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Update to Current Policy for Treatment of Depleted Uranium Chemical Toxicity

Catherine E. Shuster

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About This Publication

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Executive Summary

Depleted uranium (DU) is 40% less radioactive than natural uranium and therefore poses a chemical toxicity threat rather than a radiological threat.¹ While DU has few industrial uses, certain military personnel may be affected by its chemical toxicity as a result of operations involving DU munitions and vehicle armor. The U.S. Department of Defense (DOD) policy regarding depleted uranium exposure has not been updated since 2004. New knowledge from the last 15 years of scientific research and long-term studies on exposed veterans has not yet been incorporated into the DOD policy. The Institute for Defense Analyses produced this paper for the U.S. Army Office of the Surgeon General (OTSG) to review the scientific literature and policies regarding depleted uranium that have been published since 2004 to determine if changes to the current DOD policy are necessary, and to make appropriate recommendations.

Most scientific research and non-DOD policy regarding DU published since 2004 supports and adds to previous knowledge. While no major changes or updates have occurred, there are potential improvements that could be implemented in DOD policy to ensure that depleted uranium exposure is appropriately addressed as exposed personnel age. Exposed personnel should be monitored for changes in bone density and composition because bone is a target organ of depleted uranium and has a tendency to lose density as people age. While clinical effects have not yet been observed, high-exposure personnel (who typically have embedded DU fragments) in Department of Veterans Affairs (VA) follow-up studies frequently have observed changes in bone markers.²

Key recommendations for updating DOD policy are to:

- add regular skeletal scans to the current monitoring routine, and
- as necessary, consider adapting monitoring protocol if exposed personnel begin presenting with new symptoms (e.g., kidney dialysis).

¹ Carlos E. Corredor et al., “Ionizing Radiation,” in Timothy M. Mallon, ed., *Occupational Health and the Service Member* (Fort Sam Houston, TX: Office of the Surgeon General, Borden Institute, 2019), 414.

² Melissa A. McDiarmid et al., “The U.S. Department of Veterans’ Affairs Depleted Uranium Exposed Cohort at 25 Years: Longitudinal Surveillance Results,” *Environmental Research* 152 (2017): 178; M.A. McDiarmid et al., “Surveillance Results of Depleted Uranium-Exposed Gulf War I Veterans: Sixteen Years of Follow-Up,” *Journal of Toxicology and Environmental Health* 72, no. 1 (2009): 22.

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1. Introduction

Depleted uranium (DU) is used in medical and industrial shielding, radioactive material transport,³ radiation detection devices and shielding, parts of aircraft ailerons, ballasts, elevators, landing gear, and rotor blades, and in armor-piercing munitions. It is a high-density material with self-sharpening and pyrophoric (spontaneous ignition upon contact with air) properties,⁴ which led to its use in munitions. The Persian Gulf War was the first time DU munitions were used on a large scale; when exploded, these munitions produce DU dust, smoke, fumes, and particles that can cause internal and external exposure.⁵

Approximately 10 tons of DU were used by the U.S. military in Kosovo and 300 tons were used in the Persian Gulf War.⁶ In February 1991, U.S. forces accidentally fired upon about 115 fellow Service members in six Abrams tanks and fourteen Bradley fighting vehicles, resulting in 11 fatalities and approximately 50 casualties requiring medical attention. The Department of Veterans Affairs (VA) began biennial surveillance of these casualties in late 1993.⁷

DU is chemically and toxicologically the same as natural uranium, though it is 40% less radioactive. Its primary physiological action is as a heavy metal rather than a radioactive element.⁸ DU toxicity is dose-dependent, which therefore depends on exposure route. Embedded fragments can leach particles into the blood stream and excrete constantly

³ Adna Asic et al., “Chemical Toxicity and Radioactivity of Depleted Uranium: The Evidence from In Vivo and In Vitro Studies,” *Environmental Research* 156 (2017): 665.

⁴ Department of Defense, “Attachment 3: Depleted Uranium: Information for Clinicians,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 15, 2003), 2; World Health Organization (WHO), “Health Effects of Depleted Uranium,” A54/19 Addendum 1 (Geneva: WHO, April 26, 2001), 3.

⁵ U.S. Army Public Health Center, “Depleted Uranium – Medical,” Fact Sheet 26-004-1116 (Aberdeen, MD: Army Public Health Center, November 1, 2016), 1.

⁶ Xabier Arzuaga, Susan H. Rieth, Ambika Bathija, and Glinda S. Cooper, “Renal Effects of Exposure to Natural and Depleted Uranium: A Review of the Epidemiologic and Experimental Data,” *Journal of Toxicology and Environmental Health, Part B* 13, no. 7-8 (2010): 533.

⁷ Katherine S. Squibb and Melissa A. McDiarmid, “Depleted Uranium Exposure and Health Effects in Gulf War Veterans,” *Philosophical Transactions of the Royal Society B* 361, no. 1468 (2006): 639.

⁸ Carlos E. Corredor et al., “Ionizing Radiation,” in Timothy M. Mallon, ed., *Occupational Health and the Service Member* (Fort Sam Houston, TX: Office of the Surgeon General, Borden Institute, 2019), 414.

for months to years.⁹ Primary exposure routes are inhalation (due to explosion of DU munitions), ingestion (due to DU-contaminated food/water or children eating contaminated soil), and dermal (due to wound contamination or fragments).¹⁰

A. Scopes and Methods

To determine if changes to current Department of Defense (DOD) policy are necessary, the IDA research team conducted a qualitative literature review of policy, doctrine, and scientific literature. While the focus was policy and scientific literature published since 2004, some older literature was reviewed to better understand the historical context and reasoning for existing policies.

Papers or policies referenced in current DOD policy and doctrine were reviewed. In addition, military/government-related documents were retrieved from the Army Publishing Directorate and the Textbooks of Military Medicine, and scientific literature was retrieved from Google Scholar, PubMed, and ProQuest. The World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) guidance and publications were reviewed to the extent they were relevant. Search terms included “depleted uranium,” “depleted uranium policy,” “depleted uranium toxicity,” “depleted uranium chemical toxicity,” “depleted uranium treatment,” and “depleted uranium DOD.” When applicable, relevant resources were taken from papers found in the initial search. Papers written in non-English languages were not reviewed.

In this paper, chapter 2 discusses the current DOD policy and the updates made since 2004. Chapter 3 discusses historical and current scientific literature, including the Veterans Affairs (VA) follow-up studies. Chapter 4 provides the conclusions of the analysis and presents policy update recommendations.

⁹ Army Surgeon General Policy, “Policy for the Treatment of Personnel Wounded by Depleted Uranium,” (Washington, DC: DOD Health Affairs, February 26, 1999), 2.

¹⁰ WHO, “Health Effects of Depleted Uranium,” A54/19 Addendum 1 (Geneva: WHO, April 26, 2001), 3.

2. Updates to DOD Policy

A. Context for the Current DOD Policy

At the time the original DOD DU policy was published—and for the most part, since then as well—there has been limited research into the specific health effects related to military exposure to DU. Depleted uranium exposure typically does not cause clinical effects, and there has been no established link between DU and increased cancer risk.¹¹ Respiratory and renal effects are the most common, though it is unclear if low-level exposure can cause renal disease.¹² Over 95% of DU is not absorbed by the body before being excreted; if any does enter the bloodstream, 67% will be filtered by the kidneys within 24 hours.¹³ Very high doses (at least 15 mg/kg,¹⁴ which is similar to the LD₅₀ of cyanide¹⁵) are necessary to cause kidney damage, and a study that has followed DU-exposed Gulf War veterans since 1993 showed that by 1999, none had abnormal kidney function.¹⁶ Furthermore, although long-term exposure may impair kidneys, research has shown that kidney function may return to normal once exposure stops.¹⁷ In 2003, the genotoxicity, mutagenicity, and reproductive effects were just beginning to be studied.¹⁸

¹¹ WHO, “WHO Guidance on Exposure to Depleted Uranium for Medical Officers and Programme Administrators,” (Geneva: WHO, 2001), 7.

¹² Department of Defense, “Attachment 3: Depleted Uranium: Information for Clinicians,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 15, 2003), 3–4.

¹³ WHO, “Health Effects of Depleted Uranium,” A54/19 Addendum 1 (Geneva: WHO, April 26, 2001), 3.

¹⁴ Laura Vicente-Vicente et al., “Nephrotoxicity of Uranium: Pathophysiological, Diagnostic and Therapeutic Perspectives,” *Toxicological Sciences* 118, no. 2 (2010): 329.

¹⁵ ATSDR, *Toxicological Profile for Cyanide* (Atlanta: Department of Health and Human Services, July 2006): 20.

¹⁶ Army Surgeon General Policy, “Policy for the Treatment of Personnel Wounded by Depleted Uranium,” (Washington, DC: DOD Health Affairs, February 26, 1999), 3.

¹⁷ WHO, “Health Effects of Depleted Uranium,” A54/19 Addendum 1 (Geneva: WHO, April 26, 2001), 4.

¹⁸ Department of Defense, “Attachment 3: Depleted Uranium: Information for Clinicians,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 15, 2003), 4.

While these effects were monitored in the VA studies, 2001 was the only year in which changes were observed¹⁹ and monitoring of genotoxic effects stopped after 2007.²⁰

Despite its main effects being heavy metal toxicity, chelation therapy²¹ is not recommended as treatment for DU exposure because its efficacy against DU is largely unknown.²² Most documents recommend treating by removing embedded DU fragments, treating other wounds and burns as normal, and monitoring kidney function.²³ According to U.S. Navy Bureau of Medicine and Surgery (BUMED) Instruction 6470.10B, “there are no approved methods to reduce the chemical toxicity of DU in the body.”²⁴ WHO guidance agrees that there is no specific treatment,²⁵ but suggests sodium bicarbonate perfusion to bind and excrete DU (since chelation therapy may or may not be helpful) in cases of renal tubulopathy (i.e., disease of the kidney’s nephron tubules), in addition to monitoring kidney and liver function.²⁶ At this time, there is no consensus on potentially effective specific treatment options, though various organizations suggest options that might be effective. Until some consensus is reached and more research is done, the DOD should not alter its treatment recommendations.

Depleted uranium munitions create DU oxide aerosols and metal shards upon impact. Personnel within 50 meters (m) are likely to receive DU fragments and inhale DU aerosols. According to the Baltimore VA DU Program protocol, all other injuries should be treated as normal and kidney function should be monitored in personnel with contaminated

¹⁹ Melissa A. McDiarmid et al., “Health Effects of Depleted Uranium on Exposed Gulf War Veterans: A 10-Year Follow-Up,” *Journal of Toxicology and Environmental Health, Part A* 67, no. 4 (2004): 288–91.

²⁰ M.A. McDiarmid et al., “Surveillance Results of Depleted Uranium-Exposed Gulf War I Veterans: Sixteen Years of Follow-Up,” *Journal of Toxicology and Environmental Health* 72, no. 1 (2009): 14–29.

²¹ Chelation therapy is the administration of specific chemical molecules to bind and aid excretion of toxins or heavy metals from the body. See United Healthcare Oxford, “Chelation Therapy for Non-Overload Conditions,” 2, updated March 1, 2019, accessed March 24, 2020, <https://www.uhcprovider.com/content/dam/provider/docs/public/policies/oxford/chelation-therapy-ohp.pdf>.

²² Army Surgeon General Policy, “Policy for the Treatment of Personnel Wounded by Depleted Uranium,” (Washington, DC: DOD Health Affairs, February 26, 1999), 4.

²³ Department of Defense, “Attachment 3: Depleted Uranium: Information for Clinicians,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 15, 2003), 8–9.

²⁴ Department of the Navy, Bureau of Medicine and Surgery, “BUMED Instruction 6470.10B,” Enclosure 8 (Washington, DC: Department of the Navy, September 26, 2003), 2.

²⁵ WHO, “Health Effects of Depleted Uranium,” A54/19 Addendum 1 (Geneva: WHO, April 26, 2001), 5; WHO, “Depleted Uranium: Sources, Exposure and Health Effects,” accessed December 2, 2019, https://www.who.int/ionizing_radiation/pub_meet/en/DU_Eng.pdf.

²⁶ WHO, “WHO Guidance on Exposure to Depleted Uranium for Medical Officers and Programme Administrators,” (Geneva: WHO, 2001), 5.

wounds or embedded fragments.²⁷ In general, peacetime military risk of DU exposure is low and exposed patients do not pose a risk to others.²⁸ WHO says healthy personnel can be sent into “DU conflict areas without fear of adverse health consequences from DU exposure.”²⁹

The VA has monitored DU fragmentation since 1993 and divided patients into three exposure categories:³⁰

- Level I: people who were in, on, or near (within 50 m) vehicles that were hit with DU munitions or immediately entered the wreckage to begin rescue operations;
- Level II: people who regularly entered DU-damaged vehicles or fought DU-related fires as part of their job duties; and
- Level III: all other exposures, such as people who were driving near a DU-hit vehicle but were not hit themselves.

In cases of aerosol exposure, approximately 60–90% of DU aerosols are smaller than 10 μm (within the respirable range) and 90% of airborne DU particles remain within 50 m of a DU-hit vehicle.³¹

B. Current DOD Policy

The original DOD strategy regarding DU exposure was to coordinate with the VA on training and education, medical surveillance, post-deployment screening, risk communication, treatment, and medical follow-up; this guidance applies to all DOD and Coast Guard personnel (including civilians and volunteers) during deployment and combat operations.³² The Services were directed by Health Affairs (HA) Policy 03-012 to identify all personnel who served in Operation Iraqi Freedom and received Level I or II exposures.

²⁷ Army Surgeon General Policy, “Policy for the Treatment of Personnel Wounded by Depleted Uranium,” (Washington, DC: DOD Health Affairs, February 26, 1999), 2–4.

²⁸ Department of the Navy, Bureau of Medicine and Surgery, “BUMED Instruction 6470.10B,” Enclosure 8 (Washington, DC: Department of the Navy, September 26, 2003), 1.

²⁹ WHO, “WHO Guidance on Exposure to Depleted Uranium for Medical Officers and Programme Administrators,” (Geneva: WHO, 2001), 3.

³⁰ Department of Defense, “Policy for the Operation Iraqi Freedom Depleted Uranium (DU) Medical Management,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 30, 2003), 1.

³¹ Department of the Navy, Bureau of Medicine and Surgery, “BUMED Instruction 6470.10B,” Enclosure 8 (Washington, DC: Department of the Navy, September 26, 2003), 3.

³² Department of Defense, “Policy for the Operation Iraqi Freedom Depleted Uranium (DU) Medical Management,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 30, 2003), 1–3.

Commanders and medical personnel decide whether bioassays are required for Level I and II exposures and optional for Level III exposures. Level I hospital patients are given priority, while Level II bioassays must be collected within 180 days and Level III bioassays are given at a physician's discretion based on medical history or the patient's request.³³ Medics at the Role 1 and 2 levels should note DU exposure on medical records, while physicians at Roles 3 and 4³⁴ should determine the need for a urinary bioassay.³⁵ While there is no specific treatment for DU, urinary bioassays can determine exposure and guide future care by alerting the physician and patient to potential clinical signs and markers of concern.³⁶

To perform a bioassay according to Army Surgeon General Policy (1999) and HA Policy 03-012 (2003), an initial urine sample is collected at some point between 1 and 180 days post-exposure; as much urine as possible should be collected over a 24-hour period, but if that is not possible, at least 120 mL of the initial sample is collected. If the initial sample was collected 24–48 hours post-exposure, a secondary urine sample is taken 7–10 days after exposure. Urine samples are processed to normalize to creatinine and sample volume and are analyzed for isotopic uranium.³⁷

HA Policy 04-004 corroborated and updated HA Policy 03-012: it clarified which form should be used to identify potential DU exposures, and it clarified that a secondary urine sample is not necessary if the initial sample was taken more than 48 hours after exposure. It also stated that any removed fragments should be sent to a laboratory for medical composition testing and should be included in medical records, and that all assay results and potential risk should be communicated to the patient and included in medical records; it also provided a suggested “script” detailing how to communicate this information to

³³ Department of Defense, “Policy for the Operation Iraqi Freedom Depleted Uranium (DU) Medical Management,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 30, 2003), 3–4.

³⁴ Role 1 = first responder care. Role 2 = forward resuscitative care. Role 3 = in-theater hospital. Role 4 = definitive US-based hospital care. See Joint Chiefs of Staff, “Joint Health Services,” JP 4-02 (Washington, DC: Joint Chiefs of Staff, September 28, 2018), II-1–II-4.

³⁵ Army Surgeon General Policy, “Policy for the Treatment of Personnel Wounded by Depleted Uranium,” (Washington, DC: DOD Health Affairs, February 26, 1999), 7.

³⁶ Department of Defense, “Policy for the Operation Iraqi Freedom Depleted Uranium (DU) Medical Management,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 30, 2003), 3.

³⁷ Army Surgeon General Policy, “Policy for the Treatment of Personnel Wounded by Depleted Uranium,” (February 26, 1999), 7–9; Department of Defense, “Policy for the Operation Iraqi Freedom Depleted Uranium (DU) Medical Management,” HA Policy 03-012, memorandum (Washington, DC: DOD Health Affairs, May 30, 2003), 4–5.

the patient.³⁸ A Department of the Army memo supported the current exposure categories (as listed in the previous section), but suggested that urinalysis is not necessary for every deployed soldier; rather, it should be based on physician discretion and exposure history.³⁹

In 2004, the DOD requested a semi-annual report of bioassay results to assess the impact of HA 03-012. DOD requested the number of Level I and II personnel, the source of exposed personnel (e.g., unit or operation they came from), a qualitative assessment of exposures, the percentage of personnel evaluated with a urine bioassay, the status of bioassay analysis, patient reporting status, and the number of referrals to the Baltimore VA Medical Center's Follow-Up program. This memo also clarified some points from HA Policy 03-012, as follows:

- the DD Form 2796 should not be the only source consulted (involved units should be contacted to identify other possible exposed personnel);
- people should be referred to and evaluated by healthcare workers based on in-theater experiences, DU Questionnaire, and Health Survey Forms before being assigned an exposure category;
- urinary bioassays must be tested within 180 days and laboratories must store a 250 mL sample indefinitely;
- detailed relevant information should be collected to aid follow-on investigations and evaluations (and compared with confirmed exposures so consistent evaluations are performed); and
- the Deployment Health Clinical Center at Walter Reed shall be the central DU exposure archive that stores lab results, questionnaires, referrals, and qualitative summaries.⁴⁰

The 2004 DOD memo also outlined a more detailed urinalysis protocol,⁴¹ as depicted in Figure 1 and Figure 2.

³⁸ Department of Defense, "Department of Defense Deployment Biomonitoring Policy and Approved Bioassays for Depleted Uranium and Lead," HA Policy 04-004, memorandum (Washington, DC: Under Secretary of Defense, February 6, 2004).

³⁹ Department of Defense, "Medical Management of Army Personnel Exposed to Depleted Uranium (DU)," memorandum (Fort Sam Houston, TX: Department of the Army, April 29, 2004).

⁴⁰ Department of Defense, "Operation Iraqi Freedom Depleted Uranium Medical Management," memorandum (Washington, DC: DOD Health Affairs, April 9, 2004), 1–2.

⁴¹ Department of Defense, "Operation Iraqi Freedom Depleted Uranium Medical Management," memorandum (Washington, DC: DOD Health Affairs, April 9, 2004), 7.

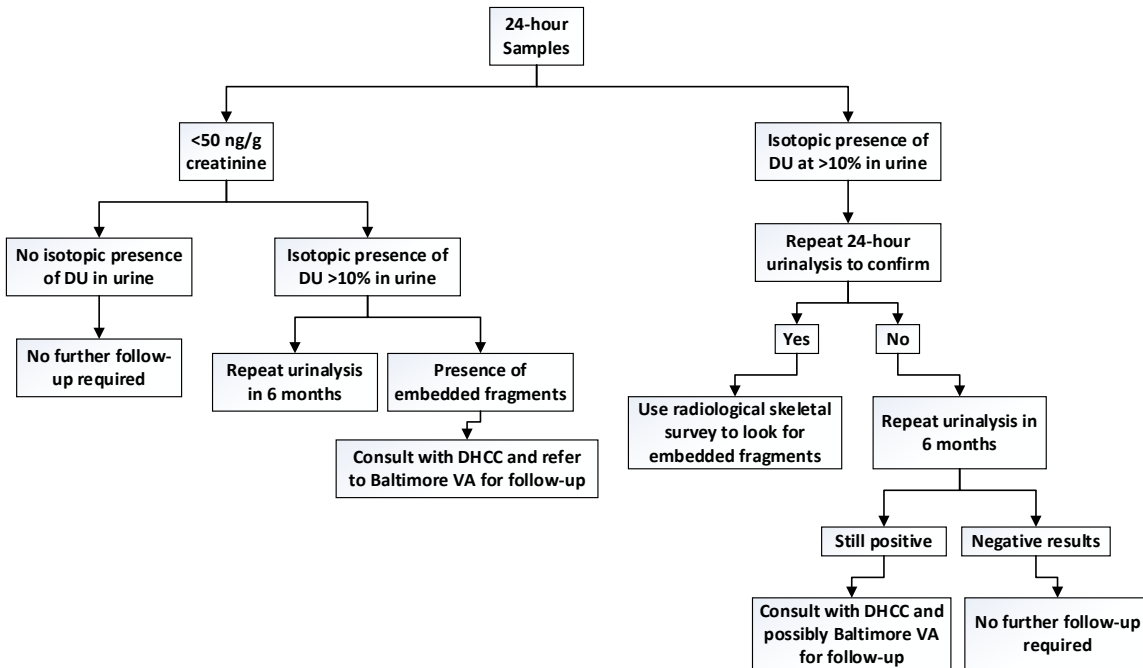


Figure 1. 24-Hour Urinary Bioassay Protocol

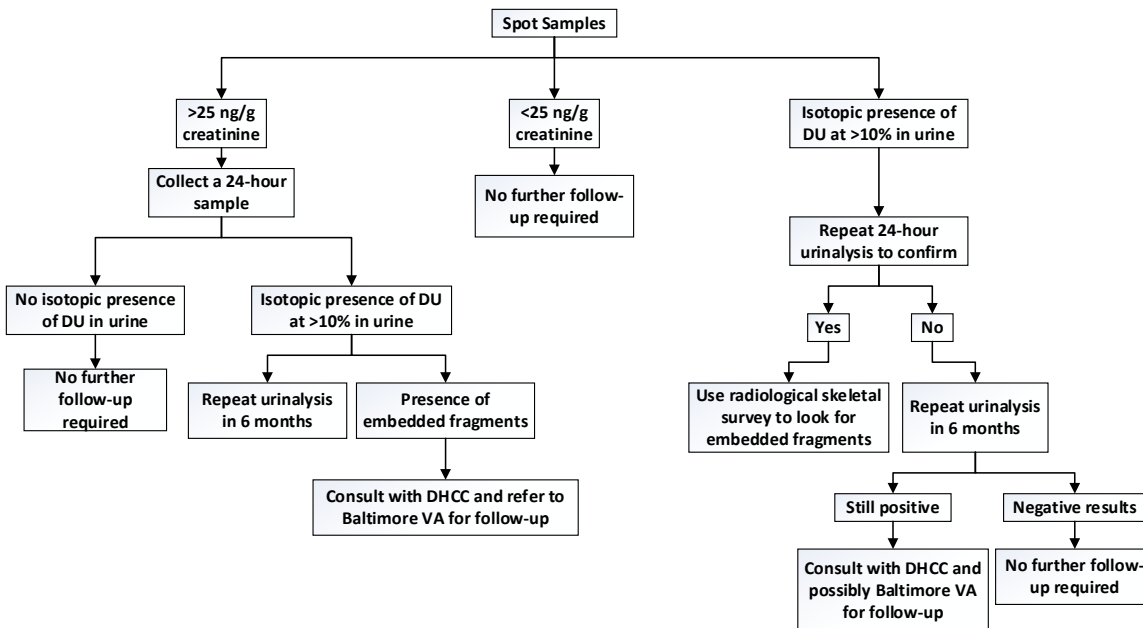


Figure 2. Spot Sample Urinary Bioassay Protocol

The Army Radiation Safety Program, as outlined in AR 11-9, only mentions DU to say that the Army Radiation Safety Officer will provide Army headquarters oversight of the DOD Executive Agency for Low-Level Radioactive Waste “to include matters

concerning depleted uranium.”⁴² AR 385-10 replaced AR 11-9 in 2007 and was most recently updated in 2017.

C. New Policy

Nearly all new policy that has been introduced since 2004 agrees with old policy and does not change the information significantly; most of the few changes made merely add clarifications or minimal new details. Most health- and CBRN-related policy (DoDIs, DoDDs, DoDMs, FMs, ATPs, etc.) fail to even mention depleted uranium. Exposure categories and criteria have remained the same: newer policy reiterates that Level I and II exposures are not expected to experience acute health effects. A recent Army fact sheet on DU stated that universal precautions are sufficient to protect healthcare workers from exposure and that chelation treatment may help clear systemic DU.⁴³

In 2012, HA Policy 12-001 stated that the Office of the Assistant Secretary of Defense for Health Affairs (OASD(HA)) would no longer require semi-annual reporting of DU bioassays, though testing would continue as necessary. For example, between 1 April and 30 September 2011, 9 Army personnel underwent DU bioassay testing, with three people in each exposure category. Between 2003 and 2012, a total of 2,701 Service members had undergone bioassays, with 10 confirmed exposures who were subsequently referred to the VA for long-term follow-up.⁴⁴ Figure 3 summarizes the bioassays from 1 June 2003 to 30 September 2011 outlined in that memo.

Level	Army	Navy/ Marine	Air Force	TOTAL	Confirmed Elevated Total Uranium	Confirmed DU Detected in Urine Specimen	Retained Fragments or Fragment- Type Injury ^{a,b}
I	365	71	3	439	6	9 ^c	29
II	588	98	14	700	0	0	5
III	339	92	10	441	0	0	10
Uncat	1,108	13	0	1,121 ^d	0	1 ^c	33
TOTAL	2400	274	27	2701	6	10^f	77

Figure 3. Service Summary of DU Bioassays from 2003–2011

Source: Department of Defense, “Operation IRAQI FREEDOM/Operation NEW DAWN Depleted Uranium Bioassay Results – 16th Semi-Annual Report and Policy on Future Data Submissions,” HA Policy 12-001 (memorandum, Washington, DC: DOD Health Affairs, January 23, 2012).

⁴² Department of the Army, *The Army Radiation Safety Program*, AR 11-9 (Washington, DC: Headquarters, Department of the Army, 28 May 1999), 8.

⁴³ U.S. Army Public Health Center, “Depleted Uranium – Medical,” Fact Sheet 26-004-1116 (Aberdeen, MD: Army Public Health Center, November 1, 2016), 2.

⁴⁴ Department of Defense, “Operation IRAQI FREEDOM/Operation NEW DAWN Depleted Uranium Bioassay Results – 16th Semi-Annual Report and Policy on Future Data Submissions,” HA Policy 12-001, memorandum (Washington, DC: DOD Health Affairs, January 23, 2012), 1.

VHA Directive 1303 states that each VA medical facility must offer DU screening for eligible veterans and coordinate with the Baltimore program for referrals. However, as of 2017, no significant adverse effects were reported in the 80 Gulf War veterans being followed by the Baltimore DU Follow-up Program. These results indicate that inhalation-only exposure presents a low risk of significant body burden.⁴⁵

Army Regulation AR 385-10 replaced the older AR 11-9 and describes the Army Radiation Safety Program. The only mention of DU in this updated regulation is that the Commanding General of the Training and Doctrine Command will develop and include “appropriate radiation safety training” and mission essential task lists for military occupational specialties and table of organization and equipment units that use radiation commodities and DU munitions and/or armor.⁴⁶

⁴⁵ Department of Veterans Affairs, “Evaluation Protocol for Veterans with Potential Exposure to Depleted Uranium (DU),” VHA Directive 1303 (Washington, DC: Department of Veterans Affairs, April 6, 2017), 1–2.

⁴⁶ Department of the Army, *The Army Safety Program*, AR 385-10 (Washington, DC: Headquarters, Department of the Army, 24 February 2017), 7.

3. Updates in Scientific Literature

A. Historical Research

At the time the original policy was written, there was a dearth of DU-specific scientific research that had been done. However, it had been determined that DU preferentially resides in the lungs, kidneys, bones, and liver, and that the kidneys can excrete about 90% of soluble DU within 3 days. In military applications, about 10–35% of DU becomes aerosolized and 60–69% of that portion is respirable (i.e., aerosols are a size that have the potential to be taken into and retained by the respiratory system); those respirable particles oxidize into many compounds, primarily depleted U_3O_8 with some UO_2 and UO_3 . About 90% of particles greater than 10 μm deposit in the upper respiratory tract (leading to prolonged lung exposure), while DU particles under 0.5 μm primarily deposit in the alveoli, where they are cleared by macrophages or transferred into the bloodstream (and potentially to other target organs). A dose of milligrams can cause kidney toxicity, although it typically does not lead to long-term damage; most exposures are acute, asymptomatic, and can possibly lead to reversible glomerular and tubular damage.⁴⁷

A 1999 study assessed the health effects of a National Guard company that had “potential” exposure by working on contaminated vehicles for weeks without protective gear. The results determined that no increase in detectable urinary uranium excretion was measured,⁴⁸ indicating that exposure risk for peripheral personnel is minimal and that standard protective gear is likely sufficient to protect against exposure.

B. Updated Research

1. Health Effects and Treatment

Recent research has added more clarity to the aerosol properties of DU particles and their fate in the body. Inhalation depends on particle size and solubility; typically, only

⁴⁷ Naomi H. Harley, Ernest C. Foulkes, Lee H. Hilborne, Arlene Hudson, and C. Ross Anthony, *A Review of the Scientific Literature as it Pertains to Gulf War Illnesses, Volume 7: Depleted Uranium* (Santa Monica, CA: RAND, 1999): 6, 26–27, 60.

⁴⁸ Naomi H. Harley, Ernest C. Foulkes, Lee H. Hilborne, Arlene Hudson, and C. Ross Anthony, *A Review of the Scientific Literature as it Pertains to Gulf War Illnesses, Volume 7: Depleted Uranium* (Santa Monica, CA: RAND, 1999): 53.

0.76–5% of particles that are inhaled will reach the bloodstream through the lungs.⁴⁹ DU munitions create 0.2–15 µm particles, which can be trapped in the oropharynx then swallowed or reach the alveoli and then be absorbed into the bloodstream.⁵⁰ Alveolar absorption is biphasic: an early rapid absorption causes peak plasma levels, then tapers to a slower, steadier absorption. The pulmonary half-life of DU is approximately 4 years.⁵¹ Soluble inhaled DU compounds will be taken up into the bloodstream within a few days, while insoluble DU compounds will remain in the lungs or lymph nodes for weeks.⁵² This is an important factor because one of the main effects of DU (and uranium in general) exposure is lung cancer, based on some observed effects in small cohort long-term uranium exposure studies.⁵³

Approximately 67–70% of uranium (including DU) is filtered by the kidneys within 24 hours.⁵⁴ DU can damage proximal tubular cells and glomeruli during tubular reabsorption; this damage can increase urinary β₂-microglobulin and retinol binding protein concentrations, though it is still unknown exactly how well these markers correlate to clinical damage.⁵⁵ Short-duration high-dose DU exposure has been shown to cause decreased glomerular filtration rates and increased serum creatinine, urine protein, and urine catalase levels. The mechanism by which DU causes nephrotoxicity is still largely unclear, but reactive oxygen species formation and oxidative stress are likely causes.⁵⁶ The

⁴⁹ ATSDR, *Toxicological Profile for Uranium* (Atlanta: Department of Health and Human Services, February 2013): 4.

⁵⁰ Wayne Briner, “The Toxicity of Depleted Uranium,” *International Journal of Environmental Research and Public Health* 7, no. 1 (2010): 304.

⁵¹ Wayne Briner, “The Toxicity of Depleted Uranium,” *International Journal of Environmental Research and Public Health* 7, no. 1 (2010): 305.

⁵² National Research Council of the National Academies, *Review of Toxicologic and Radiologic Risks to Military Personnel from Exposure to Depleted Uranium During and After Combat* (Washington, DC: The National Academies Press, 2008), 19.

⁵³ Geir Bjørklund, Olav Albert Christophersen, Salvatore Chirumbolo, Olle Selinus, and Jan Aaseth, “Recent Aspects of Uranium Toxicology in Medical Geology,” *Environmental Research* 156 (2017): 527.

⁵⁴ ATSDR, *Toxicological Profile for Uranium* (Atlanta: Department of Health and Human Services, February 2013): 12; Geir Bjørklund, Olav Albert Christophersen, Salvatore Chirumbolo, Olle Selinus, and Jan Aaseth, “Recent Aspects of Uranium Toxicology in Medical Geology,” *Environmental Research* 156 (2017): 526.

⁵⁵ Geir Bjørklund, Olav Albert Christophersen, Salvatore Chirumbolo, Olle Selinus, and Jan Aaseth, “Recent Aspects of Uranium Toxicology in Medical Geology,” *Environmental Research* 156 (2017): 529.

⁵⁶ Yuhui Hao et al., “Zinc Protects Human Kidney Cells from Depleted Uranium-Induced Apoptosis,” *Basic & Clinical Pharmacology & Toxicology* 114, no. 3 (2014): 271.

current LD₅₀ of uranium (including DU) is 14 mg/kg for humans, but that value is being reassessed;⁵⁷ such a high dose is unlikely to be obtained from an accidental exposure.

DU primarily forms carbonate and citrate complexes, which makes it more bioavailable to various tissues; this leads to higher concentrations in the kidneys and lower concentrations in the blood and plasma. In the kidneys, the proximal tubules are the most sensitive.⁵⁸ DU undergoes various processes in the body to form different oxide, hydroxide, and carbonate compounds.⁵⁹ Cell line studies indicate that renal toxicity depends on the formation of uranyl phosphate complexes. DU may also inhibit cellular metabolism processes and alter genes that are necessary to calcium-dependent cell signaling in renal cells.⁶⁰ Twenty years of *in vitro* studies show that DU-induced carcinogenic changes to cell lines is due to its heavy metal toxicity rather than its radioactivity. One study used two cell lines to show that uranium can “directly interact with and bind to the DNA” to cause genetic changes.⁶¹

Systemic distribution and storage favors the bone (66%), liver (16%), and kidneys (8%).⁶² Once systemic distribution occurs, DU can have long residence times in different tissues: DU can remain in bone for months and inhaled DU particles can stay in the lungs for months to years.⁶³ DU may affect bone deposition due to the replacement of calcium cations and may alter vitamin D metabolism.⁶⁴ Though DU rapidly enters the bloodstream,

⁵⁷ Adna Asic et al., “Chemical Toxicity and Radioactivity of Depleted Uranium: The Evidence from In Vivo and In Vitro Studies,” *Environmental Research* 156 (2017): 666.

⁵⁸ M.A. McDiarmid et al., “Longitudinal Health Surveillance in a Cohort of Gulf War Veterans 18 Years after First Exposure to Depleted Uranium,” *Journal of Toxicology and Environmental Health* 74, no. 10 (2011): 685, 687.

⁵⁹ Adna Asic et al., “Chemical Toxicity and Radioactivity of Depleted Uranium: The Evidence from In Vivo and In Vitro Studies,” *Environmental Research* 156 (2017): 666.

⁶⁰ Xabier Arzuaga, Susan H. Rieth, Ambika Bathija, and Glinda S. Cooper, “Renal Effects of Exposure to Natural and Depleted Uranium: A Review of the Epidemiologic and Experimental Data,” *Journal of Toxicology and Environmental Health, Part B* 13, no. 7-8 (2010): 539–40.

⁶¹ Adna Asic et al., “Chemical Toxicity and Radioactivity of Depleted Uranium: The Evidence from In Vivo and In Vitro Studies,” *Environmental Research* 156 (2017): 670.

⁶² ATSDR, *Toxicological Profile for Uranium* (Atlanta: Department of Health and Human Services, February 2013): 13.

⁶³ Geir Bjørklund, Olav Albert Christophersen, Salvatore Chirumbolo, Olle Selinus, and Jan Aaseth, “Recent Aspects of Uranium Toxicology in Medical Geology,” *Environmental Research* 156 (2017): 528–29.

⁶⁴ Yong-Chao Yue, Ming-Hua Li, Hai-Bo Wang, Bang-Le Zhang, and Wei He, “The Toxicological Mechanisms and Detoxification of Depleted Uranium Exposure,” *Environmental Health and Preventive Medicine* 23 (2018): 3.

it is not well-retained by the liver.⁶⁵ DU can also cross the blood-brain barrier: rat studies have shown that DU can cause brain lipid peroxidation, which can lead to behavioral changes (which have occasionally been observed in humans).⁶⁶ However, it is still unclear how and where DU deposits in the brain. In addition to these tissues, DU can also affect the immune system by causing macrophage apoptosis and modifying gene expression and signal transduction.⁶⁷

There is currently not enough data to determine definitive treatment options.⁶⁸ One suggested treatment approach is to increase the DU elimination rate or block absorption. Though not generally recommended, one study stated that chelating agents might be effective against DU, and would ideally be lipophilic selective DU scavengers; various types of chelating agents were studied and compared. Polyaminocarboxylic acids, such as DTPA and EDTA, may be effective; however, DTPA requires prompt administration and may have side effects and EDTA may require acidic conditions to be most effective. Ca-DTPA and Zn-DTPA have fewer side effects, but are unstable and have lower selectivity for DU in physiological conditions than other experimental therapeutic options. Siderophores like CBMIDA and HOPO might also be effective—CBMIDA performed better than DTPA—but only certain forms of HOPO are stable enough to be considered.⁶⁹ CBMIDA increases excretion and aids in detoxification, but it relies on acidic conditions to be effective.⁷⁰ Polyphosphonates such as EHBP may be selective for DU deposited in bone and may reduce renal lesions, as shown in rat studies. Sodium bicarbonate has a long history in DU chelation therapy and can be given orally or as an IV infusion; it is believed to increase the pH in proximal tubules and bind with uranyl ions to filter DU out of the kidneys. Zinc might be able to inhibit DU-induced apoptosis.⁷¹ Some experimental

⁶⁵ Yong-Chao Yue, Ming-Hua Li, Hai-Bo Wang, Bang-Le Zhang, and Wei He, “The Toxicological Mechanisms and Detoxification of Depleted Uranium Exposure,” *Environmental Health and Preventive Medicine* 23 (2018): 3.

⁶⁶ Wayne Briner, “The Toxicity of Depleted Uranium,” *International Journal of Environmental Research and Public Health* 7, no. 1 (2010): 305.

⁶⁷ Yong-Chao Yue, Ming-Hua Li, Hai-Bo Wang, Bang-Le Zhang, and Wei He, “The Toxicological Mechanisms and Detoxification of Depleted Uranium Exposure,” *Environmental Health and Preventive Medicine* 23 (2018): 4.

⁶⁸ Wayne Briner, “The Toxicity of Depleted Uranium,” *International Journal of Environmental Research and Public Health* 7, no. 1 (2010): 306, 308.

⁶⁹ Yong-Chao Yue, Ming-Hua Li, Hai-Bo Wang, Bang-Le Zhang, and Wei He, “The Toxicological Mechanisms and Detoxification of Depleted Uranium Exposure,” *Environmental Health and Preventive Medicine* 23 (2018): 4–6.

⁷⁰ Yuhui Hao et al., “Zinc Protects Human Kidney Cells from Depleted Uranium-Induced Apoptosis,” *Basic & Clinical Pharmacology & Toxicology* 114, no. 3 (2014): 272.

⁷¹ Yong-Chao Yue, Ming-Hua Li, Hai-Bo Wang, Bang-Le Zhang, and Wei He, “The Toxicological Mechanisms and Detoxification of Depleted Uranium Exposure,” *Environmental Health and Preventive Medicine* 23 (2018): 7.

treatment options that have been studied include high-dose melatonin, zinc, and ginkgo biloba.⁷² Various plant and animal studies have been performed to assess other treatment options, with varying success.⁷³

2. VA Follow-Up Studies

After the Gulf War, the DOD Deployment Health Support Directorate, U.S. Army Heavy Metals Office, and the U.S. Army Public Health Center joined together to establish the Capstone DU Project to provide rigorous peer-reviewed scientific research into DU health risks, focusing on personnel in munition-hit vehicles. In 2005, the “U.S. Army Capstone Depleted Uranium Aerosols Study & Human Health Risk Assessment” found that there were little to no health effects for Service members who breathed DU particles while inside DU munition-hit vehicles. The Aerosols Study portion assessed the types of vehicles hit with DU rounds in the Gulf War (e.g., Abrams tanks and Bradley fighting vehicles) and found that the ventilation systems are very effective in reducing DU particle concentrations and therefore exposure; the study also found that quickly exiting the vehicle significantly minimized exposure. The Human Health Risk Assessment portion used Aerosol Study data and scientific reviews to calculate DU concentrations in the body based on the time spent inside the vehicle; it was determined that inhalation health risks are very low, even if a person is inside a munition-hit vehicle, and long-term health effects are not expected. Regardless, the DOD policy still requires that personnel in or near vehicles to be tested for exposure and referred to the Baltimore VA Medical Center follow-up program if exposed.⁷⁴

Most human toxicity data comes from the Gulf War veterans studies, which have shown that DU has little to no clinical effect on liver, bone, hematological function, neuroendocrine hormones, or reproductive function; at times, non-statistically significant kidney changes have been observed, mostly in patients with embedded fragments who had a high exposure. In the majority of cases, the exposure category is too low to cause clinical effects. A United Kingdom Gulf War veterans study showed that 13-years post-exposure, 7% self-reported DU exposure and had a non-statistically significant mortality rate increase. This study found non-significant indicators of potential disruption in the bone turnover process (decreased serum alkaline phosphatase and increased vitamin D) and non-

⁷² Geir Bjørklund, Olav Albert Christophersen, Salvatore Chirumbolo, Olle Selinus, and Jan Aaseth, “Recent Aspects of Uranium Toxicology in Medical Geology,” *Environmental Research* 156 (2017): 529.

⁷³ Yuhui Hao et al., “Zinc Protects Human Kidney Cells from Depleted Uranium-Induced Apoptosis,” *Basic & Clinical Pharmacology & Toxicology* 114, no. 3 (2014): 272.

⁷⁴ Deployment Health and Family Readiness Library, “U.S. Army Capstone Depleted Uranium Aerosols Study & Human Health Risk Assessment,” (San Antonio, TX: Air Force Institute for Operational Health, March 10, 2005): 1–2.

significant indicators of potential early kidney damage (increased urinary retinol binding protein and β 2-microglobulin); all of these changes were not statistically significant and still fell within the normal range. Furthermore, there were no significant hepatic, neurocognitive, or genotoxic effects.⁷⁵ Studies following uranium miners have also shown that chronic exposure poses little to no risk of increased lung, bone, or kidney disease.⁷⁶

People with embedded fragments tend to have higher DU retention as shown by urinary concentration, while those without fragments have urinary DU concentrations comparable to the general population. This is likely caused by a total clearance of systemic exposure or any remaining DU has moved into long-term storage sites such as bone, leading to a steady-state DU burden accompanied by minimal DU release.⁷⁷

In the 2001 VA follow-up (10 years after initial exposure in the Gulf War), 39 patients participated in the assessment and were divided into high-exposure and low-exposure groups. There were no significant neurocognitive or hematological differences, though the high-exposure group had slightly lower (but still normal) hematocrit and hemoglobin levels, which was a new development from prior assessments. There was a significant difference for some renal indicators: serum creatinine was higher in the low-exposure group, and retinol binding protein and urine total protein levels were higher in the high-exposure group. This new development could indicate decreased protein reabsorption or increased glomerular filtration by the kidneys, but it did not present as a clinical change in renal function. There was a significant difference in chromosomal aberrations: the high-exposure group had marginally higher chromosomal aberration frequency per cell. However, this was the only year that significant genotoxic effects were observed. Finally, there were some significant immunological differences: the high-exposure group had a higher percent (but not absolute number) of CD4+ T cells and lower percent (but not absolute number) of CD8+ T cells, but all were within normal ranges.⁷⁸

In the 2003 VA follow-up, 32 of 70 veterans participated; about 25% of the cohort had embedded fragments. Urinary uranium concentration assessments are a good indicator of exposure and fragment presence: inhalation-only exposures likely only has a small amount of long-term DU storage in bone, while embedded fragments provide a chronic exposure due to tissue depots. There were no clinically significant differences between the

⁷⁵ ATSDR, *Toxicological Profile for Uranium* (Atlanta: Department of Health and Human Services, February 2013): 17, 44, 176, 179–81, 184.

⁷⁶ Melissa A. McDiarmid et al., “Health Effects of Depleted Uranium on Exposed Gulf War Veterans: A 10-Year Follow-Up,” *Journal of Toxicology and Environmental Health, Part A* 67, no. 4 (2004): 278.

⁷⁷ Melissa A. McDiarmid et al., “Health Effects of Depleted Uranium on Exposed Gulf War Veterans: A 10-Year Follow-Up,” *Journal of Toxicology and Environmental Health, Part A* 67, no. 4 (2004): 292.

⁷⁸ Melissa A. McDiarmid et al., “Health Effects of Depleted Uranium on Exposed Gulf War Veterans: A 10-Year Follow-Up,” *Journal of Toxicology and Environmental Health, Part A* 67, no. 4 (2004): 277–96.

low- and high-exposure groups. Serum phosphorus levels, a measure of renal function, was significantly different between the groups but was still within the normal range; urinary phosphate levels were not abnormal, so serum phosphorus changes alone are not likely to indicate impaired renal function. Retinol binding protein was slightly higher, but still normal and insignificant, in the high-exposure group. There were no hematological or sister chromatid exchange differences; no data on chromosomal aberration was available in 2003.⁷⁹

In the 2005 VA follow-up, the cohort was comprised of 74 participants separated into low- and high-exposure groups; there were no consistent clinically significant differences between the groups. Retinol binding protein levels were slightly higher in the high-exposure group (which tends to have people with embedded fragments), but the levels still fell within the normal range. There was no significant increase of bone cancer risk within the cohort, despite the fact that bone is a target organ of DU. In the 14 years post-exposure, urinary DU concentrations have not significantly dropped in patients with DU fragments, indicating that the fragments are constantly releasing DU.⁸⁰

In the 2007 VA follow-up, 35 of 77 veterans participated; 40% of these veterans had embedded DU shrapnel. There were little to no observed clinical effects: all renal, neurocognitive, hematology, genotoxic, and reproductive indicators were within the normal range, and there were no significant differences of neuroendocrine measures between the high- and low-exposure groups. The high-exposure group had slightly decreased osteoblast activity and slightly increased urinary calcium concentration, possibly indicating an effect on bone turnover processes. The 2007 follow-up was the final year that sister chromatids, hypoxanthine-guanine phosphoribosyltransferase, and chromosomal aberrations were assessed, and there were no significant changes or differences between groups.⁸¹

In the 2009 VA follow-up, 35 of 79 veterans participated; the low-exposure group mostly consisted of people who had inhalational exposures and the high-exposure group primarily consisted of people who had embedded DU fragments. The high-exposure group had no significant differences in blood and plasma DU concentrations from the low-exposure group, although there were higher calcium and sodium excretion rates (but still within a normal range). The low-exposure group had plasma DU concentrations

⁷⁹ M.A. McDiarmid et al., “Biological Monitoring and Surveillance Results of Gulf War I Veterans Exposed to Depleted Uranium,” *International Archives of Occupational and Environmental Health* 79, no. 1 (2006): 11–21.

⁸⁰ Katherine S. Squibb and Melissa A. McDiarmid, “Depleted Uranium Exposure and Health Effects in Gulf War Veterans,” *Philosophical Transactions of the Royal Society B* 361, no. 1468 (2006): 639–48.

⁸¹ M.A. McDiarmid et al., “Surveillance Results of Depleted Uranium-Exposed Gulf War I Veterans: Sixteen Years of Follow-Up,” *Journal of Toxicology and Environmental Health* 72, no. 1 (2009): 14–29.

approximately four times greater than blood DU concentrations. There were no significant differences between the groups in renal, hematology, neuroendocrine, or neurocognitive measures.⁸²

In the 2015 VA follow-up, 36 of 80 veterans participated and 18 had embedded fragments. Even 25 years after exposure, there were no clinically significant effects. There were no significant hematological, neurocognitive, renal, or pulmonary effects or differences between the low- and high-exposure groups. The high-exposure group had renal indicators on the higher end of the normal range, but they were still within normal and were not significantly different than the low-exposure group.⁸³

An independent evaluation corroborated the 2005 Capstone Report results, showing that the kidneys are the primary chemical target. However, there was some uncertainty in the data used to determine health effects: it was either difficult to attribute the health effects solely to DU or there was uncertainty or inconsistency in the model estimates. The independent evaluation recommended that personnel whose duties may cause Level II exposures limit their time in contaminated vehicles or wear respirators and other PPE to minimize cumulative DU exposure.⁸⁴

⁸² M.A. McDiarmid et al., “Longitudinal Health Surveillance in a Cohort of Gulf War Veterans 18 Years after First Exposure to Depleted Uranium,” *Journal of Toxicology and Environmental Health* 74, no. 10 (2011): 678–91.

⁸³ Melissa A. McDiarmid et al., “The U.S. Department of Veterans’ Affairs Depleted Uranium Exposed Cohort at 25 Years: Longitudinal Surveillance Results,” *Environmental Research* 152 (2017): 175–84.

⁸⁴ National Research Council of the National Academies, *Review of Toxicologic and Radiologic Risks to Military Personnel from Exposure to Depleted Uranium During and After Combat* (Washington, DC: The National Academies Press, 2008), 99.

4. Conclusions

Policy and scientific research have not significantly changed since the enactment of the original depleted uranium policy in 2004. Most scientific research only adds small details rather than upending previously held knowledge, and the testing protocols and exposure category guidelines have not changed. Therefore, the current DOD policy remains in line with current scientific knowledge and requires no significant changes to continue to keep in step with the knowledge base.

However, as veterans who were exposed to depleted uranium age and potentially encounter new physiological effects, a few minor changes could be made to current policy to ensure that the policy adapts and ensures appropriate care. Because bone is one of the target organs of depleted uranium, and because it has a tendency to lose density as people age, exposed personnel should be monitored for changes in bone density and composition. While clinical effects have not yet been observed, the high-exposure groups (who typically have embedded DU fragments) in the VA follow-up studies frequently have observed changes in bone markers (e.g., blood estradiol levels).⁸⁵ Adding regular skeletal scans to the existing monitoring routine would not require major changes. Similarly, the DOD should be prepared to make similar changes if other physiological changes occur; while depleted uranium exposure has not caused clinical effects in the last 25 years or so, there is not enough data to predict what changes might arise as the exposed population ages. Policy should be flexible enough to incorporate new tests into the existing monitoring routine or create different protocols for different milestones if clinical effects arise and change over time. In summary, recommended adaptations include:

- adding regular skeletal scans to the current monitoring routine, and
- as necessary, consider adapting monitoring protocol if exposed personnel begin presenting with new symptoms (e.g., kidney dialysis).

⁸⁵ Melissa A. McDiarmid et al., “The U.S. Department of Veterans’ Affairs Depleted Uranium Exposed Cohort at 25 Years: Longitudinal Surveillance Results,” *Environmental Research* 152 (2017): 178; M.A. McDiarmid et al., “Surveillance Results of Depleted Uranium-Exposed Gulf War I Veterans: Sixteen Years of Follow-Up,” *Journal of Toxicology and Environmental Health* 72, no. 1 (2009): 22.

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Appendix A. Illustrations

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Appendix C. Abbreviations

BUMED	U.S. Navy Bureau of Medicine and Surgery
CDC	Centers for Disease Control and Prevention
DOD	Department of Defense
DNA	deoxyribonucleic acid
DU	depleted uranium
HA	Health Affairs
kg	kilogram
LD ₅₀	lethal dose in 50% of the population
m	meter
mg	milligram
U.S.	United States
VA	Department of Veterans Affairs
WHO	World Health Organization

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14. ABSTRACT Depleted uranium is a form of uranium that poses a chemical toxicity risk. Depleted uranium has a few military applications, such as in vehicle armor and munitions. Exposure to depleted uranium in the battlefield poses inhalational and fragment risks because of its chemical toxicity. The U.S. Department of Defense (DOD) policies for dealing with depleted uranium exposure have not been updated since 2004. Therefore, there is a risk that patients who are exposed to depleted uranium will not receive medical care that is in sync with the last decade-plus of scientific research. Other associated policies, such as U.S. Veterans Administration and World Health Organization guidelines, may have changed in the interim as well. This paper reviews scientific literature and policies published since 2004 to determine whether or why any changes to the current DOD policies are warranted, and makes recommendations accordingly.					
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