THE TOXICITY OF ORAL INFECTIONS AND AMALGAMS

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The Concept of Oxidative Stress, Why is it so Common as a Symptom of Many Systemic Illnesses?

- Basically oxidative stress is identified as the over production of reactive oxygen species, e.g. hydroxyl free radical ($OH^{\cdot}$), due to some malfunction of the body's metabolism. This over production first consumes the reduced glutathione (GSH) converting it to oxidized glutathione (GSSG) as follows:
- $GSH + OH^{\cdot} \rightarrow GS^{\cdot} + H_2O$
- $2\ GS^{\cdot} \rightarrow GSSG$ and the free radical is abolished until all of the GSH is consumed.

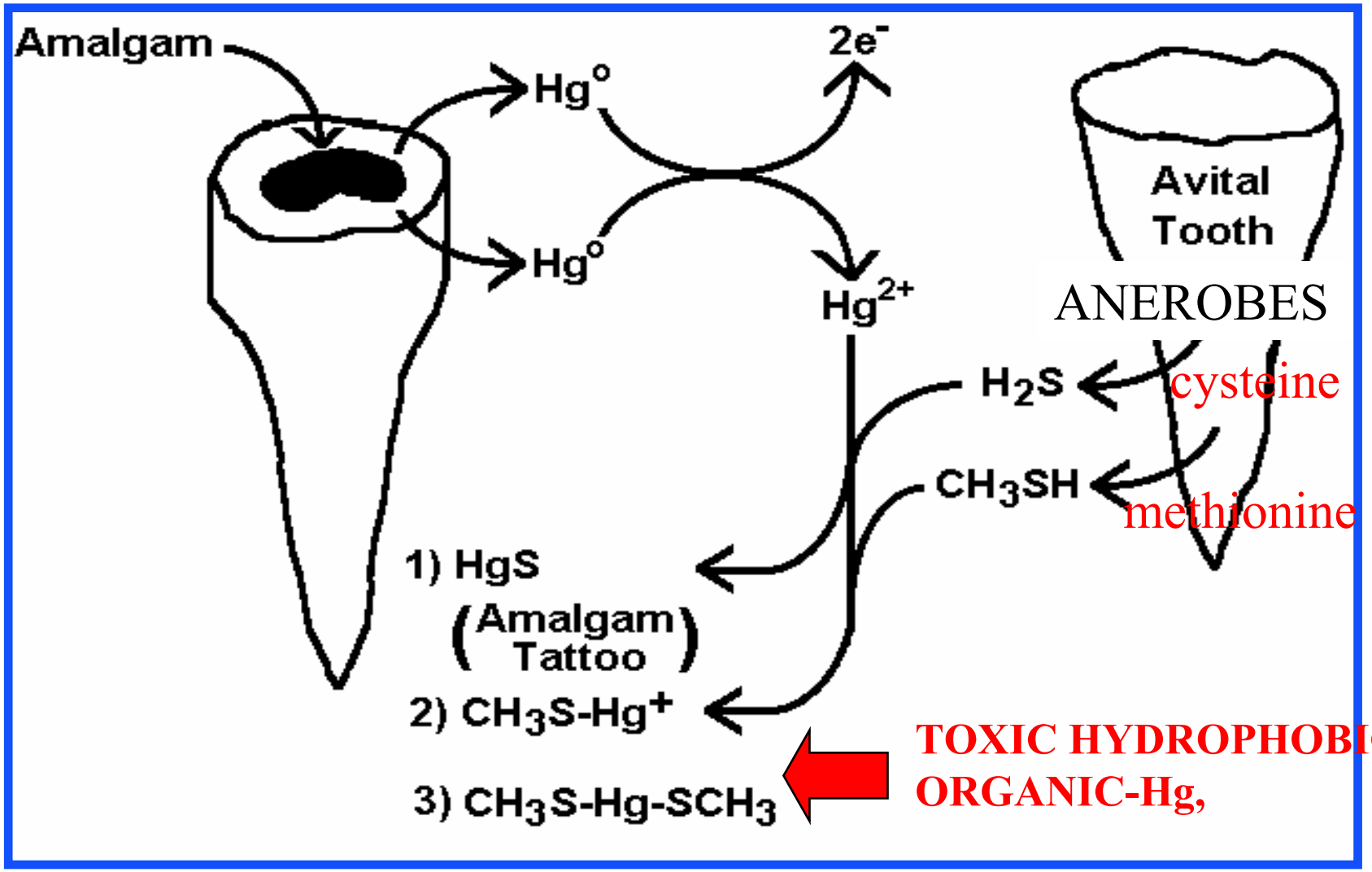
The Concept of Oxidative Stress, Why is it so Common as a Symptom of Many Systemic Illnesses?

- After consumption of protective GSH the $OH^{\cdot}$ radical starts chemically reacting with lipids, DNA, RNA and proteins causing extensive damage and cell death. The produced GSSG is the first step in apoptosis or programmed cell death that is not natural.
- Most cases of oxidative stress are elicited by damage to the electron transport system of the mitochondria, which when damaged, transfers electrons to H_2O catalytically producing $OH^{\cdot}$.

The Concept of Oxidative Stress, Why is it so Common as a Symptom of Many Systemic Illnesses?

- It is the unusual biochemical structures of the electron transport system, e.g. the iron sulfur centers, that make it susceptible to damage.
- Any sulfur reactive toxin, e.g. bacterial, yeast, or fungal produced oral toxins and heavy metals, would disrupt this system and allow catalytic production of reactive oxygen species damaging specific cells in specific locations eliciting different systemic illnesses.
- One molecule of toxin can cause the production of orders of magnitude of ROSs, e.g.$OH^{\cdot}$.

Amalgam Mercury Can Combine With Bacterial Toxins To Produce Even More Toxic Species



ORAL CHEMISTRY OF MERCURY

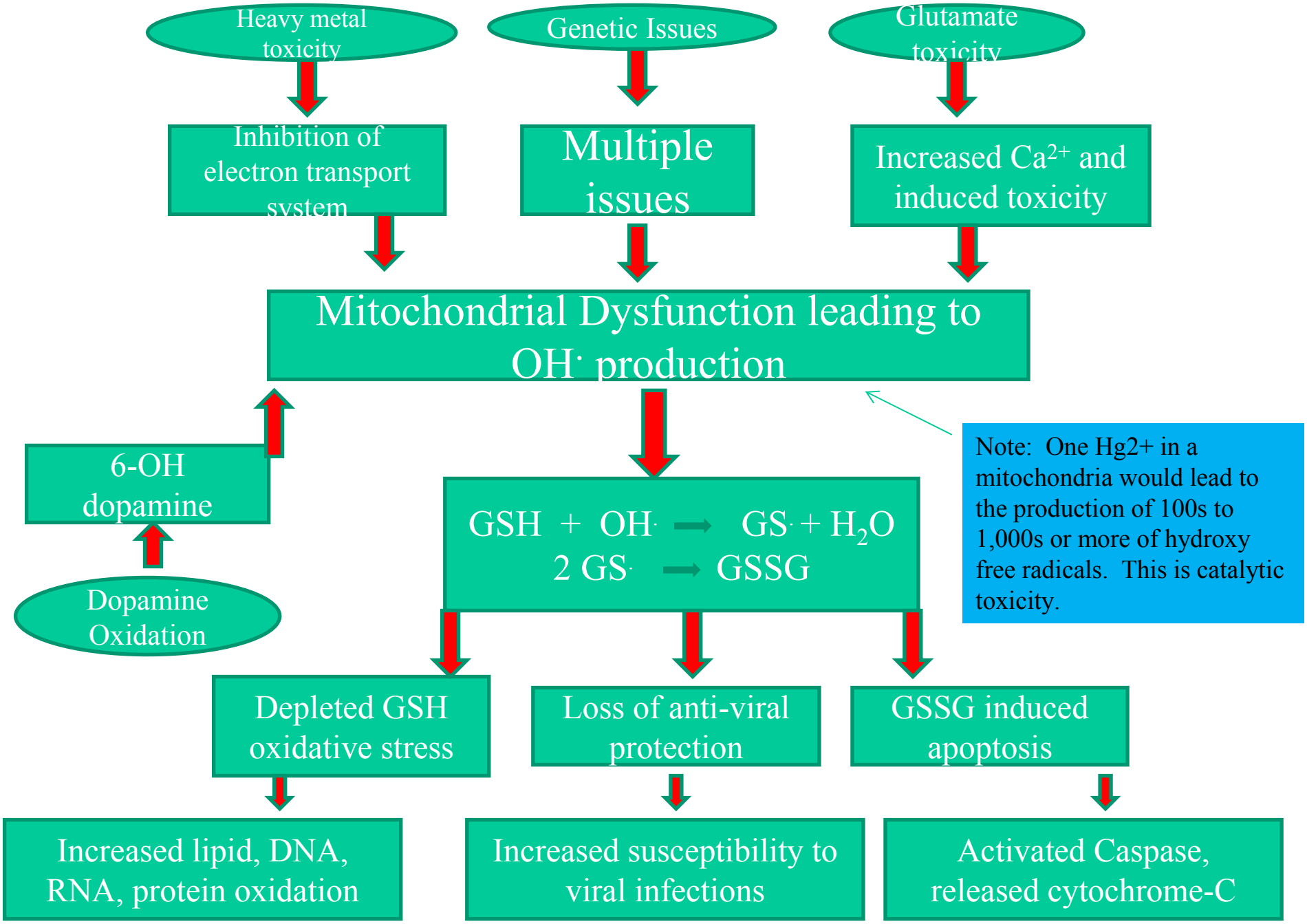
MERCURY RELEASED FROM DENTAL AMALGAMS WOULD REACT WITH ORGANIC THIOLS TO PRODUCE HYDROPHOBIC TOXINS MORE POTENT THAN Hg^{2+} DUE TO THEIR ABILITY TO PENETRATE CELL MEMBRANES AND CROSS THE BLOOD BRAIN BARRIER.

Oxidative Stress

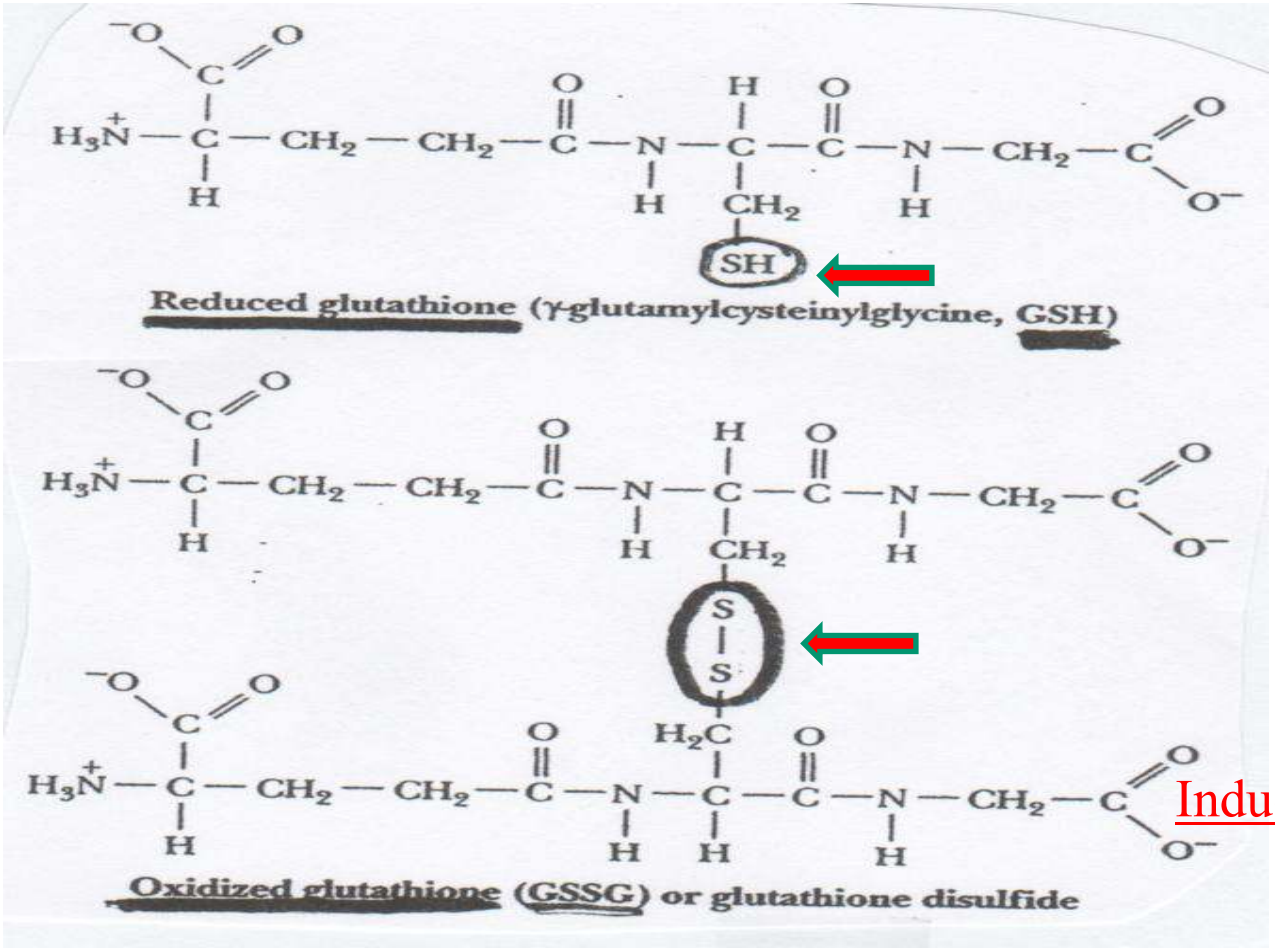
- OXIDATIVE STRESS IS PRIMARILY CAUSED BY OVER PRODUCTION OF FREE RADICALS THAT CONSUME THE MAJOR ANTIOXIDANT OF THE BODY WHICH IS CALLED REDUCED GLUTATHIONE (GSH).
- IT IS BOTH THE TOTAL AMOUNT OF GLUTATHIONE AND THE RATIO OF REDUCED (GSH) VERSUS OXIDIZED (GSSG) FORMS (GSH/GSSG) THAT ARE OF CONCERN IN HEALTH.
- THE GSH/GSSG RATIOS CONTROL PROGRAMED CELL DEATH.
- TOTAL BLOOD GLUTATHIONE LEVELS ARE OBTAINABLE FROM COMMERCIAL LABS.

The Importance of Glutathione (GSH) Levels

1. GSH serves as a frontline reducing agent keeping all our enzymes protected from oxidation.
2. GSH serves as a "natural chelator" for excretion of many heavy metals including Hg, Pb, Cd, etc.
3. GSH is attached to many water insoluble toxicants by glutathione-S-transferase (GST) allowing them to become water soluble and excretable as **GS-toxin** complexes. GSH with GST is used as an organic toxin remover.
4. GSH can react with certain yeast, fungal toxins (e.g. gliatoxin) decreasing their activity. It is a toxin inhibitor.
5. **GSH prevents viral infections** by binding to the viral coat surface preventing cell penetration. The influenza and HIV virus are two that are susceptible to GSH inhibition.
6. GSH conversion to GSSG **controls apoptosis**.


Heavy metal toxicity
Genetic Issues
Glutamate toxicity
Inhibition of electron transport system
Multiple issues
Increased Ca^{2+} and induced toxicity
Mitochondrial Dysfunction leading to $OH^{\cdot}$ production
6-OH dopamine
Dopamine Oxidation
$GSH + OH^{\cdot} \rightarrow GS^{\cdot} + H_2O$
$2\ GS^{\cdot} \rightarrow GSSG$
Note: One Hg2+ in a mitochondria would lead to the production of 100s to 1,000s or more of hydroxy free radicals. This is catalytic toxicity.
Depleted GSH oxidative stress
Loss of anti-viral protection
GSSG induced apoptosis
Increased lipid, DNA, RNA, protein oxidation
Increased susceptibility to viral infections
Activated Caspase, released cytochrome-C

Structures and General Chemistry of Glutathione



GOOD

BAD

Induces apoptosis

Note the number of charges on GSH. This makes it unlikely that it could enter any hydrophobic location in a tissue where much of the damaging oxidation occurs as caused by many

Structures and General Chemistry of Glutathione

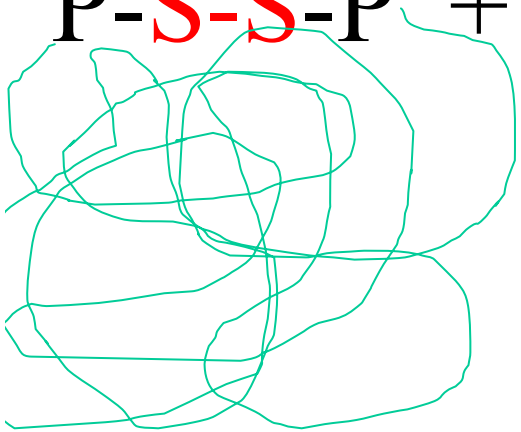
Glutathione (GSH) occurs in all tissues and is the most abundant sulfhydryl (-SH) containing compound in cells. It protects many enzymes from inhibition by reactive oxygen species (ROS) and heavy metals.

1. $Enzyme\text{-}SH_{(active)} + ROS + RSH \Longleftrightarrow Enzyme\text{-}S\text{-}S\text{-}R_{(inactive)} + H_2O_2$
2. $Enzyme\text{-}S\text{-}S\text{-}R_{(inactive)} + GSH \Longleftrightarrow Enzyme\text{-}SH_{(active)} + G\text{-}S\text{-}S\text{-}R$
3. $Enzyme\text{-}SH_{(active)} + Hg^{2+} \Longleftrightarrow Enzyme\text{-}S\text{-}Hg^{+}_{(inactive)} + H^{+}$
4. $Enzyme\text{-}S\text{-}Hg^{+}_{(inactive)} + GSH \Longleftrightarrow Enzyme\text{-}SH_{(active)} + GS\text{-}Hg^{+}$
5. $GS\text{-}Hg^{+} + GSH \Longleftrightarrow GS\text{-}Hg\text{-}SG_{(excreted\ form)} + H^{+}$

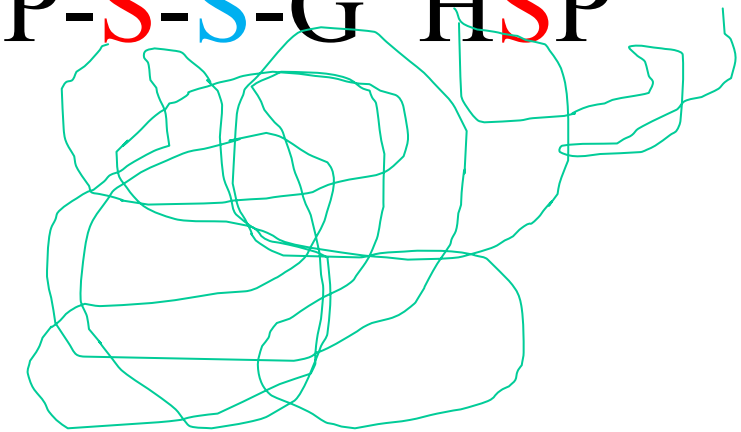
GSH PROTECTS THE BODY FROM OXIDATION AND HEAVY METAL TOXICITY! GS-Hg-SG is probably the major form of mercury that is excreted from the body by natural means. It leaves through the bilary transport system of the liver into the feces, not through the kidney. Low GSH levels (oxidative stress) in effect cause increased enzyme inhibition by ROS and decreases the ability to remove many toxic metals as well as organic type toxins. YOU CANNOT INCREASE BODY GLUTATIONE LEVELS BY EATING GLUTATHIONE!

GSH INSERTS INTO THE VIRAL COAT PROTEIN MARKING IT FOR REMOVAL FROM THE BLOOD STREAM .

P-S-S-P + GSH → P-S-S-G + HSP



VIRAL COAT PROTEIN WITH DISULFIDE LINKAGE



VIRAL COAT PROTEIN WITH GLUTATHIONE INSERTED IN BY A DISULFIDE EXCHANGE REACTION. THE –SG MARKS IT FOR REMOVAL.

GSH IS THE MOST EFFECTIVE INHIBITOR OF VIRAL REPLICATION IN CULTURED CELLS KNOWN. IT DOES SO WITHOUT ANY DISPLAYED TOXICITY.

INHIBITION OF INFLUENZA INFECTION BY GLUTATHIONE

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*Department of Biochemistry, †Department of Microbiology and Immunology, Emory University School of Medicine, Atlanta, GA, USA; and
‡Nutri-Quest, Inc., Chesterfield, MO, USA (*Received 27 August 2002; Revised 23 December 2002; Accepted 9 January 2003)*

Abstract—Infection by RNA virus induces oxidative stress in host cells. Accumulating evidence suggests that cellular redox status plays an important role in regulating viral replication and infectivity. In this study, experiments were performed to determine whether the thiol antioxidant glutathione (GSH) blocked influenza viral infection in cultures of Madin-Darby canine kidney cells or human small airway epithelial cells. Protection against production of active virus particles was observed at a low (0.05– 0.1) multiplicity of infection (MOI). **GSH inhibited expression of viral matrix protein and inhibited virally induced caspase activation and Fas upregulation.** In BALB/c mice, inclusion of GSH in the drinking water decreased viral titer in both lung and trachea homogenates 4 d after intranasal inoculation with a mouse-adapted influenza strain A/X-31. Together, **the data suggest that the thiol antioxidant GSH has an anti-influenza activity in vitro and in vivo. Oxidative stress or other conditions that deplete GSH in the epithelium of the oral, nasal, and upper airway may, therefore, enhance susceptibility to influenza infection.**

Most likely even the Swine or Avian influenza types are susceptible to GSH

Glutathione deficiency is associated with impaired survival in HIV disease.

Herzenberg, LA, De Rosa, SC, Dubs, JG, Roederer, M, Anderson, MT, Ela, SW, Deresinski, SC, Herzenberg, LA.

Department of Genetics, Stanford University Medical School, CA ,USA.

Glutathione (GSH), a cysteine-containing tripeptide, is essential for the viability and function of virtually all cells. In vitro studies showing that low GSH levels both promote HIV expression and impair T cell function suggested a link between GSH depletion and HIV disease progression.

Clinical studies presented here directly demonstrate that low GSH levels predict poor survival in otherwise indistinguishable HIV-infected subjects. Specifically, we show that GSH deficiency in CD4 T cells from such subjects is associated with markedly decreased survival 2-3 years after baseline data collection (Kaplan-Meier and logistic regression analyses, $P < 0.0001$ for both analyses). **This finding, supported by evidence demonstrating that oral administration of the GSH prodrug N-acetylcysteine replenishes GSH in these subjects and suggesting that N-acetylcysteine administration can improve their survival, establishes GSH deficiency as a key determinant of survival in HIV disease.**

Further, it argues strongly that the unnecessary or excessive use of acetaminophen, alcohol, or other drugs known to deplete GSH should be avoided by HIV-infected individuals.

Source: *Proc Natl Acad Sci USA*, **1997**, 94 (5), 1967-72.
URL Accessed: 12/5/2008, http://www.ncbi.nlm.nih.gov/pubmed/9050888?dopt=Abstract.

Molecular Mechanism of Decreased Glutathione Content in Human Immunodeficiency Virus Type 1 Tat-transgenic Mice.

Jinah Choi, Rui-Ming Liu, Ramendra K. Kundu, Frank Sangiorgi,
Weicheng Wu, Robert Maxson, and Henry Jay Forman.

Human immunodeficiency virus (HIV) progressively depletes GSH content in humans. Although the accumulated evidence suggests a role of decreased GSH in the pathogenesis of HIV, significant controversy remains concerning the mechanism of GSH depletion, especially in regard to envisioning appropriate therapeutic strategies to help compensate for such decreased antioxidant capacity.

Tat, a transactivator encoded by HIV, is sufficient to cause GSH depletion *in vitro* and is implicated in AIDS-associated Kaposi's sarcoma and B cell lymphoma. In this study, we report a decrease in GSH biosynthesis with Tat, using HIV-1 Tat transgenic (Tat+) mice. A significant decline in the total intracellular GSH content in liver and erythrocytes of Tat+ mice was accompanied by decreased γ-glutamylcysteine synthetase regulatory subunit mRNA and protein content, which resulted in an increased sensitivity of γ-glutamylcysteine synthetase to feedback inhibition by GSH. Further study revealed a significant reduction in the activity of GSH synthetase in liver of Tat+ mice, which was linearly associated with their GSH content.

Therefore, Tat appears to decrease GSH *in vivo*, at least partially, through modulation of GSH biosynthetic enzymes.

Source: *J Biol Chem*, **2000,** 275 (5), 3693-3698.

URL Accessed: 12/5/2008, http://www.jbc.org/cgi/content/abstract/275/5/3693.

This research implies that oxidative stress, i.e. low GSH levels must be induced for effective HIV replication to occur and that low GSH levels must be a risk factor for HIV infection.

Glutathione inhibits HIV replication by acting at late stages of the virus life cycle.

Palamara, AT, Perno, CF, Aquaro, S, Buè, MC, Dini, L, Garaci, E.
Department of Experimental Medicine and Biochemical Sciences, University of Rome, Italy.

We investigated the effect of glutathione on the replication of human immunodeficiency virus (HIV) in chronically infected macrophages, a known reservoir of the virus in the body.

We found that exogenous GSH strongly suppresses the production of p24gag protein as well as the virus infectivity. This is related to a dramatic decrease in both budding and release of virus particles from chronically infected cells (either macrophages or lymphocytes), together with a selective decrease in the expression of gp120, **the major envelope glycoprotein, rich in intrachain disulfide bonds and thus potentially sensitive to the effect of a reducing agent such as GSH.**

Overall data suggest that GSH can interfere with late stages of virus replication. This would be in agreement with data obtained in cells exposed to herpesvirus type 1 (a DNA virus) or to Sendai (an RNA virus), showing that the suppression of virus replication by GSH is related to the selective inhibition of envelope glycoproteins.

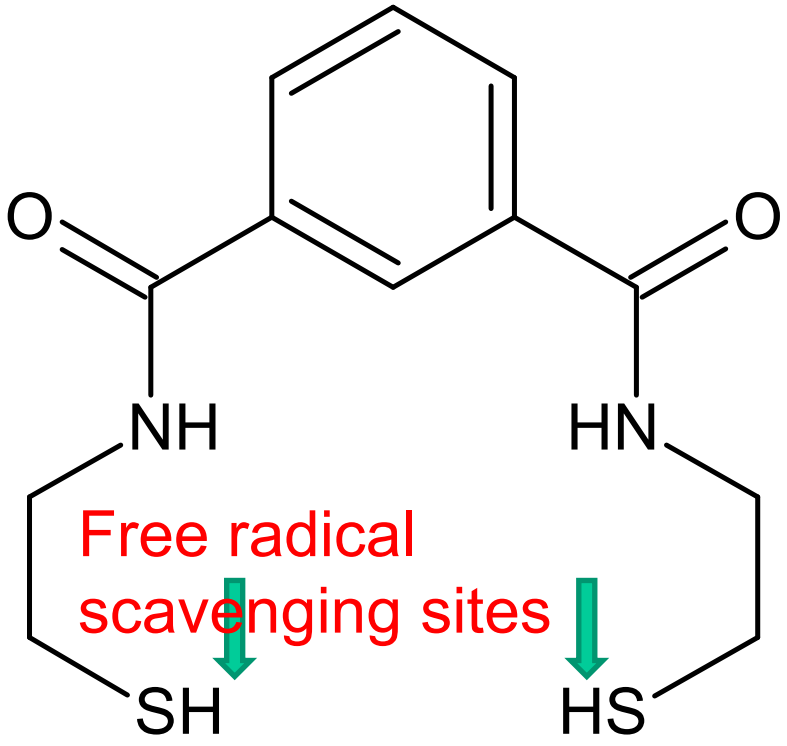
These results suggest a potential role of GSH in combination with other antivirals in the treatment of virus-related diseases.

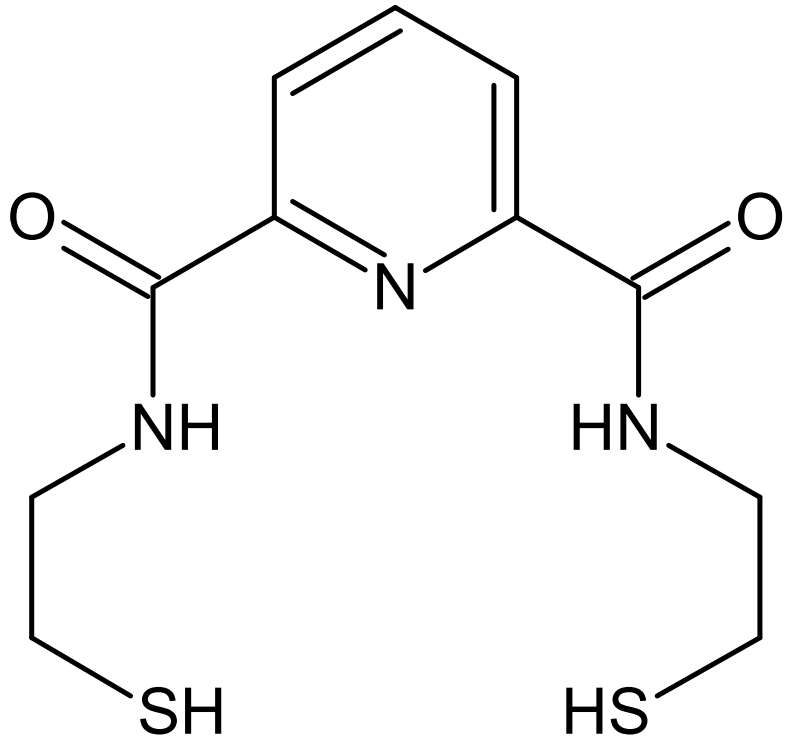
Source: *AIDS Res Hum Retroviruses,* **1996,**12 (16), 1537-41.
URL Accessed: 03/14/2009, http://www.ncbi.nlm.nih.gov/pubmed/8911579.

ANTIOXIDANT CONCEPT: HELPING TO MAINTAIN A HEALTHY TOTAL AND REDUCED GLUTATIONE LEVEL

- IT IS OF MAJOR CONCERN THAT TOXICITIES AND SPORADIC OR CHRONIC ILLNESSES OR INFECTIONS CAN REDUCE TOTAL OR REDUCED GLUTATHIONE FOR SUCH A PERIOD OF TIME THAT RECOVERY IS MADE DIFFICULT BECAUSE OF THE BUILD UP OF MANY TOXINS THAT REQUIRED A CONSISTENT HIGHER LEVEL OF GSH FOR EFFECTIVE REMOVAL.
- IF A SIGNIFICANT PERCENTAGE OF MITOCHONDRIA ARE DYSFUNCTIONAL OR DAMAGED THEY CAN CONTINOUSLY CATALYTICALLY PRODUCE HYDROXYL FREE RADICALS AT A RATE THAT PREVENTS GLUTATHIONE RECOVERY TO A NORMAL LEVEL.
- WHEN SUCH CONDITIONS EXIST THE BODY WILL SURVIVE WITH SUB-ADEQUATE LEVELS OF GSH AND WILL BE SUSCEPTIBLE TO MANY OTHER ILLNESSES AND INFECTIONS.
- BOTH MEDICAL/DENTAL AND DIETARY APPROACHES ARE NEEDED TO HELP THE BODY MAINTAIN A HEALTHY GLUTATHIONE LEVEL IN ORDER FOR AFFLICTED INDIVIDUALS TO REGAIN AND MAINTAIN NORMALITY.

New Hydrophobic Antioxidant Agents

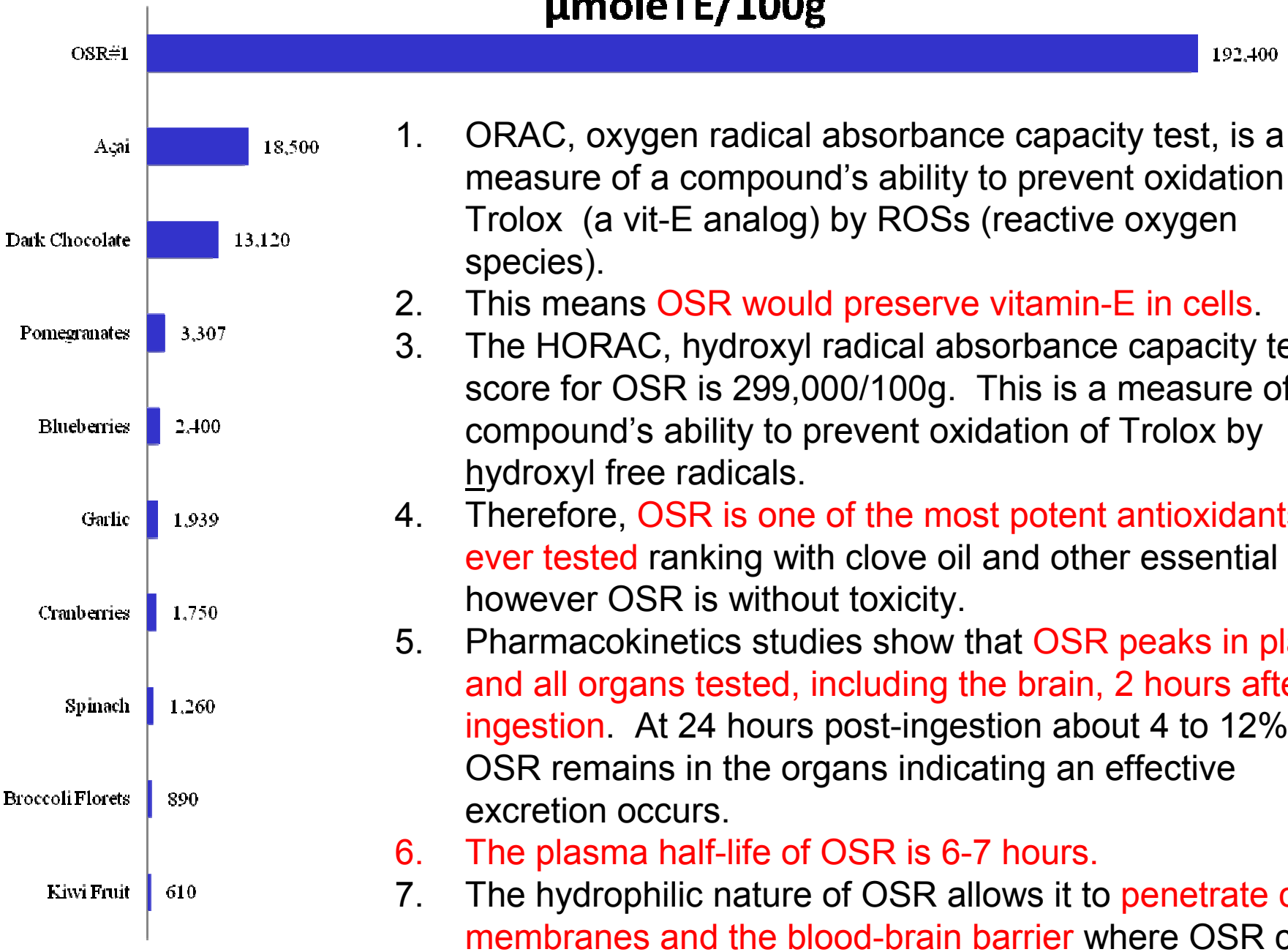




Potent scavengers of hydroxyl radicals in lipophilic areas.

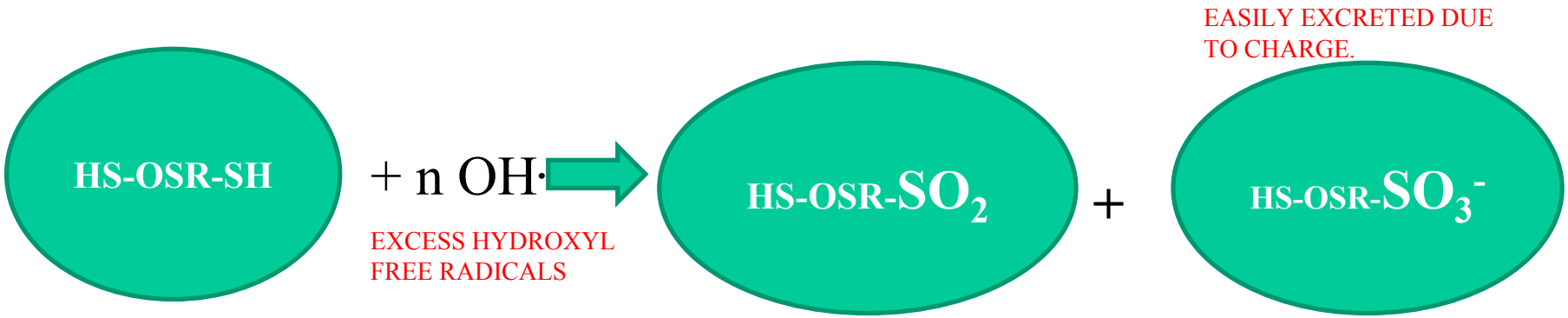
A New Antioxidant Called OSR that consists of two natural non-toxic compounds (benzoate, found in cranberries, and cysteamine, found in all mammalian cells and on the terminal end of CoEnzyme-A).

Comparative ORAC Scores
µmoleTE/100g



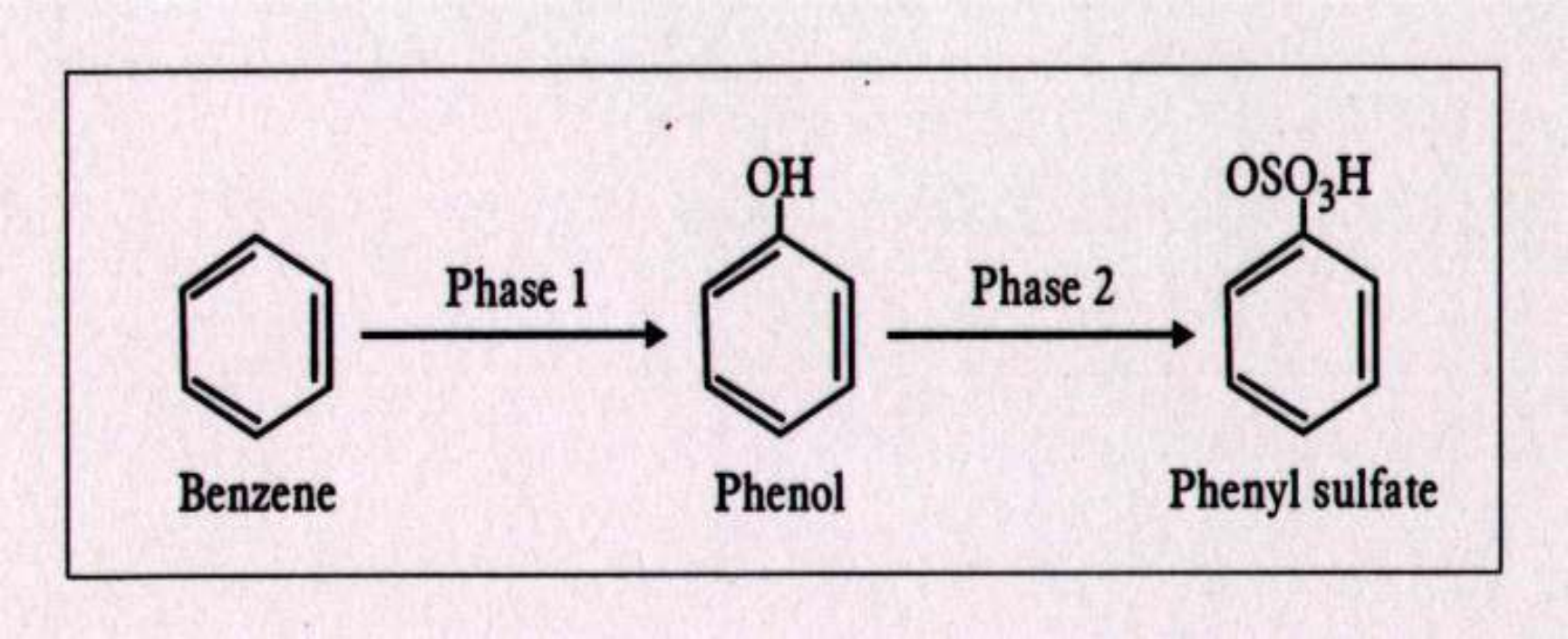
1. ORAC, oxygen radical absorbance capacity test, is a measure of a compound's ability to prevent oxidation of Trolox (a vit-E analog) by ROSs (reactive oxygen species).
2. This means OSR would preserve vitamin-E in cells.
3. The HORAC, hydroxyl radical absorbance capacity test, score for OSR is 299,000/100g. This is a measure of a compound's ability to prevent oxidation of Trolox by hydroxyl free radicals.
4. Therefore, OSR is one of the most potent antioxidants ever tested ranking with clove oil and other essential oils, however OSR is without toxicity.
5. Pharmacokinetics studies show that OSR peaks in plasma and all organs tested, including the brain, 2 hours after ingestion. At 24 hours post-ingestion about 4 to 12% of OSR remains in the organs indicating an effective excretion occurs.
6. The plasma half-life of OSR is 6-7 hours.
7. The hydrophilic nature of OSR allows it to penetrate cell membranes and the blood-brain barrier where OSR can

INCUBATION OF OSR WITH HUMAN AND RAT LIVER HOMOGENATES



DETERMINED BY ICP MASS SPECTROMETRY WITH HPLC SEPARATION AND FRAGMENTATION. NO SINGLE OXYGEN PRODUCT WAS DETECTED, THE THREE OXYGEN SPECIES PREDOMINATED. IT SEEMS AS IF ONLY ONE –SH PER OSR WAS OXYGENATED AS NO SPECIES WAS DETECTED THAT HAD OXYGEN ON BOTH SULFURS OF OSR. IT APPEARS AS IF THE EXTRAORDINARY ORAC SCORES OF OSR IS DUE TO –SH TO –SH INTERACTION THAT MAKES ONE OF THE –SHs MORE REACTIVE WITH HYDROXYL FREE RADICAL.

P-450 Detoxification Chemistry



DIETARY SAFETY OF ORAL OSR#1

- A commercial toxicology laboratory has confirmed that the new antioxidant has **an LD50 greater than 5grams/kg body weight** when given orally, the highest testing level! **This is equivalent to a 100 lb person taking 227grams.**
- Nor did mice given 1.0g/kg (2.2lbs) body weight for 28 straight days demonstrate any toxic effects on any organ.
- The compounds are not mutagenic as determined by a FDA approved laboratory and low endotoxin levels.
- **These compounds are dietary antioxidants and are not FDA approved to treat any illness or disease.**

OSR: GSH and Thiol Data in ASD

Peach colored samples hemolyzed- disregard

	8 yo wm ASD			9 yo wf ASD Severe			9 yo wf ASD gd recovery			11 yo wm ASD		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
Total GSH/GSSG	40.3	53.6	87.1	42.9	37.5	87.7	24.8	32.3	64.5	14.8	22.1	28.6
Free GSH/GSSG	15.7	18.0	24.3	13.5	8.2	26.2	8.7	14.1	29.5	5.3	6.9	12.2
Glu-Cys	2.1	2.4	3.4	3.6	3.3	4.0	2.2	3.0	3.9	2.5	2.9	3.2
Cys-Gly	37.9	38.1	33.3	41.2	36.8	46.9	35.0	35.6	34.0	51.7	42.4	35.8
Cysteine	200.4	212.2	201.9	170.2	166.8	169.1	240.2	231.3	260.0	237.1	250.5	185.8
Homocys	4.6	5.5	5.3	5.7	5.1	5.0	5.2	5.9	6.3	7.9	8.4	9.2
Methionine	14.8	15.4	16.4	20.7	22.7	26.0	22.1	22.6	26.3	22.2	19.4	30.9

OSR: GSH and Thiol Data Seniors

Peach colored samples hemolyzed- disregard

	72 yo wm			71 yo wf			73 yo wf		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
Total GSH/GSSG	**11.4**	**16.9**	**48.8**	**17.2**	**36.2**	**28.7**	**15.8**	**42.8**	**69.6**
Free GSH/GSSG	**3.5**	**5.3**	**17.0**	**8.9**	**12.1**	**15.6**	**8.0**	**17.3**	**25.4**
Glu-Cys	3.2	3.3	3.6	2.9	2.8	4.0	1.8	3.2	4.1
Cys-Gly	63.0	59.1	61.2	45.0	51.4	48.0	39.8	41.9	51.5
Cysteine	344.2	255.4	317.9	304.7	243.6	290.0	288.2	253.7	324.2
Homocys	21.2	13.9	12.8	9.7	9.3	9.1	11.4	12.6	16.1
Methionine	20.5	28.3	31.2	15.4	17.2	25.4	21.1	23.1	33.7

GST is an enzyme that attaches GSH to organic toxicants making a covalent complex of Toxin-SG that is charged, water soluble and marked for cell excretion and elimination from the blood by the bilary transport system of the liver.

HUMAN FOOD SAFETY STUDIES: Effect of OSR on Glutathione-S-transferase (GST) levels (ng/ml)

	GST		
Time (months)	0	1	2
Patient #			
1	L	L	0.48
2	L	L	0.48
3	L	0.46	0.43
4	L	L	0.53
5	L	L	0.43
6	L	L	0.37
7	L	L	0.32
8	L	0.58	0.43
9	L	L	0.63
10	L	L	0.43

GST activities increased in every patient. Detection levels were 0.4 for normals to 3.1 for a high level for GST.

CONCLUSIONS

- A NON-TOXIC, LIPID SOLUBLE, FREE RADICAL SCAVENGING ANTIOXIDANT HAS BEEN DEVELOPED AND FOUND TO BE WITHOUT DETECTABLE TOXICITY.
- THIS ANTIOXIDANT EFFECTIVELY SCAVENGES HYDROXYL RADICALS.
- THIS ANTIOXIDANT IS EFFECTIVE IN HELPING MAINTAIN A HEALTHY GLUTATHIONE LEVEL.
- A HEALTHY GLUTATHIONE LEVEL IS IMPORTANT FOR HEALTH.

Hg Induces the Aberrant Biochemistry of AD

- Khatoon, S., Campbell, S.R., Haley, B.E. and Slevin, J.T. **Aberrant GTP β-Tubulin Interaction in Alzheimer's Disease. Annals of Neurology 26, 210-215 (1989).**
- Gunnersen, D.J. and Haley, B.E. **Detection of Glutamine Synthetase in the Cerebrospinal Fluid of Alzheimer's Diseased Patients: A Potential Diagnostic Biochemical Marker. Proc. Natl. Acad. Sci. USA, 89 pp. 11949-11953 (1992).**
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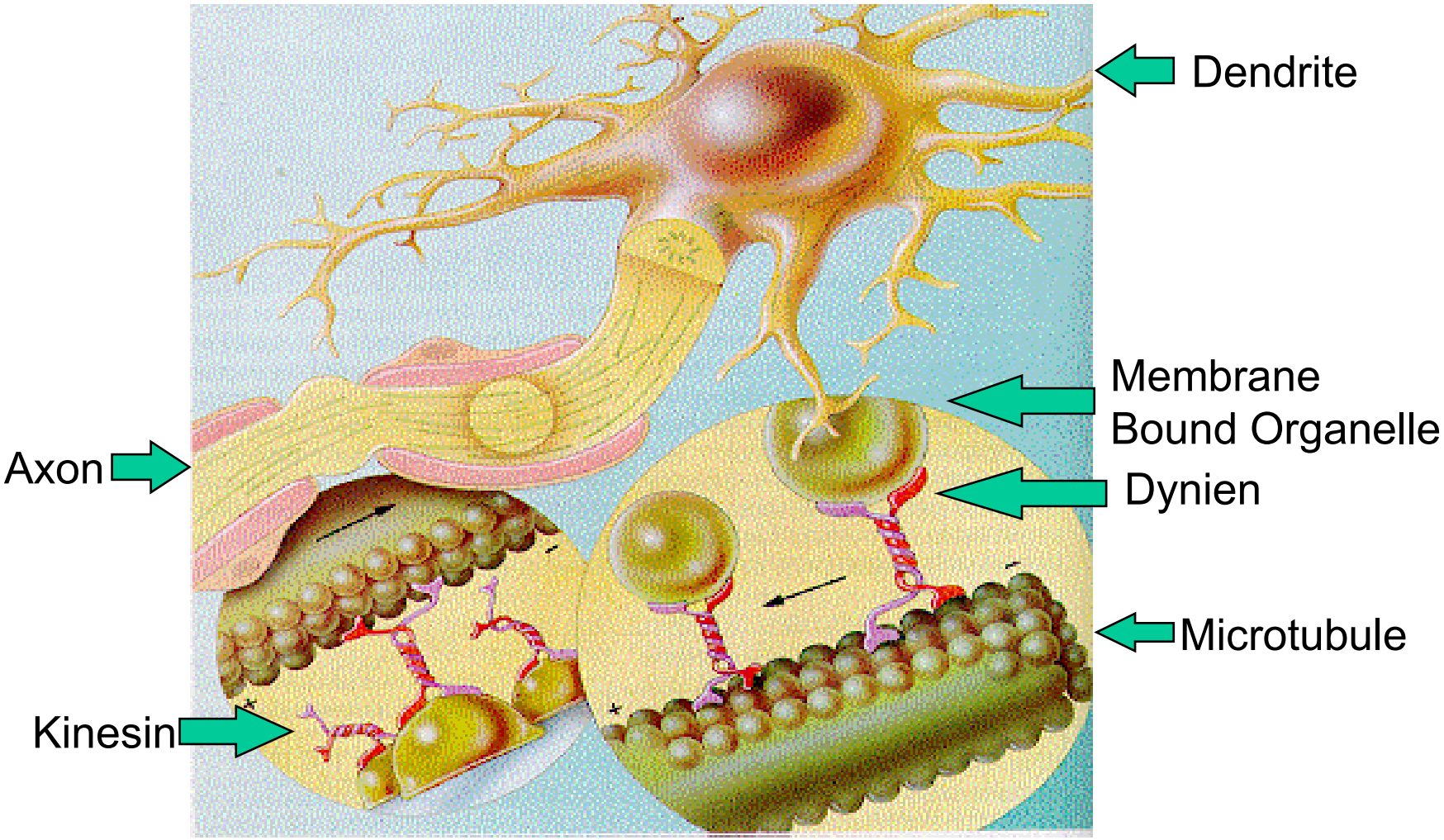
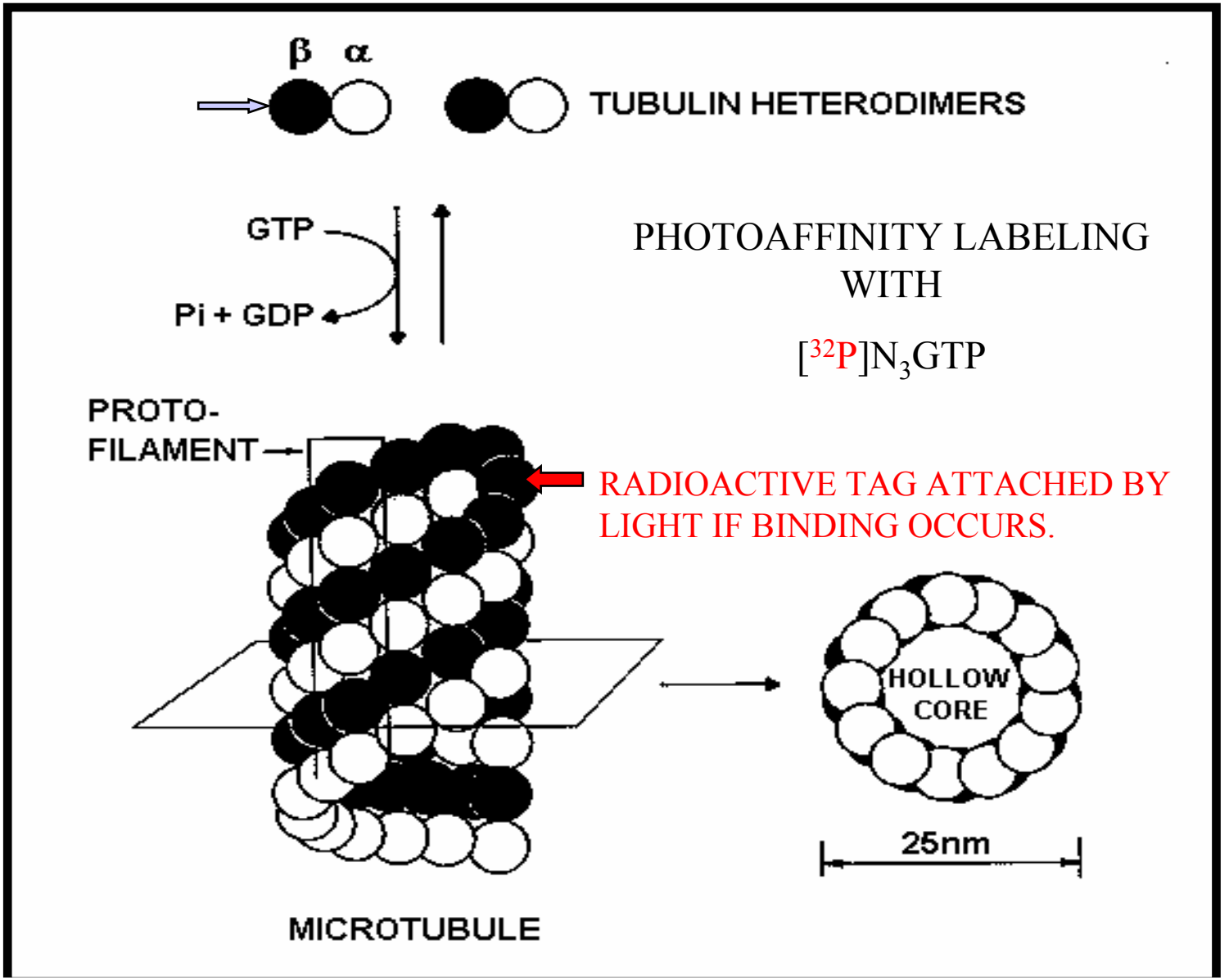
- Haley, B. **The Relationship of the Toxic Effects of Mercury to Exacerbation of the Medical Condition Classified as Alzheimer's Disease. Nordic J. of Biological Medicine, June-July 2003**

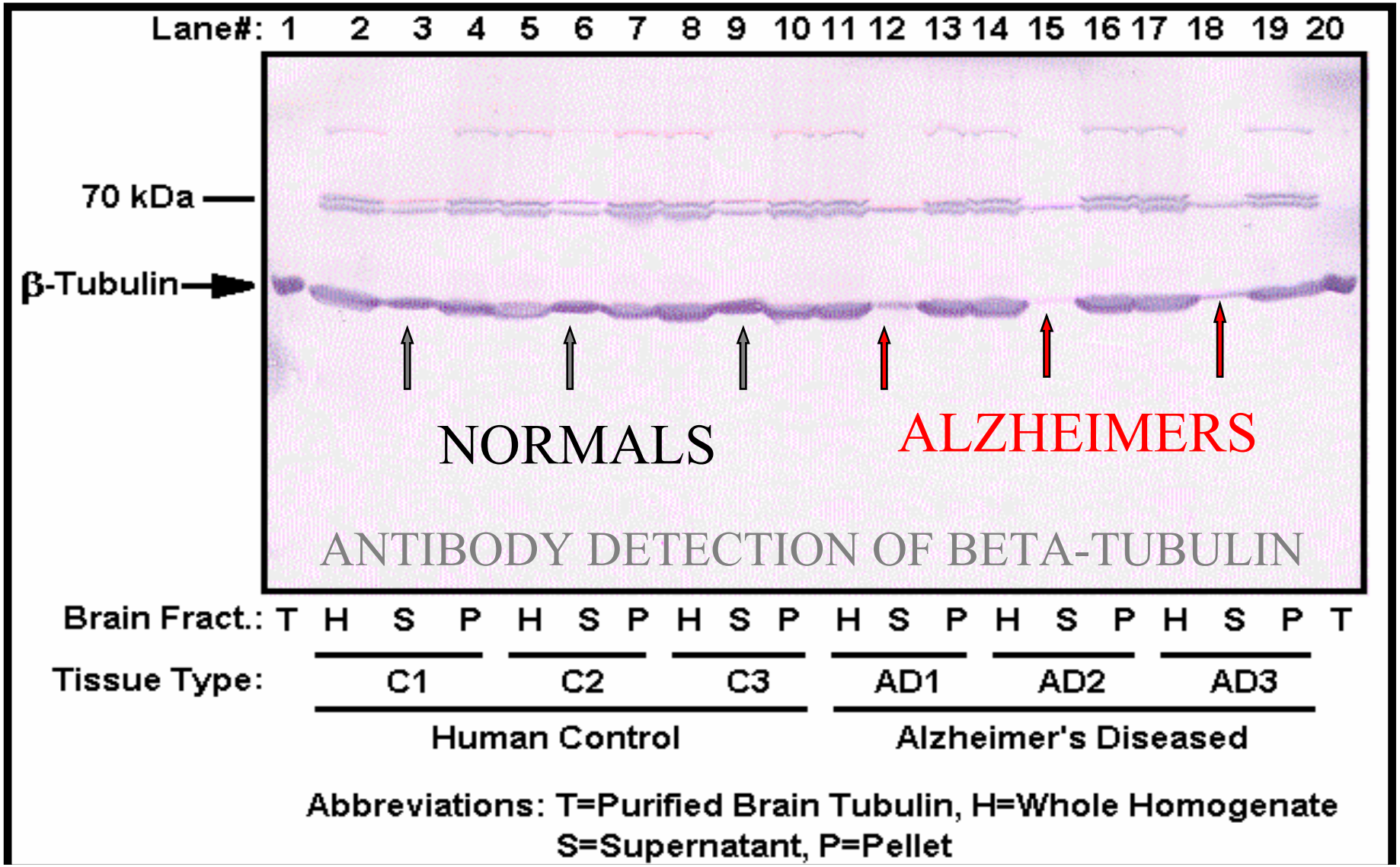
Axonal Transport - A Process Essential for the Survival of Neurons



Structure of Neuronal Microtubules



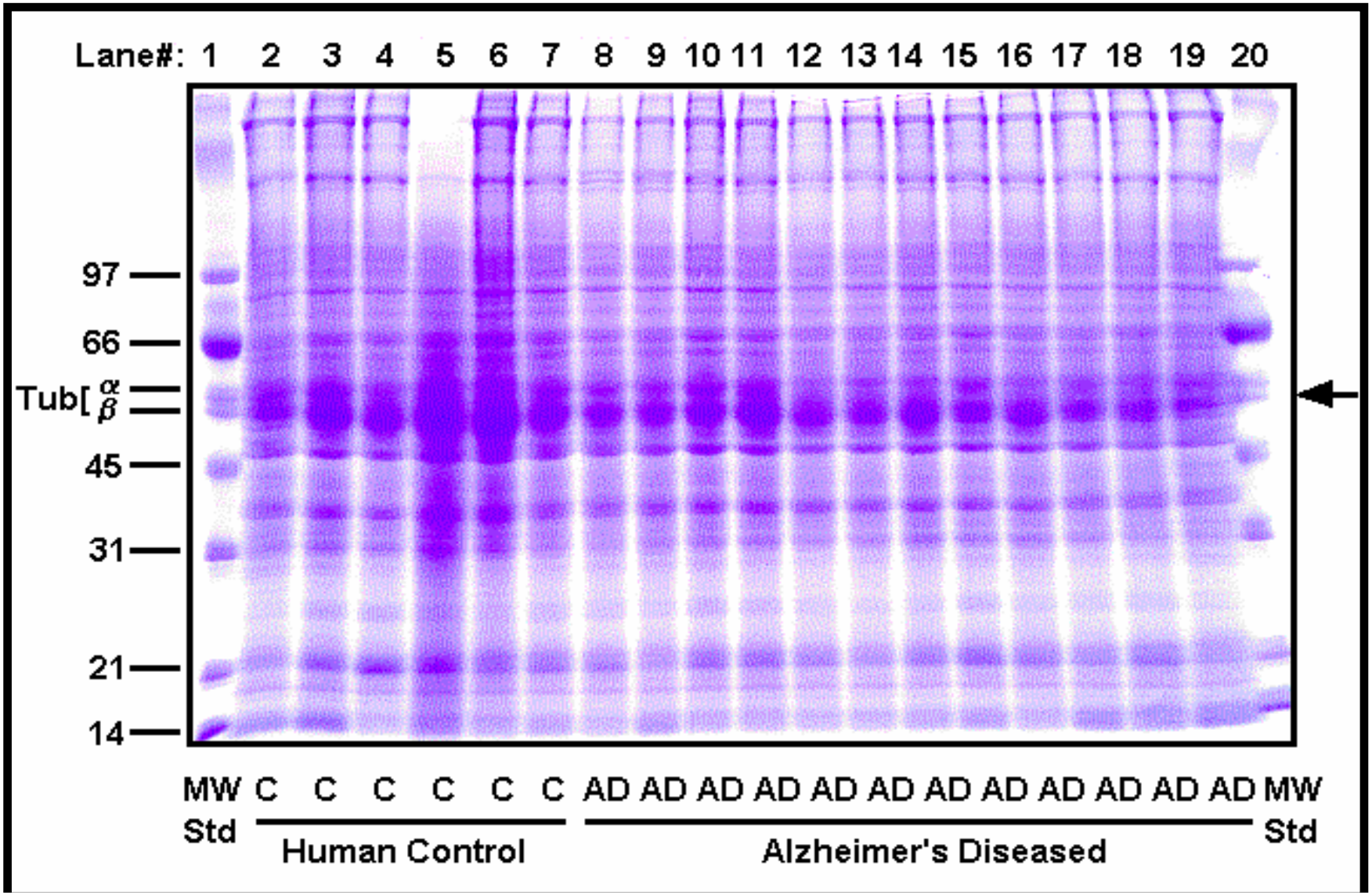
Partitioning of ß-Tubulin is Aberrant in Alzheimer's Diseased Brain Homogenates



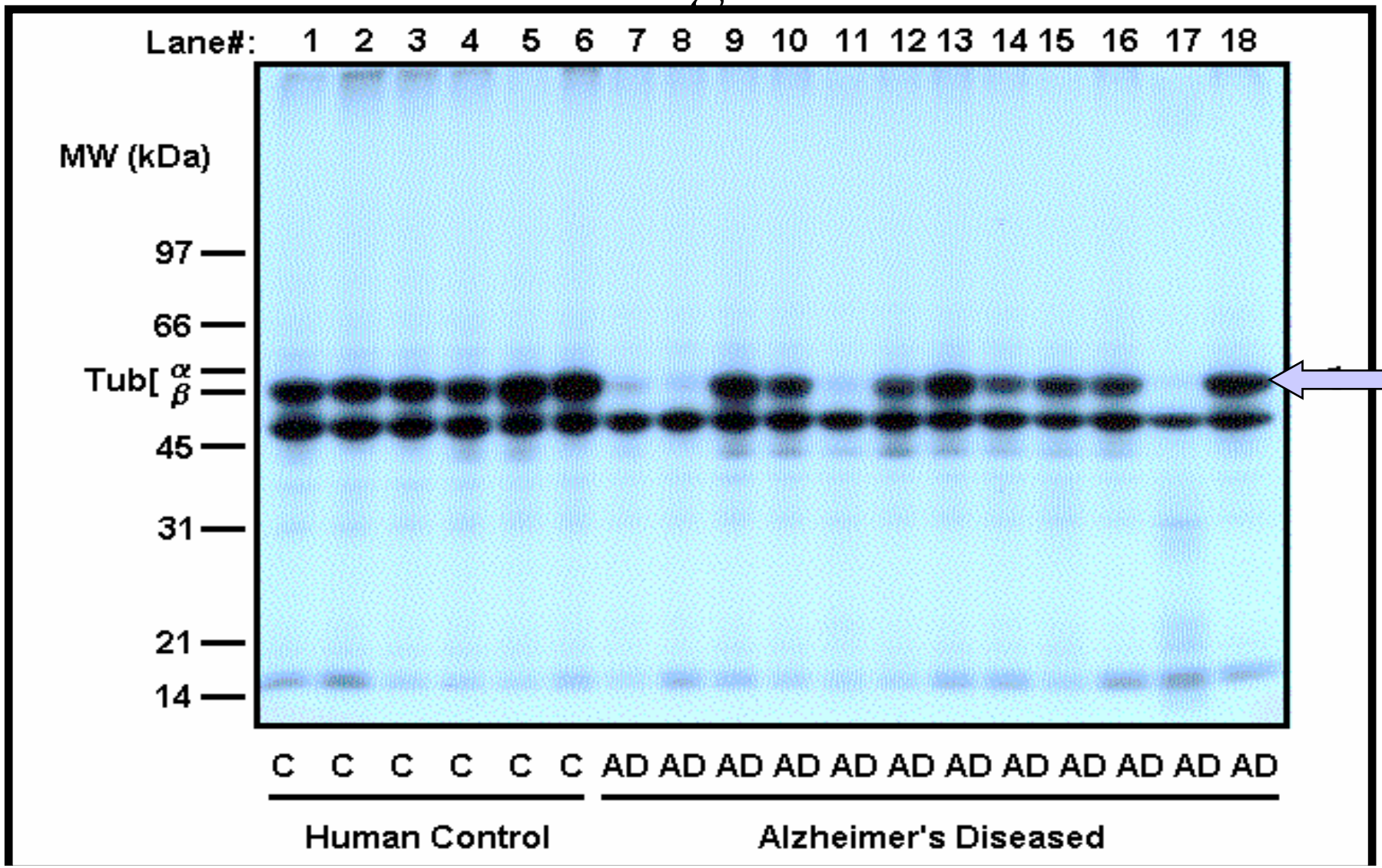
Result:

Human Brain Tubulin of Alzheimer's Subjects is Diminished in the Soluble Fraction and Higher in the Particulate Fraction. It appears to be abnormally polymerized.

SDS-PAGE Separation of Human Control and AD Brain Hippocampus Homogenates



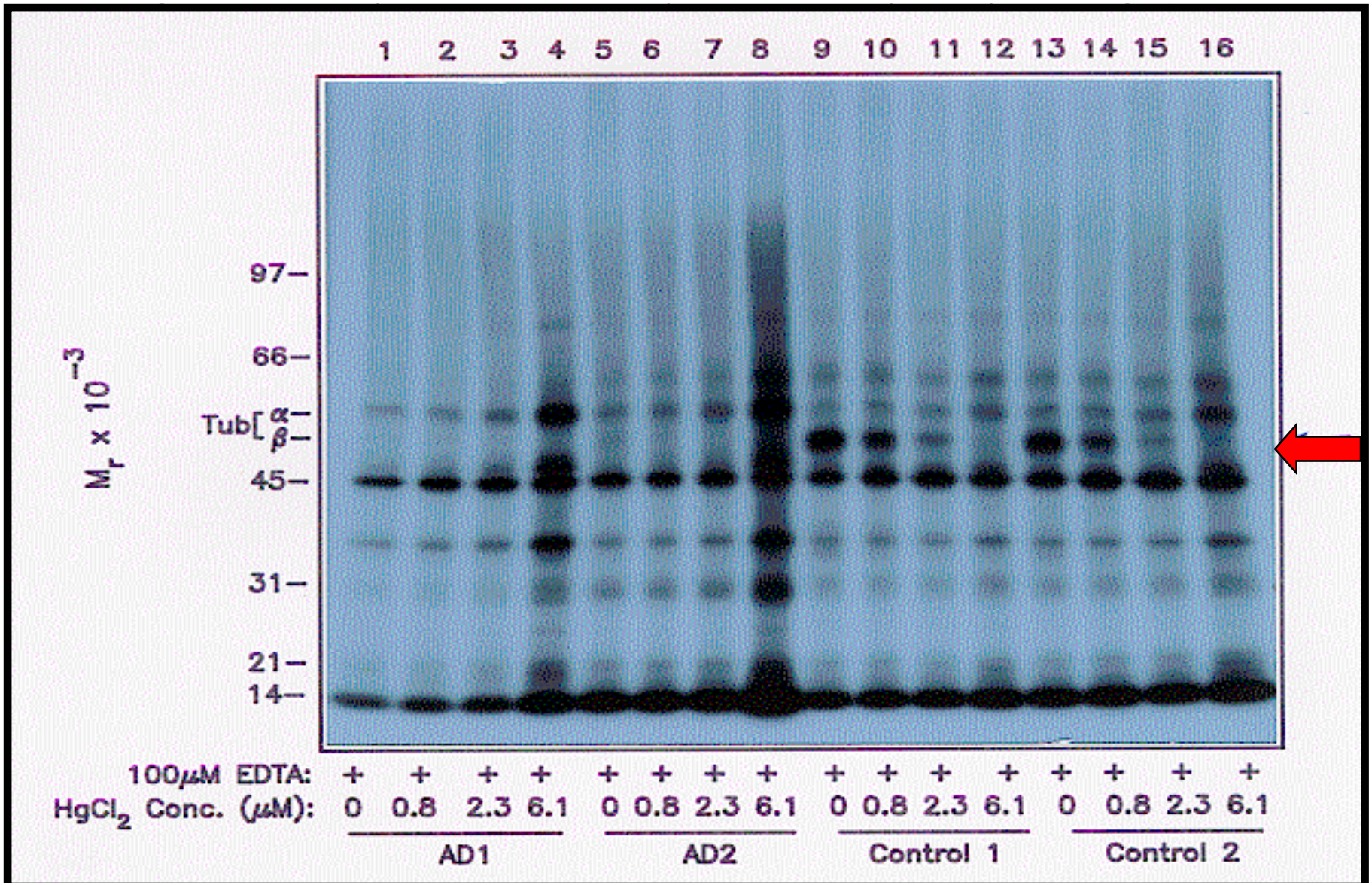
Autoradiogram of [^{32}P]8N$_3$GTP Photolabeled Control & AD Brain Hippocampus Homogenates



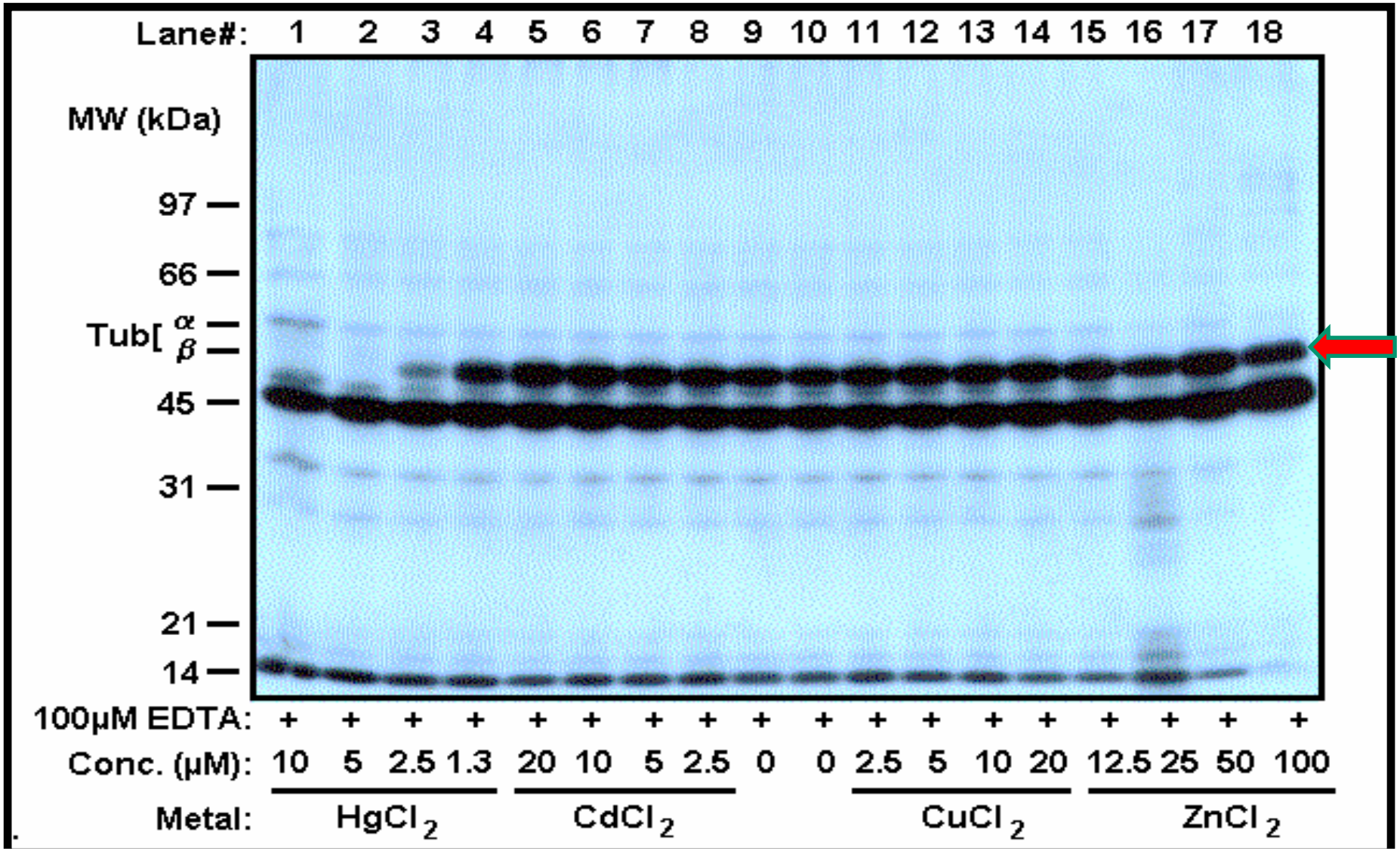
Result:

Human Brain Tubulin of Alzheimer's Subjects is Diminished in its Ability to Bind GTP that Induces Normal Polymerization.

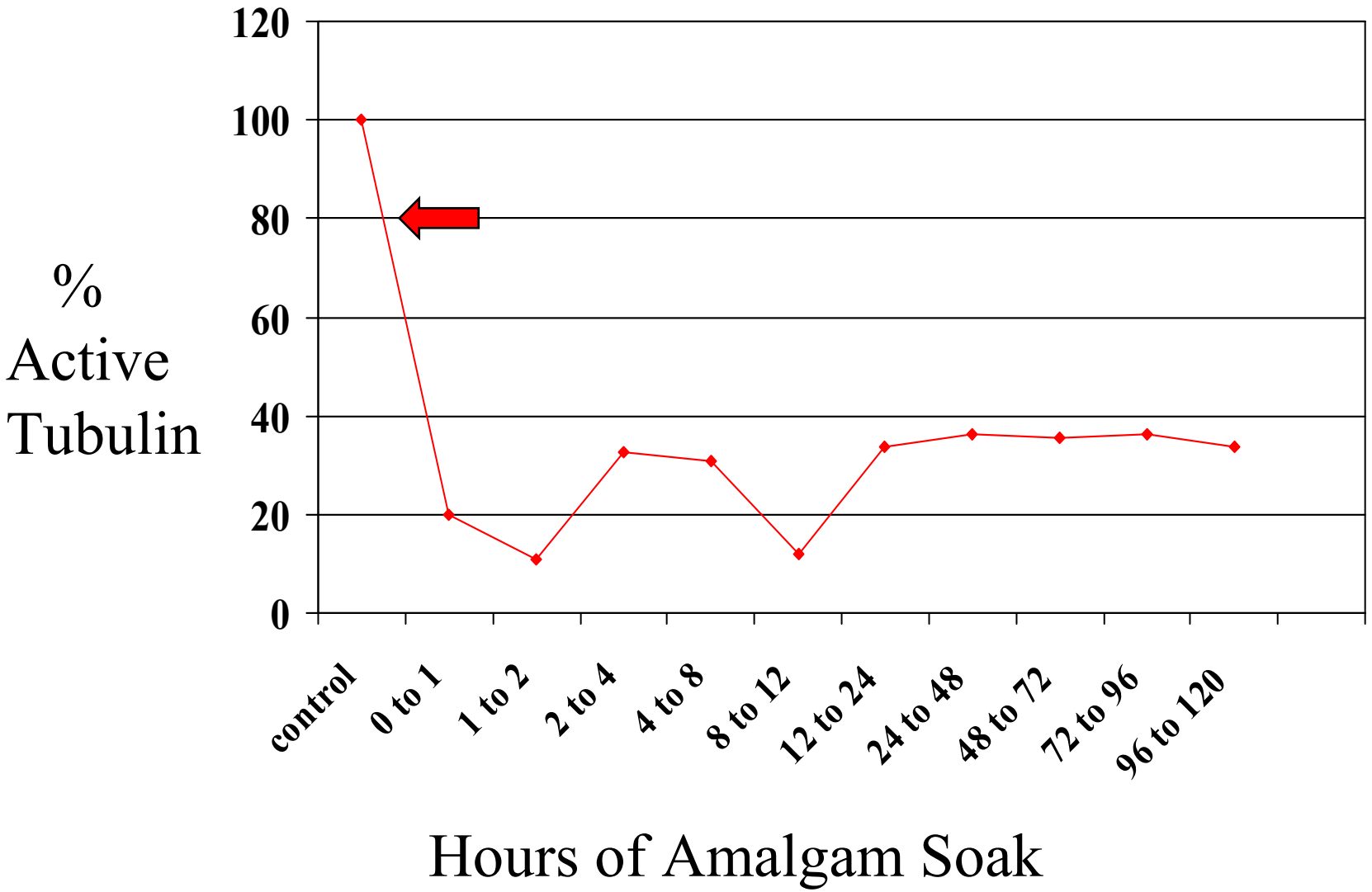
HgEDTA Induces Aberrant [^{32}P]8N$_3$GTP-



EDTA Prevents Cd, Cu & Zn, But Not Hg Inhibition, of [^{32}P]8N$_3$GTP Photolabeling of Brain ß-Tubulin



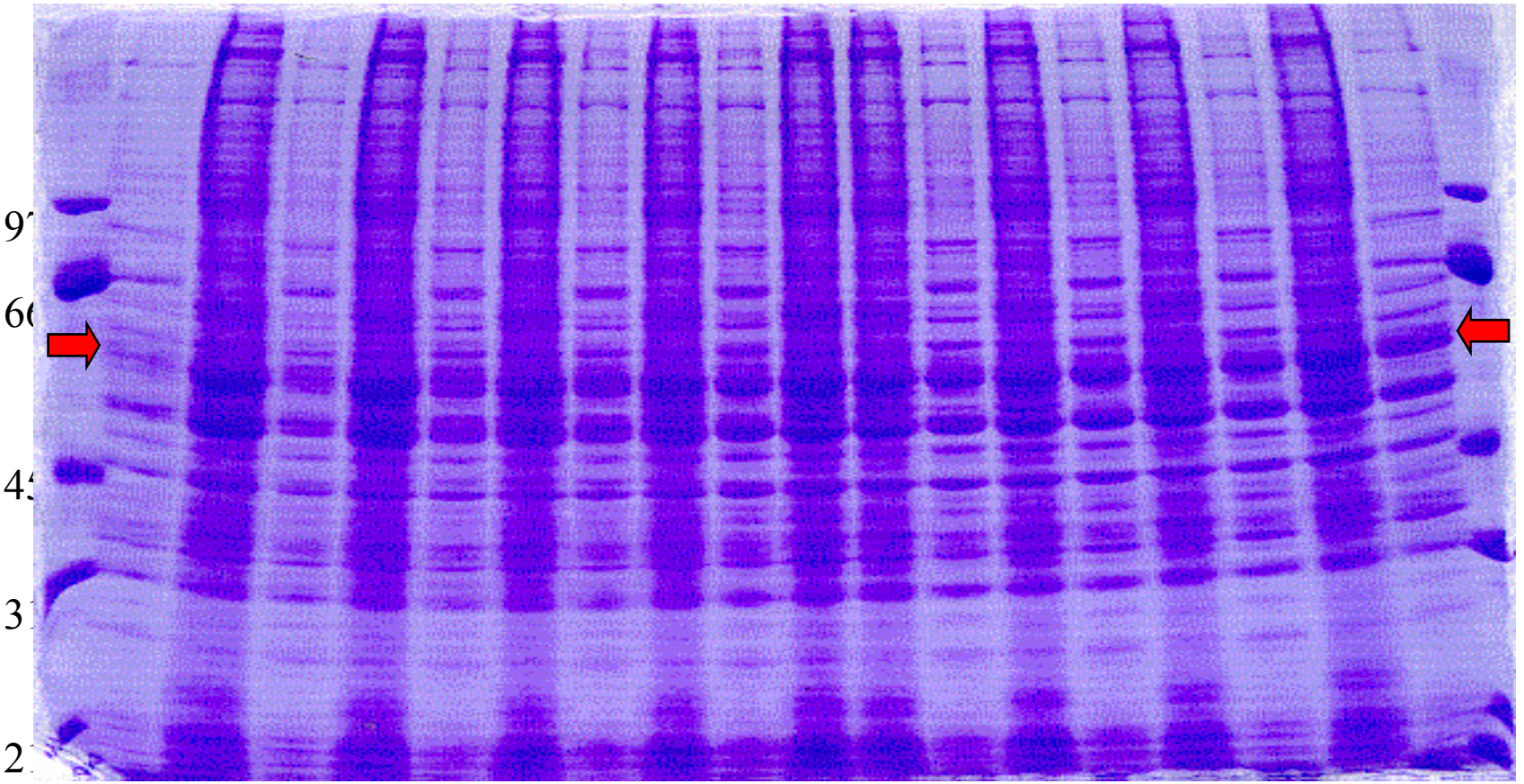
EFFECT OF SEQUENTIAL AMALGAM EXTRACTION SOLUTIONS ON THE VIABILITY OF BRAIN TUBULIN



Results:

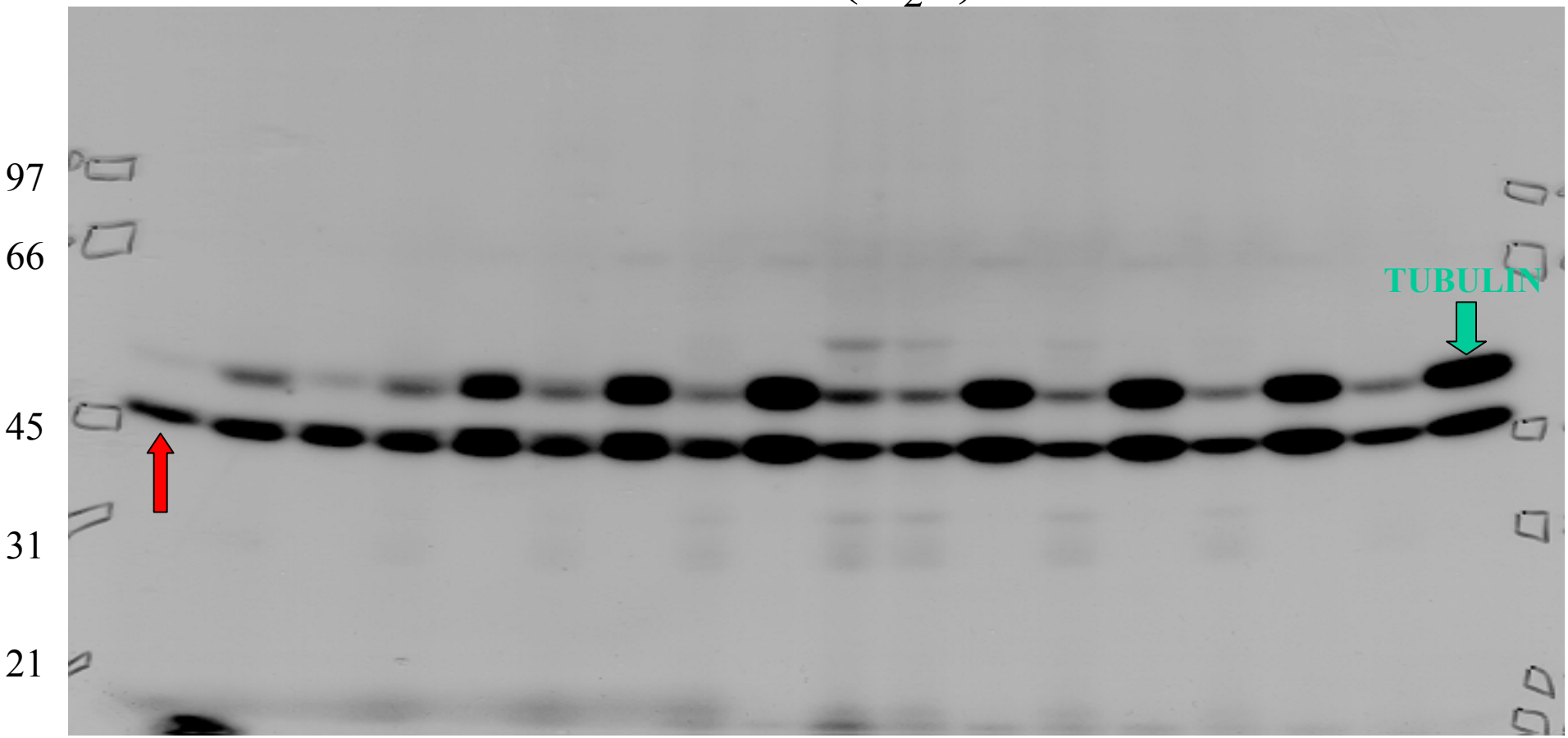
1. Of all metals tested, only Hg^{2+}, when Added to Normal Brain Tissues, Produces Tubulin that Biochemically Behaves Like Tubulin of Alzheimer's Diseased Brain.
2. Material released from dental amalgam causes the same effect.

SDS-PAG ON WHICH BRAIN PROTEINS HAVE BEEN SEPARATED AFTER EXPOSURE TO ROOT CANAL TOOTH TOXIN OR H_2S



	S	P	S	P	S	P	S	P	S	P	P	S	P	S	P	S	P	S
TOXIN µL	20		10		5.0		2.5		0		-		-		-		-	
H_2S µM	-		-		-		-		-		100		200		400		800	

AUTORADIOGRAPH COMPARING EFFECTS OF EXTRACTED TOOTH TOXIN TO HYDROGEN SULFIDE (H_2S) ON TUBULIN



	S P	S P	S P	S P	S P	P S	P S	P S	P S
TOXIN µL	20	10	5.0	2.5	0	-	-	-	-
H_2S µM	-	-	-	-	-	100	200	400	800

Results:

1. Solutions made from an infected tooth with a root canal had the same effect on normal brain tubulin as adding Hg^{2+}.
2. Both Hg^{2+} and toxins from infected teeth inhibit thiol (-SH) containing proteins/enzymes.

Effects Of Mercury And Methyl-mercury On MICROTUBULIN In Cell Cultures

- CH_3Hg^+ (5μM) causes complete microtubulin disruption in fibroblast cultures. Prevented by DMSA. Sager et al., Exptl. Cell Res. 146, 127-137, 1983.
- CH_3Hg^+ (5μM) or Hg^{2+} (50μM) resulted in complete microtubulin disassembly. Miura et al., Toxicol. Appl. Pharmacol. 73, 218-231, 1984.
- Cd (75μM) or As (100μM) for 1.5 hrs results in microtubulin disassembly. Chou, I.N., Biomed. Environ. Sci. 2, 358-365, 1989.
- Thimerosal causes complete inhibition of the viability of brain tubulin in a manner similar to Hg^{2+}. B. Haley

MERCURY AND ALZHEIMER'S DISEASE

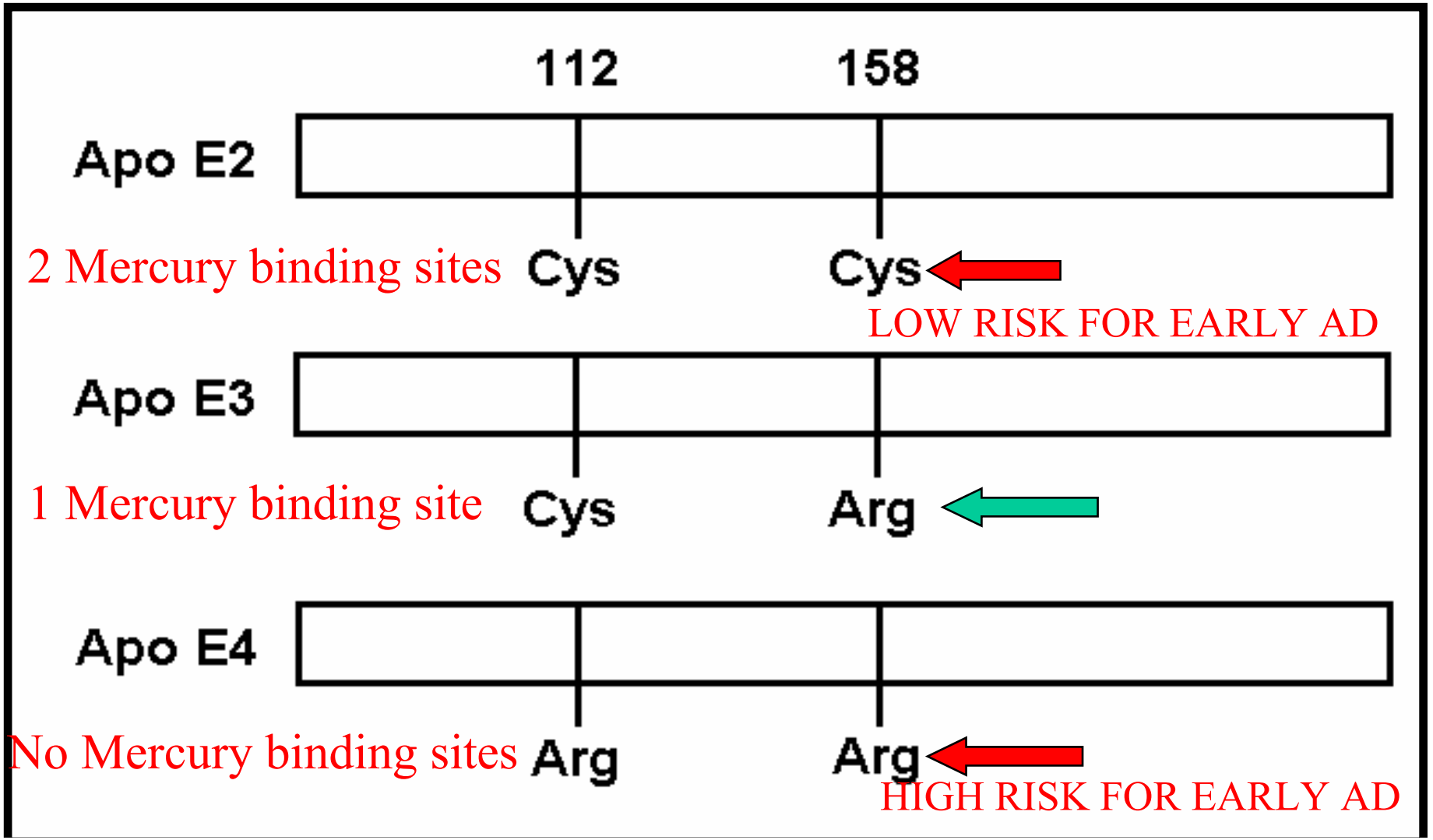
- Exposure of neuroblastoma cells to 10^{-9} molar mercury increases ***Tau phosphorylation and secretion of beta-amyloid.*** Both of these events occur in Alzheimer's diseased brain. Amyloid plaque formation is the "diagnostic hallmark" of Alzheimer's disease. Olivieri et al. J. Neurochemistry, 74, 231, 2000.
- Exposure of cultured neurons to 10^{-7} to 10^{-10} molar mercury rapidly causes *the stripping of tubulin* from the neurofibrils forming the neurite processes ***leading to the formation of neurofibillary tangles*** **(NFTs),** a "diagnostic hallmark" of Alzheimer's disease. Leong et al. NeuroReports 12(4), 733, 2001
- **Therefore, Hg exposure can create many of the diagnostic hallmark factors and the aberrant biochemistry observed in Alzheimer's Disease!**

Apolipoprotein E Genotype Alters the Susceptibility to the Development of AD

APOE Genotype	% U.S. Population	Age of AD Onset (yr.)
2/2	<1	?
2/3	11	>90
2/4	5	80-90
3/3	60	80-90
3/4	21	70-80
4/4	2	<70

Adapted from Roses, A.D. (1995) *Sci. Am. Science & Med*. 16-25.

Biochemical Differences Between the Three Most Common Apolipoprotein E Isoforms is Reflected in Hg Binding Capacity



RELATIONSHIP TO NUMBER OF APO-E –SH GROUPS AND AGE OF AD ONSET

APO-E→ ↓	2	3	4
2	4 (>90)	3 (>90)	2 (80-90)
3	3 (>90)	2 (80-90)	1 (70-80)
4	2 (80-90)	1 (70-80)	0 (<70)

RED = APO-E GENOTYPE COMBINATION

BLUE = NUMBER OF –SH GROUPS

BLACK = APPROXIMATE AGE OF ONSET OF AD

APO-E is a lipid binding housekeeping protein that is being excreted from the brain through the CSF into the blood for removal by the liver. As it leaves it could sequester Hg^{2+} and remove it from the CSF. The second highest concentration of APO-E in the human body is in the CSF.

MOST IMPORTANT CONCLUSION

- THERE APPEARS TO BE A SUBSET OF THE ELDERLY POPULATION THAT CANNOT EFFECTIVELY EXCRETE MERCURY AND ARE AT GREATER RISK FROM EXPOSURES TO MERCURY THAN ARE THE GENERAL POPULATION.
- APO-E4 CARRIERS MAY REPRESENT SOME OF THESE PATIENTS.

OBSERVATIONS

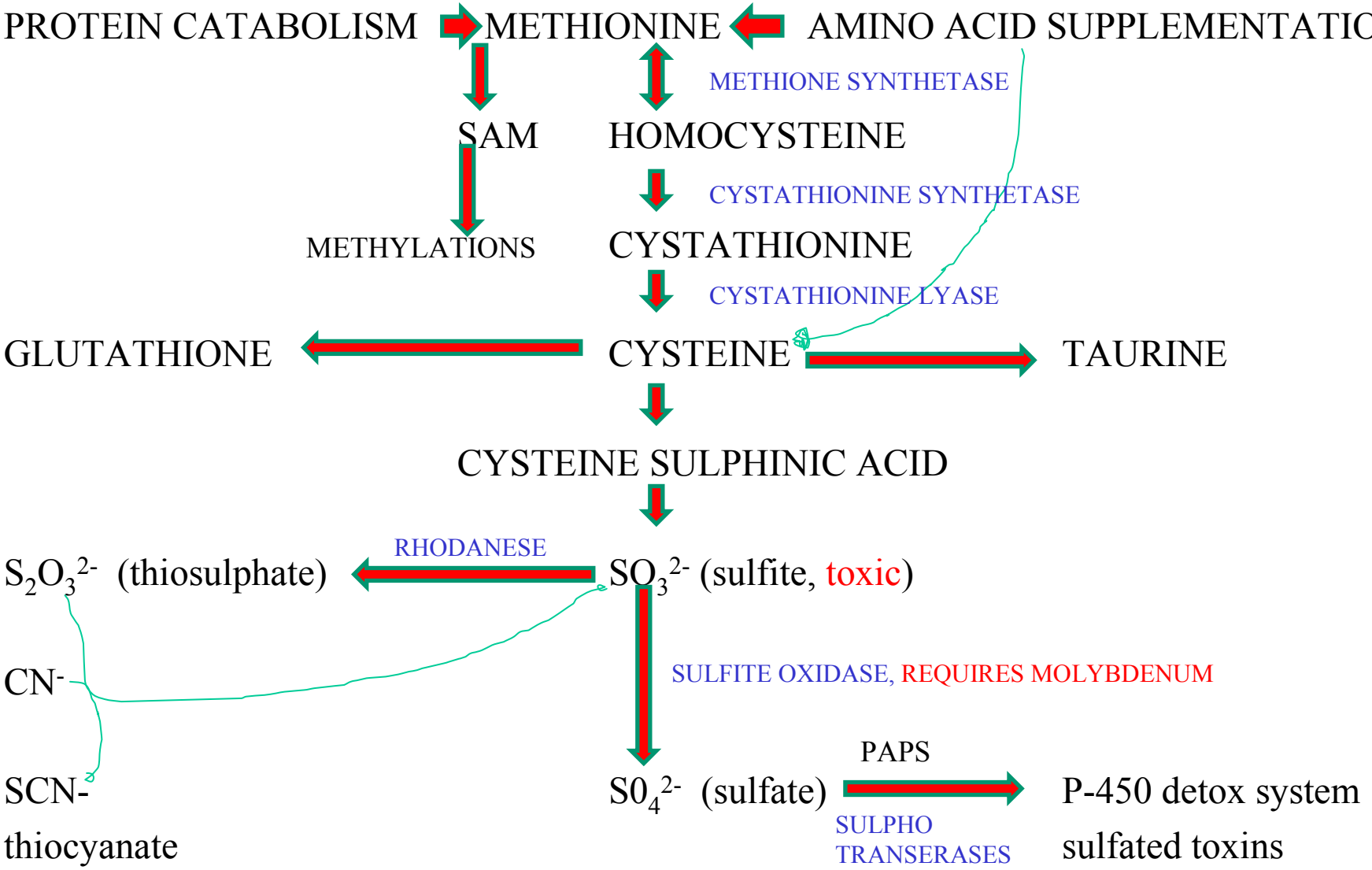
- ALZHEIMER'S DISESASE (AD) AND OTHER NEUROLOGICAL DISEASES APPEARED AFTER THE INTRODUCTION OF AMALGAM FILLINGS.
- A MAJOR ABNORMALITY IN AD BRAIN IS A MOLECULAR LESION THAT DESTROYS AXONS.
- THE MAJOR BIOCHEMICAL LESIONS OF AD BRAIN CAN BE PRODUCED IN NORMAL BRAIN SAMPLES BY THE ADDITION OF MERCURY, AND ONLY MERCURY, OR EXTRACTIONS OF INFECTED TEETH.
- THE NEUROTOXICITY OF MERCURY AND MERCURY CONTAINING COMPOUNDS, **INCLUDING DENTAL AMALGAM,** IS WELL DESCRIBED IN THE SCIENTIFIC LITERATURE.

SULFITE TOXICITY AND CORRESPONDING ABNORMAL MYELINATION OF WHITE MATTER OF THE CNS

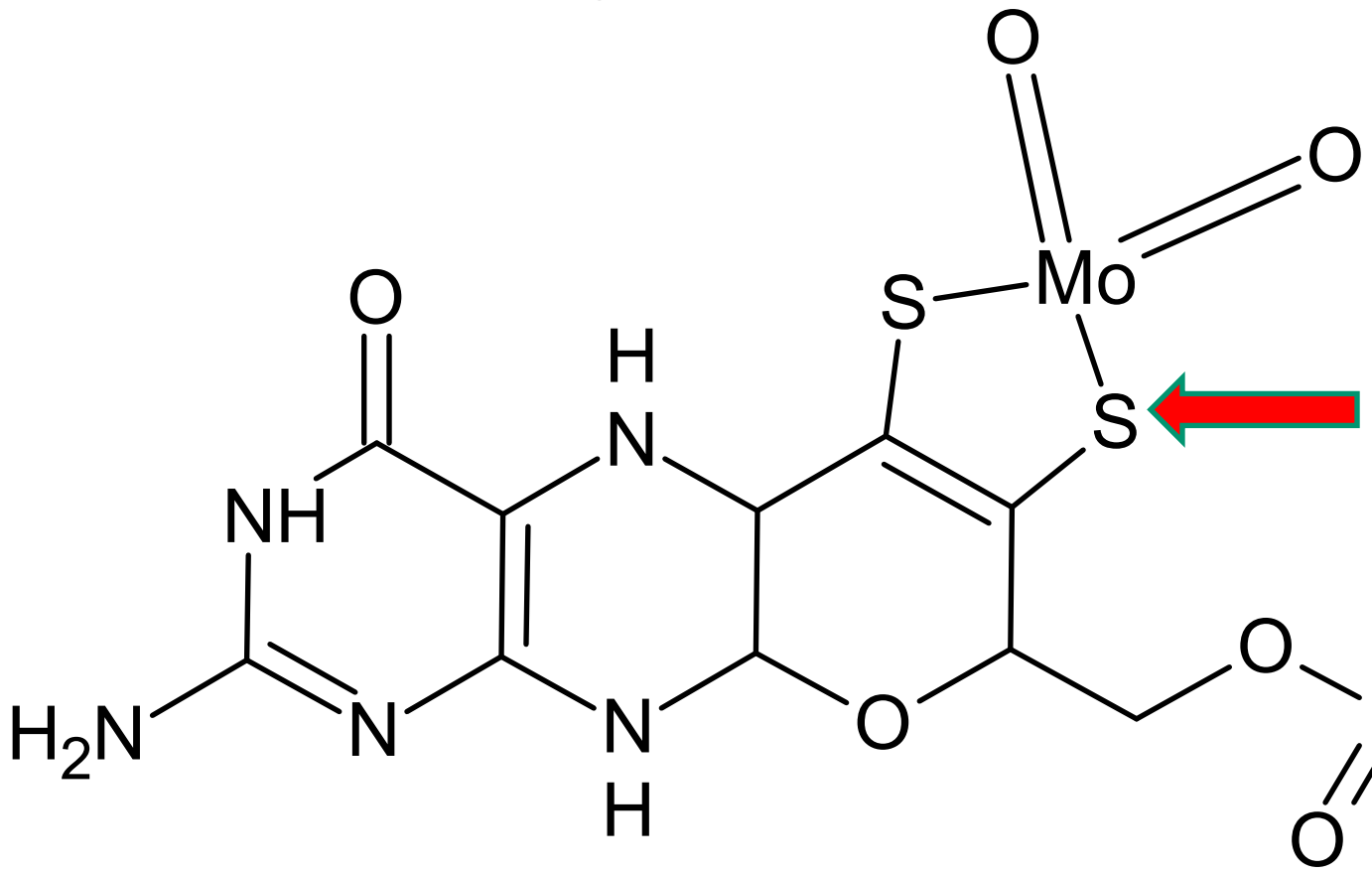
INFANTS BORN WITH DEPLETED SULFITE OXIDASE (SO) ACTIVITY, DUE TO LACK OF MOLYBDOPTERIN OR POLYMORPHISM OF LOW ACTIVITY SO DIE OF SEIZURES EARLY IN LIFE. SEIZURES WERE ASSUMED TO BE CAUSED BY INADEQUATE MYLENIZATION OF THE WHITE MATTER OF THE CNS. (see Shih, V.E. et al. Sulfite Oxidase Deficiency New England J. Medicine (1977) 10:1022-8)

ALSO, HUMAN SENSITIVITY TO SULFITE HAS LEAD TO WARNING LABELS ON WINE STATING "CONTAINS SULFITE". IT IS ALSO AGAINST THE LAW IN THE USA TO SPRAY SULFITE ON VEGATABLES TO KEEP THEM LOOKING FRESH AS THIS HAS CAUSED MEDICAL EMERGENCIES AT THE SALAD BAR.

METABOLISM OF SULFUR CONTAINING AMINO ACIDS



Molybdopterin



High Hg^{2+} , Pb^{2+}, Cd^{2+} and arsenic affinity.

Mo is a essential mineral for conversion of sulfite to sulfate by the enzyme sulfate oxidase. Autistic children are lower in Mo and sulfate than control children, and higher in excreted

Excretion of Urinary Protein and Anions in Autism: R.H. Waring and L.V. Klovrza, J. Nutritional & Environmental Medicine (2000) 10, 25-32.

	Autism (n=232)	Controls (n=68)
Age (years)	**7.6±2.4**	**8.5±3.7**
Protein µg/ml	**103.2±89.9***	**64.5±27.5**
Sulphite	**106.9±162.9***	**2.1±6.3 (A 53-FOLD INCREASE)**
Thiosulfate	**130.8±148.1***	**18.6±25.0**
Thiocyanate	**6.4±16.9***	**44.0±101.0**
Sulfate	**6819.0±6712.3***	**3030.8±1461.0**

Anion excretion is given in nmoles/ml, mean ±SD* p<0.001 (Wilcoxon rank sum test). Sulphate and sulphite were estimated by standard colorimetric methods.

"Reduction in urinary sulphite was associated with improvement in clinical symptoms as reported by parents and carers." Molybdenum supplementation caused 36% (14/38) of children to have improved sulfite levels.

WHAT WOULD REPLACEMENT OF Mo BY Hg ON MOLYBDOPTERIN DO?

1. Inhibits the enzyme sulfite oxidase leading to decreased sulfate levels and higher toxic sulfite levels.
2. Cause a depletion of Mo.
3. Cause a more rapid breakdown of Molybdopterin to neopterin.
4. Decrease the removal of toxins, like tylenol, which require sulfation for removal.
5. Inhibit other pathways that require sulfation.
6. Increase sensitivity to sulfhydryl containing foods by increasing sulfite levels which causes abnormal myelination of nerves of the white matter in the CNS.

Conclusions

- TOXIC METALS ARE INCREASING IN THE BLOOD OF AMERICANS AND OTHERS MORE RAPIDLY THAN EVER BEFORE.
- TOXIC METALS LEAD TO OXIDATIVE STRESS WHICH MAKES THE POPULATION MORE SUSCEPTIBLE TO INFECTIONS, ESPECIALLY VIRAL INFECTIONS.
- THE ELIMINATION OF EXPOSURES TO TOXINS AND MAINTAINING A HEALTHY REDOX STATUS BY DIET AND MEDICAL TREATMENT ARE NEEDED TO ATTAIN AND KEEP HUMAN AND ANIMAL HEALTH.
- IT IS IMPORTANT TO CONSIDER SULFITE TOXICITY IN NEUROLOGICAL ILLNESSES, SUCH AS MULTIPLE SCLEROSIS, WHICH ARE EPISODIC AND INVOLVE ABNORMAL MYLENIZATION OF NEURONS.
- DIETARY RESTRICTIONS FOR –SH CONTAINING FOODS MAY BE IMPORTANT.

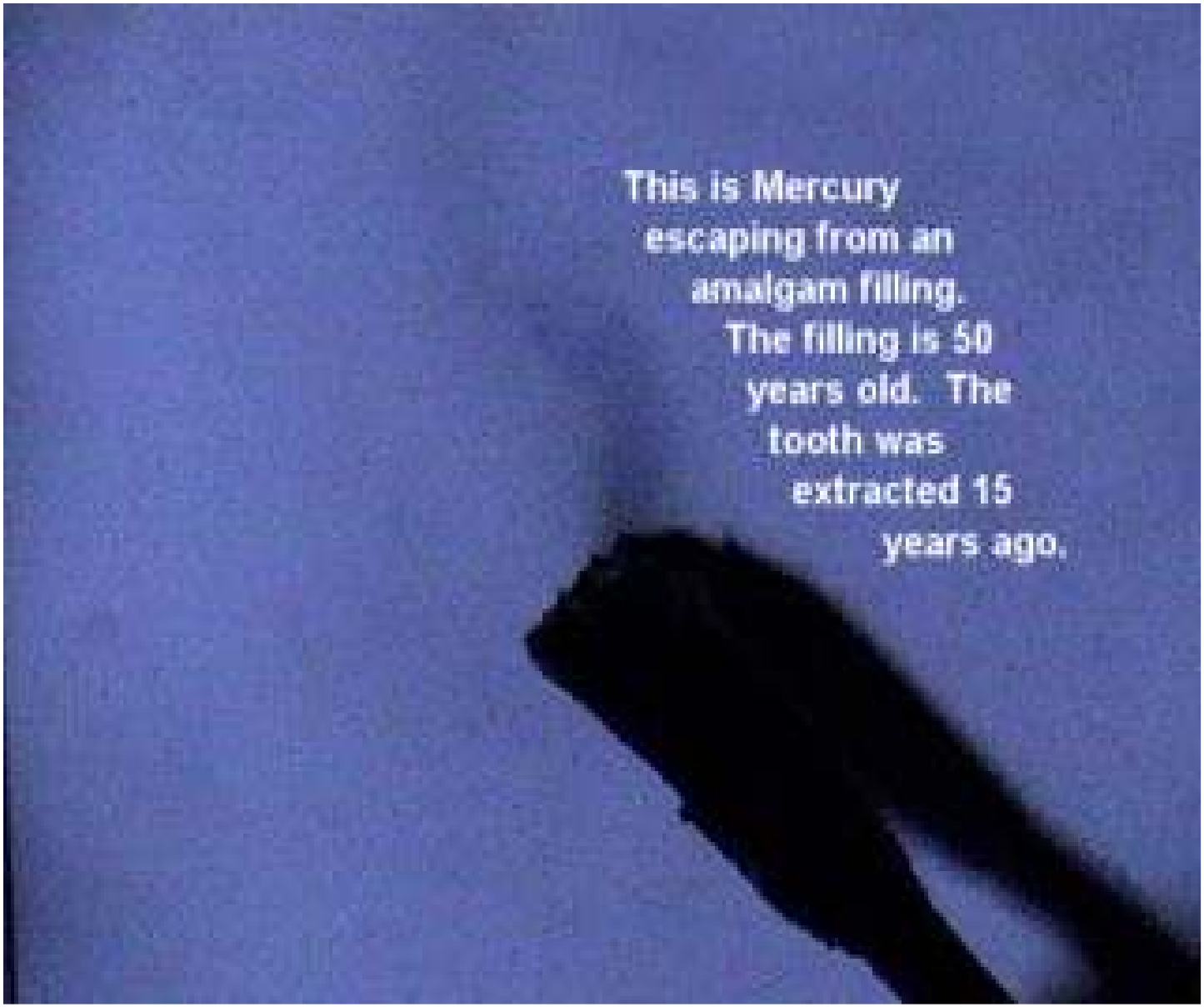
IS MERCURY RELEASED FROM DENTAL AMALGAMS?

- In a study of long-term dissolution of mercury from a non-mercury releasing amalgam it was determined that 43.5±3.2 μg/cm^2/day Hg was released and this remained constant for 2 years. Chew et al., Clin. Prev. Dent. 13(3):5-7, 1991.
- In a study of 1,127 soldiers by NIH the level of mercury in the urine of amalgam bearers was 4.5 times that of amalgam free controls. Some with extensive amalgams had levels 8 times or higher than controls. Kingman et al. J. Dental Research 77(3) 461, 1998.

VISUALIZATION OF HG EMITTING FROM A DENTAL AMALGAM THAT IS 50 YEARS OLD.

- From: www.uninformedconsent.com
- David Kennedy's www.IAOMT.org tape

IN SPITE OF THE OBVIOUS EMISSION OF Hg VAPORS FROM DENTAL AMALGAM THE FDA HAS STEADFASTLY REFUSED TO TEST THEM FOR SAFETY!



Mercury from Dental Amalgam

1. Pro-amalgam ADA spokespersons "estimate" that about 0.03 mcg mercury are emitted from a single amalgam per day. Estimate that it would take several hundred amalgams to provide a toxic exposure. "Hijacking Science Example"
2. A new IAOMT study shows that different amalgam types emit more mercury and that a single spill (very small amalgam) emits between 4.0 to 20 mcg of mercury per day at room temperature and without abrasion of any sort. This is about 133 to 666 times more than was estimated by the ADA!

Mercury in saliva and feces after removal of amalgam fillings.

Björkman L, et al. Toxicol Appl Pharmacol. 1997 May;144(1):156-62. Department of Basic Oral Sciences, Karolinska Institutet, **Stockholm, Sweden**.

The toxicological consequences of exposure to mercury (Hg) from dental amalgam fillings is a matter of debate in several countries. The purpose of this study was to obtain data on Hg concentrations in saliva and feces before and after removal of dental amalgam fillings. In addition Hg concentrations in urine, blood, and plasma were determined. Ten subjects had all amalgam fillings removed at one dental session. **Before removal, the median Hg concentration in feces was more than 10 times higher than in samples from an amalgam free reference group consisting of 10 individuals (2.7 vs 0.23 mumol Hg/kg dry weight, p < 0.001).** A considerable increase of the Hg concentration in feces 2 days after amalgam removal (median 280 mumol Hg/kg dry weight) was followed by a significant decrease. **Sixty days after removal the median Hg concentration was still slightly higher than in samples from the reference group.** In plasma, the median Hg concentration was 4 nmol/liter at baseline. Two days after removal the median Hg concentration in plasma was increased to 5 nmol/liter and declined subsequently to 1.3 nmol/liter by Day 60. In saliva, there was an exponential decline in the Hg concentration during the first 2 weeks after amalgam removal (t 1/2 = 1.8 days). **It was concluded that amalgam fillings are a significant source of Hg in saliva and feces.** Hg levels in all media decrease considerably after amalgam removal. The uptake of amalgam mercury in the GI tract in conjunction with removal of amalgam fillings seems to be low.

Human exposure to mercury and silver released from dental amalgam restorations.

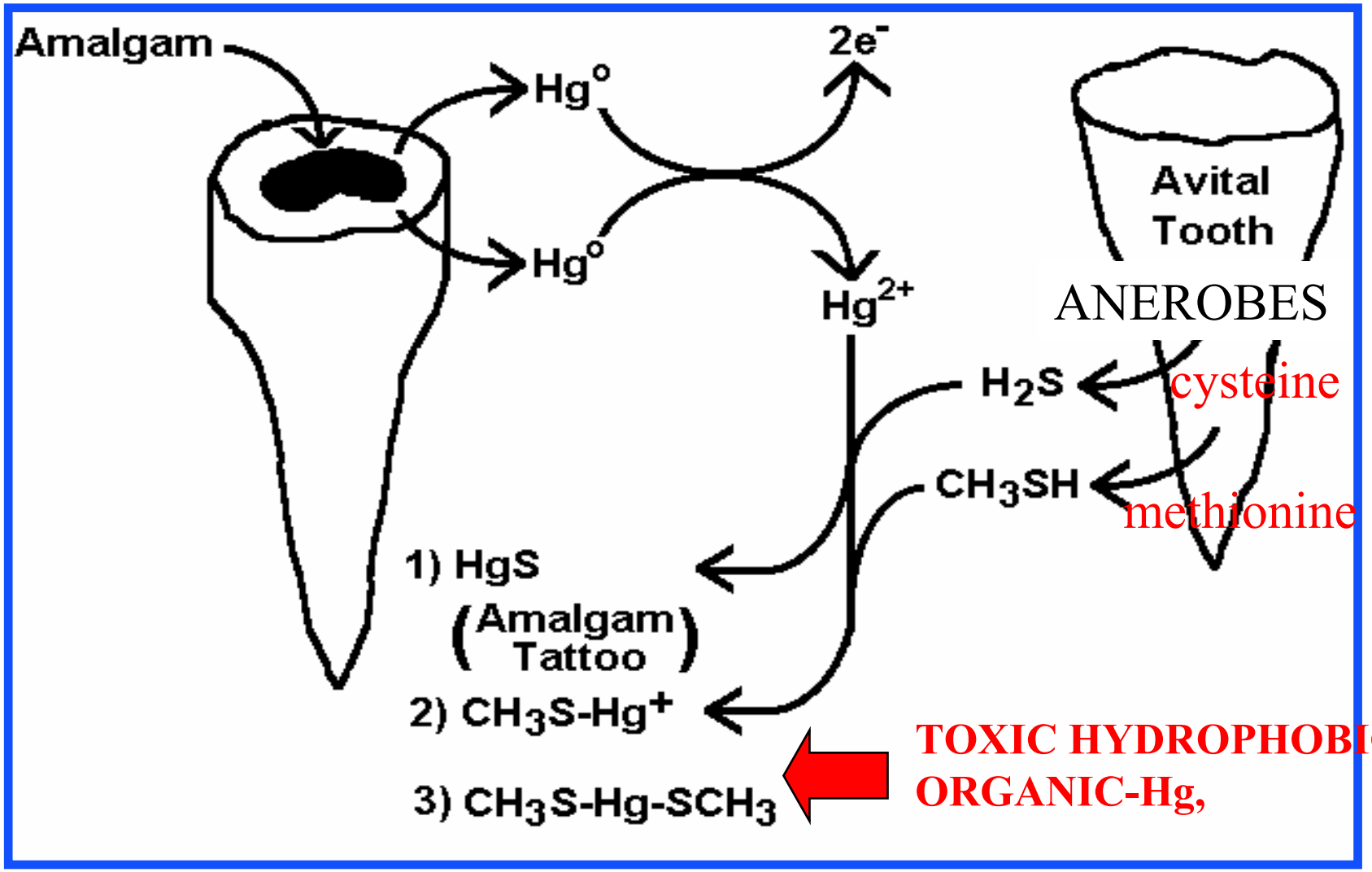
Skare, I and Engqvist, A. Arch Environ Health. 1994 Sep-Oct;49(5):384-94. National Institute of Occupational Health **Stockholm, Sweden**.

In 35 healthy individuals, the number of amalgam surfaces was related to the emission rate of mercury into the oral cavity and to the excretion rate of mercury by urine. Oral emission ranged up to 125 micrograms Hg/24 h, and **urinary excretions ranged from 0.4 to 19 micrograms Hg/24 h.** In 10 cases, urinary and fecal excretions of mercury and silver were also measured. **Fecal excretions ranged from 1 to 190 micrograms Hg/24 h** and from 4 to 97 micrograms Ag/24 h. Except for urinary silver excretion, a high interplay between the variables was exhibited. The worst-case individual showed a fecal mercury excretion amounting to 100 times the mean intake of total Hg from a normal Swedish diet. **With regard to a Swedish middle-age individual, the systemic**

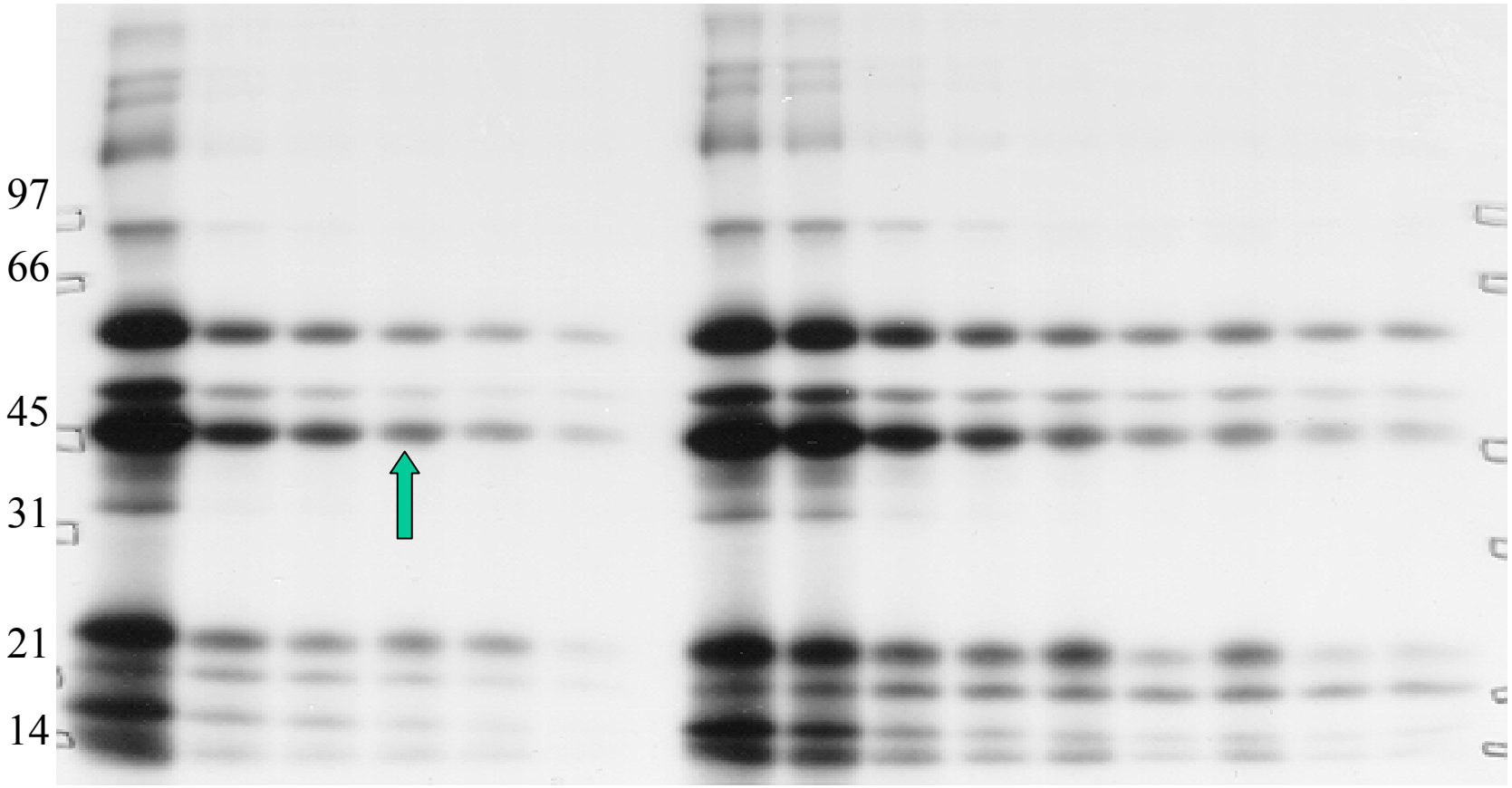
A Study of the Toxicants Associated with Avital Teeth and Osteonecrotic Materials

Early studies showed that the toxicants released by bacteria and microbes of periodontal disease were thiol based such as H_2S, CH_3SH and others. We found the toxicity of teeth with root canals was directly associated with a colorimetric assay for –SH groups and the conversion of crevicular fluid of low protein level to an exudate of high protein level. –SH groups are known to react rapidly with Hg^{2+}.

Amalgam Mercury Can Combine With Bacterial Toxins To Produce Even More Toxic Species



A COMPARISON OF THE TOXICITY OF A ROOT CANALED TOOTH EXTRACT (MS) AND HYDROGEN SULFIDE (H_2S)



RESULT

- SOLUTIONS OF LOW ODOR PRODUCED BY SOAKING INFECTED TEETH IN WATER PRODUCED A TOXIC SOLUTION MORE POTENT THAN A SOLUTION OF HYDROGEN SULFIDE, THE MOST COMMON TOXICANT PRODUCED BY PERIODONTAL DISEASE.
- THIS TOXIN COULD NOT BE REMOVED BY ANION OR CATION RESINS BUT WAS TOTALLY REMOVED BY CHARCOAL INDICATING A HYDROPHOBIC NATURE.

DETECTION OF MICROBES IN DENTIN OF PERIODONTAL INFECTED AREAS.

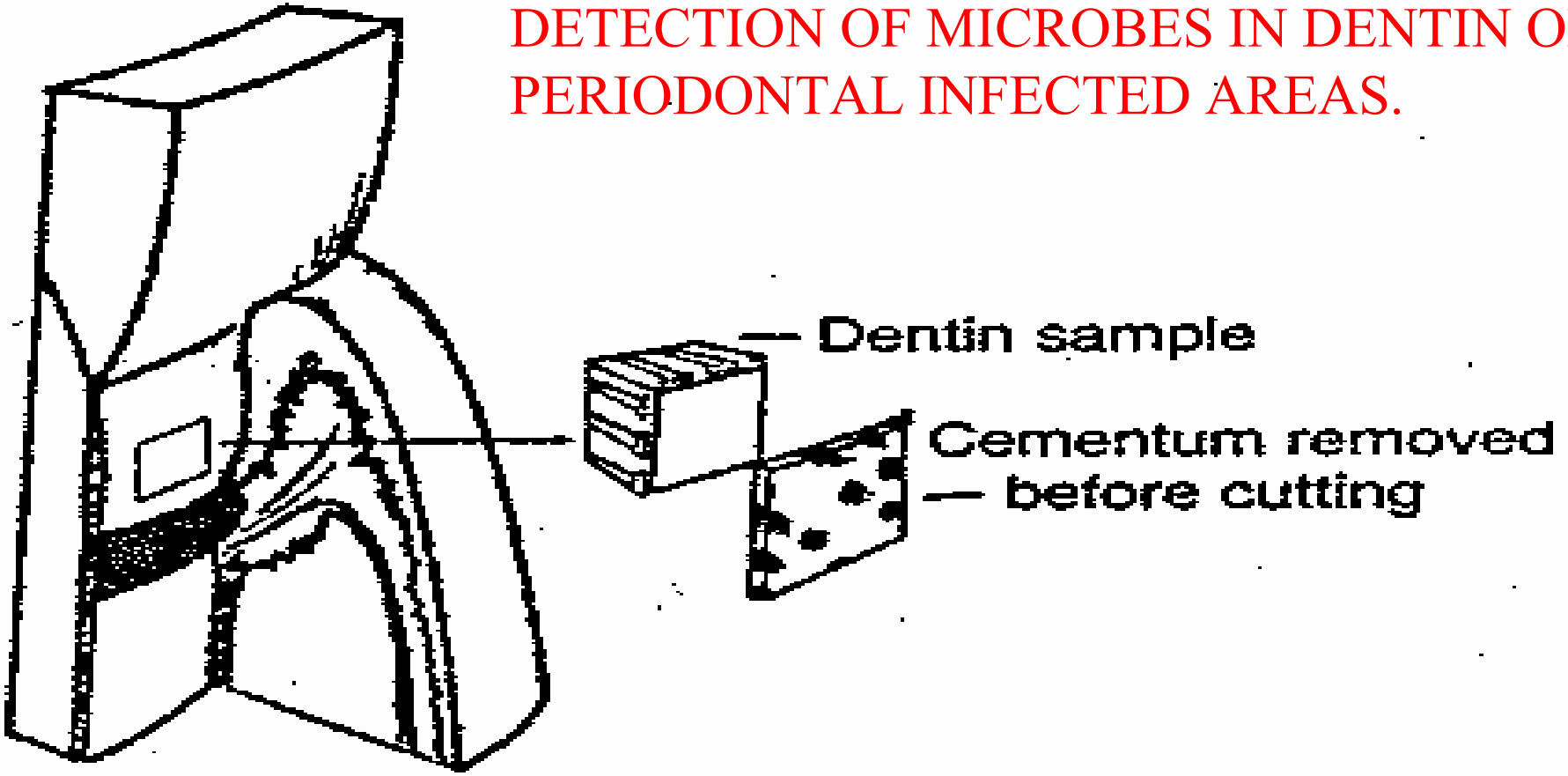


Fig. 1. Preparation of dentin samples. Root surfaces were sampled after cementum removal. The samples were taken from the middle dentin layer and none of them were in contact with the pulp.

Giuliana *et al*., (1997). *J. Clin. Periodontol*. **24**, 478-485.

Table 1. Frequency distribution of total viable counts (TVC) recovered from test and control samples before homogenization

Total viable counts (CFU/0.1 ml)	Test samples (n=26)	Control samples Cervical (n=14)	Medial (n=14)	Apical (n=14)
0	3	9	12	14
≤100	5	5	2	0
101–500	12	0	0	0
501–1000	1	0	0	0
1001–1500	3	0	0	0
1501–2000	1	0	0	0
2001–2500	1	0	0	0

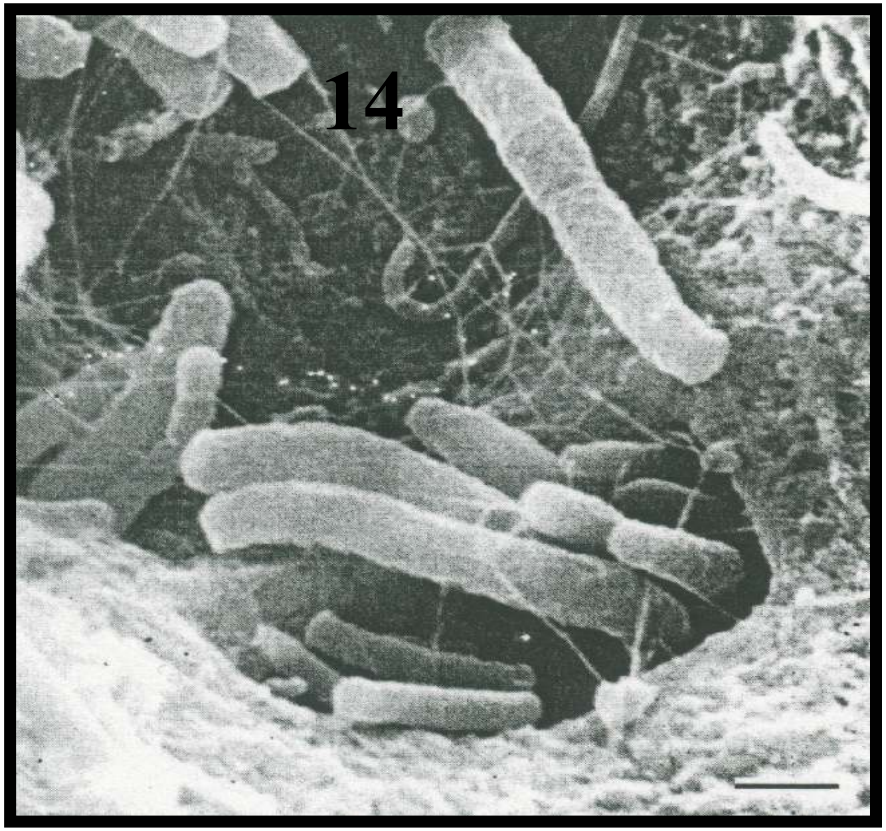
Table 2. Differences in total viable counts (TVC) recovered from test and control samples before and after homogenization

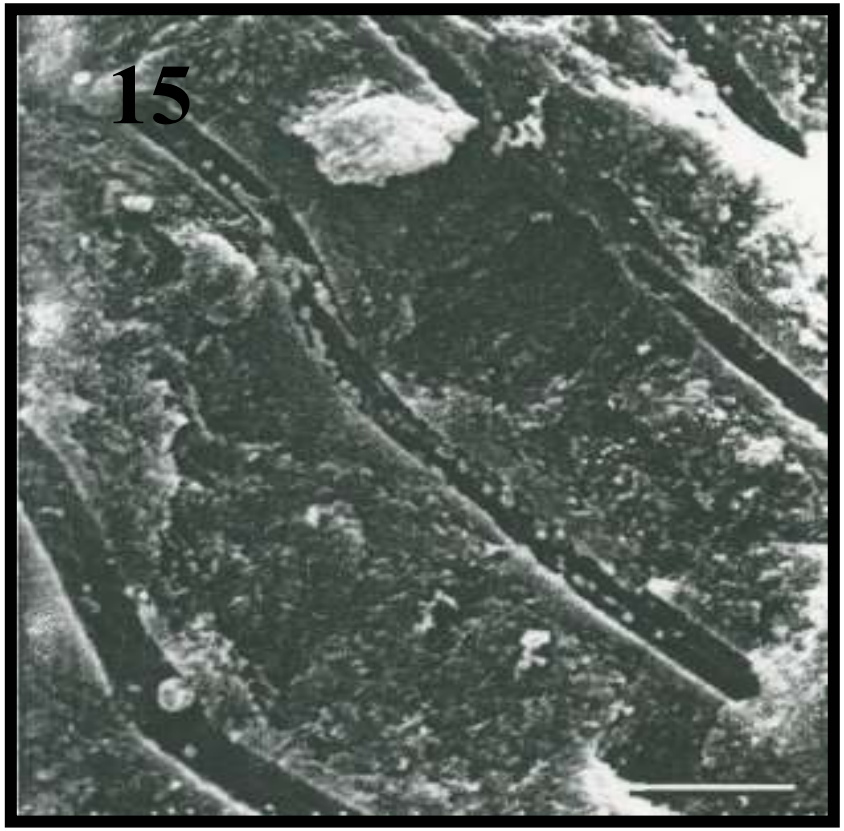
	Total viable counts (CFU/0.1 ml)		Wilcoxon test
	before homogenization	after homogenization	two-sided p-value
test samples (n=26)	501.08±659.75	3463.08±5029.69	0.00022*
control samples (n=42)	12.33±29.34	13.59±31.86	0.2183

Results are expressed as mean±standard deviation (SD) * Significant differences, $p<0.01$.

Giuliana *et al.*, (1997). *J. Clin. Periodontol.* **24**, 478-485.

Adriaens et al., (1988). *J. Clin. Periodontol.* **59**:493-503.



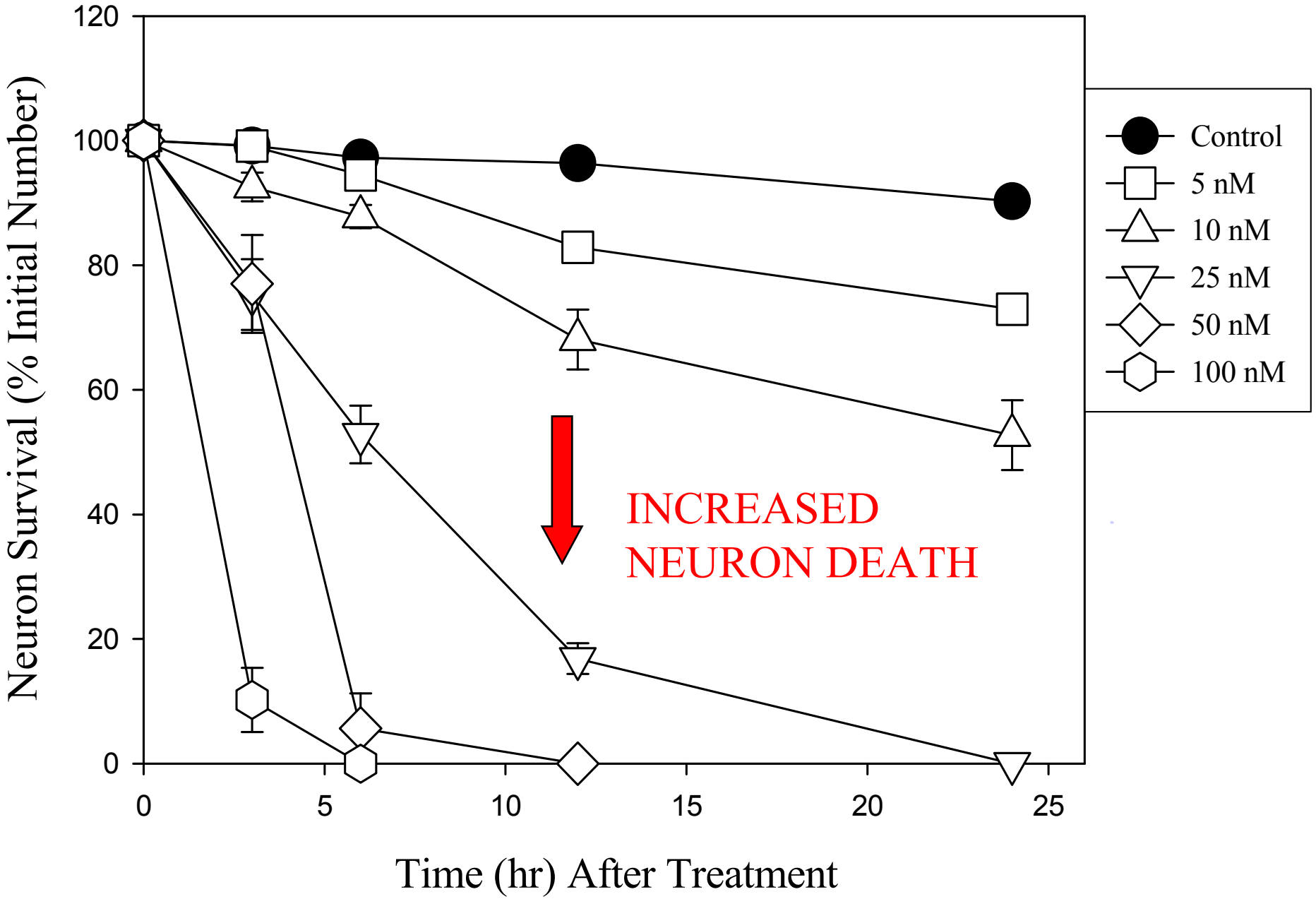


- "Figure 14. Filamentous bacteria invading the dentinal tubules at their orifices in the bottom of a resorption lacuna."
- "Figure 15. Longitudinally fractured dentinal tubules in the radicular dentin area corresponding to the exposed subgingival root surface. Bacteria are present in the dentinal tubules."

RESULTS

- ANAEROBIC BACTERIAL THAT CAUSE PERIODONTAL DISEASE AND TOOTH INFECTIONS RESIDE IN THE DENTIN OF TEETH.
- THESE BACTERIA RELEASE THIOL (-SH) BASED TOXICANTS.
- THESE INFECTIONS CAN LEAD TO BLOOD BACTEREMIA AND SYSTEMIC DISEASES.

Response of Primary Hippocampal Neurons to Mercury Chloride



SYNERGISTIC EFFECTS OF HEAVY METALS IS QUITE COMPLEX AND CAN GREATLY ENHANCE TOXICTY OF MERCURY

Shubert et al. Combined Effects in Toxicology--A Rapid systematic Testing Procedure:Cadmium, Mercury & Lead. J. of Toxicology & Environmental Health 4:763, 1978.

1. "the administration of an essentially no response level (LD1) of a mercury salt together with a 1/20 of the LD1 of a lead salt **killed all of the animals**." 2. "Generally, **a combination was synergistic when the most toxic member was present at or near its LD1 dose in the presence of a much less toxic member."**
2. **Recently, lead exposures from new dish plates have been reported.**

OBSERVATIONS

- MERCURY IS RELEASED FROM AMALGAM FILLINGS AT TOXIC LEVELS.
- MERCURY WOULD REACT WITH ANAEROBIC PRODUCED TOXICANTS TO PRODUCE VERY TOXIC ORGANIC-THIOL-Hg BASED COMPOUNDS.
- TOXICANTS ISOLATED FROM AVITAL TEETH WHEN ADDED TO NORMAL BRAIN TISSUES PRODUCE THE SAME BIOCHEMICAL ABNORMALITIES WITH BRAIN TUBULIN, CAUSING ABNORMAL PARTITIONING AND INABILITY TO REACT WITH GTP AS SEEN IN AD BRAIN. IS THIS CH_3-S-Hg-S-CH_3 LIKE?
- MERCURY, AND MERCURY COMPOUNDS, CAUSE NEURONAL DEATH AT LOW NANOMOLAR CONCENTRATIONS.

AD and Olfactory Deficits

- Devanand, D.P., Michaels-Marston, K.S., Liu, X., Pelton, G.H., Padilla, M., Marder, K., Bell, K., kStern, Y., and Mayeux, R. Olfactory Deficits in Patients with Mild Cognitive Impairment Predict Alzheimer's Disease at Follow-up. Am. J. Psychiatry 157(9): 1399-1405, 2000.
- Kovacs, T., Cairns, N.J., Lantos, P.L. Olfactory Centres in Alzheimer's disease: Olfactory Bulb is Involved in Early Braak's Stages. Neuroreport 12(2): 285-288, 2001.
- Gray, A.J., Staples, V., Murren, K., Dahariwal, A. and Bentham, P. Olfactory Identification is Impaired in Clinic-Based Patients with Vascular Dementia and Senile Dementia of Alzheimer's type. Int. J. Geriatr. Psychiatry 16(5):513-517, 2001.

Hg levels in hair & nails of AD

- Ehmann, Markesbery et al. Neurotoxicology 9(2)197-208. Trace Element Imbalances in Hair and Nails of Alzheimer's Diseased Patients.
- "The concentrations of 17 elements in the hair and nails of 180 Alzheimer's disease (AD) and control subjects have been determined by instrumental neutron activation analysis (INAA)".
- **Quote "Mercury is decreased in the nail of AD subjects compared to controls."**
- "Perhaps one reason for the lowering of nail Hg in AD subjects could be the presumably lower exposure rate of the AD patients to environmental Hg. This would not explain the elevated brain Hg, however."

Hg in nails of AD subjects

- Ehman, Markesbery et al. Biological Trace Element Research, pp461-470. Editor:G.N. Schrauzer, 1990 by the Humana Press, Inc.
- A Search for Longitudinal Variations in Trace Element Levels in Nails of Alzheimer's disease patients. **A three year study.**
- **Quote "Mercury tended to decrease in nail with increasing age of patient, and with the duration and severity of the dementia."**
- **This is a sign of decreasing ability to excrete mercury as the patient ages.**

Hg in nails of AD subjects

- Ehman, Markesbery et al. Biological Trace Element Research, pp461-470. Editor:G.N. Schrauzer, 1990 by the Humana Press, Inc.
- A Search for Longitudinal Variations in Trace Element Levels in Nails of Alzheimer's disease patients.
- Quote: **"This decrease is counter to the elevated levels of Hg observed in AD brain, as compared to age-matched controls."**

Hg Levels in Human Brain

- **Saxe et al, with Ehmann and Markesbery in Alzheimer's Disease, Dental Amalgam and Mercury, JADA v130, p191-199, 1999, determined Hg levels in the brains of 101 human subjects, both AD and normals.**
- **The histogram in this paper showed 6 of 101 subjects with brain Hg levels above 200 ng/g wet weight (C=236, 248, 319: AD=394, 622, 698). This minimally represents between 1.2 & 3.5 micromolar levels of Hg in 6% of these subjects. THESE ARE HIGHLY TOXIC LEVELS! At 100 ng/g Hg this increases to about 15% of subjects who died with highly toxic levels of brain mercury. Levels 100 to 500 times lower than these cause adverse effects on neurons.**
- **????Where does this Hg come from???? Are we to assume it is not doing any damage???? Note: these subjects were mostly Nuns. DOES THIS REPRESENT GENETIC SUSCEPTIBILITY TO BEING UNABLE TO EXCRETE MERCURY?**
- **Note: Control olfactory tissue in this study had *TWICE* the level of mercury as did the AD subjects! They found no correlation between amalgam exposure and brain Hg**

OBSERVATIONS

- AS PREDICTED, TISSUES EXPOSED TO Hg VAPOR VIA AMALGAMS, SUCH AS THE OLFACTORY BULB, HAVE DECREASED NEURONAL ACTIVITY.
- UNEXPECTEDLY (??), THE NAILS OF AD SUBJECTS HAD LESS Hg THAN NORMALS WHEREAS THEIR BRAIN AND OLFACTORY TISSUES HAD HIGHER Hg LEVELS.
- IN THE JADA ARTICLE IT WAS REPORTED THAT 6-15% OF THE NUNS HAD HIGHLY TOXIC Hg LEVELS IN THEIR BRAINS. THIS IS 18 TO 45 MILLION OUT OF A 300 MILLION POPULATION!
- AS THESE NUNS ATE AND SLEPT IN THE SAME LOCATION CONSIDER THIS AS EVIDENCE OF A "GENETIC SUSCEPTIBILITY" TO Hg RETENTION ?
- IS THERE OTHER EVIDENCE FOR THIS?

From a study funded by NIH done on orphans in Lisbon, Portugal which concluded amalgams were safe for use in children!

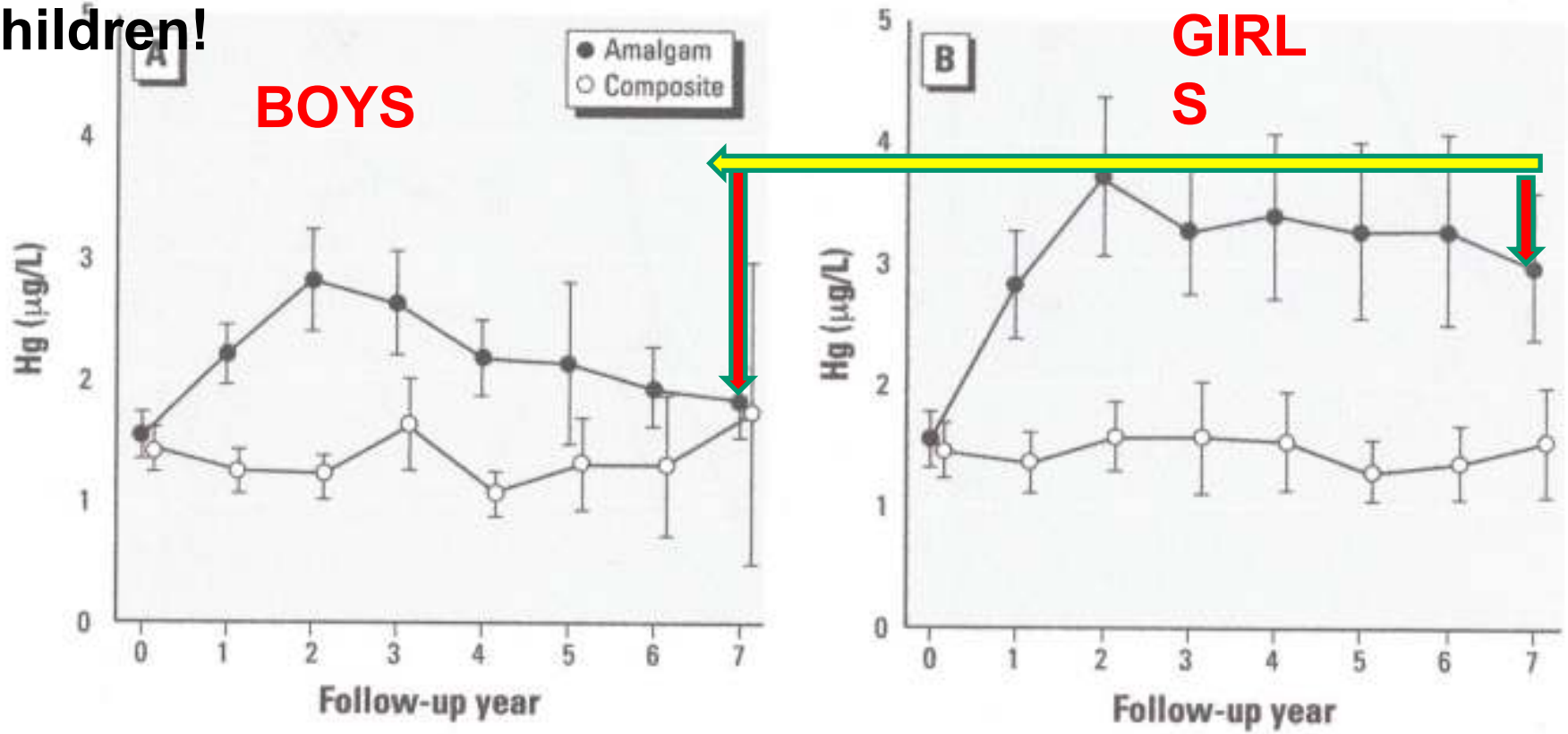


Figure 3. Mean urinary mercury concentrations for the amalgam group and composite group separately for male (*A*) and female (*B*) participants. Error bars show 95% confidence intervals for the group means. Differences between males and females in the amalgam group were statistically significant ($p < 0.05$) at all follow-up years except follow-up year 3. The sex comparisons were not altered significantly by adjustment for creatinine (results not shown).

J. Woods, et al., Environmental Health Perspectives (2007) 115:10, 1527-1531.

ELEVATED MERCURY IN IDIOPATHIC DILATED CARDIOMYOPATHY (IDCM).

WHERE DOES THE Hg COME FROM?

LEVELS ng/g	Hg	Sb
Controls	8.0	1.5
IDCM	178,400	19.260

Frustaci et al., J. of American College of Cardiology, 33, (6) 1578, 1999. Controls were patients with valvular or ischemic heart disease.

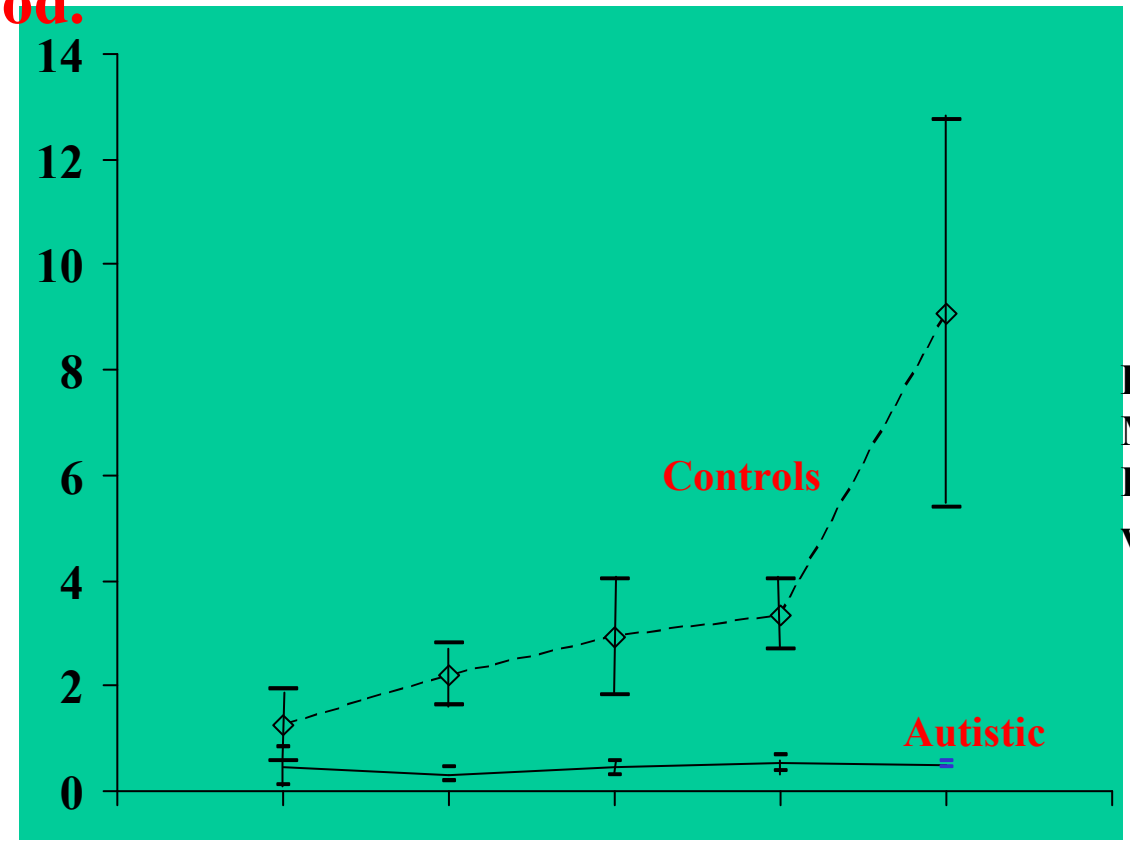
ATHLETIC YOUTH DIE OF IDCM.

WHY HASN'T NIH REQUESTED PROPOSALS FOR RESEARCH TO STUDY THIS??

THIS IS PROOF THAT MERCURY CAN CONCENTRATE IN SPECIFIC TISSUES OR ORGANS OF THE BODY, EVEN IF Hg BLOOD LEVELS ARE FOUND TO BE IN THE NORMAL RANGE.

MERCURY BIRTH HAIR LEVELS VS. AMALGAM FILLINGS IN AUTISTIC AND CONTROL GROUPS

Conclusion, autistic fetuses do not effectively excrete mercury into their blood. Note, fetal blood mercury is about 1.7 times the mother's blood.

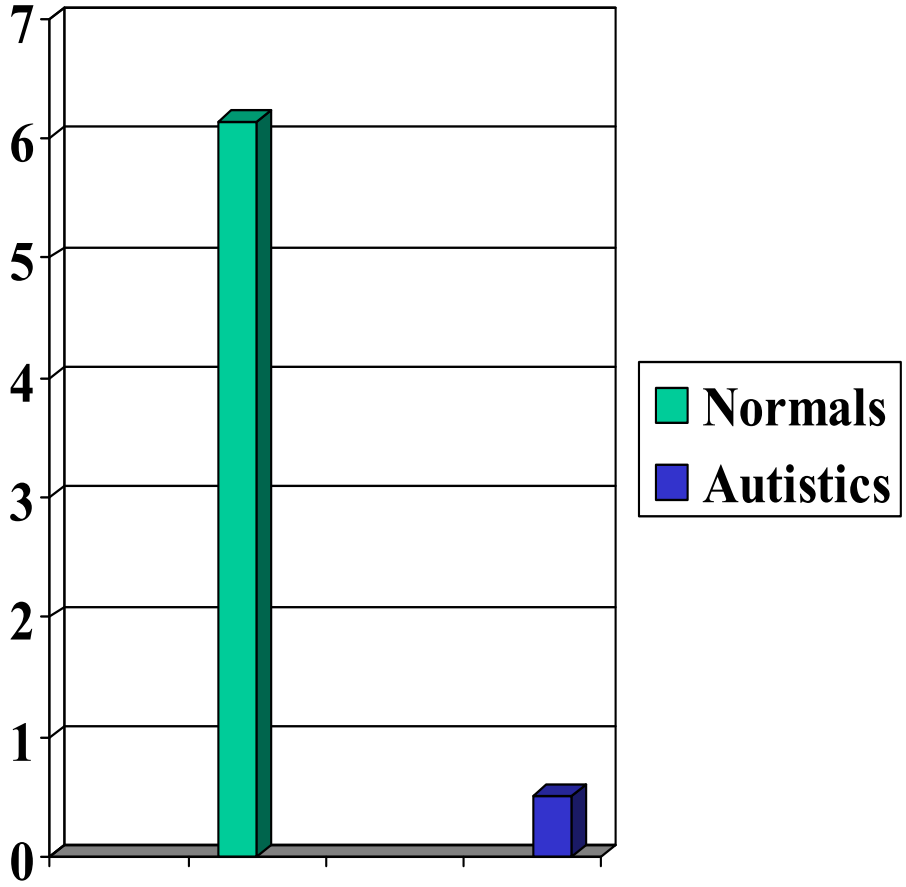


Data from A. Holmes, M. Blaxill & B. Haley, Int. J. of Toxicology v22, 2003

Number of amalgams:	0-3	4-5	6-7	8-9	≥10
Control: autistic ratio:	2.64	6.93	6.70	6.32	17.91
N:	15	22	29	30	43

Birth-Hair Hg Levels In Infants From Mothers With More Than Eight Amalgams

- Data (Hg ppm) was selected from only mothers who had 8 to 15 amalgam fillings to determine if these extremes showed a more definite trend on the differences between autistic and normal infants. The ratio was 12:1.



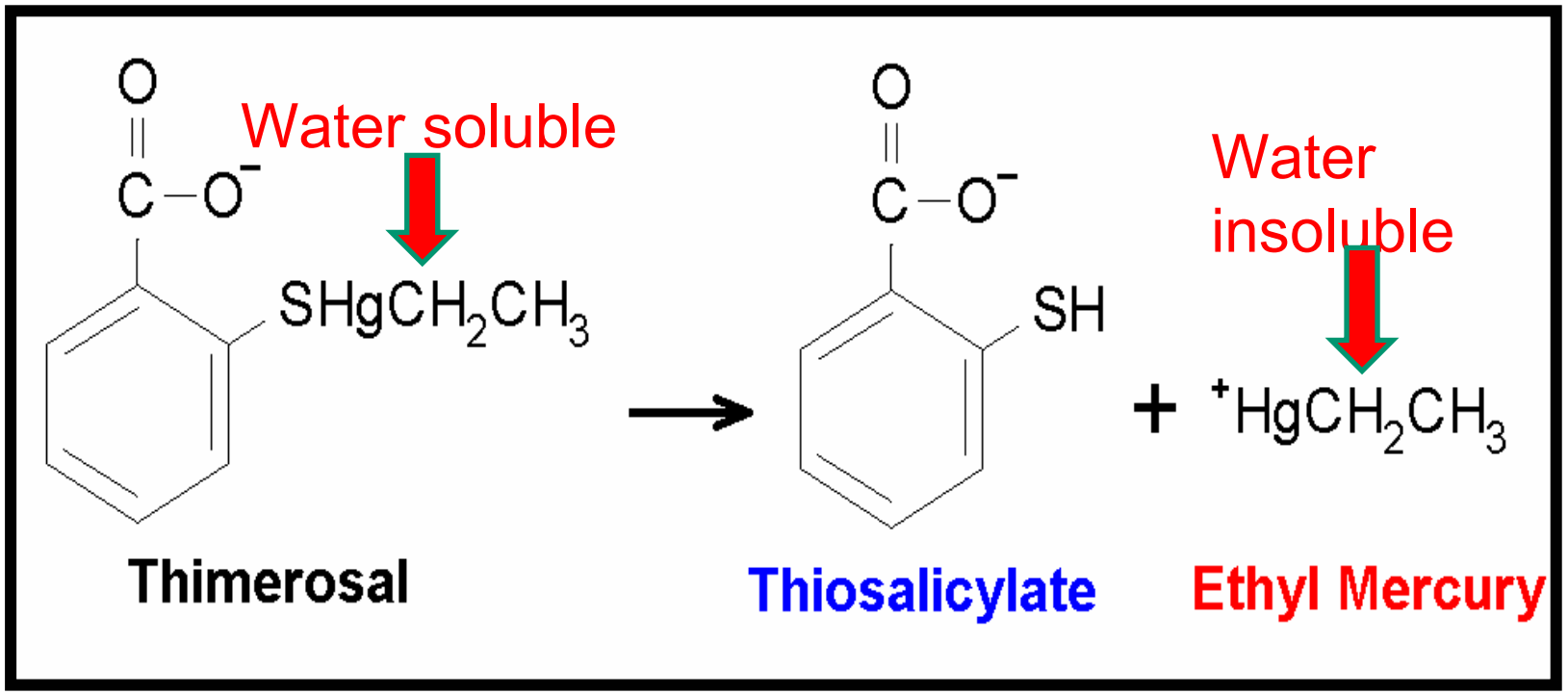
Epidemiological Studies

- A study on seven-year-old children in the Faeroe Islands found that blood pressure problems increased with decreased blood Hg. This implies retention toxicity effects of Hg in this comparison.
- In the Sechylles study of >700 children, boys with higher levels of hair mercury performed better on some tests as the Boston Naming test. This implies that ability to excrete increases hair Hg levels, not exposure, in this comparison.
- CONCLUSION: Blood and hair Hg levels are not a measure of exposure at low levels, but rather a measure of both exposure and ability to excrete mercury.

OBSERVATIONS

- IDCM DATA PROVES THAT Hg CAN COLLECT IN TISSUE AT LEVELS WAY ABOVE BLOOD LEVELS. THIS HAS TO BE DUE TO INABILITY TO EXCRETE Hg.
- ALZHEIMER'S SUBJECTS ANDAUTISTIC CHILDREN APPEAR TO HAVE THE SAME IMPAIRED ABILITY TO EXCRETE Hg WHEN COMPARED TO NORMAL CONTROLS.
- **NEW CONCEPT: Low mercury levels in the blood, hair and urine do not imply lack of toxic mercury exposure or retention in the body!**

Thimerosal Is Composed of Thiosalicylic Acid And Ethyl Mercury, A Known Neurotoxicant

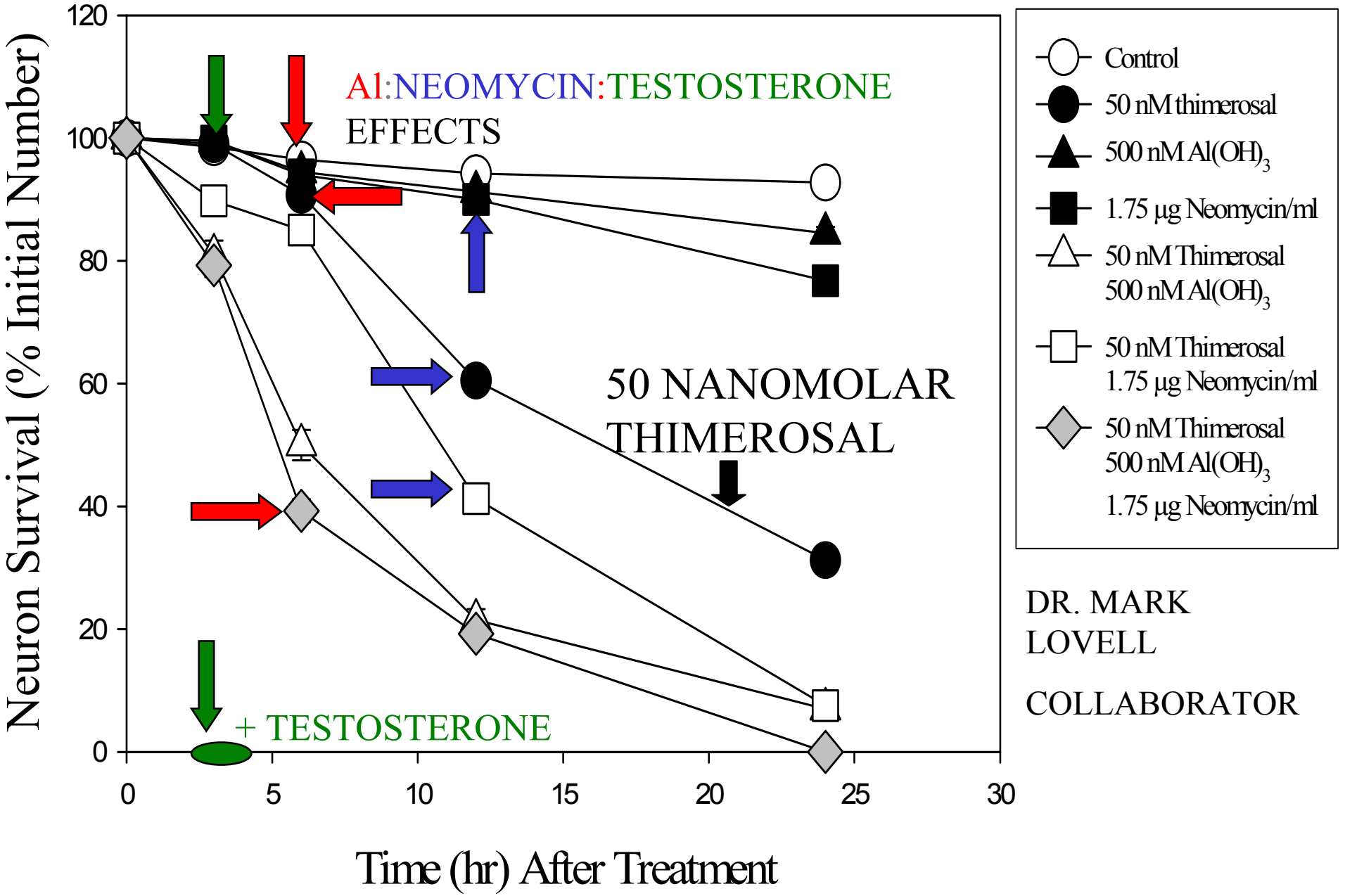


1. The Merck Index, 12th ed., p. 1590, #9451 (199
2. Martindale The Extra Pharmacopoeia, 30th ed.

Organ Mercury Levels in Infants with Omophaloceles Treated with Thimerosal. Fagan et al. Archives of Disease in Childhood 52, 962-64, 1977

- Between 1969-75, 13 cases were treated, 10 died. Mercury analysis of organs ranged from 65 to 2,700 times normal levels. This appears to be from 9 to 48 topical applications of 0.1% thimerosal applications. **NOTE; These children were most likely on antibiotics. Consider the effect on their immune system!**
- "Paradoxically, (in another study) 3 infants exposed postnatally (Iraq, Methyl-Hg by ingestion) did not exhibit signs or symptoms, though their blood levels were >1,000ppb, and one was >1,500ppb." **No antibiotics involved and this was Methyl-Hg!**
- **CONCLUSION IN 1977: "Organic mercurial antiseptics should be heavily restricted or withdrawn from hospital use, and the fact that mercury readily penetrates intact membranes and is highly toxic seems to have been forgotten."**
- **Result: Mercurochrome and Merthiolate were removed from the market by the FDA.**

SYNERGISTIC TOXICITIES



DR. MARK
LOVELL

COLLABORATOR

Estradiol Reduces Cumulative Mercury and Associated Disturbances in the Hypothalamus-Pituitary Axis of Ovariectomized Rats. Oliveria et al. Ecotoxicol. Environ. Safety Jan.10, 2006

- Methyl-mercury induced a decrease in LHRH in the medial hypothalmus and a decrease in plasma levels of LH. These decreases in LHRH and LH were abolished by estrogenic replacement therapy.
- **"The estrogenic effects were associated with a reduction of mercury content of the anterior pituitary gland and medial hypothalmus, suggesting a protective estrogenic effect."**
- **Could this explain the increased male susceptibility to autism? Recent studies show that autistics have very high testosterone levels.**

Mercury Effects on the Immune System

- The mitotic spindle is built on tubulin quite similar to that found in axons of neurons. Therefore, since the cells of the immune system must divide for an effective immune response Hg inhibits this and actively suppresses the immune system.
- Thimerosal is a **very potent inhibitor of phagocytosis** by mononuclear phagocytes, inhibiting the process at low nanomolar levels. (Rampersad et al., Transfusion 45(3):384-93,2005). This prevents removal of microbes and ethyl-Hg damaged cells and proteins leading to greater susceptibility for microbe infection and widespread autoimmune problems.

Mercury induces inflammatory mediator release from human mast cells.

Kempuraj D, Asadi S, Zhang B, Manola A, Hogan J, Peterson E, Theoharides TC. J Neuroinflammation. 2010 Mar 11;7(1):20.

INTRO: Mercury is known to be neurotoxic, but its effects on the immune system are less well known. Mast cells are involved in allergic reactions, but also in innate and acquired immunity, as well as in inflammation. Many patients with Autism Spectrum Disorders (ASD) have "allergic" symptoms; moreover, the prevalence of ASD in patients with mastocytosis, characterized by numerous hyperactive mast cells in most tissues, is 10-fold higher than the general population suggesting mast cell involvement. We, therefore, investigated the effect of mercuric chloride (HgCl2) on human mast cell activation.

RESULTS: $HgCl_2$ induced a 2-fold increase in beta-hexosaminidase release, and also significant VEGF release at 0.1 and 1 microM (311+/-32 pg/10*6 cells and 443+/-143 pg/10*6 cells, respectively) from LAD2 mast cells compared to control cells (227+/-17 pg/10*6 cells, n=5, $p<0.05$). Addition of HgCl2 (0.1 microM) to the proinflammatory neuropeptide substance P (SP, 0.1 microM) had synergestic action in inducing VEGF from LAD2 mast cells. $HgCl_2$ also stimulated significant VEGF release (360 +/- 100 pg/10*6 cells at 1 microM, n=5, $p<0.05$) from hCBMCs compared to control cells (182 +/- 57 pg/10*6 cells), and IL-6 release (466+/-57 pg/10*6 cells at 0.1 microM) compared to untreated cells (13+/-25 pg/10*6 cells, n=5, $p<0.05$). Addition of HgCl2 (0.1 microM) to SP (5 microM) further increased IL-6 release.

CONCLUSIONS: $HgCl_2$ stimulates VEGF and IL-6 release from human mast cells. This phenomenon could disrupt the blood-brain-barrier and permit brain inflammation. As a result, the findings of the present study provide a biological mechanism for how low