Comparative Toxicity of Ethyl and Methyl Mercury

- Exposure and toxicity issues for methylmercury.
- Risk assessments for methylmercury.
- Comparative pharmacokinetics of ethyl and methylmercury.
- Comparative toxicities of ethyl and methylmercury.
- General conclusions.

General Toxicity and Risk Assessment Issues

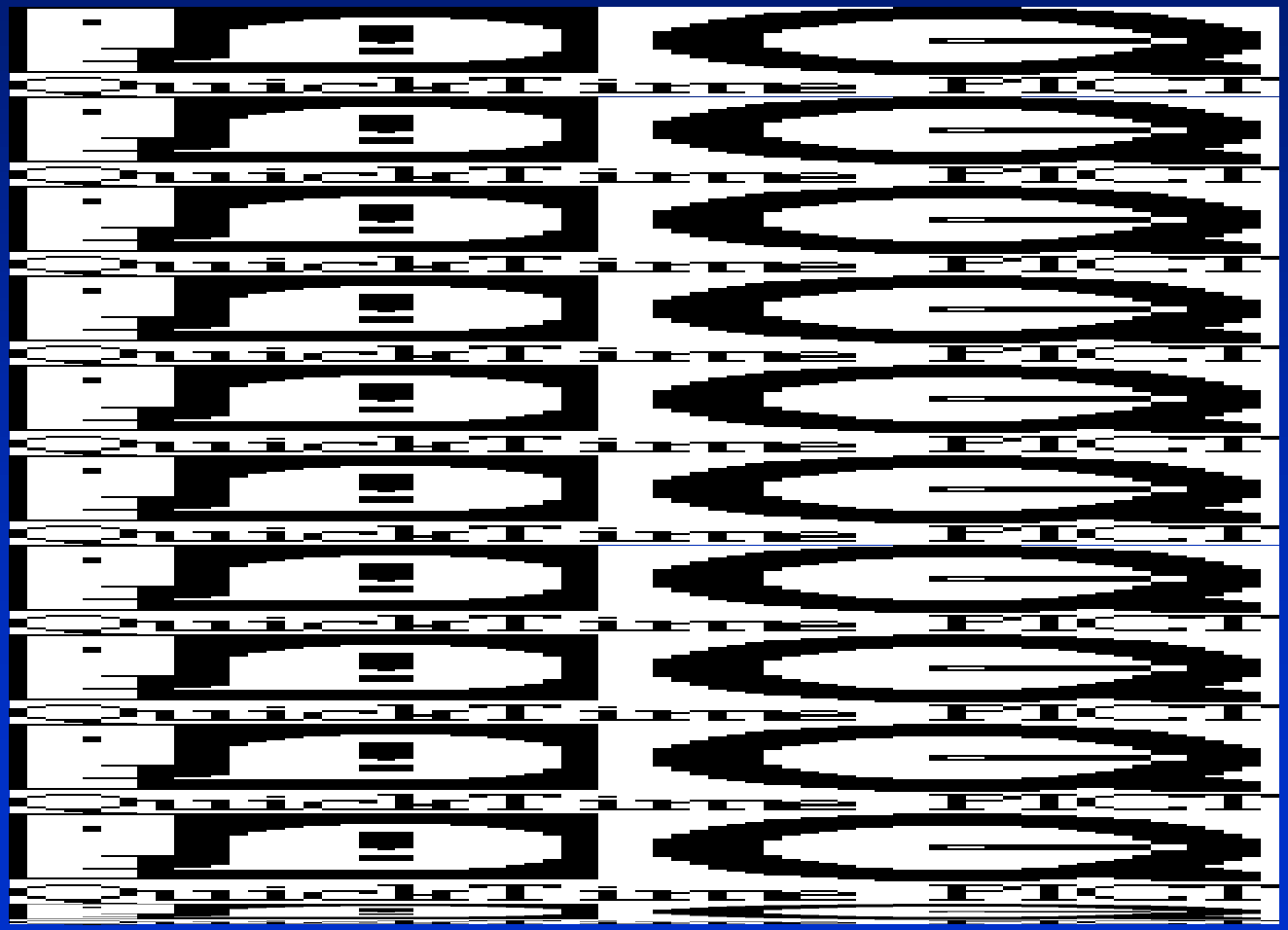
- Methylmercury is a developmental neurotoxin in people.
- The developing fetus is roughly 5 - 10 times more sensitive than adults.
- The relative sensitivity of infants to methylmercury is unknown but they are likely more sensitive than adults.
- Effects at low level exposures are difficult to evaluate.
- Pattern of exposure (peak exposures vs chronic exposures) are important.
- Methylmercury is ubiquitous and nearly everyone has some exposure.
- Initial efforts to establish safe exposure levels acknowledged the need for further studies on populations with low levels of exposure.

Mercury Air Emission Point Sources

- Electric utility
- Medical waste incineration
- Municipal waste combustion
- Manufacturing processes
- Chlor~alkali plants
- Pulp and paper
- Numerous other uses

Life Cycle of Mercury

Predicted Effect of Reduced Mercury Local Deposition Rates on Fish Methylmercury Levels*



* Provided by R. Harris, Tetra Tech Environmental

Some Existing Risk/Health Assessments for Methylmercury

EPA RfD	0.1 µg/kg/day
ATSDR MRL	0.3 µg/kg/day
WHO	0.47 µg/kg/day
North Carolina	0.17 µg/kg/day
NAS	~ 0.1 µg/kg/day

Blood and Hair Levels of Methylmercury

		Blood (ppb)	Hair (ppm)
NAS-2000	Benchmark (0.05)	58	12
	Benchmark/10	5.8	1.2
CDC-2001	Women 16 - 49 (mean)	1.2	
	Children 1 - 5 (mean)	0.3	
	Women 16 - 49 (90th%)	6.2	1.4
	Children 1 - 5 (90th%)	1.4	0.4
Seychelles	Maternal (mean)		6.8
Faroes	Maternal (mean)		4.3
	Cord	22.9	
North Carolina Fish Eaters	Adults (mean)		3.3
North Carolina Non-fish Eaters	Adults (mean)		0.4

North Carolina Hair Mercury Levels*

* Provided by Dr. Gregory Smith, NC DHHS

Toxicity of Thiomersal

Adult squirrel monkeys were administered thiomersal equivalent to ethylmercury doses of 1 or 6 μg/kg/day (Blair et al, 1975).

- Significant conversion to inorganic mercury.
- High levels in kidney-lower levels in brain.
- No evidence of toxicity.

Toxicity of Ethylmercury and Methylmercury

Adult male and female rats were administered 5 daily doses of equimolar concentrations of ethyl or methylmercury by gavage and tissue distribution, neurotoxicity and nephrotoxicity assessed (Magos et al, 1985).

- Neurotoxicities of methyl and ethylmercury were similar although higher levels of inorganic mercury were seen in brains of ethylmercury treated rats.
- Renal damage was greater in ethylmercury treated rats.
- Neither time-course nor dose response attempted.

Biological Half Life in People

Methylmercury	40 - 70 days
Ethylmercury	30 - 50 days

Note: Little or no information on differences between infants, children, or adults.

Infant Exposure to Methyl and Ethylmercury

Dietary exposure to methylmercury		0.02 - 0.2 µg/kg/day
Ethylmercury exposure by thiomersal vaccines		
– 2 months		4 - 18 µg/kg
– 4 months		3 - 11 µg/kg
– 6 months		3 - 11 µg/kg
Averaged over 4 months		0.1 - 0.3 µg/kg/day
EPA RfD	Women of child-bearing age	0.1 µg/kg/day
Faroe Islands	Women of child-bearing age	0.3 µg/kg/day

Some Toxicological Comparisons of Interest

		Brain:Blood Concentration Ratio	
		MeHg	EtHg
3 days	Male	0.066	0.029
	Female	0.089	0.023
10 days	Male	0.078	0.028
	Female	0.116	0.026

Methylmercury passes the blood brain barrier
3 - 4 times faster than ethylmercury

From Magos, 1985 and 2001

Clinical Manifestations of Ethylmercury Poisoning Episodes

- Speech disorders
- Vision disorders
- Tremor
- Ataxia
- Spasticity
- Delerium
- Death

Blood levels greater than 500 ppb can produce adverse effects.

Subtle measures of developmental neurotoxicity (as done for Methylmercury) have not been evaluated.

Ethylmercury Toxicity

- Ethylmercury is a neurotoxin.
- Infants may be more susceptible than adults.
- Ethylmercury is approximately 5 times less acutely toxic than methylmercury.
- Data are not adequate to compare potencies of ethylmercury and methylmercury for developmental neurotoxicity.
- The mechanisms responsible for organomercurial - caused developmental neurotoxicity are unknown and this also complicates evaluation of structure/ activity relationships.

Comparative Critical Toxicology Studies on Thiomersal - Ethylmercury and Methylmercury

- Developmental neurotoxicity - assessing dose response and age dependent responses.
- Mechanistic studies - focused on critical changes in gene function and cellular pathways.
- Evaluation of possible sensitive subpopulations based on genetic predisposition, diet, and cumulative risk.
- Biomarkers of exposure including hair need to be evaluated.

Conclusions

- Ethylmercury is probably slightly less toxic than methylmercury.
- However, the database for ethylmercury is weak which creates considerable uncertainty in risk assessment comparisons.
- Ethylmercury should be considered equipotent to methylmercury as a developmental neurotoxin. This conclusion is clearly public health protective.
- Ethylmercury exposure from vaccines (added to dietary exposures to methylmercury) probably caused neurotoxic responses (likely subtle) in some children.