Mercury and The Human Detoxification System

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Mercury and The Human Detoxification System

1. What are the key forms of Hg
2. How the Detoxification System Works
3. Methylmercury Accumulation as a hidden danger in Amalgam toxicity
4. Intestinal Metals Detox System to repair and amplify the bodies detoxification mechanisms and safely remove mercury

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Transport of mercury

- Hg^0
  - 80% uptake in lungs, crossed BBB, diffuses in to tissues; moderate uptake from intestines
- Hg^{II}
  - Very poor uptakes in intestines; poor mobility; does not cross BBB
- MeHg
  - 95% uptake from intestines, good mobility, crosses BBB
- EtHg
  - 100% absorbtion (inj), good mobility, crosses BBB

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The Heart of the Toxicity

1. Inappropriate Binding
2. Oxidative Damage and related Inflammation

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The Heart of the Toxicity

- Thiol Binding and Redox Reaction
  - Reduced sulfur groups, R-SH,
  - Hg replaces proton and binds to sulfur
    - $R\text{-}SH + Hg^{2+} = R\text{-}SHg^{+} + H^{+}$
  - Enzymes use thiols to anchor functional metals (Zn, Ni, Cu, Fe)
  - Bind and alter membrane or trigger membrane reorganization and consequent auto-oxidation
  - Oxidize ***Thioredoxin*** (protein repair molecule)
  - Deplete ***Glutathione*** system

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Defense – Glutathione System

Antioxidant, Detoxification, Protein Repair

- Glutathione (GSH) - A thiolic tripeptide composed of glutamate, cysteine, and glycine
- The system involves
  - Synthetases (synthesize GSH from precursors)
  - Transpeptidases (take apart and reassemble)
  - Transferases (conjugation)
  - Peroxidases (radical quenching)
  - Reductases (repair after quenching)
  - Redoxins (using GSH as reducing equivalent for protein repair)

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The Human Detoxification System

- Detoxification ***Phases I, II, III***
  - ***Phase I*** is an activation,
  - ***Phase II*** is conjugation
  - ***Phase III*** is transport

The Human Detoxification System

- ***Phase I -*** an oxidative activation, usually the Cytochrome P450 system
  - Prepares toxin for conjugation in ***Phase II*** with GSH, Glucuronic acid, Sulfate, Gycine or other amino acid, Taurine, Methyl group
  - **Not needed for metals,** but very important to have coupled to ***Phase II***
    - ***Creates Essentially Free-Radicals***

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The Human Detoxification System

- ***Phase II*** – conjugation makes toxin more water soluble and recognizable by transporters
  - ***Glutathione S-Transferases (GST)*** responsible for GSH conjugation
  - Low in people with high MeHg and with sensitivity to Thimerosal (EthylHg)

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The Human Detoxification System

- ***Phase III*** **is the transport out!**
  - Several transport proteins (**cMOAT, OAT, MRP1, MRP2, GS-X**)
  - Same transporters for many pathways (glucuronide, sulfate, glycinate, GSH)
  - In cells, liver, intestines, kidneys – biggest in liver then intestines

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Breakdown of the defense system

- GSH deficiency – genetic and/or environmental
- GST problems – genetic and/or environmental
- ***Phase III can get blocked and then downregulates Phase II enzymes***
  - ***Can stop multiple detoxification pathways!***

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Biggest Reason for *Phase III* Dysfunction

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Biggest Reason for *Phase III* Dysfunction

Inflammation in Gut!

-Hallmark of Autism cases

-Easily caused by heavy metal induced oxidative damage

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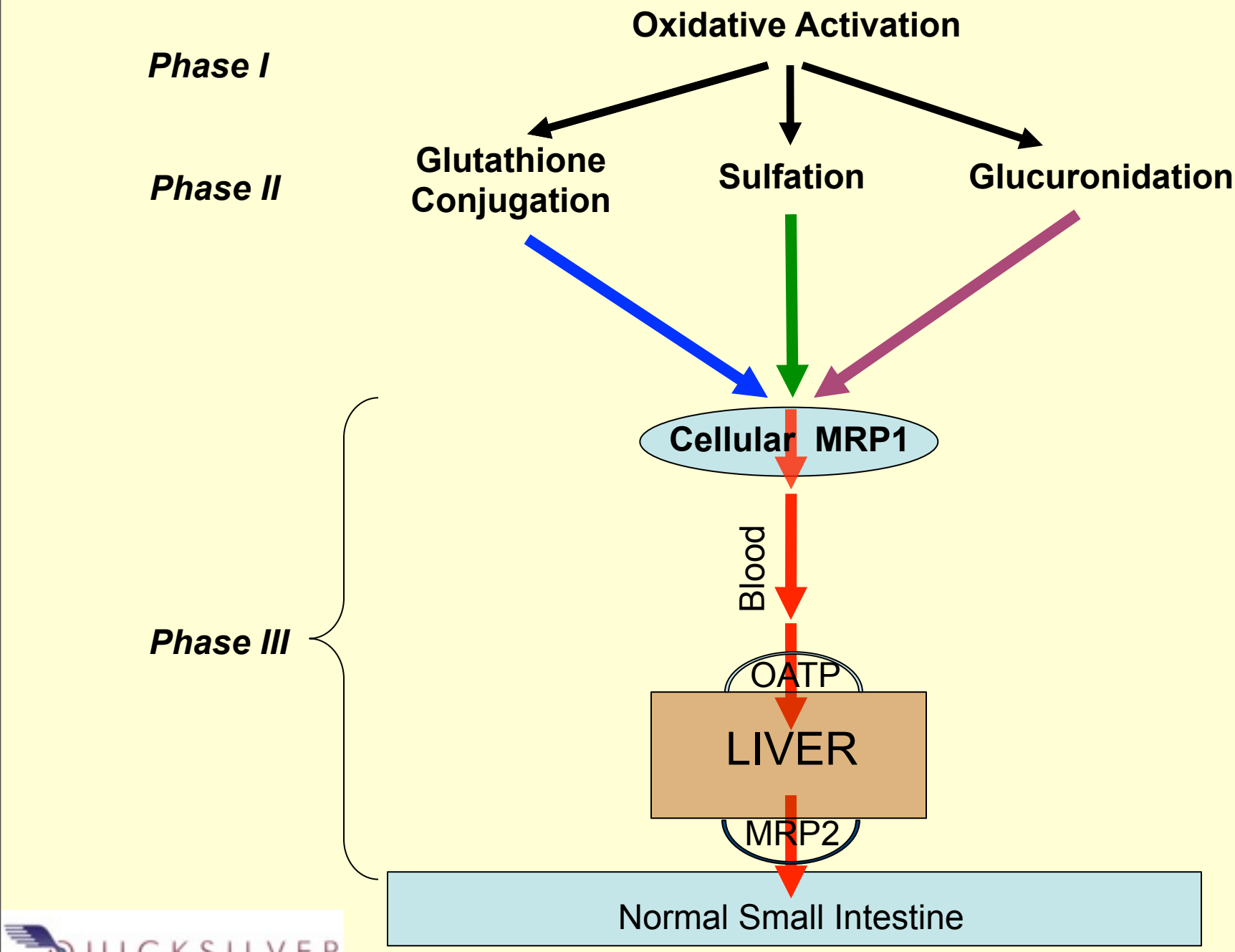
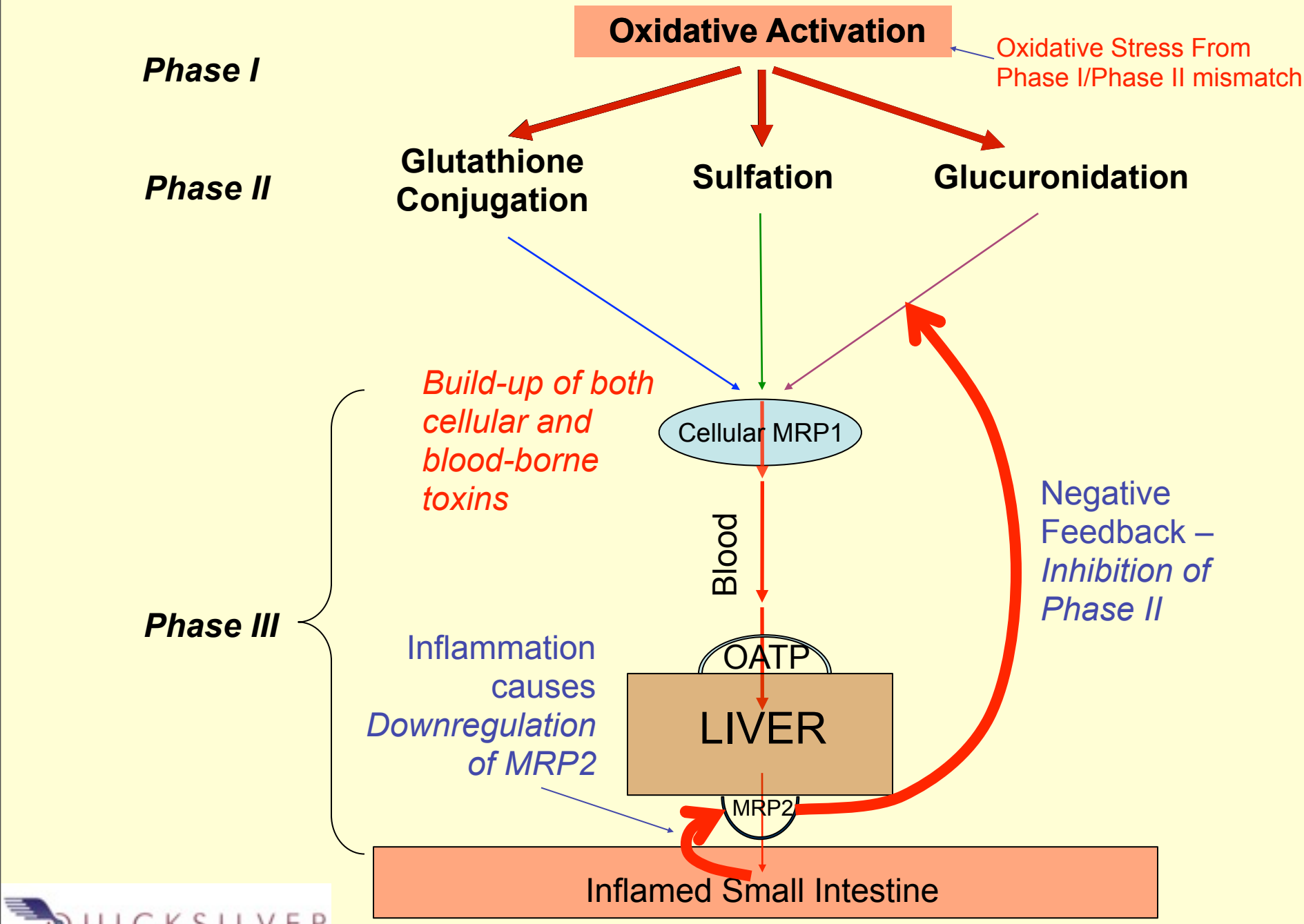

Phase I
Oxidative Activation
Phase II
Glutathione Conjugation
Sulfation
Glucuronidation
Cellular MRP1
Blood
Phase III
OATP
LIVER
MRP2
Normal Small Intestine


Phase I
Oxidative Activation
Oxidative Stress From
Phase I/Phase II mismatch
Phase II
Glutathione
Conjugation
Sulfation
Glucuronidation
Build-up of both
cellular and
blood-borne
toxins
Cellular MRP1
Blood
Negative
Feedback –
Inhibition of
Phase II
Phase III
Inflammation
causes
Downregulation
of MRP2
OATP
LIVER
MRP2
Inflamed Small Intestine

Accumulation

- Retention Toxicity – ***Phase II, III*** problem?
  - *Genetic difficulties*: GS, GST deletions
  - *Acquired Dysfunctions*: Transporter impairment, severe oxidative stress

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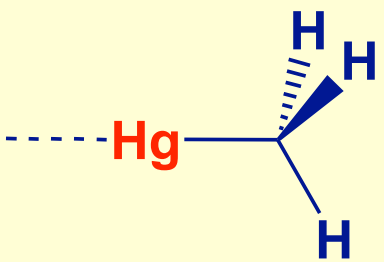
MethylMercury

The Unsuspected Factor



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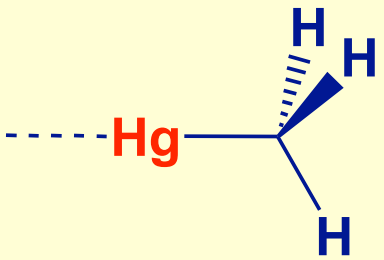
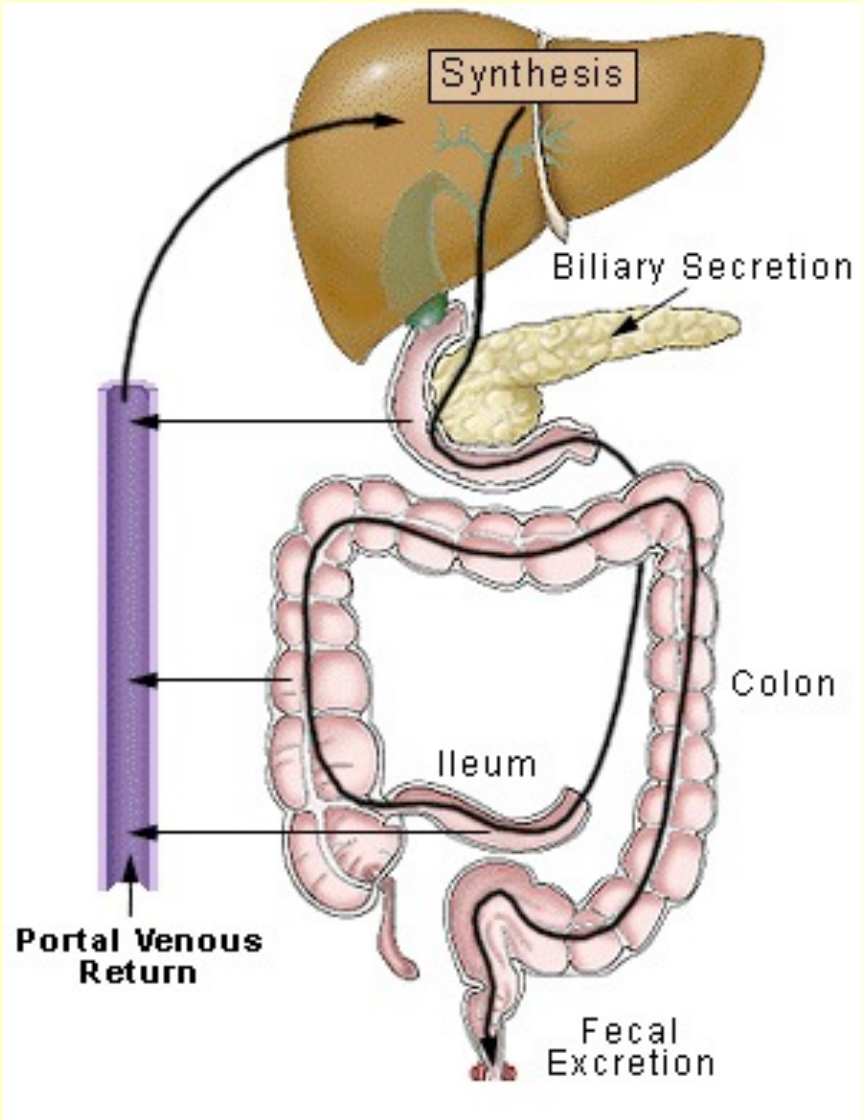


Enterohepatic Circulation of MeHg



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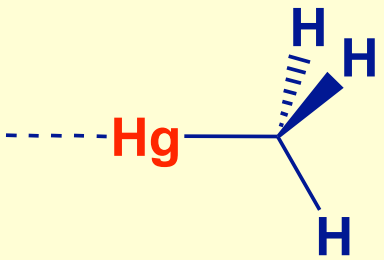

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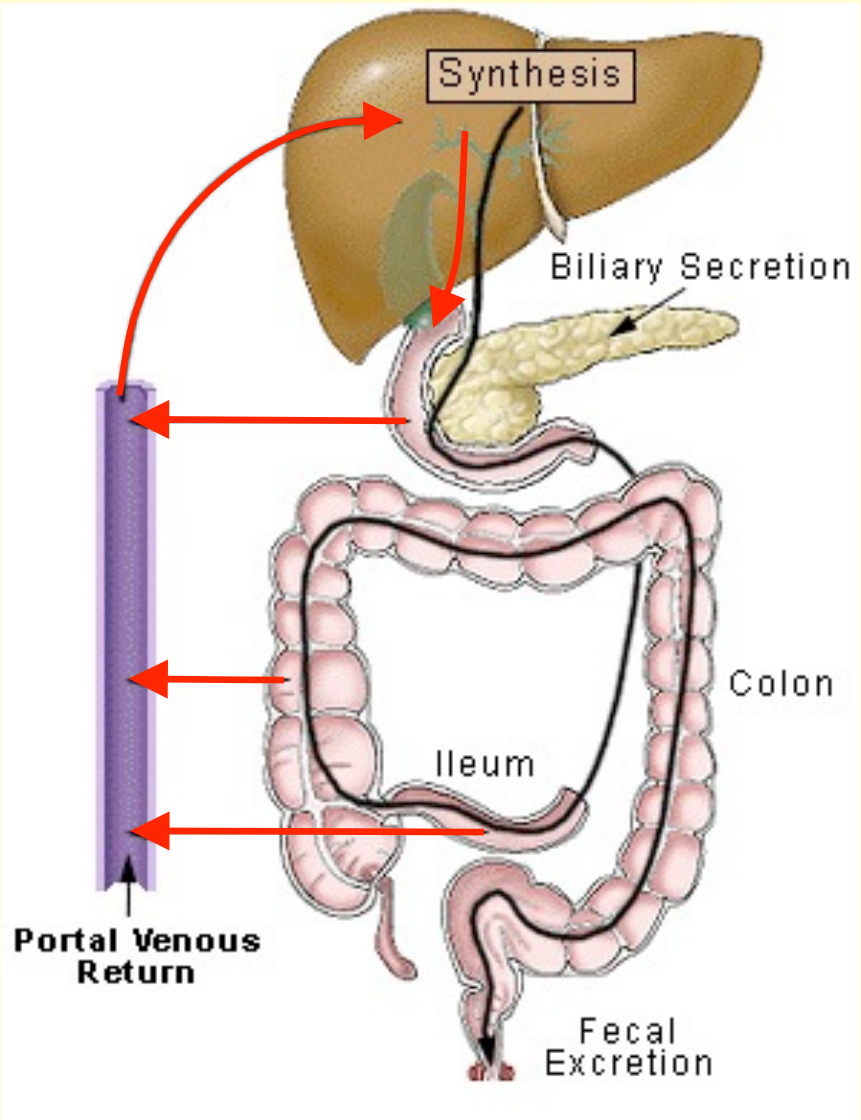

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Synthesis of Methylmercury from Amalgam-Derived Hg

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Experimental Results in Monkeys

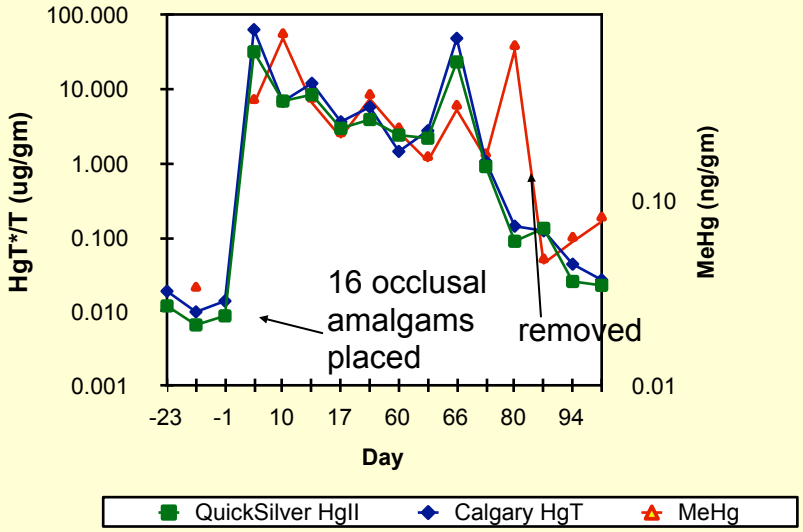
w/ Dr. Anne Summers, University of Georgia

Continuous In Vivo Synthesis of CH_3HgX from Amalgam Hg by Intestinal Bacteria in Live Monkeys

Time course

CH_3HgX as a fraction of total Hg

F78



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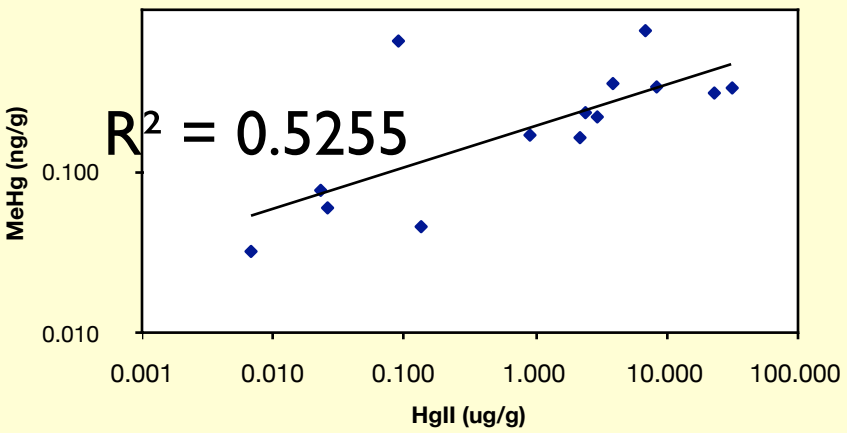
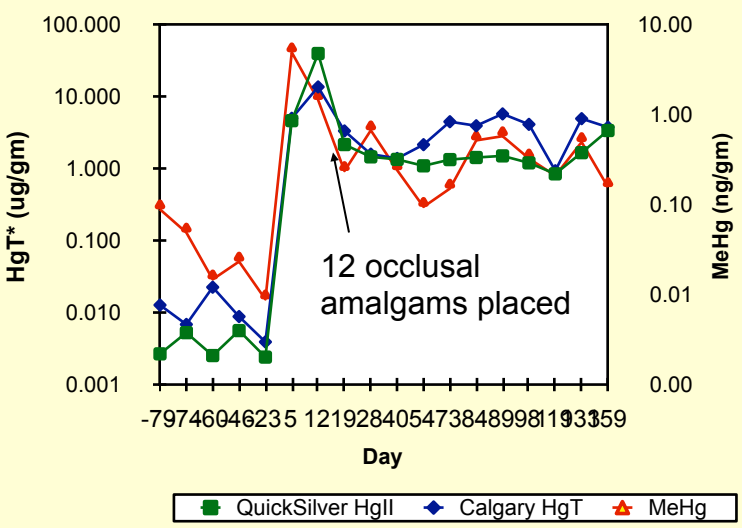


R87



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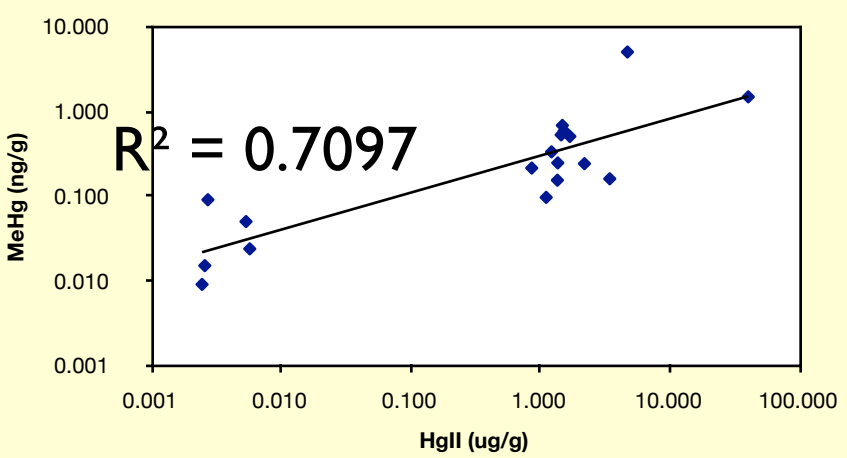
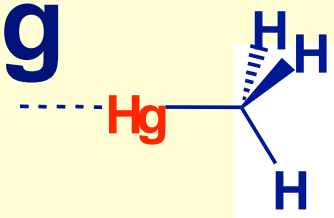


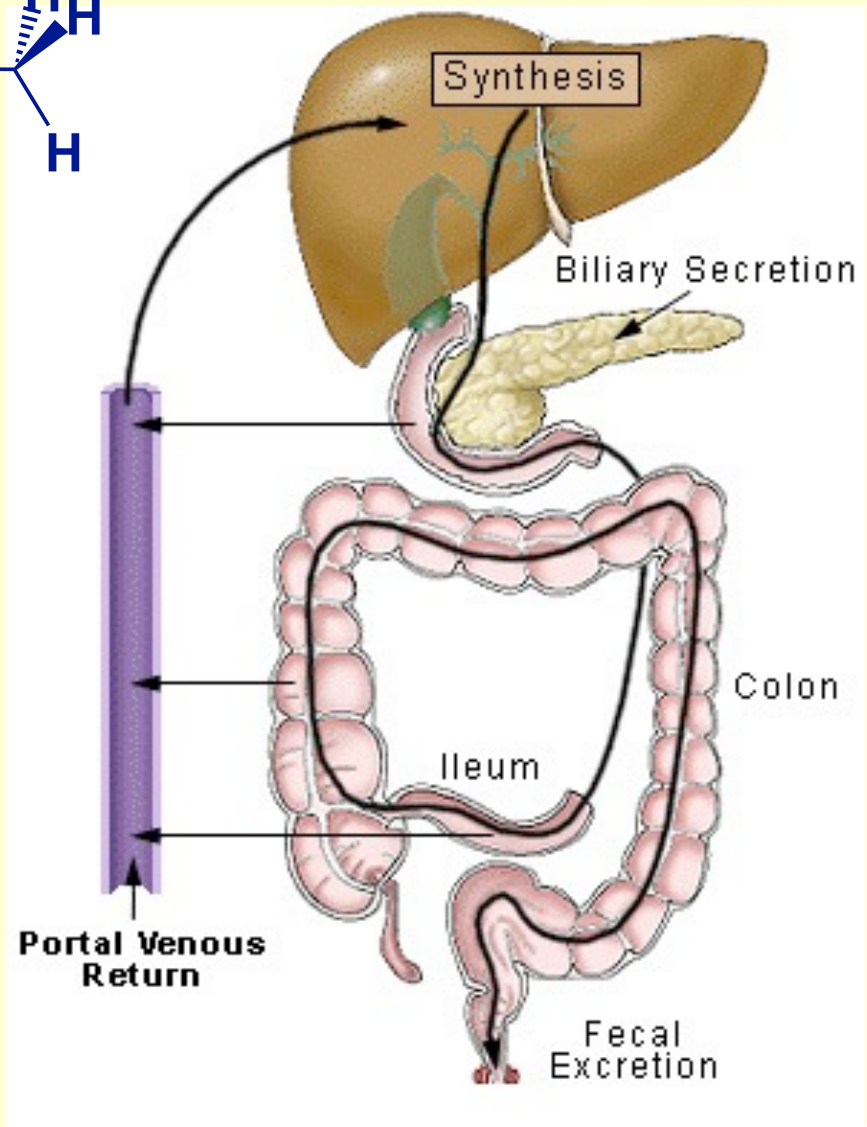
In-Gut MeHg Synthesis



MeHg synthesized from Hg^{II} derived from amalgam corrosion.

MeHg absorbed ~95% efficiency versus the 5-10% of Hg^{II}.

Continuous Synthesis plus recirculation can lead to high body burden of MeHg



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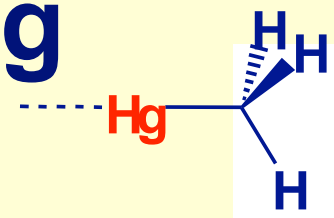

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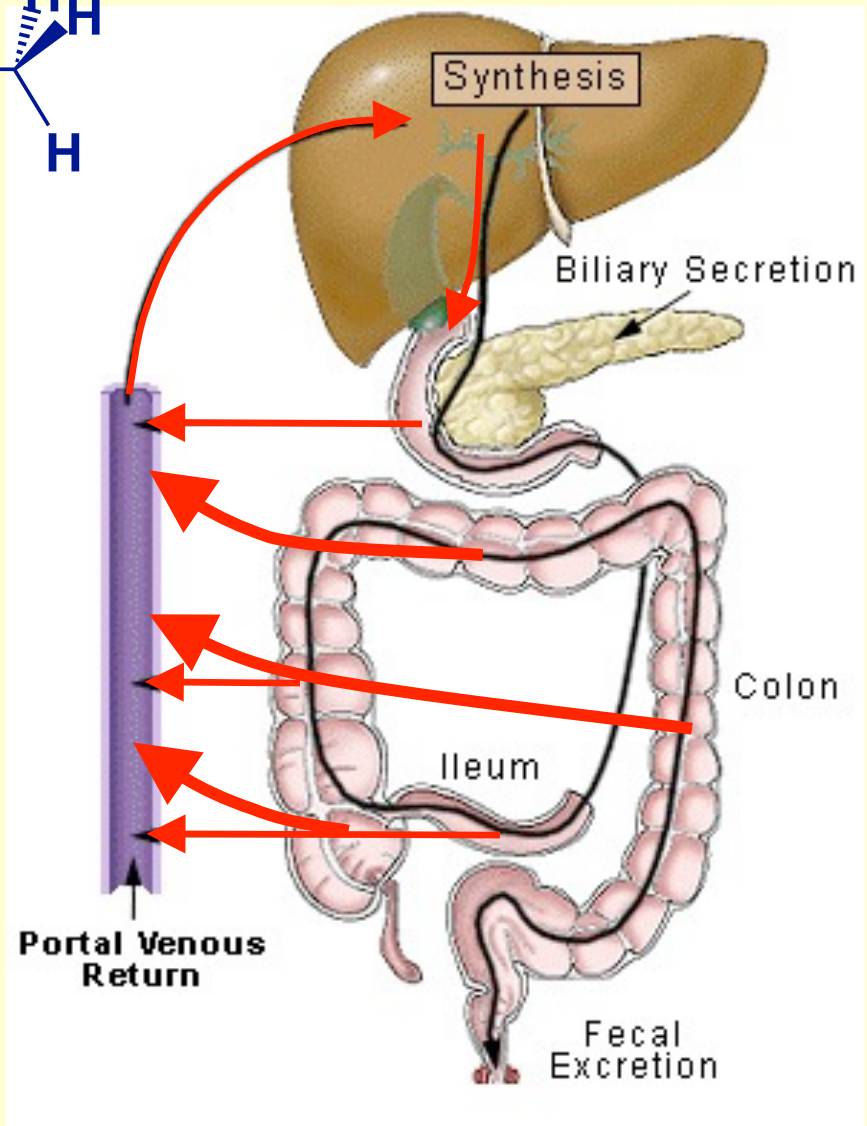

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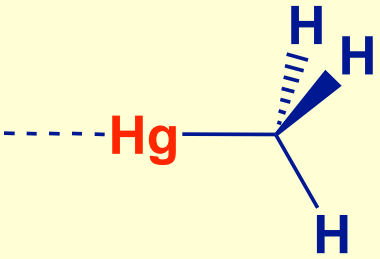
Testing for MeHg



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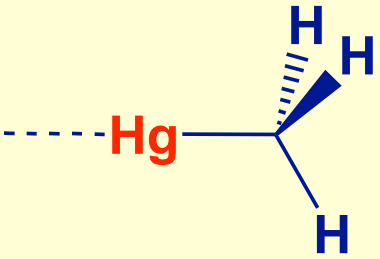

- ***Old Dictum*** – blood is only recent exposure, 3-days

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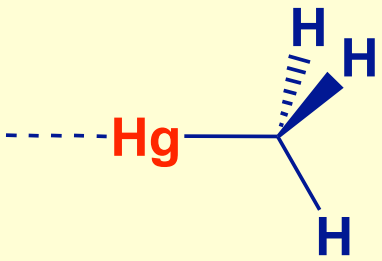

- ***Old Dictum*** – blood is only recent exposure, 3-days
- **Reality**

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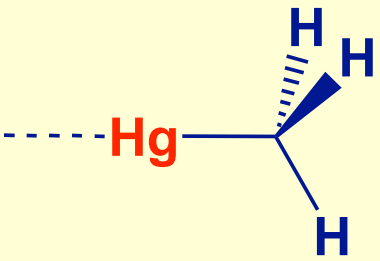

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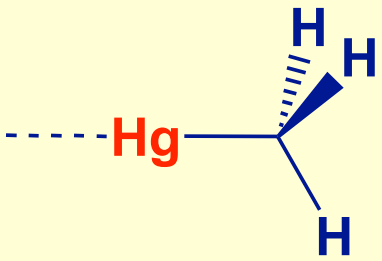

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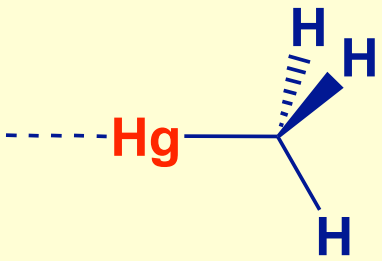

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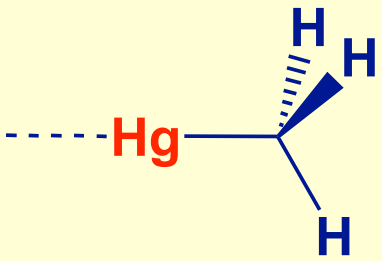

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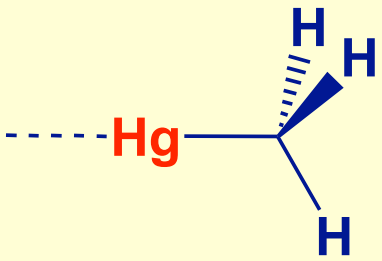

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- **Real Problem**
  - Most labs detection limits too high to see dynamics
  - ***Need sensitive equipment!***

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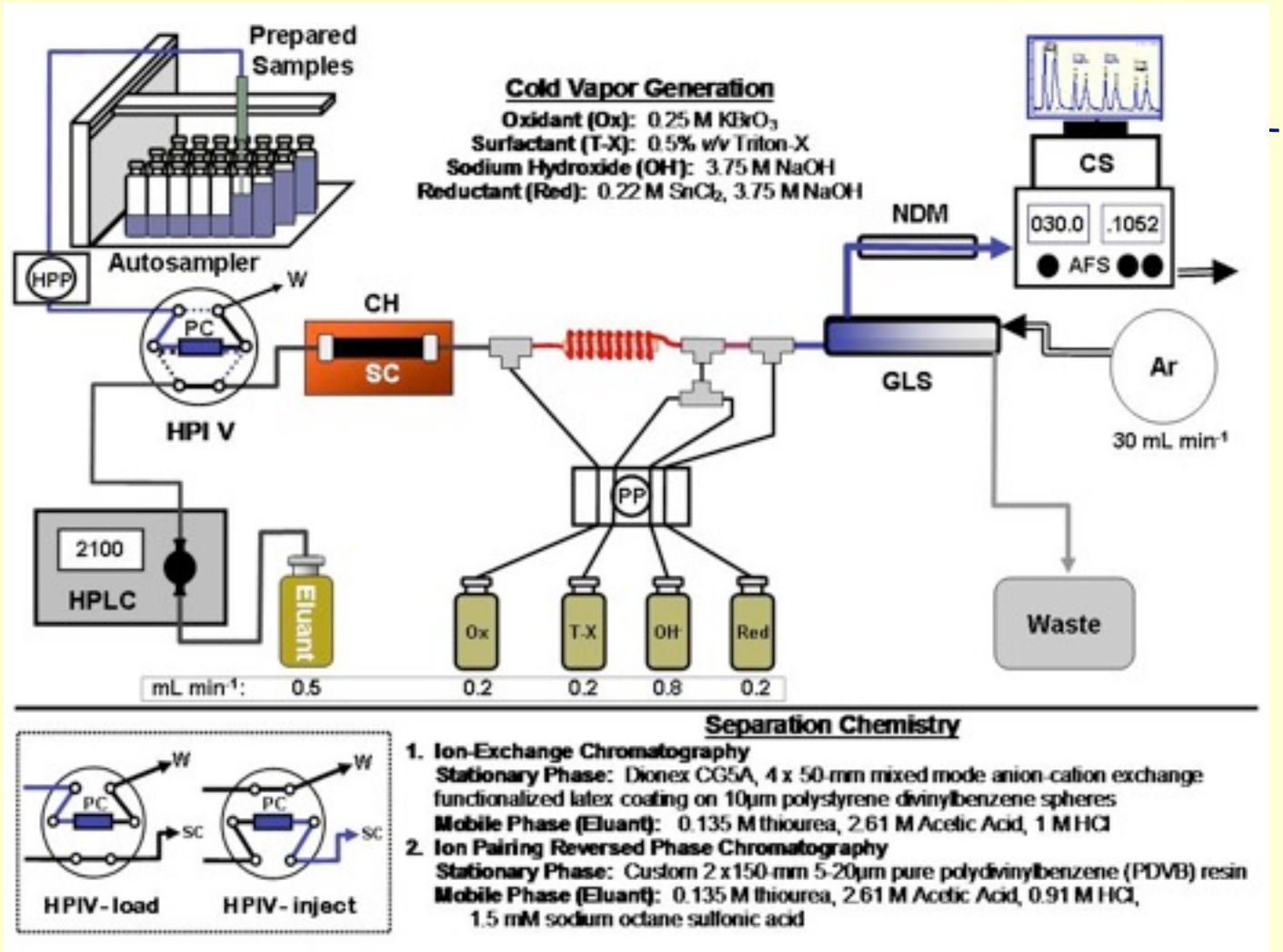

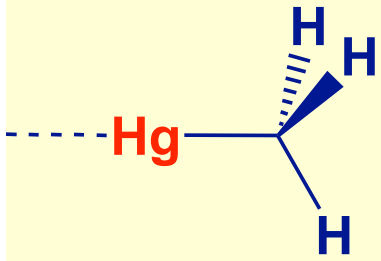

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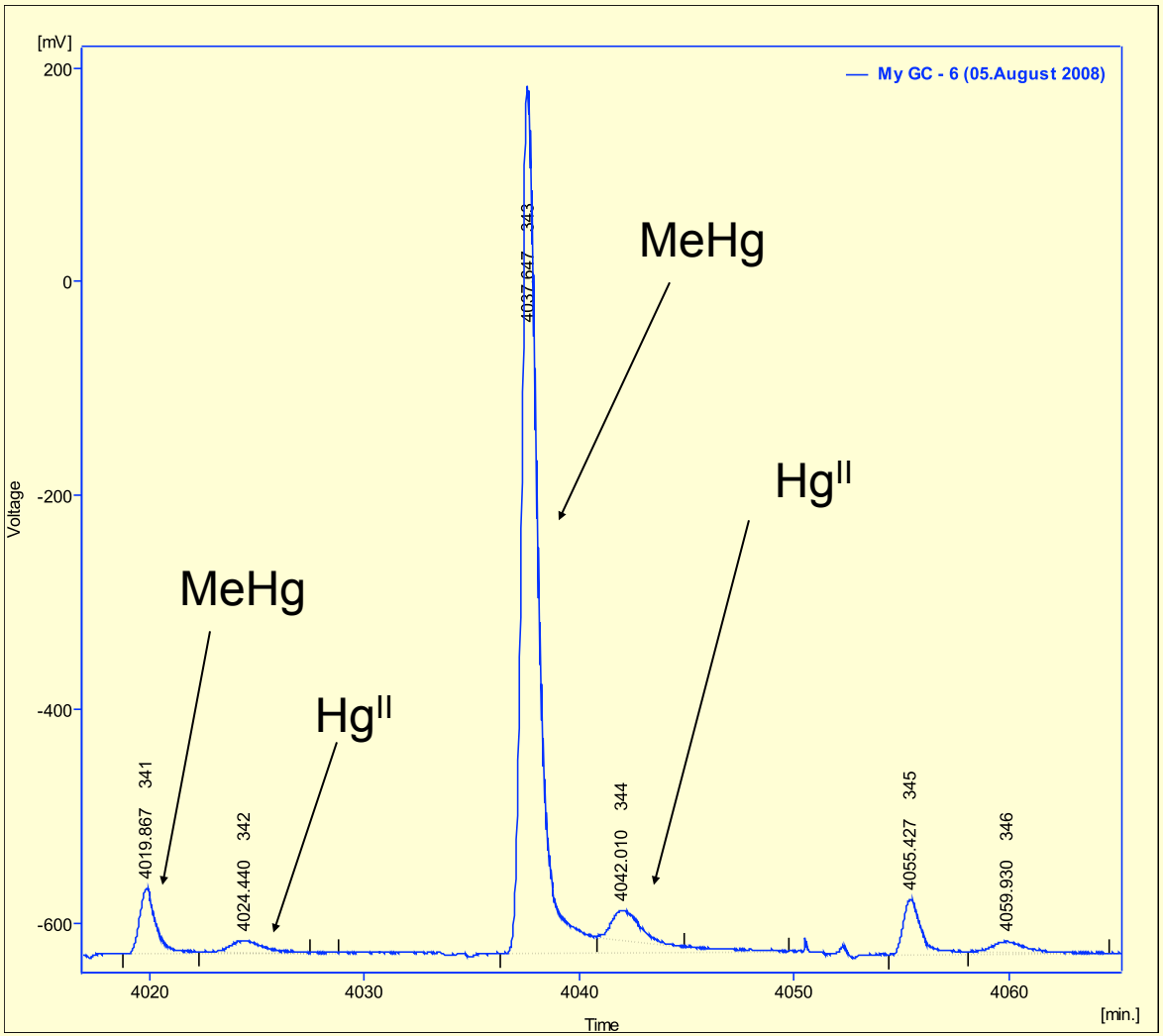

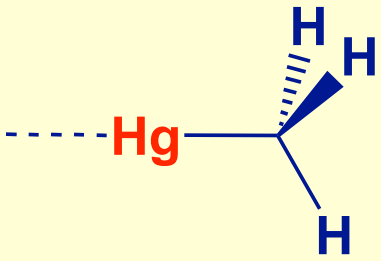

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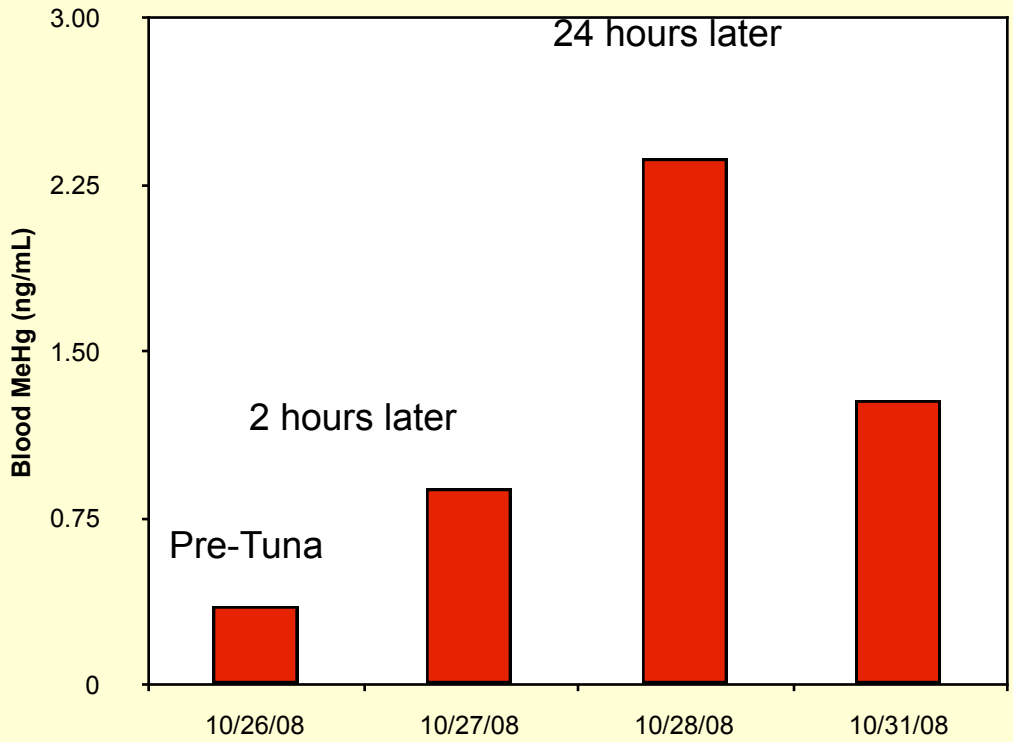
The Great Tuna Experiment

- Wade Wimer – 2 cans of Albacore Tuna in one sitting



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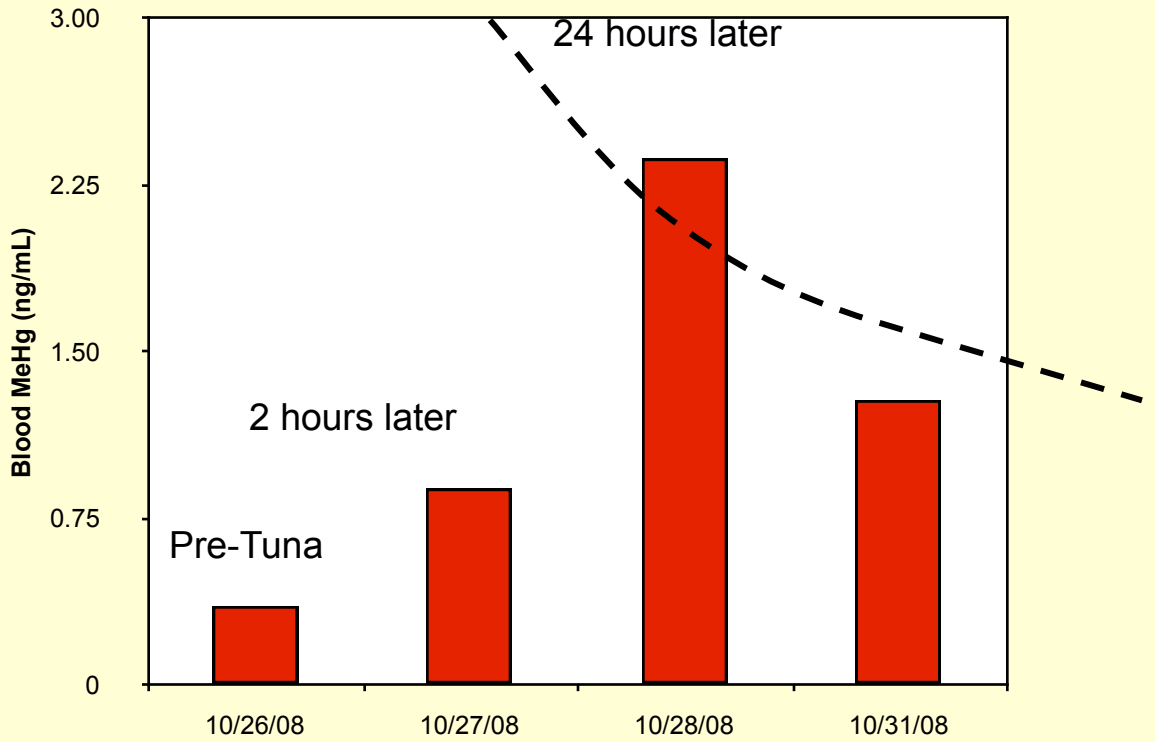

Decay – Excretion? Redistribution to Tissues?
Or some of Both?

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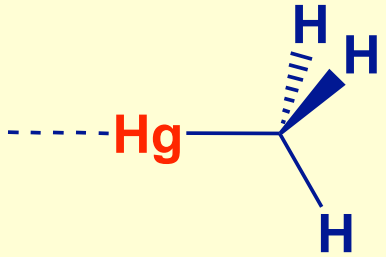
Testing for MeHg



Dr. Huggins Observation

Patients with high MeHg take much longer to recover!

-testing can give indication of rate of recovery

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Removal of Hg

Amplifying and Augmenting Natural Systems

Product/System for Intestinal Detoxification

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- **MicroSilica (IMD)**

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  - Use Intestines NOT Kidneys for Metal Removal

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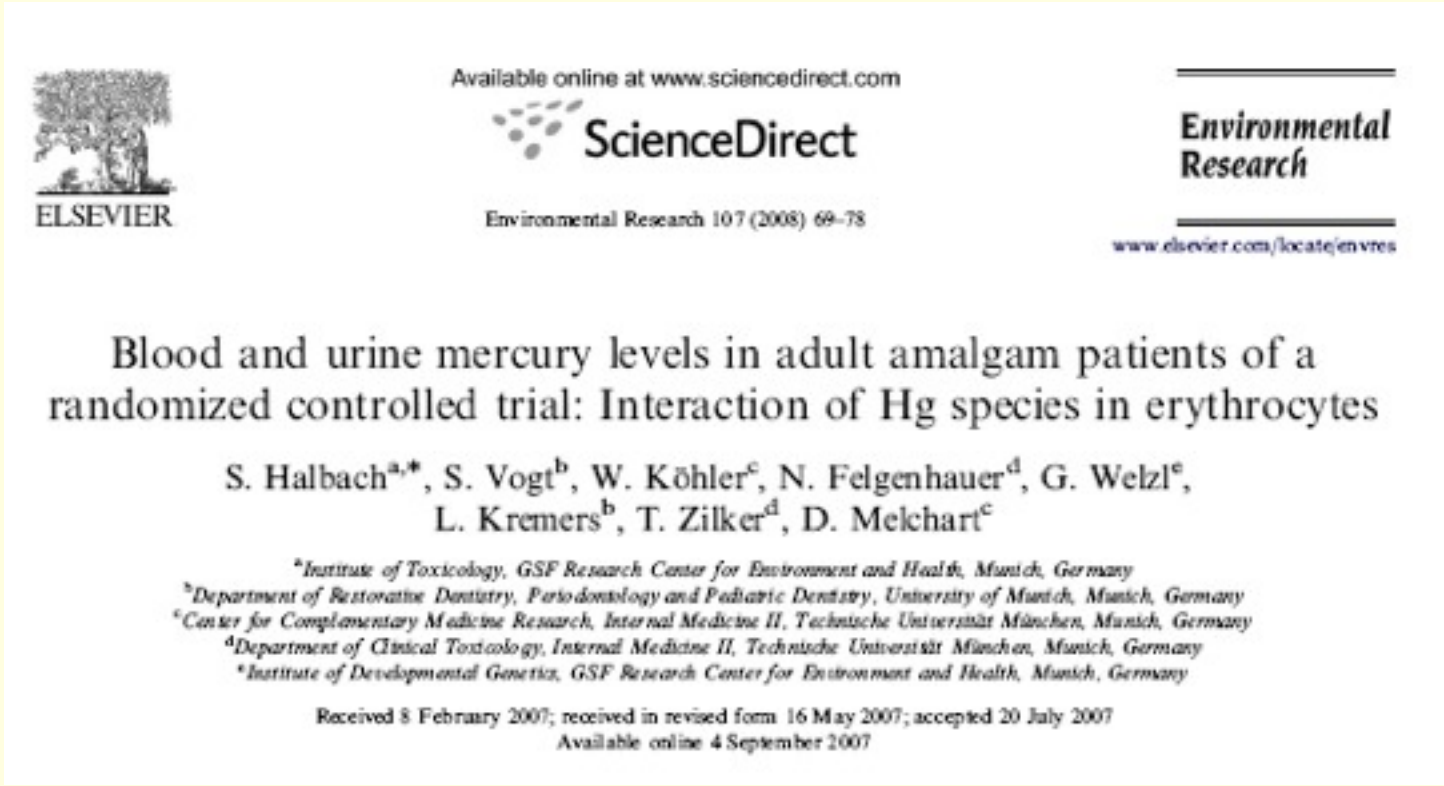
  - Binds Mercury in Intestines and moves out of Body
- Stops Enterohepatic Circulation
- Opens Phase III transporters
  - Bilirubin levels fall dramatically too!
- System adds **Phytonutrients** that enhance *Phase II enzymes* and *strengthen the vascular system* and **Liposomal GSH** to raise GSH levels (Phospholipid Exchange)

A Look at Natural Attenuation Post-Revision



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Environmental Research 107 (2008) 69–78
Environmental Research
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Blood and urine mercury levels in adult amalgam patients of a randomized controlled trial: Interaction of Hg species in erythrocytes

S. Halbach[a,*], S. Vogt[b], W. Köhler[c], N. Felgenhauer[d], G. Welzl[e], L. Kremers[b], T. Zilker[d], D. Melchart[c]

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[b]Department of Restorative Dentistry, Periodontology and Pediatric Dentistry, University of Munich, Munich, Germany
[c]Center for Complementary Medicine Research, Internal Medicine II, Technische Universität München, Munich, Germany
[d]Department of Clinical Toxicology, Internal Medicine II, Technische Universität München, Munich, Germany
[e]Institute of Developmental Genetics, GSF Research Center for Environment and Health, Munich, Germany

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Halbach et al., **2008**, *Environ Research* 107:69-78

Changes in RBC Hg after Dental Revision

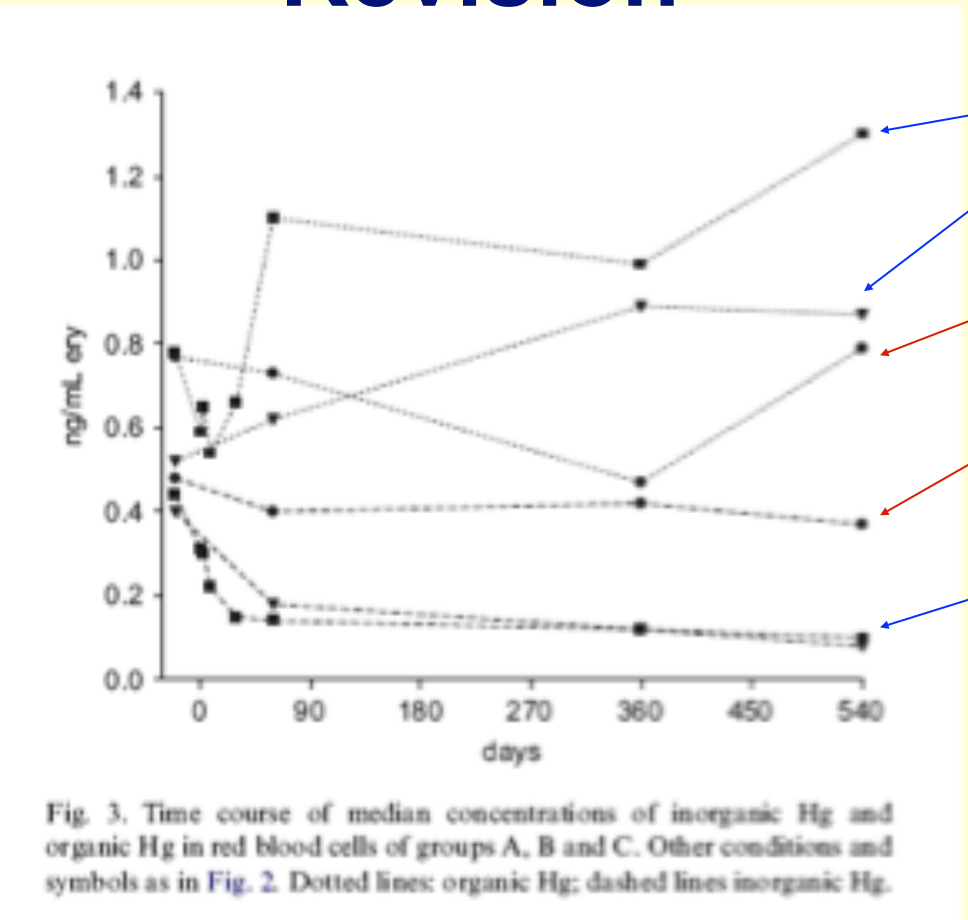


Fig. 3. Time course of median concentrations of inorganic Hg and organic Hg in red blood cells of groups A, B and C. Other conditions and symbols as in Fig. 2. Dotted lines: organic Hg; dashed lines inorganic Hg.

Revision-MeHg

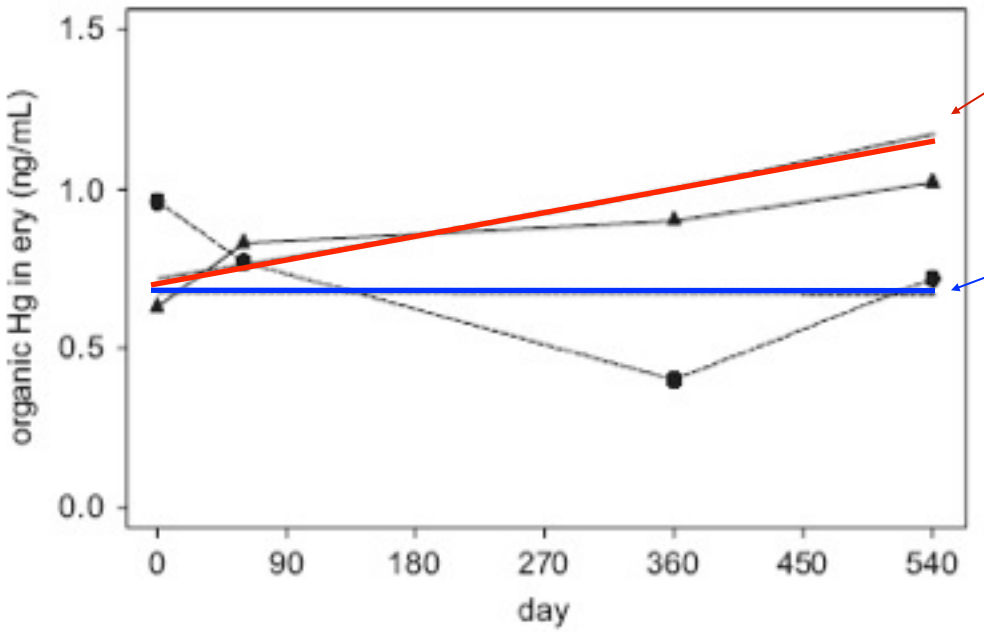
No Revision - MeHg

No Revision - Hg^{II}

Revision- Hg^{II}

Halbach et al., **2008**, *Environ Research* 107:69-78

MeHg Moving from tissues to Bloodstream… But NOT Out!



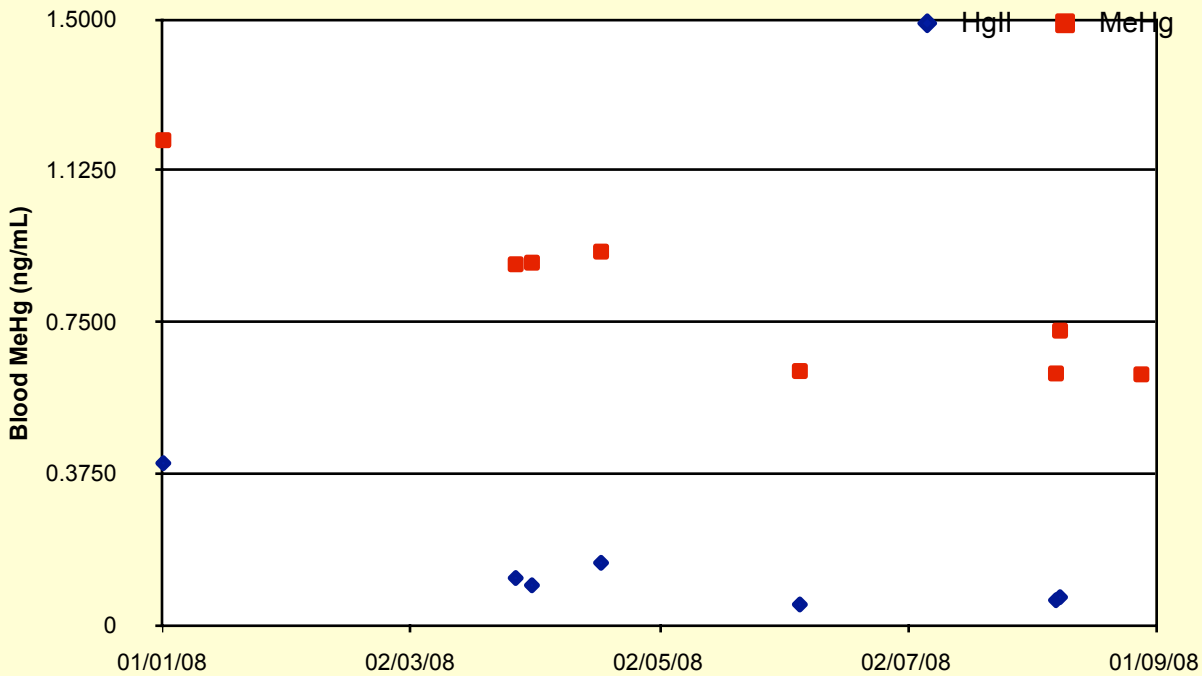
Modeled Trend - Revision

Modeled Trend - No Revision

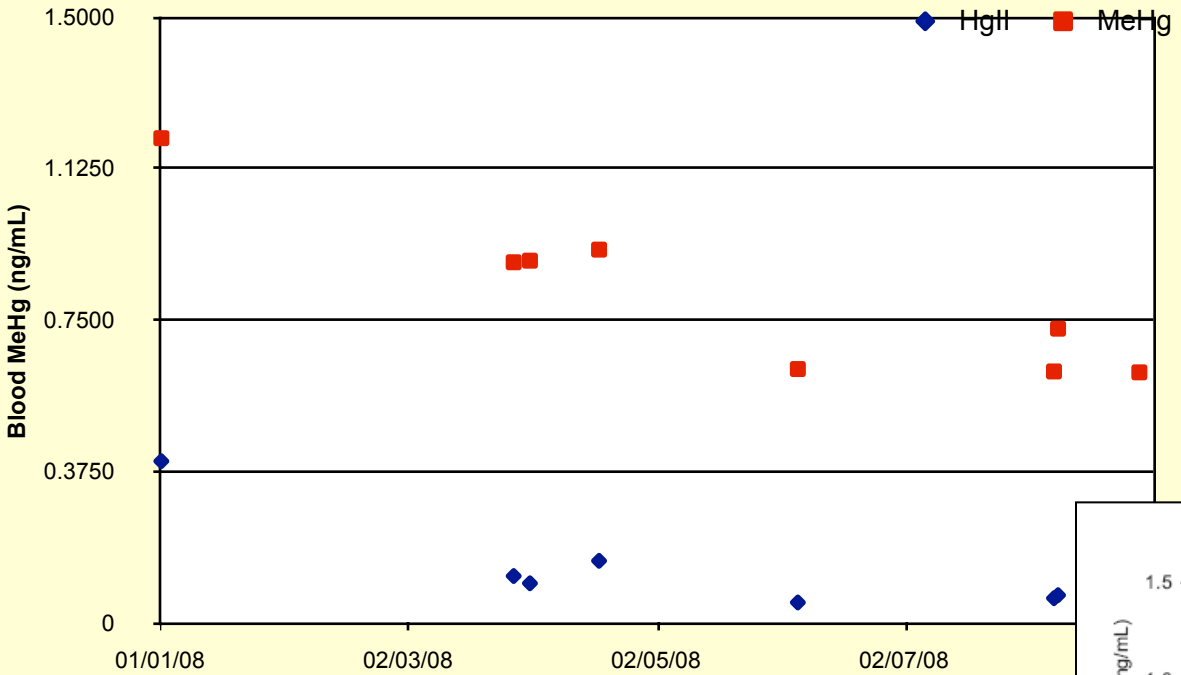
Fig. 6. Linear-mixed-effects (LME) model for the effect of amalgam removal on the concentration of organic Hg in erythrocytes. The data of groups A and B were combined (removal, medians, triangles, $n = 39$) and compared to those of group C (no removal, circles, $n = 19$). Lines without symbols show regressions of the LME model: solid line for group A + B, dashed line for group C.

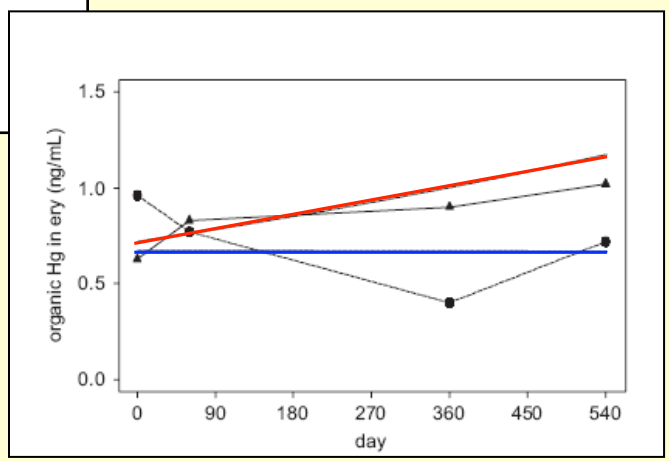
Halbach et al., **2008**, *Environ Research* 107:69-78

Blood Stream *Decrease* with MicroSilica (IMD)



Blood Stream *Decrease* with MicroSilica (IMD)





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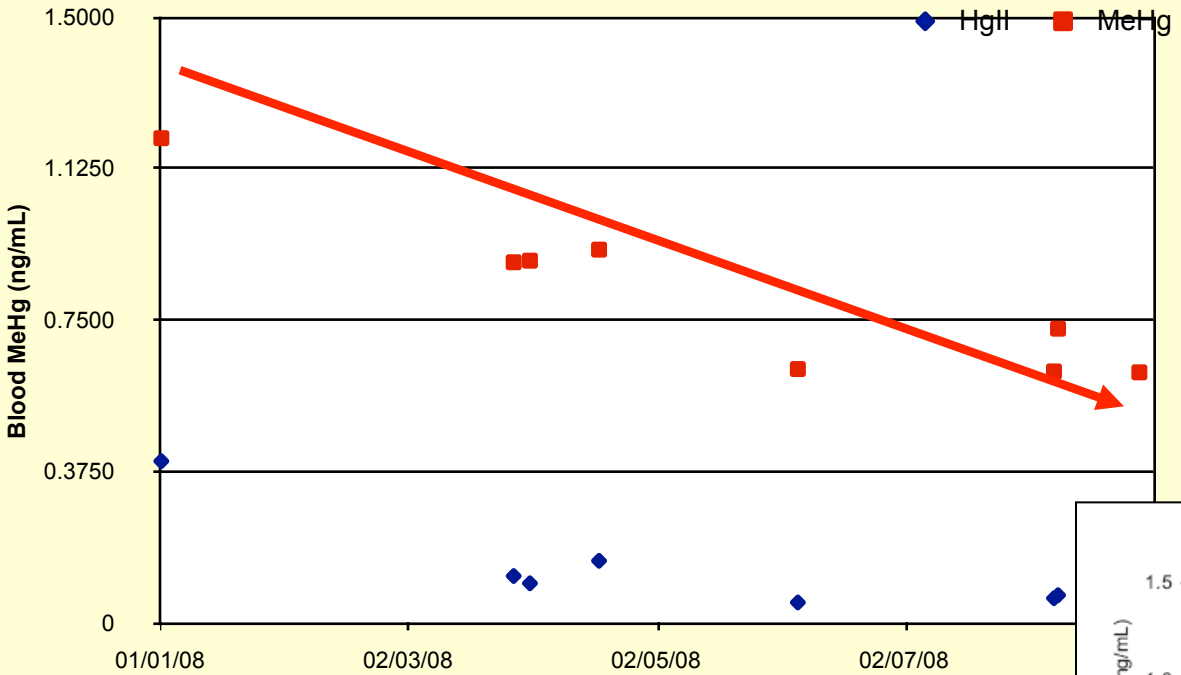

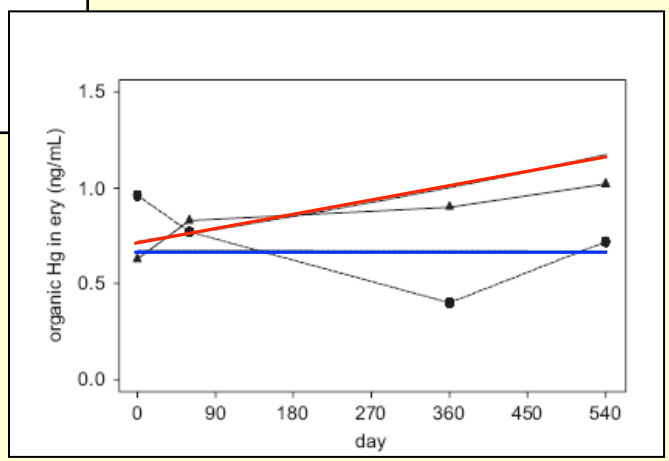

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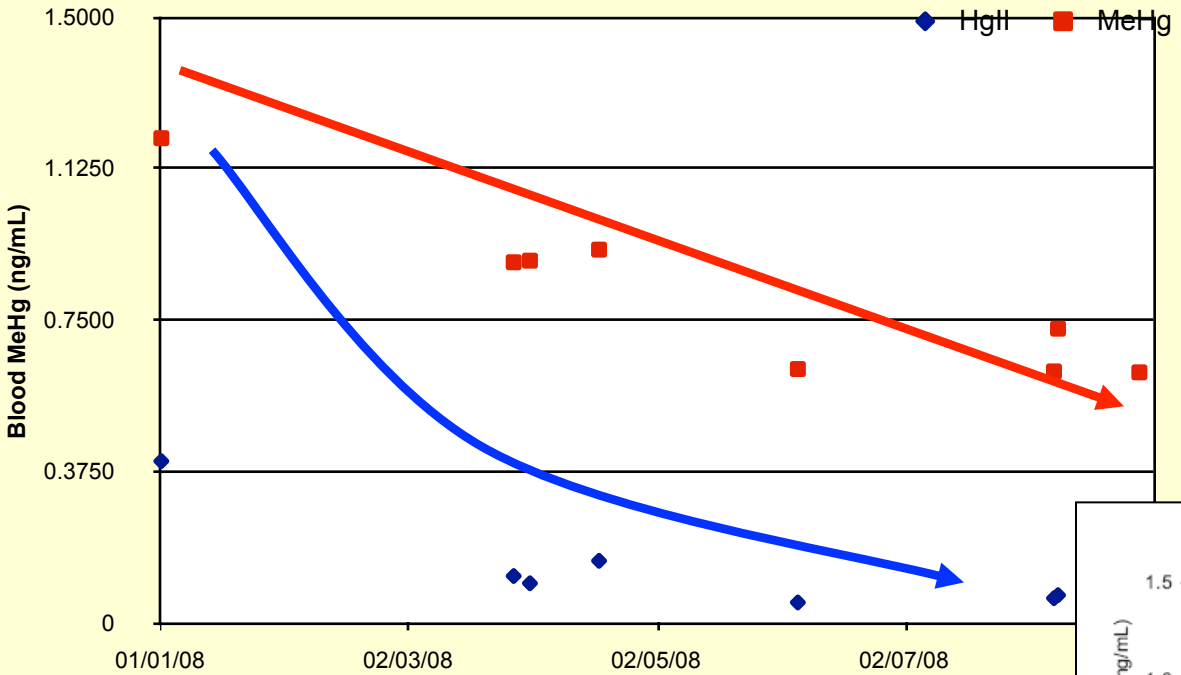

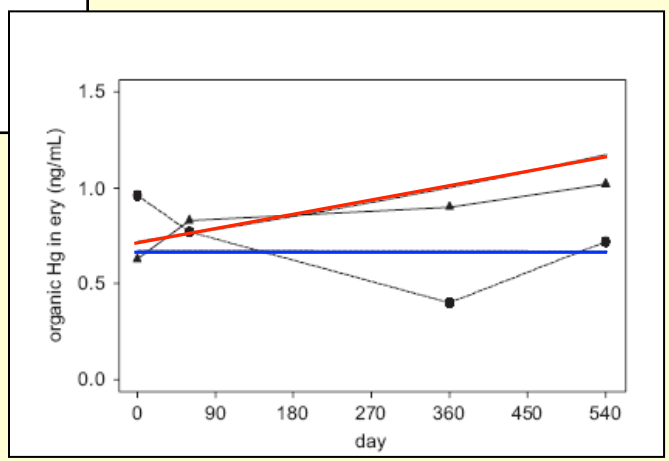

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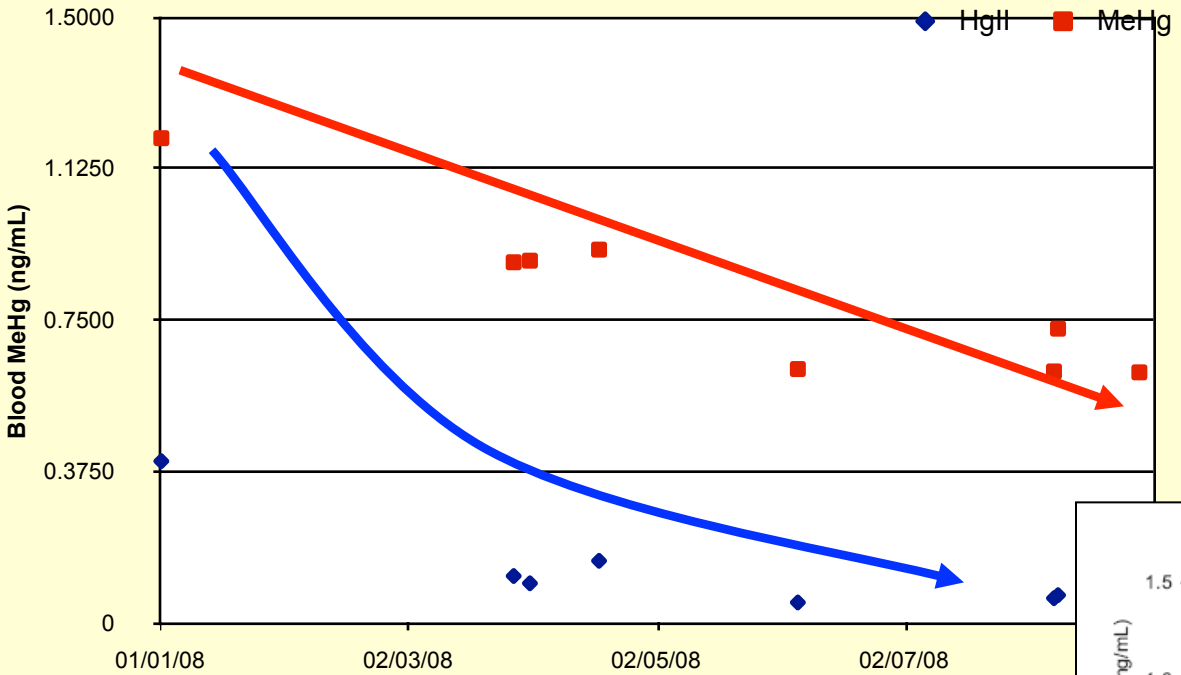
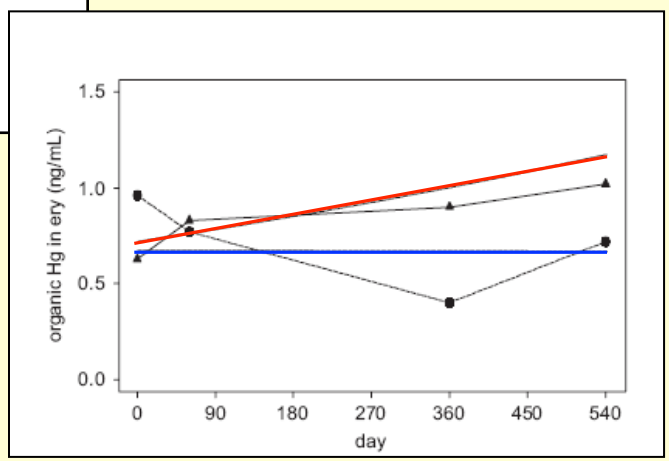




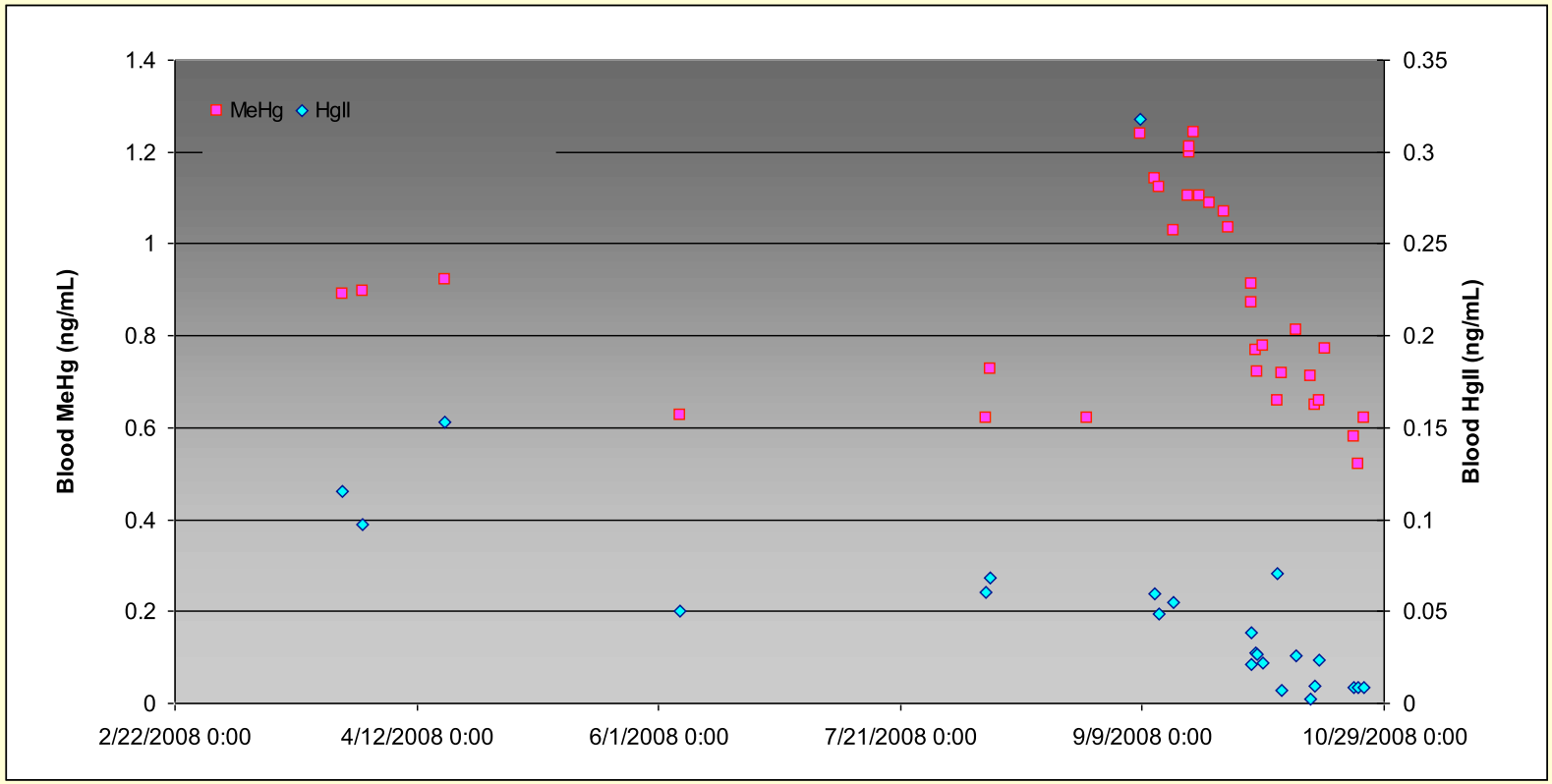
Depressed Phase II Transferases keep MeHg in cells; Once they kick in again, enterohepatic circulation retards excretion from body

Small Clinical Trial Results

Table 3.1 Changes in blood mercury levels during 7-10 day intervention with amalgam revision and nutritional support.

	Clinic 1		Clinic 2	
	IMD (n=8)	**No Treatment (n=4)**	**IMD only (n=5)**	**IMD+OSR (n=7)**
%Decr HgT	23.9	0.4	16.3	17.5
%Decr MeHg	22.9	5.1	15.9	32.3
%Decr HgII	12.4	-4.1	7.1	-15.0

Effect of Liposomal GSH enhancing cocktail (Phospholipid Exchange)



Enhancing Both Organ Drainage
and Blood Drainage

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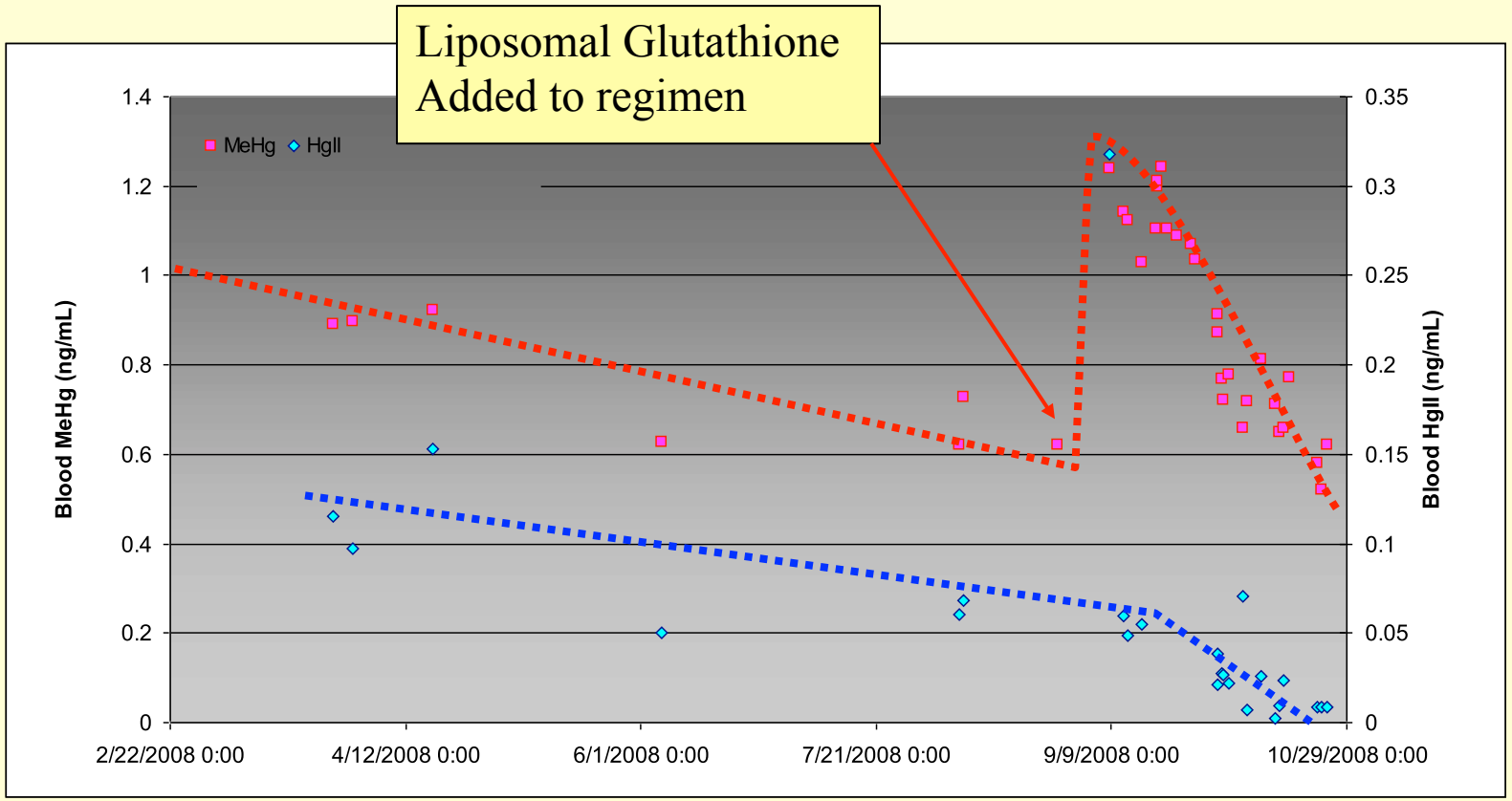
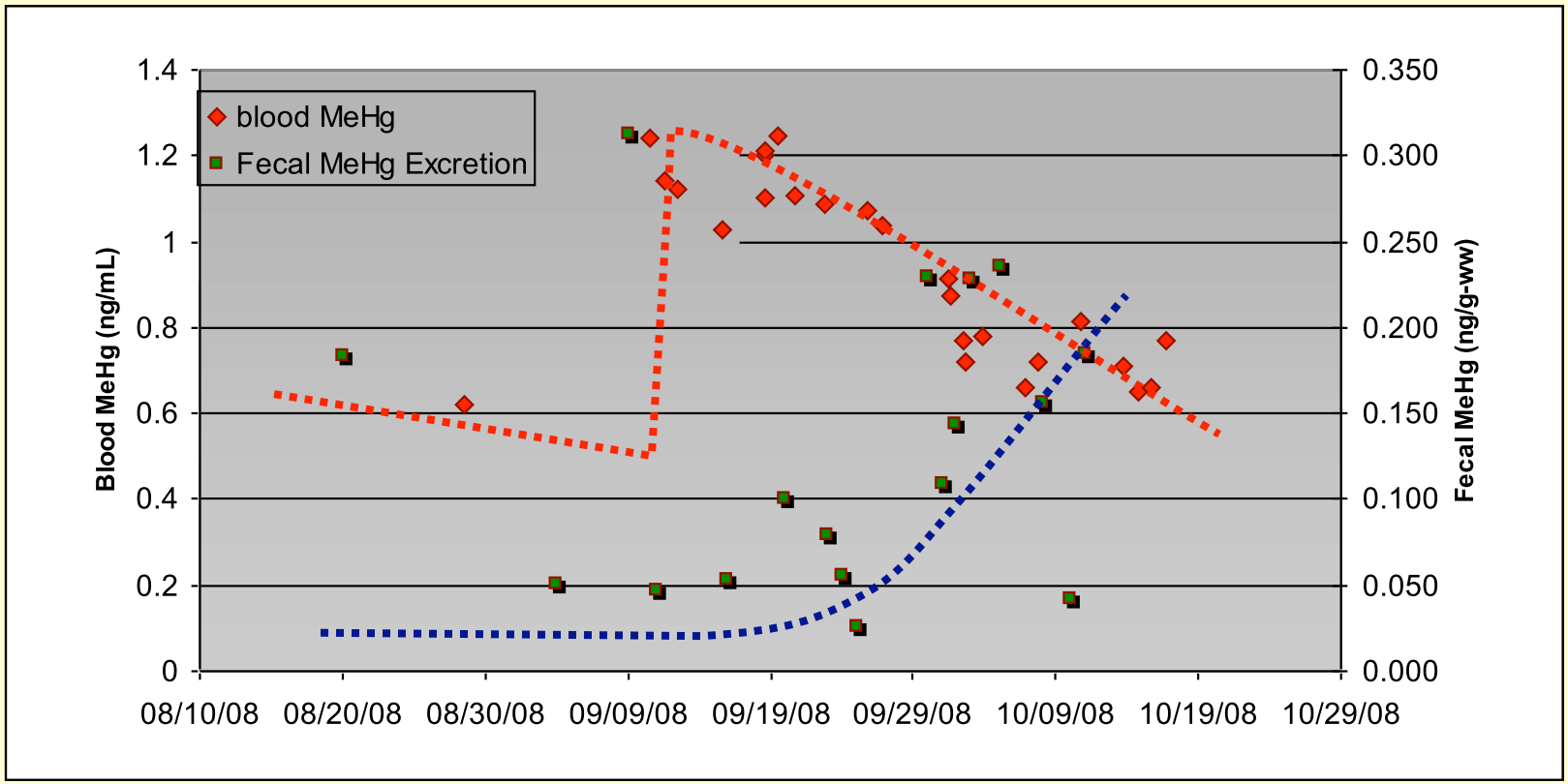


Enhancing Both Organ Drainage
and Blood Drainage

Excretion Rates
Liposomal GSH Supplementation



A truly effective chelation based on the natural detox system!

Summary

- Retention Toxicity Related to Dysfunction of Natural Glutathione Detox System, **BUT** Affects other detox systems

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Summary

- Retention Toxicity Related to Dysfunction of Natural Glutathione Detox System, **BUT** Affects other detox systems
- Inflamation as major trigger
- **MeHg** big hidden danger with amalgam
- Blood MeHg testing way to monitor detox
- IMD safe effective supplement to open up the detox channels and drain retained toxicity

Thank You

Dr. Klinghardt