Nutricia Learning Center

Recognition and Management of Gastrointestinal (GI) and Nutritional Issues in Children with Autism Spectrum Disorder (ASD)

Dr. Timothy Buie
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NUTRICIA

Webinar Presenter:

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Webinar Objectives

1. Recognize the prevalence of GI issues in children with ASD and how these issues may be identified.
2. Describe the most commonly occurring GI symptoms and potential nutritional deficits in children with ASD.
3. Discuss assessment needs and management strategies for children with ASD and GI and/or nutrition issues.
4. Identify 2 ways in which AA-based formula/AA-based semi-solid food may be indicated for children with ASD with GI and/or nutrition issues.

2014 U.S. Autism Prevalence Data

Centers for Disease Control
MMWR Morbidity and Mortality Weekly Report
Surveillance Summaries/Vol 63/No.2 March 23.2014

Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2010

1 in 42 boys have ASD

1 in 189 girls have ASD

CDC Press Release. March 27, 2014
http://www.cdc.gov/media/releases/2014/p0327-autism-spectrum-disorder.html

- ASD is ~5 times more common among boys than girls

Background: Autism diagnosis by DSM V

Must meet criteria A, B, C, and D: (ASD term eliminated)

A. Persistent deficits in social communication and social interaction across contexts, not accounted for by general developmental delays

B. Restricted, repetitive patterns of behavior, interests, or activities

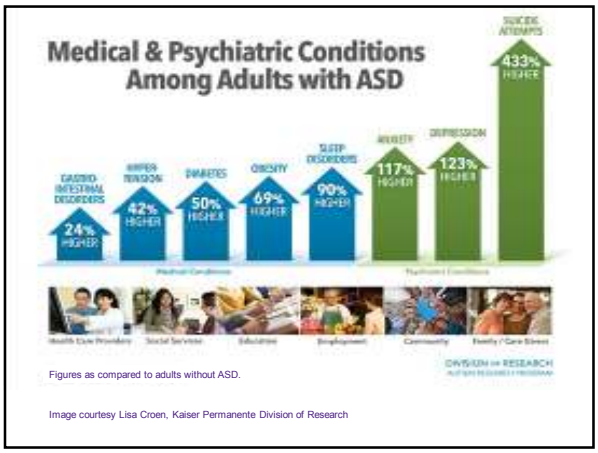
C. Symptoms must be present in early childhood (but may not become fully manifest until social demands exceed limited capacities)

D. Symptoms together limit and impair everyday functioning

Autism is Heterogeneous

Co-morbidity in Autism commonly discussed:

1. Genetic syndromes
2. Associated psychopathology
3. Medical conditions:
   - Epilepsy
   - GI Disorders
   - Food Allergy
   - Immune Dysregulation
   - Catatonia



Medical Issues: GI and Autism

Findings	References
Valicenti-McDermott, 2006, evaluated children with ASD and 2 control groups matched for age, sex and ethnicity (50 children/group) ▪ 70% of children with ASD had GI Issues compared to. . . ▪ 42% of children with developmental disorder other than ASD ▪ 28% of children with typical development	Valicenti-McDermott M et.al. *J Dev Behav Pediatr* 2006 Apr;27(2 Suppl):S128-36.
Horvath, 2002 identified at least one GI complaint in 84% of children with ASD compared with 31% of unaffected siblings	Horvath K et al. *Curr Gastroenterol Rep* 2002 Jun; 4(3):251-8.
Vanderbilt/MGH reviewed the AGRE database in 2009 found higher frequency of GI issues in ASD (385 in ASD compared with 75 in unaffected siblings) ▪ 43% in ASD vs. 4% unaffected siblings	Campbell D et al. *Pediatrics* 2009 (123): 1018-24.
Mazefsky, Minshew et al., 2013 reported that 61% of children with ASD had GI symptoms and associated features of affective and behavioral symptoms	Mazefsky CA et al. *Autism*. 2013. Oct 8; 18(5):493-501.
GI issues in ASD are common and parent-reported concerns correlate well with physician assessment.	Gorrindo P et al. *Autism Res*. 2012 Apr; 5(2):101-8.

Traditional vs. unconventional symptom recognition

Typical Child	Autism/Non-Verbal Child
Hurts to swallow	Intermittent or continuous tantrum, feeding refusal
Hard to swallow	Banging on chest, textural preferences
Something stuck in throat	Pointing to throat, tapping site of distress
Have heartburn Stomach hurts after eating	Irritability after meals or at bedtime
Reports pain	Self-injury, aggression

Odyssey of GI issues and Autism


PEDIATRICS


PEDIATRICS

Medical Issues: GI and Autism

Findings	References
Inflammation	▪ Horvath K et al. *Curr Gastroenterol Rep* 2002 Jun; 4(3): 251-8.
Increased intestinal permeability	▪ D'Eufemia P et al. *Acta Paediatr* 1996 Sep;85(9):1076-9.
Impaired digestion of carbohydrates	▪ Horvath K et al. *Curr Gastroenterol Rep* 2002 Jun;4(3): 251-8. ▪ Kushak RI et al. *Autism.* 2011 May;15(3):285-94. ▪ Williams BL. *PLoS ONE* 2011 6(9): e24585.
Disruption of typical microbiota	▪ Finegold SM et al. *Anaerobe*. 2010 Aug;16(4):444-53. ▪ Williams BL. *PLoS ONE* 2011 *6(9): e24585.* ▪ Kang DW, el al. *PLoS One*. 2013 Jul 3;8(7):e68322.
Altered immune response to inflammation	▪ Ashwood P et al. *Clin Dev Immunol.* 2004 Jun;11(2):165-74

Recent Support for GI - Autism Link

PEDIATRICS

Gastrointestinal Symptoms in Autism Spectrum Disorder: A Meta-analysis
Barbara O. McElhanon, Courtney McCraken, Saul Karpen and William G. Sharp
Pediatrics 2014; 133:872; originally published online April 28, 2014

- McElhanon et al. >3-fold risk of general GI concerns, constipation and diarrhea over the unaffected comparison groups.
- Supports consensus findings (2010) suggesting **access to GI and nutrition experts was extremely valuable to assess possible underlying issues.**

Medical Issues: GI

Prevalence of GERD in Typically Developing Children

- Children ages 3 - 9 years old: 24% have history of symptoms consistent with GERD
- Children ages 10 - 17 years old: 8%-25% experienced GERD symptoms (child or parent report)

Children with Autism have the right to have commonly occurring medical conditions

GERD and Autism:

- Horvath (1999) evaluated 36 patients with ASD and chronic GI symptoms (diarrhea, gas, abdominal pain/distention) by endoscopy
- **69%** had Grade 1-2 reflux esophagitis histologically
  - These patients had no clinical symptoms of GERD reported

Horvath K et al. *J Pediatr.* 1999. Nov;135(5):559-63.

Medical Issues: GI and Autism

Historical Review: hypotheses of causation. . .

Currently unsupported

- **Opioid Peptide Theory:** Reichelt (1991) and Shattock (2002) - peptides from milk and gluten caused childhood schizophrenia (ASD)
- **Autistic Enterocolitis:** Wakefield (1999, 2000) increased intestinal permeability induced by measles virus; caused immune disruption

Reichelt KL. 2002. *Biol Psychiatry.* 1991 Mar 1;29(5):515-7.
Shattock P et al. 2002. *Expert Opin Ther Targets.* 2002 Apr;6(2):175-83.
Wakefield AJ. *Lancet.* 1999 Sept 11;354(9182):949-50.
Wakefield AL et al. *Am J Gastroenterol.* 2000 Sep;95(9):2285-95.
Retraction in: *Am J Gastroenterol.* 2010 May;105(5):1214.

How food might affect Autism

- Celiac Disease
- Carbohydrate maldigestion
- Non-digestible components of food
- Food allergy
- Altered intestinal flora
- Altered intestinal permeability

Medical issues: Food Allergy US. Population and Autism

Findings	References
6-8% pediatric food allergy prevalence	Gupta RS, et al. *J Pediatr.*2011; 128.
Food allergy may be 2X more common in boys	Liu AH et al. *J Allergy Clin Immunol.*2010; 126: 798-806.
Food allergy was reported in 36% of 36 children with ASD	Lucarelli S et al. *Panminerva Med.* 1995 Sep;37(3):137-41
Families report their children with ASD had a food allergy or sensitivity in over 40%	Horvath K et al. *Curr Gastroenterol Rep.* 2002 Jun;4(3):251-8
Higher frequency of IgE mediated food allergy in children with ASD compared to unaffected siblings	Trajkovski V et al. *Focus Autism Other Dev Disabl.* 2008;23: 176–185

Sensitivity may = allergy, "drug-like" effect of food, maldigestion

Allergy testing

- Debate re: best measures for allergy diagnosis: skin testing
  IgE testing, IgG testing

Medical Issues: Impaired carbohydrate digestion, transport and dysbiosis

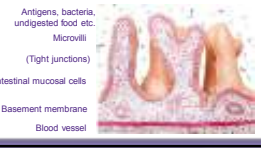
- Williams et al. (2011) surveyed gene expression and the microbiota in intestinal biopsies from children with ASD and GI disease and children with GI disease alone.
  - Disaccharidases and hexose transporters were deficient in children with ASD, indicating impairment of the primary pathway for carbohydrate digestion, transport and creating a setting for dysbiosis.

Williams BL et al. *PLoS* 2011;6(9)e24585.

- **Disaccharidase deficiencies may be common**

Intestinal Permeability in Autism

- Altered intestinal permeability has been frequently reported
  - Food-related immune modulation
  - Inflammation or other factors
- 2014 MGH abstract ***did not*** show increased permeability in our children with ASD compared to unaffected children; abnormal permeability was ***not correlated*** with inflammation noted in intestinal biopsies done contiguously with the permeability testing



Microbiota plays important role in many physiologic functions

Metabolism:
- Vitamin synthesis
- Digestion of harmful compounds
- Fermentation of non-digestible substances
- Energy production

Protection:
- Immune system stimulation
- Antimicrobial effect
- Physical barrier against pathogenic bacteria

Can we eat our way back into balance?

GI Microbiota: If the balance is upset. . .

Current efforts are directed to refine our understanding . . .

. . . of the relationship between human intestinal gene expression and the bacterial community structure in order to provide insights into the pathophysiology of GI disturbances in children with ASD.

Williams BL et al. *PLoS* 2011;6(9):e24585.

Some Consequences of Gut Dysbiosis

- Localized gut inflammation
- Systemic inflammation
- Increased oxidative stress
- Increased endotoxins & other biotoxins
- **Altered production/synthesis of neurotransmitters**
- Intestinal permeability
- Chronic infections
- Impaired detoxification/regulation oxidative stress (eg. sulfation)
- Impaired energy metabolism
- **Impaired nutrient synthesis (eg. vitamins, minerals, short-chained fatty acids**
- Impaired enzyme activity
- Autoimmunity

GI Microbiota: Dysbiosis in Autism

- Reduced incidence of Prevotella (gram negative bacteria) and other fermenters in intestinal "microflora" of children with ASD

  Kang DW, et al. *PLoSOne* 2013 Jul 3:8(7):e68322.
- Characteristics of the microbiota in ASD:
  - Diminished diversity of species
  - Diminished lactose fermenter population
- Concern about predominance of specific species (Sutterella, Desulfovibrio)
- ? Altered microbiota as a result of dietary selectivity or alteration
- May lead to altered gut **metabolome**
  - These small bacterial byproducts may alter nervous system communication

Case Study: 3.5 year old boy

- **Irritable infant at 2 weeks**, initially fed cow milk formula, mom unable to breast feed; PPI trial (failed)
- **At 4 weeks, no symptom improvement** – initiated hydrolyzed protein formula
- **At 6 weeks, slight symptom improvement** - still fussy and sleepless
- **2 months, initiated amino acid-based formula** (Neocate® Infant), sustained symptom improvement
- **11 months**, **gradually reintroduced milk products** without obvious worsening of symptoms

Case Study: 3.5 year old boy

- **15 months**: on target development and social progress – had some words
- **17 months:** ear infection + fever; less interactive – language regressed, behavioral withdrawal
- Loose stools; skin (which was normal before) got "rashy"
- **20 months:** Pediatrician referred for a developmental assessment and was diagnosed with ASD

Case Study: 3.5 year old boy

- **24 months**: Family initiated gluten-free and milk-free diet & requested GI evaluation for:
  - Diarrhea
  - Diet related questions
- Stools improved; seemed "more focused" while on diet
- Skin rashes continued; had RAST allergy testing; Celiac testing (had gluten exposure within past 2 months)
- All testing was negative

NOW WHAT?....
Do I continue his current diet?
Should one consider additional restrictions?

Case Study: 3.5 year old boy

- **RD consult** (removed additives, preservatives, colorings)
  Considerations:
  - Further food restriction for allergens? SCD?
  - Add milk substitute? What are concerns?
  - Initiate amino acid-based formula?
- **Plan:** Re-initiated amino acid-based formula (Neocate® Junior/ E028 Splash) and restricted diet
  Formula Rationale:
  - Familiarity and well tolerated
  - Reduced antigen load
  - Multiple flavor options including unflavored (can creatively flavor per individual preference)
- **Outcome:** Rash and stools improved

He is making progress with many interventions in place.

Celiac Disease

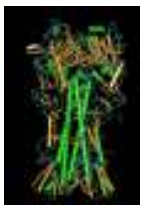
- Celiac disease is a digestive, autoimmune disorder characterized by intolerance to gluten, a protein found in wheat, rye, barley and triticale.
- When gluten is ingested, the immune system forms antibodies that bind to parts of the villi of the small intestine, resulting in inflammation, damage to the intestine

Celiac Disease and Autism

Findings	Reference
No link in a limited population of children with ASD	Pavone L et al. *Biol Psychiatry.* 1997 Jul 1:42(1):72-5.
Swedish nationwide study of the association of Celiac Disease and the risk of ASD; no higher among ASD and general population ▪ Higher risk of **positive screening markers:** IgA/IgG gliadin, endomysium, tissue transglutaminase	Ludvigsson JF et al. *JAMA Psychiatry.* 2013Nov; 70(11):122-30.

Does abnormal antibody response reflect OTHER RISK?

Gluten and Non-Digestibles



- **Gliadin** and **glutenin**, proteins in gluten cannot be completely digested
- **Lectins**, carbohydrate-binding proteins may be “gut toxic”, associated with a variety of autoimmune conditions
- **Phytic acid** binds minerals affecting zinc and iron absorption (and to a lesser extent, calcium and magnesium)
- **FODMAPS**, short-chained carbohydrates and sugar alcohols found in foods naturally or as food additives, strong link to IBS, pain

Gluten Concerns and Autism Go Way Back . . .

1943 - Autism was originally described by Leo Kanner

1944 - A compendium of articles including one penned by Asperger suggested the link of autism behaviors to gluten exposures

Asperger, H. 1944. In Frith U. 1991. *Autism and Asperger syndrome*. Cambridge University Press. pp. 37–92.

1961 – Dohan observed a remarkable increase in gluten exposure in post WWII diet along with an increase in schizophrenia diagnosis

Dohan FC. *Arch Environ Health*. 1961 Oct;3:387-95.

1970s to present – Plethora of publications evaluating diets for ASD

- Milk and gluten-free are prominent

Where there is smoke . . .???

New symptom development …think medical/GI Issues

Case Study: Teenage Boy

- Has non-verbal autism and is now in his late teens
- He had onset of severe behaviors including agitation and screaming especially after meals. He also had episodes of violent throat clearing and progressive self injury.
- 13 yo-initial pediatric GI evaluation (endoscopy) revealed distal (reflux) esophagitis and constipation
- Treatment for GI issues helped, but the throat clearing got worse over the years, and he began **posturing** during meals
- Repeat endoscopy revealed progression to eosinophilic esophagitis (EoE)
- Allergy evaluation for foods was negative

Symptoms drive medical evaluation . . .

Case Study: Teenage boy

- A limited restrictive diet (no milk, eggs) was initiated-standard therapy, 6FED was not feasible)
- Remarkable symptom and histologic improvement in weeks
- The elimination diet combined with his restrictive eating patterns made attainment of adequate nutritional intake extremely difficult...
- Therefore, HCPs should strongly consider the use of an Amino Acid Formula/semi-solid (Nutra®) in children with Autism and GI issues
- 2 potential benefits:
  1. Ensures balanced nutrient support
  2. Provides adequate intake while reintroducing foods

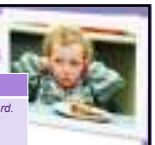
Feeding Disorders in Autism

Multi-factorial issues that influence eating are well described . . .

Social interaction challenges	Sensory processing	Medical diagnoses
Communication challenges	Praxis	GI concerns
Rigidity	Sleep disturbances	Allergies or sensitivities
Relationships	Anxiety	Medication

- Children with ASD have more feeding problems and food selectivity compared to their peers. Bandini LG et al. *Pediatr.* 2010 Aug;157(2):259-64.
- Food refusal based on food characteristics has been reported in ASD; need to routinely screen in order to prevent dietary inadequacies. Hubbard KL et al. *J Acad Nutr Diet.* 2010 Aug;157(2):259-64.

Nutritional Issues/Deficits in Autism



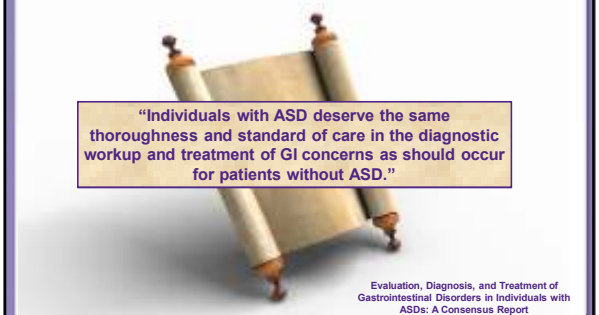
Findings	References
Reported nutrient inadequacies include: -Calcium, Vitamins B12, A,D, protein, fiber	Sharp WG et al. *J Autism Dev Disord. 2013 43:2159-2173.* Bandini LG et al. *J Pediatr.* 2010 Aug;157(2):259-64.
In individual cases, food selectivity can create isolated deficiencies (E.g. Vit C-scurvy), but large scale studies show surprisingly adequate energy intake for most children despite restrictive eating patterns.	Graf-Myles J et al. *Dev Behav Pediatr.* 2013 Sep;34(7):449-59.
Children with ASD consume more energy-dense foods	Evans EW et al. *Res Autism Spectr Disord.* 2012 6(1):399-405.
Prevalence of obesity in children with ASD is at least as high as seen in typically developing children	Curtin C et al. *Harv Rev Psychiatry.* 2014 Mar-Apr 22(2):93-103.
Reported decreased bone mineralization in ASD	Hediger ML et al. *J Autism Dev Disord.* 2008 38(5):8484-56. Neumeyer AM et al. *J Autism Dev Disord.* 2013 Jul;43(7):1623-9.

Summary

- I believe a distinct sub-group of individuals with Autism and GI issues will be identified where GI symptoms, behaviors, and perhaps even core autism features will improve when managed using dietary modulation.
- Referral to a pediatric dietitian to assess potential benefit and nutritional adequacy of a restricted diet is **essential** in the individualized management of Autism and GI issues.
- Amino acid-based formulas/semi solid foods provide key nutritional support for many of these children with Autism and GI issues.

- **Healthcare professionals need to consider the child with Autism in a medical light.**
- **Until proven otherwise, behaviors should be considered medically-based.**
- **Problem or self-injurious behaviors may require medical or behavioral management. Attention to underlying medical factors may mitigate the requirement of pharmacological management for some individuals.**

Bill of Rights for Individuals with Autism



"Individuals with ASD deserve the same thoroughness and standard of care in the diagnostic workup and treatment of GI concerns as should occur for patients without ASD."

Evaluation, Diagnosis, and Treatment of Gastrointestinal Disorders in Individuals with ASDs: A Consensus Report
Buie T et al. Pediatrics 2010;125;S1

Key recommendations for HCPs caring for children with Autism and GI issues

In clinical settings, healthcare providers should:
1. Include assessment of feeding problems and nutrient intake as part of early routine medical evaluations.
2. Not rely exclusively on typical anthropometrics (HT, WT, BMI) to assess overall heath status.
3. Educate parents/caregivers regarding potential empirical, detrimental non-proven interventions.
4. Refer to a Registered Dietitian/Nutritionist to guide dietary intervention strategies.
5. Assess for potential over supplementation.
6. Foster interdisciplinary collaboration and communication to help improve the level of care provided.
7. Consider increased risk for diet-related chronic diseases that may develop in adulthood.

Question & Answer Session

Nutricia North America would like to thank **Dr. Timothy Buie**, for his expertise in the development of this presentation.

Thank you. . .
Questions?

- **Registered Dietitians (RDs) interested in obtaining a Certificate of Attendance for 1 CEU credit please visit:**
  http://www.NutriciaLearningCenter.com

  Information needed:

  Event code = **GWASD1**

  Event date = 9.23.14

- **For other healthcare professionals, contact Carol.Henderson@Nutricia.com to obtain a certificate of attendance for your licensing board**