



Mending Autism

May 25, 2012

Jerry J Kartzinel MD FAAP

Kartzinel Wellness Center
www.MendingAutism.com
 16263 Laguna Canyon Road
 Suite 150, Irvine, CA
 (949) 398-7654



We Treat: Underlying Medical Problems

DIAGNOSE AND MANAGE

- GI ISSUES
- SLEEP ISSUES
- ALLERGIC ISSUES
- IMMUNE ISSUES
- NEUROLOGIC and PSYCHIATRIC ISSUES
- ENDOCRINE ISSUES
- INFLAMMATORY AND OXIDATIVE ISSUES
- TOXIC ISSUES



Physical Signs Long Forgotten:

- **Case 1:** "Eating has always been a problem for him. He has never shown a normal appetite."
- **Case 2:** "...large and ragged tonsils."
- **Case 3:** diarrhea and fever following smallpox vaccination healthy except for large tonsils and adenoids.
- **Case 4:** vomited a great deal during his first year... feeding formulas were changed frequently ... tonsils were removed...
- **Case 5:** nursed very poorly ... quit taking any kind of nourishment at three months... tube-fed five times daily up to one year of age...At camp she slid into avitaminosis and malnutrition but offered almost no verbal complaints."
- **Case 7:** vomited all food from birth through the third month....
- **Case 8:** feeding formula caused ...concern. ... colds, bronchitis, streptococcus infection, impetigo...
- **Case 9:** none of the usual children's diseases."
- **Case 10:** frequent hospitalizations because the feeding problem ... repeated colds and otitis media
- **Case 11:** was given anterior pituitary and thyroid preparations for 18 months

Leo Kanner 1943



Autism: Parents Perspective

- Mismanagement of incoming stimuli:
 - External environment
 - The five senses which bring information to the brain
 - Internal environment
 - Response to the senses
 - Regulation of the response to the stimuli
 - Inappropriate response to internal cues
 - Responses are all biochemically mediated!



The Main Ingredients



- Case History
- Overall approach
- Team work, education
- Broad picture
- Patterns
- Details
- Biochemical aberrations



Parent's Concerns

- Foul smelling loose yellow green stools
- Bloating belly
- No language
- NOT SLEEPING: hard to get down, mom has to sleep with him
- Does not do well with running errands as he tantrums with each transition
- Covers ears
- Strange "eeeeee" sounds
- Tantrums severely, sometimes triggered, sometimes no clue
- Fevers can come and go
- Not potty trained, no interest
- Odd body movements



Commonly Seen During an Office Visit

- Poor eye contact
- Non-stop moving
- Climbing on everything
- Language deficit
- Repetitive play on office Brio train
- Restricted diet: loves bread, cheese, juice, milk, chips (grazing in office)
- Physical exam:
 - Dark circles below eyes
 - Dry, pale, translucent skin
 - Dull hair, straw-like
 - White tongue
 - Dilated pupils
 - Low muscle tone
 - Tender “mass” in LLQ
 - Enlarged lymph nodes



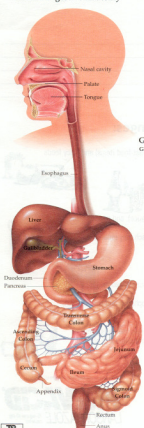
Listing What's Biologically Different

- **Gut Problems**
 - Inflammatory Bowel Disease
 - Reflux Esophagitis
 - Gastritis
 - Dysbiosis
 - Leaky gut
 - Malabsorption
- **Immunologic**
 - Persistent Viral/bacterial Infection
 - Food allergy
 - Recurring illnesses
 - Auto immune
 - Inflammation
- **Neurologic**
 - Seizures/Sensory Issues
 - Low muscle tone- especially trunk
 - Perfusion Defects- SPECT
 - Opiate effect
- **Metabolic/Detoxification Pathway Disruption**
 - Purine disorders
 - Elevated ammonia
 - Omega 3 deficits
 - Sulfation defect
 - Methylation disorders
 - Serotonin/Melatonin deficit
 - Dopamine defect
 - Heavy metal burden
- **Chromosomal issues**



Time to Translate Physical Findings Into Meaningful Medical Interventions

Normal Digestive Anatomy



Genetics Let's Look at One Pathway: The Methylation Pathway

- The methylation pathway is an intracellular biochemical pathway, that moves a carbon group (CH_3) that ultimately produces a MAJOR antioxidant, glutathione
- Individuals who are genetically programmed to poorly methylate are a set up for a host of different disease entities



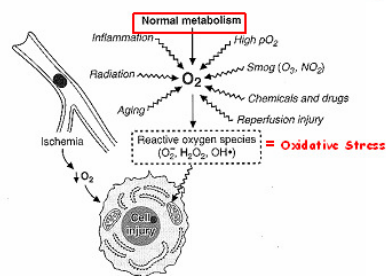
Defects in Methylation: decrease in glutathione production

- Alcoholism
- Bipolar disease
- Schizophrenia
- Depression
- Attention deficit disorder
- Autism
- Constipation
- Diabetes
- Cardiovascular disease
- Thyroid dysfunction
- Neuro-inflammation
- Multiple sclerosis
- Alzheimer's
- Parkinson's



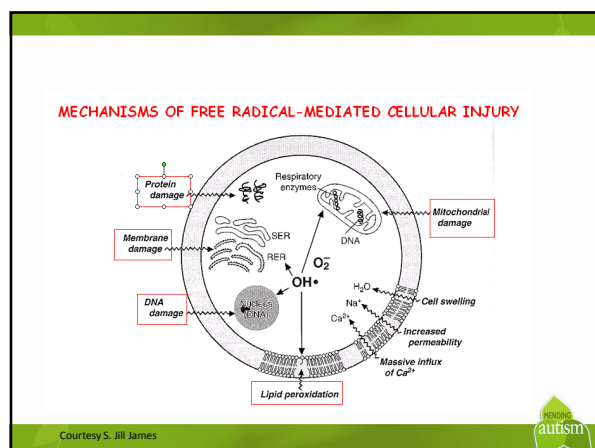
Physiology: Mechanisms of Cell Injury

SOURCES OF OXYGEN FREE RADICALS AND CELL INJURY



Courtesy S. Jill James

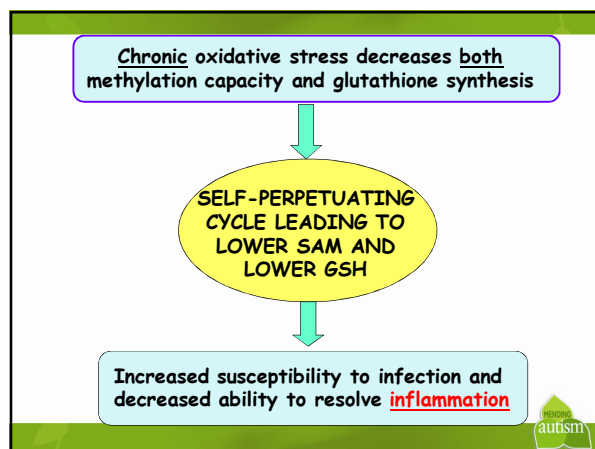




Comparison of methionine cycle and transsulfuration metabolites between autistic children and control children¹

	Control children (n = 33)	Autistic children (n = 20)
Methionine (μmol/L)	31.5 ± 5.7 (23–48)	19.3 ± 9.7 (15–25) ²
SAM (nmol/L)	96.9 ± 12 (77–127)	75.8 ± 16.2 (68–100) ²
SAH (nmol/L)	19.4 ± 3.4 (16–27)	28.9 ± 7.2 (14–41) ²
SAM:SAH	5.2 ± 1.3 (4–8)	2.9 ± 0.8 (2–4) ²
Adenosine (μmol/L)	0.27 ± 0.1 (0.1–0.4)	0.39 ± 0.2 (0.17–0.83) ⁴
Homocysteine (μmol/L)	6.4 ± 1.3 (4.3–9.0)	5.8 ± 1.0 (4.0–5.8) ²
Cystathionine (μmol/L)	0.17 ± 0.05 (0.1–0.27)	0.14 ± 0.06 (0.04–0.2) ²
Cysteine (μmol/L)	202 ± 17 (172–252)	163 ± 15 (133–189) ²
tGSH (μmol/L)	7.6 ± 1.4 (3.8–9.2)	4.1 ± 0.5 (3.3–5.2) ²
Oxidized glutathione (nmol/L)	0.32 ± 0.1 (0.11–0.43)	0.55 ± 0.2 (0.29–0.97) ²
tGSH:GSSG	25.5 ± 8.9 (13–49)	8.6 ± 3.5 (4–11) ²

¹ All values are $\bar{x} \pm SD$; range in parentheses. SAM, S-adenosylmethionine; SAH, S-adenosylhomocysteine; tGSH, total glutathione; GSSG, oxidized glutathione.
²⁻⁵ Significantly different from control children: ² $P < 0.001$, ³ $P < 0.01$, ⁴ $P < 0.05$, ⁵ $P < 0.002$.



Methylation Defects: therapeutic intervention

- Methyl B 12 appears to work best when given sub-cutaneously, by the parents (this is a prescription). We tend to add folic acid and N- acetyl cysteine to the injection.
- TMG or DMG
- Folic/folinic acid
- Glutathione transdermally twice daily is prescribed as well

Consequences of Abnormal Immune Shifting

Clinical Clues to Immune Dysregulation	Evidence of Immune Dysregulation
<ul style="list-style-type: none"> • Allergic Shiners • Eczema • Fungal skin infections • Oral thrush • Molluscum contagiosum • Warts • Scratch/itch 	<ul style="list-style-type: none"> • Autoimmunity markers • Increased IgE • Abnormal natural killer cell function • IgG, IgA, IgM deficiency • Low WBC counts • T cell abnormalities

Consequences of Abnormal Physiologic Functions:

- Immune System- shift toward allergy and autoimmunity
- **Gastrointestinal- stripping the gut of its ability to keep foreign things inside, dysbiosis, inflammation, maldigestion**
- Neurologic- inflammation, alterations in serotonin, dopamine, norepinephrine
- Endocrine: abnormal feedback controls of the thyroid, adrenal, pituitary glands, and many other glandular functions

Gut Disorders in Autism

Historical Clues:

Difficulty breastfeeding
Persistent Colic
Gastro-esophageal reflux
Infantile eczema
Food sensitivities
Failure to thrive
Frequent antibiotics (abnormal flora)
Abnormal posturing
Self injurious behavior
Poor sleep

Physical/Lab Clues:

Abnormal stools
Abnormal cytokine profile
Lymphonodular
Hyperplasia of ileum
Esophagitis
Gastritis



When bowels improve.....

- Stools improve
- Sleep improves
- Eye contact improves
- Word approximations may start
- Tantrums improve
- Appetite improves; trying new things
- Just seems "happier in the skin he/she is in"
- Health improves



Abnormal Bowels



- Soiling
- Constipation
- Diarrhea
- Anorexia
- Nocturnal awakenings
- Reflux
- Foul Smelling Stools
- Foul Smelling Breath
- Protuberant Belly



Laboratory Evaluation

- Urine Organic Acids
- Urine Opiates/Peptides
- Comprehensive Stool Cultures and Parasitology
- Food Sensitivity Profile
- Inflammatory Markers, ie IBD profile, CRP, ESR, Calprotectin
- Yeast
- Dysbiotic Bacteria
- Parasites
- Overall digestion
- X ray/KUB
- Endoscopy



Undigested Food in Stool

- **Gastrointestinal Abnormalities in Children with Autistic Disorder**
- **RESULTS:** Histologic examination in these 36 children revealed grade I or II reflux esophagitis in 25 (69.4%), chronic gastritis in 15, and chronic duodenitis in 24. The number of Paneth's cells in the duodenal crypts was significantly elevated in autistic children compared with non-autistic control subjects. Low intestinal carbohydrate digestive enzyme activity was reported in 21 children (58.3%)
- Horvath K, Papadimitriou JC, Rabstzyn A, Drachenberg C, Tildon JT. J Pediatr 1999 Nov;135(5):559-63. Department of Pediatrics, University of Maryland School of Medicine, Baltimore, USA. PMID: 10547242 [PubMed - indexed for MEDLINE]



Very Large Stools

- **Constipation With Acquired Megarectum in Children With Autism**
Conclusions: Constipation is a frequent finding in children with gastrointestinal symptoms and autism, particularly in the rectosigmoid colon, often with acquired megarectum.
- PEDIATRICS Vol. 112 No. 4 October 2003
Nadeem Afzal, MRCPCH*; Simon Murch, PhD*; Kumran Thirrupathy, MBBS*; Leslie Berger, FRCP†; Andrew Fagbemi, MRCPCH*; and Robert Heuschkel, FRCPCH



Large Amount of Flatulence

- Fermenting organisms
- Incomplete breakdown of polysaccharides
- Air swallowing
- Old stool



What is Stool?

- 10 parts water
- 1 part bacteria
- 1 part fiber
- 1 part mucous, fat, dead cells, protein



Soft Serve

- Poor absorption and digestion
- Fructose
- Lactose
- Gluten/sprue



Snake Stools

- Baring down against a partially closed sphincter
- Straining



Pebble Stool

- Small pebbles often result due to the lack of fiber.
- Decreased fluid intake



Rainbow Stools

- Yellow: fat in stool
- Red: blood, beets
- Green: GI infection
- Black: blood, Bismuth, iron
- White/grey: lack of bile flow
- Reddish-black: intussusception (currant jelly)



Diarrhea

- 1-6 (or more) liquid movements per day
- Some can be explosive
- Can be very foul
- Can have varied colors



Management of Diarrhea

- Diet: remove gluten, dairy, consider removing fruits and fruit juices
- Digestive Enzymes
- Antibiotics
- Antifungals
- Antiparasitics
- Zinc: adding 20-60mg per day
- Fiber: soluble 1 to 4 tsp per day



Constipation

- Can be daily to once weekly
- Can be small balls, pellets, to soft ball sized
- Very foul smelling
- Don't forget about Hirschsprung's Disease



Treatments for Constipation

- Enemas daily for up to a week if necessary
- Glycerin suppository
- Polyethylene glycol
- Aloe
- Fiber (may require larger amounts)
- Vitamin C 2000-10,000mg daily as tolerated (buffered)
- Magnesium 200-600mg as tolerated
- Magnesium citrate
- Water soluble contrast enema (in radiology suite)
- Admit, NG tube, etc



Fiber

- **Soluble Fiber** helps prevent [constipation](#), which in turn, diminishes the potential for dysbiosis.
- Fiber choices:
KH Fiber mixes easily with drink and virtually undetectable



Dysbiosis

- Stools studies can give information of many aerobic overgrowths as well as current probiotic bacterial counts
- Urine organic acid studies can give information on anaerobic bacterial growth
- Fungal cultures with sensitivities will point to antifungal medication preferences
- Parasitology studies, when positive, can help with therapeutic interventions



Treatment for Bacteria:

Gram Negative Bacteria and Some Parasites

- Metronidazole and Metronidazole Benzoate (suspension form of metronidazole) 30mg/kg/d divided three times daily for 7-10 days
- Nitaoxanide suspension: use published tables for 3 days...or longer



Inflammatory Bowel Disease

- Mesalamine: individual dosing, starting with 250mg twice daily.
- Budesonide 3mg twice daily for up to 8 weeks
- Oral steroids
- Dietary changes
- Regular bowel movements
- Zinc 40-60 mg per day
- Purified distilled Aloe
- Fiber
- Probiotics



Inflammatory Bowel Disease

- Antiviral therapies
- IV Immunoglobulin therapy
- Curcumin
- Omega 3's
- Pain/discomfort management such as compounded ibuprofen
- Pyruvate



Reflux

- This is a common allergic/noxious stimuli response
- Associated with otitis media, sinusitis, asthma
- Dietary changes help
- Antacids: promote healing
- Gastric motility/constipation



Reflux Treatments

- Remove exogenous allergens
- Famotidine 20 to 40 mg once daily
- Ranitidine 5-10mg/kg/day divided twice daily
- Omeprazole 5-10kg give 5mg per day, 10-20kg give 10mg per day, over 20 kg, give 20mg per day
- Cimetadine 20-25mg/kg divided in 4 doses
- Esomeprazole : 1-10yrs 10mg once daily, 11yrs and older, 20-40mg once daily



Dietary Recommendations

- Removal of dairy: that's anything that comes from a cow's udder! No casein, whey, etc
- Removal of Gluten is next
tacanow.org
gfcfdiet.com
- Selective removal of specific foods your child may be sensitive to
- True addictions may make these transitions difficult!



Diets

- There are many, many different diets
- The **best** diet: the one that works for your child
- Laboratory investigations can point direction
- Trial and error may be the only way to find out what really works for your child
- As organic as possible, cook from “scratch”
- Medically prescribed diets are a tax deduction!!



Eicosanoids as Inflammatory Mediators – the Sugar Link to Mood and Bad Behaviors.

- Generally underemphasized influence, over the inflammatory response in your child, is the eicosanoid pathway.
- the consumption of certain fats and/or sugar (starch/carbohydrates) influences the production of these inflammatory mediators (Diet Link)
- Vascular effects of eicosanoids, are likely part of the observed perfusion (blood flow) abnormalities in autism



Primary Goals of Supplementation

- **Optimization of Normal Physiology**
- **Improve Function of the Immune System**
- **Enhance Cognitive Abilities**
- **Improve Red Cell Membrane Function**
- **Reduction of Autistic Behaviors**
- **Improve Gastrointestinal Function**
- **Minimize our NEGATIVE genetic influences**



Starting with Nutritional Supplements

- Vitamins and Minerals: need replenishment due to usual self limited diet
- Digestive Enzymes: well known and well described deficiency
- Omega 3's: crucial to start these
- Soluble Fiber: very important for bowel health



Vitamins

- **Vitamins:** Vitamins are micronutrients that are critical for normal cellular metabolism and function. They must be consumed regularly as our bodies are not able to synthesize these vital nutrients in sufficient amounts. Vitamins are required for proper cell signaling, mediators of cell growth, as antioxidants, and even as hormones
- We recommend KH Multivitamins with Minerals



Minerals

- **Minerals:** The main electrolytes are Sodium, Potassium, Calcium, Magnesium and Chloride. Proper levels of these minerals in the body allow the body to have energy, better muscle and nerve function (including faster stress recovery) and improved function in many other areas. The so called trace minerals (such as selenium, iodine, chromium, magnesium, molybdenum, just to name a few) need to be replenished daily, ideally through the diet.



We have to address the Vitamins and Minerals

ELEMENTS	RESULT	REFERENCE RANGE	PERCENTILE (50%)				
			25 th	50 th	75 th	84 th	97 th
Calcium	24	8 - 11					
Magnesium	43	36 - 64					
Potassium	77	65 - 95					
Phosphorus	595	480 - 745					
Copper	0.7	0.52 - 0.89					
Zinc	7.7	0 - 14.5					
Iron	794	745 - 1050					
Manganese	0.015	0.007 - 0.33					
Chromium	0.021	0.012 - 0.37					
Selenium	0.15	0.13 - 0.33					
Boron	0.09	0.005 - 0.11					
Vanadium	0.0011	0.001 - 0.002					
Molybdenum	0.0009	0.0005 - 0.002					



Digestive Enzymes

- **Digestive Enzymes** break down the foods that we eat into smaller compounds that can be readily absorbed and put into the blood-stream. The enzyme class of proteases breaks down proteins to amino acids. The enzyme class of lipase is responsible of breaking down fats to fatty acids, and the carbohydrases break down carbohydrates into simple sugars.
- We recommend KH Enzymes



Omega 3's

- **Omega 3** : the fatty acids, maintain the fluidity and stability of cell membranes and protect the body from harmful substances such as bacteria and viruses. They must be obtained through diet or supplementation with EFA-rich food oils.
- They have an amazing affect on behaviors, mood, focus and concentration.
- We recommend KH Omega Oil



Consequences of Abnormal Physiologic Functions:

- Immune System- shift a balance between TH1 and TH2 heavily to TH2 (allergy and autoimmunity)
- Gastrointestinal- stripping the gut of its ability to keep foreign things inside, dysbiosis, inflammation, maldigestion
- Neurologic- inflammation, alterations in serotonin, dopamine, norepinephrin
- **Endocrine: abnormal feedback controls of the thyroid, adrenal, pituitary glands, and many other glandular functions**



Thyroid Symptoms

- Lethargy
- Abnormal weight gain
- Constipation
- Mental slowness
- Dry skin
- Thin hair
- Poor growth parameters



Thyroid

- Labs: T3 Free, T4 Free, TSH, reverse T3
- Many aberrations found with feedback control
- Ideally, TSH is considered normal if falls within 1.0 and 2.0
- Insure daily amount of Iodine:
Children Tolerable Upper Intake Levels (UL):
200mcg/day for ages 1-3 years; 300mcg/day for 4-8 years; 600mcg/day for 9-13 years; 900mcg/day for 14-18 years
- Use compounded porcine thyroid for replacement/augmentation as indicated
- Remove sources of fluoride, chlorine



Sleep:

Decreased Melatonin Activity

- Subgroup of children with very poor sleep cycles in autism
- Biol Psychiatry 1990 Nov 1;28(9):773-93. **A novel biochemical model linking dysfunctions in brain melatonin, proopiomelanocortin peptides, and serotonin in autism.**
Chamberlain RS, Herman BH



Sleep

- Melatonin: 1-3mg before bedtime (Start with lower dose, also useful in chronic pain)
- 5-HTP: 100mg 5-hydroxytryptophan before bedtime. Especially useful when taken with vitamin B6 and magnesium
- Calcium/magnesium: can really be helpful
- Vitamin D3 1000 IU and up
- GABA 125mg or Gabapentin
- Cortisol replacement
- Vitamin B6/niacinamide: 50mg B6 and 500 mg niacinamide before bedtime
- Pantothenic acid (Vitamin B5): 50 mg daily. (good for relieving stress)
- Inositol: 100-1000mg daily (Enhances REM sleep)
- Herbs: milk thistle, valerian, chamomile tea



Sleep

- Benadryl dye free/compounded 1-2mg/kg
- Ibuprofen 10mg/kg
- Clonidine 0.1mg: ¼ -2 tabs at bedtime
- Trazadone: 0.75mg-1mg/kg at bedtime
- Risperidone: 0.25mg-1mg at bedtime
- Buspirone: 2.5mg -5 mg divided twice daily
- Synthesized Tetrahydrocannabinol 2.5mg 1-3 times per day
- Clonazepam: 0.01-0.03 mg/kg/d divided three times daily
- HBOT
- Neurontin



Inflammation

Disease States

- Allergies
 - environmental sources
 - food sources
- Reflux disease
- Small bowel disease
- Large bowel disease
- Chronic viral activation
- Low grade bacterial infections

Laboratory Findings

- Inflammatory markers: elevated platelets, elevated erythrocyte sedimentation rate, elevated C-reactive protein
- Endoscopy/pathology findings
- Viral titers: HHV 1,2,6, and CMV, EBV
- Stool cultures, anaerobic markers



Inflammation

Allergies

- Claritin Redi-Tabs
- Zyrtec
- Singulair
- Nasonex
- Gastrocrom
- Quercetin
- Provocation-Neutralization-Desensitization
- LDA

Inflammatory Bowel

- Antacids
 - Nexium
 - Prilosec
 - Pepcid
- Anti-inflammatories
 - Colazal
 - Pentasa
 - Rowasa
 - Steroids
 - 6 mercapto purine



Inflammation

Infections

- Antibiotics
- Antifungals
- Antiparasitics
- Antivirals

Anti-inflammatory

- Motrin/Advil
- Celebrex
- Naprosyn
- Actos
- Steroids
- LongVida/Neuroprotek
- Natural agents
 - Curcumin
 - Omega oils
 - Pycnogenols



In Summary

- Prioritize what needs to be done: dietary changes, sleep, and treatment of the bowel issues is always a good place to start
- Maximize nutrition: organic foods and supplements
- Then target issues such as allergies, inflammation, chronic infections, focus/concentration, language development, etc.

