Autistic Spectrum Disorders
And Intestinal Health
MIND THE GUT

MINDD
Sydney, Australia
August, 2011
Nancy O’Hara, M.D.
www.ihealthnow.org

Vicious Cycles

Intestinal Inflammation and Malabsorption

GI/Autism Issues: How Prevalent

GI/Autism: How Prevalent?

GI Symptoms: Prospective Studies
GI/Autism Issues: How prevalent

- MGH/Vanderbilt review of the AGRE database supports high frequency of GI issues
- In 460 children, 385 ASD, 75 unaffected siblings - frequency of GI complaints is 43% in ASD vs. 4% in unaffected siblings
- This compares to previous reports of higher prevalence than “controls”

Specific Conditions

- Problems seen in children with ASD
  - Gastroesophageal Reflux
  - Food allergy
  - Irritable Bowel Syndrome
  - Colitis
  - Constipation/Motor disorder

Pathological Mucosal Alteration Observed with Autistic Subjects

- Increased size and number of lymphoid follicles particularly in ileum
- Merging of lymphoid follicles
- Luminal infiltration of neutrophils, and eosinophils
- Crypt cell proliferation
- Ulceration of epithelium*
- Thickening of basement membrane
- Decreased production of brush border associated digestive enzymes
- Up-regulated Th2 and Th1 response.

All above responses are consistent with the establishment of a chronic inflammatory condition.

What do we see?

- Bloating, gassy
- Constipation – huge, hard stools; small pebbles; infrequent
- Diarrhea, encopresis
- Muscle wasting and failure to thrive
- Foul smelling stools and gas
- Foul breath, body odor, foul stools
- Pain or pain behaviors, SIB
- Posturing
- Irritability (especially just prior to bowel movements)
- Probing and smearing
- Behavioral changes

Extra-esophageal Symptoms of GERD in Children

- Hoarseness
- Dental erosions
- Otitis/sinusitis
- Extra Esophageal Manifestations of GERD
- Chronic sore throat
- Apnea/bradycardia
- Chronic Cough
GERD and Autism

- Russell (1989) reported 2 patients with SIB unresponsive to psycho-pharmacological intervention who had resolution on antiemetics.
- Horvath (1999) evaluated 36 patients: 69% had Grade 1-2 esophagitis histologically.
- Lindsay (2001) described 4 of 9 children randomized to famotidine (Pepcid) therapy showed improved behavior.

Food Allergy

- Food allergy is common, 5-8% prevalence in pediatric patients (Sampson, 1999).
- Food allergy is reported in 36% of autistic children (Lucarelli, 1995).
- Food allergy may present as skin rash, GI symptoms of diarrhea, pain and constipation and behavioral changes.
- Up to 50% of surveyed families report their autistic children had a food allergy or sensitivity (Horvath 2002).

Mechanisms by which it contributes to symptoms:
- Inflammatory effect
- Pain
- Chemical mediator release and altered neurotransmission, histamine, cytokines and opioid effect.

Gluten and Casein in Autism

- In patients with co-morbidity of celiac disease and autism, improvements in autistic symptoms coincide with exclusion of gluten and deteriorate again when gluten is reintroduced (Goodwin et al 1971).
- Elimination of milk and gluten from the diet resulted in improvement in social, cognitive and communication skills, commensurate with reduction of urinary exorphin level. (Knivsberg et al 1990)
- Elder et al (J. Autism Dev Disorders 2006) double blind crossover in 12 week study of 15 children with ASD no benefit [parents reported benefits not identified by study].

Allergy Testing

- All allergy testing has limited accuracy.
- IgE tests (skin test, RAST blood tests and patch testing) can be negative even if clinical symptoms of food allergy.
- IgG tests and IgE tests can be positive but not correlate to a clinical symptom.
- Any testing is a guide to think about what foods may be worthy to consider a problem.
Upper GI Problem
- Gastro-esophageal Reflux
- Gastritis/Peptic Ulcers
- Allergic Esophagitis/Gastritis/Enteritis
- Delayed Gastric Emptying/Motility disorder
- Intestinal or pancreatic malabsorption
- Inflammatory Bowel Disease
- Overgrowth of microbes (bacteria etc.)

Lower GI Problems
- Chronic Recurrent Abdominal Pain
- Irritable Bowel Syndrome
- Constipation
- Diarrhea
- Colitis
- Toilet training issues

Irritable Bowel Syndrome
- Irritable Bowel Syndrome (IBS) is a motor and sensory condition of the colon, an example of visceral sensitivity
- Abdominal pain +/- constipation +/- Diarrhea
- Painful stimuli outside the bowel are tolerated better than in patients without IBS; but bowel distention or contraction may be excruciating
- This makes IBS a "sensory processing disorder of bowel"

Impaired CHO Digestion and Germogrowth
- Williams, IMFAR 2010 Abstract 130.073
- In AUT-GI subjects, ileal transcripts for the disaccharidases sucrase isomaltase, maltase glucoamylase, and lactase, and the monosaccharide transporter, and glucose transporter 2 were significantly decreased
- This study supports our previous enzymatic findings of disaccharide deficiency and goes further to show associated flora alteration is present
- This supports rational for overgrowth syndrome (so called dysbiosis of bacteria, yeast, clostridia)

Impaired CHO Digestion and Germogrowth
- Bacterial 16S rRNA gene pyrosequence analysis of biopsy material from ileum and cecum revealed significantly decreased Bacteroides, increased Firmicutes and Proteobacteria, and increased Betaproteobacteria in AUT-GI as compared with Control-GI biopsies
- The findings support Dr. Feingold’s work suggesting overgrowth in children with autism

Some Guiding Principles
- What does each child need to:
  - Get
  - Get rid of
  - Treatment pyramid
  - Dietary interventions
  - Correct nutritional deficiencies
  - Treat gastrointestinal problems
What do we need to give to or get out of our children?

- Exercise/Activity
- Basic nutritional changes (change in diet...)
  - Fresh, unprocessed, unrefined, unadulterated, organic (chix, rice)
  - Varied and rotational (try to vary day to day)
  - Non-allergenic (chose which most sensitive to)
  - Protein (every 4-5 hours; not necessarily meat)
  - Vegetable juicing
  - Fermented foods
- 3 R’s (not just as it applies to the gut)
  - Remove – sugars, junk food, preservatives, toxins, germs, allergenic foods
  - Replenish – healing diets, probiotics, enzymes, nutrients, zinc
  - Repair/Restore
    - Oxidative stress (alkalinize, antioxidants, HBOT)
    - Immune modulation (EFAs, gamma globulins)
    - Hormonal (thyroid, adrenal)

Treatment of Constipation

- Fiber
- Fluids
- Exercise, especially swimming
- Vitamin C: 1000-2000 mg/day, sometimes up to 6000 mg/day
- Magnesium Citrate (100-500 mg/day)
- Aloe Vera: 1 oz (children) to 2 oz (teens) (George's Always Active)
- Senna (Smooth Move Tea)
- Oils
- Enemas if impacted

Prescription Treatment for Constipation

- Carnitine (Carnitor)
- Lactulose
- Glycolax (now available OTC)
- Colace (OTC)
- IBS treatments: Fiber, Antispasmodics
- Misoprostil (Miralax)

Core GI Evaluation

- CBC
- ESR
- Iron/Ferritin
- Standard Chemistry Profile including Liver Function
- Vitamin D levels (25 OH)
- Immunoglobulins and subclasses
- Celiac Panel (TTG, Gliadin, HLA)
- Food Allergies (IgG and IgE)

Core GI Evaluation

- Urine Metabolic Analysis (OAT)
- Stool for blood
- Stool for H Pylori
- Stool for culture, ova and parasite, and C Difficile
- Stool for Elastase
- CDSA (beneficial flora, inflammatory markers, absorption markers)
- Abdominal X ray
- Scope

What To Do

- Treat constipation (Mg, Vitamin C, fiber, senna, diet changes)
- Remove stressors (e.g., allergenic foods, gluten, casein, toxins)
- Supply nutrients (e.g., vitamin A & C, zinc, pantothenic acid, folic acid, L-glutamine)
- Supply immunoglobulin production (nutrients, probiotics, saccharomyces boulardii)
- Treat germ overgrowth (bacteria, fungus, parasites)
- Treat inflammation - Anti-inflammatory (Ibuprofen, Mesalamine, Sulfasalazine, Steroids, EFAs, Minocycline)
- Treat underlying conditions (reflux, motility)
What to do
Consequences of Zinc Deficiency

- Limited appetite, decreased taste
- Oxidative stress
- Dysfunctional metallothionein
- Impaired brain function
  - poor short term memory, decreased cognition
- Behavioral changes
  - hyperactivity, aggression
- Acne, canker sores, spots on nails

What to do
Zinc

- Zinc supplementation tightens leaky gap junctions in Crohn’s disease (Sturniolo et al, Inflammatory Bowel Dis., May 2001)
- Piccolinate, Acetate
- Best given at night, alone
- Zinc taste test

What To Do

- Probiotics
  - Discourage pathogens
  - Support digestion
  - Produce SCFAs, reduce pH, synthesize vitamins
  - Control inflammation and promote oral tolerance
  - Encourage peristalsis
  - Minimum of 10 billion CFU/day (50 billion), taken on empty stomach

What To Do

- Saccharomyces boulardii
  - Discourages pathogens, including Candida
  - Stimulates IgA production & mucosal repair
  - Natural yeast, skin of lychee fruit
  - Destroyed by antifungals, not antibiotics
  - Dose: 5 billion cells (250 mg) 2 X day

What To Do: Treat Germ Overgrowth

- Bacteria (history of positive response to antibiotics, OCD, tics)
- Antibiotics
  - Gram Negative bacteria (Klebsiella, Enterobacter)
    - Bactrim
    - Gentamycin
  - Anti-clostridial (smearing, probing, diarrhea after abx, OCD, temper)
    - Metronidazole
    - Alinia
    - Vancomycin
  - If response is significant, may need to extend treatment past 14 days

What To Do – Treat Parasites

- Parasites (bizarre behavior, insatiable appetite, aggression, worse at full moon, picking/biting/itching/grinding/smearing)
  - Blastocystis hominis (treat with Bactrim and Humatin)
  - Probiotics
  - Antiparasitics (Metronidazole, Paromomycin, Mebendazole)
  - Natural remedies (artemesia, pumpkin seeds, coconut)
  - TSO therapy
What To Do – Treat Germ Overgrowth

The Antifungal Parade

(mood swings, inappropriate laughter, thickened nails, sugar cravings, urinary frequency, spaciness)

- Non-absorbable
  - *S.boulardii*: 3 months (at least 3-9/day)
  - Nystatin: 1,000,000 units 4X day
  - Amphotericin B: 250mg 4X day x 10 days, then 500mg 4X day x 10 days

- Systemic
  - Sporanox (Itraconazole): 100mg 2X day x 10 days, then 200mg x 10 days
  - Diflucan (Fluconazole): 5 mg/kg/day up to 200mg day x 10 days, then 400mg day x 10 days
  - Lamisil (Terbinafine): 200mg day x 10 days, then 400mg day x 10 days
  - Nizoral (Ketoconazole): 200mg day x 10 days, then 400mg day x 10 days

May need to extend treatment longer
Follow liver and kidney function at least every 2 months

What To Do – Natural

- Natural Antimicrobials and Antifungals
  - Oil of Oregano (0.2 ml 2x/day)
  - Grapefruit Seed Extract (1/3 adult dose)
  - Caprylic acid (500-1000 mg with meals)
  - Biocidin
  - Berberine
  - Plant Tannins
  - Garlic (1-2 fresh cloves or pills/day)

Allergy Treatment

- Gastrocrom
- Singular
- Digestive Enzymes
- Antihistamines
- Probiotics
- Bioflavinoids

Anti-inflammatory

- Ibuprofen
- Mesalamine
- Sulfasalazine
- Steroids
- Omega-3 essential fatty acids
- Actos, spironolactone, curcumin
- Immune Therapy (TSO, IVIG)

Treatment for UGI Conditions

- For H. Pylori: Antibiotics and a Proton Pump Anti-Acid, course is 2 weeks
- For GE reflux: Anti-Antiacids including H2 blockers like Zantac or Pepcid or Proton Pump Blockers like Prilosec or Prevacid
- Carafate is a topical binding RX
- Motility drugs including Reglan, E-mycin, Baclofen, Carnitine

What Does It Mean

- Digestive enzyme impairment
- Inflammation, leaky gut
- Immune dysreguation → greater susceptibility to germs, inflammation, and food sensitivities → further immune deficiency (vicious cycle)
- Germ overgrowth
The Gut-Brain Axis of Pathology in Autism

Intestinal permeability
Inflammation

In autism patient

Dietary Protein
Defective enzyme/Microbial environment

Opioid peptides excess
Systemic carriage

Low active tissue peptidase with antagonism endorphines

High TNF-α titre
High IL-1 and IL-6 titre
Skewing to Th2
Depression of Th1 immunity
Decreased NK cell
Decreased Th1 CD cell
Decreased IgA

Low sensitivity to pain
Repetitive behavior
Social deficiencies
Genes mutation in Cognitive development

Conclusions

GI issues are common in autism
GI conditions in autism may promote autistic behaviors.
Willingness to consider underlying medical factors in children with autism may impact autism
Ideal methods to identify flora disruption, Inflammatory markers is needed
Treat the child as individual not a label