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OXFORD BIBLIOGRAPHIES IN ECOLOGY
"HEAVY METAL TOLERANCE"
By
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Introduction

The operation of biological systems is challenged by various environmental factors that interfere with or interrupt biological processes (creating stress). Some heavy metals have important physiological roles, but high doses of these essential heavy metals or exposure to other heavy metals that lack physiological roles in organisms may create stress through interference with the function of enzymes or with the information-coding molecules (DNA or RNA) in cells. Some organisms are less susceptible to these effects than others, and this heavy metal tolerance has become an important example of core biological concepts such as adaptation and evolution. Heavy metal tolerance is also of interest because organisms can be tolerant to more than one stress: understanding this phenomenon (termed “co-tolerance” or “cross-tolerance”) can provide insights into the mechanisms of tolerance and allow applications of this knowledge in solving environmental problems. Heavy metal tolerance also has vital practical and applied aspects, since human industry relies greatly on various metals (some of which are quite toxic) and these industries have resulted in pollution that can have severe impacts on the health of humans, other organisms, and entire ecosystems. Current studies explore the physiological mechanisms of heavy metal tolerance in many groups of organisms, investigate its underlying genetic basis, and use that knowledge to create genetically engineered organisms that may be useful to solve environmental problems caused by heavy metal pollution.

General Overviews

General information on heavy metal tolerance is often included in sources that cover heavy metal toxicity, as tolerance is essentially the ability of organisms to avoid the toxic effects of heavy metals. The toxicological literature is vast, but Anderson, et al. 2005 is a good example of a general resource that can provide toxicological information on heavy metals. A general toxicological text, such as Stine and Brown 1996, can provide a helpful introduction to underlying principles and approaches of toxicology. Heavy metals are generally found at relatively small concentrations in organisms, and Pais and Jones 1997 and Kabata-Pendias 2010 provide useful summaries on specific heavy metals and their interactions with soils and biota. A number of edited volumes have chapters that cover particular aspects of heavy metal tolerance: a recent example targeting cellular mechanisms affected by heavy metals is Bánfalvi 2011. Pollution by heavy metals is an important environmental problem, and sources that focus on heavy metal pollution often contain information about heavy metal tolerance (Sánchez 2008 is a recent example). Finally, there are sources that focus on a specific group of organisms and provide overviews that are taxonomically limited to that group. For example, Shaw 1990 and Gupta and Sandallo 2011 focus on heavy metal tolerance (or toxicity) in plants, a group that has been heavily researched, partly because of the applied uses of heavy metal tolerant plants in restoration and phytoextraction/phytomining operations.

Anderson, Bruce, Ann de Peyster, Shayne C. Gad, et al., eds. 2005. Encyclopedia of toxicology. 2d ed. Amsterdam: Elsevier.

A four-volume set that contains over eleven hundred entries on an extensive set of subjects relevant to toxicology, including entries on individual heavy metals.

Bánfalvi, Gáspár, ed. 2011. Cellular effects of heavy metals. New York: Springer.

A collection of sixteen chapters on aspects of heavy metal toxicity, the book includes a useful introductory chapter on general cellular effects of heavy metals. Other chapters focus on specific metals or experimental systems that reflect the expertise of the contributors.

Gupta, Dhamendra K., and Luisa M. Sandallo, eds. 2011. Metal toxicity in plants: Perception, signaling and remediation. London: Springer.

Recent summary of advances in the study of metal toxicity (and its opposite, tolerance), this book includes twelve chapters on a wide variety of topics including physiology, new advances stemming from “omics” approaches (transcriptomics, proteomics, metabolomics), gene expression, and applied fields such as phytoextraction using metal tolerant plants.

Kabata-Pendias, Alina. 2010. Trace elements in soils and plants. 4th ed. Boca Raton, FL: CRC Press.

Highlights the role that anthropogenic factors play in changing the heavy metal and other trace element status in soils and plants. Chapters cover natural/background levels of biologically relevant heavy metals in soils and plants, chemical phenomena relevant to the mobility of heavy metals, and the remediation of heavy metal–contaminated soils.

Pais, István, and J. Benton Jones Jr. 1997. The handbook of trace elements. Boca Raton, FL: St. Lucie.

Provides an overview of trace elements in biology, and then lists each of forty-one trace elements and provides a summary of its concentration in various materials (soil, water, foods, fertilizers) as well as in plants and animals.

Sánchez, Mikel L., ed. 2008. Causes and effects of heavy metal pollution. New York: Nova Science.

An edited volume covering a wide range of topics regarding heavy metal pollution, the book is a good example of a volume on pollution. It includes information in some chapters pertinent to heavy metal tolerance.

Shaw, A. Jonathan, ed. 1990. Heavy metal tolerance in plants: Evolutionary aspects. Boca Raton, FL: CRC Press.

This extensive treatment summarizes ecological, physiological, and evolutionary aspects of heavy metal tolerance research in plants, fungi, protists, and animals. The twenty-one chapters provide a useful synthesis of the heavy metal tolerance literature prior to 1990.

Stine, Karen E., and Thomas M. Brown. 1996. Principles of toxicology. Boca Raton, FL: CRC Press.

An example of a general toxicology text, it covers the breadth of toxicology, from molecular/cellular to physiological and to environmental/ecological levels.

Journals

Papers regarding heavy metal tolerance can be found in a wide variety of journals because the topic is pertinent to the broad fields of ecology, evolution, genetics, and physiology. Important journals in these areas that publish papers involving heavy metal tolerance include Evolution and Genetics. The number of journals is magnified because the topic applies to various groups of organisms (plants, fungi, bacteria, invertebrate animals, and vertebrate animals) and so pertinent papers can be found in journals with specialized taxonomic coverage, such as Plant Physiology. Even greater breadth stems from the environmental aspects of metal tolerance, such as the effects of heavy metal pollutants on organisms or communities: these can be covered in journals with environmental or pollution themes, such as Environmental Pollution or those focusing on plant-soil interactions, such as Plant and Soil. Many aspects of the environmental impacts of pollutants, including mechanisms that underlie both metal toxicity and metal tolerance, are explored in journals with a more toxicological theme, such as Journal of Applied Toxicology. Applied aspects of metal tolerance, such as using tolerant plants for phytoremediation, have specialized journals such as International Journal of Phytoremediation. A new journal, Metallomics, may develop into a major source of information pertinent to heavy metal tolerance.

Environmental Pollution.

Example of a journal with a wide coverage of the ecological effects of pollution of air, water, and soil environments, including pollution by heavy metals.

Evolution.

Published by the Society for the Study of Evolution, this journal publishes widely on evolutionary topics, including occasional papers regarding the evolution of heavy metal tolerance.

Genetics.

Publishes papers in all areas of genetics, including those covering the genetic basis of heavy metal tolerance.

International Journal of Phytoremediation.

Specializes in papers regarding phytoremediation, including papers on phytoremediation of areas polluted with heavy metals, as wells as papers on phytomining.

Journal of Applied Toxicology.

As an example of a journal that focuses on the toxicological aspects of heavy metals, this journal covers a wide range of topics, varying from mechanistic to applied areas and from molecular to environmental levels.

Metallomics.

This new journal (begun 2009) focuses on the role of metals in biological systems. Topic areas related to heavy metal tolerance include the physiological mechanisms of metal uptake/accumulation/metabolism, metal exchange between organisms and the environment, and the regulation of metal uptake and metabolism.

Plant and Soil.

This journal covers fundamental and applied aspects of plant-soil interactions, including those relating to heavy metals.

Plant Physiology.

A leading plant journal publishing papers on a wide range of plant physiological topics, including heavy metal tolerance.

Defining Heavy Metal Tolerance

The term “heavy metal tolerance” is not used uniformly. A large part of the problem is that “heavy metal” is an imprecise and inconsistently used term, with a number of definitions being offered. Duffus 2002 reviews uses of this term, finding that it has been variously defined based on density, atomic mass, atomic number, or other properties including toxicity, and suggests that definitions based on the chemical properties of elements would be more useful. Appenroth 2010 recognizes the term’s ubiquity and suggests that, instead of abandoning it, a more careful description when it is used would be helpful. The second difficulty is to define “tolerance.” First, it is a relative concept and relies on comparisons between organisms. Second, there are at least two aspects to tolerance: avoidance and resistance. One way to tolerate an application of a heavy metal is avoidance (to not take it up). Another (resistance) is to absorb that metal but to possess mechanisms to either prevent it from affecting physiology or tie it up, sequester it in a safe compartment, or eliminate it rapidly. In some cases, the word “tolerance” is applied interchangeably to these phenomena, whereas the more specific term would be more accurate. An important aspect of heavy metals is their toxicity, and much effort has been expended in determining toxicological parameters such as Lethal Dose 50% (LD50) values for these metals. A useful (and searchable) online resource for toxicological information on metals is the Agency for Toxic Substances & Disease Registry, which links to sources that can provide LD50 and other information about specific heavy metals. Ibrahim, et al. 2006 provides information about heavy metal poisoning in humans and is a good resource for information about symptoms and treatment for some important heavy metal pollutants. Finally, heavy metal pollution is usually viewed as a stress that must be tolerated by organisms, but in some cases small amounts of heavy metal pollutants can have positive effects. Lefcort, et al. 2008 provides a recent example of this phenomenon (termed “hormesis”) from a polluted freshwater system.

Agency for Toxic Substances & Disease Registry.

On this site, after performing a search for a specific metal and clicking on the substance name, one can scroll down to a link in the Toxicological and Health Professionals section called ToxGuide that provides a summary of toxicological information for that metal.

Appenroth, Klaus-J. 2010. Definition of “heavy metals” and their role in biological systems. In Soil heavy metals. Edited by I. Sheramati and A. Varma, 19–29. Soil Biology 19. Berlin: Springer-Verlag.

In addition to discussing the imprecise meaning of the term “heavy metal,” the author provides an overview of heavy metal toxicity and the effects of heavy metals on major cellular processes.

Duffus, John H. 2002. “Heavy metals”: A meaningless term?. Pure and Applied Chemistry 74:793–807.

Summary of the varied uses and meanings of the term “heavy metal” and its inconsistent use in scientific papers.

Ibrahim, Danyal, Blake Froberg, Andrea Wolf, and Daniel E. Rusyniak. 2006. Heavy metal poisoning: Clinical presentations and pathophysiology. Clinics in Laboratory Medicine 26:67–97.

Focusing on human health, this paper presents information on toxicity, symptoms, and treatment of heavy metals that are commonly involved in poisoning incidents.

Lefcort, Hugh, Zachary Freedman, Sherman House, and Mathew Pendleton. 2008. Hormetic effects of heavy metals in aquatic snails: Is a little bit of pollution good? EcoHealth 5:10–17.

This paper provides a brief review of the concept of hormesis and presents experiments that investigate it from a freshwater system. Snails from a polluted site showed hormesis, although the mechanism for the effect was unknown.

Physiological Mechanisms

Some metals have important physiological roles in organisms and are therefore essential macro- or micronutrients, whereas others have no known physiological functions. In a broad sense, animals and plants have similar general strategies that can lead to heavy metal tolerance. For example, chelation, binding metals so that they are not available to interact with sensitive cellular processes, is a common strategy. Cobbett and Goldsbrough 2002 provides a summary of two important classes of metal-binding compounds, metallothioneins and phytochelatins, that have been widely studied in eukaryotic organisms. Although phytochelatins were once thought to be specific to plants and metallothioneins to animals, recent work has shown both present in eukaryotes. Another mechanism of tolerance involves sequestration: placing metals into compartments that spatially remove them from vital tissues or processes. Vijver, et al. 2004 reviews these mechanisms. Efflux transporters can also play important roles in regulating metal concentrations in cells, as illustrated in a review of transporters of arsenic and antimony in eukaryote cells by Maciaszczyk-Dziubinska, et al. 2012. Heavy metals can also cause oxidative stress in cells, so that mechanisms that provide resistance to oxidative stress are important to heavy metal tolerance. Hossain, et al. 2012 provides a recent review of this mechanism, as well as many others, for plants.

Cobbett, Christopher, and Peter Goldsbrough. 2002. Phytochelatins and metallothioneins: Roles in heavy metal detoxification and homeostasis. Annual Reviews in Plant Biology 53:159–182.

This review provides a good introduction to these two important groups of compounds involved in metal tolerance.

Hossain, Mohammad A., Pukclai Piyatida, Jaime A. Teixeira da Silva, and Masayuki Fujita. 2012. Molecular mechanism of heavy metal toxicity and tolerance in plants: Central role of glutathione in detoxification of reactive oxygen species and methylglyoxal and in heavy metal chelation. Journal of Botany 2012:1–37.

Recent review that provides a good overview of heavy metal toxicity and how antioxidant defense tactics can lead to heavy metal tolerance in plants.

Maciaszczyk-Dziubinska, Ewa, Donata Wawrzycka, and Robert Wysocki. 2012. Arsenic and antimony transporters in eukaryotes. International Journal of Molecular Sciences 13:3527–3548.

Arsenic and antimony are toxic metalloids and all organisms have developed pathways for their detoxification. The review highlights recent advances in the understanding of arsenic and antimony transport pathways in eukaryotes, including the dual role of aquaglyceroporins in uptake and efflux of metalloids.

Vijver, Martina G., Cornelis A. M. Van Gestel, Roman P. Lanno, Nico M. van Straalen, and Willie J. G. M. Peijnenburg. 2004. Internal metal sequestration and its ecotoxicological relevance: A review. Environmental Science and Technology 38:4706–4712.

The review summarizes current knowledge on metal compartmentalization in organisms and identifies metal fractions that are indicators of toxicity. Guidance is provided on future improvement of models, such as the Biotic Ligand Model (BLM), for risk assessment of metal stress to biota.

Bacteria

Bacteria can tolerate heavy metals by regulating transport into and out of their cells or compartmentalizing them within cells, as well as other mechanisms, including production of siderophores (chelators known to detoxify heavy metals in bacteria). Schalk, et al. 2011 reviews the roles of siderophores in metal tolerance by bacteria, whereas Nies 1999 provides an overall review of the tactics used by bacteria to tolerate heavy metals. Long, et al. 2012 illustrates the importance of efflux transporters as a metal tolerance tactic by bacteria. Gillera, et al. 2009 provides a general overview of microbe-metal interactions in soils, while Nies 2003 compares the metal resistance physiology in a bacterium with sixty-three species of prokaryotes to examine protein-level similarities that may exist among metal-tolerant microorganisms. The heavy metal tolerance of some bacteria has useful applications: for example, Nies 2000 suggests that some metal resistant bacteria can be developed into metal pollution biosensors.

Gillera, Ken E., Ernst Witterb, and Steve P. McGrath. 2009. Heavy metals and soil microbes. Soil Biology and Biochemistry 41:2031–2037.

This review discusses recent advances in studies of the toxicology of metals and their effects on soil organisms. It highlights major gaps in our understanding of microbe-metal interactions and discusses the need for long-term experiments and basic research to establish relevant environmental protection policies and enhance knowledge of microbe-metal relations.

Long, Feng, Chih-Chia Su, Hsiang-Ting Lei, Jani R. Bolla, Sylvia V. Do, and Edward W. Yu. 2012. Structure and mechanism of the tripartite CusCBA heavy-metal efflux complex. Philosophical Transactions of the Royal Society B: Biological Sciences 367:1047–1058.

The authors describe the structure of efflux proteins known to expel metals in bacteria and document that one such efflux system uses methionine residues to bind and export Cu and Ag. Their studies suggest that the efflux system is capable of picking up metals from the periplasm and the cytoplasm.

Nies, Dietrich H. 1999. Microbial heavy-metal resistance. Applied Microbiology and Biotechnology 51:730–750.

This review describes metal-resistance systems in microorganisms. After a summary of the basic principles of homeostasis for all biologically relevant heavy metals, the physiology and genetics of microbial tolerance to the seventeen most important heavy metals are compared.

Nies, Dietrich H. 2000. Heavy metal-resistant bacteria as extremophiles: Molecular physiology and biotechnological use of Ralstonia sp. CH34. Extremophiles 4:77–82.

The review summarizes the molecular physiology of heavy metal tolerance in the extremophile bacterium Ralstonia sp. CH34. The use of this bacterium as a biosensor of heavy metal contamination and in biotechnological processes relating to metal resistance is also discussed.

Nies, Dietrich H. 2003. Efflux-mediated heavy metal resistance in prokaryotes. FEMS Microbiology Reviews 27:313–339.

Mechanisms of action, physiological functions, and distribution of metal-exporting proteins are outlined for sixty-three prokaryotes and are compared with the heavy metal resistant bacterium Ralstonia metallidurans. The comparison shows that heavy metal tolerance results from multiple resistance systems, some widespread among prokaryotes, and others found only in some heavy metal resistant bacteria.

Schalk, Isabelle J., Mélissa Hannauer, and Armelle Braud. 2011. New roles for bacterial siderophores in metal transport and tolerance. Environmental Microbiology 13:2844–2854.

This article examines how siderophores can play a role in protecting bacteria against heavy metal toxicity and discusses the possible contribution of these chelators to the detoxification and transport of biologically relevant metals.

Plants and Other Non-Animal Eukaryotes

General references on plant nutrition often contain useful information on the roles of metals in plant physiological processes: two authoritative sources are Epstein and Bloom 2005 and Marschner 2012. Although some heavy metals, such as nickel, copper, iron, manganese, and zinc, regulate various biological processes in plants, when they occur in excess these metals may interact directly with biomolecules, disrupting critical biological processes. Thus, most plants exclude metals at the root level by binding them to organic acids or ligands or storing them within vacuoles in the roots where they cannot interfere with important physiological processes. Bothe 2012 provides a recent overview of the general physiological mechanisms that plants use to tolerate heavy metals in soils at both whole plant and cellular levels. Some plants, called hyperaccumulator plants, take up large amounts of heavy metals into their aboveground tissues and thus are extremely metal tolerant (see Rascio and Navari-Izzo 2011, cited under Ecological Aspects: Plants). Studies of hyperaccumulator plants have been particularly useful in illustrating the physiological mechanisms of tolerance in plants. Callahan, et al. 2006 summarizes metal binding ligands in plants that hyperaccumulate metals. Other non-animal eukaryotic organisms have mechanisms similar to plants and are summarized by Backor and Fahselt 2008 (for lichens) and Gadd 1993 (for fungi).

Backor, M., and D. Fahselt. 2008. Lichen photobionts and metal toxicity. Symbiosis 46:1–10.

Symbiotic algae or cyanobacterial partners, photobionts, associated with fungi, mycobionts, in a lichen are sensitive to heavy metal stress. The review discusses biochemical and physiological mechanisms associated with heavy metal tolerance in lichens, pointing out that metal tolerance depends upon the metal, its concentration, and the strain of photobiont.

Bothe, Hermann. 2012. Plants in heavy metal soils. In Detoxification of heavy metals. Edited by I. Sheramati and A. Varma, 35–57. Soil Biology 30. Berlin: Springer-Verlag.

Provides good general coverage of the mechanisms employed by plants to tolerate heavy metals and so makes an excellent gateway to the literature. The article also extends into applied uses of metal tolerant plants in phytoremediation situations.

Callahan, Damien L., Alan J. M. Baker, Spas D. Kolev, and Anthony G. Wedd. 2006. Metal ion ligands in hyperaccumulating plants. Journal of Biological Inorganic Chemistry 11:2–12.

Mini-review covering molecules involved in sequestering, transporting, or storing metal accumulated by these types of plants. Includes a section on metallothioneins and phytochelatins,

concluding that normal plants use phytochelatins to bind metals, whereas the specialized hyperaccumulator plants do not.

Epstein, Emanuel, and Arnold J. Bloom. 2005. Mineral nutrition of plants: Principles and perspectives. 2d ed. Sunderland, MA: Sinauer.

This authoritative treatment of mineral nutrition in plants discusses the role that macro- and micronutrients play in plant growth and metabolism. Heavy metals that are also considered as micronutrients are listed and discussed with respect to the roles they play in nutrition and the symptoms that arise from their deficiencies.

Gadd, Geoffrey M. 1993. Interactions of fungi with toxic metals. New Phytologist 124:25–60.

The review examines mechanisms of heavy metal toxicity in fungi, including resistance and tolerance to metals brought about by biochemical and physiological processes at the cellular and extracellular levels. Significant interactions between heavy metals and mycorrhizal fungi and macrofungi are summarized, including environmental influences on metal toxicity toward fungi.

Marschner, Petra, ed. 2012. Marschner's mineral nutrition of higher plants. 3d ed. London: Academic Press.

This definitive reference of plant mineral nutrition covers all aspects of plant-ion interactions, including essential metals important as micronutrients for plant growth.

Animals

Heavy metal tolerance in animals is often studied in vertebrates, as that group includes humans as well as many species important to human activities, but there are specialized sources that cover invertebrates as well. Hopkin 1989 provided an early focus on heavy metal effects on invertebrates and set the stage for much future research. Janssens, et al. 2009 provides a more recent review of invertebrate heavy metal tolerance mechanisms. Besides the general mechanisms shared by plants and animals (see Physiological Mechanisms), animals can also eliminate heavy metals through their excretory systems. Some metal tolerant herbivore insects studied by Augustyniak, et al. 2008, for example, appear to be able to tolerate a diet of hyperaccumulator plant tissue partly through efficient elimination (in this case via their Malpighian tubules). Heavy metals may also cause toxicity to animals via indirect pathways: for example, metals can influence immune function (Lawrence and McCabe 2002) and thus metal tolerance can be complicated by these indirect effects on animal health.

Augustyniak, M., W. Przybylowicz, J. Mesjasz-Przybylowicz, et al. 2008. Nuclear microprobe studies of grasshopper feeding on nickel hyperaccumulating plants. X-Ray Spectrometry 37:142–145.

A pioneering work that examines tissue levels of metals as an indicator of heavy metal tolerance mechanisms, this paper is an example of the use of a sophisticated imaging tool for studying the tissue-level distribution of metals.

Hopkin, Stephen P. 1989. Ecophysiology of metals in terrestrial invertebrates. New York: Elsevier Applied Science.

This book is an early synthesis of information on the physiological effects of metals in terrestrial invertebrates and is a good introduction to the field prior to 1989.

Janssens, Thierry K. S., Dick Roeloefs, and Nico M. van Straalen. 2009. Molecular mechanisms of heavy metal tolerance and evolution in invertebrates. Insect Science 16:3–18.

Review focusing on insects and other invertebrates, highlighting recent work on metallothioneins and how their overexpression promotes cadmium tolerance in springtails (Collembola).

Lawrence, David A., and Michael J. McCabe Jr. 2002. Immunomodulation by metals. International Immunopharmacology 2:293–302.

An overview of how metals can increase or decrease activity of the immune system and thus modify effects of metals on an animal. The paper focuses on mercury as an example of these heavy metal effects.

Genetics and Evolution

Yang, et al. 2005 discusses how the advent of novel genetic tools has contributed to a renewed interest in understanding the genetic basis for heavy metal tolerance. Roux, et al. 2011 examines the role that heavy metal tolerant genes play, either directly or through pleiotropy and linkage, in reproductive isolation, that is, speciation. Research to date, across all life-forms, shows that heavy metal tolerance can evolve rapidly and repeatedly in populations exposed to heavy metal stress, as reviewed by O'Dell and Rajakaruna 2011 (cited under Genetics and Evolution: Plants). Courbot, et al. 2007 shows that major genes or loci of large effects are often responsible for metal tolerance, and Kay, et al. 2011 (cited under Genetics and Evolution: Plants) discusses how these loci often also contribute to reproductive isolation. The genetic relationship between heavy metal tolerance, an adaptive trait, and traits driving reproductive isolation, confirms the role that extreme ecologies play in the origin of species. In addition to revealing the genetic basis for speciation, studies on the genetics of heavy metal tolerance have also contributed greatly in remediation/restoration of metal-contaminated landscapes, primarily through the creation of genetically modified plants, as discussed by Maestri and Marmiroli 2011 (cited under Genetic Engineering for Metal Tolerance), that are able to tolerate and hyperaccumulate heavy metals. As with other stresses, adaptations that confer metal tolerance to organisms impose costs: Mireji, et al. 2010 illustrates this with a study of a freshwater mosquito, and McKenzie, et al. 2012 provides another example for a marine bryozoan. These costs are important factors that counterbalance heavy metals as a selective factor and limit the evolution and spread of heavy metal tolerance in organisms. Study of the genetic basis of heavy metal tolerance has benefited from application of Quantitative Trail Loci (QTL) techniques: for example, Frérot, et al. 2010 shows that both metal tolerance and hyperaccumulation traits in a model plant species have partially overlapping genetic bases and may have evolved simultaneously. Study of the genetic mechanisms underlying metal tolerance is further complicated by the many factors that can affect gene expression: van Straalen, et al. 2011 illustrates this with a study of the genetics of metal tolerance in a springtail species: they conclude that the concept of single-gene based tolerances should be replaced with a more complex ("tangled bank") model of genomic evolution.

Courbot, Mikael, Glenda Willems, Patrick Motte, et al. 2007. A major quantitative trait locus for cadmium tolerance in Arabidopsis halleri colocalizes with HMA4, a gene encoding a heavy metal ATPase. Plant Physiology 144:1052–1065.

The study confirms that HMA4, a major gene, contributes to enhanced Cd/Zn tolerance in plants under conditions of Cd/Zn toxicity by maintaining low cellular metal concentrations in the cytoplasm.

Frérot, Hèléne, Michel-P. Faucon, Glenda Willems, et al. 2010. Genetic architecture of zinc hyperaccumulation in Arabidopsis halleri: The essential role of QTL X environment interactions. New Phytologist 187:355–367.

Quantitative trait loci (QTLs) were mapped using an interspecific Arabidopsis halleri X A. lyrata petraea F2 population to determine the genomic regions that control Zn hyperaccumulation. The findings suggest that Zn tolerance and hyperaccumulation partially share a common genetic basis and may have simultaneously evolved on heavy metal–contaminated soils.

McKenzie, Louise A., Emma L. Johnston, and Robert Brooks. 2012. Using clones and copper to resolve the genetic architecture of metal tolerance in a marine invader. Ecology and Evolution 2:1319–1329.

Study of copper tolerance in a widespread invasive marine bryozoan, Watersipora subtorquata, suggests that there is considerable potential for adaptation to copper, but this comes at a cost to growth in unpolluted environments.

Mireji, Paul O., Joseph Keating, Ahmed Hassanali, et al. 2010. Biological cost of tolerance to heavy metals in the mosquito Anopheles gambiae. Medical and Veterinary Entomology 24:101–107.

Anopheles gambiae were selected for cadmium, copper, and lead tolerance through chronic exposure of larvae to metals for three successive generations. Study confirms the mosquito's potential to develop tolerance to heavy metals, particularly copper, and that tolerance comes at a significant biological cost, which can adversely affect its ecological fitness.

Roux, Camille, Vincent Castric, Maxime Pauwels, Stephen I. Wright, Pierre Saumitou-Laprade, and Xavier Vekemans. 2011. Does speciation between Arabidopsis halleri and Arabidopsis lyrata coincide with major changes in a molecular target of adaptation? PLoS One 6.11: e26872.

The study suggests that the split between two closely related species of Arabidopsis coincides with adaptive processes related to heavy-metal homeostasis.

van Straalen, Nico M., Thierry K. S. Janssens, and Dick Roelofs. 2011. Micro-evolution of toxicant tolerance: From single genes to the genome's tangled bank. Ecotoxicology 20:574–579.

The invertebrate Orchesella cincta from metal-polluted sites has a higher constitutive expression of the cadmium-induced metallothionein (Mt) gene and its promoter appears to include a large degree of polymorphism. Additionally, evolution of metal tolerance is not via a single gene adaptation but rather by a molecular network, including trans-acting factors.

Yang, Xiao-E., Xiao-Fen Jin, Ying Feng, and Ejazul Islam. 2005. Molecular mechanisms and genetic basis of heavy metal tolerance/hyperaccumulation in plants. Journal of Integrative Plant Biology 47:1025–1035.

The paper reviews what is known about the genetic basis for molecular/cellular mechanisms that underlie the uptake and detoxification of heavy metals by plants.

Bacteria

Bacteria may have genes that code for metal tolerance on the bacterial chromosome, but they also may have genes that code for metal tolerance on plasmids, small circular pieces of DNA that are inherited separately from the bacterial chromosome. Furthermore, as reviewed by Gogartin, et al. 2002, bacteria may transfer plasmids or other genetic material between species and thus spread traits such as heavy metal resistance between relatively distantly related species. This horizontal gene transfer allows evolution of heavy metal tolerance in bacteria to differ from that of eukaryotes. A recent example, Nongkhlaw, et al. 2012, studies tolerance of uranium by a bacterium isolated from mine ores in India. In some cases, evolution of heavy metal tolerance can affect agricultural activities. A classic example is the use of Bordeaux mixture, which contains copper sulfate, to control bacterial diseases of various crops. Evolution of copper resistant strains of bacteria has followed, as illustrated by the study by Cazorla, et al. 2002 of mango trees repeatedly treated with Bordeaux mixture. Co-tolerance of stresses in bacteria is interesting, as it may reveal similar modes of action of different stresses or similar mechanisms of tolerance to different stresses. The phenomenon of co-tolerance in bacteria has an important human health implication: pollution by metals may create conditions that help to maintain antibiotic resistance. Baker-Austin, et al. 2006 reviews this concept, which is generating concern as an additional and indirect threat of heavy metal pollution to human health. Finally, Olsson-Francis, et al. 2010 suggests that metal tolerance genes evolved very early in the evolution of life, since microbes in early volcanic environments needed to acquire nutrients such as iron from rockbound minerals but in doing so would be exposed to a mix of heavy metals. Thus tolerance to heavy metals evolved long before the recent human inputs of heavy metals to the environment have provided new habitats for metal tolerant bacteria.

Baker-Austin, Craig, Meredith S. Wright, Ramunas Stepanauskas, and J. V. McArthur. 2006. Co-selection of antibiotic and metal resistance. Trends in Microbiology 14:176–182.

Addresses the concern that metal contamination may aid the evolution of antibiotic resistance in bacteria because selection for metal tolerance can be linked to selection for antibiotic resistance. Thus, contamination by metals may promote the spread of antibiotic resistance and the authors point to future research directions needed to further explore this phenomenon.

Cazorla, Francisco M., Eva Arrebola, Ane Sesma, et al. 2002. Copper resistance in Pseudomonas syringae strains isolated from mango is encoded mainly by plasmids. Phytopathology 92:909–916.

The authors document evolution of copper resistance in a bacterial pathogen after repeated use of copper as a disease control agent. They demonstrate that the resistance is plasmid encoded and suggest that rapid heavy metal tolerance is responsible for disease control failures in the mango plantations they studied.

Gogartin, J. Peter, W. Ford Doolittle, and Jeffrey G. Lawrence. 2002. Prokaryotic evolution in light of gene transfer. Molecular Biology and Evolution 19:2226–2238.

Overview of how bacterial gene transfer may occur and its significance for bacterial evolution and classification.

Nongkhlaw, Macmillan, Rakshak Kumar, Celin Acharya, and Santa Ram Joshi. 2012. Occurrence of horizontal gene transfer of PIB-type ATPase genes among bacteria isolated from the uranium rich deposit of Domiasiat in North East India. PLoS One 7.10: e48199.

A study of the tolerance of bacteria to uranium, this paper provides evidence of horizontal transfer of certain genes that allow heavy metal tolerance between and among bacterial phyla.

Olsson-Francis, Karen, Rob van Houdt, Max Mergeay, Natalie Leys, and Charles C. Cockell. 2010. Microarray analysis of a microbe–mineral interaction. Geobiology 8:446–456.

DNA microarray technology is used to determine putative genes involved in weathering and sequestering of iron, using the heavy metal–resistant bacterium, Cupriavidus metallidurans CH34. The bacterium does not depend on siderophores for tolerance, but up-regulation of porins and transporters which are utilized alongside genes associated with biofilm formation.

Plants

Most evolutionary biologists are familiar with the series of classic papers titled “Evolution in closely adjacent plant populations,” reviewed in Antonovics, et al. 1971, that explored the evolution of metal tolerance in populations of grass species found on and off heavy metal–enriched mine tailings in Europe. Their work provides a classic demonstration of how natural selection can maintain distinct subpopulations (i.e., ecotypes) despite the potential for gene flow between ecologically divergent populations. Such reproductive isolation, followed by further divergence, sets the foundation for the origin of new plant species. Since this early treatment, much research has been directed at examining intraspecific variation with respect to heavy metal tolerance, as reviewed by O’Dell and Rajakaruna 2011. Additionally, Bone and Farres 2001 examines trends and rates in the evolution of heavy metal tolerance, Kay, et al. 2011 reviews speciation in response to adaptation to metal-enriched soils, and Ernst 2006 discusses evolutionary trends in metal tolerance among angiosperms. Species-level studies by Ryser and Sauder 2006 investigate the effects of heavy metals on the biology of particular species, and those by Eränen, et al. 2009 examine the effects of heavy metals on the ecology of particular species. Wright and von Wettberg 2009 discusses recent advances in ionomics and related fields that have provided the means to establish genetic relationships between adaptations to heavy metals and those mechanisms contributing to speciation.

Antonovics, Janis, Anthony D. Bradshaw, and Roger G. Turner. 1971. Heavy metal tolerance in plants. Advances in Ecological Research 7:1–85.

This review helped to establish metal tolerance in plants as a classic example of natural selection. It also emerged at a time when the effects of metal contamination (especially that originating from lead in gasoline) and revegetation of metal mining sites were generating public concern and attention from regulatory agencies.

Bone, Elizabeth, and Agnes Farres. 2001. Trends and rates of microevolution in plants. Genetica 112–113:165–182.

The authors estimate rates of evolution for heavy metal tolerance and other stressors, using data from past studies to examine trends and rates of microevolution in plants. Their analyses suggest that population differentiation in response to tolerance to metals such as Zn, Cu, and Pb may take from twenty to one thousand years.

Eränen, J. K., J. Nilsen, V. E. Zverev, and M. V. Kozlov. 2009. Mountain birch under multiple stressors: Heavy metal-resistant populations co-resistant to biotic stress but maladapted to abiotic stress. Journal of Evolutionary Biology 22:840–851.

Tolerance to heavy metals did not confer co-tolerance to other abiotic stressors, but resulted in a tradeoff of reduced performance under drought. Additionally, tolerance to heavy metals resulted

in co-resistance to insect herbivory, although the metal-induced co-resistance was not directly related to metal accumulation in plant tissue.

Ernst, Wilfried H. O. 2006. Evolution of metal tolerance in higher plants. Forest Snow and Landscape Research 80:251–274.

Written by one of the founders of the field, this review provides a good overview of the genetics and evolution of metal tolerance in plants, including plants of naturally metal-enriched sites as well as polluted sites.

Kay, Kathleen M., Kimiora L. Ward, Lorna R. Watt, and Douglas W. Schemske. 2011. Plant speciation. In Serpentine: Evolution and ecology in a model system. Edited by Susan P. Harrison and Nishanta Rajakaruna, 71–96. Berkeley: Univ. of California Press.

The chapter evaluates the theory and evidence for the mechanisms of plant speciation on heavy metal–enriched serpentine soils. It highlights how studies of serpentine plants have contributed to the general understanding of speciation processes and suggests directions for future research.

O'Dell, Ryan E., and Nishanta Rajakaruna. 2011. Intraspecific variation, adaptation, and evolution. In Serpentine: Evolution and ecology in a model system. Edited by Susan P. Harrison and Nishanta Rajakaruna, 97–137. Berkeley: Univ. of California Press.

The chapter reviews how adaptation to chemically harsh soil conditions, including heavy metal–enriched mine tailings and serpentine soils, can contribute to ecotypic differentiation and subsequent speciation. The discussion includes a useful summary of major trends in plant adaptation as demonstrated by examples of intraspecific variation found among serpentine-tolerant species.

Ryser, Peter, and Wendy R. Sauder. 2006. Effects of heavy-metal-contaminated soil on growth, phenology and biomass turnover of Hieracium piloselloides. Environmental Pollution 140:52–61.

The authors investigate the effects of heavy metals on growth, biomass turnover, and reproduction. Although the effect on growth was minimal, the delayed and reduced reproduction detected may have large effects at population, community, and ecosystem levels, and contribute to rapid evolution of metal tolerance.

Wright, Jessica W., and Eric von Wettberg. 2009. "Serpentinomics": An emerging new field of study. Northeastern Naturalist 16 (Suppl. 5): 285–296.

The review describes recent advances in the fields of ionomics, metabolomics, proteomics, transcriptomics, and genomics that can be utilized to uncover the mechanistic and genetic basis for the tolerance of and adaptation to serpentine and other heavy metal–enriched soils.

Animals

Because of its relevance to human health (see Järup 2003), heavy metal tolerance in animals has been relatively well studied. In some cases, sources provide information on the effects of specific heavy metals on genes: for example, Johnson 1998 regarding lead. Genes that code for heavy metal tolerance traits are often found to be present in many other types of organisms, indicating that they evolved early in the history of life and have been conserved over time. Preveral, et al. 2009 illustrates this point for a cadmium tolerance gene. Much work on the evolution of metal tolerance has been done using invertebrate animals from polluted sites, in part because the rapid life cycles of many of them allow adaptation to occur relatively quickly. Classic work on Collembola (springtails), as included in a review by Posthuma and van Straalen 1993, is an example. The rapid life cycles of many invertebrates are also useful for laboratory studies of heavy metal tolerance in invertebrates from both terrestrial habitats, as covered by Spurgeon and Hopkin 2000, and aquatic habitats, illustrated by Vidal and Horne 2003 and Ross, et al. 2003. Hedrickx, et al. 2008 demonstrated that exposure to cadmium affected the genetic architecture of growth rate in a spider species, but also that long-term metal pollution can have evolutionary impacts by affecting life history traits.

Hendrickx, Frederick, Jean-P. Maelfait, and Luc Lens. 2008. Effect of metal stress on life history divergence and quantitative genetic architecture in a wolf spider. Journal of Evolutionary Biology 21:183–193.

> This paper shows that metal stress can not only affect life history variation in natural populations of the wolf spider Pirata piraticus but also decreases the expression and the amount of genetic variation for particular life history traits.

Järup, Lars. 2003. Hazards of heavy metal contamination. British Medical Bulletin 68:167–182.

> The article summarizes the main threats to human health from exposure to lead, cadmium, mercury, and arsenic.

Johnson, F. M. 1998. The genetic effects of environmental lead. Mutation Research 410:123–140.

> Illustrating the many effects of this particularly toxic heavy metal on biological molecules, this overview includes a helpful section on adaptations to lead exposure that illustrates some pathways by which metal tolerance can evolve.

Posthuma, Leo, and Nico M. van Straalen. 1993. Heavy-metal adaptation in terrestrial invertebrates: A review of occurrence, genetics, physiology and ecological consequences. Comparative Biochemistry & Physiology Part C: Comparative Pharmacology and Toxicology 106:11–38.

> A wide-ranging review of heavy metal tolerance in invertebrates, this article provides access to the early literature on this topic.

Preveral, S., L. Gayet, C. Moldes, et al. 2009. A common highly conserved cadmium detoxification mechanism from bacteria to humans: Heavy metal tolerance conferred by the ATP-binding cassette (ABC) transporter Sphmt1 requires glutathione but not metal-chelating phytochelatin peptides. Journal of Biological Chemistry 284:4936–4943.

> Cadmium poses a significant threat to human health. The paper demonstrates that a common, highly conserved cadmium detoxification mechanism, via ATP-binding cassette transporters after conjugation to glutathione, has been selected during the evolution from bacteria, including plants and yeast, to humans.

Ross, Kirstin, Naomi Cooper, Joseph R. Bidwell, and John Elder. 2003. Genetic diversity and metal tolerance of two marine species: A comparison between populations from contaminated and reference sites. Marine Pollution Bulletin 44:671–679.

> This study uses genetic and physiological approaches to examine tolerance to heavy metals in a prawn and an isopod species. The two species differ with respect to diversity and tolerance, pointing to the need to examine more than one species when genetic diversity analyses are used to determine remediation success.

Spurgeon, David J., and Stephen P. Hopkin. 2000. The development of genetically inherited resistance to zinc in laboratory-selected generations of the earthworm Eisenia fetida. Environmental Pollution 109:193–201.

> The study documents the evolution of zinc and copper tolerance in earthworms over two generations and investigates the mechanisms underlying the increased resistance.

Vidal, Dora E., and Alex J. Horne. 2003. Inheritance of mercury tolerance in the aquatic oligochaete Tubifex tubifex. Environmental Toxicology and Chemistry 22:2130–2135.

> This study shows that adaptation to mercury occurs rapidly in oligochaete worms, and the metal tolerance appears to be due to both phenotypic and genotypic mechanisms. Their findings suggest that developing resistance to heavy metals may be a common phenomenon in aquatic benthic invertebrates.

Coevolutionary Relationships

Given the importance of metal tolerance as a selective factor in the environment, it is unsurprising that metal tolerance by one species may affect the metal tolerance of another. Coevolutionary studies have emphasized plants and species associated with them, particularly at the root/soil interface. Cetin, et al. 2012 explores how plant growth promoting bacteria and fungi often can increase plant metal tolerance and how these relationships may be important for phytoremediation applications. Schechter and Bruns 2008 suggests that coevolution between arbuscular mycorrhizal fungi (AMF) and plants may account for differences in community structure of mycorrhizae in serpentine and non-serpentine soils, and Hassan, et al. 2011 reports similar adaptation between plants and arbuscular mycorrhizal fungi in metal-polluted soils. In some cases, these coevolutionary relationships have practical applications: Adriaensen, et al. 2005 shows that a copper-adapted mycorrhizal fungus is able to protect pine trees from copper toxicity so that they can be grown on mine spoils. Some metal tolerant plants hyperaccumulate metals, and their high-metal tissues provide a food source for herbivores that can evolve tolerance of the metal. For example, some nickel hyperaccumulator plants host "high-nickel" insects that have relatively large amounts of Ni in their bodies. Boyd 2009 defines the term "high-nickel" insect and provides a review of the literature about these insects that presumably have evolved metal tolerance in order to be able to exploit hyperaccumulator plant tissues as a food source.

Adriaensen, Kristin, Trude Vralstad, Jean-P. Noben, Jaco Vangronsveld, and Jan V. Colpaert. 2005. Copper-adapted Suillus luteus, a symbiotic solution for pines colonizing Cu mine spoils. Applied and Environmental Microbiology 71:7279–7284.

The study shows that the Cu tolerant ectomycorrhizal fungus Suillus luteus is able to protect pine trees against Cu toxicity. The findings suggest that the Suillus-Pinus coevolutionary relationship with respect to metal tolerance might be useful for large-scale land reclamation efforts of metal-enriched industrial sites.

Boyd, Robert S. 2009. High-nickel insects and nickel hyperaccumulator plants: A review. Insect Science 16:19–31.

Providing a definition for "high-nickel" insect, this review documents a number of cases in which nickel hyperaccumulator plants are fed upon by specialist insects that have relatively high nickel levels in their bodies.

Cetin, Sema C., Ayten Karaca, Ridvan Kizilkaya, and Oguz C. Turgay. 2012. Role of plant growth promoting bacteria and fungi in heavy metal detoxification. In Detoxification of heavy metals. Edited by I. Sheramati and A. Varma, 369–388. Soil Biology 30. Berlin: Springer-Verlag.

Provides an up-to-date survey of how bacteria and fungi associated with plant roots impact plant metal tolerance. Some of the relationships described presumably involve coevolution between plants and these root associates.

Hassan, Saad El Din, Eva Boon, Marc St-Arnaud, and Mohamed Hijri. 2011. Molecular biodiversity of arbuscular mycorrhizal fungi in trace metal-polluted soils. Molecular Ecology 20:3469–3483.

The study finds a decreased diversity of native arbuscular mycorrhizal fungi in soils and Plantago major (plantain) roots harvested from metal-polluted habitats compared with soils and roots of

unpolluted habitats. Furthermore, community structure was also modified by metal contamination, suggesting a close relationship between fungi and plants in distinct soils.

Schechter, Shannon P., and Thomas D. Bruns. 2008. Serpentine and non-serpentine ecotypes of Collinsia sparsiflora associate with distinct arbuscular mycorrhizal fungal assemblages. Molecular Ecology 17:3198–3210.

The authors examine AMF assemblages associated with serpentine and nonserpentine ecotypes of Collinsia sparsiflora and find that ecotypes are associated with distinct AMF assemblages: Acaulospora dominated plants from metal rich serpentine soils, and Glomus dominated plants from nonserpentine soils, suggesting possible coevolution of plants and fungi in relation to soil.

Ecological Aspects

The ability to tolerate heavy metals can provide organisms with ecological advantages. For example, environmental stresses such as those caused by heavy metals can modify competitive relationships. Areas contaminated by heavy metals often have a distinctive biota composed of heavy metal tolerant organisms, and many studies have compared organisms from polluted and non-polluted sites to explore the ecological consequences heavy metal pollution. For example, Kozlov, et al. 2009 provides wide-ranging coverage of the effects of point source pollution (often heavy metals) on terrestrial biotas. Pollution by metals is often associated with mining and smelting operations, and there are many cases of severe metal pollution that occurred from these activities prior to the advent of pollution controls. A classic case study from North America is described in detail by Wirth 2000, and many other examples can be found on other continents. But the reliance of industrial society on metals provides additional opportunities for metal pollution. Kabir, et al. 2012 provides a global overview of the industries responsible for heavy metal pollution and the metals most often released by these activities. Certain metals have specific additional pollution sources: a recent case is that of lead used in munitions that can be accidentally ingested by wildlife. Finkelstein, et al. 2012 reports that the apparent recovery of the California Condor, an iconic bird that scavenges carcasses and is one of the world's rarest, is being undermined by lead poisoning from ammunition used by hunters. Lead is also a good example of a heavy metal that has been widely spread by vehicles due to the use of lead in gasoline, creating roadside pollution that persists well after lead was banned as a gasoline additive. Kovarik 2005 gives a historical account of how early warnings of the toxicity of lead were ignored so that leaded gasoline became widely used and the long struggle that resulted in the eventual ban on its use. In addition to polluted sites, naturally occurring high levels of some heavy metals can be found in some areas. For example, serpentine soils are derived from ultramafic rocks that often have high levels of some heavy metals. These soils often have distinctive plant communities, and much has been written about the ecology of these sites, mostly from a botanical perspective. Brooks 1987 was an early work on serpentine ecology: more recent overviews are provided by Alexander, et al. 2007 and Harrison and Rajakaruna 2011.

Alexander, Earl B., Robert G. Coleman, Todd Keeler-Wolf, and Susan P. Harrison. 2007. Serpentine geoecology of Western North America: Geology, soils and vegetation. New York: Oxford Univ. Press.

Although geographically restricted, this recent book explores the ecology of serpentine habitats, focusing on soils and plants but including information on other organisms (animals, fungi, microorganisms) where feasible.

Brooks, Robert R. 1987. Serpentine and its vegetation: A multidisciplinary approach. Portland, OR: Dioscorides.

A classic overview of serpentine geology and ecology, this volume provides a summary of early work on this habitat type and includes information on soils, plants, animals, agriculture, and vegetation.

Finkelstein, Myra E., Daniel F. Doak, Daniel George, et al. 2012. Lead poisoning and the deceptive recovery of the critically endangered California condor. Proceedings of the National Academy of Sciences of the United States of America 109:11449–11454.

As an example of heavy metal pollution via use of munitions impacting recovery of an endangered species, this widely publicized article illustrates the difficult political decisions that can be created by heavy metal pollution (in this case, whether lead bullets should be replaced by those made from other metals).

Harrison, Susan P., and Nishanta Rajakaruna, eds. 2011. Serpentine: Evolution and ecology in a model system. Berkeley: Univ. of California Press.

The nineteen chapters discuss how metal-enriched serpentine habitats have been used or can be used to address major questions in earth history, evolution, ecology, conservation, and restoration.

Kabir, Ehsanul, Sharmila Ray, Ki-Hyun Kim, et al. 2012. Current status of trace metal pollution in soils affected by industrial activities. Scientific World Journal 2012. Article id 916705

Global overview of heavy metal pollution and contributions of various industries to the problem. This paper also summarizes regulatory standards by various countries and illustrates use of the Geoaccumulation Index to judge the relative contribution of industrial contamination versus naturally occurring contributions of metals in determining metal levels at particular sites.

Kovarik, William. 2005. Ethyl-leaded gasoline: how a classic occupational disease became an international public health disaster. International Journal of Occupational and Environmental Health 11: 384–397.

In this fascinating historical account of the development, marketing and eventual ban of lead as a gasoline additive, the author describes how the deleterious effects of lead pollution were discounted or ignored because of profit motives.

Kozlov, Michail V., Elena L. Zvereva, and Vitali Zverev. 2009. Impacts of point polluters on terrestrial biota: Comparative analysis of 18 contaminated areas. New York: Springer.

This book relies on data collected from eighteen polluted sites in six countries to generate information on the response of soils, plants, and animals to severe cases of pollution (often by heavy metals) and is a good introduction to the often severe impacts of pollution upon terrestrial communities.

Wirth, John D. 2000. Smelter smoke in North America: The politics of transborder pollution. Lawrence: Univ. Press of Kansas.

Highlighting a case involving international borders (Canada and the United States), this book illustrates the severe pollution caused by heavy metal smelters before environmental regulations were created and the social and political conflicts that can arise from that pollution's effects on the environment.

Bacteria

High metal substrates, either created through pollution or those that have naturally high metal levels, provide habitat for metal tolerant bacteria. Sites used for metal mining have been a source of many metal-resistant bacteria, as recently illustrated in the study by Choudhary, et al. 2012 of bacteria from a uranium mine. Heavy metal tolerance genes may have been useful to some bacteria by preadapting them for antibiotic resistance, as mentioned in a review of evolution and ecology of antibiotic resistance by Aminov and Mackie 2007. Metal tolerant hyperaccumulator plants may concentrate metal in the soil under their canopies and create high metal habitats in which metal-resistant bacteria strains may be found, as demonstrated by Schlegel, et al. 1991. It has also been recognized relatively recently that the tissues of hyperaccumulator plants also may provide a niche for metal-tolerant bacteria, as shown by Mengoni, et al. 2010. In some cases, however, metal hyperaccumulation provides a defense against pathogenic bacteria. Fones, et al. 2010 shows that hyperaccumulation of cadmium, nickel, or zinc protected the model plant species Thlaspi (Noccaea) caerulescens from attack by some (unadapted) strains of a bacterial pathogen. This study also shows, interestingly, that bacterial populations from a field site where the plant naturally occurred had apparently evolved metal tolerance and were able to colonize plant leaves. Finally, it should be noted that besides the physiological mechanisms that contribute the bacterial heavy metal tolerance (see Physiological Mechanisms: Bacteria), bacterial community properties can provide tolerance to stresses (including heavy metal stress). Formation of biofilms by bacterial communities is an important feature in bacterial ecology, and Harrison, et al. 2007 provides a helpful review of the contribution of biofilms to bacterial heavy metal tolerance.

Aminov, Rustam I., and Roderick I. Mackie. 2007. Evolution and ecology of antibiotic resistance genes. FEMS Microbiology Letters 271:147–161.

Some genes that encode resistance to stress factors, including some heavy metals, also provide resistance to antibiotics. An example involving resistance to mercury and subsequent interest in dental amalgams containing mercury is discussed.

Choudhary, Sangeeta, Ekramul Islam, Sufia K. Kazy, and Pinaki Sar. 2012. Uranium and other heavy metal resistance and accumulation in bacteria isolated from uranium mine wastes. Journal of Environmental Science and Health, Part A: Toxic/Hazardous Substances and Environmental Engineering 47:622–637.

The authors discover several strains of bacteria tolerant to uranium but also co-tolerant to cadmium, cobalt, copper, and nickel from samples taken from mine wastes. The strains also produced chemicals that might be useful for mining or pollution remediation efforts in the future.

Fones, Helen, Calum A. R. Davies, Arantza Rico, Fang Fang, J. Andrew C. Smith, and Gail M. Preston. 2010. Metal hyperaccumulation armors plants against disease. PLoS Pathogens 6:e1001093.

Testing the elemental defense hypothesis for metal hyperaccumulation, the authors demonstrate that hyperaccumulated metals inhibit the growth of a bacterial pathogen through direct effects of tissue metals on bacterial cells. They also show that pathogens from field sites have likely evolved metal tolerance as a counterdefense tactic.

Harrison, Joe J., Howard Ceri, and Raymond J. Turner. 2007. Multimetal resistance and tolerance in microbial biofilms. Nature Reviews Microbiology 5:928–938.

This review suggests that biofilms can resist metals through chemical, physical, and physiological processes that are affected by variation among biofilm cells. The authors propose that cellular diversification within a biofilm provides multimetal resistance properties to microbial biofilms.

Mengoni, Alessio, Henk Schat, and Jaco Vangronsveld. 2010. Plants as extreme environments? Ni-resistant bacteria and Ni-hyperaccumulators of serpentine flora. Plant and Soil 331:5–16.

This paper reviews the niches that hyperaccumulator plants can provide for Ni tolerant bacteria, including the rhizosphere (niche surrounding a plant root) and the newly explored endosphere (niche inside the tissues of a plant).

Schlegel, H. G., J.-P. Cosson, and Alan J. M. Baker. 1991. Nickel-hyperaccumulating plants provide a niche for nickel-resistant bacteria. Botanica Acta 104:18–25.

In a pioneering investigation of the soil under hyperaccumulating plants, the authors find nickel resistant bacteria in soils that are enriched in nickel by hyperaccumulators.

Plants

Some soils have naturally elevated levels of heavy metals, and plants that can tolerate those soils are generally termed metallophytes. Baker 1981 classified the ability of metallophytes to tolerate metals into two major strategies: accumulators and excluders. Accumulators concentrate metals in plant parts, whereas excluders keep shoot levels low over a wide range of soil metal concentrations. The International Society for Serpentine Ecology maintains an online database of information on metallophytes and is a good resource for information about these species. Some metallophytes, termed hyperaccumulators by Brooks, et al. 1977, take up and sequester relatively large amounts of metals in their aboveground tissues. Brooks 1998 provides an early overview of many aspects of hyperaccumulator plants, while van der Ent, et al. 2012 provides a very recent summary of the definitions of hyperaccumulation of various heavy metals. Rascio and Navari-Izzo 2011 provides a broad summary of the physiology and ecology of metal accumulating plants, including hyperaccumulators.

Baker, Alan J. M. 1981. Accumulators and excluders: Strategies in the response of plants to heavy metals. Journal of Plant Nutrition 3:643–654.

An early review by a leader in the field of plant metal tolerance, this paper defined accumulators and excluders as well as indicators, plants that have proportional relationships between soil metal content and metal concentration in plant tissues.

Brooks, Robert R., ed. 1998. Plants that hyperaccumulate heavy metals: Their role in phytoremediation, microbiology, archaeology, mineral exploration and phytomining. Wallingford, UK: CAB International.

The fifteen chapters in this edited volume provide a broad coverage of hyperaccumulator plants and the many fields of study in which they play a role.

Brooks, Robert R., Julian Lee, Roger D. Reeves, and Tanguy Jaffré. 1977. Detection of nickeliferous rocks by analysis of herbarium specimens of indicator plants. Journal of Geochemical Exploration 7:49–77.

This paper first used the term “hyperaccumulator” for plants that take up extraordinary quantities of metals into their tissues. It also illustrates the value of such plants for bioprospecting, use of such plants as an indicator of the presence of metal ores, a topic that continues to generate interest today.

International Society for Serpentine Ecology.

This website contains a link to a global database of information regarding metallophyte plants. Most of the information pertains to plants from serpentine soils.

Rascio, Nicoletta, and Flavia Navari-Izzo. 2011. Heavy metal accumulating plants: How and why do they do it? And what makes them so interesting? Plant Science 180:169–181.

The paper reviews the physiology, genetics, ecology, and applied aspects of metal tolerant plants, especially those known to hyperaccumulate heavy metals. The figures illustrate transport systems constitutively overexpressed and/or with enhanced affinity to heavy metals and their role in uptake, root-to-shoot translocation, and vacuolar sequestration.

van der Ent, Antony, Alan J. M. Baker, Roger D. Reeves, A. Joseph Pollard, and Henk Schat. 2012. Hyperaccumulators of metal and metalloid trace elements: Facts and fiction. Plant and Soil 362:1–16.

A timely review clarifying the circumstances in which the term “hyperaccumulator” is appropriate, outlining the conditions to be met when the term is used. It summarizes the main considerations for establishing metal hyperaccumulation in plants and redefines some of the terminology, including thresholds for the hyperaccumulation of various metals.

Animals

The impacts of heavy metal pollution on animals has been an important area of study at least since the 1960s, when increasing environmental awareness began to highlight the issue of pollution in general, and has resulted in many investigations of fauna of metal polluted sites. Results of these studies imply that heavy metal pollution has decreased biodiversity in polluted areas: Ficken and Byrne 2012 describes a recent case for frog species in Australia. Studies of metal polluted sites have described many cases of disruption of ecological relationships stemming from the toxic effects of heavy metals on members of terrestrial and freshwater communities. Lürling and Scheffer 2007 describes a relatively subtle way that some pollutants (including heavy metals) can disrupt ecological relationships among aquatic organisms: info-disruption. By interfering with animal sensory systems, metals can have important effects on organismal interactions at concentrations that are less than those used to define toxicity. Thus toxicity is not the only danger from pollutants such as heavy metals. Byzitter, et al. 2012 shows that low concentrations of two heavy metals in aquatic snails can impede memory formation, but only when the metals were applied in combination. As pointed out by Yang 1994, much toxicological literature has developed around studies that examine heavy metals singly: it is clear that more emphasis needs to be placed on determining effects of mixtures. An interesting connection between heavy metals and ecology is the potential use of heavy metals to indirectly study animal ecology. For example, Das, et al. 2000 shows that heavy metal concentrations of the tissues of marine top predators can be useful in describing their feeding niches.

Byzitter, Jovita, Ken Lukowiak, Vikram Karnik, and Sarah Dalesman. 2012. Acute combined exposure to heavy metals (Zn, Cd) blocks memory formation in a freshwater snail. Ecotoxicology 21:860–868.

Illustrating the importance of considering mixtures as well as studies of sublethal effects of metal pollutants, the authors show that memory formation is inhibited by metals only when a mixture of the two metals is applied.

Das, Krishna, Gilles Lepoint, Véronique Loizeau, Virginie Debacker, Patrick Dauby, and Jean-Marie Bouquegneau. 2000. Tuna and dolphin associations in the North-east Atlantic: Evidence of different ecological niches from stable isotope and heavy metal measurements. Marine Pollution Bulletin 40:102–109.

Studies of these marine top predators show that heavy metal levels in tissues of some populations can be used to infer both diet preferences and feeding locations. This information is helpful to management efforts for these species.

Ficken, Kristina L. G., and Phillip G. Byrne. 2012. Heavy metal pollution negatively correlates with anuran species richness and distribution in south-eastern Australia. Austral Ecology.

Recent study showing a negative correlation of frog species richness with water heavy metal concentration, implying that intolerant species were declining in response to heavy metal pollution. This study adds heavy metals to a host of environmental features that are causing a global biodiversity crisis in amphibians.

Lürling, Miquel, and Marten Scheffer. 2007. Info-disruption: Pollution and the transfer of chemical information between organisms. Trends in Ecology and Evolution 22:374–379.

This review established the concept of info-disruption, which suggests that low (sublethal) levels of pollutants (including metals) may affect the ecological relationships of organisms by interfering with their ability to gather information from their environment.

Yang, Raymond S. H., ed. 1994. Toxicology of chemical mixtures: Case studies, mechanisms, and novel approaches. London: Academic Press.

Although not focused solely upon metals, this edited volume contains twenty-five chapters covering a wide range of topics regarding the toxicology of mixtures. It illustrates the importance of studying chemical mixtures, the approaches that can be used, and provides some case studies.

Environmental Health

Because of the toxicity of heavy metals, heavy metal pollution can be a major environmental threat. Han, et al. 2002 quantifies anthropogenic inputs of heavy metals into the environment by human activities on a global scale, indicating the magnitude of this challenge to environmental health. In some cases, particular groups of organisms can be important indicators (bioindicators) of heavy metal pollution, either because they are tolerant of the metals and accumulate them in their bodies (in which case analysis of their bodies can show that an area is polluted), or because they are not tolerant and their absence from an area can be used to indicate that the area is polluted. A classic example is lichens: Garty 2001 provides a comprehensive introduction to this topic. Biomagnification is a phenomenon that can result from pollutants (including heavy metals) in ecosystems. It is generally defined as the increase in concentration of a pollutant in the tissues of organisms as trophic level increases in a food web, and if it occurs may have important impacts on top carnivores if they are not relatively tolerant of the pollutant. Gray 2002 provides a critical review of this topic and of the approaches used to study biomagnification of pollutants (including heavy metals), focusing on marine ecosystems, while Langdon, et al. 2003 explores the possibility of arsenic transfer via earthworms living in metal-contaminated mine spoils. Human health threats of heavy metals depend on the metal, and a useful overview of heavy metal pollution effects on humans is provided by Järup 2003 (cited under Genetics and Evolution: Animals). High levels of metals can be found naturally in some locations that are not polluted by humans, and the metal levels of these sites can lead to potential human health hazards. An example of this is the study of Miranda, et al. 2009, which reports on levels of heavy metals in cattle raised on serpentine soils in Europe. Additional examples in which insect herbivores mobilize heavy metals by feeding on metal hyperaccumulator plants are provided by Petersen, et al. 2003 and Boyd, et al. 2006. Other human health issues can arise from heavy metals in medicinal plants, as discussed by Street 2012.

Boyd, Robert S., Michael A. Wall, and Tanguy Jaffré. 2006. Nickel levels in arthropods associated with Ni hyperaccumulator plants from an ultramafic site in New Caledonia. Insect Science 13:271–277.

> This survey reveals some high-Ni insects that apparently are specialist feeders on hyperaccumulator plants and can move Ni into local food webs.

Garty, Jacob. 2001. Biomonitoring atmospheric heavy metals with lichens: Theory and application. Critical Reviews in Plant Sciences 20:309–371.

> A review of the use of lichens to monitor atmospheric heavy metal pollution, this paper explores how lichens acquire metals, where they store them, and discusses the practical uses of lichens to monitor two important heavy metal pollutants with important human health consequences: lead and mercury.

Gray, John S. 2002. Biomagnification in marine systems: The perspective of an ecologist. Marine Pollution Bulletin 45:46–52.

The author reviews studies of biomagnification in marine systems, finding that for metals it is only well documented for mercury. He further suggests that changes be made in how some studies document biomagnification, as they may not actually be measuring the correct parameters.

Han, Fengxiang X., Amos Banin, Yi Su, et al. 2002. Industrial age anthropogenic inputs of heavy metals into the pedosphere. Naturwissenschaften 89:497–504.

This interesting review article quantifies human inputs of seven important heavy metals into the global environment during the Industrial Age, and provides some general estimates of per capita metal burdens over time and metal inputs to soils.

Langdon, Caroline J., Trevor G. Piearce, Andrew A. Meharg, and Kirk T. Semple. 2003. Interactions between earthworms and arsenic in the soil environment: A review. Environmental Pollution 124:361–373.

The review discusses the relationships between earthworms and arsenic-rich mine spoil wastes, examining possible mechanisms of tolerance to the heavy metal and potential routes for transfer of arsenic across trophic levels.

Miranda, M., J. L. Benedito, I. Blanco-Penedo, C. Lo´pez-Lamas, A. Merino, and M. López-Alonso. 2009. Metal accumulation in cattle raised in a serpentine-soil area: Relationship between metal concentrations in soil, forage and animal tissues. Journal of Trace Elements in Medicine and Biology 23:231–238.

The paper evaluates chromium, copper, and nickel accumulation in cattle raised in a serpentine area in southwestern Europe. A relatively high percentage of cattle showed tissue levels of nickel and copper indicative of risk of toxicity. Accumulation of chromium in tissues was generally low and within the normal range.

Peterson, Lynsey R., Victoria Trivett, Alan J. M. Baker, Carlos Aguiar, and A. Joseph Pollard. 2003. Spread of metals through an invertebrate food chain as influenced by a plant that hyperaccumulates nickel. Chemoecology 13:103–108.

One of the first demonstrations that heavy metal plants can mobilize metals into food webs (in this case, nickel). This phenomenon has implications for phytoremediation/phytomining, which might mobilize metals and cause unanticipated environmental impacts.

Street, Renée A. 2012. Heavy metals in medicinal plant products: An African perspective. South African Journal of Botany 82:67–74.

Discusses potential impacts of heavy metals in African medicinal plants, including examples of heavy metal poisoning caused by medicinal plants used in Africa, as well as discussion of the need for international standards and regulation to prevent additional incidents.

Habitat Reclamation and Restoration

Reclamation or restoration of sites damaged by mining activity is an important applied aspect of heavy metal tolerance. Plant heavy metal tolerance was famously reported by Bradshaw 1952 for the grass Agrostis tenuis, focusing on plants that were able to grow on metal-polluted soil near Roman-era metal mines in Great Britain. He realized the practical importance of this discovery and how it might apply in other cases of human-caused metal pollution. As reviewed by Sheoran, et al. 2010, reclamation/revegetation of mines is a complex task, with metal-tolerant plants playing an important role by being able to colonize the often high metal substrates left behind. O'Dell and Claasen 2011 provides an overview of methods useful for aiding in the recovery of sites characterized by harsh environmental conditions, including high levels of heavy metals. As pointed out by Khan, et al. 2000, one also has to consider the role of mutualists (particularly mycorrhizae) in contributing to plant metal tolerance under field conditions. Whiting, et al. 2004 and Baker, et al. 2010 provide useful summaries of the importance of conservation of plants with metal-tolerance capabilities for future reclamation and restoration efforts.

Baker, Alan J. M., Wilfried H. O. Ernst, Antony van der Ent, Françoise Malaisse, and Rosanna Ginocchio. 2010. Metallophytes: The unique biological resource, its ecology and conservational status in Europe, central Africa and Latin America. In Ecology of industrial pollution. Edited by Lesley C. Batty and Kevin B. Hallberg, 7–40. Cambridge, UK: Cambridge Univ. Press.

A broad overview of heavy metal tolerant plants from particular geographic regions, this chapter brings attention to the need to conserve these plants for their scientific values as well as their value in developing applied technologies.

Bradshaw, Anthony D. 1952. Populations of Agrostis tenuis resistant to lead and zinc poisoning. Nature 169:1098.

Bradshaw's first report of heavy metal tolerance in this grass species. Further research would show that the tolerance was due to a relatively small genetic difference and had evolved fairly rapidly, making this a classic example of plant evolution.

Khan, A. G., C. Kuek, T. M. Chaudhry, C. S. Khoo, and W. J. Hayes. 2000. Role of plants, mycorrhizae and phytochelators in heavy metal–contaminated land remediation. Chemosphere 41:197–207.

Review of bioremediation of contaminated land, presenting the potential roles of arbuscular mycorrhizae and ectomycorrhizae as well as natural and synthetic chelators that can influence metal availability in soils.

O'Dell, Ryan E., and Victor Claasen. 2011. Restoration and revegetation of harsh soils. In Serpentine: Evolution and ecology in a model system. Edited by Susan P. Harrison and Nishanta Rajakaruna, 383–416. Berkeley: Univ. of California Press.

The chapter focuses on the restoration and revegetation of heavy metal-enriched serpentine ecosystems. The discussion highlights soil and vegetation manipulation methods used to restore partially degraded serpentine soils and focuses on steps that are critical to successful revegetation of severely degraded serpentine and other edaphically harsh settings.

Sheoran, V., A. S. Sheoran, and P. Poonia. 2010. Soil reclamation of abandoned mine land by revegetation: A review. International Journal of Soil, Sediment and Water 3.2:1–20.

A broad overview of the challenges faced during mine land restoration, including the importance of metal resistant plants because of their ability to survive the difficult conditions on those restoration sites.

Whiting, Stephen N., Roger D. Reeves, D. Richards, et al. 2004. Research priorities for conservation of metallophyte biodiversity and their potential for restoration and site remediation. Restoration Ecology 12:106–116.

This paper stresses the need to protect heavy metal tolerant plants because they and their genes provide the basis for reclamation/restoration of heavy metal–contaminated sites. The authors discuss six important questions about knowledge gaps, threats to metallophytes, their uses, and ethical issues raised by those uses.

Phytoextraction of Heavy Metals

Heavy metal tolerant plants have important potential uses as a mechanism to remove metals from soils (phytoextraction). The soils may either be contaminated with the metals through pollution by human activity (phytoremediation) or have naturally elevated metal levels (phytomining): in either case, the plant material could be harvested to remove the metal from the site. In either case, but particularly for phytomining, harvested material could then be used to generate bioenergy and the metals recovered and put into the smelter stream or, if the recovery of the metal is not economically feasible, disposed of in a landfill. Chaney, et al. 2007 provides an overview of these uses of tolerant plants while a recent review by Tang, et al. 2012 reports that phytomining may be most economically feasible for nickel. Bhargava, et al. 2012 provides ideas about techniques that can be used to develop new genotypes of metal extracting plants, while Meier, et al. 2012 points out that mutualists such as mycorrhizal fungi may be able to aid with phytoextraction efforts. The Phytoremediation of Organics Action Team provides an online searchable database of phytoremediation-oriented publications that can be a useful information search tool. As with any new technology, phytoremediation/phytomining may involve potential environmental risks; these are reviewed by Angle and Linacre 2005.

Angle, J. Scott, and Nicholas A. Linacre. 2005. Metal phytoextraction: A survey of potential risks. International Journal of Phytoremediation 7:241–254.

Summary of problems that may be created by phytoextraction technologies, including creating new weeds, toxicity to plants and native animals, and transfer of genetic material from phytoextraction crops to native plants.

Bhargava, Atul, Francisco F. Carmona, Meenakshi Bhargava, and Shilpi Srivastava. 2012. Approaches for enhanced phytoextraction of heavy metals. Journal of Environmental Management 105:103–120.

The review provides an update with respect to heavy metal tolerance and accumulation mechanisms in plants, as well as the environmental and genetic factors affecting metal uptake. Possible strategies for developing novel genotypes with increased metal accumulation and tolerance to toxicity are also discussed.

Chaney, Rufus L., J. Scott Angle, C. Leigh Broadhurst, Carinne A. Peters, Ryan V. Tappero, and Donald L. Sparks. 2007. Improved understanding of hyperaccumulation yields commercial phytoextraction and phytomining technologies. Journal of Environmental Quality 36:1429–1443.

This paper connects advances in knowledge about hyperaccumulation with the uses of hyperaccumulator plants in emerging technologies that use that feature to remove heavy metals from either contaminated soils or naturally high-metal soils.

Meier, Sebastian, Fernando Borie, Nanthi Bolan, and Pablo Cornejo. 2012. Phytoremediation of metal-polluted soils by arbuscular mycorrhizal fungi. Critical Reviews in Environmental Science and Technology 42:741–775.

Heavy metal tolerant microbes are able to enhance the ability of plants to remediate contaminated soils. The review summarizes the use of arbuscular mycorrhizal fungi (AMF) in the promotion of phytoremediation processes by, for example, enhancing plant biomass in polluted soils and stimulating phosphorous nutrition under metal stress.

Phytoremediation of Organics Action Team.

This searchable database of information sources regarding phytoremediation is a useful resource for those interested in heavy metals as well as organic pollutants. The database is no longer being updated but currently is predicted to remain available online until at least 2015.

Tang, Y. T., T. H. B. Deng, Q. H. Wu, et al. 2012. Designing cropping systems for metal-contaminated sites: A review. Pedosphere 22:470–488.

Recent review covering the use of plants on contaminated sites. Proper selection of plant species can result in production of: (1) edible plants that have low metal levels (due to phytoexclusion), (2) plants that can limit the movement of metals into food chains (phytostabilization), or (3) plants that can remove metals from the soil (phtyoremediation/phytomining).

Genetic Engineering for Metal Tolerance

Our increasing understanding of the mechanisms of heavy metal tolerance and their genetic basis allows the use of genetic engineering to increase metal tolerance in some organisms. Because metal tolerance is an important feature of plants used for mine reclamation/restoration or phytoremediation/phytomining, there has been great interest in using genetic engineering to improve or establish metal tolerance in plants used in these activities. Jez 2011 and Maestri and Marmiroli 2011 provide complementing coverage of recent progress in using genetic engineering to improve phytoremediation efforts, including phytoremediation of heavy metal pollution. Bacteria can also be very important tools for metal mining, as reviewed by Rawlings 2002, and also are useful for remediation of pollution. Because bacteria can be relatively easy to genetically modify, efforts have been made to genetically engineer heavy metal tolerant bacteria as well. Singh, et al. 2011 provides a recent review of genetic engineering of bacteria for environmental remediation and is a good entry point into the literature for bacteria. Compared with plants and bacteria, there is relatively less interest in genetic engineering for heavy metal tolerance into other groups of organisms, including animals, but Pócsi 2011 provides a recent review of heavy metal tolerance in fungi that considers future approaches to genetic engineering metal tolerance in this group of organisms.

Jez, Joseph M. 2011. Toward protein engineering for phytoremediation: Possibilities and challenges. International Journal of Phytoremediation 13 (Suppl. 1): 77–89.

> The review summarizes molecular methods for altering or improving protein function, highlighting examples of how these methods have addressed bioremediation problems. The author proposes the use of protein engineering technologies combined with genomic information and metabolic engineering strategies to design plants and microbes to remediate both organic and inorganic pollutants.

Maestri, E., and N. Marmiroli. 2011. Transgenic plants for phytoremediation. International Journal of Phytoremediation 13 (Suppl. 1): 264–279.

> The paper reviews transgenic approaches for metal tolerance and discusses recent efforts to transform plant species to hyperaccumulate heavy metals and organic pollutants for more efficient phytoremediation. Tables and figures provide useful summaries for sources of transgenes, target genes and recipient plants, and the results of recent transformations.

Pócsi, István. 2011. Toxic metal/metalloid tolerance in fungi: A biotechnology-oriented approach. In Cellular effects of heavy metals. Edited by Gáspár Bánfalvi, 31–48. New York: Springer.

> In this recent review of mechanisms of heavy metal tolerance in fungi, the author includes suggestions for approaches that might be used to genetically engineer heavy metal tolerant fungi.

Rawlings, Douglas E. 2002. Heavy metal mining using microbes. Annual Review of Microbiology 56:65–91.

Reviews the importance of bacteria as tools for the mining industry.

Singh, J. S., P. C. Abhilash, H. B. Singh, R. P. Singh, and D. P. Singh. 2011. Genetically engineered bacteria: An emerging tool for environmental remediation and future research perspectives. Gene 480:1–9.

A review of the important uses that are being considered for genetically engineered bacteria and the biosafety challenges of using genetically engineered organisms to solve environmental problems.

Model Organisms

Many advances in biology have been made by focusing research efforts on particular species that are widely studied by many groups of researchers. Emphasis on these model organisms allows a deeper understanding of phenomena such as heavy metal tolerance. Among animals, Drosophila is an important model organism, as illustrated by the work of Balamurugan, et al. 2004 comparing metal tolerance between Drosophila and mammalian cells. Springtails (Collembola) have emerged as an invertebrate group about which much has been learned about metal tolerance mechanisms, as summarized by Janssens, et al. 2009 (cited under Physiological Mechanisms: Animals). The utility of the Noccaea caerulescens species as a model organism is summarized by Milner and Kochian 2008, and discussion of other model hyperaccumulator plants is found in Krämer 2010. Model organisms in the algae that have been studied for their metal tolerance include Chlamydomonas reinhardtii, as summarized by Hanikenne 2003. Among bacteria, the human gut bacterium Escherichia coli is a widely used model organism for bacterial genetics and ecology and has been studied for its heavy metal tolerance (Nies 1999, cited under Physiological Mechanisms: Bacteria).

Balamurugan, K., D. Egli, A. Selvaraj, B. Zhang, O. Georgiev, and W. Schaffner. 2004. Metal-responsive transcription factor (MTF-1) and heavy metal stress response in Drosophila and mammalian cells: A functional comparison. Biological Chemistry 385:597–603.

Vertebrate and Drosophila MTF-1, involved in the tolerance to heavy metals, are highly conserved in the region for zinc tolerance but are quite divergent in most other parts. The paper describes a series of experiments to determine similarities and differences in the heavy metal response between insects and mammals.

Hanikenne, Marc. 2003. Chlamydomonas reinhardtii as a eukaryotic photosynthetic model for studies of heavy metal homeostasis and tolerance. New Phytologist 159:331–340.

The review examines a common algal species as a model for studies of heavy metal tolerance. Recent molecular advances, including molecular mapping and whole genome and extended expressed sequence tag (EST) sequencing, have made this taxon an extremely valuable model for studying heavy metal homeostasis and tolerance in photosynthetic organisms.

Krämer, Ute. 2010. Metal hyperaccumulation in plants. Annual Review of Plant Biology 61:517–534.

The paper reviews the history of metal hyperaccumulator research, highlighting metal hyperaccumulating species, including recent advances using model plants such as Arabidopsis halleri and Noccaea caerulescens. The physiological, molecular, and genetic basis underlying metal hyperaccumulation and its evolution and future research needs and opportunities are also discussed.

Milner, Matthew J., and Leon V. Kochian. 2008. Investigating heavy-metal hyperaccumulation using Thlaspi caerulescens as a model system. Annals of Botany 102:3–13.

The review highlights recent advances in molecular and genetic techniques in examining the physiological mechanisms underlying tolerance to heavy metals such as Zn, Cd, and Ni in the model plant Thlaspi (Noccaea) caerulescens. Furthermore, the use of this taxon for better understanding of micronutrient homeostasis and nutrition is also discussed.