

Bioremediation and Tolerance of Humans to Heavy Metals through Microbial Processes: a Potential Role for Probiotics?

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The food and water we consume are often contaminated with a range of chemicals and heavy metals, such as lead, cadmium, arsenic, chromium, and mercury, that are associated with numerous diseases. Although heavy-metal exposure and contamination are not a recent phenomenon, the concentration of metals and the exposure to populations remain major issues despite efforts at remediation. The ability to prevent and manage this problem is still a subject of much debate, with many technologies ineffective and others too expensive for practical large-scale use, especially for developing nations where major pollution occurs. This has led researchers to seek alternative solutions for decontaminating environmental sites and humans themselves. A number of environmental microorganisms have long been known for their ability to bind metals, but less well appreciated are human gastrointestinal bacteria. Species such as *Lactobacillus*, present in the human mouth, gut, and vagina and in fermented foods, have the ability to bind and detoxify some of these substances. This review examines the current understanding of detoxication mechanisms of lactobacilli and how, in the future, humans and animals might benefit from these organisms in remediating environmental contamination of food.

Heavy metals are a unique group of naturally occurring compounds released into the environment by various processes (15, 107). The recent expansion of human industrial activity, including mining, smelting, and synthetic compound creation, has led to an exponential increase in the amounts of heavy metals released into the atmosphere, water, and soil (62). Many countries have regulatory guidelines for heavy-metal presence and exposure as well as remediation and treatment options. Screening of soil and water sources is conducted frequently to prevent overconsumption, but many of these programs and technologies are not readily available in developing nations, where the burden is greatest (2, 55, 56). The net result is that people around the globe are exposed, and new approaches are required to reduce the adverse consequences of accumulation of these compounds.

BACTERIAL INTERACTIONS WITH METALS: WHAT WE CAN LEARN FROM ENVIRONMENTAL STUDIES

Geomicrobiology is the study of how microbial processes interact with geological and geochemical processes. Studies in the early 1980s (9–11) explained how *Bacillus subtilis* was able to interact with a range of toxic metals, including copper, iron, magnesium, gold, and lead. This ability was attributed to differences between the net negative charge of bacteria and the cationic charge of many metals. The theory stated that nucleation sites on the cell surface had the ability to bind metals of opposite charge. Once bound to the cell wall, this resulted in a nucleation site where a large concentration of metals could bind and precipitate on the cell wall (8). In support of this, Fein et al. (28) showed through potentiometric titration of *B. subtilis* that changing the pH of the environment, and thus altering the cell surface charge, affected the ability of bacterial species to bind metal in solution. Based on this work, it was proposed that a neutral pH 7 had the optimum binding potential of cationic metal species, because at this pH, reactive functional groups would not be ionized (28). However, this is not true for all bacterial species or all interactions with metals. In many environments, such as acid mine tailings, bacterial species exist

with the ability to not only survive in extreme pH conditions but also cope with high metal concentrations that are toxic to humans and the majority of other species. These unique microbes have the ability to cope with metals through a variety of mechanisms but most notably through the precipitation of metal particles and active efflux.

The unique observation by the U.S. Geological Survey (USGS) that bacterial species, along with some eukaryotic organisms (fungi and yeasts), were interacting with both metals and other toxic compounds developed the theory of bioremediation (67). This was not actively used until 1992 when the USGS added nutrients to contaminated soils in Hanahan, SC, to activate bacterial species in the soil (58). Within a year, 75% of the toxic compounds in the soil had been removed. The use of natural microorganisms found in soil, water, and sludge pioneered the field of bioremediation. Further improvements in capabilities of bacteria to degrade environmental toxins and bind metals arose through the use of genetically engineered microorganisms (GEM). *Pseudomonas fluorescens* strain KH44, designed by the University of Tennessee and Oak Ridge National Laboratory, is one such example. The strain was able to sense toxic polycyclic aromatic hydrocarbons and degrade them (90). Attempts have been made to use GEM to increase heavy-metal remediation in contaminated sites. One approach was the transformation and expression of metallothionein (MT) by bacterial cells. Valls et al. (114) managed to successfully engineer MT to be expressed on the surface of *Escherichia coli* as an attempt to increase metal binding sites, leading to increased Cd accumulation. However, strict regulatory guidelines by the Environmental Protection Agency make the use of GEM difficult, and

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a better understanding of how these microbes work and their safety and environmental containment is needed before they will be used for bioremediation (30).

The interaction of bacterial species with metals and their use to remove metals from contaminated sites represent a unique process. As heavy metals are natural elements and in the most basic level are just atoms, degradation and metabolism are not possible. Instead, microorganisms have evolved coping strategies to either transform the element to a less-harmful form or bind the metal intra- or extracellularly, thereby preventing any harmful interactions in the host cell. Plus, they are able to actively transport the metal out of the cell cytosol (41, 66, 121). Resistance mechanisms are often plasmid encoded, but in some instances, the genes are found on the chromosome, suggesting an important evolutionary pressure to keep these genes; examples include mercury (Hg^{2+}) resistance in *Bacillus*, cadmium (Cd^{2+}) efflux in *Bacillus*, and arsenic efflux in *E. coli* (16, 96). Unfortunately, much of the data regarding these phenomena come from *in vitro* studies rather than large-scale field trials on metal absorption in contaminated soil and water.

HEAVY-METAL MEASUREMENT AND BIOSORPTION IN THE HUMAN BODY

In environmental ecosystems, there is an intricate interaction between heavy-metal contaminants and native microorganisms. These organisms have developed unique resistance mechanisms which allow them to survive and, in some instances, remove/reduce the concentrations of contaminants in their environments. The question remains: how are humans affected by the contaminants to which they are exposed daily? In addition, with the human body home to a large microbial population, especially in the oral and gastrointestinal (GI) microbiotas, what role might these constituents play in interacting with metals?

The gut microbiota comes into contact with metals and other contaminants as they are ingested through diet (110). This microbiota comprises the largest microbial community in the human body and contains at least two orders of magnitude more genes than are found in the human genome (79); thus, the genetic and enzymatic diversity is immense. It is well accepted that the gut microbiota has key roles in regulating digestion by providing enzymes required for metabolic breakdown by processing and metabolizing compounds as they enter the host through normal diet (61, 93). It is therefore likely that microbes are presented with metals in water and food and may play a role in protecting the host from their adsorption.

The relative bioavailability of ingested contaminants following oral exposure is traditionally calculated using *in vivo* animal experiments that monitor the percentage of an ingested dose that is absorbed into the bloodstream (23). The physiologically based extraction test, an *in vitro* gastrointestinal (GI) model that simulates the physical, chemical, and enzymatic conditions of the human GI tract, was first developed for the calculation of lead bioaccessibility from contaminated soils (86). Contaminant bioaccessibility refers to the fraction/percentage of an ingested contaminant that is released into simulated GI fluids (82). Since contaminant dissolution is typically required prior to the absorption of the substance across the GI epithelium, bioaccessibility is considered to be a conservative predictor for *in vivo* bioavailability (75). One of the more accepted and newer models of bioavailability is the simulator of

the human intestinal microbial ecosystem (SHIME), an *in vitro* GI model that is unique because it incorporates the activity of the human GI microbiota (21, 115). No other tests or standard models take into account the effect of the human GI microbiota in altering the bioavailability of metals.

Microbial sequestering of heavy metals by the intestinal microbiota is strongly supported by studies that show that when these contaminants are consumed at much higher concentrations, there is a lower detection in clinical samples, excluding absorption and dilution factors (29, 128). Only 40 to 60% of ingested metals are absorbed across the intestinal barrier into the body (113, 120). An exception to this is methylmercury, which can be absorbed upwards of 90% (59). This variance in bioaccessibility is unique for each metal and depends on the route of entry, the foodstuff consumed, and the type of host microbiota (105). While the SHIME system has been important in showing the effect of the gut microbiota on liberating metals for bioaccessibility, it has not answered the question of what effect the gut microbiota may have on binding and sequestering metals, thus imparting protection to the host.

MICROBIAL MECHANISMS OF ACTION

Three main mechanisms for the binding of metals to bacterial cell walls are known: (i) ion exchange reactions with peptidoglycan and teichoic acid, (ii) precipitation through nucleation reactions, and (iii) complexation with nitrogen and oxygen ligands (10, 11, 67). Gram-positive bacteria, particularly *Bacillus* spp., have high adsorptive capacity due to high peptidoglycan and teichoic acid content in their cell walls. Gram-negative bacterial cell membranes are lower in these components and are poorer metal absorbers (32). The phylum *Firmicutes* represents a major proportion of the microbiota in the colon (127); it is largely composed of Gram-positive species, such as *Bacillus* and *Clostridium*, and includes *Lactobacillus* as a major group (118). Thus, within the human intestinal tract, there are large populations of bacterial cells with the potential to bind and sequester metals that enter the body.

Detoxification is the ability to remove drugs, mutagens, and other harmful agents from the body. This is in contrast to detoxication, which is the mechanism of preventing entry of damaging compounds into the body (46). Detoxication usually occurs in the human intestinal tract, the liver, and the kidneys before compounds can spread and reach target sites where damage ensues (7). It is by this process that the gut microbiota, lactobacilli, and potentially probiotic bacteria may have the largest role in binding metals, preventing their entry to the body and, thus, protecting the host.

Many of the species used in environmental remediation—for example, chemolithotrophic bacteria that use inorganic sources of energy, such as metals, for electrons and production of ATP—are not applicable to human physiological metal removal. Free forms of metals, especially iron (Fe), are rare in the body and, thus, are a limiting nutrient for growth (92). Second, many soil bacteria can be opportunistic or obligate pathogens inside the human body (6, 19). Third, many of the most-effective species for bioremediation are genetically engineered or modified to enhance their innate ability (4, 101).

SEQUESTERING HEAVY METALS BY LACTOBACILLI AND OTHER PROBIOTIC BACTERIA

Certain members of the gut microbiota, such as lactobacilli used in food applications, may potentially be an adjunct for reducing metal toxicity in humans. This is because they have

TABLE 1 Negative effects associated with heavy-metal exposure and toxicity

| Metal | Negative effects of: ^a | | Reference(s) |
|----------|---|---|--------------------|
| | Acute toxicity | Chronic toxicity | |
| Arsenic | Bloody urine, GI discomfort, diarrhea, headaches, vomiting, convulsions, coma, and death | Skin lesions, blisters, Blackfoot disease; organ failure/damage; diabetes; cancer and mutagenic properties | 18, 44, 49, 109 |
| Cadmium | Hepatic, pulmonary, and testicular injury | Renal and bone injury (osteoporosis); carcinoma (primarily prostate and renal); toxicity to other organs | 63, 89, 119 |
| Chromium | Vomiting and diarrhea; hemorrhage and blood loss in GI Tract | Liver/kidney necrosis; skin ulcers, "chrome holes," irritative dermatitis; ulceration and perforation of the nasal septum; nasal, pharyngeal, and gastrointestinal carcinomas | 20, 126 |
| Lead | Neurobehavioral problems: impulsivity, distractibility, and short attention span; mild fatigue; headaches, nausea, vomiting | Antisocial behaviors; impaired hemoglobin synthesis; impaired renal function; deafness, blindness, retardation; decreased IQ, memory loss; decreased libido, fatigue | 5, 37, 65, 83, 95 |
| Mercury | Impaired neurodevelopment; loss of IQ; decrease in memory, attention, language, and visual-spatial perception tests; associations with autism and ALS | Impaired neurodevelopment; loss of IQ; decrease in memory, attention, language, and visual-spatial perception tests; associations with autism and ALS | 33, 38, 48, 57, 84 |

^a ALS, amyotrophic lateral sclerosis.

resistance mechanisms which are effective in preventing damage to their cells (98) and they can bind and sequester heavy metals to their cell surfaces, thus removing them through subsequent defecation (81). Heavy-metal and antibiotic resistance genes are often encoded together on the same plasmid, so a selective pressure exists to keep the plasmid in the intestinal tract (22).

Lactobacilli have a long history of safe use in food (43) and, more recently, as probiotics (27). Of importance is the ability of lactobacilli to reduce oxidative stresses caused by metal toxicity *in vitro* (12, 51) and detoxification abilities against other dietary toxins (104). The ability of lactobacilli to bind and sequester metals depends on the strain's resistance mechanisms. In coping with arsenic and mercury, the main method of resistance is through active expulsion of toxic metals from the cytosol. This has been shown by the presence of *mer* and *ars* operons in *Lactobacillus* and other gut-associated species (76, 116) which encode efflux transporters. Bacteria which have the ability to export metals out of their cell reduce damage to the organism by lowering the cellular concentration. However, such a mechanism is not ideal for detoxification of the gastrointestinal tract, as it results in the cycling of metals. Possibly the ideal species for detoxification are those which lack the genes encoding metal transporters and thus only bind and sequester heavy metals.

REMOVAL OF ARSENIC

One of the most toxic and common contaminants is arsenic, a metalloid element that is colorless and tasteless, widely distributed throughout the Earth's crust, and found in groundwater in a number of countries (1, 13). Natural contamination of groundwater is a health problem globally but especially in India (88) and Bangladesh (100). It has been estimated that in these two countries alone, 60 million to 100 million people are at risk because of consumption of arsenic-contaminated drinking water. The World Health Organization states that the acceptable level of arsenic in drinking water should not exceed 10 ppb.

However, this limit is difficult to maintain and may be exceeded, especially in developing regions in which water treatment technology is not readily available (99).

The route of arsenic entry into the body is through consumption of food/water and inhalation. Absorption of arsenic through the skin is minimal, and thus, hand washing and bathing with water containing arsenic does not pose human health risks (72, 124) (Table 1). Arsenic can reach dangerous levels in food; this occurs when arsenic-contaminated water is used for irrigation and accumulates in crops prior to consumption. A major threat comes from arsenic restriction limits for water, with no acceptable levels when the water is used in food. Studies have attempted to determine the exposure of the population to arsenic, but a multitude of factors, including geographic location and diet, affect this. Bangladeshi men have the highest arsenic intake, with studies showing 214 $\mu\text{g}/\text{person}/\text{day}$, while the consumption in the United States and Canada is at 88 and 59.2 $\mu\text{g}/\text{person}/\text{day}$, respectively (100). This may be both an exposure issue and a feature of differences in the gut microbiota compositions of people in these countries.

Unlike the other heavy metals discussed here, arsenic is an anionic negatively charged species; this is problematic for bacterial metal-binding interactions, as it is believed that the large amount of metal absorbed by microbes is due to charge attractions between the net negative bacterial cell and the positively charged metal. Halttunen et al. (40) attempted to overcome the charge issue of arsenic and bacterial surfaces by methylating a selection of lactobacilli in order to neutralize surface negative charges to foster more attraction between positively charged amino groups on the cell wall and negatively charged metals. Lyophilized cultures of lactobacilli were resuspended, incubated with As(III) or As(V), and observed for metal reduction. The amino groups were the most probable binding sites of As(V), and therefore, the methylation did not have a significant effect in reducing all negative charges on all observed strains. Although anionic carboxylic and

phosphate groups are the most-abundant ionic groups and give lactobacilli their net negative charge, peptidoglycan layer and surface proteins, such as S-layer proteins, are known to contain positively charged groups. *Lactobacillus acidophilus* strains and *Lactobacillus crispatus* DSM20584 are known to produce S-layer proteins, which may explain their activity against arsenic (91). Singh and Sharma (97) showed that *L. acidophilus* was able to bind and remove arsenic from water at concentrations of 50 to 1,000 ppb, and the maximum removal occurred within 4 h of exposure in a concentration-dependent manner. It is not inconceivable that home- or community-based yogurt containing lactobacilli able to remove arsenic may be of practical use in countries like India and Bangladesh (64, 79).

REMOVAL OF LEAD AND CADMIUM

Throughout history, lead has been widely used in construction and industrial projects; this has resulted in the metal being ubiquitous in the environment in soils and dust (36, 54). For the majority of people, exposure to lead occurs from secondary sources. It can be inhaled; it may enter the atmosphere through burning at industrial sources, through smelting, and until recently, through emissions of vehicles with leaded gasoline (80). Lead can also enter drinking water through older lead pipes (77), some home paints, and contaminated soils, with all causing an ongoing source of exposure and danger, especially for children.

Lead toxicity and exposure can also occur through consumption of contaminated food/water or the intake of lead particles. Lead has the ability to bioaccumulate in both the blood and bones (102). Its half-life in the blood is about 30 days, but it can remain in the skeletal system for years, and for this reason, lead toxicity is a persistent problem (42, 60) (Table 1). Lead exposure is most severe for children; thus, many reports focus on child blood lead levels (BLLs). From 1999 to 2002, an estimated 310,000 (1.6%) U.S. children had BLLs greater than 10 $\mu\text{g}/\text{dl}$ and 1.4 million (almost 14%) had BLLs of 5 to 9 $\mu\text{g}/\text{dl}$ (17). It is difficult to pinpoint sources, as there are a multitude of exposure points from the environment, diet, and even consumer goods (122), but the problem is not inconsiderable.

Cadmium generally occurs in low concentrations with other metals in the ecosystem, but it can be found in high concentrations, such as in association with zinc ore (125). Dispersion into the environment occurs from multiple sources, including inadequate disposal of electronic waste and industrial production. Sources of exposure and release in industrialized countries have been better controlled recently, but in many areas, exposures still exceed the number that occurred before industrialization. The human diet is the main source of environmental cadmium exposure in nonsmokers in most parts of the world. Atmospheric deposition of cadmium, mining activities, and the application of cadmium-containing fertilizers on farm land may lead to the contamination of soils and increased cadmium uptake by produce and livestock (14).

Cadmium is present in almost all foods, but the concentrations vary depending on the type of food and the level of environmental contamination (87). Food from plants generally contains higher concentrations of cadmium than meat, eggs, milk, dairy products, and fish (24, 73). Smoking is another major source of cadmium exposure. One cigarette may contain 1 to 2 μg cadmium, but this varies based on the brand. It is estimated that a person smoking 20 cigarettes per day will absorb about 1 μg of cadmium daily.

Recent studies based on provisional tolerable weekly intake examined cadmium accumulation in the kidneys and liver of environmentally exposed subjects. These suggested that the safe intake level for an adult is $<30 \mu\text{g}/\text{day}$ (89). Cadmium can accumulate in humans and has a long half-life in tissues of 10 to 30 years, particularly in the kidneys (47). In high-exposure areas, such as Toyama, Japan, chronic poisoning of the population from a contaminated river led to the onset of what has been called Itai-itai disease (50, 71). This is characterized by a softening of the bones, resulting in joint pain and failure of the kidneys, and other complications.

In contrast to arsenic, lead and cadmium are cationic. Although they are unique elements with differing molecular weights, occurrences in nature, and physiological effects, studies on lead and cadmium are often conducted together, as the elements seem to react with bacterial species in similar ways. Much emphasis has been put on the ability to bind and sequester these metals because of their high occurrence in the environment and in the human diet and their toxic effects.

Halttunen et al. (39) showed that *Lactobacillus* and *Bifidobacterium* species can bind lead and cadmium in solution. They observed a rapid binding phenomenon across all studied species, with the largest amounts of both lead and cadmium bound within 5 min to 1 h (39, 106). Most importantly, the metal remained strongly sequestered by the cell and did not disassociate, even 48 h after testing.

The rapid absorption of the metals from solution indicates cell surface binding. Ibrahim et al. (45) also compared the abilities of *Lactobacillus rhamnosus* LC-705 and *Propionibacterium freudenreichii* to bind and absorb lead and cadmium in solution. They reported a rapid effect of the bacteria to bind maximal amounts of metal after only 1 h of exposure; this was influenced by pH, as in *B. subtilis* and *E. coli* (52). Involvement of anionic surface groups in heavy-metal binding has been reported for the Gram-positive *B. subtilis*. *Lactobacillus rhamnosus* GG and some *Bifidobacterium longum* strains are also known to produce exopolysaccharides (53, 69), which contain different charged groups, including carboxyl, hydroxyl, and phosphate, which make a greater percentage of negatively charged groups increase the number of ligands capable of binding cationic metals such as cadmium and lead. Using electron microscopy and Fourier transform infrared spectroscopy (FTIR) with two *Lactobacillus kefir* strains, CIDCA 8348 and JCM 5818, the precipitation of metals in the cell S-layer and changes in the secondary structure of the S-layer in terms of protein arrangement and structure after metal absorption have been observed (34).

Ibrahim et al. (45) compared the abilities of two common probiotics, *L. rhamnosus* LC-705 and *Propionibacterium freudenreichii*, to bind and absorb lead and cadmium in solution. There was a rapid ability of the bacteria to bind maximal amounts of metal after 1 h of exposure. Recently, a larger study examining 53 different lactic acid bacteria isolated 11 strains shown to have high tolerance and the ability to bind cadmium and lead from water and MRS medium (21). It appeared that *Enterococcus faecium* EF031 and probiotic *E. faecium* M74 also sequestered heavy metals (36, 108). Again, the complexes formed with these strains occurred rapidly, were sufficiently long lasting (at least 48 h), and were able to be eliminated with the strains upon defecation (118).

REMOVAL OF CHROMIUM

Chromium is a metal that can be found in numerous alloys and salts. It has been used industrially for more than a century and can be detected in concentrations ranging from less than 0.1 g/m³ in air to 4 g/kg in soils. “Naturally occurring” chromium is usually present as Cr(III), and hexavalent chromium in the environment is derived from human activities (123). Trivalent Cr(III) and hexavalent Cr(VI) forms are the most important for human health, though they are poorly absorbed through the intestine (3, 24).

Studies in mice showed that gut microbiotas provided the first line of defense to the body by converting toxic Cr(VI) to a less-toxic Cr(III). *Pseudomonas* spp. obtained from the Cr-stressed rat had the highest MIC values, while *Lactobacillus* spp. and *E. coli* had lower values than bacteria from the normal control rats. This indicated that bacterial tolerance in the Cr-stressed animals contributed to the host's defense (111). However, a separate study conducted by Upreti et al. (112) showed that the exposure of lactobacilli to chromium over time can generate resistant strains able to better tolerate metals. In a similar study, Shrivastava et al. (94) showed that lactobacilli and other gut-associated bacteria, along with some human immune cells, can transform chromium to its less-toxic form. Human fecal bacteria can also bind and sequester chromium (74, 103). This is interesting, as strains of *Bacillus* species, even when dead, can perform this activity in soil. It is possible that in geographical areas in which heavy-metal contamination is high, humans inadvertently ingest these organisms. *Bacillus* species used as probiotics may be useful if they, too, have high metal-binding activity.

REMOVAL OF MERCURY

Mercury has a long history of use in human applications, although its presence in many products has been phased out due to high toxicity (Table 1). This metal can be found in both inorganic and organic forms, but it is the latter form that is most toxic. Organic mercury is fat soluble, absorbed readily across the intestinal epithelium, and able to bioaccumulate. This occurs most commonly in fish, specifically large species such as sharks and tuna that are near the top of the food chain; this bioaccumulation poses a risk to humans who consume seafood as a regular part of their diet. The detoxification of organic mercury in bacteria involves conversion of methylated mercury to inorganic Hg²⁺, which is less well absorbed in the GI tract, and then to Hg⁰, which is poorly absorbed. Organic mercury is internalized via passive means, while inorganic mercury is actively imported by the cell via mercury-specific transporters. This sequestration reduces the opportunity for it to be reabsorbed by the intestinal epithelium (85).

Unfortunately, no published scientific data on the ability of lactobacilli or gut bacteria to bind and absorb mercury exist. Preliminary studies in our laboratory have shown that certain strains of lactobacilli appear to sequester mercury and may also have mechanisms for its degradation. Although mercury is a cationic species most commonly found in a +2 oxidation state as Hg(II), we cannot assume a system of binding to the cell surface that is similar to that for lead and cadmium. However, the possibility that the large net negative charge of lactobacilli and other species of the gut will be able to bind and sequester mercury in the human gastrointestinal tract does remain.

CONCLUSIONS AND PROSPECTS FOR FUTURE STUDIES

Contamination of metals in the environment and human diet represents a persistent problem that will continue to be a burden on human health (26). While many developed countries have taken some action to monitor and reduce the problem, it remains an ongoing issue, as industrial activity is inevitably tied to the release of toxic metal (70). In the rest of the world, especially nations without the proper technologies and infrastructure, the burden of metal exposure occurs unabated and often without safeguards for their citizens. While bioremediation projects using bacterial species are now an established and active field, the application of microbes for bioprotection and detoxification of the human body of heavy metals and other contaminants is still in its infancy.

Lactobacilli and potentially other bacterial types used in the food industry or as probiotics are ideal organisms to use as an adjunct tool to prevent/reduce heavy-metal toxicity and prevent absorption of metals into the human body. Lactobacilli have a strong track record of safe application in the food industry and as probiotics, and they have the ability to bind and sequester metals. The use of lactobacilli as a tool to reduce the burden of metal exposure is advantageous, as it can be applied almost immediately; there is no requirement for expensive technology or infrastructure setup, as fermentation capability is either already available or easily set up.

Future studies should focus on the ability of lactobacilli to bind an array of heavy metals at human physiologically relevant concentrations and assess in humans the extent to which levels can be reduced over time. If such interventions can encompass locally produced foods, such as yogurt made in the home or community, this may potentially provide an affordable option for billions of people around the world who are consuming these toxic metals inadvertently on a daily basis (79).

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Jeremy Burton has always worked in the field of human microbial ecology and probiotics. His appreciation of the area was sparked as a student of Professor Gerald Tannock in the Department of Microbiology and Immunology, University of Otago. Part of his Ph.D. work was also undertaken with Nestle in Switzerland. As a postdoctoral fellow at the University of Western Ontario in the early 2000s, he was fortunate enough to study the vaginal microbiota with then-emerging non-culture-based techniques. These studies were the first to show that difficult-to-culture organisms, such as *Lactobacillus iners*, were frequent inhabitants of woman but were not often detected by bacteriological culture-based methods. After undertaking studies with the *Streptococcus salivarius* probiotics for upper-respiratory-tract applications, he has returned to the Lawson Health Research Institute and the Canadian Research and Development Centre for Probiotics to continue working on the exciting area of translating microbial ecological research into real-world applications.



Gregor Reid developed an interest in microbiology while earning his B.Sc. honors at Glasgow University. Through an International Rotary scholarship, he obtained a Ph.D. at Massey University, working on *E. coli* uropathogens. In 1982, he joined Bill Costerton's team in Canada and began collaborating with Andrew Bruce in Toronto. Together, he and Dr. Bruce studied the vaginal microbiota and the ability of lactobacilli to restore and maintain health, publishing a number of "firsts" and developing a probiotic that has subsequently been used by millions of women worldwide. Dr. Reid moved to the University of Western Ontario in 1990 as the Director of Research Services and then to the Lawson Health Research Institute in 1996. He received an M.B.A. from Monash University in 1998 and an honorary doctorate in biology from Orebro University in 2008. He has published over 400 papers and given over 500 talks in 50 countries, and he has a lab currently comprising 16 students.

