Dear APGNN Meeting Participant:

Welcome to Fabulous Las Vegas! We are proud to present the 26th Annual APGNN Meeting, and are so glad you chose to join us! Maureen Egan, Program Chair, and her committee members have planned an informative conference. We hope you find the program educational and invaluable to your ongoing education. Please take time to complete the course evaluation. Your feedback is a valuable part of ensuring that our meetings are always of high quality. We also appreciate your topic suggestions and ask that you let us know what you would like to see at future programs by indicating this on your post-conference evaluations.

Our keynote speaker Minta Albietz, RN, MSN a Vegas local from Kindred Hospital will present on Leadership – Strategies for Life. Throughout the rest of the two-day meeting, there will be multiple concurrent sessions allowing you to tailor your experience to your personal and professional interests. All meeting participants can also chose attend NASPGHAN and CPNP lectures that are of interest to you.

The Annual Business Meeting will be held at 8:00 on Friday, November 3rd. The Annual Report will be presented at that time and we will be introducing you to your new board members during the meeting as well. Also, please plan to attend a committee meeting Friday afternoon (please see the schedule for details). We are sure you will find at least one APGNN committee that interests you. All levels of knowledge and expertise are welcome, and we look forward to learning from you and your expertise to improve the organization. This is a great way to become involved in APGNN. Our annual APGNN Social Event will be Friday evening, please plan to attend as several awards will be presented and this is a great time to network with your fellow members.

Speaking of membership, if you are not an APGNN member, please consider joining. Information about our organization as well as membership applications can be found at the APGNN Membership booth in the exhibit hall and on our website www.apgnn.org.

Lastly, a special thank you to the NASPGHAN staff: Margaret Stallings, Kim Rose, Donna Murphy, Pat Chirinos and Christy Norcross. We know we cannot do this without their support and are grateful for their assistance.

Sincerely,

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The Mission of APGNN

The formation and ongoing mission of the Association of Pediatric Gastroenterology and Nutrition Nurses is to:

- Promote the professional development and recognition of pediatric nurses as experts in their field
- Promote excellence in the care of families with children with gastroenterology, hepatology and nutritional illnesses

Our Goals

- The APGNN was founded upon and recognizes the following organizational goals:
- Promote nursing research and publication of findings
- Promote education for patients, families, nurses, allied health professionals, and physicians
- Establish standards of practice
- Create a Pediatric Gastroenterology/Nutrition Network
- Support role development through attendance and participation in conferences and development of teaching materials

The APGNN web site is:

www.apgnn.org

A membership application is also available through this web site. Please be patient as this site continues to evolve.

For changes in your membership database go through the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

NASP GHAN web site:

www.naspghan.org

Helpful practice guidelines and patient and family brochures are also accessible through this website.
2017 APGNN Educational Conference
Supported in part through restricted educational grants from:
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
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<tbody>
<tr>
<td>7:30am - 8:00am</td>
<td>REGISTRATION/BREAKFAST/WELCOME</td>
</tr>
<tr>
<td>8:00am - 8:45am</td>
<td>BUSINESS MEETING</td>
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<tr>
<td>8:45am - 9:30am</td>
<td>LEADERSHIP: STRATEGIES FOR LIFE</td>
</tr>
<tr>
<td></td>
<td>Minta Albietz, RN, MS, Kindred Hospital</td>
</tr>
<tr>
<td></td>
<td>Learning objectives:</td>
</tr>
<tr>
<td></td>
<td>1. Identify leadership styles to consider in variable work place environments</td>
</tr>
<tr>
<td></td>
<td>2. Describe how leadership styles impact team dynamics</td>
</tr>
<tr>
<td></td>
<td>3. Illustrate best practices for team integration</td>
</tr>
<tr>
<td>9:30am - 10:00am</td>
<td>FUSSY BABY</td>
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<tr>
<td></td>
<td>Jon Vanderhoof MD, Boston Children’s Hospital</td>
</tr>
<tr>
<td></td>
<td>Learning objectives:</td>
</tr>
<tr>
<td></td>
<td>1. Understand why infants cry</td>
</tr>
<tr>
<td></td>
<td>2. Learn appropriate intervention in crying infants</td>
</tr>
<tr>
<td>10:00am - 10:15am</td>
<td>BREAK</td>
</tr>
<tr>
<td>10:15am - 12:00pm</td>
<td>CELIAC: THE LAS VEGAS TEAM</td>
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<tr>
<td>10:15am - 11:15am</td>
<td>LIVING WITH CELIAC DISEASE</td>
</tr>
<tr>
<td></td>
<td>Teresa Carroll, APRN, Pediatric Gastroenterology and Nutrition Associates</td>
</tr>
<tr>
<td></td>
<td>Learning objectives:</td>
</tr>
<tr>
<td></td>
<td>1. Identify both GI and non-GI symptoms</td>
</tr>
<tr>
<td></td>
<td>2. Discuss updated in celiac health surveillance</td>
</tr>
<tr>
<td></td>
<td>3. Discuss food contamination risk in the home</td>
</tr>
<tr>
<td></td>
<td>4. Identify how to plan for social events, eating out and travel</td>
</tr>
<tr>
<td>11:15am - 11:45am</td>
<td>EATING GLUTEN FREE: SEPARATING THE WHEAT FROM THE CHAFF</td>
</tr>
<tr>
<td></td>
<td>Holly Brewer MS, RDN, LD, Pediatric Gastroenterology and Nutrition Associates</td>
</tr>
<tr>
<td></td>
<td>Learning objectives:</td>
</tr>
<tr>
<td></td>
<td>1. List gluten-containing food groups</td>
</tr>
<tr>
<td></td>
<td>2. Name safe starches/grains that are gluten free</td>
</tr>
<tr>
<td></td>
<td>3. Identify cross-contamination risks and how to avoid</td>
</tr>
<tr>
<td>11:45am - 12:00pm</td>
<td>QUESTIONS</td>
</tr>
<tr>
<td>12:00pm - 1:00pm</td>
<td>POSTERS AND LUNCH</td>
</tr>
</tbody>
</table>
1:00pm - 3:00pm  NUTRITION MODULE

1:00pm - 1:30pm  MALNUTRITION A TEAM APPROACH
Natalie Navarre MS, RD, LD and Maureen Egan, APRN Nemours DuPont Pediatrics Division of Gastroenterology
Learning objectives:
1. Discuss common causes for malnutrition/FTT
2. Identify initial interventions to address nutrition concerns

1:30pm - 2:00pm  THE NUTRITIONIST PHYSICAL EXAM
Carly Leon RD, Children’s Hospital of Wisconsin
Learning objectives:
1. Identify at least 3 components of the Dietitian’s Nutrition-Focused Physical Exam
2. Discuss the value of nutrition physical exam findings as they pertain to promoting and implementing nutrition recommendations.
3. Explain value of the mid-upper arm circumference and how it pertains to growth and pediatric malnutrition

2:00pm - 2:30pm  BLENDERIZED TUBE FEEDINGS (BTF): WHAT NURSES NEED TO KNOW
Margaret Girten, RD, CSP, LDN, Children’s Hospital of Philadelphia
Learning objectives:
1. Identify and compare commercial and home blended diets
2. Recognize traits of patients who might be suited for BTF
3. Recognize benefits and challenges BTF for the family and medical team

2:30pm - 3:00pm  REFEEDING SYNDROME AND LAB VALUES
Stacie Townsend MS, RD, LDN, CSP, National Institutes of Health
Learning objectives:
1. Describe what refeeding syndrome is, to include signs, symptoms, lab assessment
2. Identify who is at risk for refeeding syndrome
3. Recognize how to prevent refeeding syndrome
4. Identify recommended treatments and standard of care to prevent and treat refeeding syndrome

3:00pm - 3:15pm  BREAK

3:15pm - 4:15pm  FPIES MODULE

3:15pm - 3:45pm  FPIES
Glenn Furuta MD, Children’s Hospital Colorado
Learning objectives:
1. Recognize the differential diagnosis of diarrhea in infancy
2. Identify role of gastroenterology in diagnosis of FPIES
3:45pm - 4:15pm  FPIES: A PARENT’S PERSPECTIVE
Joy Meyer and Amanda Lefew Co-Directors The FPIES Foundation
Learning objectives:
1. Define Food Protein Induced Enterocolitis Syndrome
2. Recognize the parent perspective of having a child diagnosed with FPIES
3. Describe the quality of life adjustments for families living with FPIES

4:15pm - 5:15pm  ARE YOU SMARTER THAN A 5TH GRADER
Norberto Rodriguez-Baez MD, University of Texas Southwestern Medical Center
Learning objectives:
1. Know diagnostic and radiological studies used in common gastrointestinal diseases
2. Understand the mechanism of action of common medications used in pediatric gastroenterology and hepatology
3. Describe different pathogens causing diseases in the gastrointestinal tract

5:15pm  CONFERENCE WRAP UP

5:15pm - 6:00pm  COMMITTEE MEETINGS

6:00pm  APGNN SOCIAL EVENT  Neopolitan 3 - 4
8:00am - BREAKFAST AND REGISTRATION

8:15am - 9:45am - IBD MODULE

8:15am - 9:00am - UPDATE ON IBD MEDICATIONS
Andrew Grossman MD, Children’s Hospital of Philadelphia
Learning objectives:
1. Understand the various pharmacologic therapies used to treat IBD
2. Recognize the importance of nutritional therapy for IBD
3. Implement different treatment strategies (step up vs. top down approach)

9:00am - 9:45am - PSYCHOLOGICAL HEALTH IN PEDIATRIC IBD: OPPORTUNITIES FOR MULTIDISCIPLINARY CARE
Bonney Reed-Knight PhD, Emory University School of Medicine
Learning objectives:
1. Describe psychosocial difficulties experienced by pediatric patients diagnosed with IBD
2. List evidence-based psychotherapies for pediatric anxiety, depression
3. Describe basic tenets of cognitive-behavioral therapy for anxiety and depression
4. Discuss treatment of anxiety and depression effectively with fellow providers and patients

9:45am - 10:00am - BREAK

10:00am - 11:30am - MOTILITY MODULE

10:00am - 10:30am - CECOSTOMY AND CONE ENEMA
Jason Dranove MD, Levine Children’s Hospital
Learning objectives:
1. Understand the different types of cecostomy tubes (intermittent catheterization, indwelling button, Chait Cecostomy) and large volume enema types (cone enema and Peristeen)
2. Discuss patient most likely to benefit for cone enema or Peristeen and briefly discuss their use
3. Understand timing and advancement of flushes after placement of cecostomy
4. Understand the different types of cecostomy flush regimens available
5. Learn how to assess response to flushes and whether they are working
6. Identify some common complications of cecostomies

10:30am - 11:00am - ESOPHAGEAL MOTILITY
Samuel Nurko MD, Boston Children’s Hospital
Learning objectives:
1. Identify indications for esophageal manometry testing
2. Gain a better understanding of the esophageal manometry procedure
3. Understand first line treatment for abnormal findings on manometry
11:00am - 11:30am  **RUMINATION**
Julie Snyder Christiana Psy.D, Boston Children’s Hospital
Learning objectives:
1. Describe the rationale behind incorporating psychological/behavioral interventions into the treatment plan for a diagnosis of rumination
2. Identify specific psychological strategies that can be utilized for the management of rumination syndrome

11:30am – 11:45am  **ZEBRA: RICKETT’S, ITCHING AND POOR FEEDING: WHAT’S THE COMMON LINK?**
Shabina Virani RN, MSN, CPNP
Learning objectives:
1. Discuss different ways liver disease presents in the GI clinic
2. Recognize cholestasis even if there is not jaundice present

11:45am - 12:30pm  **AWARDS/CONFERENCE WRAP UP**
Susan G Moyer Nursing Research Award
Excellence in Education
Posters of Distinction

12:30pm - 2:00pm  **LUNCH AND POSTERS**

2:00pm - 3:30pm  **CONCURRENT SESSION - RESEARCH SKILLS**  
Milano 5 - 6
Moderators: Edaire Cheng MD and Michael Rosen MD
PATHS TO SUCCESS IN CLINICAL TRANSLATIONAL RESEARCH
Samuel Nurko MD and Rachel Rosen MD, Boston Children’s Hospital
PATHS TO SUCCESS IN QUALITY IMPROVEMENT SCIENCE
Shehzad Saeed MD, Dayton Children’s Hospital and Chelly Dykes MD, Cincinnati Children’s Hospital Medical Center

3:30pm - 3:45pm  **BREAK**

3:45pm - 5:15pm  **CLINICAL PRACTICE FORUM: CREATING A HIGHLY RELIABLE**  
Octavius 11
MULTIDISCIPLINARY TEAM
THE PEDIATRIC GASTROENTEROLOGIST AND MULTIDISCIPLINARY CARE
Ricardo Caicedo MD, Levine Children’s Hospital/Carolinas HealthCare System

CREATING A CULTURE OF CARE
Jennifer Schurman PhD, ABPP, BCB, Children's Mercy Hospital

FIVE STRATEGIES FOR NAVIGATING AN MD/NP PARTNERSHIP IN A MULTIDISCIPLINARY TEAM
Robyn Robinson CPNP, CHOC Children's Gastroenterology and Nutrition

OVERCOMING CHALLENGES TO MULTIDISCIPLINARY CARE: THE RD PERSPECTIVE
Why Babies Fuss And Cry

- Human babies are neither mobile to follow their mothers nor can they hold on to their mothers (like primates)
- Fuss/cry is an evolutionary adaptation to secure
  - Safety
  - Feeding
  - Growth
  - Communication
Most fussing and crying occurs in the evening.


Fig. 1. Hourly incidence of fussiness of 68 infants at time of post-natal check.

**Fuss/Cry and colic across countries**

**Fuss/Cry**
- In the first 6 weeks around 117-133 mins/day (on average)
- Fuss/cry reduces significantly after 8-9 weeks of age to about 60-70 mins from then on
- There are large individual variations

**Excessive Crying (Colic)**
- 10-20% of babies in the first 3 months fuss/cry 3 or more hours per day
- Colic prevalence is higher in the first 6 weeks than in subsequent weeks

**Normal versus abnormal fuss/cry**

Universal fuss/cry curve in Developed Countries

Prevalence (%) of colic (Fuss/cry > 3hrs/day) in Developed Countries in the first 12 weeks of life

Outcomes of colic in infants

- Weight gain delay
- Allergy
- Crying
- Behavior disturbances
- Temperament difficult
- Sleep problems
- Negative reactivity

- Transient
- None
- Much reduced
- None, small
- None
- None
- None


4. When excessive fuss/cry continues beyond 3 months of age: Regulatory Problems:

- Mostly co-occurring with sleeping or feeding problems: multiple regulatory problems
- Often persist into second year of life
- Associated with increased behavior problems in childhood (ADHD, externalizing, internalizing)


Consequences for parents of colic crying

- Increased tiredness, stress, and anxiety (e.g., Postert et al., 2012; Vida et al., 2008; Kurth et al., 2012)
- Increased risk of postnatal depression symptoms (30-45%) (e.g., Martin et al., 2007; McMahon et al., 2001)
- Reduced Partner Relationship Quality

Danger Signs for a stressed relationship

Multiple Family Stressors

Consequences of abnormal crying in the first 3 months: Colic

For the infant
- Colic is usually self-limiting with most infants remitting by 4 months of age
- There are usually no long-term ill effects on the infant
- Some perceptions of ‘difficult temperament’ may linger in parents’ perceptions

For parents
- Tiredness, depression and anxiety symptoms, loss of control – usually transient

BUT
- Increased risk of Abusive Head Trauma (Shaken Baby Syndrome)
Only a "fit" mother can help her infant.

Pediatricians often respond with reflex actions.

Reflex number one

- Start acid suppression
  - PPI
  - H2 receptor antagonist
Gastroesophageal Reflux

- Common cause of regurgitation, emesis
- Uncommon cause of irritability
- Overdiagnosed cause of irritable baby

PPI Impact on Irritability

<table>
<thead>
<tr>
<th>% of patients</th>
<th>Lansoprazole (n=81)</th>
<th>Placebo (n=81)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom within 1 hour after feeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crying, fussing, or irritable</td>
<td>-19.9% (21.1)</td>
<td>-19.9% (22.8)</td>
</tr>
<tr>
<td>Spitting up/vomiting</td>
<td>-14.1% (24.4)</td>
<td>-11.4% (17.3)</td>
</tr>
<tr>
<td>Stopping feeding after starting</td>
<td>-6.8% (19.8)</td>
<td>-7.5% (14.8)</td>
</tr>
</tbody>
</table>


GER and Crying Duration

\[ y = 252.3 - 0.29x \]
\[ r^2 \text{(adjusted)} = 0.0064 \]
\[ p = 0.84 \]
Conclusions: Investigation and treatment of GER in infants with persistent crying should be primarily directed at infants presenting with frequent regurgitation or feeding difficulties.

Reflex number two

- Change the formula
  - Lactose-free
  - Hypoallergenic

Does Lactose Cause Irritability in Babies?

TABLE 2. Baseline and follow-up measures of caregiver-reported infant behavior and caregivers’ distress by formula group.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Control</th>
<th>Milk LF</th>
<th>Soy LF</th>
<th>Change in LF</th>
<th>Change in Milk</th>
<th>F</th>
<th>df</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant difficultness (Baseline)</td>
<td>4.17 (0.12)</td>
<td>4.24 (0.10)</td>
<td>4.29 (0.10)</td>
<td>0.83</td>
<td>2,277</td>
<td>0.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infant difficultness (Follow-up)</td>
<td>3.79 (0.08)</td>
<td>3.64 (0.09)</td>
<td>3.67 (0.09)</td>
<td>0.74</td>
<td>2,282</td>
<td>0.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenting efficacy (Baseline)</td>
<td>3.01 (0.05)</td>
<td>2.99 (0.05)</td>
<td>2.92 (0.06)</td>
<td>1.07</td>
<td>2,285</td>
<td>0.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenting efficacy (Follow-up)</td>
<td>3.22 (0.04)</td>
<td>3.23 (0.04)</td>
<td>3.28 (0.04)</td>
<td>0.80</td>
<td>2,285</td>
<td>0.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver psychological well-being (Baseline)</td>
<td>4.00 (0.10)</td>
<td>3.95 (0.10)</td>
<td>4.11 (0.10)</td>
<td>0.57</td>
<td>4,570</td>
<td>0.63</td>
<td></td>
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</tr>
<tr>
<td>Caregiver psychological well-being (Follow-up)</td>
<td>4.32 (0.07)</td>
<td>4.37 (0.08)</td>
<td>4.48 (0.08)</td>
<td>0.80</td>
<td>2,285</td>
<td>0.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver psychological distress (Baseline)</td>
<td>2.19 (0.09)</td>
<td>2.18 (0.08)</td>
<td>2.26 (0.09)</td>
<td>0.90</td>
<td>2,285</td>
<td>0.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caregiver psychological distress (Follow-up)</td>
<td>1.98 (0.05)</td>
<td>1.96 (0.05)</td>
<td>1.98 (0.05)</td>
<td>0.90</td>
<td>2,285</td>
<td>0.36</td>
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</tbody>
</table>
Why Lactose Matters

- It is the carbohydrate in breast milk
- It is nature's prebiotic
- It has a low glycemic index preventing large postprandial changes in blood glucose

Switching Formulas Seems to Work

- Allergy or intolerance to CMP is not common (2-5%)
- Regardless of the initial feeding routine or potential CMP allergy or intolerance diagnosis:
  1. A high percentage of infants (estimated 30-50%) are switched to an alternate CMBF or experience a change to 1 or more nonstandard formulas due to parental perception of common infant symptoms
  2. Up to 80% of parents reported improved or resolved feeding intolerance due to formula replacement
Reasons for Switching Formula- USA

Source: NQF IF Usage and Experience Research, 2002

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Results – Fussiness Score Week 1

Mean ± SEM

P<0.001, Compared to baseline (B)

PHWC = Partially Hydrolyzed 60:40 Whey:Casein
Purple = Soy

Teal = PHWC


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Crying

Mean ± SEM

P<0.05 compared to baseline (B)

Teal = Partially Hydrolyzed
Purple = Soy

Possible explanations for results

• Underlying allergy
• Placebo effect

Sixty colicky infants were given a cow’s milk containing formula and a cow’s milk-free soy formula. Symptoms of 17 infants (29%) could not be related to the diet. Eleven infants (18%) were free of symptoms while receiving soy formula. Symptoms of 32 infants (53%) were unchanged or worse when they were fed cow’s milk formula and soy formula, but symptoms disappeared when they were fed a formula containing hydrolyzed casein. A challenge with cow’s milk-based formula after one month (at approximately age 3 months) produced symptoms of infantile colic in 22 infants (36%). At age 6 months, a challenge with cow’s milk was positive in 11 infants (18%) with epidermal and gastrointestinal symptoms. Eight infants (13%) at 12 months of age and five infants (8%) at 16 months of age were still intolerant to cow’s milk.

TABLE 1. Reaction to Cow’s Milk-Based Formula and Soy-Based Formula Twiced Double Blind in Infants with Infantile Colic

<table>
<thead>
<tr>
<th></th>
<th>No. of Infants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous recovery</td>
<td>17 (29%)</td>
</tr>
<tr>
<td>Adverse reaction to cow’s milk formula</td>
<td>11 (19%)</td>
</tr>
<tr>
<td>Adverse reaction to cow’s milk and soy formula</td>
<td>33 (55%)</td>
</tr>
<tr>
<td>Total</td>
<td>90 (100%)</td>
</tr>
</tbody>
</table>
Effect of a Low-Allergen Maternal Diet on Colic Among Breastfed Infants: A Randomized, Controlled Trial

<table>
<thead>
<tr>
<th>Infant</th>
<th>6 Months</th>
<th>12 Months</th>
<th>Other Foods Causing Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.G.</td>
<td>Abdominal pain</td>
<td>Abdominal pain, diarrhea</td>
<td>Orange, fish, egg, strawberry, soy, milk</td>
</tr>
<tr>
<td>S.Y.</td>
<td>Abdominal pain, diarrhea</td>
<td>Abdominal pain, diarrhea</td>
<td>Fish, egg, milk, soy</td>
</tr>
<tr>
<td>K.C.</td>
<td>Abdominal pain, diarrhea, vomiting</td>
<td>Diarrhea, vomiting</td>
<td>Tomato, soy, milk</td>
</tr>
<tr>
<td>P.K.</td>
<td>Vomiting, diarrhea, constipation</td>
<td>Diarrhea, vomiting</td>
<td>Soy, milk, egg, beef, pork, wheat, corn</td>
</tr>
<tr>
<td>J.A.</td>
<td>Vomiting</td>
<td>Diarrhea, constipation</td>
<td>Soy, milk, egg, beef, pork, wheat, corn</td>
</tr>
<tr>
<td>R.C.</td>
<td>Vomiting</td>
<td>Diarrhea, constipation</td>
<td>Tomato, egg, milk</td>
</tr>
<tr>
<td>M.C.</td>
<td>Vomiting</td>
<td>Diarrhea, constipation</td>
<td>Orange, tomato, beef</td>
</tr>
<tr>
<td>A.A.</td>
<td>Diarrhea, constipation</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>H.G.</td>
<td>Diarrhea, constipation</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>K.</td>
<td>Abdominal pain, diarrhea</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>M.W.</td>
<td>Diarrhea</td>
<td>Diarrhea, constipation</td>
<td>Fruits</td>
</tr>
</tbody>
</table>
Duodenal Bulb Nodularity: An Endoscopic Sign of Cow Milk Protein Allergy in Infants

Allergy vs Colic

<table>
<thead>
<tr>
<th>Allergy</th>
<th>Colic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal Stools</td>
<td>Normal stools</td>
</tr>
<tr>
<td>Poor weight gain</td>
<td>Normal weight gain</td>
</tr>
<tr>
<td>Feeds poorly</td>
<td>Feeds fine</td>
</tr>
<tr>
<td>Cries after eating</td>
<td>Cries in evening</td>
</tr>
<tr>
<td>Spits up a lot</td>
<td>Spits up rarely</td>
</tr>
<tr>
<td>Non-distractible</td>
<td>Soothable</td>
</tr>
</tbody>
</table>

When To Try Hypoallergenic Formula

- Failure to thrive
- Unremitting symptoms
- Presence of other symptoms
  - Diarrhea
  - Vomiting
  - Bloody stools
  - Feeding refusal
Clinical approach to fussy baby

- Careful history and physical
- Establish differential diagnosis
- Evaluate based on history and physical examination
- Treat appropriately once diagnosis is established

Does the baby have infantile colic?

- Does the history fit?
- Are there any red flags? (other symptoms, poor weight gain)
- Are there danger signs for infant suggesting risk?

If you suspect something else...

- Diagnostic evaluation as indicated especially if red flags
  - Reflux??????????
  - Metabolic disease
  - CNS
  - Renal, Other
  - Parental Issues
- Dietary restriction or hypoallergenic formula (AA or EHF) if symptoms suggest allergy
If the baby has infantile colic...

- Explain why babies cry
- Reassure the parents regarding other conditions
- Explain options to reduce crying (swaddling, soothing, repetitive stimulation)
- Explain other potential treatment options
- Schedule appropriate follow-up
- Be certain parents understand you are taking them seriously
- Other options
  - Probiotic
  - Placebo
  - Formula change

**Lactobacillus reuteri DSM 17938 for the Management of Infantile Colic in Breastfed Infants: A Randomized, Double-Blind, Placebo-Controlled Trial**

<table>
<thead>
<tr>
<th>Table 1: Probiotic vs. Placebo Group Comparison for Infantile Colic Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration (minutes)</strong></td>
</tr>
<tr>
<td><strong>Total crying time</strong></td>
</tr>
<tr>
<td><strong>Total time spent on the floor</strong></td>
</tr>
<tr>
<td><strong>Total time spent on the bed</strong></td>
</tr>
</tbody>
</table>

Hania Szajewska, MD, Ewa Gyrczuk, MD, and Andrea Horvath, MD; *J Pediatr* 2013;162:257-62

**Probiotics for Infantile Colic: A Randomized, Double-Blind, Placebo-Controlled Trial Investigating Lactobacillus reuteri DSM 17938**

<table>
<thead>
<tr>
<th>Table 2: Probiotic vs. Placebo Group Comparison for Infantile Colic Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration (minutes)</strong></td>
</tr>
<tr>
<td><strong>Total crying time</strong></td>
</tr>
<tr>
<td><strong>Total time spent on the floor</strong></td>
</tr>
<tr>
<td><strong>Total time spent on the bed</strong></td>
</tr>
</tbody>
</table>

Kim Chau, MSc, Eddy Lau, MD, Saul Greenberg, MD, Sheila Jacobson, MD, Parvaneh Yazdani-Brojeni, MD, Natasha Verma, MD, and Gideon Koren, MD; *J Pediatr* 2015;166:74-8.
Treating infant colic with the probiotic *Lactobacillus reuteri*: double blind, placebo controlled randomized trial

- What is already known on this topic
  - Previous small trials suggest that the probiotic *Lactobacillus reuteri* effectively treats colic in breastfed infants
  - These studies, however, had limitations as they examined a highly selective group of infants with colic
  - The effects of *L. reuteri* on formula fed infants with colic are unknown

- What this study adds
  - *L. reuteri* treatment did not reduce crying or fussing in infants with colic, nor was it effective in improving infant sleep, maternal mental health, family or infant functioning, or quality of life
  - Probiotics therefore cannot be routinely recommended for all infants with colic
  - Further research is needed to identify which subgroups of infants with colic may benefit from probiotics

---

*Canis lupus familiaris*

---

*Synbiotic in the management of infantile colic: A randomized controlled trial*
Probiotics in infantile colic

LGG in Infants with Cow’s Milk Allergy
Fecal Calprotection

• 26 infants with cow’s milk allergic colitis
• Randomized to receive EHCF + or - LGG
• Calprotectin was significantly reduced with LGG, compared to control

Baldassarre ME et al. J Pediatr 2010;156:397-401

Oral hypertonic glucose solution in the treatment of infantile colic

<table>
<thead>
<tr>
<th>Symptom score</th>
<th>Glucose treatment</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nm</td>
<td>%</td>
</tr>
<tr>
<td>0 = getting worse</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 = no improvement</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>2 = mild improvement</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>3 = moderate improvement</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>4 = marked improvement</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>5 = completely well</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Nutritional Supplements and Other Complementary Medicines for Infantile Colic: A Systematic Review

- Few RCTs of CAM for IC are available, and many have methodological problems
- Although some encouraging results exist for fennel extract, mixed herbal tea, and sugar solutions, design flaws and the absence of independent replications preclude practice recommendations.
- The evidence for probiotic supplements and manual therapies does not indicate an effect.

Chiropractic spinal manipulation for infant colic: a systematic review of randomized clinical trials

Practical algorithms for managing common gastrointestinal symptoms in infants
Proposed Approach Fussy Infant

Important messages for caregivers about infant colic

• Baby is not sick – point out normal growth and development; parents are capable of caring for her

• Talk about variation in crying patterns in infants and differences in sensitivity and soothability

• Crying can be reduced by changes in how the infant is handled

• Does not need to be picked up each time she whimpers; needs to be put down when overtired

• Does need more soothing and to learn to self-soothe
Celiac disease is an immune-mediated enteropathy caused by a permanent sensitivity to gluten in genetically susceptible individuals. It occurs in symptomatic subjects with gastrointestinal and non-gastrointestinal symptoms, and in some asymptomatic individuals, including subjects affected by:

- Type 1 diabetes
- Down syndrome
- Turner syndrome
- Williams syndrome
- Selective IgA deficiency
- First degree relatives of individuals with celiac disease

Celiac disease is an autoimmune condition that occurs in genetically susceptible individuals. DQ2 and/or DQ8 positive HLA haplotype is necessary but not sufficient. A unique autoimmune disorder because:

- Both the environmental trigger (gluten) and the autoantigen (Tissue Transglutaminase) are known
- Elimination of the environmental trigger leads to a complete resolution of the disease
Clinical Manifestations

- Gastrointestinal ("classical")
- Non-gastrointestinal ("atypical")
- Asymptomatic

In addition, Celiac Disease may be associated with other conditions, and mostly with:
- Autoimmune disorders
- Some syndromes

The Celiac Iceberg

- Symptomatic Celiac Disease
- Manifest mucosal lesion
- Silent Celiac Disease
- Latent Celiac Disease
- Normal Mucosa

Genetic susceptibility: - DQ2, DQ8
Positive serology
Gastrointestinal Manifestations ("Classic")

Most common age of presentation: 6-24 months

- Chronic or recurrent diarrhea
- Abdominal distension
- Anorexia
- Failure to thrive or weight loss

Rarely: Celiac crisis

Abdominal pain
Vomiting
Constipation
Irritability

Typical Celiac Disease

Non Gastrointestinal Manifestations

Most common age of presentation: older child to adult

- Dermatitis Herpetiformis
- Dental enamel hypoplasia of permanent teeth
- Osteopenia/Osteoporosis
- Short Stature
- Delayed Puberty
- Iron-deficient anemia resistant to oral Fe
- Hepatitis
- Arthritis
- Epilepsy with occipital calcifications
Dermatitis Herpetiformis

- Erythematous macule > urticarial papule > tense vesicles
- Severe pruritus
- Symmetric distribution
- 90% no GI symptoms
- 75% villous atrophy
- Gluten sensitive


Dental Enamel Defects

Involves the secondary dentition
May be the only presenting sign of Celiac Disease

Osteoporosis

Low bone mineral density improves in children on a gluten-free diet.
Short Stature/Delayed Puberty
• Short stature in children / teens:
  - ~10% of short children and teens have evidence of celiac disease
• Delayed menarche:
  - Higher prevalence in teens with untreated Celiac Disease

Fe-Deficient Anemia Resistant to Oral Fe
• Most common non-GI manifestation in some adult studies
• 5-8% of adults with unexplained iron deficiency anemia have Celiac Disease
• In children with newly diagnosed Celiac Disease:
  - Anemia is common
  - Little evidence that Celiac Disease is common in children presenting with anemia

Hepatitis
• Some evidence for elevated serum transaminases (ALT, AST) in adults with untreated Celiac Disease
  - Up to 9% of adults with elevated ALT, AST may have silent Celiac Disease
  - Liver biopsies in these patients showed non-specific reactive hepatitis
  - Liver enzymes normalized on gluten-free diet
Arthritis and Neurological Problems

- Arthritis in adults
  - Fairly common, including those on gluten-free diets
- Juvenile chronic arthritis
  - Up to 3% have Celiac Disease
- Neurological problems
  - Epilepsy with cranial calcifications in adults
  - Evidence for this condition in children with Celiac Disease is not as strong

3 – Asymptomatic

Silent \[\rightarrow\] Latent

**Silent:**
No or minimal symptoms, “damaged” mucosa and positive serology

Identified by screening asymptomatic individuals from groups at risk such:
- First degree relatives
- Down syndrome patients
- Type 1 diabetes patients, etc.

3 – Asymptomatic

Silent \[\rightarrow\] Latent

**Latent:**
No symptoms, normal mucosa

May show positive serology. Identified by following in time asymptomatic individuals previously identified at screening from groups at risk. These individuals, given the “right” circumstances, will develop at some point in time mucosal changes (± symptoms)
Asymptomatic

- Asymptomatic patients are still at risk of osteopenia/osteoporosis

- Treatment with a gluten-free diet is recommended for asymptomatic children with proven intestinal changes of Celiac Disease who have:
  - type 1 diabetes
  - selective IgA deficiency
  - Down syndrome
  - Turner syndrome
  - Williams syndrome
  - autoimmune thyroiditis
  - a first degree relative with Celiac Disease

Associated Conditions

The prevalence of Celiac Disease is higher in patients who have the following:

- Certain genetic disorders or syndromes
- Other autoimmune conditions
- Relative of a biopsy-proven celiac
Genetic Disorders

- Down Syndrome: 4-19%
- Turner Syndrome: 4-8%
- Williams Syndrome: 8.2%
- IgA Deficiency: 7%
   - Can complicate serologic screening

Prevalence of Celiac Disease is Higher in Other Autoimmune Conditions

- Type 1 Diabetes Mellitus: 3.5 - 10%
- Thyroiditis: 4 - 8%
- Arthritis: 1.5 - 7.5%
- Autoimmune liver diseases: 6 - 8%
- Sjögren’s syndrome: 2 - 15%
- Idiopathic dilated cardiomyopathy: 5.7%
- IgA nephropathy: 3.8%
Relatives

- Healthy population: 1:133
- 1st degree relatives: 1:18 to 1:22
- 2nd degree relatives: 1:24 to 1:39


Type 1 Diabetes

Patients are often asymptomatic
Nocturnal hypoglycemia with seizures
TTG may be falsely positive
Gluten-free diet challenging

2 U.S. studies in pediatrics:

- 218 patients. 7.7% EMA+. 4.6% biopsy + (Aktay et al. JPGN 2001;33:462-465)
- 185 patients. 5% EMA+. 4/5 biopsy + (Talal et al. AJG 1997;92:1280-84)

Which Came First?
Celiac Disease and Autoimmunity

- Prevalence of autoimmune disorders in celiac disease related to duration of gluten exposure
  - Diagnosed before 2 years of age: 5%
  - Age 2-10 years: 17%
  - Greater than age 10 years: 24%
- Increased incidence of autoimmune disease in patients with IDDM and "silent" Celiac Disease and their first degree relatives who were EMA+

Ventura et al, Gastro 1999; Not, Diabetologia 2001

Complications

Major Complications of Celiac Disease

- Short stature
- Dermatitis herpetiformis
- Dental enamel hypoplasia
- Recurrent stomatitis
- Fertility problems
- Osteoporosis
- Gluten ataxia and other neurological disturbances
- Refractory celiac disease and related disorders
- Intestinal lymphoma
Mechanisms of Celiac Disease Complications

- Intestinal malabsorption
  - protein-caloric malnutrition
  - deficiency of specific nutrients
- Genetic background
- Autoimmunity
- IEL clonal proliferation

Celiac Disease Associated Disorders

- Autoimmune diseases: type 1 diabetes, Hashimoto's thyroiditis, autoimmune hepatitis, adrenal failure
- Down syndrome
- IgA deficiency
- Turner syndrome
- Williams syndrome

Recurrent Aphtous Stomatitis

By permission of C. Mulder, Amsterdam (Netherlands)
Dermatitis Herpetiformis

Low Bone Mineral Density (DXA) in a Child With Untreated Celiac Disease

CT Scan Showing Occipital Calcifications in a Boy with Celiac Disease and Epilepsy
Epidemiology

The “old” Celiac Disease Epidemiology:

- A rare disorder typical of infancy
- Wide incidence fluctuates in space (1/400 Ireland to 1/10000 Denmark) and in time
- A disease of essentially European origin
The availability of sensitive serological markers made it possible to discover Celiac Disease even when the clinical suspicion was low. The Changing Celiac Epidemiology

<table>
<thead>
<tr>
<th>AGA</th>
<th>EMA</th>
<th>TTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>1990</td>
<td>2000</td>
</tr>
</tbody>
</table>

"Mines" of Celiac Disease Were Found Among:

- Relatives
  - Patients with short stature, anaemia, fatigue, hypertransaminasemia
  - Associated diseases: autoimmune disorders, Down's, IgA deficiency, neuropathies, osteoporosis, infertility
  - "Healthy" groups: blood donors, students, general population
**The First Picture of the Celiac Iceberg**

**Celiac Disease Epidemiological Study in USA**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive 31</td>
<td>Negative 4095</td>
<td>Positive 81</td>
</tr>
<tr>
<td>Positive 205</td>
<td>Negative 4303</td>
<td>Positive 33</td>
</tr>
</tbody>
</table>

**Symptomatic subjects: 3236**

**1st degree relatives: 4508**

**2nd degree relatives: 1275**

**Healthy Individuals: 4126**

**Risk Groups: 9019**

Projected number of celiacs in the U.S.A.: 2,115,954

Actual number of known celiacs in the U.S.A.: 40,000

For each known celiac there are 53 undiagnosed patients.


---

**Celiac Disease Prevalence Data**

<table>
<thead>
<tr>
<th>Geographic Area</th>
<th>Prevalence on clinical diagnosis*</th>
<th>Prevalence on screening data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>1:600</td>
<td>1:600</td>
</tr>
<tr>
<td>Denmark</td>
<td>1:9,990</td>
<td>1:500</td>
</tr>
<tr>
<td>Finland</td>
<td>1:202</td>
<td>1:122</td>
</tr>
<tr>
<td>Germany</td>
<td>1:5,306</td>
<td>1:500</td>
</tr>
<tr>
<td>Italy</td>
<td>1:1,000</td>
<td>1:184</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1:7,000</td>
<td>1:175</td>
</tr>
<tr>
<td>Norway</td>
<td>1:975</td>
<td>1:250</td>
</tr>
<tr>
<td>Slovenia</td>
<td>1:15</td>
<td>1:76</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1:184</td>
<td>1:122</td>
</tr>
<tr>
<td>Sweden</td>
<td>1:190</td>
<td>1:190</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1:122</td>
<td>1:175</td>
</tr>
<tr>
<td>World (average)</td>
<td>1:2,345</td>
<td>1:265</td>
</tr>
</tbody>
</table>

*based on classical, clinical presentation

Fasano & Catassi, Gastroenterology 2001; 120:636-651.
Celiac Societies Data in Europe and USA (approximate estimates)

<table>
<thead>
<tr>
<th>Country</th>
<th>Celiac Society members (n)</th>
<th>Population</th>
<th>Frequency of CD membership</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>48,000</td>
<td>55,000,000</td>
<td>1:1146</td>
</tr>
<tr>
<td>Italy</td>
<td>20,000</td>
<td>57,000,000</td>
<td>1:283</td>
</tr>
<tr>
<td>Sweden</td>
<td>12,500</td>
<td>8,500,000</td>
<td>1:638</td>
</tr>
<tr>
<td>Germany</td>
<td>12,000</td>
<td>83,000,000</td>
<td>1:6833</td>
</tr>
<tr>
<td>Finland</td>
<td>15,000</td>
<td>4,000,000</td>
<td>1:264</td>
</tr>
<tr>
<td>Spain</td>
<td>6,000</td>
<td>38,000,000</td>
<td>1:6312</td>
</tr>
<tr>
<td>Norway</td>
<td>6,000</td>
<td>4,300,000</td>
<td>1:716</td>
</tr>
<tr>
<td>Netherlands</td>
<td>4,500</td>
<td>15,000,000</td>
<td>1:3333</td>
</tr>
<tr>
<td>France</td>
<td>3,700</td>
<td>37,000,000</td>
<td>1:15405</td>
</tr>
<tr>
<td>Belgium</td>
<td>1,600</td>
<td>10,000,000</td>
<td>1:6255</td>
</tr>
<tr>
<td>Austria</td>
<td>2,400</td>
<td>7,500,000</td>
<td>1:3125</td>
</tr>
<tr>
<td>Switzerland</td>
<td>2,200</td>
<td>6,900,000</td>
<td>1:3049</td>
</tr>
<tr>
<td>Iceland</td>
<td>2,000</td>
<td>3,000,000</td>
<td>1:1515</td>
</tr>
<tr>
<td>Denmark</td>
<td>1,100</td>
<td>5,200,000</td>
<td>1:4727</td>
</tr>
<tr>
<td>Europe</td>
<td>149,200</td>
<td>354,600,000</td>
<td>1:2377</td>
</tr>
<tr>
<td>USA</td>
<td>40,000</td>
<td>281,421,906</td>
<td>1:7035</td>
</tr>
</tbody>
</table>

Celiac Disease Icebergs

In Italy the Celiac Case-Finding is Increasingly Efficient

Incidence of CD on 1000 newborns in the March (Middle Italy)
**The Size of the Submerged Iceberg is Decreasing in Many Countries Due to Active Case-Finding**

Even an intensive policy of Celiac Disease case-finding will leave at least 50% of celiacs without a diagnosis.

**Natural History Of Celiac Disease At Glance**

- **BIRTH**
  - Genetically predisposed subject
  - Development of celiac enteropathy
- **ENVIRONMENTAL TRIGGERS**
  - Gluten "load"
  - Intestinal infections
  - Pregnancy
cancer
- **DEATH**
  - CD complications
  - Persistently silent CD

**Where Have The Aging Celiacs Gone?**

The proportion of symptomatic cases increases with age.
Increased Overall Mortality In Adult Life

Causes of Death in Patients With Celiac Disease in a Population-Based Swedish Cohort

Mortality in patients with celiac disease and their relatives: a cohort study

Risk Factors

The Grains

The Genes

Spread of Agriculture and Celiac Disease

1 Cereals domestication started 10,000 years ago in the Fertile Crescent...

2 Catalhoyuc, the first town in the world was built 8,000 y ago

3 Agriculture slowly spread with an East-West gradient (1 km/y)...

4 CD genes confer disadvantage in areas of high cereal consumption

INVERSE RELATIONSHIP BETWEEN CD FREQUENCY AND LENGTH OF TIME SINCE THE INTRODUCTION OF AGRICULTURE ?

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INVERSE RELATIONSHIP BETWEEN CD FREQUENCY AND LENGTH OF TIME SINCE THE INTRODUCTION OF AGRICULTURE ?
**Celiac Disease in the Saharawis**
- 1:18 children are affected with Celiac Disease
- Diarrhea, stunting, anemia
- EMA pos, typical jejunal damage
- High frequency of DR3/DR3 and DR3/DR4
- High mortality (especially in summer)

**Celiac Disease in Iran**
- The prevalence of Celiac Disease among 2000 Iranian blood donors is one of the highest in the world (1:166).
- Celiac Disease is a common finding among patients labelled as irritable bowel syndrome (11%).
- The theory on the East-West increasing gradient of Celiac Disease prevalence does not hold.

**Celiac Disease in India**
- Common cause of chronic diarrhea both in children and in adults
- Long diagnostic delay
- “Hypertypical” clinical presentation
- Strong association with DQ2 heterodimer and with DR3 Asian haplotypes (A26-B8-DR3)
Celiac Disease in Developing Countries

- Worldwide circulation of gluten-containing food could cause epidemics of Celiac Disease
- Largely underestimated (e.g. along the “silk road”)
- Typical symptoms and stunting (nutritional dwarfism)
- Celiac Disease serological markers still reliable
- Formidable treatment difficulties

The Global Village of Celiac Disease

- In many areas of the world Celiac Disease is one of the commonest, lifelong disorders affecting around 1% of the general population.
- Most cases escape diagnosis and are exposed to the risk of complications.
- Active Celiac Disease case-finding is needed but mass screening should be considered.
- The impact of Celiac Disease in the developing world needs further evaluation.

Pathogenesis
Pathogenesis

- Genetic predisposition
- Environmental triggers
  - Dietary
  - Non-dietary?

Pathogenesis

Genetics
- Strong HLA association
- 90 - 95% of patients HLA-DQ2 – also found in 20 - 30% of controls
  - Most of the remainder are HLA-DQ8
- 10% of patients have an affected first degree relative

Genetics
- Gluten
- Necessary Causes
- Gender
- Infant feeding
- Infections
- Others
- Risk Factors

Celiac disease
Genetics

• Concordance in monozygotic twins is 70%
• Concordance in HLA-identical siblings 30 - 40%, suggesting other genes involved
• Protein binding receptors on antigen presenting cells

Several genes are involved
• The most consistent genetic component depends on the presence of HLA-DQ (DQ2 and/or DQ8) genes
• Other genes (not yet identified) account for 60% of the inherited component of the disease
• HLA-DQ2 and/or DQ8 genes are necessary (No DQ2/8, no Celiac Disease!) but not sufficient for the development of the disease

Be aware DR3 should now be referred to as DR17

Genes

HLA

Gluten

Celiac Disease

DQA1*0501
DQB1*0201
DQ2

{DQA1*0201

{DR3 DR3/DR3 DR5/DR7

DQA: Any

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DR17

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DR17

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

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DR3

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DQB1*0201

DQ2

DQ8

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DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

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DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3

DQA1*0501

DQB1*0201

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DQ8

Be aware DR3 should now be referred to as DR17

DR3

DQA1*0501

DQB1*0201

DQ2

DQ8

Be aware DR3 should now be referred to as DR17

DR3
Genetics

• Non-HLA Related Factors
  – Concerns about HLA factors
    • < 2% of all DQ2 carriers have Celiac Disease
    • concordance for HLA matched siblings (30-40%) is lower than for monozygotic twins (~70%)
  – Data suggests additional non HLA genes
  – Inheritance of Celiac Disease most likely multigenic
  – Conflicting data for non HLA genes

Genetics

• Genetic factors associated with effector T-cell reactivity
  – CTLA-4 - negative regulation of T-cell activation
  – CTLA-4/CD28 gene locus linked to autoimmune disease (IDDM, Graves, Celiac Disease)
  – CTLA-4 polymorphism in Finnish and French patients with Celiac Disease but not in Italian and Tunisian families

Dietary Factors

The Grass Family - (GRAMINEAE)

Subfamily
Festucaeeae

Tribe
Zizaneeae
Oryzaeeae
Hordeaceae
Aveneeae
Festucaeeae
Chlorideae

Wild rice
Rice
Oat
Wheat
Rye
Barley
Teff
Finger millet (ragi)
Dietary Factors

- Wheat - (15% protein, 75% starch)
- Rye prolamines - secalins
- Barley prolamines - hordeins
- Oats prolamines - avenins

Gluten
Gliadin (alcohol soluble) Prolamine
Glutenin (alcohol insoluble)

Amino acid sequence of A-gliadin is rich in proline (P) and glutamine (Q).

P = 15%
Q = 30%

No specific peptide activates disease in all Celiac Disease patients.

- 33 amino acid peptide in gliadin contains critical epitopes – high in glutamine and proline
- Resistant to digestion in lumen
- Penetrates epithelial barrier
- Modified by the enzyme tissue transglutaminase – deamidates glutamine residues to glutamic acid
- Resulting higher affinity binding to HLA DQ2 molecule on the surface of antigen-presenting cells
Toxic Peptides Digestion

33-mer PEP

Shan L. et al Science 2002
Matysiak-Budnik et al Gastroenterology 2003

Non Dietary Factors

- Infections
  - Viral infections
    - sequence homology between α-gliadin & adenovirus type 12 & 7, rubella and human herpesvirus 1
  - Parasitic infestations
    - sequence homology between α-gliadin & Plasmodium yoelli
  - Other?

Role of Cytokines

- Mucosal cytokines
  - upregulation of IL2 receptor expression
  - increased γ interferon mRNA expression
  - involvement of IL15
  - in vitro gluten stimulation of mucosa from treated Celiac Disease patients
    - γ interferon mRNA
    - IL2 mRNA
T Cells Activation

- Presentation of modified gliadin peptide in context of HLA-DQ2 leads to activation of CD4+ lamina propria T cells
- Gliadin-specific T cells have a Th1 functional phenotype with high secretion of IFN-γ

Mucosal Events

- Epithelial cell infiltration
  - increased IEL's - (>90% CD8, <10% CD4)
  - increased mucosal γδ T cells (nl <10%)
  - role of γδ T cells in Celiac Disease unknown
- Mucosal surface alterations
  - loss of epithelial cells
  - proliferation of crypt epithelial cells

Humoral Response

- Humoral response
  - enhanced antibody production
    - Anti-tissue transglutaminase
    - Anti-gliadin
    - ? other autoantigens (anti-actin)
  - mechanism of antibody production unknown
Tissue Transglutaminase (TTG)

- Normal gut enzyme released during injury and stabilizes the cross-linking of proteins in granulation tissue
- Role in Celiac Disease
  - Modification of gliadin epitopes
  - Autoantibodies against TTG correlate with active Celiac Disease - ? involved in pathogenesis

Pathophysiology Sequelae

- Malabsorption of nutrients, especially iron, folate, calcium, and vitamin D
- Increased intestinal permeability may permit entry of other toxins which might induce autoimmune diseases

Hypothesis
Proposed Zonulin Mechanism of Action


Intestinal lumen
Submucosa

Intestinal Lumen
Submucosa
Pathogenesis:

Unanswered Questions

Questions:

- Mechanisms for failure of gliadin tolerance
- Role of innate immunity
- What are immunodominant epitopes
- Does gluten have direct effect on mucosa
- How is mucosal TH1 response induced/maintained
- Mechanism and role of IELs
- How is mucosal remodeling induced
- What is the role of autoantibodies
Diagnosis

Diagnostic principles
• Confirm diagnosis before treating
  – Diagnosis of Celiac Disease mandates a strict gluten-free diet for life
  • following the diet is not easy
  • QOL implications
• Failure to treat has potential long term adverse health consequences
  • increased morbidity and mortality

Diagnosis

• Diagnosis of Celiac Disease requires:
  – characteristic small intestinal histology in a symptomatic child
  – complete symptom resolution on gluten-free diet
• Serological tests may support diagnosis
• Select cases may need additional diagnostic testing

ESPGAN working group. Arch Dis Child 1990;65:909
Serological Tests

Role of serological tests:
• Identify symptomatic individuals who need a biopsy
• Screening of asymptomatic “at risk” individuals
• Supportive evidence for the diagnosis
• Monitoring dietary compliance

Serological Tests

• Antigliadin antibodies (AGA)
• Antiendomysial antibodies (EMA)
• Anti tissue transglutaminase antibodies (TTG)
  – first generation (guinea pig protein)
  – second generation (human recombinant)
• HLA typing

Antigliadin Antibodies

• Antibodies (IgG and IgA) to the gluten protein in wheat, rye and barley
• Advantages
  – relatively cheap & easy to perform
• Disadvantages
  – poor sensitivity and specificity
**Endomysial Antibody - EMA**

- IgA based antibody against reticulin connective tissue around smooth muscle fibers
- **Advantages**
  - high sensitivity and specificity
- **Disadvantages**
  - false negative in young children
  - operator dependent
  - expensive & time consuming
  - false negative in IgA deficiency

**Tissue Transglutaminase - TTG**

- IgA based antibody against tissue transglutaminase (Celiac Disease autoantigen)
- **Advantages**
  - high sensitivity and specificity (human TTG)
  - non operator dependent (ELISA/RIA)
  - relatively cheap
- **Disadvantages**
  - false negative in young children
  - false negative in IgA deficiency
  - possibly less specific than EMA
Serological Test Comparison

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGA-IgG</td>
<td>69 – 85</td>
<td>73 – 90</td>
</tr>
<tr>
<td>AGA-IgA</td>
<td>75 – 90</td>
<td>82 – 95</td>
</tr>
<tr>
<td>EMA (IgA)</td>
<td>85 – 98</td>
<td>97 – 100</td>
</tr>
<tr>
<td>TTG (IgA)</td>
<td>90 – 98</td>
<td>94 – 97</td>
</tr>
</tbody>
</table>

Serum IgA Level

- Individuals with IgA deficiency are at increased risk for Celiac Disease
- IgA deficient individuals will have negative EMA-IgA & TTG-IgA
- Check IgA levels with Celiac Disease serology in all symptomatic individuals
- Consider IgG based tests (EMA-IgG & TTG-IgG) in IgA deficiency
HLA Tests

HLA alleles associated with Celiac Disease
• DQ2 found in 95% of celiac patients
• DQ8 found in remaining patients
• DQ2 found in ~30% of general population

Value of HLA testing
• High negative predictive value
  – Negativity for DQ2/DQ8 excludes diagnosis of Celiac Disease with 99% confidence

HLA Tests

• Potential role for DQ2/DQ8
  • asymptomatic relatives
  • Down, Turner & Williams syndrome
  • type 1 diabetes
  • diagnostic dilemmas

Endoscopic Findings

Normal Appearing  Scalloping  Nodularity

Scalloping
Biopsy Diagnosis

- Histologic Features:
  - Increased IEL’s (> 30/100 enterocytes)
  - Loss of nuclear polarity
  - Change from columnar to cuboid
  - Lamina propria cellular infiltrate
  - Crypt elongation and hyperplasia
  - Increased crypt mitotic index
  - Progressive villous flattening

Patterns of Mucosal Immunopathology

<table>
<thead>
<tr>
<th>Type</th>
<th>Normal Celiac Disease (latent)</th>
<th>Infiltrative Celiac</th>
<th>Hyperplastic Celiac</th>
<th>Flat destructive Celiac</th>
</tr>
</thead>
</table>

Diagnostic Pitfalls

- Poor Orientation

Nutritional Exam and Review of Systems

- Dimorphic Anemia
- Peripheral Neuropathy
- Rickets in Children
- Bone Pain
- Tetany
- Acrodermatitis
- Peripheral Neuropathy
- Easy bruising
- Coagulopathy
- Night Blindness

Fantastic Voyage

- Celiac
- Normal
### Treatment

- Only treatment for celiac disease is a gluten-free diet (GFD)
  - Strict, lifelong diet
  - Avoid:
    - Wheat
    - Rye
    - Barley

### Gluten-Containing Grains to Avoid

<table>
<thead>
<tr>
<th>Grains</th>
<th>Bulgar</th>
<th>Couscous</th>
<th>Durum</th>
<th>Einkorn</th>
<th>Barley</th>
<th>Barley Malt/Extract</th>
<th>Rye</th>
<th>Filler</th>
<th>Graham flour</th>
<th>Kamut</th>
<th>Matzo</th>
<th>Emmer</th>
<th>Faro</th>
<th>Triticale</th>
</tr>
</thead>
</table>
Sources of Gluten

- OBVIOUS SOURCES
  - Bread
  - Bagels
  - Cakes
  - Cereal
  - Cookies
  - Pasta / noodles
  - Pastries / pies
  - Rolls

Sources of Gluten

- POTENTIAL SOURCES
  - Candy
  - Communion wafers
  - Cured Pork Products
  - Drink mixes
  - Gravy
  - Imitation meat / seafood
  - Sauce
  - Self-basting turkeys
  - Soy sauce

Ingredients to Question (may contain gluten)

- Seasonings and spice blends or mixes
- Modified food starch
- Malt/ malt extract/ flavoring
- Modified hop extract and yeast-malt sprout extract
- Dextrin
- Caramel color
### Gluten-Free Grains and Starches

- Amaranth
- Arrowroot
- Buckwheat
- Corn
- Flax
- Millet
- Montina
- Oats*
- Potato
- Quinoa
- Rice
- Sorghum
- Tapioca
- Teff
- Flours made from nuts, beans and seeds

*for possible cross-contamination with gluten containing grains

### Safe Ingredients

- Starch
- Maltodextrin
  - Made from cornstarch, potato starch, or rice starch, but not from wheat
- Vinegar and Alcohol
  - Distilled vinegar and distilled spirits are gluten-free, however avoid malt vinegar and malt beverages (e.g. beer)

### Other Items to Consider

- Lipstick/Gloss/Balms
- Mouthwash/Toothpaste
- Play Dough
- Stamp and Envelope Glues
- Vitamin, Herbal, and Mineral preparations
- Prescription or OTC Medications
Potential Nutritional Complications in Untreated Celiac Disease

- Low Iron
- Low Folate
- Low Vitamin B-12
- Low Vitamins ADEK
- Low Thiamine
- Low Niacin
- Low B6 (rare)
- Low Beta-carotene
- Low Zinc
- Essential Fatty Acid Deficiency
- Prolonged PT
- Hypocalcaemia
- Elevated PTH
- Increased Alkaline Phosphatase
- Hypophosphatemia
- Hypomagnesaemia
- Hypoalbuminemia
- Re-feeding syndrome

Anemia in Celiac Disease

- Microcytic anemia - iron absorption most efficient in the duodenum
- Megaloblastic/Macrocytic anemia – folate is absorbed primarily in the proximal third of the small intestine (location of folate hydrolases)
- Vitamin B-12 deficiency occurs rarely
Importance of Folic Acid Supplementation

- Folate hydrolases are needed in the brush border for absorption
- Best absorbed in proximal 3rd of duodenum.
- Increased use of folate in apoptosis
- Low folate impairs cell division

Importance of Folic Acid Supplementation

- Low folate increases irritability & forgetfulness
- Celiac Disease increases risk of GI malignancies
  - Folate supplement may have anti-cancer effect as needed for DNA replication
- Supplement Celiac Disease patients with 1 mg folic acid

Bone Disease in Celiac Disease

- Arthritis
- Osteoporosis
- Osteopenia
- Osteomalacia
- Rickets
Calcium and Vitamin D Requirements

- 800 to 1200 mg/day of Calcium for low bone mineral density (LBMD) in males
- 1200-1500 mg/day of Calcium for treatment of LBMD in females
- 400 IU of Vitamin D daily
- Up to 2/3 of patients on a gluten-free diet have suboptimal calcium intake

Lactose Intolerance & Celiac Disease: Incidence

- Secondary lactase deficiency is estimated to be 20-40%
- Increasing lactose intolerance with delayed diagnosis
- Increased incidence in patients with GI symptoms in Celiac Disease
- Decrease calcium and vitamin D intake in lactose intolerance

Lactose Intolerance & Celiac Disease: Treatment

- Gluten free diet
- Temporary lactose-reduction
- Lactase enzymes
- Lactose-free milk
- Gluten-free milk substitute
- Supplement with calcium & vitamin D where appropriate
Nutrients Speculated to Play a Role in Celiac Disease Infertility and Pregnancy Outcomes

Low Levels of:
- Iron
- Zinc
- Folic Acid
- Vitamin B-12
- Protein
- Vitamin K
- Vitamin B-6
- Vitamin E

Nutritional Exam and Review of Systems

- Dimorphic Anemia
- Peripheral Neuropathy
- Rickets in Children
- Bone Pain
- Tetany
- Acrodermatitis
- Peripheral Neuropathy
- Easy bruising
- Coagulopathy
- Night Blindness

Nutritional Exam and Review of Systems

- Amenorrhea, Infertility
- Impotence
- Cheilosis
- Glossitis
- Stomatitis
- Purpura
- Follicular Hyperkeratosis
- Hyperpigmented dermatitis
- Edema
- Ascites
Possible Causes of GI Symptoms on a Gluten-Free Diet

- Acidic foods
- Sorbitol
- Olestra
- Guar gums
- Antibiotics
- Lactose
- Alternate flours made from beans or nuts
- Food Allergens such as Milk Protein, Soy, Nuts, Egg, Corn
- Food Intolerance to fructose Foods high in salicylates and amines

Eating Healthy on the Gluten-Free Diet

- Similar to a normal diet
  - Moderate cholesterol
  - Moderate protein
  - Low fat, sodium, alcohol, and concentrated sugars
  - High fiber
- Variety of foods for good nutrient balance

Improving Nutrient Density

- Nutrient density and quality of the gluten-free diet can be improved:
  - Use nutrient-rich grains/seeds
    - Amaranth
    - Bean
    - Buckwheat
    - Teff
    - Millet
    - Montina
    - Rice Bran
    - Quinoa
    - Sorghum
    - Soy
  - These grains are:
    - higher in protein and amino acids
    - moderate carbohydrates
    - good sources of calcium
    - some are higher in iron than wheat
    - low sodium.
Improving Nutrient Density

• When limiting the use of gluten-free flours to the most common sources (rice, corn), nutrient deficiencies may occur due to low fiber content and excess calories.

• Rapid increases in fiber intake may lead to increased GI distress.

Living Gluten-Free

• You can have a positive outlook.

• Learning to live:
  – Gluten-free foods are better tasting than ever before.
  – The diet gets easier as patients adjust to it.
  – It is not necessary to restrict the patient's lifestyle, it is just a different way of eating.

• Don't make it harder than it needs to be
  – Why following a strict gluten-free diet is vital to living a full, healthy life.

• Weight management may become a concern.

Dietary Adherence: A Common Problem

• Only 50% of Americans with a chronic illness adhere to their treatment regimen including:
  – diet
  – exercise
  – medication

• Dietary compliance can be the most difficult aspect of treatment.
Health Beliefs of Adults with Celiac Disease

- Survey of 100 people in Celiac Disease support group (Buffalo, NY)
  - Number of people who agreed with following statements:
    - “If I eat less gluten I will have less intestinal damage.” – 51%
    - “I’ve lived this long eating gluten, how much will the gluten-free diet really help me now?” – 33%
    - “My doctor should be the one to tell me when I need follow up testing.” – 26%
    - “Scientist/diagnosis still haven’t proven that gluten really hurts them.” – 10%

Barriers to Compliance

- Ability to manage emotions – depression, anxiety
- Ability to resist temptation – exercising restraint
- Feelings of deprivation
- Fear generated by inaccurate information

Barriers to Compliance

- Time pressure – time to plan, prepare food is longer
- Planning – work required to plan meals
- Competing priorities – family, job, etc.
- Assessing gluten content in foods/label reading
- Eating out – avoidance, fear, difficult to ensure food is safe
Barriers to Compliance

- Social Events – Not wanting to look/be different
- Support of Family and Friends – “Just a little bit – it won’t hurt you”

Factors that Improve Adherence

Internal Adherence Factors Include:
- Knowledge about the gluten-free diet
- Understanding the risk factors and serious complications can occur to the patient
- Ability to break down big changes into smaller steps
  - Ability to simplify or make behavior routine
- Ability to reinforce positive changes internally
- Positive coping skills
- Ability to recognize and manage mental health issues
- Trust in physicians and dietitians

The Key to Dietary Compliance is Follow Up Care

- NASPGHAN Guidelines apply to adults and children
- The health effects are motivation
  - When one believes they are real
  - Testing measures the health effects of eating gluten
- Follow up testing provides important feedback
The Key to Dietary Compliance is Follow Up Care

- Test results are a powerful motivator, especially those who do not have symptoms when they eat gluten.
- Patients/parents look to the physician to tell them when follow-up testing is needed.
- Proactive follow-up measures can reinforce adherence.

Resources

- Reputable websites
  - Celiac.Com (www.celiac.com)
  - National Institutes of Health (www.niddk.nih.gov)
  - American Dietetic Association (www.eatright.org)
- Local Support Groups
  - Celiac.Com (www.celiac.com)
- National Support Groups
  - The Gluten Intolerance Group – GIG (www.gluten.net)
  - Celiac Disease Foundation – CDF (www.celiac.org)
- Research and Information
  - Center for Celiac Research (www.celiaccenter.org)

Resources

- Cookbooks
  - Hagman, Bette, “The Gluten-Free Gourmet Cooks Fast and Healthy”
  - Saros, Connie, “Wheat-free Gluten-free Cookbook for Kids and Busy Adults”
- Books and Magazines
- Gluten-Free Living
- Sully’s Living Without (www.livingwithout.com)

- Product information
  - www.glutenfreemall.com
Prevention & Future Directions

Celiac Disease-Diagnosis: The Future

• Diagnosis Strategies
  – Mass population screening
    • Not cost effective (research tool)
    • Benefits uncertain
• Active case finding
  – Selective serological testing
  – Biopsy confirmation

Celiac Disease-Diagnosis: The Future

• Non biopsy diagnosis
  – Characteristic clinical subgroups
  – Refined (standardized) serological tests
  – Use of HLA typing
  – Discovery of biomarkers
  – Specific gene identification
Celiac Disease-Management: The Future

- Gluten free diet remains best treatment
- Refined understanding of “gluten free”
- FDA mandates better food labeling
- Commercial recognition of the “value” of gluten free products
Pediatric Malnutrition:
Identification, Assessment, & Intervention

Maureen Egan, APRN, MSN
Natalie Navarre, MA, RD, CSP, LDN

Objectives

- Define pediatric malnutrition/FTT and identify common causes
- Discuss methods of identifying and classifying pediatric malnutrition
- Identify initial nutrition interventions to address malnutrition
- Coordinating Care: GI & Nutrition

Disclosure

- We do not have any financial disclosures.
Defining Malnutrition

- Pediatric malnutrition (undernutrition) is "an imbalance between nutrient requirements and intake that results in cumulative deficits of energy, protein or micronutrients that may negatively affect growth, development and other relevant outcomes" - Mehta et al., 2013

- Prevalence rates reported between 24% and 50% worldwide

Malnutrition vs. Failure to Thrive (FTT)

<table>
<thead>
<tr>
<th>Malnutrition</th>
<th>Failure to Thrive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can be used as a diagnosis</td>
<td>A sign of malnutrition (undernutrition), not a diagnosis</td>
</tr>
<tr>
<td>- E44.1 = mild malnutrition</td>
<td>FTT is a term used to describe inadequate growth or the inability to maintain growth</td>
</tr>
<tr>
<td>- E44.0 = moderate malnutrition</td>
<td>Lacks a clear definition</td>
</tr>
<tr>
<td>- E43 = severe protein/calorie malnutrition</td>
<td>No consensus on what criteria should be used to define FTT</td>
</tr>
<tr>
<td>Has a clear definition</td>
<td></td>
</tr>
<tr>
<td>Consensus on indications for identifying and documenting malnutrition</td>
<td></td>
</tr>
</tbody>
</table>

Look at full clinical picture, not just the growth chart!

- Children of small parents growing to their genetic potential (short stature)
- LGA infants who regress toward the mean
- Children with constitutional delay in growth (versus stunting)
- Premature infants with normal growth when corrected for age
- Children with special needs
- Children who are growing to their genetic potential
- 24 wk premie, now 4 mo, CA of ~1.2mo Growing to genetic potential
- 36 wk premie, now 4 mo, CA of ~1.3mo Growing to genetic potential

Look at full clinical picture, not just the growth chart!
### Common Causes for Malnutrition

#### Etiology of malnutrition
- Illness related: disease or trauma
- Non-illness related: environmental or behavioral

#### Increased caloric demand
- Cancer
- Chronic infection (HIV)
- Chronic lung disease
- Congenital heart defects
- High muscle tone
- Hyperthyroidism
- Thyroid disease

#### Inadequate caloric intake
- Compromised feeding skills
- Food aversion
- Food insecurity
- GERD
- Medication-induced anorexia
- Pyloric stenosis

#### Inadequate caloric absorption, metabolism, or utilization
- Celiac disease
- Cystic fibrosis
- Diabetes
- Inborn errors of metabolism
- Inflammatory bowel disease
- Liver disease
- Milk protein allergy
- Short gut

### Screening Labs

- Common initial diagnostic screening labs:
  - CBC with diff and plt
  - Comprehensive metabolic panel
  - Sed rate
  - Celiac Panel
  - Lead level
  - Urinalysis and culture
  - Fecal Calprotectin
  - Stool studies if indicated

- Adjust to meet individualized needs of the patient

### Identifying Malnutrition

- In 2014, Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) published a consensus statement on the identification and documentation of pediatric malnutrition

- Indicators:
  - Food/Nutrient intake
  - Assessment of energy and protein needs
  - Growth parameters
  - Weight gain velocity
  - Mid-upper arm circumference (MUAC)
  - Handgrip strength
  - Documentation of tanner stage
1. Food/Nutrient Intake

- Major determinant of nutritional status
- Accurate assessment of intake and estimation of adequacy is critical
  - Necessary in order to determine the degree of the deficit and the extent/acuity of the deficit
- Primary concern: Is the child’s current intake adequate to meet his/her nutrition needs in the context of his/her current clinical situation, growth pattern, and developmental level?

2. Assessment of Nutrient Needs

- Equations are estimates
- GOLD STANDARD: Indirect Calorimetry
- Calories:
  - RDA for infants and toddlers 0-3yr
  - WHO REE x Activity Factor for children older than 3 years of age
- Protein:
  - RDA for all ages
- Catch-up growth:
  - 0-3 yrs: Calorie and protein needs based on RDA x ideal body weight / actual weight
  - Calories for children older than 3 = Activity factor of 1.5-1.7
- Vitamin/Minerals:
  - Dietary reference intakes (DRI) for age
    - Recommended Dietary Allowance (RDA), Adequate Intakes (AI), UL (Tolerable Upper Intake Level)

3. Growth Parameters

- Growth is the primary outcome measure of nutritional status in children
- Children 0-2 years:
  - length-for-age
  - weight-for-age
  - head circumference-for-age (up to 36 months)
  - weight-for-length
- Children 2-20 years:
  - standing height-for-age
  - weight-for-age
  - BMI-for-age
Growth Charts
- Designed to observe growth trends over time and for early detection of growth problems
  - Not intended as a sole diagnostic instrument
- WHO growth charts for children ages 0-2 years
  - Developed in 2006, multicenter study, 6 countries
  - Depicts normal human growth under optimal environment conditions (BF for at least 4 months, still BF at 12 months)
- CDC Growth charts for children ages 2-20 years
  - Data obtained from NHANES surveys from 1963-1994
  - Measurements of height change from recumbent length to standing height
  - Reference for typical growth in US
- Premature infants
  - Plot for corrected age, weight (until 24mo), length (until 40mo), HC (36mo)

Growth Charts: Percentiles vs Z-scores
Percentiles
- Indicates the portion of the reference population that lies above or below the child being measured
- Does not reveal the degree of deviation from population norms

Z-scores
- If above or below “average,” it measures how “atypical” the data point is
- Reveals the degree of deviation from the mean
- Allows for more precision describing anthropometric status compared to percentiles

Z-Scores
- Recommendation for monitoring and assessing nutritional status in pediatric population
- “A statistical measure that tells how a single data point compares with normal data and, if above or below “average,” how atypical the measurement is” - Becker et al., 2015

Adapted from Ehrenfeld, 2009
4. Weight Gain Velocity
- Growth velocity: rate of change in weight or length/height over time
- Can be used as an early sign of healthy or unhealthy response to the nutritional environment

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight (grams per day)</th>
<th>Length/Height (cm per wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 months</td>
<td>23-34</td>
<td>0.80-1.00</td>
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<tr>
<td>4-8 months</td>
<td>10-16</td>
<td>0.37-0.47</td>
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<tr>
<td>8-12 months</td>
<td>6-11</td>
<td>0.28-0.37</td>
</tr>
<tr>
<td>1-3 years</td>
<td>4-10</td>
<td>0.18-0.25</td>
</tr>
<tr>
<td>4-6 years</td>
<td>5-6</td>
<td>0.10-0.18</td>
</tr>
</tbody>
</table>

*Ages 2-6 years, average gain of 2-3 kg/year and growth of 5-8 cm/year*

Pediatric Nutrition Reference Guide. 10th Ed. Texas Children’s Hospital.

Classification of Malnutrition
- Previous Recommendations:
  - Percentage of ideal body weight (Gomez Classification and Waterlow Criteria)
  - Defining undernutrition and FTT as decreases in 2 percentiles or faltering growth as weight below the 5th%ile

- Current Recommendations:
  - Using Z-score, decline in Z-score, and negative Z-score to identify and document pediatric malnutrition

Classification of Malnutrition
- Acute Malnutrition:
  - Less than 3 months
  - Weight loss or lack of weight gain
- Chronic Malnutrition:
  - 3 months or longer
  - Stunting in height-for-age

- Mild
  - Usually due to acute event
  - Presentation: unintentional weight loss or suboptimal weight gain velocity

- Moderate
  - Undernutrition of a significant duration
  - Presentation: weight-for-length or BMI-for-age below normal range

- Severe
  - Prolonged undernutrition
  - Presentation: declines in rates of linear growth that result in stunting
Key Elements in Assessment of Growth for Malnutrition

- Decline in Z-score greater than -1 SD
- Height-for-age Z-score less than -2.0
- Suboptimal weight gain for age
- Weight-for-length or BMI Z-score less than -1.0
- Concern for Malnutrition
- Trending away from established growth curve

Mild Malnutrition: Decline in z-score

- Use of growth trends
- 5/23/2017
  - Weight-for-length z-score of -1.56
- 6/8/2017
  - Weight-for-length z-score of -2.63
- Decline in z-score of 1.07 standard deviations = MILD MALNUTRITION

Degree of Malnutrition Growth Trends: Decline in Weight
- Mild: Decline of 1.0 to 1.9 z-score
- Moderate: Decline of 2.0 to 2.9 z-score
- Severe: Decline of 3.0 z-score or greater

Nutrient Intake
- Inadequate nutrient intake (energy/protein)
  - 51-75% estimated need
  - 26-50% estimated need
  - <25% estimated need

Weight loss (2 – 20 years)
- Loss of 5 to 7.49% usual body weight
- Loss of 7.5 to 9.99% usual body weight
- Loss of 10% or greater usual body weight
Moderate Malnutrition: BMI-for-Age

- Use of individual growth point
- **BMI-for-age z-score of -2.82 = MODERATE MALNUTRITION**

Severe Malnutrition: % Weight Loss

- 3/13/17 – 14.5y
  - 68.9kg
- 7/18/17 - 14.8y
  - 60.2kg
  - % Weight Loss: **13%**

<table>
<thead>
<tr>
<th>Degree of Malnutrition</th>
<th>Growth Trends: Weight Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>~5% usual body weight</td>
</tr>
<tr>
<td>Moderate</td>
<td>~7.5% usual body weight</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;10% usual body weight</td>
</tr>
</tbody>
</table>

Initial Interventions

- Treat and manage any underlying medical etiology for malnutrition
- Improve nutrition status
Nutrition Interventions:
Breastfed Infants 0-3 months

Breastfeeding Support
- Lactation consultation
- Pump after feedings to stimulate production
- Feed entirely on one breast before switching to ensure intake of both fore and hindmilk
- Maintain positive feeding environment

Increase calorie intake
- Offer fortified expressed breast milk/formula after each feeding
- Offer supplemental fortified formula feeds if breast milk supply is low
- If production is adequate but intake is minimal, offer hind milk prior to foremilk
- Give 1-2 30-60mL high calorie bottles in between breastfeeding

Adequacy of intake
- Document intake of expressed breast milk
- Document frequency and length of feedings
- Monitor frequency of wet diapers and stools
- Implement feeding schedule with a daily minimum goal and guidelines for frequency and volume per feed
- Wake up for overnight feedings if sleeping thru the night

Nutrition Interventions:
Formula Fed Infants 0-3 months

Increase calorie intake
- Increase calorie concentration of formula (will need to provide mixing instructions)

Tolerance of formula
- Consider changing formula if indicated
  - Sensitive varieties, Hydrolyzed varieties, Elemental varieties
  - Offer less volume, more frequently (especially if spitting up)

Adequacy of intake
- Implement feeding schedule with a daily minimum goal and guidelines for frequency and volume per feed
- Wake up for overnight feedings if not waking up

Nutrition Interventions:
Infants 4-12 months

- Prior recommendations
- Always offer breast milk or formula before solid foods
- Make rice cereal with fortified breast milk
- Add rice cereal or formula powder to purees
- Add oil to baby foods (1/4 to 1/2 tsp per 2oz)
- Offer high calorie infant foods
  - avocado, bananas, mango, sweet potatoes, squash
Nutrition Interventions: Toddlers/Older Children

**Feeding Environment**
- Structured meal schedule to minimize grazing – 2 meals + 2-3 snacks
- Maintain positive eating environment
  - Ignore non-preferred behaviors; avoid negative reinforcement
- Minimize distractions
  - Offer both preferred and non-preferred foods at meals

**Meatline Behaviors**
- Positive reinforcement of preferred behaviors
- Limit juice to no more than 6-8oz/day

**Optimizing Calorie Intake**
- Switch to full fat milk and dairy – 2-3 servings daily
- Utilize calorie boosting techniques (slides to follow)

---

**Nutrition Interventions: Toddlers/Older Children**

- Increasing caloric density of meals/snacks
  - Add fats wherever possible – big calorie bang for your buck!
    - Add a splash of heavy cream to milk
    - Butter toast before adding jelly or peanut butter, butter toasted hot dog or burger buns
    - Add oil to frozen foods before baking
    - Toss pasta in butter or olive oil before adding red sauce
  - Promote naturally higher calorie foods
    - Whole milk, full fat yogurt, cheese
    - Nuts, nut butters, trail mix
    - Granola
    - Avocado, guacamole, hummus, sour cream
  - Fine tune healthy foods
    - Pair raw veggies with dip or a higher calorie food (ex. cheese)
    - Add butter/cheese to cooked veggies
    - Pair fresh fruit with cheese, yogurt, or peanut butter
    - Add heavy cream, butter, brown sugar to oatmeal

---

**Calorie boosters: Increasing the caloric density of each bite/sip of food/beverage**

<table>
<thead>
<tr>
<th>Heavy whipping cream</th>
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<tr>
<td>1 Tbsp = 90kcal</td>
</tr>
<tr>
<td>Oil and butter:</td>
</tr>
<tr>
<td>1 tbsp = 30-40 calories</td>
</tr>
<tr>
<td>Dry milk powder:</td>
</tr>
<tr>
<td>1/4 cup = 60kcal, 5gm protein</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Half and Half</th>
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<tbody>
<tr>
<td>1 Tbsp = 20kcal</td>
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<table>
<thead>
<tr>
<th>Canned coconut milk</th>
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<tbody>
<tr>
<td>1 Tbsp = 25kcal</td>
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</table>

<table>
<thead>
<tr>
<th>Ground flaxseed</th>
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<tr>
<td>1 Tbsp = 39kcal, 1.5gm protein</td>
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<table>
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<tr>
<th>Cheese, mayo, avocado, nut butters, cream cheese, sour cream, ghee</th>
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Nutrition Interventions: Toddlers/Older Children

- **Oral supplementation**
  - Only after other strategies have been exhausted
  - Can result in decreased intake of age appropriate foods
  - Should not be a first line intervention
    - Special consideration: severe malnutrition, developmental delay limiting food intake, severe food refusals in setting of malnutrition

- **Intended as an oral "supplement"**
  - Should be providing additional calories in the diet, NOT replacing calories

Medical Nutrition Therapy – Toddlers/Older Children

**Nutrition Supplements – Standard Cow’s Milk Based**

- **Pediasure**
  - 240 calories
  - 7g protein
  - $1.83 per bottle

- **Parent’s Choice (WALMART) Nutritional Shake**
  - 240 calories
  - 7g protein
  - $1.41 per bottle

- **Carnation Breakfast Essentials**
  - 280 calories
  - 13g protein
  - $0.61 per serving

  **based on mixing 1 packet with 1 cup whole milk**

**Medical Nutrition Therapy – Toddlers/Older Children**

**Nutrition Supplements – Soy Milk Based, Clear Liquid, Modular**

- **Bright Beginnings Soy Formula**
  - 240 calories
  - 7g protein
  - $1.42 per can

- **Boost Breeze**
  - Milk Protein/Clear Liquid
  - 250 calories
  - 9g protein
  - $1.50 per container

- **Duocal Hypoallergenic**
  - 25 calories
  - 1g protein
  - $0.95 per can - $0.31 per scoop

  **must purchase online**
Case Study – BS

GI Visit #1, November 2016
- Age: 6 months
- Referred to GI at 6 months for FTT
- PO Diet: Breast milk + expressed breast milk (estimating 25-30oz/day) + some baby foods
- History of reflux, taking omeprazole
- Diagnoses: FTT, Gastroesophageal reflux disease in infant
- Recommendations:
  - UGI
  - Stool studies: fecal fat, parasites, fecal elastase
  - Blood work: CBC, serum chemistries, serum lactate, thyroid function tests
  - Referral to dietitian – parent preference for alternative to formula for fortification
  - Optimize omeprazole dose
  - Consider 1tsp cereal/oz expressed breast milk

Case Study – BS

GI Visit #2, January 2017
- Age: 7 months
- Anthropometrics:
  - Weight gain of 215gm x ~2 months (avg of +4gm/day)
  - W-for-L Z-score = -2.41
  - Moderate malnutrition for -2.41 W-for-L Z-score + less than 50% of expected weight gain for age
- Workup unremarkable
- Vomiting daily, several times per daily
- Recommendations:
  - Optimize treatment of reflux:
    - Start EES suspension prior to meals and bedtime
    - Continue Omeprazole
  - Weekly weight checks
  - Nutrition visit in 1 week

Case Study – BS

Nutrition Visit #1, January 2017
- Age: 7 months
- Anthropometrics:
  - Slight improvement in weight and W-for-L Z-score since GI visit x 1 week
- PO intake:
  - Breastfeeding at home x 3
  - ~18oz EBM during the day (adding 1tsp rice cereal:1oz)
  - Increased intake of purees; Adding oil
  - Small, frequent feeds to avoid emesis
- Parent preference to avoid use of formula to fortify expressed breast milk
- Recommendations:
  - Add ½ to 1 tsp oil to 2oz puree (d/c if increased emesis)
  - At home, add ½ Tbsp oatmeal cereal to 2oz of puree
  - Add 1tsp of duocal : 3oz EBM to make 24kcal/oz
  - Start poly-vi-sol 1mL/day
**Case Study – BS**

Coordinated GI (#3) and Nutrition (#2), February 2017

- **Age:** 8 months
  - Weight gain of 17.8 gm/day (meeting catch-up goals)
  - W-for-L Z-score increased from -2.06 to -1.44
    - Malnutrition improved from moderate to mild
- **Intakes:**
  - Increased intake of purees and finger foods; Intake of breastmilk remains the same
  - Increased reflux with increased oil; now only adding it to large homemade mixture
  - Adding 1/2 Tbsp of oatmeal cereal to each puree
  - Adding 1 scoop duocal per puree, but not to EBM
  - Continued emesis and reflux
- **RD impression:** likely inadequate caloric intake due to frequent daily emesis
- **Recommendations:**
  - Wean EES due to no improvement in symptoms
  - Continue omeprazole
  - Continue duocal + oatmeal cereal + oil added to purees

---

**Case Study – BS**

Coordinated GI (#4) and Nutrition (#3), April 2017

- **Age:** 10 months
- **Gained average of 21.3 gm/day since February f/u – exceeding catch-up weight gain goal**
- **Age appropriate growth velocity in length**
- **W-for-L Z-score increased from -1.44 to -0.56 – no longer meeting criteria for malnutrition**
- **Intake of breast milk decreased by ~3oz, intake of age appropriate solids increased**
- **RD had discontinued duocal in March due to improved rate of weight gain based on weight checks at PCP office**
- **No longer adding oils to purees**
- **Adding oatmeal cereal to purees**
- **Recommendations:**
  - Wean oatmeal cereal with transition off of purees
  - Wean omeprazole at 12 months of age to every other day
  - Continue weight checks for 2-3 months with weaning of calorie modulars

---

**Case Study – BS in Summary**

- Catch-up weight gain was achieved
- No longer meeting criteria for malnutrition
- Interventions: optimization of reflux management and caloric intake
Case Study B: Weight-for-Age

Initial Visit 11/2016
Final Visit 4/2017

Case Study B: Length-for-Age

Initial Visit 11/2016
Final Visit 4/2017

Case Study B: Weight-for-Length

Initial Visit 11/2016
Final Visit 4/2017
Initial Visit
11/2016

Final Visit
4/2017

Resources

DISCLOSURES

- Trainer for Hands on Training Nutrition Focused Physical Exam Workshop for the Academy of Nutrition and Dietetics
- Speaker for Abbott Nutrition Speaker Bureau
- Medical Nutrition Therapy for Pediatric Liver Disease

WHAT IS NFPE AND WHY DO IT?

- Physical Exam designed to identify changes with body specifically linked to nutrition
  - Provides invaluable information when...
  - Laboratory values may not reflect nutrition status
  - Anthropometric measurements may be inaccurate, unreliable or unavailable
  - Integral part of completing a thorough nutrition assessment
  - Monitor responses to nutrition intervention
  - Adds complexity and depth to our nutrition recommendations
  - Provides backbone for nutrition recommendations
  - Standard of Practice

DIETITIAN RESPONSIBILITY

**Identify**
- Dietitians are uniquely positioned to identify malnutrition.

**Document**
- Thoroughly document our findings in the medical record.
- Apply indicators of malnutrition to diagnosis.

**Discuss**
- Communication with the larger medical team.
- Diagnosis and recommended nutrition-based treatment.

**Ensure Proper Coding**
- Choosing the best fit with the ICD-10 terminology.
- Mild, moderate, or severe protein-calorie malnutrition.

---

DIETITIAN TRAINING

- Training occurs …
  - Undergraduate programs & supervised internship curriculums
  - On the job training
  - Continuing education programs
    - Academy of Nutrition and Dietetics (AND) and Associate for Enteral and Parenteral Nutrition (ASPEN)
    - Various programs available via medical and formula companies

**Focused Techniques:**
- Inspection & Palpation
  - Observation: movement, color, shape, size, edema, affect, behavior
  - Tactile Examination: texture, size, tenderness, temperature
- Verbal interview and chart review

---

NUTRITION FOCUSED PHYSICAL EXAM

**Comprehensive Assessment**
- Subcutaneous Fat
- Muscle Mass

**Focused Assessment**
- Nutritional Status
- Edema
- Eschar

---

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SUBCUTANEOUS FAT, WHAT AM I LOOKING FOR?

- **Fat Loss**
  - Assessing fat "pads" under the skin and usually cover bony prominences or muscle
  - Use bones or muscles as landmarks to accurately assess
  - Bones prominent? Muscular outlines?
  - Look for loose or hanging skin
  - Assessing space between fingers when you are pinching
  - Should feel like "bread dough"
  - Subjective

---

SUBCUTANEOUS FAT

**Orbital:**
- Palpate fat pads around eye socket
- Checking for loss of fat pad under the eye
- Loose or sagging skin, dark circles

**Buccal:**
- Palpate fat pad between the cheek bone and jaw
- Looking for hollowing or sunken appearance
- Spindle-like dimple

**Triceps:**
- Palpate fat pads (left & right) between elbow and upper arm
- Checking for pinched double layer of fat
- Assessing pinch depth (fat loss) of fat that lays over triceps

**Ribs (Mid-Axillary Line):**
- Palpate fat pad at iliac crest and assess for gaps between ribs (anterior and axillary)
- Assessing for fat loss between ribs and at lower back

---

MUSCLE WASTING, WHAT AM I LOOKING FOR?

- **Upper Body**
  - Temporals
  - Pectoralis
  - Deltoid
  - Latissimus Dorsi & Trapezius
- **Lower Body**
  - Quadriceps
  - Knee
  - Calf

- Bulk and tone in musculature
- Should be firm and give bounce/resistance when palpated
- Prominent or protruding bones
- Muscle Atrophy
  - Flat or concave muscle
  - "Squared-off" appearance
- Upper Body usually looses mass before lower body
MUSCLES: UPPER BODY

Temporalis
- Palpate with a scooping motion
- Temporal muscle is assessed for tone and thinning of the muscle

Pectoralis
- Palpate in a scooping motion
- Assessing the muscle tone below the clavicle
- Fingers should not slide under the clavicle if there is good tone

Deltoid
- Gently squeeze the muscle at shoulder
- Assess tone & musculature (Anterior & Posterior)
- Arms should be down at side
- Look for "squared" vs "rounded" shape

Latissimus Dorsi & Trapezius
- Palpate the muscles along the edge of the scapula
- Assessing musculature of muscles surrounding shoulder blade
- Maybe helpful to have patient push against an object
- Look for "squared off" appearance or protrusion of bone

Image by: Anatomography (http://creativecommons.org/licenses/by-sa/2.1/jp/deed.en) and Dr. Johannes Sobotta

MUSCLES: LOWER BODY

Quadriceps
- Palpate to differentiate muscle from fat
- Assessing the 4 muscles that make the larger quadriceps
- Look for rounded musculature and rounded shape going into the knee joint
- Prop leg up and assess from front

Knee
- Visual assessment, anterior view
- Looking for prominence of joint and squared appearance

Calf
- Grasp the back of the calf muscle to assess tone and bulk
- Assessing the "bulb" of the muscle
- Looking for symmetry of both legs
- Important with assessment of edema
- Have patient stand if able or push against your palm or bed

MID-UPPER ARM CIRCUMFERENCE

- Incorporated in standard assessment
- Does not require weight
- Not affected by fluid status
- Simple and accurate
- Reflection of malnutrition
- MUAC is more sensitive to changes in muscle and fat than BMI
- Z Scores available for 6-59 months (WHO Standards)
- Peditools.org
- Reference Tables available for > 5 years of age
- Located at www.cdc.gov/nchs/data

MUAC TECHNIQUE

Step 1
• Ask patient to face away from you
• Bend right arm at 90 degree angle at elbow with palm facing up
• Measure from posterior acromion process to elbow (olecranon process)
• Average two measurements
• Mark midpoint

Step 2
• Relax marked arm at side
• Locate midpoint marking on arm
• Wrap tape around the arm at midpoint
• Flush with arm
  • Do not compress fat or have fat “spilling” over tape measure
  • Ensure it’s not loose or gapping
• Record circumference in nearest 0.1 cm

MUAC

MICRONUTRIENTS
• Micronutrient Deficiency
  • Primary or secondary deficiency
• Is there a medical reason for a deficiency?
  • Medications, medical diagnosis
• Is Inflammation Present?
  • An elevation in inflammatory markers may warrant delay in checking for nutrient levels
  • Markers: CRP, SED rate, WBC

Litchford M. Nutrition Focused Physical Assessment: Making Clinical Connections. 2013
**MICRONUTRIENT EXAM**

- **Hair**
  - Assess hair from root to tip
  - Look for dry, brittle, lackluster hair
  - Can it be plucked easily?
  - Bald or thinning spots
  - Assess scalp
  - Healthy skin or any waxy build-up?
  - Seborrheic dermatitis

- **Eyes**
  - Assessing the sclera of the eye
  - Color, dryness, or plaques
  - Look at patient at eye level and have them move eyes to one side
  - Make a sweeping "W" motion with Penlight
  - Switch sides
  - Assessing Conjunctiva of the eye
  - Assess color or paleness of lower eye lid
  - Gently roll/pull lower eye lid down

- **Nails**
  - Assessing uniformity, texture and shape
  - Check for artificial nails
  - Clinical finding should appear on all nails
  - 1 or 2 nails more likely trauma related

- **Skin**
  - Assessing the skin
  - Temperature
  - Texture
  - Color
  - Integrity
  - Assessed in conjunction w/other areas of NFPE

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By Lynn McCleary
By Bierenard
By Mijane (http://www.gnu.org/copyleft/fdl.html)
https://www.flickr.com/photos/quinndom


Images: CDC Image Library, PHIL.
**Oral Cavity**
- Assessing the mouth & lips
  - Ask patient to open wide
  - Observe oral hygiene
  - Dry or cracking lips
  - Sores
- Assessing Teeth and Gums
  - Dental plaque or missing teeth
  - Full saliva test for white, yellow, green
  - Sore or inflamed gums

**Assessing Tongue**
- Ask patient to stick out tongue
- Cheek for color and texture of the tongue
- In infants and small children may see signs of teething and/or thrush

**Hydration Status**

**Dehydration**
- Laboratory
  - ↑ Serum Na, Cl
  - ↑ BUN/Creat
  - ↑ Serum osmolality & Spec Gravity
- Clinical Findings
  - ↓ BP, ↑ Heart Rate
  - ↑ Temp and prolonged capillary refill
- Physical Findings
  - Clammy skin, cracked lips
  - Poor Skin Turgor
  - Sunken eyes
  - Dark urine, decreased UOP

**Overhydration**
- Laboratory
  - ↓ Serum Na, Cl
  - ↓ BUN/Creat
  - ↓ Serum osmolality & Spec Gravity
- Clinical Findings
  - ↑ BP, Central Venous Pressure
- Physical Findings
  - Puffy eyes, moist skin
  - Light Colored Urine
  - Anasarca
  - ↑ Weight

**Edema & Malnutrition**

- Bilateral Assessment
  - Identify Mild, Moderate or Severe Edema
  - Assessment based on depth and/or rebound time
  - Most commonly assess at feet (pedal)
  - Other sites: scrotal
  - Not all fluid accumulation is nutrition related

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**Micronutrients**

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**Images:** CDC Image Library, PHIL.
FUNCTIONAL STATUS & DEVELOPMENTAL MILESTONES

- Assess Functional status: Hand Grip Strength (Dynamometer)
  - Correlates with loss of total protein and BMI
  - Shows earlier response to nutritional changes than labs or anthropometrics in adults
  - Does not quantify severity of malnutrition
  - There are physical and/or mental limitations
- Alternative to using a dynamometer
  - Collaboration with physical therapy or occupational therapy
- Monitor Developmental Milestones
  - www.milestonemoments.cdc.gov
- Ask Questions!
  - Is your child able to do things that he enjoys?
  - Has your child needed some help doing things they used to do on their own?
  - How is your child’s energy level?

References

- Beer, S., Juarez, M. Pediatric Malnutrition: Putting the New Definition and Standards into Practice. NCP, October 2015 30(5)
References

- NFPE Pocket Guide
BLENDERIZED TUBE FEEDINGS... WHAT NURSES NEED TO KNOW

Mimi Gitten, RD, CSP, LDN
Pediatric Dietitian
The Children’s Hospital of Philadelphia
November 3, 2017

DISCLOSURES

Nothing to Disclose

OBJECTIVES

Understand rationale for using blended tube feedings (BTF).
Recognize traits of patients who might be a candidate for BTF.
Identify & compare commercial and home blended diets.
Recognize benefits and challenges of blended tube feedings for family and medical team.
Blended tube feeding (BTF) is defined as whole foods that are liquefied in a blender with water, juice, broth, or other types of liquids and administered by syringe bolus in feeding tubes.
COMMERCIAL PRODUCTS

Use:
- Natural / Holistic Option
- Formula Intolerance
- Volume Tolerant
- Oral Aversions / Delayed Oro-motor skill

Description:
- Medium/Thin Liquid
- Moderate Free Water
- 20-30 kcal/oz Formula
THICK BLENDS

Use:
• Gagging
• Refluxing
• Nissen Fundoplication
• Volume Intolerance

Description:
• Thick/Pasty Liquid
• High Caloric Density (> 30 kcal/oz)
• Minimal Free Water

PUREED BY GASTROSTOMY TUBE (PBGT) DIET IMPROVES GAGGING AND RETCHING IN CHILDREN WITH FUNDOPLICATION

- 52% reported a 76 to 100% decrease in gagging and retching.
- Symptoms resolved almost immediately after beginning a PBGT diet.
- No parents reported a worsening in symptoms.
- 57% reported an increase in oral intake on PBGT.

WHO IS A GOOD FIT

...
Liquid Hope® is a nutritionally complete, organic, real-food, whole foods enteral formula and oral meal replacement. Perfect for anyone who may be looking to increase daily nutrition. This product is plant based, dairy free, gluten free, soy free, corn free, non-GMO and packaged in a BPA free pouch. Liquid Hope® has a two year shelf life with no preservatives. Liquid Hope® meets all food safety requirements and meets all GRAS, HACCP, CGMPs standards. Liquid Hope® is processed in a FDA/USDA registered facility with USDA inspector on site. SID#: 2013-06-12/001

**SUMMARY POINTS**

<table>
<thead>
<tr>
<th>Features</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher fiber content</td>
<td>Nutrient content not as complete</td>
</tr>
<tr>
<td>Non-GMO</td>
<td>Less free water</td>
</tr>
<tr>
<td>Dairy, soy, com, gluten free</td>
<td>Higher fiber content</td>
</tr>
<tr>
<td>Higher caloric/ml (1.3)</td>
<td>Contains nuts</td>
</tr>
</tbody>
</table>
COMPLEAT®

Overview-Compleat®

A blend of ingredients from real foods.

Contains protein from dehydrated chicken powder, milk protein concentrate, and pea protein isolate.

No corn or soy ingredients.

A convenient alternative to blenderized, homemade tube feedings.

Meets the 2011 IOM recommendations for calcium and vitamin D.

SUMMARY POINTS

Features

- Covered by insurance
- No corn or soy products
- Nutritional complete
- Blend of real foods

Considerations

- Not vegetarian
- Less fiber than some blended products
- Contains milk

- Covered by insurance
- No corn or soy products
- Nutritional complete
- Blend of real foods
SUMMARY POINTS

**Features**
- Covered by insurance
- Nutritional complete
- No corn or soy products
- Lower calorie/ml available

**Considerations**
- Not vegetarian
- Less fiber than some blended products
- Contains milk

OVERVIEW-REAL FOOD BLENDS

These blended meals are intended to give tube-fed people easy access to real food. Blended meals give a convenient option when blending isn't possible or becomes a logistical challenge (traveling, hospitalized, at work or school, etc.). 4 meal varieties with 7 real food ingredients. Produced in an FDA and USDA regulated facility. No refrigeration required. No corn syrup or preservatives. Covered by insurance and often regulated by insurance.
NOURISH®

Functional Formulas

Perfect for anyone who may be looking for a more balanced nutrition. The product is plant-based, dairy-free, nut-free, gluten-free, soy-free, corn-free, non-GMO and packaged in a BPA-free pouch.

NOURISH® has a two-year shelf life without preservatives.
**SUMMARY POINTS**

**Features**
- Higher fiber content
- Non-GMO
- Dairy, nut, soy, com, gluten free
- Higher calorie/ml (1.1)

**Considerations**
- Not consistently covered by insurance at this time
- Documented to meet DRI’s of only 4 to 8 yr. old
- Less free water
- Processed in a plant that process gluten and nuts

---

**Overview-Kate Farms® Core Essentials 1.0®**

A ready-to-use oral and tube-feeding formula.

- Each 325 mL carton provides 325 calories and delivers 24 vitamins and minerals and 29 antioxidant-rich superfoods.

- Does not contain any of the common allergens (milk, wheat, soybeans, eggs, peanuts, tree nuts, fish, shellfish, corn products).

- CHO: Brown rice syrup, agave.
- Pro: organic pea, rice protein.
- Fat: coconut, sunflower.

- Pending Organic, Non-GMO, Kosher, Halal.
### CLOSER LOOK

<table>
<thead>
<tr>
<th>Formula</th>
<th>Price / Unit, $</th>
<th>Price / 100 kcal</th>
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</thead>
<tbody>
<tr>
<td>Homemade, Conventional</td>
<td>2.48 per daily</td>
<td>0.16</td>
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<tr>
<td>Homemade, Organic</td>
<td>4.29 per daily</td>
<td>0.61</td>
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<tr>
<td>Standard pediatric formula</td>
<td>2.04 per can</td>
<td>0.05</td>
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<tr>
<td>Compleat (Nestle Nutrition)</td>
<td>3.99 per tetra</td>
<td>1.50</td>
</tr>
<tr>
<td>Compleat Pediatric (Nestle Nutrition)</td>
<td>3.12 per tetra</td>
<td>1.25</td>
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<tr>
<td>Real Food Blend</td>
<td>4.16 per pouch</td>
<td>1.26</td>
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<tr>
<td>Liquid Hope (Functional Formularies)</td>
<td>7.99 per pouch</td>
<td>1.78</td>
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<tr>
<td>Nourish (Functional Formularies)</td>
<td>12.50 per pouch</td>
<td>3.13</td>
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<tr>
<td>Kate Farms® Core Essentials 1.0®</td>
<td>3.88 per tetra</td>
<td>1.19</td>
</tr>
</tbody>
</table>


### Product Comparison

#### 3 yr. old female (1260 kcal/day)
- **Compleat Pediatric**
  - Below DRI's: Vitamin E
- **Nourish**
  - Below DRI's: Vitamin C, Biotin, Phosphorus
- **Kate Farms**
  - Meets 100% DRI's
- **Real Foods**
  - Below DRI's: Calcium, Phosphorus, Vit D=ZERO, Vit B's, Folate, Vit K, Zinc, Selenium
- **Liquid Hope**
  - Below DRI's: Calcium, Vitamin D, Vitamin E, Magnesium, Phosphorus

#### 10 yr. old male (1800 kcal/day)
- **Compleat Pediatric**
  - Below DRI's: Vitamin E
- **Nourish**
  - Below DRI's: Calcium, Phosphorus, Vit D=ZERO
- **Kate Farms**
  - Meets 100% DRI's
- **Real Foods**
  - Below DRI's: Calcium, Phosphorus, Vit D=ZERO, Vit B's, Folate, Vit K, Zinc, Selenium
- **Liquid Hope**
  - Below DRI's: Calcium, Vitamin D, Vitamin E, Magnesium, Phosphorus
**Product Comparison**

14 yr. old male (2200 kcal/day)

**BM:**
- Below DRI's: 
  - Vitamin E
  - Phosphorus
  - Chromium

**Kate Farms**
- Meets 1000% DRI's
- Above DRI's: 
  - Vitamin C
  - Folate
  - Vitamin D=ZERO
  - Vitamin K
  - Vitamin B's
  - Calcium
  - Iron
  - Magnesium
  - Phos
  - Zinc
  - Selenium

**Liquid Hope**
- Below DRI's: 
  - Vitamin C
  - Vitamin E
  - Calcium
  - Magnesium
  - Phosphorus
  - Selenium
  - Zinc

---

**BENEFITS OF BTF**

**Physiologic**
- May aid in transition to oral diet
- Considered a natural product
- Adds variety
- Improve GI symptoms
- Improve quality of life
- Tailor to meet specific nutritional needs
- Inclusive with family meals

**Prospective cross-sectional study in 54 enterally fed adults**

- 50% used BTF
- 80% expressed a desire to use BTF

**Motivation for using BTF**
- Natural (43%)
- Eating what the family eats (33%)
- Better tolerance (30%)
CHALLENGES...FOR THE FAMILY

• Medical team
• Insurance reimbursements
• Supplies
• Recipe development
• TIME

BUMPS IN THE ROAD...

Inpatient admissions
Insurance issues
Emergencies
BUMPS IN THE ROAD…

Tube clogging/degradation
Reactions/Intolerance
Nutrient shortfalls

CHALLENGES… FOR PROVIDERS

Variability in nutritional content
Microbial contamination
Increase clinician time
CHALLENGES…FOR PROVIDERS

- Tube clogging and degradation
- Provider/facility support
- Insurance issues
- Noncompliance

NURSING PEARLS

**Need RD Support**
- For adequacy and management

**Constipation**
- Many products have a greater fiber content than standard formulas
- Less free water in products

**Fluids**
- Assure adequate free water is being provided

**Calories**
- Often 15-20% more calories are required when using a BTF

Bolus Syringe
- 60-90 ml slowly over 10-15 minutes

Gravity Syringe
- Must be very thin to flow easily

Tubes
- ASPEN safe practices for enteral nutrition recommends at least a 14F to minimize clogging risks
NURSING PEARLS

Pump
- Feeding pump manufacturers (Moog and Medtronic) specify only commercially prepared feeding solutions
- BTF are not recommended for use on these pumps
- Infusion providers are noting pump failure due to use of BTF against manufacturer recommendations

Hang Time
- Hang times are listed on individual products
- Food Safety Standards recommend no longer than 2 hours

FUTURE OF BTF
- There is and will continue to be increasing popularity
- More education and training for clinicians needed
- More research is needed

'Alone we can do so little. Together we can do so much.' - Lincoln
QUESTIONS

References
Refeeding Syndrome in the Pediatric Patient

STACIE TOWNSEND, MS, RDN, CSP, LDN
THE NATIONAL INSTITUTES OF HEALTH CLINICAL CENTER, BETHESDA, MD
STACIE.TOWNSEND@NIH.GOV

I do not have any disclosures to report.

All material presented should not be interpreted as representing the viewpoint of the U.S. Department of Health and Human Services, the National Institutes of Health or the Clinical Center. All views presented are my own.

Outline
- Definition and Incidence of Refeeding Syndrome (RS)
- Who is at risk for Refeeding Syndrome
- How to spot Refeeding Syndrome
- How Refeeding Syndrome occurs
- How to prevent Refeeding Syndrome
- How to manage and treat Refeeding Syndrome
What is Refeeding Syndrome?

- Group of metabolic and clinical complications that occur to a malnourished and/or starved individual once nutrition rehabilitation/support is initiated
- If severe, can lead to death
- Usually seen symptoms 2-5 days after nutrition is re-initiated
- First discovered in the 1940s in World War II prisoners of war (cardiac failure, edema)
- Discrepancies exist re: definition, symptoms, evaluation, and treatment
  - Difficult to study Refeeding Syndrome in pediatrics
  - Poor recognition of the condition

Incidence of Refeeding Syndrome

- Difficult to determine
- Up to 25% of oncology patients receiving nutrition support
- Up to 10% of ICU eating disorder patients (Vignaud et al. 2010)
- UK study – only 50% of those identified at risk for RS were correctly identified
- Some elements of RS can be seen in up to 50% of high-risk patients
- 80% of patients experience hypophosphatemia, hypokalemia and hypomagnesemia if vigorously refed

Who is at risk for Refeeding Syndrome?

**Conditions associated with increased risk of RS:**

1. Low nutrient intake
   - Eating disorders
   - Depression
   - Chronic drug/ETOH use
   - Failure to thrive
   - Cancer + associated treatments
   - Chronic inflammatory disease
   - Chronic kidney disease, diuretic use
   - Catabolic illness
   - Post-op
   - Uncontrolled DM
   - Social issues
   - Extreme dieting
   - Critically ill

2. **Increased nutrient losses / decreased nutrient absorption**
   - Chronic pancreatitis
   - Chronic liver disease
   - Congenital heart disease
   - Chronic septic state
   - Chronic high-dose diuretics

**Symptoms associated with increased risk of RS:**

1. Weight status
   - >10% loss in 1-2 months*
   - <70-80% IBW*
   - Muscle wasting

2. Low nutrient intake
   - Poor PO/EN/PN intake 7 days*
   - Persistent N/V/D limiting PO intake

* May be less in infants/small child
Symptoms of Refeeding Syndrome

- Hallmark of RS – hypophosphatemia (usually see 2-3 days after re-feeding)
- Also see hypokalemia, hypomagnesemia, thiamine deficiency, BG intolerance
- Possibly see hyponatremia and fluid overload
- Decreases in K+, Mg and Phos occur due to increase in basal metabolic rate
- How to diagnose?
  - Onset of clinical symptoms?
  - But many fluid and electrolyte abnormalities happen in absence of clinical symptoms

Can occur with reinitiating any type of nutrition (PO, EN, PN, dextrose IV)

Characteristics of Refeeding Syndrome

- Electrolyte Disturbances
  - Hypophosphatemia
  - Hypomagnesemia
  - Hypokalemia
  - Hypoglycemia
- Cardiac issues
  - Hypertension
  - Arrhythmia
- Respiratory issues
  - Dyspnea
  - Fluid overload
  - Difficulties weaning from mechanical vent
- Hematologic issues
  - Anemia
  - Necrosis
- Immunologic issues
  - Immune suppression
  - Infection risk / complications
- Neurologic issues
  - Wernicke’s encephalopathy
- Musculoskeletal issues
  - Weakness
  - Rhabdomyolysis

From Byrnes and Stangenes 2011

Incidence of Hypophosphatemia

- Increased incidence w/eating disorders, <68% of IBW or BMI <15.1 kg/m2
- Up to 27.5% of eating disorder pts within 1st week of nutrition rehabilitation
- All-cause mortality of 18.2% compared with 4.6% among those w/no hypophosphatemia
- In adult ICU-level care: increased rates of mechanical ventilation and LOS with hypophosphatemia (Oud 2009)
- 30-38% of patients receiving parenteral nutrition (who were previously unfed)
  - 100% of these patients will develop hypophosphatemia if no Phos is added to PN
### HYPOPHOSPHATEMIA

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cardiac</th>
<th>Pulmonary</th>
<th>Musculoskeletal</th>
<th>Neurologic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>sudden death, arrhythmia, heart failure, hypotension, shock</td>
<td>respiratory failure</td>
<td>weakness, myalgia, rhabdomyolysis</td>
<td>confusion, delirium, paresthesias, paralysis, seizures, hallucinations, tetag, coma</td>
<td>metabolic acidosis, insulin resistance, acute tubular necrosis, lethargy</td>
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</tbody>
</table>

### HYPOKALEMIA

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cardiac</th>
<th>Pulmonary</th>
<th>Musculoskeletal</th>
<th>GI</th>
<th>Neurologic</th>
<th>Other</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>arrhythmia</td>
<td>respiratory failure</td>
<td>weakness</td>
<td>nausea, vomiting, diarrhea</td>
<td>paralysis</td>
<td>death</td>
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</table>

### HYPOMAGNESEMIA

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<th>GI</th>
<th>Neurologic</th>
<th>Other</th>
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<tbody>
<tr>
<td></td>
<td>arrhythmia</td>
<td>weakness</td>
<td>nausea, vomiting, diarrhea</td>
<td>tremor, tetag, seizures, AMS, coma</td>
<td>refractory hypokalemia and hypocalcemia, death</td>
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### HYPERGLYCEMIA

<table>
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<tr>
<th>Symptom</th>
<th>Cardiac</th>
<th>Pulmonary</th>
<th>Musculoskeletal</th>
<th>GI</th>
<th>Neurologic</th>
<th>Other</th>
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<tbody>
<tr>
<td></td>
<td>hypotension</td>
<td>respiratory failure</td>
<td>weakness, rhabdomyolysis, muscle necrosis</td>
<td>nausea, vomiting, constipation</td>
<td>paralysis</td>
<td>infection, death</td>
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</table>

### THIAMINE DEFICIENCY

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cardiac</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>encephalopathy</td>
<td>lactic acidosis, death</td>
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</tbody>
</table>

### FLUID OVERLOAD / SODIUM RETENTION

<table>
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<tr>
<th>Symptom</th>
<th>Cardiac</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>heart failure</td>
<td>death</td>
</tr>
</tbody>
</table>

### TRACE ELEMENT DEFICIENCY

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cardiac</th>
<th>Neurologic</th>
<th>Other</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>arrhythmia, heart failure</td>
<td>encephalopathy</td>
<td>metabolic acidosis</td>
</tr>
</tbody>
</table>

Adapted from A.S.P.E.N. Fluids, Electrolytes, and Acid-Base Disorders Handbook 2015; Pulcini, Zettle and Srinath 2016.
Starvation – first 72 hours

1. BG levels decrease
2. Decrease insulin, increase in glucagon and growth hormone
3. Liver uses non-CHO sources to produce glucose
   • glycogen for energy
   • skeletal muscles break down → release amino acid for gluconeogenesis
4. Goal: maintain BG levels for brain, erythrocytes, renal medulla

Starvation - Prolonged

- Prolonged starvation (30+ days) → muscle catabolism of lean muscle → death
- Decreased basal metabolic rate by 20‐25%
- Vitamins/minerals also become depleted
- Body tries to maintain serum electrolyte levels (decrease excretion, volume constriction)
- Phos plays major role in glucose metabolism
- Muscle wasting affects vital organ function
  Atrophy of myocardium; liver wasting; GI atrophy; kidneys lose ability to concentrate urine
- Ketones are produced to obtain energy
- Free fatty acids are increased to prevent further skeletal muscle breakdown
- Glycogen stores are depleted, so metabolic pathways shift

Initiating Nutrition After Starvation

- Increase in insulin secretion
- Inhibit glucagon release
- Slowed anabolic pathways increase
- Shift from lipolysis to lipogenesis

This causes electrolytes to migrate intracellularly (severity depends on degree of malnutrition – electrolyte depletion)
Alkalosis leads to reduced renal excretion of sodium and water
Electrolyte demand increases
ICF expansion / fluid retention / pulmonary edema / CHF
Why is Phosphorus so important?

- Involved in all intracellular processes and structural integrity of all cells (phospholipids, nucleoproteins, nucleic acids)
- Required for the production of energy (ATP)
- Structural component of 2,3-diphosphoglycerate (2,3-DPG)

Treatment of Refeeding Syndrome

- Prevent it!
- First and foremost determine who is at risk for refeeding syndrome!
- Then - check serum electrolytes and correct any electrolyte abnormalities before initiating any type of nutrition support (whether PO, EN, PN)
- Do not begin nutrition support just to treat electrolyte and acid-base abnormalities
  - Adjustments can be made to your PN regimen to more adequately meet electrolyte needs and reverse abnormalities
- Once electrolytes are repleted, maintain homeostasis (especially with K+, Phos, Mg, Na, fluid)
- Rule of Thumb: low and slow
- Multidisciplinary Team is KEY

Treatment of Refeeding Syndrome: Macronutrients (PO, EN, PN)

START:
- At maximum of 25 – 33% of kcal goal for high risk patients
- Can start at 50% of goal for lower risk patients
- EN/PO is preferred over PN
- Lack of consensus for initiating / advancement
- Don’t forget kcals from Propofol, IVF
- Macronutrients: 50-60% CHO, 15-25% PRO, 20-30% FAT

ADVANCE:
- Over at least 3 – 5 days, but can go as slow as 7 – 10 days (depending on clinical response)
- Typically advance kcals by 10 – 25% daily
- OK to still increase macronutrients even if:
  - Minor and asymptomatic electrolyte abnormalities
  - Active treatment of low electrolytes
  - Gradual increase in kcal intake
Macronutrient advancement cont’d:

**ENTERAL FEEDS**
- Start at 25-50 mL/hour
- Advance 10-25 mL q8-24 hours as tolerated to goal

**Monitor**
- free water
- pulse
- BP

**PO DIET**
- *Calorie intake:*
  - Start at 1000 kcal/day
  - Advance by 200-250 kcal/day to goal
- *Fluid intake:*
  - Start fluids at ~50% of goal (~1200 mL in adolescent)
  - Advance by 200 mL/day as tolerated to goal

**A.S.P.E.N. Pediatric Core Curriculum, 2nd edition 2015**

---

**What to do if you see RS as you advance?**

<table>
<thead>
<tr>
<th>Decrease / suspend</th>
<th>Decrease / suspend nutrition until symptoms are corrected / resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct</td>
<td>Correct electrolyte abnormalities and give supportive measures</td>
</tr>
<tr>
<td>Restart</td>
<td>Once symptoms improve, restart at 50% of 50% of previous rate (when you started to see symptoms)</td>
</tr>
<tr>
<td>Monitor</td>
<td>Monitor electrolytes, vital signs</td>
</tr>
</tbody>
</table>

---

**Treatment of sodium / fluid**

Those at risk for RS may accumulate Na and fluid, so monitor fluid intake daily

**For pediatric patients:**
- No specific recommendations
- Start with maintenance fluid needs, but no more than 1000 mL/day
- May need to restrict Na to <20 mEq/L
- Monitor Na intake; restrict fluid if edema develops

**For adolescents / adults:**
- Maintenance = 1-2 mEq/kg/day Na
- For those at risk for fluid overload (cardiac, pulmonary issues), limit Na to 1 mEq/kg/day and fluid to <1500 mL/day

---
Treatment of Refeeding Syndrome: Electrolytes, Vitamins, Minerals

IN GENERAL
- Patients at risk for RS may need 120–150% of requirements for K⁺, Mg, and Phos to maintain WNL.
- May need to adjust goals based on underlying disease, renal function and replacement therapy, abnormal losses.
- May need IV replacement due to common GI side effects of PO/EN K⁺, Mg and Phos supplements (and if risk for malabsorption).
- Check for other nutrient deficiencies.

Monitoring
SERUM LEVELS:
- q 8-12 hours for the first 5–7 days, then daily.
- All electrolytes, but specifically Na, K⁺, Mg and Phos.
- May need to decrease repletion PRN.
- Most electrolyte abnormalities occur within the first 2–3 days of refeeding, but can occur for up to 7–10 days.
- Also monitor BC, renal function daily.
- Baseline and weekly hepatic enzymes, lipid panel, coags, and TG if on PN.
- Prealbumin, albumin, zinc, urinary electrolytes.

OTHER:
- Continuous cardiorespiratory monitor (concerning cases) and full vital signs q 4 hours and adjust PRN.
- Daily: detailed physical (focus on neuro and cardiac).
- U&L.
- Calorie count.
- Weight.

Treatment of hypophosphatemia

For children:
- Maintenance dose = 0.3–0.6 mEq/kg/day.
- Repletion dose = 0.3–0.6 mEq/kg/day.
- Varies by patient and BMD.
- May need to decrease Ca to allow increase in Phos.
- Typical Al content in CaPhos is less than in K⁺Phos.

For adolescents / adults:
- Maintenance = 10–15 mmol/L in PN or 20–40 mmol/L/day (assumes adequate renal function).
- Varies by patient and BMD.
- May need to decrease Ca to allow increase in Phos.
- Typically AlPhos contains less aluminum than K⁺Phos.

Recall:
- 1 mEq AlPhos = 1.47 mEq K⁺.
- 1 mEq NaPhos = 1.33 mEq K⁺.

* Decrease by 50% for impaired renal function.
**Treatment of hypokalemia**

Different levels of deficiency but repletion does not differ. For children:
- **PO:**
  - Maintenance dose = 1 – 2 mEq/kg/day
  - Repletion dose = IV repletion recommended
- **IV:**
  - Repletion dose = 0.3 – 0.5 mEq/kg/day, as long as urine output is >/= 0.5 mL/kg/hour
  - Maximum dose = 30 mEq/dose (ONCE)
  - Infuse over >/= 1 hour
  - Measure K+ level 2 hours after infusion ends

**For adolescents / adults:**
- **IV:**
  - Repletion = 0.3 – 0.5 mEq/kg/dose
  - Maximum dose = 30 mEq/dose (assumes adequate renal function)
  - Maintenance = 1 – 2 mEq/kg/day

**Vitamin/minerals**

- Magnesium sulfate (1 gm = 8.1 mEq Mg)

**Treatment of hypomagnesemia**

For children:
- **PO:**
  - Maintenance dose = 0.2 mEq/kg/day
  - Repletion dose = 25 – 50 mg/kg per PO dose (0.2 – 0.4 mEq/kg per dose; decrease by 50% if impaired renal function)
  - Maximum dose = 36 mEq (ONCE) PO
- **IV:**
  - No recs given but infuse over 4 hours

**For adolescents / adults:**
- **IV:**
  - Repletion = 1 gm Mg over 4 doses (0.5 mg/kg; 10 – 1.2 mg/mL)
  - 1 gm Mg over 2 doses (1 mg/mL; 1.2 mg/mL)
  - 0.2 – 0.3 mg/kg/day (assumes adequate renal function)

**PO:**
- Maintenance = 0.2 – 0.4 mEq/kg/day
- Maximum = 16 mEq (ONCE)

**Vitamin/minerals**

- Magnesium sulfate (1 gm = 8.1 mEq Mg)

**Treatment of other deficiencies**

**Thiamine supplementation**

Typically empiric:
- **Pediatric patients:**
  - 10 – 25 mg/day or 500 mg/L (extremely ill)
  - Then 500 mg/L for 2 weeks and then 50 mg/day x 1 month
- **Adolescents / adults:**
  - 5 – 10 mg/day 3 x week or 40 mg/day (extremely ill)
  - Then 20 mg/day 3 x week

**Vitamins/minerals**

Empiric supplementation of folic acid = 1 mg/day x 3-7 days

Multivitamins (or iron) should be administered orally or IV ARAF

**Pediatric patients:**
- Supplement prior to dextrose administration and electrolyte supplementation to prevent electrolyte depletion
Acid-base issues
Evaluate for acid-base disturbances
Minimize underlying acid-base disorders
Normal Cl:acetate = 1:1 to 1.5:1
If giving PN for those at risk for RS:
- if pt at risk for metabolic acidosis:
  ▪ Increase acetate
  ▪ Decrease chloride
  ▪ Keep Cl:acetate to < 1.2:1
- if pt at risk for metabolic alkalosis:
  ▪ Increase chloride
  ▪ Decrease acetate
  ▪ Keep Cl:acetate to > 2:1

In Summary
- Refeeding Syndrome is complex!
- Know what patients are at risk
- Feed at low kcal, low fluid and slowly
- Check and replete electrolytes prior to initiating re-feeding
- Team / communication is key!

Thank you!
QUESTIONS / CONCERNS / COMMENTS:
STACIE.TOWNSEND@NIH.GOV

Adapted from A.S.P.E.N. Fluids, Electrolytes, and Acid-Base Disorders Handbook 2015; Pulcini, Zettle and Srinath 2016
References

Food Protein Induced Enterocolitis Syndrome -

What are the goals of the gastroenterology team?
APGNN Annual Meeting
Las Vegas, NV
November 3, 2017

Glenn T. Furuta
University of Colorado School of Medicine
Digestive Health Institute
Gastrointestinal Eosinophilic Diseases Program
Children’s Hospital Colorado
Aurora, CO

Disclosure

Co-Founder of EnteroTrack LLC
Research Funding from National Institutes of Health and Nutricia
Consultant for Shire and GSK
Royalties from UpToDate
Not an allergist

Learning objectives

• Review differential diagnosis of infants with vomiting and diarrhea
• Recognize the clinical manifestations of FPIES
• Identify role of gastroenterologist and nurses in diagnosis of FPIES
Causes of infantile vomiting

Common
- Gastroesophageal reflux
- Eosinophilic Esophagitis
- Allergic disease
- Infections

Rare
- Anatomic malformations
- Metabolic diseases / inborn errors in metabolism
- Increased intracranial pressure
- FPIES

Causes of infantile diarrhea

Common
- Infectious enteropathy
- Post-infectious enteropathy
- Allergic enteropathy

Rare
- Transport defects
  - chloride-bicarbonate exchanger (chloride-losing diarrhea)
  - sodium-hydrogen exchanger (congenital sodium diarrhea)
  - ileal bile acid receptor defect
- Sodium-glucose co-transporter (glucose-galactose malabsorption)
- Micronutrient deficiency
- Acrodermatitis enteropathica (zinc deficiency)
- Enzyme deficiency
- Enterokinase deficiency
- Inflammatory bowel disease
- Microvillus inclusion disease
- Tufting enteropathy
- Autoimmune enteropathy / IPEX syndrome
- FPIES

Food Protein Induced Enterocolitis Syndrome (FPIES)

Gastroenterologists view
Milk Induced Colitis in an Infant

Chronic diarrhea and the passage of blood and mucus in the stools are frequent manifestations of cow’s milk allergy. In 1940, Rubin first presented the classical description of intestinal hemorrhage in the newborn as a manifestation of allergy to cow’s milk. More recently, Wilson, Heiner, and Lahy have related anemia and occult blood loss in the stools of infants to the ingestion of cow’s milk. Although these findings are highly suggestive of disease of the large bowel, the reaction of the colon of the allergic infant to the ingestion of milk has not been well defined.

The following report describes an infant who developed shock and fulminating colitis on three occasions after the ingestion of commercial infant formulas which contained cow’s milk proteins.

CASE REPORT

N. L., a Caucasian male infant, was delivered after a normal full-term pregnancy and weighed 3,600 gm. He took Similac formula well and had no difficulties until 1 week of age when his stools became loose. The stools gradually increased in frequency and in water content until by 37 days of age he was having 15 blood-streaked mucoid stools per day. He became severely dehydrated.

Hospital course

- Developed pneumonia and made NPO
- Physical examination-distended abdomen
- Treated with antibiotics
- Day 6-cow’s milk formula started
Hospital course

Within 2 hours he was in shock. His pulse rose to 150 per minute and his abdomen became distended and tense. He passed an explosive movement of blood and mucus which contained identifiable sheets of tissue. Sigmoidoscopy to 8 cm visualized a rough, purple-red hemorrhagic mucosa. During the procedure thin sheets of tissue exuded from the rectum about the sigmoidoscope.

Hospital course

- Stabilized and made NPO

- Sigmoidoscopy improved 3 days later

- Stool cultures negative

Hospital course

He gained weight slowly while taking Nutramigen and had normal formed stools until the twenty-first hospital day when Enfamil was unintentionally substituted for a feeding. Within 30 minutes he passed copious liquid stools and within 1 hour he became ashen, hypothermic, and passed blood, mucus, and colonic tissue per rectum. Transfusion and
3 month old male

- Son of an otolaryngologist who was exclusively breastfed
- 4 weeks- ingestion of cows milk formula
- One month later- Persistent vomiting, intermittent loose stools and poor weight gain
- Seen by pediatrician and changed back to breastfeeding alone

3 month old male

- 3 months of age- challenged with cow’s milk formula
- 1 hour later- developed profuse and repetitive vomiting, dehydration and lethargy
- Metabolic disease ruled out, sepsis work up unremarkable, UGI was normal
- Intravenous resuscitation and antibiotic administered
- Changed to an elemental diet

3 month old male

- 1 year later-Re-challenged with cows milk was tolerated
- 2 year follow up- normal growth and development
Author composition and process

- Allergists, Gastroenterologists (4), Dietitians, Advocates
- International
- Review of the literature and expert opinion
- 30 Summary statements
Food protein–induced enterocolitis (FPIES) is a non-IgE cell-mediated food allergy that can be severe and lead to shock. Despite the potential seriousness of reactions, awareness of FPIES is low; high-quality studies providing insight into pathophysiology, diagnosis, and management are lacking; and clinical outcomes are poorly established.

**FPIES Definition**

- Typically less than 9 months of age
- Exposure to food elicits delayed severe vomiting and diarrhea
- Removal of causative food results in resolution of symptoms
- Re-exposure or oral food challenge elicits typical symptoms within 4 hrs

Nowak-Wegrzyń et al JACI 2017
### FPIES Subtypes

#### TABLE 1: Proposed defining features for subclassification of FPIES

<table>
<thead>
<tr>
<th>FPIES Subtype</th>
<th>Defining Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute FPIES</td>
<td>- Acute onset of symptoms following ingestion of cow’s milk X 3 in an infant</td>
</tr>
<tr>
<td></td>
<td>- Rapid, severe, life threatening</td>
</tr>
<tr>
<td></td>
<td>- Responsive to removal of cow’s milk</td>
</tr>
<tr>
<td>Chronic FPIES</td>
<td>- &lt;4 months</td>
</tr>
<tr>
<td></td>
<td>- Cow’s milk or soy protein</td>
</tr>
<tr>
<td></td>
<td>- Vomiting and diarrhea +/- failure to thrive</td>
</tr>
<tr>
<td></td>
<td>- More common in Japan and Korea</td>
</tr>
</tbody>
</table>
Clinical features

- Vomiting: 1-4 hours

- Diarrhea: 5-10 hours

- Lethargy and pallor, hypotension and hypothermia

- ER visit(s)

- Well when not eating offending food

Table 2. Incidence of common symptoms in acute food-protein-induced enterocolitis syndrome

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Mehr et al. [14] (n = 66 all FPIES)</th>
<th>Katz et al. [3*] (n = 28 CM-FPIES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Lethargy</td>
<td>85%</td>
<td>77%</td>
</tr>
<tr>
<td>Pallor</td>
<td>67%</td>
<td>14%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>24%</td>
<td>25%</td>
</tr>
<tr>
<td>Bloody diarrhea</td>
<td>4.5%</td>
<td>NA</td>
</tr>
<tr>
<td>Temperature &lt;36°C</td>
<td>NA</td>
<td>24%</td>
</tr>
</tbody>
</table>

CM, cow's milk; FPIES, food-protein-induced enterocolitis syndrome.
Clinical manifestations

- First few days of life to 6 months
  - Early onset- Cow / soy milk- 30 days
  - Later onset- Solid food- 5.5 months

- Of 35 children with 66 acute episodes seen over a 16 year period, 2 received correct diagnosis at initial presentation.

- Otherwise well who has repeated episodes of GI symptoms of undetermined etiology

Mehr et al Pediatrics 2009
Morita et al Allerg Intl 2013
Fiocchi et al Curr Opin Allergy Clin Immunol 2014

Clinical manifestations

- 75% appear severely ill and 15% develop hypotension

- Responds to elimination of commonly ingested proteins (cow’s milk, soy, rice)

- Atopic diseases- atopic dermatitis-65%, asthma- 20%,

- FH of atopic disease- 40-80%

Mehr et al Pediatrics 2009
Morita et al Allerg Intl 2013
Fiocchi et al Curr Opin Allergy Clin Immunol 2014

Prevalence

- 13,019 infants

- Dx criteria-sxs, <9 months of age, no other IgE mediated problems, removal lead to remission, OFC positive

- 0.34% had FPIES
  - Vomiting, lethargy
  - First 6 months
  - Cows milk

Katz et al JACI 2011
Age of onset

Course of response

Rice: a common and severe cause of food protein-induced enterocolitis syndrome

- Rice (n=14) compared to cow’s milk (n=17)
- Longer delay in diagnosis
- More severe reactions

Mehr et al Arg Dis Child 2009
Caminti et al Ital J Pediatr 2013
Cow’s milk and soy induced responses are outgrown by 10 months to 3 years

• 60%-3 years in US
• 60% by 10 months in Korea
• 90% by 3 years in Israel
• 100% by 2 years in Italy

Onset of tolerance

• 2001-2011
• 160 subjects
• 6 months to 45 years
• 54% male
• 15 months (median age at diagnosis)
Onset of tolerance

- Median age when tolerance developed
  - Milk: 5.1 years
  - Soy: 6.7 years
  - Rice: 4.7 years
  - Oat: 4 years


Laboratory testing is non-specific

- Labs
  - Dehydration
  - Peripheral eosinophilia
  - Methemoglobinemia
  - Thrombocytosis
  - Stool PMN or Eos, heme positive

- IgE levels may not be elevated
  - Cows milk/soy: 30%

Endoscopic and Histologic are non-specific

- Friable mucosa, normal
- Villous atrophy
- Crypt abscesses
- Lymphocytes, mast cells and eosinophils
**Endoscopic and Histologic are non-specific**

Ishige et al. Gastro Endoscopy 2014

---

**Management-acute**

- Oral rehydration fluids, if mild
- Intravenous fluids, if moderate to severe: 20 ml/kg boluses of isotonic saline
- Intravenous steroids: methylprednisolone 1 mg/kg (max 60–80 mg)
- Vasopressors for hypotension if severe or unresponsive to fluids
- Bicarbonate for acidemia
- Methylene blue for methemoglobinemia

Janvinen et al. J Allergy Clin Immunol 2013

---

**Management-chronic**

- Removal of causative food from diet
- Intravenous fluids if dehydrated
- For cow’s milk-FPIES: use soy alternative (following a supervised oral food challenge), casein hydrolysate or elemental formula
- Bicarbonate for acidemia
- Methylene blue for methemoglobinemia

*Observation for feeding difficulties
Letter for family to carry with them*

Meyer et al. J Gastrointest Hospitil 2014
Differential diagnoses

- Infections / Sepsis-febrile
- Anaphylaxis—minutes
- Allergic proctocolitis -not as sick
- Celiac sprue—respond to gluten removal

Differential diagnoses

- Inflammatory bowel diseases—systemically ill
- Autoimmune—diarrhea severe and systemically ill
- Obstruction/pyloric stenosis / Hirschprung disease
- Eosinophilic gastrointestinal disease—not as sick
What is the role of the gastroenterologist and nurse in the care of the patient with presumed FPIES?

a. Recognize symptoms and initiate evaluation
b. Provide consultation to identify alternative diagnosis for symptoms
c. Contribute to understanding the pathogenesis of FPIES
d. Refer to allergist for long term management
e. All of the above
Slide 1

FPIES: A Parent Perspective
Presented by:
Amanda LeFew and Joy Meyer
Co-Directors of The FPIES Foundation

Learning objectives:
• Describe the quality of life adjustments for families living with FPIES
• Recognize the parent perspective of having a child diagnosed with FPIES
• Learn ways you can help a family living with FPIES

Slide 2

About the Presenters:
Amanda LeFew has a Bachelor’s degree in Music Therapy and is a board-certified music therapist (MT-BC), with additional training in Neurological Music Therapy. She is a mom to two energetic daughters; both girls, ages 5 and 8, have FPIES. Amanda is a Foundation founding member and Executive Co-Director of The FPIES Foundation.

Joy Meyer has an Associate degree in Nutrition and is a Registered Dietetic Technician (DTR). Joy is a busy wife and mother of four sons, the youngest of which continues to live with FPIES on a limited diet. Joy has a love for Nutrition and a passion for helping others. Joy is a Foundation founding member and Executive Co-Director of The FPIES Foundation.

Slide 3

What is FPIES?
Food Protein-Induced Enterocolitis Syndrome (FPIES) is a Non-IgE mediated food allergy affecting the gastrointestinal (GI) tract.
Finding Our Voices: A Patient Registry

As a parent of children affected by FPIES, advocacy quickly becomes a 24hr-a-day job!

We parents are always seeking new ways for our voices to be heard in hopes of bettering day-to-day life for our kids.

Affected families often express:
- Feelings of isolation,
- Being misunderstood
- Experiencing inadequate care

Altavoice’s free patient registry platform gave us the opportunity to create a home-base for our community’s voices—a place to be seen and heard by practitioners and researchers, worldwide.

A Foundation for FPIES Voices

The Registry in Numbers

- 600+ registered participants
- Participants connect from 48 states, from six different continents
- Seven available surveys can be completed more will be added
- Participation is free for patients, providers, and researchers!

www.fpiesregistry.com

Meaningfulness of Quality of Life (QOL) Survey

Offers a snapshot of life with this chronic health condition to practitioners and researchers on the registry portal

Offers validation and solidarity to affected families sharing their experiences and reflecting on the shared challenges of other families

Reported FPIES Impact:
- Experiences of Pain
- Developmental Milestones
- Emotional/ Coping skills
- Social/Community Life
- Financial resources
A Life Altering Diagnosis

- The Diagnosis
  - Easily misunderstood
  - No medical tests
  - Few specialists

- Not your Typical Food Allergy
  - Delayed food allergy
  - Less treatment plans
  - Rare/"Invisible Illness"

- Advocate and Educate
  - Family/Friends
  - Community
  - Daycare/school
  - Doctors

FPIES In The Everyday

- Accidental exposure risk
- ED aware
- Food trial anxiety
- Shopping & label reading
- Creative food prep
- No simple meals
- Always plan ahead

Living on an Island

"FPIES isn’t a diagnosis for us, it’s an island".
Alliyson, parent of a child with FPIES
Though acute FPIES reactions may be brief in nature, management of FPIES is an ongoing, daily process that is best addressed with multifaceted approaches, as is often the case with chronic conditions.

A Multifaceted Approach for a Chronic Condition

- **FPIES at Home**—Explore potential modifications in family life
- **FPIES in the Community**—Explore ways to educate community members and to create safe spaces for children to engage with their communities
- **FPIES at School/Age-Appropriate Social Settings**—Encourage inclusion and support education of child’s peers and adult facilitators

Because FPIES impacts multiple aspects of daily life, viewing it as a chronic condition (until the time it is outgrown) can help clinic communities to better explore the nature of support needed by families between and during reactions.
Slide 13

How to Help

- Help prevent accidental exposures
- Treating reactions
- Empower
- Validate
- Referrals
- Individualize care

Slide 14

Offer Words of Encouragement

- Acknowledge
- Be optimistic but realistic
- Choose your words carefully

Slide 15

The Positive Impact

- Healthy eating
- Celebrating food passes
- New recipes
- Family meals
- Food free events
- Inclusion
- Validation
Slide 16

Resources

- FPIES Registry
- FPIES Provider Database
- Patient & Provider packets
- Websites:
  - www.fpiesfoundation.org
  - www.acaai.org
  - www.foodallergy.org
  - www.globalgenes.org
  - www.rarediseases.org
  - www.themighty.com
- Support groups

FPIES Toolbox:

- Awareness
- Food Journals
- Healthcare professionals
- Medical Literature
- Cooking & Nutrition
- Emergency care
- For Kids/School
- Webinars & online learning
- Bilingual resources

Slide 17

Questions or Comments?
Update on Pediatric IBD Therapy

Andrew B. Grossman MD
Co-Director, Center for Pediatric Inflammatory Bowel Disease
Associate Professor of Clinical Pediatrics
Division of Gastroenterology, Hepatology, and Nutrition

Disclosures

• None

Objectives

• Review pharmacologic options available for treatment of pediatric IBD
• Discuss nutritional therapies and diets for pediatric IBD
• Present basis for “top-down” therapy
• Introduce recently approved therapies
• Review most recent safety data
Pediatric IBD: Shifting Therapeutic Goals

**Previous Goals**
- Induce and maintain clinical remission
- Improve quality of life
- Minimize drug toxicity
- Optimize surgical outcomes

**Newer Goals**
- Heal mucosa
- Modify natural course of disease
  - To prevent disease complications

---

Traditional Pediatric IBD “Step-Up” Algorithm

---

Efficacy of 5-ASA’s

**Ulcerative Colitis**
- Oral therapy effective for induction and maintenance of remission
- Rectal, oral + rectal → More effective than just oral for distal disease

**Crohn’s disease**
- Efficacy unclear for induction or maintenance of remission
Systemic Corticosteroids

• Oral (prednisone), IV (methylprednisolone), rectal
• Suppress active inflammation
• Indication: Acute UC or Crohn’s flare
• Provide immediate symptomatic relief
  – Do not promote healing of GI tract
• *Not* indicated for maintenance therapy
  – Lose efficacy, side effects

Budesonide

Immunomodulators

• Suppress immune response that triggers intestinal damage in IBD
• Maintenance of remission
• Steroid-sparing
  
  **6-MP/Imuran**
  • Daily dosing
  • Oral administration
  • 3-4 months for max. efficacy
  • CD and UC
  
  **Methotrexate**
  • Once weekly dosing
  • Oral or subcutaneous
  • 6-8 weeks for max. efficacy
  • Minimal UC data
**Enteral Nutrition**

- Improves nutrition for **all** IBD
- Effective **therapy** for pediatric Crohn’s
- Replace **all** or **the majority** of calories with formula and excluding/limiting food
- UC → Not shown to be effective
- Often requires NG tube
- Proposed mechanism: Modulation of intestinal bacteria

---

**Bacterial populations in pediatric IBD subjects on semi-elemental diet**

(16S rDNA sequencing)

Conclusion: Rapid change in gut bacterial populations upon initiating diet

---

**Enteral Nutritional Therapy: Traditional Protocol**

**Induction**
- Exclusive enteral nutrition with an elemental, semi-elemental, or polymeric formula
  - Duration: 4 – 12 weeks

**Maintenance**
- **Nutritional therapy**: Repeat 4 week cycle of exclusive enteral nutrition every 3 – 4 months or 50% EN daily
- **Medical therapy**: 6-MP/AZA/MTX
Enteral Nutrition vs. Steroids for Active Crohn’s Disease

- Enteral Nutrition → As effective as steroids for improving symptoms, more effective for healing of GI inflammation

**CHOP Partial EN Experience**

- 80%-90% of estimated caloric needs from formula
  - 10-20% from food (limited)
- Nocturnal NG feeds
- Induction
  - 7 days per week for 8-12 weeks
- Maintenance
  - Lower calories (decrease days, volume)
  - Simultaneously increase calories from food

Greater Mucosal Healing with More Restrictive Diet During Induction Phase
How Prevalent is EN Implementation?

NASPGHAN Survey

<table>
<thead>
<tr>
<th></th>
<th>U.S</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>30%</td>
<td>20%</td>
</tr>
<tr>
<td>Never</td>
<td>70%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Currently (OR 38.5) or previously (OR 7.9) working at center that uses EN regularly increases EN use

The Specific Carbohydrate Diet

- Principle that disaccharides and polysaccharides pass undigested into the colon, which causes bacterial and yeast overgrowth, thereby leading to overproduction of mucus and intestinal injury

- Mostly anecdotal evidence supporting efficacy
- Scientific literature includes only small, uncontrolled studies in children (7-10 patients)
- No well-designed randomized trials

Other Exclusion Diets

- Semi-vegetarian diet
- IBD-AID
- Crohn’s Disease Exclusion Diet
- Paleolithic diet
- Low FODMAP diet
- UC diet
**Anti-TNF Biological Therapies for IBD**

- Certolizumab pegol
- Adalimumab
- Golimumab
- Infliximab

**REACH (Pediatric Crohn’s Disease Study)**

**Clinical Remission**

<table>
<thead>
<tr>
<th>Week 10</th>
<th>Week 54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response*</td>
<td>Remission**</td>
</tr>
<tr>
<td>88%</td>
<td>64%</td>
</tr>
<tr>
<td>59%</td>
<td>56%</td>
</tr>
</tbody>
</table>

* ↓ from baseline of ≥ 15 points in PCDAI score & PCDAI score ≤ 30
** PCDAI score ≤ 10


**REACH**

**Improved Growth with Infliximab**

- All Patients
- No Baseline Steroids
- Steroids at Baseline

Anti-TNF Therapy in Pediatric IBD

- Moderate to severe Crohn’s disease
  - Decreases steroid requirement
  - Mucosal healing
  - Healing of perianal disease
  - Improvement of growth
  - Bone health
  - Prevention of post-operative recurrence

- Ulcerative colitis
  - Treatment of moderate to severe disease
  - Prevention of surgery

Anti-TNF Therapeutic Monitoring

- Measure trough level/antibodies against medicine
  - “Sub-therapeutic drug level”
    - Less likely to be effective
    - Increase dose and/or decrease interval

- Antibodies against medication
  - Less likely to be effective
  - Can optimize dose
  - Might have to switch agents
  - Add immunomodulator

Factors Affecting Pharmacokinetics of Monoclonal Antibodies

<table>
<thead>
<tr>
<th>Factors Affecting Pharmacokinetics</th>
<th>Impacting pharmacokinetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of AOAs</td>
<td>Decrease clearance of drug</td>
</tr>
<tr>
<td>Constant arterial blood pressure</td>
<td>Increase clearance of drug</td>
</tr>
<tr>
<td>High baseline TNF-α</td>
<td>May decrease (may by increasing clearance)</td>
</tr>
<tr>
<td>Low albumin</td>
<td>May decrease clearance</td>
</tr>
<tr>
<td>High baseline CRP</td>
<td>Increase clearance</td>
</tr>
<tr>
<td>Body size</td>
<td>High body mass index may increase clearance</td>
</tr>
<tr>
<td>Gender</td>
<td>Male have higher clearance</td>
</tr>
</tbody>
</table>

AOA: anti-inflammatory; CRP: C-reactive protein; TNF: tumor necrosis factor; Clearance: clearance
Assessing Optimal Anti-TNF Levels for Mucosal Healing
Retrospective, observational cohort adult study (n=145; 78 IFX, 67 adalimumab; 111 CD; 34 UC)

Proactive vs. Reactive TDM in Clinical Practice
Multi-center, retrospective cohort of adult IBD patients (n=264) who responded to IFX induction therapy
- Proactive: TDM prior to active disease; titrate to goal trough
- Reactive: TDM due to active symptoms or intolerance

What Are Biosimilars?
• WHO: “Biotherapeutic product similar in terms of quality, safety, and efficacy to a licensed biotherapeutic product”
• Primary amino acid sequences of biosimilar and originator are same, but are not identical
  – Differences in glycosylation, protein structure
• Must not be clinically different in quality, safety, efficacy, or potency from originator biologic agent
How Do Biosimilars Differ from Generics?

- **Generics**
  - Small molecule drugs
  - Identical to original drugs

- **Biosimilars**
  - Much larger molecular structure
  - Heterogeneous from originator
  - Sensitive to changes in manufacturing (living cell lines)

---

Current Biosimilars

- Inflectra™ (infliximab-dyyb) – First FDA Approved Biosimilar for IBD
  - From same cell line as infliximab
    - Same amino acid sequence
    - Comparable pharmacokinetics, anti-TNF binding, and cytotoxic activity to infliximab
  - Studied in RA
  - Extrapolated to current GI indications for infliximab
    - Adult and pediatric Crohn’s disease
    - Adult UC
Crohn’s and Colitis Foundation Position Statement on Biosimilars (Endorsed by NASPGHAN)

Safety and Effectiveness:

- Human testing
- Interchangeability
- Immunogenicity and cross-reactivity
- Unique name/identifier

Undergo thorough human testing and meet highest safety standards. Provide reasonable proof that switching would not incur immunogenicity or loss of response to innovator agent (vice versa). Risk of cross-reactivity of anti-drug antibodies from innovator agent to biosimilar must be clearly understood, defined, and listed on the label and prescribing information.

Each biosimilar should have unique identification number, name, or else use international non-proprietary name standards to eliminate patient and provider confusion.

http://www.crohnscolitisfoundation.org/assets/pdfs/advocacy/biosim-position.pdf

Crohn’s and Colitis Foundation Position Statement on Biosimilars (Endorsed by NASPGHAN)

Shared-Decision Making and Transparency:

Notification to Prescribing Provider

Prevention of Substitution

The provider should be able to prevent substitution by indicating “Dispense as written” or “Brand medically necessary.”

http://www.crohnscolitisfoundation.org/assets/pdfs/advocacy/biosim-position.pdf

Does Early Use of Biological Therapy Improve Efficacy? Growth?

- Biologic therapy
- 6-MP/AZA/Methotrexate
- Steroids
- Surgery

Early

Late
Risk of Treating vs. Not Treating

Long-Term Evolution of Pediatric Crohn Disease is Structural Damage

SONIC Trial
Corticosteroid-Free Clinical Remission at Week 50
**SONIC Trial**

### Mucosal Healing at Week 26

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Proportion of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZA + placebo</td>
<td>16.5</td>
</tr>
<tr>
<td>IFX + placebo</td>
<td>30.1</td>
</tr>
<tr>
<td>IFX + AZA</td>
<td>41.9</td>
</tr>
</tbody>
</table>

* p<0.001
* p=0.023
* p=0.055

**Early Anti-TNF Therapy in Pediatric Crohn Disease**

- Observational cohort of pediatric CD patients (inflammatory)
- Propensity score analysis matched patients on baseline characteristics in 68 triads
  - Early anti-TNF (<3 mo)
  - Early immunomodulator
  - Neither
- Early anti-TNF
  - Higher remission rate
  - Improved height z-score

*Remission: PCDAI≤10, steroid free, no surgery*

**Immunomodulators and Biologics – Common Toxicities**

- Leukopenia
- Liver toxicity
- Increased infection risk
- Slightly increased risk of malignancy
  - HSTCL
**Pediatric IBD Risk of Serious Infection: A Systematic Review**

**Serious Infections per 10,000 Patient-Years**

- **Ped Anti-TNF**: 325
- **Ped IM**: 352
- **Adult Anti-TNF**: 654
- **Ped Steroids**: 790

**Meta-Analysis: Biological Therapies and Risk of Infection**

- 49 randomized, placebo controlled trials
  - 14,590 participants
- For all studies, patients on biological therapy:
  - 19% increased risk of “all infections”
  - Serious infections not increased
  - Higher risk of opportunistic infections (including Tb)
- For studies deemed “low risk of bias”
  - Serious infections decreased in biologic exposed

**Vaccination**

- Ensure that vaccines are up to date at time of diagnosis
- All non-live vaccines should be given
  - Annual flu shot
  - HPV vaccine
- Avoid live vaccines if immunosuppressed
  - MMR, Varicella, intranasal flu, others
  - Try to confirm Varicella immunity prior
  - Consider pneumococcal vaccine
Pediatric Develop Registry

- Largest prospective pediatric IBD safety cohort
  - Patients assessed every 6 months, followed for 20 years
  - 5,691 patients enrolled with > 20,000 PY of F/U
- Infliximab exposed do not have higher rate of malignancy than non-exposed
- Statistically significant increased rate of malignancy in thiopurine exposed

Malignancy Risk in Pediatric IBD

Standardized Incidence Ratios (SIR)

<table>
<thead>
<tr>
<th>Year</th>
<th>Observed # of cases</th>
<th>Expected # of cases</th>
<th>SIR</th>
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Risk of Disease Often Greater than Risk of Treatment

Risk of Disease

Risk of Treatment

169
201 cases PML after natalizumab became available for prescription in July 2006

Vedolizumab (Entyvio) – CHOP Experience
Gut selective anti-integrin α4β7 (approved 2014)

Ustekinumab (Stelara®) for Active Crohn Disease
Prevents binding of IL-12 and IL-23 to receptors
• Showed promise for adult CD patients with anti-TNF failure
• 09/2016: Approved for treatment of Crohn disease
• Side effect profile seems favorable
• Induction: Single IV weight-based dose
• Maintenance: 90 mg SQ q8 weeks
Ustekinumab for Crohn’s disease: UNITI-1 and UNITI-2

UNITI-1 & 2: Clinical Response Through Week 8

UNITI-1 & 2: Clinical Remission Through Week 8

The Key to the Future: Targeting Therapy

Gene I  IBD 1  Bacteria X
Gene II  IBD 2  Bacteria Y
Gene III  IBD 3  Bacteria Z

Rx IBD1  Rx IBD2  Rx IBD3

Mild  Severe
“There is nothing permanent except change”
-Heraclitus, c. 500 BC
Psychosocial Health in Pediatric IBD: Opportunities for Multidisciplinary Care

Bonney Reed-Knight, PhD
Pediatric Psychologist

Learning Objectives

1. Describe psychosocial difficulties experienced by pediatric patients diagnosed with IBD
2. List evidence-based psychotherapies for pediatric anxiety, depression
3. Describe basic tenets of cognitive-behavioral therapy for anxiety and depression
4. Discuss treatment of anxiety and depression effectively with fellow providers and patients

Disclosures
No conflicts of interest or disclosures
I'm Tired  
By Kristen Ottesen

I'm tired. 
Tired of the constancy, 
Tired of hiding who I really am. 
Tired of pretending, 
Tired of being put down, 
Tired of remembering, 
Tired of failing. 
I'm tired. 
Tired of the people I felt closest to. 
Tired of not being good enough. 
Tired of crying, 
Tired of dreaming, 
Tired of not being happy. 
Source: http://www.familyfriendpoems.com/poem/im-tired-4

---


National Survey on Drug Use and Health

- 29.9% high school students
- 39.8% females
- 20.3% males
- 35.3% Hispanic
- 28.3% white non-Hispanic
- 25.2% black non-Hispanic

---

Single-Item Response: Felt So Sad or Helpless for ≥ 2 Weeks In Prior Year (2011)

Youth Risk Behavior Survey (YRBS)
Sadness ≠ Depression

• Sadness is a normal response to difficult life events.
• Depression affects our emotions, thoughts, behaviors, and physiology in pervasive and chronic ways.
• The Loss of Sadness: How Psychiatry Transformed Normal Sorrow into Depressive Disorder
  – By Allan V. Horwitz, Jerome C. Wakefield
Inflammatory Bowel Disease

Emotional Functioning

- Emotional functioning
- Compared to healthy children:
  - More symptoms of anxiety/depression (internalizing symptoms)
  - Separately, symptom domains not higher
  - Higher risk for diagnosis of depression
  - Rates up to 25%
- Adults
  - Higher risk for anxiety disorders (OR = 2.18)

Emotional Functioning Table

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Healthy 69%</th>
<th>Anxiety 13-31%</th>
<th>Depression 10-59%</th>
<th>Anxiety 6-28%</th>
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</thead>
<tbody>
<tr>
<td>Depressive Symptoms</td>
<td>3-25%</td>
<td>13-31%</td>
<td>10-59%</td>
<td>6-28%</td>
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<tr>
<td>Depression Disorder</td>
<td>5-30%</td>
<td>20%</td>
<td>25%</td>
<td>11-28%</td>
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<td>Anxiety Symptoms</td>
<td>10-59%</td>
<td>13-31%</td>
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<tr>
<td>Anxiety Disorder</td>
<td>6-28%</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Depression and Anxiety (Internalizing Symptoms)</td>
<td>10-31%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Fuller-Thompson, E., et al., Robust association between inflammatory bowel disease and generalized anxiety disorder. Inflamm Bowel Dis. 2015.


Inflammatory bowel disease

- Psychosocial functioning and adherence
  - Symptoms of depression, anxiety, and behavioral/emotional problems associated with worse adherence
  - High depression/anxiety – barriers predict much worse adherence

Leake et al. Rates and predictors of oral medication adherence in pediatrics with IBD. Inflamm bowel dis. 2013;19:832-

Emotional Functioning

- Risk factors for depression
  - Stressful life events
  - Maternal depression
  - Family dysfunction
  - Parenting Stress
  - Steroid treatment
  - Ostomy
  - Disease Activity (mixed findings)

Classifying Depressive Episode

**ESSENTIAL FEATURES**
- Depressed mood OR irritability
- Anhedonia
- Low energy/fatigue

**OTHER SYMPTOMS**
- Change in appetite
- Hypersomnia or insomnia
- Psychomotor agitation or retardation
- Guilt/worthlessness
- Difficulty concentrating
- Suicidal ideation/thoughts of death

Mild: 2+ essential feature + 1-2 other symptoms
Moderate: 2+ essential feature + 2-3 symptoms
Severe: 3 essential features and >3 other symptoms with severe functional impairment
Assessment Logistics
Screen for depressive symptoms using validated questionnaire (e.g., PHQ-9)
Score in clinic, additional assessment, and triage
Education, Safety Planning, Refer as needed
Document and Rescreen

Triage
- Use shared decision making to determine most desirable course of action
  - Mild: Monitor/Education, Self-help, Therapy
  - Moderate: Medication, Therapy, Medication, Safety Planning, Hospitalization
  - Severe: Medication, Therapy, Safety Planning, Hospitalization

How can I make a difference with my IBD patients?
Symptom Presentation

- Younger children more likely to present with somatic symptoms (e.g., aches and pains); adolescents more likely to present with cognitive symptoms (e.g., sense of worthlessness, guilt, suicidal ideation)

- In adolescence, females more likely to present with symptoms than males

- Does my patient have risk factors for depression/anxiety in IBD?

Course of Depression

- 50-75% depressive episodes triggered by recent exacerbating event
- 50-80% remission in 12 months
- 30-70% relapse within 5 years

Effective treatment associated with quicker recovery and lower relapse rates

Assessment Logistics

- When possible, assess apart from caregiver
- Review limits of confidentiality
- Normalize
- Be direct & ask open-ended questions (e.g., “tell me the last time you had thoughts of killing yourself” vs. “have you ever…”)
Post-Assessment Youth Talking Points

- **Remove fault:** Depression isn’t your fault.
- **Destigmatize:** Depression is often associated with an imbalance of neurotransmitters, or chemicals in the brain. It can also be associated with stress, traumatic life experiences, a family history of depression, IBD symptoms, etc. Depression can happen to anyone.
- **Support:** I will help you with this.
- **Empower:** There are things you can do to support yourself in getting better. This is not forever.

Prophylactic/Tier 1 Advice for Teens

- Behavioral activation
- Get enough sleep
- Find an outlet to express your feelings
- Limit social media
- Be physically active
- Associate with friends who have positive goals
- Identify and target barriers to adherence for IBD

Caregiver Assessment
**Assessment Logistics**

- Concordance rate between parent and youth report of mental health functioning is fair at best.
- Parents have unique insights into youth functioning (may counteract impression management)
- Opportunity for clinicians to model healthy communication between teens and parents.

**Caregiver Talking Points**

- **Educate:**
  - Depression is the most common mental health disorder in the U.S. among teens and adults.
  - Patients with IBD are at higher risk for symptoms of anxiety and depression
  - Depression is associated with other at-risk behaviors.
  - Depression may re-occur.

  **Emphasize importance:** Treatment is successful in 80% of teens but only 1 in 3 teens gets help.

**Prophylactic/Tier 1 Advice for Caregivers**

- Listen
- Don’t minimize child’s subjective experience
- Normalize distress within context of development and disease
- Allow child to make mistakes
- Keep the lines of communication open
- Elicit support from close friend or family member your child is close with
- Be firm in setting rules and calm in enforcing them
- Manage your own mental health issues as needed
Referring for treatment

Referring for Treatment

- Active support and monitoring
  - Mild depressive symptoms

- Evidence-based psychotherapies
  - Moderate/Severe depressive symptoms

- Antidepressant medications
  - Moderate/Severe depressive symptoms

- American Academy of Pediatrics
  - Policy Statements on Guidelines for Adolescent Depression

- Improve Care Now
  - Depression Screening Toolkit

Cognitive Behavioral Therapy

- How we Think (Cognition)
- What we Do (Behavior)
- How we Feel
Treatment Efficacy: Anxiety and Depression

- Anxiety:
  - CBT > wait-list or active controls
  - CBT = Sertraline (but less side effects!)
  - CBT + Sertraline > single modality

- Depression:
  - CBT and IPT > supportive therapy
  - CBT = Fluoxetine by 18 weeks
  - CBT + Fluoxetine initially > single modality


Summary

Acknowledgments

- GI Teams at Children’s Healthcare of Atlanta
- Society of Pediatric Psychology: GI Special Interest Group
- ImproveCareNow Psychosocial Professionals’ Group
References

High Yield Bowel Evacuation: Cecostomy and Trans-anal Irrigation

Jason E. Dranove MD FAAP
Pediatric Gastroenterology, Hepatology, Nutrition
Levine Children’s Hospital
Carolinas Healthcare System
Charlotte, NC

Overview
• Suppositories/Standard Enemas
• Cecostomy Overview
  • Post Op
  • Getting Started
  • Maintenance
  • Troubleshooting
• Trans-anal Irrigation (large volume enemas)
  • Cone Enema
  • Peristeen
  • Q / A

Basic Rectal Therapy -- Suppository
• Suppositories
  • Solid Glycerin Suppository
    • < 2 YO = ½ Pediatric Size Glycerin Supp
    • 2-5 YO = 1 Pediatric Size Glycerin Supp
    • 6 YO and up = 1 Adult Sized Glycerin Supp
  • Liquid bulb Glycerin Suppository
    • 2-5 YO = Pediatric Size Liquid Glycerin Supp
    • 6 YO and up = Adult Size Liquid Glycerin Supp
  • Bisacodyl Suppository
    • One Size only = 10 mg
    • If Glycerin Supp ineffective use ½ to 1 suppository
Basic Rectal Therapy -- Enemas

- Sodium Phosphate Enema
  - < 2 YO = not recommended
  - 2.5 YO = ½ of a Pediatric Enema (33 ml)
  - 6-11 YO = 1 Pediatric Enema (66 ml)
  - 12 YO and up = 1 Adult Enema = 133 ml

- Bisacodyl Enema
  - 10 mg/37 ml
  - No concrete dosing instructions
    - Roughly 0.2 mg/kg, but in general can start with ½ bottle in younger patients < 5-6 YO and use whole bottle if older

What is a cecostomy

Who has a cecostomy

- Myelomeningocele
- Spinal Cord Injury
- Tethered Spinal Cord
- Anorectal Malformations / Imperforate Anus
- Hirschsprung’s Disease
- Functional Constipation +/- Fecal Incontinence
- Nonretentive Fecal Incontinence
The Golden Hammer

"I suppose it is tempting, if the only tool you have is a hammer, to treat everything as if it were a nail."

ABRAHAM MASLOW
THE PSYCHOLOGY OF SCIENCE

What I feel like

Goals of Cecostomy Flushes

- Eliminate or Greatly Improve Fecal Incontinence
- Prevent Recurrent Hospitalizations / Manual Disimpaction
- Improve Quality of Life
- Prevent or delay more invasive surgeries such as ostomy or resections
- Minimum Age
  - Technically no minimum age or size, but relatively very rare less than 3 YO
- Relative Contraindications
  - Older / larger child unable to sit on toilet
    - May tolerate enemas better
Methods of Cecostomy Administration

**Placement**
- Surgical
  - Approximate Cecum to Abdominal Wall and create a tunnel
  - Appendiceo-cecostomy
    - Most commonly known as MACE
    - Malone Antegrade Continent Enema
- Endoscopic
  - Percutaneous Endoscopic Cecostomy
  - Interventional Radiology Placement

**Administration**
- Intermittent Catheterization
- Indwelling Gastrostomy button or Regular Button Gastrostomy
- Chait Cecostomy

In and Out Catheterization

- More common in Spina Bifida or patients with poor sensation
- Usually 8 to 10 French Catheter (can be smaller or larger)
- Must be able to tolerate
  - Anxiety
  - Visceral hypersensitivity

Indwelling Button

- Initial placement may be with a standard Gastrostomy balloon or with a Foley with a balloon
- Allows for eventually changing at home and low profile for improved aesthetics
Chait Trapdoor Cecostomy

- Some surgeons prefer
- Change once q 6 months
  - Some require anesthesia
  - Hard to replace at home if comes out
  - Tract is only 10 Fr so can close up easier if removed
  - Very low profile for aesthetics
  - Anecdotally less granulation tissue and leakage problems

Variation in Management

- ~22% did not require minimum age. Range from any age, 1, 4, or 7
- ~only 26% required colonic manometry. Less than 60% require ARM or biopsy
- ~variation in when to start flushes, whether to use additive, duration of infusion, time on toilet

Pre-operative

- Educational material
- Consultation with surgeon
- Possible admission for cleanout prior to surgery
Post-operative

• Typically 1-2 day stay after surgery
• Will have either a long button gastrostomy, a low profile gastrostomy, a Chait Cecostomy, or rarely a foley catheter through the stoma
• Start 10 ml NS flush bid day after surgery x 2 weeks, then advance to larger volume flushes
• Continue PO meds until closer to goal volume
• Order Supplies

Necessary Supplies

• 60 ml syringes (2 per month)
• Extension set (2 per month)
• Gravity Bag with Roller Clamp (1 per day)
• Split Gauze
• Paper tape
• Replacement button (as soon as know button size)
• Tegaderm for swimming

Initial Followup

• Hands on Demonstration
• If long tube is in, patient will be sized by surgeon and appropriate button placed or ordered by surgeon
• If I/O catheterization, indwelling tube can be removed and I/O caths started
• Make plan to start and/or advance flushes
• Plan to wean off of PO meds
Antegrade Enema (Washout)

- Recommend after dinner
- Flush runs in over 5 to 15 minutes
- Total sitting time at least 30 mins, Avg 45 minutes

Flush Composition
- Base of the flush is warm water mixed with salt (1/2 to ¾ tsp per 500 ml)
- Start 300 to 500 ml depending on size
  - Good initial goal is 20 to 25 ml/kg
  - Advance to goal by 50 ml increase q 3 days
  - Usually Max 600-700 no matter size, but can go up to 1000 ml
- Avoid water alone as will have higher chance of being reabsorbed and ineffective
- Rare cases can cause water intoxication
- Some advocate always starting with stimulant in flush
- More necessary in pts with idiopathic Constipation

Possible Additives
- Osmotic
  - PEG 3350
    - For little extra strength, short of using a stimulant
    - Substitute Golytely for Saline if fail Saline + additive flushes
- Stimulant
  - Bisacodyl
    - 5 mg tablets
    - Can crush and mix directly into the flush solution
    - Can mix 1 or 2 crushed tablets with 10 to 30 ml and flush directly before or after the main flush
    - Can use Liquid Enema 10 mg/37 ml
    - More inconvenient as usually need to order online and usually not covered
  - Glycerin
    - 5 to 30 ml
Initial Flush not working

- Rule out Fecal Impaction
- Rule out severe backup in 2 week post op before flushes begin
- May need manual disimpaction vs. inpatient cleanout
  - Depending on timing post op, might need a large volume cleanout per cecostomy

Complications

**Early**
- Separation of cecum from abdominal wall
- Granulation Tissue
- Perforation or false tract with I/O cath
- Leakage while healing
- Infection / Abscess
- Retraction of tube into tract if too short

**Later**
- Granulation Tissue
- Leakage
- Inability to flush
- Stenosis of tract for I/O
- Perforation or false tract with I/O cath
- Retraction of tube into tract if too small
- Infections can be tricky to dx
  - Pain with flush even though flush works
  - Hyoscyamine
  - Gabapentin

General Troubleshooting

**Poor Output**
- Increase Volume
- Add Stimulant before or after
- Flush bid (difficult logistically)
- Add PEG 3350 or Change to Golytely
- Empiric Cleanout
- Compliance
- Dysmotility preventing movement of flush through colon

**Leakage**
- Button tube or Chait Too long
- Tube too short
  - Fluid comes out in tract and moves retrograde through tract
- Granulation Tissue
- Poorly Healed tract
- Fecaloma in cecum
- Balloon underfilled
Flush not going in

<table>
<thead>
<tr>
<th>No Pain</th>
<th>Pain</th>
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<tbody>
<tr>
<td>• Tube clogged or blocked</td>
<td>• Tube pulled up into tract</td>
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<tr>
<td>• Try to change tube</td>
<td>• Too Short</td>
</tr>
<tr>
<td>• IMHO</td>
<td>• Balloon deflated and retracted</td>
</tr>
<tr>
<td>• Being backed up should not cause the flush to not go in</td>
<td>• Similar concept to buried bumper of a PEG tube</td>
</tr>
<tr>
<td></td>
<td>• Chait coils visible</td>
</tr>
<tr>
<td></td>
<td>• False tract or perforation</td>
</tr>
<tr>
<td></td>
<td>• Difficulty flushing with pain can be from cecal distension</td>
</tr>
</tbody>
</table>

Cone Enema

- Less Invasive option than Cecostomy
- Better for Spina Bifida / Tethered Cord due to poor sensation
- Hard for highly anxious kids
- Not palatable long term solution for many
- Failure does not preclude a cecostomy

Peristeen®

- How does Peristeen work?
- Peristeen allows the evacuation of stool from the bowel by introducing water into the rectum via a suppository that releases saline solution in a controlled manner.
- Other characteristics:
  - Easy to use:
  - Can be used while lying down or sitting up
  - Can be used in any position:
  - Can be used at any time of the day or night
  - Can be used as a means to keep the stool soft or to empty the colon.
**Team**

- Gastroenterologist
- Invested and Interested Surgeon
- Radiology for Chait Changes
- GI RN
- Home Health Nursing / Discharge Planners
- Motility Nurse
- Social Worker for 504 plan
- RD on occasion
- Need to educate colleagues who will cover patients on call
Esophageal manometry

Samuel Nurko MD MPH
Center for Motility and Functional Gastrointestinal Disorders
Boston Children’s Hospital

OBJECTIVES
• Discuss when esophageal manometry should be used in the clinical setting
• Advances in the performance of esophageal manometry (HRM)
• Discuss the relevance of combining impedance testing and high-resolution manometry.

DYSPHAGIA
• Difficulty swallowing is very common
• It may be related to anatomic/mechanical or functional problems
• History is an important part of clinical assessment, but bedside assessment alone is often inadequate in achieving a diagnosis
IS THERE A MOTILITY DISORDER?

- Exclude anatomic obstruction
- Evaluate transit
- Look for an etiology
- Motility testing

EVALUATION

- X-ray studies
  - Anatomy
- Endoscopy
  - Anatomy and mucosal disease
- Scintigraphy
  - Transit
- Motility testing
  - Esophageal function
  - Transit

DYSPHAGIA

- These symptoms may be indicative of an underlying esophageal motility disorder potentially caused by impaired esophageal propulsion or
- Increased resistance to bolus flow at the esophago-gastric junction (EGJ).
ESOPHAGEAL MANOMETRY

- Manometry is the most sensitive and accurate technique to diagnose esophageal motility disorders.
- Three functional regions of interest:
  - Upper esophageal sphincter (UES)
  - Esophageal body
  - Lower esophageal sphincter (LES) & Gastro-esophageal junction (GEJ)

THE BOUNDARIES OF THE ESOPHAGUS ARE DEFINED BY SPHINCTERS

<table>
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<th>Pressures</th>
<th>Muscle Type</th>
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<tbody>
<tr>
<td>Atmospheric = 0 mmHg</td>
<td>Striated muscle</td>
</tr>
<tr>
<td>Upper esophageal sphincter (UES) = 100 mmHg</td>
<td>Smooth muscle</td>
</tr>
<tr>
<td>Intraesophageal = -5 mmHg</td>
<td>Mixed striated and smooth muscle</td>
</tr>
<tr>
<td>Lower esophageal sphincter (LES) = 20 mmHg</td>
<td>Smooth muscle</td>
</tr>
<tr>
<td>Intragastric = +5 mmHg</td>
<td></td>
</tr>
</tbody>
</table>

-Sphincters prevent influx of air and reflux of gastric contents into the esophagus.

EFFECTIVE NEURAL PATHWAYS DIFFER IN STRIATED AND SMOOTH MUSCLE REGIONS OF THE ESOPHAGUS

- Dorsal motor nucleus
- Nucleus ambiguous
- Vagus nerve
- Intramural ganglia
- Mixed striated and smooth muscle
- Smooth muscle
Conventional manometry evaluates peristaltic function in the esophagus over a series of pressure transducers spaced at defined intervals (2-5 cm depending on the size of the patient).

Standard esophageal manometry

- Lack of standardization and lack of consensus regarding the optimal spacing
- Problems with inter-observer variability
- Achieving consensus on what is normal or abnormal is at times difficult
- Very few diseases are well defined (achalasia and problems with movement)
- Difficulty in correlating esophageal motor patterns and symptoms
  - Inability to assess esophageal transit

**NEED FOR IMPROVEMENT TO INCREASE ACCURACY AND CLINICAL UTILITY**
The basic concept being that by vastly increasing the number of recording sites and decreasing the spacing between them, one can completely define the intraluminal pressure environment without spatial gaps between recording sites and, consequently, with minimal movement-related artifacts.

HRM recordings with esophageal pressure topography (EPT) enable features of peristalsis, such as the pattern and integrity of the contraction, as well as the extent of EGJ relaxation to be more easily determined via objective metrics.
Proposed Advantages of HRM

- Simultaneous assessment of sphincters and esophageal body
  - Separation of LES, crural diaphragm

- Hiatal hernia

Proposed Advantages of HRM

- Simultaneous assessment of sphincters and esophageal body
  - Separation of LES, crural diaphragm
  - New parameters
  - More standardized measures of peristalsis and sphincter function

HRM

- Easier to perform
- Eliminates movement artifact
- Provides functional anatomy
- Improve measurement of GEJ junction
  - Separation of LES, crural diaphragm
- New parameters that were not previously apparent
  - Transition zone
  - Different segments
  - New variables
    - IRP (integrated relaxation pressure)
    - CVF (contractile front velocity)
    - DCI (distal contractile integral)
    - Others
Proposed Advantages of HRM

- Simultaneous assessment of sphincters and esophageal body
- More comprehensive approach
- New parameters
- More standardized measures of peristalsis and sphincter function
- Decreased movement-related artifact

CHICAGO CLASSIFICATION v3.0

- Hierarchical approach, sequentially prioritizing:
  - (i) disorders of esophagogastric junction (EGJ) outflow,
  - (ii) other major disorders of peristalsis, and
  - (iii) minor disorders of peristalsis.

A higher percentage of patients with type II achalasia are treated successfully with PD or LHM than patients with types I and III achalasia. Success rates in type II are high for both treatment groups but significantly higher in the PD group. Patients with type III can probably best be treated by LHM.
Proposed Advantages of HRM

- Simultaneous assessment of sphincters and esophageal body
  - Separation of LES, crural diaphragm
  - New parameters
- More standardized measures of peristalsis and sphincter function
- Decreased movement-related artifact
- *Easier to perform and shorter study duration*

HRM in children

- Easy to perform
- Advances:
  - Microperfused catheters
  - Solid state catheters
- Limited information in pediatrics
  - Do we need to use the adult measurements?

Is the Chicago Classification applicable to children?
Younger patient age and shorter size correlated significantly with greater IRP4s (p < 0.05), shorter DL (p < 0.001) and smaller break size (p < 0.05).

NGM 2014; 26:1333

---

Chicago classification
Adjusted criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Abnormal motility</th>
<th>Abnormal criteria based on age in months</th>
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<td>Category 1</td>
<td>Achalasia</td>
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<td>Achalasia type 2</td>
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<td>Achalasia type 5</td>
<td>3.0 (4)</td>
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NGM 2014; 26:1333

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CC IN CHILDREN

- 66% of pediatric cohort showed abnormal motility when applying standard CC criteria.
- Adjustment for age and size reduced this to 50% and 53% respectively, with the largest reduction being in the IRP4s- and DL dependent disorders EGJ outflow obstruction and diffuse esophageal spasm (13% to 7% and 5% and 14% to 1 and 5%, respectively).
Chicago classification

• Applying the 2012 Chicago Classification (CC) of esophageal motility disorders to pediatric patients may be problematic as it relies upon adult-derived criteria

IS IT REPRODUCIBLE?

• Intra- and inter-rater reliability of software generated CC diagnosis was substantial (mean $\kappa=0.69$ and 0.77 respectively) and moderate-substantial for subjective CC diagnosis (mean $\kappa=0.70$ and 0.58 respectively).
• Agreement on software-generated and subjective diagnosis of Normal motility was high ($k=0.81$ and $k=0.79$). Intra- and inter-rater agreement was excellent for IRP4, DCI and BS.
• Amongst experts the agreement for the subjective diagnosis of achalasia and EGJ outflow obstruction was moderate-substantial ($k=0.45 - 0.82$).

DEGLUTITIVE INHIBITION
Solids better peristalsis than liquids

Figure 1: Representative HRM pressure topography from water and solid swallows in comparison with ESMD (left) and ERMD (right). The peristaltic wave of solid, water is indicative with a clear expansion of proximal and distal swallows, whereas the wave of solid, water is observed with clear contraction in ESMD, whereas filled boluses show a significant intrabolus dephosphorylation as ERMD. Note the expansion of a 0.5 cm saline bolus in both swallows.
The relationship between esophageal contractile patterns and bolus transport disruption, leading to bolus hold up perception and symptoms, is far from clear, even in adults.

Symptoms of dysphagia correlate poorly with conventional manometric findings, and the underlying cause of these symptoms still remains unclear in a large proportion of dysphagia patients.

Manometry as a standalone technique may not be sensitive enough to elucidate esophageal motility events underlying ineffective esophageal bolus clearance and/or dysphagia.

Combining esophageal pressure patterns with bolus flow measured by intraluminal impedance was proposed to assess bolus transport throughout the esophageal lumen and across the EGJ.
HRM AND IMPEDANCE

- May allow the classification of motility abnormalities and their impact on bolus transit
- May allow the understanding of the pathophysiology of esophageal motor abnormalities, and may provide better treatments
AIM

- Bolus flow characteristics as measured by impedance are combined with esophageal contractile characteristics
- Different measures are extracted, such as the intrabolus pressure (IBP), the slope of the IBP over time, and time from nadir impedance to peak contraction.
- From these, the dysphagia risk index is derived

Automated Impedance Manometry analysis (AIM)

DYSPHAGIA
Pf index and weak peristalsis

Eur J Peds 2015
SPECIAL POPULATIONS

- Preop
- TEF
- Rumiantion

CAN BASELINE HRM PREDICT OUTCOME AFTER SURGERY?

FUNDOPPLICATION

- 10 children; 4 developed dysphagia

J Peds 2013
• Calculation of BPT and BFT may help to determine whether esophageal bolus transport to the EGJ and/or esophageal emptying through the EGJ are aberrant. For achalasia this may detect flow resistance at the EGJ, potentially improving both diagnosis and objective assessment of therapeutic effects.
ESOPHAGEAL MOTILITY

- Diagnosis of achalasia and other primary esophageal motor disorders
- Assess esophageal motor function in patients with dysphagia, odynophagia or non-cardiac chest pain
- To support the diagnosis of connective tissue diseases, or other systemic illness
- To localize LES before pH probe placement in patients with abnormal anatomy (like hiatal hernia, etc)
- To evaluate effect of pharmacologic or surgical therapy
- To diagnose rumination

Neuropsychostrual Met 2002; 14:411-420

FLIP

![Diagram of FLIP procedure]

![Graphical representation of esophageal motility]
HRM

• HRM simplifies the performance of esophageal motility in children

• Impedance measurement is a must
  – New analysis

• Will it change the diagnosis? Will it provide useful information?
Psychological Treatment of Rumination Syndrome

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Pediatric Psychologist
Department of Gastroenterology
Boston Children's Hospital

Disclosures

• I have nothing to disclose!

Rumination Defined

• Repetitive regurgitation of small amounts of food from the stomach that is then re-chewed and re-swallowed or expelled (Dalton & Czyzewski, 2009)
Describe the rationale behind incorporating psychological/behavioral interventions into the treatment plan for a diagnosis of rumination.

Identify specific psychological strategies that can be taught and utilized for the management of rumination syndrome.

Presentation Objectives

Outline of Presentation

Brief History
Diagnostic Criteria
Prevalence Rates
Pathophysiology
Making the Diagnosis/Clinical Features
Treatment

History of Rumination

Well known to occur in animals with compartmentalized stomachs (e.g., sheep, cattle, goats).

First case reports of this disorder in humans dates back to the 17th century.

Physician in the 19th century, Edouard Brown-Sequard, documented that he experienced rumination as a result of “experimenting” on himself.

Rome IV Criteria for Rumination Syndrome in Children/Adolescents

- Must include all of the following:
  1. Repeated regurgitation and re-chewing or expulsion of food that:
     a. Begins soon after ingestion of a meal
     b. Does not occur during sleep
   2. Not preceded by retching
   3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition. An eating disorder must be ruled out

Criteria fulfilled for at least 2 months before diagnosis

Prevalence Rates

- Estimated to occur in about 6-10% of patients diagnosed with developmental delays (Singh, 1981; Winton & Singh, 1983)
- Prevalence rates of 17-20% in patients previously diagnosed with bulimia (Fairburn & Cooper, 1984)

Prevalence

- Almost no studies assessing prevalence rates of rumination in typically developing children and adolescents
  - Continued difficulties with recognizing/making a diagnosis of rumination makes it harder to understand the prevalence of this disorder
  - Symptoms overlap with the symptoms of more recognizable conditions
Rajindrajith, et al. (2012)

- Prevalence of rumination in cohort of Sri Lankan children
- N=2163
  - 55% of sample were males
  - Children ages 10-16 (mean age: 13.4)
  - Excluded children with neurological problems, developmental delays/autism, and other chronic diseases

- 110 (5.1%) children fulfilled diagnostic criteria for rumination
  - 5.1% male; 5.0% female
  - 11.8% missed school because of rumination
  - 74% said they re-swallowed regurgitation; 26% said they spit it out
  - 95% reported rumination occurred within first hour after meal
  - Frequency of symptoms:
    - 63% at least once/week
    - 29% several times per week
    - 8% daily symptoms

Pathophysiology

- "Trigger" may be present right before the onset of rumination
- Illness or emotional stressor
  - Stressor resolves, but behavior persists
  - Resembles a "tic"
- Gastric motor/sensory abnormalities
  - Increased intragastric pressure that results from contracting of abdominal muscles and is associated with lower esophageal sphincter (LES) relaxation
  - When LES relaxes the regurgitation occurs
  - On high resolution manometry "r" waves are representative of increase in intra-abdominal pressure
  - Regurgitation occurs due to an increase in abdominal pressures that results in displacement of gastroesophageal junction (GEJ) into the thorax
Regurgitation serves the purpose of relieving epigastric discomfort/dyspeptic symptoms (nausea, bloating, feeling of fullness, pressure) given hypersensitivity to LES relaxation.

Rosen, Rodriguez & Nurko, 2016: 40% of patients reported sensation right before R wave

Over time, regurgitation becomes a learned response to food/liquid ingestion

“Learned anticipation or possible hypersensitivity to the sensations associated with food in the stomach causes the individual with rumination syndrome to contract the abdominal wall, opening the lower esophageal sphincter and upper esophageal sphincter with cessation of esophageal body peristalsis, prior to a regurgitation event” (Chitkara et al., 2006)

Rumination may be confused with other diagnoses

When differentiating rumination from another GI disorder, consider the following:

You can diagnose rumination by history alone

It typically starts during or immediately after a meal

Reports are that regurgitated food looks undigested and still “tastes good”

Volume of what is regurgitated is small (in comparison to vomiting)

Retching before regurgitation is not reported

Nausea also not reported (anxious, vasomotor symptoms also not reported such as heart palpitations, sweating, light-headedness)

Patients will report that the regurgitation persists after eating, sometimes up to 1-2 hours

Rumination happens with most meals, regardless of what is eaten

Liquids also result in rumination

(Mak et al., 2016)

Making the Diagnosis

Table 16.1 Differential diagnosis of rumination syndrome from other conditions presenting with onset in adolescence

- Regurgitation
  - During or minutes after meal
  - Often (nausea)
  - Not helpful
  - Not helpful

- Achalasia
  - Hours after meal
  - Often (nausea)
  - Not helpful
  - Not helpful

- GERD
  - After large meals
  - Often
  - Helpful
  - Helpful

- Gastroparesis
  - Hours after meal
  - Often
  - Helpful
  - Not helpful

- Cyclic vomiting
  - Intermittent, alternating to meal
  - During episodes
  - Not helpful
  - Not helpful

Alioto & Di Lorenzo (2013)
Potential Consequences of Rumination

- Weight loss
- Malnutrition
- Dental erosions
- Halitosis
- Electrolyte abnormalities
- Functional Disability
- Embarrassment/Anxiety
- Parental Annoyance

Treating Typically Developing Patients

- Keep in mind that you are treating a functional GI disorder
- Provide reassurance
- Take the time to describe that the diagnosis is made based on signs and symptoms
- Explain, in developmentally appropriate terms, what is happening in rumination
- Explain a biopsychosocial treatment approach

Ways to explain rumination:

- A learned “habit”
  - Patients may experience an “urge” in response to what the stomach begins to do after eating, which results in certain parts of the digestive system contracting (stomach) and relaxing (LES) - the end result is regurgitation
  - Operant conditioning: regurgitation diminishes the urge in the moment, but the positive experience of getting rid of the urge with regurgitation increases the likelihood that the person will repeat the behavior in the future
A “tic”
- Tends to make the most sense when a trigger event has been identified
- Even though the trigger has been removed, the vomiting/regurgitation behavior persists
- As a consequence, when food/liquid enters stomach, body has learned to contract abdominal muscles, which pushes food back up

Treatment of Rumination
- Medication
- Diaphragmatic Breathing
  - Reduces intragastric pressure/Increases EGJ pressure
  - Changes seen during esophageal manometry studies in adults (Halland, Parthasarathy, Bharucha, & Katzka, 2016)
- 3 non-randomized, retrospective studies in children and adolescents:
  - Chial et al., 2003: 54 patients treated for average of 3 sessions; resolution of symptoms in 30%, improvement in 55%, no change in 15% at 10 months

Khan, Hyman, Cocjin, & DiLorenzo, 2000: 12 patients, 7 of who were treated with breathing/biofeedback (other 5 treated with pain management interventions and psychopharmacological treatment)
- 10 children noted to “improve” but separate results not reported for breathing/biofeedback group
Green, Alloto, Mousa, & Di Lorenzo, 2011: 5 patients (4 female) 
- Sx occurred anywhere between 5 months and 4 years before diagnosis was made 
- Feeding sources: TPN, NJ, NG, GJ, and PO 
- All had gastroduodenal manometry prior to admission (showing the characteristic R waves) 

- Some patients discharged with continued rumination, yet able to maintain weight 
- Periods of stress resulted in occasional return of symptoms 
- At one year follow-up, 0 patients needed to return to supplemental nutrition 

Teaching Diaphragmatic Breathing 
- Learn technique in sitting or supine position 
- One hand on chest; other hand on stomach 
  - Asked to take a deep breath in (with most patients able to notice that they tend to breathe with their chest) 
  - Asked to "switch" their breathing 
  - Slowly breathe in through the nose, thinking about filling belly up with air (like blowing up a balloon) 
  - Slowly breathe out through pursed lips, thinking about deflating the balloon 
  - Place object on stomach to make sure patients sees belly moving up and down
Practice and Follow-through

- Practice daily for a few days to ensure proper use of the breathing
- Breathe mid-way, immediately after, and every time that rumination occurs

Habit Reversal Protocol

- 1. Become more aware of the behavior
  - Daily log to track rumination episodes and any sensations that happen right before rumination occurs
  - Biofeedback to note contraction of abdominal wall
- 2. Increase aversiveness of rumination
  - Swallow food back down every time
  - Get rid of garbage cans, vomit basins
- 3. Teach diaphragmatic breathing
  - Involves relaxation of abdominal muscles so it serves as a competing response to this abdominal wall contraction
  - This breathing also decreases responsiveness around [major player in functional GI diagnoses] by promoting the relaxation response
- 4. Distraction
  - Divert attention away from physical sensations to decrease anxiety (which could exacerbate rumination)
- 5. Social Support

Treating Severe Rumination

- When significant weight loss and/or functional impairment consider multidisciplinary approach
  - Inpatient or outpatient
  - Gastroenterology, Psychology, Nutrition, other disciplines
  - Alloto, Yacob, Yardley, & Di Lorenzo (2015): Retrospective analysis
  - 55 patients completing inpatient program
  - Interventions: Medical management of GI symptoms (gastroenterologist), set nutritional goals (dietician), address physical deconditioning (recreation therapist), massage, adjustment to program (child life), habit reversal combined with relaxation/diaphragmatic breathing (psychologist)
91% white females
- Average duration of illness: 22.6 months
- 58% started on enteral or parenteral nutrition
- Average length of hospitalization: 9 days
- Mental health diagnoses in patients:
  - 40% GAD
  - 27% Depression
  - 5-6% ED NOS
- Results:
  - At time of discharge 81% were retaining at least 80% of daily caloric intake requirement (but 93% continued to ruminate)
  - Comorbid mental health disorder more likely in those not achieving set intake goal
  - 9% of patients on supplemental nutrition were discharged without feeds

Benefits of gradual refeeding process
- Allows patient to practice self management skills when trying to comply with challenge of eating increasing quantities of foods
- Increases ability to tolerate discomfort associated with gastric distention
- Frequent/small food trials permits repeated exposure to stressful stimulus (food)
- Instills confidence in patients as they make progress with keeping food down

(Green, Alioto, Mousa, Di Lorenzo, 2011)

References

Rickets, itching and poor feeding: What's the common link?
Shabina Walji-Virani RN, MSN, CPNP
Children’s Health, Plano, TX

Initial Presentation
• 13 month old Hispanic male with history of rickets, eczema and poor weight gain/ “picky eater”
• Had intermittent diarrhea between birth and 4 months of age that seemed to have improved.

History
• Previously treated for eczema with creams and vitamin D deficiency by PCP
• Diagnosed with rickets by PCP in the previous month.
• Refused to eat any solids except pureed sweet potatoes. Drank about 36-42 ounces of Lactaid milk
• FHx: Gallstones: mother, eczema: brother
Physical Exam

- VS stable
- Alert and active
- WT: 7.9 kg (3.54%)
- HT: 70.7 cm (1.5%)
- WT for length: 18.87%
- Skin with scratch marks from itching.

Work up

- EGD: Normal
- Initial labs:
  - Albumin: 3.1, Alk Phos: 1407, ALT: 188, AST: 111, T.Bili: 0.7, D.Bili: 0.24, GGT: 8, Phos: 6.8,
  - Vitamin A: 0.64, Vitamin D: 16, Vitamin E: 3.0, and PT/INR: 11.2/0.8
  - Serum Bile acids: 310 (0-10)
  - Jaundice chip: Heterozygous for mutation in the ABCB11 gene

Differential

- Infective
- Obstructive
- Genetic
- Endocrine
- Metabolic

- Always obtain GGT in cholestatic children
Diagnosis
- Progressive Familial intrahepatic cholestasis type 2

Progressive Familial Intrahepatic Cholestasis (PFIC)
- Group of genetic disorders involving the hepatocanalicular transporters.
- Characterized by cholestasis, pruritus and jaundice in infancy and childhood.
- There are 3 types: PFIC 1, 2 and 3.
- PFIC1 caused by mutation in the ATP8B1
- PFIC2 caused by mutation in the ABCB11
- PFIC3 caused by mutation in the ABCB4

Progressive Familial Intrahepatic Cholestasis Type 2 (PFIC 2)
- Autosomal recessive disease caused by mutation of the ABCB11 gene on chromosome 2q24. This gene is responsible for the canalicular bile salt export protein (BSEP).
- BSEP is the main exporter of bile acid from hepatocytes to the canaliculi across different concentration gradients.
PFIC 2

- Defective or nonfunctional BSEP can result in reduced bile salt secretion followed by decreased bile flow, leading to accumulation of bile salts in hepatocytes and hepatocellular damage.
- Presents with cholestatic jaundice, pruritus and poor growth.
- Labs: elevation in alkaline phosphatase and serum bile acids, but GGT remains in normal range.

PFIC 2

- PFIC 1 and 2 are very similar with low GGT levels but PFIC 2 is more severe. The evolution and progression is faster than PFIC 1 and could be fatal in the absence of liver transplantation.

Treatment

- Nutritional support
  - Fat soluble vitamin supplement.
  - Supplemental formula with high MCT oils.
- Medical management of pruritus
  - Ursodiol, rifampin or cholestyramine.
- Surgical Intervention
  - Partial biliary diversion can delay the progression to end stage liver disease.
  - Ultimately, Liver transplantation
Prognosis

- Liver transplantation is usually successful, however, recurrences have been reported in literature