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AT A GLANCE

Clinical Evaluation for Cadmium Exposure: A Simplified Approach

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Introduction

This document is for physicians and other licenced primary care providers (e.g., nurse practitioners) who require more information on identifying and managing potentially clinically relevant metals exposure in the community setting. This is a brief guide, and not intended to be comprehensive. It should not supersede specialist or urgent care referral, where clinical judgement dictates.

Public Health Ontario (PHO) has also developed documents for lead exposure and mercury exposure.

Step 1: Enquire About Relevant Exposures

An **exposure history** should capture potential exposure in the home, community, and at the workplace:

- First and second-hand tobacco smoke; for smokers, this is the major source of exposure.[1]
- Though food is the most common source of exposure for non-smokers, such exposure is unlikely to lead to clinical toxicity.[1,2] Where this has been historically observed (e.g., Taiwan, Bangladesh), it was associated with contamination from significant nearby industrial pollution.[1]
- Hobbies such as metallurgical work, art using pigments and glazes, and electronics.[1]
- Occupations at risk: work in sawmills and saw filing, automotive and machinery repair, plastics manufacturing, Ni-Cd battery work, welding and non-ferrous metal smelting and metallurgical work.[3]

Step 2: Assess for Expected Clinical Outcomes

- Inhalational exposures to high concentrations of cadmium fumes in certain occupations can cause an acute flu-like illness followed by chemical pneumonitis and acute lung injury.[1]
- Ingestion of high concentrations of cadmium (rarely reported) can cause symptoms of acute gastric irritation (nausea, vomiting, abdominal pain, diarrhea).[1]
- Chronic cadmium exposure in sustained high concentration exposures (occupational contexts for greater than 10 years[1]) can cause kidney dysfunction leading to decreased eGFR, proteinuria, nephrolithiasis, electrolyte losses (particularly calcium), and subsequent osteopenia, osteomalacia, and fragility fractures (known as “Itai-itai” disease).[1] The levels of cadmium in urine or blood that correspond to where these effects begin are available.[1] However, they range widely and are therefore difficult to interpret at the clinical level.[1]
- Any of the above exposures in the community setting would be rare.
- Cadmium is also a recognized carcinogen, linked to the development of lung, and possibly kidney and prostate cancers, in significantly exposed workers.[4]

Step 3: Determine What Testing Should be Performed

Urine and blood cadmium are biomarkers of choice, however testing should only be done if clinicians are prepared to interpret the results.

- Urine testing more accurately reflects body burden and may be helpful in assessing long-term historical cadmium exposures.[1]
- Blood cadmium may be useful to assess whether recent exposures (e.g., several months) have occurred.[1]
- Hair testing has not been shown to be a valid biomarker for cadmium exposure.[1,5]
- Testing after administration of a chelating agent (provoked urine testing) is not interpretable and should be avoided.[6,7]

Step 4: Interpreting Results

Reported laboratory reference ranges represent population averages, and are generally much lower than levels of toxicity. Dose related individual and population level clinical effects are found in Table 1 and Table 2.

- The first principle of management is identification and cessation of exposure. If there are no obvious occupational or environmental exposures present, then an elevated level is most likely secondary to tobacco smoke exposure.
- Levels above concentrations associated with adverse effects described in Table 2 may warrant additional testing to identify end-organ (kidney) damage. The most sensitive test is urine beta-2 microglobulin level, which can identify early subclinical proteinuria. Referral to a nephrologist and an occupational medicine specialist may be necessary for ongoing management.

Cadmium Concentrations Associated with Individual and Population Level Effects

The tables below describe corresponding biomarker levels and observed outcomes, at both the population and individual level.

Table 1a: Urinary Cadmium and Population Level Effects

Urine Cadmium Concentration (µg/g Creatinine)	Outcome – Population Level
0.2	Geometric mean of Canadians aged 3–79, 2018–2019[8]
0.35	Geometric mean in Canadian adult never-smokers, 2007–2011[9]
0.46	Geometric mean in Canadian adults exposed to second hand smoke, 2007–2011[9]
0.58	Geometric mean in Canadian adult smokers, 2007–2011[9]
1.9	Lowest 5th percentile at risk for renal dysfunction (from a modelled dose-response Benchmark Dose Level or BMDL5 for lowest 5th percentile of individuals with elevated beta-2 microglobulin elevation)[10]

Table 1b: Urinary Cadmium and Individual Level Effects

Urine Cadmium Concentration (µg/g Creatinine)	Outcome – Individual Level
<3	Low risk of renal impairment[1,11]
3–7	Elevated risk of renal tubular proteinuria[11,12]
5	ACGIH BEI,* based on earliest signs of subclinical renal dysfunction (elevated urine beta-2 microglobulin)[13]
>7	Medical removal from workplace (US OSHA*)[11]
<10	If pre-existing kidney disease, may be unrelated to cadmium exposure[1]
20-30	Average concentration in cadmium-related osteomalacia patients[14]

*ACGIH BEI: American Conference of Governmental Industrial Hygienists Biological Exposure Indices; US OSHA: United States Occupational Safety and Health Administration

Table 2: Blood Cadmium – Population and Individual Level Effects

Blood Cadmium Concentration (nmol/L)	Blood Cadmium Concentration (µg/L)	Clinical Effect
1.9	0.21	50th percentile in Canadians aged 3–79 (from 2018–19 CHMS[8]*)
14.2	1.6	Geometric mean in Canadian adult smokers, 2007–2011[9]
15.1	1.7	95th percentile in Canadians aged 3-79 (from 2018–19 CHMS[8])
44.4	5	Upper limit of ACGIH BEI;* earliest signs of subclinical renal dysfunction (elevated urine beta-2 microglobulin)[13]
48	5.4	Upper limit of laboratory reference range (smokers)[15]
88.9	10	Elevated risk of developing renal tubular proteinuria over the general population[11] Medical removal from workplace (US OSHA[11]*)
95–415	10.7–46.7	Concentration range for patients with Itai-Itai Disease (severe hypocalcemia)[14]

*CHMS: Canadian Health Measures Survey; ACGIH BEI: American Conference of Governmental Industrial Hygienists Biological Exposure Indices; US OSHA: United States Occupational Safety and Health Administration

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