Celiac Disease
Who to Test & How to Test

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Disclosure Statement

I have the following financial relationship to disclose:

Astra-Zeneca - Consultant

No products or services produced by this company is relevant to my presentation.

Celiac Disease

• Case # 1 - 10 year old girl
  • Excess gas x 6-7 weeks
  • Frequent burping and malodorous flatulence
  • Preceding viral gastroenteritis - resolved
  • Abdominal cramping +/- improved off dairy
  • Examination
    • WDWN
    • Abdominal distension - tympanic ++
    • KUB - gas +++ throughout
    • Diagnosis – lactose intolerance

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Celiac Disease

- Case #2 – 7 year old boy
  - Parental concern for short stature
  - Grew well until 4 years (25-50% tile)
  - Progressive fall in height to below 5% tile
  - Weight maintained on 25% tile
  - Initial endocrine work up negative
  - Examination
    - Short but healthy (wt 25% and height < 5%)
  - Provisional diagnosis = “constitutional”

Celiac Disease

- Case #3 – 19 month old girl
  - Progressive misery since a year of age
  - Per mother – “clingy, irritable, low energy”
  - Poor appetite and weight gain
  - No vomiting or diarrhea
  - Problems began with starting regular milk
  - Examination
    - Fretful, thin appearing – height 25% tile, weight <5% tile
    - Poor muscle bulk, abdominal distension
  - Provisional diagnosis CMPI

Celiac Disease

- Celiac disease factoids!
  - Affects ~ 1% of the USA population
  - 2-3 million cases in the USA
  - 5-20 affected children in average practice
  - 90% undiagnosed
Celiac Disease

The 3 Steps to Diagnosis

Clinical suspicion

Screening Test

Confirmation

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Celiac Disease

Aims

- Identify children in need of testing
  - Symptomatic
  - Asymptomatic – but at risk
- Choose the best test for screening
  - Limitations of testing
  - Pitfalls in testing
- Confirmation of the diagnosis

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Celiac Disease

Manifestations

Early Gastrointestinal

Late Gastrointestinal

Non Gastrointestinal

Associated conditions

Asymptomatic

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Celiac Disease

- Symptomatic group
  - Gastrointestinal – early onset
  - Age – 6 mths – 2 yrs
  - Abdominal distension
  - Anorexia
  - Weight loss
  - Diarrhea
  - Steatorrhea

- Gastrointestinal – late onset
  - Age – childhood to adult
  - Transaminitis
  - Anorexia
  - Weight loss
  - Nausea
  - Vomiting
  - Diarrhea
  - Steatorrhea
  - Pain
  - Bloating
  - Flatulence
  - Abdominal distension
  - Anorexia
  - Weight loss
  - Diarrhea
  - Steatorrhea

- Non-Gastrointestinal
  - Skin
  - Hematologic
  - Short stature
  - Mucous membranes
  - Reproductive
  - Dental
  - CNS
  - Musculoskeletal

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Celiac Disease
At Risk Groups
Autoimmune  Non-autoimmune
Type 1 DM  Relatives
Thyroiditis  Down syndrome
A.I. Hepatitis  Turner syndrome
Sjogren’s  Williams syndrome
Arthritis  IgA deficiency

Celiac Disease
Who to test?

Celiac Disease
Screening recommendations
Symptomatic – consensus!
• Typical GI symptoms – first line test
• “Atypical” – second line test
Asymptomatic – schizophrenia!

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Celiac Disease
Screening - asymptomatic

- Recommendations
  - NH Consensus Development Program
  - NASPGHAN
  - American Gastroenterological Association

- Some
- All
- None

Celiac Disease
Screening

- Asymptomatic screening problems
  - Natural history unknown
  - Benefits uncertain
  - Compliance unlikely
  - QOL issues

- Concerns
  - Mortality – malignancies
  - Morbidity – osteoporosis, autoimmune diseases, growth stunting

Celiac Disease
Screening

- Static vs. dynamic disorder?

  - Fate of Five Celiac Disease-Associated Antibodies During Normal Diet in Genetically At-Risk Children Observed from Birth in a Natural History Study

- Malignancy myth?

  - Malignancies in cases with screening-identified evidence of celiac disease: a long-term population-based cohort study

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Celiac Disease

- How to test?
  Consensus!

- Commercial serological tests.
  - Antigliadin - IgG & IgA
  - Endomysial - IgA
  - Transglutaminase – IgA & (IgG)
  - Deamidated gliadin – IgA & IgG

Celiac Disease

Serological tests
- AGA (IgG & IgA)
  - Advantages - cheap & easy to perform
  - Disadvantage - variable sens/spec.
- EMA (IgA)
  - Advantages - high sens/spec.
  - Disadvantages - expensive, time consuming, operator dependent, no use in IgA deficiency

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Celiac Disease

Serological tests
- TTG (IgA)
  - Human recombinant protein
  - Advantages – cheaper than EMA, easier to perform, non operator dependent
  - Disadvantages – ? less specific than EMA, no use in IgA deficiency

Celiac Disease

Serological test comparison

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity %</th>
<th>Specificity %</th>
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</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>
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</table>


Celiac Disease

The new kid on the block?

Deamidated Gliadin antibodies

Usefulness of Antibodies to Deamidated Gliadin Peptides in Celiac Disease Diagnosis and Follow-up

Umberto Soli, Alessandro Gramito, Erica Fiumara, et al.

Dig Dis Sci 2008;53:1582-1588

<table>
<thead>
<tr>
<th></th>
<th>IgA</th>
<th>IgG</th>
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</thead>
<tbody>
<tr>
<td>Celiac subjects – 128</td>
<td>83.6%</td>
<td>84.4%</td>
</tr>
<tr>
<td>Controls – 134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>90.3%</td>
<td>98.5%</td>
</tr>
</tbody>
</table>

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Comparative Usefulness of Deamidated Gliadin Antibodies in the Diagnosis of Celiac Disease

Shadi Rashtak, Michael W. Ettore, Henry A. Homberger, Joseph A Murray

<table>
<thead>
<tr>
<th></th>
<th>Celiac subjects – 92</th>
<th>Controls – 124</th>
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<tbody>
<tr>
<td></td>
<td>IgA</td>
<td>IgG</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>74%</td>
<td>65%</td>
</tr>
<tr>
<td>Specificity</td>
<td>95%</td>
<td>98%</td>
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</table>

Celiac Disease

- The new kid on the block?
- Deamidated Gliadin antibodies

Recommendations
- Transglutaminase
- Serum IgA?
- Single test vs. panel?
- Serial testing – TTG → EMA?

Pitfalls in serological testing!
- Research setting vs. the real world
- Diabetics?
- Young children (< 2 years)

Antigliadin and antiendomysium antibody determination for celiac disease.
Arch Dis Child 1993;68:945-7

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Celiac Disease

- Pitfalls in serological testing!
  - Young children (< 2 years)

<table>
<thead>
<tr>
<th>Test</th>
<th>Under 18 mth</th>
<th>Over 18 mth</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGA-IgA</td>
<td>97%</td>
<td>94%</td>
</tr>
<tr>
<td>TG-IgA &amp; EMA-IgA</td>
<td>83%</td>
<td>99%</td>
</tr>
</tbody>
</table>

Subjects: 428 (7.5 mth to 14 yr) Controls: 216 (8.5 mth to 14.6 yr)

Celiac Disease

- Pitfalls in serological testing!
  - Consider:
    - Transglutaminase
    - Serum IgA
    - Antigliadin
    - Deamidated gliadin ???

Celiac Disease

- Definitive diagnosis
  - Always confirm before treating
  - Confirmation mandates GFD for life
    - Following a strict GFD is not easy
    - Diet has potential QOL implications
  - Failure to treat has potential long term adverse health consequences
    - Increased morbidity and mortality

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Celiac Disease

- Definitive diagnosis
  - Revised ESPGHAN criteria
    - Characteristic histology
    - Symptom resolution
    - +/- serological tests
  - Biopsy
    - Serology positive
    - Serology negative

Celiac Disease

- Biopsy technique
  - Capsule vs. Endoscope
  - Jejunum vs. Duodenal


Celiac Disease

- Biopsies
  - Endoscopic appearance
  - Magnification
    - Normal
    - Scalloping
    - Nodularity
    - Normal
    - Villous blunting
Celiac Disease

- Biopsy recommendations

- Number - minimum of 4
- Site - D2 and beyond
- duodenal bulb?


Celiac Disease

- Normal 0
- Infiltrative 1
- Hyperplastic 2

- Partial atrophy 3a
- Subtotal atrophy 3b
- Total atrophy 3c
Celiac Disease

- Diagnostic confidence
  - Marsh grade 3 - strong
  - Marsh grade 2 - moderate/weak (need additional evidence)
  - Marsh grade 1 - highly suspect (need alternative strategies)


Celiac Disease

- Conclusions
  - Diagnosis depends on:
    - High index of clinical suspicion
    - Use of appropriate serological tests
    - Multiple intestinal biopsies
    - Therapeutic response

Celiac Disease

- Suggestions for change
  - Consider celiac disease more often
  - Use “cost effective” screening protocol
  - A final plea!!!

Always confirm before you treat!
Celiac Disease

- **Resources**
  - [www.cdhnf.org or (www.celiachealth.org)]
  - Guidelines for evaluation and management
  - Patient information brochures
  - Start up diet
  - Gluten free drug list

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