Elevated Cadmium

Important Notice:

*All public health recommendations for routine investigations are based 3.3unless otherwise stated. Use the CCDM as the primary resource for case investigations that meet routine follow up. In cases of complicated situations or unique issues not addressed by this manual, please refer to the Administrative Rules of Montana (ARM) Chapter **37.114** or contact the designated subject matter expert in the Office of Epidemiology and Scientific Support at the Montana DPHHS for further clarification.*

PROTOCOL CHECKLIST

- ☐ Confirm diagnosis, see case definition (see section 3.3 and 4.1)
- ☐ Review background information on elevated cadmium (see section 2)
- ☐ Contact provider to determine plan to re-test cadmium level
- ☐ Notify state health department of case by entering available information into the Montana Infectious Disease Information System (MIDIS), if available, within the time frame for the specific disease per (ARM) **37.114.204** (see section 1.3)
- ☐ Review for use, specific technical assistance guidance documents
- ☐ Interview patient/guardian, cover the following:
  - ☐ Review health consequences of an elevated cadmium facts with patient/guardian (see section 2.2)
  - ☐ Ask about exposures to relevant risk factors to determine the risk of exposure for other household members (see section 4.3 and 4.4)
  - ☐ Educate patient/ guardian on cadmium exposure prevention (see section 6)
  - ☐ Implement Control Measures (see section 5.1)
  - ☐ Address patient's/guardian's questions or concerns
  - ☐ Determine answers to "condition specific" questions at the end of each MIDIS investigation
  - ☐ Complete the Exposure Questionnaire on Cadmium (See the CD Epi Resources)
- ☐ Follow-up on special situations (see section 5, review references and additional information or contact the Epidemiology and Scientific Support Bureau at 406-202-8866
- ☐ Attach any additional lab reports to case investigation in MIDIS
- ☐ Fax the Exposure Questionnaire on Cadmium to DPHHS 1-800-616-7460
- ☐ When done with MIDIS investigation, close the investigation

1 DISEASE REPORTING

1.1 Provider notification to Public Health Authorities

Any person, including, but not limited to a physician, dentist, nurse, medical examiner, other health care practitioner, administrator of a health care facility or laboratory, public or private school administrator, or laboratory professional who knows or has reason to believe that a case exists of a reportable disease or condition defined in the Administrative Rules of Montana (ARM) **37.114.203** must immediately report to the local health officer.

For more information on analysis and specimen collection, please contact the laboratory conducting the test.

1.2 Local Health Department Follow-up Responsibilities

Immediately after being notified of a case of a reportable condition, a local health officer must investigate per (ARM) **37.114.546** and **37. 114. 205**. See section 4.3 below.

Direct the case-patient or physician to Montana Poison Information Center Network (MPICN) (available 24/7) for more information , 1-800-222-1222.

1.3 Local Health Department Reporting to State Public Health Authorities

Total cadmium in urine $\geq$ 3 µg/L or total cadmium in blood ≥ 5 µg/dL must be reported to DPHHS within seven days.

2 THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Public Health Significance in Montana

DPHHS added cadmium poisoning to the reportable diseases list in 2020. Currently, little is known about the public health significance of cadmium exposure in Montana. Cadmium poisoning reporting and surveillance may determine cadmium sources of public health concern. The highest risk for workplace exposures occurs in occupations involved in heating cadmium-containing products, such as ore smelting operations, drying of cadmium pigments, and soldering and welding of cadmium-containing ores. Workers may have exposure to cadmium in the smelting of zinc, lead, and copper. Other exposures may come from working with fly ash, petroleum refining, and the manufacturing of batteries or plastics. Follow-up of identified cases will prevent continued or widespread exposure to cadmium sources amongst other workers or family members.

Cadmium is a naturally occurring element widely distributed in the earth's crust. Smelting metal ore can vaporize cadmium and concentrate cadmium in tailings. Cadmium can be a byproduct of zinc, lead, and copper production. Cadmium is also an impurity in iron, steel, cement, and phosphate fertilizers.

The primary use of cadmium, in the form of cadmium hydroxide, is in electrodes for Nickel-Cadmium (Ni-Cd) batteries. Because they last a long time and can be used in a wide range of temperatures, Ni-Cd batteries are used for starting and emergency power and in consumer products. Ni-Cd batteries are used in the railroad and aircraft industries, cordless power tools, cell phones, portable computers, and portable household appliances and toys. Cadmium is also used in photoelectric cells and semiconductors.

Cadmium-containing pigments may be used in various applications, including engineering plastics, glass, glazes, ceramics, rubber, enamels, and artist's paints; fireworks also use cadmium sulfide compounds due to their stability under a variety of environmental conditions.

Cadmium and cadmium alloys are corrosion resistant in alkaline or salt solutions; these alloys have a low friction coefficient and are conductive and solderable. These properties make them useful as engineered or electroplated coatings on iron, steel, aluminum, and other non-ferrous metals. These alloys are also durable, making them useful in solar cells, parts for the aerospace industry, industrial fasteners, electrical components, automotive systems, military equipment, and marine and offshore installations.

Cadmium is also produced from recycled material, such as Ni-Cd batteries, manufacturing scrap, and residues, such as cadmium-containing dust from electric arc furnaces. Recycling accounts for approximately 10-15% of the production of cadmium in developed countries.

2.2 Clinical Description of Illness

Cadmium is a heavy metal that causes adverse health effects at very low exposure levels. Cadmium affects many organ systems and induces toxicity following acute and chronic exposures. The degree and severity of effects depend on the amount of cadmium present. Toxicity is also related to the form of cadmium (cadmium oxide, cadmium chloride), the particle size (fume or aerosol), length of exposure, and route of exposure (i.e., humans more readily absorb inhaled cadmium than by ingestion.

Illness from acute exposure: Acute toxicity can occur following exposure to very high levels of cadmium in a short period. If the exposure is via inhalation, inflammation of the respiratory tree ensues, manifesting as bronchitis, pneumonitis, and pulmonary edema; pulmonary toxicity — seen primarily in occupational exposures — is often fatal. Ingestion of high doses of cadmium causes inflammation of the intestines, with symptoms of nausea, vomiting, abdominal pain, and diarrhea. Most persons recover from acute cadmium ingestion without complications.

Metal fume fever can also occur from inhalation of cadmium oxide fumes when cadmium metal and cadmium compounds are heated to high temperatures. Metal fume fever causes flu-like symptoms. Particle size is a more critical determinant of respiratory toxicity than chemical form (i.e., the smaller cadmium particles in fumes are more potent toxicants than the larger particles in dust).

Illness from chronic exposure: With chronic exposure, cadmium accumulates primarily in the kidneys, with smaller amounts accumulating in the liver and muscles. Kidney damage is the critical health effect associated with long-term cadmium exposure. The latency period between exposure and renal dysfunction may be >10 years. Cadmium damages the proximal tubules and is characterized by increased urinary excretion of low-molecular-weight proteins, including β2-microglobulin or intracellular tubular enzymes. This damage manifests clinically as proteinuria (protein in the urine). Over time, cadmium may also affect glomerular (filter) function. Skeletal complications, including osteoporosis (brittle or fragile bones) and fractures, may result from abnormal calcium loss in the renal tubules.

Bone disorders reported following chronic exposure to high levels of cadmium in food and water include osteoporosis (porous bones) and osteomalacia (adult rickets). In Japan, long-term ingestion of cadmium-contaminated water and food was associated with a crippling condition known as “itai-itai” (ouch-ouch) disease. The affliction is characterized by pain in the back and joints, adult rickets, and bone fractures.

Among cancers, the association with lung cancer is the strongest for cadmium via inhalation exposure. Cadmium exposure has been associated with prostate and kidney cancers.

Long-term cadmium inhalation exposure, at low levels, can lead to decreased lung function and emphysema. Cigarettes contain cadmium, and smoking can be an important source of exposure.
Cadmium is potentially neurotoxic and may cause testicular damage.

Cadmium affects many organ systems primarily by binding to proteins within cells and interfering with enzymes requiring zinc. Cadmium is similar to zinc in structure and function and may replace zinc in many physiological and enzymatic processes. The zinc/cadmium ratio influences cadmium toxicity and storage; zinc deficiency increases toxicity while adequate zinc levels can reduce cadmium-related tissue damage. Zinc deficiency and cadmium toxicity are more likely to occur in diets high in refined grains and flours because the zinc/cadmium ratio may be altered during the refining of grains.

Cadmium has no biological function in humans. Cadmium's biological half-life may be up to 38 years, accumulating in the liver and kidneys. A minimal amount is excreted in the urine.

Household residents (contacts) health effects
While there are few reports of cadmium poisoning in children, health effects are expected to be like those seen in adults (i.e., kidney, lung, and intestinal damage depending upon the route of exposure). These effects might mostly be seen in acute high-level exposure situations. Harmful effects on child development or behavior have not generally been observed in populations exposed to cadmium, but more research is needed [https://www.atsdr.cdc.gov/toxprofiles/tp5.pdf].

Children who do not get enough iron, calcium, zinc, or protein may absorb more cadmium from their diet. It remains unclear if cadmium causes congenital disabilities. A limited number of epidemiology studies suggest effects on birth weight, neurobehavior, and the developing immune system. However, further confirmation of these findings is needed. Studies in animals exposed to high levels of cadmium during pregnancy have harmful effects on the developing nervous system, leading to behavioral and learning deficits. Some animal data suggest that high cadmium exposures before birth can lower birth weight and affect the developing skeleton. However, dose levels used in these animal studies are higher than human exposures, and people may respond differently.

Pregnant women with low calcium, iron, or zinc levels may absorb more cadmium. Cadmium can be transferred to offspring through breast milk. Cadmium levels in breast milk can range from 5 to 10% of the levels in the mother's blood [https://www.atsdr.cdc.gov/toxprofiles/tp5.pdf].

3 CASE DEFINITION

3.1 Clinical Description

See Section 2.2.

3.2 Laboratory Criteria for Diagnosis

Confirmed

Total cadmium in urine $\geq$ 3 µg/L, or total cadmium in blood $\geq$ 5 µg/L. Only urine accurately reflects the total body burden of cadmium. Free cadmium is rapidly bound in the blood, and blood cadmium levels are useful only in the context of acute toxicity.

3.3 Case Classification

Confirmed

• A case with confirmatory laboratory test results for total cadmium in urine ≥ 3 µg/L, or total cadmium in blood ≥ 5 µg/L.

Probable

• A clinically compatible case, for whom a high index of suspicion exists (i.e., patient's exposure history regarding location and time) or an epidemiologic link exists between this case and a confirmed case.

Comment(s)

None.

4 ROUTINE CASE INVESTIGATION

In accordance with (ARM) **37.114.314** conduct an epidemiologic investigation to determine the source and possible cadmium exposure risks. Refer to the CDC/Agency for Toxic Substances and Disease Registry (ATSDR) Case Studies in Environmental Medicine (CSEM) on Cadmium Toxicity for additional resources related to cadmium investigation. Determine the information necessary to complete the investigation in MIDIS (See the CD Epi Exposure Questionnaire for Cadmium).

4.1 Confirm the Diagnosis

Review the laboratory results to confirm the diagnosis. Clinical signs and symptoms are not necessary to confirm elevated urine or blood cadmium levels.

4.2 Laboratory Requirements

See Sections 1.1 and 1.2.

4.3 Case Investigation

Public health recommendations for this investigation guideline are based on the ARMs and CDC.

Specific Control Measures

Per ARM **37.114.546**, "The health officer must gather information about the circumstances and nature of the exposure using forms developed by the department (See the CD Epi Exposure Questionnaire on Cadmium). The local health officer must ensure that the following actions are performed when a cadmium in urine ≥ 3 µg/L or total blood cadmium levels ≥ 5 µg/dL is reported. The health officer or health-care provider must provide:

(a) Counseling about health consequences of cadmium poisoning;
(b) Information about ways to eliminate cadmium exposure; and
(c) Referral of the case and household members potentially at risk of exposure to a healthcare provider for additional follow-up and urine-cadmium testing as appropriate.

4.4 Contact Investigation

Because environmental and occupational cadmium exposures may affect entire families, investigation of an individual should note whether there are additional family members (or workers) at risk of exposure to cadmium. If so, those family members or workers should be evaluated for elevated urine cadmium levels. This applies particularly to pregnant women and people who may become pregnant to protect fetuses, babies, and young children.

4.5 Environmental and Occupational Evaluation

See Sections 1.2 and 4.3(b). Conduct an environmental and occupational evaluation if an ongoing source of exposure is suspected (See the CD Epi Exposure Questionnaire on Cadmium).

5 CONTROL MEASURES

In accordance with (ARM) **37.114.501**, utilize the control measures (prevention tips) indicated in Section 6.2 for this disease. Contact the Epidemiology and Scientific Support Bureau for consultation and questions at 406-202-8866 or the 24-hour line 406-444-0273.

5.1 Case Management

See Section 1.2.

5.2 Contact Management

See Section 4.4.

5.3 Environmental and Occupational Measures

An environmental and occupational evaluation is appropriate if an ongoing source of exposure is not identified or if more than one case is associated with a venue, such as an occupational setting.

Depending on the situation, the Department of Labor and Industry (DLI) may assist with environmental investigations of public entities. The Occupational Safety and Health Administration (OSHA) may help with private and federal entities. The Billings MT OSHA contact is Art Hazen at 406-247-7494. A public entity is defined as any state or local government, department, agency, special purpose district, or other instrumentality of one or more state or local governments. Contact the Department of Labor and Industry (DLI) with any questions about public entities at 406-444-6543.

Employees should work with their employer to complete a First Report of Injury. The employer must submit the form to the company's worker's compensation insurer. The insurer will determine whether the injury or occupational disease is work-related and compensable. However, if the employee has issues working with their employer to receive compensation, they can contact the DLI at 406-444-6543 or visit their website for more information and resources http://erd.dli.mt.gov/work-comp-claims. Please refer to OSHA standard 1910.1027 – Cadmium for additional information on occupational monitoring.

There are many ways to minimize cadmium exposure in the workplace:
- Enclosure of processes that result in the production of cadmium oxide fumes;
- Use local exhaust ventilation and personal protective measures to minimize exposure to cadmium dust;
- Pay strict attention to workplace and personal hygiene to prevent chronic exposure.
- Prohibit smoking in work areas that use cadmium;
- Require air-supplied respirators in enclosed spaces where workers are welding on cadmium-treated metal or brazing with cadmium solders.

5.4 Special Circumstances

See Section 4.3

6 ROUTINE PREVENTION

6.1 Immunization Recommendations

N/A

6.2 Prevention Recommendations

Prevention of cadmium exposure:

1. Management involves stopping exposure to cadmium.
2. Advise workers to practice good occupational hygiene. Discuss concerns regarding cadmium and prevention of hazardous exposures at the workplace with the patient's employer or workplace health and safety representative. The employer should consult OSHA standard "1910.1027 - Cadmium" for detailed information on occupational cadmium exposure, including medical surveillance. Please see Section 5.3 above for additional means of preventing cadmium exposure in the occupational setting. Ensure the patient has adequate iron intake — iron deficiency enhances cadmium absorption in the gastrointestinal tract.
3. Advise a smoking patient to stop smoking quit line link. Cigarettes contain small amounts of cadmium that build up over time, especially in patients with a more diminutive stature, who might smoke more than average.

Common and less common sources of cadmium are described in the ATSDR Cadmium Toxicological Profile. Sources are described briefly on page 3 and at length on page 277 Cadmium tox profile link and summarized in the ATSDR Tox Guide pamphlet.

7 ESCALATION/ACTIVATION OF EMERGENCY OPERATIONAL PLANNING

These investigation guidelines are designed to assist local health jurisdictions in the steps and actions needed to report, investigate and control reported cases of cadmium poisoning. Suppose investigations or other reported cases of arsenic exposure appear to a cluster by person, time, and place. In that case, local health jurisdictions need to contact DPHHS under the Administrative Rules of Montana 37.114.314 and 37.114.315 so DPHHS can consider emergency operational escalation or activation under the Communicable Disease Annex to the DPHHS Emergency Operation Plan.

8 ACKNOWLEDGEMENTS

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9 REFERENCES AND ADDITIONAL INFORMATION

Important references:

A. ATSDR Case Study in Environmental Medicine Cadmium Toxicity https://www.atsdr.cdc.gov/csem/cadmium/docs/cadmium.pdf
B. Information for Health Care Professionals, Cadmium Exposure and Toxicity https://ldh.la.gov/assets/oph/Center-EH/envepi/Heavy_Metal/Documents/Cadmium_for_Health_Providers_Final_2017.pdf
C. Lewis, R. (2007). Occupational Exposures: Metals. In Joseph LaDou (Ed.) *Current Occupational and Environmental Medicine* (pp. 413-438). McGraw Hill Publishing.
D. *Cadmium and Cadmium Compounds* IARC monograph https://monographs.iarc.fr/wp-content/uploads/2018/06/mono100C-8.pdf
E. OSHA 1910.1027 – Cadmium https://www.ha.gov/laws-regs/regulations/standardnumber/1910/1910.1027

Resources for Adult Cases

A. Agency for Toxic Substances and Disease Registry (ATSDR) ToxGuide for Cadmium: A pocket guide on Cadmium sources, toxicity, health consequences, exposure, and biomonitoring, https://www.atsdr.cdc.gov/toxguides/toxguide-5.pdf
B. United States Department of Labor https://www.osha.gov/Publications/osha3136.pdf