Follow-up Management of Patients with Celiac Disease: Resource for Health Professionals

Jocelyn Silvester, MD PhD FRCPC
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Disclosures

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– Canadian Institutes of Health Research
– Canadian Association for Gastroenterology
– Children’s Hospital Research Institute of Manitoba
– Diagnostic Services of Manitoba
– Canadian Celiac Association
– National Institutes of Health (US)
Objectives

• Describe the prevalence and clinical presentation of celiac disease
• Describe the optimal testing to confirm the diagnosis of celiac disease
• Describe key elements, including the 2016 guidelines for family physicians, for management of celiac disease
What does a “gluten problem” look like?

What does a “gluten problem” look like?
Your Role: Melting the Celiac Iceberg

Symptomatic Celiac Disease

Asymptomatic Celiac Disease

Potential Celiac Disease

Genetic Susceptibility (DQ2/DQ8)

Positive Serology

Mucosal damage

Normal Mucosa
Case Finding in Primary Care to Identify patients with Celiac Disease

• A multi-center case-finding study in North America
• 4 centers
  – Manitoba
  – North Carolina
  – Virginia
  – Pittsburgh
• 2568 interviewed
  – 976 patients screened

Enrollment Criteria

• Family history of CD (first- or second-degree relative)
• Unexplained anemia or iron deficiency
• Recurrent abdominal pain or bloating
• Irritable bowel syndrome or chronic diarrhea (longer than 2 weeks)
• Chronic fatigue
• Abnormal liver function test (AST, ALT)
• Autoimmune disorders, *e.g.*, type 1 diabetes, thyroiditis
• Infertility and recurrent fetal loss
• Unexplained osteoporosis

Results

- 2.25% celiac disease prevalence among screened patients
- 4300% increase in diagnosis of celiac disease in participating centers
- 11.6/1000 during study period
- 0.27/1000 during the year prior to the study

Your Role: Think Celiac!

**Current Manitoba Screening Protocol**

**Step 1** - TTG IgA
- Most **sensitive** serologic test (~80%)
- Positive test >15

**Step 2** – IgA EMA (if TTG IgA positive)
- 95% **specificity** for celiac disease

(Anti-gliadin antibody testing no longer performed)
Diagnosis of Celiac Disease

**Biopsy**

- **The** gold standard
- **Recommended in all** individuals
  - False positive serology does occur
  - Atypical biopsies - collagenous sprue, tropical sprue, lymphoma, crohn’s disease, olmesartan

*biopsy may not be necessary for some children who meet certain criteria – refer to a pediatric gastroenterologist to sort this out!

Physician Visits Prior to Diagnosis

- 37% consulted 2 or more family doctors
- 27% consulted 3 or more physicians
- Subspecialties involved
  - Gastroenterology
  - Rheumatology
  - Dermatology
  - Neurology
  - Haematology

Delays to Diagnosis in 2017

- Manitoba Celiac Disease cohort – 151 patients
- 28% consulted 3 or more physicians
- Median 2 years before presenting to MD with symptoms
- 50% first told of celiac disease by family doctor

Canadian Guidelines: Management of Celiac Disease

Consultation with a skilled dietitian

Education about the disease and family testing

Lifelong adherence to a gluten-free diet and evaluation of compliance

Identification and treatment of nutritional deficiencies

Access to an advocacy group

Continuous long-term follow-up by health professionals with expertise in celiac disease

Gluten-free grains

Flowering plants

Monocots

Grasses

wheat
rye
barley
spelt
kamut

Dicots

quinoa
buckwheat
amaranth

Dicots

rice
corn
millet
teff
oats

Gluten (Gladiin + Glutenin)
Oats = oatstanding questions

- Oats – avenin
  - structurally similar to gluten
  - *most* celiac patients don’t react
  - 2000s studies of *pure, uncontaminated oats shown to be safe for most*
Oats = oatstanding questions

• Mechanically-optically sorted oats
  – Commodity oats with special processing...
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Manitoba Celiac Disease Cohort

• 200 adults (>16 years) with celiac disease diagnosis within 8 weeks of study entry
• 2 years prospective observational study
  – Interview
  – Diet Assessment
  – Labs
  – 24 month biopsy
Nutritional deficiencies and celiac disease in Manitoba

• Iron absorbed in duodenum

• At diagnosis in Manitoba (n = 200)
  – 23% low ferritin
  – 13% anemic
    • 5 microcytic, 1 macrocytic
  – 5% low RBC folate

Silvester and Duerksen, unpublished data.
Vitamin D and bone health

• Malabsorption of calcium leads to osteopenia
• Vitamin D deficiency also decreases calcium and phosphate absorption
• Up to 38-72% of adults with celiac disease have osteopenia/osteoporosis at diagnosis
• 50% recover normal bone mineral density on a strict gluten-free diet

Vitamin D and bone health: Manitoba

• Vitamin D
  – Deficient 8% (< 30 nmol/L)
  – Insufficient 15% (30 to 75 nmol/L)
  – Sufficient 77% (> 75 nmol/L)

• Calcium
  – 1% with low serum calcium
  – None with low albumin corrected calcium

• Phosphate
  – 7% with low serum phosphate

• Alkaline phosphatase
  – 8% with elevated serum alkaline phosphatase

Silvester and Duerksen, unpublished data.
Canadian Guidelines: Bone health in adults with celiac disease

• Correct malabsorption = GFD
• Ensure adequate (dietary PLUS supplement)
  – Calcium
  – Phosphate
  – Vitamin D
• Weight-bearing exercise
• Avoid alcohol, cigarettes

Canadian Guidelines: Who needs a DEXA scan?

• At diagnosis
  – Adults presenting with malabsorption
  – Patients without malabsorption at high risk for bone disease
    • Postmenopausal women
    • Men older than 50 years
    • History of fragility fracture
    • High tTG antibody levels

• Follow-up in 2-3 years
  – If previously abnormal

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Canadian Celiac Association

- www.celiac.ca
- Winnipeg and Brandon Chapters
- Display table
Canadian Guidelines: Management of Celiac Disease

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## Canadian Guidelines: What tests do I need?

<table>
<thead>
<tr>
<th></th>
<th>Diagnosis</th>
<th>3 months</th>
<th>6 months</th>
<th>1 year</th>
<th>Annually</th>
<th>Symptom recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight, BMI</strong></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td><strong>History &amp; Physical</strong></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<tr>
<td><strong>GFD Education</strong></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td><strong>Dietitian Referral</strong></td>
<td>●</td>
<td>●</td>
<td></td>
<td>By request</td>
<td>Ideal</td>
<td>●</td>
</tr>
<tr>
<td><strong>Serology</strong></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
</tr>
<tr>
<td><strong>ALT, AST, ALP, GGT</strong></td>
<td>●</td>
<td></td>
<td></td>
<td>If previously abnormal</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TSH</strong></td>
<td>●</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Every 2 years</td>
</tr>
</tbody>
</table>

How does serology help?

• Systematic review and meta-analysis
• Population
  – Biopsy-confirmed celiac disease
  – Follow-up biopsy and serology and gluten-free diet
• How well does serology detect persistent villous atrophy?
Sensitivity and specificity of tTG IgA for persistent villous atrophy on a GFD

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.69 [0.36, 0.90]</td>
<td>0.87 [0.79, 0.92]</td>
</tr>
<tr>
<td>0.64 [0.30, 0.88]</td>
<td>0.91 [0.68, 0.98]</td>
</tr>
<tr>
<td>0.44 [0.24, 0.67]</td>
<td>0.86 [0.71, 0.94]</td>
</tr>
<tr>
<td>0.75 [0.20, 0.97]</td>
<td>0.68 [0.39, 0.88]</td>
</tr>
<tr>
<td>0.17 [0.10, 0.26]</td>
<td>0.89 [0.83, 0.92]</td>
</tr>
<tr>
<td>0.38 [0.09, 0.78]</td>
<td>0.99 [0.95, 1.00]</td>
</tr>
<tr>
<td>0.42 [0.33, 0.52]</td>
<td>0.79 [0.67, 0.87]</td>
</tr>
<tr>
<td>0.75 [0.20, 0.97]</td>
<td>0.88 [0.62, 0.97]</td>
</tr>
<tr>
<td>0.66 [0.41, 0.84]</td>
<td>0.76 [0.60, 0.86]</td>
</tr>
<tr>
<td>0.12 [0.03, 0.38]</td>
<td>0.83 [0.70, 0.91]</td>
</tr>
<tr>
<td>0.44 [0.34, 0.54]</td>
<td>0.75 [0.67, 0.81]</td>
</tr>
</tbody>
</table>

Silvester, Duerksen et al, submitted, under review.
ROC of tTG IgA for persistent villous atrophy (Marsh 0-2 v 3)

Silvester, Duerksen et al, submitted, under review.
When do I re-refer to gastroenterology?

- Non-responsive celiac disease
  - Persistent symptoms after 6-12 months on a GFD
  - Recurrence of symptoms on a GFD
  - Recurrence of laboratory abnormalities on GFD
- Conversion from seronegative to seropositive
- Persistently abnormal serology

What to remember?

• Melt the iceberg – think celiac!
• Most patients with celiac disease are managed by their family physician
• Antibodies are a screening test - biopsy is diagnostic
• Treatment is a gluten-free diet – have a dietitian on your team
• Monitor bone health, serology and TSH
• Re-refer to your friendly local gastroenterologist if it’s not getting better...
Thank you!

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