A cluster of lead poisoning among consumers of Ayurvedic medicine

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Background: Use of alternative medications and herbal remedies is widespread in the United States and across the globe. These traditional medications can be contaminated with toxic metals. Despite several case reports of poisoning from such contamination, the epidemiological data are still limited.
Objectives: To report on a cluster of lead and mercury toxicity cases in 2011 among a community of adherents of traditional medical practice of Ayurveda.
Methods: Adherents of Ayurveda were offered heavy metals screening following the identification of the index case.
Results: Forty-six of 115 participants (40%) had elevated blood lead levels (BLLs) of 10 μg/dl or above, with 9.6% of BLLs at or above 50 μg/dl.
Conclusions: This is the largest cluster of lead and mercury toxicity following use of Ayurvedic supplements described in the literature in the US. Contamination of herbal products is a public health issue of global significance. There are few regulations addressing contamination of "natural" products or supplements.

Keywords: Ayurvedic medicine, Complementary and alternative medicine, Lead toxicity, Mercury toxicity, Public health response

Introduction

Approximately 40% of adults in the United States report using complementary and alternative medicines (CAMs).[1,2] Globally, estimates of CAM use are even higher, with the World Health Organization (WHO) finding approximately 70–80% of all people utilizing non-allopathic medicines, mainly of herbal sources, in their health care.[3,4] Prior to 1994, CAMs were not regulated in the United States, but passage of the Dietary Supplement Health and Education Act (DSHEA)[5] defined the class of dietary supplements and provided the US Food and Drug Administration (FDA) with new responsibilities, including development of manufacturing standards for supplements and compulsory regulation for "current good manufacturing practices" (cGMP).[6] However, the regulatory reach of DSHEA extends only to dietary supplement products sold in the US. Individuals traveling abroad may return with contaminated traditional medicines, pottery, or beauty aids for personal use. There are no regulatory controls over such products.

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Several cases of metal toxicity have been associated with the presence of lead, mercury, and arsenic in Ayurvedic traditional medicine. These include reports of lead poisoning in England, New Zealand, United States, and in India.[7–11] A systematic literature search for the years 1966–2007 identified five case reports of lead encephalopathy associated with Ayurvedic products.[12]

Ayurveda is the most widely practiced of the traditional Indian medical systems and has been used for over 2000 years.[7,13] Up to 80% of India's population is estimated to use Ayurveda, either exclusively or in combination with other medical therapies.[14,15] Experts in Ayurveda estimate that greater than 20% of the Ayurvedic medications contain at least one heavy metal.[16–18]

This manuscript presents results of a study of a heavy metal toxicity cluster of Ayurveda consumers in the United States. Results can be used to inform policy and raise awareness on the expanding use of CAMs in this country.

Methods

The index case of this cluster lived in a small community where a subset of the town residents obtained Ayurvedic herbal medications through

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personal travel to India or by direct importation and distribution from a clinic in India.

Study recruitment

The Iowa Department of Public Health (IDPH) and University of Iowa College of Public Health (UI CPH) investigated the public health implications of potentially contaminated Ayurvedic supplement use in the community. Participants were recruited in various ways. First, a notice was placed in the local newspaper inviting anyone using Ayurvedic medicine to get their Indian medications and supplements tested for heavy metals by the State Hygienic Laboratory at the University of Iowa. Individuals were advised to have blood lead and mercury tests. Second, emails from the researchers were forwarded to approximately 1500 clients around the globe by the Ayurvedic clinic in India selling the supplements.

Blood screening

The clinic in India advised all of their clients to cease use of all Ayurvedic products obtained through their clinic until results of an analysis for metals for their products were available. Individuals were invited to participate in blood lead screening and asked to document all complementary medicinal usage, sources of these substances, and medical symptoms. A subset was offered mercury testing based on potential for contamination of Ayurvedic products with mercury.[17] Blood lead testing was performed predominantly by the State Hygienic Laboratory, and blood mercury testing was performed by Mayo Medical Laboratories.

Blood lead concentration was measured using graphite furnace atomic absorption spectroscopy. Blood mercury concentration was measured using inductively coupled plasma-mass spectrometry (IC-PMS).[19] Individuals were immediately informed of their results and advised accordingly. They were considered to have an elevated blood lead level (BLL) if their blood lead concentration was ≥ 10 μg/dl.[20] Individuals with blood mercury level (BML) of ≥ 10 ng/ml were considered to have elevated mercury levels.[21] The results of the analysis of metals in the supplements sent to the State Hygienic Laboratory were compiled and provided as a list to all individuals within the community using Ayurvedic medications. This study was exempted from IRB approval because it was part of a public health response.

Statistical analysis

Statistical analyses were performed using Statistical Analysis System (SAS) 9.2.[22] Descriptive statistics of age, sex, BLL, BML, lead intake, and lag time are expressed as means, standard deviations, and ranges. Lead intake in grams per day for each individual was calculated using the following formula: number of Ayurvedic pills per day $\times$ 0.5 grams $\times$ lead concentration per pill (in ppm). Two pills per day and 0.5 g per pill (1 g/day total) were assumed as a baseline dose for individuals who did not specify doses of specific Ayurvedic products taken per day. Lag time was calculated since the last dose of Ayurvedic products to the measurement of BLL and BML and expressed in days.

The lower detection limit for BLL was between 3 and 5 μg/dl and for BML between 1 and 4 ng/ml, depending on the laboratory. For the statistical analysis, results below these limits ($n = 43$ for lead, $n = 38$ for mercury) were assigned non-zero values of 0.5 μg/dl and 0.1 ng/ml, respectively.

Wilcoxon rank-sum test was used to test the differences in medians of continuously distributed characteristics between genders and between those with normal versus elevated BLL. Trends in BLL by gender were tested using Cochran–Armitage chi-square test, and Fisher's exact chi-square test was used to test the differences in distribution by gender between those with normal and elevated BLL.

A p-value of <0.05 was selected as the level of statistical significance for every analysis throughout this study.

Results

One hundred and 15 individuals participated in the blood lead screenings (Table 1).

Of those tested, slightly less than half were men (47%). Forty-six (40%) of the 115 people tested had BLLs of ≥ 10.0 μg/dl. Thirty-four (30%) of the participants had BLLs of ≥ 25.0 μg/dl. Men were more likely to have elevated BLLs compared to women. Mean lead intake in grams per day was statistically significantly associated with elevated BLL (Table 2). Those with BLL of ≥ 10 μg/dl consumed on average 0.03 g of lead per day compared to 0.001 g by those with BLL below 10 μg/dl.

While elevated BLLs were the predominant abnormality seen in the clinical laboratory results, four individuals were identified with elevated BMLs of ≥ 10.0 ng/ml. One individual had an elevated blood mercury at 105 ng/ml and coincident elevation of blood lead at 42 μg/dl. The blood mercury and blood lead in this individual declined rapidly after cessation of the herbal products and a course of oral chelation with dimercaptosuccinic acid (DMSA). Their extreme fatigue improved significantly with reduction in blood lead and mercury levels.

In addition to testing BLLs, most individuals sent Ayurvedic supplement samples to be tested for metals by the University of Iowa State Hygienic Laboratory. Results of 182 of the Ayurvedic medications are available for review. Of the 182 supplements, 50 (27.5%) showed lead levels above California's maximum allowable daily level (MADL) for chemicals causing reproductive toxicity of 0.5 μg/day[23] and FDAs

Table 1 Characteristics of the screened population by sex

Characteristic	*n*	All (*n* = 115)	Male (*n* = 54)	Female (*n* = 61)	*P*
Age	115	59.4 ± 8.2	60.9 ± 5.3	58.1 ± 5.7	0.10
BLL (μg/dl)	115	16.2 ± 20.9	21.4 ± 23.2	11.7 ± 17.6	**0.03**
<5.0		53 (46.1)	20 (37.0)	33 (54.1)	**0.01**
5.0–9.9		16 (13.9)	7 (13.0)	9 (14.8)	
10.0–24.9		12 (10.4)	4 (7.4)	8 (13.1)	
25.0–49.9		23 (20.0)	16 (29.6)	7 (11.5)	
≥50.0		11 (9.6)	7 (13.0)	4 (6.5)	
BML (ng/ml)	77	3.2 ± 12.2	4.7 ± 17.2	1.9 ± 3.8	0.73
<4.0		63 (81.8)	29 (78.4)	34 (85.0)	0.31
4.0–9.9		10 (13.0)	5 (13.5)	5 (12.5)	
≥10.0		4 (5.2)	3 (8.1)	1 (2.5)	
Lead intake (g/day)	60	0.01 ± 0.02	0.02 ± 0.02	0.01 ± 0.02	0.16
Lag time (days)	65	43.1 ± 94.5	21 ± 26	61 ± 122	0.24

BLL: blood lead level; BML: blood mercury level; lead intake (g/day): umber of Ayurvedic pills per day × 0.5 g × lead concentration per pill (in ppm); lag time: time since the last dose of Ayurvedic pills to the measurement of BLL/BML (in days).
Note: *P* value estimated by comparing males to females using Wilcoxon rank-sum test for continuous variables, and Cochran-Armitage chi-square test of trend for categorical variables

Table 2 Distribution of BML, lead intake, and lag time by BLL.

	BLL < 10 μg/dl (*n* = 69)	BLL ≥ 10 μg/dl (*n* = 46)	*P*
BML (ng/ml)	46 (40.0); 2.1 ± 3.8	30 (26.1); 5.0 ± 19.0	0.95
Lead intake (g/day)	27 (23.5); 0.001 ± 0.006	33 (28.7); 0.03 ± 0.01	**<0.0001**
Lag time (days)	31 (30.0); 55 ± 125	34 (29.6); 33 ± 53	0.37

BLL: blood lead level; BML: blood mercury level; lead intake (g/day): number of Ayurvedic pills per day × 0.5 g × lead concentration per pill (in ppm).
Note: *P* value estimated by comparing participants with BLL < 10 μg/dl to participants with BLL ≥ 10 μg/dl using Wilcoxon rank-sum test.

recommended maximum level (RML) for industry of 0.1 μg/g of lead per candy,[24] assuming a minimum daily consumption of 1 g of Ayurvedic supplements. The highest content of lead in an individual supplement was 43 200 μg/g. Eighty-seven (47.8%) of the supplements showed elevated levels of elemental mercury above California's MADL for methyl mercury of 0.3 μg/day[25] with the highest concentration being 279 000 μg/g. Twenty-nine (15.9%) of the supplements had arsenic levels elevated above California's no-significant risk level (NSRL) for carcinogens[23] of 10 μg/day with the highest concentration reported at 44 800 μg/g.

Discussion

This represents one of the largest reported clusters of lead toxicity from complementary or alternative products to date. This cohort was made up of medically well-versed individuals who consume Ayurveda and other CAMs. There were several obstacles in identifying and addressing the risk for metal poisoning. The majority of the substances with toxic levels of lead and mercury came from one particular Ayurvedic clinic in India. The cooperation of respected members of the community and of the Ayurvedic clinic in India was critical to the success of this intervention and study.

One of the fundamental concepts governing Ayurvedic medical practice is that "man and the universe are composed of the same basic elements, and disease occurs if there is an imbalance."[7] It is due to this belief that heavy metals are intentionally added to several Ayurvedic medications and that processing of heavy metals results in their being non-toxic for ingestion.[8,15,16] The process of detoxifying heavy metals has been described and includes the use of heat, sesame oil, buttermilk, cow's urine, plants, tamarind, and arsenic sulfide.[15] However, numerous case reports of lead toxicity due to ingestion of Ayurvedic medications demonstrate the inadequacy of this heavy metal detoxification process.[7–9,11,12] The widespread use of herbal medications, combined with the fact that many cases of lead toxicity may not be recognized clinically, makes contamination of such herbal medication with heavy metals and other toxicants a public health concern. The prevalence and significance of mercury contamination in such preparations is not well understood.

Identification of products with unsafe levels of metals and education of the population at risk regarding these products was our primary intervention. The majority of participants was receptive to this message; however, there was a need for ongoing discussion regarding the bioavailability and significance of published acceptable limits of various metals in such products. In particular, the discrepancy between extremely elevated mercury concentrations in some of the Ayurvedic products and low prevalence of elevated blood mercury among consumers begs the question of bioavailability of specific mercury compounds

and availability of laboratory services for chemical speciation.

The implicated products were all directly imported by the users from India, and there is no regulatory public health authority in the United States for these products. Lack of quality control of herbal products represents a public health threat requiring increased recognition among Ayurvedic practitioners and consumers regarding the potential toxicity from metals in such preparations. As use of alternative medications becomes more common in the US, it is imperative that both traditional and non-traditional medical practitioners communicate effectively with their patients regarding the use and potential risks of unregulated products. The use of herbal and other CAM products is a major and, largely unregulated, industry in the US and globally. Recognition of the potential for metal toxicity from herbal products, particularly those obtained overseas, will require continued vigilance among clinicians, public health officials, and the consumers of such products. The impact on this community from Ayurvedic medications shows a need for laboratory capacity to test products for contaminants. As herbal and CAM products gain more widespread use,[1] it raises the need for testing not just for the presence of toxic metals but also for chemical speciation and bioavailability.

Disclaimer Statements

Contributors Dr. Laura E. Breeher participated in the design and data collection for the study, wrote the first draft of the paper, and participated in revising all drafts of the manuscript. Dr. Marek A. Mikulski participated in the design and data collection for the study, analyzed the data, and revised all drafts of the manuscript. Mr. Thomas. Czeczok participated in the design and data collection for the study and revised all drafts of the manuscript. Ms. Kathy. Leinenkugel provided consultation on state lead public health programs and review and revision of drafts. Dr. Laurence J. Fuortes provided scientific oversight and clinical services for the study and revised all drafts of the manuscript. All the authors have read the manuscript, agreed the work is ready for submission to a journal, and accepted responsibility for the manuscript's contents.

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Human participant protection The Human Subjects Research protocol was waived as this was a public health response to heavy metals poisoning, hence no informed consent was obtained.

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References

1 Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, *et al.* Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. JAMA. 1998;280(18):1569–75.
2 National Center for Complementary and Alternative Medicine (NCCAM). Complementary, Alternative or Integrative Health. What's in the Name. NCCAM Pub No D347; 2007.Available from: http://nccam.nih.gov/health/whatiscam
3 Akerele O. Nature's medicinal bounty: don't throw it away. World Health Forum. 1993;14:390–5.
4 World Health Organization (WHO). *Traditional Medicine Strategy 2002-2005*. 2002Available from: http://whqlibdoc.who.int/hq/2002/who_edm_trm_2002.1.pdf.
5 Dietary Supplement Health and Education Act (DSHEA). Pub L no. 103-417.108 Stat 4325; 1994.Available from: http://history.nih.gov/research/downloads/PL103-417.pdf
6 U.S. Food and Drug Administration. Current good manufacturing practice in manufacturing, packaging, labeling, and holding operations for dietary supplements. 21 CFR 111. Federal Register. 2007;72(121):34752–34958, Available from: http://www.gpo.gov/fdsys/pkg/FR-2007-06-25/html/07-3039.htm.
7 Dargan PI, Gawarammana IB, Archer JR, House IM, Shaw D, Wood DM. Heavy metal poisoning from Ayurvedic traditional medicine: an emerging problem? Int J Environ Health. 2008;2(3/4):463–73.
8 van Schalkwyk J, Davidson J, Palmer B, Hope V. Ayurvedic medicine: patients in peril from plumbism. N Z Med J. 2006;119(1233):U1958.
9 Centers for Disease Control and Prevention (CDC). Lead poisoning associated with Ayurvedic medications – five states, 2000-2003. Morb Mortal Wkly Rep. 2004;53:582–4.
10 Breeher L, Gerr F, Fuortes L. A case report of adult lead toxicity following use of Ayurvedic herbal medication. J Occup Med Toxicol. 2013;8(1):26.
11 Raviraja A, Vishal Babu GN, Sehgal A, Saper RB, Jayawardene I, Amarasiriwardena CJ, *et al.* Three cases of lead toxicity associated with consumption of Ayurvedic medicines. Indian J Clin Biochem. 2010;25(3):326–9.
12 Karri SK, Saper RB, Kales SN. Lead encephalopathy due to traditional medicines. Curr Drug Saf. 2008;3(1):54–9.
13 Chopra A, Doiphode VV. Ayurvedic medicine, core concept, therapeutic principles and current relevance. Med Clin North Am. 2002;86(1):75–89.
14 Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. Drug Saf. 2002;25(14):1005–19.
15 Thatte UM, Rege NN, Phatak SD, Dahanukar SA. The flip side of Ayurveda. J Postgrad Med. 1993;39(4):179–82.
16 Saper RB, Kales SN, Paquin J, Burns MJ, Eisenberg DM, Davis RB, *et al.* Heavy metal content of Ayurvedic herbal medicine products. JAMA. 2004;292(23):2868–73.
17 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.
18 Kales SN, Saper RB. Ayurvedic lead poisoning: an underrecognized, international problem. Indian J Med Sci. 2009;63(9):379–81.
19 Dolan SP, Nortrup DA, Bolger PM, Capar SG. Analysis of dietary supplements for arsenic, cadmium, mercury, and lead using inductively coupled plasma mass spectrometry. J Agric Food Chem. 2003;51(5):1307–12.
20 Centers for Disease Control and Prevention (CDC)/National Institute for Occupational Safety and Health (NIOSH) Adult Blood

Lead Epidemiology and Surveillance (ABLES). 2010.Available from: http://www.cdc.gov/niosh/topics/ables/description.html
21 Roberts WL, McMillin GA, Burtis CA, Burns DE. Reference information for the clinical laboratory. In: Burtis CA, Ashwood ER, Burns DE, editors. *Tietz textbook of clinical chemistry and molecular diagnostics*. 5 edn. St. Louis, MO: Elsevier Saunders; 2012; p. p.2301.
22 SAS [computer program]. Version 9.2.Cary, NC: SAS Institute Inc.; 2002-2008
23 State of California, Safe Drinking Water and Toxic Enforcement Act of 1986.Proposition 65.Chemicals known to the State of California to cause cancer or reproductive toxicity; 2013.Available from: http://www.oehha.ca.gov/prop65/pdf/safeharbor081513.pdf. [update]
24 U.S. Food and Drug Administration. Guidance for Industry. Lead in candy likely to be consumed frequently by small children: recommended maximum level and enforcement policy; 2005.Available from: http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ChemicalContaminantsMetalsNaturalToxinsPesticides/ucm077904.htm#ftn2
25 State of California Environmental Protection Agency. Proposition 65 Status Report Safe Harbor Levels; 2005.Available from: http://legacy.library.ucsf.edu/documentStore/l/p/a/lpa81g00/