, North Carolina 27710, USA. J Toxicol Environ Health B Crit Rev. Vol. 7(4), Jul-Aug, 2004 (pp. 297-317).
Depleted uranium (DU) is a by-product from the chemical enrichment of naturally occurring uranium. Natural uranium is comprised of three radioactive isotopes: (238)U, (235)U, and (234)U. This enrichment process reduces the radioactivity of DU to roughly 30% of that of natural uranium. Nonmilitary uses of DU include counterweights in airplanes, shields against radiation in medical radiotherapy units and transport of radioactive isotopes. DU has also been used during wartime in heavy tank armor, armor-piercing bullets, and missiles, due to its desirable chemical properties coupled with its decreased radioactivity. DU weapons are used unreservedly by the armed forces. Chemically and toxicologically, DU behaves similarly to natural uranium metal. Although the effects of DU on human health are not easily discerned, they may be produced by both its chemical and radiological properties. DU can be toxic to many bodily systems, as presented in this review. Most importantly, normal functioning of the kidney, brain, liver, and heart can be affected by DU exposure. Numerous other systems can also be affected by DU exposure, and these are also reviewed.

Despite the prevalence of DU usage in many applications, limited data exist regarding the toxicological consequences on human health. This review focuses on the chemistry, pharmacokinetics, and toxicological effects of depleted and natural uranium on several systems in the mammalian body. A section on risk assessment concludes the review.
[Craft200407JTEHBCRv7n4p297].

47. Depleted uranium dust from fired munitions: physical, chemical and biological properties, by RE Mitchel, et al., Atomic Energy of Canada Limited, Chalk River Laboratories, Chalk River Ontario, K0J 1J0, Canada. mitchelr@aecl.ca. Health Phys. Vol. 87(1), Jul. 2004 (pp. 57-67).
This paper reports physical, chemical and biological analyses of samples of dust resulting from munitions containing depleted uranium (DU) that had been live-fired and had impacted an armored target. Mass spectroscopic analysis indicated that the average atom% of U was 0.198 +/- 0.10, consistent with depleted uranium. Other major elements present were iron, aluminum, and silicon. About 47% of the total mass was particles with diameters <300 micrometer, of which about 14% was <10 micrometer. X-ray diffraction analysis indicated that the uranium was present in the sample as uranium oxides-mainly U3O7 (47%), U3O8 (44%) and UO2 (9%). Depleted uranium dust, instilled into the lungs or implanted into the muscle of rats, contained a rapidly soluble uranium component and a more slowly soluble uranium component. The fraction that underwent dissolution in 7 d declined exponentially with increasing initial burden. At the lower lung burdens tested (<15 microg DU dust/lung) about 14% of the uranium appeared in urine within 7 d. At the higher lung burdens tested (~80-200 microg DU dust/lung) about 5% of the DU appeared in urine within 7 d. In both cases about 50% of that total appeared in urine within the first day. DU implanted in muscle similarly showed that about half of the total excreted within 7 d appeared in the first day. At the lower muscle burdens tested (<15 microg DU dust/injection site) about 9% was solubilized within 7 d. At muscle burdens >35 microg DU dust/injection site about 2% appeared in urine within 7 d. Natural uranium (NU) ore dust was instilled into rat lungs for comparison. The fraction dissolving in lung showed a pattern of exponential decline with increasing initial burden similar to DU. However, the decline was less steep, with about 14% appearing in urine for lung burdens up to about 200 microg NU dust/lung and 5% at lung burdens >1,100 microg NU dust/lung. NU also showed both a fast and a more slowly dissolving component. At the higher lung burdens of both DU and NU that showed lowered urine excretion rates, histological evidence of kidney damage was seen. Kidney damage was not seen with the muscle burdens tested. DU dust produced kidney damage at lower lung burdens and lower urine uranium levels than NU dust, suggesting that other toxic metals in DU dust may contribute to the damage.
[Mitchel200407HPv87n1p57]. PMID: 15194923 [PubMed - indexed for MEDLINE]

Chapter III

The Effects of Low Level Ionizing Radiation Exposure on Living Tissue, Cells, Chromosomes and DNA

Summary

Every living thing on this planet is exposed to low-level ionizing radiation (LLIR) from both natural and man-made sources. Natural uranium, radium and radon and their radioactive decay products are present in low concentrations throughout our air, water and earth. Since the advent of the nuclear age, and particularly as a result of atmospheric nuclear testing from 1945 through 1972, many biologically active radioactive isotopes have been produced and have been dispersed around the world. Nuclear accidents such as those at Chernobyl, Windscale and Three Mile Island have been responsible for world-wide releases of radioactive substances. LLIR is an ever-present issue in the immediate neighborhood of nuclear power plants and all mining, manufacturing and processing plants that deal with radioactive materials.

Unlike ultraviolet radiation from the sun and other sources of low-energy electromagnetic radiation which must actually strike a molecule to do damage, ionizing radiation creates a path of disrupted molecules in its wake. Alpha and beta particles, emitted as ionizing radiation from radioactive sources, are electrically charged. It is this electrical charge that rips electrons out of neighboring molecules when the charged particle passes nearby. This "force at a distance" effect is similar to moving a magnet above a pile of iron filings. X-rays and the more energetic gamma rays, though not charged, are also ionizing radiation through what is known as the Compton effect. When one of these high-energy photons strikes a molecule, it causes one of the molecule's own electrons to fly off from the molecule as a high-energy beta particle, destroying the molecule in the process. Furthermore, along with the released electron, a new gamma or X-ray having a somewhat lower energy than the original, is also given off, allowing the process to repeat several more times. Thus a single sufficiently energetic gamma ray can be responsible for the release of many ionizing beta particles.

The Bystander Effect and Low Dose Effects in Radiation Induced Cytotoxicity. The following articles show that radiation damage can induce signals in cells that are sent to neighboring cells that have not received direct radiation. This "bystander effect" can result in far more cellular damage than expected for the number of cells that are directly hit by alpha and beta particles. This information has been neglected in most arguments that suggest that internalized depleted uranium would not have sufficient radiation effects to produce a significant increase in cancers. These papers discuss the implications of this effect for radon gas exposure, but it would also apply to ionizing particles emitted by any radioactive element, including uranium or plutonium. It has been argued "If DNA damage were to occur in bystander cells in vivo, and these cells survived such damage, these results would impact significantly on the assessment of cancer risk initiated by low fluence exposures to alpha radiation." [Azzam et al., PNAS, 98, 478, 2001, see below].

Details

Batchelor (1), in 1980, demonstrated that when enriched uranium (with higher concentration of fissionable U-235 than depleted uranium) was introduced into rat lungs by injection or inhalation, and the rat subjected to neutron bombardment (thus initiating nuclear fission of the U-235), squamous cell carcinomas developed at the site containing enriched uranium. Injected depleted uranium oxide did not show this effect, and adenocarcinomas were observed in rats subjected to enriched uranium oxide exposure even without neutron bombardment, clearly demonstrating that alpha particle radiation from uranium oxides in pulmonary tissue is carcinogenic.

Sister chromatid exchange (SCE) is generally believed to lead to increased genetic mutations in daughter cells. Nagasawa (2) observed SCE in hamster ovary cells in 1992 after low-dose alpha particle irradiation and found that 30% of the cells were affected even though only 1% of the cells had been directly exposed.

In 1996, Chen (3) reported developing a computer simulation to predict radiation-induced chromosome abberations. Using FISH (fluorescent in-situ hybridization) to visualize a wide variety of chromosome aberrations, Chen (11) compared the results obtained from a computer simulation and found a good correlation.

Brenner (4) reports in 1996 that chromatid exchanges observed in Hiroshima A-bomb blast victims points to neutrons, rather than gamma radiation as previously thought, as being the dominant exposure vector. This in turn calls to question previous conclusions on which dose and exposure risk data have been based.

RC Miller (5), of Columbia U, found that oncogenic transformation in cells from direct exposure to radon gas (which emits alpha particles with a variety of energies) was comparable to that produced from exposure to a spectrum of energy-tuned alpha particles from an accelerator, lending credence to the use of laboratory methodology for determining exposure limits for radon gas.

Sachs (6) calculates that irradiation therapy to kill cancer cells must take into account the growth rate of the cancer cells between treatments and concludes that concentrating irradiation dosage earlier in the program is best. Sachs also calculates the proximity effects (7) that give rise to chromosome aberrations when a damaged DNA molecule attempts to repair itself after being exposed to ionizing radiation and further reported (9) that comparing the ratio of intraarm vs. interarm chromatid exchanges might provide a means of deducing extent of initial radiation exposure. He concludes (10) that at low radiation dosage, the linear quadratic model is the best predictor of resulting molecular damage. Brenner (8) also defended the use of the linear quadratic model as appropriate in clinical radiation oncology and later reported (13) that this model and others commonly used in radiation therapy for time-dose relationships produce similar results.

Hei (12) reported that single alpha particle exposure to a cell resulted in less than 20% mortality but a high mutagenicity (110 cells out of 100,000 survivors), with both figures being dose dependent. Miller (15) reported oncogenic transforming potential to cells traversed by single alpha particles and multiple alpha particles and found risks to be much lower than anticipated for single particle exposure. One conclusion from this study was that extrapolating radon risk from population studies of uranium miners to risks associated with domestic radon exposure might tend to overestimate domestic risk.

Sachs (14) reported in 1998 on the observed clustering of DNA double strand breaks (DSB) along a chromosome and on creating a model relating the extent of clustering to the intensity of radiation dose. Johnson (16) reported that DNA cleavage from radiation exposure was non-random, with certain chromosomes as well as certain specific regions within chromosomes experiencing greater likelihood of damage. However, Cornforth (30) reported in 2002 that his experiments pointed to essentially random damage within the irradiated chromosomes.

Brenner (24) showed that chromosome damage can serve as a reliable biomarker for previous exposure to radiation. Hande (31), using a new technique to detect chromosome damage, found that blood cells of plutonium workers showed a long-lasting signature of previous radiation exposure, even among workers whose exposure had ended many years before.

Lehnert (28f) reported on the influence of reactive oxygen species initiated within cells by ionizing radiation and/or chemical exposure and the possible beneficial and detrimental effects resulting from such exposure.

Smith (20) studied low radiation doses to determine if they might be more effective in destroying tumor cells than higher doses, but found no significant deviation from the linear quadratic model even for the low radiation dose experiments. RC Miller (21), (22) showed that low energy neutron irradiation of cells result in oncogenic transformations.

Nagasawa (19) observed the bystander effect at low radiation doses on Chinese hamster ovarian cells. Sawant (25), Brenner (26), (29), (32), Azzam (27), Iyer (22m), (28m) and Zhou (23), (28), (33) reported on their detailed studies of bystander effects. Goldberg (29m) published a review in 2002 detailing studies on the bystander effect.

Brenner (34) published a review in 2003 on risks associated with low energy radiation exposure and proposed that the minimum exposure level demonstrated to date that results in cancer formation is 10-50 msev for acute exposure and 50-100 msev for protracted exposure and suggested that the linear no-threshold model is appropriate for extrapolating dose/risk relationships to extremely small dose levels.

1. The carcinogenic effect of localized fission fragment irradiation of rat lung, by AL Batchelor, et al.. Int J Radiat Biol Relat Stud Phys Chem Med. Vol. 37(3), Mar. 1980 (pp. 249-66).
In a preliminary investigation of 'hot particle' carcinogenesis uranium oxide particles were introduced into the lungs of rats either by intubation of a liquid suspension of the particles or by inhalation of an aerosol. Subsequently the animals were briefly exposed to slow neutrons in a nuclear reactor, resulting in localized irradiation of the lung by fission fragments emitted from 235U atoms in the oxide particles. The uranium used in the intubation experiments was either enriched or depleted in 235U. Squamous cell carcinomas developed at the site of deposition of the enriched uranium oxide in many cases but no lung tumours occurred in the rats with the depleted uranium oxide, in which the lung tissue was exposed to very few fission fragments. Only enriched uranium oxide was used in the inhalation experiments. Pulmonary squamous cell carcinomas occurred after the fission fragment irradiation but were fewer than in the intubation experiments. Adenocarcinomas of the lung were seen in rats exposed to uranium oxide without subsequent irradiation by neutrons in the reactor and in rats irradiated with neutrons but not previously exposed to uranium oxide. It is concluded that (i) fission fragments were possibly implicated in the genesis of the squamous cell carcinomas, which only developed in those animals exposed to enriched uranium oxide and neutrons and (ii) the adenocarcinomas in the rats inhaling enriched uranium oxide only were likely to have been caused by protracted irradiation of the lung with alpha-rays emitted from the enriched uranium.
[Batchelor198003IJRBv37n3p249]. (PMID: 6966271 [PubMed - indexed for MEDLINE])

2. Induction of sister chromatid exchanges by extremely low doses of alpha-particles, by H. Nagasawa, et al., Cancer Research Vol. 52, 1992 (pp. 6394-6396).
Chinese hamster ovary cells grown in culture were irradiated with low doses of alpha-particles (31 mrads) during G1 ((pre-DNA synthesis) phase. Found that 30% of cells had increased frequency of sister chromatid exchange (SCE), even though less than 1% of cells would have been traversed by an alpha-particle. Although the significance of SCE isn't clear, it is generally recognized that SCE can lead to increased genetic mutations in daughter cells. Authors suggest that intercellular communication may be responsible for this phenomenon. [Nagasawa1992xxCRv52nxp6394].

3. Proximity effects for chromosome aberrations measured by FISH, by AM Chen, et al., Department of Mathematics, University of California, Berkeley 94720, USA. Int J Radiat Biol. Vol. 69(4), Apr. 1996 (pp. 411-420).
A Monte Carlo simulation computer program for radiation-produced chromosome aberrations, based on the breakage-and-reunion model, was extended to include proximity effects due to localization of chromosomes and limited range for break-break interactions. Two adjustable parameters were used. One corresponds to total dose: the other determines proximity effects by specifying the number of 'interaction regions' in a cell nucleus. The use of additional adjustable parameters was avoided by assuming randomness of break induction and aberration production. FISH chromosome painting data were obtained from 1.9 Gy 60Co gamma-rays-irradiated human lymphocytes. The data were compared with the computer simulation results, taking individual chromosome lengths into account. With about 13 interaction regions, agreement between the experiment and the simulation was good, even when detailed categories of damage were scored. An estimated average dsb-dsb interaction distance, based on 13 interaction regions, is about 1.3 micron. Monte Carlo methods give useful quantitative estimates of relative aberration yields, with a minimum of adjustable parameters and the theoretical assumptions, and indicated proximity effects. Computer simulation of FISH experiments can be adapted to any number of colours, any scoring criteria and any method of grouping aberrations into categories. Simulation allows systematic extrapolation of aberration data on painted chromosomes to whole-genome aberration frequencies.
[Chen199604IJRBv69n4p411]. (PMID: 8627123 [PubMed - indexed for MEDLINE]).

4. Direct biological evidence for a significant neutron dose to survivors of the Hiroshima atomic bomb, by Brenner DJ, Center for Radiological Research, Columbia University, New York 10032, USA. Radiat Res. Vol. 145(4), Apr. 1996 (pp. 501-7). Erratum in: Radiat Res. Vol. 145(5), May 1996 (pp. 653). Comment in: Radiat Res. Vol. 147(4), Apr. 1997 (pp. 506-510).
In the past few years much physical evidence has accumulated that the A-bomb survivors at Hiroshima were exposed to significant doses of neutrons, in contrast to the predictions of the current DS86 dosimetry. We discuss some biological measurements of exchange-type chromosomal aberrations in survivors at Hiroshima, which also strongly imply that the survivors received a significant neutron dose. Specifically, the ratio of translocations (an interchromosomal aberration) to pericentric inversions (intra-chromosomal interarm aberration), the F value, was significantly smaller than would be expected from a gamma-ray exposure, and was consistent with the majority of the effective dose coming from neutrons. If this biological evidence and the previous physical evidence are correct, the effective neutron dose at relevant locations at Hiroshima dominated the total effective dose, from which it may be concluded that (1) the risk coefficient for gamma rays may have been considerably overestimated, and (2) there is a possibility of deriving from the A-bomb data, with reasonable confidence limits, the relative biological effectiveness (RBE) for carcinogenesis by neutrons.
[Brenner199604RRv145n4p501] (PMID: 8600511 [PubMed - indexed for MEDLINE]).

5. The biological effectiveness of radon-progeny alpha particles. V. Comparison of oncogenic transformation by accelerator-produced monoenergetic alpha particles and by polyenergetic alpha particles from radon progeny, by RC Miller, et al., Center for Radiological Research, Columbia University, New York, New York 10032, USA. Radiat Res. Vol. 146(1), Jul. 1996 (pp. 75-80).
Generation of estimates of risk caused by exposure to radon in the home, either from miner data or from A-bomb data, requires several scaling factors such as for dose, dose rate and radiation quality, and possible synergisms. Such scaling factors are best developed from laboratory-based studies. Two possible sources of alpha particles for such studies are (1) a polyenergetic spectrum, generated directly by radon and its progeny, or (2) a series of monoenergetic alpha particles. We compare here the results of oncogenic transformation from studies using both systems. At the Columbia University Radiological Research Accelerator Facility (RARAF), C3H 10T1/2 cells were irradiated with alpha particles of various energies, with defined LETs from 70 to 200 keV/mum. At Pacific Northwest Laboratory, cells from the same stock were exposed to alpha particles from radon gas and its progeny, which were in equilibrium with the culture medium. There was good agreement between the results of oncogenic transformation experiments using the two different exposure systems. Apart from the experimental transformation frequencies themselves, such a comparison requires (1) reliable dosimetry at both facilities and (2) estimated LET distributions for the polyenergetic alpha-particle irradiator. Thus this good agreement gives some confirmation to the technique which is used to fold together oncogenic transformation rates from monoenergetic alpha particles to yield a predicted rate for a spectrum of alpha particles.
[Miller199607RRv146n1p75]. (PMID: 8677301 [PubMed - indexed for MEDLINE]).

6. Dose timing in tumor radiotherapy: considerations of cell number stochasticity, by RK Sachs , et al., Department of Mathematics, University of California, Berkeley, USA. sachs@math.berkeley.edu. Math Biosci. Vol. 138(2), Dec. 1996 (pp. 131-46).
A typical tumor radiotherapy regimen using external beam X rays consists of doses on weekdays for 4-7 weeks. During the final weeks, the tumor may contain only a few cells capable of regenerating the tumor and may be growing exponentially between

doses. Stochastic fluctuations of the cell number can influence the optimal time pattern of dose delivery. If the total dose is fixed, a deterministic model of exponential tumor growth, neglecting stochastic effects, predicts that the way the radiation dose is spread out in time does not affect the average number of tumor cells at the end. However, we here show, within the framework of a birth-death model, that when stochastics are taken into account, the earlier the dose is given (consistent with other constraints imposed by quite different considerations), the better. The proof uses a transformation that simplifies the characteristic equation of the partial differential equation governing the probability generating function for a birth-death process with time-dependent rates. The theorem that earlier is better holds for any statistical distribution of cell number from patient to patient at the start of the exponential growth phase and for virtually any cell-killing model. Numerical results indicate the stochastic effects, although not dominant, are not negligible.
[Sachs199612MBv138n2p131] (PMID: 8987356 [PubMed - indexed for MEDLINE]).

7. Review: proximity effects in the production of chromosome aberrations by ionizing radiation, by RK Sachs, et al., Department of Mathematics, University of California, Berkeley 94720, USA. sachs@math.berkeley.edu. Int J Radiat Biol. Vol. 71(1), Jan. 1997 (pp. 1-19).
After ionizing radiation has induced double-strand DNA breaks (dsb), misrejoining produces chromosome aberrations. Aberration yields are influenced by "proximity' effects, i.e., by the dependence of misrejoining probabilities on initial dsb separations. We survey proximity effects, emphasizing implications for chromosome aberration-formation mechanisms, for chromatin geometry, and for dose-response relations. Evidence for proximity effects comes from observed biases for centric rings and against three-way interchanges, relative to dicentrics or translocations. Other evidence comes from the way aberration yields depend on radiation dose and quality, tightly bunched ionizations being relatively effective. We concludes (1) that misrejoining probabilities decrease as the distance between dsb at the time of their formation increases, and almost all misrejoining occurs among dsb initially separated by < 1/3 of a cell nucleus diameter; (2) that chromosomes occupy (irregular) territories during the G0/G1 phase of the cell cycle, having dimensions also roughly 1/3 of a cell nucleus diameter, (3) that proximity effects have the potential to probe how much different chromosomes intertwine on move relative to each other: and (4) that incorporation of proximity effects into the classic random breakage-and-reunion model allows quantitative interrelation of yields for many different aberration types and of data obtained with various FISH painting methods or whole-genome scoring. [Sachs199701IJRBv71n1p1]

8 The use of the linear-quadratic model in clinical radiation oncology can be defended on the basis of empirical evidence and theoretical argument, by DJ Brenner, et al., Columbia University, Center for Radiological Research, New York, New York 10032, USA. djb3@columbia.edu. Med Phys. Vol. 24(8), Aug. 1997 (pp. 1245-1248). Comment in: Med Phys. Vol. 24(8), Aug. 1997 (pp. 1329). [Brenner199708MPv24n8p1245]. (PMID: 9284247 [PubMed - indexed for MEDLINE]).

9. Intra-arm and interarm chromosome intrachanges: tools for probing the geometry and dynamics of chromatin, by RK Sachs, et al., Department of Mathematics, University of California, Berkeley 94720, USA. Radiat Res. Vol. 148(4), Oct. 1997 (pp. 330-40.)
Many chromosome-type, exchange-type chromosomal aberrations produced by radiation are intrachanges, i.e. involve only one chromosome. It is assumed such intrachanges are formed by illegitimate reunion of two double-strand breaks (DSBs) on the chromosome. The yield of intra-arm intrachanges (acentric rings or paracentric inversions) relative to that of interarm intrachanges (centric rings or pericentric inversions) is larger than would occur if production and illegitimate reunion of DSBs were spatially random. The excess of intra-arm intrachanges is presumably due to proximity effects for illegitimate reunions, i.e. enhancement of the intrachange probability when two DSBs are formed close to one another. Radiation track structure may also play a role. Using a polymer description for "large-scale" chromatin geometry (>2 Mb), and using two alternate (rapid or slow motion) models for the way that DSBs move after they are produced, theoretical estimates are given for size distributions of intrachanges at low or high linear energy transfer (LET). The ratio of intra-arm to interarm intrachanges is derived from the size distribution and compared with data from the literature on centric rings, inversions, interstitial deletions and excess acentric fragments. Proximity effects enhance yields of intra-arm relative to interarm intrachanges at least severalfold and perhaps as much as 10-fold compared to expectations based on spatial randomness. We argue that further measurements of intra-arm and interarm intrachanges would be informative about large-scale chromatin structure and chromosome motion. Because inversions are more frequent than estimates of randomness would indicate, and are transmissible to daughter cells, their size distribution could also help characterize past exposure to high-LET radiation. [Sachs199710RRv148n4p330] (PMID: 9339949 [PubMed - indexed for MEDLINE]).
10. The link between low-LET dose-response relations and the underlying kinetics of damage production/repair/misrepair, by RK Sachs, et al., Department of Mathematics, University of California, Berkeley 94720, USA. Int J Radiat Biol. Vol. 72(4), Oct. 1997 (pp. 351-74).
PURPOSE: To review current opinion on the production and temporal evolution of low-LET radiobiological damage. METHODS: Standard cell survival models which model repair/misrepair kinetics in order to quantify dose-response relations and dose-protraction effects are reviewed and interrelated. Extensions of the models to endpoints other than cell survival, to multiple or compound damage processing pathways, and to stochastic intercellular damage fluctuations are surveyed. Various molecular mechanisms are considered, including double strand breaks restitution and binary misrepair. CONCLUSIONS: (1) Linking dose-response curves to the underlying damage production/processing kinetics allows mechanistic biological interpretations of observed curve parameters. (2) Various damage processing pathways, with different kinetics, occur. (3) Almost every current kinetic model, whether based on binary misrepair or saturable repair, leads at low or intermediate doses to the LQ (linear-quadratic) formalism, including the standard (generalized Lea-Catcheside) dependence on dose protraction. (4) Two-track (beta) lethal damage is largely

due to dicentric chromosome aberrations, but one-track (alpha) lethal damage is largely caused by other mechanisms such as point mutations in a vital gene, small deletions, residual chromosome breaks, induced apoptosis, etc. (5) A major payoff for 50 years of radiobiological modelling is identifying molecular mechanisms which underly the broadly applicable LQ formalism.
[Sachs199710IJRBv72n4p351] PMID: 9343102 [PubMed - indexed for MEDLINE]).

11. Computer simulation of data on chromosome aberrations produced by X rays or alpha particles and detected by fluorescence in situ hybridization, by AM Chen, et al., Department of Mathematics, University of California, Berkeley 94720, USA. Radiat Res. Vol. 148(5 Suppl), Nov. 1997 (pp. S93-101).
With fluorescence in situ hybridization (FISH), many different categories of chromosome aberrations can be recognized-dicentrics, translocations, rings and various complex aberrations such as insertions or three-way interchanges. Relative frequencies for the various aberration categories indicate mechanisms of radiation-induced damage and reflect radiation quality. Data obtained with FISH support a proximity version of the classic random breakage-and-reunion model for the formation of aberrations. A Monte Carlo computer implementation of the model, called the CAS (chromosome aberration simulator), is generalized here to high linear energy transfer (LET) and compared to published data for human cells irradiated with X rays or 238Pu alpha particles. For each kind of radiation, the CAS has two adjustable parameters: the number of interaction sites per cell nucleus and the number of reactive double-strand breaks (DSBs) per gray. Aberration frequencies for various painted chromosomes, of varying lengths, and for 11 different categories of simple or complex aberrations were simulated and compared to the data. The optimal number of interaction sites was found to be approximately 13 for X irradiation and approximately 25 for alpha-particle irradiation. The relative biological effectiveness (RBE) of alpha particles for the induction of reactive DSBs (which are a minority of all DSBs) was found to be approximately 4. The two-parameter CAS model adequately matches data for many different categories of aberrations. It can use data obtained with FISH for any one painting pattern to predict results for any other kind of painting pattern or whole-genome staining, and to estimate a suggested overall numerical damage indicator for chromosome aberration studies, the total misrejoining number.
[Chen199711RRv148n5SupppS93] (PMID: 9355862 [PubMed - indexed for MEDLINE]).

12. Mutagenic effects of a single and an exact number of alpha-particles in mammalian cells, by T.K. Hei, et al., Proceedings of the National Academy of Sciences Vol. 94, 1997 (pp. 3765-3770).
Using hamster-human hybrid cells in culture, showed that single alpha-particle traversal was only slightly cytotoxic (>80% survival) but highly mutagenic (110 mutants/100,000 survivors). Cytotoxicity and mutant induction were both dose dependent. [Hei1997xxPNASv94nxp3765].

13. The linear-quadratic model and most other common radiobiological models result in similar predictions of time-dose relationships, by DJ Brenner, et al., Center for Radiological Research, Columbia University, New York, New York 10032, USA. Radiat Res. Vol. 150(1), Jul. 1998 (pp. 83-91).
One of the fundamental tools in radiation biology is a formalism describing time-dose relationships. For example, there is a need for reliable predictions of radiotherapeutic isoeffect doses when the temporal exposure pattern is changed. The most commonly used tool is now the linear-quadratic (LQ) formalism, which describes fractionation and dose-protraction effects through a particular functional form, the generalized Lea Catcheside time factor, G. We investigate the relationship of the LQ formalism to those describing other commonly discussed radiobiological models in terms of their predicted time-dose relationships. We show that a broad range of radiobiological models are described by formalisms in which a perturbation calculation produces the standard LQ relationship for dose fractionation/protraction, including the same generalized time factor, G. This approximate equivalence holds not only for the formalisms describing binary misrepair models, which are conceptually similar to LQ, but also for formalisms describing models embodying a very different explanation for time-dose effects, namely saturation of repair capacity. In terms of applications to radiotherapy, we show that a typical saturable repair formalism predicts practically the same dependences for protraction effects as does the LQ formalism, at clinically relevant doses per fraction. For low-dose-rate exposure, the same equivalence between predictions holds for early-responding end points such as tumor control, but less so for late-responding end points. Overall, use of the LQ formalism to predict dose-time relationships is a notably robust procedure, depending less than previously thought on knowledge of detailed biophysical mechanisms, since various conceptually different biophysical models lead, in a reasonable approximation, to the LQ relationship including the standard form of the generalized time factor, G.
[Brenner199807RRv150n1p83] (PMID: 9650605 [PubMed - indexed for MEDLINE]).

14. A formalism for analysing large-scale clustering of radiation-induced breaks along chromosomes, by RK Sachs, et al., Department of Mathematics, University of California, Berkeley 94720, USA. Int J Radiat Biol. Vol. 74(2), Aug. 1998 (pp. 185-206).
PURPOSE: To model intra-chromosomal clustering of DSB (DNA double strand breaks) induced by ionizing radiation. That DSB are located non-randomly along chromosomes after high LET irradiation, with clustering even at extremely large scales, has been confirmed by recent pulsed field gel electrophoresis data for size distributions of DNA fragments. We therefore extend the standard random-breakage model for DNA fragment-size distributions to a more general 'clustered-breakage' formalism, which can take correlations of DSB locations along a chromosome into account. METHODS: The new formalism is based mainly on a one-track probability distribution, describing the DNA fragment-size pattern due to a single primary high-energy particle, a pattern determined by track structure and chromatin geometry. Multi-track fragment-size distributions are derived mathematically from the one-track distribution, so that dose response relations are obtained. RESULTS: The clustered-breakage formalism is applicable to any

chromosomal geometry and any radiation track structure. It facilitates extrapolations of high-dose data to the much lower doses of interest for most applications. When applied to recently published data for irradiation of mammalian cells with ions of LET approximately 100 keV microm(-1) it indicates a pattern of Mbp-scale DSB clusters, each containing a number of DSB and corresponding to a very large-scale, multiply-damaged chromatin site. Although DSB are bunched, DSB clusters are scattered almost at random throughout the genome. Estimates of DSB yield are markedly increased by resolving such clusters into individual DSB. The dose response relation for fragments of a given size becomes non-linear when clusters from different tracks interlace or adjoin, as can occur for high doses and large sizes. CONCLUSIONS: DSB clustering along chromosomes, which influences important radiobiological endpoints, is described quantitatively by the clustered-breakage formalism.
[Sachs199808IJRBv74n2p185] (PMID: 9712548 [PubMed - indexed for MEDLINE]).

15. The oncogenic transforming potential of the passage of single alpha particles through mammalian cell nuclei, by RC Miller, et al., Center for Radiological Research, Columbia University, 630 West 168th Street, New York, NY 10032, USA. Proc Natl Acad Sci USA Vol. 96(1), Jan. 1999 (pp. 19-22).
Domestic, low-level exposure to radon gas is considered a major environmental lung-cancer hazard involving DNA damage to bronchial cells by alpha particles from radon progeny. At domestic exposure levels, the relevant bronchial cells are very rarely traversed by more than one alpha particle, whereas at higher radon levels-at which epidemiological studies in uranium miners allow lung-cancer risks to be quantified with reasonable precision-these bronchial cells are frequently exposed to multiple alpha-particle traversals. Measuring the oncogenic transforming effects of exactly one alpha particle without the confounding effects of multiple traversals has hitherto been unfeasible, resulting in uncertainty in extrapolations of risk from high to domestic radon levels. A technique to assess the effects of single alpha particles uses a charged-particle micro-beam, which irradiates individual cells or cell nuclei with predefined exact numbers of particles. Although previously too slow to assess the relevant small oncogenic risks, recent improvements in throughput now permit micro-beam irradiation of large cell numbers, allowing the first oncogenic risk measurements for the traversal of exactly one alpha particle through a cell nucleus. Given positive controls to ensure that the dosimetry and biological controls were comparable, the measured oncogenicity from exactly one alpha particle was significantly lower than for a Poisson-distributed mean of one alpha particle, implying that cells traversed by multiple alpha particles contribute most of the risk. If this result applies generally, extrapolation from high-level radon risks (involving cellular traversal by multiple alpha particles) may overestimate low-level (involving only single alpha particles) radon risks.
[Miller199901PNASv96n1p19]. (PMID: 9874764 [PubMed - indexed for MEDLINE]).

16. Radiation-induced breakpoint misrejoining in human chromosomes: random or non-random? by KL Johnson, et al., Center for Radiological Research, Columbia University, New York, NY 10032, USA. kj77@columbia.edu. Int J Radiat Biol. Vol. 75(2), Feb. 1999 (pp. 131-141).
PURPOSE: To investigate whether radiation-induced misrejoining of chromosome breakpoints is randomly or non-randomly distributed throughout the human genome. MATERIALS AND METHODS: Data were combined from as many published cytogenetic studies as possible. The percentage of radiation-induced breaks per megabase (Mb) of DNA between all human chromosomes was calculated, and the observed and expected numbers of breakpoints based on DNA content between and within chromosomes were compared. RESULTS: A DNA-proportional distribution of breakpoints in 14 autosomes and a statistically significant deviation from proportionality in the other eight autosomes and the sex chromosomes was found.
Regression analysis showed no significant change in breakpoint frequency per Mb of DNA relative to autosome size. Analysis between chromosome arms showed a non-random distribution of induced breakpoints within certain autosomes, particularly the acrocentrics. In cases of non-random distributions, a prevalence of events was found at heterochromatic regions and/or telomeres, and a clustering of breakpoints was found near the centromeres of many chromosomes.
CONCLUSIONS: There is an approximately linear proportionality between autosomal DNA content and observed breakpoint number, suggesting that subsets of autosomes can be used to estimate accurately the overall genomic frequency of misrejoined breakpoints contingent upon a carefully selected subset. However, this conclusion may not apply to the sex chromosomes. The results also support the influence of chromatin organization and/or preferential DNA repair/misrejoining on the distribution of induced breakpoints. However, these effects are not sufficient at a global level to dismiss the value of cytogenetic analysis using a genome subset for biodosimetry.
[Johnson199902IJRBv75n2p131] (PMID: 10072174 [PubMed - indexed for MEDLINE]).

17. Does fractionation decrease the risk of breast cancer induced by low-LET radiation? by DJ Brenner, Center for Radiological Research, Columbia University, New York, New York 10032, USA. Radiat Res. Vol. 151(2), Feb. 1999 (pp. 225-229). Comments in: Radiat Res. Vol. 151(2), Feb. 1999 (pp. 123-124). Radiat Res. Vol. 152(1), Jul. 1999 (pp. 104-105). Radiat Res. Vol. 152(5), Nov. 1999 (pp. 567).
Whether fractionation decreases the risk of breast cancer induced by low-LET radiation is a question of some importance. Analyses of the data for TB cohorts who were exposed to multiple fluoroscopies show an apparently similar breast cancer risk compared with those for the acutely exposed A-bomb survivors. However, the fluoroscopy cohorts were subjected to very much lower-energy photons (60-80 kVp) compared with the A-bomb survivors; the increased RBE associated with the low photon energies to which these fluoroscopy cohorts were exposed suggests that, in comparison to the risk estimates for the A-bomb survivors, the risk estimates from the X-ray fluoroscopy cohorts are increased because of the lower-energy X rays and decreased by a similar amount due to fractionation, resulting in an overall apparent equality of risk. Thus the results from the most powerful epidemiological data

sets available for assessing breast cancer risks after fractionated exposure to low-LET radiation (the fluoroscopy cohorts) are quite consistent with a lower radiation risk for a fractionated exposure in comparison to an acute exposure. In general, for any cancer site, estimates of the dose-rate effectiveness factor (DDREF) generated by comparing the results for A-bomb survivors with those for the TB fluoroscopy cohorts should probably be roughly doubled from their apparent values because of the increased RBE of the fluoroscopy X rays.
[Brenner199902RRv151n2p225]. (PMID: 9952308 [PubMed - indexed for MEDLINE]).

18. Chromosome aberrations of clonal origin in irradiated and unexposed individuals: assessment and implications, by KL Johnson, et al., Center for Radiological Research, Columbia University, 630 West 168th Street, New York, New York 10032, USA. Radiat Res. Vol. 152(1), July 1999 (pp. 1-5).
Chromosome painting has proven useful for the detection of chromosomal rearrangements, although the presence of cells containing clonal aberrations can have an effect on the outcome of cytogenetic analyses (e.g. aberration frequency and chromosomal distribution studies). Cells with clonal chromosomal changes have been found in studies of both radiation-exposed Chernobyl cleanup workers ("liquidators") and healthy unexposed human subjects. We have used a simple statistical method to aid in the identification of individuals from distinct Chernobyl radiation-exposed and unexposed control populations who may possess cells containing clonal rearrangements. A chi2 value determined from the observed number of aberrations and the expected number based on chromosome length that corresponds to a probability less than 0.005 appears to be an indicator of clonality. These selected individuals can be analyzed further for clonality, thereby sparing detailed examination of the entire population. Here we present an analysis of individuals possessing clonal aberrations to assess the influence of clonality on the results of cytogenetic studies. Our results show that the subtraction of clonal events from the chi2 calculation for the "outliers" results in nearly all of these values losing their statistically significant deviation from proportionality. These adjustments can also be made to prevent the overestimation of frequencies of chromosome aberrations for biodosimetry. The frequency of clonal aberrations appears to increase as a function of age in control subjects, whereas an age effect was not evident in Chernobyl liquidators. This suggests that spontaneous and radiation-induced clonal expansion are occurring in control subjects and liquidators, respectively.
[Johnson199907RRv152n1p1]. (PMID: 10381835 [PubMed - indexed for MEDLINE]).

19. Unexpected sensitivity to the induction of mutations by very low doses of alpha-particle radiation: evidence for a bystander effect, by H. Nagasawa, et al., Radiation Research Vol. 152, 1999 (pp. 552-557).
Found a linear dose response for radiation induced mutations in Chinese hamster ovary cells in culture in the dose range of 5 cGy to 1.2 Gy (>20 fold range), but the response was not linear below 5 cGy, instead it was much higher than expected from extrapolation of the linear data. There was a nearly 5 fold increase in mutations over expected response at lowest doses studied. This supports the bystander effect, i.e., mutations arising in non-irradiated cells through signals from neighboring cells exposed to radiation. [Nagasawa1999xxRRv152nxp552].

20. Investigation of hypersensitivity to fractionated low-dose radiation exposure, by LG Smith, et al., Department of Radiation Oncology, College of Physicians and Surgeons of Columbia University, New York, NY, USA. Int J Radiat Oncol Biol Phys. Vol. 45(1), Aug. 1999 (pp. 187-91).
PURPOSE: Hypersensitivity to cell killing of exponentially growing cells exposed to X-rays and gamma rays has been reported for doses below about 0.5 Gy. The reported results have been interpreted to suggest that a dose of 0.5 Gy or less is not sufficient to trigger an inducible repair mechanism. The purpose of this study was to examine this suggested hypersensitivity after multiple low doses (0.3 Gy) of gamma rays where a) the effect would be expected to be significantly magnified, and b) the effect might be of clinical relevance. METHODS AND MATERIALS: C3H 10T1/2 mouse embryo cells were grown to confluence in culture vessels. While in plateau phase of growth, cells were exposed to 6 Gy of gamma rays, delivered in either 6 Gy, 3 Gy, 2 Gy, 1 Gy, or 0.3 Gy well-separated fractions. Corresponding experiments were performed with V-79 and C3H 10T1/2 cells in exponential growth. Cells were replated at low density and assayed for clonogenicity. RESULTS: The results of this study were not inconsistent with some hypersensitivity at low doses, in that 20 fractions each of 0.3 Gy produced a slightly lower (though nonsignificant) surviving fraction compared with the same dose given in 2-Gy fractions. However, the results of the 20 x 0.3 Gy exposures also agreed well with the standard linear-quadratic (LQ) model predictions based on high dose per fraction (1-6 Gy) data. In addition, effects of cellular redistribution were seen which were explained quantitatively with an extended version of the LQ model. CONCLUSIONS: These experiments were specifically designed to magnify and probe possible clinical implications of proposed "low-dose hypersensitivity" effects, in which significant deviations at low doses from the LQ model have been suggested. In fact, the results at low doses per fraction were consistent with LQ predictions based on higher dose per fraction data. This finding is in agreement with the well-documented utility of the LQ approach in estimating isoeffect doses for alternative fractionation schemes, and for brachytherapy.
[Smith199908IJROBPv45n1p187]. (PMID: 10477023 [PubMed - indexed for MEDLINE]).

21. Neutron-energy-dependent cell survival and oncogenic transformation, by RC Miller, et al., Center for Radiological Research, College of Physicians and Surgeons of Columbia University, New York, NY 10032, USA. miller@rsna.org. J Radiat Res (Tokyo) Vol. 40 (Suppl.), Dec. 1999 (pp. 53-59).
Both cell lethality and neoplastic transformation were assessed for C3H10T1/2 cells exposed to neutrons with energies from 0.040 to 13.7 MeV. Monoenergetic neutrons with energies from 0.23 to 13.7 MeV and two neutron energy spectra with average energies of 0.040 and 0.070 MeV were produced with a Van de Graaff accelerator at the Radiological Research Accelerator Facility (RARAF)

in the Center for Radiological Research of Columbia University. For determination of relative biological effectiveness (RBE), cells were exposed to 250 kVp X rays. With exposures to 250 kVp X rays, both cell survival and radiation-induced oncogenic transformation were curvilinear. Irradiation of cells with neutrons at all energies resulted in linear responses as a function of dose for both biological endpoints. Results indicate a complex relationship between RBEm and neutron energy. For both survival and transformation, RBEm was greatest for cells exposed to 0.35 MeV neutrons. RBEm was significantly less at energies above or below 0.35 MeV. These results are consistent with microdosimetric expectation. These results are also compatible with current assessments of neutron radiation weighting factors for radiation protection purposes. Based on calculations of dose-averaged LET, 0.35 MeV neutrons have the greatest LET and therefore would be expected to be more biologically effective than neutrons of greater or lesser energies.
[Miller199912JRRv40nsuppp53]. (PMID: 10804994 [PubMed - indexed for MEDLINE]).

22. Oncogenic transformation in C3H10T1/2 cells by low-energy neutrons, by RC Miller, et al., Center for Radiological Research, Columbia University, New York, NY 10032, USA. Int J Radiat Biol. Vol. 76(3), Mar. 2000 (pp. 327-33).
PURPOSE: Occupational exposure to neutrons typically includes significant doses of low-energy neutrons, with energies below 100 keV. In addition, the normal-tissue dose from boron neutron capture therapy will largely be from low-energy neutrons. Microdosimetric theory predicts decreasing biological effectiveness for neutrons with energies below about 350 keV compared with that for higher-energy neutrons; based on such considerations, and limited biological data, the current radiation weighting factor (quality factor) for neutrons with energies from 10 keV to 100 keV is less than that for higher-energy neutrons. By contrast, some reports have suggested that the biological effectiveness of low-energy neutrons is similar to that of fast neutrons. The purpose of the current work is to assess the relative biological effectiveness of low-energy neutrons for an endpoint of relevance to carcinogenesis: in vitro oncogenic transformation. METHODS: Oncogenic transformation induction frequencies were determined for C3H10T1/2 cells exposed to two low-energy neutron beams, respectively, with dose-averaged energies of 40 and 70 keV, and the results were compared with those for higher-energy neutrons and X-rays. RESULTS: These results for oncogenic transformation provide evidence for a significant decrease in biological effectiveness for 40 keV neutrons compared with 350 keV neutrons. The 70 keV neutrons were intermediate in effectiveness between the 70 and 350 keV beams. CONCLUSIONS: A decrease in biological effectiveness for low-energy neutrons is in agreement with most (but not all) earlier biological studies, as well as microdosimetric considerations. The results for oncogenic transformation were consistent with the currently recommended decreased values for low-energy neutron radiation weighting factors compared with fast neutrons.
[Miller200003IJRBv76n3p327] (PMID: 10757312 [PubMed - indexed for MEDLINE])

22m. Factors underlying the cell growth-related bystander responses to alpha particles, by R Iyer, et al., Bioscience Division, Los Alamos National Laboratory, New Mexico 87545, USA. Cancer Res. Vol. 60(5), Mar. 2000 (pp. 1290-1298).
Increases in cell proliferation are widely viewed as being of importance in carcinogenesis. We report that exposure of normal human lung fibroblasts to a low dose of alpha particles like those emitted by radon/radon progeny stimulates their proliferation in vitro, and this response also occurs when unirradiated cells are treated with supernatants from alpha-irradiated cells. We attribute the promitogenic response to superoxide dismutase- and catalase-inhibitable a particle-induced increases in the concentrations of transforming growth factor beta1 (TGF-beta1) in cell supernatants. TGF-beta1 at concentrations commensurate with those in the supernatants capably induces increases in intracellular reactive oxygen species (ROS) in unirradiated cells. Furthermore, the addition of supernatants from alpha-irradiated cells to unirradiated cells decreases cellular levels of TP53 and CDKN1A and increases CDC2 and proliferating cell nuclear antigen in the latter. Like the increased intracellular ROS bystander effect, this "decreased TP53/CDKN1A response" can be mimicked in otherwise untreated cells by the addition of low concentrations of TGF-beta1. Our results indicate that alpha particle-associated increases in cell growth correlate with intracellular increases in ROS along with decreases in TP53 and CDKN1A, and that these cellular responses are mechanistically coupled. As well, the proliferating cell nuclear antigen and CDC2 increases that occur along with the decreased TP53/CDKN1A bystander effect also would expectedly favor enhanced cell growth.
Such processes may account for cell hyperplastic responses in the conducting airways of the lower respiratory track that occur after inhalation exposure to radon/ radon progeny, as well as, perhaps, other ROS-associated environmental stresses.
[Iyer200003CRv60nfp1290].

23. Induction of a bystander mutagenic effect of alpha particles in mammalian cells, by H. Zhou, et al., Proc. Natl. Acad. Sci. Vol. 97, 2000 (pp. 2099-2104).
Showed that genetic mutations were about 3 fold higher than expected if one assumes no bystander effect. Also showed that the types of mutations induced were different from those occurring spontaneously (without radiation). Radical scavengers had no effect on mutagenicity. These results further support intercellular communication inducing the bystander effect.
[Zhou2000xxPNASv97nxp2099].

24. Bio-markers specific to densely-ionising (high LET) radiations, by DJ Brenner, et al., Center for Radiological Research, Columbia University 630 West 168th Street, New York, NY 10032, USA. djb3@columbia.edu : Radiat Prot Dosimetry Vol. 97(1), 2001 (pp. 69-73).
There have been several suggestions of bio-markers that are specific to high LET radiation. Such a bio-marker could significantly increase the power of epidemiological studies of individuals exposed to densely-ionising radiations such as alpha particles (e.g.

radon, plutonium workers, individuals exposed to depleted uranium) or neutrons (e.g. radiation workers, airline personnel. We discuss here a potentially powerful high LET bio-marker (the H value) which is the ratio of induced inter-chromosomal aberrations to intra-arm aberrations. Both theoretical and experimental studies have suggested that this ratio should differ by a factor of about three between high LET radiation and any other likely clastogen, and will yield more discrimination than the previously suggested F value (ratio of inter-chromosomal aberrations to intra-chromosomal inter-arm aberrations). Evidence of the long-term stability of such chromosomal bio-markers has also been generated. Because these stable intra-arm and inter-chromosomal aberrations are (1) frequent and (2) measurable at long times after exposure, this H value appears to be a practical bio-marker of high LET exposure, and several in vitro studies have confirmed the approach for unstable aberrations. The approach is currently being tested in a population of Russian radiation workers exposed several decades ago to high- or low LET radiation.
[Brenner2001xxRPDv97n1p69]. (PMID: 11763360 [PubMed - indexed for MEDLINE]).

25. The bystander effect in radiation oncogenesis: I. Transformation in C3H 10T1/2 cells in vitro can be initiated in the unirradiated neighbors of irradiated cells, by SG Sawant, et al., Center for Radiological Research, Columbia University, New York, New York 10032, USA. Radiat Res. Vol.155(3), Mar. 2001 (pp. 397-401).
It has long been accepted that radiation-induced genetic effects require that DNA be hit and damaged directly by the radiation. Recently, evidence has accumulated that in cell populations exposed to low doses of alpha particles, biological effects occur in a larger proportion of cells than are estimated to have been traversed by alpha particles. The end points observed include chromosome aberrations, mutations and gene expression. The development of a fast single-cell micro-beam now makes it possible to expose a precisely known proportion of cells in a population to exactly defined numbers of alpha particles, and to assay for oncogenic transformation. The single-cell micro-beam delivered no, one, two, four or eight alpha particles through the nuclei of all or just 10% of C3H 10T1/2 cells. We show that (a) more cells can be inactivated than were actually traversed by alpha particles and (b) when 10% of the cells on a dish are exposed to alpha particles, the resulting frequency of induced transformation is not less than that observed when every cell on the dish is exposed to the same number of alpha particles. These observations constitute evidence suggesting a bystander effect, i.e., that unirradiated cells are responding to damage induced in irradiated cells. This bystander effect in a biological system of relevance to carcinogenesis could have significant implications for risk estimation for low-dose radiation.
[Sawant200103RRv155n3p397] (PMID: 11182789 [PubMed - indexed for MEDLINE]).

26. The bystander effect in radiation oncogenesis: II. A quantitative model, by DJ Brenner, et al.,Center for Radiological Research, Columbia University, New York, New York 10032, USA. Radiat Res. Vol. 155(3), Mar. 2001 (pp. 402-408).
There is strong evidence that biological response to ionizing radiation has a contribution from unirradiated "bystander" cells that respond to signals emitted by irradiated cells. We discuss here an approach incorporating a radiobiological bystander response, superimposed on a direct response due to direct energy deposition in cell nuclei. A quantitative model based on this approach is described for alpha-particle-induced in vitro oncogenic transformation. The model postulates that the oncogenic bystander response is a binary "all or nothing" phenomenon in a small sensitive subpopulation of cells, and that cells from this sensitive subpopulation are also very sensitive to direct hits from alpha particles, generally resulting in a directly hit sensitive cell being inactivated. The model is applied to recent data on in vitro oncogenic transformation produced by broad-beam or micro-beam alpha-particle irradiation. Two parameters are used in analyzing the data for transformation frequency. The analysis suggests that, at least for alpha-particle-induced oncogenic transformation, bystander effects are important only at small doses-here below about 0.2 Gy. At still lower doses, bystander effects may dominate the overall response, possibly leading to an underestimation of low-dose risks extrapolated from intermediate doses, where direct effects dominate.
[Brenner200103RRv155n3p402] (PMID: 11182790 [PubMed - indexed for MEDLINE]).

27. Direct evidence for the participation of gap junction-mediated intercellular communication in transmission of damage signals from alpha-particle irradiated to non-irradiated cells, by El Azzam, et al., Proc. Natl. Acad. Scis. Vol. 98, 2001 (pp. 473-478).
Using genetically engineered cells with compromised gap junctions, showed that the bystander effect is mediated by gap junctions, i.e., non-irradiated cells respond to radiation induced damage in neighboring cells. They found increased expression/activation of specific biochemical markers that are induced by stress which also correlated with induction of DNA damage, seen in the increased number of micronuclei in cells arising from DNA double-strand breaks.
[Azzam2001xxPNASv98nxp473].

28. Radiation Risk to low fluences of alpha-particles may be greater than we thought, by H. Zhou, et al., Proc. Natl. Acad. Sci. Vol. 98, 2001 (pp. 14410-14415).
It was shown in this paper that when 10% of cells in a confluent population were hit with a single alpha-particle the result was similar to that observed when all cells are irradiated. It was found that the bystander effect could be eliminated by treating the cell culture with octanol, a chemical that blocks intercellular communication through gap junctions (direct communication channels between contiguous cells).
[Zhou2001xxPNASv98nxp14410].

28f. Exposure to low-level chemicals and ionizing radiation: reactive oxygen species and cellular pathways, by BE Lehnert, et al., Bioscience Division, Los Alamos National Laboratory, New Mexico 87545, USA. lehnert@telomere.lanl.gov. Hum Exp Toxicol. Vol. 21(2), Feb., 2002 (pp. 65-69).
Reactive oxygen species (ROS), which contribute to the energy landscapes in and around cells, play numerous roles in maintaining normal cell homeostasis as components of signaling pathways. Excessively high levels of ROS, on the other hand, can lead to pronounced DNA damage and a variety of cellular responses, including cell cycle arrests, senescence, apoptosis and possibly cancer. Far less is known, however, about how supra-basal levels of ROS that can be generated in response to low doses of ionizing radiation or chemicals in the environment may bring about untoward or perhaps even beneficial cellular responses. Even so, some evidence suggests that adaptive responses that have been associated with ROS-generating stimuli can have protective effects by fundamentally altering subsequent cellular dose-response profiles to otherwise detrimental stresses. Yet, even these seemingly favorable 'adaptive' effects may have longer-term untoward consequences. Other effects that have been associated with supra-basal levels of ROS, such as enhanced states of cell proliferation, potentially could have a protective function. But again, such increases in cell growth, which may be accompanied by greater than normal ROS-mediated damage to DNA, as well may ultimately favour the expansion of cells with heritable mutations. Unfortunately, the state of the art of our current understanding of how elevated but still low-level increases in ROS that may be induced by environmental stimuli presently precluded incorporation of supra-basal ROS-associated mechanisms in predictive risk assessment models, both at the population level and at the level of individualized risk assessment.
[Lehnert200202HETv21n2p65].

28m Low dose, low-LET ionizing radiation-induced radioadaptation and associated early responses in unirradiated cells, by R Iyer, et al., Bioscience Division, MS 888, Los Alamos National Laboratory, Los Alamos, NM 87545, USA. Mutat Res.
Vol. 503(1-2), Jun., 2002 (pp. 1-9).
Numerous investigators have reported that irradiation of cells with a low dose of ionizing radiation (IR) can induce a condition of enhanced radioresistance, i.e. a radioadaptive response. In this report, we investigated the hypothesis that a radioadaptive bystander effect may be induced in unirradiated cells by a transmissible factor(s) present in the supernatants of cells exposed to low dose gamma-rays. Normal human lung fibroblasts (HFL-1) were irradiated with a 1 cGy dose of gamma-rays and their supernatants were transferred to unirradiated HFL-1 as a bystander cell model. Compared with the directly irradiated cells, such treatment resulted in increased clonogenic survival following subsequent gamma-irradiation with 2 and 4 Gy. This radioadaptive bystander effect was found to be preceded by early decreases in cellular levels of TP53 protein, increase in intracellular ROS, and increase in the redox and DNA repair protein AP-endonuclease (APE). The demonstration that radioadaptation can occur in unirradiated cells via a fluid-phase, transferable factor(s) adds to the complexity of the current understanding of mechanisms by which radioadaptive responses can be induced by low dose, low-LET IR.
[Iyer200206MRv503n1to2p1].

29. Do low dose-rate bystander effects influence domestic radon risks?, by Brenner DJ, et al.,Center for Radiological Research, Columbia University, 630 West 168th Street, New York, NY 10032, USA. djb3@columbia.edu. Int J Radiat
Biol. Vol. 78(7), Jul. 2002 (pp. 593-604).
PURPOSE: Radon risks derive from exposure of bronchio-epithelial cells to high-linear energy transfer (LET) alpha-particles. alpha-particle exposure can result in bystander effects, where irradiated cells emit signals resulting in damage to nearby unirradiated bystander cells. This can result in non-linear dose-response relations, and inverse dose-rate effects. Domestic radon risk estimates are currently extrapolated from miner data, which are at both higher doses and higher dose-rates, so bystander effects on unhit cells could play a large role in the extrapolation of risks from mines to homes. Therefore, we extend an earlier quantitative mechanistic model of bystander effects to include protracted exposure, with the aim of quantifying the significance of the bystander effect for very prolonged exposures. MATERIALS AND METHODS: A model of high-LET bystander effects, originally developed to analyse oncogenic transformation in vitro, is extended to low dose-rates. The model considers radiation response as a superposition of bystander and linear direct e. It attributes bystander effects to a small subpopulation of hypersensitive cells, with the bystander contribution dominating the direct contribution at very low acute doses but saturating as the dose increases. Inverse dose-rate effects are attributed to the replenishment of the hypersensitive subpopulation during prolonged irradiation. RESULTS: The model was fitted to dose- and dose-rate-dependent radon-exposed miner data, suggesting that one directly hit target bronchio-epithelial cell can send bystander signals to about 50 neighbouring target cells. The model suggests that a naive linear extrapolation of radon miner data to low doses, without accounting for dose-rate, would result in an underestimation of domestic radon risks by about a factor of 4, a value comparable with the empirical estimate applied in the recent BEIR-VI report on radon risk estimation. CONCLUSIONS: Bystander effects represent a plausible quantitative and mechanistic explanation of inverse dose-rate effects by high-LET radiation, resulting in non-linear dose-response relations and a complex interplay between the effects of dose and exposure time. The model presented provides a potential mechanistic underpinning for the empirical exposure-time correction factors applied in the recent BEIR-VI for domestic radon risk estimation.
[Brenner200207IJRBv78n7p593] (PMID: 12079538 [PubMed - indexed for MEDLINE]).

29m. Radiation-induced effects in unirradiated cells: a review and implications in cancer, by Z Goldberg, et al., Department of Radiation Oncology, University of California, Davis, Sacramento, CA 95817, USA. zelanna.goldberg@ucdmc.ucdavis.edu. Int J Oncol. Vol. 21(2), Aug. 2002 (pp. 337-349).

A long-held central dogma of radiation biology has been that the carcinogenic effects of ionizing radiation (IR) are induced by the direct and radiolytic actions of IR on nuclear DNA. Numerous investigations, however, have revealed that several cancer relevant effects of IR can occur in cells that have received only cytoplasmic or plasmalemmal membrane exposure to IR. Further, mounting evidence now indicates that many effects that have been attributed to IR-induced damage to nuclear DNA or that occur following irradiation of the cytoplasmic compartment of cells can also occur in cells that have received no direct exposure to IR per se. These so-called <bystander effects>, i.e., radiation-induced effects in unirradiated cells, include cell killing, increases in intracellular reactive oxygen species, the induction of mutations, enhanced cell growth, the induction of apoptosis, the induction of genomic instability and neoplastic transformation. In this report, we summarize the evidence that demonstrates IR can cause this array of effects in non-irradiated cells, and we discuss recent findings concerning the potential mechanisms that may underlie IR-induced effects in unirradiated, or cells. Additionally, we discuss IR-induced bystander effects and their possible relationship to some in vivo observations, how bystander effects may pertain to carcinogenesis the treatment of tumors with radiotherapy, and how effects in bystander cells contribute to uncertainties in assessing cancer risks associated with exposure to IR.
[Goldberg200208IJOv21n2p337].

30. Chromosomes are predominantly located randomly with respect to each other in interphase human cells, by MN Cornforth, et al., Department of Radiation Oncology, University of Texas Medical Branch, Galveston, TX 77555, USA. J Cell Biol. Vol. 159(2), Oct. 28 2002 (pp. 237-44).
To test quantitatively whether there are systematic chromosome-chromosome associations within human interphase nuclei, interchanges between all possible heterologous pairs of chromosomes were measured with 24-color whole-chromosome painting (multiplex FISH), after damage to interphase lymphocytes by sparsely ionizing radiation in vitro. An excess of interchanges for a specific chromosome pair would indicate spatial proximity between the chromosomes comprising that pair. The experimental design was such that quite small deviations from randomness (extra pairwise interchanges within a group of chromosomes) would be detectable. The only statistically significant chromosome cluster was a group of five chromosomes previously observed to be preferentially located near the center of the nucleus. However, quantitatively, the overall deviation from randomness within the whole genome was small. Thus, whereas some chromosome-chromosome associations are clearly present, at the whole-chromosomal level, the predominant overall pattern appears to be spatially random.
[Cornforth200210JCBv159n2p237] (PMID: 12403811 [PubMed - indexed for MEDLINE]).

31. Past exposure to densely ionizing radiation leaves a unique permanent signature in the genome, by MP Hande, et al., Center for Radiological Research, Columbia University, New York, NY 10032, USA. Am J Hum Genet. Vol. 72(5), May 2003 (pp. 1162-70).
Speculation has long surrounded the question of whether past exposure to ionizing radiation leaves a unique permanent signature in the genome. Intra-chromosomal rearrangements or deletions are produced much more efficiently by densely ionizing radiation than by chemical mutagens, x-rays, or endogenous aging processes. Until recently, such stable intra-chromosomal aberrations have been very hard to detect, but a new chromosome band painting technique has made their detection practical. We report the detection and quantification of stable intra-chromosomal aberrations in lymphocytes of healthy former nuclear-weapons workers who were exposed to plutonium many years ago. Even many years after occupational exposure, more than half the blood cells of the healthy plutonium workers contain large (>6 Mb) intra-chromosomal rearrangements. The yield of these aberrations was highly correlated with plutonium dose to the bone marrow.
The control groups contained very few such intra-chromosomal aberrations. Quantification of this large-scale chromosomal damage in human populations exposed many years earlier will lead to new insights into the mechanisms and risks of cytogenetic damage.
[Hande200306AJHGv72n5p1162] (PMID: 12679897 [PubMed - indexed for MEDLINE]).

32. Domestic radon risks may be dominated by bystander effects--but the risks are unlikely to be greater than we thought, by Brenner DJ, et al., Center for Radiological Research, Columbia University, 630 West 168th Street, New York, NY 10032, USA. djb3@columbia.edu. Health Phys. Vol. 85(1), Jul. 2003 (pp. 103-8).
Radon risks derive from exposure of bronchio-epithelial cells to alpha particles. Alpha-particle exposure can result in bystander effects when irradiated cells emit signals resulting in damage to nearby unirradiated bystander cells. Bystander effects can cause downwardly-curving dose-response relations and inverse dose-rate effects. We have extended a quantitative mechanistic model of bystander effects to include protracted exposure, with inverse dose-rate effects attributed to replenishment, during exposure, of a subpopulation of cells which are hypersensitive to bystander signals. In this approach, bystander effects and the inverse dose-rate effect are manifestations of the same basic phenomenon. The model was fitted to dose- and dose-rate dependent radon-exposed miner data; the results suggest that one directly-hit target cell can send bystander signals to about 50 neighboring cells and that, in the case of domestic radon exposures, the risk could be dominated by bystander effects. The analysis concludes that a naive linear extrapolation of radon miner data to low doses, without accounting for dose rate/bystander effects, would result in an underestimation of domestic radon risks by about a factor of approximately 4. However, recent domestic radon risk estimates (BEIR VI) have already applied a phenomenological correction factor of approximately 4 for inverse dose-rate effects, and have thus already implicitly taken into account corrections which we here suggest are due to bystander effects. Thus current domestic radon risk estimates are unlikely to be underestimates as a result of bystander effects.
[Brenner20037HPv85n1p103]

33. Interaction between radiation-induced adaptive response and bystander mutagenesis in mammalian cells, by Zhou H, et al., Center for Radiological Research, College of Physicians and Surgeons, Columbia University, New York, New York 10032, USA. hz63@columbia.edu. Radiat Res. Vol. 160(5), Nov. 2003 (pp. 512-6).
Two conflicting phenomena, the bystander effect and the adaptive response, are important in determining biological responses at low doses of radiation and have the potential to have an impact on the shape of the dose-response relationship. Using the Columbia University charged-particle micro-beam and the highly sensitive AL cell mutagenic assay, we reported previously that non-irradiated cells acquired mutagenesis through direct contact with cells whose nuclei had previously been traversed with either a single or 20 alpha particles each. Here we show that pretreatment of cells with a low dose of X rays 4 h before alpha-particle irradiation significantly decreased this bystander mutagenic response. Furthermore, bystander cells showed an increase in sensitivity after a subsequent challenging dose of X rays. Results from the present study address some of the pressing issues regarding both the actual target size and the radiation dose response and can improve on our current understanding of radiation risk assessment.
[Zhou200311RRv160n5p512] (PMID: 14565832 [PubMed - indexed for MEDLINE])

34. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know, by DJ Brenner, et al., Center for Radiological Research, Columbia University, 630 West 168th Street, New York, NY 10032, USA. djb3@columbia.edu. Proc Natl Acad Sci USA Vol. 100(24), Nov.25, 2003 (pp. 13761-13766).
High doses of ionizing radiation clearly produce deleterious consequences in humans, including, but not exclusively, cancer induction. At very low radiation doses the situation is much less clear, but the risks of low-dose radiation are of societal importance in relation to issues as varied as screening tests for cancer, the future of nuclear power, occupational radiation exposure, frequent-flyer risks, manned space exploration, and radiological terrorism. We review the difficulties involved in quantifying the risks of low-dose radiation and address two specific questions. First, what is the lowest dose of x- or gamma-radiation for which good evidence exists of increased cancer risks in humans? The epidemiological data suggest that it is approximately 10-50 mSv for an acute exposure and approximately 50-100 mSv for a protracted exposure.
Second, what is the most appropriate way to extrapolate such cancer risk estimates to still lower doses? Given that it is supported by experimentally grounded, quantifiable, biophysical arguments, a linear extrapolation of cancer risks from intermediate to very low doses currently appears to be the most appropriate methodology. This linearity assumption is not necessarily the most conservative approach, and it is likely that it will result in an underestimate of some radiation-induced cancer risks and an overestimate of others.
[Brenner200311PNASv100n24p13761] PMID: 14610281 [PubMed - in process])

Chapter IV

Epidemiological and Population Studies I: Exposure to Uranium, Depleted Uranium and Low-Level Ionizing Radiation

Summary

Epidemiological and population studies provide conclusions based on statistical evaluation of data rather than on reproducible experimental results. It is therefore incumbent on the reader to evaluate the parameters defining a study and the statistical methodology used to arrive at given conclusions.

For example, generally speaking, the larger the population studied (sample size), the better. But it is essential that the individual members of the population share a commonality with respect to whatever alleged causitive factor is being scrutinized if the purpose of the study is to determine whether or not a cause/effect relationship exists. It is also important that the control population be as closely identical as possible to the population under study except in that single causitive factor. Obviously, studies in which multiple factors might compete or interfere with the alleged causitive factor are less reliable and may in some cases be of little value.

Suppose, for example, that 40 individuals living within a five-mile radius of a nuclear facility appear to have a cancer rate that is 25% higher than average (say 10 cancers as opposed to 8). By extending the radius under study to 10 miles, the sample size might be increased ten-fold, to 400, and the results may now show no statistically significant increase in cancer rate. But the fallacy with this study is that the additional 360 individuals are not experiencing the same exposure rates as the 40 living closest to the plant. A more appropriate way to increase the sample size would be to include 10 different nuclear plants and keep the five-mile radius parameter. Now you have 400 people in the sample, all of whom live within the presumably high exposure area. If the cancer rate in this population is not significantly higher than the general population (the control), one might conclude with greater reliability that living near nuclear plants entails no increase in cancer risk.

Because data can be so easily manipulated in population studies that rely on statistical results, it should come as no surprise that conclusions reported in the studies in this and the following two chapters vary so widely, with authors even arriving at directly opposing results. Only a careful analysis of the details presented in the full paper will reveal any flaws in the methodology or conclusions, and this challenge is left to the reader.

In this chapter, several reports on Iraqi civilians following the 1991 Gulf war claim an increase in cancers and congenital defects and point to exposure to depleted uranium as a causitive factor. Other studies of veterans and NGO workers from the Balkan conflict showed no increased levels of urinary uranium. A study of a population living in an area in India with high background radiation found no increased cancer risk while another similar study in China showed increased cancer mortality. And one study determined that civilian exposure to DU remains following a military confflict created sufficient risk that cleanup efforts should be undertaken to minimize that risk.

Details

In 1998, Birchard (1) reported in Lancet the results of Bill Griffin's studies on the increasing cases of childhood leukemia, adult cancers and congenital malformations in Iraq between 1989 and 1993, suggesting that the use of DU weapons in 1991 were a causitive factor. Kido (2) and Ishikawa (3) report on the radiation effects of Thorotrast, a drug containing radioactive thorium-232. Benign and malignant lung tumors were shown by Collier (4) to result from inhalation exposure of radon by rats.

Nair (5) reports on a study of 100,000 residents in India exposed to high levels of background radiation and showing no increased cancer risk. On the other hand, Bolviken (6) reports on a study in China where increased mortality from nasopharyngeal carcinoma was observed in a region with high background concentrations of uranium and radon. McDiarmid (7) published an article supporting her take on DU and public health in 2001, following years of study into the small contingent of US troops who had been exposed to DU fragments from "friendly fire". (See Chapter V for other articles by McDiarmid specifically related to Gulf War veterans.)

Pranjik (8) in 2002 published a review (in Croatian) dealing with the toxicological effects of DU and concluded that more research needed to be done, particularly epidemiological studies of veterans and civilians exposed to DU through military use. Meddings (9) reported findings based on urinary analysis of International Red Cross and Red Crescent workers in Kosovo that suggest these NGO workers did not have body burdens of uranium above those expected from background exposure. Ough (10) studied 103

Canadian veterans who might have been exposed to DU in the 1991 Gulf War and in Kosovo and reported no increased incidence of urinary uranium and only natural uranium in hair samples.

Abu-Qare (11) reviews the overriding health concerns resulting from exposure to DU. Giannardi (12) determined that civilian exposure to soil contaminated with DU could, over time, provide a substantial health risk, particularly to children, and that every effort should be made to clean up after its use. Shawky (13) reported in 2003 on a statistical evaluation of causes of mortality in Middle Eastern countries as compared with the rest of the world. Sumanovic-Glanuzima (14) reported no statistically significant increase in birth abnormalities or mortalities in the Mostar hospital of Bosnia-Herzegovina from before hostilities and after hostilities in which DU had been used.

1. Does Iraq's depleted uranium pose a health risk? by K. Birchard. Lancet Vol. 351, Feb. 28, 1998 (pp. 657).
Reports that Bill Griffin, an Irish petrochemical engineer, compiled a literature review and sent it to the UN Commissioner for Human Rights hypothesizing that the current health and environmental problems in Iraq may be linked to DU weapons use in the 1991 conflict. The report notes that the death rate per 1000 Iraqi children under 5 years rose from 2.3 in 1989 to 16.6 in 1993. Cases of lymphoblastic leukemia more than quadrupled. In men, lung, bladder, bronchus, skin and stomach cancers show the greatest increase. In women, the greatest increases are in breast and bladder cancer, and non-Hodgkin lymphoma. Congenital malformations have also increased, as have diseases of the immune system.
[Birchard199802Lv351n9103p657]. (PMID: 9500343 [PubMed - indexed for MEDLINE])

2. Cancer mortality of Thorotrast patients in Japan: the second series updated 1998, by C Kido, et al., Radiation Research Vol. 152, 1999 (pp. S81-S83).
[Kido199900RRv152nxpS81].

3. Revised organ partition of thorium-232 in Thorotrast patients, by Y Ishikawa, et al., Radiation Research Vol. 152, 1999 (pp. S102-S106).
[Ishikawa199900RRv152nxpS102].

4. Effects of continuous inhalation exposure of rats to radon and its progeny at various levels of dose and dose rate: Interim results, by CG Collier, et al., Radiation Res Vol. 152, 1999 (pp. S141-S144).
Shows that exposure to radon and radon progeny causes elevated incidences of both benign and malignant lung tumors. The study was not yet complete at time of publication.
[Collier1999xxRRv152nxpS141].

5. Population study in the high natural background radiation area in Kerala, India, by MK Nair, et al., Radiation Res. Vol. 152, 1999 (pp. S145-S148).
High radiation level due mostly to Th. Of total 400,000 population, 100,000 lived in high radiation areas. Preliminary analysis shows no significant increase in cancer for high exposure group.
[Nair1999xxRRv152nxpS145].

6. Relationships between nasopharyngeal carcinoma and radioactive elements in soils in China, by B Bølviken, Medical Hypotheses Vol. 55, 2000 (pp. 513-516).
Epidemiological and geochemical maps of China indicate association between high mortality from nasopharyngeal carcinoma (NPC) and low Mg in soil, but high levels of U and Th are also present in regions with high NPC. The author suggests radioactivity from radon and daughter nuclides may be a contributing factor, but neglects the possibility that U or Th chemical toxicity may play a role.
[Bolviken2000xxMHv55nxp513].

7. Depleted uranium and public health, by MA McDiarmid. BMJ (Clin. Res. Ed.) Vol. 322(7279), Jan. 20, 2001 (pp. 123-124).
[McDiarmid200101BMJv322n7279p123].

8. Internal contamination with depleted uranium and health disorders. [Article in Croatian], by N Pranjic, et al., Zavod za Medicinu rada, Medicinski fakultet Univerziteta u Tuzli. Med Arh. Vol. 56(1), 2002 (pp. 39-42).
In this review we used the published data on depleted uranium (experimental and epidemiological) from the current literature. Depleted uranium is a toxic heavy metal that in high dose may cause poisoning and health effects as those caused by lead, mercury, and chromium. It is slightly radioactive. The aim of this review was to select, to arrange, to present references of scientific papers, and to summarise the data in order to give a comprehensive image of the results of toxicological studies on depleted uranium that have been done on animals (including carcinogenic activity). We have also used epidemiological posted study results related to occupational and environmental exposure to depleted uranium. The toxicity of uranium has been studied extensively.
The results of the studies indicated primarily its chemical toxicity, particularly renal effects, but depleted uranium is not radiological hazard. Uranium is not metal determined to be carcinogenic (the International Agency of Research on Cancer).

The military use of depleted uranium will give additional insight into the toxicology of depleted uranium. The present controversy over the radiological and chemical toxicity of depleted uranium used in the Gulf War requests further experimental and clinical investigations of its effects on the biosphere and human beings.
[Pranjic2002xxMAv56n1p39]. (PMID: 11917690 [PubMed - indexed for MEDLINE]).

9. Depleted uranium in Kosovo: an assessment of potential exposure for aid workers, by DR Meddings, et al., Unit of the Chief Medical Officer, International Committee of the Red Cross, Geneva, Switzerland. dmeddings@icrc.org. Health Phys. Vol. 82(4), Apr. 2002 (pp. 467-472).
BACKGROUND: During the Kosovo conflict approximately 11 tons of depleted uranium munitions were used against armored targets, predominantly in the west. Potential exposure to uranium amongst employees of the International Red Cross and Red Crescent Movement in western Kosovo was assessed. METHODS: Individuals (n = 31) who had resided at least 3 months in western Kosovo provided 24-h urine collections and completed an administered questionnaire. Specimens were analyzed for creatinine concentration, and uranium concentration was determined using inductively coupled mass spectrometry. FINDINGS: Subjects ranged in age from 22 to 45 y, and 77% were male. Mean duration of residency was 11 months, and 14 individuals were in western Kosovo throughout the hostilities. Almost three quarters of subjects reported seeing destroyed tanks or vehicles, predominantly while passing by within a vehicle. Two individuals spent time within 50 m of a destroyed tank or vehicle while outside of a vehicle. Urinary uranium concentrations ranged from 3.5 to 26.9 ng of uranium per liter of urine (median 8.9 ng L(-)). Creatinine normalized values ranged from 2.9 to 21.1 ng of uranium per gram of creatinine (median 7.4 ng g(-1) creatinine). These results fall toward the lower end of urinary uranium determinations made amongst non-exposed populations drawn from a literature review. INTERPRETATION: These results do not indicate an increased exposure to uranium amongst adults living and working in western Kosovo who do not spend time in proximity to destroyed vehicles. Environmental sampling and replication of these results amongst a sample including children and individuals reporting intensive exposure to destroyed vehicles would further develop the exposure assessment.
[Meddings200204HPv82n4p467]. (PMID: 11906135 [PubMed - indexed for MEDLINE]).

10. An examination of uranium levels in Canadian forces personnel who served in the Gulf War and Kosovo, by EA Ough, et al., Department of Chemistry and Chemical Engineering, Royal Military College of Canada, Kingston, ON. ough-e@rmc.ca. Health Phys. Vol. 82(4), Apr. 2002 (pp. 527-532).
A uranium bioassay program was conducted involving 103 active and retired Canadian Forces personnel. The total uranium concentrations in each of two 24-h urine collections were analyzed separately at independent commercial laboratories by inductively coupled plasma mass spectrometry (ICP-MS) and by instrumental neutron activation analysis (INAA). The mean and median concentrations were determined to be 4.5 ng L(-1) and 2.8 ng L(-1), respectively, from ICP-MS and 17 ng L(-1) and 15 ng L(-1), respectively, from INAA. The total uranium concentrations were sufficiently low so that isotopic (238U:235U ratio) assays could not be performed directly from urine samples.
Isotopic assays were performed on hair samples from 19 of the veterans participating in the testing. The isotopic hair assays were scattered around the natural 238U:235U ratio of 137.8, ranging from 122 +/- 21 to 145 +/- 16 (1sigma). Due to concern expressed in the media over possible depleted uranium exposure and long-term retention in bone, a single bone sample (vertebrate bone marrow) from a deceased member of the Canadian Forces was also analyzed for total uranium content and isotopic ratio by ICP-MS. The sample was shown to have 16.0 +/- 0.3 microg kg(-1) uranium by dry weight and a 238U:238U isotopic ratio of 138 +/- 4, consistent with natural uranium.
[Ough200204HPv82n4p527]. (PMID: 11908516 [PubMed - indexed for MEDLINE]).

11. Depleted uranium--the growing concern, by AW Abu-Qare, et al., Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC 27710, USA. J Appl Toxicol. Vol. 22(3), May-June 2002 (pp. 149-152).
Recently, several studies have reported on the health and environmental consequences of the use of depleted uranium. Depleted uranium is a heavy metal that is also radioactive. It is commonly used in missiles as a counterweight because of its very high density (1.6 times more than lead). Immediate health risks associated with exposure to depleted uranium include kidney and respiratory problems, with conditions such as kidney stones, chronic cough and severe dermatitis. Long-term risks include lung and bone cancer. Several published reports implicated exposure to depleted uranium in kidney damage, mutagenicity, cancer, inhibition of bone, neurological deficits, significant decrease in the pregnancy rate in mice and adverse effects on the reproductive and central nervous systems. Acute poisoning with depleted uranium elicited renal failure that could lead to death. The environmental consequences of its residue will be felt for thousands of years. It is inhaled and passed through the skin and eyes, transferred through the placenta into the fetus, distributed into tissues and eliminated in urine. The use of depleted uranium during the Gulf and Kosovo Wars and the crash of a Boeing airplane carrying depleted uranium in Amsterdam in 1992 were implicated in a health concern related to exposure to depleted uranium. Copyright 2002 John Wiley & Sons, Ltd.
[AbuQare200205JATv22n3p149]. (PMID: 12015793 [PubMed - indexed for MEDLINE]).

12. Military use of depleted uranium: assessment of prolonged population exposure, by C Giannardi, et.al., Fisica Ambientale, Dipartimento di Firenze ARPAT. Journal of Environmental Radioactivity Vol.64(2,3), 2003 (pp. 227-236).
This work is an exposure assessment for a population living in an area contaminated by the use of depleted uranium (DU) weapons. RESRAD 5.91 code was used to evaluate the average effective dose at depths of 1, 10, 20 cm of contaminated soil in a residential

farming scenario. Critical pathways and groups are identified in soil inhalation and ingestion; critical group is identified in children playing with the soil. From the available information on DU release at targeted sites, both critical and average exposure can produce toxicological hazards. The annual dose limit for the population can be exceeded within a few years from DU deposition for soil inhalation. As a result, clean up at targeted sites must be planned on the basis of measured concentration, when available, while special measures must be adopted anyway to reduce unaware exposures.
[Giannardi200302JERv64n2p227]. (PMID: 12500807 [PubMed - indexed for MEDLINE]).

13. Causes of death in the Eastern Mediterranean Region during the years 1998-2000, by S Shawky, PO Box 115, Jeddah 21411, Kingdom of Saudi Arabia. Tel. +966 (2) 6318318. Fax. +966 (2) 6323142. E-mail: shshawky@hotmail.com. Saudi Med J. Vol. 24(4), Apr. 2003 (pp. 380-387).
OBJECTIVE: This paper aims to consider the available mortality data as an insight to epitomize the mortality pattern and the main leading causes of death specific to the Easter Mediterranean Region (EMR) in order to set priorities for future research in the region. METHODS: Data was taken from the last 3 World Health Organization (WHO) mortality statistics. Crude mortality rates were compared between the 6 WHO regions for the years 1998, 1999 and 2000.
Proportional mortality and standardized proportional mortality ratios were calculated for the causes of death and types of malignant neoplasm deaths and compared between the EMR and the other regions of the world. Spearman coefficient rank-order correlation was calculated to detect significant correlation between the ranking of the main causes of death in EMR and the 3 basic demographic, socio-economic and health care indicators in the 6 regions of the world. RESULTS: The results of this study showed that approximately 9 per 1,000 of the world's population die annually. Africa and Europe have the highest mortality rates. The main causes of death worldwide are cardiovascular diseases, infectious or parasitic diseases, malignant neoplasm, infectious respiratory diseases and other respiratory diseases. In EMR, approximately 8 per 1,000 die annually. The causes of death in EMR can be classified into 3 categories. 1) Non-prominent in EMR as compared to other regions of the world. 2) Prominent in EMR and significantly correlated to the basic indicators. 3) Prominent in EMR but not related to the basic indicators. These include deaths due to wars, congenital anomalies, perinatal conditions, genitourinary diseases, endocrine disorders, road traffic accidents, cancer bladder, lymphoma leukemia CONCLUSION: The results of this study emerged the need for extensive epidemiological studies to investigate thoroughly the main causes of death influencing mortality in EMR, specially that they coincide with the health consequences of depleted uranium. Also, most of these health conditions were previously described among the United States and European veterans who served in the Gulf War.
[Shawky200304SMJv24n4p380]. (PMID: 12754539 [PubMed - in process]).

14. Incidence of major congenital malformations in a region of Bosnia and Herzegovina allegedly polluted with depleted uranium, by D Sumanovic-Glamuzina , et al., Department of Pediatrics, Mostar University Hospital, Mostar, Bosnia and Herzegovina. dara.glamuzina@tel.net.ba. Croat Med J. Vol. 44(5), Oct. 2003 (pp. 579-584).
OBJECTIVES: To determine 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. METHODS: 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. Malformations were recorded according to the recommendations of the EUROCAT protocol. RESULTS: 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. In both cohorts, anomalies of the musculoskeletal system were the most common, followed by anomalies of the digestive system (in 1995) and the cardiovascular system (in 2000). The prevalence of malformations and the organ systems involved were essentially comparable with those in other populations not affected by military activities. CONCLUSION: Despite 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.
[SumanovicGlamuzina200310CMJv44n5p579]. (PMID: 14515417 [PubMed - in process]).

Chapter V

Epidemiological and Population Studies II: Gulf War Veterans and Gulf War Syndrome

Summary

Following the first Gulf War in 1991 in which depleted uranium weapons were used in a battlefield arena for the first time, US and UK veterans in large numbers began reporting an unusual set of illnesses that later became known as "Gulf War Syndrome" (GWS). Unfortunately, these soldiers had been exposed to a large number of potentially toxic agents in addition to depleted uranium. These included pyridostigmine bromide, numerous immunizations of which some were not approved for human use, chemical and biological warfare agents, pesticides and heavy smoke from oil well fires. Not surprisingly, the reported symptoms vary greatly among the affected veterans. It has thus been difficult to pin down a single causative factor in these illnesses.

It is a documented fact that the US military has every intention of continuing the use of depleted uranium weapons and has actively and purposefully opposed efforts to study what effects, if any, inhalation of aerosolized depleted uranium particles might have on human health. After the 1991 Gulf War, the contingent of veterans being studied for DU exposure was restricted to 33 soldiers who were suspected of having embedded DU fragments resulting from friendly fire. MA McDiarmid and her coworkers at the Veterans' Administration Medical Center in Baltimore have issued several papers relating to this limited group of veterans while ignoring the more than 200,000 other veterans who have now been awarded disability pensions as a result of their Gulf War experiences.

It is also a fact that given reassurances from the Department of Defense in the US and the Ministry of Defense in Great Britain that exposure to depleted uranium is relatively harmless, studies into causative factors for GWS (and its related Balkan syndrome resulting from the conflict in Bosnia, Kosovo, Serbia and Yugoslavia in the late 1990s) have often purposely omitted DU as one possible culprit. Unfortunately, the few population studies that have been done on US veterans have been performed by the Veterans' Administration and by military research labs, neither of which can be construed to be free of a conflict of interest.

Careful scrutiny of the studies presented in Chapters I through III in this volume should convince even the casual reader that this oversight is not warranted. Recent court rulings in Scotland and Italy on behalf of veterans exposed to DU have finally opened the door to official recognition that exposure to depleted uranium may have drastic consequences to human health.

Details

In 1994, Douce (1) summarized much of the anecdotal reports that had been appearing relating to soldiers' ill health and the appearance of an undiagnosed "wasting disease" among Iraqi children and suggests that, whatever the cause, it appears that one of the targets is the immune system. McDiarmid (2) reported in 1995 the presence of sister chromatid exchanges in soldiers deployed to Kuwait, a common result of radiation exposure. In 1997, Korenye-Both (3) reported searching for causitive factors of Al-Eskan disease and concludes that inhalation of ultra-fine sand particles (less than 1 micron in diameter) found in Saudi Arabia and Kuwait can lead to immunodepression and many of the symptoms associated with GWS. Charp (4) submitted a comment on this article later that year. Jamal's (5) 1998 review of studies into GWS emphasized the complexity of the issue and conluded that much more research and epidemiological studies needed to be done.

McDiarmid (6), in her continuing studies at the US Veterans Administration of 1991 Gulf War veterans with embedded fragments, determined that for low concentrations of urinary uranium, spot uranium urinary analysis showed poor correlation with the more accurate 24-hour timed collection samples. Petruccelli (7) writes on the health effects of veterans' exposure to the oil fires during that conflict. Hooper (8), also of the VA, notes that the 33 veterans being studied showed significantly higher urinary uranium both 2 years and 4 years after the conflict, but none showed renal disfunction. In 2000, McDiarmid (9), (15) reported that elevated urinary uranium in 29 of the veterans still in the embedded fragment study was observed 7 years following the conflict, still with no renal disfunction, but with definite signs of neurocognitive degeneration and "subtle perturbations in the reproductive and central nervous systems". In 2001, McDiarmid (10) expanded the original cohort under study to 169 veterans, divided into 19 groups based on probable DU exposure levels during the Gulf War (based on answers given in questionaires) and found 12 veterans with elevated urinary uranium levels (later reduced to 9 veterans after a second round of tests). Her conclusion was that only those with embedded DU fragments showed any statistical correlation to elevated urinary uranium.

McClain (12), of the Armed Forces Radiobiology Research Institute (AFRRI), in 2001 published a review of on-going research into the effects of embedded DU fragments in rats and reported extensive distribution of DU throughout the body over time, including in bone, kidney, muscle and liver tissues, and that it could enter fetal tissue by crossing the placental barrier and that it exhibited neurophysiological deterioration in the subjects. He also reviewed Miller's work that showed DU to be mutagenic and capable of transforming human osteoblast cells to a tumorigenic phenotype. As a result of these investigations, McClain (16) proposed altering existing medical protocol that avoids surgical removal of embedded fragments if those fragments contain DU. These observations help explain those of Durakovic (11) who had been working with veterans complaining of GWS since the early 1990s and had concluded early on that DU might be one causitive factor.

In December of 2001, McDiarmid (13) reported on a cohort of 50 embedded DU fragment veterans, all showing elevated urinary uranium and statistically correlated "perturbations in central nervous system function and a general measure of mutagen exposure" and concluded that "Observations in this group of veterans prompt speculation about the health effects of DU in other exposure scenarios." Hodge (14), of AFRRI, proposed using ICP-MS to assay veterans' urine samples and use isotope ratios to identify DU specifically in order to "mitigate the concerns of exposed individuals."

The British Royal Society (17) published a summary in 2002 of two papers compiled by their Working Group on the Health Hazards of Depleted Uranium Munitions covering the potential radiotoxicity and chemotoxicity of DU exposure. Horan (18) used mass spectroscopy to determine specific presence of DU in 27 American, Canadian and British Gulf War veterans and identified its presence in 14 of the 27 patients. Bolton (19) of the British Surgeon General's office, presented a review of health effects resulting from exposure to DU and concludes that although potential renal and lung cancer risks exist, in military use context they are low.

In 2003, Toohey (20) reported attempting to correlate urinary uranium excretion data from the VA studies with time and/or fragment characteristics and was unable to determine significant correlations. Lagercrantz (21) studied Swedish veterans of the Balkan conflict and could identify no increase in cancer among Swedish veterans by 2002.

1. Desert Storm syndrome: sick soldiers and dead children? by I. Douce, Medical Educational Trust, London, Med War. Vol. 10(3), Jul-Sep. 1994 (pp. 183-194).
Ill-health has been reported by many soldiers and others deployed in the Persian Gulf during the Gulf War of 1991. Iraqi children have also been reported as suffering from an undiagnosed wasting disease. Little conclusive information has come to light; this paper reviews what is known at present, largely from anecdotal reports. Symptoms reported differ from post-traumatic stress syndrome as reported after previous conflicts; some are suggestive of a direct effect on the immune system. Various possible causes are examined, including post-traumatic stress disorder, infection, prophylactic medication, exposure to chemical and biological warfare agents, exposures resulting from oil spills and fires, and exposure to depleted uranium ammunition. The latter was used extensively for the first time in the Gulf War, and is manufactured and test-fired in Britain. The passive role of the British government in following up such reports is noted, in contrast with the more active official responses in the United States. It is suggested that Desert Storm Syndrome is one example of multiple assault upon the body's immune system.
[Douce199407MWv10n3p183]. (PMID: 7935166 [PubMed - indexed for MEDLINE])

2. Increased frequencies of sister chromatid exchange in soldiers deployed to Kuwait, by MA McDiarmid, et al., Mutagenesis Vol. 10, 1995 (pp. 263-265).
[McDiarmid1995xxMv10nxp263].

3. Al Eskan disease: Persian Gulf syndrome, by AL Korenyi-Both, et al., Office of the State Surgeon, Pennsylvania National Guard, Department of Military and Veteran's Affairs, Commonwealth of Pennsylvania 17003-5003, USA. Mil Med. Vol. 162(1), Jan. 1997 (pp. 1-13).
This article examines the potential relationship between Al Eskan disease and the Persian Gulf syndrome. Al Eskan disease, reported in Military Medicine in 1992, is a novel and previously unreported condition triggered by the exceptionally fine sand dust of the Central and Eastern Saudi Arabian peninsula. We repeat our study of the pathogenesis of Al Eskan disease to include the ultrastructural and microanalytical study of the sand, aerobiological studies of the Kingdom of Saudi Arabia, and the etiology, symptoms, and prevalence of the disease. We conclude that immunodepression resulting from the continued presence of sand particles less than 1 micron in diameter in the lungs and bodies of Persian Gulf veterans explains not only the symptoms of the hyperegic lung condition of phase I and the symptoms of phase II of Al Eskan disease, but also provides an important clue to a common factor in most cases of Persian Gulf illnesses. We include a discussion of most of the commonly suspected agents in the Persian Gulf syndrome. In this case, we conclude that each of these factors, such as oil well fires, old-world diseases, or depleted uranium, are probably adjuvant or contributing causes. The only common exposure that would lead to recognition of the Persian Gulf syndrome as a single medical condition, rather than a catch-all phrase for unrelated conditions, appears to be exposure to the ubiquitous, fine sand of the area, and a resulting immunosuppression that is aggravated by opportunistic infections and other nonmicrobial ailments.
[KorenyiBoth199701MMv162n1p1]. (PMID: 9002695 [PubMed - indexed for MEDLINE])

4. Al Eskan disease: Persian Gulf syndrome, by PA Charp. Mil Med. Vol. 162(3), Mar. 1997 (pp. ii). Comment on: Mil Med. 1997 Jan;162(1):1-13.
[Charp199703MMv162n3pii]. (PMID: 9121655 [PubMed - indexed for MEDLINE])

5. Gulf War syndrome--a model for the complexity of biological and environmental interaction with human health, by GA Jamal.University Department of Neurology, Southern General Hospital NHS Trust, Glasgow. Adverse Drug React Toxicol Rev. Vol. 17(1), Mar. 1998 (pp. 1-17).
Since the end of the Gulf War, tens of thousands of American, Canadian and British soldiers who participated in that war have claimed to be suffering from a variety of incapacitating symptoms which are generally termed as Gulf War Syndrome (GWS).
The symptoms are multiple but mainly consist of excessive tiredness, muscle and joint pain, loss of balance, sensory symptoms, neurobehavioural manifestations, diarrhoea, bladder dysfunction, sweating disturbances, and respiratory, gastrointestinal, musculoskeletal and skin manifestations. These veterans have been exposed to a variety of damaging or potentially damaging risk factors including environmental adversities, pesticides such as organophosphate chemicals, skin insect repellents, medical agents such as pyridostigmine bromide (NAPS), possible low-levels of chemical warfare agents, multiple vaccinations in combinations, depleted uranium, and other factors. A large number of basic research findings, clinical epidemiological studies, and case control studies are reviewed to try and link them together to produce a coherent picture and to demonstrate the complexity of the interaction of biological systems, environmental and genetic factors, combinations of drugs and toxins with human health. The findings of these studies so far have demonstrated that many of the previous assumptions made about the 'safety' of certain drugs and toxic substances or vaccines must be radically reviewed. Many of the findings have far reaching implications not only in terms of explanation of what might have gone wrong during the Gulf War, but also have wider implications for many occupational groups who are exposed daily to some of these risk factors. More open-mindedness and much less prejudice are required concerning the basic biology of interactions of the above factors and their effects on cell functions and wider intelligent research is urgently required with high priority. This review highlights the importance of intelligent research for answers for a new phenomenon, and demonstrates the necessity for a combination of this approach with high quality epidemiological research. The reader will notice an emerging clear picture that the majority (if not all) of these advances have been achieved from studies funded by independent or charity organizations rather than by the responsible authorities who are supposed and are duty bound to take on this task.
[Jamal199803ADRTRv17n1p1]. (PMID: 9638279 [PubMed - indexed for MEDLINE])

6. The utility of spot collection for urinary uranium determinations in depleted uranium exposed Gulf War veterans, by MA McDiarmid, et al., Occupational Health Project, Baltimore, MD 21201, USA, Health Phys. Vol. 77(3),
Sept. 1999 (pp. 261-264).
The utility of spot urine collections for uranium bioassay determinations was examined in a small cohort of depleted uranium exposed Gulf War veterans. Some members of the group are excreting elevated concentrations of urinary uranium resulting from the metabolism of retained metal fragments, the residua of several friendly fire incidents. Uranium determinations were performed on both 24-h timed collections and spot urine samples using kinetic phosphorescence analyzer (KPA) methodology. Results ranged from non-detectable to 30.7 mcg g(-1) creatinine in a 24-h collection. A creatinine-standardized spot sample and a 24-h uncorrected sample both correlated highly (R2=0.99) with a creatinine corrected 24-h collection, presumed to be the best estimate of the urinary uranium measure. This relationship was upheld when the population was stratified by uranium concentration into a high uranium group (> or = 0.05 mcg U/g creatinine) but for the lower uranium group (< 0.05 mcg U/g creatinine) more variability and a lower correlation was seen. The uncorrected spot sample, unadjusted for volume, concentration or creatinine had the lowest correlation with the 24-h creatinine adjusted result, especially at lower urinary uranium concentrations. This raises questions regarding the representativeness of such a sample in bioassay programs.
[McDiarmid199909HPv77n3p261]. (PMID: 10456496 [PubMed - indexed for MEDLINE]).

7. Health effects of the 1991 Kuwait oil fires: a survey of US army troops, by B.P. Petruccelli, et al., Journal of Occupational and Environmental Medicine Vol. 41, 1999 (pp. 433-439).
[Petruccelli1999xxJOEMv41nxp433]

8. Elevated urine uranium excretion by soldiers with retained uranium shrapnel, by FJ Hooper, et al., Baltimore Veterans Administration Medical Center, Department of Medicine, University of Maryland School of Medicine, 21201, USA., Health Phys. Vol. 77(5), Nov. 1999 (pp. 512-519).
The use of depleted uranium in munitions has given rise to a new exposure route for this chemically and radioactively hazardous metal. A cohort of U.S. soldiers wounded while on or in vehicles struck by depleted uranium penetrators during the Persian Gulf War was identified. Thirty-three members of this cohort were clinically evaluated, with particular attention to renal abnormalities,
approximately 3 y after their injury. The presence of retained shrapnel was identified by x ray, and urine uranium concentrations were measured on two occasions. The absorption of uranium from embedded shrapnel was strongly suggested by measurements of urine uranium excretion at two time intervals: one in 1993/1994 and one in 1995. Mean urine uranium excretion was significantly higher in soldiers with retained shrapnel compared to those without shrapnel at both time points (4.47 vs. 0.03 microg g(-1) creatinine in 1993/1994 and 6.40 vs. 0.01 microg g(-1) creatinine in 1995, respectively). Urine uranium concentrations measured in 1995 were consistent with those measured in 1994/1993, with a correlation coefficient of 0.9. Spot urine measurements of uranium excretion were also well correlated with 24-h urine collections (r = 0.95), indicating that spot urine samples can be reliably used to

monitor depleted uranium excretion in the surveillance program for this cohort of soldiers. The presence of uranium in the urine can be used to determine the rate at which embedded depleted uranium fragments are releasing biologically active uranium ions. No evidence of a relationship between urine uranium excretion and renal function could be demonstrated. Evaluation of this cohort continues.
[Hooper199911HPv77n5p512]. (PMID: 10524504 [PubMed - indexed for MEDLINE])

9. Health effects of depleted uranium on exposed Gulf War veterans, by MA McDiarmid, et al., Department of Veterans Affairs Medical Center, Baltimore, Maryland, USA. mmcdiarm@medicine.umaryland.edu. Environ Res. Vol. 82(2), Feb. 2000 (pp. 168-180).
A small group of Gulf War veterans possess retained fragments of depleted uranium (DU) shrapnel, the long-term health consequences of which are undetermined. We evaluated the clinical health effects of DU exposure in Gulf War veterans compared with nonexposed Gulf War veterans. History and follow-up medical examination were performed on 29 exposed veterans and 38 nonexposed veterans. Outcome measures employed were urinary uranium determinations, clinical laboratory values, and psychiatric and neurocognitive assessment.
DU-exposed Gulf War veterans with retained metal shrapnel fragments are excreting elevated levels of urinary uranium 7 years after first exposure (range 0.01-30.7 microg/g creatinine vs 0.01- 0.05 microg/g creatinine in the nonexposed). The persistence of the elevated urine uranium suggests on-going mobilization from a storage depot which results in a chronic systemic exposure.
Adverse effects in the kidney, a presumed target organ, are not present at this time, though other effects are observed. Neurocognitive examinations demonstrated a statistical relationship between urine uranium levels and lowered performance on computerized tests assessing performance efficiency. Elevated urinary uranium was statistically related to a high prolactin level (>1.6 ng/ml; P=0.04). More than 7 years after first exposure, DU-exposed Gulf War veterans with retained metal fragments continue to excrete elevated concentrations of urinary uranium. Effects related to this are subtle perturbations in the reproductive and central nervous systems. Copyright 2000 Academic Press.
[McDiarmid200002ERv82n2p168]. (PMID: 10662531 [PubMed - indexed for MEDLINE]).

10. Urinary uranium concentrations in an enlarged Gulf War veteran cohort, by MA McDiarmid, et al., Occupational Health Project, Baltimore 21201, USA. Health Phys. Vol. 80(3), Mar. 2001 (pp. 270-273).
Depleted uranium was first used on a large scale as a major component of munitions and armaments employed by the U.S. armed forces during the Gulf War in 1991. In response to concern that exposure to depleted uranium may have been a cause of health problems suffered by returning veterans of that war, an already existing surveillance program following depleted uranium "friendly fire" victims was enlarged to assess the wider veteran community's exposure to depleted uranium. Between August 1998 and December 1999, 169 Gulf War veterans submitted 24-h urine samples for determination of urinary uranium concentration and questionnaires describing their potential exposures to depleted uranium while in the Gulf War theatre. Depleted uranium exposure assessment was determined from 30 separate questionnaire items condensed into 19 distinct exposure scenarios.
Results of urine uranium analysis were stratified into high and low uranium groups with 0.05 microg uranium/g creatinine being the cut point and approximate upper limit of the normal population distribution. Twelve individuals (7.1%) exhibited urine uranium values in the high range, while the remaining 157 had urine uranium values in the low range. A repeat test of urine for 6 of these 12 produced uranium results in the low range for 3 of these individuals. Exposure scenarios of the high and low uranium groups were similar with the presence of retained shrapnel being the only scenario predictive of a high urine uranium value. Results emphasize the unlikely occurrence of an elevated urine uranium result and consequently any uranium-related health effects in the absence of retained depleted uranium metal fragments in the veterans.
[McDiarmid200103HPv80n3p270]. (PMID: 11219540 [PubMed - indexed for MEDLINE]).

11. On depleted uranium: gulf war and Balkan syndrome, by A. Durakovic, Nuclear Medicine Division and Clinical PET, King Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia, TAhaideb@kfshrc.edu.sa. Croat Med J. Vol. 42(2), Apr. 2001 (pp. 130-134).
The complex clinical symptomatology of chronic illnesses, commonly described as Gulf War Syndrome, remains a poorly understood disease entity with diversified theories of its etiology and pathogenesis. Several causative factors have been postulated, with a particular emphasis on low level chemical warfare agents, oil fires, multiple vaccines, desert sand (Al-Eskan disease), botulism, Aspergillus flavus, Mycoplasma, aflatoxins, and others, contributing to the broad scope of clinical manifestations. Among several hundred thousand veterans deployed in the Operation Desert Storm, 15-20% have reported sick and about 25,000 died. Depleted uranium (DU), a low-level radioactive waste product of the enrichment of natural uranium with U-235 for the reactor fuel or nuclear weapons, has been considered a possible causative agent in the genesis of Gulf War Syndrome. It was used in the Gulf and Balkan wars as an armor-penetrating ammunition. In the operation Desert Storm, over 350 metric tons of DU was used, with an estimate of 3-6 million grams released in the atmosphere. Internal contamination with inhaled DU has been demonstrated by the elevated excretion of uranium isotopes in the urine of the exposed veterans 10 years after the Gulf war and causes concern because of its chemical and radiological toxicity and mutagenic and carcinogenic properties. Polarized views of different interest groups maintain an area of sustained controversy more in the environment of the public media than in the scientific community, partly for the reason of being less than sufficiently addressed by a meaningful objective interdisciplinary research.
[Durakovic200104CMJv42n2p130]. (PMID: 11259733 [PubMed - indexed for MEDLINE]).

12. Biological effects of embedded depleted uranium (DU): summary of armed forces radiobiology research institute research, by DE McClain, et al., Armed Forces Radiobiology Research Institute, Bethesda, MD 20889-5603, USA. mcclain@mx.afrri.usuhs.mil . Sci Total Environ. Vol. 274(1-3), Jul. 2001 (pp. 115-118).
The Persian Gulf War resulted in injuries of US Coalition personnel by fragments of depleted uranium (DU). Fragments not immediately threatening the health of the individuals were allowed to remain in place, based on long-standing treatment protocols designed for other kinds of metal shrapnel injuries. However, questions were soon raised as to whether this approach is appropriate for a metal with the unique radiological and toxicological properties of DU. The Armed Forces Radiobiology Research Institute (AFRRI) is investigating health effects of embedded fragments of DU to determine whether current surgical fragment removal policies remain appropriate for this metal. These studies employ rodents implanted with DU pellets as well as cultured human cells exposed to DU compounds. Results indicate uranium from implanted DU fragments distributed to tissues far-removed from implantation sites, including bone, kidney, muscle, and liver. Despite levels of uranium in the kidney that were nephrotoxic after acute exposure, no histological or functional kidney toxicity was observed. However, results suggest the need for further studies of long-term health impact, since DU was found to be mutagenic, and it transformed human osteoblast cells to a tumorigenic phenotype. It also altered neurophysiological parameters in rat hippocampus, crossed the placental barrier, and entered fetal tissue. This report summarizes AFRRI's depleted uranium research to date.
[McClain200107STEv274n1to3p115]. (PMID: 11453287 [PubMed - indexed for MEDLINE]).

13. Surveillance of depleted uranium exposed Gulf War veterans: health effects observed in an enlarged "friendly fire" cohort, by MA McDiarmid, et al.; Depleted Uranium Follow-Up Program., Department of Medicine, University of Maryland School of Medicine, 405 W. Redwood Street, Baltimore, MD 21201, USA. mmcdiarm@medicine.umaryland.edu . J Occup Environ Med. Vol. 43(12), Dec. 2001 (pp. 991-1000).
To determine clinical health effects in a small group of US Gulf War veterans (n = 50) who were victims of depleted uranium (DU) "friendly fire," we performed periodic medical surveillance examinations. We obtained urine uranium determinations, clinical laboratory values, reproductive health measures, neurocognitive assessments, and genotoxicity measures. DU-exposed Gulf War veterans with retained metal shrapnel fragments were excreting elevated levels of urine uranium 8 years after their first exposure (range, 0.018 to 39.1 micrograms/g creatinine for DU-exposed Gulf War veterans with retained fragments vs 0.002 to 0.231 microgram/g creatinine in DU exposed but without fragments).
The persistence of the elevated urine uranium suggests ongoing mobilization from the DU fragments and results in chronic systemic exposure. Clinical laboratory outcomes, including renal functioning, were essentially normal. Neurocognitive measures showing subtle differences between high and low uranium exposure groups, seen previously, have since diminished. Sister chromatid exchange frequency, a measure of mutation in peripheral lymphocytes, was related to urine uranium level (6.35 sister chromatid exchanges/cell in the high uranium exposure group vs 5.52 sister chromatid exchanges/cell in the low uranium exposure group; P = 0.03). Observed health effects were related to subtle but biologically plausible perturbations in central nervous system function and a general measure of mutagen exposure. The findings related to uranium's chemical rather than radiologic toxicity. Observations in this group of veterans prompt speculation about the health effects of DU in other exposure scenarios.
[McDiarmid200112JOEMv43n12p991]. (PMID: 11765683 [PubMed - indexed for MEDLINE]).

14. Detection of depleted uranium in biological samples from Gulf War veterans, by SJ Hodge, et al., Armed Forces Radiobiology Research Institute, 8901 Wisconsin Avenue, Bethesda, MD 20889-5603, USA. Mil Med. Vol. 166(12 Suppl.), Dec. 2001 (pp. 69-70).
During the Persian Gulf War, soldiers may have inhaled, ingested, and/or experienced wound contamination by depleted uranium (DU), which is used in military projectiles and armor. DU is produced by depleting natural uranium of 234U and 235U during the uranium-enrichment process. Although the long-term effects of significant DU exposures require investigation, many veterans express fears about its impact on health. An assay by which DU exposure can be assessed would not only be a useful research tool, but the information could help mitigate the concerns of exposed individuals. In this study, urine samples from individuals enrolled in the Depleted Uranium Follow-Up Program at the Baltimore Veterans Administration Medical Center were examined for uranium content. Isotopic composition of urine uranium was determined by measuring the 235U/238U ratio, using an inductively coupled plasma mass spectrometer. Using this method, natural and depleted uranium could be readily differentiated.
By demonstrating the absence of DU in soldiers who suspect exposure by inhalation or ingestion, the assay should reduce psychological stress in these individuals.
[Hodge200112MMv166n12Suppp69]. (PMID: 11778443 [PubMed - indexed for MEDLINE]).

15. Health effects and biological monitoring results of Gulf War veterans exposed to depleted uranium, by MA McDiarmid, et al., Department of Veterans Affairs Medical Center, 10 North Greene Street, Baltimore, MD 21201, USA. Mil Med. Vol. 167(2 Suppl), Feb. 2002 (pp. 123-124).
A small group of Gulf War veterans have retained fragments of depleted uranium (DU) shrapnel, the long-term health consequences of which are undetermined. We evaluated the clinical health effects of DU exposure in Gulf War veterans compared with nonexposed Gulf War veterans. History and follow-up medical examinations were performed on 29 exposed veterans and 38 nonexposed veterans. Outcome measures used were urinary uranium determinations, clinical laboratory values, and psychiatric and neurocognitive assessment. Gulf War veterans with retained DU metal shrapnel fragments were found to be still excreting elevated levels of urinary uranium 7 years after first exposure to DU (range for exposed individuals is 0.01-30.7 micrograms/g creatinine vs. 0.01-0.05 microgram/g creatinine in the nonexposed). The persistence of the elevated urine uranium suggests ongoing mobilization

of uranium from a storage depot, resulting in chronic systemic exposure. Adverse effects in the kidney, a presumed target organ, were not seen at the time of the study; however, other subtle effects were observed in the reproductive and central nervous systems of the DU-exposed veterans.
[McDiarmid200202MMv167n2suppp123]. (PMID: 11873493 [PubMed - indexed for MEDLINE]).

16. Depleted uranium: a radiochemical toxicant?, by DE McClain, Armed Forces Radiobiology Research Institute, 8901 Wisconsin Avenue, Bethesda, MD 20889-5603, USA. Mil Med. Vol. 167(2 Suppl), Feb. 2002 (pp. 125-126).
The first large-scale combat use of depleted uranium (DU) weapons occurred during the Gulf War, and some U.S. personnel were wounded by DU fragments. Established fragment removal policies dictated that embedded metal fragments be left in place unless doing so posed unacceptable additional risks. However, questions were raised as to whether these policies are appropriate for a metal that--unlike lead, steel, or others--is chemically toxic and emits low-level radiation. Data from research currently under way indicate that long-term exposure to embedded DU fragments may present a level of risk that requires modification of established policies. Our understanding of DU health effects and of the possible mechanisms by which DU might affect tissues is evolving.
Understanding more about the long-term response of tissues exposed to DU could facilitate future development of treatments for DU injuries.
[McClain200202MMv167n2suppp125]. (PMID: 11873494 [PubMed - indexed for MEDLINE]).

17. The health effects of depleted uranium munitions: a summary, by Royal Society Working Group on the Health Hazards of Depleted Uranium Munitions., The Royal Society, London, UK. J Radiol Prot. Vol. 22(2), Jun. 2002 (pp. 131-139).
There has been a substantial amount of public discussion on the health effects of the use of depleted uranium (DU) munitions. In response to this concern the Royal Society set up an independent, expert working group to investigate the health effects of DU munitions. The Royal Society has now produced two reports, and this summary covering the key conclusions and recommendations from both reports. The part I report considered the increased risks of radiation-induced cancer from exposures to DU on the battlefield. Part II dealt with the risks from the chemical toxicity of uranium, non-malignant radiation effects from DU intakes, the long-term environmental consequences of the deployment of DU munitions and responses to part I including issues arising at a public meeting to discuss the part I report.
[RoyalSoc200206JRPv22n2p131]. (PMID: 12148788 [PubMed - indexed for MEDLINE]).

18. The quantitative analysis of depleted uranium isotopes in British, Canadian, and U.S. Gulf War veterans, by P Horan, et al., Department of Earth Sciences, Memorial University of Newfoundland, St. Johns, Canada. horan@morgan.ucs.mun.ca. Mil Med. Vol. 167(8), Aug. 2002 (pp. 620-627).
The purpose of this work was to determine the concentration and ratio of uranium isotopes in allied forces Gulf War veterans. The 27 patients had their 24-hour urine samples analyzed for 234U, 235U, 236U, and 238U by mass spectrometry. The urine samples were evaporated and separated into isotopic dilution and concentration fraction by the chromatographic technique. The isotopic composition was measured by a thermal ionization mass spectrometer using a secondary electron multiplier detector and ion-counting system. The uranium blank control and SRM960 U isotopic standard were analyzed by the same procedure. Statistical analysis was done by an unpaired t test. The results confirm the presence of depleted uranium (DU) in 14 of 27 samples, with the 238U:235U ratio > 207.15. This is significantly different from natural uranium ($p < 0.008$) as well as from the DU shrapnel analysis, with 22.22% average value of DU fraction, and warrants further investigation.
[Horan200208MMv167n8p620]. (PMID: 12188230 [PubMed - indexed for MEDLINE]).

19. Battlefield use of depleted uranium and the health of veterans, by JP Bolton, et al., Surgeon General's Department, St Giles Court, St Giles High Road, London WC2H 8LD. J R Army Med Corps. Vol. 148(3), Sept. 2002 (pp. 221-229).
Depleted uranium munitions have been used in recent military operations in both the Gulf and the Balkans and there have been concerns that exposure to depleted uranium may be a cause of 'Gulf War Syndrome' and cancer clusters. We recount the properties of depleted uranium, its military uses and the situations in which personnel may be exposed. Following a review of scientific literature, the health effects of depleted and natural uranium exposure are described and the major outcomes of research into Gulf Veterans' Illnesses are summarised. We conclude that, although there is the potential for uranium exposures to cause renal damage or lung cancer, the risk of harm following depleted uranium exposure in military settings seems to be low. We advise on the management of casualties exposed to depleted uranium and suggest control measures that may be appropriate to protect personnel who provide casualty care.
[Bolton200209JRAMCv148n3p221]. (PMID: 12469421 [PubMed - indexed for MEDLINE]).

20. Excretion of depleted uranium by Gulf War veterans, by RE Toohey, Oak Ridge Institute for Science and Education, Oak Ridge, TN 37830, USA. tooheyr@orau.gov. Radiat Prot Dosimetry. Vol. 105(1-4), 2003 (pp. 171-174).
During the Persian Gulf War, in 1991, approximately 100 US military personnel had potential intakes of depleted uranium (DU), including shrapnel wounds. In 1993, the US government initiated a follow-up study of 33 Gulf War veterans who had been exposed to DU, many of whom contained embedded fragments of DU shrapnel in their bodies. The veterans underwent medical evaluation, whole-body counting, and urinalysis for uranium by kinetic phosphorescence analysis (KPA). Data are available from seven individuals who exceeded the detection limit for whole-body counting and also had elevated urinary uranium. Urinary excretion rates, in microg U g(-1) creatinine, were determined in 1997 and 1999. The body contents, in mg DU, were determined in 1997; it is

assumed there were no significant decreases in total body content in the interim. For the 1997 data, the mean fractional excretion was (2.4 +/- 2.8) x 10(-5) g(-1) creatinine, and for the 1999 data, the mean was (1.1 +/- 0.6) x 10(-5) g(-1) creatinine. However, these means are not significantly different, nor is there any correlation of excretion rate with body content. Thus, human data available to date do not provide any basis for determining the effects of particle surface area, composition and solubility, and biological processes such as encapsulation, on the excretion rate.
[Toohey2003xxRPDv105n1to4p171]. (PMID: 14526951 [PubMed - in process]).

21. Depleted uranium a cancer risk that disappeared. Leukemia alarm regarding Balkan veterans came to nothing. [Article in Swedish], by B Lagercrantz, barbro.lagercrantz@hkv.mil.se. Lakartidningen Vol. 100(4), Jan. 2003 (pp. 219-221).
After alarming reports in the international press in January 2001, about leukemia in war veterans returning from the Balkans after possible exposure to depleted uranium, a follow-up was conducted of the Swedish personnel that had served in the Balkans. Questionnaires, analysis of uranium in urine, and coordination with The National Board of Health and Welfare's cancer register showed no correlation between service in the Balkans and cancer or other illnesses. Several did however experience anxiety, insomnia and fatigue that may have been caused by the stressful environment and/or the anxiety arising from the depleted uranium-debate. To lower the risk for unjustified anxiety and to be better prepared for the physical environment, the Swedish Armed Forces are working on better risk analysis before mission as well as increased health examinations both before and after mission.
[Lagercrantz200301Lv100n4p219]. (PMID: 12580006 [PubMed - indexed for MEDLINE]).

22. Undiagnosed illnesses and radioactive warfare, by A Durakovic, Uranium Medical Research Center, 3430 Connecticut Avenue/11854, Washington, DC 20008, USA. asaf@umrc.net. Croat Med J. Vol. 44(5), Oct. 2003 (pp. 520-532).
The internal contamination with depleted uranium (DU) isotopes was detected in British, Canadian, and United States Gulf War veterans as late as nine years after inhalational exposure to radioactive dust in the Persian Gulf War of 1991. DU isotopes were also identified in a Canadian veteran's autopsy samples of lung, liver, kidney, and bone. In soil samples from Kosovo, hundreds of particles, mostly less than 5 micrometer in size, were found in milligram quantities. The Gulf War in 1991 resulted in 350 metric tons of DU deposited in the environment and 3-6 million grams of DU aerosol released into the atmosphere. Its legacy, Gulf War disease, is a complex, progressive, incapacitating multiorgan system disorder.
The symptoms include incapacitating fatigue, musculoskeletel and joint pains, headaches, neuropsychiatric disorders, affect changes, confusion, visual problems, changes of gait, loss of memory, lymphadenopathies, respiratory impairment, impotence, and urinary tract morphological and functional alterations. Current understanding of its etiology seems far from being adequate. After the Afghanistan Operation Anaconda (2002), our team studied the population of Jalalabad, Spin Gar, Tora Bora, and Kabul areas, and identified civilians with the symptoms similar to those of Gulf War syndrome. Twenty-four-hour urine samples from 8 symptomatic subjects were collected by the following criteria: 1) the onset of symptoms relative to the bombing raids; 2) physical presence in the area of the bombing; and 3) clinical manifestations. Control subjects were selected among the sympotom-free residents in non-targeted areas. All samples were analyzed for the concentration and ratio of four uranium isotopes, (234)U, (235)U, (236)U and (238)U, by using a multicollector, inductively coupled plasma ionization mass spectrometry. The first results from the Jalalabad province revealed urinary excretion of total uranium in all subjects significantly exceeding the values in the nonexposed population. The analysis of the isotopic ratios identified non-depleted uranium. Studies of specimens collected in 2002 revealed uranium concentrations up to 200 times higher in the districts of Tora Bora, Yaka Toot, Lal Mal, Makam Khan Farm, Arda Farm, Bibi Mahro, Poli Cherki, and the Kabul airport than in the control population. Uranium levels in the soil samples from the bombsites show values two to three times higher than worldwide concentration levels of 2 to 3 mg/kg and significantly higher concentrations in water than the World Health Organization maximum permissible levels. This growing body of evidence undoubtedly puts the problem of prevention and solution of the DU contamination high on the priority list.
[Durakovic200310CMJv44n5p520]. (PMID: 14515407 [PubMed - in process]).

23. Detection of depleted uranium in urine of veterans from the 1991 Gulf War, by Roberto H. Gwiazda, et al., Environmental Toxicology, University of California, Santa Cruz, CA 95064, USA. gwiazda@etox.ucsc.edu. Health Phys. Vol. 86(1), Jan. 2004 (pp. 12-18).
American soldiers involved in "friendly fire" accidents during the 1991 Gulf War were injured with depleted-uranium-containing fragments or possibly exposed to depleted uranium via other routes such as inhalation, ingestion, and/or wound contamination. To evaluate the presence of depleted uranium in these soldiers eight years later, the uranium concentration and depleted uranium content of urine samples were determined by inductively coupled plasma mass spectrometry in (a) depleted uranium exposed soldiers with embedded shrapnel, (b) depleted uranium exposed soldiers with no shrapnel, and (c) a reference group of deployed soldiers not involved in the friendly fire incidents. Uranium isotopic ratios measured in many urine samples injected directly into the inductively coupled plasma mass spectrometer and analyzed at a mass resolution m/delta m of 300 appeared enriched in 235U with respect to natural abundance (0.72%) due to the presence of an interference of a polyatomic molecule of mass 234.81 amu that was resolved at a mass resolution m/delta m of 4,000. The 235U abundance measured on uranium separated from these urines by anion exchange chromatography was clearly natural or depleted. Urine uranium concentrations of soldiers with shrapnel were higher than those of the two other groups, and 16 out of 17 soldiers with shrapnel had detectable depleted uranium in their urine. In depleted uranium exposed soldiers with no shrapnel, depleted uranium was detected in urine samples of 10 out of 28 soldiers. The median uranium concentration of urines with depleted uranium from soldiers without shrapnel was significantly higher than in urines with no depleted uranium, though substantial overlap in urine uranium concentrations existed between the two groups. Accordingly,

ssessment of depleted uranium exposure using urine must rely on uranium isotopic analyses, since urine uranium concentration is not an unequivocal indicator of depleted uranium presence in soldiers with no embedded shrapnel.
[Gwiazda200401HPv86n1p12]

24. Health effects of depleted uranium on exposed Gulf War veterans: a 10-year follow-up, by MA McDiarmid, et al., Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA. mmcdiarm@medicine.umaryland.edu. J Toxicol Environ Health A. Vol. 67(4), Feb. 27, 2004 (pp. 277-296).
Medical surveillance of a group of U.S. Gulf War veterans who were victims of depleted uranium (DU) "friendly fire" has been carried out since the early 1990s. Findings to date reveal a persistent elevation of urine uranium, more than 10 years after exposure, in those veterans with retained shrapnel fragments.
The excretion is presumably from ongoing mobilization of DU from fragments oxidizing in situ. Other clinical outcomes related to urine uranium measures have revealed few abnormalities. Renal function is normal despite the kidney's expected involvement as the "critical" target organ of uranium toxicity. Subtle perturbations in some proximal tubular parameters may suggest early although not clinically significant effects of uranium exposure. A mixed picture of genotoxic outcomes is also observed, including an association of hypoxanthine-guanine phosphoribosyl transferase (HPRT) mutation frequency with high urine uranium levels. Findings observed in this chronically exposed cohort offer guidance for predicting future health effects in other potentially exposed populations and provide helpful data for hazard communication for future deployed personnel.
[McDiarmid200402JTEHAv67n4p277]. (PMID: 14713562 [PubMed - indexed for MEDLINE]).

Chapter VI

Epidemiological and Population Studies III: Uranium Miners & Mill Workers

Summary

Concern over the risk to health of uranium miners has been studied for over 60 years. In mining natural uranium (mostly U-238), the minor is exposed not only to uranium, but to many of the thirteen daughter isotopes, all radioactive, that appear in uranium's decay chain. These include radium-226 and radon-222. In the process of breaking up rock deposits, radon, a gas, is released and inhaled.

Radon-222 is of particular concern because it is a gas and has a half-life of 3.8 days and the next four radioactive isotopes in the decay chain have half-lives measured in minutes. So when a radon atom decays, emitting one alpha particle, within minutes two additional alpha particles and two beta particles are also produced. This greatly amplifies the radiotoxicity of radon, and the product of these five decay steps is a radioactive isotope of lead, a heavy metal with a chemotoxicity vector as well. Thus when inhaling even minute quantities of radon, some of those radon atoms will statistically decay while deep in the miner's lungs, changing from a gas (which would otherwise be exhaled) to a metal which becomes deposited within the lung tissue, and within minutes that deposited metal has undergone four more decay steps, further irradiating lung tissue, and ultimately becoming atoms of radioactive lead.

Uranium mill workers are also exposed to uranium, but in a much more concentrated form than uranium miners. Uranium ore contains many other minerals besides uranium, so the miner encounters uranium in a very dilute form. At the mill, this ore is treated chemically and pure uranium metal is extracted. The two main isotopes of uranium metal (as hexafluorides) are then partially separated at a uranium enrichment facility. This results in two uranium fractions. One, called enriched uranium, is enriched in the U-235 isotope, making it a useful fuel for nuclear power plants and for use in atomic weapons. The other fraction is essentially a left-over, waste product that is depleted in this isotope and is roughly 99.8% U-238. This is radioactive depleted uranium.
Finally, there are the uranium fabrication facilities where DU munitions are manufactured.

Details

In 1944, Lorenz (1) published a critical review of uranium miner's lung cancer and concluded that radon by itself wasn't the sole cause of the lung cancer. Twenty years later, Wagoner (2) reported on cancer mortality patterns in uranium miners and millers over a twelve year period and found no mortality increase among millers, but a nearly 50% mortality increase among miners, with a 10-fold increase in respiratory neoplasms. His study eliminated most suggested causes for this increase except exposure to airborne radiation. The following year, Wagoner (3) reported similar findings based on a much larger sample consisting of 3415 miners.

In 1992, Shields (8) reported increased birth defects among children of Navajo women living near uranium mine tailings and waste dumps near Shiprock, NM. Brugge (17) in 2002 published a review on the overall health affects of uranium mining among the Navajos.

In 1997, Zaire (12) compared 75 non-HIV Namibian uranium miners with 31 non-miners and reported finding a six-fold increase in urinary uranium, lower testosterone levels and neutrophil count, and a three-fold increase in chromosome aberrations. Wesch (13) reported studying over 17,000 uranium miner autopsy cases from the Erzgebirge, Germany mines over the 1946 to 1990 period and reported considerably higher rates of lung cancer (vs. general population) but no increase in solid cancers or leukemias. Tomaseck (14) studied a population of Czech miners and determined that cancer risk was age related, being greater for the younger miners.

In 1983, Allard (5) studied skin exposure to radiation and provided a dose-related model that compared well with actual measurements. West (4) discovered a group of uranium mill workers who exhibited exceptionally long retention of uranium in their lungs. In 1987, Dupree (6) reported statistically significant higher mortality in 995 workers at a uranium processing plant in New York, compared to the general population, with the greatest difference being in mortality due to laryngeal cancer and pneumonia. Dupree expanded these studies to include four uranium processing facilities and reported his findings in 1995 (10). Meanwhile, Madley (9) reported on urinary uranium levels in uranium mill workers' urine specimens.

Henderson (7) reported a study in workers' exposure to DU in 1991 at an Oak Ridge facility that resulted in procedural changes to reduce exposure levels. In 1996, Loomis (11) presented a report on mortality rates at an Oak Ridge DU processing plant. McGeoghegan (15), (16) published two reports in 2000, the first reporting mortality studies of nearly 14,000 radiation workers from

1946 to 1995 at British Nuclear Fuel's Springfield plant and the second on 3244 radiation workers from 1946 to 1995 at British Nuclear Fuel's Capenhurst plant.

1. Radioactivity and lung cancer: a critical review of lung cancer in the miners of Schneeberg and Joachimsthal, by E Lorenz, J. Nat. Cancer Inst. Vol. 5, 1944 (pp. 1-15).
Concludes that radon cannot be the sole cause of lung cancer in miners, but may also include pneumoconiosis produced from dust in the mines, chronic irritation caused by respiratory diseases, arsenic, radioactive substances and perhaps hereditary susceptibility.
[Lorenz1944xxJNCIv5nxp1].

2. Cancer mortality patterns among U.S. uranium miners and millers, 1950 through 1962, by JK Wagoner, et al., J. Nat. Cancer Inst. Vol. 32, 1964 (pp. 787-801).
Report cancer mortality patterns for a group of US uranium miners and millers, with comparison of age-race-cause specific mortality with that of the general male population of the Colorado Plateau. Among white millers, there was no difference in cause-specific mortality relative to general population. Among white uranium miners with 5 or more years experience, there were 218 deaths compared with 148.7 expected, with respiratory neoplasms about 10 fold higher (11 vs 1.1 expected). The excess neoplasms was not attributable to age, smoking, nativity, heredity, urbanization, self-selection, diagnostic accuracy and prior hard-rock mining or other ore constituents including silica dust. The evidence implicates airborne radiation in the genesis of this increase in resp. cancer among US uranium miners.
[Wagoner1964xxJNCIv32nxp787].

3. Radiation as the cause of lung cancer among uranium miners, by JK Wagoner, et al., New Engl. J. Med. Vol. 273, 1965 (pp. 181-188).
Studied 3415 underground, white U miners compared with general white male population of the Colorado Plateau. Excess mortality attributed to respiratory neoplasms (22 obs. v 5.7 expected). Conclude that airborne radiation causes respiratory cancers. From dose-response relationship, even when other factors, e.g., cigarette smoking are taken into consideration. Conclude that pathology of U miners was unlike age-smoking-resident matched control group, but was similar to that observed in factory workers exposed to "radiomimetic" agent, mustard gas.
[Wagoner1965xxNEJMv273nxp181].

4. A comparison of uranium cases showing long chest burden retentions, by CM West, et al., Health Physics Vol. 12, 1966 (pp. 1545-1555).
This paper describes a small percentage of uranium industry workers who have unusually slow clearance of uranium from lungs. The authors can't explain the reason for this phenomenon.
[West1966xxHPv12nxp1545].

5. Beta dosimetry experiences at a depleted uranium metal fabrication facility, by DJ Allard, et al., Nuclear Metals, Inc., Concord, MA. Proc. Int. Beta Dosim. Symp., 1983 (pp. 509-531).
Extensive evaluation via physical measurements and calculations is presented for 3 exposure scenarios, with emphasis on skin doses. The scenarios are compared with actual experiences.
[Allard1983xxPIBDSp509].

6. Mortality among workers at a uranium processing facility, the Linde Air Products Company ceramics plant, 1943-1949, by EA Dupree,et al., Scandanavian J. of Work and Environmental Health Vol. 13, 1987 (pp. 100-107).
A mortality study of 995 white males employed at this U processing facility in western New York State compared with the white male population of the U.S. and also compared separately with white males in Erie and Niagara counties of New York State shows statistically increased standardized mortality ratios (SMR) for all causes (118), laryngeal cancer (447), all circulatory diseases (118), arteriosclerotic heart disease (119), all respiratory diseases (152) and pneumonia (217) [note, 100 would be the SMR if there is no difference in mortality between exposed workers and controls]. There was also a statistically signif increase in number of death above expected for laryngeal cancer (5) and pneumonia (17). [Note: although all investigators were affiliated with U.S. institutions, this work was published in a Scandanavian journal].
[Dupree1987xxSJWEHv13nxp100].

7. Evaluation of radiation exposure in metal preparation depleted uranium process areas, by MD Henderson, Oak Ridge Y-12 Plant, Oak Ridge, TN. Gov. Rep. Announce. Index (US) Vol. 16(8), 1991 (abstr. no. 19829).
Research in DU operations at the Y-12 plant to assess the magnitude of nonuniform and extremity exposures in order to reduce such exposures and design optimum dosimetry protocol to assure compliance. As a result of the research, operational changes were made that lowered the dose equiv. to the employees.
[Henderson1991xxGRAIv16n8p19829].

8. Navajo birth outcomes in the Shiprock uranium mining area, by LM Shields, et al., Health Physics Vol. 63, 1992 (pp. 542-551).
Statistically significant association between uranium operations and unfavorable birth outcome was identified with the mother living near tailing or mine dumps. Indicates birth defects increased significantly when either parent worked in Shiprock electronics assembly plant. Authors indicate weak association between birth outcomes and radiation exposure. No discussion of possible chemical toxicity from living near mine tailings or mine dumps.
[Shields1992xxHPv63nxp542].

9. Diurnal urinary volume and uranium output in uranium workers and unexposed controls, by DW Madley, et al., Health Physics Vol. 67, 1994 (pp. 122-130).
[Madley1994xxHPv67nxp122].

10. Uranium dust exposure and lung cancer risk in four uranium processing operations, by EA Dupree, et al., Epidemiology Vol. 6, 1995 (pp. 370-375).
[Dupree1995xxEv6nxp370].

11. Mortality of workers at a nuclear materials production plant at Oak Ridge, Tennessee, 1947-1990, by DP Loomis, et al., American Journal of Industrial Medicine Vol. 29, 1996 (pp. 131-141).
[Loomis1996xxAJIMv29nxp131].

12. Unexpected rates of chromosomal instabilities and alterations of hormone levels in Namibian uranium miners, by R Zaire, et al., Radiation Res Vol. 147, 1997 (pp. 579-584).
Shows a much higher prevalence of cancer among open pit U miners in Namibia rel to general population. Measured U excretion in urine, neutrophil counts and serum levels of FSH, LH and testosterone, and chromosomal aberrations in whole blood cells. Compared 75 non-smoking, HIV-negative miners with 31 individuals with no occupational mining history. There was 6 fold increase in U excretion among miners, with reduction in testosterone levels and neutrophil count. Also a 3 fold increase in chromosomal aberrations in miners rel to controls. Cells with multiple aberrations among miners, i.e., rogue cells, found for the first time among U miners. Previously only found among acute radiation dose victims in Hiroshima and Chernobyl.
[Zaire1997xxRRv147nxp579].

13. German uranium miner study - historica background and available histopathological material, by H Wesch, et al., Radiation Research Vol. 152, 1999 (pp. S48-S51).
Gives historical background on the Erzgebirge area of Saxony in Germany where many metal ores were mined. About 400,000 workers produced a total of 220,000 tons uranium during 1946-1990. Documents contain protocols for 28,975 autopsy cases and about
400,000 slides collected from 1957-92, about 66,000 tissue blocks, and 238 whole lungs. From autopsy cases, about 17,466 could be identified as workers of uranium mining. Shows significantly higher incidence of lung cancer in miners relative to area residents. No significant difference for other solid cancers and leukemias.
[Wesch1999xxRRv152nxpS48].

14. Radon exposure and lung cancer risk: Czech cohort study, by L Tomášek, et al., Radiation Res Vol. 152, 1999 (pp. S59-S63).
Analyzed 2 main factors for radiogenic risk, time since exposure and age at exposure. Find that increasing age at initial exposure to radiation in mines results in less lung disease (lower risk).
[Tomasek1999xxRRv152nxpS59].

15. The mortality and cancer morbidity experience of workers at the Springfields uranium production facility, 1946-95, by D. McGeoghegan, et al., Westlakes Scientific Consulting Ltd, Cumbria, UK. david.mcgeoghegan@westlakes.ac.uk. J Radiol Prot. Vol. 20(2), June 2000 (pp. 111-37).
The results presented here are from the follow-up of the cohort of workers ever employed at the Springfields site of British Nuclear Fuels plc (BNFL) between 1946 and 1995. The main activity of the site is uranium fuel fabrication and uranium hexafluoride production. The study cohort consists of 19454 current and former employees, 13 960 of which were classified as radiation workers, and contains 479146 person-years of follow-up. The mean follow-up period is 24.6 years. To the end of 1995 there have been 4832 deaths recorded for this cohort, 3476 of which were amongst radiation workers and 1356 were amongst non-radiation workers. The standardised mortality ratios (SMRs) for all causes were 84 and 98 for radiation workers and non-radiation workers respectively. For all cancers the SMRs were 86 and 96 respectively. For cancer morbidity the standardised registration ratios (SRRs) for all cancers were 81 and 81 respectively.
Significant associations were noted for both mortality and morbidity due to Hodgkin's disease and cumulative external dose. A strong association was also noted for morbidity, but not mortality, due to non-Hodgkin's lymphoma. These associations, however, are unlikely to be causal. The excess relative risk estimates for cancer other than leukaemia and for leukaemia excluding chronic lymphatic leukaemia are consistent with other occupationally exposed cohorts and estimates from the high-dose studies.
[McGeoghegan200006JRPv20n2p111]. (PMID: 10877261 [PubMed - indexed for MEDLINE]).

16. The mortality and cancer morbidity experience of workers at the Capenhurst uranium enrichment facility 1946-95, by D McGeoghegan, et al., Westlakes Scientific Consulting Ltd, Cumbria, UK. david.mcgeoghegan@westlakes.ac.uk. J Radiol Prot. Vol. 20(4), Dec. 2000 (pp. 381-401).
The results presented here contain the follow-up of the cohort of workers ever employed at the Capenhurst site of British Nuclear Fuels plc or its predecessors between 1946 and 1995. The main activity of the plant is isotopic, 235U, enrichment of uranium. The study cohort consists of 12,540 employees and contains 334,473 person-years of follow up. This is a relatively mature cohort, with a mean follow-up period of 26.7 years, that has been exposed to low levels of radiation. The collective external radiation dose received by the 3244 radiation workers was 31.95 person-sieverts, with mean cumulative dose 9.85 mSv.
To the end of 1995 there have been 3841 deaths recorded for this cohort, 585 of which were amongst radiation workers. The standardised mortality ratios (SMRs) for all causes were significantly low, 83 and 91 respectively, for radiation and non-radiation workers, indicating the usual 'healthy worker' effect. The cancer mortality was less than that expected, though not significantly so, with SMRs for all cancers of 88 and 97, for radiation and non-radiation workers respectively. The cancer registration rates were significantly low, with standardised registration ratios (SRRs) for all cancers of 82 and 88, for radiation and non-radiation workers respectively. An association between bladder cancer registrations and cumulative external radiation exposure was noted when the cumulative external dose was lagged by 20 years.
[McGeoghegan200012JRPv20n4p381]. (PMID: 11140711 [PubMed - indexed for MEDLINE]).

17. The history of uranium mining and the Navajo people, by D Brugge, et al., Amer. J. Public Health Vol. 92, 2002 (pp. 1410-1419).
Gives a good review of health risks from uranium mining and describes health effects of U mining on Navajo people.
[Brugge2002xxAJPHv92nxp1410].

Chapter VII

Uranium, Depleted Uranium and the Environment

Summary

Natural uranium is ubiquitous in our environment. It is present in the earth, the air we breath and the water we drink. As a species, we have thus always been subjected to uranium exposure. It is likely that this background radiation and heavy-metal exposure is responsible for a certain on-going "base" level of human disease and death experienced by our species since the dawn of time. However, uranium does not appear in nature in its purified metallic form, nor does it manifest itself in particulates of dust so fine (less than 5 microns in diameter) as to become deeply embedded in the lungs, nor does it take on the particularly insoluble crystalline structure of a ceramic. Unfortunately, all three of these characteristics describe the nature of depleted uranium when it is used in munitions. When U and DU burn (as happens when a DU shell strikes a hard object), an aerosol of these ultra-fine particles of uranium oxide ceramic form and can become dispersed far beyond the battlefield in which they were used.

Details

Several reports and articles have been published characterizing the nature of uranium and depleted uranium munitions. In 1980, Glissmeyer (1) reported characteristics of airborne DU (size distribution, quantity and dispersion) from test firing 105-mm penetrators and Ensminger (2) reported on procedures to calculate health risks resulting from these airborne particulates. Elder (3) studied the oxidation features of the burning DU aerosols and estimated that complete oxidation of a sample could take place in a sustained fire. In 2003, Chazel (30) reported the results of studying actual aerosol samples resulting from DU penetrator strikes on tank armour and found the average particle size to be 1 to 2 microns in diameter, and aerosol concentration to be 8.5 mg of DU per cubic meter of air. Parkhurst (31) described the parameters and testing procedures used for a comprehensive analysis of DU aerosols produced inside a tank hit by a DU penetrator, with results to be published in a later paper.

Hooker (5) and Robitaille (6) determined that the radiological exposure to tank crews from DU munitions stored in the tank was within occupational accepted levels. Shinn (8) reported on the metal particle dispersion resulting from explosion of a DU test round.

Trzaskoma (4) and McIntyre (7) studied the corrosion properties of DU and DU alloys in air, moist salt air (7% wt. loss in 30 days), and salt water. Graham (12) modeled mobilization and transport of DU in surface waters while Grsic (20) and Mitsakou (41) have modeled dispersion of DU aerosols. In 2002, Chen (25) reported modelling the subsurface behavior of DU. Durante (26), (39) used models to asses the health risks associated with use of DU munitions and concluded that radiological risk could be ignored and that chemical toxicity from DU use in the Balkans was most likely to occur through water contamination rather than air and was well within acceptable limits of exposure.

In 1990, Erickson (9) published a review on the environmental behavior of DU from DU penetrators, and Ebinger (10) reported on the fate of DU from testing at Aberdeen and Yuma Proving Grounds.

In 1995, Bou-Rabee (11) analyzed soil and air samples in Kuwait for DU and determined that not enough uranium would be inhaled by residents to impose a health risk. In 1999, Fetter (14) reported that rescuers and cleanup crews working around equipment hit by DU penetrators were at high risk from heavy-metal toxicity from DU aerosols.

In 1992, a Boeing 747 cargo plane with DU counterweights crashed in Amsterdam, and 330 pounds of DU were never recovered from the crash site. In 2000, Uijt de Haag (17) used models to report an assessment of the risk to residents' health posed by the resulting DU contamination of their environment and determined the health risk to be negligible.

NATO's use of DU in the Balkans initiated numerous studies on the behavior of DU in this region. In 1999, Sitaras (13) looked into the impact of DU munitions use by NATO in the Yugoslavia. Duric's (15) review attempted to determine a zero-state biological reference for uranium in the region in order to ascertain future risks and damage associated by DU contamination. Pavlovic (16) ran DU analyses of food and drinking water for DU following the war. In 2001, Kerekes' (18) use of alpha spectrometry on airborne samples in Hungary to detect DU resulting from NATO bombing in northern Yugoslavia came up negative for DU, but he reported an increase in the background level of natural uranium in the soil that he attributed to fallout from the bombing.

Sansone (19) analyzed soil surrounding DU penetrator impact sites and found elevated uranium levels within a 2-meter radius and 10 to 20 cm deep into the soil. He also reported (24) on water, soil, tree bark and lichen samples taken from Kosovo. The soil

samples ranged from 10 mg/kg of DU to as much as 18 grams of DU per kilogram of soil. All bark and lichen samples tested positive for DU (probably from aerosolized DU), even in locations where the soil samples showed no DU. On the other hand, Loppi (40) reported finding no DU in lichens retrieved from the Balkans. Orlic (21) wrote on the health and environmental effects expected from NATO's bombing of Yugoslavia. Papachristodoulou (38) used gamma spectroscopy to analyze for DU in Kosovo samples.

Boulyga (22), analyzed soil samples and a penetrator shell from Kosovo with ICP-MS and alpha spectrometry and discovered both plutonium and amerecium mixed with the DU in the penetrator, indicating that the DU had come from nuclear reactor waste material. Desideri (27), Pollanen (33), and McLaughlin (35) reported similar results while Danessi (32), of the International Nuclear Energy Agency disagreed, concluding that the plutonium levels could be explained from nuclear testing fallout. Danessi (34) reported in another paper that the DU particles in soil samples were generally less than 5 microns in diameter, with 50% of the particles smaller than 1.5 microns. In mid 2002, Papastefanou (28) reviewed these data, and at the same time Uyttenhove (29) reported gamma spectroscopy on 50 Kosovo samples taken from sites where DU use had been reported and found no trace of DU in any sample.

Salbu (36) studied samples from Kosovo soil and determined that 50% of the particles (avg. size 2 microns) were the more insoluble UO2 (vs. U3O8).

Hamilton (23) writes in 2001 that concerns about DU contamination in the environment result from poor understanding of basic geologic distribution principles and ignorance of general health physics. Meinrath (37) describes the Erzgebirge region in Germany where a great deal of uranium was mined for the former USSR and the 6.5 billion Euros that have been expended since 1991 for environmental cleanup.

1. Characterization of airborne uranium from test firing of XM774 ammunition, by JA Glissmeyer, et al., Battelle Pac. NW Lab, Richland, WA. Energy Res. Abstr. Vol. 5(5), 1980 (abstr. no. 7563)
The airborne DU resulting from the test firings of 105-mm APFSDS-t XM774 ammunition was determined to evaluate the human inhalation exposure to the DU. The size distribution of airborne DU; the quantity of airborne DU, the dispersion of airborne DU from the target vicinity, the amount of DU deposited on the ground, the solubility of airborne DU compounds in lung fluid and oxide forms of airborne and fallout DU were studied.
[Glissmeyer1980xxERAv5n5p7563].

2. Procedures to calculate radiological and toxicological exposures from airborne releases of depleted uranium, by DA Ensminger, et al., Anal. Sci. Corp., Reading MA. Gov. Rep. Announce. Index (US) Vol. 81(10), 1981 (p. 2091).
The 105-mm XM774 and M735A1 shells containing a DU penetrator are analyzed for their radiological and chemical toxicities.
[Ensminger1981xxGRAIv81n10p2091].

3. Oxidation of depleted uranium penetrators and aerosol dispersal at high temperatures, by JC Elder, Los Alamos Sci. Lab, Los Alamos, NM. Energy Res. Abstracts Vol. 6(8), 1981 (abstr. no. 11536).
Oxidation of DU aerosols in the respirable range was min. at 700 degrees in air and 800 degrees in 50/50 air CO2, indicating some self-protection at higher temperatures. There was no evidence of self-sustained burning, though complete sample oxidation can be expected in a sustained blaze.
[Elder1981xxERAv6n8p11536].

4. A comparison of the corrosion and stress corrosion resistance of two depleted uranium alloys: DU-0.75Ti and DU-2Mo, by PP Trzaskoma, Nav. Res. Lab, Washington, DC. Gov. Rep. Announce. Index (US) Vol. 81(21), 1981 (p. 4599).
The observed corrosion rates in moist air were low, but that for the titanium alloy in salt fog increased sharply. Approx. 7% weight loss was observed in 30 days.
[Trzaskoma1981xxGRAIv81n21p4599].

5. Radiological assessment of cartridge 120-mm APFSDS-T XM829 ammunition, by CD Hooker, et al., Pac. NW Lab, Richmond, WA. INIS Atomindex Vol. 15(17), 1984 (abstr. no. 15:052427).
Shielding on the XM-829 rounds effectively block beta radiation, leaving gamma radiation the predominant emission. These are low such that military personnel are not likely to exceed the maximum permissable nonoccupational dose (Army Reg. 40-14) and properly packaged munitions may be exempted from special marking and labeling requirements.
[Hooker1984xxINISAv15n17p052427].

6. Gamma-ray exposure hazard due to storage of M-774 APFSDS rounds in a Leopard C-1 main battle tank, by HA Robitaille, Defence Res. Establ., Ottawa, On, Can. Gov. Rep. Announce Index (US) Vol. 84(7), 1984 (p. 56).
Concludes that 29 of the M-744 shells (with 3.4 kg Duper round) exposes the loader's position to 0.17 mrad/hr, or 29 mrad/week (168 hours), ¼ the max. currently allowed by Canadian fources regulators, so therefore is not a significant gamma radiation hazard to Leopard C1 crew members.

[Robitaille1984xxGRAIv84n7p56].

7. Galvanic corrosion behavior of depleted uranium in synthetic seawater coupled to aluminum, magnesium and mild steel, by JF McIntyre, et al., Naval Surf. Weapons Center, Silver Spring, MD, Corrosion Vol. 44(8), 1988 (pp. 502-10).
[McIntyre1988xxCv44n8p502].

8. An environmental analysis of metal particle dispersion from an explosive test at Tonopah Test Range, by JH Shinn, Lawrence Livermore Natl. Lab, Livermore, CA, Energy Res. Abstr. Vol. 13(16), 1988 (Abstract 37713).
[Shinn1988xxERAv13n16p37713].

9. A review of the environmental behavior of uranium derived from depleted uranium penetrators, by R. Erikson, et al., Pac. Northwest Lab, richland, WA. Energy Res. Abstr. Vol. 15(7), 1990 (abstr. no. 16179).
[Erikson1990xxERAv15n7p16179].

10. Long-term fate of depleted uranium at Aberdeen and Yuma Proving Grounds: Final Report, Phase 1: Geochemical transport and modeling, by MH Ebinger, et al., Los Alamos Natl. Lab, Los Alamos, NM. Energy Res. Abstr. Vol. 15(16), 1990 (abstr. no. 36795).
Soil samples beneath a penetrator fragment at humid APG site showed 12% DU in the surface horizon and significantly above background to a depth of 20 cm, and while surface water showed only background levels of U, bottom sediments were contaminated with DU. At arid YPG site, only 0.5% of U in the surface horizon and background concentrations of U and DU to 20 cm depth were found. Concluded that at APG, water dissolution and transport was primary cause of transport, while at YPG dispersion was due mainly to erosion.
[Ebinger1990xxERAv15n16p36795].

11. Estimating the concentration of uranium in some environmental samples in Kuwait after the 1991 Gulf War, by F Bou-Rabee, Dept. of Geology, Kuwait Univ, Safat, Kuwait. Appl. Radiat. Isot. Vol. 46(4), 1995 (pp. 217-220).
Soil and air samples in Kuwait have been analyzed using ICP-MS. Avg. U in soil samples is 0.7 microgram/gram, half that of solid fall-out and air particulate matter samples. Total per capita annual intake of U via inhalation was appraised to be about 0.05 Bq, less than 0.2% of max. allowed annual intak for general population.
[BouRabee1995xxARIv46n4p217].

12. Mobilization and transport of depleted uranium in surface waters, by PN Graham, et al., Georgia Inst. of Tech., Atlanta, GA. 212th ACS Nat'l Meeting Abstracts, Aug. 25, 1996.
A model using experimental oxidation and dissolution rate equations is developed to determine long-range potential for DU transport.
[Graham1996xxACSNMA].

13. Environmental impact of the NATO air strikes in Yugoslavia, by IE Sitaras, et al., Dept. Chem., Natl. and Capodistrian Univ., Athens, Greece. Chemika Chronika, Genike Ekdose Vol. 61(6), 1999 (pp. 180-184).
Sources and health impacts of organic pollutants and DU resulting from NATO air strikes are examined, with attempts at estimating their transport and future dispersion in the environment.
[Sitaras1999xxCCGEv61n6p180).

14. After the dust settles, by S Fetter, et al., The Bulletin of the Atomic Scientists Vol. 55, 1999, (pp. 42-45).
The authors conclude that radiological effects from DU exposure will be minor, but people exposed to vehicles hit by DU munitions, their rescuers, and individuals who spent prolonged time in the vehicles as part of cleanup details without adequate respiratory protection could be at high risk for heavy-metal toxicity from inhalation of DU dust.
[Fetter1999xxBASv55nxp42].

15. Uranium in the environment, (in Serbian), by GD Duric, et al., Univ. of Belgrade, Belgrade, Yugoslavia. Hemijska Industrija Vol. 54(2), 2000 (pp. 50-52).
A review with 20 references with emphasis on determining an appropriate "zero state" biological reference in order to assess risks and damage that may be caused by future environmental contamination from DU.
[Duric2000xxHIv54n2p50].

16. Assessment of the environmental radioactive contamination levels by depleted uranium after a war, by S Pavlovic, et al., VINCA Inst. of Nuclear Sciences, Belgrade, Yugoslavia. Bilten Instituta za Nuklearne Nauke Vinca Vol. 5(1to4), 2000 (pp. 25-31).
Radioactivity analysis of food, drinking water, etc. were carried out following wartime assault with DU weapons.
[Pavlovic2000xxBINNVv5n1to4p25].

17. Evaluating the risk from depleted uranium after the Boeing 747-258F crash in Amsterdam, 1992, by PA Uijt de Haag, et al., RIVM, P.O. Box 1, 3720 BA, Bilthoven, Netherlands. paul.uijt.de.haag@rivm.nl J Hazard Mater. Vol. 76(1), Aug. 2000 (pp. 39-58).
On 4 October 1992, a large cargo plane crashed into an apartment building in the Bijlmermeer quarter of Amsterdam. In the years following the accident, an increasing number of people started reporting health complaints, which they attributed to exposure to dangerous substances after the crash. Since the aircraft had been carrying depleted uranium as counterbalance weights and about 150 kg uranium had been found missing after clearance of the crash site, exposure to uranium oxide particles was pointed out as the possible cause of their health complaints.Six years after the accident, a risk analysis was therefore carried out to investigate whether the health complaints could be attributed to exposure to uranium oxide set free during the accident. The scientific challenge was to come up with reliable results, knowing that - considering the late date - virtually no data were available to validate any calculated result. The source term of uranium was estimated using both generic and specific data. Various dispersion models were applied in combination with the local setting and the meteorological conditions at the time of the accident to estimate the exposure of bystanders during the fire caused by the crash.
Emphasis was given to analysing the input parameters, inter-comparing the various models and comparing model results with the scarce information available.Uranium oxide formed in the fire has a low solubility, making the chemical toxicity to humans less important than the radiotoxicity. Best-estimate results indicated that bystanders may have been exposed to a radiation dose of less than 1 microSv, whereas a worst-case approach indicated an upper limit of less than 1 mSv. This value is considerably less than the radiation dose for which acute effects are to be expected. It is therefore considered to be improbable that the missing uranium had indeed led to the health complaints reported.
[UijtdeHaag200008JHMv76n1p39]. (PMID: 10863013 [PubMed - indexed for MEDLINE]).

18. Did NATO attacks in Yugoslavia cause a detectable environmental effect in Hungary?, by A Kerekes, et al., Frederic Joliot-Curie National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary. kerekes@hp.osski.hu Health Phys. Vol. 80(2), Feb. 2001 (pp. 177-178).
Because of the intensive NATO bombardment of the neighboring region to Hungary, i.e., Vojvodina, North Yugoslavia, air monitoring for detection of depleted uranium particles supposed to be used as a component of bullets was extended to the Southern region of the country. Alpha spectrometry was applied as a sensitive analytical technique able to detect uranium. Though no depleted uranium was detected in air by the sensitive technique of alpha-spectrometry, the increased uranium content in natural ratio as a component of normal soil, natural gas, etc., is suggested to originate from well dispersed dust (2.5 microm size) emitted to the atmosphere by explosions during bombing. This observation is supported by the geographical distribution and the relatively rapid decrease of pollution after the bomb attacks ceased.
[Kerekes200102HPv80n2p177]. (PMID: 11197468 [PubMed - indexed for MEDLINE]).

19. Levels of depleted uranium in Kosovo soils, by U Sansone, et al., ANPA-Agenzia Nazionale per la Protezione dell'Ambiente, Italian National Environmental Protection Agency, Rome. sansone@anpa.it. Radiat Prot Dosimetry. Vol. 97(4), 2001 (pp. 317-320).
The United Nations Environment Programme (UNEP) has performed a field survey at 11 sites located in Kosovo, where depleted uranium (DU) ammunitions were used by the North Atlantic Treaty Organization (NATO) during the last Balkans conflict (1999). Soil sampling was performed to assess the spread of DU ground contamination around and within the NATO target sites and the migration of DU along the soil profile. The 234U/238U and 235U/238U activity concentration ratios have been used as an indicator of natural against anthropogenic sources of uranium. The results show that levels of 238U activity concentrations in soils above 100 Bq x kg(-1) can be considered a 'tracer' of the presence of DU in soils. The results also indicate that detectable ground surface contamination by DU is limited to areas within a few metres from localised points of concentrated contamination caused by penetrator impacts. Vertical distribution of DU along the soil profile is measurable up to a depth of 10-20 cm. This latter aspect is of particular relevance for the potential risk of future contamination of groundwater.
[Sansone2001xxRPDv97n4p317]. (PMID: 11878410 [PubMed - indexed for MEDLINE]).

20. Estimation of depleted uranium aerosol distribution through the atmosphere after hitting of a solid target by ammunition, in Serbian, by Z Grsic. Hemijska Industrija Vol. 55(7-8), 2001 (pp. 335-338).
Using a Gaussian “puff” trajectory diffusion model, the effects of meteorological conditions was demonstrated.
[Grsic2001xxHIv55n7to8p335].

21. Estimation of consequences to the population and the environment due to the use of ammunition with depleted uranium in Yugoslavia, in Serbian, by M Orlic. Hemijska Industrija Vol. 55(7-8), 2001 (pp. 349-357).
[Orlic2001xxHIv55n7to8p349].

22. Optimization and application of ICP-MS and alpha spectrometry for determination of isotopic ratios of depleted uranium and plutonium in samples collected in Kosovo, by SF Boulyga, et al., Research Center Juelich, Juelich, Germany. Journal of Analytical Atomic Spectroscopy Vol. 16(11), 2001 (pp. 1283-1289).

The limits of quantification for U-236 and Pu-239 using these two methods was 0.6 pg/liter (aq. soln.) and 0.13 pg/gram (soil). DU was detected in Kosovo soil samples, along with Pu-240, and Pu-239, (total Pu at 0.5 pg/gram), though the samples containing Pu were not the same as those containing DU, leading to the possible conclusion that the Pu detected as background contamination from nuclear testing fallout and from the Chernobyl accident of 1986. However, Plutonium, Am-241 (1.7 pg/gram), and U-236 (0.031 mg/gram) were all detected in a sample taken from a penetrator shell.
[Boulyga2001xxJAASv16n11p1283].

23. Depleted uranium (DU): a holistic consideration of DU and related matters, by EI Hamilton, Phoenix Research, Marldon, Paignton, UK. Sci Total Environ. Vol. 281(1-3), Dec. 2001 (pp. 5-21).
Following the use of depleted uranium (DU) during the Gulf and Balkan conflicts, unnecessary and costly confusion has existed for some 11 years concerning the hazard it constitutes, despite the fact that sufficient data are available to answer most of the relevant questions. In tracing the significance of uranium in the environment and humans, too much reliance is still placed upon the extrapolation of animal data. The existing radiological nomenclature is far too involved and complex to understand, let alone implement. The excellence of early health physics seems to have been lost, and hence there is a failure to utilise the large body of knowledge, and the manner in which it was obtained, in other disciplines. Health physics has failed to understand the nature of some natural processes that ultimately control radiation dose to the environment and humans.
Examination of three types of DU, in particular the highly radioactive and potentially hazardous unprocessed, spent-reactor uranium fuel debris (UDU), alluded to as hot particles, has been poorly studied on the basis of scarcity in the environment. Fundamental geological processes are described which illustrate that, as a consequence of routine operation of nuclear reprocessing plants, especially in the past, and following reactor accidents, natural processes can result in an enrichment of DU particles in most types of sediment. Failure to grasp essential geological processes in relation to the dispersion of radionuclides in the environment is detrimental to public acceptance of an essential form of energy in association with others.
[Hamilton200112STEv281n1to3p5]. (PMID: 11778960 [PubMed - indexed for MEDLINE]).

24. Radioecological survey at selected sites hit by depleted uranium ammunitions during the 1999 Kosovo conflict, by U Sansone, et al., Agenzia Nazionale per la Protezione dell'Ambiente, Rome, Italy. sansone@anpa.it. Sci Total Environ. Vol. 281(1-3), Dec. 17, 2001 (pp. 23-35).
A field study, organised, coordinated and conducted under the responsibility of the United Nations Environment Programme (UNEP), took place in Kosovo in November 2000 to evaluate the level of depleted uranium (DU) released into the environment by the use of DU ammunition during the 1999 conflict.
Representatives of six different scientific organisations took part in the mission and a total of approximately 350 samples were collected. During this field mission, the Italian National Environmental Protection Agency (ANPA) collected water, soil, lichen and tree bark samples from different sites. The samples were analysed by alpha-spectroscopy and in some cases by inductively coupled plasma-source mass spectrometry (ICP-MS). The 234U/238U and 235U/238U activity concentration ratios were used to distinguish natural from anthropogenic uranium. This paper reports the results obtained on these samples.
All water samples had very low concentrations of uranium (much below the average concentration of drinking water in Europe). The surface soil samples showed a very large variability in uranium activity concentration, namely from approximately 20 Bq kg(-1) (environmental natural uranium) to approximately 2.3 x 10(5) Bq kg(-1) (approximately 18000 mg kg(-1) of depleted uranium), with concentrations above environmental levels always due to DU. The uranium isotope measurements refer to soil samples collected at places where DU ammunition had been fired; this variability indicates that the impact of DU ammunitions is very site-specific, reflecting both the physical conditions at the time of the impact of the DU ammunition and any physical and chemical alteration which occurred since then. The results on tree barks and lichens indicated the presence of DU in all cases, showing their usefulness as sensitive qualitative bio-indicators for the presence of DU dusts or aerosols formed at the time the DU ammunition had hit a hard target. This result is particularly interesting considering that at some sites, which had been hit by DU ammunition, no DU ground contamination could be detected.
[Sansone200112STEv281n1to3p23]. (PMID: 11778955 [PubMed - indexed for MEDLINE]).

25. Modeling of Depleted Uranium in subsurface systems, by PJ Chen, et al.,Department of Chemical and Environmental Engineering, National University of Singapore, Singapore, Singapore. Water, Air and Soil Polution, Vol. 140(1-4), 2002 (pp. 173-201).
“Equilibrium modelling studies showed that DU sorption increased sharply from 0 to 100% at pH 3.5-5.0 and max immobilization was established at pH >5. Kinetic simulations indicated that the sorption of DU in subsurface systems is a rapid process.”
[Chen200201WASPv140n1to4p173]

26. Estimates of radiological risk from depleted uranium weapons in war scenarios, by M Durante, et al., Department of Physics, University Federico II, Napoli, Italy. durante@na.infn.it. Health Phys. Vol. 82(1), Jan. 2002 (pp. 14-20).
Several weapons used during the recent conflict in Yugoslavia contain depleted uranium, including missiles and armor-piercing incendiary rounds. Health concern is related to the use of these weapons, because of the heavy-metal toxicity and radioactivity of uranium. Although chemical toxicity is considered the more important source of health risk related to uranium, radiation exposure has been allegedly related to cancers among veterans of the Balkan conflict, and uranium munitions are a possible source of

contamination in the environment. Actual measurements of radioactive contamination are needed to assess the risk. In this paper, a computer simulation is proposed to estimate radiological risk related to different exposure scenarios. Dose caused by inhalation of radioactive aerosols and ground contamination induced by Tomahawk missile impact are simulated using a Gaussian plume model (HOTSPOT code). Environmental contamination and committed dose to the population resident in contaminated areas are predicted by a food-web model (RESRAD code). Small values of committed effective dose equivalent appear to be associated with missile impacts (50-y CEDE < 5 mSv), or population exposure by water-independent pathways (50-y CEDE < 80 mSv). The greatest hazard is related to the water contamination in conditions of effective leaching of uranium in the groundwater (50-y CEDE < 400 mSv). Even in this worst case scenario, the chemical toxicity largely predominates over radiological risk. These computer simulations suggest that little radiological risk is associated to the use of depleted uranium weapons.
[Durante200201HPv82n1p14]. (PMID: 11768794 [PubMed - indexed for MEDLINE]).

27. Chemical and radiochemical characterization of depleted uranium (DU) in Kosovo soils, by D Desideri, et al., Centre of Applied Radiochemistry, Urbino University, Piazza Rinascimento 6, 61029 Urbino, Italy. d.desideri@uniurb.it. Ann Chim. Vol. 92(4), Apr. 2002 (pp. 397-405).
As is well known ammunitions containing depleted uranium (DU) were used by NATO during the Balkan war. The paper deals with the determination of uranium alpha emitting radiosotopes in Kosovo soils by chemical separation and alpha spectrometry. The samples were collected by CISAM (Centro Interforze Studi ed Applicazioni Militari, S. Piero a Grado, Livorno) in the period November 1999-April 2000. The DU distribution in soil appeared very disomogeneous; the isotope weight percentages for U-238, U-235 and U-234 resulted 99.76, 0.24 and 7.24.10(-4) respectively; consequently the activity distribution was 86.42%, 1.31%, 11.63% and the isotope ratios were 1.52.10(-2) and 0.134 for U-235/U-238 and U-234/U-238 showing clearly the presence of DU. A small peak at 4.49 MeV (U-236) in the alpha spectrum indicated that the used DU was the by-product of exhausted uranium reprocessing. In order to determine the chemical and physiological solubility of uranium a fractionation study was carried out by using the Tessier method: 55% of uranium showed a fair solubility, but 45% was solubilized only by 8 M HNO3.
[Desideri200204Acv92n4p397]. (PMID: 12073885 [PubMed - indexed for MEDLINE]).

28. Depleted uranium in military conflicts and the impact on the environment, by C Papastefanou, Aristotle University of Thessaloniki, Nuclear Physics Department, Greece. papastefanou@physics.auth.gr. Health Phys. Vol. 83(2), Aug. 2002 (pp. 280-282).
Kosovo was bombarded by fired shells (bullets) with depleted uranium (DU) during April 1999. Around 30,000 depleted uranium rounds (projectiles) were fired, and about 10 tons of the DU debris were scattered across Kosovo. In reviewing the data on environmental measurements for depleted uranium collected by field missions in the Kosovo area during the period of 5-19 November 2000 (1.5 years following the 1999 conflict), evidence of depleted uranium was found only in soil samples at localized points of concentrated contamination. Concentrations varied from a few mg (2.34 mg) DU per kg soil (29 Bq DU/kg soil) at depths of 39.5-44.5 cm up to about 18 g DU per kg soil (225,760 Bq DU/kg soil) at depths of 0-5 cm surface soil. There were no signs of depleted uranium in waters. However, in most (80%) of the 145 soil (core) samples reported by UNEP, 238U was lower than 100 Bq per kg soil (the lowest was 8.8 Bq per kg soil) in 112 locations of widespread contamination.
[Papastefanou200208HPv83n2p280]. (PMID: 12132716 [PubMed - indexed for MEDLINE]).

29. Depleted uranium in Kosovo: results of a survey by gamma spectrometry on soil samples, by J Uyttenhove, et al., Ghent University, Physics Lab, Gent, Belgium. jozef.uyttenhove@rug.ac.be. Health Phys. Vol. 83(4), Oct. 2002 (pp. 543-548).
The presence of depleted uranium in the soil of former Yugoslavia after the 1999 conflict raised great public concern all over the world. The so-called Balkan-syndrome is often linked with depleted uranium contamination. An excellent compilation of data about DU and its possible impact on health and environment can be found in the 1999 UNEP report and publications from the Swedish Radiation Protection Institute. Unfortunately, very few systematic and reliable data on the possible depleted uranium concentrations were until now available. Some of these rare data are only available on the web, without adequate information about the experimental procedure used. To clarify the situation, a systematic survey was started in the summer of 2000 as a collaborative effort between Ghent University (Physics Laboratory) and the Belgian Ministry of Defense (Medical Service). From 50 sites selected all over Kosovo, 150 soil samples were measured in the laboratory with a high-resolution gamma-spectrometer. Some sites (14) were explicitly selected based on military information on the use of depleted uranium munitions in the vicinity. After careful analysis we can conclude that there is no indication of any depleted uranium contamination on these 50 sites with a minimal detectable activity of 15 Bq; this corresponds approximately to 1 mg depleted uranium in a typical sample (100-150 g).
[Uyttenhove200210HPv83n4p543]. (PMID: 12240731 [PubMed - indexed for MEDLINE])

30. Characterisation and dissolution of depleted uranium aerosols produced during impacts of kinetic energy penetrators against a tank, by V Chazel, et al., Institut de Radioprotection et de Surete Nucleaire, Departement de Protection de la Sante de l'Homme et de Dosimetrie, Service de Dosimetrie, LEAR, BP 166, F 26702 Pierrelatte Cedex, France. valerie.chazel@irsn.fr. Radiat Prot Dosimetry Vol. 105 (1-4), 2003 (pp. 163-166).
Aerosols produced during impacts of depleted uranium (DU) penetrators against the glacis (sloping armour) and the turret of a tank were sampled. The concentration and size distribution were determined. Activity median aerodynamic diameters were 1 microm (geometric standard deviation, sigma(g) = 3.7) and 2 microm (sigma(g) = 2.5), respectively, for glacis and turret. The mean air concentration was 120 Bq m(-3), i.e. 8.5 mg m(-3) of DU. Filters analysed by scanning electron microscopy (SEM) and X ray

diffraction showed two types of particles (fine particles and large molten particles) composed mainly of a mixture of uranium and aluminium. The uranium oxides were mostly U3O8, UO2.25 and probably UO3.01 and a mixed compound of U and Al. The kinetics of dissolution in three media (HCO3-, HCl and Gamble's solution) were determined using in-vitro tests. The slow dissolution rates were respectively slow, and intermediate between slow and moderate, and the rapid dissolution fractions were mostly intermediate between moderate and fast. According to the in-vitro results for Gamble's solution, and based on a hypothetical single acute inhalation of 90 Bq, effective doses integrated up to 1 y after incorporation were 0.54 and 0.56 mSv, respectively, for aerosols from glacis and turret. In comparison, the ICRP limits are 20 mSv y(-1) for workers and 1 mSv y(-1) for members of the public. A kidney concentration of approximately 0.1 microg U g(-1) was predicted and should not, in this case, lead to kidney damage.
[Chazel2003xxRPDv105n1to4p163]. (PMID: 14526949 [PubMed - in process]).

31. Measuring aerosols generated inside armoured vehicles perforated by depleted uranium ammunition, by MA Parkhurst, Pacific Northwest National Laboratory, PO Box 999, Richland, WA 99352, USA. maryann.parkhurst@pnl.gov. Radiat Prot Dosimetry Vol. 105(1-4), 2003 (pp. 167-170).
In response to questions raised after the Gulf War about the health significance of exposure to depleted uranium (DU), the US Department of Defense initiated a study designed to provide an improved scientific basis for assessment of possible health effects on soldiers in vehicles struck by these munitions. As part of this study, a series of DU penetrators were fired at an Abrams tank and a Bradley fighting vehicle, and the aerosols generated by vehicle perforation were collected and characterised. A robust sampling system was designed to collect aerosols in this difficult environment and monitor continuously the sampler flow rates. The aerosol samplers selected for these tests included filter cassettes, cascade impactors, a five-stage cyclone and a moving filter.
Sampler redundancy was an integral part of the sampling system to offset losses from fragment damage. Wipe surveys and deposition trays collected removable deposited particulate matter. Interior aerosols were analysed for uranium concentration and particle size distribution as a function of time. They were also analysed for uranium oxide phases, particle morphology and dissolution in vitro. These data, currently under independent peer review, will provide input for future prospective and retrospective dose and health risk assessments of inhaled or ingested DU aerosols. This paper briefly discusses the target vehicles, firing trajectories, aerosol samplers and instrumentation control systems, and the types of analyses conducted on the samples.
[Parkhurst2003xxRPDv105n1to4p167]. (PMID: 14526950 [PubMed - in process]).

32. Isotopic composition and origin of uranium and plutonium in selected soil samples collected in Kosovo, by PR Danesi, et al., International Atomic Energy Agency (IAEA), Seibersdorf Laboratories, Wagramer Strasse 5, PO Box 100, A-1400 Vienna, Austria. P.R.Danesi@iaea.org. J Environ Radioact. Vol. 64(2-3), 2003 (pp. 121-131).
Soil samples collected from locations in Kosovo where depleted uranium (DU) ammunition was expended during the 1999 Balkan conflict were analysed for uranium and plutonium isotopes content (234U, 235U, 236U, 238U, 238Pu, (239 + 240)Pu). The analyses were conducted using gamma spectrometry (235U, 238U), alpha spectrometry (238Pu, (239 + 240)Pu), inductively coupled plasma-mass spectrometry (ICP-MS) (234U, 235U, 236U, 238U) and accelerator mass spectrometry (AMS) (236U)). The results indicated that whenever the U concentration exceeded the normal environmental values (approximately 2 to 3 mg/kg) the increase was due to DU contamination. 236U was also present in the released DU at a constant ratio of 236U (mg/kg)/238U (mg/kg) = 2.6 x 10(-5), indicating that the DU used in the ammunition was from a batch that had been irradiated and then reprocessed. The plutonium concentration in the soil (undisturbed) was about 1 Bq/kg and, on the basis of the measured 238Pu/(239 + 240)Pu, could be entirely attributed to the fallout of the nuclear weapon tests of the 1960s (no appreciable contribution from DU).
[Danesi2003xxJERv64n2to3p121]. (PMID: 12500799 [PubMed - indexed for MEDLINE]).

33. Characterisation of projectiles composed of depleted uranium, by R Pollanen, et al., STUK-Radiation and Nuclear Safety Authority, P.O. Box 14, 00881 Helsinki, Finland. roy.pollanen@stuk.fi. J Environ Radioact. Vol. 64(2-3), 2003 (pp. 133-142).
Projectiles suspected to be composed of depleted uranium (DU) were found in Kosovo. Their properties were analysed using alpha and gamma ray spectrometry, mass spectrometry and electron microscopy. They were found to be composed of DU with small amounts of other elements such as Ti. 236U was detected in the penetrators, reflecting the use of reprocessed fuel. No transuranium elements were detected. The typical external dose rate meter is not the best option for mapping the location of penetrators from the ground. Monte Carlo calculations were performed in estimating possible skin doses. Penetrators in long-lasting contact with skin may cause a notable equivalent dose to skin.
[Pollanen2003xxJERv64n2to3p133]. (PMID: 12500800 [PubMed - indexed for MEDLINE]).

34. Depleted Uranium particles in selected Kosovo samples, by PR Danesi, et al., International Atomic Energy Agency (IAEA), Seibersdorf Laboratories, IAEA, Vienna, Austria. Journal of Environmental Radioactivity, Vol. 64(2-3), 2003 (pp. 143-154).
Selected soil samples, collected in Kosovo locations where DU ammunition was expended during the 1999 Balkan conflict, have been investigated by secondary ion mass spectroscopy (SIMS), X-ray fluorescence imaging using a micro-beam (micro-XRF) and scanning electron microscopy equipped with an energy dispersive X-ray fluorescence detector (SEM-EDXRF), with the objective to test the suitability of these techniques to identify the presence of small DU particles and measure their size distribution and the 235U/238U isotope ratio (SIMS). Although the results do not permit any legitimate extrapolation to all the sites hit by the DU rounds used during the conflict, they indicated that there can be “spots” where hundreds of thousands of particles may be present in a few milligrams of DU contaminated soil. The particle size distribution showed that most of the DU particles were <5 micrometer in diameter and more than 50% of the particles had a diameter <1.5 micrometer. Knowledge of DU particles is needed as a basis for

the assessment of the potential environmental and health impacts of military use of DU, since it provides information on possible re-suspension and inhalation.
[Danesi200302JERv64n2p143] (PMID: 12500801 [PubMed - indexed for MEDLINE]).

35. Actinide analysis of a depleted uranium penetrator from a 1999 target site in southern Serbia, by JP McLaughlin, et al., Department of Experimental Physics, University College Dublin, Belfield, Dublin 4, Ireland. james.mclaughlin@ucd.ie. J Environ Radioact. Vol. 64(2-3), 2003 (pp. 155-165).
Following the detection of 236U in depleted uranium (DU) ammunition used during the Balkans conflict in the 1990s, concern has been expressed about the possibility that other nuclides from the nuclear fuel cycle and, in particular, transuranium nuclides, might be present in this type of ammunition. In this paper, we report the results of uranium and plutonium analyses carried out on a depleted uranium penetrator recovered from a target site in southern Serbia. Our data show the depleted nature of the uranium and confirm the presence of trace amounts of plutonium in the penetrator. The activity concentration of (239+240)PU, at 45.4+/-0.7 Bq kg(-1), is the highest reported to date for any penetrator recovered from the Balkans. This concentration, however, is comparable to that expected to be present naturally in uranium ores and, from a radiological perspective, would only give rise to a very small increase in dose to exposed persons compared to that from the DU itself.
[McLaughlin2003xxJERv64n2to3p155]. (PMID: 12500802 [PubMed - indexed for MEDLINE]).

36. Oxidation states of uranium in DU particles from Kosovo, B by Salbu B, et al., Isotope Laboratory, Department of Soil and Water Sciences, Agricultural University of Norway, P.O. Box 5028, N-1432 As, Norway. brit.salbu@ijvf.nlh.no. J Environ Radioact. Vol. 64(2-3), 2003 (pp. 167-173.
The oxidation states of uranium contained in depleted uranium (DU) particles were determined by synchrotron radiation based micro-XANES, applied to individual particles in soil samples collected at Ceja Mountain, Kosovo. Based on scanning electron microscopy (SEM) with XRMA prior to micro-XANES, DU particles ranging from submicrons to about 30 microm (average size: 2 microm or less) were identified. Compared to well-defined standards, all investigated DU particles were oxidized. About 50% of the DU particles were characterized as UO2, the remaining DU particles present were U3O8 or a mixture of oxidized forms (ca. 2/3 UO2, 1/3 U3O8). Since the particle weathering rate is expected to be higher for U3O8 than for UO2, the presence of respiratory U3O8 and UO2 particles, their corresponding weathering rates and subsequent remobilisation of U from DU particles should be included in the environmental or health impact assessments.
[Salbu2003xxJERv64n2to3p167]. (PMID: 12500803 [PubMed - indexed for MEDLINE]).

37. Uranium ores and depleted uranium in the environment, with a reference to uranium in the biosphere from the Erzgebirge/Sachsen, Germany, by A Meinrath, et al., Klinikum, Bischof-Pilgrim Str.1, 94032 Passau, FRG, Germany.
Journal of Environmental Radioactivity, 64(2-3), 2003 (pp. 175-193).
The Erzgebirge ('Ore Mountains') area in the eastern part of Germany was a major source of uranium for Soviet nuclear programs between 1945 and 1989. During this time, the former German Democratic Republic became the third larges uranium producer in the world. The high abundance of uranium in the geological formations of the Erzgebirge are mirrored in the discovery of uranium by M. Klaproth close to Freiberg City in 1789 and the description of the so-called 'Schneeberg' disease, lung cancer caused in minors by the accumulation of the uranium decay product, radon, in the subsurfaces of shafts. Since 1991, remediation and mitigation of uranium at production facilities, rock piles and mill tailings has taken place. In parallel, efforts were initiated to assess the likely adverse effects of uranium mining to humans. The costs of these activities amount to about 6.5 billion Euro. A comparison of depleted uranium at certain sites is given.
[Meinrath200300JERv64n2p175]. (PMID: 12500804 [PubMed - indexed for MEDLINE]).

38. Use of HPGe gamma-ray spectrometry to assess the isotopic composition of urnanium in soils, by CA Papachristodoulou, et al. Nuclear Physics Laboratory, Dept. of Physics, The University of Ioannina, 45110 Ioannina, Greece. Journal of Environmental Radioactivity 64(2-3), 2003 (pp 195-203).
Gamma-ray spectrometry was used to determine uranium activity and investigate the presence of depleted uranium in soil samples collected from camping sites of the Greek expeditionary force in Kosovo. Assessment of 238U concentrations was based on measurements of the 63.3 keV and 92.38 keV emissions of its first daughter nuclide, 234Th. To determine the isotopic ratio of 238U/235U, secular equilibrium along the two radioactive series was first ensured and thereby the contribution of 235U under the 186 keV peak was deduced. The uranium activity in the samples varied from 48 to 112 Bq kg(-1), whereas the activity ratio of 238U/235U averaged 23.1 +/-4.3.
[Papachristodoulou200302JERv64n2p195]. (PMID: 12500805 [PubMed - indexed for MEDLINE]).

39. Depleted uranium residual radiological risk assessment for Kosovo sites, by M Durante, et al., Department of Physics, University Federico II, Monte S. Angelo, Via Cintia, 80126 Napoli, Italy. durante@na.infn.it J Environ Radioact. Vol. 64(2-3), 2003 (pp. 237-45).
During the recent conflict in Yugoslavia, depleted uranium rounds were employed and were left in the battlefield. Health concern is related to the risk arising from contamination of areas in Kosovo with depleted uranium penetrators and dust. Although chemical toxicity is the most significant health risk related to uranium, radiation exposure has been allegedly related to cancers among veterans of the Balkan conflict. Uranium munitions are considered to be a source of radiological contamination of the environment.

Based on measurements and estimates from the recent Balkan Task Force UNEP mission in Kosovo, we have estimated effective doses to resident populations using a well-established food-web mathematical model (RESRAD code). The UNEP mission did not find any evidence of widespread contamination in Kosovo. Rather than the actual measurements, we elected to use a desk assessment scenario (Reference Case) proposed by the UNEP group as the source term for computer simulations. Specific applications to two Kosovo sites (Planeja village and Vranovac hill) are described. Results of the simulations suggest that radiation doses from water-independent pathways are negligible (annual doses below 30 microSv). A small radiological risk is expected from contamination of the groundwater in conditions of effective leaching and low distribution coefficient of uranium metal. Under the assumptions of the Reference Case, significant radiological doses (>1 mSv/year) might be achieved after many years from the conflict through water-dependent pathways. Even in this worst-case scenario, DU radiological risk would be far overshadowed by its chemical toxicity.
[Durante2003xxJERv64n2to3p237]. (PMID: 12500808 [PubMed - indexed for MEDLINE])

40. Lichens as biomonitors of uranium in the Balkan area, by S Loppi, et al., Department of Environmental Science, University of Siena, Italy. loppi@unisi.it Environ Pollut. Vol. 125(2), 2003 (pp. 277-280).
The contribution of the conflict of 1999 to the environmental levels of uranium in the Balkan area was evaluated by means of lichens used as biomonitors. The average U concentration found in lichens in the present study was in line with the values reported for lichens from other countries and well below the levels found in lichens collected in areas with natural or anthropogenic sources of U. Measurement of isotopic ratios 235U/238U allowed to exclude the presence of depleted uranium. According to these results, we could not detect widespread environmental contamination by depleted uranium in the Balkan area.
[Loppi2003xxEPv235n2p277]. (PMID: 12810321 [PubMed - indexed for MEDLINE]).

41. Modeling of the dispersion of depleted uranium aerosol, by C Mitsakou, et al., Institute of Nuclear Technology-Radiation Protection, N.C.S.R. Demokritos, 15310 Ag. Paraskevi, Attiki, Greece. Health Phys. Vol. 84(4), 2003 (pp. 538-544).
Depleted uranium is a low-cost radioactive material that, in addition to other applications, is used by the military in kinetic energy weapons against armored vehicles. During the Gulf and Balkan conflicts concern has been raised about the potential health hazards arising from the toxic and radioactive material released. The aerosol produced during impact and combustion of depleted uranium munitions can potentially contaminate wide areas around the impact sites or can be inhaled by civilians and military personnel. Attempts to estimate the extent and magnitude of the dispersion were until now performed by complex modeling tools employing unclear assumptions and input parameters of high uncertainty. An analytical puff model accommodating diffusion with simultaneous deposition is developed, which can provide a reasonable estimation of the dispersion of the released depleted uranium aerosol. Furthermore, the period of the exposure for a given point downwind from the release can be estimated (as opposed to when using a plume model). The main result is that the depleted uranium mass is deposited very close to the release point. The deposition flux at a couple of kilometers from the release point is more than one order of magnitude lower than the one a few meters near the release point. The effects due to uncertainties in the key input variables are addressed. The most influential parameters are found to be atmospheric stability, height of release, and wind speed, whereas aerosol size distribution is less significant. The output from the analytical model developed was tested against the numerical model RPM-AERO. Results display satisfactory agreement between the two models.
[Mitsakou200304HPv84n4p538]. (PMID: 12705453 [PubMed - indexed for MEDLINE]).

Chapter VIII

Testing and Analysis Procedures for Uranium and Depleted Uranium

Summary

Simple laboratory procedures are not sufficient for identifying and quantifying depleted uranium in samples taken from the environment, from body tissues, or from body fluids. First, there is the problem of concentration. Typically, samples being tested for DU have such low concentrations of DU that any successful procedure must have a very high level of sensitivity. Second, there is the problem of natural uranium (NU), which permeates our natural environment, requiring special procedures to differentiate between NU and DU.

Despite these difficulties, several methods have been developed to accomplish this task. Since NU and DU, by definition, differ in the ratio of uranium isotopes contained within their respective samples, methods utilizing various types of mass spectroscopy (MS) have been the most frequently used. With MS, a spectrum is produced containing a peak for each different mass ion detected, with each peak's height being proportional to the abundance of that ion. The spectrum of a pure NU sample would show a peak at 238 mass units that was 142 times as large as the peak at 235 mass units due to the natural abundances of U-238 and of U-235 being 99.3% and 0.7%. For a DU sample with 99.8% U-238 and 0.2% U-235, the spectrum would show a peak at 238 mass units that was close to 500 times as large as the peak at 235 mass units. In most real samples, NU and DU are mixed, so the peak ratios lie between these two extremes and the actual concentrations of each must be calculated from the observed ratio.

Other methods rely on alpha or gamma radiation spectra analysis of the radiation emitted by uranium samples. Spectra of gamma emissions can be analyzed to reveal isotope abundances, since different isotopes release packets of gamma rays having a spectrum of certain specific energies. Since several different isotopes are usually present in a given sample, their individual spectra are overlapped, requiring the researcher to recognize each overlapping signature. Computer analysis plays an important role in these analyses.

Neutron activation analysis may also be employed, since one of the isotopes of concern, U-235, is fissionable. Bombarding the sample with neutrons will cause U-235 to undergo fission and produce radioactive fission products which have more intense gamma ray emissions that are easier to detect and quantify. This technique may lower the detection limits for U-235 and allow more accurate analysis of samples containing very low concentrations of uranium.

Finally, finding appropriate biomarkers for uranium make it possible to pinpoint environmental contamination with greater accuracy. Knowing which plants readily incorporate uranium from water or soil and the degree to which they are prone to do this gives the researcher a handle for assessing uranium contamination.

Details

Larsen's paper of 2000, (8), and Fortuna's paper of 200, (20), both present some general notes relating to determining of isotope ratios and items to consider when drawing conclusions from these ratios. Fortuna also addresses the problem of environmental remediation.

Coleman (1) published depth-dose curves in Mylar for DU in 1983 to measure workers' exposure levels. Cassorla (2) compared gamma ray spectrometry and neutron activation analysis for the determination of uranium isotope ratios. In 1989, Camins (3) reviewed DU detection methods for aerosol and soil samples, while Miyajima (4) and Flynn (5) reported methods for detecting and measuring low concentrations of DU.

In 1999, Baglan (7) published protocols for inductively-coupled plasma mass spectroscopy (ICP-MS) monitoring of uranium workers' urine specimens and found ICP-MS to provide better sensitivity to low U-235 concentrations than alpha spectrometry. In February of 2000, Ejnik, (11), of the Armed Forces Radiobiology Research Institute (AFRRI) in Bethesda, MD used ICP-MS to identify DU in veterans' urine samples while Kalinich (12), (21) in the same labs, developed a rapid colorimetric method for identifying uranium in shrapnel. Desideri , (22), reported comparison of ICP-MS and alpha spectroscopy for the analysis of various actinides, including plutonium, amerecium and U-236, obtained from sample penetrator shells used by NATO. The presence of these isotopes in DU penetrators clearly show that the DU being used to manufacture DU munitions underwent neutron bombardment (activation) in a

nuclear reactor. Montaser (16) compared the sensitivities of two different types of ICP-MS instrumentation for analysis of DU in biological matrices.

Goldstein (6) reported that preparing samples for uranium isotope analysis by first using extraction chromatography and ion exchange before performing the alpha spectroscopy resulted in greater sensitivity. Chandler (9) determined that bismuth germinate detectors were more sensitive than sodium iodide detectors in the gamma ray detection of embedded DU fragments in wounds. Spaic (10) reported the optimum instrument settings for gamma ray detection. Shoji (18) used gamma ray spectroscopy of Th-234, the daughter isotope of U-238 with a stronger gamma ray spectrum to differentiate between natural uranium and depleted uranium. In 2003, Bikit (24) reported a gamma ray detection method using U-238 and Ra-226 to identify and quantify depleted uranium from approximately 90 soil samples.

Abu-Qare (19) first derivitized uranium in rats urine with dibenzoylmethane and used UV spectroscopy to identify and quantify uranium, finding 2 ng/ml to be the limit for detection of uranium and 10 to 100 ng/ml to be the effective range of quantification.

Barrata (13) and Forte (14) look into methodologies for analyzing food and water samples for uranium isotopes. Roth (23) assesses the difficulties of determining a time-zero body burden of depleted uranium from urine samples taken some time after exposure.

Magnoni (15) analyzed mollusk samples from the Adriatic sea for DU, and Edmands (17) analyzed uranium levels and isotope ratios in black oak trees near the Concord, MA DU penetrator fabrication facility and found that, once incorporated into tree sap, uranium ions are highly mobile through cellular tissue. He also determined that uranium concentrations in black oak sapwood reflect concentrations in shallow ground water feeding the tree.

1. Depth-dose curves for strontium-90 and natural and depleted uranium in Mylar, by RL Coleman, Health Physics Serv., Tennessee Valley Auth., Muscle Shoals, AL, Health Physics Vol. 44(4), 1983 (pp. 395-402).
[Coleman1983xxHPv44n4p395].

2. Comparative studies for determination of the uranium-235/uranium-238 ratio in solutions of natural and depleted uranium using gamma spectrometry and neutron activation analysis, by F Cassorla, et al., Nucleotecnica Vol. 8(14), 1988 (pp. 7-15).
[Cassorla1988xxNv8n14p7].

3. Analysis of Beryllium and depleted uranium: An overview of detection methods in aerosols and soils, by I. Camins, Lawrence Livermore Natl. Lab, Livermore, CA, Report, Energy Res. Abstr. Vol. 14(14), 1989 (Abstract 28146).
[Camins1989xxERAv14n14p28146].

4. RIS and detection of isotopes of low abundance, by M Miyajima, et al., Natl. Lab. High Energy Physics, KEK (Japan), 1989.
[Miyajima1989Report].

5. Use of the USRADS system for real time radiation survey measurements for depleted uranium environmental contamination, by CR Flynn, et al., Chemrad Tennessee Corp., Oak Ridge, TN. Waste Management Vol. 2, 1989 (pp. 603-607).
[Flynn1989xxWMv2nxp603].

6. Measurement and application of uranium isotopes for human and environmental monitoring, by SJ Goldstein SJ, et al., Inorganic Trace Analysis Group, Chemical Science and Technology Division, Los Alamos National Laboratory, NM 87545, USA. Health Phys. Vol. 72(1), Jan. 1997 (pp. 10-18).
An improved method is described utilizing extraction chromatography, anion exchange, and alpha spectroscopy for measurement of uranium isotopes in human and environmental surveillance studies. These methods provide a sensitivity of approximately 0.7 mBq per isotope per sample and are generally accurate within the precision of the measurements. The extraction chromatography methods greatly simplify separation of uranium from iron in silicate matrices and provide increased sample throughput and data quality for water, soil, and air filter samples. For bioassay samples, the coprecipitation/anion exchange/alpha spectrometric methods provide rapid throughput and sufficient sensitivity to meet new analytical performance standards in human monitoring studies. In addition, the 234U:238U data can be used as a fingerprint of natural vs. anthropogenic sources of uranium. For 1995 data from our laboratory, a large percentage (79-94% by matrix) of samples appear to be of natural 234U:238U isotopic composition. For all matrices, samples with higher uranium concentration generally have more depleted isotopic composition (smaller 234U:238U). A small percentage of soil (11%), air filter (3%), urine (3%), and water (3%) samples have depleted isotopic signatures at the 95% confidence interval, indicating anthropogenic contributions of uranium to these samples.
[Goldstein199701HPv72n1p10]. (PMID: 8972822 [PubMed - indexed for MEDLINE])

7. Implementation of ICP-MS protocols for uranium urinary measurements in worker monitoring, by N Baglan, et al., Institut de Protection et de Sureté Nucléaire, Département de Protection de la santé de l'Homme et de Dosimetrie, IPSN, Fontenay-aux-Roses, France. nicolas.baglan@ipsn.fr Health Phys. Vol. 77(4), Oct. 1999 (pp. 455-461).

The uranium concentration in human urine spiked with natural uranium and rat urine containing metabolized depleted uranium was determined by ICP-MS. The use of ICP-MS was investigated without any chemical treatment or after the different stages of a purification protocol currently carried out for routine monitoring. In the case of spiked urine, the measured uranium concentrations were consistent with those certified by an intercomparison network in radiotoxicological analysis (PROCORAD) and with those obtained by alpha spectrometry in the case of the urine containing metabolized uranium. The quantitative information which could be obtained in the different protocols investigated shows the extent to which ICP-MS provides greater flexibility for setting up appropriate monitoring approaches in radiation protection routines and accidental situations. This is due to the combination of high sensitivity and the accuracy with which traces of uranium in urine can be determined in a shorter time period. Moreover, it has been shown that ICP-MS measurement can be used to quantify the 235U isotope, which is useful for characterizing the nature of the uranium compound, but difficult to perform using alpha spectrometry.
[Baglan199910HPv77n4p455]. (PMID: 10492353 [PubMed - indexed for MEDLINE])

8. Some notes and comments regarding natural and processed uranium isotopes, by IL Larsen, Teledyne-Brown Engineering, Knoxville, TN. Radioactivity and Radiochemistry Vol. 11(2), 2000 (pp. 6-10).
Discusses using isotope ratios to ascertain DU concentration in samples and considerations to take into account when deriving conclusions from these measurements.
[Larsen2000xxRRv11n2p6].

9. Comparison of scintillation detection efficiencies of depleted uranium in wounds, by SZ Chandler, et al., Hill AF Base, Utah. Journal of Radioanalytical and Nuclear Chemistry Vol. 243(2), 2000 (pp. 451-457).
Determined that bismuth germinate (BGO) detectors had higher efficiency and lowest minimum detectable activity (MDA=5.8 kBq) relative to NaI crystal detectors for both shallow, medium and deep depth wounds containing embedded DU fragments.
[Chandler2000xxJRNCv243n2p451].

10. Bullet Scintigraphy: Can gamma camera be used for depleted uranium accident measurements? by R Spaic, et al., Inst. of Nuclear Med., Med. Military Acad., Belgrade, Yugoslavia. Bilten Instituta za Nuklearne Nauke Vinca Vol. 5(1-4), 2000 (pp. 15-17).
For detection of DU, X-rays with an energy of 100 keV and 20% window width are used (about 40% of DU gamma emissions are within this limit).
[Spaic2000xxBINNVv5n1to4p15].

11. Determination of the isotopic composition of uranium in urine by inductively coupled plasma mass spectrometry, by JW Ejnik, et al., Armed Forces Radiobiology Research Institute, Bethesda, MD 20889-5603, USA. ejnik@mx.afrri.usuhs.mil Health Phys. Vol. 78(2), Feb. 2000 (pp. 143-146).
A simple method based on inductively coupled plasma mass spectrometry (ICP-MS) was developed to identify exposure to depleted uranium by measuring the isotopic composition of uranium in urine. Exposure to depleted uranium results in a decreased percentage of 235U in urine samples causing measurements to vary between natural uranium's 0.72% and depleted uranium's 0.2%. Urine samples from a non-depleted uranium exposed group and a suspected depleted uranium exposed group were processed and analyzed by ICP-MS to determine whether depleted uranium was present in the urine. Sample preparation involved dry-ashing the urine at 450 degrees C followed by wet-ashing with a series of additions of concentrated nitric acid and 30% hydrogen peroxide. The ash from the urine was dissolved in 1 M nitric acid, and the intensity of 235U and 238U ions were measured by ICP-MS. After the samples were ashed, the ICP-MS measurements required less than 5 min. The 235U percentage in individuals from the depleted uranium exposed group with urine uranium concentrations greater than 150 ng L(-1) was between 0.20%-0.33%, correctly identifying depleted uranium exposure. Samples from the non-depleted uranium exposed individuals had urine uranium concentration less than 50 ng L(-1) and 235U percentages consistent with natural uranium (0.7%-1.0%). A minimum concentration of 14 ng L(-1) uranium was required to obtain sufficient 235U to allow calculating a valid isotopic ratio. Therefore, the percent 235U in urine samples measured by this method can be used to identify low-level exposure to depleted uranium.
[Ejnik200002HPv78n2p143]. (PMID: 10647980 [PubMed - indexed for MEDLINE]).

12. A procedure for the rapid detection of depleted uranium in metal shrapnel fragments, by JF Kalinich, et al., Armed Forces Radiobiology Res. Inst., Bethesda, MD. Military Medicine Vol. 165(8), Aug. 2000 (pp. 626-629).
Treating a shrapnel fragment for 5 minutes in nitric acid in an ultrasonic cleaner, sufficient metal is solubilized to allow for colorimetric detection using a pyridylazo dye. Using masking agents as sodium citrate and EDTA, the reaction can be made specific for depleted uranium.
[Kalinich200008MMv165n8p626].

13. Determination of isotopic uranium in food and water, by EJ Baratta, et al., USFDA, Winchester, MA. Journal of Radioanalytical and Nuclear Chemistry Vol. 248(2), 2001 (pp. 473-475).
Discusses the methodology used for the determination of isotopic uranium in the analysis of food and water samples and results from sample surveys.
[Baratta2001xxJRNCv248n2p473].

14. Determination of uranium isotopes in food and environmental samples by different techniques: a comparison, by M Forte, et al., ARPA Lombardia, Division of Radiological Protection Milan, Italy. Radiat Prot Dosimetry. Vol. 97(4), 2001 (pp. 325-328).
The uranium concentration in 59 samples of bottled and tap water, mainly from northern Italy, was measured by different techniques. Results obtained by inductively coupled plasma mass spectrometry (ICP-MS), semiconductor alpha spectrometry and low level liquid scintillation counting with alpha/beta discrimination (LSC) have been compared. High resolution gamma spectrometry and semiconductor alpha spectrometry have been used to analyse uranium in a variety of organic and inorganic samples. Isotopic secular equilibrium in the 238U series may be lacking or hidden by auto-absorption phenomena, so caution should be used in evaluating gamma spectrometry data. Alpha spectrometry has also been used to ascertain the possible pollution from depleted uranium in the environment.
[Forte2001xxRPDv97n4p325]. (PMID: 11878412 [PubMed - indexed for MEDLINE]).

15. Variations of the isotopic ratios of uranium in environmental samples containing traces of depleted uranium: theoretical and experimental aspects, by M Magnoni, et al., ARPA Piemonte-Dipartimento di Ivrea, Italy. m.magnoni@arpa.piemonte.it. Radiat Prot Dosimetry Vol. 97(4), 2001 (pp. 337-340).
The possibility of using conventional analysis, such as gamma spectrometry and alpha spectrometry, for the detection of traces of depleted uranium (DU) in environmental samples has been investigated. The expected values have been compared with the experimental results obtained by using mollusc samples gathered in the Adriatic Sea. The analysis has shown that it is possible to detect DU. if the percentage composition is about 20% depleted uranium and 80% natural uranium, for a sample containing 10 Bq x kg(-1) of 238U. The possibility of extending this approach to samples with any given uranium concentration is investigated.
[Magnoni2001xxRPDv97n4p337]. (PMID: 11878415 [PubMed - indexed for MEDLINE]).

16. Ultratrace and isotopic analysis of long-lived radionuclides and depleted uranium by direct liquid introduction-inductively coupled plasma mass spectrometry, by A Montaser, et al., George Washington U, Washington, DC. ACS Abstracts 2001, 221st NUCL-176.
An analysis of the performance of a double-focusing inductively coupled plasma mass spectrometer (ICP-DFMS) and a quadrupole-based ICPMS (ISP-QMS) in the analysis of long-lived radionuclides, including isotopes of uranium, using direct injection high efficiency nebulizers. Samples included radioactive waste samples and detection of depleted uranium in biological matrices.
[Montaser2001xxACSANUCL176].

17. Uptake and mobility of uranium in black oaks: implications for biomonitoring depleted uranium-contaminated groundwater, by JD Edmands, et al., Department of Earth Sciences, Boston University, MA 02215, USA. Chemosphere Vol. 44(4), Aug. 2001 (pp. 789-795).
In a preliminary study, the uptake and the mobility of uranium (U) by black oak trees (Quercus velutina) were assessed by measuring the isotopic composition of tree rings in two mature oak trees in a heavy metal contaminated bog in Concord, MA. The bog is adjacent to a nuclear industrial facility that has been processing depleted uranium (DU) since 1959. Over the past 40 years, DU has been leaking from an onsite holding basin and cooling pond down gradient to the bog where the oaks are located. Because DU has no source outside the nuclear industry, contamination from the industrial facility is readily discernable from uptake of natural U by measuring isotopic compositions. Isotope ratio analysis confirms the occurrence of DU in bark, sapwood and heartwood tree rings dating back to 1937, pre-dating the introduction of DU at the site by at least 20 years. Isotope dilution analysis indicates high concentrations of U (>3 ppb) in sapwood that drop rapidly to relatively constant concentrations (0.3-0.4 ppb) in heartwood. These data indicate that once incorporated into tree cells, U is mobile, possibly by diffusion through the tree wood. Concentrations of U in sapwood are approximately equal to average U concentrations in groundwater onsite over the past 10 years, suggesting that oak trees can be used as present-day bioindicators of U-contaminated groundwater. We suggest that regional sampling of oak bark and sapwood is a reasonable, inexpensive alternative to drilling wells to monitor shallow groundwater U contamination.
[Edmands200108Cv44n4p789]. (PMID: 11482670 [PubMed - indexed for MEDLINE]).

18. A convenient method for discriminating between natural and depleted uranium by gamma-ray spectrometry, by M Shoji, et al., Radioisotope Research Center, Toyama Medical and Pharmaceutical University, Sugitani, Japan. shojim@ms.toyama-mpu.ac.jp . Appl Radiat Isot. Vol. 55(2), Aug. 2001 (pp. 221-227).
A convenient method for discriminating between natural and depleted uranium reagent was developed by measuring and analyzing the gamma-ray spectra of some reagents with no standard source. The counting rates (R) of photoelectric peaks of gamma-rays from nuclides with the same radioactivity divided by their emission probability (B) are expressed as a function of gamma-ray energy. The radioactivities of 234Th and 234mPa and 21.72 times that of 235U are equal to the radioactivity of 235U in natural uranium. Therefore, the plot of 21.72-fold R/B for 235U should be on a curve fitted to the points for 234Th and 234mPa in natural uranium. Depleted uranium with a 235U isotopic composition of less than 0.68% could be discriminated from natural uranium in the case of a reagent containing 4.0 g of uranium.
[Shoji200108ARIv55n2p221]. (PMID: 11393763 [PubMed - indexed for MEDLINE]).

19. Determination of depleted uranium, pyridostigmine bromide and its metabolite in plasma and urine following combined administration in rats, by AW Abu-Qare , et al., Department of Pharmacology and Cancer Biology, Duke University Medical Center, PO Box 3813, Durham, NC 27710, USA. J Pharm Biomed Anal. Vol. 26(2), Sept. 2001 (pp. 281-289).

A simple and reliable method was developed for the quantification of depleted uranium, the anti nerve agent drug pyridostigmine bromide (PB;3-dimethylaminocarbonyloxy-N-methyl pyridinium bromide) and its metabolite N-methyl-3-hydroxypyridinium bromide in rat plasma and urine. The method involved using solid phase extraction and spectrophotometric determination of uranium, and high performance liquid chromatography (HPLC) with reversed phase C(18) column, and UV detection at 280 nm for PB and its metabolite. Uranium was derivatized using dibenzoylmethane (DBM) then the absorbance was measured at 405 nm. PB and its metabolite were separated using a gradient of 1--40% acetonitrile in 0.1% triflouroacetic acid water solution (pH 3.2) at a flow rate of 0.8 ml/min in a period of 14 min. Limits of detection were 2 ng/ml for uranium and 50 ng/ml for PB and its metabolite. Limits of quantitation were between 10 and 100 ng/ml for uranium and the other two analytes, respectively. Average percentage recovery of five spiked plasma samples were 83.7+/-8.6, 76.8+/-6.7, 79.1+/-7.1, and from urine 82.7+/-8.6, 79.3+/-9.5 and 78.0+/-6.2, for depleted uranium, PB and N-methyl-3-hydroxypyridinium bromide, respectively. The relationship between peak areas and concentration was linear for standards between 100 and 1000 ng/ml for all three analytes. This method was applied to analyze the above chemicals and metabolites following combined administration in rats.
[AbuQare200109JPBAv26n2p281]. (PMID: 11470205 [PubMed - indexed for MEDLINE]).

20 Practical aspects of the detection of radioactive contamination caused by the use of ammunition with depleted uranium, in Serbian, by D Fortuna, et al., Hemijska Industrija Vol. 55(7-8), 2001 (pp. 346-348).
In addition to covering detection of DU in the environment, decontamination methods are also analyzed.
[Fortuna2001xxHIv55n7to8p346].

21. Staining of intracellular deposits of uranium in cultured murine macrophages, by JF Kalinich, et al., Applied Cellular Radiobiology Department, Armed Forces Radiobiology Research Institute, Bethesda, MD 20889-5603, USA.
kalinich@mx.afrri.usuhs.mil. Biotech Histochem. Vol. 76(5-6), Sept. – Nov. 2001 (pp. 247-252).
In our studies of the health effects of internalized depleted uranium, we developed a simple and rapid light microscopic method to stain specifically intracellular uranium deposits. Using J774 cells, a mouse macrophage line, treated with uranyl nitrate and the pyridylazo dye 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol, uranium uptake by the cells was followed. Specificity of the stain for uranium was accomplished by using masking agents to prevent the interaction of the stain with other metals. Prestaining wash consisting of a mixture of sodium citrate and ethylenediaminetetraacetic acid eliminated staining of metals other than uranium. The staining solution consisted of the pyridylazo dye in borate buffer along with a quaternary ammonium salt, ethylhexadecyldimethylammonium bromide, and the aforementioned sodium citrate/ethylenediaminetetraacetic acid mixture. The buffer was essential for maintaining the pH within the optimum range of 8 to 12, and the quaternary ammonium salt prevented precipitation of the dye. Staining was conducted at room temperature and was complete in 30 min. Staining intensity correlated with both uranyl nitrate concentration and incubation time. Our method provides a simple procedure for detecting intracellular uranium deposits in macrophages.
[Kalinich20009BHv76n5to6p247]. (PMID: 11871745 [PubMed - indexed for MEDLINE]).

22. Determination of (236)U and transuranium elements in depleted uranium ammunition by alpha-spectrometry and ICP-MS, by D Desideri, et al., General Chemistry Institute, Urbino University, Urbino, Italy. Anal Bioanal Chem. Vol. 374(6), Nov. 2002 (pp. 1091-1095). Epub 2002 Oct 16.
It is well known that ammunition containing depleted uranium (DU) was used by NATO during the Balkan conflict. To evaluate the origin of DU (the enrichment of natural uranium or the reprocessing of spent nuclear fuel) it is necessary to directly detect the presence of activation products ((236)U, (239)Pu, (240)Pu, (241)Am, and (237)Np) in the ammunition. In this work the analysis of actinides by alpha-spectrometry was compared with that by inductively coupled plasma mass spectrometry (ICP-MS) after selective separation of ultratraces of transuranium elements from the uranium matrix. (242)Pu and (243)Am were added to calculate the chemical yield. Plutonium was separated from uranium by extraction chromatography, using tri-n-octylamine (TNOA), with a decontamination factor higher than 10(6); after elution plutonium was determined by ICP-MS ((239)Pu and (240)Pu) and alpha-spectrometry ((239+240)Pu) after electroplating. The concentration of Pu in two DU penetrator samples was 7 x 10(-12) g g(-1) and 2 x 10(-11) g g(-1). The (240)Pu/(239)Pu isotope ratio in one penetrator sample (0.12+/-0.04) was significantly lower than the (240)Pu/(239)Pu ratios found in two soil samples from Kosovo (0.35+/-0.10 and 0.27+/-0.07). (241)Am was separated by extraction chromatography, using di(2-ethylhexyl)phosphoric acid (HDEHP), with a decontamination factor as high as 10(7). The concentration of (241)Am in the penetrator samples was 2.7 x 10(-14) g g(-1) and <9.4 x 10(-15) g g(-1). In addition (237)Np was detected at ultratrace levels. In general, ICP-MS and alpha-spectrometry results were in good agreement.The presence of anthropogenic radionuclides ((236)U, (239)Pu,(240)Pu, (241)Am, and (237)Np) in the penetrators indicates that at least part of the uranium originated from the reprocessing of nuclear fuel. Because the concentrations of radionuclides are very low, their radiotoxicological effect is negligible.
[Desideri200211ABCv374n6p1091]. (PMID: 12458425 [PubMed]).

23. Assessment of exposure to depleted uranium, by P Roth, et al., GSF-National Research Center for Environment and Health, Institute of Radiation Protection, Ingolstadter Landstr. 1, 85764 Neuherberg, Germany. Roth@gsf.de. Radiat Prot Dosimetry. Vol. 105(1-4), 2003 (pp. 157-161).

In most circumstances, measurement of uranium excreted in urine at known times after exposure is potentially the most sensitive method for determining the amount of depleted uranium (DU) incorporated. The problems associated with this approach are that natural uranium is always present in urine because of the ingestion of natural uranium in food and drink, and that the uncertainties in the intakes as assessed from excretion measurements can be quite large, because many assumptions concerning the exposure characteristics (time pattern of exposure, route of intake, chemical form, solubility, biokinetics within the body) must be made. Applying currently available methods and instruments for the measurement of uranium in urine samples, DU incorporations of levels relevant with respect to potential health hazards can be detected reliably, even a long time after exposure.
[Roth2003xxRPDv105n1to4p157]. (PMID: 14526948 [PubMed - in process]).

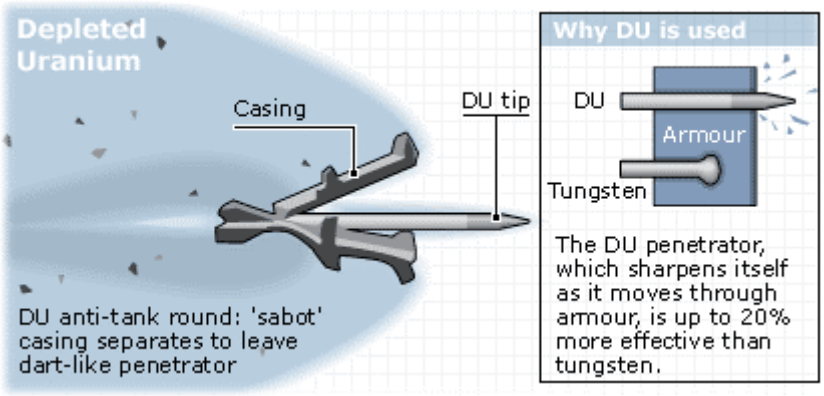
24. Simple method for depleted uranium determination, by I Bikit, et. al., Institute of Physics, Faculty of Sciences, University of Novi Sad, Serbia and Montenegro, Yugoslovia. Japanese Journal of Applied Physics, Part 1, Vol. 42(8), 2003 (pp.5269-5273).
When the issue of depleted uranium (DU) presence in the environment emerged, methods for analytical discrimination of DU against natural uranium should be developed. We present here a simple gamma-spectrometric method, based on the 238U-226Ra activity (non) equil. The detection limit of the method for DU is of the order of magnitude 10 Bq/kg (for about 50 ks counting), thus the method is appropriate for the detection of small amounts (=100 Bq/kg) of DU in environmental samples. The method is tested on about 90 soil samples.
[Bikit200308JJAPv42n8p5269]

Chapter IX

Civil and Military Uses of Depleted Uranium

Natural uranium consists principally of two uranium isotopes: 99.3% U-238 and 0.7% U-235. It is the U-235 that is fissionable and useful for powering nuclear reactors and for use in nuclear weapons. But to be operational, the concentration of U-235 must be increased to at least 3% for nuclear fuel and much higher for nuclear bombs. The uranium enrichment process accomplishes this and in the process leaves a radioactive waste product behind which now contains 99.8% U-238 and only 0.2% U-235. This waste product has been given the name depleted uranium. It is uranium that has been depleted of the more radioactive U-235 isotope. Nevertheless, it still retains 60% of the radioactivity of natural uranium.

Because of the nature of the uranium enrichment process, prodigious quantities of depleted uranium are produced. By 1999 the United States alone had stockpiled over 250,000 tons of waste depleted uranium, much of it in the form of uranium hexafluoride, the chemical form used in the enrichment process. Being a low-level radioactive material, its storage and disposal have been subjected to relatively strict requirements. This is beginning to change, however, and current regulations are being proposed that would lift these restrictions and make depleted uranium available for a wide variety of commercial uses and allow its disposal in non-regulated community landfills. Although this would provide an instant solution to a major headache facing the Nuclear Regulatory Agency and the Environmental Protection Agency in the United States, it completely ignores the potential health and environmental liabilities such a move might impose on our entire civilization (13), (15). As long as any valid question exists regarding the safety of depleted uranium, the Precautionary Principle and simple common sense would demand that this material continue to be sequestered.



Current military uses of depleted uranium include its use in anti-tank penetrators (2) fired from Abrams (US) and Challenger (UK) tanks and in a variety of smaller munitions usually designed to be rapid-fired from Gatling guns (20 mm shells in the Navy Phalanx system, and 30 mm shells in the Army's A-10 planes) (4), (5). In addition, plates of depleted uranium armor have been incorporated into the Abrams tank, rendering them nearly impenetrable to enemy fire. US patents include the use of DU in cruise missiles (Raytheon) and various "bunker buster" bombs (Lockheed-Martin). Whether such weapons containing DU have actually been manufactured and/or deployed and used remains a subject of some controversy. The US military has denied using DU use in cruise missiles.

Current civilian uses (16), (17) of depleted uranium include addition to aggregates that are mixed with cement to form a high density concrete (6), (11), (12). The commercial product Ducrete contains depleted uranium. Depleted uranium makes an excellent radiation shielding material, and has been used in this capacity for shipping and storage containers for nuclear wastes (1), (14) and in the medical arena as radiation shielding in instruments containing radioactive materials (such as cobalt-60). Because of its high density, (1.7 times the density of lead) a lot of weight can be packed into a smaller space than for materials such as lead, making depleted uranium an ideal candidate for counterweights in airplane and missile control systems and in sailing vessels (8). Depleted uranium is also incorporated into the drill bits used by the oil drilling industry.

DU has been proposed as a suitable material for magnets based on its ferromagnetic properties (7). Waste DU/graphite blocks from nuclear reactors have been proposed as a source of carbon for plastics and composites (9). Various coatings and coverings have been studied for items made of DU to reduce corrosion and air oxidation of this reactive material (3), (10).

1. Versatile composite radiation shield, by KH Defrane, et al., US Patent No. 4914306, 1990 (7 pp.)
Described is a radiation shield for use in transport containers wherein DU rods provide shielding for radioactive materials being transported.
[Defrane1990xxUSPatent4914306].

2. High velocity performance of a uranium alloy long rod penetrator, by MJ Keele, Army Ball. Res. Lab., Aberdeen Proving Ground, MD. Gov. Rep. Announce. Index (US) Vol. 91(19), 1991 (27 pp.). Abstr. No. 153650.
The high velocity (1.7 – 2.4 km/s) performance of a 120-mm projectile (aspect ratio 20:1) against armor targets was evaluated.
[Keele1991xxGRAIv91n19pxx].

3. Assessment of corrosion-resistant coating for a depleted uranium-0.75 titanium alloy, by F Chang, et al., US Army Mater. Technol. Lab, Watertown, MA. Surface and Coatings Tech. Vol. 48(1), 1991 (pp. 31-31).
Al-Zn and Al-Mg sacrificial coatings were found best of several tested for increasing corrosion resistance of the DU-Titanium alloy.
[Chang1991xxSCTv48n1p31].

4. High strength and ductile depleted uranium alloy, by WT Nachtrab, et al., Nuclear Metals Inc. US Patent No. 5273711, 1993 (7 pp.)
Use of molybdenum and titanium mixtures at alloy up to 2% with DU.
]Nachtrab1991xxUSPatent5273711].

5. Development of high-density ceramic composites for ballistic applications, by NL Rupert, et al., US Army Res. Lab., Aberdeen Proving Ground, MD. Proc. Int. Conf. Adv. Compos. Mater., 1993 (pp. 141-146).
Armor applications of DU ceramics is described, including fabrication, analysis and ballistic evaluation.
[Rupert1993xxPICACMp141].

6. Method for producing heavy concrete for manufacturing of radioactivity-shielding concrete casks for storing spent nuclear fuels, by C Ito, et al, Nuclear Fuel Industries, Ltd. Japan. Japanese Patent No. 11038181, 1999 (5 pp.)
Described is a process for molding DU oxides and mixing with concrete to produce heavy concrete with high mechanical strength.
[Ito1997xxJPatent11038181].

7. Magnetic material containing uranium and usage of depleted uranium, by H. Kaneko, Mito Kagaku Gijutsu Kyokai, Japan. Japanese Patent No. 11154603, 1999 (6 pp.)
Described is a process for making magnets out of the DU from spent nuclear fuel.
[Kaneko1997xxJPatent11154603].

8. Benefits of the use of depleted uranium metal as the source for industrial counterweights, by T Roberts, Uranium Research and Products Corp., Paducah, KY. WM 99 Conference Proceedings, Feb. 28, 1999 (pp. 1745-1752).
[Roberts1999xxWM99CPp1745].

9. Use of graphite from blocks of depleted urannium-graphite reactors, by YSVirgilyev, MIIGrafit, Russia. Perspectivnye Materialy Vol. 2000(2), (pp. 41-44).
Reviews the possible use of DU-graphite blocks from reactors in manufacture of carbon-based composites.
[Virgilyev2000xxPMv2000n2p41].

10. Dupoly process for treatment/recycling of depleted uranium and use in molded products, by PD Kalb, et al., Brookhaven Science Associates. US Patent 6030549, 2000.
Described is a method for encapsulating DU in thermoplastic polymer and molding the product into various shapes for use in shielding, counterweights, etc.
[Kalb2000xxPatent6030549].

11. Process for producing an aggregate suitable for inclusion into a radiation shielding product, by PA Lessing, et al., Bechtel BWXT Idaho, LLC. US Patent 6120706, 2000.
Describes a one-step process for conversion of uranium hexafluoride into uranium silicide aggregate suitable for mixing with concrete for use in a radiation shielding product.
[Lessing1998xxPatent6120706].

12. Ducrete: a cost effective radiation shielding material, by WJ Quapp, et al., Starmet, USA. Spectrum 2000 Internat'l. Conf. on Nuclear and Hazardous Waste Management, Sept. 24, 2000 (pp. 336-342).
Describes Ducrete, the ceramic DU aggregate used to make high density concrete for gamma ray and neutron radiation shielding, and mentions U leaching characteristics of Ducrete.
[Quapp2000xxICNHWMp336].

13. Civilian and military uses of depleted uranium: environmental and health problems, by C Cantaluppi, et al., Istituto di Chimica e delle Tecnologie Inorganiche e dei Materiali Avanzati, CNR C.so Stati Uniti 4, 35127, Padova. Ann Chim. Vol. 90(11-12), Nov.-Dec. 2000 (pp. 665-676).

Depleted uranium is a by-product of the process of enrichment of natural uranium and is classified as a toxic and radioactive waste; it has a very high density (approximately 19 g cm-3), a remarkable ductility and a cost low enough to be attractive for some particular technical applications. Civilian uses are essentially related to its high density, but the prevailing use is however military (production of projectiles). From the radioactive point of view, the exposure to depleted uranium can result from both external irradiation as well as internal contamination. The associated risks are however mainly of chemical-toxicological kind and the target organ is the kidney. In the present note the recent military uses and the possible effects of its environmental diffusion are discussed.
[Cantaluppi200011Acv90n11to12p665]. (PMID: 11218253 [PubMed - indexed for MEDLINE]).

14. Cermet waste packages using depleted uranium dioxide, by CW Forsberg, Oak Ridge National Laboratory, Oak Ridge, TN. Proc. Internat'l. High-Level Radiation Waste Mgmt. Conf., Apr. 29, 2001 (pp. 378-381).
Discusses use of a steel/DU/cermet structure for use as containers in the nuclear waste repository site.
[Forsberg2001xxPIHLRWMp378].

15. Depleted uranium: a study of its uses in the UK and disposal issues, by B Russ, J Radiol Prot. Vol. 22(1), Mar. 2002 (pp. 99-100).
[Russ200203JRPv22n1p99]. PMID: 11929123 [PubMed - indexed for MEDLINE]

16. Military and non-military use of depleted uranium, by PA Assimakopoulos, Journal of Environmental Radioactivity Vol. 64(2-3), 2003 (pp. 87-88).
[Assimakopoulos200302JERv64n2p87]

17. Civil use of depleted uranium, by M Betti, European Commission, Joint Research Centre, Institute for Transuranium Elements, P.O. Box 2340, 76125 Karlsruhe, Germany. betti@itu.fzk.de. J Environ Radioact. Vol. 64(2-3), 2003 (pp. 113-119).
In this paper the civilian exploitation of depleted uranium is briefly reviewed.
Different scenarios relevant to its use are discussed in terms of radiation exposure for workers and the general public. The case of the aircraft accident which occurred in Amsterdam in 1992 involving a fire, is discussed in terms of the radiological exposure to bystanders. All information given has been obtained on the basis of an extensive literature search and are not based on measurements performed at the Institute for Transuranium Elements.
[Betti2003xxJERv64n2to3p113]. (PMID: 12500798 [PubMed - indexed for MEDLINE]).

Chapter X

Biological and Environmental Remediation Techniques for DU Contamination

One of the more unfortunate situations resulting from the official industry-government-military dogma that DU is relatively harmless is that not nearly enough research is being focused on effective treatment for various forms of uranium poisoning or on techniques for environmental remediation. The government of Kuwait has spent tens of millions of dollars since the 1991 Gulf War in an attempt to clean up their contaminated environment, a needless expense if the Kuwaiti officials truly believed that DU poses no risk. British officials expressed grave concern when a small amount of DU appeared to have been stolen, saying that the DU might be used in a "dirty bomb" if it got into the hands of terrorists. But if DU is truly innocuous, of what use would it be in a dirty bomb? And what should one make of the UK Ministry of Defense issuing warning cards concerning DU to each of its soldiers deployed to Iraq in 2003?

Of course, environmental remediation begins at home at decommissioned DU manufacturing facilities (4), (7), (8), and DU testing ranges (3). Filtration through micropore filters (5) and through a bed of iron (12) have shown some success for removal of DU from contaminated water. Reicevic proposes that in-situ techniques be developed to immobilize DU in water and soil to facilitate removal (13). Miller discusses removal of DU shell fragments from soil (11), while Biwer reviews options for dealing with the vast stockpiles of uranium hexafluoride (10).

Finneran reports on studies involving bioremediation of uranium contaminated soil and water (15).

Citrates have been shown to be useful antidotes in cases of uranium poisoning (1), (2). Chelation therapies have been studied for reducing the nephrotoxicity of DU (6), (9) and for facilitating body repair following exposure to damaging doses of radiation (14).

1. The stimulating influence of sodium citrate on cellular regeneration and repair in the kidney injured by uranium nitrate, by GL Donnelly, et al., Journal of Pharmacology and Experimental Therapeutics Vol. 75, 1942 (pp. 11-17)
[Donnelly1942xxJPETv75nxp11]

2. Effect of sodium citrate on uranium poisoning in dogs, by GE Gustafson, et al., Archives of Internal Medicine Vol. 74, 1944 (pp. 416-423).
[Gustafson1944xxAIMv74nxp416]

3. Depleted uranium test range fragment reclamation, by MJ Waltz, Nuclear Metals, Inc., Concord, MA. Gov. Rep. Announce. Index (US) Vol. 83(7), 1983 (pp. 1367).
DU fragments recovered from testing GAU-8 penetrators at Eglin Air Force Base, Florida, were melted and recast into new GAU-8 penetrators and other products.
[Waltz1983xxGRAIv83n7p1367].

4. Challenges in decontamination of a depleted uranium manufacturing facility, by LW Cole, et al., Aerojet Ordnance, Jonesborough, TN. Waste Management Vol. 2, 1989 (pp. 567-570).
Cleanup of the Compton, CA facility where over 18 million GAU-8 penetrators had been manufactured was accomplished at a cost of $4 million and over 40,000 man-hours.
[Cole1989xxWMv2nxp567].

5. Filtration system for removal of depleted uranium from water, by PT Barlett, TTI Eng. and Waste Management, Tucson, AZ. Waste Management Vol. 2, 1989 (pp. 659-663).
Three cross-flow membrane module microfiltration systems were tested on DU contaminated water to remove DU particles greater than 0.1 microns in size. The best system removed 34% of the solids with a 50% reduction in radiation.
[Barlett1989xxWMv2nxp659].

6. Treatment of experimental acute uranium poisoning by chelating agents, by A Ortega, et al., Pharmacology and Toxicology Vol. 64, 1989 (pp. 247-251).
[Ortega1989xxPTv64nxp247].

7. Laboratory characterization and leaching of uranium and hazardous materials from Oak Ridge Y-12 Plant wastes contaminated with depleted uranium, by JL Collins, et al., Oak Ridge Nat'l. Lab, Oak Ridge, TN. Energy Research Abstracts Vol. 16(4), 1991.
[Collins1991xxERAv16n4px].

8. Mixed Wastes management during decommissioning at a DOD depleted uranium-conatminated facility, by RG Shimko, et al.. Tech. and Programs for Rad. Waste Mgmt and Env. Restoration Vol. 1, 1993 (pp. 701-704).
Discussion of planned mixed waste stabilization on-site at the Army Materials Technology Lab in Watertown, MA in preparation for that site's decommissioning.
[Shimko1993xxTPRWMERv1nxp701].

9. Comparative effects of the chelators sodium 4,5-dihydroxybenzene-1,3-disulfonate (Tiron) and diethylenetriaminepentaacetic acid (DTPA) on acute uranium nephrotoxicity in rats, by J.L. Domingo, et.al., Toxicology Vol. 118, 1997 (pp. 49-59).
Tiron was more effective than DTPA in reducing the nephrotoxic effects of uranyl acetate through increasing urea and creatinine excretion, but had little or no ameliorative effect on urine volume, total protein excretion or NAG (N-acetyl-$-D-glucosaminidase) excretion.
[Domingo1997xxTv118nxp49].

10. Depleted uranium disposal options, by BM Biwer, et al., Argonne Nat'l. Lab., Argonne, IL. Hazardous, Toxic and Radioactive Waste Management Vol. 4(2), 2000 (pp. 65-72).
A study concluding that UF6 stockpiles must be converted to a more stable form (such as U3O8) prior to disposal as a low-level waste at authorized LLW disposal facilities.
[Biwer2000xxHTRWMv4n2p64].

11. An alternative for cost-effective remediation of depleted uranium (DU) at certain environmental restoration sites, by M Miller, et al. Health Phys. Vol. 78(2 suppl), Feb. 2000 (pp. S9-12).
Numerous sites in the United States and around the world are contaminated with depleted uranium (DU) in various forms. A prevalent form is fragmented DU originating from various scientific tests involving high explosives and DU during weapon development programs, at firing practice ranges, or war theaters where DU was used in armor-piercing projectiles. The contamination at these sites is typically very heterogeneous, with discreet, visually identifiable DU fragments mixed with native soil. That is, the bulk-averaged DU activity is quite low, while specific DU fragments, which are distinct from the soil matrix, have much higher specific activity. DU is best known as a dark, black metal that is nearly twice as dense as lead, but DU in the environment readily weathers (oxidizes) to a distinctive bright yellow color that is readily visible. While the specific activity (amount of radioactivity per mass of soil) of DU is relatively low and presents only a minor radiological hazard, the fact that it is radioactive and visually identifiable makes it desirable to remove the DU "contamination" from the environment. The typical approach to conducting this DU remediation is to use radiation detection instruments to identify the contaminant and separate it from the adjacent soil, packaging it for disposal as radioactive waste. This process can be performed manually or by specialized, automated equipment. Alternatively, in certain situations a more cost-effective approach might be simple mechanical or gravimetric separation of the DU fragments from the host soil matrix. At SNL/NM, both the automated and simple mechanical approaches have recently been employed. This paper discusses the pros/cons of the two approaches.
[Miller200002HPv78n2supppS9]. (PMID: 10651397 [PubMed - indexed for MEDLINE]).

12. Removal kinetics of trace level depleted uranium using elemental iron determined with a kinetic phosphorescence analyzer, by M Wazne, et al., Env. Eng., Stevens Inst. of Tech., Hoboken, NJ. ACS Nat'l. Mtg. Abstracts, Aug. 2001.
Filtration with an elemental iron filter may be a viable option in remediation of DU contaminated water.
[Wazne2001xxACSNMAvxnxpx].

13. Remediation of uranium contaminated water and soil using phosphate-induced metal stabilization (PIMS), by S Raicevic, Inst. Nucl. Sci., Vinca, Yugoslavia. Hemijska Industrija Vol. 55(6), 2001 (pp. 277-280).
A review of in-situ remediation involving minimizing the mobility of contaminants by chemically converting them to stable, non-labile phases
[Raicevic2001xxHIv55n6p277].

14. Cu, Fe, Mn, and Zn chelates offer a medicinal chemistry approach to overcoming radiation injury, by JR Sorenson, Division of Medicinal Chemistry, College of Pharmacy, Department of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for Medical Sciences Campus, Little Rock, Arkansas 72205, USA. sorensonjohnrj@uams.edu. Curr Med Chem. Vol. 9(6), Mar. 2002 (pp. 639-662).
This review points out that treatment with essential metalloelement (Cu, Fe, Mn, and Zn) chelates facilitate tissue repair processes required for recovery from radiation injury including survival of lethally irradiated mice and rats. Results of studies pertaining to successful uses of bioavailable essential metalloelement chelates and combinations of them as well as aminothiols, Ca-channel blockers, acyl Melatonin homologs, substituted anilines, and curcumin radioprotectants are included in this review to suggest their

use as chelates in overcoming radiation injury. Additional reports document that non-toxic doses of essential metalloelement chelates are effective in increasing survival and repairing radiation injury when administered before irradiation, in the radiation protection paradigm, and effective in increasing survival when used to treat after irradiation, in the radiorecovery paradigm.
There are no other agents known to be effective in increasing survival when they are used to treat after irradiation. These approaches to radioprotection and radiorecovery offer promising approaches to facilitating recovery from radiation-induced injury experienced by patients undergoing radiation therapy for their neoplastic disease and by individuals who experience environmental, occupational, or accidental exposure to ionizing radiation. These individuals include those exposed to radiation resulting from nuclear accidents, the use of depleted uranium missiles, and astronauts undertaking space travel. Since there are no existing safe and effective treatments of radiation injury, studies of essential metalloelement chelates and combinations of them, as well as combinations of them with existing radioprotectant aminothiols, Ca-channel blockers, acyl Melatonin homologs, substituted anilines, and curcumin as radioprotectants seem worthwhile.
[Sorenson200203CMCv9n6p639]. (PMID: 11945129 [PubMed - indexed for MEDLINE]).

15. Multiple influences of nitrate on uranium solubility during bioremediation of uranium-contaminated subsurface sediments, by KT Finneran, et al., Department of Microbiology, University of Massachusetts Amherst, USA. dlovley@microbio.umass.edu. Environ Microbiol. Vol. 4(9), Sept. 2002 (pp. 510-516).
Microbiological reduction of soluble U(VI) to insoluble U(IV) has been proposed as a remediation strategy for uranium-contaminated groundwater. Nitrate is a common co-contaminant with uranium. Nitrate inhibited U(VI) reduction in acetate-amended aquifer sediments collected from a uranium-contaminated site in New Mexico. Once nitrate was depleted, both U(VI) and Fe(III) were reduced concurrently. When nitrate was added to sediments in which U(VI) had been reduced, U(VI) reappeared in solution. Parallel studies with the dissimilatory Fe(III)-, U(VI)- and nitrate-reducing microorganism, Geobacter metallireducens, demonstrated that nitrate inhibited reduction of Fe(III) and U(VI) in cell suspensions of cells that had been grown with nitrate as the electron acceptor, but not in Fe(III)-grown cells. Suspensions of nitrate-grown G. metallireducens oxidized Fe(II) and U(IV) with nitrate as the electron acceptor. U(IV) oxidation was accelerated when Fe(II) was also added, presumably due to the Fe(III) being formed abiotically oxidizing U(IV). These studies demonstrate that although the presence of nitrate is not likely to be an impediment to the bioremediation of uranium contamination with microbial U(VI) reduction, it is necessary to reduce nitrate before U(VI) can be reduced. These results also suggest that anaerobic oxidation of U(IV) to U(VI) with nitrate serving as the electron acceptor may provide a novel strategy for solubilizing and extracting microbial U(IV) precipitates from the subsurface.
[Finneran200209EMv4n9p510]. (PMID: 12220407 [PubMed - indexed for MEDLINE]).

Chapter XI

Biochemical Studies - DNA and Protein Binding

Summary

Uranium (uranyl salts) has been used for more than 40 years to stain DNA for electron microscopy. Other stains were favored by electron microscopists, which may be due to the more recent findings (1990s) that uranyl ion can catalyze hydrolysis of DNA (strand breaks) in the presence of light. The long-recognized fact that uranium binds to nucleic acids and nucleotides and catalyzes the chemical modification of these molecules would clearly implicate this heavy metal as a cytotoxin.

Details

Zobel (1) presents the effects of pH, salt concentration and structural integrity of DNA on the chemical interaction of DNA with uranyl salts.

Huxley (2) showed in 1961 that DNA can take up nearly its own dry weight of uranyl acetate from fixing solution, indicating high affinity for uranium. Constantinescu (3) demonstrated that the uranyl ions bind through the phosphate groups forming the backbone of DNA.

Nielson (4) showed that visible light can cleave single-strand DNA that has been pretreated to uranyl ions. Nielson (5), Mollegard (6) and Sonnichsen (7) all reported studies showing further details relating to this reaction.

Tracz (8) in 1997 showed that uranyl ion binds to paired helical filaments in nerve tissue, suggesting that uranyl ions may have neurological effects.

Ananyev (9) demonstrated that uranyl ion strongly inhibits photooxidation of Mn2+ in photosystem II indicating a potentially debilitating effect of uranium contamination in the environment and photosynthesis in exposed plants.

1. Electron Stains: I. Chemical Studies on the Interaction of DNA with Uranyl Salts, by R Zobel, et al., J. Biophys. Biochem. Cytol. Vol. 10, 1961 (pp. 336-346).
Discusses the effects of pH, salt concentration and structural integrity of DNA on the chemical interaction of uranyl salts, using spectrophotometric characterization of binding.
[Zobel1961xxJBBCv10nxp336]

2. Preferential staining of nucleic acid-containing structures for electron microscopy, by HE Huxley, et al., J. Biophys. Biochem. Cytol. Vol. 11, 1961 (pp. 273-296).
Used uranyl acetate staining to reveal excellent fine structure in nucleohistone fibers. Purified DNA can take up nearly its own dry weight of uranyl acetate from 2 % fixing solution, indicating high affinity.
[Huxley1961xxJBBCv11nxp273]

3. Metachromasia through uranyl ions: a procedure for identifying the nucleic acids and the nucleotides, by DG. Constantinescu, et al., Anal. Biochem. Vol. 62, 1974 (pp. 584-587).
Describe binding of uranyl ions through phosphate groups of nucleic acids and nucleotides.
[Constantinescu1974xxABv62nxp583]

4. Uranyl salts as photochemical agents for cleavage of DNA and probing of protein-DNA contacts, by PE Nielsen, et al., FEBS Letts. Vol. 235, 1988 (pp. 122-124).
Used uranyl acetate and nitrate to bind uranyl ion to single stranded DNA and induce nicks (cleavage) with visible light at 420 nm. Nicks are random, but proteins bound to DNA protect that region.
[Nielsen1988xxFEBSLv235nxp122]

5. DNA binding and photocleavage by uranyl salts, by PE Nielsen, et al., J. Amer. Chem. Soc. Vol. 114, 1992 (pp. 4967-4975).
Describe binding of uranyl ion in the minor groove of DNA to induce photocleavage. The binding constant is estimated to be 1010 M-1 at pH 4. Photocleavage not influenced by O2 and occurs either 3' or 5' to the deoxyribose.

[Nielsen1992xxJACSv114nxp4967]

6. Uranyl photoprobing of a four-way DNA junction: evidence for specific metal ion binding, by NE Møllegaard, et al., EMBO J. Vol. 13, 1994 (pp. 1508-1513).
Indicates uranyl, hexaminecobalt(III) and spermidine compete for the same high affinity binding site at a four-way DNA junction.
[Mollegaard1994xxEMBOJv13nxp1508].

7. Enhanced uranyl photocleavage across the minor groove of all (A/T)4 sequences indicates a similar narrow minor groove conformation, by SH Sönnichsen, et al., J. Molec. Recogn. Vol. 9, 1996 (pp. 219-227).
Shows preferential cleavage of dsDNA in the minor groove at AT rich regions, i.e., least polar region of DNA molecules.
[Sonnichsen1996xxJMRv9nxp219]

8. Paired helical filaments in corticobasal degeneration (CBD): the fine fibrillary structure with NanoVan, by E Tracz, et al., Brain Res. Vol. 773, 1997 (pp. 33-44).
Discuss using uranyl acetate, aurothioglucose, and NanoVan (vanadium compd) to identify CBD filaments by electron microscopy. This shows that uranyl ion binds to paired helical filaments in nerve tissue. It isn't certain what effect uranyl ion may have on neurodegenerative diseases.
[Tracz1997xxBRv773nxp33]

9. Remarkable affinity and selectivity for Cs+ and uranyl (UO22+) binding to the manganese site of the apo-water oxidation complex of photosystem II, by GM Ananyev, et al., Biochemistry Vol. 38, 1999 (pp. 7200-7209).
Studied binding of several different alkali and alkaline earth (divalent) metal ions to apo-water oxidizing complex of PSII in spinach (that had Mn(II), Ca(II) and Cl- removed). Uranyl ion strongly inhibits photooxidation of Mn2+ in PSII. Uranyl Kd = 15.3 :M. They argue that uranyl may block first or second photo-activation step, or alternatively accelerate the decay of IM1 (first oxidized intermediate). One must keep in mind that uranyl is a strong oxidant, just like the photooxidized Mn complex in PSII.
[Ananyev1999xxBv38nxp7200]

Appendix A.

Author Index

Each listing is coded as follows: **LastnameYYYYmmJOURNALv##n#p##**, where:
Lastname is the last name of the first author listed for the article
YYYYmm is the year and month (if known) that the article was published
JOURNAL is the initials of the principal words in the journal's name
v##n##p## are the volume and issue number and page number for the article

'x' or '0' is used wherever a number is not available.

(Note: There may be more than one journal with the same set of initials. Refer to Appendix B for a list of journals.)

Appendix B

Journal Index

Key Code	Journal Name
AB	Anal Biochem
AC	Ann Chim
ABC	Anal Bionanal Chem
ACSANUCL	ACS Abstracts NUCL
ACSNMA	ACS Natl Meeting Abstracts
ADRTR	Adverse Drug React Toxicol Rev
AIHOM	Archives of Industrial Hygiene and Occ Med
AIM	Archives of Internal Medicine
AJIM	Amer J Industrial Medicine
AJPH	Amer J Public Health
AMAAIH	AMA Archives of Industrial Health
ARI	Appl Radiat Isot
AZ	Ai Zheng (China)
B	Biochemistry
BAS	Bulletin of the Atomic Scientists
BH	Biotech Histochem
BINNV	Bilten Instituta za Nuklearne Nauke Vinca
BJIM	British J Industrial Medicine
BJR	British J Radiology
BMJ	BMJ
BR	Brain Research
C	Carcinogenesis
C	Chemosphere
C	Corrosion
CCGE	Chemika Chronika, Genike Ekdose
CMC	Curr Med Chem
CMJ	Croat Med J
CR	Cancer Research
CRT	Chemical Research in Toxicology
E	Epidemiology
EHP	Environ Health Perspect
EM	Environ Micorbiol
EMBOJ	EMBO J
EP	Environ Pollution
ER	Environ Research
ERA	Energy Research Abstracts
ETC	Environ Toxicol Chem
FEBSL	FEBS Letters
GLF	Git Labor-Fachzeitschrift
GRAI	Gov Rep Announce Index (US)
HERA	Human and Ecological Risk Assessment
HI	Hemijska Industrija
HP	Health Phys

HT	Human Toxicology
HTRWM	Hazardous, Toxic and Radioactive Waste Management
ICNHWM	Int Conf on Nuclear and Haz Waste Mgmt
IJEB	Indian J Experimental Biology
IJRB	Int J Radiat Biol
IJROBP	Int J Radiat Oncol Biol Phys
INIS	INIS Atomindex
JAAS	J of Analytical Atomic Spectroscopy
JACS	J Amer Chem Soc
JAT	J Appl Toxicol
JBBC	J Biophys Biochem Cytol
JCB	J Cell Biol
JER	J Environmental Radioactivity
JHM	J Hazard Mater
JIB	J Inorganic Biochemistry
JJAP	Japanese J of Appl Physics
JMR	J Molec Recogn
JNCI	J Nat Cancer Inst
JOEM	J Occup Environ Med
JPBA	J Pharm Biomed Anal
JPET	J Pharmacology and Experimental Therapeutics
JRAMC	J R Army Med Corps
JRNC	J Radioanalytical and Nuclear Chemistry
JRP	J Radiol Prot
JTEHA	J Toxicol Environ Health A
Kh	Khimiya (Sofiya, Bulgaria)
L	Lakartidningen (Sweden)
L	Lancet
M	Mutagenesis
MA	Med Arh (Croatia)
MB	Math Biosci
MCB	Mol Cell Biochem
MH	Medical Hypotheses
MIBM	Metal Ions in Biology and Medicine
MM	Military Medicine
MP	Med Physics
MR	Mutation Research
MW	Med War
N	Neurotoxicology
N	Nucleotecnica
NEJM	New Engl J Med
PBB	Pharmacology, Biochemistry and Behavior
PIBDS	Proc Int Beta Dosim Symposium 1983
PICACM	Proc Int Conf Adv Compos Mater
PIHLRW	Proc Int High-Level Rad Waste Mgmt Conf
PM	Perspectivnye Materialy (Russia)
PNAS	Proc Natl Acad Sci
PT	Pharmacology and Toxicology

PTUC	Pharmacology and Toxicology of Uranium Compounds
RPD	Radiat Prot Dosimetry
RR	Radiation Research
RT	Reprod Toxicol
SCT	Surface and Coatings Technology
SJWEH	Scandanavian J Work and Environmental Health
SMJ	Saudi Med J
STE	Sci Total Environ
T	Toxicology
TIH	Toxicol Ind Health
TL	Toxicology Letters
TPRWMER	Tech and Programs for Rad Waste Mgmt and Env Restoration
TS	Toxicol Sci
VMZ	Voen Med Zh (Russia)
WASP	Water, Air and Soil Polution
WM	Waste Management