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

1 in 42 boys have ASD
1 in 189 girls have ASD

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

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<thead>
<tr>
<th>Findings</th>
<th>References</th>
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<tr>
<td>70% of children with ASD had GI issues compared to 42% of children with developmental disorder other than ASD</td>
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<td>28% of children with typical development</td>
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Traditional vs. unconventional symptom recognition

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<thead>
<tr>
<th>Typical Child</th>
<th>Autism/Non-Verbal Child</th>
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<tr>
<td>Hurts to swallow</td>
<td>Intermittent or continuous tantrum, feeding refusal</td>
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<tr>
<td>Hard to swallow</td>
<td>Banging on chest, textural preferences</td>
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<tr>
<td>Something stuck in throat</td>
<td>Pointing to throat, tapping site of distress</td>
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<tr>
<td>Have heartburn</td>
<td>Irritability after meals or at bedtime</td>
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<tr>
<td>Stomach hurts after eating</td>
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<tr>
<td>Reports pain</td>
<td>Self-injury, aggression</td>
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### Medical Issues: GI and Autism

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**Recent Support for GI - Autism Link**

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.
### 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)

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### 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

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### 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
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

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<tbody>
<tr>
<td>Food allergy may be 2X more common in boys</td>
<td>Lucarelli S, et al. Allergy. 2013; 68: 786-891</td>
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<tr>
<td>Food allergy was reported in 36% of 36 children with ASD</td>
<td>Guéguen E, et al. Pediatrics. 2011; 128(3): e717-723</td>
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<tr>
<td>Sensitivity may = allergy, “drug-like” effect of food, maldigestion</td>
<td>© 2014 PediGI, LLC</td>
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Allergy testing

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

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Medical Issues: Impaired carbohydrate digestion, transport and dysbiosis

- 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.

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 nondigestible substances
    - Energy production
  - Protection:
    - Immune system stimulation
    - Antiinflammatory effect
    - Physical barrier against pathogenic bacteria

Can we eat our way back into balance?
GI Microbiota: If the balance is upset...

Some Consequences of Gut Dysbiosis
- Localized gut inflammation
- Systemic inflammation
- Increased oxidative stress
- Increased endotoxins & other biotoxins
- Altered neurotransmitter synthesis
- Intestinal permeability
- Chronic infections
- Impaired detoxification/elimination of oxidative stress (e.g., sulfation)
- Impaired energy metabolism
- Impaired nutrient synthesis (e.g., vitamins, minerals, short-chain fatty acids)
- Impaired enzyme activity
- Autoimmunity

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.


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GI Microbiota: Dysbiosis in Autism

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

NOW WHAT?....

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

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

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<tr>
<td>Swedish nationwide study of the association of Celiac Disease and the risk of ASD; no higher among ASD and general population</td>
<td>Ludvigsson JF et al. JAMA Psychiatry. 2013 Nov; 70(11):122-30.</td>
</tr>
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</table>

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


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


1970s to present – Plethora of publications evaluating diets
for ASD
  • Milk and gluten-free are prominent

Where there is smoke . . .???

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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

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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.
- Food refusal based on food characteristics has been reported in ASD; need to routinely screen in order to prevent dietary inadequacies.
Nutritional Issues/Deficits in Autism

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<tr>
<td>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.</td>
<td>Bandini LG et al. J Pediatr. 2010 Aug;157(2):359-64.</td>
</tr>
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Findings References

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.

Conclusions

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

“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.”

Bill of Rights for Individuals with Autism
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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 health 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

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