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Wholistic Pediatrics and Family Care

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Gastrointestinal Issues and Autism

December 2014

Why won't my kid eat?

Medical issues

Sensory Issues

Behavioral Issues

There could be a combination of these

Hunger is not always a motivator to eat.

Medical Reasons for Poor Eaters

- Chronic congestion, making it difficult to breath and eat at same time
 - Motor problems coordinating the feeding activity
 - GERD
 - Gastritis/ulcers
 - Swallowing issues
 - Chronic abdominal discomfort
 - Colitis
 - Celiac Disease
 - Food sensitivities
 - Constipation
-
- Refer to GI or allergy specialist if unable to evaluate or manage

Sensory Reasons for Poor Eaters

Does patient frequently gag?

Does patient have aversions to certain types of tastes, textures, temperatures or colors?

Does patient have other sensory issues?

Does the patient exhibit oral defensiveness.....not wanting to put anything in his/her mouth?

This can be very time consuming to properly manage, consider referring to sensory based OT

Behavioral Reasons for Poor Eaters

- This (along with bowel habits) are one of the few things that kids have “real” control over in their lives.
- Is it difficult to get child to attend to the meal?
- Does the child get easily distracted at the table?
- Does the child frequently get up from the table?
- Does the child know that he will get his food choice eventually if he “holds out”?

- Again, this can be time consuming to manage, consider referral to Behavioral Therapist

What you MUST know about the Autism Gut

- The medical literature supports multiple abnormalities of GI function
- Abnormal ecosystem favoring less variety of organisms = abnormal metabolic pathways provided by the autism gut microbiome
- Interfering organic acids (e.g., HPPHA and toxic phenolic cresol)
- Persistent chronic inflammatory changes in many regions of the gut
- Abnormal motility with GERD and constipation +/- diarrhea present
- Deficient disaccharidase activity = poor digestion of carbohydrates
- Deficient pancreatic enzyme response = secretin deficiency
- “Leaky Gut” = breakdown of zonulin attachments at tight junctions
- Gliadin intolerance unrelated to celiac disease
- IgE allergies and IgG intolerance of many common foods
- **Combining all of these issues together is a major challenge to anyone’s clinical skills**

Gastrointestinal abnormalities in children with autistic disorder

Karoly Horvath, MD, PhD, John C. Papadimitriou, MD, PhD, Anna Rabsztyrn, Cinthia Drachenberg, MD, and J. Tyson Tildon, PhD

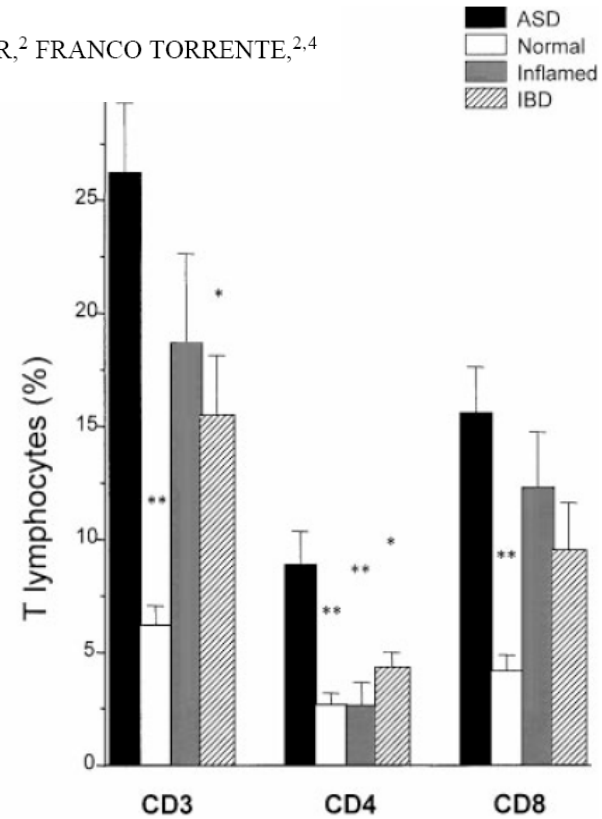
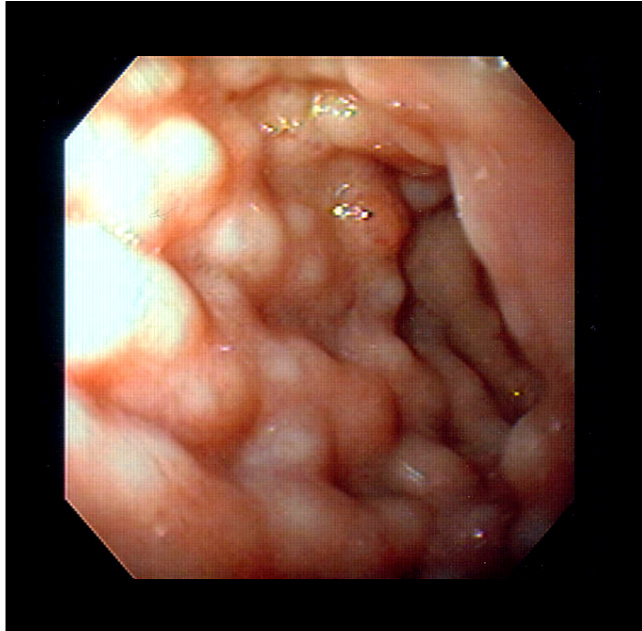
The most frequent gastrointestinal complaints were chronic diarrhea, gaseousness, and abdominal discomfort and distension. Histologic examination in these 36 children revealed grade I or II reflux esophagitis in 25 (69.4%), chronic gastritis in 15, and chronic duodenitis in 24. Low intestinal carbohydrate digestive enzyme activity was reported in 21 children (58.3%), although there was no abnormality found in pancreatic function. CONCLUSIONS: Unrecognized gastrointestinal disorders, especially reflux esophagitis and disaccharide malabsorption, may contribute to the behavioral problems of the non-verbal autistic patients

Horvath et al., 1999 J Pediatr 135(5):559-63

Intestinal Lymphocyte Populations in Children with Regressive Autism: Evidence for Extensive Mucosal Immunopathology

Journal of Clinical Immunology, Vol. 23, No. 6, November 2003 (© 2003)

PAUL ASHWOOD,^{1,2,6} ANDREW ANTHONY,^{1,3} ALICIA A. PELLICER,² FRANCO TORRENTE,^{2,4}
JOHN A. WALKER-SMITH,² and ANDREW J. WAKEFIELD^{1,5}



CASE REPORT

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Clinical Presentation and Histologic Findings at Ileocolonoscopy in Children with Autistic Spectrum Disorder and Chronic Gastrointestinal Symptoms

Arthur Krigsman¹, Marvin Boris², Alan Goldblatt³ and Carol Stott⁴

¹Assistant Professor of Pediatrics, New York University School of Medicine Director of Gastroenterology Services, Thoughtful House Center for Children, 3001 Bee Caves Rd, Austin, Texas, 78746, USA. ²Associate Clinical Professor of Pediatrics, New York University School of Medicine, 550 1st Ave., New York, NY 10016, USA. ³Adjunct Professor Touro College, 27-33 West 23rd St, New York, NY 10010, USA. ⁴Thoughtful House Center for Children, 3001 Bee Caves Rd, Austin, Texas, 78746, USA. Email: drcarolstott@impexus.co.uk

Table 1. Frequency of gastrointestinal symptoms in 143 children undergoing ileocolonoscopy.

Gastrointestinal symptom	n	%
Diarrhea (alone)	83	58%
Constipation (alone)	22	15.4%
Diarrhea (alone, or in combination with constipation)	112	78.3%
Constipation (alone, or in combination with diarrhea)	51	35.7%
Both diarrhea and constipation	29	20.3%
Abdominal pain	85	59.4%
Abdominal distension	30	21.0%
Muroid stool	27	18.9%
Hematochezia	11	7.7%



Esophageal Problems

Symptoms
of
Esophageal
Lesions:
ASD

Irritability and tantrums
Banging on chest
Pointing to throat
Sticking fingers down throat
Pinching throat
Food avoidance
Irritability after meals
Bad breath
Sandifer syndrome

**GASTROESOPHAGEAL REFLUX IN
CHILDREN WITH AUTISM: HOW DO CHILDREN
PRESENT AND CAN ONE TEST
THESE CHILDREN?**

Timothy M. Buie. Pediatric GI, MGH, Boston, MA.

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.

Buie, 2005 J Pediatr Gastroenterol Nutr 41(4):505

Natural Treatments for GE Reflux

- Apple Cider Vinegar – 5 to 15cc in small amount of water before meals
- Aloe Vera Juice – 1 to 2 ounces before meals
- DGL (deglycyrrhizinated licorice) - in chewable tabs or powder before meals
- Digestive enzymes before meals
- Probiotics
- Baking Soda (not baking powder) 5 to 15 cc in 4 ounces of water prn
- Slippery elm and marshmallow root – Lozenges and capsules



Stomach Problems

Symptoms Related to Stomach Issues

Irritability, tantrums
Food avoidance
Posturing
Head banging
Banging / poking stomach
Night time awakening
Vomiting
Sweating / pallor
Reflux symptoms

Agitation and weight loss in an autistic boy

Rachel Conyers¹ and Daryl Efron^{1,2}

An 11 year old boy with autism presented with a 2-month history of agitated behaviour with associated weight loss. On examination he was wasted and distressed. He had severe hypoalbuminaemia. Gastrointestinal imaging revealed a gastric bezoar. At operation a large phytobezoar extending into the jejunum was identified and removed. Postoperatively he required intensive nutritional resuscitation and support, including treatment of multiple micronutrient deficiencies. Malnutrition is common in children with developmental disabilities, with a number of possible contributing factors. Gastric bezoar is a rare cause, which should be considered in mobile children who may engage in pica.



Maldigestion

Intestinal disaccharidase activity in patients with autism: Effect of age, gender, and intestinal inflammation

Rafail I. Kushak, Gregory Y. Lauwers, Harland S. Winter and Timothy M. Buie

Autism published online 17 March 2011

DOI: 10.1177/1362361310369142

Intestinal disaccharidase activities were measured in 199 individuals with autism to determine the frequency of enzyme deficiency. All patients had duodenal biopsies that were evaluated morphologically and assayed for lactase, sucrase, and maltase activity. Frequency of lactase deficiency was 58% in autistic children \leq 5 years old and 65% in older patients. As would be expected, patients with autism at age 5 > years demonstrated significant decline in lactase activity (24%, $p = .02$) in comparison with \leq 5 years old autistic patients. Lactase deficiency not associated with intestinal inflammation or injury is common in autistic children and may contribute to abdominal discomfort, pain and observed aberrant behavior. Most autistic children with lactose intolerance are not identified by clinical history.

Kushak et al., 2011 *Autism*, in press

Gastrointestinal abnormalities in children with autistic disorder

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Horvath et al., 1999 J Pediatr 135(5):559-63

Gluten sensitivity

may not be the sole protagonist in this disease.

Gluten sensitivity as a neurological illness

M Hadjivassiliou

From gut to brain

THE NEUROLOGY OF COELIAC DISEASE

It has taken nearly 2000 years to appreciate that a common dietary protein introduced to the human diet relatively late in evolutionary terms (some 10 000 years ago), can produce human disease not only of the gut but also the skin and the nervous system. The protean neurological manifestations of gluten sensitivity can occur without gut involvement and neurologists must therefore become familiar with the common neurological presentations and means of diagnosis of this disease.

published a landmark study of patients with neurological disease and adult CD.⁸ This systematic review of the literature identified 100 patients with neurological disease and CD. Ten of these patients had peripheral neuropathy. All

Autism and Coeliac Disease

**Giulia Barcia · Annio Posar · Margherita Santucci ·
Antonia Parmeggiani**

Five out of one hundred and fifty subjects (3.3%) were diagnosed with CD on the basis of positive serologic tests and histopathological findings. This is significantly higher ($p = .014$) in comparison to CD prevalence for the general paediatric population of 1:106 (Binomial Test). In conclusion, our data suggest that, within the context of research, the screening for CD is recommended in all children with autism, even if no gastrointestinal symptoms are present.

Association of Family History of Autoimmune Diseases and Autism Spectrum Disorders

Hjördís Ó. Atladóttir, Marianne G. Pedersen, Poul Thorsen, Preben Bo Mortensen, Bent Deleuran, William W. Eaton and Erik T. Parner

Pediatrics 2009;124:687-694; originally published online Jul 5, 2009;

DOI: 10.1542/peds.2008-2445

The study cohort consisted of all of the children born in Denmark from 1993 through 2004 (689 196 children). RESULTS: A total of 3325 children were diagnosed with ASDs, of which 1089 had an infantile autism diagnosis. Increased risk of ASDs was observed for children with a maternal history of rheumatoid arthritis and celiac disease. Also, increased risk of infantile autism was observed for children with a family history of type 1 diabetes. A significant association between maternal history of celiac disease and ASDs was observed for the first time.

Atladdottir et al., 2009 *Pediatrics* 124(2):687-94



Intestinal permeability

Abnormal intestinal permeability in children with autism

P D'Eufemia, M Celli, R Finocchiaro, L Pacifico, L Viozzi, M Zaccagnini, E Cardi and O Giardini

Institute of Pediatrics, "La Sapienza" University of Rome, Italy

We determined the occurrence of gut mucosal damage using the intestinal permeability test in 21 autistic children who had no clinical and laboratory findings consistent with known intestinal disorders. An altered intestinal permeability was found in 9 of the 21 (43%) autistic patients, but in none of the 40 controls. Compared to the controls, these nine patients showed a similar mean mannitol recovery, but a significantly higher mean lactulose recovery (1.64% +/- 1.43 vs 0.38% +/- 0.14; P < 0.001). We speculate that an altered intestinal permeability could represent a possible mechanism for the increased passage through the gut mucosa of peptides derived from foods with subsequent behavioural abnormalities.

D'Eufemia et al., 1996 Acta Paediatr 85(9):1076-9

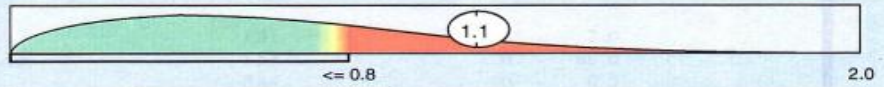
Alterations of the Intestinal Barrier in Patients With Autism Spectrum Disorders and in Their First-degree Relatives

OBJECTIVES: Intestinal permeability (IPT) was investigated in patients with autism as well as in their first-degree relatives to investigate leaky gut hypothesis. **RESULTS:** A high percentage of abnormal IPT values were found among patients with autism (36.7%) and their relatives (21.2%) compared with normal subjects (4.8%). Patients with autism on a reported gluten-casein-free diet had significantly lower IPT values compared with those who were on an unrestricted diet and controls. Gastrointestinal symptoms were present in 46.7% of children with autism: constipation (45.5%), diarrhoea (34.1%), and others (alternating diarrhoea/constipation, abdominal pain, etc: 15.9%).

Intestinal Permeability

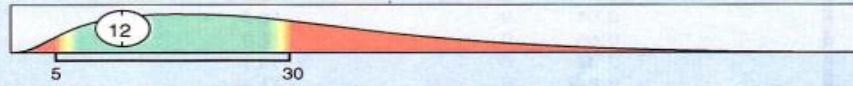
Lactulose Percent Recovery

Ref Range
%



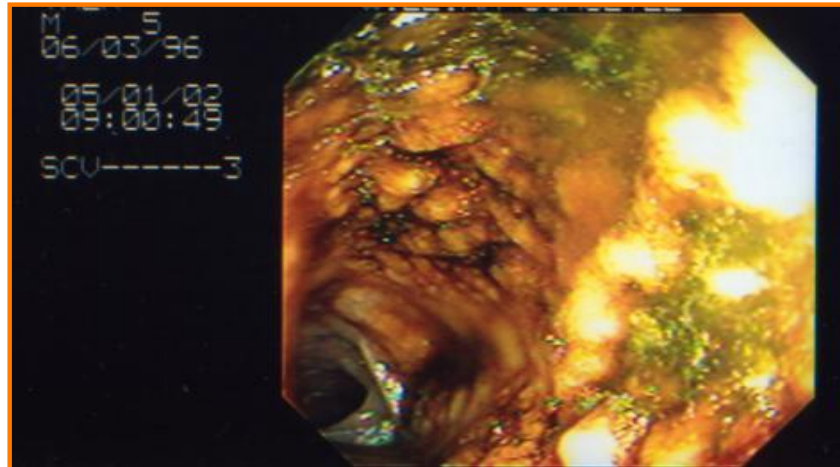
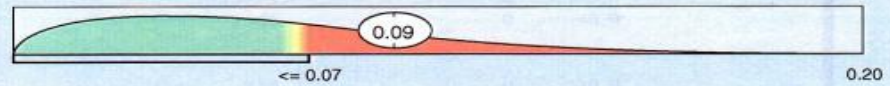
Mannitol Percent Recovery

Ref Range
%



Lactulose/Mannitol Ratio

Ref Range





Constipation

Constipation With Acquired Megarectum in Children With Autism
Nadeem Afzal, Simon Murch, Kumran Thirrupathy, Leslie Berger, Andrew Fagbemi
and Robert Heuschkel
Pediatrics 2003;112;939-942
DOI: 10.1542/peds.112.4.939

Moderate or severe constipation was more frequent in the autistic group than in the control subjects (36% vs 10%). Analysis of recto-sigmoid 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.

Afzal et al., 2003 *Pediatrics* 112(4):939-42



Fluids, Fluids, Flueids

A good clean out (Oxypowder and others)

Magnesium citrate, sulfate, etc

Fiber if inadequate (while maintaining fluids)

Vitamin C

Aloe vera juice

Carnitine

Lactulose

Enemas

Is the Opioid Hypothesis Correct?

Autism and Schizophrenia: Intestinal Disorders

ROBERT CADE*, MALCOLM PRIVETTE, MELVIN FREGLY, NEIL ROWLAND, ZHONGJIE SUN,
VIRGINIA ZELE, HERBERT WAGEMAKER† and CHARLOTTE EDELSTEIN

Departments of Medicine, Physiology, Psychology and Psychiatry, University of Florida, Gainesville, FL 32610-0204, USA

(Received 12 February 1999)

Nutritional Neuroscience, Vol. 3, pp. 57–72

We examined Dohan's hypothesis that schizophrenia is associated with the absorption of "exorphins" contained in gluten and casein. In addition, because of the work of Reichelt *et al.* (Reichelt, K.L., Saelid, G., Lindback, J. and Orbeck, H. (1986) *Biological Psychiatry* 21:1279–1290) and Rodriguez *et al.* (Rodriguez, Trav, A.L., Barreiro Marin, P., Galvez, Borrero, I.M., del Olmo Romero-Nieva, F. and Diaz Alvarez, A. (1994)

A gluten-casein free diet was accompanied by improvement in 81% of autistic children within 3 months in most of the behavior categories. Our data provide support for the proposal that many patients with schizophrenia or autism suffer due to absorption of exorphins formed in the intestine from incomplete digestion of gluten and casein.

Gluten / Casein Peptides Test

Peptides	Peptide (P) ng/ml	Creatinine (C) mg/dl	Relative Ratio (P/C)	Relative Ratio Normal	
Casomorphin (Milk)	175.4	82	2.13	<0.56	H
Gliadorphin (Wheat)	4.8	82	0.06	<0.58	

If either of the peptide results is abnormal, a gluten-free and casein-free diet should be considered for the person who was tested. If both peptide results are normal, further testing with IgG food allergy tests should be done before adopting a diet containing gluten and/or casein. If both peptide and IgG food allergy tests are normal, then the person can probably tolerate gluten and casein but a one-month elimination diet trial without these foods might still be useful.

Children on gluten and/or casein free diets may have normal values of the peptides in urine. Children with high values may benefit from gluten/casein free diets and/or peptidase supplementation. Children with normal peptide values may still have wheat and/or milk allergies that can be detected by allergy tests.

People on a diet containing soy proteins or who are consuming soy "milk" may also have high peptides in their urine. Soy proteins are used as emulsifiers, extenders, binders and stabilizers in meat, poultry, snack foods, sausage, frozen spaghetti, and whipped toppings. Textured vegetable protein (TVP) is soy based and many meat substitutes are soy-based. We have found that individuals on soy may have high values for gliadorphin and/or casomorphin presumably because of peptides from soy that are similar or identical to those in gluten or casein (Zhang XZ, Wang HY, Fu ZQ, WuXX, XuGL. Bioactive small peptides from soybean protein. Ann N Y Acad Sci 1998 Dec 13; 864: 640-5).



Pediatric Gastroenterologist told parents this was nothing to be concerned about. “Normal for child with autism.” Is it?



Krigsman, 2007 Medical Veritas 4:1528-36

Gastrointestinal flora and gastrointestinal status in children with autism -- comparisons to typical children and correlation with autism severity

James B Adams^{1*}, Leah J Johansen¹, Linda D Powell¹, David Quig², Robert A Rubin³

Gastrointestinal symptoms (assessed by the 6-GSI) were strongly correlated with the severity of autism (assessed by the ATEC), ($r=0.59$, $p<0.001$). Children with 6-GSI scores above 3 had much higher ATEC Total scores than those with 6-GSI-scores of 3 or lower (81.5 ± 28 vs. 49.0 ± 21 , $p=0.00002$). Children with autism had lower levels of species of Bifidobacter (-43% , $p=0.002$) and higher levels of species of Lactobacillus ($+100\%$, $p=0.00002$), but similar levels of other bacteria and yeast using standard culture growth-based techniques. The strong correlation of gastrointestinal symptoms with autism severity indicates that children with more severe autism are likely to have more severe gastrointestinal symptoms and vice versa.

Adams et al., 2011 BMC Gastroenterol 11(1):22

Gastrointestinal Symptoms in Children with an Autism Spectrum Disorder and Language Regression

Children with language regression more frequently exhibited an abnormal stool pattern (40% vs 12%, $P = 0.006$) and had an increased family history of celiac disease or inflammatory bowel disease (24% vs 0%, $P = 0.001$) and of rheumatoid arthritis (30% vs 11%, $P = 0.03$). Among 35 children with a family history of autoimmune disease, an abnormal stool pattern was reported more frequently in those with language regression (78% vs 15%, $P = 0.001$) than in those without. An association was observed between children with language regression, a family history of autoimmune disease, and gastrointestinal symptoms

Valicenti-McDermott et al., 2008 *Pediatr Neurol* 39:392-398

Short-Term Benefit From Oral Vancomycin Treatment of Regressive-Onset Autism

11 children with regressive-onset autism were recruited for an intervention trial using a minimally absorbed oral antibiotic. Entry criteria included antecedent broad-spectrum antimicrobial exposure followed by chronic persistent diarrhea, deterioration of previously acquired skills, and then autistic features. Short-term improvement was noted using multiple pre- and post-therapy evaluations. These included coded, paired videotapes scored by a clinical psychologist blinded to treatment status; these noted improvement in 8 of 10 children studied. Unfortunately, these gains had largely waned at follow-up.

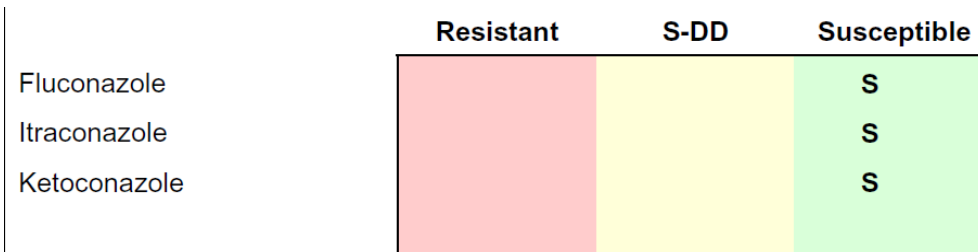
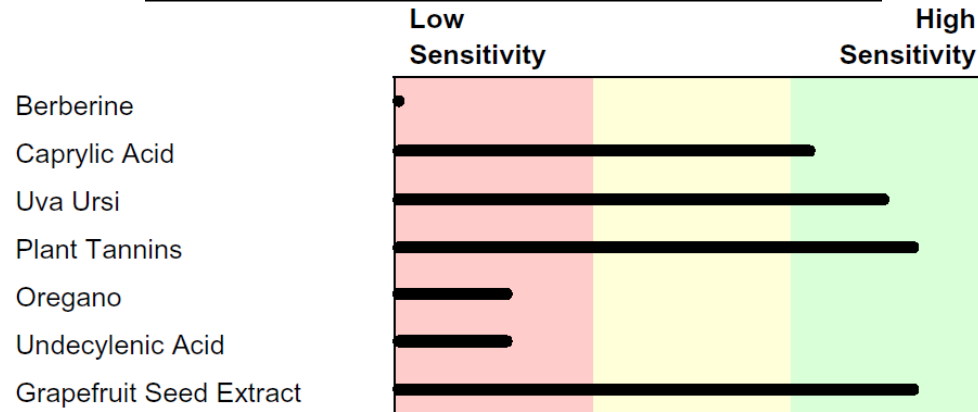
Sandler et al., 2000 J Child Neurol 15(7):429-35

BACTERIOLOGY CULTURE		
Expected/Beneficial flora	Commensal (Imbalanced) flora	Dysbiotic flora
NG Bacteroides fragilis group 4+ Bifidobacterium spp. 3+ Escherichia coli 3+ Lactobacillus spp. 4+ Enterococcus spp. NG Clostridium spp. NG = No Growth		4+ Citrobacter braakii 4+ Klebsiella pneumoniae ssp pneumoniae

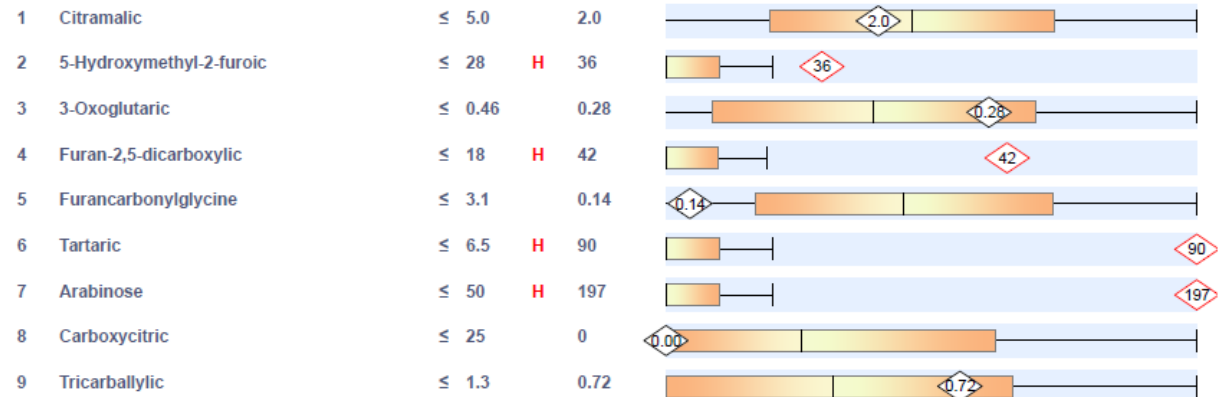
YEAST CULTURE	
Normal flora	Dysbiotic flora
	2+ Candida lusitaniae

MICROSCOPIC YEAST	
Result:	Expected:
Rare	None - Rare
<p>The microscopic finding of yeast in the stool is helpful in identifying whether there is proliferation of yeast. Rare yeast may be normal; however, yeast observed in higher amounts (few, moderate, or many) is abnormal.</p>	

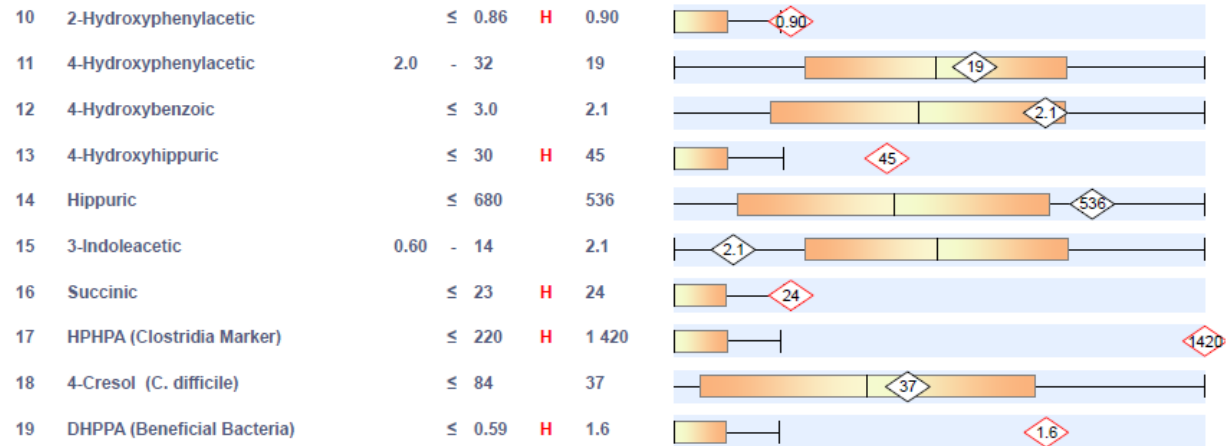
Yeast Susceptibilities: *Candida lusitaniae*



Yeast and Fungal Markers



Malabsorption and Bacterial Markers



Clostridia - Evidence

Increased urinary excretion of a 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA), an abnormal phenylalanine metabolite of Clostridia spp. in the gastrointestinal tract, in urine samples from patients with autism and schizophrenia

Nutritional Neuroscience, Volume 13, Number 3, June 2010 , pp. 135-143(9). William Shaw

- A compound identified as **3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA)** was found in higher concentrations in urine samples of children with autism compared to age and sex appropriate controls and in an adult with recurrent diarrhea due to *Clostridium difficile* infections.

More Clostridia Evidence

Urinary p-cresol in autism spectrum disorder.

Neurotoxicol

Teratol. 2012 Sep 10. Persico AM, Napolioni V.

- Environmental exposure to the organic aromatic compound p-cresol (4-methylphenol) is relatively common and occurs through the skin, as well as the gastrointestinal and respiratory systems. However, the largest and most widespread source of this compound is represented by some gut bacteria which express p-cresol synthesizing enzymes not found in human cells. Potential sources of p-cresol excess in ASD, such as gut infection, chronic constipation, antibiotics, abnormal intestinal permeability, and environmental exposure, are being investigated. P-cresol may contribute to worsen autism severity and gut dysfunction, often present in autistic children. It may also contribute to a multibiomarker diagnostic panel useful in small autistic children.

Treatment Options for Dysbiosis

- There is a general lack of published studies on the treatment of dysbiosis in ASD.
- Rationale for treatment cannot therefore be based on published outcome studies.
- It rather requires **reasoned** care to restore normal fermentation producer balance.
- Intervention would therefore be based on some measure of history, physical and objective (biomarker) findings. **Goal is to remove bad bugs and restore healthy ones** – Easier said than done!

Treatment Options for Dysbiosis: Anaerobic Summary

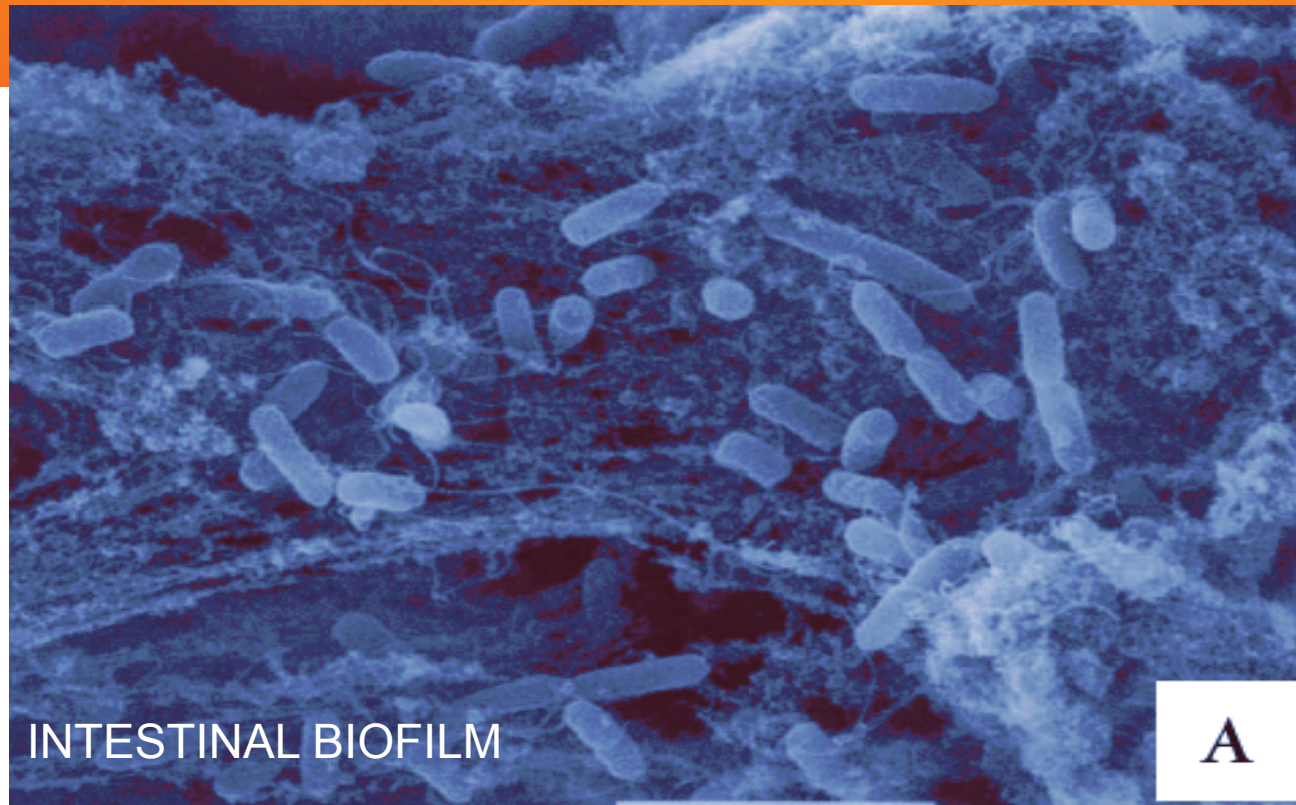
- Hi dose lactobacillus and saccharomyces boulardii.
- Vancomycin, Nitazoxanide, or Metronidazole all offer reasonable approaches.
- Treatment length should be 10 or more days and likely repeated several times since anaerobes are **spore forming** and colonize the child's environment.
- Follow clinical responses as well as appropriate biomarkers on urinary organic acid tests.

Treatment Options for Dysbiosis: Anaerobic Antibiotics – top 3 in my practice

- **Vancomycin:** 125mg tid age 4 and under, 250mg tid >4 y/o.
J Child Neurol. 2000 Jul;15(7):429-35.
- **Metronidazole** (benzoate optional compd liquid) 250 metronidazole = 400 of benzoate version. TID dosing based on 30mg/kg/d of Flagyl.
- **Nitazoxanide** (Alinia[®]) suspension 5-10 ml bid for 10 days – off label (tablet 500mg). Often very effective where others failed, but expensive if not covered by insurance.

Treatment Options for Dysbiosis: Candida

- Pharmacological: Harriet Lane Guide
- Nystatin: no systemic absorption. Need frequent dosing. Consider ORAL powder used for compounding. Liquid high in sugar.
- Azole antifungals: hepatic risks are uncommon but not unknown. Ketoconazole is problematic for numerous drug interactions. Also note the recent FDA Ketoconazole warnings
- Lamisil: 125mg if < 25kg, 187.5mg if 25-35kg, 250mg if > 35kg
- Amphotericin: Not systemic and serious reactions related to IV use are not an issue.



Arq Gastroenterol. 2011 Jul-Sep;48(3):199-204

Dietary Approaches for Normalizing Gut Balance

Specific Carbohydrate Diet - starve out the yeast. Monosaccharides only carbs allowed.

Body Ecology Diet: Optimize the diet so the body can have a natural balance of flora, which maintains/restores intestinal health, and that a healthy intestine is critical for a healthy body. Accomplished via: adding cultured foods, giving good quality fats, and dramatically reducing carb/sugar intake.

GAPS: **1) Heal the gut**, by avoiding all foods that irritate it, and by consuming only foods that will nourish and heal it. **2) Repopulating the gut with beneficial bacteria** by avoiding all foods that feed opportunistic (bad) bacteria/gut flora. Give high quality probiotic foods and supplements, and **3) Get rid of toxins-** by limiting the diet to only foods that can be easily digested and eliminated, by strengthening the gut and the beneficial bacteria so that they can deal with toxins thoroughly, and by fresh juicing to speed up the elimination of toxins.