Medical Problems Potentially Contributing to Autism

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Disclaimer

While Dr. Rossignol has attempted to make the information in this presentation as accurate as possible, the information is provided without any expressed or implied warranty. The purpose of this lecture is to provide information about different conditions or treatments that may affect individuals with autism and other conditions. Please be advised that Dr. Rossignol is not giving medical advice and that circumstances may dictate different treatments. All of the reviewed treatments in this lecture are considered off-label and not FDA-approved. Before beginning any treatment, please consult with your or your child’s physician.
The use of every treatment in autism is “off-label” except for Risperidone and Aripiprazole for the treatment of irritability.
What is Autism?

- Is diagnosed *solely* based on behavioral observations (which are *subjective*)
- Is a spectrum disorder – some children are mild, some are severe
- There are no blood or other biological tests for identifying autism
- Therefore, a diagnosis of autism tells us *nothing* about the potential *contributors or causes* of the disorder
- Testing and treatments can potentially start *before* a diagnosis of autism is made
Autistic Behaviors

- Autistic behaviors may have a medical cause or contributor (which are objective), e.g.:
  - Seizures or seizure-like (epileptiform) activity may contribute to hyperactivity, aggressive behaviors, irritability, speech delay, self-stimulatory behaviors and sleep problems [Malow, 2004; Mulligan, 2014; Viscidi, 2013]
  - Gastrointestinal problems may lead to aggressive behaviors or self-injurious behaviors [Buie, 2005; Buie, 2010]

- Key Concept: Treatment of these medical problems may lead to behavioral improvements
Aims: To evaluate autistic children with GI complaints and aggression or self-injurious behavior in order to determine if these behaviors may be symptoms of GER. Methods: Six consecutive autistic children (ages 8–19 years) undergoing endoscopy and scheduled for BRAVO (wireless) pH probe were evaluated for histology and pH meter results. Findings: GER was identified in 5 of 5 patients tested by BRAVO pH testing. Esophagitis was seen in 3 of 6 patients biopsied. Conclusions: Aggressive or self-injurious behavior may be a manifestation of pain from GER and should prompt consideration of further investigation.

Important Concept

- Several **metabolic abnormalities** have been reported to contribute to or cause a **potentially reversible** form of autism — e.g., Cerebral Folate Deficiency (CFD)
- The goal, from day one of evaluation, is to rapidly screen for these abnormalities and start treating them
- Testing can be done by measuring certain **biomarkers** (laboratory tests that may identify abnormalities)
Treatments
Impossible number of autism “treatments”

11/13/13

autism treatment - Google Search

autism treatment

Web Images Maps Shopping News More Search tools

About 66,500,000 results (0.31 seconds)

Ads related to autism treatment

Autism/Meditation Webinar - David Lynch Foundation Presents
www.eventbrite.com/Autism-Meditation
Free Webinar on Autism & Meditation

It's Not Autism - It's Sensory Processing Disorder - spdstar.org
www.spdstar.org/
Find out why SPD gets misdiagnosed.
Impossible number of autism “treatments”

4/12/2014

autism treatment

About 94,400,000 results (0.33 seconds)

Sauna Autism Therapy - Sunlighten.com
Ad www.sunlighten.com/AutismTherapy
Proud partner of the National Autism Association. Free info!
Infrared Saunas - Pricing - Compare Saunas - Portable Infrared Sauna

Autism Therapy Center - kennedykrieger.org
Ad autism.kennedykrieger.org/
Internationally recognized program for children with autism
Participate in Research - KKI's Center for Autism
Approved medications: ASD

- Risperidone (Risperdal®)
- Aripiprazole (Abilify®)
- Both are antipsychotic medications approved for treating irritability associated with ASD and thus do not treat core autistic symptoms or behaviors
- There are currently no FDA approved medications for the core symptoms of ASD
Choosing a treatment

- We treat **metabolic or biochemical abnormalities** that may be **contributing** to behavior; in that sense, we are not treating “autism” or “ADHD”
  - e.g., autism is treated with ABA therapy
- Use proven treatments based upon **biomarkers** (laboratory tests or other tests like EEGs) and/or **evidence-based medicine** (choosing the best treatments based on the published medical literature)
Best & worst cell phone deals

- Top carriers
- Best phones
- Contract traps to avoid

ALSO iPhone vs. Palm vs. BlackBerry
<table>
<thead>
<tr>
<th>Speech/communication</th>
<th>Carnitine</th>
<th>Carnosine</th>
<th>GFCF diet</th>
<th>Alpha-2 adrenergic agonists</th>
<th>Cyproheptadine</th>
<th>Glutamate antagonists</th>
<th>AIT</th>
<th>Tetrahydrobiopterin</th>
<th>B6/magnesium</th>
<th>Al</th>
<th>HBOT</th>
<th>Famotidine</th>
<th>Music therapy</th>
<th>Neurofeedback</th>
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<tr>
<td>Autistic behavior</td>
<td>Carnosine</td>
<td>B$_6$ / magnesium</td>
<td>Probiotics</td>
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<td>Piracetam</td>
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<td>Carnosine</td>
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<td>Naltrexone</td>
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<td>Stereotypy</td>
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<th>Hyperactivity</th>
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<tr>
<th>Eye contact</th>
<th>Tetrahydrobiopterin</th>
<th>Omega 3 fatty acids</th>
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<td>AI</td>
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<td>Famotidine</td>
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<th>Attention</th>
<th>Omega 3 fatty acids</th>
<th>AI</th>
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<tr>
<th>Sleep</th>
<th>Melatonin</th>
<th>Carnitine</th>
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<td></td>
<td>Multivitamin</td>
<td>Iron</td>
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<td></td>
<td>Alpha-2 adrenergic agonists</td>
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AI: Acetylcholinesterase inhibitors; AIT: auditory integration training; GFCF: gluten-free, casein-free diet; HBOT: hyperbaric oxygen treatment;
Targeting medical comorbidities (conditions) in autism
Gastrointestinal problems
INSANITY PROCEEDING FROM THE COLON.

Read before the Chicago Medical Society, July 15, 1889.
BY HAROLD N. MOYER, M.D.,
LECTURER ON PHYSIOLOGY, RUSH MEDICAL COLLEGE, CHICAGO.
Von der Kolk was himself affected with this disorder. While suffering from constipation and fatigue from overwork, hallucinations and phantasms appeared to him and continued for three days. A large clyster was administered, which was followed by a copious evacuation of foul-smelling faecal matter; immediately the hallucinations disappeared and his mind became tranquil. There are no distinguishing symptoms of this condition, but an intellectual disturbance which has its origin in this source, is said by Schroeder to be characterized by a peculiar depression of spirits, by anguish of mind, and by the patient’s self-accusations of wretchedness and baseness. The disease has a very slow course, and generally the mental anguish has existed some time before the physician is consulted.
Common GI problems in autism

- Constipation
- Diarrhea
- Malabsorption
- Maldigestion
- Inflammation
- Dysbiosis
Statement 6: Individuals with ASDs and GI symptoms are at risk for problem behaviors.

Statement 8: Education of caregivers and health care providers is necessary to impart knowledge of how to recognize typical and atypical signs and symptoms of GI disorders in individuals with ASDs.

Buie et al., 2010  Pediatrics 125:S1-S18
GI problems and autism

- GI problems correlated with autism severity [Adams, 2011; Chaidez, 2014]
- Oxidative stress in ASD correlated with GI problems [Gorrindo, 2013]
- Constipation associated with language impairment [Gorrindo, 2012]
- GFCF diet lessens leaky gut [de Magistris 2010]
To compare gastrointestinal (GI) problems among children with: (1) autism spectrum disorder (ASD), (2) developmental delay (DD) and (3) typical development (TD), GI symptom frequencies were obtained for 960 children from the CHildhood Autism Risks from Genetics and Environment (CHARGE) study. Compared to TD children, those with ASD [aOR 7.92 (4.89-12.85)] and DD [aOR 4.55 (2.51-8.24)] were more likely to have at least one frequent GI symptom. Restricting to ASD children, those with frequent abdominal pain, gaseousness, diarrhea, constipation or pain on stooling scored worse on irritability, social withdrawal, stereotypy, and hyperactivity compared with children having no frequent GI symptoms.

Moderate or severe constipation was more frequent in the autistic group than in the control subjects (36% vs 10%). Analysis of rectosigmoid loading showed more striking differences (54.4% of autistic children had moderate/severe loading or acquired megarectum compared with 24.1% of control subjects). Multivariate regression analysis showed consumption of milk to be the strongest predictor of constipation in the autistic group. **CONCLUSIONS:** Constipation is a frequent finding in children with gastrointestinal symptoms and autism, particularly in the rectosigmoid colon, often with acquired megarectum.
Treatment of constipation

- Magnesium citrate
- Vitamin C
- Aloe vera juice
- Carnitine
- Lactulose
- Miralax
- Saline enemas
Diarrhea: Causes

- Severe constipation
- Infections
- Food
- Medications
- Nutritional supplements
- Functional diarrhea
- Dysbiosis
Dysbiosis

- Yeast
- Clostridia
- Other bacteria
- Parasites
- Parasitic worms
Some cases of late-onset (regressive) autism may involve abnormal flora because oral vancomycin, which is poorly absorbed, may lead to significant improvement in these children. Fecal flora of children with regressive autism was compared with that of control children, and clostridial counts were higher. The number of clostridial species found in the stools of children with autism was greater than in the stools of control children. Children with autism had 9 species of Clostridium not found in controls, whereas controls yielded only 3 species not found in children with autism. In gastric and duodenal specimens, the most striking finding was total absence of non-spore-forming anaerobes and microaerophilic bacteria from control children and significant numbers of such bacteria from children with autism.
Clostridia: Potential Treatments

- **Probiotics (Consider higher potency)**
  - Lactobacillus
  - Saccharomyces boulardii
  - Lactobacillus rhamnosus GG
  - Lactobacillus plantarum
  - VSL #3
- **Carnitine**
- **IVIG**
- **HBOT**
Clostridia: Potential Treatments

- Antibiotics
  - Metronidazole (Flagyl)
  - * Vancomycin (Vancocin) (*non-absorbed)
  - Nitazoxanide (Alinia)

- May need to also treat yeast at the same time
A graph showing the CDAD recurrences (%) on the right y-axis and Vancomycin dosage (mg day⁻¹) on the left y-axis. The x-axis represents different dosing regimens: 10 days (Standard), 10 days (High dose), Over 25 days (Tapered), and One every 3 days (Pulsed). The graph indicates a decrease in Vancomycin dosage with a corresponding decrease in CDAD recurrences.

Yeast: Potential Treatments

- Limit carbohydrates and sugar
- Probiotics
- Saccharomyces Boulardii
- Herbals
  - Berberine
  - Grapefruit Seed Extract
  - Oil of Oregano
  - Garlic
  - Others
Yeast: Potential Treatments

- Antifungals
  - Fluconazole (Diflucan)
  - Ketoconazole (Nizoral)
  - Nystatin *
  - Amphotericin B *
  - Itraconazole (Sporanox)
  - Terbinafine (Lamisil)
* not absorbed
The potential of Lactobacillus plantarum WCSF1 (a probiotic) to modulate the gut microbiota of autistic subjects was investigated during a double-blind, placebo-controlled, crossover-designed feeding study. The faecal microbiota, gut function and behaviour scores of subjects were examined throughout the 12-week study. Lactobacillus plantarum WCFS1 feeding significantly increased Lab158 counts (lactobacilli and enterococci group) and significantly reduced Erec482 counts (Clostridium cluster XIVa) compared to placebo. Probiotic feeding also resulted in significant differences in the stool consistency compared to placebo and behaviour scores (total score and scores for some subscales) compared to baseline.

Nutritional deficiencies
Deficiencies and autism

- Vitamin D deficiency correlated with more severe autism [Gong, 2014; Mostafa, 2012]
- Low vitamin D correlated with antibodies to brain tissue [Mostafa, 2012]
Iron deficiency and autism

- **Iron deficiency** more common in children with autism [Dosman, 2006; Latif, 2002]
- A study of 2,957 patients with iron deficiency found an increased risk of autism (3.1-fold) [Chen, 2013]
- Lower ferritin correlated with more sleep problems in autism and limb movements [Youssef, 2013]
- Low ferritin correlated with more severe speech problems in autism [Dosman, 2006]
- Iron supplementation improves sleep in autism [Dosman, 2007]
- Iron supplementation increases attention compared to placebo in ADHD (when ferritin <30) [Konofal, 2008]
Cholesterol deficiency

- In one study, 19/100 children with ASD had a cholesterol <100 [Tierney, 2006]
- Children with cholesterol <145 are 3 times more likely to be suspended or expelled from school [Zhang, 2005]
- Cholesterol supplementation lowered autistic behaviors, irritability, hyperactivity, aggression, self-injury and temper outbursts [Aneja, 2008]
Sleep problems
Sleep problems in autism

- In a study of 166 ASD children: 47% had at least one sleep problem, including bedtime resistance (2.7 x), insomnia (4.1 x), and daytime sleepiness (7.6 x) compared to their unaffected siblings [Park, 2012]
- A study of 1,583 children with autism found that anxiety, autism symptom severity, sensory sensitivities, and GI problems were associated with sleep disturbance [Hollway, 2013]
- Sleep problems are associated with video game use at night [Engelhart, 2013]
- Decreased production of melatonin correlated with autism severity [Tordjman, 2005]
Abnormal melatonin synthesis in autism spectrum disorders

Melke et al., 2008 Mol Psychiatry 13(1): 90-98
Abnormal melatonin synthesis in autism spectrum disorders

Melke et al., 2008 Mol Psychiatry 13(1): 90-98
Melatonin in autism

Six randomized, double-blind, placebo-controlled studies have demonstrated improvements in the amount of time to fall asleep, number of nighttime awakenings, and/or length of sleep compared to both baseline and/or to placebo in children with autism.

Cortesi et al., 2012  J Sleep Res 21(6):700-709
McArthur and Budden, 1998  Dev Med Child Neurol 40:186-92
Garstang and Wallis, 2006  Child Care Health Dev 32(5):585-9
Wasdell et al., 2008  J Pineal Res 44:57-64
Wirojanan et al., 2009  J Clin Sleep Med 5:145-50
Wright et al., 2011  J Autism Dev Disord 41(2):175-84
Treatments for sleep problems

- Melatonin (typically 1-3 mg) at bedtime
- 5-HTP 50-100 mg 1 hr before bedtime
- GABA 250-750 mg at bedtime
- Omega-3 fatty acids
- Iron [Dosman, 2007]
- Clonidine [Ingrassia, 2005]
Glutathione and oxidative stress abnormalities
We investigated the relationship of the MTHFR polymorphisms (C677T and A1298C) and the risk of ASD by meta-analysis. Up to December 2012, eight case-control studies involving 1672 patients with ASD and 6760 controls were included for meta-analysis. The results showed that the C677T polymorphism was associated with significantly increased ASD risk in all the comparison models [T vs. C allele (frequency of allele): odds ratio (OR) = 1.42, 95% confidence interval (CI): 1.09-1.85; CT vs. CC (heterozygote): OR = 1.48, 95% CI: 1.09-2.00; TT vs. CC (homozygote): OR = 1.86, 95% CI: 1.08-3.20; CT+TT vs. CC (dominant model): OR = 1.56, 95% CI: 1.12-2.18; and TT vs. CC +CT (recessive model): OR = 1.51, 95% CI: 1.02-2.22], whereas the A1298C polymorphism was found to be significantly associated with reduced ASD risk but only in a recessive model (CC vs. AA+AC: OR = 0.73, 95% CI: 0.56-0.97).
Plasma methionine and the ratio of S-adenosylmethionine (SAM) to S-adenosylhomocysteine (SAH), an indicator of methylation capacity, were significantly decreased in the autistic children relative to age-matched controls. Plasma levels of cysteine, glutathione, and the ratio of reduced to oxidized glutathione, an indication of antioxidant capacity and redox homeostasis, were significantly decreased. We propose that an increased vulnerability to oxidative stress (endogenous or environmental) may contribute to the development and clinical manifestations of autism.
Based on reports of abnormal methionine and glutathione metabolism in autistic children, it was of interest to examine the same metabolic profile in the parents. The results indicated that parents share similar metabolic deficits in methylation capacity and glutathione-dependent antioxidant/detoxification capacity observed in many autistic children.

James et al., 2008  J Autism Dev Disord 38(10):1966-75
### Effectiveness of Methylcobalamin and Folinic Acid Treatment on Adaptive Behavior in Children with Autistic Disorder Is Related to Glutathione Redox Status

Thirty-seven children diagnosed with autistic disorder and abnormal glutathione and methylation metabolism were treated with twice weekly 75 microg/Kg methylcobalamin and twice daily 400 microg folinic acid for 3 months.

<table>
<thead>
<tr>
<th>Vineland Subscale</th>
<th>Baseline Age Equivalent Months (mean ± SE)</th>
<th>Post-Intervention Age Equivalent Months (mean ± SE)</th>
<th>Change (months) (mean; 95% CI)</th>
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</thead>
<tbody>
<tr>
<td>Receptive Language</td>
<td>23.1 ± 1.8</td>
<td>31.4 ± 3.4</td>
<td>8.3 (2.9, 13.7)</td>
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<tr>
<td>Expressive Language</td>
<td>20.6 ± 1.9</td>
<td>27.5 ± 2.9</td>
<td>6.0 (3.3, 9.4)</td>
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<tr>
<td>Written Language</td>
<td>40.5 ± 3.8</td>
<td>46.7 ± 4.0</td>
<td>6.2 (3.4, 9.0)</td>
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<tr>
<td>Personal Skills</td>
<td>30.5 ± 2.3</td>
<td>40.5 ± 3.8</td>
<td>10.0 (3.8, 16.2)</td>
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<tr>
<td>Domestic Skills</td>
<td>30.3 ± 4.1</td>
<td>39.3 ± 5.9</td>
<td>9.0 (-1.4, 19.4)</td>
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<tr>
<td>Community Skills</td>
<td>32.9 ± 2.9</td>
<td>36.1 ± 3.8</td>
<td>2.0 (-3.0, 6.9)</td>
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<tr>
<td>Interpersonal Skills</td>
<td>18.7 ± 2.7</td>
<td>24.1 ± 3.9</td>
<td>5.4 (0.0, 10.9)</td>
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<tr>
<td>Play/Leisure Skills</td>
<td>22.0 ± 4.5</td>
<td>34.0 ± 4.1</td>
<td>12.0 (4.1, 19.6)</td>
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<tr>
<td>Coping Skills</td>
<td>25.8 ± 2.5</td>
<td>34.3 ± 4.0</td>
<td>11.5 (4.9, 18.0)</td>
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Increasing Glutathione

- Antioxidants
- Pycnogenol 1-2 mg/kg/day
- Methylcobalamin injections 65 mcg/kg 3 times per week
- Folinic acid 400 mcg twice a day
- Glutathione 10-50 mg/kg/day
- NAC (N-acetylcysteine) 10-50 mg/kg/day
- Vitamins C (100 mg/kg PO) and E (400 IU)
Mitochondrial dysfunction
Mitochondria

- Possible descendant of an ancestral purple, non-sulfur, photosynthetic bacteria
- Found in every cell, generate ATP (energy)
- Has its own DNA (genome)
- Many cells contain 500 to 2000 mitochondria
- Liver mitochondria detoxify ammonia
Symptoms / Signs of mitochondrial dysfunction

- “Any symptom in any organ at any age”
- Developmental or growth delay
- Motor delay
- Clumsiness
- Developmental regression
- Seizures
- Hypotonia (low muscle tone)
- Migraines
- GI Abnormalities (diarrhea, constipation)
- Slow cognitive processing speed
- Fatigue / lethargy
- Ataxia
- Cardiomyopathy
- Myopathy
- Oxidative stress
Mitochondrial Dysfunction in ASD

- Prevalence of mitochondrial disease in ASD ~5% (probably an underestimation)
- Biomarker data suggest that mitochondrial dysfunction is present in ~1/3 children with ASD
- Mitochondrial dysfunction correlated with autism severity [Minshew, 1993; Mostafa, 2005]
- The significant variability in biomarkers suggests that a spectrum of mitochondrial dysfunction in ASD exists
- Mitochondrial dysfunction in many cases may be secondary in nature (e.g., non-genetic)

Rossignol and Frye, 2012 Mol Psychiatry 17(3):290-314
Labs: Mitochondrial dysfunction (blood)

- Elevated lactic acid and pyruvate
- Elevated ammonia (>40 µg/dL)
- Low ubiquinone (CoEnzyme Q10)
- Low carnitine, free and total
- Elevated creatine kinase (>150 U/L)
- Fasting plasma amino acids: alanine (>450 µmol/L); alanine/lysine (>2.5)
- Fasting plasma acylcarnitine analysis (3 or more elevations)
- AST / ALT > 2.0
Treatments for mitochondrial dysfunction associated with autism spectrum disorders

Table 2
Recommend doses of vitamin supplements

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<th>Vitamin</th>
<th>Dose</th>
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<td><strong>Electron Transport Chain Support</strong></td>
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<tr>
<td>Co-enzyme Q10: Ubiquinol</td>
<td>5–30 mg/kg/day divided in 2 doses per day</td>
</tr>
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<td>10–30 mg/kg/day divided in 2 doses per day</td>
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<tr>
<td><strong>Energy Storage and Transportation</strong></td>
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<tr>
<td>Creatine monohydrate</td>
<td>0.1 g/kg/day divided in 1–2 doses per day</td>
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<tr>
<td><strong>Fatty Acid Oxidation Support</strong></td>
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<tr>
<td>L-carnitine</td>
<td>30–100 mg/kg/day divided in 2–3 doses per day</td>
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<tr>
<td>Acetyl-L-carnitine</td>
<td>250–1000 mg/day divided in 2 doses per day</td>
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<tr>
<td>Biotin (B7)</td>
<td>5–10 mg/day given once per day</td>
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<tr>
<td><strong>B-Vitamins</strong></td>
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<tr>
<td>Thiamine (B1)</td>
<td>50–100 mg/day given once per day</td>
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<tr>
<td>Riboflavin (B2)</td>
<td>100–400 mg/day given once per day</td>
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<tr>
<td>Niacin (B3)</td>
<td>50–100 mg/day given once per day</td>
</tr>
<tr>
<td>Pyridoxine (B6)</td>
<td>200 mg/day given once per day</td>
</tr>
<tr>
<td><strong>Antioxidants</strong></td>
<td></td>
</tr>
<tr>
<td>Acetyl-L-carnitine</td>
<td>250–1000 mg/day divided in 2 doses per day</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>200–400 IU/day given once per day</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>100–500 mg/day given once per day</td>
</tr>
<tr>
<td>alpha-lipoic acid</td>
<td>50–200 mg/day given once per day</td>
</tr>
<tr>
<td><strong>Oxidative Stress Support</strong></td>
<td></td>
</tr>
<tr>
<td>Methylcobalamin (B12)</td>
<td>5–1000 mcg/day given once per day</td>
</tr>
<tr>
<td>Folinic Acid / leucovorin (B9)</td>
<td>400–800 ug/day given once per day</td>
</tr>
<tr>
<td>5-methyltetrahydrofolate (B9)</td>
<td>400–800 ug/day given once per day</td>
</tr>
<tr>
<td>N-acetyl-L-cysteine (NAC)</td>
<td>10–70 mg/kg/day divided in 1–3 doses</td>
</tr>
</tbody>
</table>

Cerebral folate problems
Folate transport into the brain

- 5-methyltetrahydrofolate (5MTHF): binds to a Folate Receptor 1 (FR1) in the choroid plexus and then undergoes endocytosis, storage and then delivery into the CSF. It is then transported into the CSF and neurons by the reduced folate carrier (RFC).
- In this process, folate transport by FR1 is ATP-dependent.
- Low levels of 5MTHF in the brain can cause cerebral folate deficiency (CFD).
CFD represents one of a few progressive neurological disorders that is treatable and potentially reversible. To date, three studies have reported an association between CFD and Rett syndrome, seven studies have reported that CFD is associated with autism spectrum disorders (ASD) in some children, and five studies have reported FRα autoantibodies in children with ASD, some of whom also had CFD. One study of 93 children with ASD reported that FRα autoantibodies were found in 75.3%. From these studies of children with concomitant ASD and CFD, treatment with oral folinic acid (leucovorin, 0.5 to 2 mg/kg/day) resulted in various improvements ranging from partial improvements in communication, social interaction, attention and stereotypical behavior to complete recovery of both neurological and ASD symptoms.
Twenty-five patients with early-onset low-functioning autism with or without neurological deficits, were evaluated for serum folate, cerebrospinal fluid (CSF) 5MTHF, and serum FR autoantibodies of the blocking type to determine the significance of folate receptor (FR) autoantibodies with respect to folate transport across the blood-CSF barrier. In spite of normal serum folate, CSF 5MTHF was low in 23 of 25 patients. The reduced CSF folate in 19 of these 23 patients could be explained by serum FR autoantibodies blocking the folate binding site of the membrane-attached FR on the choroid epithelial cells. Oral folinic acid supplements led to normal CSF 5MTHF and partial or complete clinical recovery after 12 months.

Ramaekers et al., 2007  Neuropediatrics 38(6):276-81
“Two patients (patients 2, 4) who were diagnosed early and received treatment were cured with full recovery from autism and neurological deficits. In the whole group these two patients were among the youngest and were detected at 2 years 8 months and at 3 years and 2 months. Three older patients (patients 11, 23, 25), diagnosed and treated from the age of 4.9, 8 and 11.9 years, did not recover from autism but showed improvement of their neurological deficits. The remaining thirteen patients in the age range of three and seven years showed a good response after treatment with improvement of most neurological deficits, but only partial recovery from their autism. The partial recovery in the latter group of 13 patients consisted of amelioration of social impairment in 4 of 13 patients, reversal of impaired communication in 9 of 13 patients and disappearance of perseverative behaviour and restricted interests in 6 of 13 patients.”

Ramaekers et al., 2007  Neuropediatrics 38(6):276-81
Seizures
Seizures: Definition

- Episodes of disturbed brain function that cause changes in attention or behavior
- Caused by abnormally excited electrical signals that disrupt the smooth-running pattern of electrical activity in the brain causing overload
- Epilepsy: recurrent seizures (at least 2)
Seizures: Symptoms and signs

- Subclinical (silent)
- Staring spells
- Rapid blinking, holding of the hands to the ears, unprovoked crying episodes
- Loss of consciousness
- Violent convulsions
- Aura: strange sensation (such as tingling, emotional change, or smell of odor not there)
Seizures in autism

- Prevalence of seizures ranges from 8-42%, with most estimates at 25-30%
- Prevalence of EEG epileptiform (seizure-like) activity 60% or more [Chez 2006; Valvo, 2013]
- Children over 10 years old 2.4 times more likely to have epilepsy [Viscidi, 2013b]
- Children with seizure-like activity more likely to have stereotypes and aggressive behaviors [Mulligan, 2014]
- ASD children with epilepsy are more irritable and hyperactive [Viscidi 2013a]
Seizures in autism

- Seizure-like activity can often progress to epilepsy [Kanemura 2013]
- Children with seizure-like activity often improve with seizure meds [Frye, 2010]
- Seizure-like activity can impair attention [Kawatani, 2012]
- When seizures go up, sleep goes down [Malow, 2004]
- Tall children with autism more likely to have seizures [Valvo, 2013]
Several lines of evidence point to valproate, lamotrigine and levetiracetam as the most effective and tolerable AEDs for individuals with ASD. Limited evidence supports the use of traditional non-AED treatments, such as the ketogenic and modified Atkins diet, multiple subpial transections and immunomodulation and neurofeedback treatments. Limited evidence supports L-carnitine, multivitamins and N-acetyl-L-cysteine in mitochondrial disease and dysfunction, folinic acid in cerebral folate abnormalities and early treatment with vigabatrin in tuberous sclerosis complex. Finally, there is limited evidence for a number of novel treatments, particularly magnesium with pyridoxine, omega-3 fatty acids, the gluten free casein-free diet and transcranial magnetic simulation.
DIAGNOSIS AUTISM: NOW WHAT?
A SIMPLIFIED BIOMEDICAL APPROACH

By Dan Rossignol, MD, FAAFP

Rossignol, 2009  Autism File 32:8-11
Training Physicians

Medical Academy of Pediatric Special Needs
MAPS Curriculum

Focused on 6 major areas:

1. Neurology
2. Metabolic
3. Immunology
4. GI / nutrition
5. Toxicology
6. Integration into clinical care / cases

Partnering with Parent Groups