



## **Autism 2002 : Mercury, Heavy Metals... Toxicity**

### **Physical Health in Autism and How to Improve It**

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Dedicated to **Irene (Vicky) Colquhoun (1920-2000)**

As true discoverer in the parental tradition, Vicky reported fatty acid deficiency in hyperactive children twenty years ago. Thousands of families report benefits from zinc, evening primrose oil and food avoidance espoused by the Hyperactive Children's Support Group.

### **Physical Health in Autism and How to Improve It**

Gastrointestinal pathology, suboptimal nutrient status, food intolerance, chronic infections and toxic accumulations typify children with autistic symptoms. Laboratory testing and clinical observation complement empiric treatment of these physical problems, often with substantial improvement in behavior.

From the Autism Research Institute perspective, autism and ADHD occur as a result of underlying physical problems. We recognize that these physical problems are multiple and variable among children. We find that many of the physical problems are identifiable within our current technology and that nutrition is central to treatment and complimentary to other modalities.

Clinical treatment is years ahead of research science in this area. Published outcome studies exist for some of our treatments (Vitamin B6 and magnesium, gluten/casein-free diet), while other useful interventions are based primarily on outcome reports from parents and clinicians. Research science can help us measure these outcomes and elucidate mechanism, especially when multiple interventions are involved.

Current thinking about autism and ADHD necessarily converges on the gut. **Most autistic children have significant gut disease.**

### **Gut problems seen in autism**

**Inflammation of the entire alimentary canal is common in autism.** Horvath found esophagitis and duodenitis in about seventy-percent of autistic children, and Wakefield

found enterocolitis and lymphonodular hyperplasia (LNH) in about ninety-percent of the regressed autistic subgroup. Chronic inflammation implies ongoing oxidative stress in the gastrointestinal tissue.

Consistent with the physical pathology, **functional gut problems abound**. Low intestinal digestive enzyme activity in about sixty percent of autistics is reported, and this is understandable in the context of gut disease, since these enzymes are made in the intestinal brush border. A malabsorbing, leaky, protein-losing autistic gut is documented in the literature, and IgG food intolerance and steatorrhea is found by clinicians in the majority of autistic children. Abdominal pain, chronic diarrhea, constipation or alternating diarrhea and constipation are common in autism, and well-documented.

**Suboptimal nutrient status, microbial overgrowth, food allergens, and toxins all cause inflammation of the gut.** In promoting gut inflammation, these factors have additive, inter-related effects. Mercury and cadmium bind avidly to gut membrane and are notoriously caustic to gut mucosa. Mucosal degradation is accompanied by microbial overgrowth and production of microbial toxins. Increasing toxin accumulation can affect immune function, permeability, digestion and assimilation of nutrients, and further erode microbial balance.

### **Results of gut injury:**

- Suboptimal nutrient status due to impaired digestion and assimilation.
- Excess circulating peptides due to impaired brush-border and paneth cell peptidase production.
- IgG food allergy due to increased intestinal permeability.
- Increased production of toxins such as organic acids due to local immune disruption.
- Increased uptake of toxins due to increased permeability.

**Gut mucosa is especially sensitive to oxidative stress** via the production of superoxide and hydroxyl radicals, as demonstrable in ischemia / reperfusion studies showing stomach and intestinal ulceration under conditions of stress. Inflammation from microbial infection, food allergy, endogenous and exogenous toxins, and suboptimal nutrient status means less resistance to oxidative stress in the sensitive gut tissue. Gastrointestinal autoimmunity should not be overlooked as a possible contributor to chronic inflammation in the gut, especially in the context of heavy metals, which are highly oxidative by nature.

### **Factors which aggravate oxidative stress in the gut**

- **Microbial overgrowth:** protozoal, bacterial, fungal, viral and consider chlamydia and mycoplasma.
- **Low immune-boosting nutritional factors:** especially Zn, B6, Vitamin A and GLA.

- **Compromised immune function** with low IgA, C4b, NK- and T-cell activity, more infections and more antibiotics.
- **Inadequate anti-oxidant nutrients** with low vitamin C, vitamin A, Zn, Se, and glutathione-supporting methionine, vitamin B6, Mg, and lipoic acid. Uric acid plays a key anti-oxidant role in the plasma, and low levels seen in autism may be a reflection of oxidizing stress. [Glutathione, lipoic acid, glutathione-reductase, and superoxide dismutase levels would be of interest in autism].
- **Endogenous toxins:** Organic acids (example: arabinose from yeast or maldigestion forms pentosidine cross linkages to block B6, biotin and lipoic acid; tartaric from yeast blocks Krebs Cycle); Pyrroles (Maue Factor) blocks p450, heme synthesis, extremely reactive.
- **Exogenous toxic load:** Pica of contaminated soils and objects, toxicants in food and water, insecticides, PCB's, organic solvents, food dyes, excitotoxic flavor-enhancers, and NSAIDs.
- **Floral-derangement:** Antibiotic-altered flora eliminate less heavy metal in feces, concentrate greater metals in tissue; suckling detoxification is much weaker than weaned state, probably due to flora; lactobaccilli induce IgA and may be key to detox capability. There is ample suggestion of significant derangement of the autistic flora, but no formal study.

## **Pilot study: nutritional status of autistic children**

DAN Think-Tank 2000, Phoenix AZ

### **Most autistic children demonstrate:**

- Poor B6-binding, with low or low-normal intracellular magnesium
- Low intracellular zinc
- Low serum Vitamin A
- Low biotin, B1, B3 and B5 function on microbiological assay
- Low urinary vitamin C
- Low RBC membrane EPA (derivative omega-3)
- Low RBC membrane GLA and DGLA (derivative omega-6)
- Elevated RBC membrane arachidonic acid (inflammatory)
- Low taurine
- Elevated casomorphine and gliadomorphine
- Elevated urinary yeast metabolites
- Elevated IgG to milk
- Floral imbalance

## Many autistic children demonstrate:

- Low serum selenium (50%)
- Low folate and B12 on microbiological assay
- Elevated RBC membrane trans fatty acids
- IgG to grains
- Elevated urinary bacterial metabolites (50%)
- Overly acidic stool

Waring reports **low blood sulfate** and high urinary sulfate loss (**and proteinuria**) in most autistic children. For a review of the published studies on the nutritional status of autistic and ADHD children and heavy metals in autism review refer to <[www.woodymcginis.com](http://www.woodymcginis.com)>

## Current successful gut-related interventions

- **Gluten / Casein-Free Diets**

Key peptidase is produced by the intestinal membrane.

- **Anti-viral agents and IV gamma globulin**

May affect chronic intestinal infection.

- **Digestive Enzymes**

Multiple choices, including special peptidase and prescription microencapsulated forms.

- **Floral Remediation**

Antifungal, antibacterial and regular probiotic are mainstay treatment.

- **Secretin**

Produced by the small intestine, stimulates digestive enzymes, trophic and stimulates blood flow to the intestine, triggers digestive juices from the pancreas, increases immune levels in bile.

- **Cod liver oil**

Vitamin A supports gastrointestinal membranes and mucin production. EPA in cod liver oil is anti-inflammatory.

- **Bethanecol**

Stimulates all-important acid production by the stomach, tightens gastroesophageal sphincter to stop reflux esophagitis, stimulates digestive enzymes, trophic to pancreas, stomach, small and large bowel mucosa, stimulates defensins release by paneth cells for local immunity, promotes ordered peristalsis.

- **DMSA and Lipoic Acid**

Remove heavy metals, which have particularly high affinity for intestine. Mercuric cation at nanomolar concentrations completely inhibits activation of B6 in the intestinal mucosa. Floral alterations may affect heavy metal recirculation and heavy metal levels in the lumen may affect floral composition.

- **Zinc**

Last line of defense in protection of cell membrane sulfhydryls from oxidation; inhibits bacterial lipase; lessens intestinal permeability; increases intestinal PGE1 for immune function. Necessary for stomach acid production and Vitamin A metabolism.

### **Strategy: assure generous levels of the key nutrients**

- **Vitamin B6.** Pyridoxal-5-phosphate is activated form.
- **Magnesium.** Glycinate form most absorbable.
- **Zinc.** Picolinate form most absorbable. Dose away from minerals and food which block absorption. Balance with manganese. Warts, stretch marks, flecks subside.
- **Calcium.** Assure RDA of about one gram daily plus some require extra.
- **Selenium.** Doses up to 200 mcg daily as anti-oxidant and to bind mercury.
- **Vitamin A.** Cod liver oil for all behavioral children unless allergic to cod.
- **Vitamin C.** Twice-daily dosing rationale; also helps regularize bowel movement.
- **Vitamin E.** Important chain-breaking anti-oxidant.
- **Fish Oil.** Quiet inflammation with EPA. High EPA / DHA preparations available.
- **Evening Primrose Oil.** Good for the gut, growth and immunity.
- **Particularly Important for Immunity:** Zn, Vitamin A, GLA.

## **Management of nutrition and gut**

### **History and Physical**

Dry skin and hair, allergies, thirst, frequent infections and dyspraxia suggest fatty acids; nail flecks and lighter hair from low zinc; indirect gaze for low Vitamin A; rashes and carbohydrate cravings for fungal overgrowths; abnormal stool consistency and frequency; response to food challenges

### **Laboratory**

Select sensitive lab measurements for nutritional assessment, such as RBC (intracellular) mineral levels, RBC-membrane fatty acids, functional vitamin assay; for key nutrients, treat low-normal lab ranges and do follow-up studies to verify correction.

**Newer testing modalities** such as IgG food allergy blood testing and urinary organic acids are useful.

- **Routine chemistry profile, thyroid, complete blood count and urinalysis**
- **Stool studie:** Culture and sensistivity, parasitology, steatocrit
- **Urinary organic acids**
- **Urinary pyrroles.** Elevation in twenty-five percent implies primary Zn and B6 need. Off Zn and B6 prior to collection.
- **Urinary peptides.** Or, empiric trial gluten/cassein-free
- **IgG blood test for food allergies.**
- **RBC mineral levels**
- **Sensitive vitamin assay**
- **RBC membrane fatty acids**
- **Amino acid levels** Methionine, taurine, and glutamine very important
- **Heavy metals levels** and **MELISA** for allergic reactivity to metals

## Treatment guidelines

- **Principle:**
  - If rationale exists for an intervention, continue it unless there is a reason to stop or change it. Nutrients, floral remediation, digestive enzymes and detoxification take time to work and they work together.
- **Combination formulations can be beneficial.**
- **Tailored nutritional programs**
  - Include B6 (P5P) and magnesium, zinc, calcium, vitamin C, vitamin E, selenium, cod liver oil and fatty acids.
  - Add one nutrient at a time, sometimes trying lower doses.
  - In the allergy-prone child, start with fish-oil, then balance with evening primrose oil.
- **Assure anti-oxidant coverage before administering oils.**
  - Zinc and biotin co-factors for conversion of GLA from EPO.
- **Effective levels of anti-oxidant nutrients**
- **Reduce over-all oxidative stress, which is additive.**
  - Avoid exposure to classical allergens such as pets and pollens as associated with hay fever and asthma.
- **Floral remediation**
  - **Anti-parasitics**, nystatin and other **anti-fungals** and **regular probiotics** are key. Lactobacillus GG especially effective for clostridia. Some stool overgrowths may require specific antibiotics;
  - antibiotics generally should be avoided to promote healthy flora.
- **Address food intolerance**
  - **Avoid aggravating foods** to halt IgG (and IgE) reactivity to food antigens which keeps the bowel inflamed.
  - Gastrocrom, quercitin, EPA (fish oil), vitamins C and E all quiet inflammation.
- **Digestive enzymes** with all meals and snacks.
- **Avoid NSAIDS** (non-steroidal anti-inflammatory medication) to lessen leaky gut.
- **Glutamine** as nutrient for the enterocyte.
- **Decrease toxic burden**
  - **Organic food** free of insecticides, antibiotics, flavor enhancers, artificial sweeteners, colors, and preservatives.
  - **Purified water**, clean home and school environments.

- Assure **bowel regularity** (fiber, magnesium citrate, vitamin C, bethanecol) to reduce toxins. The autistic child should eat regularly, several meals per day.
- **Detoxification with DMSA / lipoic acid**
  - Precede by nutritional and gut enhancement.
  - Floral influence on metals retention may be significant.
  - Fluctuations in dysbiosis may be related to changes in heavy metals levels.
- **Outcomes**
  - Autistic children respond to improved nutrient status and reduction of microbial overgrowths, aggravating food antigens, ingested toxins and body burdens of toxins, all of which decrease oxidative stress on gastrointestinal tissue and reduce inflammation.

## Future directions

**Stool mercury levels**, or differences in **species** of mercury in stool are of interest and stool mercury levels are relatively inexpensive. Mercury metabolism and sulfate reduction in the gut flora may be linked, maybe even via **mucin degradation**. Mercury metabolism in the gut may generate **toxic sulfides**. Antibiotic exposure may select mercury-resistant flora with detrimental mercury-metabolizing traits. Common mercury **methylators include candida, staph, strep and E. coli**. Mercury volatilizers may emerge after antibiotic exposure.

**Small Bowel Overgrowth (SBO)**, for which either stasis or LNH are risk factors, is diagnosed by hydrogen breath-test, which presents a practical challenge in autistic children. SBO may be diagnosable by other means in autism. Microbial action could produce toxic bile acids metabolites in the feces of autistic children. One known bile metabolite, lithocholic acid, is highly toxic in animals, has not been assayed in autism. Sub-groups autistic should be evaluated for excess fecal d-lactate production.

About half of incinerator and fossil-fuel mercury fall-out is in salt form, for which gut has very high binding affinity. This form of inorganic mercury as well as cadmium are concentrated in effluent sludge, used to fertilize food crops. **Intestinal biopsy** may demonstrate higher mercury or cadmium levels in autism, particularly recent regressions.

There is strong logic for **development of a good sequestrant** to bind heavy metal in the gut of autistic children.