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Mercury Contamination and its Potential Roles in Antibiotic Resistance and Infectious Diseases

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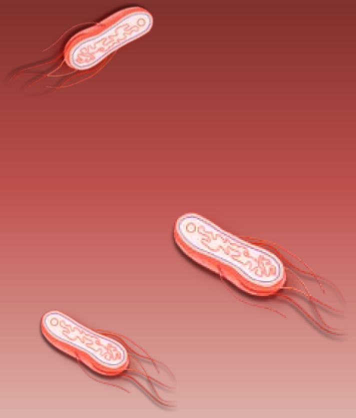

Adapted from a presentation first delivered at the

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Introduction

- During this era of increasing use of antibiotics in medicine and agriculture releases of mercury to the environment have also increased significantly.
- Many bacterial pathogens important in human health and agriculture are now developing resistance to multiple antibiotic drugs.
- There is also some evidence that parasitic diseases such as malaria may be reemerging in areas where increasing releases of mercury from mining are occurring.
- Increasing levels of mercury contamination in both outdoor and indoor environments may be an important contributor to these trends.

This presentation will describe the mechanisms of action and potential relationships of environmental mercury contamination to infectious diseases.

Mechanism of Action: Bacterial Resistance to Antibiotics

- Mercury contamination in an environment favors selection and proliferation of resident bacteria that are resistant to mercury's toxicity.
- In bacteria, the genes for resistance to both mercury toxicity and antibiotics are often located close together on mobile genetic elements – transposons and plasmids.
  - Transposons or "jumping genes" are sequences of DNA that can move around to different positions within the genome of a single cell.
  - Plasmids are DNA molecules outside the chromosome, usually double stranded and circular in shape, that often carry genes for resistance to chemicals in the surrounding environment.

Bacterial Resistance to Antibiotics

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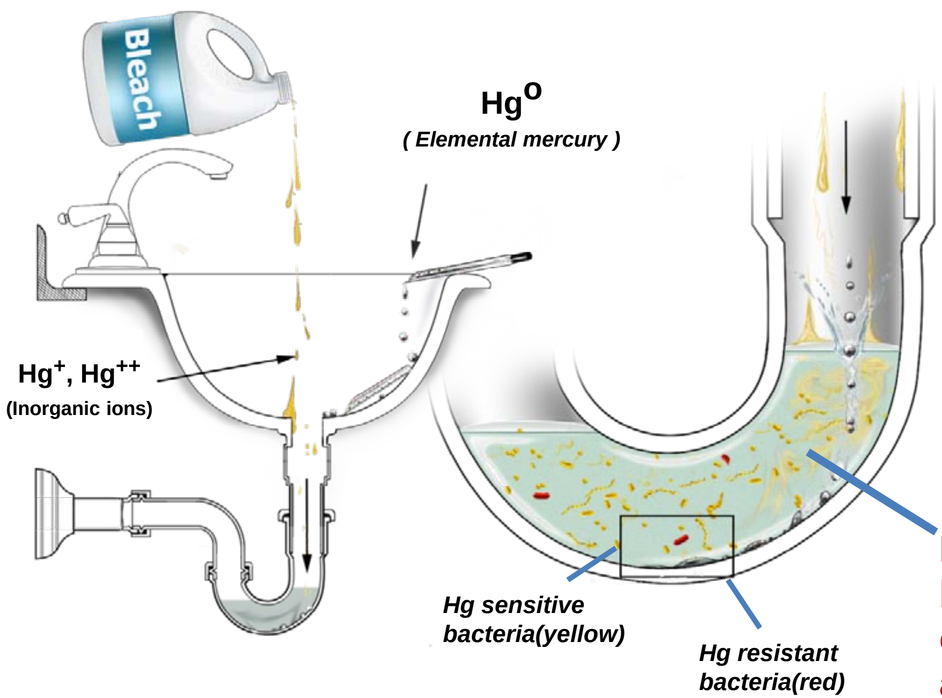
- Because resistance genes are located on these mobile genetic elements they can be easily transferred between different bacteria.
- Bacteria that are sensitive to mercury and antibiotics can rapidly acquire resistance from resistant bacteria by plasmid transfer.

These processes are illustrated in the following slides depicting a contamination scenario that may occur in the microenvironment of a hospital or laboratory sink trap.

Discharge into the Wastewater System

Common sources of mercury (Hg) in wastewater systems include contaminated janitorial products like some types of bleach, amalgam from dental clinics and spills from broken thermometers.

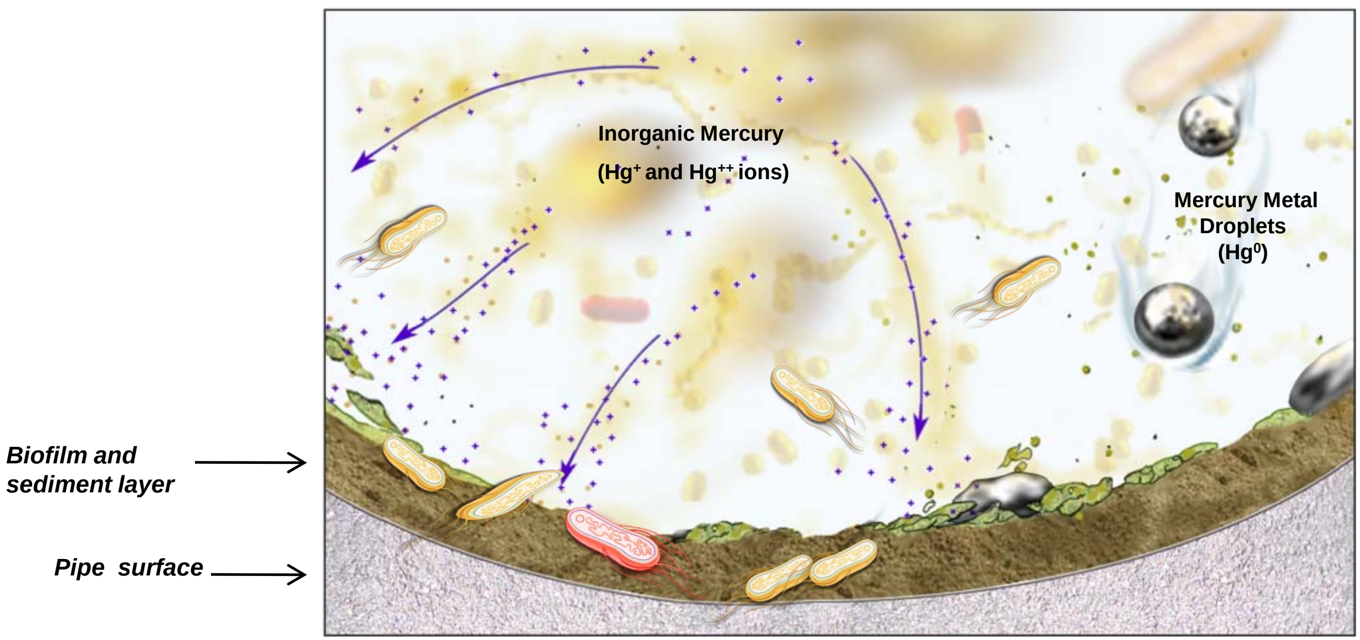


Most of the initial population of bacteria in the wastewater environment is sensitive to antibiotics and not resistant to mercury's toxic effects.

Accumulation in Biofilms and Sediments

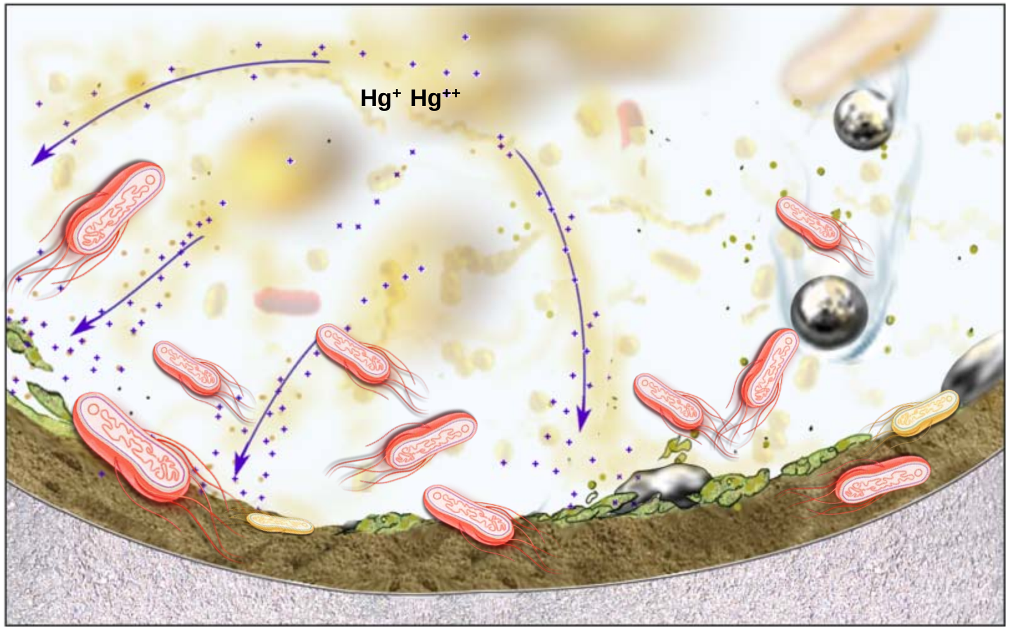
Inorganic forms of mercury concentrate in biofilms and sediment. Heavy liquid mercury metal settles rapidly by gravity deposition and may form solid amalgams on contact with some other metals such as copper.

<u>Plumbing Surfaces and Sediments</u>



Alteration of the Microbial Population

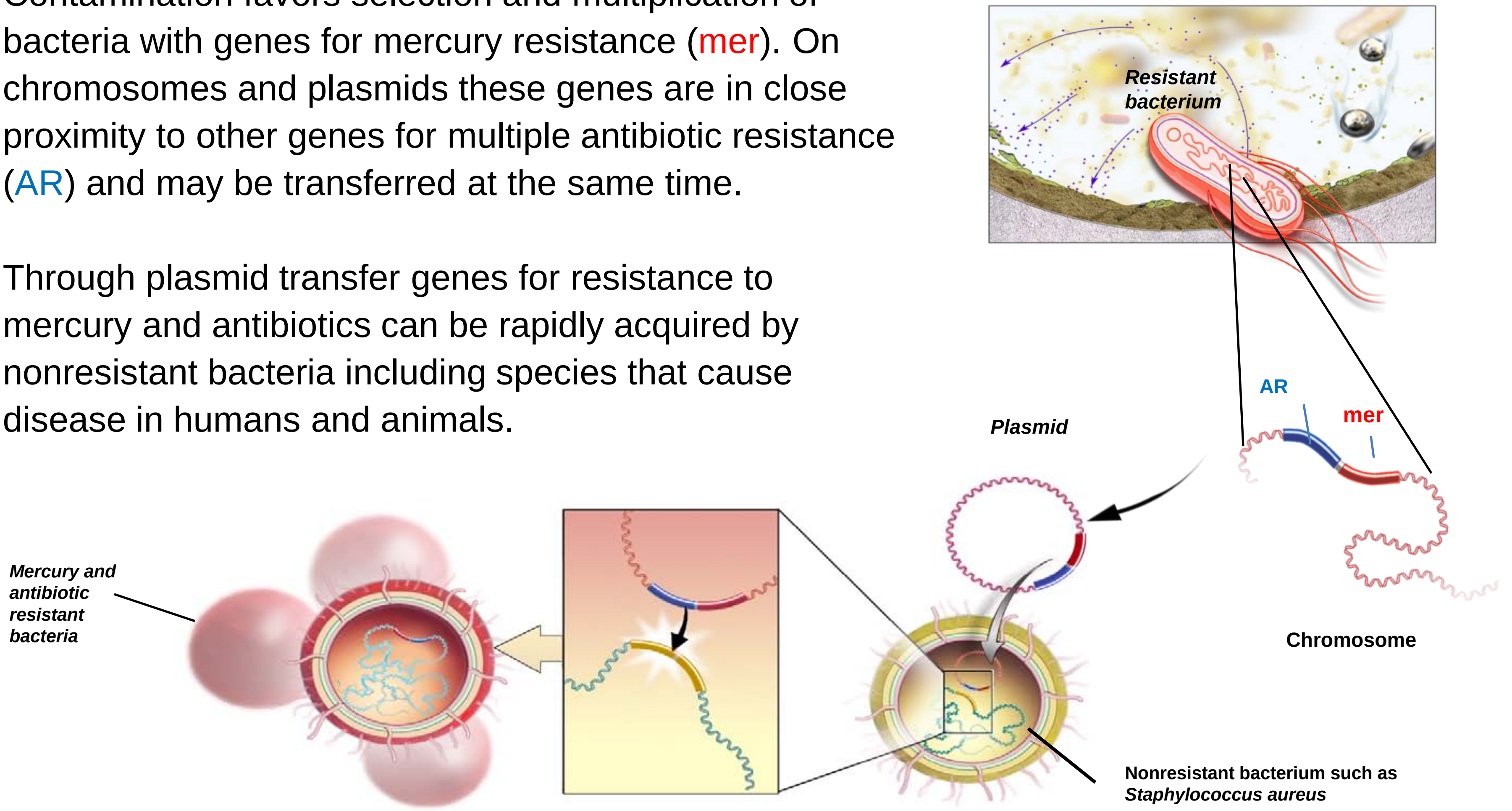
Bacteria that are not resistant to the toxicity of inorganic mercury compounds die off or are unable to grow. Resistant bacteria (shown here in red) survive and become dominant.



Genes for Mercury and Antibiotic Resistance Can be Transferred to Nonresistant Bacteria

Contamination favors selection and multiplication of bacteria with genes for mercury resistance (mer). On chromosomes and plasmids these genes are in close proximity to other genes for multiple antibiotic resistance (AR) and may be transferred at the same time.

Through plasmid transfer genes for resistance to mercury and antibiotics can be rapidly acquired by nonresistant bacteria including species that cause disease in humans and animals.



Evidence from Environmental Monitoring

Numerous studies have consistently shown significant association between levels of mercury contamination in an environment and the prevalence of resistance to both mercury and multiple antibiotics in resident bacteria.

The data are for bacterial pathogens isolated from diverse environments:

- Fresh, brackish and marine water
- Sediments
- Wastewater
- Health care facilities
- Clinical specimens from patients

Mechanisms of Action: Impairment of Immune Response

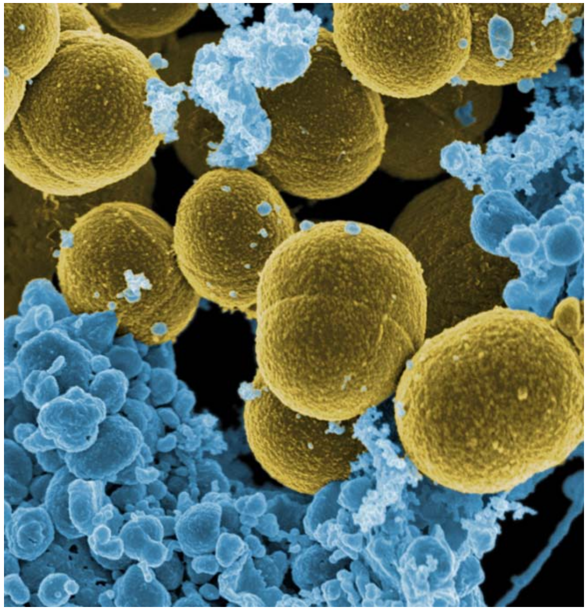
- In addition to its well known neurotoxicity, mercury is a potent immunomodulator that can impair the body's response to infectious agents such as parasites.
- Immunotoxic effects of mercury have been observed in animals at some of the lowest dose to effect ratios yet described (0.04µg/kg body weight).
- Human body burdens of mercury, particularly in populations that consume above average amounts of fish are increasing.
- Effects on the human immune response to infectious agents at these increased mercury levels are not well established. However, other adverse health effects associated with mercury related immunotoxicity have been confirmed.

Impacts on Human Health

- Development of multiply antibiotic resistant bacteria reduces options for treatment of infectious diseases and greatly increases health care costs. Some resistant bacteria are becoming serious public health problems.

- For example, in the U.S. the mortality rate from infections caused by methicillin resistant *Staphylococcus aureus* (MRSA) bacteria may now be greater than that caused by the human immunodeficiency virus (HIV).

- Clinical isolates of *S. aureus* with resistance to methicillin almost always have resistance to mercury; methicillin sensitive strains do not.



MRSA bacteria surrounded by dead white cell. Photo credit NIAID/RML

Impacts on Human Health
(Continued)

- Mercury may reduce the immune response to diseases in exposed populations.

- For example, there is some evidence that resurgence of malaria in some areas of the Amazon river basin may be associated with increased human exposure to mercury pollution from mining activities.

- Farm raised fish are an increasingly important source of food. Mercury contamination in aquaculture systems and feed may increase fish losses to infectious and parasitic diseases.

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Impacts may be Greatest in Developing Countries

- Mercury control regulations may not be in place or ineffective.
- Less awareness of mercury hazards.
- Continuing intentional use of mercury and its compounds as medicines and in religious practices.
- Limited availability of non-mercury alternatives for thermometers and sphygmomanometers.
- Higher prevalence of infectious diseases requiring treatment with antibiotics.
- Availability and greater potential misuse of antibiotics acquired without medical supervision favors development of resistance.

Impacts in Biomedical Facilities

- Mercury contamination from breakage of thermometers and other sources is common in clinics, hospitals and biomedical research facilities.
- While direct uses of mercury in the U.S. are declining there is still continuing use of mercury in medical and dental procedures, and diagnostic reagents.
- Mercury is also a contaminant in some commonly used disinfectants and cleaning products.
- High or inappropriate use of antibiotics also favors development of resistant bacteria in these facilities.
- Some patients may have a depressed immune response from other causes and/or open wounds susceptible to infection.

Conclusions

- Mercury contamination in indoor and outdoor environments favors development of bacterial resistance to multiple antibiotics.
- Increasing human exposure from environmental and dietary sources of mercury may also depress the immune response to infectious agents.
- These effects may result in fewer effective options for treatment of bacterial infections, increase the prevalence of hospital acquired infections and the potential for reemergence infectious diseases.

Conclusions

(Continued)

- These potential impacts provide strong, additional public health justifications and increased urgency for international collaboration in reducing mercury emissions to the general environment and the elimination of all unnecessary uses of mercury in medical facilities.
- Concerns about these impacts on biomedical research activities contributed to an agency wide ban on most uses of mercury added and mercury contaminated products at the National Institutes of Health in September 2008.

Join Our Campaign for a Mercury Free ~~NIH~~ World