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**Integrating Medical Care
And The Behavioral
Treatment of Autism**




Allen T. Lewis, MD
1090 Beecher Crossing N, Suite C
Gahanna, Ohio 43230
614-245-4750

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**The Road to
Integrative Pediatrics**

Medical Training

- Medical School
U. of Washington School of Medicine,
Seattle, WA, 1986 – 1990
- Pediatric Residency
Primary Children's Medical Center,
Salt Lake City, UT, 1990 – 1993

Practice Experience

- General Pediatrics
Salt Lake City, UT, 1993 – 1999.
Billings, MT, 1999 – 2003
- Medical Director, Pfeiffer Treatment Center
Warrenville, IL, 2003 – 2010
- Integrative Pediatric Medicine
Gahanna, OH, 2010 - present

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Integrative Pediatric Medicine
is healing-oriented medicine:

- Patient & Family-centered care focusing on healing the whole child.
- Makes use of all appropriate therapeutic approaches and evidence-based global medical modalities to achieve optimal health and well-being – an optimal balance of mind, body and spirit.
- Recognizes that children strive for mastery and thereby are integral participants in their own care. Development of appropriate self-care skills are important throughout their lifetime.
- Utilizes natural, less invasive interventions before more costly, invasive and potentially more risky one whenever possible.
- Encourages healing partnerships between the providers, patient, and family as well as other key decision makers; thereby, supporting the individualization of care.
- Neither rejects conventional medicine or embraces complementary alternative medicine therapies uncritically, recognizing and differentiates many valid but different "ways of knowing."

Culbert T and Oiness K. *Integrative Pediatrics*, 2010. Oxford University Press, New York, p.4.




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Coherent Wholeness

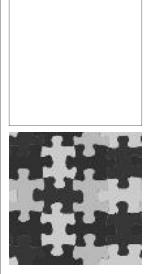
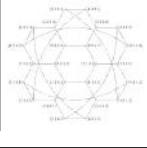
A Principal of Systems-Biology Describing The Obligatory Interconnectedness of Biology and Behavior.

"A systems-medicine model rests on the conceptualization of health and illness as part of a continuum in which all components of the human biological system interact dynamically with the environment."

"This model of practice emphasizes that chronic disease is almost always preceded by a period of declining function in one or more of the bodies organizing systems. Returning patients to health requires reversing (or substantially improving) the specific dysfunctions that have contributed to the disease state. Those dysfunctions are, for each of us, the result of lifelong interactions with our environment, our lifestyle, our belief systems, and our genetic predispositions."

More far-reaching than homeostasis, balance within a system, coherence describes an even greater order of connectedness across multiple organ systems, neuropsychology and cognition/emotion, i.e. everything is connected to everything.

Jones, DS. Needed: A Coherent Architecture For 21st-Century Clinical Practice And Medical Education. *Alt Therapies*. 2010; 16(4), pp 78-79.

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Why talk about autism?

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Autism Prevalence

| Year | Prevalence |
|------|---|
| 2009 | 1 in 91 ⁴ |
| 2004 | 1 in 166 ¹ |
| 2001 | 1 in 250 ² or 1 in 149 for ASD ² |
| 1998 | 1 in 1000 ³ |
| 1966 | 1 in 2500 ³ |

1 out of 6 (~17%) of children will be diagnosed with a developmental disorder and/or behavioral problem.¹

1. Autism A.I.A.R.M. For more information: www.medicalhomeinfo.org
2. Bertrand, J. et al. Prevalence of Autism in a United States population: The Birch Run Township, New Jersey, Investigation. *Pediatrics*. 2000; 105(5):1-16.
3. Technical Report: The Pediatrician's Role in the Diagnosis and Management of Autistic Spectrum Disorder in Children. *Pediatrics*. 2001; 107(5):1-18.
4. Kogan, M. et al. Prevalence of Parent-Reported Diagnosis of Autism Spectrum Disorder Among Children in the US. 2007. *Pediatrics*. 2009;124(4).

Lecture Objectives

- 1) Introduce a workable paradigm for better understanding and thereby treating autism.
- 2) Introduce an integrative pediatric medicine model for treating autism.
- 3) Review the biochemistry and the importance of oxidative stress in autism.
- 4) Introduce medical concepts to help identify biologic processes that may negatively impact a child's readiness for and traction of educational and behavioral therapies.



Questions:

- 1) What is autism?
- 2) How did it happen?
- 3) What can be done?



Understanding a Disease Process

What does it look like?

- Diagnostic criteria
- Level of functioning
- Clinical manifestation

What is broken?

- Genetic and Epigenetic influences
- Physiology and Biochemistry
- Review of systems

Identifying Affected Systems

Systemic, Regional, or Local:

For example, in the brain is it:

- Global brain
- Individual hemisphere
- One or more foci

Organ Systems:

- Brain
- Bowel
- Immune system

General Metabolic Pathways:

- Oxidative Stress
- Inflammation
- Immune dysfunction
- Autoimmunity

Individual Biochemical Pathways:

- Trace metal chemistry
- Methylation
- Pyrrole chemistry
- Vitamin D chemistry

Autism: Diagnostic Criteria

Autism is defined by observational impairments in all of the following with onset prior to age 3 years*:

- 1) Social interaction,
- 2) Language, and
- 3) Symbolic or imaginative play.

* And cannot be described by Rett's Disorder or Childhood Disintegrative Disorder.

Autism: Clinical Manifestations

Social interaction:

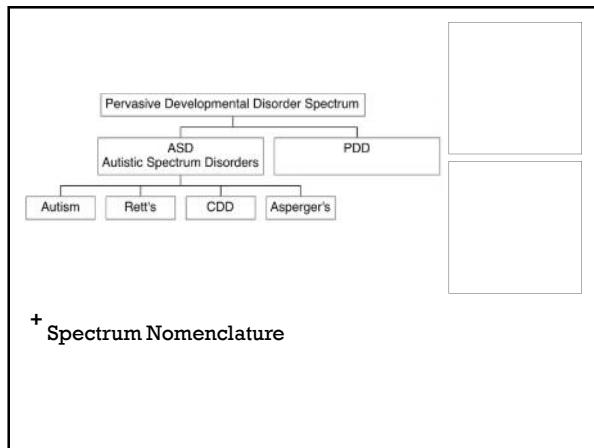
- Poor eye contact
- Inability to regulate social interaction
- Inability to develop age appropriate relationships

Language:

- Delay or lack of spoken language
- Abnormal or absence of imitative play

Symbolic or imaginative play:

- Rituals
- Repetitive mannerisms (aka "stims")
- Restricted areas of interest



+ Spectrum Nomenclature

+ Autism Subtypes: History of Onset

Plateau Autism:

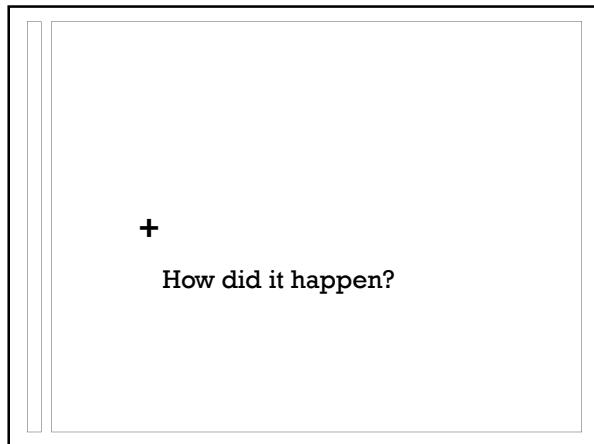
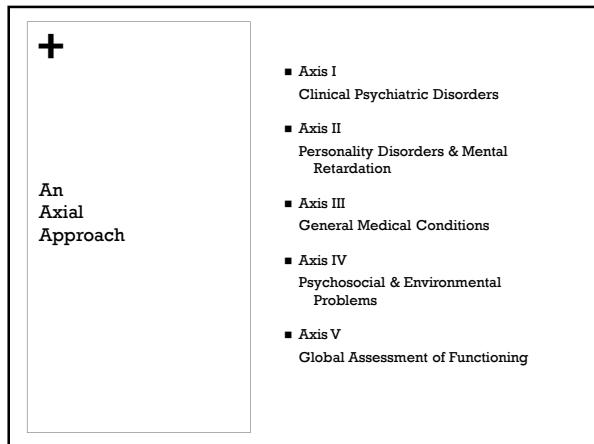
- Predominant type seen today
- Development seems normal from birth; however, is characterized by a gradual or more abrupt plateau in developing new milestones.
- Diagnosis may be delayed waiting to see if child will catch up with peers.

Regressive Autism:

- Initial development is normal and then is characterized by regression and loss of milestones, often speech.

Classic Autism:

- First described by Kanner
- Abnormal from birth



+ Theories of Causality

■ Genetics

- Cannot by itself describe increase in prevalence
- Polygenic is most likely
- Twin Studies
 - Monozygotic twins have 60% concordance
 - Dizygotic twins have 6% concordance
- Siblings have a 2-8% recurrence risk

■ Better Diagnosis

- Cannot account for increased prevalence
- Prevalence in older ages lacking
- Doesn't account for the predominant types on the increase – plateau and regression

■ Environmental Exposure

- Varied presentation unlikely due to single agent exposure

+ Genetics

- Chromosome 2
Hox genes: control growth & development very early in life
 - Chromosome 7
AUTS1: related to speech and language disorders
MET: signals neocortical & cerebellar growth and maturation, immune function, and gastrointestinal repair
 - Chromosome 17
Genes involved in synthesis of GABA & the serotonin transporter
 - Cytogenetic
Duplications of the imprinted domain on chromosome 16q11-13
- Russo AJ. Autism etiology: Genes and the Environment. *Autism Insights* 2009;1, 1-2.

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Oxidative Stress

+ Oxidative Stress

- | | |
|---|---|
| Definition: | Consequences: |
| <ul style="list-style-type: none"> ■ An excess of free-radicals that can damage proteins and essential fats, as to disrupt normal cellular processes. ■ Oxygen free-radicals are one of many free-radicals that lead to oxidative damage. Nitrogen species and ionized metals are also important free-radicals. | <ul style="list-style-type: none"> ■ Inflammation ■ Poor immune function ■ Neurodegeneration ■ Impaired methylation and other cellular processes ■ Increased sensitivity to toxic influences ■ Depletion of glutathione and metallothionein |

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Three Critical Strikes

It is a triad of:

1. genetic susceptibility in light of
2. critically-timed environmental insults of
3. sufficient severity and quantity to trigger:
the disease processes that manifest as a neurodevelopmental disorder (i.e. ASD, ADHD, etc).

Hornig M and Lipkin W. *Ment Retard Dev Disabil Res Rev* 2001;7(3):200-10.



+ Oxidative Injury

Genetic susceptibility sets the stage for critically-timed environmental insult(s) that likely determine the extent of the injury and subsequently the severity of disease.

Mild Injury



PDD or speech delay

Severe Injury



ASD or autism

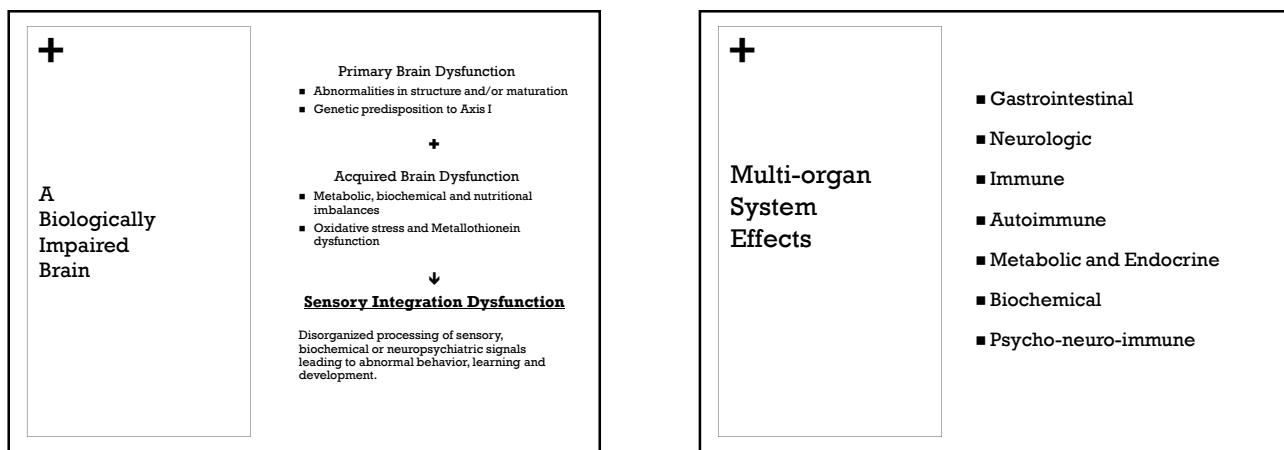
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Oxidative Damage And Brain Development

1. Similar genotype increases susceptibility of individual to oxidative stress/damage
2. Timing of critical insults determine natural history of presentation

Alzheimer's Disease => cumulative oxidative stress/damage over a lifetime resulting in end-stage neurodegeneration.

Autism => early, critically-timed oxidative stress/damage in a developing brain resulting in abnormal development and maturation.



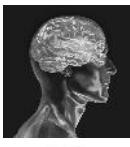
An Integrative Pediatrics Description of ASD

ASD is a medical illness with:

1. a biological impaired brain
2. multi-organ system involvement and thereby multiple medical problems
3. genetic and acquired factors

Resulting in abnormal behavior, learning and development that is:

treatable.





Evidence of Oxidative Stress

+ Evidence of Oxidative Stress

Vascular Damage in the Kidney

| | |
|-----------|---------------|
| Research: | Implications: |
|-----------|---------------|

Treatment-naïve patients with autism vs. age-matched controls:

- Evidence of increased oxidative markers in the urine.
- Evidence of oxidative damage to vascular tissues.

Yao Y et al. Altered vascular phenotype in autism: correlation with oxidative stress. *Arch Neurol.* 2006 Aug;63(8):1181-4.

Increased oxidative damage of fats, vascular tissues, and other molecules may be present in many tissues and organs of the body - brain, bowel, immune tissue.

Antioxidant therapy may be helpful for patients with ASD.

Oxidative Stress in WBC/Leukocyte

| | |
|-----------|---------------|
| Research: | Implications: |
|-----------|---------------|

Study of treatment-naïve patients with autism vs. age-matched controls:

- Increased oxidative stress in the white blood cell (WBC).
- Increased inflammation
- Decreased immune function
- Significant disturbance in methylation.

Soh J et al. Altered Sulfur Amino-acid Metabolism in Immune Cells of Children Diagnosed With Autism. *Am J Biochem Biotechnol.* 2008 4(2):105-113.

Similar disturbances in cellular function extend beyond the kidney to other tissues.

Oxidative stress plays an important role in the disruption of normal cellular processes.

Biochemical abnormalities exist in autism.

+ Oxidative Injury in the Brain

Research:

Study of autism brain samples for evidence of oxidative injury in comparison to control brain samples.

- Direct evidence of oxidative damage was found in all samples of autism brain, and in none of the controls.

Evans T et al. The Autistic Phenotype Exhibits a Remarkably Localized Modification of Brain Proteins by Products of Free Radical-Induced Lipid Oxidation. *Am J Biochem Biotechnol* 2008 4(2):81-72.

Implications:

- Oxidative injury of proteins in the brain would likely be associated with neurological abnormalities.
- Oxidative injury of brain tissue likely plays a role in autism.
- A better understanding of oxidative injury in the brain and other tissue is needed and would likely lead to improvements in the treatment of autism.

+ Neuroinflammation

Study of autism and control brain tissue for evidence of immune-mediated differences.

- Evidence of active neuroinflammation of the cerebral cortex, white matter and cerebellum of autism brain tissue.
- Evidence of a pro-inflammatory response in the cerebrospinal fluid of patients with autism.

Vargas D et al. Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism. *Ann Neurol*. 2005; 57(1):87-91.

+ What can be done?

+ An Integrative Look at Autism

Affected Systems

- Physical
- Behavioral
- Developmental
- Neuropsychiatric

Pieces of the Autism Puzzle

- Physical
- Gastrointestinal
- Immunologic
- Neurologic
- Biochemical
- Consequences of Physical Illness affect:
 - Behavior
 - Development
 - Neuropsychiatric issues

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Biochemical Individuality and Behavior

The basis for Targeted Nutrient Therapy



+ Nutrients and Neurotransmission

The Brain is a Chemical Factory

Provided with all necessary precursors and co-factors the brain can manufacture all it needs. The source of these building blocks is dietary:

- Zinc is required for GABA synthesis
- Vitamin B6 is required for Serotonin (5-HT) synthesis
- Copper (Cu^{++}) is a cofactor in the conversion of Dopamine (DA) to Norepinephrine (NE).
- The methyl:folate ratio impacts the levels of Dopamine, Norepinephrine and Serotonin.

+ Biochemical Individuality Matters

Individuality

Due to genetic and epigenetic influences individuals may be:

- Deficient in several nutrients, as well as
- Overloaded in others.

Multi-vitamins are rarely effective, as they may:

- Contribute to nutrient excess in pre-existing overload states (i.e. copper, folate) and/or
- Induce another nutrient imbalance.

Targeted Nutrient Therapy

Treatment focuses on correcting specific imbalances that manifest with specific and consistent clinical symptoms.

- Genetic nutrient deficiencies may require many times the RDA to achieve normalization/optimization.
- Genetic overloads may require nutrient/biochemical therapy to eliminate the nutrient excess.

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Violent Behavior Outcome Study

Walsh WJ et al. Reduced violent behavior following biochemical therapy. *Physiol Behav*. 2004 Oct 15;82(3):835-8.

Study Details:

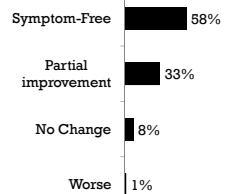
- 207 behavior-disordered subjects
- Diagnosis of biochemical imbalances
- Targeted nutrient therapy to correct imbalances
- Measurement of frequency of physical assaults and property destruction before and after treatment

Study Compliance:

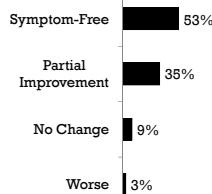
- 12% failed to initiate treatment
- 11% were non-compliant with treatment
- 77% achieved compliance throughout the study period

+ Response to Targeted Nutrient Therapy

Assaultive Behavior



Destructive Behavior



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Differential Diagnosis of Biochemistry in Autism

- Oxidative Stress
- Inflammation
- Mitochondrial Dysfunction
- Disordered Trace Mineral Chemistry
 - Zinc Deficiency
 - Copper Excess
- Metallothionein Dysfunction
- Pyrrole Disorder
- Vitamin D Deficiency
- Disordered Sulfation
- Disordered Methylation
- Iodine Deficiency

+ Zinc Deficiency

Clinical Features:

- Explosive temper
- Mental lethargy & poor memory
- Poor & delayed growth
- Frequent infections
- Poor wound healing
- Acne
- Hypoguesia
- White spots on fingernails

Metabolic Consequences:

- Reduced defense against oxidative stress
- Decreased GABA formation
- Altered copper homeostasis
- Impaired cell-mediated immunity
- Poor energetics

+ Copper Excess

Clinical Features:

- Hyperactivity
- Temper tantrums
- Learning problems
- Agitation
- Tinnitus
- Depression (dysthymic or refractory)
- Post-partum Depression

Metabolic Consequences:

- Increased oxidative stress
- Increased inflammatory responses and stressors
- Increased Norepinephrine effects due to increased conversion from Dopamine
- Increased strain on zinc requirements

+ Pyrrole Disorder

Clinical Features:

- Fear and anxiety
- Mood swings
- Stress intolerance (emotional, biochemical, & physical)
- Misperceptions
- Sensory issues (light, sound, & tactile)
- Increased risk of PTSD-related triggers

Metabolic Consequences:

- Increased oxidative stress
- Functional Vitamin B6 deficiency
- Impaired serotonin synthesis
- Zinc deficiency
- Low blood arachidonic acid levels
- Physiologic stress (i.e. adrenal fatigue)

+ Low Blood Histamine

Clinical Features:

- Generalized anxiety
- Depression
- Panic
- Agitation & paranoia
- Racing thoughts
- Underachievement
- Good response to benzodiazepine medication

Metabolic Consequences:

- Relative folate deficiency
- Tendency to high dopamine, serotonin and norepinephrine
- AKA "over-methylation;" however, metabolic consequences are not most accurately so simply described.
- Higher risk of negative effects from SSRIs and medications with anti-histaminic effects.

+ Elevated Blood Histamine

Clinical Features:

- ADHD
- OCD, perfectionism
- Blank-mind
- Rumination
- Addictive behavior
- Migraine headaches
- Seasonal allergies

Metabolic Consequences:

- Methyl deficiency
- Clinically associated with low levels of dopamine and serotonin
- AKA "undermethylation"
- Typically good response to SSRI medications
- Higher risk of negative effects with moderate or higher doses of folic acid

+ Metallothionein Dysfunction

At the biochemical level:

Disturbances in zinc and copper are directly related to problems with MT and can be broken down into two main categories:

- Quantitative depletion
As zinc is one of the primary inducers of MT, zinc deficiency leads to lower levels of MT, decreased zinc transport, and delivery of zinc to tissues.
- Functional impairment
Excess copper displaces zinc from MT and thereby reduces zinc availability to the tissues.

MT dysfunction and Autism:

- Brain structure and function
- Impaired immune modulation and T-cell function
- Impaired digestive enzyme function
- Impaired functioning of the Blood-Brain Barrier and the barrier function of the bowel wall
- Impaired or crippled protection from oxidative stress

+ Metallothionein Family of Proteins

Metallothionein (MT) are short, linear, cysteine-rich proteins present in all tissues of the body that are required for trace metal chemistry, as well as other functions:

Metallothionein III:

- are present mostly in the brain
- carry a predominance of copper, rather than zinc
- act as a neuronal-growth inhibitory factor in the development, organization, and apoptosis of brain cells.

Metallothionein I & II:

- are present in all tissues and regulate zinc and copper; thereby
- cell transcription, immune function, and more.
- Highest concentrations are in the intestinal and blood-brain barriers prevent penetration of toxic metals and other ions.

Metallothionein IV:

- Are present primarily in the gastrointestinal tract
- Regulate stomach acid pH
- Are involved in taste and texture discrimination by the tongue.

+ Oxidative Stress in Autism

Pro-oxidant Influences:

- Elevated Copper
- Emotional Stress
- Environmental toxins
 - Inhaled
 - Ingested
 - Transdermal
- Physical injury

Overwhelmed Defenses:

- Glutathione Deficiency
- Zinc Deficiency
- Impaired MT function
- Selenium deficiency
- Sulfation problems
- Malnutrition
- Impaired methylation

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Autism Research at the Pfeiffer Treatment Center

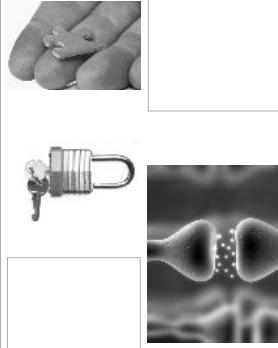
Since 1989 the Pfeiffer Treatment Center has evaluated approximately 22,000 patients; 6,000 or more of which had ASD.

Analysis of the data on biochemical findings in the ASD patients has shown:

- 1999 Undermethylation
- 2000 Elevated copper: zinc
- 2001 Elevated unbound copper
- 2001 & 2003 Metallothionein deficiency
- 2003 Confirmation of these biochemical findings in treatment-naïve patients
- 2006 & 2008 Increased oxidative stress
- 2008 Vitamin D Deficiency

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An Integrative Pediatric Approach to Autism



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Integrative Management

Comprehensive medical evaluation and re-evaluation of response to treatment focusing on the differential diagnosis of the medical and biochemical issues in context of:

- the unique strengths and needs of the child and family
- the social, emotional, behavioral, and developmental challenges faced by the child and parents
- the unique and often rough path that the child and family are walking
- and recognizing the need for a multi-disciplinary team of open and innovative professionals looking to unlock a child's best

The doctor's role:

- Complete the differential diagnosis of affected systems
- Guide and monitor integrative medical treatment
- Collaborate with other professionals
- Advocate for the child to grow, develop, and live to his/her fullest potential

Key to success:

"When serving children with autism, one must first **reach**, and then **teach** the child."

Lynette Scutese-Wojila, 2009
The S.U.C.C.E.S.S. Approach

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Goals of Treatment

- Identification of broken systems
 - Systemic, regional, and/or local
 - Organ systems
 - Metabolic and/or biochemical
 - Mind, body, and spirit
- Restoration of normal function
- Protection of re-injury
- Promotion of normal physical, emotional, and mental health
- Restoration of more normal learning and development

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Overview of Treatment

- Dietary Intervention
 - Ensure optimal nutrition
- Normalization of bowel function
 - Ensure regular, effective stooling
 - Treat dysbiosis, if present
- Correct biochemical imbalances and oxidative stress
- Maximize learning by helping anxiety, sensory problems, focus, attention, inattentive and attention avoidance factors:
 - Methyl-B12
 - Oxytocin
 - Indicated pharmaceuticals
- Expect new insights along the way

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Tantrums

| | |
|--|--|
| Associated Findings: | Underlying Etiologies: |
| <ul style="list-style-type: none"> ■ Fear and anxiety ■ Stress intolerance ■ Sensory overload ■ Pain ■ Poor ability to communicate desires ■ Change in routine | <ul style="list-style-type: none"> ■ Biochemistry <ul style="list-style-type: none"> ■ Pyrrole Disorder ■ High Copper ■ Gastrointestinal <ul style="list-style-type: none"> ■ Constipation ■ GERD ■ Food allergy ■ Immunologic <ul style="list-style-type: none"> ■ Occult infection ■ PANDAS ■ Neurologic <ul style="list-style-type: none"> ■ Seizures |

+ Poor Sleep

Associated Findings:

- Pain
- Sensory overload
- Hyperacusis
- Agitation
- Poor regulation of circadian rhythm

Underlying Etiologies:

- Gastrointestinal
 - Fecal retention
 - GERD
 - Food allergy
- Biochemistry
 - Pyrrole Disorder
 - High Copper
- Pulmonary
 - Sleep apnea
 - Sleep phase disorder
 - Inhalant allergies
- Endocrine
 - Relative hypoglycemia
 - Adrenal fatigue

+ Self-stimulatory Behaviors

Associated Findings:

- Anxiety
- Fear
- Excitement
- Dysinhibition
- Core deficits
- Obsession/compulsions

Underlying Etiologies:

- Neurologic
 - Seizures
- GI disturbances
 - Retained stool
 - Food allergy
 - Bowel overgrowth
- Immunologic
 - PANDAS
 - Occult infection
- Biochemistry
 - Low zinc
 - High copper
 - Pyrrole disorder



There is Hope!

Educate yourself about autism

Assemble your team

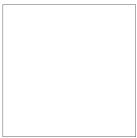
Develop a plan that fits your child's and your family's needs and abilities.

Take one step at a time
Don't do too much too fast, it is exhausting for the child, the siblings and the parents

Trust your instinct

Focus on the whole family

- Health begins at the dinner table
- Respite for the parents and siblings
- Attention to siblings



+ Minimize Pro-oxidant Behaviors

■ Minimize environmental toxic exposures – EWG.org

- Cleaning products
- Building materials (i.e. low VOC paint)
- Plastics and other materials

■ Reduce emotional, physical and emotional stresses.

- Electronics are very potent neuroactivators
- Find quiet time
- Walk in nature

■ Eat locally grown organic food; avoid nitrates, preservatives, and artificial additives; and know the heavy metal content of the fish you eat.

+ Health Begins at the Dinner Table

Nourishing Food

- Organic, whole foods
- Consciously prepared

Family Time and Fellowship

- Relationship building
- Consciously enjoyed (i.e. slow down)

Life Skills Building

- Emotionally grounding
- Family building and role model development

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Contact Information

Allen T. Lewis, MD, FAAP
Integrative Pediatrics of Ohio, LLC
1090 Beecher Crossing N, Suite C
Gahanna, OH 43230

614-245-4750
614-855-8820 fax

integrativpediatricsohio@gmail.com
www.integrativpediatricsohio.com



integrative
medicine

