



# **DEVELOPMENTAL LEAD EXPOSURE AND ALZHEIMER'S DISEASE (AD)**

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# DEFINITIONS & PREVALENCE

- Early-onset AD (EOAD) (Wang *et al.*, 2008  
Campion *et al.*, 1999)
- Late-onset AD (LOAD) (Lahiri *et al.*, 2008)
- AD is the most common neurodegenerative disorder
- An estimated 5.3 million people have AD and this number is expected to triple by 2050 (Herbert *et al.*, 2003)

# SCIENCE

- Only long-term survivor of childhood lead encephalopathy with exhaustive neuropathological and toxicological studies

(Nicklowitz and Mandybur, 1975)

**TABLE I**  
*Brain Tissue Levels of Pb and Al in Human Autopsy Material Expressed in  $\mu\text{g}$  Per Gram Wet Weight*

No.	Patient	Age in Years	Diagnosis	Frontal Cortex		Temporal Lobes		Hippocampus		Cerebellum	
				Pb	Al	Pb	Al	Pb	Al	Pb	Al
1	NP72-120	44	Present Case*	3.3	3.0	4.2	3.6	1.8	5.3	.9	2.8
2	NP72-106	68	Alzheimer's Disease	.3	2.2	.5	2.2	.8	2.7	.6	2.1
3	U72-45	69	Recent Embolism, Hemorrhagic Infarct	.4	1.7	.5	2.1	.4	1.6	.4	2.0
4	VAN74-23	72	Congenital Spinal Malformation	.1	1.0	.4	1.7	1.4	2.1	1.3	.9
5	4090/73	3	Lead Encephalopathy	2.1†	.3†						

\* Pb of the storage medium (formalin) < .05  $\mu\text{g}/\text{ml}$ .  
† Samples were taken from unidentified cortex.

# SCIENCE

- Historical Etiology of LOAD Research; ‘protein only’ (Lahiri, *et al.*2007)
- Amyloid- $\beta$  peptide plaque build-up causes the symptoms of AD (Hardy and Higgins, 1992; Selkoe, 2003; Hardy and Selkoe, 2002)
- Reasons for New Directions of Research
- The ‘Barker Theory’ (Barker, *et al.*2002; Cheung; *et al.*2000; Eriksson, *et al.*2000, Osmand and Barker, 2000)
- Epigenetics

<http://www.sciencedaily.com/releases/2009/04/090401181447.hm>

# SCIENCE

- Bolin *et al.* 2006  
Rat Study
  - Exposed as pups to Lead Acetate
  - Two experimental groups (Pb-E, Pb-L) and one control
  - Animals with Early Pb exposure had increased AD genetic by-products and increased oxidative damage (Bolin *et al.*, 2006)

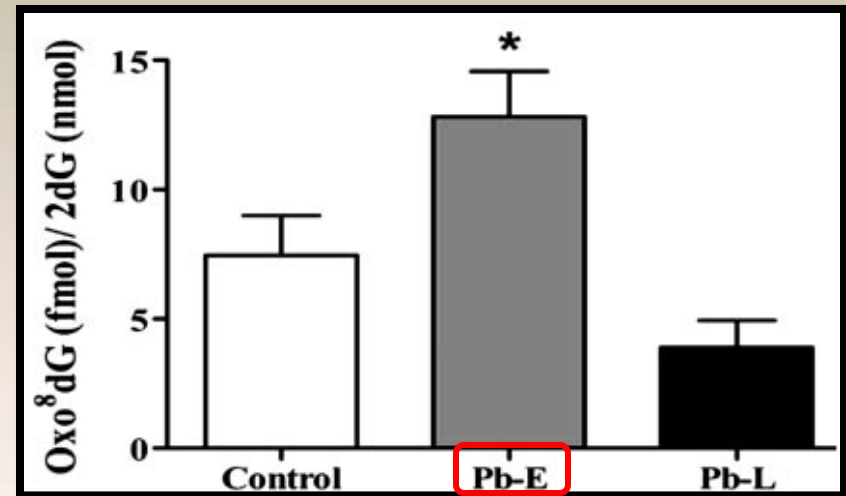


Figure 1. Changes in the oxo8dG activity profiles in the rat cerebral cortex during the life span.

# SCIENCE

- Wu *et al.* 2008  
Monkey Study
  - Link Bolin *et al.* results with pathological evidence of AD
  - Obtain results more homologous to humans
  - Exposed monkeys had increased levels of amyloid- $\beta$
  - Conclusions  
(Wu, *et al.* 2008)

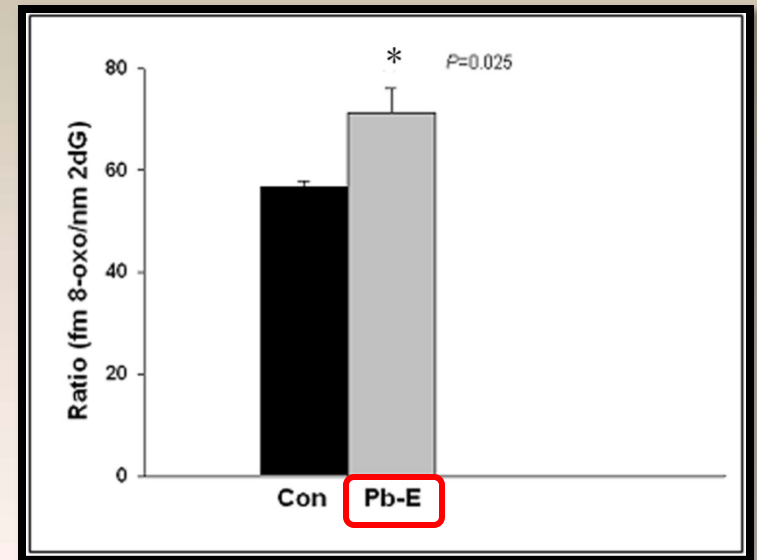


Figure 5. Oxidative DNA damage in control and infantile-exposed aged monkey brains

# SCIENCE

- The Latent Early-Life Associated Regulation Model (LEARn)
- Environmental agents and dietary factors can alter gene regulation
- Alterations begin in developmental stages
- Manifestations are not seen until later in life

(Lahiri *et al.*, 2008)

# POLICY AND PREVENTION

- **Clean Air Act of 1970** (Clean Air Act of 1970. Public Law 91-604)
- **Phasing out of Unleaded Gasoline**
- **Residential Lead-Based Paint Hazard Reduction Act of 1992** (Residential Lead-Based Paint Hazard Reduction Act of 1992. Public Law 102-550)
- **2008 Renovation, Repair and Painting Rule** <http://www.epa.gov/lead/pubs/renovation.htm>



# PROPOSED INTERVENTIONS

- Nationwide AD Registry
- Improve and Expand Toxicity Testing Measures
- Conduct Prospective Epidemiologic and Genetic Studies

(Landrigan *et al.*, 2005)

# SUMMARY

- Researchers have been unable to uncover a clear genetic link to LOAD
- Exposure hypothesis
- Early animal research results support the early exposure theories (LEARn)
- Air, housing and renovation policies in place
- Specific AD exposure focused surveillance, tracking and testing are still lacking

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**QUESTIONS?**

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