Agency for Toxic Substances and Disease Registry
Case Studies in Environmental Medicine (CSEM)
Uranium Toxicity

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Table of Contents

Key Concepts	• Everyone is exposed to uranium in food, air, and water as part of the natural environment. Most exposures do not warrant monitoring or treatment. • Populations most heavily exposed to uranium are those employed in mining and milling operations, or in uranium enrichment and processing activities. • Natural and depleted uranium are primarily chemical toxicants, with radiation playing a minor role or no role at all. • Outcomes that may occur with uranium overexposure, based on both observed human effects and animal studies, include non-malignant respiratory disease (fibrosis, emphysema) and nephrotoxicity. • Nephrotoxicity should reverse as overexposure ceases. • Alpha radiation (such as that from uranium) is classified as a human carcinogen. However, human studies have not found elevated rates of cancer from uranium exposure, and high-dose animal studies have not found cancer following inhalation, oral, or dermal exposure to uranium.
About This and Other Case Studies in Environmental Medicine	This educational case study document is one in a series of self-instructional modules designed to increase the primary care provider's knowledge of hazardous substances in the environment and to promote the adoption of medical practices that aid in the evaluation and care of potentially exposed patients. The complete series of Case Studies in Environmental Medicine is located on the

	ATSDR Web site at www.atsdr.cdc.gov/csem/. In addition, the downloadable PDF version of this educational series and other environmental medicine materials provides content in an electronic, printable format, especially for those who may lack adequate Internet service.
How to Apply for and Receive Continuing Education Credit	See Training and Continuing Education Online for more information about continuing medical education credits, continuing nursing education credits, and other continuing education units.
Acknowledgments	We gratefully acknowledge the work that the physician writers, editors, and reviewers have provided to produce this educational resource. Listed below are those who have contributed to development of this version of the *Case Study in Environmental Medicine.* **Please Note:** Each content expert for this case study has indicated that there is no conflict of interest to disclose that would bias the case study content. **ATSDR Authors:** Kim Gehle MD, MPH **ATSDR Planners:** Charlton Coles, PhD; John Doyle, MPA; Bruce Fowler, PhD; Kimberly Gehle, MD; Sharon L. Hall, PhD; Michael Hatcher, DrPH; Kimberly Jenkins, BA; Ronald T. Jolly; Barbara M. Riley, RN; Delene Roberts, MSA; Oscar Tarrago, MD, MPH, CHES; Brian Tencza, MS. **Contributors:** Sam Keith, SB, MS; Association of Occupational and Environmental Clinics (AOEC) contractors: Denece Kesler, MD, Madu Arora, MD, Kerrie Seger, MD, Philip Wagner, MD, Monica Pourrat, MD, Joanne Keefe, RN, Joyce Van Dellen, CNP, Melanie Valdez, RN, Jean Jones, NP, Patti Austin, NP, Tom White, PA, Herman J. Gibb, PhD, Joseph Burnell, PhD, Ed Maibach, PhD, M. Haider, PhD. **Peer Reviewers:** Sam Keith, SB, MS, ATSDR; Dr. Gayle Debord, PhD, NIOSH; and Mary E. Mortensen, MD, NCEH/DLS.
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	U.S. Department of Health and Human Services **Agency for Toxic Substances and Disease Registry** **Division of Toxicology and Environmental Medicine** **Environmental Medicine and Educational Services Branch**

How to Use This Course

Introduction	The goal of the *Case Studies in Environmental Medicine* (CSEM) is to increase the primary care provider's knowledge of hazardous substances in the environment and to help in evaluation and treating of potentially exposed patients. This CSEM focuses on uranium toxicity.
Availability	Two versions of the Uranium Toxicity CSEM are available. • The HTML version www.atsdr.cdc.gov/csem/uranium/ provides content through the Internet. • The downloadable PDF version provides content in an electronic, printable format, especially for those who may lack adequate Internet service. The HTML version offers interactive exercises and prescriptive feedback to the user.
Instructions	To make the most effective use of this course • Take the Initial Check to assess your current knowledge about uranium toxicity. • Read the title, learning objectives, text, and key points in each section. • Complete the progress check exercises at the end of each section and check your answers. • Complete and submit your assessment and posttest response online if you wish to obtain continuing education credit. Continuing education certificates can be printed immediately upon completion.
Instructional Format	This course is designed to help you learn efficiently. Topics are clearly labeled so that you can skip sections or quickly scan sections you are already familiar with. This labeling will also allow you to use this training material as a handy reference. To help you identify and absorb important content quickly, each section is structured as follows:

Section Element	Purpose
Title	Serves as a "focus question" that you should be able to answer after completing the section
Learning Objectives	Describes specific content addressed in each section and focuses your attention on important points
Text	Provides the information you need to answer the focus question(s) and achieve the learning objectives
Key Points	Highlights important issues and helps you review
Progress Check	Enables you to test yourself to determine whether you have mastered the learning objectives
Answers	Provide feedback to ensure you understand the content and can locate information in the text

Learning Objectives Upon completion of the Uranium Toxicity CSEM, you will be able to

Content Area	Objectives
Overview	• Describe uranium • Identify where uranium exists in the United States today
Exposure Pathways	• Identify the most common route of exposure to uranium
Who Is at Risk	• Identify the populations most heavily exposed to uranium • Describe who is at risk for uranium exposure
Standards and Regulations	• Describe the U.S. Occupational Safety and Health Administration's (OSHA) permissible exposure limit (PEL) for uranium for workers • Describe the U.S. Environmental Protection Agency's (EPA) maximum contaminant level (MCL) for uranium in drinking water
Biological Fate	• Identify where uranium is most likely to be retained in the body
Pathogenic Changes	• Identify the mechanism by which uranium induces pathogenic changes
Physiologic Effects	• Describe the medical conditions associated with uranium exposure
Clinical Assessment	• Identify the primary focus of the exposure and medical history • Describe the most typical biomarkers of effect
Treatment and Management	• Identify two primary strategies for managing uranium-exposed patients

Initial Check

Instructions	This Initial Check will help you to assess your current knowledge about uranium toxicity. To take the Initial Check, read the case below, and then answer the questions that follow.
Case	A 57-year-old man presents to his physician for a routine health maintenance visit. He believes that he is in good health. His review of systems reveals that he has a 3-year history of cough. Over the last 6 months, the cough has been productive of small amounts of green or brownish material. He has a 40+ pack-year history of smoking. When asked about his work history, he indicates that he has been employed in a uranium milling plant for approximately 15 years and has been told that his occupational exposure to uranium may be harmful. There is no evidence of renal impairment.
Initial Check Questions	1. What information should be obtained during the examination? 2. What additional tests should be conducted to assist with diagnosis and evaluation of exposure? 3. Which diseases are linked to dusts or specifically uranium exposure? 4. What risk factors may make the patient more likely to develop a uranium-related illness?
Answers	1. What information should be obtained during the examination? The physician should take a full exposure and work history, including • job duties, • potential exposures at the work site, • frequency, source, and duration of exposure, • use of personal protective equipment at the work site, • other potential sources of exposure, including residential exposures (drinking water source, hobbies, etc.) and exposures to other hazardous materials in this and prior jobs, and • a history of tobacco use. *More information for this answer can be found in the "Clinical Assessment" section.* 2. What additional tests should be conducted to assist with diagnosis and evaluation of exposure? • Renal function studies. • Pulmonary function studies. • Chest X-ray. *More information for this answer can be found in the "Clinical Assessment" section.* 3. Which diseases are linked specifically to uranium exposure? Uranium exposure in the occupational setting has been associated

with relatively few medical problems. Renal disease is related to over-exposure to uranium, but it s not specific to uranium. Pulmonary disease is related to dust exposure and is also not specific to uranium. These problems are also not related to exposure to radiation; such problems would not be expected unless the individual were handling highly enriched uranium.

More information for this answer can be found in the "What Are the Physiologic Effects of Uranium Exposure?" section.

4. What risk factors may make the patient more likely to develop a uranium-related illness?

    - Smoking status.
    - Prior renal disease.
    - Intensity, frequency, and duration of exposure.

    More information for this answer can be found in the "Clinical Assessment" section.

What Is Uranium?

Learning Objectives	Upon completion of this section, you will be able to • describe uranium.
Definition	Uranium is a natural and commonly occurring radioactive element.
Where Found	Uranium is found in very small amounts in nature in the form of minerals, but it may be processed into a silver-colored metal. Rocks, soil, surface and underground water, air, and plants and animals all contain varying amounts of uranium. Typical concentrations in most materials are a few parts per million.
Milling and Radioactive Wastes	If the amount and concentration of uranium is great enough, it may be commercially mined. After the uranium-bearing ore is mined, it is converted into uranium dioxide or other chemical forms by a series of chemical processes known as milling. The residue remaining after the uranium has been extracted is called mill tailings. Mill tailings contain smaller concentrations of uranium, other naturally radioactive waste products such as radium and thorium, and process chemicals. The milled uranium is then processed to further purify it and prepare a portion for manufacture into nuclear reactor fuel or weapons material. The residual is used in industry and military applications. Specific information regarding locations and status of uranium mill sites and tailings can be found at the U.S. Nuclear Regulator Commission *Fact Sheet on Uranium Mill Tailings* [NRC 2006].
Three Types of Natural Uranium	Natural uranium is a mixture of three types (or isotopes) of uranium, written as ^{234}U, ^{235}U, and ^{238}U, or as U-234, U-235, and U-238, and read as uranium two thirty-four, etc. All three isotopes behave the same chemically, so any combination of the three would have the same chemical effect on a person's health. But they are different radioactive materials with different radioactive properties. That is why we must look at the actual percentages of the three isotopes in a sample of uranium to determine how radioactive it is. Although natural and depleted uranium (discussed next) are primarily chemical hazards, the next few paragraphs describe the radiological nature of the toxicologically important uranium isotopes, because isotopes are addressed in some of the health effects studies. Radioactive elements are those that undergo spontaneous transformation (decay), in which energy is released (emitted) either in the form of particles, such as alpha or beta particles, or as electromagnetic radiation with energies sufficient to cause ionization, such as gamma or X-rays. This transformation or decay results in the formation of different elements, some of which may themselves be radioactive, in which case they will also decay. The process continues until a stable (nonradioactive) state is reached. When an atom of any of these uranium isotopes decays, it emits an alpha particle (the nucleus of a helium atom) and transforms into a

	radioactive isotope of another element. The process continues through a series of radionuclides until reaching a stable, non-radioactive isotope of lead. The radionuclides in these transformation series (such as radium and radon) emit alpha, beta, and gamma radiations with energies and intensities that are unique to the individual radionuclide [ATSDR 2008b]. In addition, each isotope has a different radiological half-life or the amount of time it takes for one-half of the atoms of the radionuclide to transform. ^{234}U has the shortest half-life and is, therefore, the most radioactive, followed by ^{235}U and ^{238}U.
Processing	The processing of uranium for industrial and governmental use changes the ratios of the different isotopes. If the fraction of ^{235}U is increased, it is called enriched uranium. However, if the portion of ^{235}U is decreased, it is called depleted uranium. Depleted uranium is less radioactive than natural uranium, and enriched uranium is more radioactive than natural uranium. When enriched uranium is 97.5% pure ^{235}U, the same weight of enriched uranium is about 75 times more radioactive than natural uranium. This is because enrichment also increases the concentration of ^{234}U, which is the most radioactive of the three uranium isotopes. Natural uranium is typically about two times more radioactive than depleted uranium. Industrial processes produce other isotopes of uranium called ^{232}U, ^{233}U and ^{236}U. These are also much more radioactive than natural uranium.
Natural Uranium	Natural uranium is radioactive but poses more of a chemical hazard because its half-life is very long. When uranium gives off radiation, it transforms into another substance (such as radon). Unlike other kinds of radiation, the alpha radiation ordinarily given off by uranium cannot pass through solid objects, such as paper or human skin. Very small amounts of natural uranium are used to make some ceramic ornament glazes, light bulbs, photographic chemicals, and household products. Some fertilizers contain slightly higher amounts of natural uranium.
Enriched Uranium	Enriched uranium contains more of the fissionable ^{235}U that is the energy source for reactors and weapons. Low-enriched uranium is used in civilian reactors. High-enriched uranium is used in Naval reactors and for weapons production.
Depleted Uranium	Depleted uranium (DU) is created as a byproduct of the uranium enrichment process and possesses about 60% of the radioactivity of natural uranium. Due to its high density, it can be used as radiation shielding material, as penetrators in cannon rounds, and as counterweights for aircraft control surfaces. Therefore, DU is used on helicopters and airplanes. It is also used by the armed forces as shielding to protect Army tanks and as parts of bullets and missiles to help them go through enemy armored vehicles. DU can contaminate wounds and become imbedded in soft tissue where direct contact with its high-energy alpha particles can be a source of systemic exposure over time.

Key Points	• Uranium is a naturally occurring radioactive element. • Uranium emits alpha particles and gamma rays. • Uranium is enriched for nuclear fuel or weapons production. • DU is a highly dense byproduct of the uranium enrichment process. It is less radioactive than natural uranium, but is an important source of exposure to high-energy alpha radiation when embedded in soft tissues (*i.e.*, shrapnel). • Uranium has both chemical and radiological properties.
Progress Check	1. Uranium is A. A radioactive element. B. A naturally occurring substance. C. Used in defense programs. D. All of the above. *To review relevant content, see "Definition" and "Where Found" in this section.*

Answers

1. The correct answer is D, all of the above. Uranium is a naturally occurring radioactive substance that is used in defense programs.

Where Is Uranium Found?

Learning Objectives	Upon completion of this section you will be able to • identify where uranium exists in the United States today.
Introduction	Uranium occurs naturally in the earth's crust. In the United States, it is found most abundantly in the western states [EPA 2006a, b, c; Lide 1994; USGS 2009b]. Enrichment of uranium for nuclear weapons began in the 1940s and for energy production in the 1950s. Gaseous diffusion was developed by the War Department (precursor to the Atomic Energy Commission and the Department of Energy (DOE)) as a way to enrich uranium. Uranium is currently used to fuel nuclear power plants, create medical isotopes, and for industrial and defense purposes. Detailed information on where uranium is found in the United States is available using the National Geologic Map Database [USGS 2008].
The Natural Environment	Uranium is naturally present in the world's environment. It is commonly found in • plants, • rock, • soil, • water, and • animals in small quantities. Uranium is present in the earth at approximately 3 parts per million (ppm). The most important uranium ores for commercial production include • autunite, • carnotite, • coffinite, • pitchblend, • tobernite, • tyuyamunite, and • uraninite, The majority of the uranium deposits in the United States are found in the western states of • Arizona, • Colorado, • Nebraska, • New Mexico, • Texas, • Utah, and • Wyoming. Uranium is radioactive and contributes to the natural background radiation levels in the environment [EPA 2009b]. For information on the location of uranium deposits in other areas of the United States, please

visit U.S. Geological Surveys website on Uranium Resources and Environmental Issues [USGS 2009a].

Uranium is redistributed on the Earth through various natural and anthropogenic processes. Volcanic eruptions, wind and water erosion, and other weathering processes can mobilize uranium into the atmosphere and redeposit it into other media.

Industrial Processes

Some industrial processes also contribute to the movement of uranium, including

- extraction of phosphorus from phosphate ores to produce phosphate fertilizers,
- uranium enrichment,
- uranium mine tailings disposal, and
- uranium mining and milling to produce uranium oxides.

DOE and Civilian Reactor Sites

Uranium processing (enrichment and reprocessing) occurred at a number of DOE sites beginning in 1943 and continues to the present day. DOE sites also store uranium and uranium wastes. Spent fuel rods are stored at civilian reactor sites. For information on the location of uranium sites in the United States, please visit the U.S. Geological Survey website Uranium Resources-Uranium Information System [USGS 2009b].

Key Points

- Uranium occurs naturally in the Earth's crust, water, air, and living organisms.
- Uranium has been processed at U.S. government facilities since 1943 and at commercial facilities since the 1950s.
- Uranium enrichment and reprocessing still occurs in the United States.
- DOE sites throughout the United States store uranium and uranium wastes.
- Nuclear reactor fuel is uranium. The spent fuel rods stored at government and commercial sites retain a fraction of the original uranium.

Progress Check

2. Where is uranium found in the United States today?

   A. In residential and commercial products.
   B. Naturally occurring in the environment (including mine and mill tailings).
   C. At nuclear fuel production facilities.
   D. A and B
   E. All of the above.

   To review relevant content, see "Introduction" in this section.

Answers	2.	The correct answer is E, all of the above. Uranium can be found in residential and commercial products, naturally occurring in the environment, at nuclear fuel and weapons production sites, and at civilian and government reactor sites. The majority of the uranium deposits in the United States are found in the western states, *i.e.*, Arizona, Colorado, Nebraska, New Mexico, Texas, Utah, and Wyoming.

What Are the Routes of Exposure for Uranium?

Learning Objectives	Upon completion of this section, you will be able to • identify the most common route of exposure to uranium
Introduction	Exposure to uranium in the natural environment occurs most commonly via oral exposures. Uranium enters the body by eating contaminated food or drinking water that contains uranium. Dermal exposures occur through skin contact with uranium powders or metals. Usually only those working with products or processes using uranium would be exposed in this way. Another possible route of exposure is from retained depleted uranium metal fragments (shrapnel) that embed in soft tissue. These fragments oxidize in situ and provide a source of ongoing systemic absorption. Inhalation of uranium powder can also occur and is the primary exposure route for workers. As discussed later in this section, inhalation may be an important route of exposure for individuals in "at risk" communities.
Ingestion	Ingestion is the most common pathway of exposure to naturally occurring uranium for the general public. Exposures can occur through • ingesting food or drinking water containing naturally occurring uranium and/or • ingesting food or drinking water contaminated through uranium mining or waste activities. Uranium is found in drinking water at an average concentration of 2.5 micrograms/Liter (µg/L) throughout United States [Drury 1981; EPA 2006a]. Uranium also adsorbs to plant roots and can be ingested during food intake. Overall, the daily estimated oral intake for both food and water is about 3.0 µg/day of natural uranium. In areas of the country where natural uranium concentrations are elevated, populations can be exposed to higher average doses of uranium. For information on the location of uranium deposits in the United States, please visit U.S. Geological Surveys website on Uranium Resources and Environmental Issues [USGS 2009a].
Inhalation	Inhalation of uranium powder is the primary exposure route for workers. However, inhalation of uranium is a very minor source of exposure for the general population. Exposure scenarios include inhalation of contaminated air and dust from • communities where remediation activities are ongoing, • enrichment, or recycling, • mining and milling, • site remediation activities, • the combustion of coal (since it contains uranium), and • worker's skin, hair, and clothing.

In areas where uranium enrichment processes occur, atmospheric concentrations of uranium have been measured at 200 times higher than normal background levels. Mining activities can increase air concentrations of uranium, exposing mine workers to elevated levels of uranium. Uranium enrichment processing also has potential to release additional uranium into the atmosphere. Both mining and processing of uranium have significantly decreased since the early 1990s, so that the highest exposures would have likely occurred prior to this. However, uranium mining for the purpose of either building or providing supplies for new nuclear power plants did increase some in the late 1990's as sources of alternative energy were sought. Many of the Department of Energy mining and milling facilities have undergone or are undergoing remediation activities, which can also lead to increases in airborne uranium concentrations. This is currently the most likely exposure scenario for inhalation exposures

Dermal

Dermal contact with uranium is also a possible exposure pathway for naturally occurring uranium. Dermal exposure scenarios include

- workers exposed to uranium powders or metals and
- workers coming in contact with uranium wastes.

It is not likely that community members would be exposed to elevated levels of uranium via direct skin contact, though children playing in contaminated areas may be at risk for this type of exposure.

Key Points

- The ingestion pathway, eating food and drinking water, is the most common route of exposure to natural uranium for the general public.
- Inhalation of uranium also occurs and is the most common route of exposure for uranium workers.
- Dermal contact is not usual outside the work setting.

Progress Check

3. The most common route of exposure for uranium workers is

   A. Inhalation.
   B. Ingestion.
   C. Dermal contact.
   D. A and B.

   To review relevant content, see "Introduction" and "Ingestion" in this section

Answers	3.	The correct answer is A. The air pathway (inhalation of contaminated air and particles) is the most common route of occupational exposure to uranium and the route that most commonly leads to illness. Ingestion is the most common route of non-occupational exposure.

Who Is at Risk of Exposure to Uranium?

Learning Objectives	Upon completion of this section, you will be able to • identify the populations most heavily exposed to uranium and • describe who is at risk for uranium exposure.
Introduction	The occupations most heavily exposed to uranium are those employed in mining and milling operations, or in uranium enrichment and processing activities. Communities living near Department of Energy (DOE) facilities and mining sites and those living in areas where naturally occurring uranium levels are elevated are most at risk for significant environmental exposure.
Past Occupational Exposures	In the past, uranium exposure has been associated mainly with mining and milling of the raw material, with workers engaged in uranium enrichment, and processing (DOE sites). In the 1980s, the United States stopped recycling and reprocessing uranium for antiproliferation purposes (other than for military fuel), increasing the need for mining and material production.
Past Paraoccupa-tional Exposures	In the past, industrial hygiene practices may not have been adequate to protect workers from bringing contamination home with them, resulting in possible exposures to family members. At DOE sites in the 1950s, in particular, workers often did not know the hazards they were working with due to the secrecy of the atomic weapon projects. While it is expected that workers became more aware of the industrial hazards after the end of World War II, industrial hygiene practices in general did not improve significantly until the mid-1970s. In addition, some releases from DOE facilities during the 1950s and 1960s may have exposed nearby communities to elevated levels of radiation, including uranium.
Current Occupational Exposures	Very little mining or processing of uranium for the purpose of fuel or weapons development is currently underway. Occupational activities with potential for uranium exposure include workers involved in • using armor-piercing weapons, • decommissioning uranium-contaminated areas (*e.g.*, handling wastes or debris suspected of containing uranium while decommissioning uranium contaminated areas), • processing nuclear fuel, • maintenance and/or repair activities at applicable U.S. government facilities, • mining or milling of uranium, silver, phosphorus, coal, etc., • producing phosphate fertilizer, • operating power plants, • repairing, storing, transporting and using uranium weapons, • working with gyroscope, helicopter rotor counterbalances, or control surfaces of aircraft containing uranium metal weights, or • using uranium-containing glazes as artists, hobbyists, and glass workers.

Direct Domestic Exposures	As noted earlier, the most common non-occupational exposures are primarily a result of drinking water, eating food, and breathing air contaminated by naturally occurring uranium sources. Communities located near contaminated sites may be exposed through accidental releases during remediation activities. Essentially no uranium is released from nuclear power plants because of the fuel assembly design and the chemical and physical nature of the uranium oxide fuel [ATSDR 2008b].
Background Exposures	Background exposures to uranium occur throughout the United States and the world because uranium is a naturally occurring element in the soil, water, and air. Average daily ingestion of uranium (both food and water) is estimated to be 3 micrograms (µg)/day in the United States. According to the Third National Report on Human Exposure to Environmental Chemicals, urine uranium levels were measured in a subsample of the National Health and Nutrition Examination Survey (NHANES) participants aged 6 years and older during 1999–2002. The 95th percentile of urinary uranium concentrations was 0.034 µg/gram (gram) creatinine in the 1999–2000 survey years and 0.040 µg/g creatinine in the 2001–2002 survey years for the U.S. population aged 6 years and older [CDC 2009].
Key Points	• Populations most heavily exposed to uranium are those employed in mining and milling operations, or in uranium enrichment and processing activities. • The most common nonoccupational exposures occur from exposure to naturally occurring uranium sources such as contaminated well water. • Communities located near mining sites or other potential sources of uranium contamination may also be at risk.

Progress Check

4. In the past, occupations that entailed exposure to uranium included which of the following?

   A. Mining and milling of uranium.
   B. Repair and maintenance functions at uranium enrichment facilities.
   C. Processing nuclear fuel.
   D. All of the above.

   To review relevant content, see "Past Occupational Exposures" in this section.

5. Of the following, who is **LEAST** likely to be at current risk of significant environmental uranium exposure? A person

   A. Living downwind of a uranium processing facility.
   B. Whose primary source of drinking water is a well contaminated by naturally occurring uranium.
   C. Living near a mine undergoing remediation activities.
   D. Living near a nuclear power plant.

   To review relevant content, see "Direct Domestic Exposures" in this section.

Answers

4. The correct answer is D, all of the above. In the past, various occupational exposures may have occurred during worker activities such as uranium mining and milling, repair and maintenance functions at facilities with exposure risk to uranium (such as uranium enrichment facilities), and nuclear fuel processing at uranium facilities.

5. The correct answer is D. Of the choices listed, a person living near a nuclear power plant would be **LEAST** likely to be at current risk of significant environmental uranium exposure. Essentially no uranium is released from nuclear power plants because of the fuel assembly design and the chemical and physical nature of the uranium oxide fuel.

What Are the Standards and Regulations for Uranium Exposure?

Learning Objectives

Upon completion of this section you will be able to

- describe the U.S. Occupational Safety and Health Administration's (OSHA) permissible exposure limit (PEL) for uranium for workers and
- describe the U.S. Environmental Protection Agency's (EPA) maximum contaminant level (MCL) for uranium in drinking water.

Introduction

Uranium exposures are limited on the basis of both its chemical and radiological toxicities. In occupational settings, the Occupational Safety and Health Act regulates the limits of worker exposures based on the solubility of the uranium compound. The Department of Energy (DOE) has issued regulations applicable to its facilities that limit environmental discharges and worker exposure to uranium isotopes [DOE 2000, 2009]. The Nuclear Regulatory Commission (NRC) has also established standards and provisions for non-DOE environmental discharges and worker exposure to uranium isotopes [NRC 2009].

In addition, EPA has established standards for uranium concentrations in drinking water [EPA 2006a].

Workplace Standards

OSHA established the permissible exposure level (PEL) for airborne *insoluble* uranium in the workplace as 0.25 milligram (mg)/cubic meter (m^3) time weighted average (TWA). A TWA is the "average" exposure in any 8–hour work shift of a 40–hour work week. The PEL is the TWA concentration to which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect. Put another way, an employee's exposure to a given substance in any 8–hour work shift of a 40–hour work week, shall not exceed the 8–hour TWA limit given for that substance. This current limit was set based upon early animal study results [Voegtlin and Hodge 1953]. For more information on the OSHA PEL for insoluble uranium, please visit either OSHA's TABLE Z-1 Limits for Air Contaminants–1910.1000 TABLE Z-1 [OSHA 2006] or Safety and Health Topics Uranium (as U), Insoluble compounds [OSHA 2004].

Uranium is primarily an alpha-emitter. Workers exposed to various alpha-emitting uranium compounds protect themselves by wearing anti-contamination clothing, eye protection, and respirators when appropriate. These protective barriers are designed to eliminate external alpha radiation exposure, for such barriers easily block alpha radiation.

The OSHA PEL for airborne soluble uranium is 0.05 mg/m^3. This is lower because *soluble* uranium compounds are absorbed to a greater extent by the body. For the same exposure, soluble uranium compounds are more likely to cause chemical effects than insoluble uranium. For more information on the OSHA PEL for soluble uranium , please visit either OSHA's TABLE Z-1 Limits for Air Contaminants–1910.1000 TABLE Z-1 [OSHA 2006] or Safety and Health Topics Uranium (as U), Insoluble compounds [OSHA 2004].

	The NRC and DOE limit external radiation exposure to 5 REM per year. This is applicable to all sources combined, less background. The REM (**R**oentgen **E**quivalent **M**an) is the unit of dose actually absorbed taking biological effects into account. Both NRC and DOE have adopted internal exposure limits termed annual limits on intake (ALIs). The ALIs for inhalation or ingestion of uranium-238 are 10 microcurie/year for ingestion and 0.04-1 microcurie/year for inhalation of soluble and insoluble forms. For more information on the NRC and DOE ALIs, please visit NRC's Appendix B to Part 20–Annual Limits on Intake (ALIs) and Derived Air Concentrations (DACs) of Radionuclides for Occupational Exposure; Effluent Concentrations; Concentrations for Release to Sewerage [NRC 2009].
Environmental Standards	EPA has established a maximum contaminant level (MCL) for uranium of 30 micrograms per liter (µg/L) in drinking water. The MCL is the maximum permissible level of a contaminant in water that is delivered to any user of a public water system. EPA finalized this MCL for uranium of 30 µg/L in December 2000. Before this time, EPA did not have a limit specific to uranium in drinking water and instead regulated uranium content through gross alpha and gross beta limits. EPA's rule became effective in 2003. For more information on the EPA MCL, please visit either EPA's Radionuclides in Drinking Water [EPA 2006a] or Radiation Protection–Uranium [EPA 2009b]. EPA established the Reportable Quantity Accidental Release standard, which requires that accidental uranium waste releases containing 0.1 curies of radioactivity be cleaned up. In addition, EPA issued two standards for controlling uranium mill tailing hazards in 1983 and amended these in 1993. For more information on these standards, please see EPA's Laws We Can Use Summary [EPA 2009a]. They provide for the clean-up and disposal of mill tailings at abandoned sites and at licensed sites after operations cease. They require disposal and cleanup that will limit radium concentration in soil and radon emissions (decay products of uranium), protect groundwater, and prevent misuse.
Key Points	• OSHA's PEL for insoluble uranium in the workplace is 0.25 mg/m^3 (8–hour TWA)). • OSHA's PEL for soluble uranium in the workplace is 0.05 mg/m^3 (8–hour TWA). • EPA's MCL for uranium in drinking water is 30 µg per liter of drinking water. • EPA regulates releases of uranium above 0.1 curie • EPA regulates the clean-up of closed uranium mill tailings sites.

Progress Check

6. All of the following are true regarding the OSHA PEL of 0.05 mg/m^3 for airborne soluble uranium in the workplace **EXCEPT**

   A. It is an 8–hour TWA.
   B. It is lower than the insoluble uranium OSHA PEL because *soluble* uranium compounds are absorbed to a greater extent by the body.
   C. It is higher than the insoluble uranium OSHA PEL.
   D. For the same exposure, soluble uranium compounds are more likely to cause chemical effects than insoluble uranium.

   To review relevant content, see "Workplace Standards" in this section.

7. EPA's MCL of 30 micrograms per liter of uranium in drinking water refers to which of the following?

   A. The EPA marginal clean-up level for drinking water.
   B. The EPA maximum contaminant level allowed in drinking water.
   C. The EPA minimum contaminant level allowed in drinking water.
   D. None of the above.

   To review relevant content, see "Environmental Standards" in this section.

Answers	6.	The best choice is C. OSHA's PEL for soluble uranium in the workplace is **lower not higher** than the insoluble uranium OSHA PEL because *soluble* uranium compounds are absorbed to a greater extent by the body than insoluble compounds.
	7.	The correct answer is B. EPA's MCL for uranium is 30 µg per liter of drinking water.

What Is the Biologic Fate of Uranium in the Body?

Learning Objectives	Upon completion of this section, you will be able to • identify where uranium is most likely to be retained in the body.
Introduction	Health effects related to natural and depleted uranium exposures are related to the chemical properties of uranium, while effects from highly enriched uranium include a radiological component, since it is much more radioactive. Overall, absorption of uranium in the body is low, regardless of the route of exposure.
Inhalation Exposure	Inhaled uranium deposits in the various portions of the respiratory tract and the lungs based on particle size (*i.e.*, larger particle size deposited higher in respiratory tract). Most of the deposited uranium clears rapidly via mucociliary transport to the throat. Once there, the uranium is cleared via sputum or swallowing and primarily fecal excretion. Soluble uranium dissolves and is absorbed into the circulatory system more rapidly than insoluble forms. A portion of the uranium can reside in the lungs for years. An analysis of uranium mill crushermen (workers in the dustiest section of the mill) found that 1–5% of inhaled uranium was absorbed systemically and excreted in urine and 95% was excreted in the feces [Fisher *et al.* 1983]. Other studies have suggested that only a small portion of inhaled uranium penetrates to the alveolar region, where it can remain for years [West and Scott 1969].
Ingestion Exposure	From 0.5–5% of ingested uranium is absorbed into the blood in adults, with solubility of the compound influencing the portion that is absorbed.
Fate of Ingested Uranium	Animal studies indicate that absorbed uranium moves into the blood, where it is distributed first through soft tissues. Nearly 70% of the uranium absorbed in blood is filtered through the kidneys and cleared within 24 hours in urine. The remaining portion of uranium is distributed to other organs. After a few days, the majority of uranium exists in the kidneys and skeleton [Bhattacharyya *et al.* 1989]. A study of humans exposed to uranium showed the skeleton to be the primary long-term depot site for ingested uranium and all but the most insoluble forms of the element. Soft tissue sites of deposition include the liver and kidneys. For inhaled uranium, the pulmonary lymph nodes are the chief deposition site. Uranium deposition in bones first occurs on the surface, but the uranium eventually diffuses into the bone. Human exposure studies have shown that approximately 80–90% of bone deposition is cleared within 1–2 years [ATSDR 2008b]. Overall, most ingested uranium is excreted in feces (95%) with the remainder eliminated in urine [Wrenn *et al.* 1985].

Key Points	• Most inhaled uranium is cleared through mucociliary transport, swallowed, and excreted in the feces. • A small portion of inhaled uranium is absorbed into the blood. • An even smaller fraction of ingested uranium is absorbed into the blood. • Ingested uranium is primarily excreted in feces.
Progress Check	8. Most inhaled uranium that reaches the lungs A. Becomes lodged and is retained in lung tissue. B. Is eliminated via mucociliary clearance. C. Is absorbed. D. Is exhaled. *To review relevant content, see "Inhalation Exposure" in this section.*

Answers	8.	The correct answer is B. Most inhaled uranium that reaches the lungs is eliminated via mucociliary clearance. A very small fraction is absorbed into the blood stream, where it is distributed throughout the soft tissues and skeleton of the body.

How Does Uranium Induce Pathogenic Changes?

Learning Objectives	Upon completion of this section you will be able to • identify the mechanism by which uranium induces pathogenic changes.
Introduction	The body of evidence points to both natural and depleted uranium as being primarily chemical toxicants, with radiation playing a minor role or no role at all. Uranium has not been associated with human cancer, but if cancer were to occur, bone would be the most likely location. The primary target of uranium exposure is the kidney. However, most of the effects noted in humans have been due to high acute exposures. There is human evidence that kidney damage caused by occupational uranium overexposure can eventually heal after the excessive exposure ends [Hursh and Spoor 1973]. Uranium can cause acute renal failure in experimental models, and the pathologic changes are consistent with acute tubular necrosis. Recent studies in humans have not shown the same nephrotoxic effects as those in experimental animal studies [Kurttio *et al.* 2002, 2006].
Mechanisms	A well-accepted theory for renal toxicity is the release of uranium from serum bicarbonate complex in the kidney that allows uranium to bind to available phosphate and protein. Irritation from overexposure produces most damage in the proximal convoluted tubule, followed by the glomerulus. Another theory includes uranium inhibition of mitochondrial ATPase activity and sodium transport mechanisms that can reduce the functionality and repair capacity of the epithelium [Keith *et al.* 2007]. The mechanism for lung damage is deep lung irritation that can degrade into fibrosis or emphysema. This can be associated with oxidative stress, altered gene expression, and inhibition of sodium-dependent phosphate and glucose transport systems [Keith *et al.* 2007].
Primary Sites Affected	Uranium exposure primarily affects the kidneys (renal tubules), and inhalation exposure can also affect the lungs (alveolar changes).
Carcinogenicity	Alpha radiation, such as that from uranium, has been designated a human carcinogen. Therefore, since uranium is radioactive, exposure to uranium increases a person's calculated risk of developing cancer. However, the Committee on the Biological Effects of Ionizing Radiation (BEIR IV) reported that eating food or drinking water that has background amounts of uranium will most likely not cause cancer or other health problems in most people. No human cancer of any type has ever been seen as a result of exposure to natural or depleted uranium. The chance of developing cancer is greater with exposure to enriched uranium, because it is more radioactive than natural uranium [ATSDR 2008b]. The primary mechanism of toxicity would be direct damage to DNA from alpha particle interactions. If cancer were to occur, the most likely site would be bone (resulting in bone sarcomas). However, as previously mentioned, cancer has not been associated with uranium exposure.

The International Agency for Research on Cancer (IARC) and the U.S. National Toxicology Program (NTP) have no carcinogenicity ratings for uranium. The U.S. Environmental Protection Agency has withdrawn its carcinogenicity classification for uranium. The National Institute of Occupational Safety and Health (NIOSH) considers insoluble and soluble uranium compounds to be potential occupational carcinogens as defined by the U.S. Occupational Safety and Health Administration (OSHA) carcinogen policy [29 CFR 1990]. For more information, please see NIOSH's Uranium (soluble compounds, as U) [NIOSH 1996].

The American Conference of Industrial Hygienists (ACGIH) considers insoluble and soluble uranium compounds Confirmed Human Carcinogens (A1).

Carcinogenicity ratings are summarized on these OSHA websites:

- Safety and Health Topics–Uranium (as U), Insoluble Compounds [OSHA 2004] and
- Chemical Sampling Information–Uranium (as U), Soluble Compounds [OSHA 1999].

Cancer among uranium miners has not been associated with exposure to uranium, but instead with exposure to radon progeny, diesel exhaust particles, arsenic, and other elements in the mine air which they breathe [ATSDR 1999 (updated 2008)].

Key Points

- The process believed to account for uranium's pathogenicity is uranium ion effects in the kidneys.
- Alpha radiation (such as that from uranium) is classified as a human carcinogen. However, human studies have not found elevated rates of cancer from uranium exposure, and high-dose animal studies have not found cancer following inhalation, oral, or dermal exposure to uranium.

Progress Check

9. Some of the primary mechanisms by which natural and depleted uranium are theorized to induce pathogenic changes in tissue include

   A. Hepatic enzyme inhibition.
   B. Inflammation of the alveolar epithelium.
   C. Reactive uranyl ions released in kidney tubules.
   D. Both B and C.
   E. All of the above.

   To review relevant content, see "Mechanisms" in this section.

Answers	9.	The correct answer is D. Some of the primary mechanisms by which natural and depleted uranium are theorized to induce pathogenic changes in tissue include inflammation of the alveolar epithelium and the release of reactive uranyl ions in the kidney tubules. Uranium has not been reported to affect hepatic enzymes.

What Are the Physiologic Effects of Uranium Exposure?

Learning Objectives

Upon completion of this section, you will be able to

- describe the medical conditions associated with uranium exposure.

Introduction

The majority of adverse health outcomes related to uranium exposure have been observed in uranium mine, mill, and fabrication workers. Outcomes that may occur with uranium exposure based on both observed human effects and animal studies include

- non-malignant respiratory disease (fibrosis, emphysema) and
- nephrotoxicity
    - elevated β_2 microglobulin, BUN, Non-protein nitrogen (NPN),
    - glucosuria,
    - proteinuria,
    - tubule degeneration, lesions and
    - cell necrosis.

Extremely high acute exposures have also been lethal due to renal failure (from oral or inhaled exposure) or pulmonary failure (from inhalation exposure).

In addition, uranium overexposure by either inhalation or ingestion is associated with renal abnormalities, regardless of solubility. However, there is some question as to whether the same cytotoxic effects to the kidney from exposure to uranium in experimental settings occurs in humans [Kurttio *et al.* 2002, 2006].

Additional health effects involving the reproductive/developmental systems and indicating potential neurologic effects from uranium exposure have been reported at higher doses in the literature and more studies have been indicated for some of them [ATSDR 1999].

Nephrotoxicity in Experimental vs. Non-Experimental Settings

Recent studies have raised questions concerning the cytotoxic effects on the kidney from exposure to uranium in experimental animal settings vs. in humans. In one study of people drinking well water with high natural uranium concentrations, the median urinary concentration was 0.078 microgram/Liter (μg/L) (ranging up to 5.65 μg/L). Here, a subtle effect of uranium on calcium and phosphate fractional clearance was indicated (within the normal range of these measures), but without effect on other biochemical or traditional markers of renal function [Kurttio *et al.* 2002]. In another study, uranium was measured in 193 people who used drinking water from drilled wells for an average of 16 years. Possible toxic effects of uranium on kidney cells and renal function were evaluated by measuring

- urinary *N*-acetyl-gamma-D-glucosaminidase,
- alkaline phosphatase,
- lactate dehydrogenase,
- gamma-glutamyltransferase and glutathione-S-transferase,

- serum cystatin C,
- urinary and serum calcium phosphate,
- glucose, and
- creatinine.

The study concluded that continuous uranium intake from drinking water, even at relatively high exposures, was not found to have cytotoxic effects on kidneys in humans [Kurttio *et al.* 2006].

Health Effect Differences between Children and Adults

It is not known whether exposure to uranium affects children differently. No cases have been reported where exposure to uranium is known to have caused health effects in children. Very young animals absorb more uranium than adults do when fed uranium, but we do not know if this happens in children.

It is also not known whether exposure to naturally occurring uranium can affect the developing human fetus. In laboratory animals, extremely high doses of uranium in drinking water resulted in birth defects and an increase in fetal deaths. We do not think that uranium can cause these problems in pregnant women who are exposed to background levels of uranium in food, water, and air.

There is not a significant amount of information to suggest that children are affected differently than adults when exposed to uranium.

Key Points

- The majority of adverse health outcomes related to uranium exposure have been observed in uranium mine, mill, and fabrication workers.
- Outcomes that may occur with uranium exposure based on both observed human effects and animal studies include non-malignant respiratory disease (fibrosis, emphysema) and nephrotoxicity.
- Abnormalities consistent with nephrotoxicity include elevated β_2 microglobulin, BUN, Non-protein nitrogen (NPN), glucosuria, proteinuria, tubule degeneration, lesions and cell necrosis.
- Nephrotoxicity should reverse as overexposure ceases.

Progress Check

10. Uranium may cause which of the following nephrotoxic effects?

    A. Cell necrosis.
    B. Tubule degeneration.
    C. Elevated β_2 microglobulin.
    D. All of the above.

    To review relevant content, see "Introduction" in this section.

Answers	10.	The correct answer is D, all of the above. Nephrotoxic effects of uranium exposure may include cell necrosis and tubule degeneration, leading to elevated levels of β_2 microglobulin, BUN, and NPN, as well as proteinuria and glucosuria. As the dose increases, renal effects increase from none to elevated β2 microglobulin, to tubular degeneration (potentially reversible), to cellular necrosis.

Clinical Assessment

Learning Objectives

Upon completion of this section, you will be able to

- identify the primary focus of the exposure and medical history and
- describe the most typical biomarkers of effect.

Introduction

In general, uranium at levels typically encountered in the community or in the workplace when normal protective measures are enforced has not been found to result in adverse health effects. Workers in the uranium milling industry have been shown to have early signs of renal toxicity, but these usually resolve after exposure is ended. Autopsies of highly exposed workers who died years after exposure ended found apparent complete repair of affected renal tissues.

Uranium exposures in industrial settings often occur in the presence of other known toxicants such as

- silica dust,
- diesel exhaust particles,
- radon, and
- radium.

Individuals who are exposed to uranium in an occupational setting may need to be assessed for these types of concurrent exposures. A typical patient evaluation should include

- an exposure history,
- a medical history,
- a physical exam, and
- an assessment of biomarkers of exposure and effect.

Exposure History

A detailed exposure history is an important step in evaluating a patient who may be at risk for health outcomes related to uranium exposure. In general, uranium at levels typically encountered in the community or in the workplace when normal protective measures are enforced has not been found to result in short-term or long-term adverse health effects. However, other concurrent exposures may be significant and could result in more serious health outcomes requiring further evaluation and treatment. Uranium exposure can result in reversible lung or kidney damage.

A work history, including past occupations in which the patient may have been exposed directly or indirectly, is relevant in evaluating their exposures. Additionally, exposure histories should be evaluated in communities where naturally occurring uranium is elevated in air and water or where milling operations occur. Contact the local or state health department for assistance with finding information on uranium levels in air and water, especially levels in local aquifers likely to be tapped by private wells.

	ATSDR's case study *Taking an Exposure History* provides more information on taking an exposure history [ATSDR 2008a].
Medical History	Knowing the complete medical history of a patient who has been exposed to uranium can help in making an accurate diagnosis. It is especially important to ask about renal function, since the kidney is the target organ for inhaled, ingested, and dermally absorbed uranium. In the case study, the findings are very nonspecific because uranium has no specific biomarkers of effect. The health care provider may wish to consider the possibility of bronchial irritation or pulmonary fibrosis associated with respective current and past inhalation overexposure to uranium.
Physical Exam	The primary toxic effect of uranium exposure is nephrotoxicity. There are very few physical findings associated with renal disease unless it is very severe. However, it is important to check patients for hypertension and edema.
Biomarkers of Exposure and Effect	Finding a measurable amount of uranium in urine does not mean that the level of uranium causes an adverse health effect. According to the Third National Report on Human Exposure to Environmental Chemicals, urine uranium levels were measured in a subsample of the National Health and Nutrition Examination Survey (NHANES). Participants in this survey were aged 6 years and older during 1999–2002. Participants were selected within the specified age range to be a representative sample of the U.S. population. The analytical method measured only levels of the U-238 isotope (99% naturally occurring) and not levels of the U-235 isotope (U-235 is higher in enriched uranium used as nuclear fuel). The 95th percentile of urinary uranium concentrations was .034 micrograms/gram (µg/g) creatinine in the 1999–2000 survey years and .040 µg/g creatinine in the 2001–2002 survey years for the U.S. population aged 6 years and older [CDC 2009]. These urinary uranium levels provide physicians with a reference range so that they can determine whether people have been exposed to higher levels of uranium than are found in the general population. Whether uranium at these levels is cause for health concern is unknown. More research is needed. Urinary uranium analyses are not routinely available at typical hospital laboratories. A study looking at 105 people exposed to well water in South Carolina containing natural uranium in the range of 1.8 to 7770 µg/Liter (L) (median 157 µg/L) showed urinary levels of uranium as high as 9.55 µg/L (median 0.162 µg/L) [Orloff *et al.* 2004]. The best way to evaluate acute uranium exposure and possible effects is through urine tests for uranium concentration (exposure) and markers of renal effects. Indicators of renal toxicity include urinary catalase, proteinuria, aminoaciduria, and clearance of β_2-microglobulin relative to creatinine. The majority of uranium is cleared quickly from the body; therefore, high uranium concentrations in the urine (>100 µg/L) reflect current or recent

exposures, while low concentrations (<40 µg/L) are most likely a result of past exposures or typical background exposure.

It is important to re-emphasize that elevated urine uranium concentrations indicate exposure, but they do not necessarily indicate adverse effects. In addition, biomarkers of effect (nephrotoxicity) are not unique to uranium exposure and should be considered in the whole of a patient's exposure and medical history.

No other laboratory tests are likely to be useful.

Differential Diagnosis

There are multiple causes of renal dysfunction; therefore, it is important to include a work history or an exposure history. If there is none, document the possibility of environmental exposure for communities with elevated levels of uranium in soil and water, as well as evaluate biomarkers of exposure and effect. In addition, there is no evidence for an effect of uranium as a carcinogen; other alpha-emitters are known to have greater effects and should be considered in evaluating cancer outcomes (*e.g.*, radon exposure in uranium miners, especially in those who also smoke).

Key Points

- The exposure history focuses on occupational exposure or community exposure where uranium is elevated in soil or water.
- The medical history focuses on renal function.
- The most typical finding is elevated β_2-microglobulin, proteinuria, and glucosuria.
- Health effects from uranium are not easily differentiated from other causes without a clear history of exposure.

Progress Check

11. The most typical biomarkers of effect for a patient with uranium nephrotoxicity is

    A. Increased β_2-microglobulin on urinalysis.
    B. Aminoaciduria.
    C. Proteinuria.
    D. All of the above.

    To review relevant content, see "Biomarkers of Exposure and Effect" in this section.

12. Why is it important to know a patient's exposure history?

    A. The biomarkers of effect are not unique to uranium exposure.
    B. Other concurrent exposures may be more toxic and more important to future patient care.
    C. It is important to determine if exposures are ongoing or occurred in the past.
    D. All of the above.

    To review relevant content, see "Exposure History" in this section.

Answers

11. The correct answer is D, all of the above. All of these biomarkers (β_2-microglobulin, aminoaciduria, and proteinuria) for renal tubule toxicity are indicative of uranium overexposures.

12. The correct answer is D, all of the above. The biomarkers of effect are not unique to uranium exposure, so an exposure history is very important in determining if uranium is indeed a cause of the health effects. It is also important to consider other concurrent exposures that may be more toxic and significant to the patient's health. The exposure history is essential to determine if exposures are continuing and how the patient should proceed to minimize possible future health effects.

How Should Patients Exposed to Uranium Be Treated and Managed?

Learning Objectives	Upon completion of this section, you will be able to • identify two primary strategies for managing uranium-exposed patients.
Introduction	All patients are exposed to uranium in food, air, and water as part of their natural environment. Most exposures to naturally occurring uranium do not warrant monitoring or treatment.
If Overexposure Is Suspected or Known	The following steps are relevant if a recent uranium overexposure poses a potential health threat. • Remove the patient from the workplace or community source of overexposure, since renal damage normally reverses after overexposure ends. • Externally decontaminate patients to reduce further overexposure if they have residue from the exposure on them. If overexposure is apparent, you can contact the Radiation Emergency Assistance Center/Training Site (REAC/TS) for medical guidance [REACTS 2008]. REAC/TS: • is available 24 hours a day, 7 day a week to deploy and provide emergency medical services at incidents involving radiation anywhere in the world, • provides advice and consultation on radiation emergency medicine from its Oak Ridge, TN headquarters or at the scene of an incident, and • can be contacted for emergency assistance at 1-865-576-1005 (ask for REAC/TS) or the Internet at orise.orau.gov/reacts/ Care of patients who have been overexposed to uranium, whether or not they are symptomatic, should include the assessment of renal function to determine if the exposure may have caused renal damage. This may include measurement of uranium excreted in the urine (biomarker of exposure) as well as abnormalities in the clinical urinalyses (biomarkers of effect), as mentioned in the previous section.
Monitoring	Daily urine samples should be collected after large accidental overexposures [Diamond 1989; Howland 1949], and should continue for at least 2 weeks. The collection of 24–hour urine samples whenever possible is recommended. These samples can be used for both assessment of uranium excretion and for clinical urinalysis. For acute uranium nephrotoxicity, oral dose or infusions of sodium bicarbonate can be administered to maintain alkaline urine [Lincoln and Voelz 1990; MacNider 1916] with frequent monitoring of urine pH. Alkaline urine prevents dissociation of the uranium-bicarbonate complex that protects the renal tubular epithelium from exposure to the reactive uranyl ion. Forcing fluids to increase urinary output is recommended.

Treatment	The use of chelation drugs for acute uranium overexposures is considered a controversial practice in the United States. No human cases of uranium overexposure have been reported as being treated with chelation in the Western world. Soviet research indicates that chelating agents can significantly reduce the risk of acute uranium injury to the kidneys [Ivannikov 1987]. However, chelation must begin within 4 hours of exposure to be effective, and it is most effective if given within a few minutes of the exposure. Some authors have advised against the use of chelation because precipitation of uranium in the kidney may cause additional damage. The avoidance of calcium DTPA for chelation is mentioned, as it can increase bone deposition.
Instructions to Patients	Patients whose exposures are a result of elevated water or food uranium concentrations from home or community sources should, as a matter of general principle, limit exposure by switching to bottled water or another water source known to contain uranium levels within U.S. Environmental Protection Agency limits.
Key Points	• Everyone is exposed to uranium in food, air, and water as part of his/her natural environment. Most exposures do not warrant monitoring or treatment. • Strategies for treatment and management of overexposed patients include removal from overexposure, decontamination, monitoring uranium biomarkers of exposure and biomarkers of effect (nephrotoxicity), administration of sodium bicarbonate to maintain an alkaline urine, and pushing fluids to increase urine output. • Nephrotoxicity should reverse as overexposure ceases. • REAC/TS is available to provide medical guidance in cases of overexposure. • Patient instructions include avoidance of overexposure by making behavioral changes in work and nonwork settings.
Progress Check	13. Standard treatment modalities in the United States for patients with acute uranium nephrotoxicity include which of the following? A. Administration of sodium bicarbonate. B. Urine monitoring for pH, uranium concentration, and biomarkers of effect. C. Chelation. D. Both A and B. E. All of the above. *To review relevant content, see "Treatment" in this section.*

Answers	13.	The correct answer is D. Treatment modalities for patients with acute uranium nephrotoxicity do include administration of sodium bicarbonate to maintain an alkaline urine, and urine monitoring for pH, uranium concentration, and biomarkers of effect. The use of chelation drugs for acute uranium overexposures is considered a controversial practice in the United States and is not recommended. Nephrotoxicity should reverse on its own as overexposure ceases.

Sources of Additional Information

Uranium Specific Information

Please refer to the following Web resources for more information on the adverse effects of uranium, the treatment of uranium-associated diseases, and management of persons exposed to uranium.

- Agency for Toxic Substances and Disease Registry (www.atsdr .cdc.gov/)
    - For chemical, emergency situations
        - **CDC Emergency Response: 770-488-7100 and request the ATSDR Duty Officer**
    - For chemical, non- emergency situations
        - CDC-INFO (www.bt.cdc.gov/coca/800cdcinfo.asp)
        - 800-CDC-INFO (800-232-4636) TTY 888-232-6348 - 24 Hours/Day
        - E-mail: cdcinfo@cdc.gov

        Please Note
        ATSDR cannot respond to questions about individual medical cases, provide second opinions or make specific recommendations regarding therapy. Those issues should be addressed directly with your health care provider.
    - Toxicological Profile for Uranium www.atsdr.cdc.gov/toxprofiles/tp150.html
    - ToxFAQs™ for Uranium www.atsdr.cdc.gov/tfacts150.html, or (Spanish) www.atsdr.cdc.gov/es/toxfaqs/es_tfacts150.html
    - Case Studies in Environmental Medicine – Radon Toxicity www.atsdr.cdc.gov/csem/radon/
- EPA's Radiation Information on Uranium www.epa.gov/radiation/radionuclides/uranium.html
- Radiation Emergency Assistance Center/Training Site (REAC/TS) orise.orau.gov/reacts/
    - Provide 24/7 availability to deploy and provide emergency medical services at incidents involving radiation anywhere in the world.
    - Provide advice and consultation on radiation emergency medicine from its Oak Ridge, TN, headquarters or at the scene of an incident.

Clinical Resources

- American College of Occupational and Environmental Medicine (ACOEM) (www.acoem.org)
  - ACOEM is the nation's largest medical society dedicated to promoting the health of workers through preventive medicine, clinical care, research, and education.
  - Its members are a dynamic group of physicians encompassing specialists in a variety of medical practices is united via the College to develop positions and policies on vital issues relevant to the practice of preventive medicine both within and outside of the workplace.
- American College of Medical Toxicologists (ACMT) (www.acmt.net)
  - ACMT is a professional, nonprofit association of physicians with recognized expertise in medical toxicology.
  - The College is dedicated to advancing the science and practice of medical toxicology through a variety of activities.
- Association of Occupational and Environmental Clinics www.aoec.org
  - The Association of Occupational and Environmental Clinics (AOEC) is a network of more than 60 clinics and more than 250 individuals committed to improving the practice of occupational and environmental medicine through information sharing and collaborative research.
- Pediatric Environmental Health Specialty Units (PEHSUs) www.pehsu.net
  - Each PEHSU is based at an academic center and is a collaboration between the pediatric clinic and the (AOEC) occupational and environmental clinic at each site.
  - The PEHSU's have been developed to provide education and consultation for health professionals, public health professionals and others about the topic of children's environmental health.
  - The PEHSU staff is available for consultation about potential pediatric environmental health concerns affecting both the child and the family. Health care professionals may contact their regional PEHSU site for clinical advice.
- Poison Control Center
  - The American Association of Poison Control Centers may be contacted for questions about poisons and poisonings. The web site provides information about poison centers and poison prevention. AAPC does not provide information about treatment or diagnosis of poisoning or research information for student papers.

  - American Association of Poison Control Centers (1-800-222-1222 or www.aapcc.org).

General Environmental Health Information

- Agency for Toxic Substances and Disease Registry (www.atsdr.cdc.gov)
  - To view the complete library of CSEMs (www.atsdr.cdc.gov/csem/).
  - Taking an Exposure History CSEM (www.atsdr.cdc.gov/csem/exphistory/).
- Environmental Protection Agency Integrated Risk Information System (IRIS) cfpub.epa.gov/ncea/iris/index.cfm
  - IRIS is a compilation of electronic reports on specific substances found in the environment and their potential to cause human health effects.
  - Initially developed for EPA staff in response to a growing demand for consistent information on substances for use in risk assessments, decision-making and regulatory activities.
  - The information in IRIS is intended for those without extensive training in toxicology, but with some knowledge of health sciences.
- National Center for Environmental Health (NCEH) (www.cdc.gov/nceh/)
  - NCEH works to prevent illness, disability, and death from interactions between people and the environment. It is especially committed to safeguarding the health of populations that are particularly vulnerable to certain environmental hazards - children, the elderly, and people with disabilities.
  - NCEH seeks to achieve its mission through science, service, and leadership.
- National Institute of Health (NIH) (www.nih.gov)
  - A part of the U.S. Department of Health and Human Services, NIH is the primary Federal agency for conducting and supporting medical research.
- National Institute of Occupational Safety and Health (NIOSH) (www.cdc.gov/niosh/)
  - NIOSH is in the U.S. Department of Health and Human Services and is an agency established to help assure safe and healthful working conditions for working men and women by providing research, information, education, and training in the field of occupational safety and health.
- National Library of Medicine's (NLM) Environmental Health and Toxicology sis.nlm.nih.gov/enviro.html

Assessment and Posttest Instructions

Introduction	ATSDR seeks feedback on this course so we can asses its usefulness and effectiveness. We ask you to complete the assessment questionnaire online for this purpose. In addition, if you complete the assessment and posttest online, you can receive continuing education credits as follows.

Accrediting Organization	Credits Offered
Accreditation Council for Continuing Medical Education (ACCME)	**CME**: The Centers for Disease Control and Prevention is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The Centers for Disease Control and Prevention designates this educational activity for a maximum of **1.75 AMA PRA Category 1 Credit(s)™**. Physicians should only claim credit commensurate with the extent of their participation in the activity.
American Nurses Credentialing Center (ANCC), Commission on Accreditation	**CNE**: The Centers for Disease Control and Prevention is accredited as a provider of Continuing Nursing Education by the American Nurses Credentialing Center's Commission on Accreditation. This activity provides **1.7** contact hours.
National Commission for Health Education Credentialing, Inc. (NCHEC)	**CHES**: The Centers for Disease Control and Prevention is a designated provider of continuing education contact hours (CECH) in health education by the National Commission for Health Education Credentialing, Inc. This program is a designated event for the Certified Health Education Specialist (CHES) to receive **2.0** Category I contact hours in health education, CDC provider number GA0082.
International Association for Continuing Education and Training (IACET)	**CEU**: The CDC has been approved as an Authorized Provider by the International Association for Continuing Education and Training (IACET), 1760 Old Meadow Road, Suite 500, McLean, VA 22102. The CDC is authorized by IACET to offer **0.2** IACET CEU's for this program.

Disclaimer	CDC, our planners, and our presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters. Presentations will not include any discussion of the unlabeled use of a product or a product under investigational use. There was no commercial support received for this activity.
Online Instructions	To complete the assessment and posttest, go to www2.cdc.gov/atsdrce/ and follow the instructions on that page. You can immediately print your continuing education certificate from your personal transcript online. No fees are charged.

Posttest

1. Uranium is found naturally in

   A. Rocks.
   B. Soils.
   C. Animals.
   D. Water.
   E. All of the above.
   F. None of the above.

2. Where can uranium be found in the United States today?

   A. Naturally occurring in the environment (including mine and mill tailings).
   B. At nuclear fuel production facilities.
   C. In residential and commercial products.
   D. All of the above.
   E. Both A and B only.

3. Enriched uranium

   A. Contains more U-235 than natural uranium.
   B. Is less radioactive than natural uranium.
   C. Has diverse therapeutic uses.
   D. Is created when meteors strike the earth.

4. Uranium is used

   A. In nuclear power plants.
   B. To counter balance helicopter blades.
   C. As armor for military vehicles.
   D. As a part of certain kinds of bullets.
   E. All of the above.
   F. None of the above.

5. In the past, occupations that entailed exposure to uranium included which of the following?

   A. Uranium miners and millers.
   B. Repairmen and maintenance workers at uranium enrichment facilities.
   C. Nuclear fuel processors.
   D. All of the above.

6. Of the following, who is **LEAST** likely to currently be at risk of significant environmental uranium exposure? A person

   A. Living downwind of a uranium processing facility.
   B. Whose primary source of drinking water is a well contaminated by naturally occurring uranium.
   C. Living near a mine undergoing remediation activities.
   D. Living near a nuclear power plant.

7. In general, exposure to uranium in the natural environment occurs primarily via

   A. Inhalation.
   B. Ingestion.
   C. Dermal contact.
   D. None of the above.

8. Which of the following is **<u>FALSE</u>** regarding the OSHA PEL of 0.05 mg/m^3 for airborne soluble uranium in the workplace?

   A. It is an 8–hour, time-weighted average.
   B. It is lower than the insoluble uranium OSHA PEL because *soluble* uranium compounds are absorbed to a greater extent by the body.
   C. It is higher than the insoluble uranium OSHA PEL.
   D. For the same exposure, soluble uranium compounds are more likely to cause chemical effects than insoluble uranium.

9. EPA's MCL of 30 micrograms per liter of uranium in drinking water refers to which of the following?

   A. The EPA marginal clean-up level for drinking water.
   B. The EPA maximum contaminant level allowed in drinking water.
   C. The EPA minimum contaminant level allowed in drinking water.
   D. None of the above.

10. Most inhaled uranium that reaches the lungs

    A. Becomes lodged and is retained in lung tissue.
    B. Is eliminated via mucociliary clearance.
    C. Is absorbed.
    D. Is exhaled.

11. The radioactivity from uranium is primarily

    A. Alpha particles.
    B. Beta particles.
    C. Gamma rays.
    D. Muons.
    E. All of the above.
    F. None of the above.

12. Exposure to natural uranium increases a person's risk of getting cancer

    A. True.
    B. False.

13. Exposure to uranium is associated with

    A. Heart disease.
    B. Emphysema.
    C. Rheumatologic disease.
    D. Renal disease.
    E. Neurodegenerative disease.
    F. All of the above.
    G. Only B and D.
    H. None of the above.

14. The most typical biomarkers of effect for a patient with uranium nephrotoxicity is

    A. Increased β_2-microglobulin on urinalysis.
    B. Aminoaciduria.
    C. Proteinuria.
    D. All of the above.

15. Why is it important to know a patient's exposure history?

    A. The biomarkers of effect are not unique to uranium exposure.
    B. Other concurrent exposures may be more toxic and more important to future patient care.
    C. It is important to determine if exposures are ongoing or occurred in the past.
    D. All of the above.

16. Biomarkers of uranium exposure include

    A. The presence of uranium in feces.
    B. Pathognomonic changes in an EMG (electromyogram).
    C. The chemical or radiological detection of uranium in the urine.
    D. Both A and C.
    E. All of the above.
    F. None of the above.

17. Standard treatment modalities in the United States for patients with acute uranium nephrotoxicity include which of the following?

    A. Administration of sodium bicarbonate.
    B. Urine monitoring for pH, uranium concentration and biomarkers of effect.
    C. Chelation.
    D. Both A and B.
    E. All of the above.

Relevant Content	To review content relevant to the posttest questions

Question	Location of Relevant Content
1	What Is Uranium?
2	Where Is Uranium Found?
3	What Is Uranium?
4	What Is Uranium?
5	Who Is at Risk of Exposure to Uranium?
6	Who Is at Risk of Exposure to Uranium?
7	What Are Routes of Exposure for Uranium?
8	What Are Standards and Regulations for Uranium Exposure?
9	What Are Standards and Regulations for Uranium Exposure?
10	What Is the Biologic Fate of Uranium in the Body?
11	How Does Uranium Induce Pathogenic Change?
12	How Does Uranium Induce Pathogenic Change?
13	What are the Physiologic Effects of Uranium Exposure?
14	Clinical Assessment
15	Clinical Assessment
16	Clinical Assessment
17	How Should Patients Exposed to Uranium Be Treated and Managed?

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