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A Case of Lead Poisoning from Traditional Medicines: Investigation, management, and solutions through multi-level public health collaboration

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Howard Shapiro, Anna Miranda (Toronto Public Health)

Bobbie Chiu, Celina Bak (Health Canada)

April 26, 2022

PHO Rounds

Learning Objectives

By the end of this session, participants will be able to:

1. Describe the clinical features of lead poisoning and possible sources of exposure to lead.
2. Describe potential health risks from Ayurvedic and other unregulated treatments.
3. Discuss the role of different health and regulatory partners in investigating natural products implicated in adverse health outcomes, using a case of lead poisoning in Ontario.

Outline

A case of lead poisoning from 3 vantage points

- Part 1: The referral (Public Health Ontario)
- Part 2: Investigating the source (Toronto Public Health)
- Part 3: Widening the scope (Health Canada)
- Part 4: Conclusions

Conflict of Interest

- None to declare

The case referral

- JinHee Kim, MD, MPH, CCFP, FRCPC - Physician Lead, Environmental and Occupational Health (EOH)
- Vincent Spilchuk, MD, FRCPC, MScCH - Occupational Medicine Consultant, EOH
- Rena Chung, Manager, MES, DABT - Director, EOH

Acknowledgments

- Dr. Howard An, Unity Health
- Dr. Margaret Thompson, Ontario Poison Centre
- Ministry of the Environment, Conservation and Parks Laboratory
- Office of the Chief Medical Officer of Health

The case referral

- A 37 year-old previously healthy woman presented to hospital for a third time in the last 4 weeks, with persistent abdominal pain, nausea and vomiting, dark stools, constipation, and fatigue which started a few days prior to her first visit.
- The initial workup identified normocytic anemia (Hb 67g/L, improved with transfusion) and a normal CT abdomen.
- Subsequent workup included **hospital admission, upper and lower endoscopy, bone marrow biopsy, and diagnostic laparoscopy**, where the gynecologist drained a simple cyst and resected possible endometriosis. Otherwise no clear cause was identified.
- After her extensive workup she was sent home with pain medications and referred to Internal Medicine as an outpatient.

The case (cont'd)

- At follow up, her abdominal pain and nausea were improving, but she reported worsening fatigue, shortness of breath, headaches, and tinnitus.
- The clinician enquired about potential exposures.
  - She was married, lived with her husband in a condo, worked in an office setting. They had no children and were trying to conceive. She did not consume any alcohol in the past year and was a non-smoker.
- She noted being prescribed medications from an Ayurvedic practitioner over the last year for infertility treatment.
- Physician ordered a blood lead level (BLL):
  - 47.8 ug/dL (2.31 umol/L), 55 ug/dL (2.69 umol/L) on repeat testing.
  - 95th percentile of CHMS Cycle 6 was 2.3 ug/dL (0.11 umol/L); geo mean 0.81 ug/dL (0.04umol/L).
  - She was chelated and her levels declined to 22.8 ug/dL (1.1 umol/L), with improvement in symptoms.

Health Canada. Sixth report on human biomonitoring of environmental chemicals in Canada. Ottawa, ON: Her Majesty the Queen in Right of Canada, represented by the Minister of Health; 2021. Available from: https://www.canada.ca/content/dam/hc-sc/documents/services/environmental-workplace-health/reports-publications/environmental-contaminants/sixth-report-human-biomonitoring/pub1-eng.pdf

Key features of lead poisoning

- Clinical lead poisoning presents with non-specific symptoms. An exposure history is key to differentiating lead from other more common causes.
- Depending on severity of poisoning, symptoms may include:
  - Abdominal pain, ranging from occasional discomfort, to diffuse pain, to “lead colic” (severe, intermittent abdominal cramps)
  - Constitutional symptoms, primarily fatigue and malaise
  - Musculoskeletal symptoms, including arthralgias and myalgias
  - Neurological dysfunction including tinnitus, headaches, poor concentration and peripheral motor/sensorimotor neuropathy

Poll: What is the most common source of lead poisoning in adults?

- ❑ Munitions (handling bullets)
- ❑ Drinking water
- ❑ Spices
- ❑ Ayurvedic medicines

258. Lead toxicity: A systematic review of recently published cases

Howard H An[1], Mila Luchak[3], Ray Copes[2]

[1]*Ontario Poison Centre, Toronto ON Canada,* [2]*Public Health Ontario, Toronto ON Canada,* [3]*University of Alberta, Edmonton AB Canada*

Results: Among 1287 articles identified, 129 cases of lead toxicity were included in the study. Patients were largely male (57%, 8.5% unreported) with an average age of 34.5 years (range 0.5 to 84 years) with 83% of patients aged 18 or over. Mean lead levels were 105.1 mcg/dL. Mean time from first exposure to presentation was 5 years 11 months with 19.3% of cases presenting within 3 months of initial exposure (acute exposure). The most common presenting symptoms were abdominal pain or discomfort (58%) and other gastrointestinal symptoms (53%) including nausea, vomiting, and constipation. The most common exposures were bullets/gun shot wounds (20%), Ayurvedic medications (19%), contaminated substances of abuse (13.1%), and paint chips (11.6%). Common lab abnormalities included anemia (62.8%) and basophilic stippling (47.3%). Among cases with lead levels above 70 mcg/dL, 13 of 13 cases (100%) with acute exposure presented with abdominal pain whereas 23 of 38 cases (60.5%) with longer exposure times presented with abdominal pain. Among cases with lead levels above 50 mcg/dL, 13 of 15 acute exposure cases (86.7%) underwent chelation therapy and 30 out of 42 chronic exposure cases (71.4%) underwent chelation therapy.

Source: An HH, Luchak M, Copes R. 258. Lead toxicity: a systematic review of recently published cases. In: 2015 Annual Meeting of the North American Congress of Clinical Toxicology (NACCT). Clin Toxicol. 2015;53(7):757-8. Available from: https://doi.org/10.3109/15563650.2015.1071025

Lead and Ayurveda

- Ayurveda is a form of traditional medicine originating in India and South Asia.
- In addition to lifestyle modification and other therapies, Ayurvedic medicine can also involve the ingestion of preparations that have been documented to contain heavy metals, particularly lead, mercury and arsenic.
- Lead toxicity from Ayurvedic medicine use has been documented in Canada and the United States. A systematic review from 2015 looking at recently published cases of lead toxicity (2004-2014) found that of the 129 reported cases, 25 (19%) were attributed to Ayurvedic medicine consumption. This source was second only to munitions exposure, which was implicated in 20% of cases.

Saper RB, Phillips RS, Sehgal A, Khouri N, Davis RB, Paquin J, et al. Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. JAMA. 2008;300(8):915-23. Available from: https://doi.org/10.1001/jama.300.8.915

An HH, Luchak M, Copes R. 258. Lead toxicity: a systematic review of recently published cases. In: 2015 Annual Meeting of the North American Congress of Clinical Toxicology (NACCT). Clin Toxicol. 2015;53(7):757-8. Available from: https://doi.org/10.3109/15563650.2015.1071025

Lead and other unregulated medicines

- Lead contamination has been identified in other unregulated medicines, as well as other privately imported products commonly sold by weight (e.g., spices, illicit drugs)
- Several previous Health Canada advisories regarding lead-contaminated traditional medicines were identified from 2005, 2006, 2008, 2015, 2016, and 2019.

Ontario Agency for Health Protection and Promotion (Public Health Ontario), Spilchuk V. Fact sheet: lead exposure from Ayurvedic medicines. Toronto, ON: Queen's Printer for Ontario; 2019. Available from: https://www.publichealthontario.ca/-/media/Documents/F/2019/fact-sheet-lead-ayurveda.pdf?sc_lang=en

Sources of lead exposure

- Population-level
  - Food
  - Dust
  - Water
- Less common, individual-level:
  - Occupation (e.g., metallurgy, metal extraction/processing, law enforcement)
  - Hobbies (e.g., stained glass; casting weights, shots; shooting ranges)
  - Traditional remedies/cosmetics (e.g., Ayurvedics, surma/kohl)
  - Paint chips, lead dust
  - Consumer products (e.g., some jewelry, toys)
  - Imported candies and foods
  - Lead-glazed ceramics, china, and leaded crystal, pewter
  - Pica

Ontario Agency for Health Protection and Promotion (Public Health Ontario), Spilchuk V. Fact sheet: lead exposure from Ayurvedic medicines. Toronto, ON: Queen's Printer for Ontario; 2019. Available from: https://www.publichealthontario.ca/-/media/Documents/F/2019/fact-sheet-lead-ayurveda.pdf?sc_lang=en

Clinical versus population health effects of lead – An important distinction

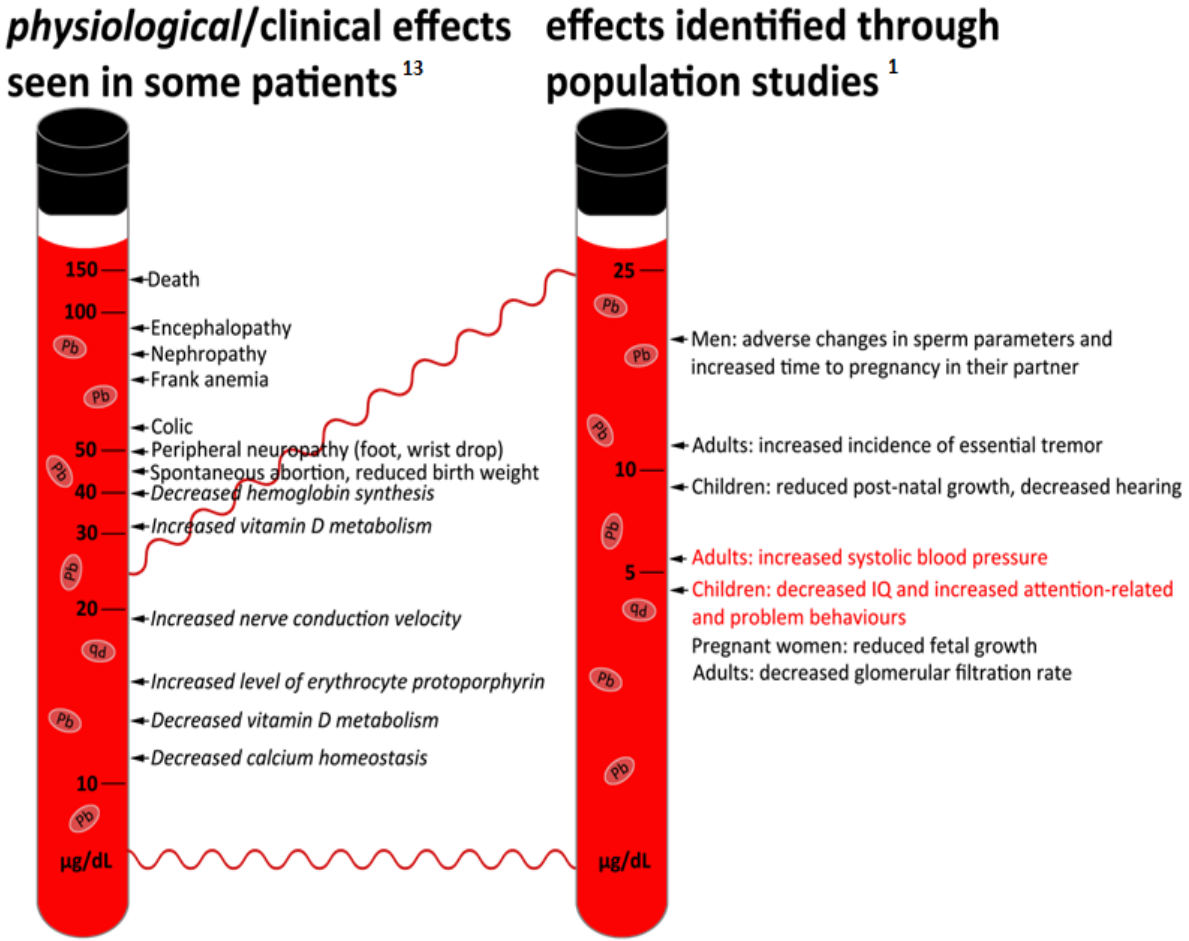


Figure 1: Health effects at varying blood lead levels.
(Modified from WHO 2010, US Dept of Health and Human Services 2012, Health Canada 2013, National Toxicology Program 2012)

Lead working group. Blood Lead Testing – Indications and Interpretation: A guide for health care providers. [Unpublished draft]. Lead Working Group. June 2014.

Continued decline in population BLLs 1970s to present

	1970s	Now
Canada	**66% <10 µg/dL** **22% 10-19 µg/dL** **3% 20-29 µg/dL** 3+ years 1978-1979 CHS	**0.81 µg/dL** 3-79 years 2018-2019 CHMS Cycle 6
U.S.	**13.9 µg/dL** 6 mos-74 years 1976-1980 NHANES	**0.75 µg/dL** ≥1 year 2017-2018 NHANES

Statistics Canada, Health and Welfare Canada. The health of Canadians: report of the Canada Health Survey. Ottawa, ON: Government of Canada; 1981. Available from: https://publications.gc.ca/collections/collection_2016/statcan/CS82-538-1981-eng.pdf

Annest JL, Mahaffey KR, Cox DH, Roberts J. Blood lead levels for persons 6 months-74 years of age: United States, 1976-80. Adv Data. 1982;(79):1-23. Available from: https://stacks.cdc.gov/view/cdc/84781

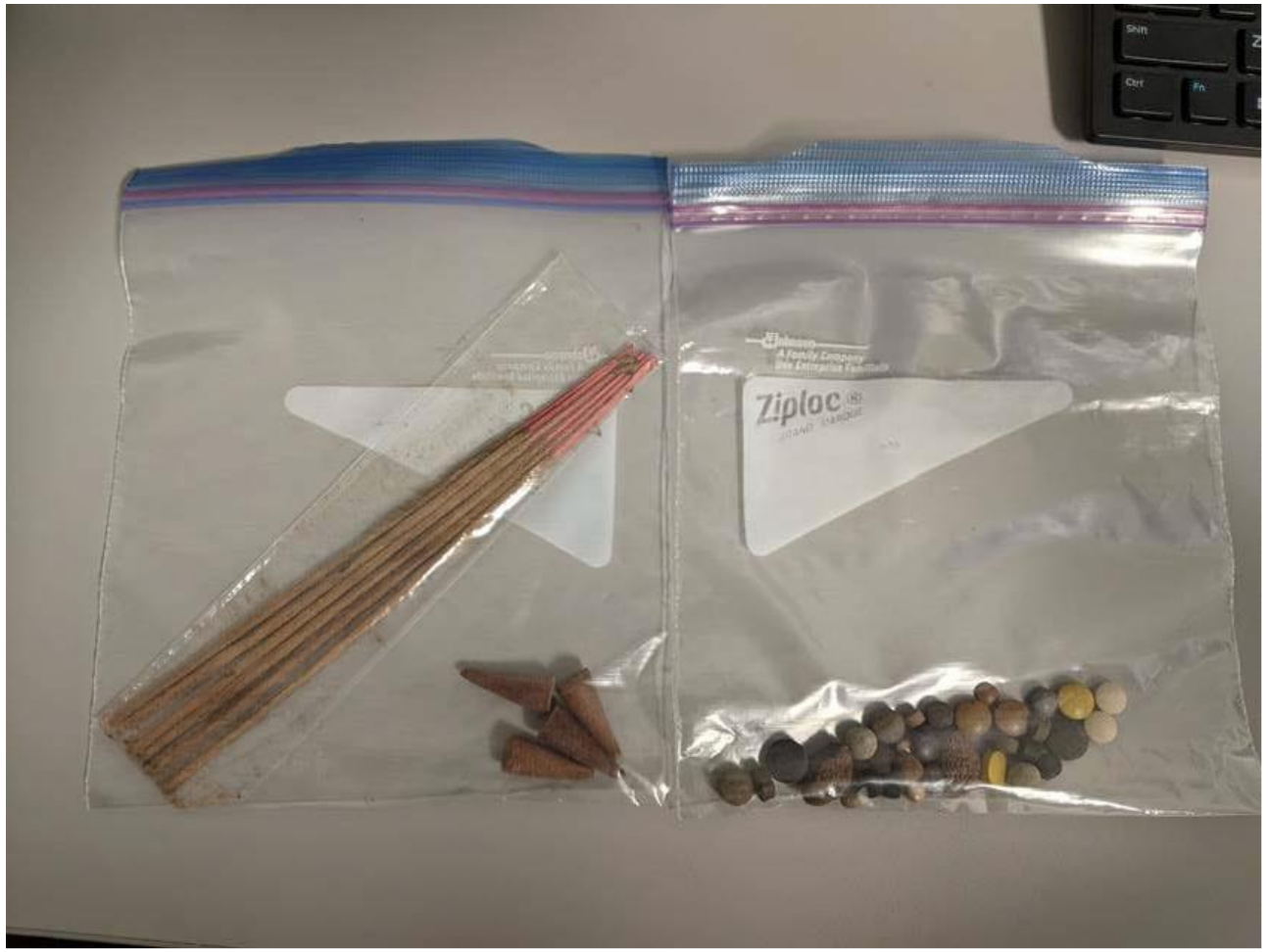
Health Canada. Sixth report on human biomonitoring of environmental chemicals in Canada. Ottawa, ON: Her Majesty the Queen in Right of Canada, represented by the Minister of Health; 2021. Available from: https://www.canada.ca/content/dam/hc-sc/documents/services/environmental-workplace-health/reports-publications/environmental-contaminants/sixth-report-human-biomonitoring/pub1-eng.pdf

Centers for Disease Control and Prevention. National report on human exposure to environmental chemicals [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2022 [cited 2022 Apr 26]. Biomonitoring data tables for environmental chemicals, blood lead (2011 - 2018), CAS number 7439-92-1. Available from: https://www.cdc.gov/exposurereport/report/pdf/cgroup2_LBXBPB_2011-p.pdf

Back to the case

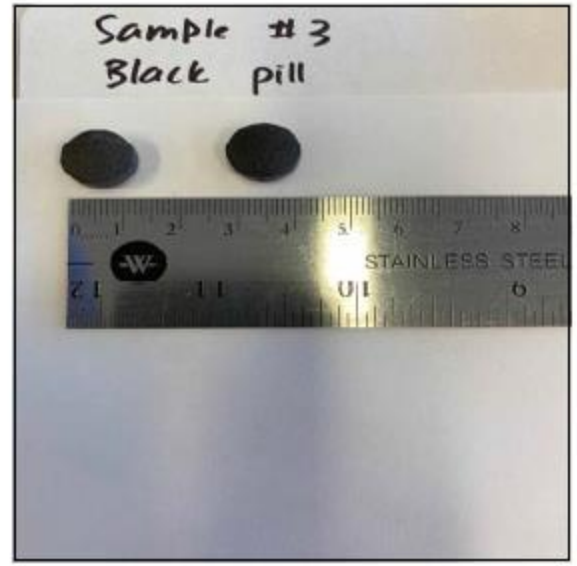
- The clinician was connected to the EOH team at PHO through the Ontario Poison Centre to facilitate testing of the Ayurvedic medications, to confirm the source.
- 19 samples were tested (including 2 types of incense provided to case by practitioner)
  - 11 contained lead levels greater than the detection limit
  - One pill's lead concentration was 129,000 ppm (i.e., almost 13% lead by weight).
- A screen for mercury was positive, leading to quantitative testing
  - 4 pills were between 7,900 and 33,000 ppm mercury (i.e., between 0.8 and 3.3% mercury by weight).
- PHO referred the situation to Toronto Public Health to consider an investigation
  - PHO provides scientific and technical advice to the Ontario government and the health care system – does not determine policy or regulate

Samples obtained from patient/delivered to PHO




Sample #1
Brown pill


Sample #2
Yellow pill


Sample #3
Black pill


Sample #13
Brown pill


Sample #14
Small black pills


Sample #15
Small reddish pill

Investigation of lead poisoning from traditional medicines: a local public health perspective

Anna M. Miranda MES, BASc, CPHI (C)

Associate Director, Healthy Environments

Toronto Public Health

Polling Question

- Have you ever been involved in an investigation involving lead in traditional medicines?

  - ❑Yes
  - ❑No
  - ❑Don’t know

- Notified by PHO of a case of lead poisoning in a 30 year old female taking Ayurvedic medicines for fertility reasons
- With our legal counsel - reviewed relevant legislation to determine which bodies could take which actions
- TPH using the HPPA had limited and specific authority (only remove the specific items that are a “health hazard” based on reasonable and probable grounds)
  - e.g. only pill type(s) tested and found to contain lead
- Health Canada- broader legal authority; able to remove natural health products not licensed for sale in Canada
- TPH MOH and Communications notified of investigation
- CMOH notified – issued letter to all ON local public health units

- Interviewed case to determine other potential sources of exposure
- Joint inspection conducted by TPH with Health Canada
- Toronto legal advised to obtain client information, using s. 41 under the HPPA (rights of entry and powers of inspection), by making copies or taking photos while in the premises (advised against removing the book)
- 203 photos were taken of every page in the “client book”, names and phone numbers only, text was written in a dialect/language that could not be deciphered
- Client names dating back to 2019
- Prepared a line list, 173 clients identified (some outside Toronto)
- Agreement with other health units that TPH would follow-up with all clients and share outcome/resources
- Advised practitioner of our investigation and “next steps”

- Rave Alert (text followed by robocall) sent to 173 contacts
- Text alerted client that they would be receiving a phone call from TPH
- Robocall message advised clients of the investigation, directed them to TPH's specific webpage and requested they contact TPH
- Successfully reached 163 (answered phone, went to voicemail)
- 10 contacts were not reached (line out of service, line busy or no answer)
- Only 3 clients proactively contacted TPH
- After the Rave Alert a team of 3 Public Health Inspectors (2 Tamil speaking) called every client on the line list
- TPH did not learn of any other elevated blood leads in clients of clinic
- Lead poisoning not reportable in Ontario; clients would have to volunteer information

Materials developed to support this investigation

- Workflow process to ensure clarity and consistency throughout this investigation
- Q and A's to support TPH staff
- Checkmarket Survey completed by Toronto Health Connections to triage calls to TPH
- Checkmarket Survey completed by Public Health Inspectors to document client interviews
- Line list with client names and contact information
- Spreadsheet to track all documentation
- Letter to Physicians in the community
- Toronto Public Health (TPH) Webpage, with link to the Health Canada Advisory
- Article in Communique Newsletter for Physicians in Toronto
- Dedicated shared drive folder "Lead and Ayurvedics Investigations Materials" to centrally store all information including all investigation materials and resources, documentation, photos

- Initial list started with 173 client names, final list has 191 client names
- 155 clients were interviewed (Check market survey completed)
- Clients were: 1. advised to discard any remaining pills/powders; 2. asked if they had experienced any signs/symptoms; 3. offered a copy of the MD Letter; 4. provided with a link to out TPH Webpage which further directs them to the HC Advisory.
- 36 clients were "lost to follow-up" (PHI's reached out on 3 separate days at 3 different times, no response).
- 66% clients indicated that they did purchase/obtain product from this Operator
- 21 clients indicated that they had been ill (leg pain, increased urination, loss of appetite, hair loss, memory loss, fatigue, headache)
- 37% of clients (including some who indicated they were never ill) were provided with an MD Letter
- 2-3 indicated that they obtained product from "another location". Referrals made to Health Canada and the local PHU for follow-up.

Helpful “take aways”

- Understand relevant legislation in order to determine their use in the investigation
- Collaboration and communication with internal and external partners
- Important to build a rapport and trust with clients (i.e., language, cultural, credible information)
- Dedicated investigation team to build expertise and ensure consistency in approach
- Materials to be available in language(s) appropriate for the clients (i.e., Punjabi, Urdu, Tamil and Hindi)
- Centralized repository of all investigation materials and resources, documentation, photos readily accessible to staff to support them during the investigation

Thank you

- Nicole Pyndiura
- Niratha Kanagaratnam
- Sudharsun Vettivelu
- Reg Ayre
- Dr. Rita Shahin
- Dr. Howard Shapiro

Health Canada Santé Canada

Canada

Compliance and Enforcement of Unauthorized Ayurvedic Products

Collaboration with Public Health Ontario and Toronto Public Health

Regulatory Operations and Enforcement Branch (ROEB)
Health Product Compliance Directorate (HPCD)
Health Product Compliance and Enforcement Program (HPCE)

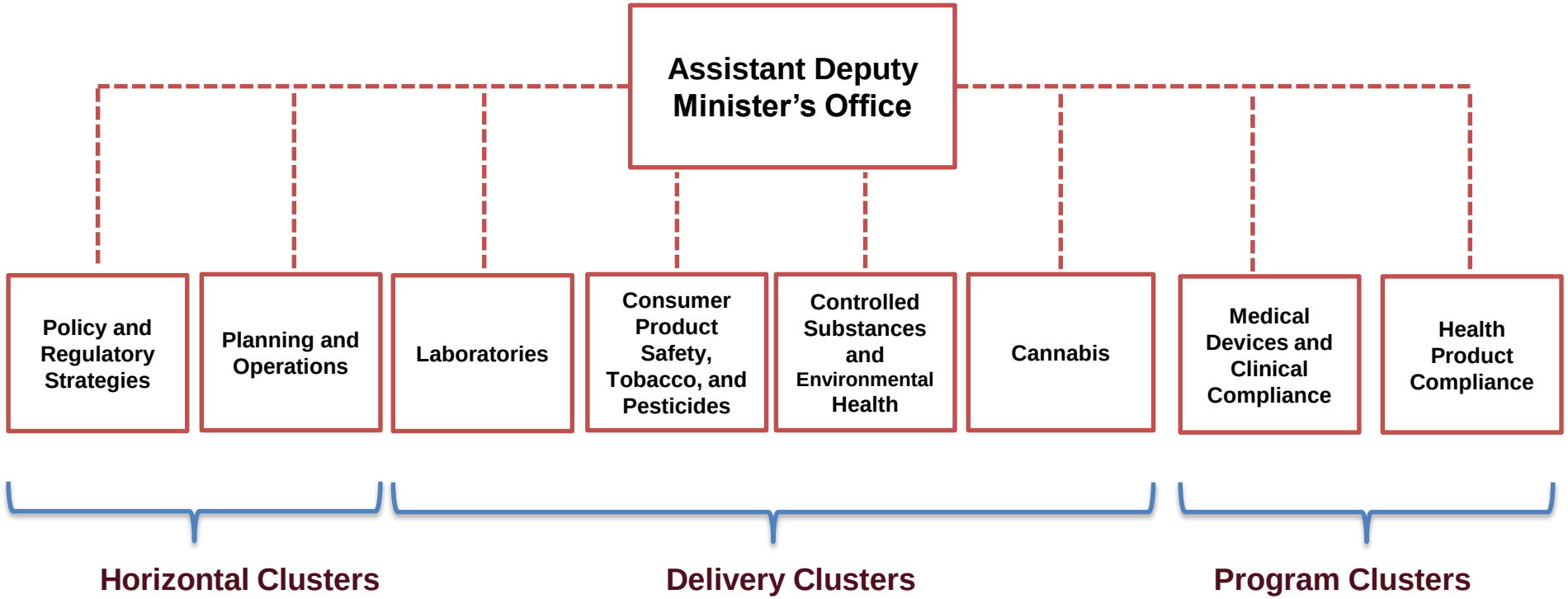
April 26, 2022

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Agenda

1. Overview of the Branch, Directorate and Division
2. Compliance Verification Process (Reactive vs. Proactive)
3. Ayurvedic Products
4. Case for Kerela Ayurvedic
5. The Path Forward

Regulatory Operations and Enforcement Branch



Health Product Compliance Directorate

The Health Product Compliance Directorate (HPCD) is one of 8 directorates in the Regulatory Operations and Enforcement Branch (ROEB) of Health Canada.

We are a virtual organization with over 200 employees located from coast to coast; our staff work at locations in:

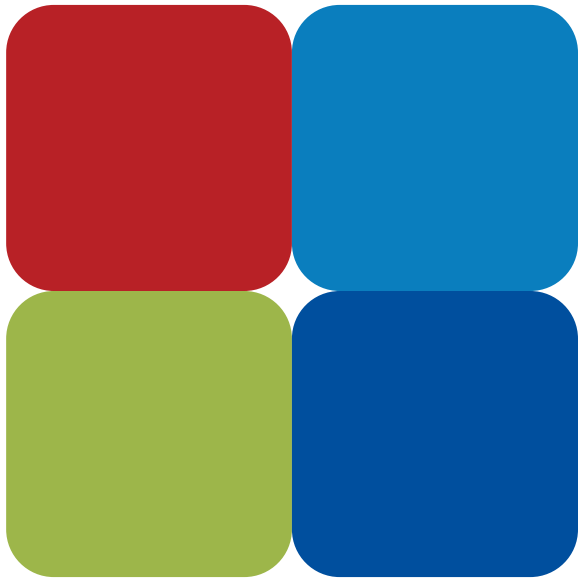
- Burnaby
- Calgary
- Edmonton
- Winnipeg
- Hamilton
- Toronto
- Mississauga
- Scarborough
- Ottawa
- Longueuil
- Halifax
- St. John’s

Health Product Compliance and Enforcement Program

- The Health Product Compliance and Enforcement (HPCE) Program is responsible for verification, monitoring and generation of compliance in the area of drug products and natural health products.

- Several key principles guide the work of the HPCE Program including
  - A risk-based compliance and enforcement approach to mitigating risk whereby the intensity and timeliness of action is proportional to the regulatory non-compliance and/or risk;
  - An integrated approach to the management of the risks and benefits of health products; and
  - A predictable, uniform, and national approach to enforcement.

Reactive Approaches to Non-Compliance



Triage

Based on complaints from internal / external partners (ex: public, industry, international partners or sister directorates)

Engage Internal Program Partners for Decision Making

Risk Assessment, Shortage Considerations etc.

Compliance and Enforcement Action and Communication

Includes stop sales, seizures, recalls and risk communication targeting public (informing them of risks)

Compliance Monitoring and Promotion

Monitors trends of non-compliance to determine appropriate long term mitigation measures
Promotion of key compliance and enforcement areas where trends show industry could use further guidance

- **What number would appear on an ayurvedic product that is authorized to be marketed in Canada?**

  a. DIN

  b. DIN-HM

  c. NDC

  d. NPN

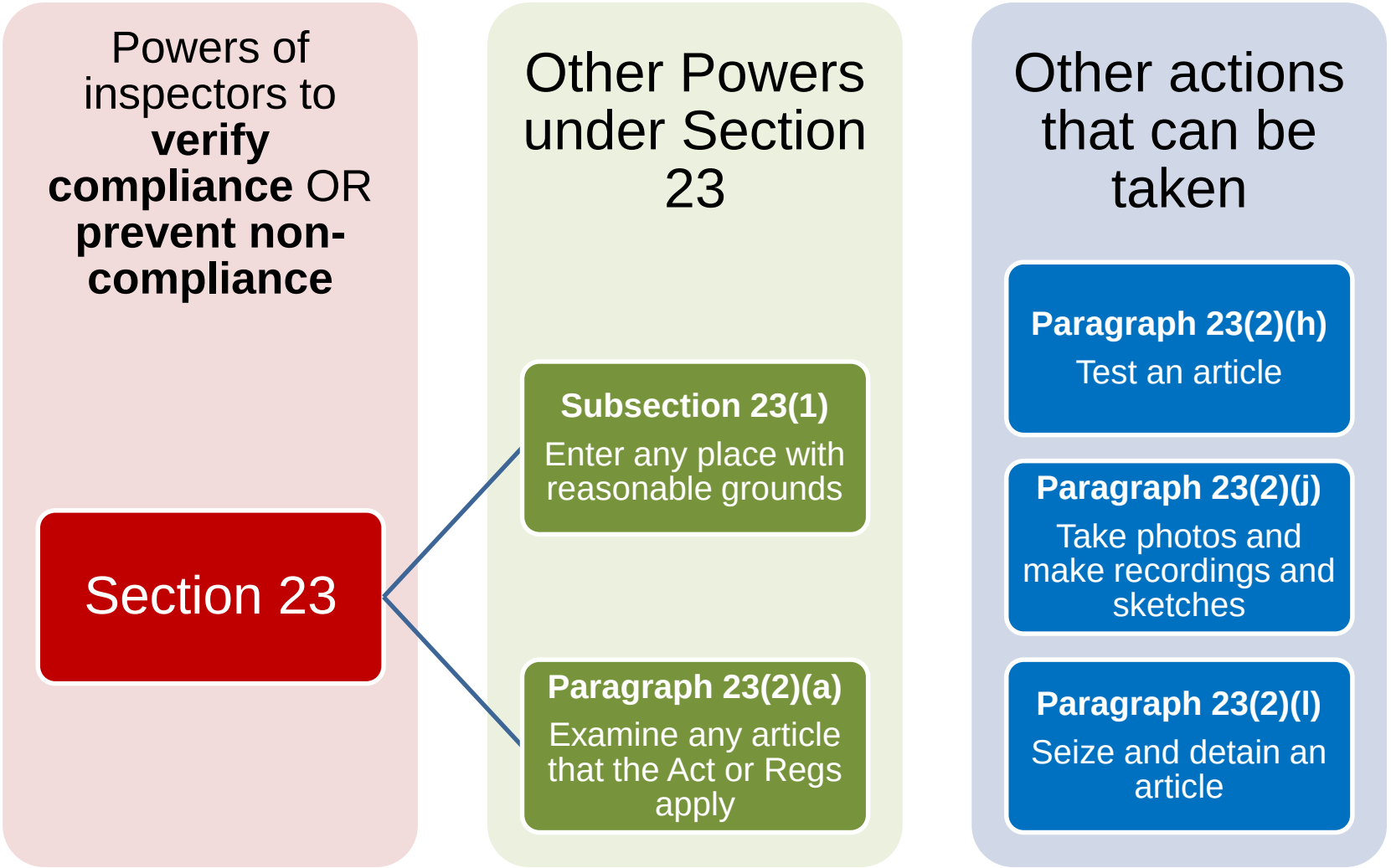
Ayurvedic medicine

- A form of traditional medicine originating in India and South Asia
- They are health products containing herbs, minerals and metals
- Documented to contain lead, mercury and arsenic
- Products are often imported into Canada for sale
- Classified as Natural Health Products (NHP) in Canada
- Sale in Canada require licensing (Product & Site Licences)
- Improper manufacturing processes may lead to high levels of heavy metals in final product

Natural Health Products (NHPs)

- NHPs are naturally occurring substances used to restore or maintain good health.
- They include probiotics, herbal remedies, vitamins and minerals, homeopathic medicines, traditional medicines, other products like amino acids and essential fatty acids
- NHPs are assessed by Health Canada before they can be sold
- NHPs require a **Product Licence** and companies require a **Site Licence** to manufacture, package/label or import NHPs
- Requirements detailed in the *Natural Health Products Regulations*

Powers of inspectors under the *Food and Drugs Act*



Kerela Ayurvedic & Natural Herbal Consultation

Verification

- Verified complainant info
- No compliance history of firm
- Importing, manufacturing vs compounding

Inspection

- Joint site visit with TPH inspector
- Seized unauthorized health products
- Informed responsible party of requirements

Testing

- Sampled 15 products for laboratory analysis
- 14 products were above limits for arsenic, mercury, and lead

Product photos

Kerela Ayurvedic & Natural Herbal Consultation …2

- HC issued a Public Advisory warning of risk of products sold at the location – Advisory made available in Hindi, Punjabi, Tamil and Urdu
- Public Advisory updated after results received from lab testing
- Further verification confirmed the clinic is no longer in operation
- TPH's engagement with the clinic's clients resulted in additional sites that may be offering unlicensed NHPs for sale
- No compliance issues were found at those sites

Recalls and safety alerts

Public advisory

Health Canada warns that products sold by Kerela Ayurvedic & Natural Herbal Consultation in Toronto, ON, may pose serious health risks

Last updated: 2022-02-01

Summary

Product: Unauthorized Ayurvedic medicinal products sold by Kerela Ayurvedic & Natural Herbal Consultation in Toronto, ON. Health Canada received a report of heavy metal poisoning following use of products obtained from this clinic.

Issue: Health products - Product safety
Health products - Unauthorized product

What to do: Stop using products sold by this clinic. Consult a health care professional if you have used any of these products and have health concerns. This Advisory is also available **on request** in Hindi, Punjabi, Tamil, and Urdu.

- **Which activities related to natural health products do Health Product Compliance Directorate (HPCD) of Health Canada *not* regulate?**

a. Manufacturing

b. Compounding

c. Distributing

d. b and c

Our Path Forward

Foster Partnerships

With our various partners to align key concerns and to jointly develop strategies to target those concerns.

Develop Strategies to be as Proactive as Possible

Continue to promote the use of proactive risk management projects to attempt to identify upcoming issues

Communicate

Continue to communicate regularly with the public, program partners, internationally and sister programs

Contact Us

Health Products Compliance and Enforcement Program

hc.hpce-cpsal.sc@hc-sc.gc.ca

Recalls and Safety Alert Database:
https://healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php?cat=3

Health Product Complaint Form:
https://healthycanadians.gc.ca/apps/radar/MD-IM-0005.08.html

Other Regulatory Operations and Enforcement Programs

Cannabis Reporting Form
https://health.canada.ca/en/health-canada/services/drugs-medication/cannabis/recalls-adverse-reactions-reporting/reporting-form.html

Medical Device Complaint Form:
https://health.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/problem-reporting/medical-device-consumer.html

Conclusions

- Lead poisoning can be an elusive diagnosis
- Clinical management focuses on exposure elimination, monitoring and appropriate treatment for identified cases of lead poisoning
  - Public health can be consulted on possible environmental investigation
- Public health intervention is focused on identifying others in the community who may be exposed including those who may need clinical management, and removing the source of exposure
  - Multiple jurisdictions may have a role (local, provincial, federal)
  - The investigation and management strategy may vary depending on situation