INTEGRATIVE MEDICINE EVALUATION AND TREATMENT OF COMMON PEDIATRIC DISORDERS

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• We do not intend to discuss an unapproved/investigative use of a commercial product/device in our presentation.
WHAT IS INTEGRATIVE MEDICINE?

- **Personalized** medical therapy and treatment of chronic disease that embraces the **best of both conventional and complementary** therapies.

- Integrative medicine reaffirms the importance of the therapeutic relationship, a focus on the **whole person**, lifestyle, biochemical (metabolic) individuality and environmental influences.

- Specific emphasis on “**Wellness**” and the body’s innate ability to heal itself utilizing “**Food as Medicine**” and “**Harnessing Resilience**"
What do these have in common?

- Eczema
- Migraines
- ADHD
- PCOS

- Frequently seen in pediatrics
- Increasing incidence
- Often not improved with conventional interventions or medications despite our best efforts
WHAT DO THESE HAVE IN COMMON?

- Eczema
- Migraines
- ADHD
- PCOS

- Frequently seen in pediatrics
- Increasing incidence
- Often not improved with conventional interventions or medications despite our best efforts

They share similar underlying pathophysiology that contributes to their manifestations
Usual sequence of events

- Conventional medical treatments are prescribed to manage the symptoms

- When symptom management fails, we do more investigations and try different medications

- When that doesn’t work, we refer to sub-specialists

- When that doesn’t work we send them to psychiatrist/psychologist
TODAY’S OBJECTIVES

- Understand the shared underlying mechanisms that contribute to common pediatric disorders
- Appreciate the role that healthy nutrition and nutritional supplements play in the treatment of these disorders
- Learn of other evidence-based integrative medicine therapies used in these disorders
ROOT CAUSES OF DISEASE
INTERACTIONS OF NEURO-ENDO-IMMUNE SYSTEMS

Neurotransmitters/Nervous system
(substance P, glutamate, aspartate, serotonin, etc)

Immune system
(neutrophils, autoantibodies, TNF-α, GALT, etc)

Endocrine system
(ACTH/cortisol, estrogen, CRH, Vitamin D, etc)
LEAKY GUT SYNDROME/INTESTINAL PERMEABILITY

Expected gut flora
(Lactobaillus, Bacteroides, etc.)
Bacteria
Beneficial bacteria
Yeast

GUT MICROBIOME

Crohn’s disease, Ulcerative colitis
Infection, Cancer

Environment

Inflammation

Neurodegenerative diseases

Autoimmunity
Allergy

Metabolism

Genes

Obesity, Insulin resistance
Typ 2 diabetes, Atherosclerosis

Microbes
Diet
Toxic Stress

Childhood Toxic Stress
Here Today, Here Tomorrow

Toxic Stress:
“The excessive or prolonged activation of the physiologic stress response systems in the absence of the buffering protection afforded by stable, responsive relationships.”

- American Academy of Pediatrics

Overactivation of the stress management system can change the architecture of the brain, disrupt metabolic regulatory systems, and alter the genome.

These changes trigger a cycle of chronic stress, compromise cognitive and behavioral functioning, and lead to chronic disease.

Adolescence & Adulthood
Problems with:
- Learning
- Memory
- Impulse control
- Regulation of emotion
- Depression
- Asthma
- Cancer
- Heart disease
- Autoimmune disease

Childhood
Economic hardship
Incarceration of a parent
Abuse
Neglect
Divorce/separation
Parental mental illness
Parental substance abuse

Source: CFSP PES Study, PES Mothers at 3 months, weighted.
© Child and Family Research Partnership at The University of Texas at Austin, All Rights Reserved.
ADVERSE CHILDHOOD EXPERIENCES (ACE)

- Number is ACEs correlate with increased risk:

  - Alcoholism and alcohol abuse
  - Chronic obstructive pulmonary disease (COPD)
  - Depression
  - Fetal death
  - Health-related quality of life
  - Illicit drug use
  - Ischemic heart disease (IHD)
  - Liver disease
  - Risk for intimate partner violence
  - Multiple sexual partners
  - Sexually transmitted diseases (STDs)
  - Smoking
  - Suicide attempts
  - Unintended pregnancies
  - Early initiation of smoking
  - Early initiation of sexual activity
  - Adolescent pregnancy

http://www.cdc.gov/violenceprevention/acestudy/findings.htm
Atopic Dermatitis (Eczema)

- Genetic risk factors
- Prenatal/Perinatal Factors
  - maternal diet/lifestyle
  - antibiotic use
  - type of delivery
  - breastfeeding
- Diet—abnormal EFA metabolism
- Skin Barrier
  - Decreased cathelicidins and beta-defensins in skin
  - Increased susceptibility to bacteria, virus, fungal infections
- Skin irritants and allergens
- Immune Dysregulation
  - Increased levels of cytokines and chemokines
  - TH-1:Th-2 imbalance
  - IgE autoreactivity
- Microbiome

ATOPIC DERMATITIS: CASE STUDY

- 8 yr old F presents with eczema recalcitrant to standard of care treatment (topical steroid ointment/moisturizing)
  - Born full-term via C-section
  - Formula fed
  - Recurrent otitis media requiring multiple antibiotics
  - Standard American Diet (SAD 😞)

- What is your next approach?
A TOPIC DERMATITIS: DIETARY ASSESSMENT

Food Sensitivity or Food Allergy?

35% atopic dermatitis may be related to food

- Diagnosis for Food Sensitivity:
  - Elimination Diet with food challenge is gold standard
  - Non-IgE food sensitivity (IgG and IgA, rxn hrs-days)

- Diagnosis for Food Allergy:
  - Skinprick Testing, IgE bloodwork (often negative)
  - Gold standard is elimination diet with food challenge

Fig. 4 A schematic diagram illustrating the hypothetical gastrointestinal and immune interface. The digestive processes and absorption of food are dependent on gastric acidity, enzymatic digestion, and tight junctions, which is followed by antigen processing via local mucosal lymphoid (Peyer’s patch) involvement, which then leads to IgE-, non-IgE-, or mixed type-mediated food hypersensitivities. There is a continuous interplay of cellular and humoral molecular factors and signaling pathways. Abbreviations: APC antigen presenting cells, TNF-α tumor necrosis factor alpha, IL-5 interleukin 5.

Figure from: Ho MHK et al. Clinic Rev Allerg Immunol 2014; 46:225-40
**HOW-TO: ELIMINATION DIET**

Removal of most common food allergies or sensitivities:
- **dairy, gluten/wheat**, corn, soy, eggs, citrus, tree nuts, peanuts, and shellfish. “Listen to your gut”.

- **Step 1. Planning Phase**: Thorough patient history and have Pt keep “Food Diary” for several weeks. Choose foods to avoid.
- **Step 2. Avoidance Phase**: Eliminate chosen foods for at least 10 days. 2-4 wks often rec. More restrictions = Less compliance. Anticipate detox and “feeling worse before it gets better”.
- **Step 3. Challenge Phase**: Reintroduce 1 food for 1 day, then stop again for 3-4 days as it may take several days for symptoms to appear (IgG).
- **Step 4. Long Term Diet Plan**: Requires Pt and family motivation. Continue elimination of food for 3-6 months, often food intolerance resolves.
- Have families note any health/physiologic changes in addition to behavioral symptoms during food challenge

Elimination Diet: Risk of Nutrient Insufficiencies

Restricted Diet may result in:
- Weight Loss
- Potential insufficiencies: Protein, Vitamin D, Calcium, folate, Iron

Strategy to avoid complications
- Utilize and Review Diet Diaries (e.g. written or Mobile Apps) to review caloric intake
- Consult Dietitian
- Supplementation with laboratory guidance during elimination diet

ATOPIC DERMATITIS: DIETARY ASSESSMENT

Fatty Acids

- Evaluate for fatty acid imbalance:
  - Dietary Intake
  - Serum Comprehensive Fatty Acid Panel
  - RBC Fatty Acid Profile

- FA Patterns in Atopic Dermatitis
  - Balance Omega-6/Omega-3 Ratio
  - Low Gamma-Linolenic Acid Levels¹,²
    - Found in evening primrose oil/borage oil
  - Low Omega-3 Fatty Acid Intake³,⁴

**Biochemistry of Eicosanoids**

- **Membrane Phospholipids**
  - Phospholipase A2
  - Arachidonic Acid
    - 5-Lipoxygenase (LOX)
    - 12-Lipoxygenase (LOX)
  - Cyclooxygenase 1 (COX)
  - Cyclooxygenase 2 (COX)
  - Prostaglandins Series 2
    - Thromboxanes A₂, B₂

- **Series 4 Leukotrienes**

- **Vitamin E, Quercitin**
- **Licorice, Turmeric**
- **Corticosteroids**
- **EPA & DHA**
- **Ginger, turmeric, Black Willow, Wintergreen**
- **Sulfasalazine**
- **NSAIDS**

- **Therapeutic Strategies**
  - NSAIDS (non-steroidal anti-inflammatory drugs)
  - Sulfasalazine
  - Vit E, Quercitin, EPA
  - Ginger, turmeric, Black Willow, Wintergreen
Atopic Dermatitis: Dietary Assessment

Zinc—Necessary for Skin Healing

- Zinc levels lower in children with AD than controls\(^1, 2, 3, 4\)
  - Evaluate Dietary Sufficiency
  - Serum Zinc Levels

Serum Zinc Levels:

<table>
<thead>
<tr>
<th>Zinc</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>48-129 mcg/dL</td>
</tr>
</tbody>
</table>

ZINC FOOD SOURCES

Dietary adequacy: Is patient meeting 100% of their need?

World's Healthiest Foods rich in zinc

<table>
<thead>
<tr>
<th>Food</th>
<th>Cals</th>
<th>DRI/DV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef</td>
<td>175</td>
<td>37.1%</td>
</tr>
<tr>
<td>Lamb</td>
<td>310</td>
<td>35.1%</td>
</tr>
<tr>
<td>Sesame Seeds</td>
<td>206</td>
<td>25.3%</td>
</tr>
<tr>
<td>Pumpkin Seeds</td>
<td>180</td>
<td>22.9%</td>
</tr>
<tr>
<td>Lentils</td>
<td>230</td>
<td>22.8%</td>
</tr>
<tr>
<td>Garbanzo Beans</td>
<td>269</td>
<td>22.8%</td>
</tr>
<tr>
<td>Cashews</td>
<td>221</td>
<td>21%</td>
</tr>
<tr>
<td>Quinoa</td>
<td>222</td>
<td>18.3%</td>
</tr>
<tr>
<td>Turkey</td>
<td>167</td>
<td>17.7%</td>
</tr>
<tr>
<td>Shrimp</td>
<td>135</td>
<td>16.8%</td>
</tr>
</tbody>
</table>

Zinc Repletion
Children 2-12 yo: 10-50 mg daily
Adults: 25-100 mg daily

Side Effects:
Nausea, vomiting, metallic taste in mouth, copper deficiency

Zinc Food sources from: [www.whfoods.com](http://www.whfoods.com)“Zinc” Natural Medicines Comprehensive Database. Apr 17, 2015
ATOPIC DERMATITIS: DIETARY ASSESSMENT

Vitamin D

- Vitamin D deficiency increases the risk of sensitization to food allergens and the severity of atopic dermatitis

- Children given 4000 IU daily for 21 days
  - Significant ↑ in cathelicidin levels
  - Reduced colonization of skin pathogens.

- Supplementation with 1,000 IU daily increased 25 OH-D levels, reduced AD severity, and reduced serum cytokine levels
  - Normalization of Th-1 and Th-2 interleukin serum patterns

- Ideal 25 OH-D level of 40-60 ng/ml

VITAMIN D REPLETION

US Endocrine Society's Clinical Practice Guideline
Vitamin D-3

- 400-1,000 IU per day may be needed for children less than 1 year old
- 600-1,000 IU per day for children aged 1 year or more
- 1,500-2,000 IU per day for adults aged 19 years or more to maintain 25(OH)D above the optimal level of 30 ng/ml.
  - [Pramyothin P Curr Opin Gastroenterol. 2012.28(2):139-150]

Each 100 IU raises the 25OHD levels by 1 ng/ml
**Atopic Dermatitis: Gut Microbiome**

- **Probiotics**
  - Double-blind RCT of 220 children\(^1\)
    - Clinical improvement of probiotics (lactobacillus sp) after 3 months
  - Meta-Analysis\(^2\)
    - Treatment with a mixture of Lactobacillus/Bifidobacterium showed greater benefit than Bifidobacterium sp. alone
  - Meta-Analysis\(^3\)
    - Probiotics have protective role in AD

**Side Effects:**
- Excessive gas, abdominal bloating, diarrhea
- *Avoid in immunocompromised patients with indwelling catheters.*

**Atopic Dermatitis:**
**Integrative Medicine Treatment**

- Determine food allergy (IgE) or sensitivity
  - Wheat, dairy, corn, soy, eggs, nuts

- Treat intestinal yeast overgrowth/skin colonization

- Probiotics
  - 10-20 billion CFU’s daily (lactobacillus & bifidobacterium)

- Supplement to balance Omega 6 and Omega 3
  - EFA 1-2 grams/day if indicated
    - [Skellchock LE. Integrative Medicine, 2nd ed. Saunders 2007, Philadelphia, PA.]
**ATOPIC DERMATITIS: INTEGRATIVE MEDICINE TREATMENT**

- **Supplement with Zinc and Vitamin C**
  - [Kim JE. Acta Derm Venereol. 2014 Sep;94(5):558-562.]

- **Increase Vitamin D**
  - Follow US Endocrine Society Guidelines
    - [Di Filippo. Int Arch Allergy Immunol. 2015;166(2):91-96.]

- **Bathe in warm water with 1-2 cups baking soda or sea salt**
  - Tea Tree essential oil 5% body wash to eradicate MRSA
    - [Dryden MS. J Hosp Infect. 2004 Apr;56(4):283-6.]

- **Use coconut or olive oil topically**
Atopic Dermatitis: Integrative Medicine Treatment

- Mind-Body Techniques
  - Hypnosis
    - [Adinolfi B. Acta Biomed. 2013 Sep 1;84(2):94-97]
  - Progressive muscle relaxation
  - Kissing
    - [Kimata H. J Psychosom Res. 2006 May;60(5):545-547]

- Chinese Herbal Medicine
  - [Chen HY. Evid Based Complement Alternat Med. 2015;2015:347164]

- Acupressure
MIGRAINE/HEADACHES

- Migraine attacks are result of **inflammation** at level of trigeminovascular connections

- Mitochondrial dysfunction

- Hormonal Imbalance/Menstrual Disorders

- Dysfunctional stress response

- Diet & Nutrition

- Majority are myofascial

- May not have “body awareness” of muscle tension/stress

- History often reveals multiple traumas
  - Physical, emotional, repeated illnesses
  - These affect body mechanics and nerve function

- PE often reveals myofascial restrictions or trigger points

Migraine Case Study

- 12 yo male with chronic migraines on beta-blocker and imitrex as needed, but still having episodes weekly
  - Standard American Diet (SAD 😞)
  - Non-restorative sleep (“addicted” to video games)
  - Bullied at school
  - Limited physical activity
  - Minimal sun exposure

- What is your next approach to help improve quality of life?
Migraine: Dietary Assessment

- Recognizing food triggers (food diary) or possible hypoglycemia
  - [Finocchi C. Neurol Sci. 2012 May;33 Suppl 1:S77-80.]
- Foods high in histamine/tyramine
- Food additives (i.e. MSG, aspartame)
- Preservatives
- IgG food sensitivity testing
  - [Alpay K et al. Cephalalgia. 2010; 30(7): 829-837]
MIGRAINE: DIETARY ASSESSMENT

Magnesium—RBC vs serum

- 98% of magnesium works intracellularly
- Serum level may be “normal”, but still be deficient

- RBC magnesium levels lower in those with migraine compared to controls
  - [Mazzotta G. Cephalalgia. 1999 Nov;19(9):802-809.]
  - [Orr S Cephalalgia. 2014; 34(8): 568-583]
MIGRAINE: MAGNESIUM

Magnesium

- over the course of 16 weeks reduced migraine frequency and severity in children
- given twice daily for 3 months was preventative of further headache episodes in children/adolescents

Magnesium Malate/Glycinate/Taurate/Citrate

- Most commonly used forms of Magnesium for GI absorption
- Dosage:
  - Children 2-12 yo: titrate up to 6 mg/kg/day or 50-600 mg
  - Adolescents and Adults: 350-750 mg
- Side effects
  - May cause diarrhea (magnesium oxide), often beneficial SE. Mag malate and glycinate causes less GI symptoms.
**MIGRAINE: DIETARY ASSESSMENT**

**Vitamin D**

- Serum vitamin D and VDR levels were found to be significantly lower in migraine patients than in controls

- Vitamin D given in addition to routine anti-migraine treatment reduced the number of migraine attacks in children compared to anti-migraine treatment alone.

<table>
<thead>
<tr>
<th>Vitamin D(25-OH)Total</th>
<th>Ref. Range</th>
<th>22 (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-80 NG/ML</td>
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</table>
MIGRAINES: DIETARY ASSESSMENT

CoQ10 deficiency

- Low CoQ10 levels common in migraine (related to mitochondrial dysfunction).
- Plasma CoQ10 (Reduced and Total)

<table>
<thead>
<tr>
<th>CoQ10 Reduced</th>
<th>Value</th>
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<tbody>
<tr>
<td></td>
<td>707.4</td>
</tr>
</tbody>
</table>

Comments:
Reference range: 320 to 1376
Unit: mcg/L
MAYO MEDICAL LABS

<table>
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<tr>
<th>Coenzyme Q10</th>
<th>786</th>
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Comments:
Reference range: 320 to 1563
Unit: mcg/L
MAYO MEDICAL LABS

<table>
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<tr>
<th>Percent Reduced</th>
<th>90 (L)</th>
</tr>
</thead>
</table>

Comments:
Reference range: 93 to 100
Unit: %
MAYO MEDICAL LABS

Interpretation
In this sample, the total coenzyme Q10 (CoQ10) concentration was in the normal range. However, in plasma, CoQ10 exists primarily in the reduced form. An imbalance of the redox status may occur as a result of oxidative stress.

<table>
<thead>
<tr>
<th>Resulting lab:</th>
<th>QUEST DIAGNOSTICS</th>
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<tbody>
<tr>
<td>Reference range:</td>
<td>0.44 - 1.64 mg/L</td>
</tr>
<tr>
<td>Value:</td>
<td>0.39 (Low)</td>
</tr>
<tr>
<td>Comment:</td>
<td>Therapeutic Range Recommended for Cardiovascular Disease &gt;2.50 mg/L</td>
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</table>

**CoQ10 Repletion**

- **CoQ10**
  - safely reduced migraine frequency and associated disability in children who were found on screening to have low clinical co-enzyme Q-10 values.

- **COQ10 Repletion**
  - 1-3 mg/kg/day in children and adolescents
  - Most common dosage forms are between 25-300 mg
  - Ubiquinol (Reduced CoQ10)
MIGRAINE: DIETARY ASSESSMENT

**Vitamin B2: Riboflavin**

- Diagnosis of Deficiency:
  - 24-hr urine riboflavin excretion of less than 10%
  - RBC riboflavin
  - Serum riboflavin
    - [Stipanuk MH & Caudill MA. Biochemical, Phys, & Molec Aspects Human Nutrition. 3rd ed. 2013]

- Common Signs/Symptoms of Deficiency:
  - Beefy red tongue, seborrheic dermatitis, cheilosis, and sore throat
MIGRAINE REPLETION

Vitamin B2: Riboflavin

- Riboflavin may be effective in migraine, with a more favorable response in boys and in individuals with severe migraine.

Treatment:

- 200-400 mg/day for migraine prophylaxis
- 10-50 mg/day for children
- Riboflavin is in a B-complex
  - [Colombo B. Neurological Sciences. 2014; 35(1): 141-144]
MIGRAINE:
INTEGRATIVE MEDICINE TREATMENT

- Migraine Journal, Elimination Diet Trial, Whole Foods & Anti-Inflammatory Diet to reduce inflammation
- Magnesium
- Co-enzyme Q10
- Riboflavin (B-2)/B-complex
- Vitamin D
- Fish Oil (Omega-3s)
MIGRAINE: INTEGRATIVE MEDICINE TREATMENT

- **Butterbur root extract**
  - at least a 50% reduction in migraine attacks in 77% of children aged 6-17.
    - [Pothmann R. Headache 2005 Mar; 45(3):196-203]

- **Mind-Body techniques**
  - Breathing/relaxation training, biofeedback and cognitive-behavioral therapy (CBT), stress management
    - [Trautmann E. Cephalalgia. 2006 Dec;26(12):1411-1426]
  - CD-ROM program (HEADSTRONG) on home computers for 4 weeks had significant improvements in headache activity above and beyond those in the control group.
**MigraIEnE: InTeGrATiVe MEdiCInE TreAtMent**

- **Diet/Sleep/Hydration/Regular meals**
  - Lifestyle factors are often primary in initiating and maintaining headache syndromes in children

- **Music Therapy**
  - music therapy was superior to placebo over 12 weeks as well as 6 months later
Migraine: Integrative Medicine Treatment

- Acupuncture/Acupressure
  - DBRPCT in 43 children with migraine or tension-type headache found a significant improvement in headache-free days for children receiving “true” acupuncture with low level laser.
MIGRAINE: INTEGRATIVE MEDICINE TREATMENT

Manual therapies
- OMT, cranio-sacral, myofascial release, massage
- “Hands on” helps where meds fall short
- Initially start with practitioner, but teach self-therapy
  - [Bronfort G. J Manipulative Physiol Ther. 2001;24:457-466]

Physical therapy/Yoga
- Therapies to improve posture
- Therapies for core strengthening
ADHD: PREVALENCE & ETIOLOGY

- Affects 11% children ages 4-17 yo¹
  - Increasing in prevalence
- Etiology
  - Genetics
  - Nutritional status
  - Oxidative stress
  - Neurotransmitter/endocrine dysregulation
  - Neurologic abnormalities (fronto-striatal and basal ganglia network)
  - Physical & emotional trauma
  - Environmental toxicity
  - Modern Media

ADHD: CASE STUDY

- 7 yo male with ADHD and anxiety trialed on multiple stimulant and non-stimulant medications, currently on Ritalin, Methylphenidate patch and Zoloft. However, grades still C’s and D’s with impulsivity and hyperactivity at school and home.

- Standard American Diet (SAD 😞)
- No physical activity
- Video games/TV
- Sleep Disturbance/Restless

- What is your next approach?
INTEGRATIVE RX FOR ADHD

- Dietary therapies
- Micronutrients
- Neurofeedback
- Probiotics/Gut Microbiome
- Biologic-based Therapies
- Mind-Body Therapies
- Pet therapy
- Music therapy

Why Dietary Therapy?

- Greater prevalence of GI symptoms among children with ADHD\(^1\)
- Hypothesis: gut-brain axis dysfunction in neuropsychiatric disorders
  - 90% neurotransmitter synthesis in gut\(^2\)
  - \(~66\text{-}75\%\) immune system in gut\(^3\)

INCA study: Impact of Nutrition in Children with ADHD

1st phase: Open label for individual nutrition guidance
- 5 Weeks
- Elimination diet group or control group
- 100 enrolled and randomized with 83 completing first phase and 32 eligible for second phase

2nd Phase: Double-blind crossover study
- 2 weeks
- Each group assigned to three foods that induce low IgG levels or three that induce high IgG levels
- IgE food allergies also considered

ELIMINATION DIET: RESULTS

- 32 (64%) of 50 children showed significant improvement in ADHD symptoms
- **64% relapsed after food challenge**
- Food IgG panel did not predict deleterious behavior
  - IgE allergens same in both group-> meaning there may be a food sensitivity component that was not detected by IgG
Sugar dysregulates neurotransmission, similar to drug addiction

Majority of studies done\(^1,2\)

- Comparing sugar to placebo of aspartame or saccharin.
- No evaluation of chronic sugar consumption

ADHD: Dietary Assessment

Iron

- Low ferritin and abnormal iron indices
  - Sleep disturbance in children with ADHD
  - Intake in ADHD is lower on medication
  - Brain iron is lower in striata and thalamus of children with ADHD

2. Abou-Khadra MK et al. BMC Pediatr 2013
IRON THERAPY

- Serum ferritin <50 ng/mL with sleep disturbance + ADHD:

  - Children six years and younger:
    - 3-6 mg/kg/day of elemental iron
    - Max 150 mg elemental iron per day

  - Children six years and older:
    - Elemental iron 45-65 mg (1-2 times daily)

- Take with Vitamin C to enhance absorption
ADHD: DIETARY ASSESSMENT

Zinc

- **Systematic Review**¹:
  - 3 out of 80 trials met inclusion criteria
  - **Conclusion:**
    - Zinc combined with methylphenidate improved total ADHD score²
    - Zinc alone decreased hyperactivity and impulsivity, but no effect on inattention³
    - Zinc did not have any effect on ADHD symptoms, but were able to lower amphetamine medication.⁴

ADHD: Dietary Assessment

Healthy Fats

- Several RCT differ in conclusions\(^1,2,3,4\)
  - Due to different doses and combinations of PUFA mixes (ALA/LA/EPA/DHA/GLA)
  - Varying placebos with nutritional properties

- Meta-analysis\(^5\)
  - Omega-3’s are 40% as effective as methylphenidate

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If not getting enough of fatty acids in diet:

- suggest dietary changes and supplementation with balanced omega oil: 3/6/9
- plus Phospholipids (phosphatidylcholine/phosphatidylserine)
EEG-based Biofeedback (Neurofeedback)

- The American Academy of Pediatrics (AAP) recently declared “biofeedback” to be an evidence-based child and adolescent psychosocial intervention with “level 1, best support”.

- “Biofeedback” is used to refer to feedback interventions to train either the brain (ie, NF) or the body (traditionally referred to as biofeedback).
Neurofeedback: EEG-based form of biofeedback emphasizes:
Positive reinforcement and operant conditioning
Retrains abnormal brain wave states back to its normal state

**Operant Conditioning**

**Reinforcement**
Increase Behavior

- **Positive**
  - Add appetitive stimulus following correct behavior
  - Giving a treat when the dog sits

- **Negative**
  - Escape
    - Remove noxious stimuli following correct behavior
    - Turning off an alarm clock by pressing the snooze button.
  - Active Avoidance
    - Behavior avoids noxious stimulus
    - Studying to avoid getting a bad grade

**Punishment**
Decrease Behavior

- **Positive**
  - Add noxious stimuli following behavior
  - Spanking a child for cursing

- **Negative**
  - Remove appetitive stimulus following behavior
  - Telling the child to go to his room for cursing

**Key Terms**

- **Positive** presence of a stimulus
- **Negative** absence of a stimulus
- **Reinforcement** increases behavior
- **Punishment** decreases behavior
- **Escape** removes a stimulus
- **Avoidance** prevents a stimulus
ADHD: Brainwave Variants

- Elevated Theta/Beta Ratio
- Dysregulation of slow cortical potentials
- QEEG (Neuromap)
  - Assessment of responders vs non-responders

Gevensleben H et al. Brain Topogr. 2013
Meta-Analysis 2012-2014:

3 out of 12 studies included

1. NF significantly improves ADHD total score on parent scale
2. NF improves both inattention and hyperactivity/impulsivity dimensions on parent scale
3. NF improves inattention on teacher scale
ADHD: INTEGRATIVE MEDICINE TREATMENT

- Dietary Therapy
  - Elimination Diet vs. Whole Foods
  - Iron
  - Zinc
  - Omega-3

- EEG Neurofeedback

- Sleep hygiene/Lifestyle modification

- Skill building tools for stress/depression/anxiety (Parent-child interaction therapy--PCIT)
ADHD: INTEGRATIVE MEDICINE TREATMENT

- Eliminate Food additives/preservatives/food allergens
  - Food coloring, mercury, high-fructose corn syrup, lead
    - Dufault R, Behav Brain Funct. 2009 Oct 27;5:44

- L-theanine 100-200 mg twice a day

- Pycnogenol 1 mg/kg (30-300mg) daily
Whole Foods = Health
MAKE IT SIMPLE:

- Healthy fat
- Healthy protein
- Complex carbs at every meal
RESOURCES LABORATORY ASSESSMENT OF NUTRITION

Test ID: B6PRO
Vitamin B6 Profile (PLP and PA), Plasma

Useful For
Determining the overall success of a vitamin B6 supplementation program
Diagnosing and evaluation of hypophosphatasia

Clinical Information
Vitamin B6 is a complex of 6 vitamin: pyridoxal, pyridoxol, pyridoxamine, and their 5'-phosphate esters. Due to its role as a cofactor in a number of enzymatic reactions, pyridoxal phosphate (PLP) has been determined to be the biologically active form of vitamin B6.

Vitamin B6 deficiency is a potential cause of burning mouth syndrome and a possible potentiating factor for carpal tunnel and tarsal tunnel syndromes. Persons who present chronic, progressive nerve compression disorders may be deficient in vitamin B6 and should be evaluated. Vitamin B6 deficiency is associated with symptoms of scaling of the skin, severe gingivitis, irritability, weakness, depression, dizziness, peripheral neuropathy, and seizures. In the pediatric population, deficiencies have been characterized by diarrhea, anemia, and seizures.

Markedly elevated PLP in conjunction with low levels of pyridoxal acid (PA) are observed in cases of hypophosphatasia, a disorder characterized by low levels of alkaline phosphatase and a range of skeletal abnormalities.

Reference Values
PYRIDOXAL 5-PHOSPHATE
5-60 mcg/L
PYRIDOXIC ACID
3-30 mcg/L

Interpretation
Levels for fasting individuals falling in the range of 3 to 30 mcg/L for pyridoxic acid (PA) and 5 to 50 mcg/L for pyridoxal 5'-phosphate (PLP) are indicative of adequate nutrition.
Health Topics A–Z

S
- 5-HTP
- Top

A
- Acai
- Acne: See Tea Tree Oil: At a Glance
- Acupuncture
- Addiction
- Adolescents (Teenagers)
- Age-related Macular Degeneration (AMD)
- Aging
- Alcohol Addiction
- Alfalfa (MedlinePlus)
- Allergies
- Aloe vera
- Alopecia Areata
- Alpha Lipoic Acid
- Alpha- linoelnic Acid
- Alzheimer's Disease
- Amino Acids
- Androstenedione (Andro): FDA Warning (FDA)

L
- L-Arginine (MedlinePlus)
- L-Tryptophan
- Labor Pain
- Lactoferrin
- Laetrile (Amygdalin)
- Lavender
- Lemon or Lemon Balm: See Aromatherapy May Make Good Scents, But Does It Work? (04/01/08)
- Licorice Root or Glycyrrhizin
- Light Therapy
- Liver Disease
- Lobelia
- Low-back Pain
- Lung or Pulmonary Disease
- Lutein
- Lycium (MedlinePlus)
- Lycopene (MedlinePlus)
- Lyme Disease: See Bismacine Not Approved for Use (FDA: 07/21/06)
- Top
RESOURCES FOR NUTRITIONAL MANAGEMENT OF COMMON DISORDERS
To be a MEMBER:
--contact Teri Salus at tsalus@aap.org
--apply online through AAP member center
--call 847/434-7920
-- contact jweydert@kumc.edu
QUESTIONS?
**Polycystic Ovarian Syndrome: Etiology**

Key contributors to pathogenesis:
- **Chronic low-grade INFLAMMATION**
- Metabolism
  - Food & Nutrition
  - Physical Activity
- Endocrine Disruptors
- Emotional Trauma

Adolescent PCOS:
- Insulin resistance
- Obesity
- Metabolic syndrome
- Sleep disorders
- Mood disorders

16 yo female with PCOS: hirsutism, ovarian cysts and painful menses, fatigue, and overweight currently on metformin and spironolactone
- Standard American Diet (SAD 😞)
- Stopped sports/activity after age 12
- History of sexual abuse (currently undergoing therapy)

What is your next approach as her goals are to lose weight and get off medicines?
PCOS: DIETARY THERAPY

Dietary Therapy¹
- Anti-inflammatory diet
- Low glycemic index/load
- Grain-free
- Ketogenic Diet²

PCOS: VITAMIN D

Vitamin D = Secosteroid

- Antimicrobial
- Antiproliferative
- Immunomodulatory
- Mediator in Chronic Disease

Metabolism & Glucose Homeostasis:
- Upregulates insulin gene transcription
- Improves insulin secretion and glucose tolerance
- Activates PPAR-δ – a transcription factor implicated in regulation of fatty acid metabolism

PCOS: DIETARY ASSESSMENT

**Vitamin D**
- Low blood levels of serum 25 (OH)D
- Intervention studies improved androgen profiles, blood pressure, glucose metabolism and menstrual frequency

**Treatment:**
- Follow US Endocrine Society Guidelines
- Maintain Vit D levels between 40-60 ng/ml

Wehr E et al. J Endocrinol Invest 2011;34: 757-763
PCOS: Dietary Assessment

Omega 3 Fatty Acids

- Imbalance of n-6/n-3 fatty acids results in inflammation
- 8-week supplementation with 720 mg EPA & 480 mg DHA/day improved insulin resistance, lipid profiles, and adiponectin levels in overweight PCOS patients

Treatment:
- 1-2 grams of Omega-3 fatty acids daily with meal

Side effects from omega-3 fish oil may include:
- A fishy taste in your mouth/Fishy breath
- Easy bruising
- Stomach upset
- Loose stools
- Nausea

PCOS: Dietary Supplement

- **Myo-Inositol and D-chiro-Inositol**
  - Systematic Review
    - Combination of contraceptives and Myo-Inositol more effective in controlling endocrine and metabolic profiles than Metformin
  - Expert Review:
    - the administration of MI/D-chiro-inositol, in the physiological plasma ratio (i.e., 40:1) ensures better clinical results, such as the reduction of insulin resistance, androgens' blood levels, cardiovascular risk and regularization of menstrual cycle with spontaneous ovulation.
  - Improves menstrual cycle regularity, Acne score, endocrine and insulin resistance profiles in young overweight PCOS patients
    - [Formuso C et al. Minerva Ginecol 2015 Feb 11 [Epub ahead of print]]
PCOS: Dietary Supplement
Myo-Inositol & D-Chiro-Inositol

- Myo-Inositol: 4 grams/day (up to 8 grams/day)
- D-chiro-inositol: approx. 1200 mg/day
  (ranges from 300 – 2400 mg/day)

- Side effects:
  may cause looser stools, nausea, headaches, and dizziness, so titrate down

Food Sources of Inositol:
Citrus fruits, Cantaloupe, Beans, Nuts, Seeds, Whole Grains
ACUPUNCTURE/ACUPRESSURE
PCOS: INTEGRATIVE MEDICINE TREATMENT

- Supplement with Vitamin D, n-3, myo-inositol/d-chiro-inositol

- Lifestyle Modification
  - 5-10% weight loss

- Chromium picolinate
  - Increases insulin sensitivity and decreases fasting blood glucose compared to metformin in clomiphene citrate-resistant patients
  - Treatment:
    - 200-1000 mcg daily

- N-acetylcysteine or liposomal glutathione
  - NAC improved ovulation rates compared to placebo
  - Treatment:
    - 600 mg twice daily
      - [Thakker D et al. Obstet Gynecol Int 2015; 817849]
PCOS: Integrative Medicine Treatment

- **Acupuncture/TCM**
  - Improved ovulation frequency in acupuncture group compared to physical therapy

- **Mindfulness**
  - Mindfulness based stress management program revealed significant reductions in stress, depression, anxiety symptoms and salivary cortisol in women with PCOS

- **Yoga**
  - A holistic 12-week yoga program improved Anti- Mullerian Hormone, LH, testosterone levels, hirsutism, and regulated menstrual frequency