

Lead and Mercury (...and Fish)

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Treatment of Lead Poisoning

Old School Approaches

“The treatment of acute [*insert metal here*]-poisoning consists in the evacuation of the stomach, if necessary, the exhibition of the sulphate of sodium or of magnesium, and the meeting of the indications as they arise. The Epsom and Glauber’s salts act as chemical antidotes, by precipitating the insoluble sulphate of [*insert metal here*], and also, if in excess, empty the bowel of the compound formed. To allay gastrointestinal irritation, albuminous drinks should be given and opium freely exhibited...”

Wood, HC: Therapeutics Materia Medica and Toxicology, 1879

Treatment of Lead Poisoning

Old School Approaches

“If possible, the rapid administration of 2 oz. (6-7 heaping teaspoonfuls) of Magnesium sulfate (Epsom Salts) or Sodium sulfate (Glauber’s Salt) in plenty of water. Alum (aluminum potassium sulfate) will also be useful in 4 gm (60 gr.) doses (dissolved) repeated. Very dilute Sulfuric acid may be employed (30 cc of a 10 % solution diluted to 1 quart). All soluble sulfates precipitate lead as an insoluble sulfate...”

Lucas, GW: The Symptoms and Treatment of Acute Poisoning; 1953

Treatment of Lead Poisoning

Old School Approaches

“Induce vomiting or gastric lavage...”

“Demulcents such as white of egg or cream or milk etc...”

“Purge with magnesium sulfate, 15 gm in 1/2 glass of warm water...”

Kaye, S: Handbook of Emergency Toxicology; 1954

Treatment of Lead Poisoning

Old School Approaches

“Demobilize lead from blood into bones with an alkaline diet and excess calcium gluconate or lactate or sodium citrate, IV plus vitamin D...”

“When symptoms have subsided, gradually mobilize the lead from the bones into circulation->kidney->excreted. This should be done by acid shift with extreme caution...”

Kaye, S: Handbook of Emergency Toxicology; 1954

Treatment of Lead Poisoning

Old School Approaches

“Do not give BAL! Calcium versenate (CaEDTA) promises to be especially effective and safe for the rapid excretion of lead...”

“Patient must avoid alcohol during treatment...”

Kaye, S: Handbook of Emergency Toxicology; 1954

Contemporary Approaches Diagnosis and Treatment of Heavy Metal Poisoning

- Differential diagnoses are enormous
- Great deal of controversy involving laboratory testing and treatment
- Presence of metal does not imply causation
- In confirmed cases, removal from source is the best and most significant part of treatment

Laboratory Testing of Heavy Metals

- Blood testing:
 - Whole blood levels for Lead and Organic Mercury
 - No consistent use for blood testing alone with other metals
- Urine testing
 - Quantitative spot analysis inconsistent
 - Significant excretion variation throughout day

Laboratory Testing of Heavy Metals

- Hair testing
 - All metals deposit in *and on* hair
 - No lab has standardized results or reference ranges
 - No correlations have ever been found between hair levels and symptoms or exposure rates
 - Severely limited in use
 - May be useful in neonatal hair
 - May be useful in population studies
- Saliva testing
 - No clinical use whatsoever
- Iridology (?)

Laboratory Testing of Heavy Metals

- GOLD STANDARD
 - 24-hour urine collection for quantitative analysis
 - Best estimate of total body burden (except Pb and organic mercury)
 - Reasonable for most metals, but best for arsenic and inorganic mercury
- Levels slightly above reference ranges must be treated with caution

Lead

Lead Poisoning Sources

- Children
 - History of pica (Iron deficiency often concurrent)
 - Paint chips, dirt, folk remedies (“Azarcon”), candy, pottery, makeup
- Adults
 - Inadvertent occupational exposure
 - Pottery, folk remedies (“Litargirio”)

Lead Poisoning

Clinical Effects

- Can affect almost every organ system.
 - Central and peripheral nervous systems
 - Cardiovascular
 - Gastrointestinal
 - Renal
 - Endocrine
 - Hematologic systems
- Teratogenicity

Lead Poisoning

Acute Toxicity

- Young children: history of pica
- Adults: inadvertent occupational exposure
- Reversible renal injury – mild-to-moderate exposure
- Acute Lead Encephalopathy:
 - Most often from rapidly absorbed lead salts
 - Hepatic injury, hemolysis, anorexia, vomiting, malaise, and seizures due to increased intracranial pressure; chronic exposure effects may also be present

Lead Poisoning

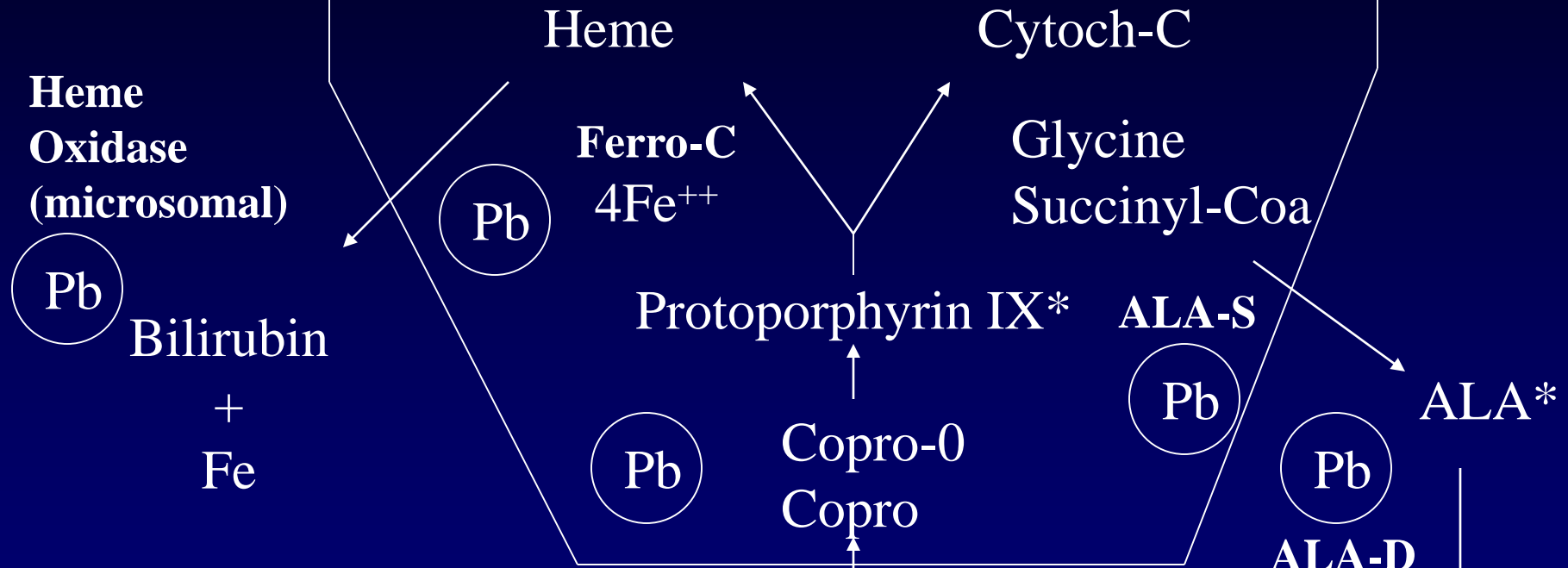
Chronic Toxicity

- Diagnosis much more vague
- Children
 - Weight loss, weakness, abdominal complaints, anemia
 - Abnormal cognitive development: first signs in children may be subtle neurobehavioral deficits adversely affecting classroom behavior and social interaction;
- Adults
 - Vague gastrointestinal and CNS complaints
 - Hypertension
 - Wrist-drop/foot-drop and colic quite rare

Chronic and Long Term Toxicity- Pathophysiology

- Lead has affinity for sulfhydryl groups and is toxic to zinc-dependent enzyme systems
 - Heme synthesis: hemoglobin, cytochromes
 - Steroid metabolism and membrane integrity
 - Interference in vitamin D synthesis in renal tubular cells (conversion of 1-hydroxyvitamin D to 1,25-hydroxyvitamin D)

Mitochondrion



ALA- aminolevulinic acid
↑ in plasma and urine
COPRO- coproporphyrinogen
↑ in urine
Protoporphyrin
↑ accumulates in the RBC

Copro* ← Uropor ← PBG

General Signs and Symptoms of Lead Toxicity

- Fatigue
- Irritability
- Lethargy
- Paresthesia
- Myalgias
- Abdominal pain
- Tremor
- Headache
- Vomiting
- Weight loss
- Constipation
- Loss of libido
- Motor neuropathy
- Encephalopathy
- Cerebral edema
- Seizures
- Coma
- Severe abdominal cramping
- Epiphyseal lead lines in children (growth arrest)
- Renal failure

Lead Poisoning

Pathophysiology

- Anemia
 - Heme synthesis – several enzymes inhibited via binding to sulfhydryl groups
 - Build-up of delta-aminolevulinic acid, coproporphyrin and zinc protoporphyrin
 - Microcytic, hypochromic; Fe deficiency
- Neuronal effects
 - Inhibition of dendritic arborization, especially in developing brains

Range of Lead-induced Health Effects in Adults and Children

Blood lead levels	Adults	Children
10 µg/dL	Hypertension may occur	<ul style="list-style-type: none"> •Crosses placenta •Impairment IQ, growth •Partial inhibition of heme synthesis
20 µg/dL	Inhibition of heme synthesis Increased erythrocyte protoporphyrin	Beginning impairment of nerve conduction velocity
30 µg/dL	<ul style="list-style-type: none"> •Systolic hypertension •Impaired hearing(↓) 	Impaired vitamin D metabolism
40 µg/dL	<ul style="list-style-type: none"> •Infertility in males •Renal effects •Neuropathy •Fatigue, headache, abd pain 	Hemoglobin synthesis inhibition
50 µg/dL	Anemia, GI sx, headache, tremor	Colicky abd pain, neuropathy
100 µg/dL	Lethargy, seizures, encephalopathy	Encephalopathy, anemia, nephropathy, seizures

Childhood Lead Poisoning

- “Childhood lead poisoning” was in the 90’s defined as a blood lead level of 10 µg/dl

Table 57-3. Interpretation of Blood Lead Test Results and Follow-up Activities: Class of Child Based on Blood Lead Concentration

Class	Blood Lead Concentration (µg/dL)	Comment
I	≤9	A child in class I is not considered to be lead poisoned.
IIA	10-14	Many children (or a large proportion of children) with blood lead levels in this range should trigger communitywide childhood lead poisoning prevention activities. Children in this range may need to be rescreened more frequently.
IIB	15-19	A child in class IIB should receive nutritional and educational interventions and more frequent screening. If the blood lead level persists in this range, environmental investigation and intervention should be done.
III	20-44	A child in class III should receive environmental evaluation and remediation and a medical evaluation. Such a child may need pharmacologic treatment of lead poisoning.
IV	45-69	A child in class IV needs both medical and environmental interventions, including chelation therapy.
V	≥70	A child with class V lead poisoning poses a medical emergency. Medical and environmental management must begin immediately.

Childhood Lead Poisoning

- The average lead level of American children is 2 $\mu\text{g}/\text{dl}$
- 8.9% of American children have lead poisoning
- Lead intoxication is more prevalent in minority groups and among those living in the northeast

Epidemiological Perspectives

- Lead toxicity is known to all cultures of the world, and efforts at reducing the prevalence of lead toxicity are common in industrialized countries

Epidemiological Perspectives USA

- National Health and Nutrition Examination Survey (NHANES) 1999-2002 gave overall prevalence of lead toxicity in the US population as 0.7% compared to 2.2% between 1991 and 1994

Epidemiological Perspectives USA

- - Non-Hispanic black and Mexican American children living in inner-city, old, dilapidated buildings are at the highest risk for developing lead toxicity
 - 1.4% in African American children and 1.5% in Mexican American children have blood lead levels higher than $0.5 \mu\text{M/L}$ in children aged 1 to 5 years compared with 0.5% for non-Hispanic white children

Epidemiological Perspectives

France

- More than 5% of adults and 2% of children aged 1 to 6 years have lead levels greater than $0.5 \mu\text{M/L}$

Epidemiological Perspectives Australia

- In mid 90s, studies of children living in non-point source areas of Sydney, NSW found over 12% had blood lead levels $> 0.5 \mu\text{M/L}$ with over 50% $> 0.5 \mu\text{M/L}$ in poorer socio-economic areas
- In 1991 in Broken Hill (a mining town located in the semi-arid region of western NSW) one quarter of children had blood lead levels $> 1.25 \mu\text{M/L}$

Why do we still consider Lead to be a significant problem?

- Emerging data on the effects of lower lead levels
 - Effect on brain development/IQ
 - Potential influence on adult behavior from childhood exposures
- Multiple sources of lead
 - Some things we can control....
 - Some things we can't...

Why do we still consider Lead to be a significant problem?

- CDC “reference level”: 5mcg/dL
- What does that mean?
- What is meant by “there is no safe level of lead?” Is it the correct thing to say?

Neurotoxicity of Lead in Childhood

- Mental retardation in severe lead intoxication
- ↓ 5 points in IQ for every 10 $\mu\text{g}/\text{dl}$ ↑ in blood lead level- population based studies
- Other adverse developmental outcomes:
 - Aggression
 - Hyperactivity
 - Antisocial behaviors
 - Learning disability- impairment in memory, auditory processing, and visual-motor integration. The IQ is normal. These effects has been demonstrated with blood lead levels as **low as 6 $\mu\text{g}/\text{dl}$**

Diagnosis

- Evaluation of clinical symptoms and signs
- CBC
- Serum iron levels, TIBC, ferritin
- Abdominal radiographs (for recent ingestion of lead-containing material)
- Whole blood lead level
- X-ray fluorescence (XRF)- to assess body burden (not widely available)

Lead Poisoning Treatment

- Removal from source of exposure
- Whole bowel irrigation for retained metal
- Chelation if indicated (BAL, EDTA, DMSA)... BAL/EDTA for encephalopathy. Role for others is still not fully determined.

Nutritional Supplementation

- Iron supplementation
- Calcium supplementation – calcium rich foods
- Phosphorus supplementation
- Frequent food consumption- regular meals + snacks

Chelation Therapy

- BLL > 70 $\mu\text{g}/\text{dl}$ or encephalopathy
 - Hospital admission
 - Administration of BAL/EDTA
- BLL > 45 $\mu\text{g}/\text{dl}$ - oral chelator (DMSA)
- BLL 25-45 $\mu\text{g}/\text{dl}$ - if these levels persist despite environmental intervention

Mercury

Mercury Poisoning Sources

- Elemental:
 - Thermometers, paints, ceramics, batteries, amalgams
 - Inhaled Hg vapor
- Inorganic:
 - Industry (photography, explosives, inking, cosmetics)
- Organic:
 - Bactericides/Fungicides
 - Fish
 - Farming
 - Embalming preparations

Mercury Poisoning

Clinical Effects

- Can affect almost every organ system.
 - Central and peripheral nervous systems
 - Cardiovascular
 - Gastrointestinal
 - Renal
 - Hematologic systems
- Teratogenicity

Mercury Poisoning

Clinical Effects

- Elemental:
 - Acute pneumonitis, corrosive bronchitis, embolism
 - May be preceded by stomatitis, colitis, lethargy, confusion, fever/chills, dyspnea, metallic taste
 - Chronic Triad: *tremor, gingivitis, erethism* (insomnia, shyness, memory loss, emotional lability, nervousness, anorexia)
 - Other findings
 - Corneoscleral junction, lens damage
 - Peripheral neuropathy

Mercury Poisoning

Clinical Effects

- Inorganic:
 - Acute corrosion – patient may die within hours
 - Shock, electrolyte imbalances, protein loss
 - Chronic effects similar to elemental mercury
 - Long-term behavioral impairment
 - Subclinical psychomotor and neuromuscular changes
 - Renal effects may resemble chronic renal failure

Mercury Poisoning

Clinical Effects

- Organic: (may take weeks)
 - Fatigue, ataxia, dyscoordination, tremor, spasticity, weakness (hands, face, legs)
 - Numbness: mouth, stocking-glove
 - Deafness, tunnel vision, visual field constriction, scanning speech, dysphagia
 - poor concentration/memory, emotional lability, depression

“Minimata Disease”

- 1956, Minamata Bay in Kumamoto Prefecture, and in 1965, in the Agano River basin in Niigata Prefecture
- Caused by the consumption of fish and shellfish contaminated by methylmercury compound discharged from the Chisso Corporation chemical plant.

“Minimata Disease”

- Numbness, ataxia, peripheral visual field loss, hearing loss, weakness
- “Dancing Cat Fever”
- At the end of March 2001, 2,955 Minamata Disease patients were certified (1,784 deaths)

Mercury Poisoning

Pathophysiology

- Binding to enzymatic sulfhydryl groups
 - Enzymes of cellular function
 - Impaired metabolism of carbohydrates at pyruvic acid level
- Binding to carboxyl, amide, amine, phosphoryl groups

Mercury Poisoning

Pathophysiology

- Elemental mercury
 - Lung is primary target for mercury vapor
 - Poor GI absorption
 - Moderate absorption via alveoli (remains in elemental form)
 - Some systemic absorption
 - Oxidized by RBC's and tissues to Hg^{2+}
 - Some elemental Hg passes through blood-brain-barrier
 - Accumulation in kidney – renal dysfunction RARE

Mercury Poisoning

Pathophysiology

- Inorganic mercury:
 - 10-15% absorbed from GI tract
 - Much remains bound to mucosa
 - Remains in ionized form post absorption
 - Very little passes into CNS
 - High renal accumulation (terminal portion of proximal tubule), leading to ATN (anuria within 24h in 50% of cases)
 - Some liver/spleen accumulation (mild)

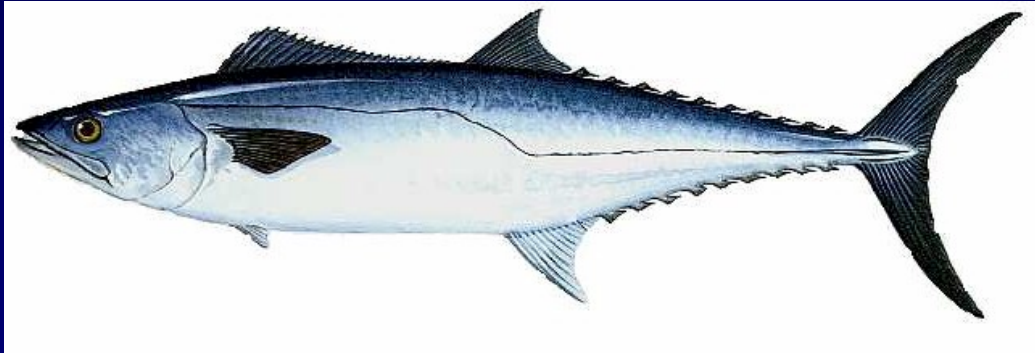
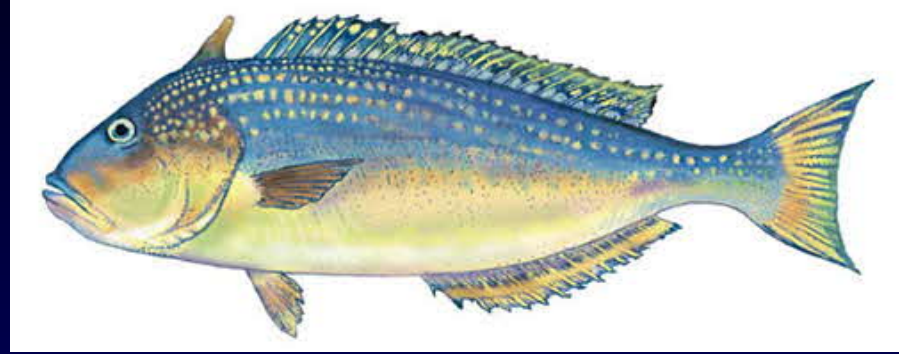
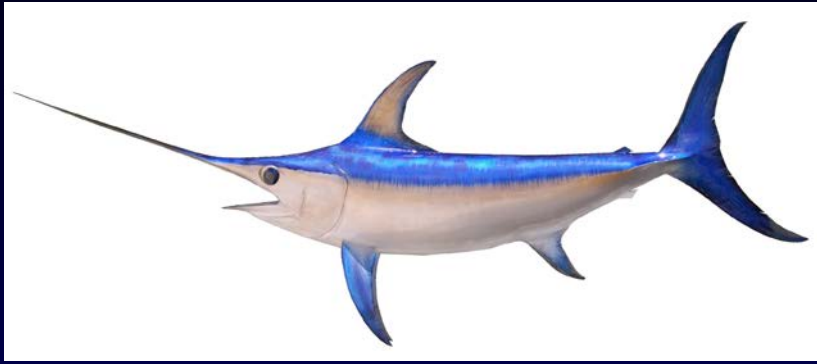
Mercury Poisoning

Pathophysiology

- Organic mercury:
 - 90% absorption from GI tract
 - Distribution: liver, kidney, RBC, brain, hair, epidermis
 - Rapid crossing over blood-brain barrier likely after conjugation to glutathione: deposition in cerebellum, occipital lobe, precentral gyrus;
 - Binds to typical enzyme moieties
 - Also inhibits choline acetyltransferase, may lead to some anticholinergic signs and symptoms, muscular weakness

Mercury Poisoning Treatment

- Removal from source of exposure
- Whole bowel irrigation for retained metal (need to perform early)
- Supportive care for fluid/electrolyte disturbances, renal failure, and pulmonary injury
- Chelation if indicated (BAL, EDTA)



GOOD CHOICES IF YOU WANT MORE FISH

Lowest-mercury fish

A 132-pound person can safely eat 36 ounces per week.

A 44-pound child can safely eat 18 ounces per week.



Shrimp
(most wild and U.S. farmed)



Scallops ①



Sardines



Wild and Alaska salmon
(canned or fresh)



Oysters ①



Squid
(domestic)



Tilapia ①

Low-mercury fish

A 132-pound person can safely eat 18 ounces per week.

A 44-pound child can safely eat 6 ounces per week.



Haddock



Pollock



Flounder and sole
(flatfish)



Atlantic croaker



Crawfish
(domestic)



Catfish ②③



Trout ①



Atlantic mackerel



Crab ①



Mullet

- ① You may want to consider country of origin and choose domestic rather than imported if possible.
- ② Always follow any local alerts regarding when shellfish can be safely harvested and eaten. Eating shellfish raw always carries additional risks of foodborne illness, and it's not recommended for vulnerable groups.
- ③ If wild caught (which includes being fished from local rivers and lakes), check with your state health department for information about PCBs especially for these fish; it's a good idea to check for anything on this list if you are concerned about PCBs.

Fish is Good Food

- ❖ American Heart Association—recommends 2 fish meals a week. Excellent source of protein and omega-3 fatty acids
- ❖ Omega-3 fatty acids may help reduce risk of heart disease, hypertension, cancer, other chronic diseases, and are important for brain & vision development



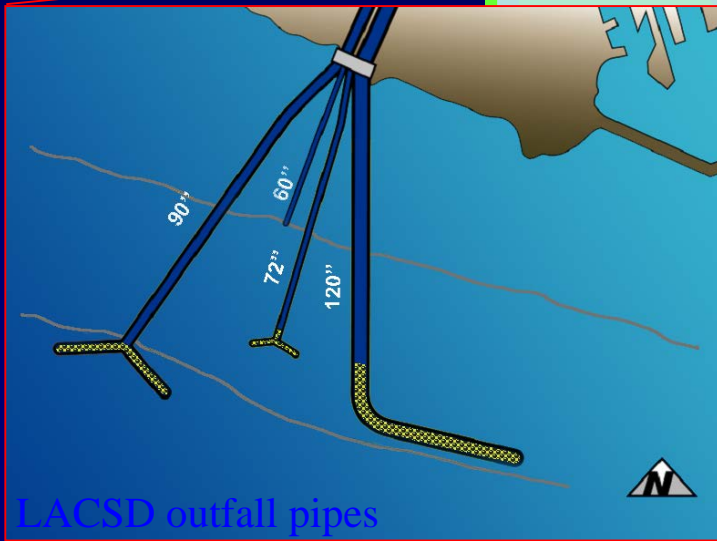
Sources of Contamination

❖ Mercury

- People and industry
- Naturally present in environment



The problem in L.A. and Orange Counties



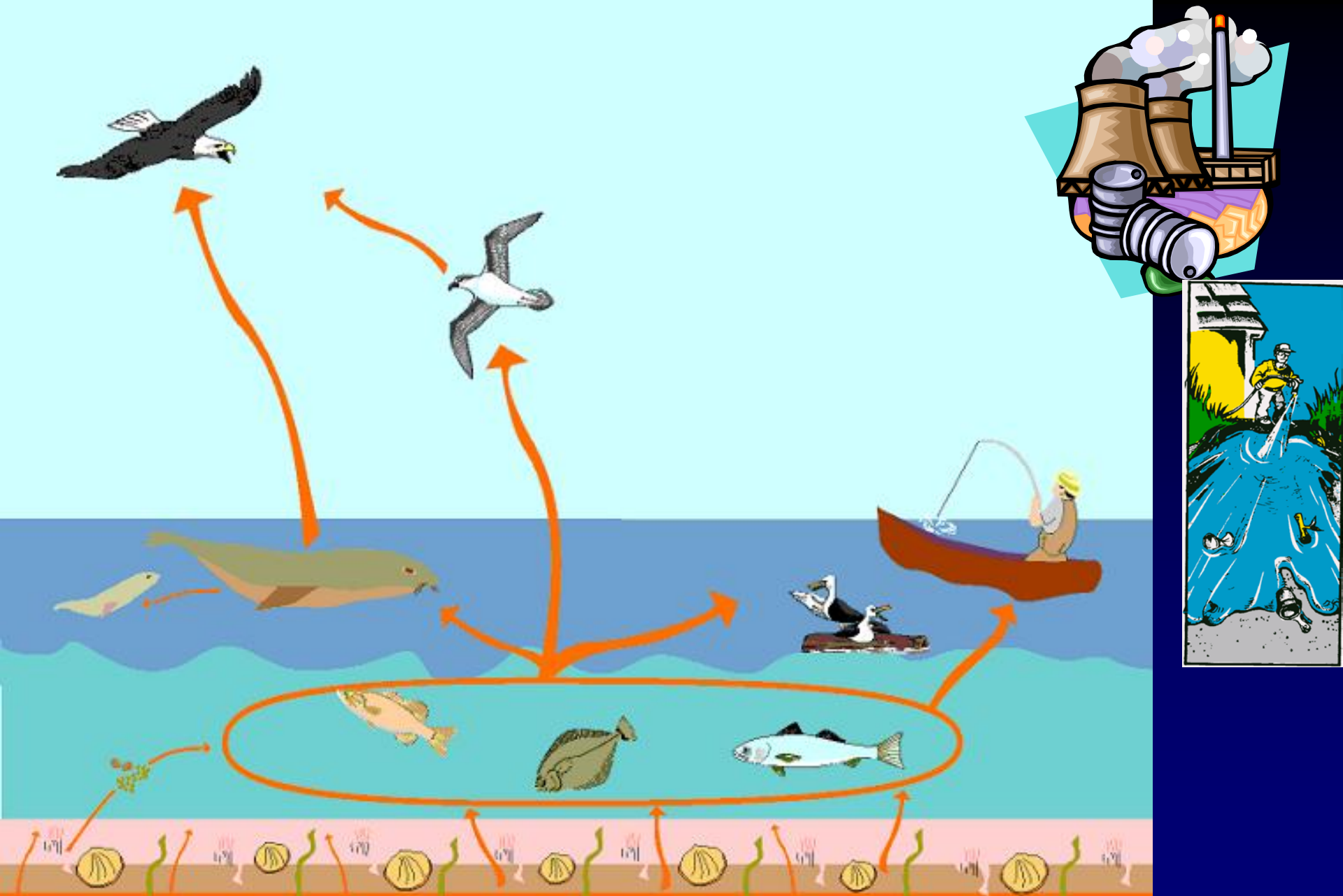
Chemicals in Fish: Mercury

- Power plants
- Incinerators, boilers
- Chlor-alkali industry
- Cement kilns
- Mining waste
- Consumer products



Builds up in fish protein tissues (ex – fillet)



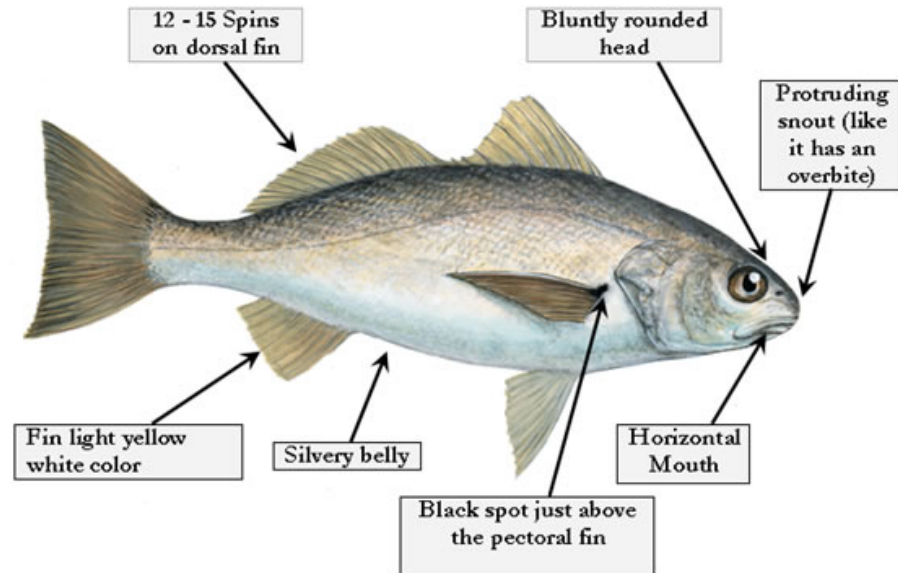


How Chemicals Get into Fish

PCBs and DDT extend the list of “Bad Fish”

❖ Do Not Eat the following fish from the Red Zone:

1. White Croaker
2. Barred Sand Bass
3. Black Croaker
4. Topsmelt
5. Barracuda



Do Not Eat



White Croaker



Barred Sand Bass



Black Croaker



Topsmelt



Barracuda

Advice only applies to fish caught in the red area below



Fish caught in this area are contaminated with harmful chemicals.

PROTECT THE HEALTH OF YOU AND YOUR CHILDREN

Join with other fishermen and follow the advice in this booklet



Visit www.pvsfish.org/health for more information on safe fish eating guidelines.



ONLY EAT THE SKINLESS FILLET



ONLY EAT ONE SERVING PER WEEK

FOR ADULTS



The recommended serving of fish is about the size your hand.

Give children smaller servings.

FOR CHILDREN



It is safe to eat the skinless fillet of these fish 1 time a week



SCORPIONFISH
Minimum Size 10 Inches



HALIBUT
Minimum Size 22 Inches



PACIFIC BONITO
Minimum Size 24 Inches



QUEENFISH



PACIFIC MACKEREL



ROCKFISH



CORBINA



OPALEYE



SURFPERCH



PACIFIC SARDINE



SHOVELNOSE GUITARFISH



No minimum size limit for fish unless otherwise indicated

Use this ruler to measure your fish



Fish Preparation & Cooking Tips

- ❖ Eat only the skinless fillet of the fish
- ❖ DDTs and PCBs build up in the fatty parts of the fish.



Health Impacts: Factors to Consider

- ❖ Continuous low level exposure to chemicals that build up in the body increases risk of developing health problems
- ❖ Factors to consider:
 - Type of chemical
 - How much of the chemical is in fish
 - How much fish is eaten
 - How often fish is eaten

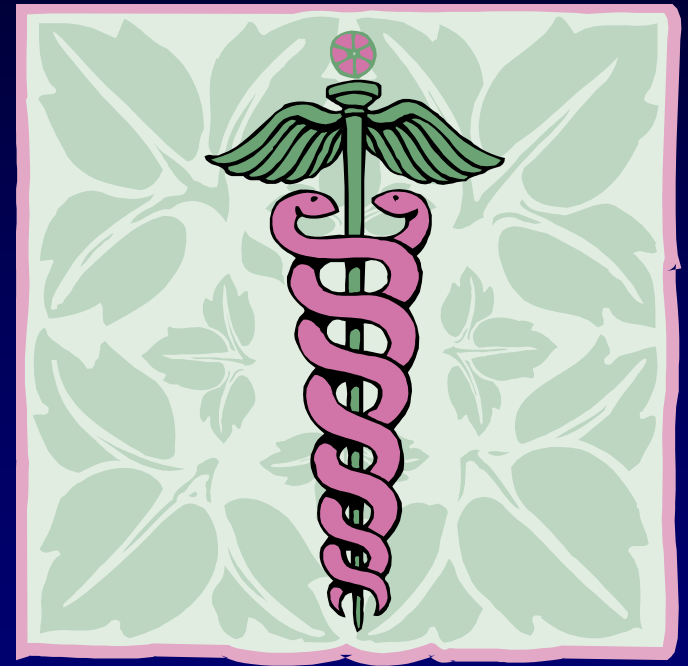
Health Effects: Sensitive Populations

- ❖ Fetuses, infants, children less than 17 years
- ❖ PCBs, DDTs, and Hg can be passed onto infants during pregnancy and through breast milk
- ❖ PCBs and Hg can affect
 - brain development and function
 - overall growth and development
 - mercury can hurt fetus before it hurts mother



Health Effects: DDTs & PCBs

- ❖ Potential for kidney, liver disease, cancer, reproductive and immune system problems
- ❖ Half life DDTs-10-20 yrs
- ❖ Half life PCBs-1-6 yrs



Fish Contamination Education Collaborative Public Messages

- ❖ Eat only the fillet of the fish, and limit total consumption
- ❖ Children and women of childbearing age are more sensitive to harmful chemicals and should be especially careful.

Resources

- ❖ Environmental Protection Agency (EPA)

<http://www.epa.gov/region09/index.html>

<http://www.epa.gov/region09/waste/sfund/index.html>

- ❖ Agency for Toxic Substances & Disease Registry (ATSDR) <http://www.atsdr.cdc.gov/>

- ❖ California Department of Toxics Substances Control (DTSC) <http://www.dtsc.ca.gov/>

- ❖ South Coast Air Quality Management District (AQMD) <http://www.aqmd.gov/>