

# ORAL FLUID TESTING FOR HEAVY METALS

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# FINANCIAL DISCLOSURES

- ① Employee of Western Slope Laboratory
- ① Pharmaceutical Sciences Advisory Board at University of Toledo
- ① Research Support Thermo Fisher Scientific



# OUTLINE

- ① Heavy metal definition
- ① Instrumentation and methods
- ① Advantages and consideration for oral fluid



# HEAVY METALS

- ⊙ loosely defined subset of elements that exhibit metallic properties
- ⊙ includes the transition metals, some metalloids, lanthanides, and actinides
- ⊙ There are twenty three metals that are deemed heavy metals



# HEAVY METALS

- ⊙ antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc



# IMPORTANT HEAVY METALS TO CLINICAL CHEMISTRY

- ⊙ arsenic, cadmium, copper, lead, mercury, and zinc
- ⊙ Aluminum though not a heavy metal can be quite toxic and is very abundant

# INSTRUMENTATION AND METHODS

- ⊙ There are three methods for testing for metals regardless of matrix:
  - ⊙ Atomic Absorption (AA)
  - ⊙ Inductively Coupled Plasma
    - Optical Emission Spectrometry (ICP-OES)
    - Mass Spectrometry (ICP-MS)

# ALUMINUM

- ⊙ Usually tested in blood, plasma, and serum
- ⊙ Has a very high LD50 and is not acutely toxic

AA	ICP-OES	ICP-MS
30ng/mL	20ng/mL	0.001ng/mL

- ⊙ Why test in oral fluid?
  - ⊙ Non-invasive and less risk of contamination
  - ⊙ With ICP-MS, the detection limits are lower



# ARSENIC

- ⊙ Usually tested in blood or urine (total arsenic)
- ⊙ US exposure limit of 35ng/mL

AA	ICP-OES	ICP-MS
300ng/mL	50ng/mL	0.001ng/mL

- ⊙ Why test in oral fluid?
  - ⊙ Non-invasive and less risk of contamination
  - ⊙ With ICP-MS, the preparation and detection limits are well below the needed limits for exposure in US
  - ⊙ Provide information on recent exposure

# CADMIUM

- ③ Usually test blood and urine

AA	ICP-OES	ICP-MS
1.5ng/mL	5ng/mL	0.0005ng/mL

- ③ Why test in oral fluid?
  - ③ The permissible limits are so low and the exposure result so vast that decreasing the detection limits would be beneficial.

# COOPER

- ③ Usually test blood and urine (24 hr collection usually)
- ③ MCL permissible levels are ~2mg/L

AA	ICP-OES	ICP-MS
3ng/mL (Cu <sup>2+</sup> )	5ng/mL	0.001-0.01ng/mL

- ③ Why test in oral fluid?
- ③ Ease of collection and correlation to plasma levels

# LEAD

- ⊙ Usually a blood test (US) or oral fluid (UK)
- ⊙ CDC 5 $\mu$ g/dL action level (children; lowered from 10 $\mu$ g/dL)

AA	ICP-OES	ICP-MS
10ng/mL	50ng/mL	0.0001-0.001ng/mL

- ⊙ Why test in oral fluid?
- ⊙ Non-invasive, inexpensive, and correlates to whole blood and plasma levels

# MERCURY

- ⊙ Usually tested for in blood and urine
  - ⊙ Ingestion limits between 0.002-1mg/L
  - ⊙ Harmful in all forms (organic, inorganic, elemental)

AA	ICP-OES	ICP-MS
145ng/mL	50ng/mL	0.001-0.01ng/mL

- ⊙ Why test in oral fluid?
  - ⊙ Ease of collection and correlation to plasma levels
  - ⊙ Repeat collection issues solved

# ZINC

- ⊙ Usually tested orally, in serum, plasma, hair, and urine
- ⊙ The US Recommended Daily Allowance is 15 mg

AA	ICP-OES	ICP-MS
1ng/mL	5ng/mL	0.001-0.01ng/mL

- ⊙ Why test in oral fluid?
  - ⊙ Simple without the subjective taste test
  - ⊙ Non invasive

Element	AAS Detection Limit (DL)	ICP-OES D. L.	ICP-MS D. L.
Antimony	40ng/mL	50ng/mL	0.0001-0.001ng/mL
Bismuth	50ng/mL	100ng/mL	0.0001-0.001ng/mL
Cerium	100µg/mL	50ng/mL	0.0001-0.001ng/mL
Chromium	0.5ng/mL	5ng/mL	0.003ng/mL
Cobalt	5ng/mL	5ng/mL	0.001-0.01ng/mL
Gallium	65ng/mL	50ng/mL	0.0001-0.001ng/mL
Gold	2ng/mL	5ng/mL	0.0001-0.001ng/mL
Iron	0.002ng/mL	5ng/mL	0.001-0.01ng/mL
Manganese	2ng/mL	1ng/mL	0.001-0.01ng/mL
Nickel	10ng/mL	5ng/mL	0.001-0.01ng/mL
Platinum	75ng/mL	50ng/mL	0.0001-0.001ng/mL
Silver	8ng/mL	50ng/mL	0.0001-0.001ng/mL
Tellurium	30ng/mL	50ng/mL	0.001-0.01ng/mL
Thallium	20ng/mL	50ng/mL	0.0001-0.001ng/mL
Tin	95ng/mL	50ng/mL	0.001-0.01ng/mL
Uranium	40µg/mL	500ng/mL	0.0001-0.001ng/mL
Vanadium	50ng/mL	5ng/mL	0.001-0.01ng/mL



# METHODS FOR ORAL FLUID

- ◎ Currently, there is one method for oral fluid heavy metals testing that has been accepted:
  - ◎ Lead
    - In the UK, this is a routine test though several different methods exist with varying efficiencies
    - In the US, there is one patented method for ICP-MS
- ◎ There is research into the other areas of heavy metals testing beginning those with the largest public health concern
  - ◎ Mercury and Aluminum





# RISK OR PITFALLS OF SALIVA METALS

- ⊙ Not all metals partition into the saliva
  - ⊙ Rate of transfer into the plasma is the determining effect
  - ⊙ Affected by binding to red blood cells and blood proteins
- ⊙ Correlation studies need to be completed in order to draw clinical conclusions about the saliva metals result
  - ⊙ And correlation needs to be statistically significant



# THINGS TO CONSIDER WHEN DOING OF METALS

- ① Age of average donor
- ① Volume needed for accurate measure
- ① Device metal content
- ① Internal standards and industry standardization
- ① Sample preparation steps and optimization
- ① Instrumentation



# PROFICIENCY TESTING

- ⊙ Programs exist for hair, urine, serum, and whole blood
- ⊙ There has been inquiries for saliva heavy metal proficiency testing programs

# SUMMARY

- ① Oral fluid can be beneficial for metals testing
  - ① Same sample size
  - ① Non-invasive
  - ① Relationship to blood levels
- ① Method exist for lead; mercury and aluminum to follow
- ① Need for proficiency testing program