Diagnosis and Management of Carbohydrate-Induced Diarrhea
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Learning Objectives

Upon completion of this activity, participants should be better able to:

- Explain the pathophysiology of carbohydrate-induced diarrhea
- Utilize current diagnostic approaches
- Provide individualized and appropriate management to meet specific patient needs
- Educate patients and parents on etiology and physiologic consequences as well as the importance of dietary modifications
Target Audience

- This activity is designed for pediatricians, pediatric and adult gastroenterologists, primary care physicians, physician assistants, nurse practitioners, dietitians, and other health care professionals who are interested in treating children and young adults with carbohydrate-induced diarrhea.
AMA PRA Statement

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Disclosures

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Faculty Disclosures

Looi Ee, MBBS has nothing to disclose.
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General Principles
Common Dietary Carbohydrates: Monosaccharides

- Glucose
- Galactose
- Fructose
Common Dietary Carbohydrates: Disaccharides and Starches

Lactose

Sucrose

Starches
Overview of Carbohydrate Digestion and Absorption

Paulev P-E and Zubieta-Calleja G. New Human Physiology. 2nd ed.
Disaccharidases

- Membrane-bound glycoproteins located within microvilli
- Luminal I active site
- Two main classes:
  - α-glycosidases
    - Sucrase-isomaltase, maltase-glucoamylase, trehalase
  - β-glycosidases
    - Lactase

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Fermentation of Malabsorbed Carbohydrate

- Incompletely digested carbohydrates pass into the colon
- Anaerobic bacteria ferment malabsorbed carbohydrate to:
  - Hydrogen and methane gas
    - Excreted in breath (basis of breath hydrogen testing)
  - Short-chain fatty acids
    - Absorbed, providing energy to colonic epithelial cells and systemically
    - Are osmotically active, contributing to diarrhea
Carbohydrate Malabsorption: Pathogenesis of Symptoms

- Malabsorbed dietary carbohydrate
  - Osmotic load
    - Luminal fluid
  - Fermentable substrate
    - Gas production

Physiologic effects

- Luminal distention
  - Diarrhea
  - Bloating
  - Pain
  - Gas

Barrett JS and Gibson PR. Pract Gastroenterol. 2007;31:51-65.
Carbohydrate Malabsorption: Diagnosis

• Signs and symptoms
  – Diarrhea
  – Abdominal pain
  – Bloating and flatulence
  – Failure to thrive in infants - rare

• History
  – Age at presentation
  – Careful nutritional history

Carbohydrate Maldigestion/Malabsorption Disorders: Typical Age of Onset

1-7 days
- Glucose-galactose malabsorption
- Congenital lactase deficiency
- Sucrase-isomaltase deficiency

3-6 months
- Fructose malabsorption
- Glucoamylase deficiency
- Sucrase-isomaltase deficiency

3-15 years
- Fructose malabsorption
- Adult-onset lactase deficiency

Carbohydrate Malabsorption Disorders: Diagnosis

- Stool testing (nonspecific)
  - pH < 6
  - Positive for reducing substances
    - Glucose, galactose, fructose
    - Not sucrose – but may be detectable from bacterial degradation to glucose and fructose
  - Increased osmotic gap > 100 mOsm/L
    - $290 - 2 ([Na+] + [K+])$
    - 290 is stool osmolality (not often measured directly)

Carbohydrate Malabsorption: Diagnosis

- Rule out inflammatory process¹
  - Occult blood
  - Calprotectin
    - Value is age-dependent²-⁴

Carbohydrate Malabsorption: Diagnosis

- Breath hydrogen tests
  - Predicated on fermentation of malabsorbed carbohydrate by colonic bacteria
  - Malabsorption defined as a specific rise in parts per million (ppm) of $H_2$ over the baseline value
Carbohydrate Malabsorption: Diagnosis

Production of $H_2$ Following Lactose Ingestion

- Lactose ingestion
  - Transit to small intestine
  - Malabsorption
    - Transit to colon
    - Intraluminal bacterial metabolism
      - Fermentation of unabsorbed carbohydrate produces $H_2$
      - Transit to lungs
- Exhaled $H_2$
  - Normal: < 20 ppm
  - Malabsorption: $\geq$ 20 ppm
Carbohydrate Malabsorption: Diagnosis

- Dietary exclusion
  - Often nonspecific because of difficulty in excluding potential offending carbohydrate
  - Often subjective response in the case of developmental lactase deficiency

Carbohydrate Malabsorption: Diagnosis

- Duodenal or jejunal biopsy - histology and disaccharidase activity (document site of biopsy)
  - Enzyme activities most commonly assayed are sucrase, lactase, and maltase
  - Isomaltase is measured using palatinase substrate
  - Gold standard for diagnosis of congenital sucrase-isomaltase deficiency (CSID)
  - Requires proper handling and processing of biopsy samples
Glucose-Galactose Malabsorption
Case Study: Alice

- 1-week-old African American female
- Infant is discharged on the day after delivery and parents immediately note watery diarrhea
Glucose-Galactose Malabsorption

- Distinguishing feature\(^1\)
  - Onset of diarrhea - first week of life
  - Selective malabsorption of glucose/galactose

- Inheritance\(^1\)
  - Autosomal recessive
    - Parents without symptoms
    - Associated with consanguinity

- Molecular basis\(^2,3\)
  - Defect sodium/glucose cotransporter protein
  - Mutation of SGLT1 gene (SLC5a1)

Glucose-Galactose Malabsorption Pathophysiology

Reproduced from Walker’s Pediatric Gastrointestinal Disease: Physiology, Diagnosis, Management, 5th ed., Volume 1 with permission of PMPH-USA, Ltd.

Glucose-Galactose Malabsorption: SGLT1 - Missense Mutations

Glucose-Galactose Malabsorption: Diagnosis

- Present with osmotic diarrhea during first week of life
  - Severe metabolic acidosis
  - Stool pH < 6, positive for reducing substances with increased osmotic gap
- Sibling with similar history
- Occasional glucosuria
- Small bowel biopsies - normal
- Selective malabsorption of glucose and galactose

Glucose-Galactose Malabsorption: Diagnosis

- Meticulous recording of intake and output
- Dietary challenge - tolerance/intolerance not subtle
  - Glucose-containing rehydration solution - diarrhea
  - Carbohydrate-free formula (RCF®) - no diarrhea
  - Carbohydrate-free formula with 6%-8% fructose - no diarrhea
  - Carbohydrate-free formula with 1% glucose - diarrhea
- Glucose breath testing - malabsorption (optional)
- SGLT1 gene sequencing - many mutations (optional)

Glucose-Galactose Malabsorption: Treatment

- Lifetime restriction of glucose and galactose (modified Atkins diet)
- Galactose - monosaccharide primarily in lactose
- Some reports of marginal improvement in glucose tolerance with age
- First 12 months of life, carbohydrate-free formula (RCF®) with addition of fructose required

Glucose-Galactose Malabsorption: Treatment

- When solids are introduced
  - Pureed food
  - Glucose-free
  - Protein/fat and fructose-based

- Many patients stay on carbohydrate-free formula with fructose beyond 12 months, but not required

- Adequate dietary calcium via supplementation must be provided

Glucose-Galactose Malabsorption: Education

• Early input of dietitian
  – May require multiple visits centering around education

• Parents need to become familiar with the amount of glucose/galactose in a broad group of foods

• Managing diet early in life relatively easy, but more difficult later
  – With independence and exploration, controlling glucose intake more difficult

Glucose-Galactose Malabsorption: Education

• Parents should be encouraged to explore level of glucose tolerance

• Make family aware that most liquid medicines are dissolved in glucose-based syrup; use crushed tablets instead

• High fat/protein and fructose-based diet not associated with obesity or other medical problems
Alice: Follow-Up

- Stool pH is 4.5
- Diarrhea induced with dietary challenge of glucose-containing formulas
- Alice is diagnosed with glucose-galactose malabsorption
- Carbohydrate-free formula with fructose for first 12 months
- Extensive education regarding carbohydrates in food and medications
Fructose Malabsorption
Case Study: Manny

- 12-year-old male

Symptoms

- Bloating, pain, and excessive flatulence after eating
- Symptoms manifest or worsen after eating/drinking:
  - Fruits and fruit juices
  - Soft drinks
  - Pizza
Dietary Fructose

- Dietary fructose
  - 64%-95% from sucrose and high-fructose corn syrup (HFCS)
  - Remainder from free fructose and fructans (linear or branched fructose polymers; perhaps 10% of total intake)
  - Pizza, pasta, cakes, and breads are sources of fructans

- Intake in United States
  - Mean 49 g/day
  - Approximately 2/3 from drinks and 1/3 from fruit

Fructose Malabsorption

• Isolated malabsorption is a rare disorder
  – Not due to mutations in protein coding region of GLUT5
  – Etiology unknown – may not be malabsorption, but possibly abnormal handling of fructose reaching the colon

• Absorption capacity increases with age

Fructose Malabsorption

- Malabsorption is directly related to dose
  - Limited ability to transport fructose
  - Malabsorption most commonly seen with excessive juice intake, with diarrheal symptoms associated with the daily consumption of > 15 mL/kg
  - GLUT5 expression is inducible by fructose, therefore slow, incremental increases in fructose may improve absorption

Fructose Malabsorption Versus Intolerance

**Fructose Malabsorption**¹
- Dose-dependent
- Diarrhea

**Hereditary Fructose Intolerance**²
- Deficiency of fructose-1,6-bisphosphate aldolase
- Liver failure
- Vomiting
- Failure to thrive
- Does not cause diarrhea

¹Shepherd SJ and Gibson PR. J Am Diet Assoc. 2006;106:1631-1639.
Fructose Malabsorption: Clinical Presentation

- Presentation related to amount of fructose ingested and individual’s sensitivity to the symptoms of malabsorption
- May be differences among individuals in the ability to absorb and/or ferment fructose in the colon
- Bloating, abdominal pain, and flatulence are characteristic
- Ingestion of fructose alone more likely to induce symptoms than when ingested with glucose

Fructose Malabsorption: Diagnosis by Breath Testing

- No consensus on appropriate dose for children
- Suggested dose 0.5 g/kg (maximum dose 15 g)
  - Positive test > 20 ppm over baseline
  - 30-min sampling interval for 3 hr
- Positive breath test along with subsequent symptoms may be most reliable
- Response to fructose alone may not reflect what happens when fructose is ingested with a meal

Fructose Malabsorption: Treatment

- Eliminate foods in which fructose is sole or main carbohydrate (fruits and honey)
  - Consumption of other foods likely to reduce symptoms
- Not all HFCSs may cause symptoms
  - HFCS-42 (42% fructose, 58% glucose) likely not to cause symptoms, as glucose in excess of fructose facilitates fructose absorption

Dietary Fermentable Substrates

- FODMAPs
  - Fermentable, Oligosaccharides (fructans/galactans), Disaccharides, Monosaccharides, And Polyols
- Ubiquitous
- Poorly absorbed, osmotically active, rapidly fermented
- Elimination from diet relieves symptoms in some adults with irritable bowel syndrome (IBS)
  - Likely related to increased gut sensitivity in IBS rather than greater malabsorption in IBS versus healthy individuals

Dietary Fermentable Substrates

- FODMAPS are hard to avoid
  - Fructo-oligosaccharides (fructans): wheat, rye, onions, garlic, artichokes
  - Galacto-oligosaccharides: legumes
  - Lactose
  - Fructose: honey, apples, pears, watermelon, mango
  - Sorbitol: apples, pears, sugar-free mints/gums, stone fruits - peaches, nectarines, plums, apricots, cherries
  - Mannitol: mushrooms, cauliflower, sugar-free mints/gums

Manny: Follow-Up

- Breath testing with 15 g of fructose resulted in 30 ppm rise of breath hydrogen over baseline
- Breath testing also induced bloating and pain
- Manny is diagnosed with fructose malabsorption
- Exclusion diet implemented to avoid foods that induce symptoms
Lactase Deficiency
Case Study: Miles

- 15-year-old male
- Symptoms
  - Occasional diarrhea
  - Abdominal pain and bloating within 1-2 hours of eating
  - No weight loss or other constitutional symptoms
Lactose

Lactose is present in milk and other dairy products

D-galactose  D-glucose

Lactose Digestion

Lactose is hydrolyzed into glucose and galactose by lactase-phlorizin hydrolase, located on the tips of villi.

Lactase Deficiency

• Primary\textsuperscript{1}
  - Congenital lactase deficiency
  - Developmental
  - Hypolactasia - ethnic variation in severity and prevalence

• Secondary\textsuperscript{2}
  - Mucosal injury; e.g., from celiac disease, infection, allergy, Crohn’s disease
  - Bacterial overgrowth

\textsuperscript{2}Bayless TM and Diehl A. Advanced Therapy in Gastroenterology and Liver Disease. 5th ed. Hamilton, Ontario, Canada: BC Decker Inc; 2005.
Lactase Deficiency: Congenital Lactase Deficiency

- Rare autosomal recessive disorder
- Most reported cases from Finland
- Diarrhea from birth when fed lactose-containing milk (e.g., breastmilk, cow or goat milk formula)
- Absent lactase activity, but histology and other disaccharidase levels normal

Lactase Deficiency: Developmental Changes in Lactase Activity

- Lactase activity increases primarily in last trimester
- Infants born < 32 weeks gestation have reduced lactase activity
- Lactase activity decreases after weaning in all mammals
- Only some humans have persistence of lactase activity after weaning

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Lactase Deficiency: Lactase Persistence

- Lactase persistence is defined by the ability to digest lactose as an adult

- Most of the world’s adult population develop hypolactasia

- Single nucleotide polymorphisms, including C/T-13910 and G/A-22018, in the coding and regulatory parts of the lactase gene have been associated with lactase expression\(^1\)

- The T allele of 13910 is strongly associated with lactase persistence in European, but not sub-Saharan African populations\(^2,3\)

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\(^1\) Troelsen JT. *Biochim Biophys Acta.* 2005;1723:19-32.


# Lactase Deficiency: Ethnic Variation in Lactase Activity

## TABLE 2
Prevalence of Primary Lactase Deficiency in Various Ethnic Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Europeans</td>
<td>2 to 15</td>
</tr>
<tr>
<td>American whites</td>
<td>6 to 22</td>
</tr>
<tr>
<td>Central Europeans</td>
<td>9 to 23</td>
</tr>
<tr>
<td>Indians (Indian subcontinent)</td>
<td></td>
</tr>
<tr>
<td>Northern</td>
<td>20 to 30</td>
</tr>
<tr>
<td>Southern</td>
<td>60 to 70</td>
</tr>
<tr>
<td>Hispanics</td>
<td>50 to 80</td>
</tr>
<tr>
<td>Ashkenazi Jews</td>
<td>60 to 80</td>
</tr>
<tr>
<td>Blacks</td>
<td>60 to 80</td>
</tr>
<tr>
<td>American Indians</td>
<td>80 to 100</td>
</tr>
<tr>
<td>Asians</td>
<td>95 to 100</td>
</tr>
</tbody>
</table>


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Lactase Deficiency: Lactose Intolerance Versus Malabsorption

- Terms are often used interchangeably but are not strictly equivalent.
- Individuals may malabsorb some degree of lactose but may not have symptoms of intolerance.
- Alternatively, people who identify themselves as severely lactose intolerant may mistakenly attribute a variety of abdominal symptoms to lactose intolerance.
- In adults, lactose intake limited to 240 mL of milk a day causes negligible symptoms.

Lactase Deficiency: Lactose Intolerance Versus Malabsorption

- Lactose malabsorption detected by breath H$_2$ test is more common than actual symptoms of lactose intolerance.
- Lactose intolerance frequency varies less among different ethnic/racial groups than does lactose malabsorption.
- Frequency of lactose malabsorption is low in children < 6 years of age.
  - Frequency of lactose malabsorption peaks between 10 and 16 years of age.

Lactose Malabsorption With Intolerance: Clinical Presentation

- Symptoms: bloating, abdominal pain, flatulence, diarrhea, and vomiting (especially in adolescents)¹
- Stools may be watery, frothy, and acidic¹
- There is significant interindividual variability in symptoms
  - Symptoms are usually minimal if intake of milk < 240 mL/day²
  - Not all patients who report these symptoms with lactose ingestion have lactose malabsorption on breath hydrogen testing³

Lactose Malabsorption: Diagnostic Testing

- **Stool testing**¹,³
  - pH < 6 and positive for reducing substances confirm carbohydrate malabsorption

- **Lactose breath hydrogen testing**²,³
  - 1 g/kg lactose (max 25 g) oral load after 6-hour fast
  - ≥ 20 ppm over baseline is positive
  - False positive if rapid intestinal transit
  - False negative if taking antibiotics

- **Duodenal biopsy and disaccharidase analysis**³

Lactase Deficiency: Diagnosis of Congenital Lactase Deficiency

- Duodenal biopsy and disaccharide analysis
  - Gold standard
  - Absent lactase activity
  - Normal histology

Lactose Malabsorption With Intolerance: Treatment

- Reduce dietary lactose intake\(^1\)
- Enzyme replacement\(^2\)
  - Commercially available lactase preparations are \(\beta\)-galactosidases derived from yeast or bacteria
  - They are either ingested prior to eating lactose-containing foods or added to lactose-containing foods to hydrolyze lactose prior to ingestion
  - Lactose hydrolysis is often incomplete with these preparations, and symptom relief can be variable

Lactose Malabsorption With Intolerance: Treatment

- Maintain adequate calcium intake
- Recommended daily intake
  - Infants < 1 years: 260 mg
  - Age 1-3 years: 700 mg
  - Age 4-8 years: 1000 mg
  - Age 9-18 years: 1300 mg

Miles: Follow-Up

- Miles was diagnosed with hypolactasia
- Over-the-counter lactase supplement recommended when dietary lactose intake leads to intolerance
- Educated on importance of calcium supplementation if milk avoidance is required
Congenital Sucrase-Isomaltase Deficiency
Case Study: Sarah

• 8-month-old Caucasian female

• History
  - Breastfed
  - 2-3 months of diarrhea and colicky discomfort
  - Faltered weight gain over same period
  - No vomiting and normal appetite
  - Abdominal distention after feeding
Sucrose

- Sucrose is present in fruits and table sugar

\[ \text{Sucrose} \]

\[ \text{Glucose} \]

\[ \text{Fructose} \]

Sucrose Digestion

• Sucrose is hydrolyzed to glucose and fructose by sucrase-isomaltase, which is located along the length of villi\(^1\)

Image reproduced with permission from The Human Protein Atlas (www.proteinatlas.org).


Congenital Sucrase-Isomaltase Deficiency

- CSID is a rare autosomal recessive disorder in which ingestion of sucrose and oligosaccharides leads to malabsorptive diarrhea.

- Found in 5% in the native population of Greenland, Alaska, and Canada and 0.02% of people of European descent.

Congenital Sucrase-Isomaltase Deficiency

- CSID is caused by mutations in the sucrase-isomaltase gene\textsuperscript{1-3}
- Several recognized phenotypes result in absence of sucrase, while isomaltase activity varies\textsuperscript{1-3}
- Unclear if milder forms exist\textsuperscript{4}


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Congenital Sucrase-Isomaltase Deficiency

- Reported sucrase-isomaltase mutations disrupt enzyme processing at multiple levels
  - Intracellular processing (glycosylation and folding)
  - Intracellular transport
  - Targeting and insertion of enzyme into brush border membrane

CSID: Clinical Presentation

- Typical presentation is in infancy, after weaning, with introduction of sucrose-containing foods or drinks (e.g., fruits, juices, and grains)
  - May present earlier if dextrins and isomaltose are present in the diet
- Symptoms include abdominal cramping, bloating, excessive gas, fermentative diarrhea, failure to thrive, and malnutrition

CSID: Clinical Presentation

- Most affected children are able to tolerate increased amounts of sucrose and maltose as they grow older.
- A number of patients are not diagnosed as children or adults and misdiagnosed as having IBS.

CSID: Diagnosis

- Stool testing\textsuperscript{1,2}
  - pH < 6 suggestive of carbohydrate malabsorption
- Sucrose breath hydrogen testing\textsuperscript{2,3}
  - 1-2 g/kg sucrose (≤ 50 g) oral load after 6-hour fast
  - ≥ 10 ppm is positive
  - False positive if rapid intestinal transit
  - False negative if taking antibiotics
- C\textsuperscript{13}-sucrose breath test\textsuperscript{4}
  - Preliminary data suggest utility

\textsuperscript{2}Ford RP and Barnes GL. *Arch Dis Child*. 1983;58:595-597.
CSID: Diagnosis

- Duodenal biopsy and disaccharidase analysis\(^1\)
  - Gold standard
  - Absent sucrase activity and marked reduction of isomaltase activity
  - Normal histology
- Unclear if milder forms exist\(^2\)

CSID: Dietary Treatment

- Adherence to a sucrose-free diet
- Reduction in starch-containing foods
  - Beetroot, peas, soybean flour, onions
  - Cereals, breads, pastas, and potatoes in the first years of life
  - Avoid glucose polymer formulas and medications with sucrose
- Tolerance improves with age

CSID: Treatment

- Lyophilized baker’s yeast
  - Has sucrase activity but low isomaltase and maltase activity
  - Effective
  - Not very palatable

CSID: Treatment

• Sacrosidase
  – Has sucrase activity but no isomaltase and maltase activity
  – Approved by US Food and Drug Administration
  – Oral liquid solution used with each meal as replacement
  – Palatable
  – Expensive

Sarah: Follow-Up

- Breath hydrogen increased by 40 ppm after weight-appropriate sucrose load
- Biopsy results:
  - Complete absence of sucrase activity
  - Reduction in isomaltase and maltase activity
Sarah: Follow-Up

- Sarah diagnosed as sucrase-isomaltase-deficient
- Restrictive diet implemented
  - Avoid sucrose- and starch-containing foods, such as cereals, peas, and sucrose-containing medications
Disaccharidase Deficiencies Related to Specific Diseases

Generalized Malabsorption
Case Study: Beverly

- 4-year-old Indian American female
- Symptoms
  - Chronic diarrhea for 5 weeks
  - Abdominal bloating and pain
Causes of Disaccharidase Deficiencies

- Brush border defect (primary deficiency: lactase deficiency, sucrase-isomaltase deficiency)
- Disordered motility, leading to small bowel bacterial overgrowth (e.g., primary dysmotility, stricture, short bowel syndrome)
- Mucosal disease (e.g., celiac disease, inflammatory bowel disease, food allergy, infection)

Dysmotility

Proximal bowel
1. Dilated bowel/stasis
2. Bacterial overgrowth
3. Secondary inflammation

Distal bowel
Normal bowel lumen diameter
Stricture

Inflammation leads to disaccharidase loss on enterocyte surface

Kastin DA and Buchman AL. Curr Opin Gastroenterol. 2002;18:221-228.
Dysmotility

Intestinal stricture (red arrow) with dilated proximal small bowel (blue arrow) in patient with short bowel syndrome.
Dysmotility

Ileal stricture from Crohn’s disease
Mucosal Disease

- Any inflammation of the small intestine epithelium can potentially lead to a secondary loss of disaccharidases
  - Food allergy
  - Inflammatory bowel disease (Crohn’s disease)
  - Celiac disease
  - Giardiasis
Mucosal Disease: Allergic

Eosinophilic infiltration of intestine due to cow’s milk protein allergy in an infant


Mucosal Disease: Crohn’s Disease

Crohn’s disease with small intestinal inflammation

May present in a manner similar to IBS
Mucosal Disease: Crohn’s Disease

Characteristic granuloma

- Inflammation diminishes disaccharidase activity of small bowel

Mucosal Disease: Celiac Disease - History

- Symptoms described by Samuel Gee in 1888\(^1\)
- Dicke and van de Kamer: identified alcohol soluble fraction of wheat gluten (gliadin) and similar residues in related barley, rye, and oats as being the damaging agents\(^2\)

\(^{1}\)Gee S.J. St Bartholomew’s Hospital Report. 1888;24:17-20.
Mucosal Disease: Celiac Disease

- Biopsy is key to diagnosis, as diagnosis cannot be solely by visual examination.
- Secondary disaccharidase deficiency due to inflammation/loss of enterocytes.

Duodenal scalloping

Mucosal Disease: Celiac Disease

- Lymphocytic infiltrate
- Areas of shortened villi

Evaluation of Dysmotility and Mucosal Disease: Potential Pertinent Tests

- **Blood tests**
  - Complete blood count, erythrocyte sedimentation rate, C-reactive protein
  - Tissue transglutaminase and immunoglobulin A (IgA)
  - T4/thyroid-stimulating hormone
- **Stool tests**
  - Culture, *C. difficile* toxin
  - Calprotectin
  - Reducing substances, pH
- **Urine culture**
- **Breath hydrogen testing**

- **Radiographic tests**
  - Abdominal x-ray
  - Abdominal ultrasound
  - Magnetic resonance enterography
  - Abdominal computed tomography
  - Upper gastrointestinal (GI) ± small bowel follow-through

ENDOSCOPY WITH BIOPSY?

Celiac Disease: Treatment

- Removal of gluten is essential
- Lifelong adherence to a gluten-free diet currently recommended
Celiac Disease: Treatment

- **Foods to avoid**
  - Grains and flours
    - All flours containing wheat, rye, barley, and oats
  - Breads
    - All breads containing wheat, rye, barley, and oats
  - Cereals
    - All cereals containing wheat, rye, barley, and oats
  - Noodles and pasta
    - Any type made of wheat, rye, barley, and oats
  - Alcohol derived from grain (adolescent/adult issue)

Celiac Disease: Treatment

- Foods to allow
  - Grains and flours
    - Almond, arrowroot starch, artichoke, corn starch, cornmeal, maize, legumes, potato starch, rice bran, rice flours, sesame, soybean flours, sunflower, tapioca starch
  - Breads
    - Only those breads with allowed gluten-free flours (see above)
  - Cereal
    - Cereal from corn, rice, or hominy
  - Noodles and pasta
    - Gluten-free corn, rice, or bean pasta
Beverly: Follow-Up

- Serum tissue transglutaminase IgA antibody positive
- Duodenal scalloping visible on upper GI endoscopy
- Characteristic findings on duodenal biopsy
- Beverly is diagnosed with celiac disease
- Started on gluten-free diet
  - No foods containing wheat, rye, or barley

Functional Diarrhea in Toddlers

Toddler’s Diarrhea/Chronic Nonspecific Diarrhea of Infancy
Case Study: Owen

- 2-year-old Caucasian male
- Symptoms
  - Intermittent diarrhea over last 3 months
    - No effect on weight gain or activity level
    - Stools shortly after eating
    - Mushy to watery
  - Drinks 5-6 cups of juice daily
  - Family friend recommended low fat diet, which made diarrhea worse
Functional Diarrhea in Toddlers: Overview

- Term first coined in 1956 by Cohlan
- Described by Davidson and Waserman in a 1966 series of 186 children
- Little research on the disorder in the last 20 years

Functional Diarrhea in Toddlers: Etiology

- Etiology not evident in all cases
- Dietary nutritional imbalance often responsible
  - Increased intake of poorly absorbed sugars, often from fruit juice
  - Reduced intake of fat and fiber

Functional Diarrhea in Toddlers: Presentation

- 12% begin between birth and 5 months of age
- > 75% begin between 6 and 20 months of age
- 88% resolve by 39 months of age
  - 98% by 48 months of age
- First stool of the day often more formed than subsequent ones

Functional Diarrhea in Toddlers: Presentation

• Daily painless passage of ≥ 3 large, unformed stools
  – May contain food and mucus
  – Often foul-smelling
• Symptoms last > 4 weeks
• Passage of stool during waking hours
• No failure to thrive if caloric intake adequate

Functional Diarrhea in Toddlers: Diagnosis

- Clinical diagnosis
- Requires very detailed history
- Exclude possibility of
  - Enteric infections (including Giardia)
  - Antibiotics
  - Laxatives
  - Celiac disease
  - Disaccharidase deficiency

Functional Diarrhea in Toddlers: Diagnosis

- Dietary history critical
- Overfeeding
  - Excessive fluid intake (> 190 mL·kg⁻¹·d⁻¹)
- Excessive fruit juice intake
  - Fructose, sorbitol
- Low fat intake
  - ≤ 27% of calories
- Food allergy

Functional Diarrhea in Toddlers: Treatment

• 80% improved on a normal diet for age
  – Appropriate fat, carbohydrate, and protein ratio
  – Limiting juice and excessive fluid intake

• Psyllium can be used as a bulking agent (1 tbsp twice daily)

Functional Diarrhea in Toddlers: Treatment

- Ask parents to keep diet and stool diary for 1 week
  - Diarrhea has been reported to resolve during the observation period
  - Use of pediatric stool chart objectifies report

Functional Diarrhea in Toddlers: Patient Education

- Balanced diet for age cornerstone of treatment
- Consultation with a dietitian may be helpful
- Reassurance that there are no known long-term consequences of the disorder
- Discussion of the utility of keeping a diet and stool diary
Owen: Follow-Up

- Growth parameters normal
- Examination of stool showed no pathogens or blood
- Owen diagnosed with functional diarrhea
- Juice intake restricted and fat and fiber dietary content increased (appropriate diet for age); stool consistency improved and normal growth continued
- Parents advised to keep daily diet/defecation diary for 1 week
Summary

• Carbohydrates are a critical dietary component, especially in growing children

• Carbohydrate malabsorption creates a barrier to development
  – Consideration of the diagnosis can quickly establish cause of symptoms
  – Appropriate treatment reduces symptoms and ensures patients receive essential nutrients

• Education on appropriate adjustment to carbohydrate intake empowers parents to regain control of their child’s nutrition