

TRAINING FOR HEALTH CARE PROVIDERS

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MERCURY

Children's Health and the Environment

WHO Training Package for the Health Sector

World Health Organization

www.who.int/ceh

July 2008 version

1

<<NOTE TO USER: Please add details of the date, time, place and sponsorship of the meeting for which you are using this presentation in the space indicated.>>

<<NOTE TO USER: This is a large set of slides from which presenters should select the most relevant ones to use in a specific presentation. These slides cover all forms of mercury, their sources and toxicities. Present only those slides that apply most directly to the local situation in your region.>>

Mercury

LEARNING OBJECTIVES

To understand, recognize and know

- ❖ Health hazards associated with exposure to the 3 different species of mercury (Hg)
- ❖ How to diagnose and manage mercury exposure and poisoning
- ❖ Public health implications
- ❖ How to prevent and reduce exposure

2

After this presentation, viewers should understand, recognize and know:

<<READ SLIDE>>

Mercury is a developmental toxicant whose effects have been known for many decades, but concern has increased in the last few years among the medical and environmental communities due to the recognition of its environmental ubiquity and persistence and the developmental effects observed at relatively low levels of exposure.

In December 2002, the United Nations Environment Programme (UNEP) published a Global Mercury Assessment, calling for immediate actions to reduce pollution. In May 2005, the first Conference of the Parties (COP 1) proposed the inclusion of mercury into the group of the Persistent Toxic Pollutants (PTPs).

Ref:

•UNEP. *Global Mercury Assessment, December 2002:*
www.chem.unep.ch/mercury/default.htm

Mercury

MERCURY

- ❖ **Is persistent and cycles globally**
- ❖ **Continues to be widely used**
- ❖ **Exposure has serious effects**
- ❖ **Has an impact on global fishing**
- ❖ **May generate bigger problems in less-developed regions**
- ❖ **Interventions can be successful**

UNEP. Global Mercury Assessment, December 2002: www.chem.unep.ch/mercury/default.htm

3

This slide states the main principles listed at the UNEP – Global Mercury Assessment, a 260-page document that responds to the specific requests made by UNEP's Governing Council (GC) and that will be the basis for considering the possibility of an international action.

UNEP: United Nations Environment Programme

Refs:

- *UNEP. Global Mercury Assessment, December 2002: www.chem.unep.ch/mercury/default.htm*
- www.who.int/phe/news/Mercury-flyer.pdf
- www.who.int/water_sanitation_health/medicalwaste/mercurypolpap230506.pdf
- *Children's Health and the Environment – A global perspective. A resource guide for the health sector, WHO, 2005.*
- *American Academy of Pediatrics Committee on Environmental Health. Pediatric Environmental Health, 2nd ed. Etzel RA, Ed. Elk Grove Village, IL: American Academy of Pediatrics, 2003.*

Mercury

OUTLINE

- ❖ Environmental origin, transport and fate of 3 species
- ❖ Routes of exposure
- ❖ Toxicokinetics
- ❖ Toxicodynamics
- ❖ Target organs/systems
- ❖ Treatment
- ❖ Prevention

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This presentation will cover the following topics:

<<READ SLIDE>>

<<NOTE TO USER: You may decide to delete certain parts of this outline if you are giving a short presentation. Please change the outline accordingly.>>

Mercury

ORIGIN: 1 ELEMENT – 3 SPECIES

- ❖ Elemental
- ❖ Inorganic
- ❖ Organic
- ❖ Different toxicity profiles

Los Alamos National Laboratory Chemistry Division

Periodic Table of the Elements

The image shows a standard periodic table of elements. A green arrow points to the element Mercury (Hg), which is located in the bottom right corner of the main table, in the 80th column and 6th row. Below the main table, there are two rows of elements: the Lanthanide series (Ce to Lu) and the Actinide series (Th to Lr). The Los Alamos National Laboratory logo and the word 'CHEMISTRY' are visible at the bottom left of the table. A small legend at the bottom right explains the color coding: blue for elements liquid at room temperature, red for elements gaseous at room temperature, and black for elements solid at room temperature.

pearl1.lanl.gov/periodic/default.htm

5

Mercury is a heavy metal, an element, and therefore cannot be created or destroyed. Natural sources of environmental emissions are volcanic eruptions, rock weathering and natural combustion. As most metals, it can exist in different forms.

Each of its 3 forms: **elemental** (or metallic), **inorganic** (e.g. mercuric chloride) and **organic** (e.g. methyl- and ethylmercury), have different toxicity profiles with different implications for children's health and development.

Picture: pearl1.lanl.gov/periodic/default.htm

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Mercury

ENVIRONMENTAL SOURCES OF EXPOSURE

- ❖ Chloralkali production
- ❖ Artisanal gold and silver mining
- ❖ Mercury mining, smelting and use
- ❖ Burning fossil fuels
- ❖ Waste incinerators
- ❖ Volcanoes



Goldman, *Pediatrics* (2001) 108:197

Courtesy of Dr. Stephan Boese-O'Reilly 2003

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<<READ SLIDE>>

Mercury has many uses, including manufacture of chlorine and caustic soda, gold and silver mining, mirror production, dental amalgams, and manometers. It is released from mercury-mining and production sources, from burning fossil fuels (especially rich in sulphur), from waste incineration (e.g. medical waste) incineration of corpses (with amalgams) and it also may be released from volcanoes.

According to the UNEP report sources are grouped as:

- Natural sources releases due to natural mobilisation of naturally occurring mercury from the Earth's crust (e.g. volcanic activity and weathering of rocks).
- Current anthropogenic (human activity-related) releases from the mobilisation of mercury impurities in raw materials (fossil fuels: specially coal but also gas and oil).
- Current anthropogenic releases from mercury intentionally used in products and processes (releases during manufacturing, leaks, disposal or spent products incineration).
- Re-mobilisation of historic anthropogenic releases previously deposited in soils, sediments, waters, landfills, waste piles.

UNEP United Nations Environment Programme

Picture: Ball mill in Rwamagasa in Tanzania to grind the ore to extract gold from ore with mercury (Courtesy of Dr. Stephan Boese-O'Reilly 2003)

Refs:

- Goldman LR et al. *American Academy of Pediatrics Committee on Environmental Health: Technical Report: Mercury in the environment: Implications for Pediatricians*, *Pediatrics* (2001) 108:197
Mercury is a ubiquitous environmental toxin that causes a wide range of adverse health effects in humans. Three forms of mercury (elemental, inorganic, and organic) exist, and each has its own profile of toxicity. Exposure to mercury typically occurs by inhalation or ingestion. Readily absorbed after its inhalation, mercury can be an indoor air pollutant, for example, after spills of elemental mercury in the home; however, industry emissions with resulting ambient air pollution remain the most important source of inhaled mercury. Because fresh-water and ocean fish may contain large amounts of mercury, children and pregnant women can have significant exposure if they consume excessive amounts of fish. The developing fetus and young children are thought to be disproportionately affected by mercury exposure, because many aspects of development, particularly brain maturation, can be disturbed by the presence of mercury. Minimizing mercury exposure is, therefore, essential to optimal child health. This review provides pediatricians with current information on mercury, including environmental sources, toxicity, and treatment and prevention of mercury exposure.
- UNEP. *Global Mercury Assessment, December 2002*: www.chem.unep.ch/mercury/default.htm

Mercury

MEDICAL WASTE

- ❖ **Medical waste incinerators**
 - ❖ ~10% of all Hg air releases

- ❖ **Health care facilities**
 - ❖ ~5% of all Hg water releases

7

<<READ SLIDE>>

Refs:

- www.who.int/water_sanitation_health/medicalwaste/mercurypolpap230506.pdf
- www.epa.gov/ttncaaa1/t3/reports/volume2.pdf

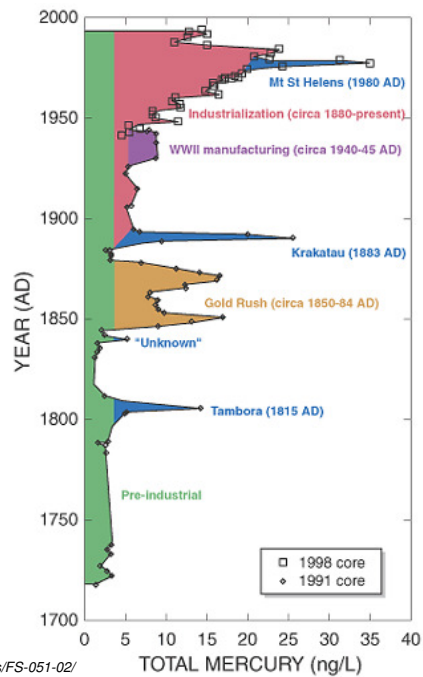
Mercury

A man made problem

Major atmospheric releases detected in the ice core

- Natural background
- Volcanic
- Gold rush
- World War II
- Industrialization

Hg released in the last 100 years: 70% from human activities



<http://toxics.usgs.gov/pubs/FS-051-02/>

Explanation of the chart:

"Atmospheric mercury deposition corresponds to volcanic and anthropogenic events over the past 270 years. Preindustrial deposition rates can be conservatively extrapolated to present time (4 ng/L; in green) to illustrate the increase during the past 100 years (in red) and significant decreases in the past 15-20 years." (US Geological Service)

Most mercury in the modern environment comes from human activities and heavy industry. Here is dramatic evidence that this problem of methylmercury contamination of our food is of our own making. This composite ice core record from Wyoming, USA shows the dramatic increase from baseline mercury levels (shown here in green) that have occurred due to human activity. In fact, 70% of the mercury released in the last 100 years has been man made (anthropogenic).

Ref:

•toxics.usgs.gov/pubs/FS-051-02/

Mercury

A LARGE ENVIRONMENTAL PROBLEM

- ❖ In small scale gold mining areas Hg is used to extract gold from ore (amalgamation process)
- ❖ 1 to 2 kg of Hg are used to process 1 kg of gold
- ❖ Most Hg is released into the environment (soil, air, water)
- ❖ More than 50% workers have high levels
- ❖ ...and their children?



© Stephan Boese-O'Reilly 2003

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In Brazil, Guyana and in some other countries, gold mining that requires large amounts of mercury is having tremendous consequences on the environment and the local community.

<<READ SLIDE>>

Ref:

•Agence France Presse, 26 October 2004.

"In the past two years, police have launched some 60 "Anaconda operations" -- named after the giant boa constrictors that inhabit this tropical French overseas department -- but they have not succeeded in squeezing the life out of the illegal gold trade that threatens the environment here.

Instead, an estimated 12,000 workers, for the most part illegal workers from across the border in Brazil, roam the rivers in search of the precious metal, poisoning the rivers with the quicksilver they use to extract the gold. Their method could not be more simple, or more brutal. From barges moored in the water, they pulverize the river banks with high-pressure hoses, pump out the resulting slurry and amalgamate the tiny specks of gold with quicksilver, or mercury.

Once the gold is extracted from the mercury, the highly toxic metal is dumped directly into the river along with the slurry. "It is an ecological disaster,"... that brings in ...the deforestation and environmental devastation left in the wake of the gold-washers... poisoning of the fish stocks, and consequently of the indigenous Indian population that depends on the fish as a dietary staple.

The gold trade has brought with it some other curses of development, including malaria, AIDS and various kinds of illegal trafficking...

... supplies needed by the gold-extracting business,... include ... mercury. With the primitive methods in use, it can take 1.3 kilos of quicksilver to process every kilo of gold, and it is estimated that at least 10 tonnes of mercury are released into the environment every year.

The impoverished Brazilian panhandlers, many living in conditions of virtual slavery, are the first victims of mercury vapor, which causes serious neurological defects. And according to a study carried out as long ago as 1997, more than half the Indians living along the river have excessive amounts of mercury in their organisms.

Picture: Liquid mercury used by miners to extract gold from ore in Tanzania (© Stephan Boese-O'Reilly 2003)

Mercury							
Continent	Stationary Combustion	Pig iron & steel production	Cement production	Waste disposal	Non-ferrous metal production	Artisanal gold mining	Sum quantified sources
Europe	186	10	26	12	15		250
Africa	197	0.5	5.2		7.9		210
Asia	860	12	82	33	87		1075
North America	105	4.6	13	66	25		210
South America	27	1.4	5.5		25		60
Australia & Oceania	100	0.3	0.8	0.1	4.4		105
Sum, quantified sources 1995	1470	30	130	110	170		~1900
Worldwide						300-100	

Drasch, Wiley VHC, Verlag, 2004, all data in metric tonnes

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<<READ SLIDE>>

Anthropogenic Sources

Estimates of global atmospheric releases of mercury (in metric tonnes) from anthropogenic sources in 1995

Explanation of the chart:

“According to the recent estimates, about 50 to 75% of total yearly input to the atmosphere is due to anthropogenic activities (Munthe, 2001). Some estimates of global atmospheric releases of mercury from a number of major anthropogenic sources in 1995 are given in the table.

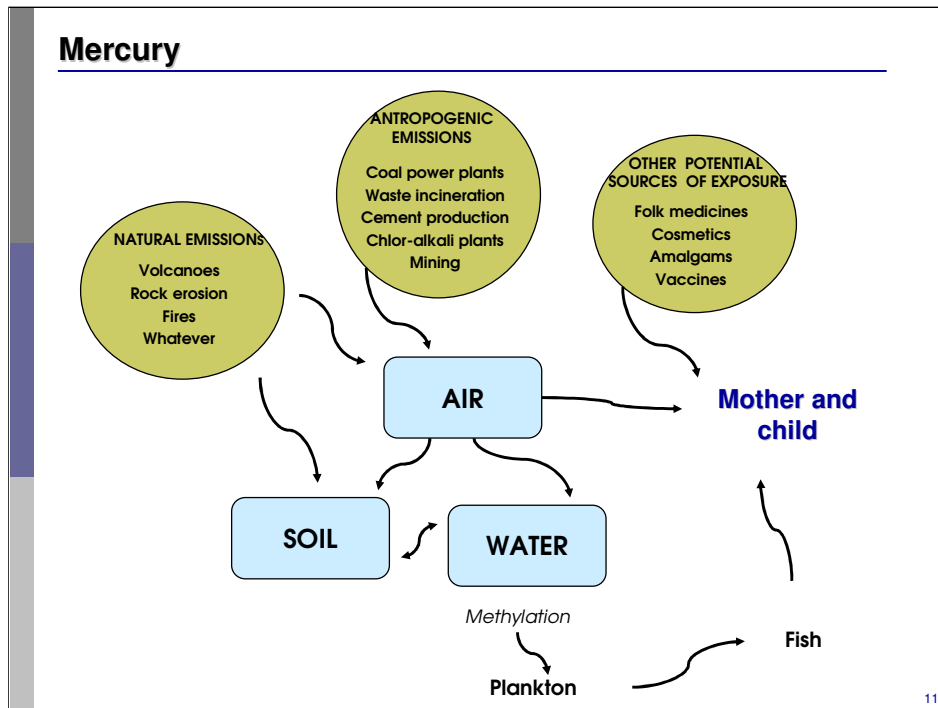
Mercury is naturally present in coal and other fossil fuels and minerals such as lime for cement production and metal ores. About 70 % of global mercury emission to the atmosphere is due to fossil fuel combustion, in particular coal (Pacyna, 2000) and incineration of wastes.

Emissions from artisanal gold mining are not included in the estimation of Pirrone, 2001.

Refs:

- *Drasch G, Mercury in: Merian E, Anke M, Ihnat M, Stoeppler M (eds) Elements and their compounds in the environment Vol 2, Wiley VHC Verlag, Weinheim, Germany, 2004.*
- *Lacerda LD, Global Mercury Emissions from Gold and Silver Mining. Water, Air and Soil Pollution (1997) 97 (3-4): 209.*
- *Munthe J, Mercury species over Europe (MOE). Relative importance of depositional methylmercury fluxes to various ecosystems. Final report for the European Commission, Directorate General XII, 2001*
- *Pacyna JM et al, Assessment of emissions/discharges of mercury reaching the Arctic environment. The Norwegian Institute for Air Research, NILU Report OR 7/2000, Kjeller, Norway, 2000*
- *Pirrone N et al, Regional differences in worldwide emissions of mercury to the atmosphere. Atmos Environ (1996) 30:2981.*
- *Pirrone N et al, Ambient Air Pollution by Mercury (Hg) – Position Paper. Office for Official Publications of the EC, 2001. (available at ec.europa.eu/environment/air/pdf/pp_mercury.pdf).*

Mercury



Picture: J. Pronczuk

Mercury

TRANSPORT: GLOBAL CYCLE OF MERCURY



Hg is emitted into the atmosphere and circulated globally

EPA

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When mercury is emitted into the atmosphere, it may deposit close to the source, or be transported long distances, as shown in this diagram.

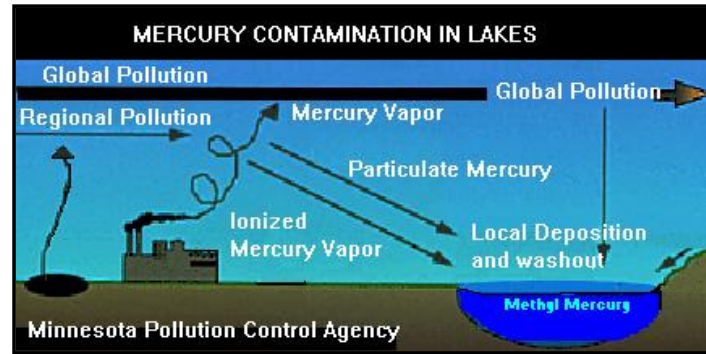
Picture: www.epa.gov/grtlakes/seahome/mercury/src/presmerc.htm (downloaded 2005)

The Environmental Protection Agency, Purdue University, and the Agricultural & Biological Engineering Department.

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Mercury

TRANSPORT: GLOBAL CYCLE OF MERCURY



EPA

Ultimately enters water bodies and deposits

- ❖ Close to source
- ❖ Long distance from source → global pollution

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Eventually, atmospheric mercury from mercury emissions ends up in water bodies where it is methylated and bioconcentrated up the food chain. The major source of methylmercury for most people is from eating contaminated fish.

High risk groups are the fetus and small children whose nervous systems are developing, and women of child bearing age because of the exposure to the fetus.

- Main source: industrial emission
- Media: air and water
- Vector: fish

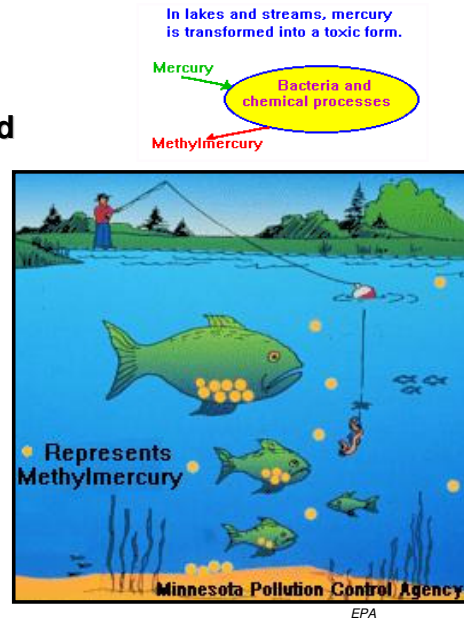
Picture: www.epa.gov/grtlakes/seahome/mercury/src/chemistr.htm (Downloaded 2005)

Mercury

FATE

Metabolic conversion and bio-accumulation through “food-chain”

- ❖ Hg in sediments converts into methylmercury (MeHg)
- ❖ MeHg enters the aquatic food chain: fish, marine and freshwater
- ❖ MeHg uptake by humans through fish consumption



For most people who are not occupationally exposed, fish is the major source of mercury exposure.

❖ Mercury attached to aquatic sediments is subject to microbial conversion to methylmercury (MeHg).

❖ Methylmercury enters the aquatic food chain, reaching highest concentration in “fish eating fish” (e.g.tuna, sharks).

- Ocean fish high in methylmercury include mackerel, shark, swordfish, tile fish, large tuna, grouper.

- Freshwater fish contamination depends more on local conditions but also is highest in long-lived, predatory fish such as pike.

<<NOTE TO USER: Insert the list of local fish which are high in mercury>>

❖ Methylmercury uptake by humans through fish consumption.

Ref:

•Clarkson TW et al, *The toxicology of mercury – current exposures and clinical manifestations*, *N Engl J Med*, 2003, 349: 1731

Picture: www.epa.gov/grtlakes/seahome/mercury/src/aquatic.htm (Downloaded 2005)

The Environmental Protection Agency, Purdue University, and the Agricultural & Biological Engineering Department.

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Mercury

ELEMENTAL (METALLIC) MERCURY – "QUICKSILVER"

Sources of exposure

❖ Environmental:

- Volcanic explosions, rock weathering, degassing

❖ Anthropogenic inadvertent:

- Combustion: fossil fuels (coal), waste incineration
- Industrial: gold/silver mining, chloralkali plants, batteries, switches, fluorescent lights, thermometers, sphyngomanometers

❖ Anthropogenic intentional:

- Dental amalgams
- Ritual and folk medicine use

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Because of the complexity of mercury chemistry, it is often easier to discuss each species separately. The following series of 6 slides recaps sources by species and briefly outlines the common routes of human exposure, toxicokinetics and major systems damaged by excess exposure.

<<READ SLIDE>>

Ref:

•Clarkson TW *et al*, *The toxicology of mercury – current exposures and clinical manifestations*, *N Engl J Med* (2003) 349: 1731

Mercury

ELEMENTAL MERCURY

Routes of exposure

- ❖ Inhalation (volatile at room temp): 75-85% absorption
- ❖ Ingestion and skin: almost no absorption

Elimination

- ❖ Urine and Feces

Toxicity

- ❖ Lungs, eyes, gingival, skin
- ❖ Also: central nervous system, kidneys, immune system

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<<READ SLIDE>>

Mercury vapour cannot be seen with the naked eye, but an educational video is available to show how it elemental mercury vapourizes. To view the video go to www.michigan.gov/mdch/0,1607,7-132-2945_5105_47868-181553--,00.html

Refs:

- *Casarett and Doull, Toxicology – The basic science of poisons. 5th Ed..Ed: Klaassen., McGraw-Hill, 1996.*
- www.michigan.gov/mdch/0,1607,7-132-2945_5105_47868-181553--,00.html

Mercury

INORGANIC MERCURY

Sources of Exposure

- ❖ Environmental
 - None
- ❖ Industrial products
 - Disinfectants, antimicrobials
 - Alternative medicines, cosmetics
 - Vapor lamps, embalming
 - Photography
 - Latex paint (pre 1990s)
- ❖ Example: mercuric chloride

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<<READ SLIDE>>

Refs:

- Drasch G, Mercury in: Merian E, Anke M, Ihnat M, Stoepler M (eds) *Elements and their compounds in the environment Vol 2.*, Wiley VHC Verlag, Weinheim, Germany, 2004
- *Global Mercury Assessment. UNEP chemicals report Geneva 2002. www.chem.unep.ch*
- Kasznia-Kocot J et al. Domestic accidental mercury vapor intoxication in families. *Public Health (Oxf)*. 2008 Mar;30(1):113.

Mercury

INORGANIC MERCURY

Routes of Exposure

- ❖ Ingestion - 10% absorbed
- ❖ Skin - can be high and deadly

Elimination

- ❖ Renal

Toxicity

- ❖ Primary: kidneys, gastrointestinal tract
- ❖ Secondary: central nervous system

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<<READ SLIDE>>

Refs:

- Clarkson TW et al, *The toxicology of mercury – current exposures and clinical manifestations*, *N Engl J Med* (2003) 349:1731
- Drasch G, *Mercury in: Merian E, Anke M, Ihnat M, Stoepler M (eds) Elements and their compounds in the environment Vol 2., Wiley VHC Verlag, Weinheim, Germany, 2004*
- Global Mercury Assessment. UNEP chemicals report Geneva 2002. www.chem.unep.ch*

Mercury

ORGANIC MERCURY

Sources of Exposure

- ❖ Environmental conversion:
 - Fish and shellfish (e.g. methylmercury)

- ❖ Industrial production:
 - Fungicides, bactericides (e.g. phenylmercury)
 - Vaccine preservatives (e.g. thiomersal)

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<<READ SLIDE>>

Refs:

- Clarkson TW et al, *The toxicology of mercury – current exposures and clinical manifestations*, *N Engl J Med* (2003) 349: 1731
- Drasch G, *Mercury in: Merian E, Anke M, Ihnat M, Stoepler M (eds) Elements and their compounds in the environment Vol 2., Wiley VHC Verlag, Weinheim, Germany, 2004*
- Global Mercury Assessment. UNEP chemicals report Geneva 2002. www.chem.unep.ch*

Mercury

ORGANIC MERCURY

Routes of Exposure

- ❖ Gastrointestinal - rapid & complete absorption
- ❖ Parenteral - 100% absorbed
- ❖ Transplacental (concentrated in cord blood)

Elimination

- ❖ Feces - $T_{1/2}$ 45 to 70 days in adults

Toxicity

- ❖ Primary: central nervous system
- ❖ Secondary: cardiovascular

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Over 95% is absorbed from the GI (gastrointestinal) tract

Widely distributed to all tissues

•It crosses the placenta.

- Cord blood : Maternal blood – 1.7 (*Mahaffey, 2004*).

•It crosses the blood brain barrier.

- Active transport on L-methionine carrier.

-It is secreted in breast milk – but in very small amounts since most is bound to red blood cells.

-It is degraded slowly by the human body.

-Half-life in adults is 45-70 days—Therefore, prospective mothers can significantly reduce mercury body burden by avoiding exposure for 6-12 months prior to pregnancy.

- Excreted in feces.

-Builds up in the brain – duration many years.

Ref:

•*Mahaffey KR et al, Blood organic mercury and dietary mercury intake: National Health and Nutrition Examination Survey, 1999 and 2000, Environ Health Perspect. (2004) 112 (5): 562*

Mercury				
Mercury	Sources	Routes of exposure	Elimination	Toxicity
Elemental (metallic)	Volcanoes Combustion Waste incineration Thermometers Amalgams Folk remedies	Inhalation	Urine and faeces	CNS Kidney Lungs Skin (acrodynia in children)
Inorganic (mercuric chloride)	Lamps Photography Disinfectants Cosmetics Folk medicine	Ingestion Dermal	Urine	CNS Kidney GI tract Skin (acrodynia in children)
Organic (methyl; ethyl)	Fish Fungicides Preservatives	Ingestion Parenteral Transplacental	Faeces	CNS Cardiovascular

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This table summarizes the different sources of mercury, routes of exposure and elimination and main effects.

<<NOTE TO USER: The relative importance of sources and particular species will vary regionally. Please highlight what is most important in your region.>>

Mercury

MERCURY: ACRODYNIA

Uncommon syndrome "Pink disease":

- ❖ Pain in the extremities
- ❖ Pinkish discoloration and desquamation
- ❖ Hypertension
- ❖ Sweating
- ❖ Insomnia, irritability, apathy

Considered as idiosyncratic reaction.



Courtesy of Professor Schwarz.

Acrodynia is a rare idiopathic chronic toxic reaction to elemental or inorganic mercury exposure, which occurs mainly in young children. It is characterized by pain in the extremities and pink discoloration with desquamation of the skin. Here are pictures of 2 children with acrodynia.

The top photo on the right side of the slide shows a child who is frequently crying, unhappy, unwilling to walk, hence sitting in the buggy. The bottom photo shows a 2 ½ year old girl with hypotonia and constant scratching. Notice that she has red lips, fingers, and soles of the feet.

<<READ SLIDE>>

Ref:

•*California Poison Control System, Poisoning and drug overdose, 3rd edition, ed: Olson, Appleton and Lange, Connecticut, 1999*

Pictures from:

Schwarz, Feersche Erkrankung (kindliche Akrodynie), Pädiatrische Praxis (1979) 21: 85 – 89. Used with permission (copyright: Hans Marseille Verlag GmbH).

Picture above: Frequently crying, unhappy, unwilling to walk, hence sitting in the buggy (acrodynia).

Picture below: 2 ½ year old girl. Hypotonia, constant scratching, with red fingers, foot soles, lips (acrodynia).

Mercury



Courtesy of Professor v. Mühlendahl



Courtesy of Professor v. Mühlendahl

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Miliary rash is typical of acrodynia. The photograph on the top shows Feer's Disease (another term for acrodynia). Notice the scaling of the skin between the fingers. The photograph on the bottom of the slides also shows Feer's Disease. Notice the exanthema, which was due to mercury intoxication from a mercury thermometer broken in the children's room four months previously.

Picture above: von Mühlendahl, Schulte-Wissermann, Grips, Hautveränderungen bei Feer'scher Krankheit. Pädiatrische Praxis (1995) 49, 647. Used with permission (copyright: Hans Marseille Verlag GmbH).

Feer's Disease (acrodynia), scaling of the skin between the fingers.

Picture below: von Mühlendahl, Schulte-Wissermann, Grips, Hautveränderungen bei Feer'scher Krankheit. Pädiatrische Praxis (1995) 49, 647. Used with permission (copyright: Hans Marseille Verlag GmbH).

Feer's Disease. Exanthema due to Hg intoxication from a mercury thermometer broken in the children's room four months previously.

Mercury



Courtesy of Professor Mühlendahl



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These are more photographs of Feer's Disease (acrodynia) exanthema due to Hg intoxication from a mercury thermometer broken in the children's room four months previously. This photo was taken 3 weeks after the first pictures.

Picture above: v.Mühlendahl, Schulte-Wissermann, Grips, Hautveränderungen bei Feer'scher Krankheit. Pädiatrische Praxis (1995) 49, 647. Used with permission (copyright: Hans Marseille Verlag GmbH).

Picture below: v.Mühlendahl, Schulte-Wissermann, Grips, Hautveränderungen bei Feer'scher Krankheit. Pädiatrische Praxis (1995) 49, 647. Used with permission (copyright: Hans Marseille Verlag GmbH).

Mercury

EXPOSURE IN INDUSTRIALIZED COUNTRIES

❖ Methylmercury

- Consumption of contaminated fish & shellfish
- Emitted to atmosphere by electric generation
- Transplacental
- Breast milk

❖ Ethylmercury

- Thiomersal

❖ Elemental - vapours

- Traditional and folk medicine uses
- Dental amalgam

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The relative importance of sources of mercury exposure vary according to the country, region, type of economic activity and level of development.

In the industrialized world, organic mercury exposure predominates in the form of methylmercury from fish consumption. Additional exposures from vaccine preservatives have substantially ceased since the late 1990s (this topic is covered later).

In some population groups, traditional uses of elemental mercury can lead to substantial exposures.

Dental amalgams also contain mercury and can be a source of exposure. (This topic is covered later).

The most critical period of vulnerability is prenatal. Small amounts of methylmercury can be transmitted by breast milk, however, this is not sufficient in quantity as to outweigh the benefits of breastfeeding (WHO strongly supports breastfeeding).

Once children are eating solid foods, dietary exposure from fish remains potentially dangerous throughout postnatal neurodevelopment.

A recent analysis on public health and the economic consequences of methylmercury toxicity to the developing brain concluded that "exposure to methylmercury emitted to the atmosphere by American electric generation facilities causes lifelong loss of intelligence in hundreds of thousands of American babies born each year and that this loss of intelligence exacts a significant economic cost to American society, a cost that amounts to at least hundreds of million dollars each year." (*Trasande, 2005*)

Refs:

- www.chem.unep.ch/mercury/Report/GMA-report-TOC.htm
- *Trasande L et al. Public health and the economic consequences of methylmercury toxicity to the developing brain, Environmental Health Perspectives (2005) 113 (5): 590*
- American Academy of Pediatrics Committee on Environmental Health. *Pediatric Environmental Health, 2nd ed.* Etzel RA, Ed. Elk Grove Village, IL: American Academy of Pediatrics, 2003.

Mercury

EXPOSURE IN DEVELOPING COUNTRIES

- ❖ “Occupational” exposures from gold/silver mining
- ❖ Traditional uses
- ❖ Eating contaminated fish

Exposure may be higher than in industrialized countries and cause overt symptoms

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Sources of exposure for children in the developing world may be quite different.

- ❖ “Occupational” exposures from gold/silver mining are usually high and may be acutely toxic. They may be seen in the context of child labour.
- ❖ Traditional uses of mercury are seen in different situations
- ❖ Preparation of cosmetics (“skin whiteners”, creams, lotions and soaps)
- ❖ Eating contaminated fish

<<READ SLIDE>>

<<NOTE TO USERS: Insert information specific to your region or locality on the most important sources and paediatric exposures>>

Refs:

- www.chem.unep.ch/mercury/Report/GMA-report-TOC.htm
- Bose-O'Reilly S et al. Mercury in breast milk – A health hazard for infants in gold mining areas? *Int J Hyg Environ Health* 2008 Feb 7.
- *Children's Health and the Environment – A global perspective. A resource guide for the health sector, WHO, 2005.*

Mercury

MERCURY: TOXIC EFFECTS

- ❖ Neurotoxicity
- ❖ Nephrotoxicity
- ❖ Teratogenicity: MeHg is a teratogen (Minamata disease)
- ❖ CVS: elevated risk of heart attack, hypertension
- ❖ Carcinogenicity: MeHg is a possible human carcinogen
- ❖ Mutagenesis: Hg seems not to be mutagen
- ❖ Reproduction: no clear evidence of effect
- ❖ Immunotoxicity: under scientific discussion

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All forms of mercury are more or less toxic to humans, because it is widely distributed in the body and many systems are affected. The toxic effects of mercury vary according to:

- Form: elemental, inorganic or organic.
- Dose: high dose acute poisonings versus low dose chronic effects.
- Timing: prenatal, infancy, childhood or adult.

In children, the central nervous system is the most vulnerable.

The International Agency for Research on Cancer (IARC) has classified methylmercury as being group 2B: the agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are possibly carcinogenic to humans.

CVS: cardiovascular system

<<READ SLIDE>>

Refs:

- Michaeli-Yossef Y et al. Mercury intoxication in a 2-year-old girl: a diagnostic challenge for the physician. *Pediatr Nephrol.* 2007 Jun;22(6):903-6

A 2-year-old girl presented with hypertension, anorexia and vomiting, restlessness, insomnia and acrodynia. Her blood pressure upon arrival was 145/98 mmHg. Ultrasound of the abdomen, CT scan of chest, abdomen and pelvis, and echocardiogram, were normal. Urinary levels of catecholamines were elevated, urine level of mercury was found to be high (33.2 microg/g creatinine), although blood level was normal (>0.5 microg/dl, reference value 0-4 microg/dl). Following a 1-month course of oral treatment with dimercaptosuccinic acid (DMSA) the child's symptoms and signs resolved, and urinary mercury and catecholamines levels normalized. Mercury intoxication should be suspected in a patient with severe hypertension, personality changes and acrodynia. Normal blood levels of mercury do not exclude this diagnosis, and catecholamine levels may serve as a surrogate marker for confirmation of the diagnosis and to evaluate response to treatment.

- IARC: www.iarc.fr/

- Clarkson TW, *The three modern faces of mercury, Environ Health Perspect.* (2002) 110 (1):11

The three modern "faces" of mercury are our perceptions of risk from the exposure of billions of people to methyl mercury in fish, mercury vapor from amalgam tooth fillings, and ethyl mercury in the form of thimerosal added as an antiseptic to widely used vaccines. In this article I review human exposure to and the toxicology of each of these three species of mercury. Mechanisms of action are discussed where possible. Key gaps in our current knowledge are identified from the points of view both of risk assessment and of mechanisms of action.

Mercury

EXPOSURE FROM FISH

- ❖ Major source of mercury burden for children in most countries
- ❖ Fish may contain methylmercury
- ❖ Children exposed
 - By eating fish
 - Transplacentally
 - Via breast milk



Rice field in the Philippines, irrigated with tailing sediments containing mercury

Courtesy of Dr. Stephan Boese-O'Reilly 1999

28

Long lived, predatory fish can contain high levels of methylmercury. It is incorporated into the muscle when fish live in polluted marine or fresh waters, such as those in the paddy field shown on this slide.

Cooking does not eliminate mercury from fish muscle.

Methylmercury is the major source of body burden in children worldwide. Not only are they exposed directly by eating contaminated fish, but they can also be exposed most importantly, transplacentally from mothers with high methylmercury blood levels. Methylmercury also passes into breast milk but at very low levels. Most methylmercury in blood is lightly bound to red blood cells and not available for transport into breast milk.

Of the three routes, transplacental exposure is potentially the most dangerous one.

Picture: Courtesy of Dr. Stephan Boese-O'Reilly. Rice field near Monkayo in Mindanao (Philippines), irrigated with tailing sediments, containing mercury from a small scale mining operation area in Diwalwal, 1999.

Ref:

•Dorea JG, *Mercury and lead during breast-feeding, Br J Nutr.* (2004) 92(1):21

Hg and Pb are of public health concern due to their toxic effects on vulnerable fetuses, persistence in pregnant and breast-feeding mothers, and widespread occurrence in the environment. To diminish maternal and infant exposure to Hg and Pb, it is necessary to establish guidelines based on an understanding of the environmental occurrence of these metals and the manner in which they reach the developing human organism. In the present review, environmental exposure, acquisition and storage of these metals via maternal-infant interaction are systematically presented. Though Hg and Pb are dispersed throughout the environment, the risk of exposure to infants is primarily influenced by maternal dietary habits, metal speciation and interaction with nutritional status. Hg and Pb possess similar adverse effects on the central nervous system, but they have environmental and metabolic differences that modulate their toxicity and neurobehavioural outcome in infant exposure during fetal development. Hg is mainly found in protein matrices of animal flesh (especially fish and shellfish), whereas Pb is mainly found in osseous structures. The potential of maternal acquisition is higher and lasts longer for Pb than for Hg. Pb stored in bone has a longer half-life than monomethyl-mercury acquired from fish. Both metals appear in breast milk as a fraction of the levels found in maternal blood supplied to the fetus during gestation. Habitual diets consumed by lactating mothers pose no health hazard to breast-fed infants. Instead, cows' milk-based formulas pose a greater risk of infant exposure to neurotoxic substances.

Mercury

METHYLMERCURY LEVELS IN FISH

Ocean fish with high levels of mercury (USA)

Species	Mercury concentration (ppm)				N° of samples
	Mean	Median	Min	Max	
Mackerel King	0.73	NA	0.23	1.67	213
Shark	0.99	0.83	ND	4.54	351
Swordfish	0.97	0.86	0.10	3.22	605
Tilefish	1.45	NA	0.65	3.73	60

US Food and Drug Administration www.cfsan.fda.gov/~frf/sea-mehg.html

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All levels of fish contamination vary with region, so it is difficult to judge risks in a particular location without local testing. The four fish usually listed as “do not eat” for women of childbearing age and children are shown on this slide. They tend to have very high methylmercury levels.

NA not available

ppm parts per million

Refs:

• www.cfsan.fda.gov/~frf/sea-mehg.html

Mercury

METHYLMERCURY: POWERFUL NEURODEVELOPMENTAL TOXICANT

- ❖ Impedes nerve cell division and migration
- ❖ Binds with microtubules required for neuronal development
- ❖ Binds to and distorts DNA & RNA



EHP

30

Toxicodynamics refers to the type of injury done to tissues.

The fetal brain is the most sensitive human tissue to damage from this powerful neurodevelopmental toxicant. In order for the brain to develop properly, an orderly process of cell differentiation and migration must occur to produce a specific and highly ordered brain architecture. Methylmercury interferes with this process by binding to critical structures such as microtubules that are crucial to normal cell division and migration. It also binds to and distorts important molecules like DNA and RNA.

Ref:

•Casarett and Doull, *Toxicology – The basic science of poisons*. 5th Ed..Ed: Klaassen., McGraw-Hill, 1996.

Picture: Environmental Health Perspectives (2002) 110 (6)

Mercury

EFFECTS OF PRENATAL MeHg EXPOSURE

- ❖ Mental retardation
- ❖ Ataxia & cerebral palsy
- ❖ Seizures
- ❖ Vision & hearing loss
- ❖ Delayed developmental milestones
- ❖ Language disorders
- ❖ Deficits in fine motor function
- ❖ Visual spatial disabilities
- ❖ Memory problems
- ❖ Low cardiac rate variability
- ❖ ? Blood pressure



DOSE

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Depending on the dose and timing of exposure during gestation, the effects may be severe and immediately obvious, or subtle and delayed.

Neurological symptoms include mental retardation, ataxia and cerebral palsy, seizures, vision and hearing loss, delayed developmental milestones, language disorders, and problems with motor function, visual spatial abilities, and memory.

Results from long-term cohort studies suggest that the cardiovascular system is also at risk—with decreased heart rate variability as methylmercury exposure increases. One study suggested diastolic blood pressure in boys may be associated with prenatal methylmercury exposure, but the association needs more study.

The full expression of these health effects of methylmercury can be delayed and deficits are often irreversible.

Ref:

• Casarett and Doull, *Toxicology – The basic science of poisons*. 5th Ed..Ed: Klaassen., Mc-Graw-Hill, 1996.

• Grandjean P et al. Cardiac autonomic activity in methylmercury neurotoxicity: 14-year follow-up of a Faroese birth cohort. *J Pediatr*. (2004) 144(2):169.

To determine whether heart function in childhood is affected by exposure to methylmercury (MeHg) from seafood. Prospective study of a Faroese birth cohort (N=1022). Examinations at ages 7 and 14 years included blood pressure, heart rate variability (HRV) and its frequency components of autonomic origin, and brainstem auditory evoked potentials (BAEPs). Mercury concentrations were determined in cord blood and in the child's hair. Results: Both low-frequency (LF) and high-frequency (HF) activities decreased by about 25% from 7 to 14 years; they correlated well with the blood pressures. A doubling of prenatal MeHg exposure was associated with a decrease in LF and HF powers of about 6.7% (P=.04) and in the coefficient of variation of the electrocardiographic R-R interval of 2.7% (P=.04) at age 14 years. No discernible effect on blood pressure was apparent. Decreased LF variability was associated with increased latency of BAEP peak III, but adjustment for MeHg exposure substantially attenuated this correlation. Conclusions: Methylmercury exposure was associated with decreased sympathetic (LF) and parasympathetic (HF) modulation of the HRV. Parallel MeHg-related delays of BAEP latencies may be caused by underlying MeHg neurotoxicity to brainstem nuclei.

• Thurston SW et al. Does prenatal methylmercury exposure from fish consumption affect blood pressure in childhood? *Neurotoxicology*. 2007 Sep;28(5):924-30.

INTRODUCTION: Prenatal exposure to organic methylmercury (MeHg) from seafood consumption has been reported to increase children's blood pressure (BP). A report from the Faroe Islands noted significantly increased diastolic and systolic BP in 7-year-old children as prenatal MeHg exposure increased. The Faroese diet includes sea mammals that contain MeHg, cadmium, and other pollutants. We examined this relationship in the Seychelles Islands to determine if it was present in a society exposed primarily to MeHg from consuming ocean fish.

METHODS: We obtained BP at ages 12 and 15 years on children with known prenatal MeHg exposure enrolled in the Seychelles Child Development Study (SCDS). We examined the association between prenatal MeHg exposure and BP using longitudinal models and linear regression adjusted for relevant covariates. **RESULTS:** Blood pressure at both ages was associated with BMI, height and maternal hypertension during pregnancy as expected. No association between prenatal MeHg exposure and BP was present in girls at either age or in either sex at age 12 years. At age 15 years diastolic BP in boys increased with increasing prenatal MeHg exposure, while systolic BP was unaffected. **SUMMARY:** It is unclear whether the association between prenatal MeHg exposure and diastolic BP seen in 15-year-old boys is of biological significance or if it is a chance finding. However, the finding is intriguing and deserves further study.

Mercury

MINAMATA DISEASE: METHYLMERCURY EXPOSURE IN PREGNANCY

- ❖ Mothers often asymptomatic
- ❖ Microcephaly
- ❖ Cerebral palsy/spasticity
- ❖ Mental deficits
- ❖ Malformation of ears, heart, skeleton, eyes



Minamata Bay, Japan

Courtesy of Dr. Stephan Boese-O'Reilly 2001

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Knowledge about the extreme vulnerability of the fetus to methylmercury began with the Minamata Bay, Japan experience. The bay was heavily contaminated with methylmercury from industrial discharge. Fish bioconcentrated the toxicant and mothers acquired high blood levels from eating fish from the bay. While the mothers were usually without symptoms of mercury poisoning, their babies were born severely damaged with microcephaly, cerebral palsy, severe mental retardation, seizure disorders, blindness, deafness and other malformations.

It is interesting to know that for many years, cats eating the fish in Minamata Bay area suffered a "strange" neurological disease.

Information on the Japanese Institute on Minamata Disease can be found at www.nimd.go.jp/english/index.htm

Picture: Courtesy of Stephan Boese-O'Reilly. Minamata Bay Japan, 2001.

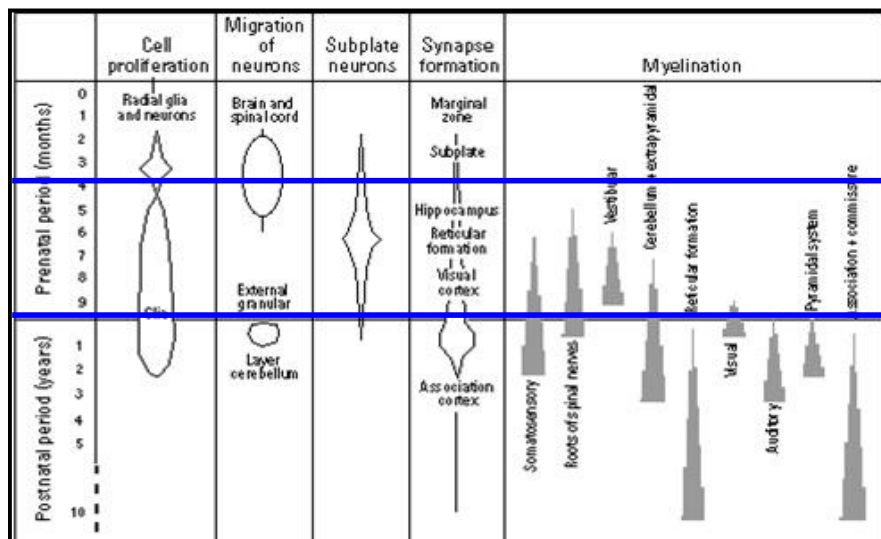
Ref:

•Yorifuji T et al. Long-term exposure to methylmercury and neurologic signs in Minamata and neighboring communities. *Epidemiology*. 2008 Jan;19(1):3-9.

BACKGROUND: It is well known that large-scale poisonings caused by methylmercury occurred in Japan (Minamata, in the 1950s) and Iraq. However, in contrast to Iraq, there have been few sound epidemiologic studies in Minamata. We evaluated the effect of methylmercury on neurologic signs using data from a 1971 population-based study. **METHODS:** Villages in 3 areas were selected for study: the Minamata area (a high-exposure area), the Goshonoura area (a medium-exposure area), and the Ariake area (a low-exposure area). We used place of residence as the exposure indicator. We examined associations between methylmercury exposure and the following neurologic signs measured on clinical examination: paresthesia of whole body, paresthesia of extremities, paresthesia around the mouth, ataxia, dysarthria, tremors, and pathologic reflexes. **RESULTS:** Total population was 1120 in the high-exposure villages, 1845 in the medium-exposure villages, and 1165 in the low-exposure villages. In the Minamata area, 87% (n=833) of the eligible population (age 10 years and older) participated in the 1971 investigations, in the Goshonoura area, 93% (n = 1450), and in the Ariake area, 77% (n = 755). Compared with subjects in the Ariake area, the subjects in the Minamata area manifested neurologic signs more frequently. The highest prevalence odds ratio was observed for paresthesia around the mouth (110; 95% confidence interval = 16-820). Although residents in the Goshonoura area had been exposed less heavily than those in the Minamata area, Goshonoura residents also had increased prevalence of neurologic signs. **CONCLUSION:** Long-term exposure to methylmercury has a strong adverse impact on neurologic signs among residents in a local community.

Mercury

NEURODEVELOPMENT



Rice, EHP, 2000 108 (3): 511

33

Recalling that mercury inhibits cell division and migration during development, it is easy to see from this schematic why the fetus and young children are particularly at risk when exposed. Note how much cell proliferation and migration occurs during the second and third trimester. Note also how much continues to occur in the first 2-3 years postnatally. Clearly, exposure to neurodevelopmental toxicants like methylmercury during these periods of rapid maturation and change can have profound consequences.

Ref:

•Rice D et al. *Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models*, *Environ Health Perspect.* (2000)108 (3):511-33.

Vulnerable periods during the development of the nervous system are sensitive to environmental insults because they are dependent on the temporal and regional emergence of critical developmental processes (i.e., proliferation, migration, differentiation, synaptogenesis, myelination, and apoptosis). Evidence from numerous sources demonstrates that neural development extends from the embryonic period through adolescence. In general, the sequence of events is comparable among species, although the time scales are considerably different. Developmental exposure of animals or humans to numerous agents (e.g., X-ray irradiation, methylazoxymethanol, ethanol, lead, methyl mercury, or chlorpyrifos) demonstrates that interference with one or more of these developmental processes can lead to developmental neurotoxicity. Different behavioral domains (e.g., sensory, motor, and various cognitive functions) are subserved by different brain areas. Although there are important differences between the rodent and human brain, analogous structures can be identified. Moreover, the ontogeny of specific behaviors can be used to draw inferences regarding the maturation of specific brain structures or neural circuits in rodents and primates, including humans. Furthermore, various clinical disorders in humans (e.g., schizophrenia, dyslexia, epilepsy, and autism) may also be the result of interference with normal ontogeny of developmental processes in the nervous system. Of critical concern is the possibility that developmental exposure to neurotoxicants may result in an acceleration of age-related decline in function. This concern is compounded by the fact that developmental neurotoxicity that results in small effects can have a profound societal impact when amortized across the entire population and across the life span of humans.

Mercury

ESTIMATED COSTS OF METHYLMERCURY TOXICITY TO THE DEVELOPING BRAIN

- ❖ 316,588 – 637,233 US children each year with cord blood Hg > 5.8 µg Hg/L, level associated with loss of IQ
- ❖ Estimated major annual cost:
Lost productivity: 8.7 billion \$US

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<<READ SLIDE.>>

A recent analysis on public health and the economic consequences of methylmercury toxicity to the developing brain concluded that "exposure to methylmercury emitted to the atmosphere by American electric generation facilities causes lifelong loss of intelligence in hundreds of thousands of American babies born each year and that this loss of intelligence exacts a significant economic cost to American society, a cost that amounts to at least hundreds of million dollars each year." (*Trasande, 2005*)

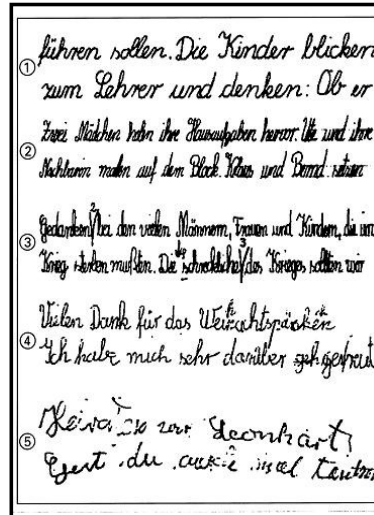
Ref:

• *Trasande L et al. Public health and the economic consequences of methylmercury toxicity to the developing brain, Environmental Health Perspectives (2005) 113 (5): 590*

Mercury

EXAMPLE OF "TREMOR MERCURIALIS"

Handwriting of
a 9 year old girl in
monthly intervals after
an accidental intake of
mercury containing
seed preservatives



Boese, Paediatr Prax (1993) 45: 183

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Handwriting of a 9 year old girl in monthly intervals after an accidental intake of mercury containing seed preservatives. This exposure was due to contaminated grain, and demonstrates that exposures well after infancy can also have serious consequences.

Picture: Courtesy of Dr. Stephan Boese-O'Reilly. 9 year old girl, handwriting example, 1989.
Boese, Chronische Metallintoxikationen als Ursache neuropaediatrischer Erkrankungen.
Paediatr Prax (1993) 45: 183

Mercury

SUBCLINICAL EFFECTS

- ❖ Susceptibility of the fetal brain is very high
- ❖ Altered neuropsychological tests in children, if prenatal Hg burden was raised by whale fish consumption (*Faroe Islands study*)
- ❖ No effects found in a similar study (*Seychelles study*)

Tolerable Intakes

- ❖ US EPA: 0.1 µg of methylmercury/kg body weight/day
- ❖ FAO/WHO JECFA: 1.6 µg/kg body weight/week

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Two important studies on mercury exposure in children rendered different results as will be seen in the next slides.

In view of mounting evidence about the adverse effects of mercury, in 2003 the Joint FAO/WHO Expert Committee on Food Additives and Contaminants (JECFA) revised the Provisional Tolerable Weekly Intake (PTWI) and reduced it to 1.6 µg/kg body weight/week in order to protect the developing fetus (Previously it was 3.3 µg/kg body weight/week.)

FAO: Food and Agricultural Organization

Refs:

- Clarkson TW et al, *The toxicology of mercury – current exposures and clinical manifestations*, *N Engl J Med* (2003) 349: 1731
- FAO/WHO. *Evaluation of certain food additives and contaminants. Sixty first report of the Joint FAO/WHO Expert Committee on Food Additives*. WHO, Geneva, 2004.
- Myers GJ, Davidson PW: *Does Methylmercury Have a Role in Causing Developmental Disabilities in Children?* *Environmental Health Perspectives* (2000) 108 (3): 413

Methylmercury (MeHg) is a potent neurotoxin that in high exposures can cause mental retardation, cerebral palsy, and seizures. The developing brain appears particularly sensitive to MeHg. Exposure levels in pregnant experimental animals that do not result in detectable signs or symptoms in the mother can adversely affect the offspring's development. Studies of human poisonings suggest this may also occur in humans. Human exposure to MeHg is primarily dietary through the consumption of fish: MeHg is present in all fresh and saltwater fish. Populations that depend on fish as a major source of dietary protein may achieve MeHg exposure levels hypothesized to adversely affect brain development. Increasing mercury levels in the environment have heightened concerns about dietary exposure and a possible role for MeHg in developmental disabilities. Follow-up studies of an outbreak of MeHg poisoning in Iraq revealed a dose-response relationship for prenatal MeHg exposure. That relationship suggested that prenatal exposure as low as 10 ppm (measured in maternal hair growing during pregnancy) could adversely affect fetal brain development. However, using the same end points as were used in the Iraq study, no associations have been reported in fish-eating populations. Using a more extensive range of developmental end points, some studies of populations consuming seafood have reported associations with prenatal MeHg exposure, whereas others have found none.

Mercury

FAROE ISLANDS STUDY

- ❖ Cohort of 1022 children born 1986-1987
- ❖ Exposure of mothers to methylmercury:
 - Pilot whale meat - episodic, and potentially high
 - Fish consumption - continuous, but low
- ❖ Neuropsychological dysfunctions (age 7)
 - Language
 - Attention
 - Memory
- ❖ Neurophysiologic dysfunctions (age 14)
 - Delayed brainstem auditory evoked potentials
 - Decreased autonomic heart rate variability
- ❖ Attributed to prenatal exposure

37

Refs:

•Grandjean P et al. Cardiac autonomic activity in methylmercury neurotoxicity: 14-year follow-up of a Faroese birth cohort, *J Pediatr.* (2004) 144(2):169.

•Grandjean P et al. Cognitive deficit in 7 year old children with prenatal exposure to methylmercury, *Neurotoxicology and teratology* (1997) 19: 417

A cohort of 1022 consecutive singleton births was generated during 1986-1987 in the Faroe Islands. Increased methylmercury exposure from maternal consumption of pilot whale meat was indicated by mercury concentrations in cord blood and maternal hair. At approximately 7 years of age, 917 of the children underwent detailed neurobehavioral examination. Neuropsychological tests included Finger Tapping; Hand-Eye Coordination; reaction time on a Continuous Performance Test; Wechsler Intelligence Scale for Children-Revised Digit Spans, Similarities, and Block Designs; Bender Visual Motor Gestalt Test; Boston Naming Test; and California Verbal Learning Test (Children). Clinical examination and neurophysiological testing did not reveal any clear-cut mercury-related abnormalities. However, mercury-related neuropsychological dysfunctions were most pronounced in the domains of language, attention, and memory, and to a lesser extent in visuospatial and motor functions. These associations remained after adjustment for covariates and after exclusion of children with maternal hair mercury concentrations above 10 microgram(s) (50 nmol/g). The effects on brain function associated with prenatal methylmercury exposure therefore appear widespread, and early dysfunction is detectable at exposure levels currently considered safe.

•Grandjean P, Neurodevelopmental disorders. In: Tamburlini G, von Ehrenstein O, Bertollini R. (eds): *Children's health and the environment: A review of evidence.* WHO, Rome, 2002.

•Murata K et al, Delayed brainstem auditory evoked potential latencies in 14-year-old children exposed to methylmercury, *J Pediatr.* (2004) 144(2):177.

To determine possible exposure-associated delays in auditory brainstem evoked potential latencies as an objective measure of neurobehavioral toxicity in 14-year-old children with developmental exposure to methylmercury (MeHg) from seafood. Prospective study of a birth cohort in the Faroe Islands, where 878 of eligible children (87%) were examined at age 14 years. Latencies of brainstem evoked potential peaks I, III, and V at 20 and 40 Hz constituted the outcome variables. Mercury concentrations were determined in cord blood and maternal hair, and in the child's hair at ages 7 and 14. Results: Latencies of peaks III and V increased by about 0.012 ms when the cord blood mercury concentration doubled. As seen at age 7 years, this effect appeared mainly within the I-III interpeak interval. Despite lower postnatal exposures, the child's hair mercury level at age 14 years was associated with prolonged III-V interpeak latencies. All benchmark dose results were similar to those obtained for dose-response relationships at age 7 years. Conclusions: The persistence of prolonged I-III interpeak intervals indicates that some neurotoxic effects from intrauterine MeHg exposure are irreversible. A change in vulnerability to MeHg toxicity is suggested by the apparent sensitivity of the peak III-V component to recent MeHg exposure.

Mercury

SEYCHELLES STUDY

- ❖ Cohort of 779 mother-infant pairs
- ❖ Exposure from mothers' high fish consumption
- ❖ At age 9: neuropsychological tests
- ❖ No support for neurodevelopmental risks due to prenatal MeHg exposure

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Refs:

•Grandjean P. Neurodevelopmental disorders. In: Tamburlini G, von Ehrenstein O, Bertollini R. (eds): *Children's health and the environment: A review of evidence*. WHO, Rome, 2002.

"A large prospective study in the Seychelles has not revealed any clear adverse effects related to maternal hair mercury concentrations"

•Myers GJ et al, Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study, *Lancet* (2003) 361:1686

Exposure to methylmercury (MeHg) before birth can adversely affect children's neurodevelopment. The most common form of prenatal exposure is maternal fish consumption, but whether such exposure harms the fetus is unknown. We aimed to identify adverse neurodevelopmental effects in a fish-consuming population. We investigated 779 mother-infant pairs residing in the Republic of Seychelles. Mothers reported consuming fish on average 12 meals per week. Fish in Seychelles contain much the same concentrations of MeHg as commercial ocean fish elsewhere. Prenatal MeHg exposure was determined from maternal hair growing during pregnancy. We assessed neurocognitive, language, memory, motor, perceptual-motor, and behavioural functions in children at age 9 years. The association between prenatal MeHg exposure and the primary endpoints was investigated with multiple linear regression with adjustment for covariates that affect child development. Mean prenatal MeHg exposure was 6.9 parts per million (SD 4.5 ppm). Only two endpoints were associated with prenatal MeHg exposure. Increased exposure was associated with decreased performance in the grooved pegboard using the non-dominant hand in males and improved scores in the hyperactivity index of the Conner's teacher rating scale. Covariates affecting child development were appropriately associated with endpoints. Interpretation: These data do not support the hypothesis that there is a neurodevelopmental risk from prenatal MeHg exposure resulting solely from ocean fish consumption.

Mercury

ANOTHER ORGANIC MERCURY: THIMEROSAL

❖ Mercury preservative used in

- Eye drops, antiseptics, other pharmaceuticals
- Multidose vaccinations

❖ 49.6% ethylmercury

- $T_{1/2}$ ~7 days in babies
- Crosses blood-brain barrier

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Thiomersal is sodium ethylmercurythiosalicylate or thimerosal. It has been used since the 1930s.

Refs:

•Pichichero ME et al. Mercury concentrations and metabolism in infants receiving vaccines containing thiomersal: a descriptive study, *Lancet* (2002) 360 (9347):1737.

•Stajich GV et al, Iatrogenic exposure to mercury after hepatitis B vaccination, *J. Pediatr.* (2000) 136: 679

Thimerosal, a derivative of mercury, is used as a preservative in hepatitis B vaccines. We measured total mercury levels before and after the administration of this vaccine in 15 preterm and 5 term infants. Comparison of pre- and post-vaccination mercury levels showed a significant increase in both preterm and term infants after vaccination. Additionally, post-vaccination mercury levels were significantly higher in preterm infants as compared with term infants. Because mercury is known to be a potential neurotoxin to infants, further study of its pharmacodynamics is warranted.

•Pichichero ME et al. Mercury levels in newborns and infants after receipt of thimerosal-containing vaccines. *Pediatrics*. 2008 Feb;121(2):e208-14.

OBJECTIVES: Thimerosal is a mercurial preservative that was widely used in multidose vaccine vials in the United States and Europe until 2001 and continues to be used in many countries throughout the world. We conducted a pharmacokinetic study to assess blood levels and elimination of ethyl mercury after vaccination of infants with thimerosal-containing vaccines. **METHODS:** Blood, stool, and urine samples were obtained before vaccination and 12 hours to 30 days after vaccination from 216 healthy children: 72 newborns (group 1), 72 infants aged 2 months (group 2), and 72 infants aged 6 months (group 3). Total mercury levels were measured by atomic absorption. Blood mercury pharmacokinetics were calculated by pooling the data on the group and were based on a 1-compartment first-order pharmacokinetics model. **RESULTS:** For groups 1, 2, and 3, respectively, (1) mean +/- SD weights were 3.4 +/- 0.4, 5.1 +/- 0.6, and 7.7 +/- 1.1 kg; (2) maximal mean +/- SD blood mercury levels were 5.0 +/- 1.3, 3.6 +/- 1.5, and 2.8 +/- 0.9 ng/mL occurring at 0.5 to 1 day after vaccination; (3) maximal mean +/- SD stool mercury levels were 19.1 +/- 11.8, 37.0 +/- 27.4, and 44.3 +/- 23.9 ng/g occurring on day 5 after vaccination for all groups; and (4) urine mercury levels were mostly nondetectable. The blood mercury half-life was calculated to be 3.7 days and returned to prevaccination levels by day 30. **CONCLUSIONS:** The blood half-life of intramuscular ethyl mercury from thimerosal in vaccines in infants is substantially shorter than that of oral methyl mercury in adults. Increased mercury levels were detected in stools after vaccination, suggesting that the gastrointestinal tract is involved in ethyl mercury elimination. Because of the differing pharmacokinetics of ethyl and methyl mercury, exposure guidelines based on oral methyl mercury in adults may not be accurate for risk assessments in children who receive thimerosal-containing vaccines.

Mercury

EXPOSURE TO THIOMERSAL IN IMMUNIZATIONS

- ❖ **Vaccine practices in the 1990s raised the body burden of mercury for small and preterm babies***
- ❖ **Thiomersal-free vaccinations for newborns ****
 - In the US, all infant vaccinations are thiomersal-free since March 2001, except some influenza
 - Still used to prevent microbial contamination of multidose vials in some countries
- ❖ **No clear cut evidence of deficits in neuropsychological functioning in children from thiomersal in vaccines *****

* Stajich 2000, ** Ball 2001, *** Heron 2004, Thompson 2007

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It is unlikely that thiomersal causes overt disease, but studies are ongoing to evaluate more subtle symptoms from the highest exposures experienced by small infants during peak use in the 1990s. According to a British study, immunizing infants with vaccines containing thiomersal may be associated with improved behavior and cognitive outcomes (Heron, 2004).

Refs:

• www.who.int/phe/news/Mercury-flyer.pdf

• WHO. (2006) Statement on Thiomersal. WHO Global Advisory Committee on Vaccine Safety. who.int/vaccine_safety/topics/thiomersal

• Ball LK et al. An assessment of thiomersal use in childhood vaccines, *Pediatrics* (2001) 107: 1147.

• Clarkson TW et al. The toxicology of mercury – current exposures and clinical manifestations, *N Engl J Med* (2003) 349: 1731

• Heron J et al. Thiomersal exposure in infants and developmental disorders: a prospective cohort study in the United Kingdom does not support a causal association, *Pediatrics* (2004) 114(3):577.

There is an established link between exposure to mercury and impaired childhood cognitive development and early motor skills. Thiomersal (also known as thiomersal), a preservative used in a number of children's vaccines, contains ethylmercury (an organic compound of mercury), and there has been concern that this exposure to mercury may be of some detriment to young children. The aim of this research was to test in a large United Kingdom population-based cohort whether there is any evidence to justify such concerns. We used population data from a longitudinal study on childhood health and development. The study has been monitoring >14,000 children who are from the geographic area formerly known as Avon, United Kingdom, and were delivered in 1991-1992. The age at which doses of thiomersal-containing vaccines were administered was recorded, and measures of mercury exposure by 3, 4, and 6 months of age were calculated and compared with a number of measures of childhood cognitive and behavioral development covering the period from 6 to 91 months of age. Contrary to expectation, it was common for the unadjusted results to suggest a beneficial effect of thiomersal exposure. For example, exposure at 3 months was inversely associated with hyperactivity and conduct problems at 47 months; motor development at 6 months and at 30 months; difficulties with sounds at 81 months; and speech therapy, special needs, and "stuttering" at 91 months. After adjustment for birth weight, gestation, gender, maternal education, parity, housing tenure, maternal smoking, breastfeeding, and ethnic origins, we found 1 result of 69 to be in the direction hypothesized-poor prosocial behavior at 47 months was associated with exposure by 3 months of age (odds ratio: 1.12; 95% confidence interval: 1.01-1.23) compared with 8 results that still supported a beneficial effect. We could find no convincing evidence that early exposure to thiomersal had any deleterious effect on neurologic or psychological outcome.

• Thompson WW et al. Early thiomersal exposure and neuropsychological outcomes at 7 to 10 years. *N Engl J Med*. 2007 Sep 27;357(13):1281-92.

BACKGROUND: It has been hypothesized that early exposure to thiomersal, a mercury-containing preservative used in vaccines and immune globulin preparations, is associated with neuropsychological deficits in children. **METHODS:** We enrolled 1047 children between the ages of 7 and 10 years and administered standardized tests assessing 42 neuropsychological outcomes. (We did not assess autism-spectrum disorders.) Exposure to mercury from thiomersal was determined from computerized immunization records, medical records, personal immunization records, and parent interviews. Information on potential confounding factors was obtained from the interviews and medical charts. We assessed the association between current neuropsychological performance and exposure to mercury during the prenatal period, the neonatal period (birth to 28 days), and the first 7 months of life. **RESULTS:** Among the 42 neuropsychological outcomes, we detected only a few significant associations with exposure to mercury from thiomersal. The detected associations were small and almost equally divided between positive and negative effects. Higher prenatal mercury exposure was associated with better performance on one measure of language and poorer performance on one measure of attention and executive functioning. Increasing levels of mercury exposure from birth to 7 months were associated with better performance on one measure of fine motor coordination and on one measure of attention and executive functioning. Increasing mercury exposure from birth to 28 days was associated with poorer performance on one measure of speech articulation and better performance on one measure of fine motor coordination. **CONCLUSIONS:** Our study does not support a causal association between early exposure to mercury from thiomersal-containing vaccines and immune globulins and deficits in neuropsychological functioning at the age of 7 to 10 years.

Mercury

CHILD LABOUR WITH MERCURY

- ❖ In small scale mining areas, children may work with mercury

- ❖ This is child labour at its worst:
 - Physically very hard and dangerous
 - High risk of injury
 - Major health hazard



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In numerous projects the United Nations Industrial Development Organization (UNIDO) has addressed the global issue of mercury as a health hazard caused by the release of the toxic metal from small-scale gold mining activities.

The UNIDO project “Removal of barriers to the Introduction of Cleaner Artisanal Gold Mining and Extraction Technologies” showed, as one of the results, a very high number of children working as miners with direct contact to mercury in Indonesia, Tanzania and Zimbabwe.

Worldwide, it is estimated by UNIDO that up to 10 000 000 people live in small scale mining areas, many of them children.

Picture: Courtesy of Dr. Stephan Boese-O'Reilly. Children in Amberose / Kadoma in Zimbabwe, where gold is extracted from ore with mercury, 2004.

Ref:

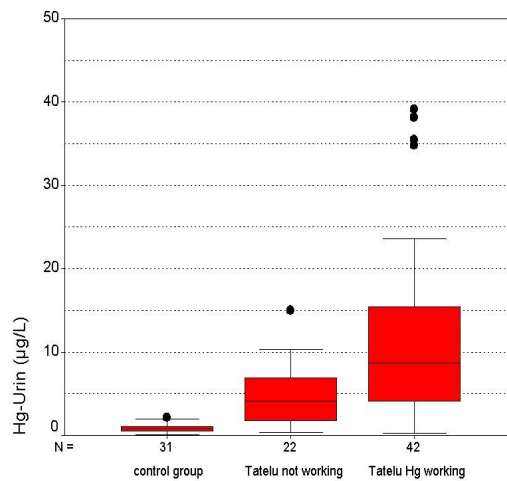
•Boese-O'Reilly S et al. Mercury as a serious health hazard for children in gold mining areas. *Environ Res.* 2008 May;107(1):89-97.

In many developing countries, mercury is used to extract gold from ore in small-scale mining areas. Exposure through mercury in these small-scale mining communities is a serious health hazard, especially to the children living and working there. Many children begin working with immediate contact to mercury from the very early age of seven. In Indonesia and Zimbabwe, 166 children were clinically examined for mercury. The mercury concentration in the blood, urine, and hair was analyzed. Compared to the control groups, the exposed children showed typical symptoms of mercury intoxication, such as ataxia. The children working with mercury had high levels of this substance in the various biomonitors. The exposure derives mainly from the liquid mercury used to bind gold, forming an amalgam. The amalgam is heated and the smelting amalgam releases mercury vapor plus the wanted gold. Mercury vapor in contrast to liquid mercury is highly toxic. This elemental, vaporized mercury is the main form of exposure. Since in over 50 countries children live in small-scale gold mining areas and are exposed in a similar way to mercury, immediate action is needed to reduce this severe chemical health hazard for children. Child labor with hazardous substances such as mercury must be stopped.

Mercury

TATELU (INDONESIA) – EXPOSED CHILDREN

Hg in urine of children aged 8 to 13 who live and/or work in the area



This slide shows results from the UNIDO projects in Indonesia by Boese-O'Reilly S., Drasch G, Rodriguez S., Beinhoff C

Tatelu is a village in Indonesia (Sulawesi). Children do work here as small scale miners with mercury. In a box plot the urine levels of mercury are shown. According to the exposure risk (control group in a different area with no specific mercury exposure, children living - but not working in the exposure area, children living and working in the exposure area) the mercury levels differ.

The coloured box represents 25-75%, the line in side is the mean mercury level. The whiskers are the 95% confidence intervals and the dots are outliers.

UNIDO: United Nations Industrial Development Organization

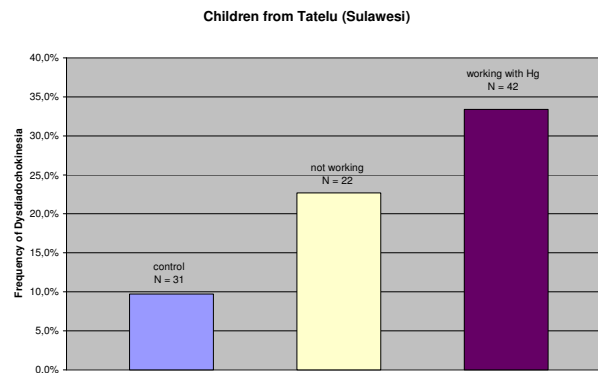
Ref:

•Boese-O'Reilly S et al. Mercury as a serious health hazard for children in gold mining areas. *Environ Res.* 2008 May;107(1):89-97.

Mercury

TATELU (INDONESIA) – DYSDIADOCHOKINESIA

Cerebellar effects in children aged 8 to 13 who live or work and live in the area



43

This slide shows results from the UNIDO projects in Indonesia by Boese-O'Reilly S., Drasch G, Rodriguez S., Beinhoff C

Dysdiadochokinesia is a clinical symptom of cerebellar damage. According to the different exposure risks the children in the highest exposure group show the highest rate of symptoms.

UNIDO: United Nations Industrial Development Organization

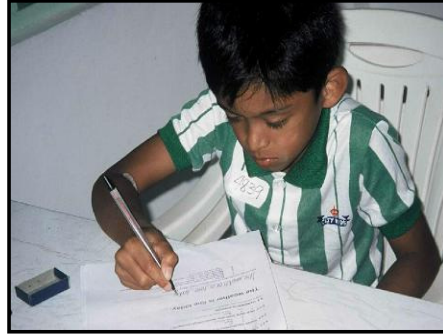
Ref:

- Boese-O'Reilly S et al. Mercury as a serious health hazard for children in gold mining areas. *Environ Res.* 2008 May;107(1):89-97.
- Rodrigues Pereira Filho S et al, *Environmental and health assessment in two small-scale mining areas – Indonesia. Final report Sulawesi and Kalimantan. Technical Final Report to UNIDO, 2004.*

Mercury

SYMPTOMS AND SIGNS OF METALLIC Hg EXPOSURE

- ❖ Tremor
- ❖ Ataxia
- ❖ Coordination problems
- ❖ Excessive salivation
- ❖ Metallic taste

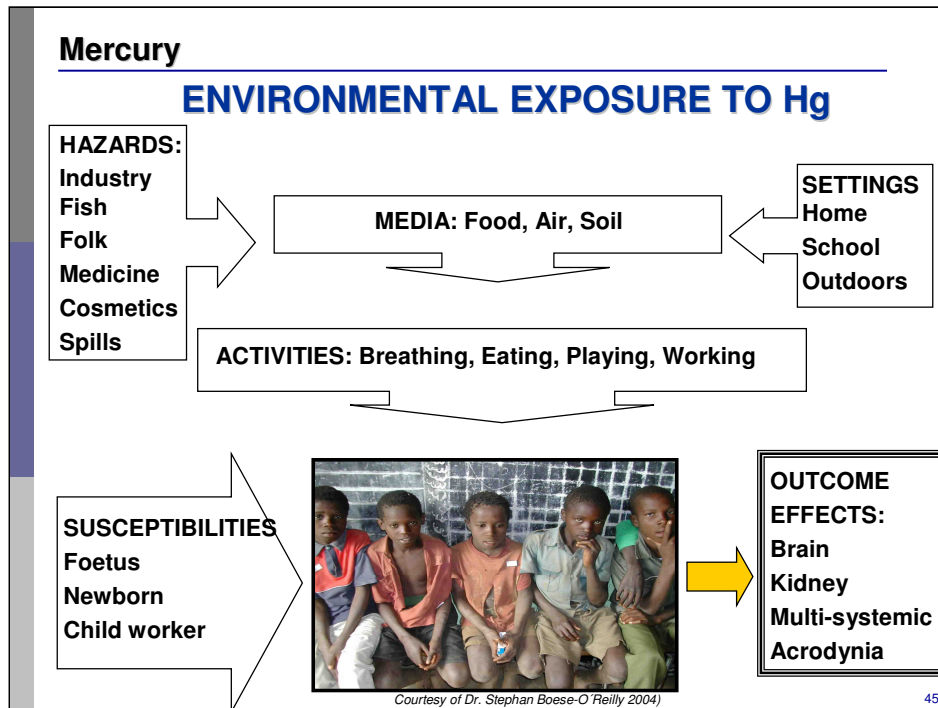


Courtesy of Dr. Stephan Boese-O'Reilly 1999)

Picture: Courtesy of Dr. Stephan Boese-O'Reilly. Boy from a small scale mining operation area near Monkayo in Mindanao (Philippines) being tested, 1999.

Ref:

•Drasch G et al, The Mt. Diwata study on the Philippines 1999 – assessing mercury intoxication of a population by small scale gold mining, Sci Total Environ (2001) 267: 151



In this summary slide, we see the complexity of the issues related to children's environmental health and mercury exposure.

- Hazards may arise from different sources (industrial pollution, fish contamination, folk medicines, cosmetics – and spills at home)
- Mercury reaches the child through food, air, soil.
- At home, school or outdoors.
- Through activities, such as eating, playing, working.
- The most susceptible are: foetus, newborn and young children.
- The outcomes depend on the form of Hg, dose and timing of exposure, but the main effects are on the central nervous system, kidney, mucosal and dermal, and also acrodynia.

<<READ SLIDE>>

Picture: Courtesy of Dr. Stephan Boese-O'Reilly. Children from Kadoma / Zimbabwe, 2004.

These children from the Kadoma area of Zimbabwe work with mercury to extract gold from ore, thereby they are exposed to mercury vapour. Some of these children have elevated levels of mercury in their urine, blood or hair, some of them already show symptoms of mercury intoxication.

Mercury

DIAGNOSIS: HAVE A HIGH INDEX OF SUSPICION!

Think about mercury!

- ❖ **Careful history taking: food, activities, environment, ...**
- ❖ **Clinical observation**
- ❖ **Urine mercury (inorganic exposure)**
- ❖ **Blood mercury (organic exposure)**
- ❖ **Hair mercury (long term exposure)**

▪ Typical signs and symptoms

+

▪ Increased mercury body burden



**MERCURY
INTOXICATION**

46

Diagnosis of mercury intoxication, particularly if it is chronic and low dose requires a high index of suspicion.

Careful history taking to find potential sources of exposure.

If symptoms are found, the analysis of blood, urine or hair should be performed.

Urine mercury typically reflects inorganic exposure.

In most cases, total blood mercury reflects organic exposure. It is difficult to speciate and to analyze methylmercury, so total blood mercury can usually be used as a surrogate.

Hair analysis is most appropriate for research because there may be problems due to possible contamination during collection and quantification by size of hair sample. When analysis in sophisticated laboratories can be done, it is an excellent indicator of total body, long term exposure.

Refs:

• *Children's Health and the Environment – A global perspective. A resource guide for the health sector, WHO, 2005.*

• American Academy of Pediatrics Committee on Environmental Health. *Pediatric Environmental Health, 2nd ed.* Etzel RA, Ed. Elk Grove Village, IL: American Academy of Pediatrics, 2003.

Mercury

MANAGEMENT

❖ REMOVE CHILD FROM EXPOSURE

❖ Chelating agents may reduce the body burden of mercury and may improve some symptoms

- DMPS simple to use (orally), has few side effects
- DMPS is effective in "mixed" and "combined" Hg exposures
- DMSA may have some advantages in MeHg poisoning

❖ Symptomatic treatment

❖ Rehabilitation

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Treatment begins with the elimination of exposure. Permanent damage may have already occurred, but ongoing damage may be reduced through chelation in some cases of exposure. No medical therapy can replace the necessity for a reduction of the external burden, but it lowers the adverse effects of a mercury intoxication.

"Mixed" exposure: acute and chronic

"Combined" exposure: elemental, inorganic and organic (as seen in gold-mining areas).

With DMSA: Multiple courses of 3 week courses separated by 4-8 weeks are usually required (This is approved only for Pb).

DMPS (Unithiol): 2,3-dimercaptopropanesulphonic acid

DMSA (Succimer): meso-2,3-dimercaptosuccinic acid

Always check the treatment indication and dosages with the local poison control centre!

Ref:

•Boese-O'Reilly S et al, *The Mt. Diwata Study on the Philippines 2000 - treatment of mercury intoxicated inhabitants of a gold mining area with DMPS (2,3-Dimercapto-1-propane-sulfonic acid, Dimaval®)*. *Sci Total Environ* (2003) 307: 71

Ninety-five inhabitants of the gold mining area of Mt. Diwata (on Mindanao, Philippines), who were diagnosed to be mercury (Hg) intoxicated, were orally treated with 2 x 200 mg of the chelating agent DMPS (Dimaval, Co. Heyl, Germany) for 14 days in the course of a UNIDO project focusing on mercury pollution abatement. Blood and urine samples before and after treatment, urine after the first application of DMPS and a hair sample were collected and analyzed for Hg. Before and after treatment extensive anamnestic data were collected, medical and neurological investigations and some neuro-psychological tests were performed. In spite of the short time of treatment most of the patients reported a marked improvement of the complaints which were stated by them before the therapy and which are characteristic for a chronic Hg intoxication, for example tremor, loss of memory, sleeplessness, metallic taste, etc. But even in some of the objective neurological parameters like hypo-mimia, Romberg test and tests for tremor/ataxia a statistical significant improvement could be found. Significant improvements could also be found in two neuro-psychological tests (pencil tapping and Frostig). In some cases an extreme high urinary Hg excretion was found under the chelating therapy with DMPS, and by this a distinct reduction of the Hg body burden. Nevertheless, in most cases Hg in blood and urine was not markedly decreased by the treatment. This shows that the duration of the treatment (14 days) was not sufficient for a permanent decrease in Hg. As DMPS excretes Hg mainly through the kidney, it can be concluded that in most cases even after 14 days of treatment there was an ongoing redistribution of Hg from other tissues to the kidney.

In conclusion, this study proves that a chelating therapy with DMPS is highly effective even in the case of a mixed chronic and acute intoxication with an unknown combination of Hg vapor, inorganic Hg and organic Hg=methylmercury (MeHg), as characteristic for gold mining areas in the third world. Adverse side effects were rarely reported. Only in one case the medication had to be terminated after the first application due to an allergic skin reaction.

Mercury

TO CONSIDER CHELATION OR NOT?

YES

- Acute elemental
- Chronic elemental
- Acute inorganic
- Chronic inorganic

NO

- Chronic low level methylmercury
(No ion to grab –
It redistributes)

MAYBE

- Acute organic
 - phenylmercury
 - methylmercury

NEVER

- Oral EDTA
- Herbals
- To “cure” autism

Consult the Poison Centre

48

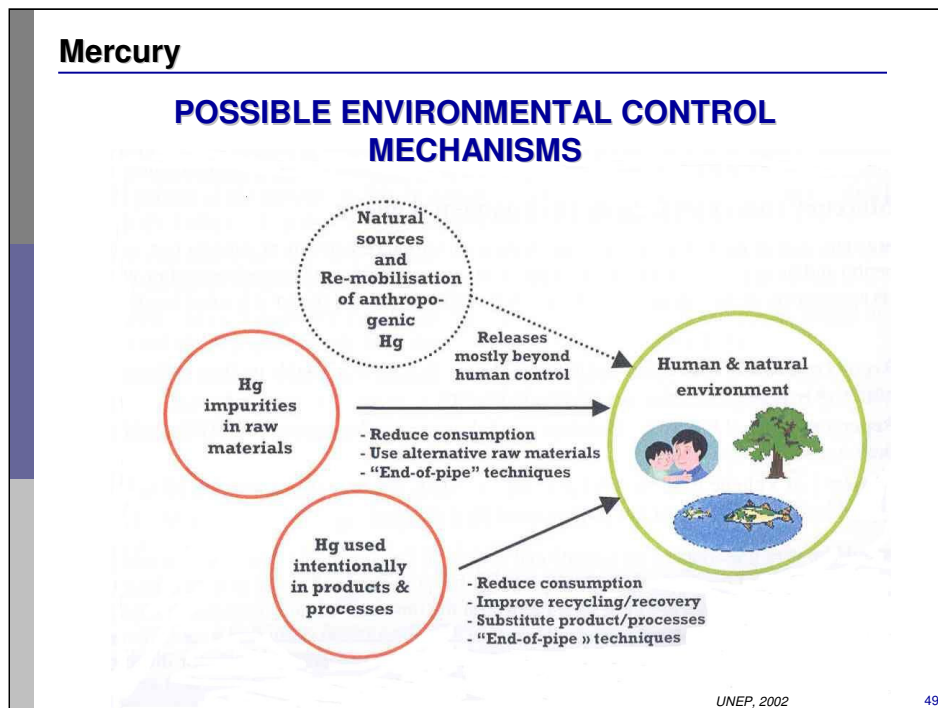
This slide summarizes the advice given to clinicians in a joint education meeting staged by the US Environmental Protection Agency (EPA) and the US Department of Health and Human Services (DHHS).

There is no indication for chelation of low level, chronic methylmercury poisoning. Courses of oral EDTA which is not absorbed, herbal preparations and claims that chelation can cure autism have not been established as effective.

When confronted with a child who has suspected symptomatic mercury intoxication it is critical to **consult your local poison centre** or clinical toxicologist before embarking on chelation treatments.

Ref:

• *Presentation at US EPA and US DHHS Conference: "Mercury: Medical and Public Health Issues." Tampa, Florida, 28-30 April 2004.*



This figure shows release categories of mercury to the biosphere with main types of possible control mechanisms.

Hg from natural sources is out of human control, but exposure to the Hg present in raw materials (e.g. fossil fuels, particularly coal and minerals) or used in products or released in processes may be controlled through:

- Reduction of use
- Use of alternative materials
- Improved recycling/recovery
- Technological improvements
- Good policies!

According to the UNEP report sources are grouped as:

- Natural sources releases due to natural mobilisation of naturally occurring mercury from the Earth's crust (e.g. volcanic activity and weathering of rocks).
- Current anthropogenic (human activity-related) releases from the mobilisation of mercury impurities in raw materials (fossil fuels: specially coal but also gas and oil).
- Current anthropogenic releases from mercury intentionally used in products and processes (releases during manufacturing, leaks, disposal or spent products incineration).
- Re-mobilisation of historic anthropogenic releases previously deposited in soils, sediments, waters, landfills, waste piles.

Ref:

- UNEP. *Global Mercury Assessment, December 2002:*
www.chem.unep.ch/mercury/default.htm

Figure: UNEP Chemicals, *Global mercury assessment*. UNEP Chemicals, Geneva, Switzerland, 2002.

Mercury

WHAT HEALTH CARE PROVIDERS CAN DO

PRIMARY PREVENTION

- ❖ Mercury-free office and hospital
- ❖ Mercury-free communities
 - Thermometer exchange
 - Hazardous waste education
 - Change high-risk behaviours
 - Folk medicines, cottage industries...**
- ❖ Advocacy
 - Request emission controls on power plants, incinerators
 - Prevent childhood exposure to artisanal mining

SECONDARY PREVENTION

- ❖ Fish consumption advice

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Prevention is pivotal because the brain has little or no ability to repair, particularly from prenatal damage to basic neuro-architecture. Since methylmercury from fish is the major world wide exposure, counseling mothers on safer fish consumption can help to protect the fetus and young children.

Primary prevention is crucial to prevent fish contamination at the source. Numerous programs are underway to reduce mercury use in medical equipment, batteries, switches and light bulbs. Regulations to control emissions and mining are also important, and health care providers have a powerful voice that can be used to influence politicians and regulators.

Mercury

EXAMPLE OF FISH CONSUMPTION GUIDELINES

For women and young children (USA)

1. Do not eat Shark, Swordfish, King Mackerel, or Tilefish
2. Eat up to 12 ounces (340 g) or two average meals per week of a variety of fish and shellfish that are lower in mercury
 - Shrimp, canned light tuna, salmon, pollock, and catfish are examples
 - Albacore ("white") tuna has more mercury than canned light tuna, you may eat up to 6 ounces (170 g) or one average meal per week.
3. Check local advisories. If no advice is available, eat up to 6 ounces (170 g) or one average meal per week of fish you catch, but don't consume any other fish during that week.

...to your young child, serve smaller portions!

From US EPA/FDA

51

Shown here is the fish consumption advisory issued by the US Environmental Protection Agency and the US Food and Drug Administration (EPA/FDA). It illustrates the complexity of the preventive messages. It only applies to women in the childbearing period and young children. Other individuals can safely eat more fish, even if it contains moderate amounts of mercury. 12 ounces is about 340 grams.

Refs:

• www.epa.gov/waterscience/fishadvice/advice.html

• Oken E et al. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. *Am J Epidemiol*. 2008 May 15;167(10):1171-81.

The balance of contaminant risk and nutritional benefit from maternal prenatal fish consumption for child cognitive development is not known. Using data from a prospective cohort study of 341 mother-child pairs in Massachusetts enrolled in 1999-2002, the authors studied associations of maternal second-trimester fish intake and erythrocyte mercury levels with children's scores on the Peabody Picture Vocabulary Test (PPVT) and Wide Range Assessment of Visual Motor Abilities (WRAVMA) at age 3 years. Mean maternal total fish intake was 1.5 (standard deviation, 1.4) servings/week, and 40 (12%) mothers consumed >2 servings/week. Mean maternal mercury level was 3.8 (standard deviation, 3.8) ng/g. After adjustment using multivariable linear regression, higher fish intake was associated with better child cognitive test performance, and higher mercury levels with poorer test scores. Associations strengthened with inclusion of both fish and mercury: effect estimates for fish intake of >2 servings/week versus never were 2.2 (95% confidence interval (CI): -2.6, 7.0) for the PPVT and 6.4 (95% CI: 2.0, 10.8) for the WRAVMA; for mercury in the top decile, they were -4.5 (95% CI: -8.5, -0.4) for the PPVT and -4.6 (95% CI: -8.3, -0.9) for the WRAVMA. Fish consumption of < or =2 servings/week was not associated with a benefit. Dietary recommendations for pregnant women should incorporate the nutritional benefits as well as the risks of fish intake.

Mercury

EXAMPLE OF FISH CONSUMPTION GUIDELINES

For women and young children in developing countries, where diets are based on fish that may have high levels of Hg

- ❑ **Recognize neurodevelopmental problems in children**
- ❑ Determine amount, type and frequency of fish consumption and provide advise
- ❑ **Encourage consumption of fish low in methylmercury, but:**
 - **Limit intake of larger, predatory fish**
 - **Greatly limit intake of marine mammals**
 - **Encourage consumption of "light" or "chunk light" tuna**

52

The advice to families in developing countries, especially those with diets based on fish, is quite different. When possible, limit intake of large fish who eat other fish. Smaller and younger fish are likely to have lower mercury levels. By eating a variety of fish, exposure is also likely to be reduced.

<<READ SLIDE>>

Refs:

- www.who.int/phe/news/Mercury-flyer.pdf
- Oken E et al. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. *Am J Epidemiol.* 2008 May 15;167(10):1171-81.

CASE STUDY

15 year old boy with rash, vomiting, muscle pain,
and “fast heartbeat”

This is a case study that describes an adolescent boy who visited the clinic because he had a rash, vomiting, muscle pain and a "fast heartbeat".

It is a case study that you may want to use in training health care providers. It can be done as an interactive exercise.

Mercury

History of Present Illness

Who else is ill?

15 friends and 3 siblings

What makes it better or worse?

Nothing noted

When did symptoms begin?

One year ago

Where did symptoms start?

At school

54

There are a number of questions that should be asked during history taking.

Who else is ill? 15 friends and 3 siblings

What makes it better or worse? Nothing noted

When did symptoms begin? One year ago

Where did symptoms start? At school

Mercury

Questions to Consider

- ❖ Is there metallic mercury in the school?
- ❖ Has mercury been spilled at school?
- ❖ Has a mercury spill been vacuumed?
- ❖ Is the boy involved in a job that involves the use of mercury?

55

These are several questions that the health care provider should consider asking the boy and his parents:

Is there metallic mercury in the school?

Has mercury been spilled at school?

Has a mercury spill been vacuumed?

Is the boy involved in a job that involves the use of mercury?

Mercury

Examination

Emotional adolescent who gives a poor history

Pulse 150, BP 140/90, Temp 37 C

Skin: sweaty, maculopapular rash, desquamation of palms and soles

Neurologic: fine tremors in eyelids and lips, moderate tremors in hands and arms

56

When the physical examination is performed, the health care provider notes an emotional adolescent who gives a poor history. Vital signs show a pulse of 150, a blood pressure of 140/90, and an oral temperature of 37 C (98.7 F)

His skin is noted to be sweaty, and he has a maculopapular rash, with desquamation of the palms and soles of his feet.

The neurologic examination is remarkable for fine tremors in the eyelids and lips, and moderate tremors in the hands and arms

Mercury

Additional History

- ❖ Brought vial of mercury to school
- ❖ He and 14 other students played with liquid mercury in the school (for ~1 year)
- ❖ School officials confiscated the mercury and removed and bagged the students' clothing

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The boy admits that he brought a vial of mercury to school over a year ago.

He and 14 other students played with liquid mercury in the school for about a year.

Finally, the school officials confiscated the mercury. They also removed and bagged the students' clothing.

Mercury

Laboratory

24-hour urine collection: 496 $\mu\text{g Hg/L}$
(normal 0-20 $\mu\text{g Hg/L}$)

School cafeteria air Hg: 5.28 to 36.6 $\mu\text{g/m}^3$
(normal $<0.5 \mu\text{g/m}^3$)

58

Ideally, one should collect urine for a 24 hour period to assess urine mercury content. This was done and the 24-hour urine collection showed 496 $\mu\text{g Hg/L}$ (Normally, 24-hour urinary mercury concentration is 0-20 $\mu\text{g Hg/L}$)

The air in the school cafeteria, where the children played with the mercury, was also measured. The level of mercury in the school cafeteria air was 5.28 to 36.6 $\mu\text{g/m}^3$. (Normally it should be $<0.5 \mu\text{g/m}^3$)

Mercury

Management

School closed and thoroughly cleaned, heated, and vented

Concentrations of mercury in air brought down to $3 \mu\text{g}/\text{m}^3$ before school reopened

Information and education of students, parents and the community about the danger of playing with mercury

59

After the school officials learned that the boy had brought mercury to school and played with it, they closed the school and thoroughly cleaned, heated, and vented it. The concentrations of mercury in the indoor air of the school were brought down to $3 \mu\text{g}/\text{m}^3$ before the school was reopened. An educational campaign was mounted to help students, parents and the community learn about the danger of playing with mercury.

WHO Guideline Value: 1 microgram/ m^3 (annual average)

Ref:

•WHO. Air Quality Guidelines for Europe, 2000.

Mercury

PRIMARY PREVENTION

Primary prevention at home

- ❖ **Avoid traditional and any other use of elemental Hg**
- ❖ **Eliminate equipment with mercury**
- ❖ **Avoid having children play with elemental Hg**
- ❖ **Dispose safely of mercury-containing products (e.g. batteries, thermometers).**

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The slide is self-explanatory. More detailed information for parents may be found at USEPA's website: www.epa.gov/epaoswer/hazwaste/mercury

<<READ SLIDE>>

Mercury

PRIMARY PREVENTION

In the medical domain:

- ❖ Hg mercury thermometers and manometers, substitution
- ❖ Promote Hg-free vaccines
- ❖ Consider dental composite (alternative to amalgam)

61

Simple clinic-based strategies for primary prevention are listed in this slide.

In the medical domain:

Since electronic thermometers may be available, and are easier and safer to use, the unnecessary risk of mercury containing thermometers could be avoided.

Since mercury free vaccinations may be available, this source of contamination could be avoided

Consider using composite (alternative to dental amalgam) when feasible.

More on reducing mercury in medical practice: www.noharm.org

<<READ SLIDE>>

Ref:

•Bellinger DC et al, Dental amalgam and psychosocial status: the New England Children's Amalgam Trial. *J Dent Res.* 2008 May;87(5):470-4.

High-dose exposures to elemental mercury vapor cause emotional dysfunction, but it is uncertain whether the levels of exposure that result from having dental amalgam restorations do so. As part of the New England Children's Amalgam Trial, a randomized trial involving 6- to 10-year-old children, we evaluated the hypothesis that restoration of caries using dental amalgam resulted in worse psychosocial outcomes than restoration using mercury-free composite resin. The primary outcome was the parent-completed Child Behavior Checklist. The secondary outcome was children's self-reports using the Behavior Assessment System for Children. Children's psychosocial status was evaluated in relation to three indices of mercury exposure: treatment assignment, surface-years of amalgam, and urinary mercury excretion. All significant associations favored the amalgam group. No evidence was found that exposure to mercury from dental amalgams was associated with adverse psychosocial outcomes over the five-year period following initial placement of amalgams.

Mercury

PRIMARY PREVENTION

In case of metallic mercury spill:

- DO NOT clean yourself if amount is greater than that contained in a thermometer: Call local health or environmental agencies.
- NEVER VACUUM or use a broom
- NEVER put mercury down the drain
- NEVER wash mercury-contaminated items in a washing machine
- NEVER walk around if your shoes might be contaminated with mercury.
- Take special measures with contaminated clothes.

www.epa.gov/epaoswer/hazwaste/mercury/spills.htm#cleanmercuryspills

62

<<READ SLIDE>>

When mercury is exposed to air, it gives off vapours that, under some circumstances, can build up in indoor air at high enough concentrations to pose health risks to occupants. Air vapours from spilled mercury can also eventually settle onto water, increasing the mercury levels in fish. Therefore, it is important to clean up mercury spills properly and to report them to the proper authorities when necessary.

During a mercury spill, you will see that mercury breaks into tiny beads that roll, and can easily become trapped in small cracks in the surface. A mercury spill can be cleaned with minimal effort, if the proper instructions are followed.

What NEVER to do with a mercury spill:

Never use a vacuum cleaner to clean up mercury. The vacuum will put mercury into the air and increase exposure. The vacuum appliance will be contaminated and have to be thrown away.

Never use a broom to clean up mercury. It will break the mercury into smaller droplets and spread them.

Never pour mercury down a drain. It may lodge in the plumbing and cause future problems during plumbing repairs. If discharged, it can cause pollution of the septic tank or sewage treatment plant.

Never wash mercury-contaminated items in a washing machine. Mercury may contaminate the machine and/or pollute sewage.

Never walk around if your shoes might be contaminated with mercury. Contaminated clothing can also spread mercury around.

Spills: Less than or equal to the amount in a thermometer: tips.

Remove everyone from the area where cleanup will take place. Shut door of impacted area. Turn off ventilation system. DO NOT allow or gain assistance from children. Remember to remove all pets as well.

Mercury can be cleaned up easily from the following surfaces: wood, linoleum, tile and any other like surfaces.

If a spill occurs on carpet, curtains, upholstery or other like surfaces, these contaminated items should be thrown away in accordance with the disposal means outlined in the US Environmental Protection Agency (EPA) website. Only cut and remove the affected portion of the contaminated carpet for disposal.

Spills: More than the amount in a thermometer. **Caution:**

The general public can clean up small mercury spills no greater than the amount contained in a thermometer from flat surfaces. If you estimate your mercury spill to be greater than the amount in a thermometer, isolate the contaminated area and call your local health or environmental agency.

These notes are taken from EPA's website. More detailed information on specific actions to be taken after spills may be found at EPA's website: www.epa.gov/epaoswer/hazwaste/mercury/spills.htm#cleanmercuryspills

Mercury

PRIMARY PREVENTION

Regulatory measures

- ❖ Control/reduce Hg release into the environment
- ❖ Enforce environmental standards
- ❖ Implement standards, actions and programmes on Hg exposure
- ❖ Eradicate child labour with mercury

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<<READ SLIDE>>

- ❖ Control/reduce Hg release into the environment through actions on:
 - Coal burning power plants
 - Medical uses and waste
 - Municipal and hazardous waste incineration
 - Factory and mining discharges
- ❖ Enforce environmental standards – control of Hg levels in drinking water, surface waters, air, soil and foodstuff –fish
- ❖ Implement standards, actions and programmes on Hg exposure - In the workplace, through fish consumption advisories and consumer safety measures.
- ❖ Eradicate child labour with mercury - In small scale mining areas and other occupations

These are more systemic approaches to prevention through regulatory measures.

<<NOTE TO USERS: If there are political strategies that are being proposed or developed in your local area, it would be ideal to insert them here.>>

Mercury

PREVENTION AND REGULATIONS

Global Mercury Assessment (UNEP, Dec 2002)

- Mercury is present throughout the environment
 - Is persistent and cycles globally
 - Has serious effects
 - Interventions can be successful
- ❖ Global actions are required because:
- Hg's global cycling increases the problem
 - Hg has an impact on global fishing
 - Hg may be more problematic in less developed regions
 - Hg is subject to significant international use and commerce
- ❖ Calls for international coordinated actions (Convention?)

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As already seen, the United Nations Environmental Programme has prepared a Global Mercury Assessment publication with very comprehensive information on mercury as a global environmental and human health threat. It calls for local, regional and global actions, and for international coordination.

Available at: www.chem.unep.ch

<<READ SLIDE>>

<<NOTE TO USERS: If there are political strategies that are being proposed or developed in your local area, it would be ideal to insert them here.>>

Ref:

•UNEP. *Global Mercury Assessment, December 2002:*
www.chem.unep.ch/mercury/default.htm

Mercury

HEALTH AND ENVIRONMENT PROFESSIONALS PLAY A CRITICAL ROLE:

- ❖ **Diagnose and treat**
- ❖ **Publish, do research**
 - Sentinel cases
 - Community-based interventions
- ❖ **Educate**
 - Patients and families
 - Colleagues and students
- ❖ **Advocate**
- ❖ **Role model**

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Health and environment professionals have a critical role to play in maintaining and stimulating changes that will restore and protect children's environmental health.

Our political and personal lives to support sustainable development, should include practices for ways to enhance the environmental health of our patients. All of us can do something to detect and avoid the effects of mercury in the environment.

Health care providers should include mercury exposure as a potential environmental etiology in differential diagnosis and preventive advice (avoiding the excess use of "idiopathic" as an etiology and looking in depth into environmental causes of disease and disability).

It is important to publish sentinel cases, detect other cases of exposure in the population and develop and write up community based interventions.

Patients, families, colleagues and students should be informed about mercury hazards and educated.

Health care providers and environmental officers can become vigorous advocates for the environmental health of children and the future generations.

As professionals with understanding of both health and the environment, we are powerful role models. Our choices will be noticed and they should be thoughtful and sustainable.

Mercury

POINTS FOR DISCUSSION

<<NOTE TO USER: Add points for discussion according to the needs of your audience.>>

Mercury

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