**Oregon Public Health Association Conference, Oct. 12, 2015**

**NW Environmental Health Conference, April 17, 2015**

**Neurodevelopmental Effects of Prenatal Exposure to Environmental toxicants**

**References for the broader issue and Pb, MeHg, and PCBs (Marjorie Kircher, MS OTR)**

**Great articles discussing neurodevelopment and environmental chemical exposures:**

1. Bellinger, David, A strategy for comparing the contributions of environmental chemicals and other risk factors to neurodevelopment of children, Environmental Health Perspectives 2012; 120(4); 501-507

Excellent discussion p. 504, about impact of many indiv not meeting criteria for dx on population burden

2. Grandjean, Philippe and Landrigan, Philip, Neurobehavioural effects of developmental toxicity, Lancet Neurology 2014; 13:330-3

“Global, silent pandemic of neurodevelopmental toxicity,” (Update of 2006 seminal article) added six more dev. neurotoxicants (manganese, fluoride, chlorpyrifos, DDT, tetrachloroethylene, PBDEs) , in addition to their previous five (lead, mercury, arsenic, PCBs, toluene) good language defining scope of the broad issue and its urgency

3. Landrigan, Philip, Lambertini, L, Birnbaum, L, A research strategy to discover the environmental causes of autism and neurodevelopmental disabilities, Environmental Health Perspec 2012; 120:258-260

Lists the chemical groups we are doing the lit search on, from Mt. Sinai workshop, supported by NIEHS and Autism Speaks,

Describes loss of cognition, dyslexia and ADHD from exposures to lead, MeHg, organophosphate insecticides, etc.

4. Rodier, Patricia, Environmental causes of Central Nervous System maldevelopment, Pediatrics 2004; 113:1076-1083

good review of developing neural architecture in utero, “MeHg is transported freely across the blood/brain barrier at any age.” p. 1080

5. Rossignol, DA, et al, Environmental toxicants and autism spectrum disorders: a systematic review, Transl Psychiatry 2014; 1-23

6. Dawson, Geraldine, Editorial: Dramatic increase in autism prevalence parallels explosion of research into its biology and causes, JAMA Psychiatry (2013); 70(1):9-10

Autism research funding by NIH in 2000 was $50 mil; by 2010, HIH funding reached $334 mil and private foundation funding $74 mil. (over $400 mil)

Growing body of evidence that autism associated with immune abnormalities—potential contributors to immune abn are a variety of env toxins, urgent need for more research on prenatal and early postnatal brain development in autism, with a focus on how genes and environm risk factors combine

**MethylMercury articles**

Excellent background info (not research studies):

1) Clarkson, Thomas W., The three modern faces of mercury, Environmental Health Perspect 2002; 110(suppl 1): 11-23

Excellent description of the way mercury gets into the environment and the human body

2) Mahaffey, Kathryn, Transactions of the Amer clinical and Climatological Assn, Vol. 116, 2005

(Theodora gave me this)

Excellent summary of the attributes of mercury: 95% of ingested methylmercury (organic) comes from the consumption of fish and other seafood

Good description of release into air as a gas, redeposited on the earth with precipitation, into earth or waterways, into sludges or sediments, where it is methylated by organisms, consumed by small fish, large fish, humans, p. 129

Blood Hg is always dominated by meHg; urinary Hg is biomarker of inorganic merc; Hair merc. is dominated by meHg.

Dental amalgams inorganic Hg

Hg vapor exposure can be life threatening, can accumulate in CNS causing irreversible damage; kidneys also affected, chest pain, etc.

Study of methylHg concentrations in US population, varies within the population; a person’s mercury intake depends on the species of fish consumed as well as quantity of fish eaten

Blood mercury values were twice as high among people who ate fish at least once a week, compared with people who ate fish twice a month or less

Adverse health effects produced by Hg exposures affects motor, sensory systems, esp. the area of sensory-motor integration;

Minamata, Iraq, p. 143

“The development of paresthesia (in adults) has been considered to be the most sensitive neurological effect of methylmercury exposure among adults,” p. 143

Other effects in adults: cardiac, endocrine, immune

Neurodevelopmental effects “the devel. Fetal Nervous system judged to be 5-10 times more sensitive to meHg than the adult NS

3) Spheres of Influence—Minamata Convention on Mercury, Environ Health Perspect, Oct. 2013, 121(10)

New controls established, 130 nations agreed to both compulsory and voluntary measures to limit mercury release

**Mercury, cont’d, mostly research studies:**

Blanchard, K., Palmer, R., Stein, Z., “The value of ecologic studies: Mercury concentration in ambient air and the risk of autism,” *Reviews on Environmental Health*, 2011; 26(2): 111-118

Boucher, O., Jacobson, S., et al, Prenatal methylmercury, postnatal lead exposure, and evidence of Attention Deficit/ Hyperactivity Disorder among Inuit children in Arctic Quebec,” *Environmental Health Perspectives (EHP)*, 2012, 120(10)

Chen, C., “Methylmercury effects and exposures: Who is at risk?”, *EHP*, 2012, 120(6)

Debes, Frodi, et al incl Philippe Grandjean, Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years, Neurotoxicology and Teratology 2006; 28:536-547

Ellefsen, Asa, et al, Autism in the Faroe Islands. An epidemiological study, J Autism Dev Disord 2007; 37: 437-444

Grandjean, P., et al, “The Faroes Statement: Human health effects of developmental exposure to chemicals in our environment,” *Basic and Clinical Pharmacology and Toxicology*; 2007, 10.1111; 1742, p 1-3

Grandjean, Philippe, et al, Cognitive deficit in 7 year-old children with prenatal exposure to methylmercury, Neurotoxicology and Teratology 1997; 19(6): 417-428

Grandjean, Philippe, et al, Neurotoxicity from prenatal and postnatal exposure to methylmercury, Neurotoxicology and teratology 2014; 43: 39-44

Grandjean, Philippe and PJ Landrigan, Developmental neurotoxicity of industrial chemicals, Lancet 2006; 368: 2167-2178

Jacobson, J.L. et al, “Relation of prenatal methylmercury exposure from environmental sources to childhood IQ,” EHP, 2015; 123(8); August 2015

Karagas, M. et al, “Evidence on the human health effects of low-level methylmercury exposure,” *EHP*, 2012; 120(6); 799-806

Mahaffey, K., et al, “Adult women’s blood mercury concentrations vary regionally in the United States: association with patterns of fish consumption (NHANES 1999-2004),” *EHP,* 2009; 117:47-53.

Miodovnik, A., “Environmental neurotoxicants and developing brain,” *Mt. Sinai Journal of Medicine 2011*, 78: 58-77

National Scientific Council on the Developing Child, “Early exposure to toxic substances damages brain architecture,”

Working Paper #4, Spring, 2006 - [www.developingchild.net](http://www.developingchild.net)

Ng, Sharon, et al, Mercury, APOE, and children’s neurodevelopment, NeuroToxicology 2013; 37 85-92

Good paper

Oken, Emily, et al, Maternal fish intake during pregnancy, blood mercury, and child cognition at age 3 years in a US cohort, Am J Epidemiol 2008; 167(10): 1171-1181

Palmer, Raymond F., Blanchard, Steven et al, Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas, Health and Place, Elsevier Ltd. 2005;

(this is rather a pilot study; see above citing Blanchard, a better study)

Razzaghi, Hilda, et al, Blood mercury concentrations in pregnant and nonpregnant women in the United States: National health and nutrition examination survey 1999-2006, American Journal of Obstetrics and Gynecology 2014; 210:357;e1-9

Data analysis from NHANES study, seafood consumption was the most signif driver of high BHg concentrations. Pregnant women had slightly but signi. lower BHg concentrations; reason may be that pregnant women consume less fish; another study revealed that pregnant women have been avoiding fish or eating less, with awareness of reducing mercury intake

Sexton et al, “Biomarker measurements of concurrent exposure to multiple environmental chemicals and chemical classes in children,” *Journal of Toxicology and Environmental Health*, 2011, Part A, 74:927-942

Trasande, Leonardo, et al, (incl Landrigan) Mental retardation and prenatal methylmercury toxicity, American J of industrial medicine 2006; 49:153-158

van Wijngaarden, Edwin, et al, Autism spectrum disorder phenotypes and prenatal exposure to methylmercury, Epidemiology 2013; 24(5): 651-659

Seychelles island (republic of, near African continent) On p. 9, level of Hg exposure in these seafood-eating islanders is 10 times the level of US mothers

They administered the Social Communication Questionnaire (p. 3,4, a 40-item parent questionnaire, the screening test of choice in previous ASD studies, not clear how this relates cross-culturally) to parents of a cohort of 1784 children, adolescents and young adults. 40% of this cohort hair samples were gathered in 1989-1990, Prenatal exposure to MeHg was measured in maternal hair samples at or near time of birth. No other neurological tests or evaluation tools were used. P. 7: They found no consistent evidence for an association between prenatal MeHg levels and total Social Comm Question or Social Respons Scale scores in their subjects. *No mention in the article of genetics*. Note: Most neurodevelopmental testing in the Seychelles, published in studies through the years shows no compromise of neuro function, despite the fact the women’s Hg blood levels are 10 times higher than US mothers. They appear to be very lucky.

Watson, Gene DDS, PhD, van Wijngaarden, Edwin, et al, Neurodevelopmental outcomes at 5 years in children exposed prenatally to maternal dental amalgam: the Seychelles child development nutrition study, Neurotoxicol Teratol 2013; 39:57-62

Prenatal mercury vapor exposure from pregnant women having their teeth filled, longitudinal cohort study; tests of cogn, language, perceptual and school achievement showed no evidence for neurodev. outcomes in children at 5 yrs.

Windham, G. et al, “Autism Spectrum Disorders in relation to distribution of hazardous air pollutants in the San Francisco Area,” *EHP*, 2006, 114(9); 1438-1444

**Lead articles**

Good one to introduce reasons to be still concerned about lead:

Barrett, Julia R., et al, Parallel outcomes –see reference below under combo chems.

“Dev. exposure to lead has been widely studied and is known to have a negative impact on cognitive function as well as on children’s behavior: across studies, cognitive flexibility, vigilance and alertness are consistently affected by lead, but also evidence exists for effects on working memory, response inhibition and planning”

Jedrychowski, W., Perera, F., et al, Gender specific differences in neurodevelopmental effects of prenatal exposure to very low-lead levels: the prospective cohort study in three-year olds, Early Human Development 2009; 85(8): 503-510

Lanphear, Bruce P., et al, Low-level environmental lead exposure and children’s intellectual function: an international pooled analysis, Environmental Health Perspec. 2005; 113(7): 894-899

Nigg, Joel T, et al, Confirmation and extension of association of blood lead with attention deficit/hyperactivity disorder and ADHD symptom domains at population-typical exposure levels, Journal of child psychology and psychiatry 2010, 51(1):58-65

Abstract only

Wang, Hui-Li, et al, Case-control study of blood levels and attention deficit hyperactivity disorder in Chinese children. Environ Health Perspec., 2009; 117(7)

**PCB articles**

Barrett, Julia R., et al, Parallel outcomes –see reference below under combo chems.

“research beginning to explore relationship between PCB and ADHD.”

Boucher, O., et al, Prenatal exposure to PCBs: A neuropsychologic analysis, Environmental Health Perspectives, Vol 117, No 1, Jan 2009

Mitchell, Michelle, et al, Levels of PCB and PBDE cogeners in human postmortem brain reveal possible environmental involvement in 15q11-q13 duplication autism spectrum disorder, Environmental and molecular mutagenesis 2012; 53(8); 589-598

Segiv, Sharon K., et al, Neuropsychological measures of attention and impulse control among 8 year-old children exposed prenatally to organochlorines, Environ Health Perspec. 2012; 120(6): 904-909

**Cadmium articles**

Early-Life Cadmium Exposure and Child Development in 5-Year-Old Girls and Boys: A Cohort Study in Rural Bangladesh. 1104431. <<http://ehp.niehs.nih.gov/1104431/>

**Multiple toxin articles—getting to be the norm for research, though they did not study synergistic action; multiple regression analyses used to determine separate chemical effects:**

Boucher, O., et al, Response inhibition and error monitoring during a visual go/no-go task in Inuit children exposed to **lead, PCBs and MeHg**, Environmental Health Perspectives. 2012, 120(4)

Barrett, Julia R., et al, Parallel outcomes: comparing effects of environmental contaminant exposures with ADHD in children, Environmental Health Perspec 2010; 118:542

Good essay (one page) explaining that deficits in executive function and attn. are key characteristics of both ADHD and dev. exposure to **lead and PCBs**

Boucher, Olivier, Jacobson, S., et al, **Prenatal methylmercury, postnatal lead exposure**, and evidence of Attention Deficit/ Hyperactivity Disorder among Inuit children in Arctic Quebec,” *Environmental Health Perspectives (EHP)*. 2012, 120(10)

Boucher, Olivier, Muckle, et al, Domain-specific effects of prenatal exposure to **PCBs, mercury, and lead** on infant cognition: results from the environmental contaminants and child development study in Nunavik, Environmental Health Perspec 2014; 122(3); 310-316

Eubig, P. A., et al, **Lead and PCBs as risk factors** for Attention deficit hyperactivity disorder, Environmental Health Perspect. 2010, 118: 1654-1667

Hackenmiller-Paradis, Rene, “Pollution in People, A study of toxic chemicals in Oregonians,” 2007; Oregon Environmental Council, www.oeconline.org

Jurewicz, Joanna, et al, Chemical exposure early in life and the neurodevelopment of children—an overview of current epidemiological evidence, Annals of agricultural and environmental medicine 2013; 20(3):465-486

**PCBs, lead, mercury, pesticides**

Kuehn, Bridget M., Increased risk of ADHD associated with early exposure to pesticides, **PCBs**, JAMA 2010; 304(1):27-28

Only have the abstract, unable to access full article from home

Llop, Sabrina, et al, Prenatal and postnatal insecticide use and infant neuropsychological development in a multicenter birth cohort study, Environment International 2013; 59:175-182--See P. 180-synnergistic effects of insecticides with Hg and PCBs

McDermott, Suzanne, et al, Are different **soil metals** (**mercury, arsenic, lead)** near the homes of pregnant women associated with mild and severe intellectual disability in children?, Developmental medicine and child neurology 2014; 56:888-897

10,051 pregnant mothers, found signif + assn. between mild intellectual disability and soil mercury; signif + assn. between severe intellect disability and soil arsenic and lead

Good explanation p. 896 how surface soil accumulates contaminants over time, deposited from air; assumes people track soil and dust into their home, rec. removal of shoes indoors.

Orenstein, Sara T.C., et al, Prenatal organochlorine and methylmercury exposure and memory and learning in school-age children in communities near the New Bedford Harbor superfund site, Massachusetts. Environmental Health Perspec. 2014; 122(11): 1253-1259

Sioen I, Den Hond E, Nelen V, Van de Mieroop E, Croes K, Van Larebeke N, Nawrot TS, Schoeters G. 2013. Prenatal exposure to environmental contaminants and behavioural problems at age 7-8 years. Environ Int. 59:225-31. <<http://www.ncbi.nlm.nih.gov/pubmed/23845936>

Winneke, Gerhard, Developmental aspects of environmental neurotoxicology: Lessons from lead and polychlorinated bephenyls, J of the Neurological Sciences 2011, 308; 9-15

Marjorie Kircher, MS OTR

April 2015