

Arsenic, Cadmium, Lead and Mercury in Sweat – A Systematic Review

Margaret E. Sears PhD,¹ Kathleen Kerr MD,² Riina Bray MHS, MD²

1. Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada.
Clinical Epidemiology, Ottawa Hospital Research Institute, Ottawa, Canada.
2. Environmental Health Clinic, Women's College Hospital, Toronto.
Department of Family and Community Medicine, University of Toronto

Corresponding Author:

Margaret Sears
RR 1, Box 9012
Dunrobin, Ontario
Canada
Telephone: 613 832-2806
Email: MegSears@ncf.ca

Keywords: arsenic, cadmium, lead, mercury, heavy metals, sweat, sauna, body burden assessment, treatment

Abstract

Arsenic, cadmium, lead and mercury exposures are ubiquitous. These toxic elements have no physiological benefits, engendering interest in minimizing body-burden. The physiological process of sweating has long been regarded as “cleansing,” and low-risk. Reports of toxicant levels in sweat were sought in Medline, Embase, Toxline, Biosis and AMED as well as reference lists and grey literature, from inception to March 22, 2011. Of 122 records identified, 24 were included in evidence synthesis. Populations, sweat collection methods and concentrations varied widely. In individuals with higher exposure or body-burden, sweat generally exceeded plasma or urine concentrations, and dermal could match or surpass urinary daily excretion. Arsenic skin excretion was several-fold higher from arsenic-exposed individuals than unexposed controls. Cadmium was more concentrated in sweat than blood plasma. Sweat lead was associated with high molecular weight molecules, and in an interventional study levels were higher with endurance compared with intensive exercise. Mercury levels normalized with repeated saunas in a case report. Sweating deserves consideration for detoxification. Research including appropriately sized trials is needed to establish safe, effective therapeutic protocols.

No person is without some level of toxic metals in their bodies, circulating and accumulating with acute and chronic lifetime exposures. An individual may take numerous measures to minimize exposures and to optimize metabolism and excretion of toxic elements in the stool and urine with diet, supplements, and chelation therapy [1,2]; however, an often overlooked route of excretion of toxicants is via the process of sweating [3].

Sweating with heat and/or exercise has been viewed throughout the ages, by groups world-wide, as “cleansing.” As part of a scoping review regarding arsenic, cadmium, lead and mercury we reviewed the scientific literature pertaining to toxicant excretion in sweat.

Arsenic, cadmium, lead and mercury - background

While many chemical elements are essential for life, arsenic, cadmium, lead and mercury have no known beneficial effect in humans. On the contrary, all four elements are confirmed or probable carcinogens, and they exhibit wide ranging toxic effects on many bodily systems, including the nervous, endocrine, renal, musculoskeletal, immunological and cardiovascular systems [4,5,6,7].

Children and the fetus are most at risk of harm, with early exposures predisposing the youngster over his/her lifetime to multisystem ailments, as well as lower IQ and dysfunctional behavior. In older populations there is increased likelihood of early cognitive decline, as well as a range of conditions including kidney and cardiovascular disease, diabetes and osteoporosis [4,5,6,7].

Some populations are exposed to elevated levels of toxic elements by virtue of geochemistry resulting in groundwater or foods with elevated levels of toxic elements (e.g. elevated arsenic in groundwater, most famously in parts of Asia such as Bangladesh but also elsewhere; cadmium that accumulates in foods grown in particular locations with high levels in soils or from fertilizers, including shellfish [8], grains[9] and brassicas [10]; and mercury in fish and seafoods). Tobacco avidly accumulates cadmium and lead from soil, making smoking a major source of exposure. In addition, valuable and unique properties of arsenic, cadmium, lead and mercury have made them integral in many products, including electronics, batteries and alloys. Modern environmental exposures arise from mining, refining and industrial processes (e.g. arsenic from precious metal mining and refining, mercury from chloralkali production, or lead and cadmium from mining, refining and recycling these and other metals such as zinc); the vestiges of older products (e.g. pesticides, leaded gasoline, paint and plumbing, mercury-containing switches and thermometers, and arsenical wood preservatives); ongoing uses (e.g. arsenical veterinary drugs, and mercury-containing dental amalgams, preservatives and lamps); as well as emissions from burning coal and other incineration (including cremation).

With toxic elements ubiquitous in our air, water, food and the physical environment, as well as in many consumer products, prudent avoidance is not always possible. Although signs and symptoms of chronic disease are consistent with effects of arsenic, cadmium, lead and/or mercury, physicians commonly have a low index of clinical suspicion, and therefore levels of toxic elements are seldom investigated. Diagnosis may be challenging because multiple chemicals may contribute to subtle effects in chronic illnesses of an individual, and the effects may be synergistic. A recent review called for mercury assessment in all patients presenting with hypertension or any vascular disease, but other toxic elements such as lead [11] may also be implicated at levels commonly observed in the population. “Interaction Profiles” [12] compiled by the US Agency for Toxic Substances and Disease Registry report that renal toxicities of mixtures of lead plus mercury are greater than would be predicted knowing the toxicity dose-response of the individual elements. Similarly, neurological toxicities of mixtures of lead plus arsenic, lead plus methylmercury, and lead plus cadmium are supra-additive [12].

Sweating – background

Increasing the thermal load on the body activates heat loss mechanisms including increased circulation throughout the skin and sweating [13], with blood flow to the skin increasing from a baseline of 5-10%, to 60-70% of the cardiac output [14]. Maximal sweating occurs within 15 minutes and the fluid loss may be as high as 2 L/h in an “acclimatized” person who regularly sweats [15].

Eccrine sweat is produced in tubular coil glands under the skin surface in response to heat and or work stress. Capillaries as well as adjacent adipose tissue may contribute to excretions from sebaceous and apocrine glands, as has been seen in research using sweat patches to detect drugs of abuse [16,17]. Sweat arises from the blood supply to the sweat gland, but is not simply an ultrafiltrate of blood plasma; sodium and chloride are lower in sweat than in serum, as salt loss is restricted by reabsorption in the gland [18]. Both the concentration and total loss of salt (sodium chloride) in sweat vary widely among individuals [19], as well as with acclimatization to exercise and heat [20]. In an early study Robinson et al. demonstrated that with serum salt depletion the kidneys responded within hours by restricting excretion into the urine, while the sweat glands responded only after days with decreased concentrations in the sweat [21]. Potassium, urea, ammonia and lactic acid concentrations are higher in sweat than in plasma, although these levels are also regulated to some extent by reabsorption in the ductal tubule of the sweat gland [22]. In one study of successive exercise sessions with cool-down breaks, over the short term sodium, potassium, calcium and magnesium excretion in sweat remained constant, while zinc excretion fell [23]. It is unclear whether reabsorption, or depletion of plasma supply resulted in diminishing zinc losses.

Children, with greater surface area in comparison to body mass, have been observed in research studies to sweat less than adults, with sweating increasing through puberty

[24]. Although some research has indicated that children's thermoregulation and heat tolerance may be less robust than adults, these findings may be at least in part an artifact of study designs and models for interpretation [25]. In research involving exercise and heat, it may be a challenge to maintain ongoing, consistent motivation among children.

Methods

Search strategy

Medline, Embase, Toxline, Biosis and AMED were searched, with no restriction on date or language, to March 22, 2011. These records were supplemented with searches for other research by key authors; searches of citations and reference lists of key reports; and "related articles."

Neither sweating nor toxic elements are modern topics of research, so in order to search older literature for all chemical forms, the online version of the Chemical Rubber Company Handbook© was searched for all arsenic, cadmium, lead and mercury compounds, and lists of keywords were extracted from these lists. Searches using these keywords yielded records that were not identified in searches using the four Chemical Abstracts Service (CAS) numbers or the Medical Subject Headings (MeSH) for arsenic, mercury, lead and mercury. CAS and MeSH are intended for specific individual chemicals or records referring to unspecified compounds – the tool cannot simultaneously be both specific and general. Toxic element records were searched for terms related to sweating, perspiration, sauna, steam baths, exercise, depuration, and secretion or excretion from skin. Bibliographic records were imported, duplicates removed and reports were screened using Zotero 2.03 (www.zotero.org).

Report screening and inclusion

Titles and abstracts were screened by one investigator (MS), for primary reports with data on one or more of the toxic elements in sweat, with at least a substantial abstract in English. Reviews were included at this level, to search reference lists. Two investigators (MS and KK) independently screened studies for inclusion, and extracted and verified data. All studies presenting quantitative human data on levels of arsenic, cadmium, lead and/or mercury were included, regardless of experimental design, or methods of sweat collection or chemical analysis.

Results

Of 122 bibliographic records identified, 70 did not meet inclusion criteria at first screening, 52 full text articles were sought for full text screening, and 50 were obtained and screened. Data from the extended abstract of a report in German [26] and the conclusion from the abstract of one peer-reviewed report in Russian [27] that was not obtained in full text were noted. Twenty-four reports of 22 or 23 trials or studies (it is unclear if two studies from one institution reported results twice for a subset of participants [22,27]) were included in evidence synthesis. Searching, screening and study inclusion is summarized in the modified PRISMA flow diagram, Figure 1.

Excretion of toxic elements in sweat

Along with essential minerals, sweat is an acknowledged excretory route for toxic metals. For instance, it is recommended to sample hair close to the scalp because content of toxic elements may be elevated along the shaft, from either environmental contamination or excreted toxins in sweat and sebum [28,29]. The minerals generally arise from blood serum [30], with contribution from dermally absorbed occupational exposures, that might not be reflected in blood or urine [31,32]. Sweating was induced by sauna, exercise or pilocarpine iontophoresis to measure the concentration of the heavy metals in the sweat, while sauna and exercise were used for therapy. Study participants included workers with occupational exposures, individuals with no occupational exposures who were well, or experiencing chronic ill health, and in two studies participants intentionally dosed with lead [32,33]. Studies that have examined the presence of toxic metals in sweat are summarized in Tables 1 to 4, for arsenic, cadmium, lead and mercury respectively.

Arsenic accumulates highly in the skin, and causes characteristic skin lesions, but little information is available on levels in sweat. Yousuf *et al.* recently found that excretion of arsenic was greatest from the skin of patients with skin lesions, slightly but not statistically significantly lower from arsenic-exposed controls, and several-fold lower in non-exposed controls [34]. Genuis *et al.* measured numerous toxic elements in blood plasma, urine and sweat of 20 study subjects (10 healthy and 10 with chronic health problems) [3]. The maximum sweat arsenic concentrations was 22 µg/L. On average sweat arsenic was 1.5-fold (in males) to 3-fold (in females) higher than in blood plasma; however arsenic was excreted at lower concentrations in sweat than in urine [3].

Cadmium in sweat was examined in six studies [3,22,28,30,35,36,37], with concentrations in sweat ranging from <0.5-10 µg/L [30] to 0.36-35.8 µg/L [3]. Stauber and Florence concluded that sweat may be an important route for excretion of cadmium when an individual is exposed to high levels [22,30], that was confirmed by observations that total daily excretion of cadmium was greater in sweat than in urine [3,28]. The maximum cadmium concentration observed in sweat was 35.8 µg/L [3].

Lead was examined in eleven studies [3,22,27,30,31,37,38,33,39,26,32]. In 1973, Hohnadel suggested that, “sauna bathing might provide a therapeutic method to increase elimination of toxic trace metals” [39]. In two males, 36% and 50% of sweat lead was of molecular weight >30,000, as measured by ultrafiltration, suggesting excretion of organic complexes rather than simple ions [22]. Lead excretion was lower in females taking birth control medications compared with females not taking medications or males [30]. Haber *et al.* found that prolonged endurance workouts (rowing) ameliorated elevated blood lead levels in exposed workers but did not alter levels in control subjects, and did not affect urine levels [26]. They suggested that the elimination route was not urine, but potentially sweat or/and bile. Omokhodion *et al.* carried out several studies of trace elements in sweat, including a study of lead ingestion by two human participants [33]. Sweat lead levels did not increase immediately with elevated blood lead, although the authors make reference to an older study with longer followup wherein lead in underarm pads doubled in the five days following ingestion. Omokhodion *et al.* also reported higher lead in sweat of exposed workers compared with unexposed controls [31], and in another study that sweat and blood lead levels were the only two variables that correlated among blood, urine, sweat and saliva [38]. The English abstract of a 1991 case report in Russian indicated that sauna increased excretion of toxic elements and resulted in clinical improvements [27]. Sweat lead levels up to 283 µg/L have been observed in non-occupationally exposed subjects [39], and up to 17700 µg/L in workers [32], where it is noted that lead in sweat may partially originate from material absorbed within the skin that is not removed by pre-test cleaning protocols [31]. Indeed, although dermal application of lead via hair follicles, sweat ducts and diffusion does not result in immediate increases in blood or urine lead concentrations, dermal absorption was demonstrated using the Pb-204 isotope [40], and lead powder and salt [32].

Mercury. In 1973 Lovejoy *et al.* noted that exposure to mercury does not always correlate with urine mercury levels and that elimination by other routes such as sweat may be an explanation [[41]. They suggested, “sweating should be the initial and preferred treatment of patients with elevated mercury urine levels.” In a 1978 case report, a severely poisoned worker was rescued with chelation therapy, followed by a regimen of daily sweats and physiotherapy over several months during which the sweat mercury level returned to normal and the patient recovered [42]. Robinson measured mercury in sweat repeatedly in two volunteers, observing sweat to urine concentration ratios ranging from less than 0.1 to greater than 5. Sweat mercury concentrations varied widely from day to day, and there was no correlation with urine levels. Sweat mercury levels of 1.5 µg/L were observed by Genuis *et al.* [3] and 1.4 µg/L by Robinson *et al.*[43]

Discussion

Arsenic, cadmium, lead and mercury may be excreted in appreciable quantities through the skin, and rates of excretion were reported matching or even exceeding urinary excretion in a 24 hour period. This is of particular interest should renal compromise limit urinary excretion of toxic elements.

Most of the research identified was over 20 years old, and collection methods varied widely. Although authors described thorough pre-cleaning methods, sweat concentrations measured in research settings are not well validated, and vary according to location on the body, collection method, and from day to day according to other variables such as hydration. Sweat contains metals not only from the blood plasma, but also evidently originating from dermal layers (particularly with significant dermal exposures, as workers in welding, smelting, or battery manufacturing). It would appear that large variabilities in measured concentrations, apart from collection methods as mentioned above, were likely the result of differences in excretion amongst widely varying individuals with ranges of body burdens, genetic polymorphisms affecting detoxification efficiency and physiological states, coupled with necessarily crude if simple experimental techniques. These were very much greater than would be expected due to limitations of analytical methods. Although analytical methods have improved over the years, analysis of these metals was commonplace at the time of the studies. Authors generally reported analytical methods rigorously or provided references to thorough descriptions, and included internal standards and some indication of sensitivity.

The observation that between a third and a half of lead in sweat may be associated with high molecular weight molecules [22] merits replication, including examination of additional toxic elements, and characterization of the associated molecules previously observed. Excretion of these large molecules also suggests that sweating may be a means of excretion of metals complexed with natural or synthetic chelating agents.

Yousef et al.'s recent study demonstrating a 2:1 molar ratio of zinc:arsenic, and increased vitamin E in skin secretions suggests potential therapeutic supplementation to accommodate these biochemical requirements. Vitamin E, zinc, and other nutrients are required for methylation and detoxification of arsenic within the body, and vitamin E supplementation improves the skin manifestations in arsenicosis [22].

From an occupational health perspective, lead, and presumably other toxic elements may be absorbed via the skin, which supports showering at work and further suggests the possibility of purging workers' skin by washing with a chelating agent (e.g. EDTA rinses extracted lead from workers' skin in methods validation experimentation [39]). It is unknown if sweating during the workday may affect dermal absorption, or if forced sweating at the end of the workday would be beneficial. It is unknown if increased blood flow to the skin could possibly enhance absorption into the bloodstream, or if worker

health could be optimized by a combination of workplace skin cleaning and sweating interventions.

Sweating has long been perceived to promote health, not only accompanying exercise but also with heat. Worldwide traditions and customs include Roman baths, Aboriginal sweat lodges, Scandinavian saunas (dry heat; relative humidity 40% to 60%) and Turkish baths (with steam). Infrared saunas heat exposed tissues with infrared radiation, while air temperatures remain cooler than in other saunas.

Sweating is a long-standing, if recently forgotten aspect of mercury detoxification. Various strategies have been used to maintain the mercury mining workforce have been explored over the centuries. In Spain, long the western world's primary source of mercury, sending ill workers to warmer climates away from the exposure, to drink weak beer (the hydrogen peroxide catalase oxidation of elemental mercury to ionic mercury is competitively inhibited by alcohol, increasing mercury in exhaled breath [44]) and to work in the heat (presumably to sweat out the "vapors"), was a common and effective strategy centuries ago; tremors, salivation and mouth ulcers resolved generally within a few weeks [45].

With acclimatization and regular use, the sauna is generally well tolerated by all ages [46], although medical supervision may be recommended during initial sessions for children or the elderly, or those with compromised health. Varying qualities of evidence indicate potential short- and long-term improvements for cardiovascular, rheumatological and respiratory conditions; contraindications include unstable angina pectoris, recent myocardial infarction, severe aortic stenosis and high risk pregnancy [14,46]. Sweating is not only observed to enhance excretion of the toxic elements of interest in this review; it may increase excretion of diverse toxicants, as observed in New York rescue workers [47], as well as persistent flame retardants [48], and bisphenol-A [49].

Optimizing the potential of sweating as a therapeutic excretory mechanism merits further research. To date the large body of research into homeostasis of the most common metals (sodium, potassium, and to a lesser extent magnesium, calcium and zinc) and conditioning or adaptation to regular sweating by athletes, has not been matched with studies of excretion of trace elements. Limited research suggests indirectly that conditioning may not restrict excretion of non-essential elements. Combination therapies, such as administration of n-acetyl cysteine, vitamin C, a chelating agent or low doses of ethanol (for mercury), to name a few possibilities, along with sauna and/or exercise therapy to induce sweating may be fruitful avenues of investigation. It has been noted that among people whose health is compromised by toxicants, heat regulatory mechanisms of the autonomic nervous system are often affected, resulting in a failure to sweat readily [3]. In these cases, along with diet and nutritional supplementation to remediate biochemical imbalances, interventions to consider include: brushing the skin; niacin to assist with vasodilation; and exercise prior to the sauna. Clinical experience is

that with persistence and ample hydration patients do eventually start to sweat – often a sign that autonomic nervous system function is beginning to improve. With enhanced ability to sweat, detoxification is facilitated, which can ultimately result in clinical improvement.

For biomonitoring and research purposes, modern validated methods are desirable to collect and measure elements in sweat, so this means of excretion may be considered in the context of other measures such as urine, blood, feces and hair. Considerations for dry and wet collection methods were recently discussed in the context of essential solutes [50,51].

Undoubtedly further research in this area would improve understanding, but the available evidence suggests that physicians could consider recommending sweating as tolerated via exercise (preferred) and/or use of a sauna as a low risk, potentially beneficial treatment for individuals who may be experiencing effects of toxic elements, or for individuals with regular exposure to or accretion of toxicants.

Conclusions

Sweating offers potential, and deserves consideration, to assist with removal of toxic elements from the body. As toxic elements are implicated in many serious chronic conditions, research is needed in patients with select conditions to evaluate the body burden, and to test the efficacy of source removal, dietary choices and supplements, interventions that induce sweating, and treatments with drugs, all to enhance excretion of toxic elements with the goal of clinical improvement. There is a clear need for robust trials, appropriately sized to assess clinical outcomes, from which therapeutic protocols can be derived. Both biochemical and clinical outcomes should be examined in order to develop and monitor clinical interventions that are both safe and effective.

Acknowledgements

The scoping review from which this work is derived was generously supported by a grant from the Canadian Institutes of Health Research, and the Social Sciences and Humanities Research Council of Canada. There are no conflicts of interest.

References

1. Institute for Functional Medicine. David S. Jones MD, Editor in Chief. Textbook of Functional Medicine. 3rd ed. Gig Harbor, WA, USA: 2010.
2. Sears M, Genuis S. Environmental determinants of chronic disease, and medical approaches: Recognition, avoidance, supportive therapy and detoxification. *J Environ Public Health*. 2012;in press.
3. Genuis SJ, Birkholz D, Rodushkin I, Beeson S. Blood, Urine, and Sweat (BUS) Study: Monitoring and Elimination of Bioaccumulated Toxic Elements. *Arch Environ Contam Toxicol*. 2010 Nov;61:334-357
4. Agency for Toxic Substances and Disease Registry. Toxicological Profile: Arsenic [Internet]. 2007 [cited 2011 Mar 18]. Available from: <http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=22&tid=3>
5. Agency for Toxic Substances and Disease Registry. Toxicological Profile: Cadmium [Internet]. 2008 [cited 2010 Dec 9]. Available from: <http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=48&tid=15>
6. Agency for Toxic Substances and Disease Registry. Toxicological Profile: Lead [Internet]. 2007 [cited 2010 Dec 9]. Available from: <http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=96&tid=22>
7. Agency for Toxic Substances and Disease Registry. Toxicological Profile: Mercury [Internet]. US Department of Health and Human Services. Public Health Service; 1999 [cited 2011 Mar 19]. Available from: <http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=115&tid=24>
8. Copes R, Clark NA, Rideout K, Palaty J, Teschke K. Uptake of cadmium from Pacific oysters (*Crassostrea gigas*) in British Columbia oyster growers. *Environ Res*. 2008 Jun;107(2):160-169.
9. Perilli P, Mitchell LG, Grant CA, Pisante M. Cadmium concentration in durum wheat grain (*Triticum turgidum*) as influenced by nitrogen rate, seeding date and soil type. *J Sci Food Agric*. 2010;90(5):813–822.
10. Liu W, Zhou Q, An J, Sun Y, Liu R. Variations in cadmium accumulation among Chinese cabbage cultivars and screening for Cd-safe cultivars. *J Hazard Mater*. 2010 Jan 15;173(1-3):737-743.
11. Health Canada. Government of Canada. Draft Human Health State of the Science Report on Lead - 2011 Health Canada Consultation Document [Internet]. 2011 [cited 2011 Sep 3]. Available from: <http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/dhssrl-rpeccepsh/index-eng.php>

12. Agency for Toxic Substances and Disease Registry. Interaction Profiles Home Page [Internet]. [cited 2010 Oct 7]; Available from: <http://www.atsdr.cdc.gov/interactionprofiles/index.asp>
13. Leppäluoto J. Human thermoregulation in sauna. *Ann Clin Res.* 1988;20(4):240-243.
14. Hannuksela ML, Ellahham S. Benefits and risks of sauna bathing. *Am J Med.* 2001 Feb 1;110(2):118-126.
15. Eisalo A, Luurila OJ. The Finnish sauna and cardiovascular diseases. *Ann Clin Res.* 1988;20(4):267-270.
16. Nerdrum P. Response to “Improvement of health after replacement of amalgam fillings” by Bjorkman et al. *J Psychosom Res.* 2005;Vol.59(3):191-192.
17. Levisky JA, Bowerman DL, Jenkins WW, Karch SB. Drug deposition in adipose tissue and skin: evidence for an alternative source of positive sweat patch tests. *Forensic science international.* 2000;110(1):35–46.
18. Cage GW, Dobson RL. Sodium Secretion and Reabsorption in the Human Eccrine Sweat Gland. *J Clin Invest.* 1965 Jul;44(7):1270-1276.
19. Dill D, Hall F, vanBeaumont W. Sweat chloride concentration: sweat rate, metabolic rate, skin temperature, and age. *J Appl Physiol.* 1966 Jan 1;21(1):96-106.
20. Dill DB, Hall FG, Edwards HT. Changes in composition of sweat during acclimatization to heat. *American Journal of Physiology.* 1938;123(2):412.
21. Robinson S, Nicholas JR, Smith JH, Daly WJ, Percy M. Time relation of renal and sweat gland adjustments to salt deficiency in men. *J Appl Physiol.* 1955 Sep;8(2):159-165.
22. Stauber JL, Florence TM. The determination of trace metals in sweat by anodic stripping voltammetry. *Sci. Total Environ.* 1987 Feb;60:263-271.
23. Montain SJ, Chevront SN, Lukaski HC. Sweat mineral-element responses during 7 h of exercise-heat stress. *Int J Sport Nutr Exerc Metab.* 2007 Dec;17(6):574-582.
24. Falk B, Bar-Or O, Calvert R, MacDougall JD. Sweat gland response to exercise in the heat among pre-, mid-, and late-pubertal boys. *Med Sci Sports Exerc.* 1992 Mar;24(3):313-319.
25. Falk B, Dotan R. Children’s thermoregulation during exercise in the heat: a revisit. *Appl Physiol Nutr Metab.* 2008 Apr;33(2):420-427.

26. Haber P, Ring F, Jahn O, Meisinger V. Influence of intensive and extensive aerobic circulatory stress on blood lead levels. [German]. Zentralblatt fur Arbeitsmedizin, Arbeitsschutz, Prophylaxe und Ergonomie. 1985;(10):303-306.
27. Parpaleš IA, Prokof'eva LG, Obertas VG. [The use of the sauna for disease prevention in the workers of enterprises with chemical and physical occupational hazards] - English abstract. Vrach Delo. 1991 May;(5):93-95.
28. Robinson J, Weiss S. The direct determination of cadmium in hair using carbon bed atomic absorption spectroscopy. Daily rate of loss of cadmium in hair, urine and sweat. J Environ Sci Health, Part A. 1980;15(6):663-697.
29. Airey D. Mercury in human hair due to environment and diet: a review. Environ. Health Perspect. 1983 Oct;52:303-316.
30. Stauber JL, Florence TM. A comparative study of copper, lead, cadmium and zinc in human sweat and blood. Sci Total Environ. 1988 Aug 1;74:235-247.
31. Omokhodion FO, Howard JM. Sweat lead levels in persons with high blood lead levels: lead in sweat of lead workers in the tropics. Sci Total Environ. 1991 Apr 15;103(2-3):123-128.
32. Lilley SG, Florence TM, Stauber JL. The use of sweat to monitor lead absorption through the skin. Sci Total Environ. 1988 Oct 15;76(2-3):267-278.
33. Omokhodion FO, Crockford GW. Sweat lead levels in persons with high blood lead levels: experimental elevation of blood lead by ingestion of lead chloride. Sci Total Environ. 1991 Oct 15;108(3):235-242.
34. Yousuf AKM, Misbahuddin M, Rahman MS. Secretion of arsenic, cholesterol, vitamin E, and zinc from the site of arsenical melanosis and leucomelanosis in skin. Clin Toxicol. 2011 Jun;49(5):374-378.
35. Omokhodion FO, Howard JM. Trace elements in the sweat of acclimatized persons. Clin Chim Acta. 1994 Nov;231(1):23-28.
36. Robinson JW, Weiss S. The direct determination of cadmium in urine and perspiration using a carbon bed atomizer for atomic absorption spectroscopy. Journal of Environmental Science and Health . Part A: Environ Sci Engineer. 1980;15(6):635.
37. Cohn JR, Emmett EA. The excretion of trace metals in human sweat (only abstract available online). Ann Clin Lab Sci. 1978 Jul;8(4):270-275.
38. Omokhodion FO, Crockford GW. Lead in sweat and its relationship to salivary and urinary levels in normal healthy subjects. Sci Total Environ. 1991 Apr 15;103(2-3):113-122.

39. Hohnadel DC, Sunderman FW, Nechay MW, McNeely MD. Atomic Absorption Spectrometry of Nickel, Copper, Zinc, and Lead in Sweat Collected from Healthy Subjects during Sauna Bathing. *Clin Chem.* 1973 Nov 1;19(11):1288-1292.
40. Stauber JL, Florence TM, Gulson BL, Dale LS. Percutaneous absorption of inorganic lead compounds. *Sci Total Environ.* 1994 May 2;145(1-2):55-70.
41. Lovejoy HB, Bell ZG, Vizona TR. Mercury exposure evaluations and their correlation with urine mercury excretions. 4. Elimination of mercury by sweating. *J Occup Med.* 1973 Jul;15(7):590-591.
42. Sunderman FW. Clinical response to therapeutic agents in poisoning from mercury vapor. *Ann Clin Lab Sci.* 1978 Jul;8(4):259-269.
43. Robinson JW, Skelly EM. The Direct Determination of Mercury in Sweat. *Spectroscopy Letters: An International Journal for Rapid Communication.* 1983;16(2):133.
44. Sallsten G, Kreku S, Unosson H. A small dose of ethanol increases the exhalation of mercury in low-level-exposed humans. *J Toxicol Environ Health Part A.* 2000 May 26;60(2):89-100.
45. Brown KW. Workers' Health and Colonial Mercury Mining at Huancavelica, Peru. *The Americas.* 2001 Apr;57(4):467-496.
46. Kukkonen-Harjula K, Kauppinen K. Health effects and risks of sauna bathing. *Int J Circumpolar Health.* 2006 Jun;65(3):195-205.
47. Dahlgren J, Cecchini M, Takhar H, Paepke O. Persistent organic pollutants in 9/11 world trade center rescue workers: Reduction following detoxification. *Chemosphere.* 2007 Oct;69(8):1320-1325.
48. Genuis SJ, Birkholz D, Ralitsch M, Thibault N. Human detoxification of perfluorinated compounds. *Public Health.* 2010 Jul;124(7):367-375.
49. Genuis S, Beeson S, Birkholz D, Lobo R. Human Excretion of Bisphenol-A: Blood, Urine and Sweat (BUS) Study. *J Environ Public Health.* 2011;In Press.
50. Weschler LB. Sweat electrolyte concentrations obtained from within occlusive coverings are falsely high because sweat itself leaches skin electrolytes. *J Appl Physiol.* 2008 Oct 1;105(4):1376 -1377.
51. Armstrong LE. Commentary on Viewpoint: Sweat electrolyte concentrations obtained from within occlusive coverings are falsely high because sweat itself leaches skin electrolytes. *J Appl Physiol.* 2008 Oct 1;105(4):1378.

Table 1. Studies of excretion of arsenic in sweat

Study	Country, Participants	Study design and intervention	Key Findings (Concentrations $\mu\text{g/L}$ unless otherwise indicated)
Yousuf 2011 [34]	Bangladesh 20 arsenicosis patients with melanosis and leucomelanosis 20 controls with As in drinking water 20 unexposed controls	Secretions from chest, back and abdomen collected for 24 h, on gauze pads (8-fold; 2x3 inches) attached to fitted T-shirt.	As secretion several-fold greater for As-exposed groups. No significant difference between patients and As-exposed controls. 2 zinc atoms excreted per As atom. Vitamin E excreted with As.
Genuis et al. 2010 [3]	Canada 10 with chronic conditions 10 healthy	Simultaneous measurement of As in blood plasma, urine and sweat. Sweating induced by exercise or sauna, collected directly into bottle.	17 participants with As detected in all samples Blood plasma mean: 2.5 (range 0.9-13 $\mu\text{g/L}$) (n=17) Urine mean: 37 (range 4.8-200 $\mu\text{g/L}$) (n=20) Sweat mean: 3.1 (range 3.7-22 $\mu\text{g/L}$) (n=20)

Table 3. Studies of cadmium excretion in sweat

Study	Country, Participants	Study design and intervention	Key Findings (Concentrations µg/L unless otherwise indicated)
Genuis 2010 [3]	Canada 10 with chronic conditions 10 healthy	Simultaneous measurement of toxic trace elements in blood plasma, urine and sweat. Exercise or sauna Sweat collected directly into bottle.	3 participants with cadmium detected in all samples Blood plasma mean: 0.03 [range 0.02-0.07] (n=11) Urine mean: 0.28 [0.18-0.39] (n=3) Sweat mean: 5.7 µg/L [0.36-36] (n=18)
Omokhodion 1994 [35]	UK 15 healthy participants	Sweat collected using modified arm bag (hand excluded) Participants exercised at room temperature.	Cadmium detected in 13 sweat samples Mean 1.9 Range 1.1-3.1
Stauber 1988[30]	Australia 24 males 13 females taking oral contraceptives 26 females not taking oral contraceptives	Forearm sweat induced by pilocarpine iontophoresis and collected on a membrane filter.	Males mean sweat cadmium 1.4 (range <0.5-10); Females not taking contraceptives 2.6 µg/L (<0.5-18); Females taking contraceptives 2.4 µg/L (<0.5-5.5).
Stauber 1987[22]	Australia 9 males 7 females taking oral contraceptives 6 not taking oral contraceptives (unclear overlap with 1988 participants)	Forearm sweat induced by pilocarpine iontophoresis and collected on a membrane filter.	Cadmium not detected in sweat (0.5 detection limit) Mean blood cadmium 0.8
Robinson 1980[36]	US 28 male university faculty members	Exercise and shower preceded sauna for sweat collection. Sweat collected as drips from forehead or nose.	Sweat cadmium range 11 - 200 Urine cadmium range ND - 67 Sweat/urine ratio range 1.0 - 16 No correlation between the concentrations in urine and sweat.
Robinson 1980[28] (companion to previous)	US 2 male university faculty members	As previous Cadmium also measured in hair segments	Daily excretion of cadmium estimated: • 30 µg/day in urine • 120 µg/day in sweat • 0.2 µg/day in hair Cadmium concentrations in hair and sweat were lower in one participant than the other.
Cohn 1978[37]	US 6 males 3 females	Total body washdown and arm bag techniques.	Mean concentration of cadmium in sweat > urine. Arm bags yielded lower levels than whole body measurements.

Table 3. Studies of lead excretion in sweat

Study	Country, Participants	Study design and intervention	Key Findings (Concentrations µg/L unless otherwise indicated)
Genuis 2010 [3]	Canada 10 with chronic health conditions 10 healthy	Analyses of blood plasma, urine and sweat. Sweating induced by exercise or sauna, collected directly into bottle.	Sweat mean 31 [range 1.5-94] (n=20) Blood plasma mean 0.12 [0.39-1.7] (n=20) Urine mean 1.8 [0.91-7.5] (n=20)
Omokhodion 1991 [33]	UK 2 participants	Blood, urine and sweat lead measured before and following ingestion of lead chloride - 1 or 2 doses of lead chloride (20mg PbCl ₂ total, in 1 or 2 divided doses)	Blood lead peaked at 4 h Sweat concentrations did not increase significantly [range 0-11] Blood concentration range 6-51 Urine concentration range 10-97 Arm sweat collections varied by more than 2-fold between arms at the same time on the same person.
Omokhodion 1991 [31]	Unidentified "tropics" 19 workers in a lead battery factory 8 controls (medical students)	Measured lead in sweat, blood and urine simultaneously. Sweating induced by exercising at room temperature Sweat collected in arm bags	Workers: • blood lead 13-36 • urine lead 28-290 µg/g creatinine. • sweat lead 72-260 Controls: • blood lead 90-120 • urine lead 9-20 µg/g creatinine • sweat lead 9-30
Omokhodion 1991 [38]	UK 24 normal, healthy subjects	Measured lead in sweat, urine, blood and saliva. Sweat collected in arm bags, sitting in a hot chamber.	• Blood lead 86 [range 60-140] • Urine lead 18µg/g creatinine (range 7.7-44 µg/g creatinine) • Mean sweat lead 5.2 [2.5-13] • Saliva lead 4.8 [2.5-10]
Parpalei 1991 [27] (In Russian – English abstract only)	Russia NR in abstract	NR in abstract	"... sauna increased excretion with sweat fluid of toxic substances [lead] that penetrated the body during work. Sauna is recommended."
Lilley 1988 [32]	Australia 9 lead workers volunteers had lead applied to skin	Lead dust 6 h/day for 4 days 20 mg Pb dust on L arm of volunteer PbNO ₃ 24 h of 60 mg PbNO ₃ on L arm of volunteer	Sweat lead in workers: 71-18000 Following exposure, sweat lead from R arm increased approx. 10x, returning to baseline after approx. 2-4 days. Saliva increased approx. 5-6x. Urine and blood levels were unchanged.
Stauber 1988 [30]	Australia 24 males 13 females taking oral contraceptives 26 not taking oral contraceptives	Sweating induced on the forearms by pilocarpine iontophoresis, and collected on a membrane filter.	Mean sweat lead: • Males 41 [range 6-87] • Females not taking contraceptives 24 [<5-66 µg/L] (difference with males p<0.01) • Females taking contraceptives 36 [<5-70]

Study	Country, Participants	Study design and intervention	Key Findings (Concentrations µg/L unless otherwise indicated)
Stauber 1987 [22]	Australia 9 males 7 females taking oral contraceptives 6 not taking oral contraceptives (unclear overlap with 1988 participants)	Sweating induced on the forearms by pilocarpine iontophoresis and collected on a membrane filter.	No significant differences among groups Mean blood lead 200 Mean blood plasma lead 10 Mean sweat lead 15
Haber 1985 [26] (In German – used extended abstract)	Germany 4 groups of 8 males 2 groups with occupational lead exposure 2 control groups	Comparison of precisely defined physical work (intensive cycling, and extended rowing in a pool), examining lead excretion in persons with elevated blood levels compared with non-exposed controls.	Aerobic endurance training (rowing) caused a significant drop in the blood lead level in the occupationally exposed group (mean 430 µg/L [range 320-580] decreased to 370 µg/L [240-450]) (p<0.05). Endurance training was more effective than shorter, more intensive training (cycling). Urine lead levels were not significantly affected by training.
Cohn 1978 [37]	US 6 males 3 females	Total body wash-down, and arm bag techniques.	The mean concentration of lead in sweat was similar to that in urine. 1. Total body sweat lead mean: • Males 24 (SD 16) µg/L • Females 53 [range 40-60] 2. Body minus 1 arm / arm bag sweat lead 60 (SD 16) [40-120] / 83 (86) [20-250]
Honandel 1973 [39]	33 healthy males 15 females	15 min arm bag collection	Mean sweat lead: • Males 51 [range 8-180] • Females 120 (SD 72)[49-280]

Table 4. Studies of mercury excretion in sweat

Study	Country, Participants	Study design and intervention	Key Findings (Concentrations µg/L unless otherwise indicated)
Genuis 2010 [3]	Canada 10 with chronic conditions 10 healthy	Sweating induced by exercise or sauna, collected directly into bottle.	16 participants had mercury detected in all samples Blood plasma mercury mean 0.61 (range 0.26-1.6) (n=16) Urine mean 0.65 (range 0.32-1.3) (n=16) Sweat mean 0.86 (range 0.48-1.5) (n=20)
Robinson 1983[43]	US 21 males at university 7 sampled more than once	Mercury in sweat dripping from forehead or nose, compared with urine	Sweat mean 0.5 (range 0.1- 1.4 µg/L)
Sunderman 1978[42]	USA 1 case with mercury intoxication	Case report of chelating agents to treat mercury intoxication, followed by a regimen of daily sweats and physiotherapy for a protracted period of several months.	Appreciable quantities of mercury were excreted in sweat. With the sweating regimen mercury levels in sweat decreased to within the normal range.
Lovejoy 1973[41]	US 3 mercury exposed workers 3 non exposed workers 1 control	Participants wore rubber chest waders from 7:30 to 9:00 am. Sweat accumulated in the feet was collected, as well as a 16 hour urine sample.	Exposed workers 1.5h sweat - 120-350 ng mercury 16 h urine - 160-190 ng mercury. Unexposed workers: 1.5h sweat - 5-8 ng mercury; 16 h urine - 5-7 ng mercury. Internal controls: 1.5h sweat - 43-70 ng mercury 16 h urine - 30-46 ng mercury Mercury concentrations in sweat > urine for exposed workers; similar for controls.

Figure 1. PRISMA flow diagram of evidence searches and inclusion

