Inorganic Chemistry of Life
Chemistry 2211a

Toxic Metals

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Course outline - on the web
Check instruct.uwo.ca/chemistry/211a

Contents of section 9:

General introduction "Toxic Metals"
Chelators
Lead
Arsenic
Cadmium
Mercury
Detailed review notes
Appendix of additional material – not tested

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2211a-TOX-MET 2010-N10f.doc

Note for mjs: Last unreduced file is 07-N8- this is reduced using tables – text in N9b

Pdf's made with 1 & 2 page format on web site. Display has 1 page format.

METAL POISONS	Substances that usually (a) combine with natural molecules (deliberately broad) or (b) disrupt chemical processes (eg due to corrosive nature, etc.) to reduce metabolic activity or biological function.
METALS POISON BY A VARIETY OF DIFFERENT MECHANISMS,	Most of which interfere with enzymes involved in ATP production directly or indirectly. A common mode of action is to tie up sulfhydryl groups of catabolic enzymes[1]. [1] Catabolic pathways break down nutrients to yield smaller molecules and capture stored energy. Key is the generation of energy in ATP and reducing power in NAPDH plus small metabolites. Anabolic pathways synthesize larger molecules from smaller precursors and use energy. Nutrients are catabolized to release and capture stored energy in form of ATP or NADH or electrochemical (chemiosmotic) gradients. Examples of the Bertrand Diagram in action.
OFTEN ARE D-BLOCK METALS	Metals on the RHS of the Periodic Table. However, many other metals are toxic; this depends on the compound they are associated with (the ligands), their exposure route (does the ligand make the metal more 'accessible' to the physiological chemistry? And, at high concentrations.
IS METAL POISONING A CURRENT PROBLEM?	Cd – yes; Hg – yes very much so; As – yes. Pb – yes. Consider: Should children with more than the "intervention level" of 10 ug/dL blood Pb be treated to lower it? Probably yes–see the Pb section below. Is this a real case value? Yes.
COMMON TOXIC METALS	Lead (Pb), arsenic (As), cadmium (Cd), mercury (Hg), copper (Cu), and chromium (Cr). But, note, Cu is essential, and Cr is thought to be essential.
HOW DO THESE METALS CONTACT HUMANS?	Cu and Cr are still used in paint pigments, considered safe at present. Pb also used to be in paint pigments and in the production of vinyl chloride but recently phased out for both of these uses. Still used in car batteries and fishing weights (see news stories – a Canadian horror story). Hg used to be used in thermometers and paints, still used in fluorescent lights, and As used to be used in rat poison and in preservatives applied to 'outside' green-wood used by the general population.. These last two uses are now phased out of all consumer products.

Toxicity Ratings and Average Lethal Doses

Toxicity Rating	LD_{50} (mg/kg body wt)	Average Lethal Dose (70kg human)	Examples
Supertoxic	< 0.01	< 1 drop	nerve gas, botulism, dioxane
Extremely toxic	< 5	< 7 drops	cyanide, heroin, nicotine
Very toxic	5-50	7 drops - 1 teaspoon	mercury salts,morphine
Toxic	50-500	1 teaspoon-1 oz	DDT, sulfuric acid, caffeine
Moderately Toxic	500 - 5000	1 oz - 1 pt	amphetamines, kerosene, aspirin
Slightly Toxic	5000-15,000 (5-15 g/kg body mass)	1 pt - 1 qt	ethanol, lysol, soap
Non-toxic	> 15,000 that's 15 g/kg	> 1 qt	water, sugar

NEXT Sources; Bioavailability; Mammalian exposure; Toxicity – long term-short term; Toxic response; Chelators

SOURCES	Metal exposure arises from several sources – we can refer to the diagrams from the GEO unit. Natural: Chemical weathering of rocks and soils; Atmospheric fallout (volcanic, wind erosion, smoke, aerosols/particulates from ocean) Human Activities - Mining operations (acid mine drainage, ore processing, smelting, refining) - Domestic effluents and storm runoff; Industrial wastes and discharges The effect of this influx of metals into the environment - both natural and man-made (home and work place) - depends on what happens to the metal-containing compounds next.
BIOAVAILABILITY	Solubility and speciation will determine whether a metal is bioavailable (particularly, the ligands the metal binds to) and whether there are mechanisms in place in the organism to absorb the complex. Acidic pH will enhance solubility – basic pH results in hydroxides and carbonates that are insoluble. Availability also depends on whether the deposited metal is mobilized by a change in its form, common causes are: Change in salt concentrations; redox conditions; pH; presence of a chelator, eg EDTA
MAMMALIAN EXPOSURE	**Respiration > ingestion > skin absorption, injection.** Through cigarette smoking; diet and water supplies. Route of exposure affects toxicity and target organs (eg Hg and Cd) Level and duration of exposure affects toxicity and target organs (eg. Pb, Cd) Nutritional status also influences toxicity of metals. Different poisons have radically different toxic dosage levels. We will see a number of these below[1], but the most common way of expressing toxic dosages is called the "LD50" of the poison. LD50 (Lethal Dosage-50%) is dosage which will kill half of the animals who are administered that quantity of poison in a single dose (no repair time). Human exposure to toxic metals[2]: Knowing about an exposure route for one metal (or even 1 compound) tells you nothing about other metals.
KEY ELEMENTS COMMONLY FOUND IN THE ENVIRONMENT AND	Arsenic, cadmium, lead, mercury, chromium, copper, cobalt and zinc. The most environmentally abundant toxic metals or metalloids (arsenic, cadmium, lead, and mercury) are each known to produce cell injury in the kidney. Each causes problems in the tubules, but by slightly

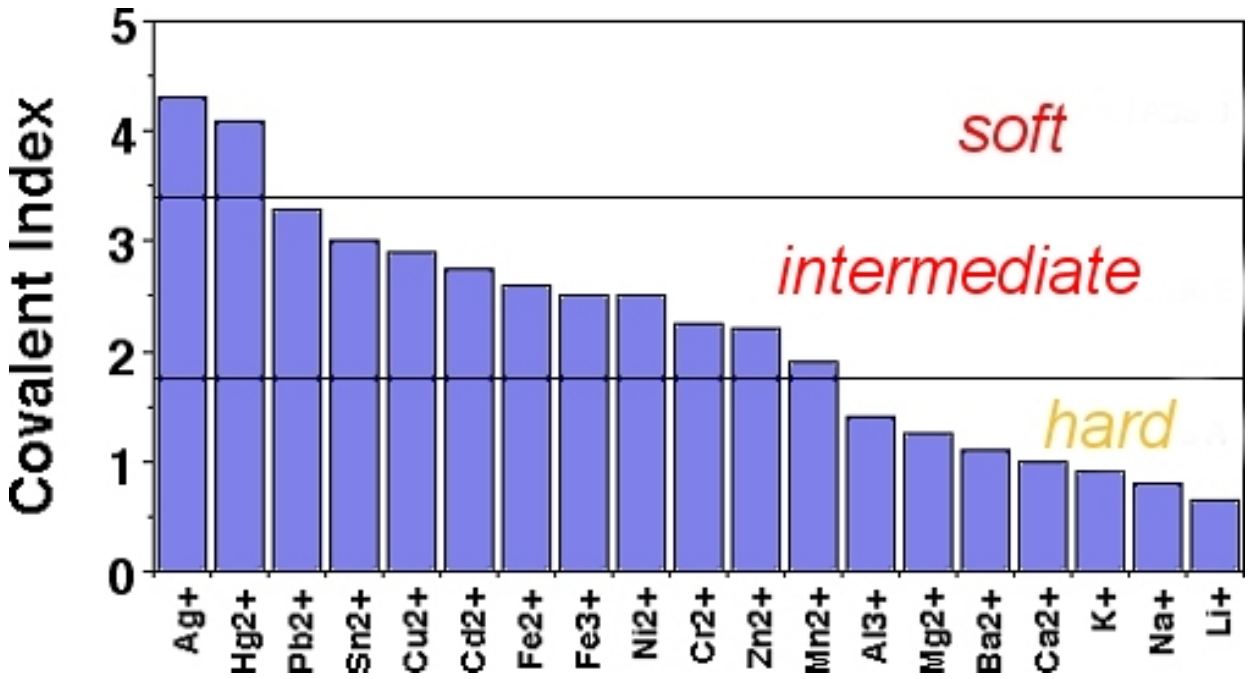
[1] See end of this section – specifics not tested – but for interest.

[2] Table 2 – Shows the distribution of 'toxic' metals is 'normal'. When is a metal toxic? The Bertrand Diagram says it all.

WORK PLACE	different mechanisms. An aside: The kidneys are part of the urinary system. The human body has two kidneys, one on either side of the middle of the back, just under the ribs. They regulate the amount and composition of the body fluids; remove waste products and excess water from the blood; produce hormones which regulate blood pressure and the amount of calcium in bone, and stimulate the formation of red blood cells by the bone marrow. The nephrotoxicity[3] of these toxic agents is due, in part, to the fact that urinary elimination is a major route of excretion from the body.
RELATIVE TOXICITIES	Hard/Soft nature of the metal[4] – soft metals will bind readily to sulfur and are potentially more toxic because formation of covalent bonds to a large biological molecule might enhance the uptake and transport of the metal. The mechanisms for controlling the metal inside the organism will affect the toxicity. Excretion requires transport in the organism; toxicity can be changed by accumulation in "sinks" of bone (Pb), hair, and even target organs (kidneys for Cd)
TOXIC RESPONSE	
ACUTE VS. CHRONIC TOXICITY	Acute – a complete overload of the organism – a usually fatal concentration. A one time event → ☠. Chronic – exposure to low concentrations over a long time period. There may even be a acclimatization – a steady state – but alternatively, metabolic functions may slowly fail → ☠ In both, the toxicity can be seen as: blockage of essential functional groups on enzymes; displacement of essential metals in enzymes; and/or modification of the conformation of key biomolecules.
WHAT MAKES METALS TOXIC?	The free ionic metal or complex of the metal is usually the toxic form Soft metals are generally more toxic than very hard metals, being most effective at binding with SH-groups (cysteine, methionine) and N- containing groups (histidine, lysine) which are commonly important in active centers of enzymes.

[3] Nephrotoxicity can be defined as renal disease or dysfunction that arises as a direct or indirect result of exposure to medicines, and industrial or environmental chemicals. From: Publication of United Nations Environment Programme, the International Labour Organisation, and the World Health Organization.
For more information see: http://www.inchem.org/documents/ehc/ehc/ehc119.htm#PartNumber:2
This is also a problem with metal-based drugs, eg cisplatin doses are limited by the nephrotoxic effects.

[4] Check back to Inorganic Unit – p 23-27 – for a refresher and details.

SOFT METAL IONS MERCURY IS AN EXCEPTION –ALL FORMS ARE SOFT METALs BUT WITH DIFFERENT CHEMICAL PROPERTIES	Soft (metal) – Int/Soft (ligands) These new metal-amino acid bonds are not accounted for in the natural metabolic processes – so may be permanent and block the protein or enzyme from subsequent chemistry. This makes the metal a metabolic poison. Particularly the case with Cd & Hg. 
SPECIFICS –USING THE GRAPH ABOVE	Soft metals: 1. Can displace/replace Intermediate/ Hard metals from metalloenzymes, causing alteration in structure and activity (redox or shape) 2. Are capable of forming organometallic ions (Hg, As, Sn, Te, Pb) -- lipid soluble and, therefore, can biomagnify, becoming much more toxic. Intermediates -- Displace/replace other intermediates or hard metals Hard metals - Displace/replace other hard metals (Be, highly oxidized dbM's) Chemical form of metal directly controls toxicity. Important for Cr (3+ vs 6+); Hg (0 vs 2+ vs CH_3Hg^+); and As (3+ vs 5+).

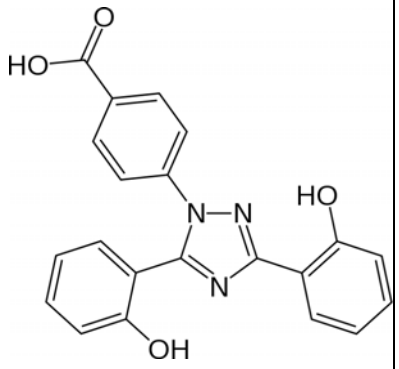
A CASE HISTORY – HG (SEE LATER FOR EFFECTS)	Hg^0 (liquid) = not toxic; used as laxative, but how to overcome what happens with the vapour. Hg^0 (vapor) = very toxic 80% absorption in the lungs no charge so crosses the membranes readily – because of catalase in the lungs this oxidises the Hg^0 to Hg^{2+} → brain → ☠☠. Hg^{1+} or Hg^{2+} = toxic at high levels – ingested → kidneys breakdown → slow ☠. alkyl-Hg = very, very toxic; lipid soluble – MeHg-Cys complex looks like Met – transported directly across the BBB so is a CNS and neurological toxin → ☠☠☠ – but in fish? (Se can protect against Hg toxicity; Zn or Ca can protect against Cd toxicity)
CHELATORS –AN OVERVIEW	Simply excreting the metals naturally may work if the metal has not done permanent damage– what does this require? Time. "Chelating agents" are substances that are extremely effective at removing heavy metals from the body. These ligands generally have 2 or more S, O, or N atoms, which bind tightly to metals and keep them from reacting with proteins. Soft or intermediate ligands are more common because they bind more toxic metals and do not bind the essential, hard metals. Chelation is the formation of a metal ion complex – usually with a strong sigma donor atom - (oxygen, nitrogen and sulfur).
THE IDEAL CHELATING AGENT	the compound should be soluble in aqueous medium should be stable in the circulation if it is given orally, it should be absorbed by the GI tract and it should be cleared by the kidney the compound should be active at physiological pH the compounds should chelate only the specific metals the chelator itself should not be toxic the chelator-metal complex should be less toxic than the metal alone
THE MOST COMMONLY USED CHELATING AGENT IS EDTA.	Also used in household cleaners to remove Ca and Mg hard water deposits from sinks, tile, and bathtubs. A very powerful metal remover. Problem with use in humans is that EDTA removes all divalent metals from the body, even the essential metals necessary for life. So to use, must supplement essential metals when treating person with EDTA to keep person alive. (Special note – how does this match what I said on the LHS? Look up EDTA from the Inorganic Unit earlier – know the structure -… but you do! – and it's on the

WHICH CHELATOR TO USE WITH WHICH METAL? -

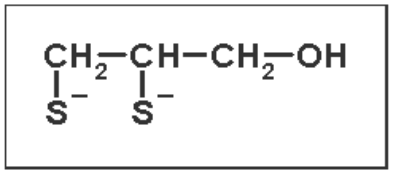
KNOW AT LEAST ONE FOR EACH METAL

HERE: BAL, DMPS, DMSA, EDTA, D-PEN, NAPA, AND FE-DFO AND A NEW ENTRY

DEFERASIROX

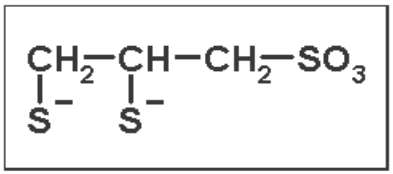


NAPA → →



2,3-dimercaptopropanol

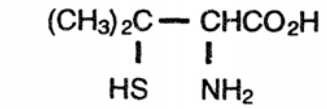
BAL



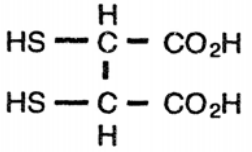
2,3-dimercaptopropylsulfonate

DMPS

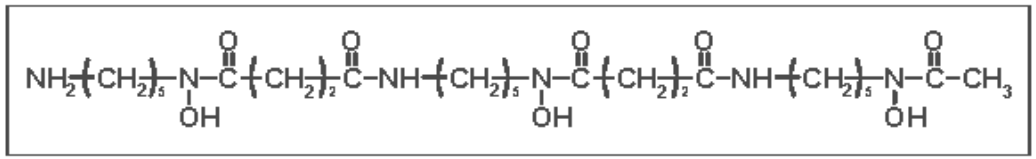
DMSA →



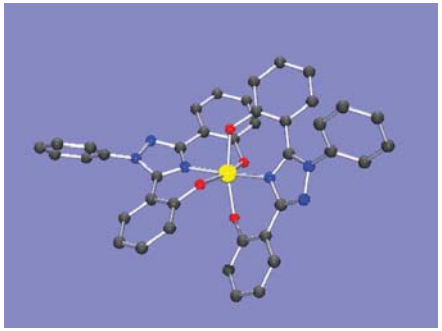
D-penicillamine

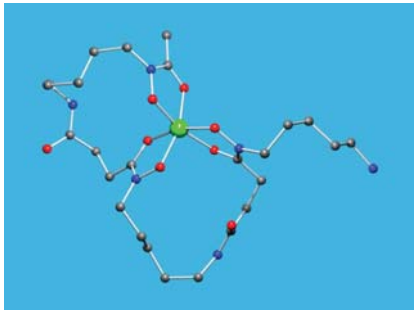


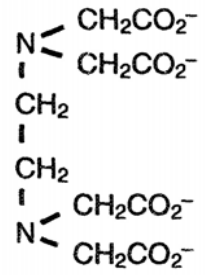
2,3-dimercaptosuccinic acid



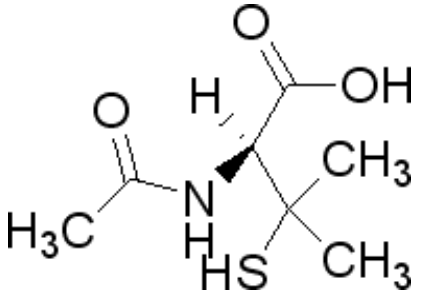
Desferrioxamine







EDTA



CURRENT – IN USE -CHELATORS	BAL - 2,3-dimercatopropanol - given IM in peanut oil Used for arsenic, mercury, antimony, lead, gold, zinc, bismuth. Half life is less than one hour. Toxicity: - CNS convulsions in high dose; increased blood pressure; constriction of arterioles.; renal toxicity; nausea, vomiting and headache EDTA given IV as the calcium disodium salt. Used as disodium EDTA to bind calcium in blood to prevent clotting- used in blood collection and storage Used for Pb: only chelates circulating metal because EDTA cannot enter inside the cell membrane; frequently used in combination with BAL or penicillamine for treatment of lead poisoning Toxicity - tubular destruction due to release of metal or the metal-EDTA complex in the kidney. d-isomer Penicillamine (Cuprimine®) given orally Used for Pb, Hg, As, and Cu (Wilson's disease where Cu^{+} is elevated) Toxicity - Fever, skin rashes, leukopenia[5], nausea, vomiting N-Acetyl-D-penicillamine (NAPA) Hg, As DMSA Can be given orally for As, Pb – Cd – minor side-effects – also chelates Zn(II). And recently, for Fe overload – DEFERASIROX.

[5] **Leucopenia** is a decrease in the number of circulating white blood cells (leukocytes) in the blood.

METAL	CHELATING AGENTS
Lead	Used to be - Ethylenediamine-tetraacetic acid ($EDTAH_4$) but side effects are significant Now the preferred chelator is 2,3-dimercaptosuccinic acid (DMSA, Succimer) 2,3-dimercaptopropanol (BAL, Dimercaprol) Penicillamine both have been used – the BAL-Pb complex is excreted through the bowel rather than the kidneys – so used when there are kidney problems
Cadmium	Overall Preferred is DMSA - BAL is more efficient but mortality is high due to renal failure; also ethylenediamine-tetraacetic acid ($EDTAH_4$)
Mercury	FDA approved – 2,3-dimercaptosuccinic acid (DMSA, Succimer) works well – has some chelating ability following CH_3Hg^+ exposure – DMSA crosses the blood-brain barrier also For serious systemic intoxication DMPS (dimercaptopropanesulphonic acid) is the treatment of choice. Also used are N-acetyl-penicillamine (NAPA) Penicillamine and older but thought very good is 2,3-dimercaptopropanol (BAL, Dimercaprol) - injections required and painful – also side effects bad
Arsenic	N-acetyl-penicillamine (NAPA) DMSA
Iron	Used to be Desferrioxamine B (DFO) Replaced in 2005 by Deferasirox – a triazole molecule quite unlike DFO – see above

Toxic effects of metals

How do metals enter the cell?

a. Passive diffusion – simply move through a channel

b. Active transport – be moved through the membrane by a 'pump' located in the membrane

c. Facilitated transport – a carrier molecule carries the metal through the membrane

d. Extracellular ionophore diffusion – specific molecule that encapsulates /chelates the metal and moves through the membrane with the metal

See diagram next page.

Once in the cell – transport to one of three routes – excretion, storage or toxic damage. Via GSH? See Arsenic section below. Possible excretion routes? See Fig 8.11

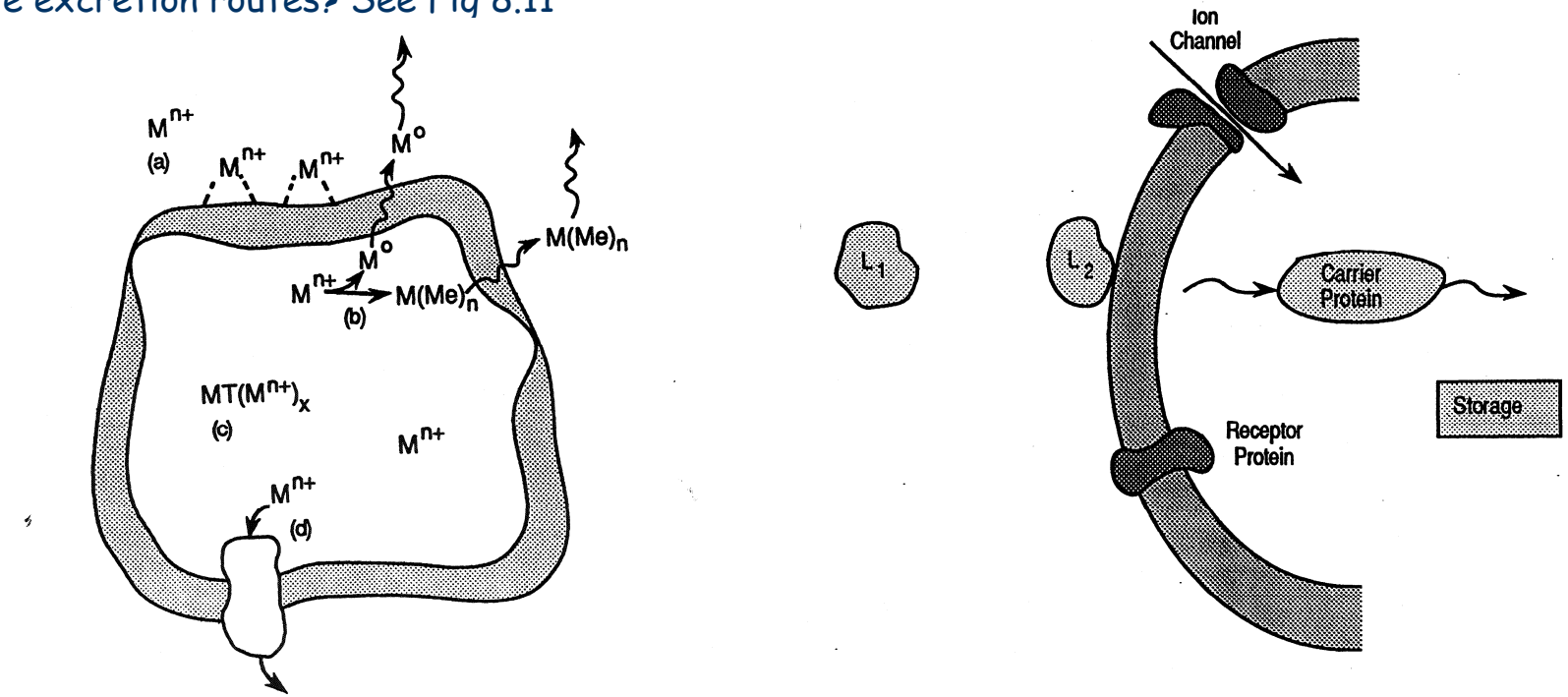
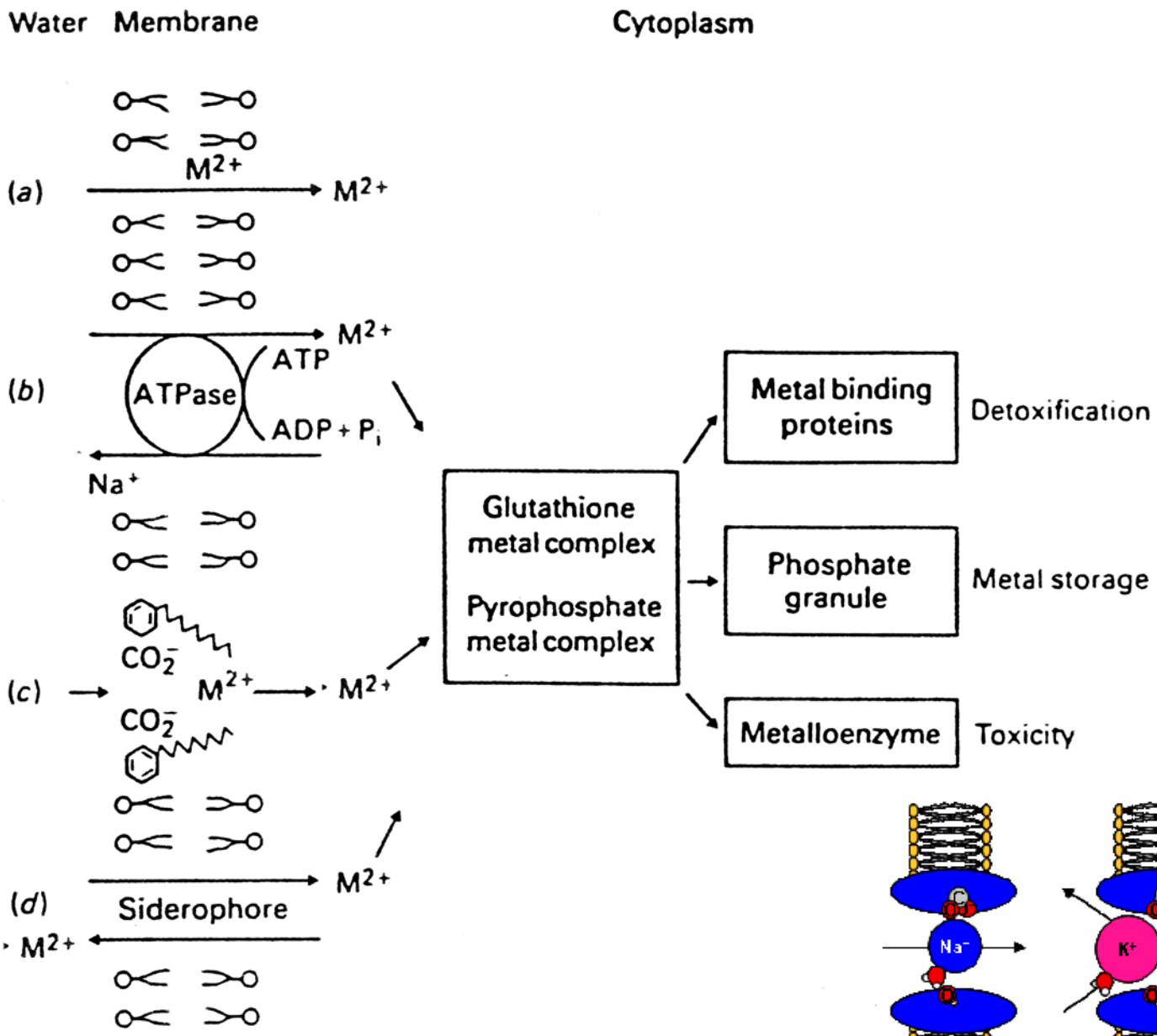
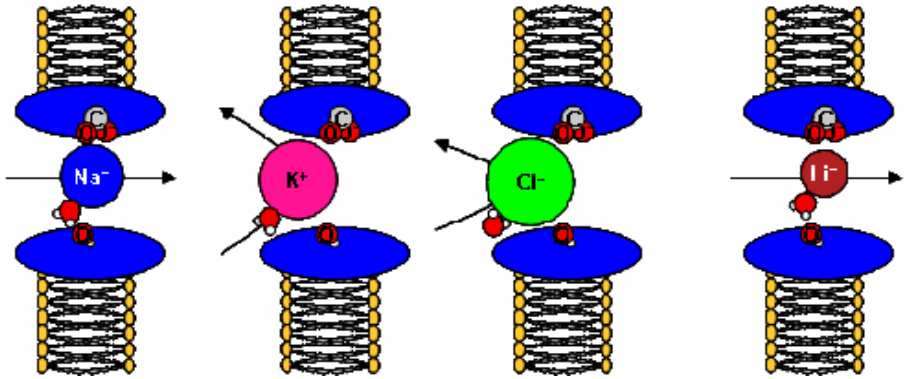


Figure 8.11 Bacterial mechanisms for disposal of heavy metals. (a) Binding to the outer membrane. (b) Chemical reduction and/or methylation to form volatile species. (c) Complexation by ligands or proteins (e.g., metallothionein, MT). (d) Export through an ion channel.

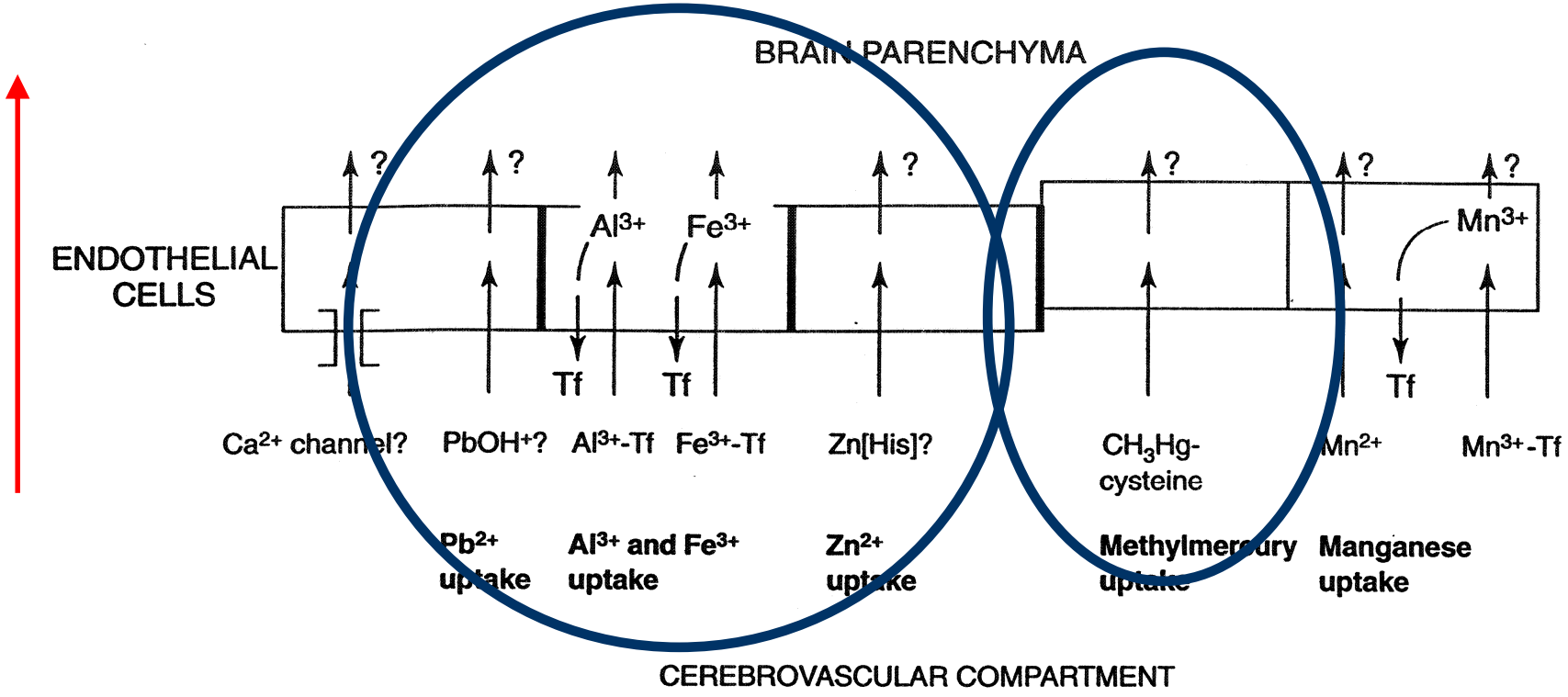




Metal uptake, transport and cell interactions in a biological cell. Transport mechanisms across the biomembrane include: (*a*) passive diffusion; (*b*) active transport; (*c*) facilitated transport; and (*d*) extracellular ionophore diffusion.

The flow of metals through the blood brain barrier Al^{3+} and Fe^{3+} use transferrin (Tf); Zn^{2+} a His complex; CH_3Hg^+ a complex with CYS – all carriers not channels

M. ASCHNER AND L.E. KERPER



ure 10.1 Mechanisms of metal transport at the blood–brain barrier. For details on each specific metal, refer to text. ? denotes unknown mechanism.

Toxicity of Metals– Pb Exposure and Health effects

Pb- so useful, from sweetening wine to soldering pipes to beautiful glazes and Pb-glass and then there's plumbing.

Pb- In diagrams with red boarders – exact details or numbers are not tested. Information mentioned in the text from these diagrams and tables IS testable. Brown text – not tested.

Lead is a potent, systemic poison that serves no known useful function in the human body.

Widely toxic because of the large number of sources for the general population and, in particular, children.

Chronic overexposure to Pb may result in severe damage to heme synthesis

Over the centuries, Pb was thought to be safe in low doses. But we know now that even extremely low levels of lead can cause health problems, especially in small children ages 6 months to 9 years.

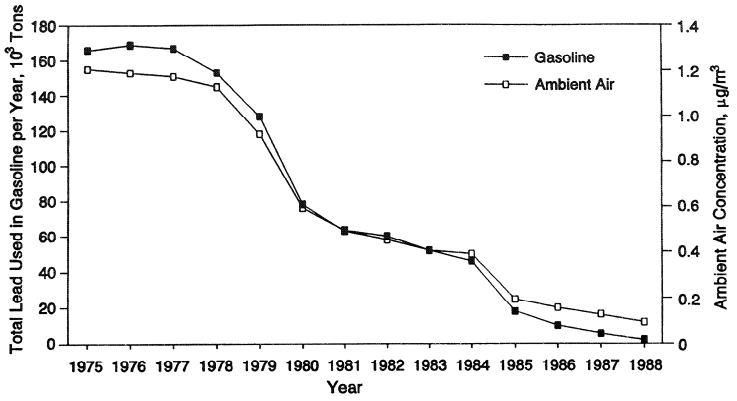


FIGURE 28.1 Gasoline lead vs. air lead levels in the U.S. (From U.S. Environmental Protection Agency, 1986, with updating.)

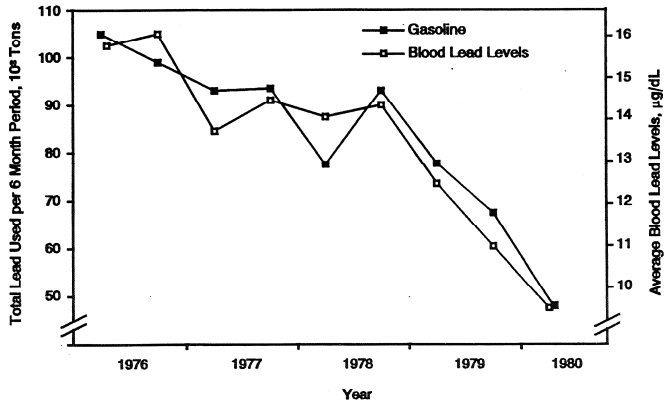


FIGURE 28.2 Gasoline lead vs. blood lead levels in the U.S. (From Annest, J.L., *Lead vs. Health: Sources and Effects of Low Level Lead Exposure*, Rutter, M. and Russell Jones, R., Eds., John Wiley & Sons, New York, 1983.)

Lead is a heavy, soft metal<	It can be found naturally in all parts of the world. Pb is released at ca. 4×10^5 tonnes/y natural sources and 3×10^6 tonnes/y due to man. The softness of lead made it very adaptable and it was bent and shaped into many useful items. Lead has been used since antiquity – especially during the Roman Empire – as above.
Pb	Soft, malleable and ductile, resistant to corrosion. Heavy – hence for fishing weights, boat ballast. Mined in northwest Wales (UK) - mining dates back to at least Roman times and continued until well into the 20th century. 2007 metal production: 127,000 tonnes.

Pb^{2+} compounds	In old pipes, paints, pottery, and up until 1970's as Et_4Pb in gasoline across the world – banned in N America – but still in the developing countries. There were 2-3g/gallon of Et_4Pb in gasoline – which became a major problem due to the particulate fallout of PbO etc. on to soils and plants. Road-side dust was rich in PbO. Pb^{2+} accumulates in bones so animals concentrate Pb^{2+} from plants but not dangerously. Note drop in Pb in fig above – this has translated into a drop in blood lead levels in children – and in number of children with depressed IQ levels.
Pb is involved in the production of many items	EG pottery glazes, lead-acid batteries – all cars!, stabilizers for PVC plastics, pigments for inks, electrical and plumbing solders, and pipes Pb use for fishing weights and ammunition spread Pb (which rapidly dissolves in the stomachs of diving birds) across Canada (see graphic below). Stained glass connections. High lead glass (approx 15% by weigth Pb) used as decanters or even glasses will leach Pd rapidly into wine and acidic drinks leading to death. X-ray shields. As a weight – balancing car wheels – scuba diving.
Pb used to be used much more frequently	White paint, lead carbonate white was used by the Japanese geisha for face-whitening make-up, typesetting. Lead was used for plumbing in Ancient Rome and as a preservative for food and drink in Ancient Rome. Tetraethyl lead in gasoline.
Exposure to Lead So that leads us to the next section -- - how does Pb exhibit toxic effects?	**Excessive exposure is usually from lead-based white paint in old houses (large amounts of lead-based paint persist in and around many older homes).** Although white lead-based paint is now not sold, yellow lead chromate paint is still available. And many toys are painted in lead-based paints if manufactured outside Europe and North America. (See Metals in the News web link on the INSTRUCT site for 2211a.) An estimated three million tons of lead remain in fifty seven million homes in the USA. Water passing through lead pipes and lead-soldered joints in newer copper water pipes (eg drinking fountains in primary schools in Ontario); road-side dust from the effects of leaded-gasoline (much of the lead from gasoline still contaminates the soil along busy roadways) and cooking or storing foods in low fired glazes. Pb is also taken up by the hair and nails. (Other uses: from batteries to lead aprons to protect from X-rays to …. the list is long.) In 1976 average BL in the USA was ca. 16 ug/dL plasma, in 1991 this fell below the critically low value of 3. However, blood lead values give an indication of only a small fraction of the total body burden Maximum dietary intake is 300 μg /day Plumbism is common in industrial workers from lead-based solder. Pb is stored in bones as well as in plasma. Lead poisoning was documented in ancient Rome, Greece, and China. Lead poisoning works on the cellular level by binding to the enzyme that inserts iron into the porphyrin ring → common symptom anemia.

THE POWER OF LEAD – THE FALL OF THE ROMAN EMPIRE

Lead (Pb) can attach tightly to proteins

Replaces metals such as zinc (Zn) or calcium (Ca), which are needed for normal metabolic function.

Lead accumulates in the soft tissues and bone[6].

Lead is particularly toxic when deposited in the brain. Lead crosses both the blood brain barrier (see earlier) and the placenta into the fetus. (Soft tissue/blood ½ life 20's days; in bone ½ life 20's years!)

In children Lead poisoning results in:

Developmental delays

Learning disabilities – even at low conc IQ is depressed

Behavior problems

In adults Lead poisoning results in:

Severe lead poisoning can damage the nervous system

Anemia – easy to understand why ... see below.

Lead poisoning is associated with male infertility

Lead is of considerable current concern[7]

Lead poisoning is usually ranked as the most common environmental health hazard for children between the ages of six months and six years.

FILE

SCIENTIFIC SPECULATION BY JUENEMAN

INNOVATIVE NOTEBOOK

A lead-pipe cinch

FOR 2,000 YEARS and more, even while using lead as a metal of commerce, we have been aware of its toxic properties. The history of lead, not to mention its discovery, fades into antiquity. And yet, how well have we learned the lessons of history? Not very.

The ancient Romans had a rather clever corps of engineers who found that lead made an easily workable and practical conduit for transporting potable water from their aqueducts and reservoirs. Moreover, lead had great staying power because it remained relatively free of corrosion. But, despite this, one of the more famous architects of the first century BC, Marcus Vitruvius Pollio, warned that lead was potentially toxic and recommended that terra-cotta pipes be used instead.

Of course, no one paid much attention to Vitruvius as lead was far too useful, especially for such items as pewter goblets, bowls, and serving dishes, as well as lead-lined copper vessels used for cooking and storage. The heavy pewter utensils, which were of an alloy of lead that could pass for antique silver, were somewhat resistant to being tipped by an inebriated guest or knocked over by gusts on a windy afternoon out on a Roman patio. The lead-lined copper pots took advantage of the thermal conductivity of the copper without introducing the metallic taste imparted by cooking in coppery vessels.

Actually, tin seems to have been the preferred metal for lining copper to keep it from discoloring or corroding, but frequently the ores of metals with low melting points were blended and reduced together, giving alloys with a high lead content. Tin had been imported from the British Isles since about the fifth century BC, but because it was more expensive, it was alloyed with cheaper ores containing zinc, lead, and probably much more than a trace of arsenic and antimony.

So, for some two millennia, with the continued and extensive use of lead and lead alloys in the culinary arts and transport of potables, plumbism (lead poisoning) became a malady of Western civilization, but this only became quantitatively characterized early in the last century.

What had finally led up to this characterization was the recognition that gout and plumbism were coincident phenomena, a condition endemic during the period of Imperial Rome and again during the 18th to 19th century among the British aristocracy. Today gout is known as a typical result of subclinical lead poisoning *(New Eng. J. Med.*, 308, 11, 1983).

There had been a suspicion in recent years that plumbism was

rampant among Roman nobility because culinary recipes of the period called for unusual amounts of salt for savoring. Chronic lead poisoning dulls the sense of taste to where the palate is pleased only by very sweet or very sour condiments, else by heavy seasoning. Chronic plumbism also is manifested by colic and constipation, not to mention gout, and makes one go funny in the head, all of which we know affected more than a few Roman Emperors.

The Roman penchant for wine is legendary, much of which had been boiled down in lead-lined pots to enhance and concentrate the sugar content. It has been said that the epicurean general, Lucius Lucullus, ordered up some 4-million liters of vino for a triumphal feast. Meanwhile, closer to our own time, England imported more than 21-million liters of fortified port wine in 1825. All contained measurable, and hence potentially toxic, lead concentrations.

Organic acids, as acetic, attack lead, and wines which have been fermented too far, forming vinegar, are "sweetened" in the presence of lead. As a questionable benefit, lead acetate is a powerful fungicide and, in addition, this property may have been the reason why lead acetate has become known as "sugar of lead."

Podagra, or gout, has been the bane of those who dined well throughout the ages. In the fourth century BC, Hippocrates—the father of medicine—made the first clinical description of saturnine gout, and although he recognized that it had to do with rich food and wine, he did not connect it with lead vessels, but recommended regular cathartics to relieve the condition. Further, he noted that the best natural relief of gout was an attack of dysentery.

Curiously, nearly 2,100 years later, a chemist named N. Grew crystallized a salt in 1695 from the brine wells near Epsom, England. The substance was magnesium sulfate heptahydrate, and became known as Epsom salt. Within a short time its purgative properties achieved international renown, and it was widely used as a serial cathartic to rid the body's vital fluids of "bad humours." An unappreciated side benefit was the scavenging of soluble lead salts and precipitation as the sulfate, whereupon it could be eliminated more readily.

In the first century AD, Dioscorides, the Greek physician, and Pliny, the Roman naturalist, both mention the addition of "gypsum" (calcined calcium sulfate, or plaster of Paris) to wine, a practice which is still customary in the Mediterranean area. It improves color and clarity while acting as a preservative, although Pliny said that it corrected acidity—meanwhile removing the lead moiety. But Dioscorides objected to the practice because it was bad for the nerves—probably since the removal of water left a higher alcohol content.

However you look at it, the lessons of history would be a cinch if we just bothered to read them from time to time.

Frederic B. Jueneman, FAIC

Exposure: after inhalation, dermal absorption, or ingestion, it enters the bloodstream and attaches to proteins that carry it to different tissues and organs.	The gastrointestinal tract absorbs about 40% on ingested lead. Almost all organs are affected by Pb poisoning - with greatest damage being to sulfhydryl enzymes. Lead tends to accumulate in the body over time as the excretion rate is low (t1/2 life from bone is 20-30 years). When lead enters the body, it replaces iron, calcium, and other minerals in the blood, which are extremely important during the stages of growth and development. Because young children require more minerals to grow and develop, they are thus more vulnerable to lead poisoning.
Symptoms of lead poisoning differ for children and adults. Pb is stored as complex with low molecular weight protein in erythrocytes, in the soft tissue, and loosely bound in bone – the major pool is tightly bound as insoluble and nontoxic Pb triphosphate in the skeleton – eventually becoming Pb-apatite (but is in equilibrium with the plasma bound Pb). Luckily, only minor amounts cross the blood-brain barrier.	High Pb leads to: iron deficiency and low Ca uptake because Pb and Ca compete for the same transport mechanism **Pb results in - anaemia due to interference in the Fe insertion reactions of heme synthesis (see next slide) and a shortened red blood cell life span.** Lead can damage the brain and nervous system -encephalitis (brain disorders) –there are several neurological disorders - in children attention disorders are common - neurologically in children - with effects of Pb poisoning quite clear at >80 ug/dl serum (4-5 uM).
Currently (2007) thought that blood Pb levels below the once-considered-safe 10-20 ug/dL in children can lead to behavioral	The US has a target of <10 µg/dL for children (& <5 by 2010) but in 2001 there were still children with BPb or BLL > 25 µ g/dL so this 2010 goal may not be achieved.

problems (this may take place in the fetus as well).	The Canadian picture is better probably because of the lower fraction of old homes[8] Normal excretion is very slow via the kidneys into the urine.
Measurement of exposure	The clearest indicator of Pb-exposure is the reduction in the activity of the delta- aminolevulinate dehydratase (ALHD or also called **Porphobilinogen Synthase**, E_2). In this reaction 2 molecules of ALA (δ-aminolevulinate) condense to form porphobilinogen (PBG) - on the pathway to formation of the heme – through a cyclization step followed by an iron insertion step.

Some details on the effects of Pb on heme synthesis.

E1= delta-aminolevulinic acid synthase → ALA

E2=PBG synthase – also called ALA dehydratase ALAD

2ALA → PBG
ALA rises when ALAD/PBGs is inhibited by Pb^{2+}.

E7 = ferrochelatase.
Inhibition raises PPIX.

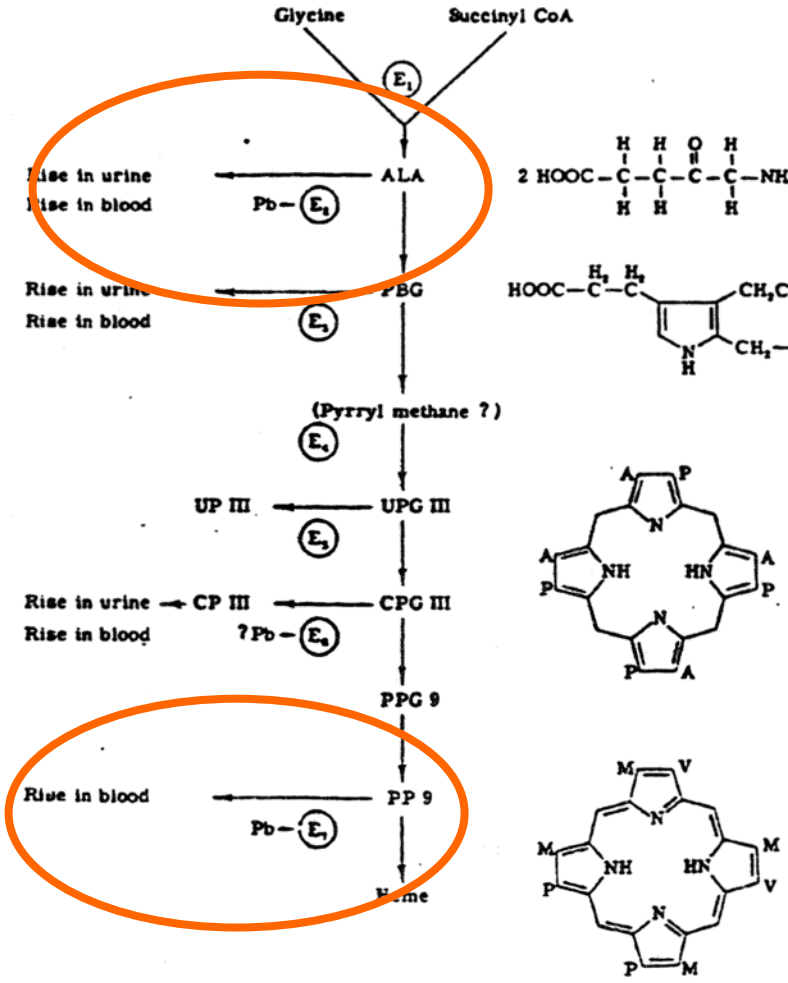


FIG. 5. The synthesis of heme. Modified from Haeger-Aronsen (1960). Reprinted from Ref. 28 by permission.

E2= Porphobilinogen (PBG) synthase or ALA-dehydratase = ALAD

The binding sites for Zn^{2+} in the homo-octomeric mammalian PBG include 2 CYS and 2 HIS ligands - these can also bind Pb^{2+}- this inhibits ALAD/PBGs.

Inhibition of PBG synthase (ALAD) by Pb^{2+} results in elevated blood ALA, which may cause some of the neurological effects of lead poisoning and that heme is not produced ➔ anemia. ALA builds up because PBG cannot be made – worse –autoxidation of ALA produces reaction oxygen radical species.

The presence of elevated ALA concentrations in blood is an excellent marker for Pb poisoning. ALA is toxic to the brain. This may be due in part to the fact that ALA is somewhat similar in structure to the neurotransmitter GABA (γ-aminobutyric acid). In the Figure we see that if E_2 is inhibited ALA rises.

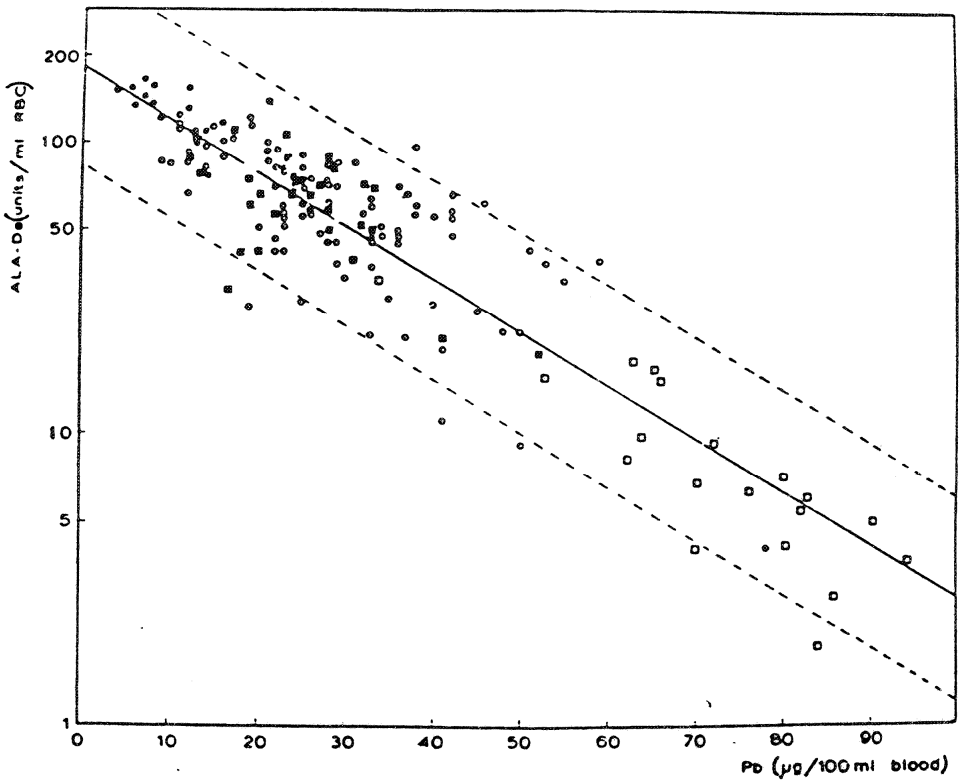
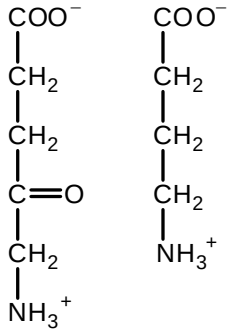
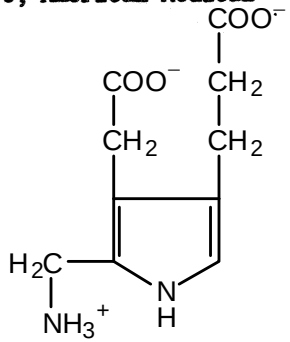


FIG. 6. Correlation between ALAD in blood and lead in blood. Solid circle = medical students. Open circle = workers in printing shops. Solid square = auto repair workers. Open square = lead smelters and ship scrappers. Reprinted from Ref. 25 by permission (copyright 1970, American Medical Association).

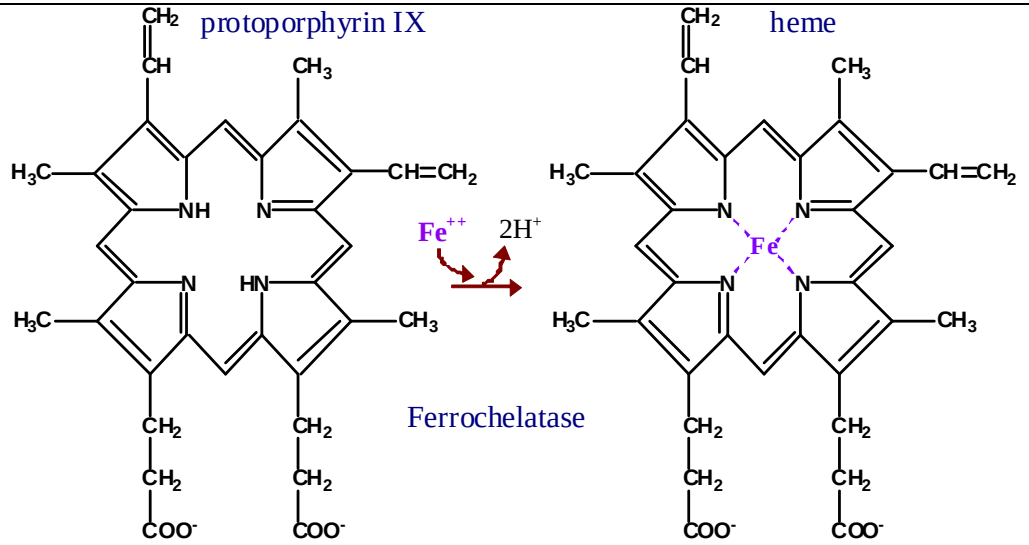


ALA

GABA



Porphobilinogen (PBG)

The porphyrin ring is formed by condensation of four molecules of porphobilinogen (PBG) –for details see Appendix – not testable.	Synthesis continues … missing a few steps that we are not concerned about until an hexapyrrole is made from the PBG`s above
Insertion of the iron – by ferrochelatase. Note – ferrochelatase is inhibited by Pb^{2+}. The porphyrin ring is formed by condensation of four molecules of porphobilinogen (PBG) The PPIX has distinctive spectral properties – amongst them fluorescence – so the artery emits light – the greater the Pb^{2+} exposure, the greater the concentration of PPIX and the brighter the emission from the tissue.	

Blood lead levels (BLL or PbB) are an important indicator of the likelihood that a person will acquire Pb-related health impairment or disease.

1. BLL are most often reported in units of milligrams (mg) or micrograms (µg) of lead (1 mg=1000 µg) per 100 grams (100 g), 100 milliters (100 ml) or deciliter (dL) of blood. These three units are essentially the same. We will quote µg/dL – where the threshold is often considered to be 5-10. Below this 'normal', above this 'to be concerned'. Current average values in the pop. are <1 µg/dL blood.

2. BLL measurements show the amount of Pb circulating in the blood stream, but do not give any information about the amount of Pb stored in various tissues. Blood Pb measurements merely show current absorption of lead, not the effect that the Pb is having on the body or the effects that past Pb exposure may have already caused.

3. **Long-term (chronic) overexposure.**

a. Chronic overexposure to Pb may result in severe damage to heme synthesis mechanisms, nervous, urinary and reproductive systems. Anemia is characterized by weakness, pallor and fatigability as a result of decreased oxygen carrying capacity in the blood. Kidney disease occurs with few, if any, symptoms appearing until extensive and most likely permanent kidney damage has occurred. Routine laboratory tests reveal the presence of this kidney disease only after about two-thirds of kidney function is lost. When overt symptoms of urinary dysfunction arise, it is often too late to correct or prevent worsening conditions, and progression to kidney dialysis or death is possible.

b. Some common symptoms of chronic overexposure to Pb include loss of appetite, metallic taste in the mouth, anxiety, constipation, nausea, pallor, excessive tiredness, weakness, insomnia, headache, nervous irritability, muscle and joint pain or soreness, fine tremors, numbness, dizziness, hyperactivity and colic. In Pb-colic there may be severe abdominal pain.

c. Chronic overexposure to Pb impairs the reproductive systems of both men and women. Overexposure to lead may result in decreased sex drive, impotence and sterility in men. Lead can alter the structure of sperm cells raising the risk of birth defects. There is evidence of miscarriage and stillbirth in women whose husbands were exposed to lead or who were exposed to lead themselves. Lead exposure also may result in decreased fertility, and abnormal menstrual cycles in women. The course of pregnancy may be adversely affected by exposure to lead since lead crosses the placental barrier and poses risks to developing fetuses.

d. Children born of parents either one of whom were exposed to excess Pb levels are more likely to have birth defects, mental retardation, behavioral disorders or die during the first year of childhood.

e. Damage to the central nervous system in general and the brain (encephalopathy) in particular is one of the most severe forms of Pb poisoning. The most severe, often fatal, form of encephalopathy may be preceded by vomiting, a

feeling of dullness progressing to drowsiness and stupor, poor memory, restlessness, irritability, tremor, and convulsions. There is a tendency for muscular weakness to develop that may progress to paralysis often observed as a characteristic "wrist drop" or "foot drop" and is a manifestation of a disease to the nervous system called peripheral neuropathy.

f. Children are at risk with elevated blood Pb levels, over 10 μg/dL – there has to be a source somewhere in their environment (old paint, water, soil).

g. The length of exposure time is an important risk factor. The longer the exposure, the greater the risk that large quantities of lead are being gradually stored in organs and tissues (body burden). The greater the overall body burden, the greater the chances of substantial permanent damage.

4. DMSA is a good chelator of blood-lead, and routine use can deplete bone-stored lead over time. EDTA inefficient though; takes time – binds Ca^{2+}. Currently DMSA is best as fewer side effects, then BAL, and d-penicillamine.

Summary - Lead

1. Lead everywhere – mobilized by Man - even though not now in gasoline or paints – smelting spreads Pb – solders in water pipe connections – electrical connections – batteries – X-ray aprons. In the home: ammunition – hence bird kill – in plastics (blinds) – cosmetics - paint in the house (if older than 40 years), coloured paints on toys; bright glazes on pottery; heavy, crystal or leaded-glass decanters[9]. Water pipes in 40+ year old houses do have high Pb. Flush water fountains due to solder. Major intake: GI tract & lungs.
2. No known biological role – always Pb^{2+} - binds readily to biological sulfur – replaces Zn^{2+} & Ca^{2+} - readily absorbed and mobilized in the body – organoPb more toxic (Et_4Pb) – dealkylation by P_{450}. Pb: bioaccumulates, is a carcinogen, causes birth defects, and reduces IQ. Pb laid down in bones, teeth and hair. RBC short term exposure indicator.
3. Most Pb intake from food and water – but for children – paint flakes, dust → 'pica' → Pb overload; inner cities paint & dust at a maximum.

4. Major neurological effects in children even below threshold of 10 µg/dL – even as low as 2-5 suspected as reducing IQ levels in children & behavioural problems[10]. Infants especially at risk → a wide range of problems, including anemia, kidney dysfunction, esp. neurological effects. Pregnant women → increased stillbirths. Adults → anemia, kidney dysfunction, peripheral neuropathy[11]. In large amounts -coma → ☠.
5. The average blood lead level of children in the US ages 6-16 years is now 1.9 µg/dL (c. 2001). Mainly due to bans on paints and gasoline. But, many recent events where Pb has been used in paints on toys (2007). Adult symptoms > ca. 40 µg/dL.
6. Pb inhibits heme synthesis. Leads to a rise in delta-aminolevulinic acid (ALA) in urine and PPIX in blood.

Toxic Metals: Arsenic. Historical events: Massive poisoning of the peoples of Bangladesh & Bengal.

Humans are exposed to arsenic (As) from air, food and water.

1. Inorganic arsenic compounds are mainly used to preserve wood. Organoarsenic compounds are used as pesticides.
2. But, arsenic has been known for thousands of years to be a toxic substance. It is best known for its acute toxicity, for example when arsenic oxide or white arsenic (As_2O_3) is administered as a lethal poison. Chronic exposure to lower concentrations can likewise lead to dramatic situations, but in this case the poisoning develops very gradually. Pure metallic arsenic is not that poisonous, but its white salt is very poisonous. The lethal dose of arsenic oxide for an adult is about 120-200 mg. Arsenic causes toxicity by combining with sulfhydryl groups (SH-groups) present on several enzymes and thereby blocking their action. Pentavalent arsenic can imitate phosphorus and replace it in the backbone of DNA, resulting in conformational changes and strand breakage. Arsenic reductases in many organisms convert pentavalent arsenic to trivalent arsenic – increasing the toxicity.

3061 Fish and shellfish can accumulate non-toxic arsenic. Particularly, cold water fin fish, crustaceans, and molluscs may contain large amounts of organo arsenic compounds – eg arsenobetaine - that have no known mammalian toxicity. In addition, certain edible marine foods, such as seaweed or kelp, may contain arsenosugars – next page- that are considered to be non toxicity.

3. BUT Inorganic arsenic cmps and synthetic organoarsenoc cmpds ARE very toxic
4. Asenic occurs in three main chemical forms in marine ecosystems: inorganic arsenic predominates in water and sediments; a group of closely related arsenicals known as arsenosugars occurs in marine algae; and arsenobetaine is the major arsenical in marine

Ironing out an arsenic problem

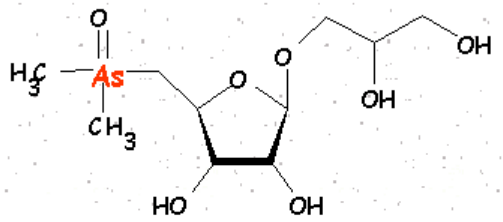
Arsenic in drinking water is a major problem in areas such as India and Bangladesh, and has a serious impact on the health of people in the region (*see Chem. Br.*, January 2003, p 10). But scientists at Oklahoma State University, US, appear to have found a tiny answer to this huge public health issue (*J. Mater. Chem.*, 2003, **13**, 983).

Allen Apblett and his coworkers used a polymer that is known to adsorb metal ions from aqueous solutions (Dowex 650C) and loaded it with Fe^{3+} ions to create spherical particles. These particles were then heated to 550 °C to generate porous spheres of haematite (Fe_2O_3) with an enormous surface area – approximately equivalent to half the size of a squash court. The iron oxide particles have an average diameter of 12 nm and their extremely small size gives them different properties to normal iron oxide particles. One of these properties is their ability to adsorb arsenic from water.

The spherical haematite powder can reduce the levels of arsenic-contaminated water from 3000 to 100 ppb in just one hour. The researchers say that their haematite powder is especially useful for 'at the tap' applications because it does not clump together when wet like loose, fine powders. However, 100 ppb is higher than the World Health Organisation's limits, so the team is investigating metal alternatives to iron in order to achieve lower arsenic concentrations. □

Smiles all round for arsenic-free water ▶

animals. **Inorganic arsenic is known to be toxic, whereas arsenobetaine (see 2 pages later) has been shown to be innocuous - that is, yes, completely harmless to mammals!** Ox. state of As is? Certain marine organisms, particularly bivalves such as clams,



Arsenosugar B

3-[5'-deoxy-5'-(dimethylarsinoyl)-β-ribofuranosyloxy] -2-hydroxypropylene glycol

Arsenic threat lurks in playground soil

BY MARTIN MITTELSTAEDT
ENVIRONMENT REPORTER

Many playgrounds across Canada are severely contaminated with arsenic that is leaching from wooden equipment treated with preservatives to resist rot, a major environmental group says.

Environmental Defence Canada tested sand in nearly 60 playgrounds in seven major Canadian cities and found more than half had arsenic concentrations exceeding federal guidelines for the protection of human health.

The highest contamination was in Toronto, where one playground had arsenic levels 12 times federal guidelines, and more than two-thirds of the other playgrounds tested had sand with elevated readings, according to a study the group is releasing today.

Arsenic contamination appears to be a national problem: The group found arsenic exceeding safety standards in every city where it conducted tests.

Soil samples were taken from playgrounds in Montreal, Halifax, Edmonton, Vancouver, Winnipeg and Ottawa. The second-most-contaminated site, with a reading more than eight times the federal safety level, was in Montreal. The group's work is some of the most comprehensive so far on arsenic in playgrounds.

"Why are we using arsenic-laced wood for playground structures?" asked Burkhard Mausberg, executive director of Environmental Defence Canada, which is based in Toronto. "There are obvious alternatives."

The report cautioned that no medical evidence links contact with contaminated sand to adverse health effects. Evaluating this risk would require testing blood and urine of the children who use the playgrounds, it said. Such tests have not been done.

"But these playgrounds are clearly a potential source of arsenic exposure, and uncertainty about the effects of that exposure should not prevent us from protecting our children from the risk," it said.

The report is recommending that municipalities paint treated wood with a sealant to prevent the arsenic from leaking out, and that they remove and replace contaminated soil. Over the longer term, it is calling for cities to replace all playground equipment built of arsenic-treated wood with safer materials.

Arsenic can cause cancer; chronic low-level oral exposure can cause loss of reflexes, liver damage, anemia and heart damage. Wood treated with chromated copper-arsenate can be immediately recognized by its greenish hue. The arsenic repels insects; the copper kills fungi.

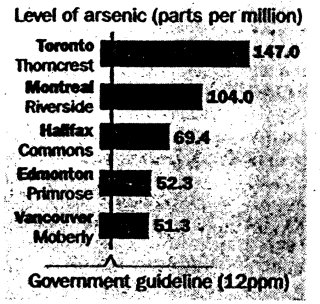
Because treated wood lasts longer and requires fewer repairs, chromated copper arsenate has become the most common wood preservative in North America.

Federal guidelines call for less than 12 parts per million of arsenic in soils used for agriculture or parkland, or around residences. The highest playground reading the group found was 147 ppm. Average urban and agricultural soil concentrations range from 4 ppm to 6 ppm. The sand the group tested was dug up within half a metre of wood posts supporting playground equipment.

Toxic playgrounds

Sixty per cent of the 58 playgrounds tested across Canada by a major environmental group had arsenic levels in sand above the federal guideline.

Canada's five playgrounds with the most toxic sand:

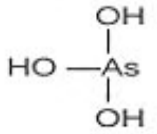


SOURCE: ENVIRONMENTAL DEFENCE CANADA

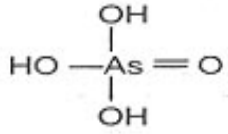
THE GLOBE AND MAIL

may contain over one hundred µg of dimethylarsonic acid in a typical serving, and may thus elevate urine As values even when the more restrictive speciation methods of analysis are used.

Toxic, naturally occurring arsenic species

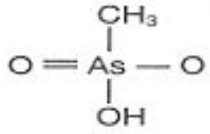


Arsenic III

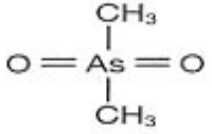


Arsenic V

Metabolic byproducts of arsenic V

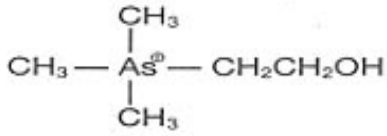


Monomethyl arsenic

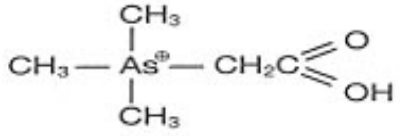


Dimethyl arsine

Nontoxic species of arsenic in food supply



Arsenocholine



Arsenobetaine

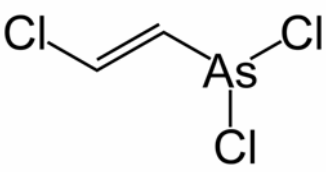
5. Arsenic exposure

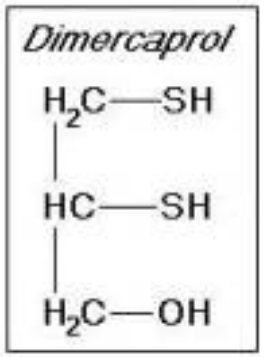
- Eating food, drinking water, or breathing air containing arsenic.
- Breathing sawdust or burning smoke from wood treated with arsenic. (Cutting arsenic-treated wood requires dust masks, gloves, and protective clothing to decrease exposure to sawdust.)
- Living in areas with unusually high natural levels of arsenic in rock.
- In air from combustion of fossil fuels
- Pesticides and Herbicides – handling or making
- Cigarettes - contain very small amounts of As – not of concern compared with the Pb and Cd and the other carcinogens.
- Most non-occupational sources are from water, food, and use of Pressure Treated Wood.

6. Danger in the playground and on the deck

- A 4 m section of pressure-treated lumber contains about an ounce of arsenic, or enough to kill 250 people (calculated from application of 0.4 lb/cu ft of wood). Applied as: Chromated Copper Arsenate (CCA).
- In less than two weeks, an average five-year-old playing on an arsenic-treated play set would exceed the lifetime cancer risk considered acceptable under US federal pesticide law. Some figures FYI:
- Total arsenic in PTW has been measured to be 0.2% i.e. 2,000 ppm or 2,000 mg kg-1 or 2 g kg-1
- To get a lethal dose: eat 3.8 g of wood – **main source of As from PTW is ingestion by licking hands.**
- If density is 0.5 g cm^{-3}. This is a 2-cm cube.[12]
- http://www.hc-sc.gc.ca/cps-spc/pest/pestprod/cca-acc_e.html

7. **Lewisite,** dichloro(2-chlorovinyl)arsine, which is an arsenic derivative, was used in World War I as a chemical weapon – see earlier unit. It acted by forming blisters on exposed skin and damaging the lungs if the vapour was inhaled. Lewisite is administered as a gas. Its common name refers to the American chemist, Lewis, who developed it. The antidote for Lewisite is British Anti-Lewisite (BAL), which is injected in peanut oil (IM). See p 26 of the INORG unit.





8. **Drinking As-rich water** – for the Canadian perspective check out this web site[13]. **– see below**

9. **Health effects of arsenic**

a. Elevated inorganic As in drinking water is the major cause of chronic As toxicity.

b. Chronic accumulation of arsenic

i. Causes nausea and vomiting, decreased production of red and white blood cells, abnormal heart rhythm, damage to blood vessels, and a sensation of "pins and needles" in hands and feet; and anaemia, peripheral neuropathy, liver enlargement, chronic lung disease, and peripheral vascular disease.

ii. Causes hyperpigmentation, depigmentation, keratosis, and peripheral vascular diseases. Resulting in a darkening of the skin and the appearance of small "corns" or "warts" on the palms, soles, and torso these are hyperkeratotic skin lesions.

iii. **Skin manifestations are the most diagnostic**

c. As measurements from urine may not be a valid reflection of As ingestion from drinking water if there has been any consumption of seafood (including seaweed products) within the past three days

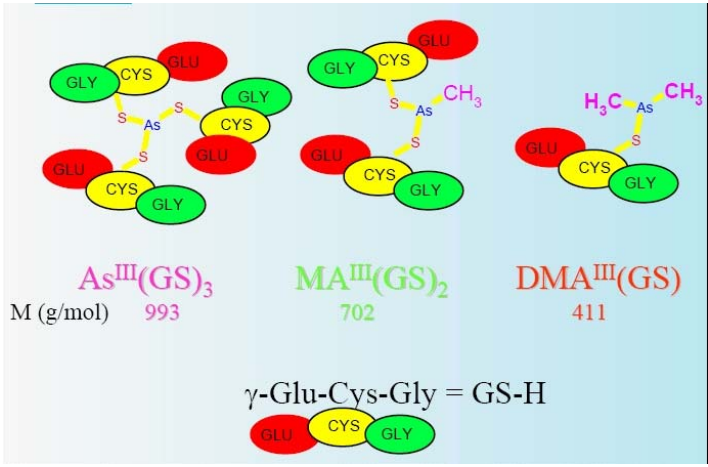
d. Acute poisoning

i. Inhalation of arsenic dusts may cause acute pulmonary oedema – fluid in the lungs.

ii. Inorganic arsenic is a strong carcinogen. Excessive and prolonged exposure to As is associated with an increased risk of skin, bladder, kidney, liver, lung and prostate cancers.

iii. Ingesting high levels of inorganic arsenic can result in death.

e. As(III) binds to 3 thiols – glutathione is a common metal transporter in cells As accumulates in soft tissue organs but clears rapidly <12 h.



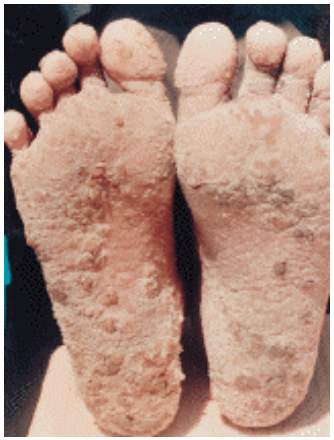
10. The Groundwater in India and Bangladesh is contaminated with As.

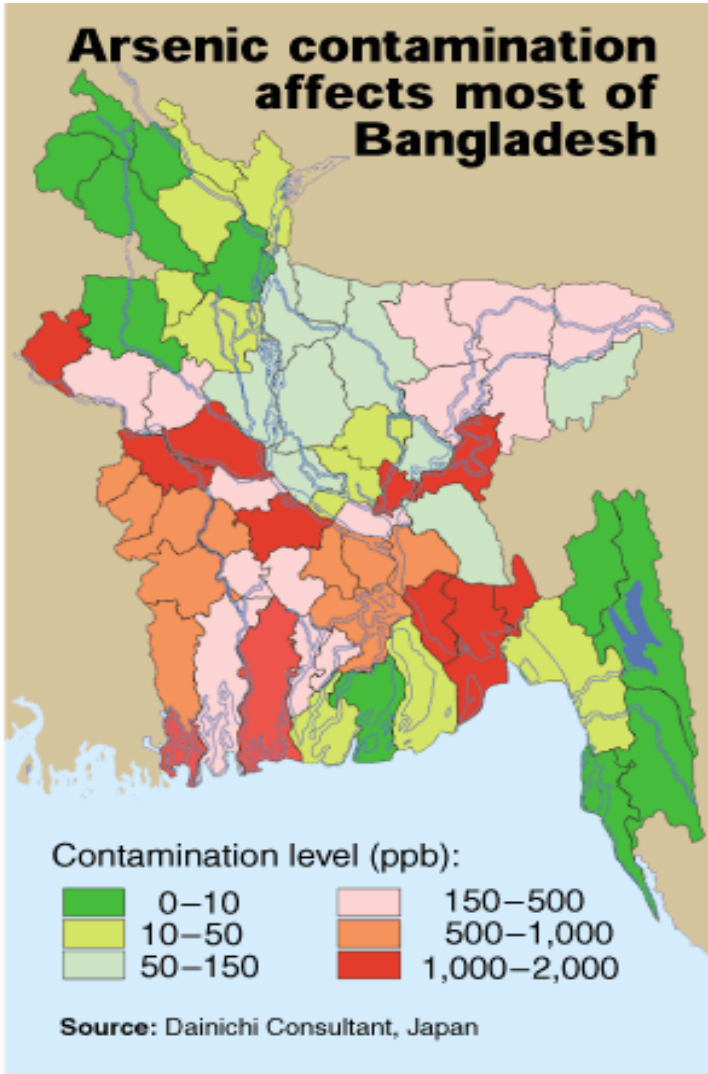
But so also is the groundwater in many other countries, including large regions of the USA – see map below.

A few notes: Major rivers deposit sediments into Bangladesh
Population of ~ 120 million (20.1% urban, 79.9% rural)

97% of the population use tube-well water during the 1970's, tube-wells were dug all over the country. A solution to contaminated surface water that was causing cholera and typhoid. Tube-wells became the main source for drinking/cooking water. Over 4 million wells were dug. In 1992, the British Geological Survey (BGS) analyzed about 150 wells to test the purity of the water.

Did not test for arsenic, but As was there…





11. The background[14]

i. In 1997, scientists from India re-tested the wells for arsenic and found the water to be contaminated

ii. The government had the safe wells painted green and the contaminated wells painted red until a solution was found. Many wells, when retested years later, were found to be marked the wrong color

b. Populations over 100 million – 30-50 million are drinking water from wells with >50 ppb As → illness and death. USA max is 10 ppb – most of Canada max is 10 ppb.

c. In one survey, out of 210 villages:

d. 83.% of hair samples were above the toxicity limit ; 94% of nail samples were above the toxicity limit. 62% of population at risk.

e. Number of Known Patients: ~ 7,000 – at risk: 50m!

f. Number of Tube-wells: ~ 4 million- affected: ~ 1.12 million

12. Source of As in tube-well water:

a. Naturally eroded from the Himalayas by the Ganges River over 20,000 years ago

b. Sediments migrate from the 4 main rivers in Bangladesh

c. Sediment deposition during the Quaternary Period, also known as the Younger Deltaic Deposition (25,000 to 80,000 years ago)

d. Geological processes: weathering, erosion, sedimentation

e. Agriculture use, irrigation, and fertilizers

f. Arsenopyrite and ferrous hydroxide are the source of the As(III).

Quoting from: United Nations Synthesis Report on Arsenic in Drinking Water
Chapter 4 : Diagnosis and treatment of chronic arsenic poisoning
By Dr. D.N. Guha Mazumder, Institute of Post Graduate Medical Education and Research, Calcutta, India

Chronic arsenic toxicity in man produces a range of clinical manifestations. However, skin manifestations are the most diagnostic and socially stigmatizing.

These are characterized by pigmentation of the body and limbs and keratosis of the palms and soles. Rain-drop like spotty pigmentation or depigmentation or diffuse melanosis affecting the whole body are the features of pigmentation. Diffuse thickening of palms and soles with or without nodular elevations **are diagnostic of keratosis.**

These features are manifested variably in different exposed populations, and may also be caused by As unrelated conditions **Hence evidence of chronic As exposure and detection of high levels of As in urine and/or in hair and nails in association with those symptoms need to be considered for the diagnosis of chronic As toxicity**.

Many of the clinical manifestations of chronic As toxicity are irreversible. Epidemiological studies have established As as an important agent which produces cancer of the skin, bladder and lung.

No specific drug for altering the natural history of the disease has yet been available. Chronic exposure will lead to death.

How to tell if a person is poisoned by arsenic? The urine test is the most reliable test for arsenic exposure within the last few days. Tests on hair and fingernails can measure exposure to high levels or arsenic over the past 6-12 months.

Keratosis of palms and soles is diagnostic for long term exposure.

Is there any hope? Very recently as the result of Canadian research work – there has been a link proposed between low Se levels and As – As binds all free Se in humans. Se deficiency results in similar skin manifestations[15]

What about North America? USA … Yes, see the map at the end of the unit.

Toxicity of Metals– As: Release into drinking water

16. What causes elevated As in ground waters?

a. Acidic metal-bearing water draining from remote, abandoned mines has been identified by the EPA as a significant environmental/health hazard in the Western United States.

b. Many of these waters contain dissolved arsenic in the trivalent and pentavalent state.

c. Similar reports and concerns from Vietnam – read for interest:[16] "Groundwater Arsenic Contamination: Can It Happen In The Mekong Delta ? A Vietnamese Perspective by *Mai Thanh Truyet, Ph. D. & Pham Phan Long, P.E.*

Iron pyrite, FeS_2 Arsenopyrite: AsFeS.

Treatment of chronic Arsenic toxicity.

Chronic arsenicosis leads to irreversible damage in several vital organs and eventually cancer.

Despite the magnitude of this potentially fatal toxicity, there is no effective therapy for this disease; patients once affected may not recover even after remediation of the As contaminated water.

Possibly give Se to 'mop up' the As.

s

The AsFeS is oxidized by the Fe^{3+} in the presence of acid and released as AsO_4^{3-}, this is soluble but attaches to $Fe(OH)_2$ – when redissolved the As is subsequently reduced to As^{3+}

$$2\ FeS_2 + 7\ O_2 + 2\ H_2O \longrightarrow 2\ Fe^{2+} + 4\ SO_4^{2-} + 4\ H^+$$

$$4\ Fe^{2+} + O_2 + 4\ H^+ \longrightarrow 4\ Fe^{3+} + 2\ H_2O$$

$$4\ Fe^{3+} + 12\ H_2O \longrightarrow 4\ Fe(OH)_3 + 12\ H^+$$

$$FeS_2 + 14\ Fe^{3+} + 8\ H_2O \longrightarrow 15\ Fe^{2+} + 2\ SO_4^{2-} + 16\ H^+$$

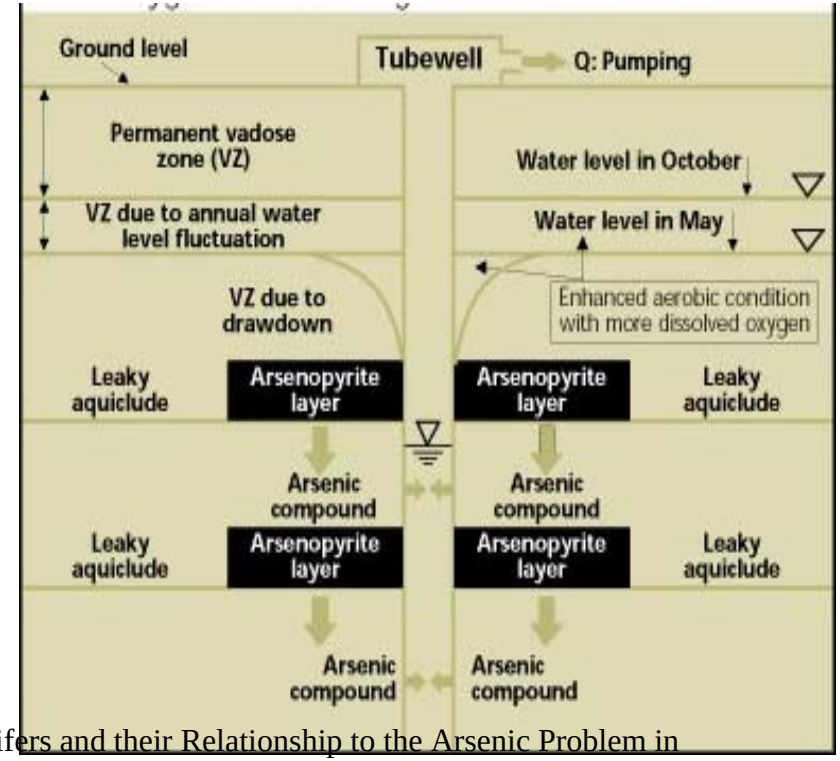
- Arsenic is available in the sediment in non-toxic form
- During discharge – the AsFeS is exposed to air
- During recharge, sediments return to the reduced environment
  - under the water table
- Non-toxic oxides of arsenic are reduced to toxic forms = As^{3+}
- Release into the water as soluble salts – As dissolves in acidic solutions

The explanation for the release of As^{3+} is controversial – it could be related to the use of fertilizers that dissolve the AsFeS more readily. The fact remains that the drinking water is heavily contaminated.

■Arsenopyrite and ferrous hydroxide
- ☐Arsenic rich
- ☐Stable in a reducing environment (under the water table)
- ☐Concentrated in organic deposits
- ☐When oxidized, arsenic is released and adsorbed onto iron hydroxide

■Cause of oxidation
- ☐Lowering of the water table below the organic deposits
- ☐Result of dry seasons, pumping of wells, and dams built in the 1970's

■Release of toxic arsenic
- ☐During recharge, the arsenic adsorbed onto iron hydroxide returns to the reduced environment under the water table
- ☐The arsenic is released and reduced to As(III)



* www.sos-arsenic.net/english/natural_origin/india.html
* Bridge, Thomas, et al. "The Increased Drawn Down and Recharge in Groundwater Aquifers and their Relationship to the Arsenic Problem in Bangladesh"

Summary of Arsenic toxicity and humans

Exposure Forms: As^{3+} and As^{5+} The 3+ is more toxic	Breathing – drinking – handling=surface contact	Breathing dust – pressure treated wood;- smoking cigarettes = small amount;	Drinking water – rocks high in As – ingestion – pesticides – herbicides Handling: walking on outside –'green' older-pressure treated wood structures
Occupational exposure	War-time – gas – Lewisite Pesticides Herbicides Handling pressure-treated wood	BAL invented for antidote	
Health effects	Many symptoms	Worst: skin pigmentation and warts, then …	Cancer - death
Cure?	No		
Major world-wide poisonings	Bangladesh and West Bengal Tube-well water	Cause: Water with As from arsenopyrites shale – As+Fe+ rocks dissolved by fertilizers possibly – certainly due to massive lowering of the water table and introduction of oxygen	Cure? Cannot reverse health effects – Response: Clean out the As with filters – eat Se in lentils
Add from your revision and poster handout			

Toxic Metals: Cadmium

Key human toxicity history: Itai Itai disease in Japan

- Very common – same triad as zinc so often replaces Zn in enzymes – $4d^{10}$ forms 4-coordination complexes with sulfur – soft – binds also to water and HIS.
- Soft – in many products – also in soils – and smoke
- Induces metallothionein in all tissues – for example in the lungs of smokers – smoking a major source of Cd.
- Has a 20-30 yr ½ in the kidneys.
- Exposure results in bone osteomalacia and renal failure.
- Itai Itai disease.
- No cure

1. Inorganic chemistry

a. Cd is a soft, silvery-white metallic element that can easily be shaped. When heated, cadmium burns in air forming CdO.

b. Only exists as the 2+ oxidation state. Like Pb, the alkyl compounds are not naturally formed.

c. Always present during Zn smelting. Present in the ore.

2. Very many industrial and consumer product uses

a. NiCd batteries, metal plating, pigments (esp. bright ones), fireworks, metal coatings, glass, porcelains and plastics (pigments and plasticizers), soft alloys, solders and brazing rods – see a longer list in the "EXTRA_MATERIALS" file.

b. CdS and CdSe photocells and photovoltaic devices.

3. Cadmium Emissions occur from natural sources and man-made or anthropogenic sources to the three major compartments of the environment - air, water and soil; there may be considerable transfer between the three compartments after initial deposition.

a. Emissions to air are considered more mobile than those to water, which in turn are considered more mobile than those to soils.

i. Volcanic activity is a major natural source of cadmium release to the atmosphere, and estimates on the amount have been placed as high as 820 mt per year.

ii. Forest fires have also been reported as a natural source of cadmium air emissions, with estimates from 1 to 70 mt emitted each year.

iii. Mining (Cd-Zn-Cu co-occur); **smelting**

iv. Burning coal and household waste, and metal mining and refining processes.

b. To soils and waters: Spills and leaks from hazardous waste sites can also cause cadmium to enter soil or water. Cadmium attached to dust particles may travel a long way before coming down to earth as dust or in rain or snow.

i. The use of cadmium-containing fertilizers and sewage sludge is considered the primary reason for the increase in the cadmium content of soils over the last 20 to 30 years in Europe.

4. Human exposure:

Smelting in China – major problems:

» **12/22/2005 13:13 CHIN**A

http://www.asianews.it/index.php?art=4940&l=en
Cadmium spill in the Beijiang River leaves millions of people without water

Yingde (AsiaNews/SCMP) – A state of emergency has been declared in the city of Yingde, in Guangdong. Residents are without drinking water because the Beijiang River has ten times the allowed concentration of cadmium after a state-owned smelting plant released cadmium waste into the river in Shaoguan Country six days ago. …

Bulletin of Environmental Contamination and Toxicology (2007) Metals Contamination in Soils and Vegetables in Metal Smelter Contaminated Sites in Huangshi, China
http://www.springerlink.com/content/7190444j341540g3/fulltext.html

This study investigated the source and magnitude of metal contamination in soils and vegetables collected in the vicinity of the Daye smelter, China. Results showed that soils and vegetables were heavily contaminated by cadmium (Cd) and lead (Pb). The average levels of Cd and Pb in vegetables were 0.21 and 3.28 mg/kg fresh weight, respectively…. The analytical results indicated that the total concentrations of metals were elevated in surface layers for all samples relative to the underlying subsoils. Furthermore, Cd contents in all soil samples were 8 to 20 times higher than the limit level; Cu and Pb concentrations slightly exceeded the limit values in some samples from the nearer sample sites to the smelter, while the other samples did not exceed the threshold value;

Smelter waste poisons farmers Shanghai Daily

By Yang Lifei | 2008-10-16 | NEWSPAPER EDITION

THE legal representatives of four smelting plants in Hubei Province have been detained after more than 1,000 farmers were diagnosed with skin ailments due to pollution from the factories.
More than 1,000 farmers in Jianli County have suffered severe rashes and other skin ailments since March, when local industrialists and their counterparts from nearby Hunan Province opened plants to smelt the highly profitable alloy vanadium, Changjiang Times reported.

There are 10 vanadium smelting plants in Jianli, six of which have been closed again since September. The other four plants had defied the government ban until yesterday, when they were shut down, the report said.
The smelting plants discharged waste containing toxic cadmium and arsenic into waterways which led to the pollution of both water and farms.
The contaminated water also spread to several villages and polluted tens of thousands of hectares of fields.
Lin said the wastewater discharged by one of the plants near the Jiangxintai Village contained vanadium 209 times above the national standard.

a. **Cadmium in Agricultural Soils** is relatively immobile under normal conditions, but could become more mobile under certain conditions such as increased soil acidity

   i. Cadmium levels may be enhanced by the use of phosphate fertilizers, manure or sewage sludge. In general, soils which have been contaminated with cadmium from industrial operations cannot be used for agricultural purposes.

   ii. Fertilizers often contain cadmium, which when transferred to soils used for growing vegetables they incorporate the Cd into S-containing peptides.

   iii. Because cadmium is also a naturally occurring component of all soils, all food stuffs will contain some cadmium and, therefore, all humans are exposed to natural levels of cadmium. Leafy vegetables and potatos accumulate higher levels of cadmium than do fruits and cereals – but rice can be particularly high in Cd.

   iv. Meat and fish normally contain lower cadmium contents, from 5 to 40 ppb – but …

   v. Animal offal such as kidneys and liver can exhibit extraordinarily high cadmium values, up to 1,000 ppb, as these are the organs in animals where cadmium concentrates.

b. **Cadmium in Water** – leads to chronic exposure – slow degeneration of the kidneys and bone tissues – also issues with food grown in the contaminated waters.

i. In the past, there have been examples of marked cadmium contamination in areas where food has been grown. This was particularly so for rice crops in Japan in the 1950s and 1960s where cadmium concentrations from 200 to 2,000 ppb were found.

ii. Consumption of a diet rich in shellfish can double the intake of dietary cadmium without producing significant impacts upon blood cadmium.

Ingestion of cadmium in food is the major source of cadmium for non-smokers.

5. **Cadmium in Tobacco Smoke** Tobacco leaves naturally accumulate and concentrate relatively high levels of cadmium, and, therefore, smoking tobacco is an important source of air cadmium exposure for smokers. Smokers generally exhibit significantly higher cadmium body burdens than non-smokers.

Food and cigarette smoke are the largest potential sources of cadmium exposure for members of the general population.

6. **Occupational exposure to cadmium is mainly by inhalation.**

a. Cadmium emits a characteristic brown fume (CdO) upon heating, which is relatively non-irritating and thus does not alarm the exposed individual.

b. Breathing air with very high levels of cadmium severely damages the lungs and can cause death.

c. Breathing lower levels for years leads to a build-up of cadmium in the kidneys that can cause kidney disease. Other effects that may occur after breathing cadmium for a long time are lung damage and fragile bones – due to depletion of Ca^{2+}.

7. **Biology**

a. **Cadmium has no known essential role.**

b. Absorption from the GI tract is followed by binding to GSH or albumin- transport to liver then to the kidneys for 20 years or so before being excreted.

c. Cadmium vapour, ions, and solutions of its compounds are highly toxic, with cumulative effects similar to those of mercury.

8. **Liver is the first binding site – to metallothionein – then the kidneys are the initial site of damage and the critical target organ for the general population as well as for occupationally exposed populations.**

a. General damaging effects of Cd are replacement of Zn in enzymes, eg carbonic anhydrase, Zn-Cu-superoxide dismutase (SOD).

b. **Cd does not cross the BBB so the CNS exhibits little damage following Cd acute poisoning.** However, the constant flux of Cu-MT in the blood in chronic poisoning eventually damages the CNS.

9. ACUTE TOXICITY

a. Respiratory damage (from inhalation), edema, fibrosis, liver, kidney failure

b. **Several deaths from acute exposure have occurred among welders who have unsuspectingly welded on cadmium-containing alloys and among silver solders.** Cadmium is also found in industrial paints and may represent a hazard when applied by spray.

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10. CHRONIC TOXICITY

a. For chronic cadmium exposure, effects occur mainly on the kidneys, lungs, and bones. The most serious consequence of chronic cadmium poisoning is cancer (lung and prostate).

b. Cd accumulates in the human body increasing with age. – see "EXTRA-MATERIALS" file for more details

c. The first observed chronic effect is generally kidney damage, manifested by excretion of excessive low molecular weight protein in the urine. Cadmium also causes pulmonary emphysema and bone disease.

d. The latter has been observed in Japan ("itai-itai" disease) where residents were exposed to cadmium in rice crops irrigated with cadmium-contaminated water. Cadmium may also cause anemia, teeth discoloration (Cd forms CdS) and loss of smell (anosmia).

e. Following exposure, within a very short period of time (<20min) >99% Cd is bound to albumin in blood

i. Circulation to the liver (the major initial site of accumulation) – see scheme on next page

ii. Albumin released in the liver cell

iii. Binds to metallothioneins - after 3 days Cd^{2+} is transported to the kidneys

iv. Necrosis takes place very slowly. The CdMT breaks down kidney cells with a ½ life of 20-30 years for release of the Cd(II). The effect of Cd(II) exposure is cumulative.

v. Bone disease (osteomalcia and osteoporosis) is also slow and irreversible – leading to very fragile bones.

11. Major concern: Current problems are from smoking and occupational exposure.

12. To come? Long term exposure from disposing of Ni-Cd batteries – industrialization of developing countries.

13. Metallothionein has 20 CYS; sequence conserved across many organisms; especially CYS-X-CYS and CYS-X-X-XYS (X another amino acid); mammalian MT binds 7 M^{2+} , eg Hg, Cd and Zn. Also binds Cu^{+}.

a. MT is an inducible protein – synthesis enhanced in the presence of these metals. Naturally binds zinc and copper.

b. Cd-Metallothionein itself is extremely toxic when injected directly into the kidneys.

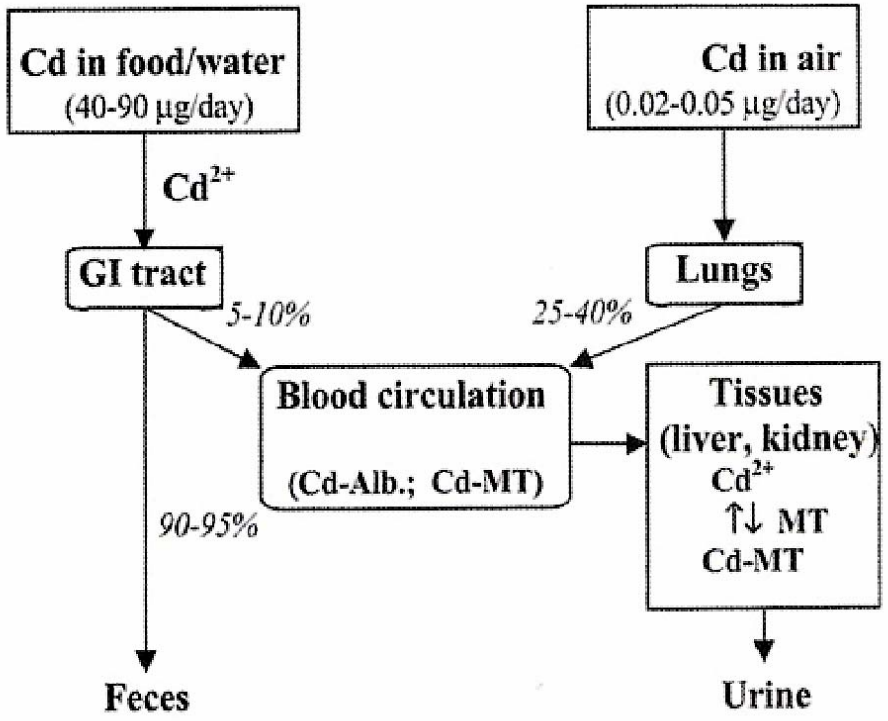
c. We do not know why metallothionein binds Cd^{2+} unless it mistakes Cd^{2+} for Zn^{2+}. Zn Metallothionein is much less

stable, releasing Zn^{2+} very readily - a temporary storage molecule for Zn?

d. With Cd^{2+}, the binding constants are so much greater that the release of Cd^{2+} does not follow the Zn^{2+} route.

14. Summary:

- Cadmium is similar to zinc.
- No known biological function.
- Major intake is from food (esp. rice) and smoking.
- Smoking dramatically increases the body-burden of Cd^{2+}.
- Cadmium toxicity generally only leads to levels of exposure sufficient to produce kidney dysfunction (shown by release of small mass proteins):
  - if the cadmium levels were significantly increased in food grown in highly contaminated agricultural areas.
  - this was the major source of food and
  - the nutritional status is low.
- More extreme exposure leads to bone disease and cancers. Does not cross the BBB.
- A situation did occur in the 1950s and 1960s in Japan where heavy cadmium contamination of rice fields, along with nutritional deficiencies for iron, zinc, calcium, and other minerals, led to renal impairment and significant bone disease (Itai Itai disease) in the exposed populations.



The most serious cases of environmental pollution by cadmium occurred in Japan after World War II. In 1946

a. Dr. Noboru Hagino noted a syndrome ("itai-itai" or "ouch-ouch" disease) that occurred in Toyama Prefecture that began with renal dysfunction and eventually resulted in painful bone changes.

b. The source of the problem was ultimately identified as cadmium in the wastes of the Kamioka mine of the Mitsui Mining and Smelting Company.

c. The cadmium was transported to rice paddies irrigated from the Jintsu River.

d. The daily cadmium intake in the endemic area was approximately 600 ug.

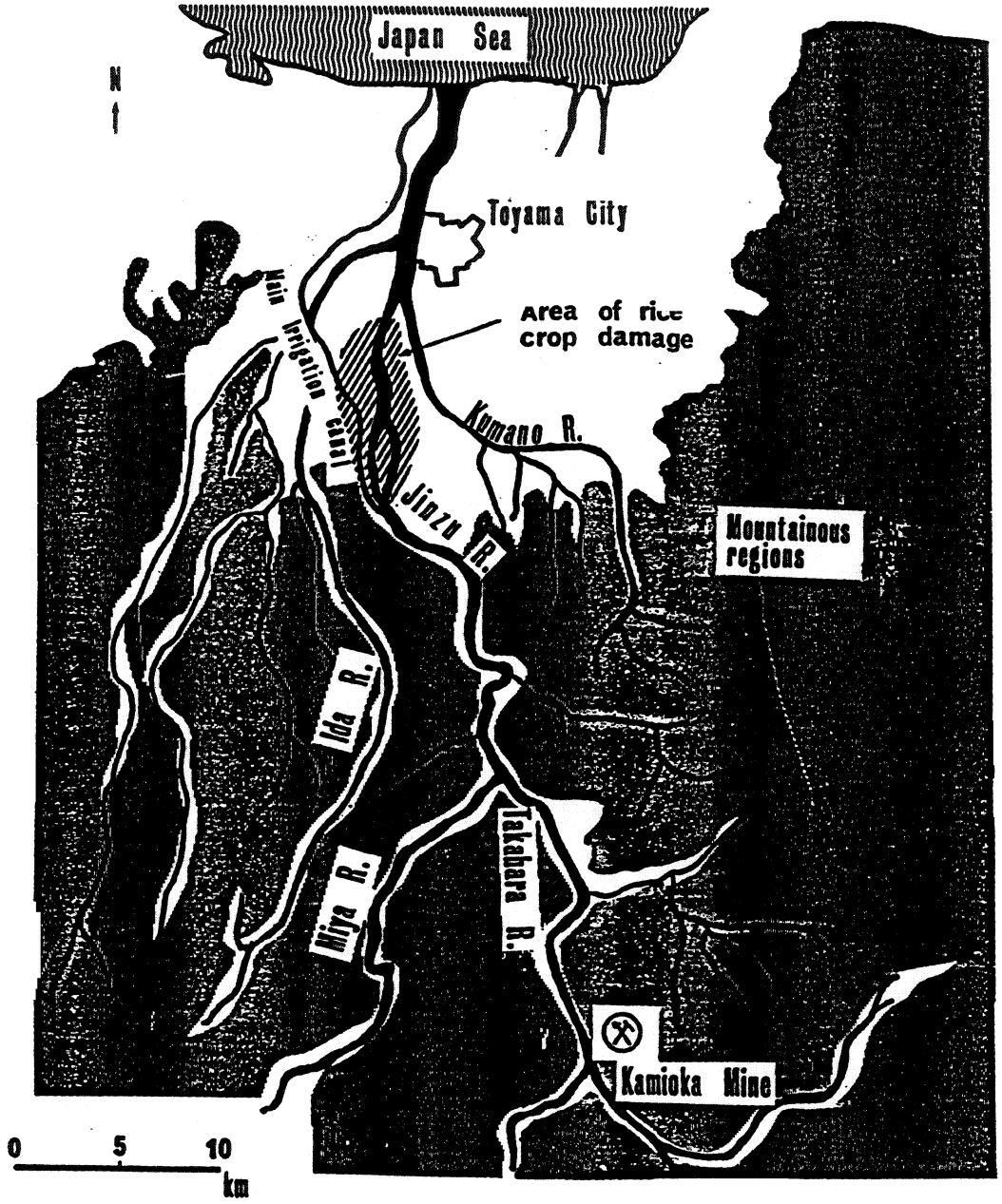


FIG. 1. Localities of the Kamioka Mine and the area of rice crop damaged.

Cd itai-itai

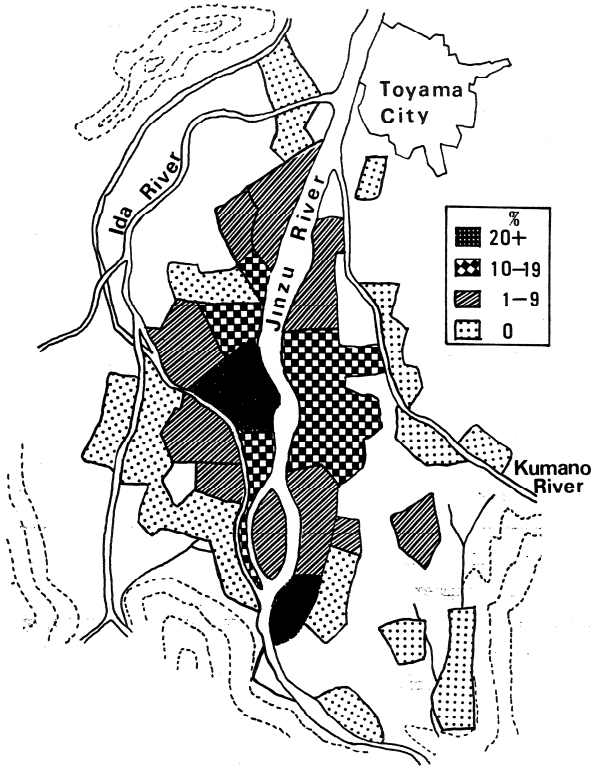


FIG. 12. Distribution of itai-itai patients (percentage of women over 50 years of age) (from Ishizaki and Fukushima [48] or Yamagata and Shigematsu [30]).

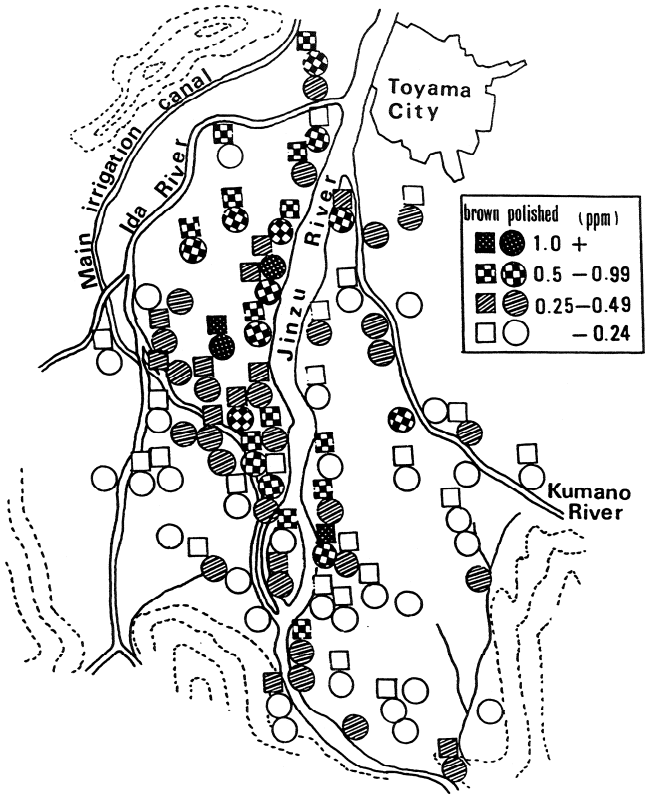


FIG. 13. Distribution of Cd in ordinary (nonglutinous) rice (from Fukushi et al. [49] or Fukushima [50]).

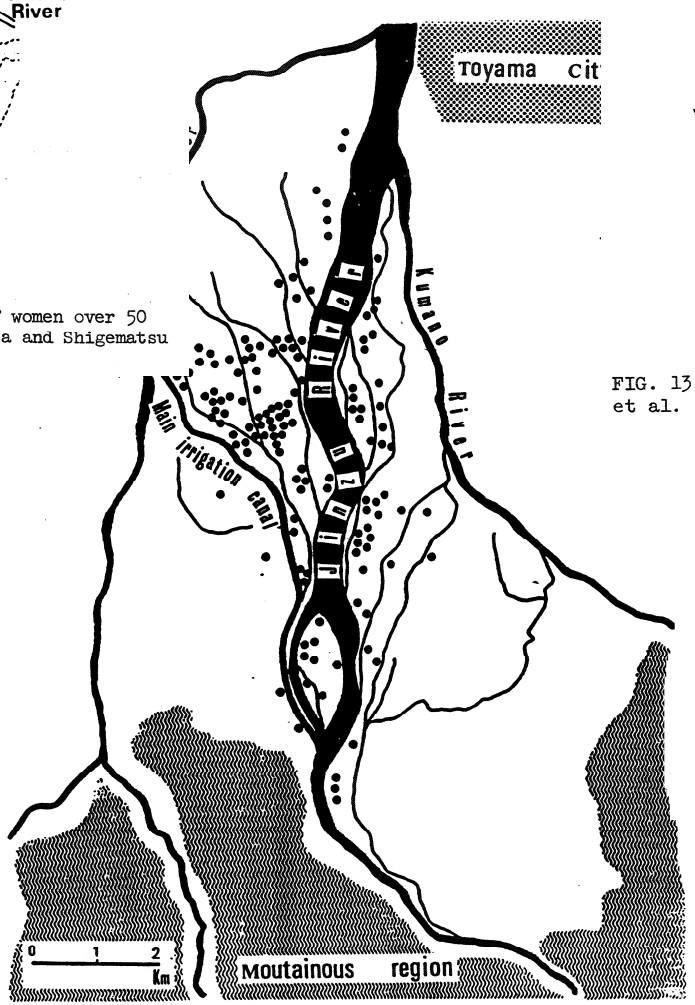


FIG. 4. The locality where the patients were found (dead patients included).

Summary of cadmium toxicity and humans			
Exposure Forms: just Cd^{2+} and fumes CdO	Breathing – drinking – eating offal - handling=surface contact	Breathing dust – smoking cigarettes – major exposure route – plus offal of large animals	Drinking water – from contaminated run-off; food grown on Cd-containing fertilizer – esp rice and leafy vegetables Liver & kdneys very high in Cd
Occupational exposure	Many products involve Cd Smelting – releases large amounts of Cd into water	Breathing fumes (CdO) from welding	
Biochemistry known?	Replaces Zn in many enzymes	Interferes with Ca deposition in bone formation	Binds first in the liver – then the kidneys – 20+ years. Does not cross BBB Binds to metallothionein
Health effects	Many symptoms – medical – kidney failure after 10-20 years leading to death.	Worst: demineralization of bones – osteomalcia - bones become very fragile - break	Cancer - death
Cure?	No	BAL used to reduce body burden – not as effective as needed – not an antidote – Cd remains bound in the liver and bones	Overall Preferred is DMSA - BAL is more efficient but mortality is high due to renal failure; also ethylenediamine-tetraacetic acid (EDTAH4)
Major world-wide poisonings	Itai Itai in Japan	Cause: Water with Cd from a Zn smelter waste that contaminated water used for rice and drinking.	Cure? Cannot reverse health effects – Response: Must remove Cd – actually – high Cd in many sources of rice in Asia
From poster handouts…			

Toxic Metals: Mercury - significant poisonings

Some of the more recent exposures include Minamata Bay in Japan (1960), mercury contaminated fish in Canada, methylmercury-treated grain in Iraq (1960 and 1970), Northern Ontario in the 1970's and, in the U.S. (1996), a beauty cream product from Mexico called "Crèma de Belleza-Manning."

1. Properties of Mercury?

a. Mercury is the only metal that is a liquid at room temperature and also a gas. Known to the Greeks and Romans. Produced from the ore cinnabar (HgS), either by roasting:

b. $HgS(s) + O_2(g) \rightarrow SO_2(g) + Hg$ or by oxidation with lime (CaO):

c. $4HgS(s) + 4CaO(s) \rightarrow 4Hg + 3CaS(s) + CaSO_4(s)$.

d. World production of mercury is about 9,000 tonnes/year and this is mostly used in the chloralkali industry.

e. Inorganic chemistry - Hg

f. Mercury exists as: elemental Hg0 and $[Hg\text{-}Hg]^{2+}$, Hg2+, and alkyl organic compounds, mono and di. The most common organic form is CH3Hg+ which toxic to the CNS - a neurotoxin.

g. Mercury is found in both organic and inorganic forms. The inorganic form can be further divided into elemental mercury and mercuric salts. Organic mercury can be found in long and short alkyl and aryl compounds.

2. Environmental aspects – Hg

a. 15 x 104 tons/year natural mobility

b. Volcanic action- degassing- dissolution of minerals into rivers

c. 18 x 104 tons/year

1. mining fossil fuel combustion - industrial & agricultural uses

d. Tuna fish can store Hg^{2+} but as $MeHg^{+}$ - 0.5 - 1 ppm in most fish - both old (in museums) and recent.

e. This high level is due to the large throughput of water

f. The biggest problem is the Hg^{2+} + B12 → CH_3Hg^{+} taking place in anaerobic sediments. Methylmercury is rapidly absorbed by fish either directly from water passing over the gills or ingested. Since fish eliminate mercury at a very slow rate, concentrations gradually accumulate. For coastal populations the problem is that shell fish concentrate Hg^{2+} very much

g. Clams 10^5 x greater conc than in sea water

3. Biological effects of Mercury

a. **Mercury in any form is toxic.**

b. The difference lies in how it is absorbed, the clinical signs and symptoms, and the response to treatment modalities.

c. Mercury poisoning can result from vapor inhalation, ingestion, injection, or absorption through the skin.

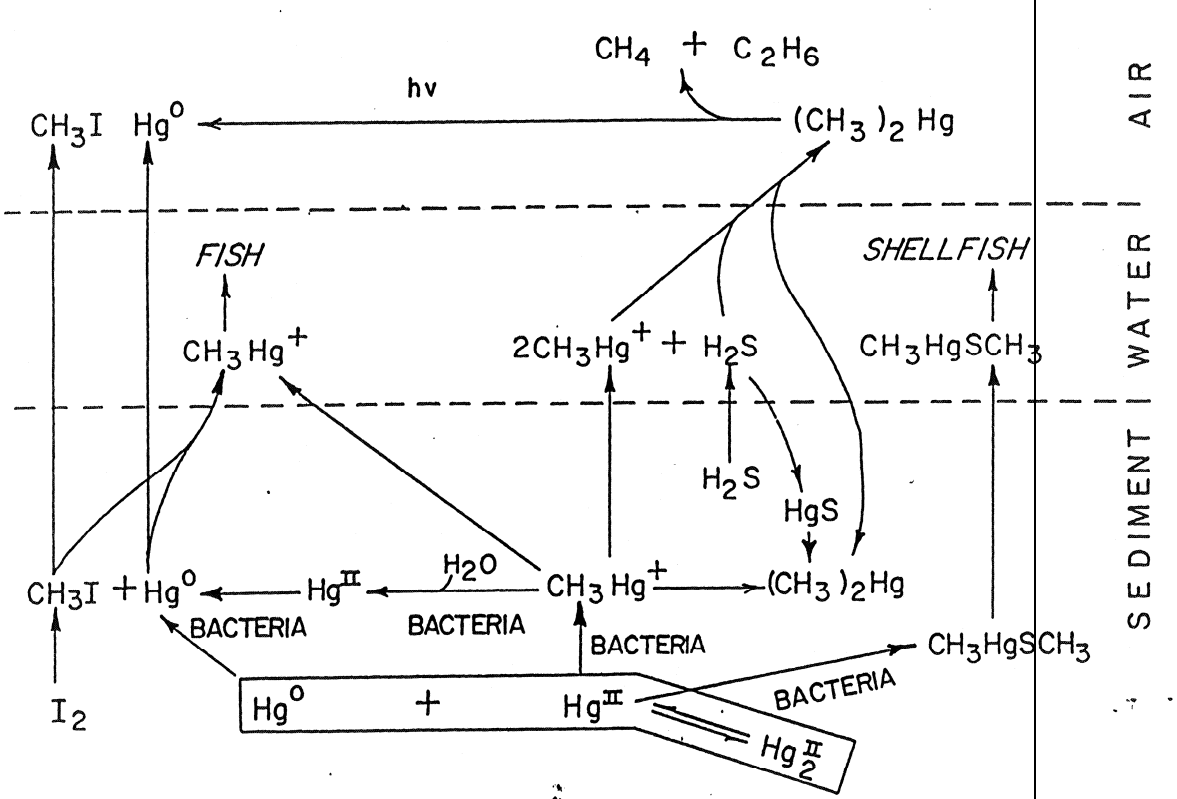


Figure 3. The mercury cycle.

d. Hg^0 vaporizes at room temperature and is readily absorbed through inhalation. It is lipid soluble, which allows for easy passage through the alveoli into the bloodstream and red blood cells. Once inhaled, it is mostly converted to the Hg^{2+} form by catalase in the erythrocytes. This Hg^{2+} has poor lipid solubility, limited permeability to the blood brain barrier, and is excreted in the feces.

e. Unfortunately, a small fraction of Hg^{2+} crosses the BBB from the blood where it reacts with catalase as well but now forming in the brain – binds to S in cysteine.

f. Hg^0 is not absorbed efficiently by the GI tract and, therefore, liquid Hg spilled due to broken thermometers, for example, is only mildly toxic.

4. Exposure to Mercury

i. For centuries, mercury was an essential part of many different medicines, such as diuretics, antibacterial agents, antiseptics, and laxatives. More recently, these drugs have been substituted and drug-induced signs of mercury toxicity are rare. Mercury toxicity in environmental pollution is a major concern because of increased usage of

fossil fuels and agricultural products, both of which contain mercury.

ii. Mercury poisoning usually is misdiagnosed due to the insidious onset, nonspecific signs and symptoms, and lack of knowledge within the medical profession.

iii. Mercury is found in many industries, such as battery, thermometer, and barometer manufacturing. Mercury can be found in fungicides used in the agricultural industry. Before 1990, paints contained mercury as an antimildew agent. In medicine, mercury is used in dental amalgams and various antiseptic agents

iv. **In the chloralkali industry, the major process is electrolysis of aqueous NaCl solution to produce NaOH and chlorine.** Mercury cells were in wide use because they are more economic; they are being replaced now by less polluting techniques. The NaOH, the spent NaCl solutions and other plant effluents from this process carry traces of mercury which are discharged into lakes and rivers. In 1970, chloralklai plants lost about 600 tonnes/year. This was the source of much of the Hg in the north of Canada.

5. But in Canada?[17]

a. In Canada, the largest anthropogenic source of mercury until the 1980s was the chloralkali industry. Although mercury is still employed in this industry to manufacture chlorine and sodium hydroxide, emissions have now declined due to antipollution measures, conversion to non-mercury processes and plant closures. In the 1970s, Canada reported 15 chlor-alkali plants in operation; however, only one Canadian facility remains in operation in New Brunswick.

Between 1990 and 1995, Canadian anthropogenic mercury emissions dropped from approximately 32 to 11 tonnes primarily as a result of process improvements in the base metal mining industry. In 1995, this industry was the largest source of mercury into the atmosphere, contributing approximately 40% of total emissions.

From 1995 to 2000, Canadian anthropogenic mercury emissions dropped to a total of just over 8 tonnes. Two sectors, electricity generation and metal smelting, were equally the largest sources of mercury into the atmosphere, each accounting for 25% of Canadian emissions.

The pie chart illustrates Canadian atmospheric mercury in 2000.

6. Compact fluorescent lamps are frequently used in place of traditional incandescent lights.

a. Compact fluorescent lamps have all the same characteristics as linear fluorescent tubes, except they have been designed to replace incandescent bulbs, which are common in residential, commercial, industrial, and accent lighting applications. Mercury content: Mercury content is generally between 1 and 25 milligrams.

7. Thermostats

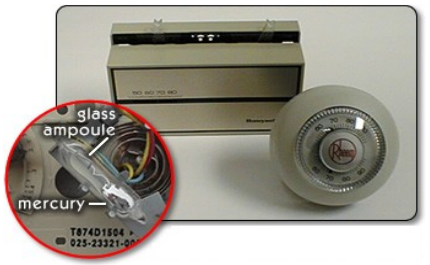
a. Mercury-containing thermostats may be used in heating and cooling systems in residential, medical, commercial and industrial settings.

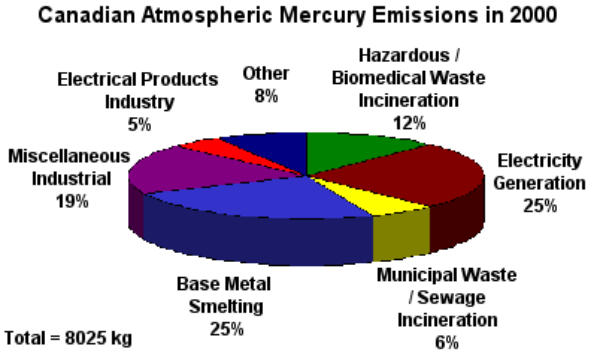
b. Thermostats comprise a tilt switch with a mercury ampoule used to activate or deactivate the heating or cooling device.

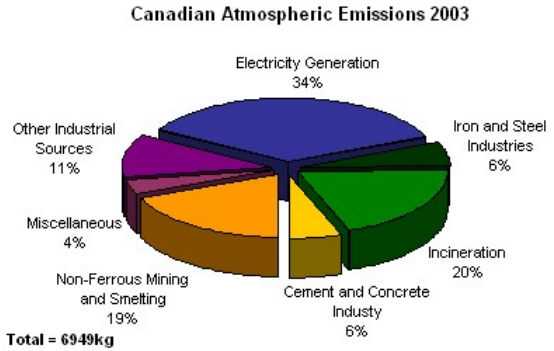
8. Dental Amalgam

a. Dental amalgam is prepared by mixing approximately equal parts of liquid mercury and alloy powder, which typically consists of silver, tin, copper, and zinc. Mercury Content: Silver coloured dental amalgams generally contain about 50% mercury.

Brazil







Guide to Eating Ontario Sport Fish 2005-2006 – **An important aside – with acknowledgement to the guide**

I quote some passages – note key statements.

"The Guide to Eating Ontario Sport Fish gives consumption advice for sport and game fish found at more than 1,700 locations in the province. The advisories continue to be based on health protection guidelines provided by Health Canada. However, advisories are now provided separately for the general population and for the sensitive population of women of child-bearing age and children under 15. This is the result of long-term epidemiological studies on mercury intake which have found developmental effects on young children at levels lower than previously thought. Since there is no evidence of any adverse effects on adults at similarly low levels, Health Canada provides two health protection guidelines, which have been incorporated into the Guide.

All users of the Guide are advised to read the Instructions section prior to proceeding to the consumption tables. This is especially important for families with women of child-bearing age and children under 15.

At inland locations, mercury is the major contaminant. Because mercury is distributed evenly throughout the fillet, in most cases the full side fillet can be consumed.

Ottawa cracks down on mercury in vehicles

BY MARTIN MITTELSTAEDT
ENVIRONMENT REPORTER

Environment Minister Rona Ambrose has told junkyards and auto makers that they're going to have to remove all mercury light switches from millions of old cars before scrap metal from the vehicles can be recycled.

The announcement, made by the federal minister yesterday at a scrapyard in Kitchener, Ont., is the final chapter in a long environmental battle over automotive use of mercury, a feared heavy metal that causes brain and nervous-system damage in children.

European car makers eliminated mercury from the switches, used for activating trunk lights, in the early 1990s, but North American manufacturers did not complete a phase-out until the 2003 model year. It would have cost companies about 12 cents extra per vehicle to switch to mercury-free devices, according to the Clean Air Foundation, a Toronto-based group that has run a voluntary program of mercury switch removal at junkyards.

Consequently, about half of the 18 million vehicles on the roads in Canada contain mercury switches, which aren't an immediate health hazard because the metal is encased. When cars are scrapped and their steel is reused, however, the mercury enters the environment.

The slow pace of Big Three automobile companies in dealing with mercury has long angered environmentalists, who had lobbied the federal government for years to order the metal out of cars, without much success.

"This is one of these totally ridiculous things that should have been done years ago. Mercury switches should have been banned," said Ken Ogilvie, executive director of Toronto-based environmental organization Pollution Probe. "We've been pushing for this for a long, long, time."

The Canadian Vehicle Manufacturers' Association, the trade group for the Big Three, said yesterday the industry will work with recyclers and dismantlers to show them how to remove switches.

Association president Mark Nantais defended mercury use because "it was used legally," and said the industry is taking responsibility by now helping to collect the switches.

He said car companies liked mercury for the cost savings and because it was reliable. "When you're producing millions of cars, everybody looks for pennies per car savings, but the key thing here is that mercury performed well," he said in an interview.

The amount of mercury in a typical switch, less than a gram, is minute, but the liquid heavy metal with the silvery hue is such a potent nerve poison that even this tiny amount would make all the fish in an eight-hectare lake unsafe to eat.

Environment Canada says there may be up to 10 tonnes of mercury in switches in the country's auto fleet, although Mr. Nantais estimated the amount may be as low as three to four tonnes.

High mercury levels threaten young loons

Vulnerable chicks preen excessively, ride less on parents' backs, Acadia study shows

MARTIN MITTELSTAEDT
The Globe and Mail

Young loons in Nova Scotia with elevated mercury levels are exhibiting unusual behaviour that appears to be putting their survival at risk, causing worries that the species could be threatened by pollution from the heavy metal.

Loon chicks with high mercury levels are engaging in excessive preening and don't ride on their parents' backs as often as chicks with lower concentrations of the contaminant, a potent nerve poison, according to research conducted by two biologists from Acadia University in Wolfville, N.S.

The researchers believe the behaviours are a sign that mercury has impaired nerve functioning in the chicks, making them vulnerable to predators.

Young loons on their parents' backs are protected from predators and conserve energy by benefiting from the warmth of their parents. Most of the high-mercury-level chicks died during the study period and were presumed to have been eaten by snapping turtles or gulls.

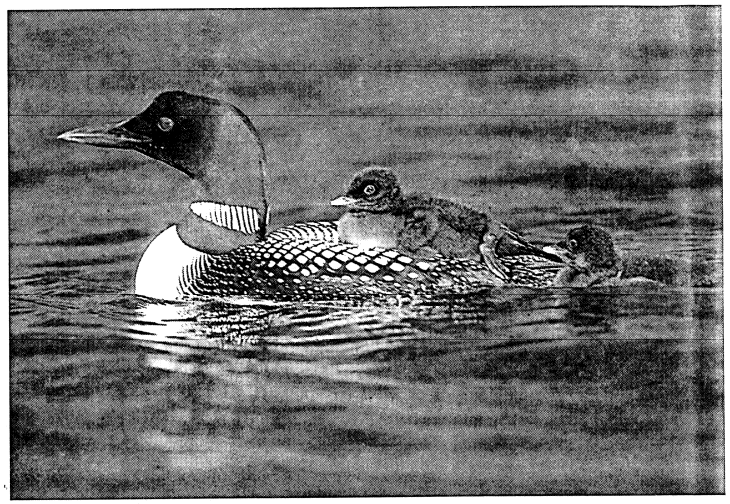
If mercury contamination becomes more widespread, it may spell major problems for the health of Canada's loon population. The birds' haunting cry is a wilderness symbol for many people, but their numbers have been in decline in recent decades, according to one of the researchers.

"Pollution, especially mercury pollution, is either aiding and abetting or enhancing the population decline that has been in evidence for the last 50 years," said Joseph Nocera, a graduate student who worked on the research project.

The researchers watched loon chicks during the past two years at Nova Scotia's Kejimkujik National Park, an area where loons have North America's highest observed mercury levels, and the Lepreau watershed in southern New Brunswick, where levels are lower.

Six of nine loon chicks in the high-mercury area disappeared and were presumed to have died during the two-year study period, a projected mortality rate of 66 per cent.

"That's not a good rate by any means," Mr. Nocera said. The reproductive rate is so low that researchers believe the area is a population sink for loons, and that the birds in this area would die out without migration from elsewhere.



Loon chicks that ride on their parents' backs are more protected from predators and are able to save valuable energy because they benefit from their parents' heat. TOM BRAKEFIELD/Corbis

Only one of six chicks in the low-mercury-level population in New Brunswick disappeared and was presumed to have died.

A research paper co-written by Mr. Nocera on the problems found in the chicks with high mercury levels has just been published in the most recent issue of Conservation Ecology.

Loons are of particular interest to scientists studying mercury pollution because they are a top predator in the aquatic food chain and are absorbing mercury from the fish they eat.

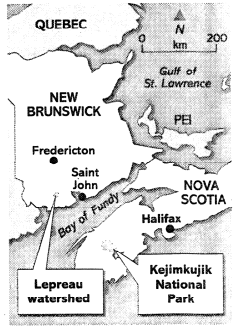
The fish, in turn, are ingesting mercury from lower on the food chain.

Concentrations of the heavy metal in the global environment are rising because of industrial pollution from such sources as coal-fired power plants and incinerators.

Mercury levels in North American loons rise from west to east, with the highest concentrations in Nova Scotia, which researchers have begun to view as a kind of tailpipe for airborne pollution from other areas of the continent.

Excessive preening is also viewed as a problem because researchers believe it wastes valuable energy, another factor that may make the chicks more vulnerable to predation.

Mr. Nocera and co-author Philip Taylor recommend more control of mercury emissions from industrial sources because it "would be a move toward prevention of further environmental degradation and adverse effects on wildlife."



The Globe and Mail

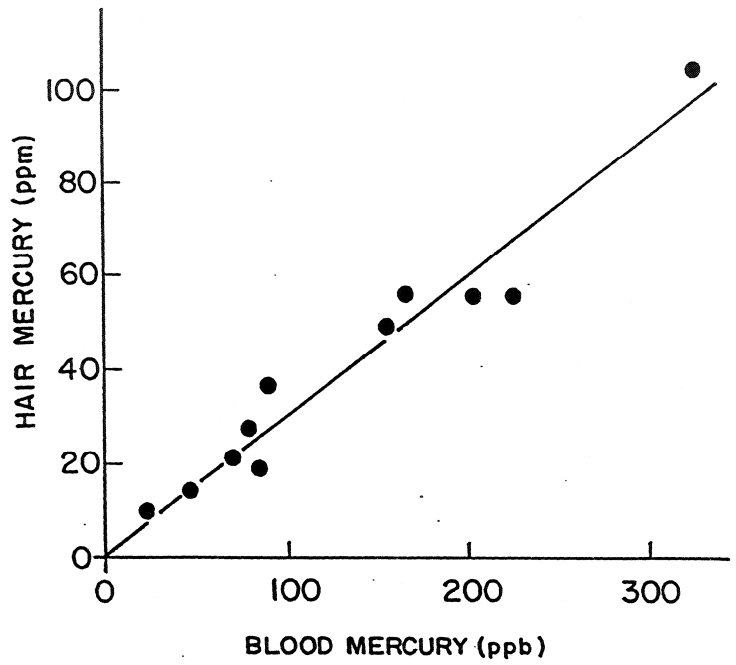


Fig. 9-5. The relationship between the concentration of total mercury in blood and in the 1-cm segment of a hair sample immediately adjacent to the scalp (from Clarkson 1976). The line was drawn by least squares linear regression analysis of the hair concentration (y, ppm) on the blood concentration (x, ppb) following the derived relationship $y = 0.49 + 0.30x$. The square of the regression coefficient is $r^2 = 0.95$. The standard error in the slope of the line is 0.02.

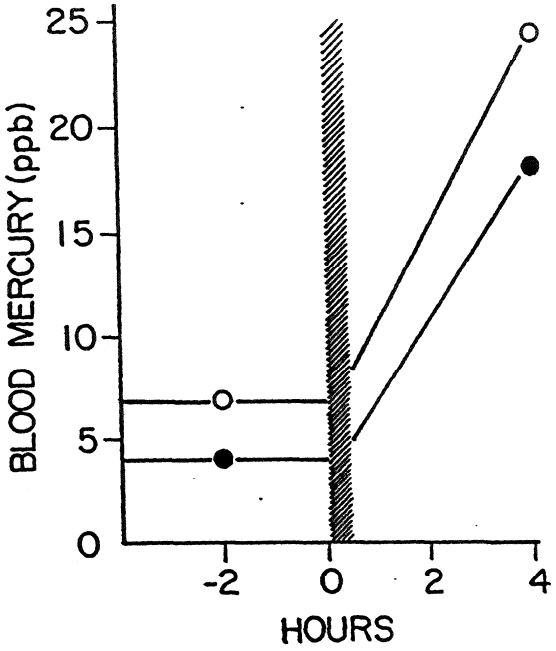


Fig. 9-6. The concentration of total mercury in blood samples before and after the consumption of one meal of fish (from Clarkson 1976). Each subject was an adult white female who consumed the cooked muscle tissue of a northern pike caught on the English River system.

● consumed approximately 0.5 lb at 2.6 µg Hg/g uncooked tissue

○ consumed approximately 0.75 lb at 2.9 µg Hg/g uncooked tissue

Top predators, such as walleye and pike, usually have the highest mercury levels. Smaller, younger fish and fish that are not top predators, such as panfish and yellow perch, are lower in contaminants. You can reduce your contaminant intake by choosing these fish to eat.

If you do wish to keep a legal-sized muskellunge for consumption, it will likely have elevated mercury levels, and should not be consumed by women of child-bearing age and children under 15. Trophy-sized muskellunge usually have very high mercury levels and should not be consumed by anyone"

Hg - Environmental exposure

Canada has a very big problem with the Hg content of fish.

"Examining Fish Consumption Advisories Related to Mercury Contamination in Canada." Prepared by MaryEllen Wood and Luke Trip, Environment Canada (2001), – reproduced with. acknowledgement to Dr Wood.

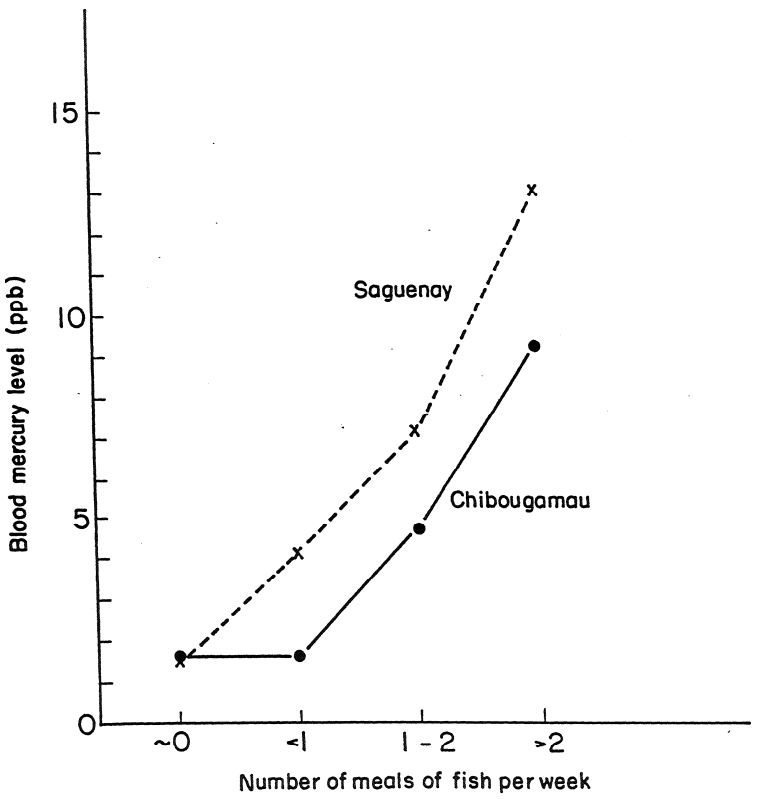


Fig. 9-2. Blood mercury levels in white Quebecois as a function of fish intake (adapted from Weber *et al.* 1978).

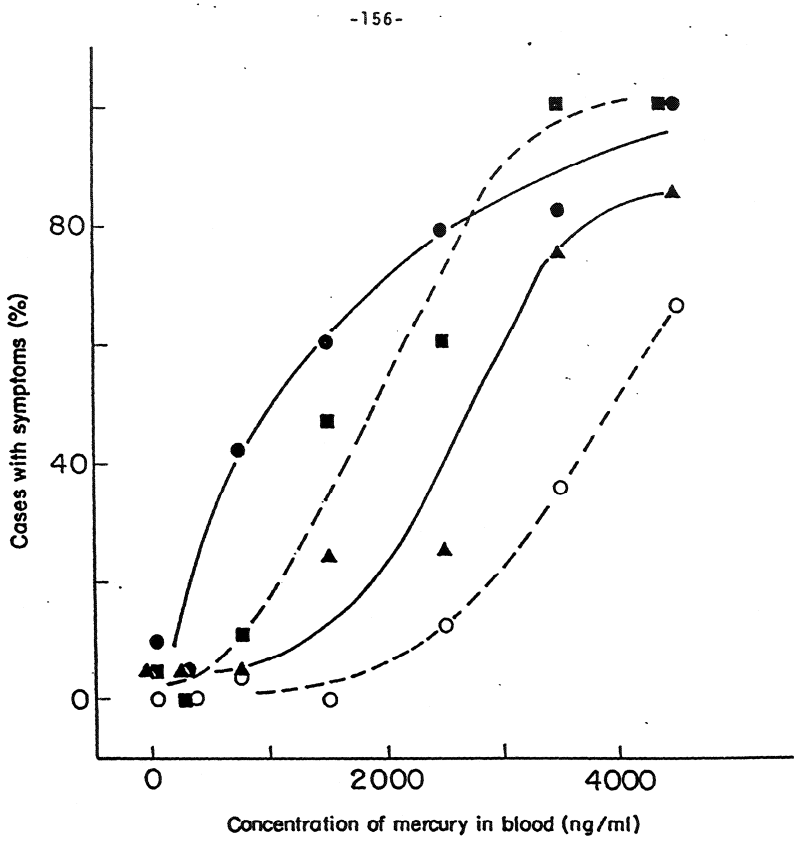
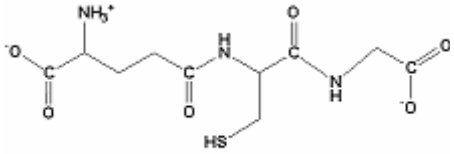
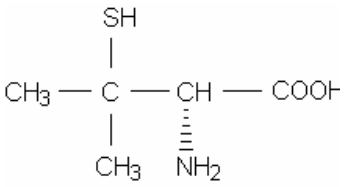


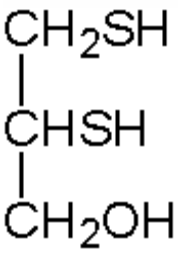
Fig. 9-7. Relation between the concentration of mercury in the blood and the incidence of symptoms (data from Bakir *et al.* 1973, Table 4). ● - paresthesia; ▲ - dysarthria; ■ - ataxia; O - hearing defects.

Her report concerned advisories issued warning of mercury bioaccumulating in the fish tissue. This is a risk for people who consume fish on a regular basis because elevated levels of mercury in fish tissue have serious implications on human health, especially for the development of unborn and young children. In 1970 Ontario, Canada, banned all fishing in the St. Clair River, Lake St. Clair, and the Detroit River. No clear data are available on numbers affected but there no known dead. Levels of mercury in fish flesh from Lake St. Clair, in 1935, were 0.07 - 0.01 ppm; but in 1970, some were 7.0 ppm, although the average was 0.5 ppm. Canadian max is 0.5 ppm.

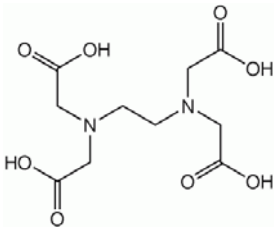
Some ligands that chelate Hg – BAL, glutathione, D-penicillamine, not EDTA,







BAL



9. Hg: Environmental exposure in Brazil[18]

As a result of gold mining in the Amazon Basin - Hg0 is used to extract the gold (estimates of nearly 2000 tonnes over an 8 year period) in the 1980's. Pollution contaminated the soil, and aquatic life.

Both miners and fishermen had elevated levels of Hg in their hair (with a mean about 40 ppm Hg) but had no symptoms - the development of MD is expected in the next decade as the effects of these high levels of Hg on the brain take place. Most of the Hg in the fish was MeHg. Recent studies have also suggested that a second cause of mercury release from the soil was the cutting and burning of trees along the river

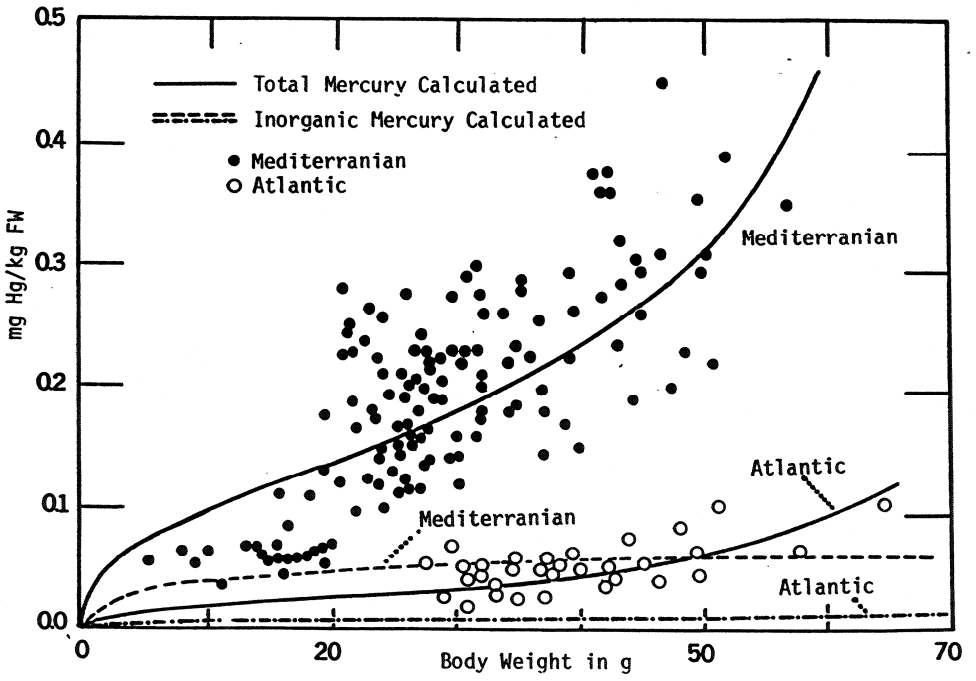


Figure 2. *Concentrations of inorganic mercury and total mercury in* ~~***Thunnus***~~ ***thynnus*** *from the Mediterranean and the Atlantic versus body weight.*

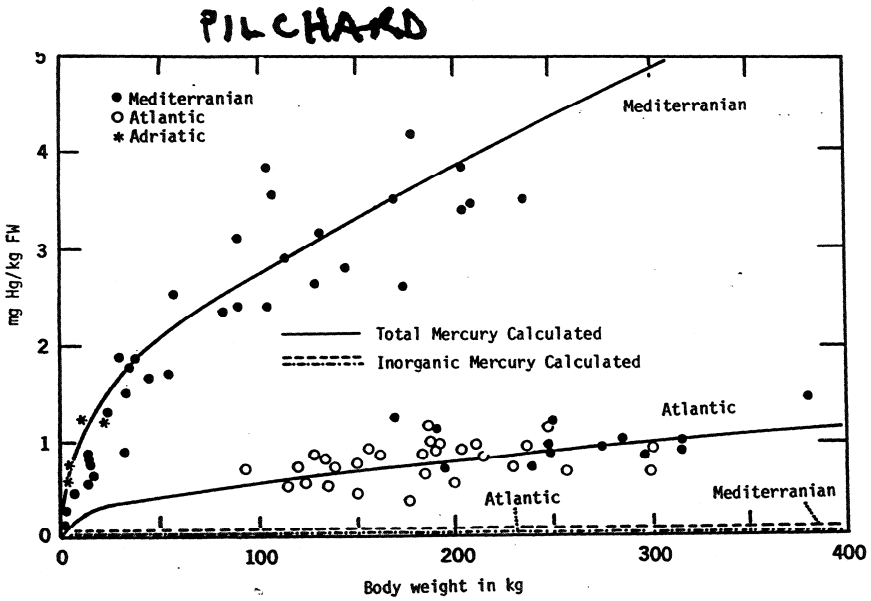


Figure 1. *Concentrations of inorganic mercury and total mercury versus body weight in* ***Thunnus thynnus*** *from the Mediterranean and the Atlantic.*

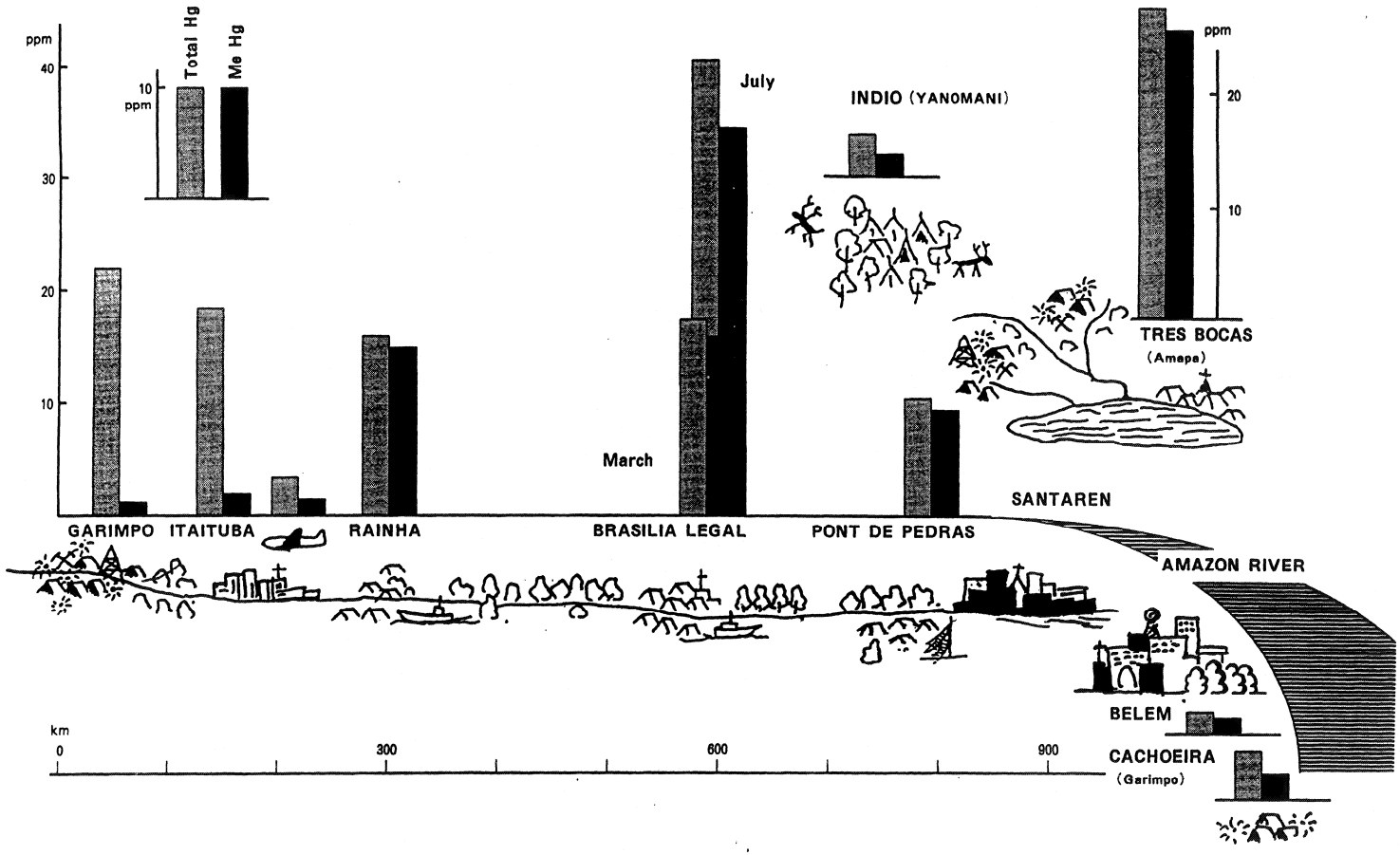


FIGURE 18.3 Total Hg and MeHg Concentration in Hair — Tapajos River Basin.

Hg: Environmental exposure in Brazil

banks, something that began 40 years ago. Once the land is deforested, rain washes soil from the top of the banks into the river-along with mercury, which naturally accumulated in the soils for up to 100 000 years.

Some areas along the Tapajós River have lost as much as 15 centimetres of surface soil.

10. Occupational exposure

a. Mercury and hatters

The felt hat industry has been traced to the mid-17th century in France, and it was probably introduced into England some time around 1830. A story passed down in the hat industry gives this account of how mercury came to be used in the process: In Turkey camel hair was used for felt material, and it was discovered that the felting process was speeded up if the fibers were moistened with camel urine. It is said that in France workmen used their own urine, but one particular workman seemed consistently to produce a superior felt. This person was being treated with a mercury compound for syphilis, and an association was made between mercury treatment of the fibers and an improved felt. Eventually the use of solutions of mercuric nitrate was widespread in the felt industry, and mercury poisoning became endemic. Danbury, Connecticut, an important center of America's hat-making industry until men's hats went out of fashion in the 1960s, developed its own reputation for madness. Regionally, the "Danbury shakes" were a commonly recognized series of ailments.

b. Throughout the 20th-century, mercury has been useful in a number of everyday items — alkaline batteries, fluorescent light bulbs, electrical switches, scientific and medical devices and the ubiquitous thermometer. Thermometers contain the less toxic elemental form of mercury and have almost never been a safety issue in peoples' homes. However, in the 1970s and '80s, workers at the Staco thermometer plant in Poultney, Vermont, began to notice a common series of health problems—headaches, bleeding or sore gums, upset digestive systems, and coordination problems. Upon investigation, mercury was detected in the air of workers' homes, on their clothing and furniture, and most tragically, in the bodies of many workers and their children. This was the first time in which the children of mercury-handling workers were proven to have been affected. The plant closed in 1984.

11. Biology - role in biological molecules - Hg

12. Metallic mercury – Hg^0

a. Unique for a metal to exhibit a liquid state - the vapour pressure is high making Hg very volatile at room temperatures, which results in significant release of Hg vapor - this is especially a problem in enclosed spaces - including our mouths. **Vapour entering the lungs is converted into oxidized forms by catalase and transported into the plasma**. Much more Hg accumulates in the brain following Hg^0 exposure through the lungs than following intravenous injections of Hg^{2+}. The whole body ½ life of inhaled mercury is about 60 days. Many symptoms results from intoxication with mercury vapour - including major neurological changes, gastrointestinal disturbances, and tremors.

13. Inorganic mercury

a. Salts are not absorbed efficiently into the gastrointestinal tract so that only an estimated 10% of $HgCl_2$ is absorbed. In the plasma Hg(II) is primarily bound to HSA (albumin). Skin absorption occurs and results in dermatitis.

b. The key problem is the extremely high binding constants for S. Glutathione – above - is thought to be the primary carrier both in plasma and in membrane transport. In critical poisoning the kidneys and GI tract are most affected. Renal failure eventually occurs. The kidneys are the primary target for inorganic mercury.

c. Chronic exposure to mercuric salts (ie low levels over a long period of time) result in the 'Mad Hatter' syndrome - neurological effects.

d. Acute exposure results in damage to the intestines and the kidneys leading to renal failure.

14. Organic mercury

The short chain alkyl mercury (methyl and ethyl) are extremely toxic to humans.

These compounds are efficiently absorbed through the GI tract. Most is bound to red blood cells - methyl mercury readily and rapidly crosses the blood brain barrier (BBB), slowly accumulating in the brain. (4 hr after ingestion and 5 min after intravenous injection reaching brain tissue.)

Although CH_3HgCl is lipid soluble - CH_3Hg^+ is bound almost completely to RSH groups in proteins and small peptides (GSH) in blood and other tissues, not free.

1) Absorption efficiency in the gastrointestinal tract for $HgCl_2$ is 20% max but $MeHg^+$ 100%
2) Eventually the Hg^{2+} is transported to the kidneys leading the renal failure.
3) The neurotoxicity is considered to occur following a series of interactions. It appears that there is a threshold level below which there is no renal damage found. Above this level, renal damage is rapid and severe.
Thiols (RSH) are the key ligands

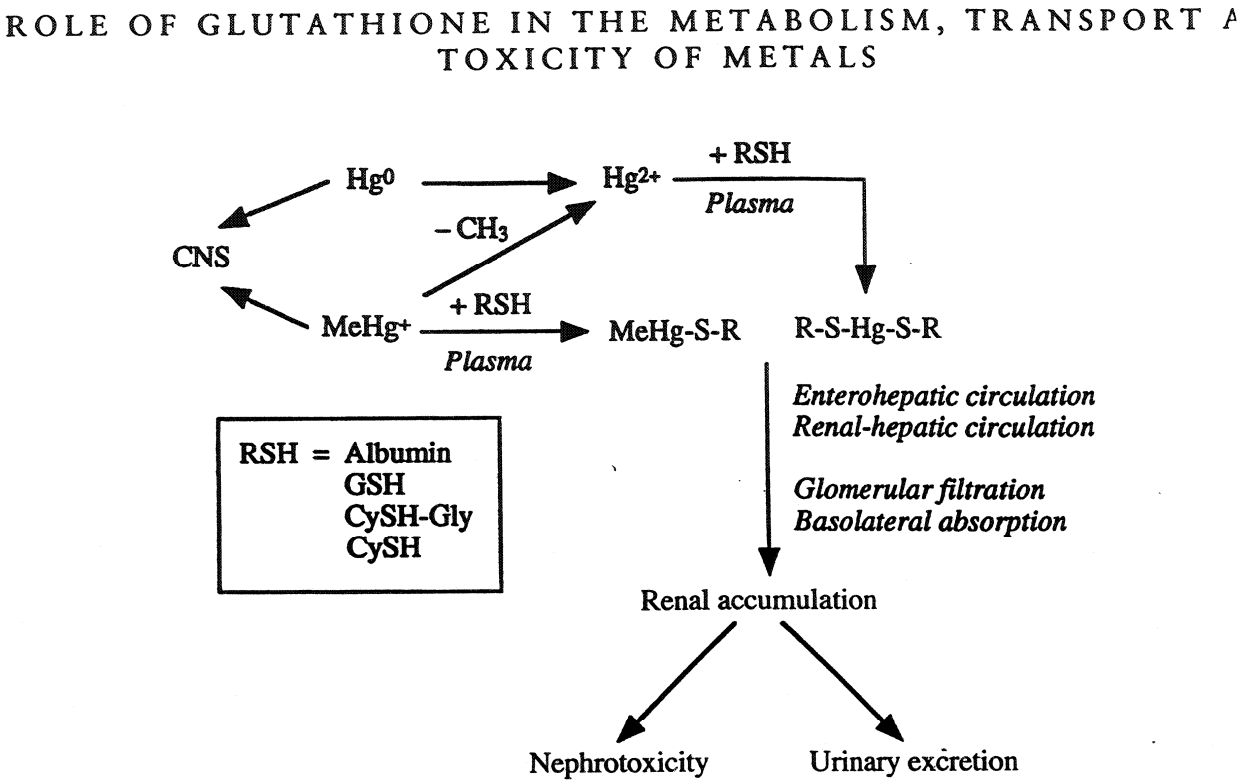


Figure 13.4 Role of sulfhydryl-containing compounds in the tissue distribution of the v forms of mercury. Elemental mercury (Hg^0) can either be accumulated in the central n system (CNS) or it can be oxidized to inorganic divalent mercury (Hg^{2+}). Hg^{2+} is bour sulfhydryl-containing ligand (R) in plasma and is translocated eventually to the kidneys. Sir methylmercury ($MeHg^+$) can accumulate in the CNS, it can be demethylated to form Hg^{2+} can be transported to tissues such as the kidneys bound to a sulfhydryl-containing Abbreviations: GSH, reduced glutathione; CySH–Gly, L-cysteinylglycine; CySH, L-cystei

Effects of mercury – once in the circulation

Alkyl mercuric salts have very high lipid solubilities & this results in significantly enhanced effects:

i. $HgCl_2$ inhibits cell growth at 7 ppb level

ii. phenylHg^+ inhibits cell growth at 0.06 ppb!

15. Health Effects of Mercury Exposure

Background: Throughout the centuries, there have been several incidents of reported mercury toxicity.

Table 17.2 Neurotoxic Effects of Mercury

Mercury species	Primary neurological effects	Primary pathological lesions
Elemental mercury vapor	Mad Hatter's Syndrome Asthenic-vegetative syndromes Erethism and micromercurialism Intentional tremor	Cerebral gray, cerebellum, brainstem nuclei
Inorganic mercury		
Mercurous salts	Pink's Disease Acrodynia	Cerebral gray, cerebellum
Mercuric salts	May resemble those of mercury vapor (rare)	Kidneys are primary targets; Neuro-lesions, if any, may resemble those induced by mercury vapor
Organic mercury		
Aryl- and alkoxyalkylmercury	ALS-like and motor neuron disease-like syndromes (rare and unconfirmed)	Kidneys are the primary organ affected Some claimed lesions in the anterior horns of the spinal cord and motor cortex
Alkylmercury	Minamata disease with sensory disturbance, constriction of visual fields, and cerebellar ataxia	Dorsal root ganglia, calcarine cortex, and cerebellum

From Chang, L.W. and Verity, M.A., *Handbook of Neurotoxicology*, Chang, L.W. and Dyer, R.S., Eds., Marcel Dekker, New York, 1995. With permission.

a. Since 1500 BC the Egyptians used mercury, as it was found in their tombs. As we have noted above, in the late 18th century, antisyphilitic agents contained mercury and during the 1800s the phrase, "mad as a hatter" was coined due to the chronic mercury exposure felters faced.

b. In the 1940s and 1950s, mercury became known as the product that caused acrodynia, also known as Pink

Disease. *Acrodynia.* This disease of infancy and early childhood is caused in most, in not all, instances by exposure to mercury. Marked by pain and swelling in, and pink coloration of, the fingers and toes and by listlessness, irritability, failure to thrive, profuse perspiration, and sometimes scarlet coloration of the cheeks and tip of the nose.

c. Methylmercury produces a much more devastating human illness than inorganic mercury, affecting primarily the central nervous system with many neurologic disturbances including paralysis, "tunnel vision" and blindness. There is no effective antidote as there is for inorganic mercury salts, nor are there any truly efficacious means for hastening its excretion from the body. Unfortunately, methylmercury is also very dangerous to a developing fetus. Offspring exposed in utero, if they survive, may have an irreversible affliction resembling cerebral palsy. Experimentally, methylmercury has been shown to cause mutations in DNA as well. **Methylmercury attacks the nervous system and the brain.** Symptoms include numbness of limbs and the area around the mouth, muscle weakness, an unsteady gait, tunnel vision, slurred speech, hearing loss, and abnormal behaviour such as sudden fits of laughter. More severe poisoning may lead to general paralysis, difficulty in swallowing, convulsions and death. **Mercury also cripples neural development in fetuses, and passes much more readily into the brains of young children than those of adults.**

16. **Poisoning has been known since 1856 and more often from 1914 when organic mercury began to be used as fungicides in agriculture** (now stopped). Causes loss of appetite, vomiting, disturbances in hearing, vision, speech and gait. Chronic intoxification begins with numbness of the extremities, loss of visual field, changes to speech and seizures. Elevated excretion into the urine - in Minamata 70-160 ug/L while exposed.

17. **Mercury and hatters**

Iraq: In 1971-72, a major epidemic occurred in Iraq in which 6,530 people were hospitalized and almost 500 died. In a well-intentioned response to famine, several nations shipped wheat grain intended for planting to Iraq. The seeds had been treated with a methylmercury-containing fungicide to hold down mold growth and preserve the viability of the seeds. The seeds were also dyed red to serve as a warning, and attempts were made to inform the natives of the hazards of eating the seeds directly. **Unfortunately, the warnings on the bags were in Spanish,**

because some of the grain had originated in Mexico, and the skull and crossbones, recognized by Westerners as meaning poison, meant nothing to the Iraqis. **In the face of starvation, many families milled the seeds directly into flour, and made and consumed the contaminated bread.** There would have been no danger in eating grain grown from the treated seeds, because the subsequent crop would contain little or no methylmercury.

18. There have been signficiant poisonings by mercury in Canada due mainly to the pulp and paper industry.

19. How to detect/quantify exposure?

    a. Hair is a good indicator of exposure to different forms of Hg. Once Hg is incorporated into hair it is trapped by the amount of RSH.

20. Detoxifying agents - Protective properties

    a. 2,3-dimercaptosuccinic acid (DMSA) is approved by FDA, 2,3-dimercaptopropane-1-sulfonate (DMPS) and NAPA are commonly used as Hg chelators in the event of poisoning. BAL is also used – although not effective for organic Hg and damaging in use to the kidneys.

    b. DMSA, DMPS and NAPA are fairly non-toxic, water-soluble, and can be administered orally. NAPA and DMSA are generally more effective in chelating organic Hg, while DMPS is more effective at chelating inorganic mercury. D-penicillamine N-acetyl-DL-penicillamine have also been used.

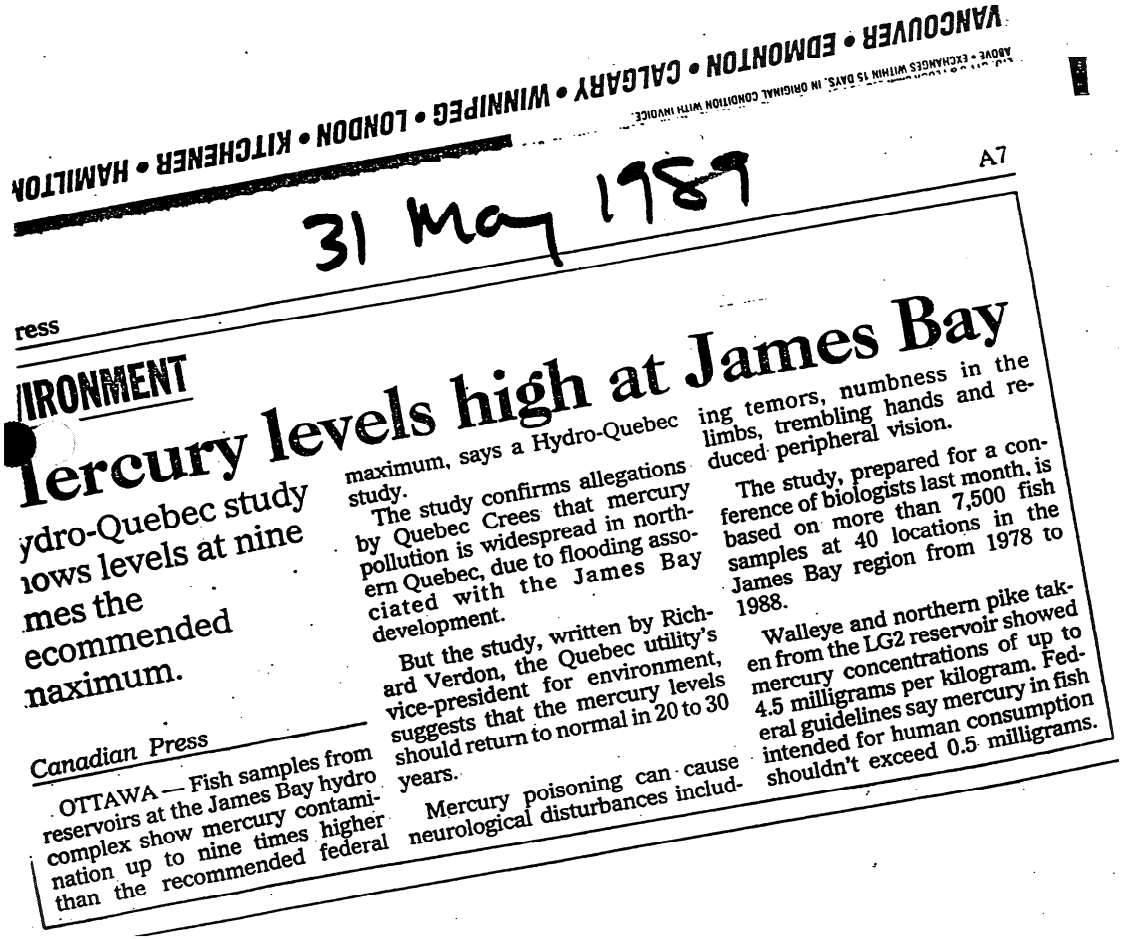
    c. It is thought that DMPS provides protection against damage by Hg^{2+} by competing for the mercury in the renal tubules.

    d. The explanation is that DMPS might be taken up in the same proximal tubular cell locations as GSH - then binds Hg - which stops the subsequent transport of the Hg to luminal side of the cells. Exogenous GSH does appear to protect against renal damage - for example, perfused GSH+Hg(II) protected renal cells from damage - oral administration of GSH did reduce the renal burden of Hg(II).

21. However, the results were not conclusive because co-administration of GSH and $HgCl_2$ in rats and mice appeared to raise the renal mercury content. This seems to suggest that the GSH is involved in transport of the Hg in the renal system.

22. Minamata Disease - MD

a. MD was first reported in 1956 in the region around Minamata Bay in Japan although probably began in 1953. The first patients were 2 young girls with serious cerebral disorders of an 'unknown' origin. The symptoms were numbness of the fingers, lips and tongue, clumsiness of the hands and strange gait. Then, deafness and constriction of the visual field, and death. Soon after, 30 similar patients were discovered in the neighbourhood of Minamata City (with 40,000 population) that faced the Minamata Bay. In addition, cats were found to exhibit the same condition after eating dead fish from the bay.



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IRONMENT

lercury levels high at James Bay

ydro-Quebec study
ows levels at nine
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naximum.

Canadian Press

OTTAWA — Fish samples from reservoirs at the James Bay hydro complex show mercury contamination up to nine times higher than the recommended federal maximum, says a Hydro-Quebec study.

The study confirms allegations by Quebec Crees that mercury pollution is widespread in northern Quebec, due to flooding associated with the James Bay development.

But the study, written by Richard Verdon, the Quebec utility's vice-president for environment, suggests that the mercury levels should return to normal in 20 to 30 years.

Mercury poisoning can cause neurological disturbances including temors, numbness in the limbs, trembling hands and reduced peripheral vision.

The study, prepared for a conference of biologists last month, is based on more than 7,500 fish samples at 40 locations in the James Bay region from 1978 to 1988.

Walleye and northern pike taken from the LG2 reservoir showed mercury concentrations of up to 4.5 milligrams per kilogram. Federal guidelines say mercury in fish intended for human consumption shouldn't exceed 0.5 milligrams.

b. MD was caused by eating fish and shellfish caught in Minamata Bay. The local fisherman were very poor and were the main patient body. These families ate large amount so of fish and sea foods.

23. Up to 1960, 111 cases of MD had been reported. 41 deaths had occurred. **MeHg readily crosses the placenta dramatically affecting the unborn leading to mental retardation, growth disorders, etc. from damage to the CNS.**

CAT DANCING

V.

by Jack Perdue

The river ran clean and clear. It had its beginnings in a sparkling lake, and tumbled between forest-clad shores on its long journey to the sea.

As time passed, settlers from Europe found it, built their communities on its shores and began shaping the wilderness to their will. Its cold northern waters became famous for fighting game fish; northern pike, walleye and the mighty muskellunge.

One day a pulp mill was built on the upper reaches of the river. It was to provide much-needed products for the growing country, and for export. And it was to provide jobs. In fact, it was to eventually provide 1,500 jobs in a town where all other industries employed less than 150 people among them. The town depended heavily on the pulp mill for its survival.

Pulp mills need great quantities of water for their operations, and this river ran fast and clear. Over the years the daily dumpings of wood fibre, together with the cleansing water that washed away the chemicals used in the pulp-making process, seemed to have little effect on the quality of the water and the downstream watershed. The river was not truly polluted at that time, although some of the game-fish species and other aquatic life began to diminish. Nearly 50 years in the future, the river would indeed become dangerously polluted, but long before that happened, it simply and quietly died. For wood fibre destroys the oxygen in a water system, and this once deep-running river was to develop a bottom layer of wood fibre up to 40 feet thick!

One of the heavy metals used extensively in the pulp-making process is mercury. For many years it was believed that organic mercury would simply sink into the sediment on the river bottom and remain there in a chemically inert form.

And then came the cat dancing.

Minamata disease, also known as 'cat dancing disease' because it was first detected through the peculiar behavior of infected cats, was originally diagnosed in Japan where 90 people died at Minamata in 1975 as the result of mercury poisoning caused by eating fish infected by the effluent from a local industry.

Mercury poisoning is nothing new. It dates back to the 15th century and even earlier, the victims at that time usually being workers in the mercury mines.

In recent times, organic mercury compounds have been used as seed dressings. The consumption of this dressed seed led to a number of severe outbreaks of mercury poisoning: in Guatemala in 1966, Pakistan in 1969 and Iraq in 1971, '72 when several thousand people died and as many became seriously ill.

An extensive monitoring program was begun in Canada as early as 1969 to detect the presence of mercury in higher-than normal quantities in bodies of water. I must be remembered, however, tha Canada has nearly one-third of th world's fresh, unsilted water in the for of hundreds of thousands of lakes an rivers. The task was all but i surmountable.

It was to be expected, however, that area in Canada would eventually be foun where mercury levels were dangerous high, and they were.

They included our river, once clean a clear. And the Indians who lived along i banks and hired out as guides to visiti sport fishermen and ate the fish in t river as their staple food were the fi residents of Ontario to show signs Minamata disease.

As you might imagine, this caused a gr deal of publicity, and government studi were immediately undertaken. The m result was the discovery that anaero bacteria in river-bottom sediment w attacking the inorganic mercury there a converting it into methyl mercury. A methyl mercury is organic and can concentrated in the fatty tissues of f and birds — and man.

The effects of mercury poisoning highly unpleasant. Mercury, toget with other heavy metals used in indus attacks the human liver, the essential p of man's immunity system. Studies suggest a definite connection betw mercury and cancer.

a. The estimates over several decades were that thousands of people were affected.

b. Initially identified as an intoxicant disease but not associated with Hg, rather Mn, Se or Tl from the marine life. Because of large amount of Mn and known neurolgical effects of Mn, Mn was initially strongly identified with the brain disorders, except that cats fed Mn did not exhibit the strange behaviours observed. In 1959, mercury was identified as the probable cause. And, then organic mercury was identified following observations of identical symptoms after oral ingestion by lab cats, again in 1959.

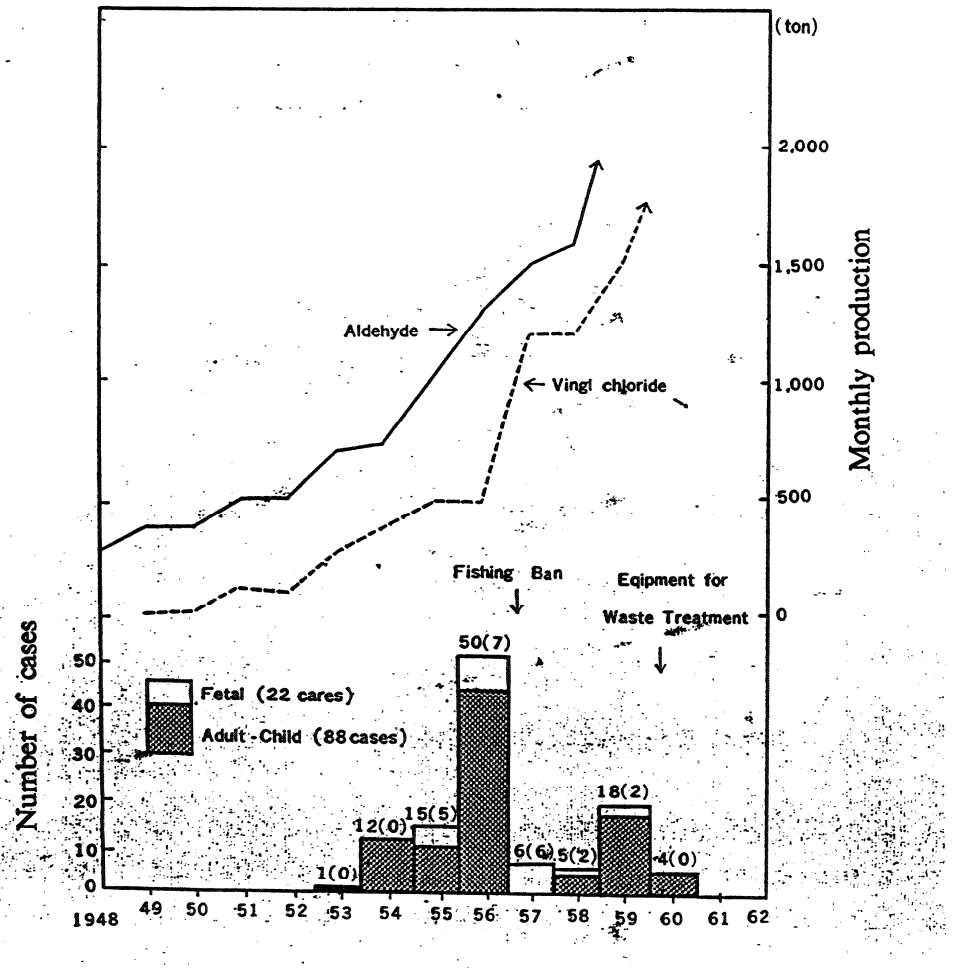
24. A series of images follow this text and in the "EXTRA-MATERIALS" file.

a. The Hg from mud and sediment in the Minamata Bay region with concentration of 2100 ppm wet weight was found at the drainage site for the Minamata factory of Shin Nihon Chisso Co.

b. In 1960, organic mercury was isolated from fish in the bay - and was shown to be $CH_3HgS.CH_3$. Methyl methylmercuric sulfide. CH_3HgCl was then isolated from the mud containing the mercury efflux of the vinyl acetate factory. .

c. The vinyl factory was identified as the source. $HgCl_2$ was used as a catalyst for vinyl chloride synthesis and $HgSO_4$ for acetaldehyde. This factory began use of mercury in 1932, producing vinyl first in 1941. The Minamata factory became the largest producer of vinyl in Japan, dumping more mercury than at any other site, directly into the Minamata River. Estimates of 500-1000 g mercury were lost for each ton of acetaldehyde made. 200 tons of mercury were used over a 5 year period ending in 1953. In 1961, waste disposal was installed and the mercury content of the effluent dropped. Treatments with EDTA and BAL were attempted. Both roughly doubled the urine concentration of Hg but did not appear to relieve symptoms. Later MD was found in other areas of Japan (Niigata) following the pollution of the Agano River - called MD-2. Directly related to eating contaminated fish. Hg levels in hair were elevated. About 200,000 people have been exposed, with 2200 officially designated MD patients

Fig. 4 Number of patients of Minamata disease and the production of chemicals at the factory



Cabinet approves Minamata disease plan

CONTINUED FROM PAGE 1

in Minamata in 1956.

However, a group of about 100 unrecognized Minamata victims who have filed damage suits with the Osaka District Court are still demanding the government accept official responsibility.

The government's statement Friday, which only expressed "regret," is unlikely to be enough for these litigants.

Under the final settlement plan, Chisso will pay ¥2.6 million to individual victims of the disease in Kumamoto and a total of ¥4.94 billion to five victims' groups to cover litigation and other costs.

In the Niigata case, the victims' group has reached an agreement with Showa Denko K.K. — the company that discharged the polluted water there — in which the company will pay ¥2.6 million to individual victims and ¥440 million to the group. Showa Denko will also pay ¥250 million to Niigata Prefecture to help revitalize the local economy.

The Cabinet agreed that medical panels designated by the prefectural governments of Kumamoto, Kagoshima and Niigata will resume accepting applications from patients in January to determine their qualifications based on medical certificates prepared by both public and private hospitals.

As a result, about 8,000 people who have not been officially recognized as Minamata disease victims are expected to be eligible.

More than 13,000 people have applied for recognition as Minamata victims to be eligible for compensation from Chisso, but the government has so far recognized only about 3,000 of them.

The Cabinet has agreed that Kumamoto Prefecture and the central government will both supply funds to financially support Chisso and revitalize the local economy.

The government will extend about ¥25 billion from the general account to the fund, while Kumamoto Prefecture will extend about ¥5 billion through a bond issue.

The fund will be used to provide ¥26 billion to Chisso and ¥4 billion for the development of the regional economy in Minamata and Ashikita, including the construction of a welfare center.

If Chisso is unable to repay the loans from the prefecture, the national government will take every possible measure to make good on them. That pledge was made in deference to a demand by the Kumamoto Prefectural Government.

Tadamori Oshima, director general of the Environment Agency, told a news conference that the agency's role now is to implement various measures approved at Cabinet meetings.

Koichi Kato, secretary general of the Liberal Democratic Party, said that the entire party supports Friday's solution to the long-running issue.

"If politicians had allowed the problem to lag on for another 10 or 20 years, it would not have been a pretty sight," he said. "It was time for us to exert leadership over administrative authorities."

He pointed out that no members of the party had opposed the plan.

25. The legal recognition of fault and a payment scheme to the living MD victims was settled on 29 October, 1995. The government officially recognized 2,265 victims - 1,435 already dead

26. **Summary**: The methylmercury was absorbed by eating fish and shellfish from contaminated water Levels of mercury in fish flesh in Minimata Bay in 1952 were 5 - 10 ppm (In Canada <0.5 ppm is the limit). The 1965 instance in Niigata, Japan was a similar case to Minimata Bay; 330 persons are known to have been affected, of which 13 died..

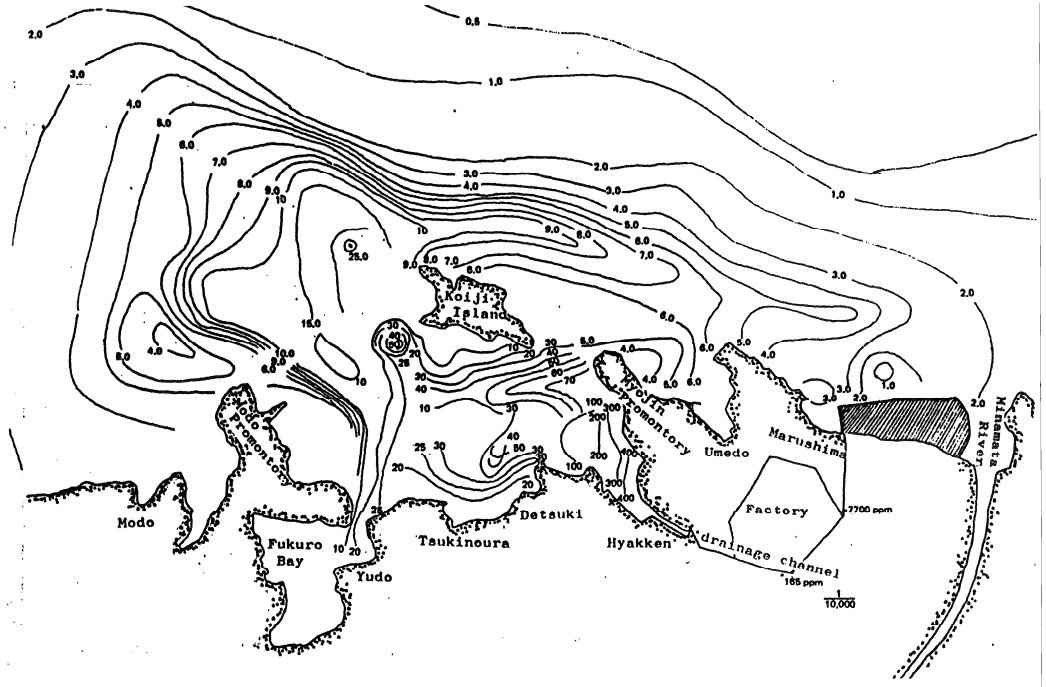


FIG. 3. Recent mercury content of sludge at the bottom of Minamata Bay. Figures = ppm Hg (dry weight) (Environmental Agency 1973).

Minamata and the search for justice

Paradise in the Sea of Sorrow: Our Minamata Disease
by Michiko Ishimure, translated from Japanese by Livia Monnet
Yamaguchi Publishing House, pp 365, 5000 yen/$35

Michael Cross

A LONG time ago and a long way away, a factory dumped sludge containing organic mercury into the sea. The mercury found its way into fish. Some people who ate the fish died in nasty ways. Others gave birth to children with almost unimaginably awful deformities. The town where this happened, Minamata, became the name of a disease and a worldwide symbol of industrial pollution.

If this explanation is simplistic, it is because there is little point in saying more about Minamata now that the classic written account of the tragedy is available in English. *Paradise in the Sea of Sorrow* appeared in Japanese in 1969, the first part of a trilogy. It spans the first 15 years of the disease, from its appearance in the early 1950s to the Japanese government's official statement that mercury pollution was to blame.

Don't expect a systematic or even chronological history. *Paradise* is the work of a passionate activist, written at the height of the struggle to win recognition of the disaster from the Japanese establishment and even people in Minamata itself.

The key word in the title is "our"—these are the participants' voices. And as so often happens when "victims" have the chance to tell their own story, the lasting impression is of human dignity. These are people who were too proud to register for compensation, who were shy about meeting delegations from Tokyo and who were diffident about making a political issue over "our little pollution incident".

They faced the prospect of an agonising premature death with anger and humour, stoicism and frustration, wisdom and stupidity. In short, as human beings. Mercifully, Ishimure leaves to our imagination most of the physical horrors. The little

W. Eugene Smith/Magnum

Eugene Smith's photographs showed the pain of Minimata disease

details she slips in become almost unbearable: a teenage boy v weighs no more than a woo Bhudda; a fisherwoman ragin the routine indignities of bein a hospital bed.

The book's format, mixing

subject ideally. The result, rendered into beautiful and economical English, lives up to the publisher's claim of "a new literary form".

Even the abrupt and anticlimatic conclusion tells a story. For, almost incredibly, the story is still not over. Nearly 35 years after the first lawsuit, arguments over responsibility and compensation for Minamata are still ploughing through the Japanese courts. The government is resisting calls for a "quick settlement" because of the principle involved. The official responsible for explaining this stance hanged himself the week before I read this book.

I do not know how easy it will be to find *Paradise in the Sea of Sorrow* outside Japan. Perhaps a canny distributor will see possibilities for three trendy niche markets, Japanism, environ-

Michael Cross is a science writer based in Japan.

Minamata sufferers win official 'regret,' redress

The government endorsed a final plan at a Cabinet meeting Friday that grants compensation to people who have not been officially designated as victims of Minamata disease but who suffer from the disease nonetheless.

Prime Minister Tomiichi Murayama released a statement expressing "regret," generally recognized as the step necessary to terminate the four-decade-long confrontation between the state and the victims.

Minamata disease has been prevalent since the 1950s and afflicts people who consumed fish and other marine life taken from Minamata Bay, Kumamoto Prefecture, after Chisso Corp. dumped mercury into the bay over several years.

The mercury attacks the nervous system, causing such problems as numbness of the extremities, sight defects, loss of hearing, ataxia and mental disablement, among other symptoms.

The plan calls for Chisso Corp. to pay compensation to the unofficial victims, who are ineligible to receive money under the existing compensation plan. It also includes loans from the national government and Kumamoto Prefectural Government to Chisso to help the financially stretched chemical company pay the redress.

Murayama is the first prime minister to admit government responsibility in the Minamata affair.

"Looking back at the history of Minamata disease, the government should honestly reflect on the fact that it took too long to determine the cause of the disease and take appropriate measures against the companies responsible for causing it, including the recurrence of Minamata disease in Niigata," Murayama said in the statement.

Murayama said he is saddened when he ponders the feelings of those who were forced to undergo years of unbearable suffering.

The National Alliance of Victims of Minamata Disease and Lawyers, the largest organization involved in the case, said it welcomes Murayama's statement, as it details the government's failure to prevent the spread of the disease. But the organization added that it will continue to work so that every victim is entitled to receive money.

With Murayama's statement and a package of measures to help Chisso pay billions of yen to thousands of victims, the disputes in Kumamoto and Niigata prefectures should now finally be settled, 39 years after the disease was officially recognized

CONTINUED ON PAGE 2

MINAMATA, Kumamoto Pref. — Kiyoto Sasaki (second from right), chairman of the Minamata Disease Patients Federation, and Teruo Kawamoto, a Minamata Municipal Assembly member and long-time activist for the patients, read on Friday a copy of the prime minister's comment on the disease. KYODO PHOTO

grams or 1.7 [illegible]
the label specified.

London Free Press. 3/Sep/82

Japanese doctors to check mercury at Indian reserves

OTTAWA (CP) — A group of Japanese doctors wants to return to the Northern Ontario reserves at Whitedog and Grassy Narrows to continue their study of the effects of mercury contamination on the Indian population.

A message was to be sent to Japan on Thursday formally inviting the Japanese contingent, headed by Dr. Kenichi Miyamoto of Osaka, said Bruce Crofts of Toronto, negotiator for the Whitedog reserve.

Miyamoto was one of the doctors who visited the two isolated reserves north of Kenora in 1975 and 1976 to study the frightening parallels between the mercury poisoning in the English-Wabigoon River system and at Minamata, a chemical company town in southern Japan.

In both cases, residents have dangerously high mercury levels from eating fish contaminated with mercury.

While there have been cases of hideous deformities and death in Japan, there haven't been any clinically proven cases of so-called Minamata disease at the two reserves.

Both reserves have been devastated financially and socially since the discovery of the mercury pollution in the early 1970s wiped out their commercial fishing industry.

Indians still eat the contaminated fish, despite warnings that they are risking their health.

Mercury levels found in the hair of some Whitedog residents tested this spring ranged from nine to 20 parts per million. Federal officials consider 30 parts per million high risk.

Crofts said he hopes the doctors can visit the reserves in October, when mercury levels will be at their peak after a summer of fishing.

Chiefs at both the reserves say they welcome the return visit, he said.

The reserves are still trying to negotiate compensation settlements with Reed Ltd. and Great Lakes Forest Products Ltd., the Dryden paper mill which contaminated the river during the 1960s.

In March, Whitedog agreed to about $2.3 million in compensation from the federal government. Grassy Narrows has yet to reach a federal settlement.

Summary of mercury toxicity and humans			
Exposure forms - Hg^0;Hg^{2+}; RHgX Non-occupational exposure to Hg – fish, shellfish; paints; fungicides; dental amalgams Hg^0 from broken thermometers, switches,	Breathing – Hg^0 - - eating fish - sea food chloralkali industry released 1000's tonnes $HgCl_2$ into water used for fishing Eating Canadian fresh water fish – still an issue	Breathing Hg from coal-power electric stations - Hg vapour–smoking cigarettes – major exposure route eating fish (all tissue – but high in muscle) – worst – sword fish - tuna -	Major difference between Hg^0, Hg^{2+}, and CH_3Hg^+ exposure Note – old sources: amalgam, paints, fungicides, thermostats, light switches, batteries. New sources: compact fluorescence lamps;
Occupational exposure	Major sources of occupational exposure to Hg – mining, refining precious metals (gold and silver ore using liquid Hg in Brazil),	And chloralkali plants in paper production, mercury contact switches; Hg in fungicides and paints	Mad hatters Gold miners
Biochemistry known?	Binds to sulphur in cysteine as well as a number of other proteins interrupting a large number of essential metabolic pathways	CH_3Hg^+ crosses the BBB Alkyl-Hg most toxic – liquid Hg^0 least toxic	Hg2+ methylated in sediments by anaerobic bacteria – via Vit B12
Health effects Organic and Hg vapour accumulate in the brain, heart and kidneys.	Many symptoms – medical – depend very much on type of Hg (0, 2+, or alkyl)	Worst: neurological – rapid coma and death	Cancer - death

Cure? Recovery? Yes, possible if not too much exposure and if not alkylmercury.	Cure? None really. Some success with Hg2+ if early with DMSA. Cannot reverse health effects – Response: Must remove Hg source. No success with chelators for CH3Hg+ poisoning.	FDA approved- 2,3-dimercaptosuccinic acid (DMSA, Succimer) – taken orally -	For serious systemic intoxication DMPS (dimercaptopropanesulphonic acid) is the treatment of choice. Also used –or N-acetyl-penicillamine (NAPA) - and 2,3-dimercaptopropanol (BAL, Dimercaprol) good but bad side effects
Major world-wide poisonings	Minamata, Japan Niigata, Japan Northern Ontario Mexico Iraq Gold miners in Brazil – on-going ..	Cause: Hg contaminated fish from Hg wastes in water; treated grain eaten; a cream.	
Add from poster handouts			
A note from a web site An essential web site to check out if you eat fish..	Many consumers are not aware, for example, that a 115 pound women consuming just two cans of albacore tuna in a week puts her 310% above what the EPA and FDA considers safe; a child weighing 45 pounds eating just one can of albacore tuna per week would get a dose 420% higher than the EPA/FDA's safe limit of .1 microgram/kilogram-day of mercury exposure. The same person consuming swordfish would have mercury level of more than three times that high. http://www.commondreams.org/news2004/0310-02.htm Source: **http://www.gotmercury.org/** **Eating seafood high in mercury is hazardous to your health, especially for women and children.** The "Got Mercury?" calculator below helps you make healthier seafood choices. Just enter your weight, the seafood type, the amount of seafood you will eat during a week, and click the calculator button. These calculations are based on EPA and FDA data (updated January 2006).		

		BACKGROUND READING FROM THE COURSE TEXT BOOKS IN THE LIBRARY	
L-B	R-M	K-S	Alternative sources of information
		As – see p 319 for a useful discussion of As toxicity Ch 17 – 'toxic metals' an excellent review chapter – might be worth photocopying this whole chapter – covers all metals and has a very similar series of figures to the lectures – highly recommended as a Final exam review source. The extra metals included are not part of the course.	See also Ch.11 in Baird's Environmental Chemistry book. Again, a very readable and useful review of each of the metals included in these lectures. Many in the class take Chem 2210, why not ask somebody for a loan of the book.

Key points from this unit

Summary: Toxic Metals

Toxic metals (including the non-metals of Se, As, etc), used to be called "heavy metals," are individual metals and metal compounds that negatively affect people's health.

Hard to determine essential at the ultra-trace level vs. toxic in all metals. But toxic accessible metals are: Sn, Pb, Hg, As, Cd, Be and Cr(VI).

In very small amounts, these metals are or may be necessary to support life. In larger amounts, they become toxic.

Toxic, accessible elements – meaning they are mobile - most of the 1st row transition metals (except Fe) - in particular, and also Sn, Pb, Hg, As, Cd, and Be. Most other transition metals are not accessible or available in high concentration - but they are toxic

For example, hexavalent chromium (not included later but of concern): calcium chromate, chromium trioxide, lead chromate, strontium chromate, and zinc chromate are known human carcinogens. An increase in incidence of lung cancers have been observed among workers in industries that produce chromate and manufacture pigments containing chromate.

Non-toxic Group 1: Li Na K Rb Mg Group 2: Ca Sr and in addition, Al, Fe, Si.

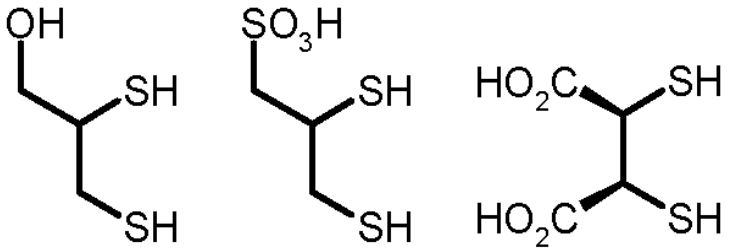
General routes into man: Respiration, ingestion (diet), skin absorption, injection, cigarette smoking

Chelators -Too few, don't work well, except for lead – now DMSA, was EDTA

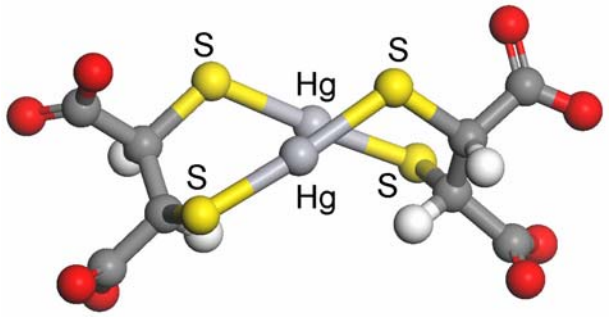
2,3-dimercaptopropanol (Dimercaprol, BAL)

2,3-dimercaptosuccinic acid (Succimer) – with 2 Hg^{2+} atoms

D-penicillamine and NAPA



BAL DMPS *meso*-DMSA



from G. George et al., in press.

1 Introduction – Toxic Metals	Metals that are toxic must cause unwanted interactions – so the most dangerous metals are classified as Soft and Intermediate Lewis acids – and these react with soft and intermediate bases - forming stronger bonding interactions is one key to the toxicity. We can itemize typical characteristics – bioavailability; reactive to biologically important ligands (CYS); lack of transporters to excrete the metal when ingested- the liver and kidneys are key target organs due to the efflux of toxic metals A number of chelators do exist – EDTA, BAL, DMSA, NAPA and D-penicillamine are most commonly used - - know the metals – know the structures – see above Key toxic metal incidents for each of Pb, As, Cd and Hg – what is/was the historical setting Summary of sources of each metal –non-occupational - occupational exposure How do metals – all metals – enter a cell? 4 routes. Computers contain toxic heavy metals such as lead, cadmium, mercury and chromium, all carcinogenic and not easily degraded. At present there is no system for dealing with such material, and a pioneering European directive to tackle the problem is being fought by the US government and the electronics industry.
2 Lead	Many exposure problems due to the low melting properties of Pb. Known since antiquity; Romans used Pb for containers; pipes and its salts to sweeten wine; Common sources – include old paint, old buildings, lead pipes, lead in solder used for copper water pipes, was in gasoline, lead batteries in cars, lead products, leaded-glass, glazes on pottery; used in plastic manufacturing; pigments ; cosmetics. Due to extensive controls on $(Et)_4Pb$ in gasoline overall environmental levels have fallen. Blood lead levels have also dropped. Blood lead used as an indicator (only of recent exposure) units micrograms/dL blood. Occupational exposure to lead is one of the most prevalent overexposures found throughout industry. Industries with high potential exposures include construction work, most smelter operations, radiator repair shops, and firing ranges. While some of the sources, such as lead-

	based paint and leaded gasoline, have been discontinued over the past few decades, their effects still show up in the environment. Primary exposure to lead is from the GI tract due to paint chips, drinking water, fertilizer, food, auto and industrial emissions, and (inhalation) dust. …and those diving ducks – those that miss the shot-gun pellets eat the shot; fishing weights; killed by lead poisoning.
2 Lead	Chronic poisoning: Major effects in children; major but different effects in adults. Can use EDTA to chelate but brings Ca^{2+} as well; and has to be done over a long period of time to remove Pb in bones. Major health concerns. Common effects: Pb accumulates in soft tissue; eventually stored in bone (relatively harmless there – but is in equilibrium with blood and tissue); neurological in children at very low levels (20-80 micrograms/dL blood); inhibition of heme biosynthesis. (we know that heme is the essential in hemoglobin, myoglobin and cytochromes). Binds to sulfhydryl groups (-SH groups) of proteins, lead inhibits the functions of the mitochondria, making cells unable to reabsorb substances. However, a major problem is damage to the brain, especially in young children from Pb in dust and paints. Major concern: exposure of children in inner city housing – disposal of Pb-based items, esp. batteries in developing world – pollution in developing world. To come: children of the developing world exposed to massive amounts of Pb.

Lead exposure routes	
Health effects – major manifestation and the most diagnostic .	
Treatment possible?	

3 As 3+ > 5+ in toxicity	**Arsenic**. Historical events: Massive poisoning of the peoples of Northern India, and Bengal. The primary route of exposure to high levels of arsenic is typically through occupational hazards, or near hazardous waste sites or areas with high natural levels. Breathing sawdust or burning smoke from arsenic-treated wood. Arsenic has also shown up in drinking water, especially among well water, and long-term exposure to arsenic in drinking water has been linked to cancer of the bladder, lungs, skin, kidney, nasal passages, liver and prostate. As (from both 3+ and 5+ oxidation states) accumulates in lung, heart, kidney, liver, muscle and neural tissue. Concentrates in skin, nails and hair. Half life is 7 to 10 hours. Humans are exposed to arsenic (As) primarily from air, food, and water. Inorganic arsenic compounds are mainly used to preserve wood (copper chromium arsenate). Organo arsenic compounds are used as pesticides. Fish and shellfish can accumulate arsenic, but the arsenic in fish is mostly in a form that is not harmful. Particularly cold water fin fish, crustaceans, and mollusks may contain large amounts of organo-arsenic compounds, that have no known mammalian toxicity. In addition, certain edible marine foods, such as seaweed or kelp, may contain arsenosugars that are without recognized toxicity. These compounds are well absorbed from the gastrointestinal tract, and in the case of arsenobetaine, are largely excreted unchanged in the urine. Exposure to low levels of arsenic can cause nausea and vomiting, decreased production of red and white blood cells, abnormal heart rhythm, damage to blood vessels, and a sensation of "pins and needles" in hands and feet, and over the long term can cause darkening of the skin and the appearance of small "corns" or "warts" on the palms, soles, and torso. Major concerns for man is As poisoning from the large amount of As_2O_3 in pesticides and fungicides
3 As	Common poisoning is by accidental ingestion from pesticides – for example, rat and ant poison High As found in run from mine tailings - the Mo mines in northern BC

	As is readily absorbed by fish - eg black bass up to 40 ppm As in their livers AsH_3 and $AsCl_3$ are hemolytic agents - meaning that these compounds break up red blood cells leading to anaemia High concentrations in man lead to lung and skin cancers As(III) inactivates sulfhydryl enzymes and acts as an antimetabolite in competing for phosphate in ADP/ATP energy storage **BUT …As deficiency in animals has been demonstrated - in goats - growth retardation, followed by death** In January 2001, the EPA revised the standard allowable level of arsenic in drinking water from 50 parts per billion (ppb) to 10 ppb. Levels must reach this lower amount by 2006. However, some experts believe that an even tougher standard of 3 parts per billion should have been adopted. **Current problem across N. India - Bangladesh where drinking water supplies are contaminated with As.** Exposure to high levels of arsenic can cause death – major problem is from drinking water where over 1000 million people are currently exposed to As level considered unsafe. **To come?** Long term exposure from use of 'green lumber'. Long term effects of polluted (natural and man-made) drinking water in North America. Arsenic occurs in three main chemical forms in marine ecosystems: inorganic arsenic predominates in water and sediments; a group of closely related arsenicals known as arsenosugars occurs in marine algae; and arsenobetaine is the major arsenical in marine animals. **Lewisite,** which is dichloro(2-chlorovinyl)arsine, was used in World War I as a chemical weapon. It acted to disable soldiers by forming blisters on exposed skin and damaging the lungs if the

	vapour was inhaled. Lewisite is administered as a gas. The antidote for lewisite is British anti-lewisite (BAL), which is injected and forms a chemical compound with the agent, thereby removing it from the body. BAL (also known as 2,3-dimercaptopropan-1-ol) is still used to treat people who have been poisoned by arsenic, mercury and other heavy metals.
3 As	Acute: At 10 ppm, arsine rapidly causes delirium, coma and death. Chronic: Chronic accumulation of arsenic in the body leads to abnormally dark, dirty grey hyperkeratotic skin lesions. Chronic arsenic toxicity in man produces a range of clinical manifestations. **However, skin manifestations are the most diagnostic.** Several studies have shown that inorganic arsenic can increase the risk of lung cancer, skin cancer, bladder cancer, liver cancer, kidney cancer, and prostate cancer. Organic arsenic compounds are less toxic than inorganic arsenic compounds. The Groundwater in India and Bangladesh is contaminated with As. A terrible tragedy – no real relief in sight. There is no effective therapy for health effects due to severe As poisoning What causes elevated As in ground waters?

Arsenic review – complete from here and the lecture text

Arsenic exposure routes	
Health effects – major manifestation and the most diagnostic .	
Why is water polluted so much?	
Treatment possible?	

4 Cd	Cadmium is one of several "trace metals" existing in nature in small quantities that have no known nutritive value and are capable of producing a toxic effect. Cadmium (Cd) is a soft, silvery-white metal that has many industrial uses. It is currently used primarily for the production of nickel-cadmium batteries (35%) and for

	metal plating (30%). It is also used for pigments in plastics as a stabilizer and for alloys and other miscellaneous uses. Several deaths from acute exposure have occurred among welders who have unsuspectingly welded on cadmium-containing alloys or working with silver solders. There are many sources of cadmium in the environment. It is released into the air from smelters (of zinc, lead, and copper); from the burning of plastics, pigments, Ni-Cd batteries, motor oil, rubber goods and tires, and other cadmium-containing items.
4 Cd	Cadmium can enter waterways from industrial waste waters (especially metal alloy and electroplating industries) and by dissolution from galvanized iron objects whose zinc coating contains cadmium. Cadmium is also widely distributed in the earth's crust at an average concentration of about 0.1 mg/kg. The toxic action of cadmium involves the replacement of zinc in enzymes by cadmium, which prevents proper functioning of the enzymes. Reduction in deposition of Ca in bones, and the breakdown of the kidneys. Know the ways Cd enters the environment – major commercial products; Consumption of a diet rich in shellfish can double the intake of dietary cadmium without producing significant impacts upon blood cadmium. Ingestion of cadmium in food is the major source of cadmium for non-smokers. Major problem from exposure of farming communities eating vegetables, fruit, rice, grown in contaminated soils. The kidney is the critical target organ for the general population as well as for occupationally exposed populations. Cadmium stays in the body for a long time (20- 40 years) and accumulates

	after long-term exposure to even low levels. Metallothionein has a low MW (6,600 daltons); 60-62 a.a. (30% are CYS); no aromatic a.a; sequence conserved across many organisms; especially CYS-X-CYS and CYS-X-X-XYS (X another amino acid); mammalian MT binds 7 M^{2+} ; binding affinity: Ag>>Hg, Cu >> Cd>Zn. MT is an inducible protein (the reason why not initially bound to MT in liver) Cd itai-itai disease – know the history
Cadmium exposure routes	
Health effects – major manifestation and the most diagnostic .	
Why is water polluted so much?	
Treatment possible?	
5 Hg	**Mercury. Historical events: Minamata; Iraq; Northern Ontario. Brazil – gold extraction from the Amazon River.** Where is Hg released from? Industrial? Commercial? In our houses? Why not eat fish? Mercury poisoning can result from vapor inhalation, ingestion, injection, or absorption through the skin. There have been several recorded instances of mercury poisoning, of which the most well-known occurred at Minimata Bay and nearby Niigata, Japan, in 1952, 1965, and 1973. Cases of mercury poisoning occurred in Iraq in 1961, in Pakistan in 1963, and in Guatemala in 1966. In 1970 Ontario, Canada, banned all fishing in the St. Clair River, Lake St. Clair, and the Detroit River. Fishing is restricted in a great many lakes and rivers. The most common significant exposure for most people is to mercury vapor from amalgam fillings. Most people with several amalgam fillings have daily exposure exceeding the U.S. government health guideline for mercury. Likewise, a major exposure source of infants and

	young children is from placental transfer from their mother's amalgam fillings and breast-feeding. Another major exposure source to infants is from thimerosal used in vaccinations as a preservative. There is considerable controversy about whether large numbers of infants are exposured above Government health guidelines for mercury, and whether there is a connection between this and theose infants suffering from neurological problems such as autism and ADD.
5 Hg	**Mercury. Historical events: Minamata; Iraq; Northern Ontario. Brazil – gold extraction from the Amazon River.** Where is Hg released from? Industrial? Commercial? In houses? Why not eat fish? Mercury poisoning can result from vapor inhalation, ingestion, injection, or absorption through the skin. There have been several recorded instances of mercury poisoning, of which the most well-known occurred at Minimata Bay and nearby Niigata, Japan, in 1952, 1965, and 1973. Cases of mercury poisoning occurred in Iraq in 1961, in Pakistan in 1963, and in Guatemala in 1966. In 1970 Ontario, Canada, banned all fishing in the St. Clair River, Lake St. Clair, and the Detroit River. Fishing is restricted in a great many lakes and rivers. The most common significant exposure for most people is to mercury vapor from amalgam fillings. Most people with several amalgam fillings have daily exposure exceeding the U.S. government health guideline for mercury. Likewise, a major exposure source of infants and young children is from placental transfer from their mother's amalgam fillings and breast-feeding. There is considerable controversy about whether large numbers of infants are exposed above Government health guidelines for mercury, and whether there is a connection between this and

	theose infants suffering from neurological problems such as autism and ADD. A major source of phenyl mercury is from mercury in paint, where many have been exposed to dangerous levels. The major source of exposure to organic(methyl) mercury is from fish and shellfish, but inorganic mercury has also been found to be methylated in the body by bacteria, yeast, etc.. Significant levels of various forms of organic mercury have also been documented from dental work such as root canals and gold crowns over amalgam base). Mercury vapor is the form that most readily crosses cellular membranes including the blood-brain barrier and placenta of pregnant women, and results in the highest levels in the major organs such as the brain, heart, and kidneys for a given level of exposure. But the average half-life of vapor in the blood is only 3 seconds so blood tests are not a good measure of such exposure. For similar reasons hair mercury is a less accurate measure of body inorganic mercury burden than for the other metals. Both mercury vapor and organic mercury have been found to be highly toxic and to have independent and synergistic effects at very low levels. However developmental effects have been found at comparable or lower levels from mercury vapor than from organic or inorganic exposure, and it has been well established that the primary exposure for most people and children is from mercury vapor.
5 Hg	Seafood and fish have often been found to have high levels of organic mercury, cadmium, and arsenic. For those eating significant amounts of sea food, the levels in the diet can be monitored by direct food testing or stool test for current exposure levels, or by hair or blood test.. Fish and seafood from areas known to contain high levels of toxic metals should be eaten only occasionally if at all, depending on levels. Those who eat a lot of freshwater fish or seafood often have levels of mercury or some other metal exceeding government guidelines. Hair tests offer a reasonable reliable low cost method of assessing the level of many toxic metals in one test. The kidneys concentrate mercury, which then reacts with other proteins and enzymes in the

	kidney cells, eventually killing the cell can also damage the central nervous system accumulates in food chains. Common sources of exposure include mining, production, and transportation of mercury, as well as mining and refining of gold and silver ores, particularly in the Amazon River in Brazil. High mercury exposure results in permanent nervous system and kidney damage. Major concerns: effects high levels in fish world-wide. Differences between inorganic and organic mercury compounds Symptoms of methylmercury poisoning, are? The history of Minamata. Methylmercury produces a much more devastating human illness than inorganic mercury, affecting primarily the central nervous system with many neurological disturbances including paralysis, "tunnel vision" and blindness.
	Overall from this unit – summarize the features of the 4 toxic metals – source, exposure, human toxicity, cure. What chelators are available?

Mercury exposure routes	
Health effects – major manifestation and the most diagnostic .	
Why is food polluted so much?	
Treatment possible?	

END OF MATERIAL DIRECTLY TESTED IN CHEMISTRY 2211A –
See the Extra Materials File for additional, but non-tested background.