



# EERC

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## ***Mercury Bioaccumulation and Toxicity are Inversely Related to Selenium***

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# Sources of Mercury Concerns

## Minamata Bay, Japan 1950s

- ~27 tons of Hg compounds released into the bay during 1932 to 1968
- grossly contaminated fish in the bay.
- Hundreds died from eating fish with high MeHg contents, unborn children were especially vulnerable.
- >3000 brain-damaged victims were diagnosed with “Minamata Disease”.



## Iraq 1971–1972

- Mercury fungicide-treated seed grain was baked into bread by starving Iraqi villagers, hundreds eventually died.
- Over 6000 were hospitalized.
- Hair Hg levels in the exposed villagers ranged as high as 674 ppm (*normal levels today are <1.4 ppm*).

<u>Present Sources</u>	<u>Hg Contents</u>
• Freshwater Fish	0.1–0.4 ppm
• Ocean Fish	0.6–0.8 ppm
• Top Predator Fish	> 1.0 ppm
• Fish in Polluted Lakes	> 10 ppm
• Fish from Minamata Bay	~ 50 ppm
• Whale Meat	~4 ppm
• Whale Liver	>1000 ppm

# The Conventional Hypothesis

## Maternal Methylmercury Exposures From Seafood Consumption Are Directly Associated with Adverse Child Neurodevelopment Outcomes

<u>Study Location</u>	<u>Exposure Outcomes</u>	<u>Results Support</u>	<u>Do Not Support</u>	<u>Results Conflict</u>
Minamata	Harm++	✓		
Iraq	Harm++	✓		
New Zealand	Harm	✓		
Faroe Islands	Harm	✓		
Seychelle Islands	No harm		✓	
United Kingdom	Benefited		✓	✓
United States	Benefited		✓	✓
Denmark	Benefited		✓	✓

Results of maternal methylmercury exposure studies do not support the conventional hypothesis, and the most appropriate studies conflict with it.

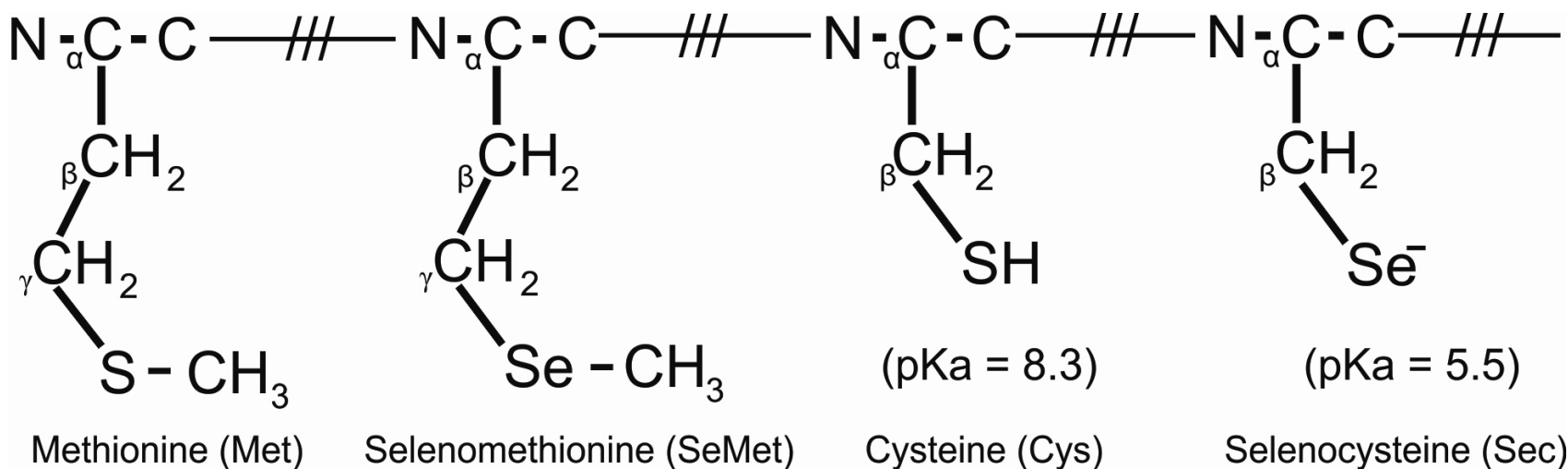
# Chemical Context

1 b	2 b	3 a	4 a	5 a	6 a	7 a	0
							He
		B	C	N	O	F	Ne
		Al	Si	P	S	Cl	Ar
Cu	Zn	Ga	Ge	As	Se	Br	Kr
Ag	Cd	In	Sn	Sb	Te	I	Xe
Au	Hg	Tl	Pb	Bi	Po	At	Rn

# Se-Physiology Background

- Selenium is essential for normal selenoenzyme functions.
- Selenoenzymes are produced in all cells of all animals.
- Selenium is the functional component of the 21st amino acid, selenocysteine (Sec), present at selenoenzyme active sites.
- Selenocysteine synthesis requires formation of selenide.
- Mercury binds to selenide better than any other partner.
- Brain selenoenzyme activities are normally unstoppable.
- Methylmercury inhibits selenoenzyme activities in brain.

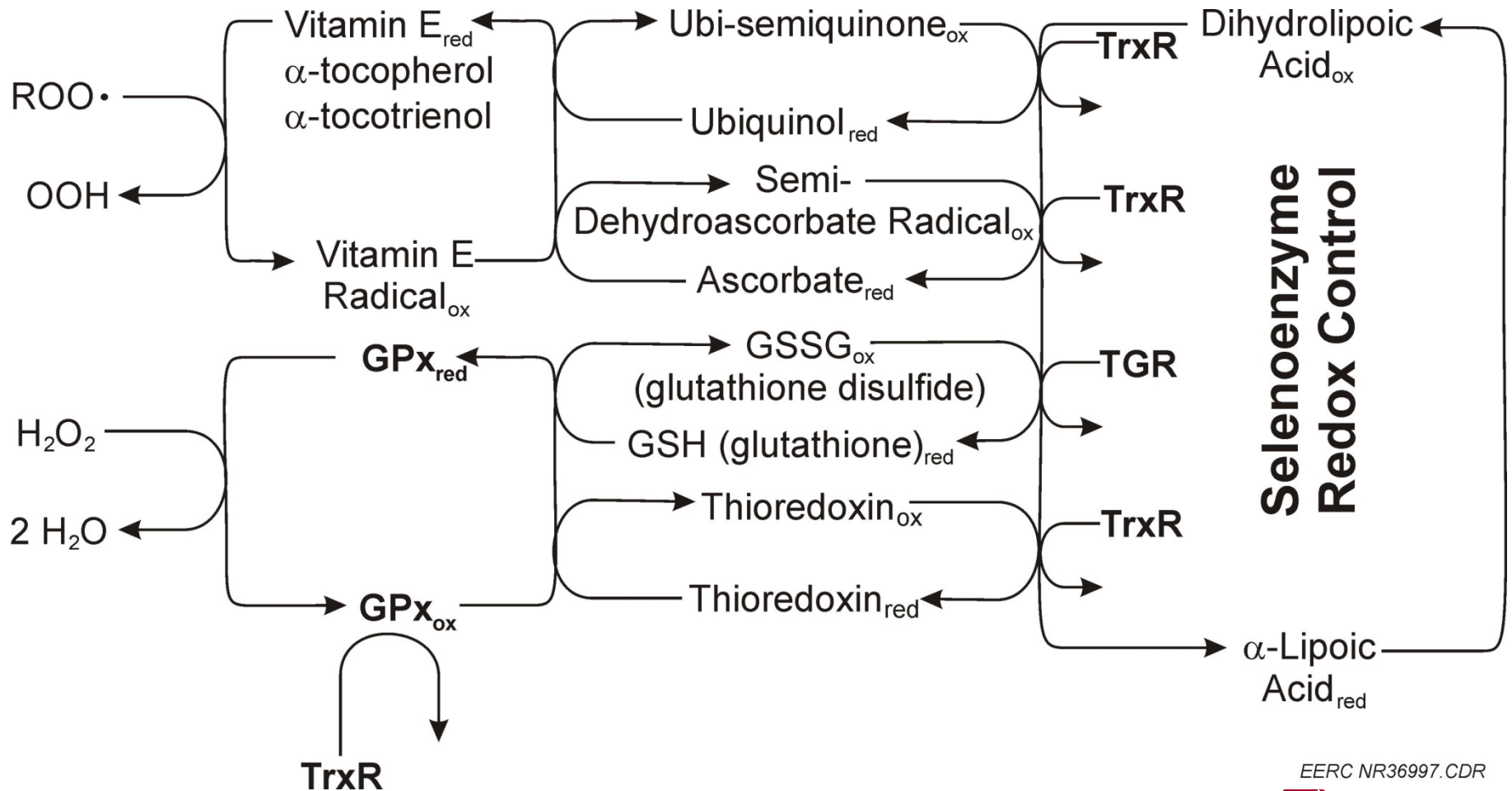
# Sulfur and Selenium Amino Acids



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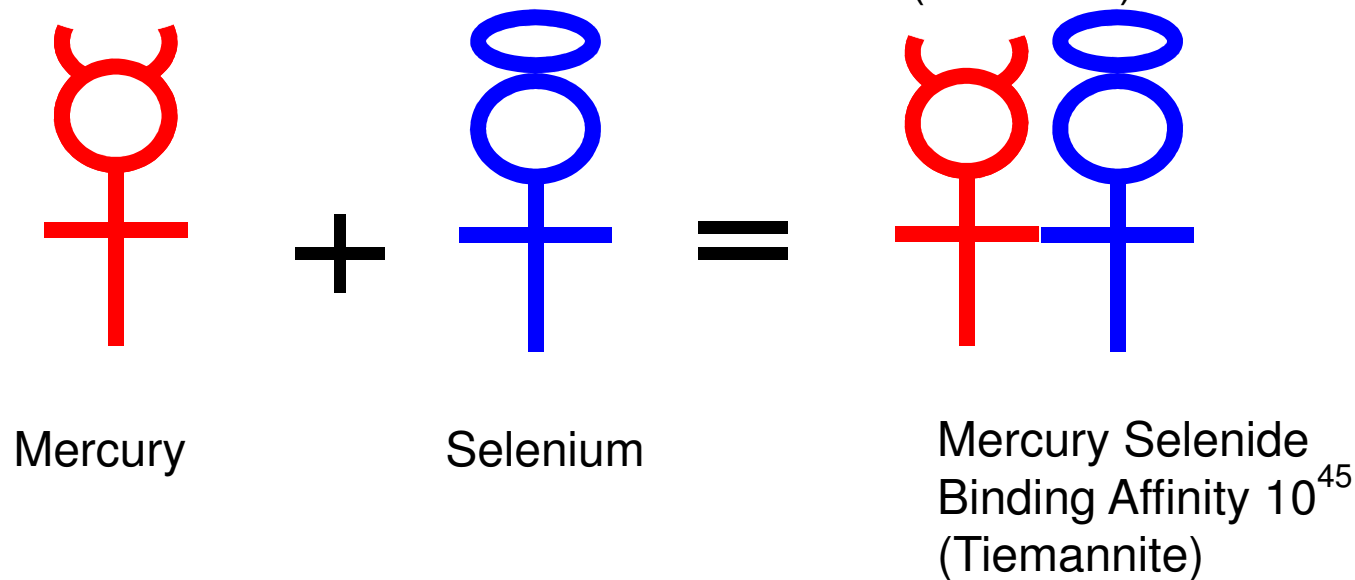
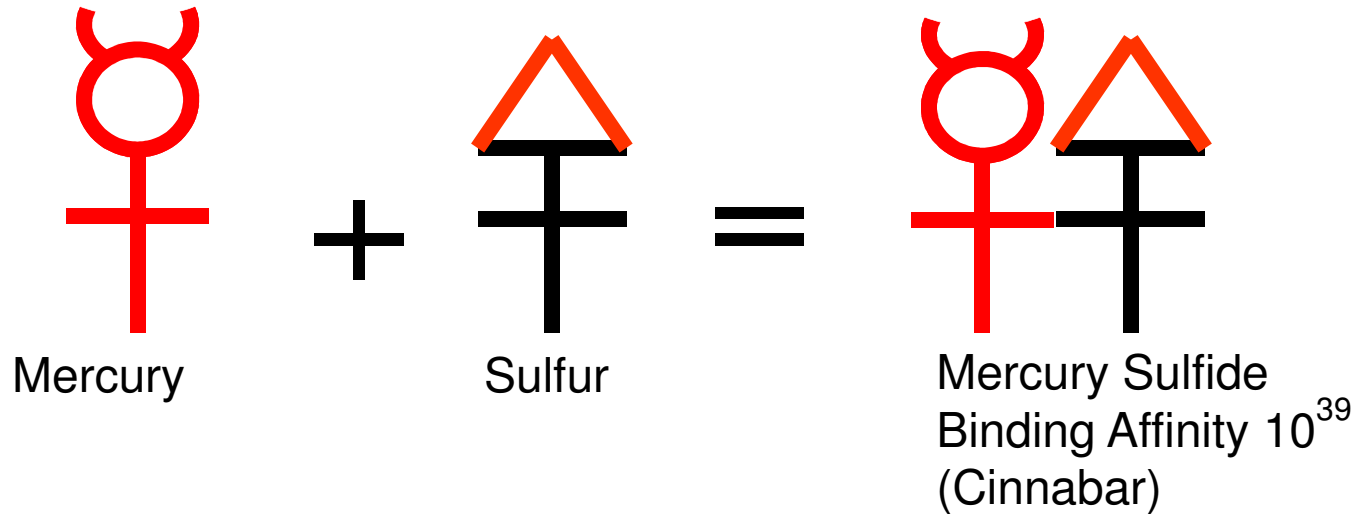
**The Se of selenocysteine is the most powerful intracellular nucleophile. Soft electrophilic toxicants selectively bind Se, irreversibly inhibiting selenoenzyme activities. This reaction is bimolecular. Assumptions that MeHg toxicity followed first-order reaction rate kinetics were incorrect, explaining why previous predictions have been unreliable.**

# Selenoenzymes in Redox Control



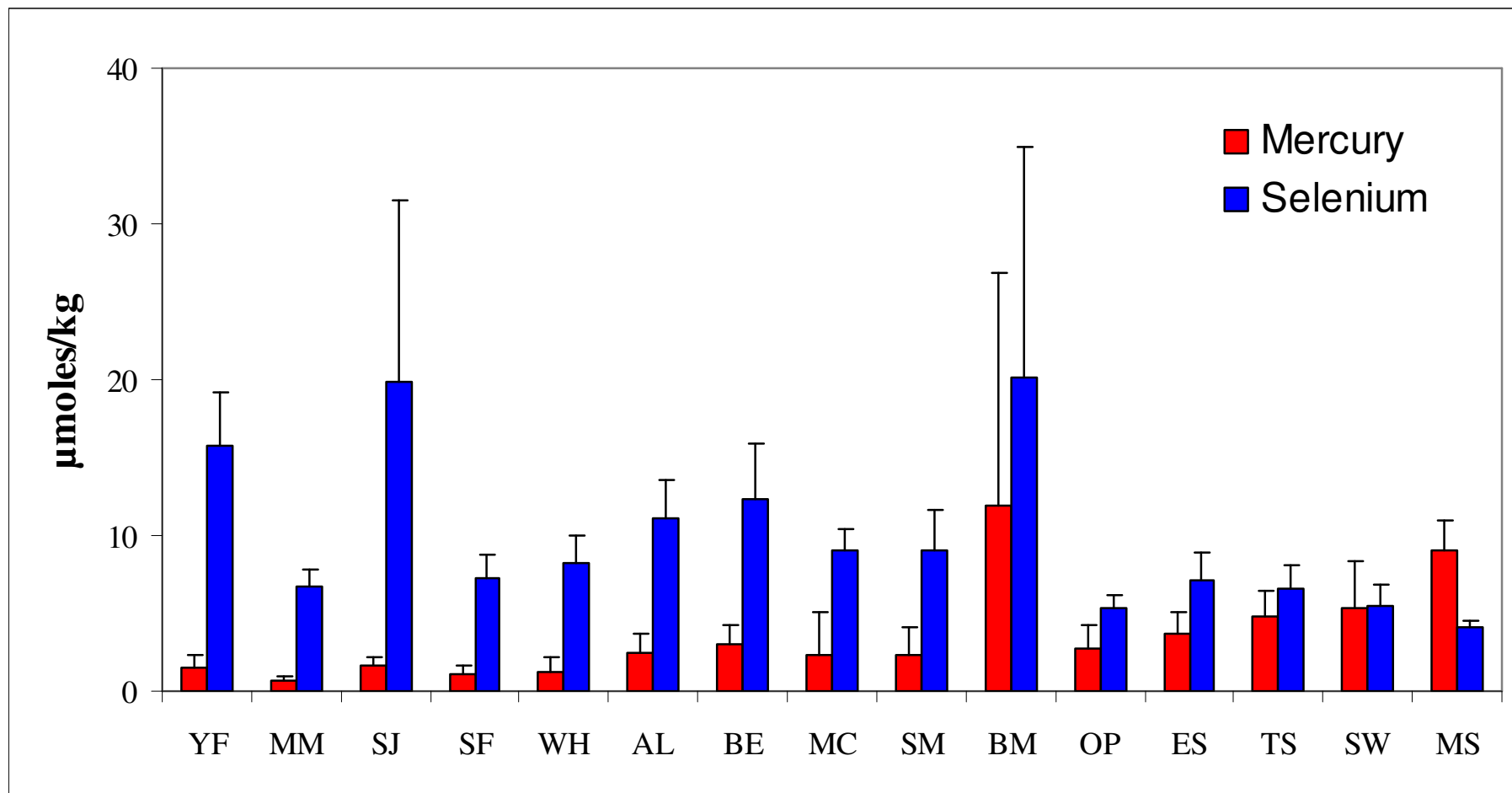
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# Mercuric Sulfide vs. Selenide



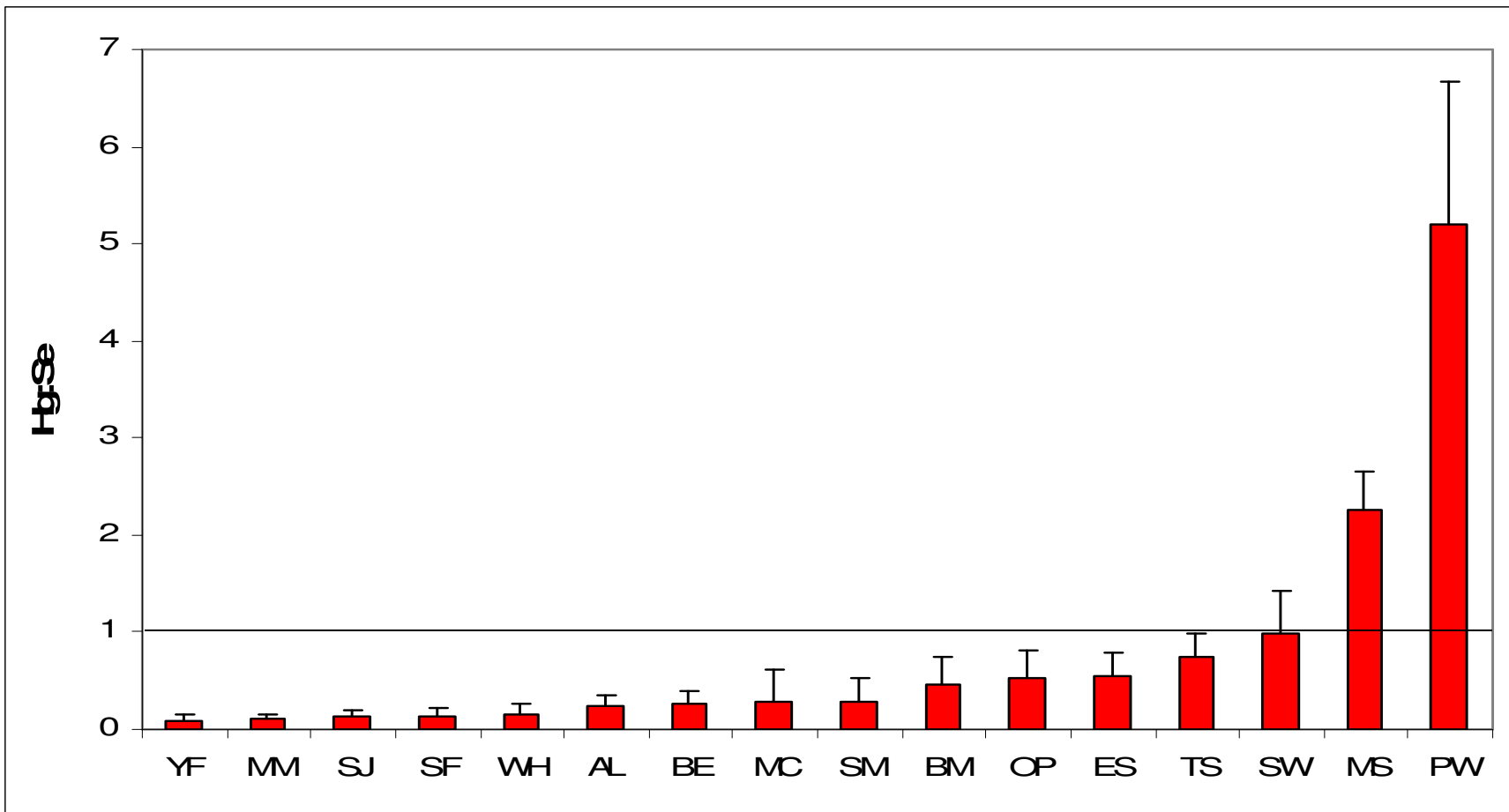


# Mercury and Selenium in Ocean Fish



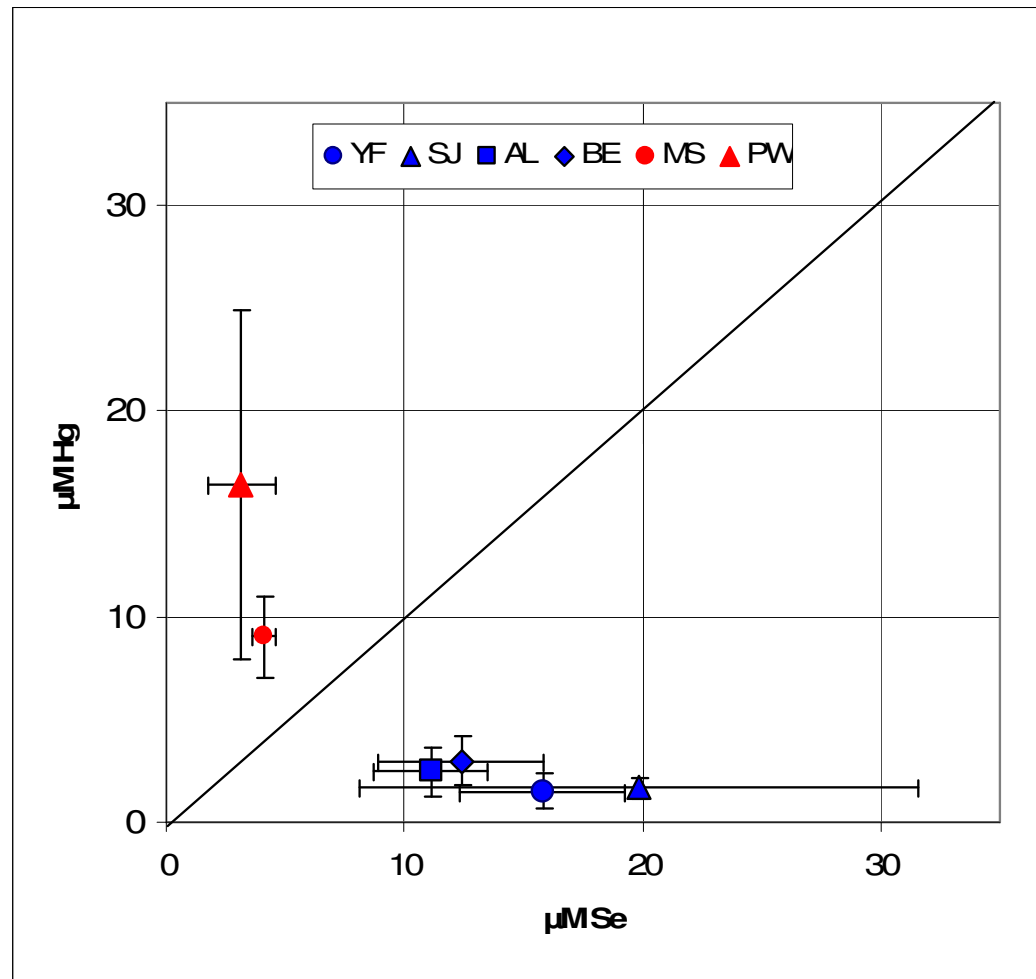
YF=Yellowfin; MM=Mahimahi; SJ=Skipjack; SF=Spearfish; WH=Wahoo; AL=Albacore; BE=Bigeye; MC=Monchong; SM=Striped Marlin; BM=Blue Marlin; OP=Opah; ES=Escolar; TS=Thresher Shark; SW=Swordfish; MS=Mako Shark

# Comparison of “Seafood” Hg and Se (molar basis)



YF=Yellowfin; MM=Mahimahi; SJ=Skipjack; SF=Spearfish; WH=Wahoo; AL=Albacore; BE=Bigeye; MC=Monchong; SM=Striped Marlin; BM=Blue Marlin; OP=Opah; ES=Escolar; TS=Thresher Shark; SW=Swordfish; MS=Mako Shark; PW=Pilot Whale

# Comparison of Seafood Hg and Se (molar basis)



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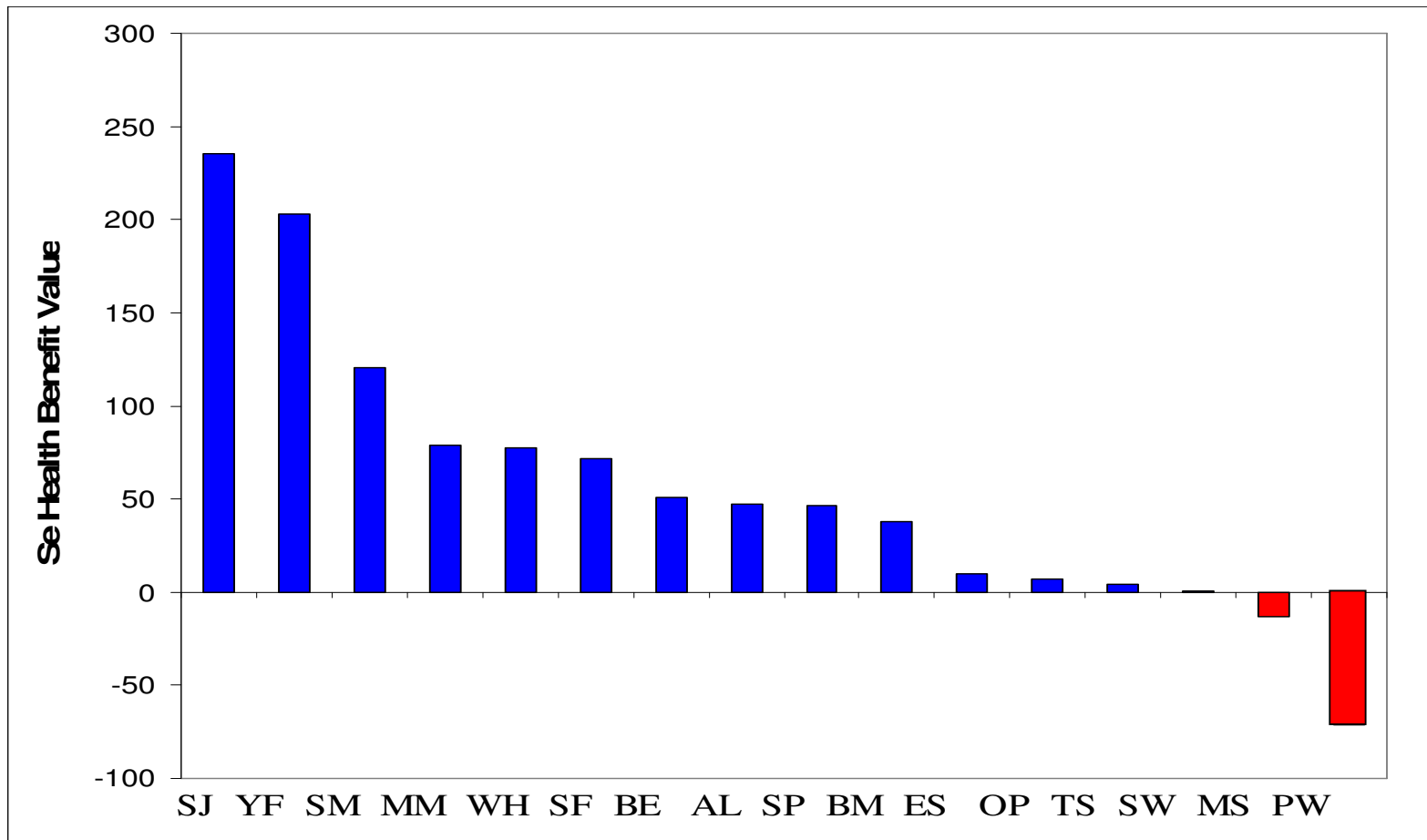
# Selenium Health Benefit Value (Se-HBV)

- Calculation:

$$\begin{aligned} & (\text{Total Se} \times \text{Se:Hg ratio}) \\ & - \underline{(\text{Total Hg} \times \text{Hg:Se ratio})} \\ & = \text{Health Benefit Value} \end{aligned}$$

- The Se-HBV allows a directly meaningful comparison of selenium's nutritional benefits in relation to the mercury present to potentially sequester it.

# Selenium Health Benefit Values



YF=Yellowfin; MM=Mahimahi; SJ=Skipjack; SF=Spearfish; WH=Wahoo; AL=Albacore;  
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# Selenoenzyme Inhibition Hypothesis

**MATERNAL METHYLMERCURY EXPOSURES IN EXCESS OF SELENIUM INTAKES ARE DIRECTLY ASSOCIATED WITH ADVERSE CHILD NEURODEVELOPMENT OUTCOMES**

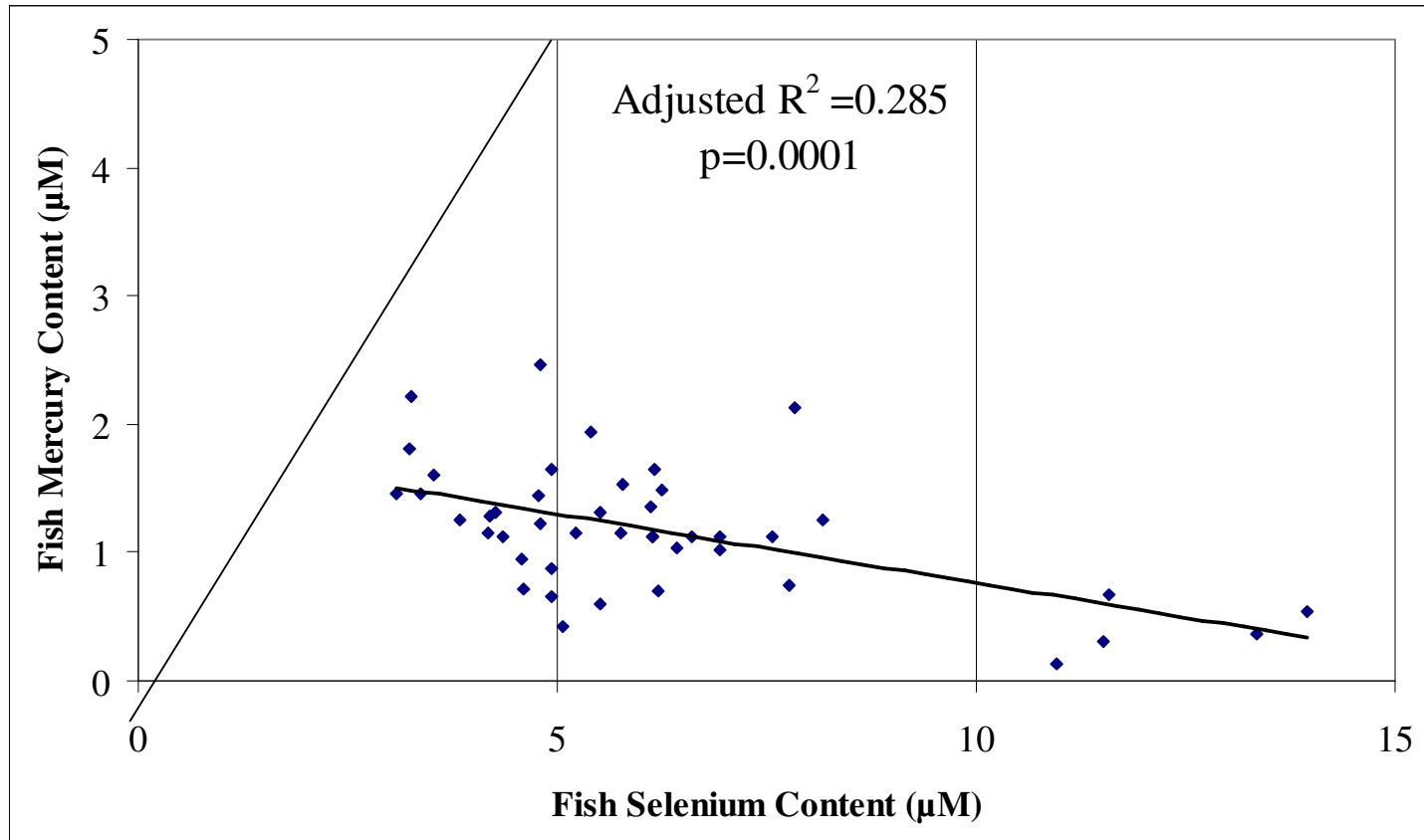
<u>Study Location</u>	<u>Exposure Outcomes</u>	<u>Calculated ~Se-HBV</u>	<u>Results Support</u>	<u>Do Not Support</u>	<u>Results Conflict</u>
Minamata	Harmed	144 to -5,000	✓		
Iraq	Harmed	-800	✓		
New Zealand	Harmed	144 to -123	✓		
Faroës	Harmed	40 to -83	✓		
Seychelles	No harm	173	✓		
United Kingdom	Benefited	202	✓		
United States	Benefited	144	✓		
Denmark	Benefited	202	✓		

Results of the major human studies of maternal methylmercury exposure are completely consistent with the selenoenzyme inhibition hypothesis.

# Selenium's Role in the Mercury Issue

- MeHg is a highly specific irreversible inhibitor of selenoenzymes.
- MeHg toxicity does not occur when adequate Se is available in MeHg-exposed neuroendocrine tissues.
- Biochemical effects of MeHg toxicity correspond with effects expected following loss of selenoenzyme activities.
- Se-protection against MeHg toxicity appears complete, indicating Se sequestration is the primary molecular mechanism of MeHg toxicity.
- Animal and human studies indicate eating Se-rich ocean fish prevents MeHg toxicity rather than causes it.
- The Faroese ate ocean fish and were protected from MeHg toxicity by their rich Se intakes. Inland populations (e.g., Finland, Florida, Rocky Mtn. States) that eat high MeHg, Se-poor freshwater fish may be at much greater risk from MeHg exposure than is currently expected.

# Mercury–Selenium in Walleye

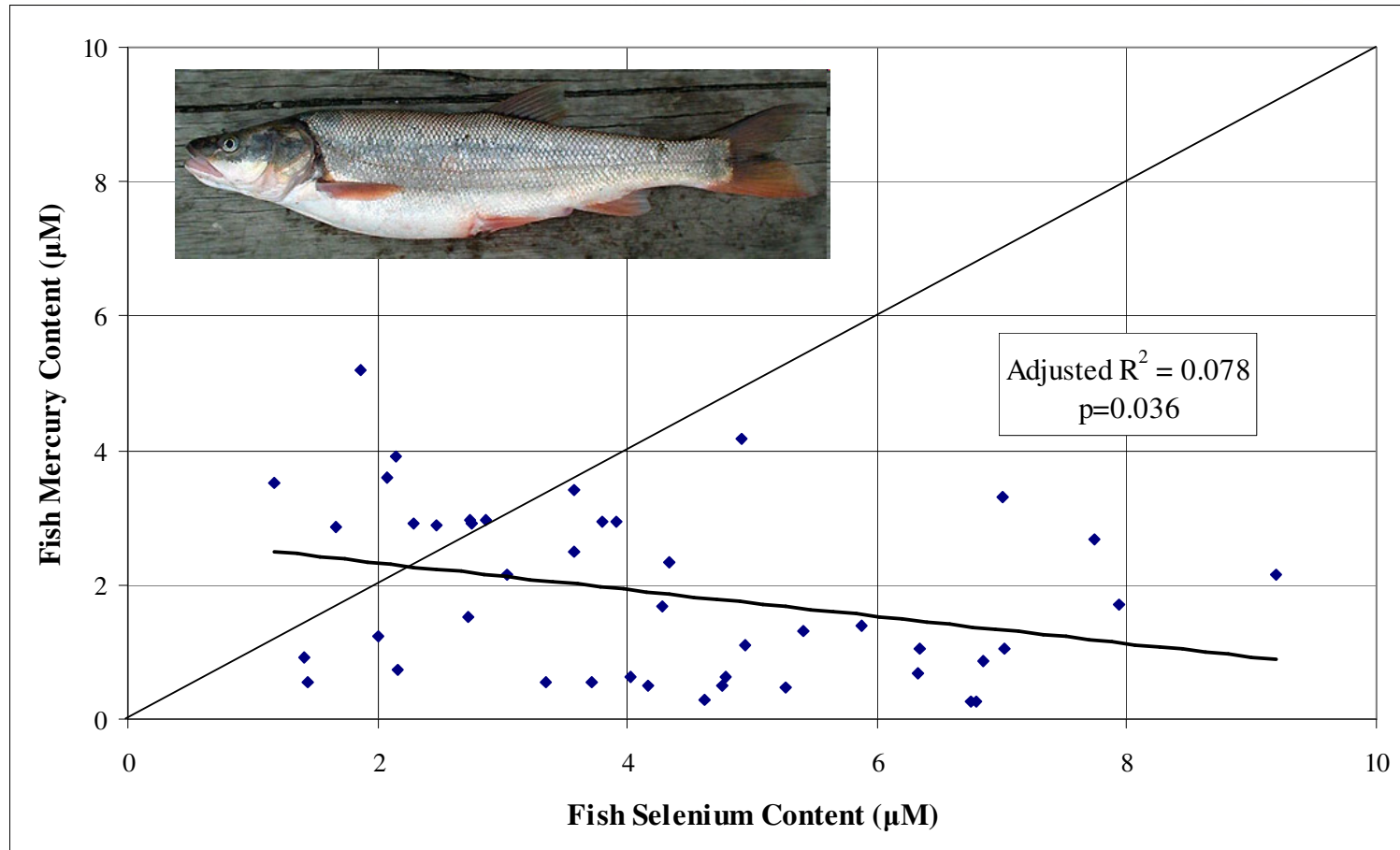


Total Hg contents of walleye is inversely related to Se content. This is a food chain effect, but the crucial reactions occur within tissues. The amount of MeHg in fish depends on Se to retire Hg as HgSe in lower trophic levels of food web.

Note: The diagonal line indicates the 1:1 Hg:Se molar ratio,  
– None of the walleye in this study contained more Hg than Se.



# Northern Pikeminnow



**In certain locations, Northern Pikeminnow (*Ptychocheilus oregonensis*), an apex predator, can contain Hg in excess of Se. Consumption of these fish could cause harm to pregnant women.**

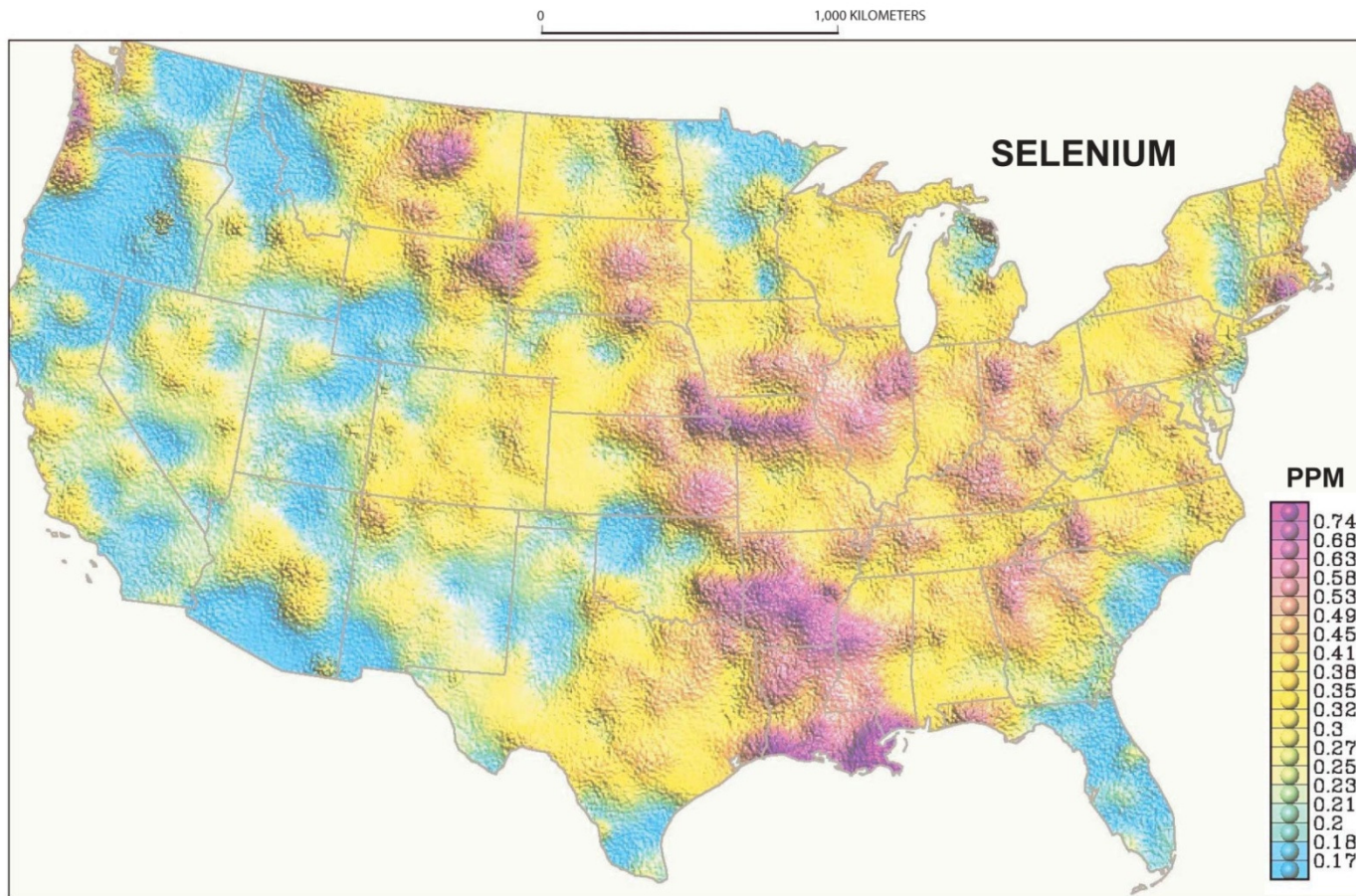
Note: these were the only fish in our study with negative SeHBV's.

# Fish Hg Contents Relative to Se

Species	n	Adjusted R <sup>2</sup>	p Value
Northern Pikeminnow	44	0.078	<0.04
Northern Pike	30	0.194	<0.01
Walleye	44	0.285	<0.0001
White Sucker	126	0.205	<0.0001
Common Carp	39	0.323	<0.0001
Short Head Redhorse	19	0.361	<0.01
Smallmouth Bass	52	-----	NS
Rainbow Trout	59	-----	NS
Brown Trout	74	-----	NS
Channel Catfish	24	-----	NS (0.14)
Large Scale Sucker	48	-----	NS (0.09)

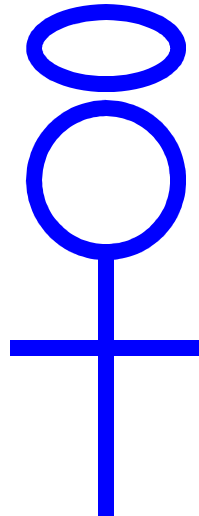
The inverse relationship between Se and Hg accumulation occurs in both top predators and non-piscivorous varieties of fish but was not uniformly observed. The reason for these species distinctions are currently being studied.

# Soil Selenium Contents



**Freshwater fish MeHg is inversely related to Se availability. Increased MeHg accumulations in low Se fish could substantially increase health risks to consumers.**

# Selenium



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