

Focusing Biomedical Treatments with Laboratory Data

Richard S. Lord, Ph.D.

Questions

- Why autism spectrum disorder epidemic
- How to treat?
- How to prevent?

A Medical Hypothesis

Regressive Autism: A neuronal disorder precipitated by the disrupting action of quinolinic acid in the brain of children with predisposing genetic, nutritional and toxicant factors and propagated by the same factors plus those created by destructive cycles, especially in the GI tract

The Three P's of Degenerative Disease

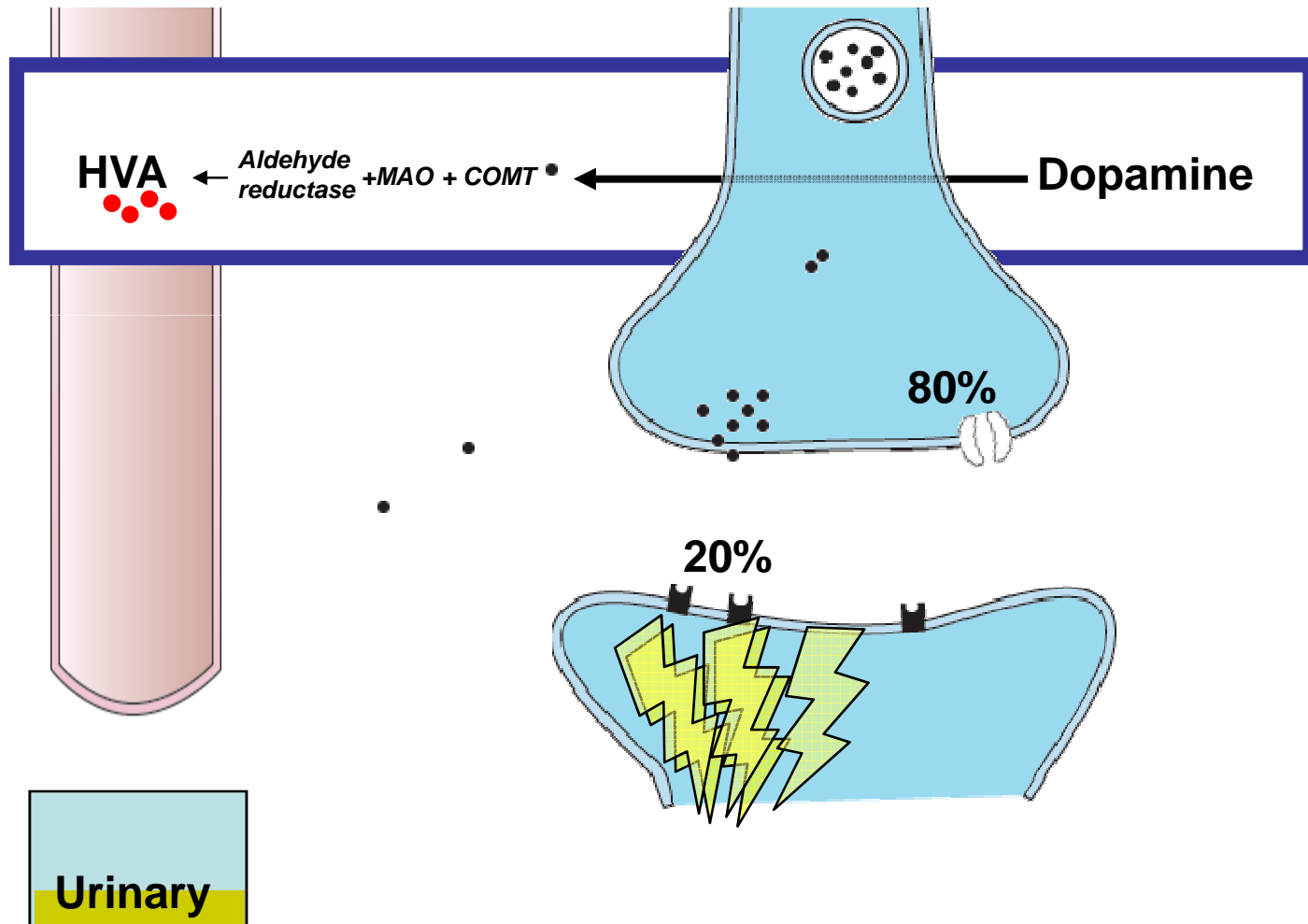
- Predisposing factors
 - Genetic, nutrient, toxicant, microbial
- Precipitating factors
 - Inflammation → Neuronal disruption
- Propagating factors
 - Genetic, nutrient, toxicant, microbial
- Prevent
 - Normalize as early as possible
- Avoid
 - Immunization
- Treat
 - Focused therapies

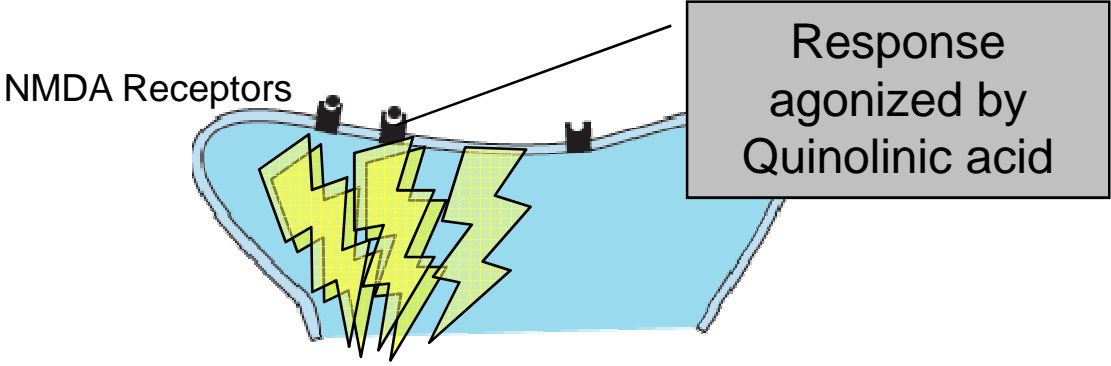
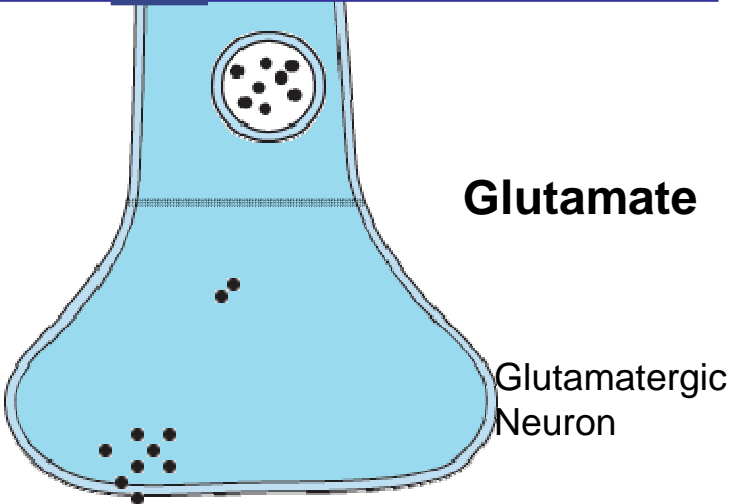
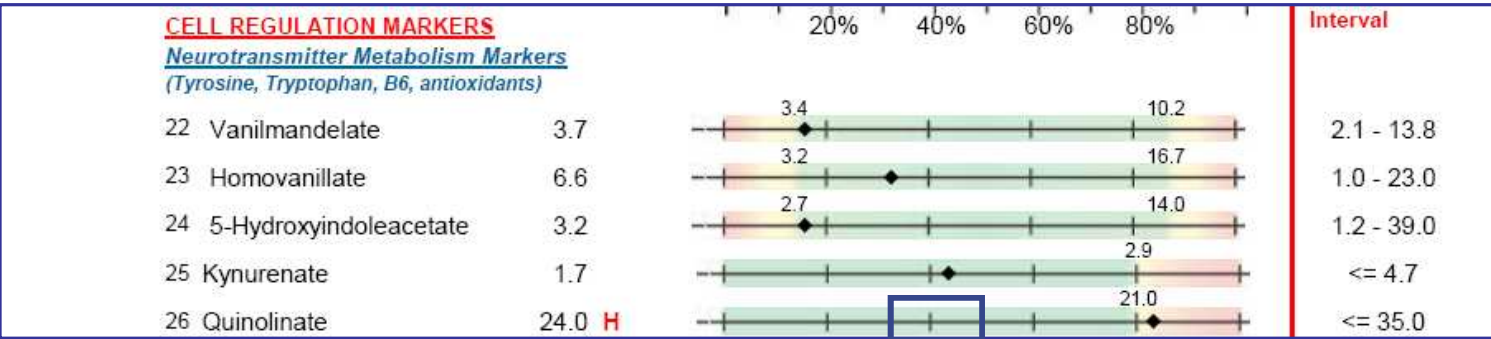
Autistic Progression

- First ~12 mo.
 - Normal development in presence of predisposing factors
 - Delicate process of learning and neuronal plasticity advancing
- Inflammatory precipitation
 - Multiple predisposing factors happen to coincide with an inflammatory incident releasing high quinolinic acid
- Regression
 - Perception and learning interrupted and destructive in the gut-associated immune system
- Healing
 - Propagating factors corrected
 - Neuronal plasticity, attention and learning restored

Neurotransmitter Function

Signal, Re-uptake, and Disposal of Neurotransmitters



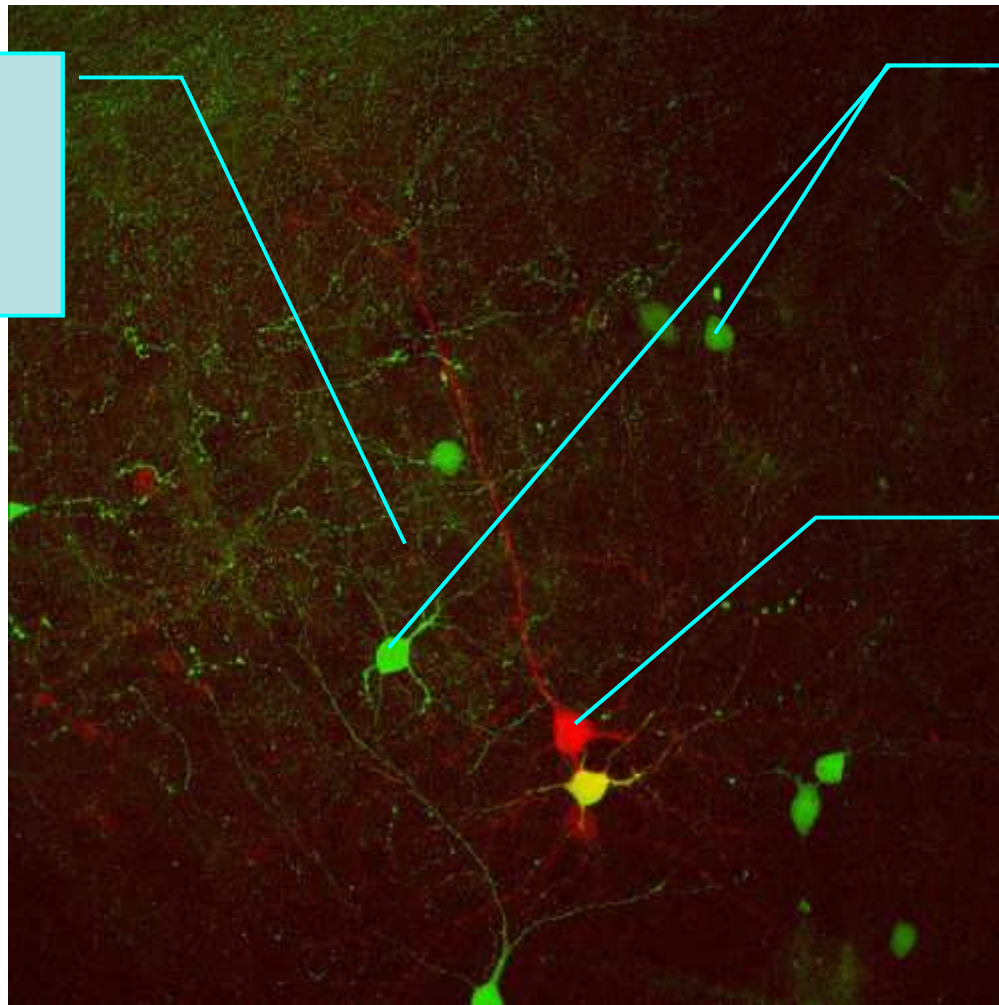


Autism is a Neuronal Disorder

Matrix of connections required for perception

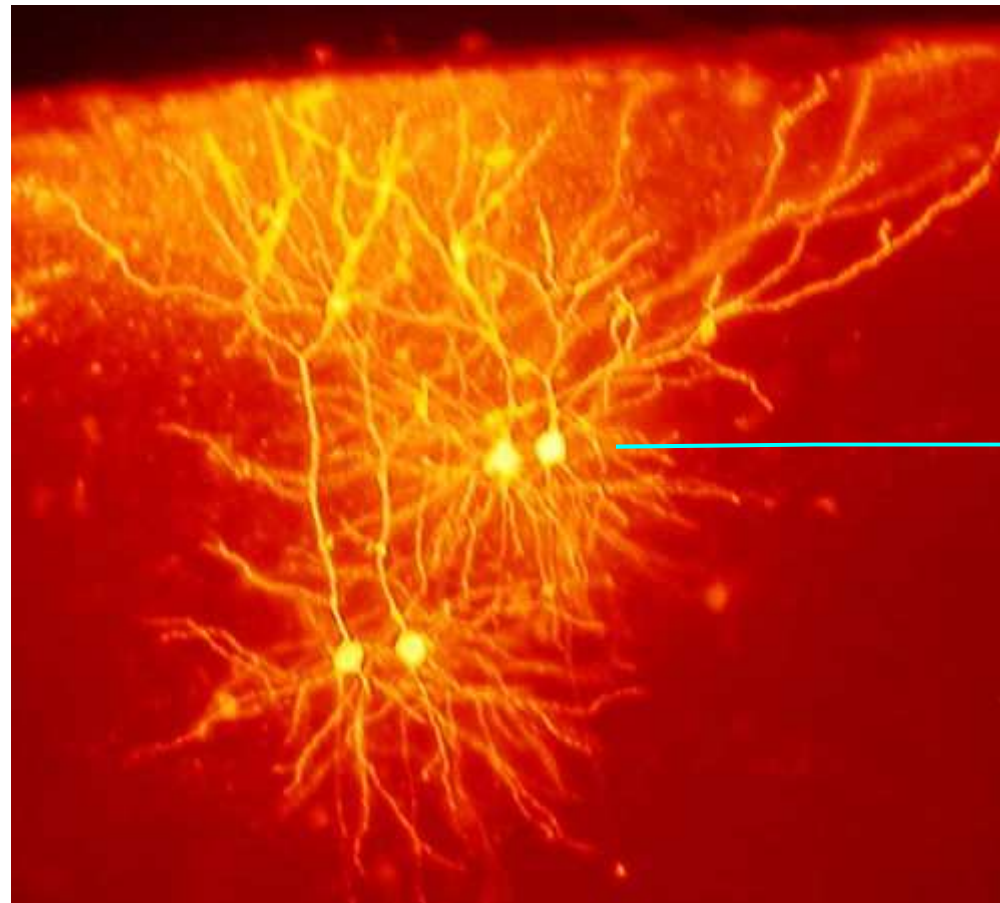
Insufficiency of Thiamin, Mg, Met, & EPA affects all (dopamine) neurons

Regulation by Quinolinic Acid in glutamate neurons



Graphical representation (not actual event capture)

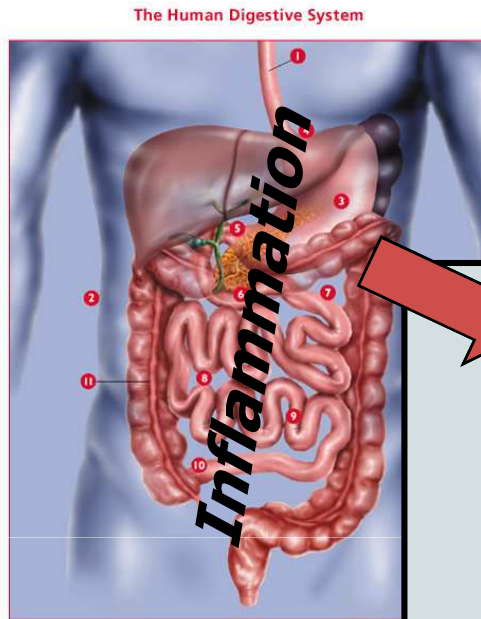
The Precipitating Factor



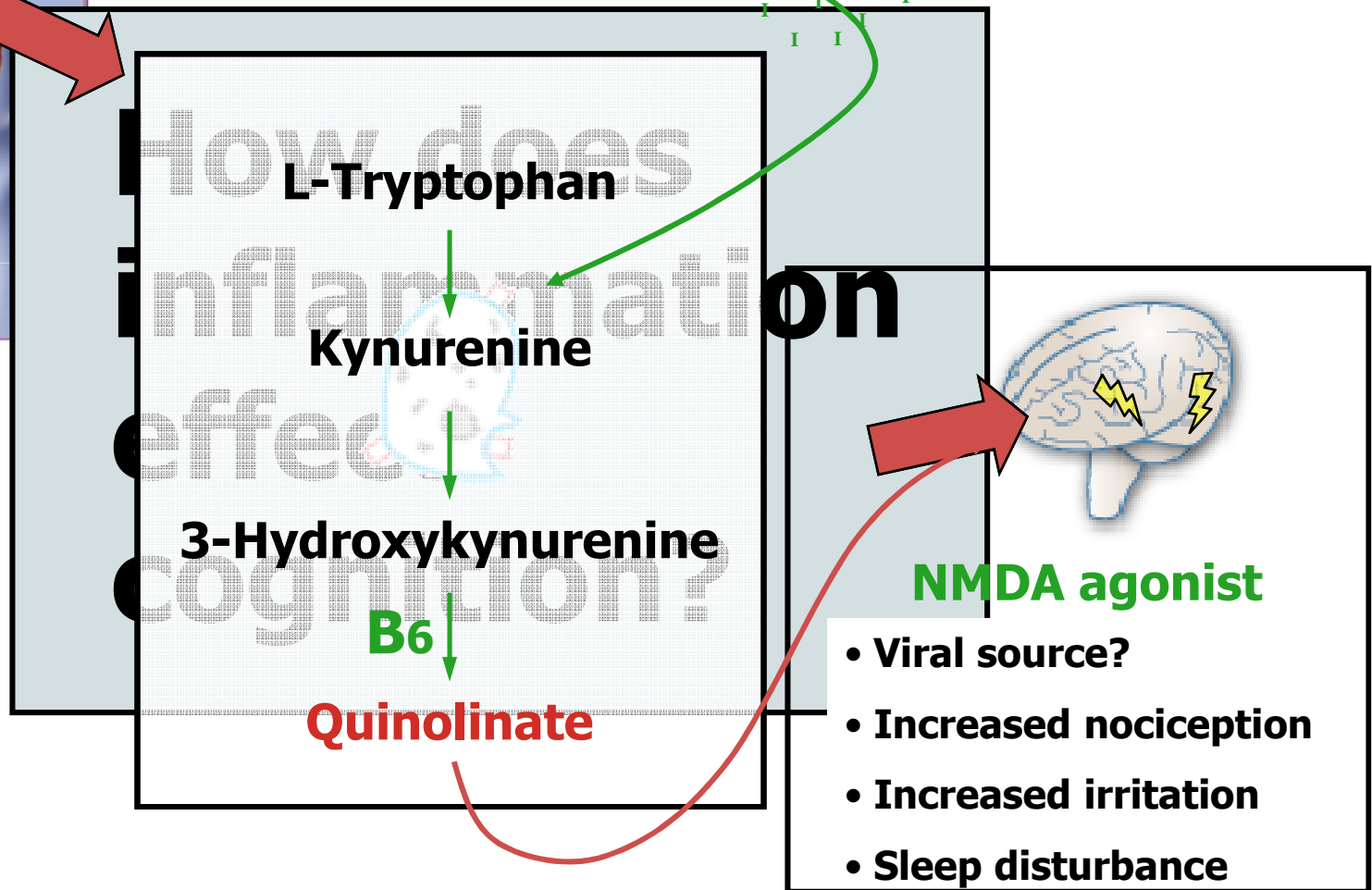
Over-
stimulation of
Quinolinic Acid
from
inflammatory
response to
viral challenge

Graphical representation (not actual event capture)

Tissue-Specific Kynurenine Pathway Effects



Interferon- γ



Neuronal Susceptibility

Deth RC. Molecular origins of human attention : the dopamine-folate connection. Boston, Mass.: Kluwer Academic; 2003.

- The DP4 Receptor
 - Coordinates activity for attention focus and learning
 - Dependent upon
 - ATP/Adenosine ratio
 - Mitochondrial efficiency – carnitine, CoQ10
 - Methyl transfer from folate
 - B-complex vitamin status and oxidative stress
 - Surrounding phospholipid methylation (fluidity)
 - Polyunsaturated fatty acid status

Nutrients

- The effect of high doses of vitamin B6 on autistic children: a double- blind crossover study
 - Rimland B, Callaway E, Dreyfus P. *Am J Psychiatry*. 1978;135(4):472-475.
- Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. II. Pervasive developmental disorder-autism
 - Mousain-Bosc M, Roche M, Polge A, Pradal-Prat D, Rapin J, Bali JP. *Magnes Res*. Mar 2006;19(1):53-62.

Nutrients

- “An increased vulnerability to oxidative stress and a decreased capacity for methylation may contribute to the development and clinical manifestation of autism.”
 - James SJ, Cutler P, Melnyk S, et al. *Am J Clin Nutr.* Dec 2004;80(6):1611-1617.
- “...a 6-year-old girl with developmental delay ... Treatment with folinic acid corrected CSF abnormalities and improved motor skills.”
 - Moretti P, Sahoo T, Hyland K, et al. *Neurology.* Mar 22 2005;64(6):1088-1090.

Environment

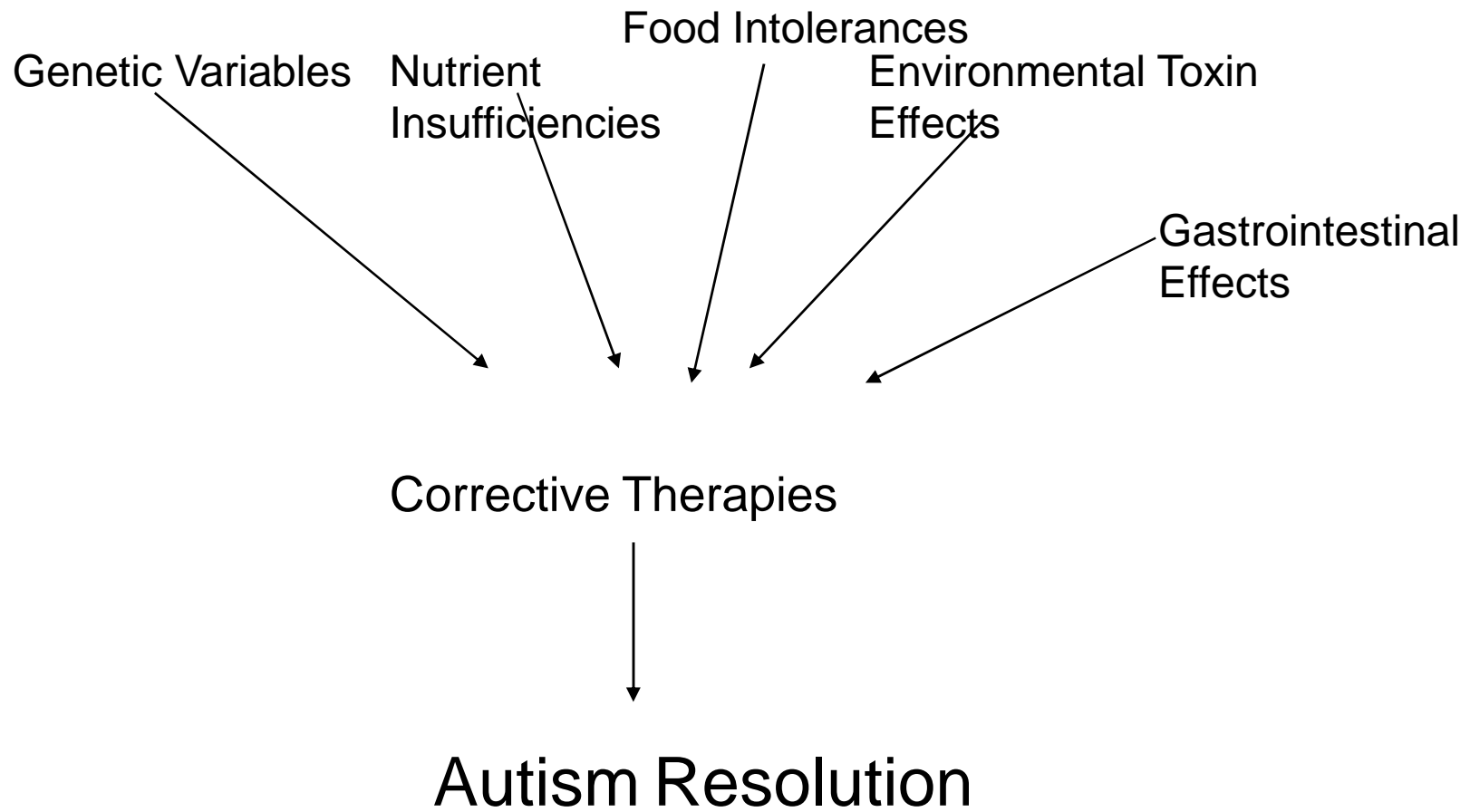
- “On average, for each 1,000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism.”
 - Palmer RF, Blanchard S, Stein Z, Mandell D, Miller C. *Health Place*. Jun 2006;12(2):203-209.
- “evidence showing a direct relationship between increasing doses of mercury from thimerosal-containing vaccines and neurodevelopmental disorders”
 - Geier DA, Geier MR. *Med Sci Monit*. Mar 2004;10(3):PI33-39.

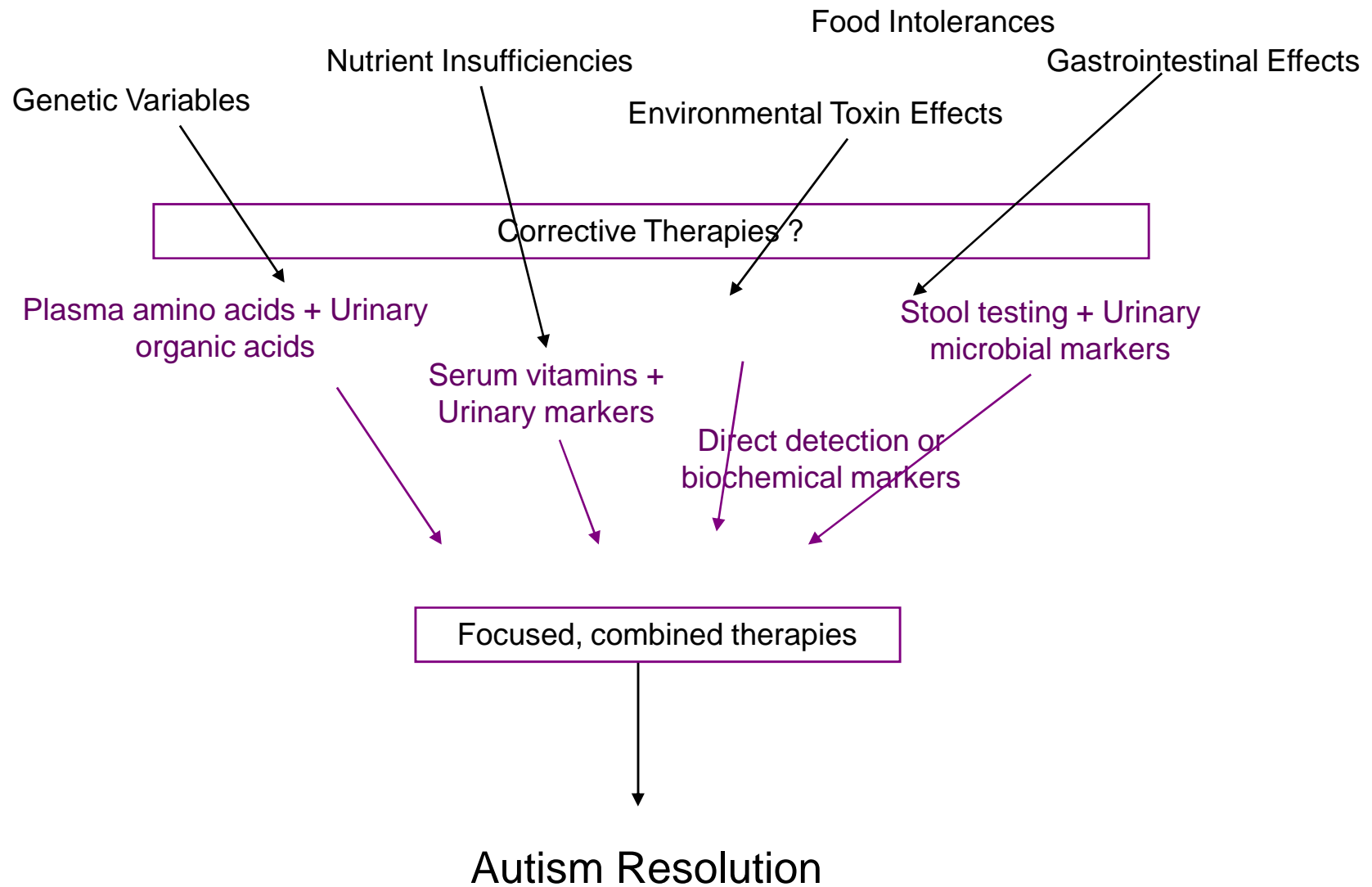
Environment

- **Institute of Medicine** of the National Academies
 - **Workshop on Autism and the Environment: Challenges and Opportunities for Research**
 - focusing on the potential relationship between autism and an array of environmental exposures
 - April 18, 2007

Gastrointestinal Effects

- “a focal CD8-dominated gastritis in autistic children”
 - Torrente F, Anthony A, Heuschkel RB, Thomson MA, Ashwood P, Murch SH. *Am J Gastroenterol*. Apr 2004;99(4):598-605.
- “... duodenal biopsies in 25 children with regressive autism ... a novel form of enteropathy”
 - Torrente F, Ashwood P, Day R, et al. *Mol Psychiatry*. 2002;7(4):375-382, 334.

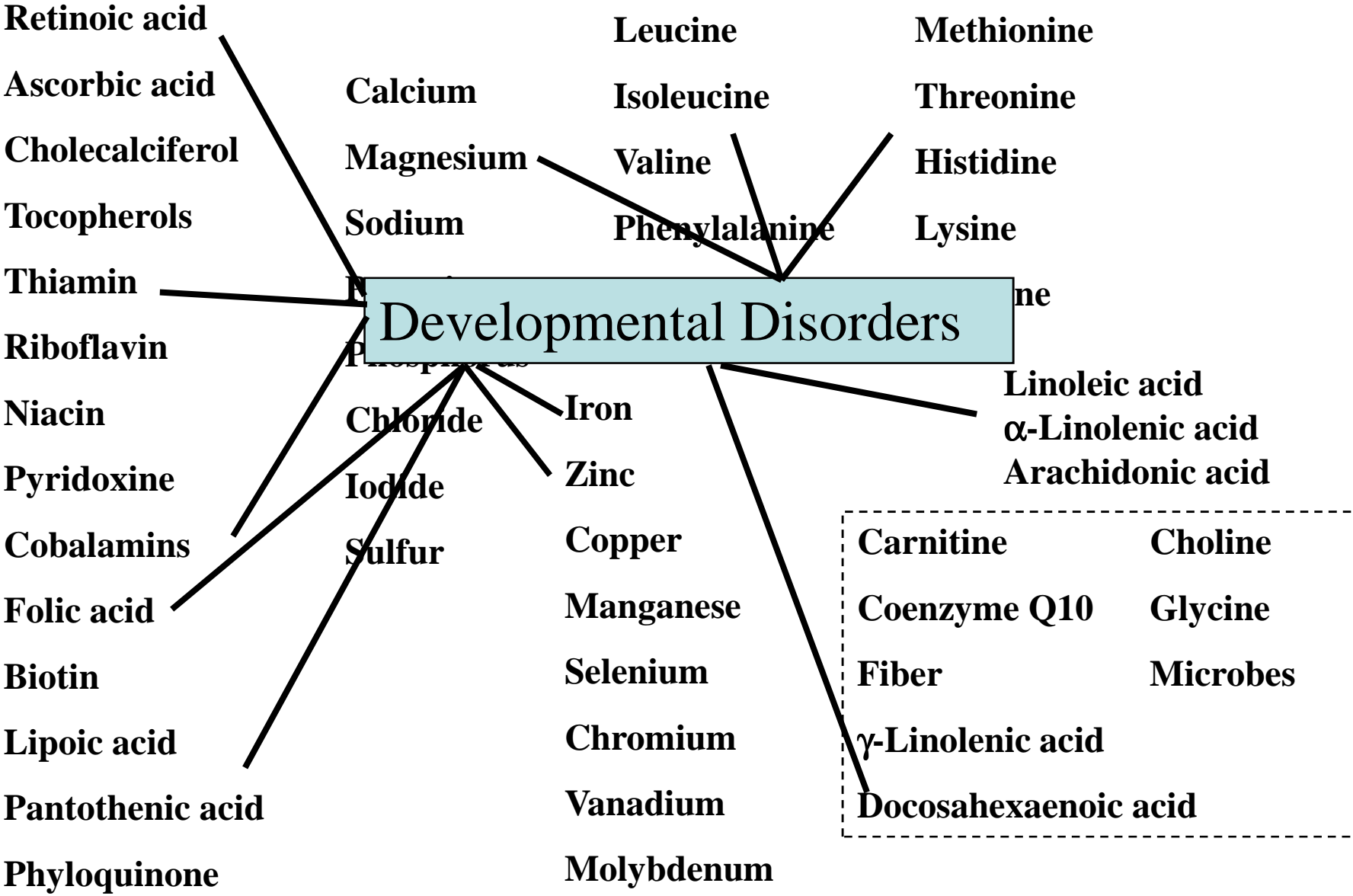




Laboratory Testing

Modifiable Genetic Factors	Urinary organic acids Plasma amino acids
Nutrient Insufficiencies	Vitamins - serum (5) Elements - blood (7) Amino Acids – plasma (10+) Fatty Acids – erythrocyte or plasma (6+) Urinary markers
Environmental Toxin Effects	Direct detection – blood or biopsy Biochemical markers - Urine
Food Intolerances	Standard allergy testing Serum immunoglobulins (IgG4)
Gastrointestinal Effects	Stool testing by for microbial gene markers Urinary microbial markers

Essential Nutrients



Answers

- Why autism spectrum disorder epidemic
 - Convergence of multi-generational diet changes and toxicant exposures
- How to treat?
 - Use testing to identify as many nutritional and toxicant factors as possible and focus aggressive interventions
- How to prevent?
 - Pre-conception testing of nutritional status
 - Screening of children prior to immunization