The prevalence of CD in Children in US is estimated to be 1 in 100.

Vested Interest

Nothing to Declare

Acknowledgements

- Special thanks to CHB Celiac Program team members: Alan Leichtner MD, Dascha Weir MD, Karen Warmen RD and CDHNF Celiac Initiative for the use of various slides.
Objectives

• Review the history of celiac disease as it relates to children.
• Describe the pathophysiology and clinical manifestations of pediatric CD.
• Explain how CD is diagnosed.
• Describe treatment of CD
• Describe management of CD in School Settings.

Celiac Disease

• Disease of the small intestine
• Immune response to ingested gluten
• Results in characteristic damage to villi
• Leading to malabsorption

• Also known as gluten intolerance, gluten-sensitive enteropathy, celiac sprue and nontropical sprue

Gluten and Celiac Disease

Dicke 1955
Grains with Gluten

The Grass Family - (GRAMINEAE)

Subfamily: Festucoideae
Tribe: Zizaneae Oryzeae Hordeae Aveneae Festuceaea Chlorideae

- wild rice
- rice
- oat
- finger millet (ragi)
- teff

The Classical Child with Celiac Disease

Onset between 6 and 24 months of:
- Chronic diarrhea
- Abdominal distension
- Poor appetite
- Failure to thrive or weight loss
- Abdominal pain
- Vomiting
- Irritability

Typical Celiac Disease

- Abdominal Distension
- Buttock Wasting
Celiac Disease in London in 1938

Celiac Disease in Boston in 2010

Our Understanding Changed with the Discovery of Blood Tests

Availability of sensitive serological markers

<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>

The Celiac Iceberg

- Symptomatic Celiac Disease
- Silent Celiac Disease
- Latent Celiac Disease
- Normal small intestine
- Damaged small intestine

Genetic susceptibility: Positive blood tests
What Children are Now being Diagnosed with Celiac Disease?

- More girls than boys
  CH 2001-5 database: 128/201 (62%) female

- Older age at diagnosis
  - Now being diagnosed at all ages
  - Average age at diagnosis increasing
  CH 2001-5 database: average age 9.3 years

- Earlier diagnosis – rare to see very sick children

### CH Database 2001-5 (n=207): Presenting Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain/cramps</td>
<td>89 (43%)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>24 (12%)</td>
</tr>
<tr>
<td>Diarrhea/loose stools</td>
<td>49 (24%)</td>
</tr>
<tr>
<td>Constipation/hard stools</td>
<td>48 (23%)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>40 (19%)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>20 (10%)</td>
</tr>
<tr>
<td>Increased fatigue</td>
<td>27 (13%)</td>
</tr>
</tbody>
</table>
| Weight loss/poor weight gain     | 72 (35%)         | Children under 3 years generally have gastrointestinal symptoms
| Short stature/poor growth        | 47 (23%)         |
| Frequent mouth ulcers            | 4 (2%)           |
| Joint symptoms                   | 7 (3%)           |
| NO SYMPTOMS                      | 28 (14%)         |
Non-gastrointestinal Manifestations

- Iron deficiency
- Osteopenia/Osteoporosis
- Dental enamel hypoplasia
- Dermatitis Herpetiformis
- Hepatitis
- Arthritis
- Epilepsy with occipital calcifications; Migraines, seizures, neuropathy, ataxia
- Infertility
- Dental enamel hypoplasia of permanent teeth
- Short Stature
- Delayed Puberty
- Behavioral problems

Most common age of presentation: older child to adult

Associated Diseases

- Patients with autoimmune diseases:
  - Type 1 diabetes mellitus (5-8% develop CD)
    CHB database 14% of patients with T1DM
  - Autoimmune thyroiditis
- Patients with genetic disorders:
  - Down syndrome (5% develop CD)
  - Turner syndrome
  - Williams syndrome

Increasing Diagnosis at CHB

- Bar chart showing increasing diagnosis from 2003 to 2009
Factors Contributing to Disease

Genetics
- HLA
- Other

Environment
- Gluten
- Infant feeding
- Infection
- Other

Celiac Disease

Pathophysiology

As best we know

Green, Cellier NEJM 2007
Genetic Basis: Overview

- ~5% of children with a parent with CD also are affected
- 10% of patients have an affected 1st relative
- Concordance in identical twins is 70 - 75%
- Strong HLA association
  - 95% of patients HLA-DQ2 – also found in 20-30% of normals
  - Most of the remainder are HLA-DQ8
- Concordance in HLA-identical siblings 30-40%, suggesting other genes involved

Environmental Factors

- Gluten
  - Possible triggering factor
  - ? Infection - Rotavirus
  - ? Toxin

Effect of Early Exposure to Gluten

- **Sweden** - Andersen, et al.
  - Era: 1950-1952
    - Gluten Intro: 9 m
    - Onset: 43 m
  - Era: 1968-1969
    - Gluten Intro: 3 m
    - Onset: 9 m
- **London** – 1975 recommendation to delay introduction of gluten until 4-6 m led to apparent decrease in incidence – probably just delay in onset
- Introduction of gluten while breast-feeding may be protective

Earlier, Larger quantity ➔ Earlier, More classical
Effect of Early Exposure to Gluten

- 1560 children with genes that increase risk for celiac disease or type 1 DM followed from birth
- Celiac disease autoimmunity defined as:
  - TTG + on 2 or more visits
  - TTG + and biopsy c/w celiac disease
- Risk based on time of gluten introduction:
  - ≤ 3 months 5x
  - 4-6 months 1x
  - > 7 months 1.8x

Major Complications of Celiac Disease

Rare in Children
- Nutritional deficiencies – calcium, iron, folate, other vitamins – leading to iron deficiency anemia, low bone density
- Refractory celiac disease
- Autoimmune disease
- Cancer

Do have decreased response to Hepatitis B vaccine

Diagnosis
Three Elements of Diagnosis

- Clinical suspicion – typical or atypical symptoms or high risk
- Blood tests
- Endoscopy

In children, Biopsy showing changes consistent with celiac disease AND Either positive blood test or response to GFD

Blood Tests

- Antigliadin antibodies (AGA)
- Antiendomysial antibodies (EMA)
- Anti tissue transglutaminase antibodies (TTG)
- Total IgA
- HLA typing

Serologic 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>

New deamidated Gliadin tests improved sensitivity and specificity
Serological Tests

- Generally recommend tissue TTG IgA level and Total IgA as best first test
- AGA not routinely recommended but may be helpful in children under age two years and children deficient in IgA
- HLA only helpful in certain situations: 1° relatives and associated diseases

HLA DQ2-DQ8

- DQ2/DQ2 have 30x risk of developing CD
- DQ2/other and DQ8/DQ8 have 10x risk
- DQ8/other have 2x risk
- DQ2/DQ8 have 14x risk

Small Bowel Biopsy

- Gold standard
- Performed by flexible endoscopy – may require general anesthesia in young or very anxious children
- May see gross abnormalities, but biopsy results most important
Endoscopic Findings

- Nodularity
- Mosaic Pattern
- Scalloping
- Normal Appearing

High Resolution Endoscopy

Degrees of Damage

- Children usually have villous atrophy
- Normal
- Partial atrophy 3a
- Subtotal atrophy 3b
- Total atrophy 3c

Studies of Biopsies at CHB

- Changes are patchy – may be missed if only 1 or 2 biopsies done – recommend 6
- 10% of children only have changes in the first part of duodenum or bulb

Can We Avoid Biopsies in Children?

Significance of High Titer TTG

<table>
<thead>
<tr>
<th>Biopsy</th>
<th>1-19 U</th>
<th>20-100 U</th>
<th>&gt;100 U</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>3</td>
<td>7</td>
<td>48</td>
<td>58</td>
</tr>
<tr>
<td>Negative</td>
<td>35</td>
<td>9</td>
<td>1</td>
<td>45</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>16</td>
<td>49</td>
<td>103</td>
</tr>
</tbody>
</table>

Current Study at Children’s Hospital

- 180 children undergoing endoscopy for suspected celiac disease
- Blood drawn when i.v. placed for procedure
- Multiple celiac blood tests performed to determine whether a combination of results might reliably predict celiac disease

Treatment

GOOD NEWS!

- Gluten free diet works!
- In children it reverses all intestinal damage
- Reduces risk of complications s.a. cancer to that of general population
Bad News!

Treatment isn't easy

Naturally Gluten Free

Less processing means fewer opportunity for gluten to slip in unnoticed.

Another White was poisoned by an apple, but saved a giant in his house, and look what happened to Alice when she ate the mushroom. And you wonder why I won't eat fruit and vegetables?
Treatment

• Gluten-free diet
  – Difficult – requires education of family
  – Expensive
  – Restricts wheat, rye, barley
  – Oats generally not toxic, but frequently contaminated
  – For life

Other Items to Consider

• Prescription or OTC Medications
• Lipstick/Gloss/Balms
• Mouthwash/Toothpaste
• Soap/shampoo
• Play Dough, art supplies
• Stamp and Envelope Glues
• Vitamin, Herbal, and Mineral preparations

Food Labeling

Food Allergen Labeling and Consumer Protection Act of 2004
(Title II of Public Law 108-282)
• Top eight allergenic foods – wheat
• Still must look for barley, rye, oats
• Does not cover inadvertent contamination
• FDA must define what is “gluten-free”
  – Less than 20 ppm = 20mg/kg product
GF Label Reading PDQ

- **Avoid:** Wheat, Barley, Rye, Malt, Malt Flavoring, Malt Extract, Beer and Ale, Brewers Yeast
- **Safe:** Caramel Flavoring made in US, Monosodium Glutamate, Vinegar(not malt), Distilled Alcohol, Maltodextrin, Dextrin
- **Check:** Brown Rice Syrup, Oats

Gluten Free????

- The Chicago Tribune: Wellshire Kids brand "gluten-free" products sold exclusively at Whole Foods contained between 116-2,200 ppm of gluten.
- The Boston Globe: Anger sizzles over seasoning used in McDonald's fries.
How Much Gluten is Safe??

- Multicenter, double-blind, placebo-controlled, randomized trial in 49 adults with biopsy-proven CD who were being treated with a gluten-free diet (GFD) ≥ 2 y.
- Daily gluten intake was < 5 mg per day
- Patients were assigned to ingest daily for 90 d a capsule containing 0, 10, or 50 mg gluten.
- Clinical, serologic, an histologic evaluations of the small intestine were performed at baseline and after the gluten microchallenge


Results

- 1 patient in the 10 mg group had ↑ clinical symptoms
- No increase in Celiac Antibody Titers
- No biopsy changes in 0mg or 10mg gluten groups
- 10 of 13 participants who had been receiving 50 mg capsules of added gluten had a worsening of their intestinal biopsy

Concluded: The ingestion of contaminating gluten should be kept lower than 50 mg/d in the treatment of CD

How Much Gluten is Safe

1/100 = 50 mg of Gluten

eating as little as 50 mg of gluten in the diet remains harmful.
< 200 ppm Gluten
8.3 servings = 50 mg gluten

< 20 ppm Gluten
83 servings = 50 mg gluten

Preventing Cross Contamination
• Separate Toaster
• Separate Spreads/Condiments
• Separate Colander
• Separate Cutting Boards
• Separate Bread Machine
• Meal Preparation

Recommended Follow-up
• See at 1-3 months to assess compliance and response to diet
• Repeat serology at 6 months
• Yearly visits to assess compliance, check serology, and screen for complications, including other autoimmune diseases
• Screen 1° relatives
Support Groups!

Children’s Family Education Series – Celiac Disease

Websites

- www.APGNN.org
- www.childrenshospital.org/celiac
- www.CDHNF.org
- www.NASPGHAN.org
- www.gastrokids.org
Five Things Teachers Need to Know

1. Student is on a restricted diet.
2. Let parent know in advance if there will be a birthday party or other snack time in the classroom, so they may send GF treat from home. (or have a GF treat stash on hand)
3. Keep student’s life as normal as possible.
4. Keep the lines of communication open.
5. Check with parent about what to say to classmates

Recommended Books for Classmates

- Eating Gluten-Free With Emily: A Story For Children With Celiac Disease
  Bonnie J. Kruszka, Richard S. Cihlar  early childhood, elementary
- The GF Kid: A Celiac Disease Survival Guide
  Melissa London, Eric Glickman  upper elementary, secondary
- The Complete Idiot's Guide to Gluten-Free Eating
  Eve Adamson, MS, RD, Tricia Thompson  upper secondary

» Available at Amazon.com
**Tips for Parents**

- Meet with teacher and school nurse asap
- Discuss school’s policy re: food in class
- Ask permission to send letter to parents of classmates
- Make list of gluten free snacks/foods
- Meet with food service director/cafeteria staff
- Ask permission to tour of cafeteria kitchen

**How does CD affect the student and classroom?**

- **Attendance:** may be an issue initially.
- **Cafeteria:** definite challenges involved in the cafeteria.
- **Off-site Events/Field Trips:** chaperones must be informed. (substitutes too!)
- **Restroom Usage:** special restroom privileges may be needed.

**Adherence to Diet**

- Difficult in older children and teens
  - Important for them to fit in and be like their peers
  - May have minimal symptoms with inadvertent gluten ingestion
  - Monitors must be informed (substitutes too!)
Early childhood & elementary settings

• Art
• Cooking and Baking
• Health Lessons
• Sensory Tables
• Snacks
• Stickers and Envelopes

Upper elementary & secondary settings

• Drama
• Visual Arts
• Health Education
• Physical Education
• Science
• Family and Consumer Sciences

Big Adjustment

“After awhile I got used to my disease. I thought of it making me special. And if you have a disease like mine, think about it in a special way.” from a second grader
**Involve the School Counselor**

- **Grief**: typical stages of grief; may observe signs of sadness, denial, shock, confusion, anger, irritability, loss of appetite, physical complaints, loss of concentration, depression, or withdrawal from friends.
- **Denial**: Even after a student has "adjusted" to having celiac disease, he or she may occasionally exhibit denial by taking risks.

**Educate the Cafeteria Staff**

- Always offer gluten free foods
- Be aware of hidden gluten in processed foods
- Clean utensils, gloves, work surfaces, etc. are imperative (Cross-contamination)
- Distribute menus in advance

90% children with CD brown bag lunch

**504 plan: yes or no?**

- Rehabilitation Act 1973 applies to all institutions receiving federal assistance
- Not designed specifically for celiac students
- Need to evaluate pros and cons
- In most cases, a student Health Care Plan is adequate
Here's the Bottom Line

Take-Home Points

• CD is being increasingly diagnosed in children
• CD should not interfere with student’s academic or social experience
• Keeping the student GF can present challenges but creative solutions abound
• Accidental exposure to gluten does not cause a life-threatening reaction

PUBLICATIONS

Thank You!