Cadmium Toxicity
Investigative Guidelines
October 2019

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance
   1. To identify persons with elevated urine cadmium levels.
   2. To identify occupational exposures for follow-up with Oregon Occupational Safety and Health (OR-OSHA).

1.2 Laboratory and Physician Reporting Requirements
   Laboratories and providers must report any finding of detectable cadmium in urine to the Oregon Health Authority (OHA) within one working day.

1.3 Local Public Health Authority Surveillance and Investigation Responsibilities
   1. Provide OHA with any reports of elevated urine cadmium they receive.
   2. Assist in case investigations during public health emergencies or when routine OHA investigations identify potential exposure to a case’s household contacts or co-workers.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent and Sources
   Cadmium is a heavy metal found naturally in the environment, typically as a component of zinc ore deposits in the Earth’s crust.

   In modern times, cadmium has been widely dispersed into the environment through mining and smelting, as well as through use in certain fertilizers, presence in sewage sludge, and various industrial uses. Occupational exposure to airborne cadmium can occur among persons who work with metals containing cadmium. Cigarettes also contain cadmium and smoking is an important source of exposure. The primary source of cadmium in non-smokers is dietary; environmental deposition of airborne cadmium enters the food chain after being absorbed by plants, particularly leafy greens, root crops, cereals and grains. It can also be ingested through meats such as liver and kidney. A secondary source of cadmium exposure comes from some products meant to be applied to the lips such as lip gloss and lipstick.

   Cadmium has no biologic function in humans. There is also no effective method of elimination, so cadmium’s biologic half-life may be up to 38 years, and it
accumulates in the liver and kidneys over time. A very small amount is excreted in the urine.

2.2 Description of Illness

Cadmium creates reactive compounds inside cells that can damage DNA. The organs most affected by cadmium are the lungs, kidneys, and the skeletal system.

Acute toxicity can occur following exposure to very high levels of cadmium in a short period. Symptoms depend upon the route of exposure. If via inhalation, inflammation of the respiratory tree ensues, manifesting as bronchitis, pneumonitis, and pulmonary edema; pulmonary toxicity — which is 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 ingestion without complications.

Chronic exposure to cadmium has been associated with a variety of conditions. Renal tubular dysfunction is the most established consequence of chronic exposure. The latency period between exposure and renal dysfunction may be >10 years. Skeletal complications, including osteoporosis and fractures, may result from abnormal calcium loss in the renal tubules. Among cancers, the association with lung cancer is the strongest.

2.3 Treatment

No treatment exists for cadmium toxicity. Chelation is not recommended, as there is little circulating cadmium to be removed, and the chelation itself may be harmful. Management involves stopping exposure to cadmium. Patients should be advised to stop smoking, practice good occupational hygiene, and — because iron deficiency enhances cadmium absorption in the GI tract — ensure adequate dietary iron intake.

Persons with end-organ damage from cadmium should be under the care of a medical provider.

3. Diagnosis, Case Definitions and Laboratory Services

3.1 Diagnosis and Case Definitions

Urine, blood, and hair can be tested for cadmium. However, only urine accurately reflects the total body burden of cadmium. Free cadmium is rapidly bound in the blood, and levels are useful only in the context of acute toxicity.

The cadmium urine concentration at which follow-up would occur is 1.0 µg cadmium per gram of creatinine. This is supported by three sources: 1) It is approximately equivalent to the 95th percentile of the National Health and Nutrition Examination Survey data that reflect exposures in US metropolitan populations (CDC, 2019); 2) data from several human exposure studies indicate
that this concentration is observed with elevations in urinary low molecular protein excretion associated with early signs of kidney toxicity (as reviewed by the Agency for Toxic Substances and Disease Registry (ATSDR), 2012); and 3) the Centers for Disease Control and Prevention (CDC) indicates that adverse health effects could be expected above this concentration (CDC, 2017)

OR-OSHA and ATSDR both indicate $\geq 300 \, \mu g$ of beta-2-microglobulin per gram creatinine in urine is associated with adverse proximal tubular renal damage. Elevated beta-2-microglobulin urinary excretion is associated with proximal tubular renal damage resulting from several potential causes that include cadmium, mercury, lithium, or aminoglycoside toxicity or pyelonephritis. Therefore, the presence of both a repeat test elevated urinary cadmium and an elevated urinary beta-2-microglobulin test are required for a confirmed case of cadmium toxicity.
Suspect Case
• A person with initial detectable urine cadmium result as measured by ≥1.0 µg cadmium per gram creatinine.

Presumptive Case
• A person with detectable urine cadmium result as measured by ≥1.0 µg cadmium per gram of creatinine on repeat testing and >300 µg of beta-2-microglobulin per gram creatinine.

Confirmed Case
A person with detectable urine cadmium result as measured by either ≥1.0 µg cadmium per gram of creatinine and ≥300 µg per gram of beta-2-microglobulin on repeat testing and renal dysfunction, evidenced by proteinuria, Fanconi’s syndrome, recurrent kidney stones, or reduced glomerular filtration rate (GFR), without another underlying condition that explains the renal dysfunction.

No Case
• A person with detectable urine cadmium result as measured by <1.0 µg cadmium per gram of creatinine on repeat testing
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Confirmed Case
A person with urinary cadmium measured at $\geq 1.0 \, \mu g$ cadmium per gram of creatinine on repeat testing, $>300 \, \mu g$ of beta-2-microglobulin per gram creatinine, and renal dysfunction, evidenced by proteinuria, Fanconi’s syndrome, recurrent kidney stones, or reduced glomerular filtration rate (GFR), without another underlying condition that explains the renal dysfunction.

Presumptive Case
A person with detectable urine cadmium as measured by $\geq 1.0 \, \mu g$ cadmium per gram of creatinine on repeat testing and $>300 \, \mu g$ of beta-2-microglobulin per gram creatinine.

Suspect Case
A person with initial detectable urine cadmium as measured by $\geq 1.0 \, \mu g$ cadmium per gram creatinine.

No Case
A person with detectable urine cadmium as measured by $<1.0 \, \mu g$ cadmium per gram creatinine on repeat testing.

3.2 Services Available at the Oregon State Public Health Laboratory
Oregon State Public Health Laboratory does not perform urine cadmium testing.

3.3 Commercial/reference laboratory urinary cadmium testing
Specimens should be collected in an acid-washed and metal-free, trace-element-free plastic container. Specimens should be refrigerated. All specimens must be properly packaged in double containers with absorbent material around them.

Patients should be instructed to collect their first urine of the day which is usually the most concentrated.

4. ROUTINE CASE INVESTIGATION
OHA will conduct routine case investigation with medical provider and/or patient to ascertain location and duration of residence, occupational history, smoking history, and any other potential hobby and lifestyle exposures.

If exposure is likely to be occupational, OHA will notify the Oregon Occupational Safety and Health Division (OR-OSHA): 503-378-3272. Note that OR-OSHA investigates cases with a detectable urine cadmium result as measured by either $\geq 3.0 \, \mu g$ cadmium per gram of creatinine or $>300 \, \mu g$ per gram of beta-2-microglobulin.

LPHAs may be asked to assist in case investigations during public health emergencies or when routine OHA investigations identify potential exposure to a case’s household contacts or co-workers.
5. CONTROLLING FURTHER SPREAD

5.1 Education

Provide basic education about cadmium, as outlined above. Advise all individuals to stop smoking. If concerned about occupational exposure (including among hobbyists), advise the person to practice good occupational hygiene, including not eating in the workspace, ensuring proper ventilation, and where indicated, using appropriate personal protective equipment.

Additional resources are available from

- OHA’s Environmental Health Assessment Program  
  (www.healthoregon.org/ehap)
- National Institute for Occupational Safety and Health (CDC): Cadmium NIOSH Resources: http://www.cdc.gov/niosh/topics/cadmium/
- Occupational Safety and Health Administration  
  https://www.osha.gov/Publications/OSHA_3675.pdf

REFERENCES

2. CDC. 2017. Cadmium Biomonitoring Summary. Available at: https://www.cdc.gov/biomonitoring/Cadmium_BiomonitoringSummary.html

UPDATE LOG

October 2019 – Clarified case definition, criteria and roles for investigation (Cude).
May 2018 – Updated roles and responsibilities (Dreher).
May 2016 – Updated case definitions and added algorithm (Hines).
February 2016 – created (Hines).