Analysis of NHANES data

CD overall 0.71% (95% CI 0.58 – 0.86%)

Among whites 1.01% (95% CI 0.78 – 1.31%)

Only 17% were aware they had CD

Very low rate of diagnosis
PATHOLOGY - THE GOLD STANDARD

- Marsh I, II
- Partial
- Subtotal
- Total
- Villous atrophy (Marsh IIIa, b, c)
DIAGNOSIS OF CELIAC DISEASE
why the underdiagnosis?
ROLE OF THE ENDOSCOPIST

• Guidelines: need 4 – 6 biopsies

Rostom A et al. Gastroenterology. 2006
• Guidelines: need 4 – 6 biopsies
• Determined degree of adherence to guidelines and the result of adherence
• Analyzed the results of biopsy specimens of 132,352 patients (Caris, Dallas, TX) 2006-2009
• Only 35% of patients had ≥4 specimens submitted

Gastrointest Endosc. 2011;74:103-9
NUMBER OF SPECIMENS OF SMALL BOWEL BIOPSIES

Gastrointest Endosc 2011;74:103-9
ADHERENCE ACCORDING TO INDICATION

<table>
<thead>
<tr>
<th>Indication</th>
<th>% with ≥4 specimens</th>
<th>OR for diagnosis of CD when ≥4 specimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>37.8</td>
<td>2.65 (2.13-3.30)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>43.9</td>
<td>1.86 (1.46-2.37)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>33.0</td>
<td>2.94 (1.94-4.43)</td>
</tr>
<tr>
<td>Heartburn</td>
<td>30.0</td>
<td>1.84 (1.33-2.55)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>38.8</td>
<td>1.83 (1.08-3.11)</td>
</tr>
<tr>
<td>Suspected celiac disease/malabsorption</td>
<td>38.5</td>
<td>7.37 (4.70-11.57)</td>
</tr>
</tbody>
</table>

DIAGNOSIS COMPARED TO NUMBER OF BIOPSY SPECIMENS
Number of Specimens and Probability of CD Diagnosis
Among those with iron deficiency, anemia, weight loss or diarrhea undergoing EGD during the years 2004-2009 (n=13,091), Only **43%** underwent small intestinal biopsy.
CONCLUSIONS

• Biopsy rates increased, in 2009 only 51% of individuals undergoing EGD with signs/symptoms of CD have a small bowel biopsy.
• Groups that are less likely to have a biopsy:
  – Non-white
  – Male
  – Indication: weight loss
Procedure volume influences adherence to celiac disease guidelines
Benjamin Lebwohl\textsuperscript{a,b}, Robert M. Genta\textsuperscript{d}, Robert C. Kapel\textsuperscript{e}, Daniel Sheehan\textsuperscript{c}, Nina S. Lerner\textsuperscript{c}, Peter H. Green\textsuperscript{a}, Alfred I. Neugut\textsuperscript{b} and Andrew Rundle\textsuperscript{b}

**European Journal of Gastroenterology & Hepatology 2013**,
• On multivariate analysis, a higher procedure volume was associated with a decreased adherence.

• An increased adherence was reported for gastroenterologists working at suites with higher numbers of gastroenterologists (OR for each additional gastroenterologist, 1.08; 95% CI, 1.04–1.13; P < 0.001).

• but not for a higher gastroenterologist density in the zip code of the practice (OR for each additional gastroenterologist per capita, 1.01; 95% CI, 0.99–1.03).

• Education, peer pressure?
Biopsies of the bulb can be assessed for villous atrophy and intraepithelial lymphocytosis

Bulb biopsies increased the yield of diagnosis by 13%
One bite or two per pass of the biopsy forceps?

M Latorre, SM Lagana, DE Freedberg, B Lebwohl, G Bhagat, SK Lewis, PH Green

DDW 2013
RESULTS

• Prospective study, N = 86
• Two bxs with one pass then in another jar
two bxs taken with two passes of forceps

<table>
<thead>
<tr>
<th></th>
<th>one pass</th>
<th>two pass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pieces</td>
<td>2.02</td>
<td>2.36</td>
</tr>
<tr>
<td>% oriented pieces</td>
<td>42%</td>
<td>66%</td>
</tr>
</tbody>
</table>
Figure 1: Percentage of Well-Oriented Specimens by Method and Sub-Group

- 1-Pass Method
- 2-Pass Method

- **ALL PATIENTS** (n=86, p<0.01)
- **KNOWN CD** (n=40, p=0.02)
- **SUSPECTED CD** (n=31, p=0.21)
- **UNKNOWN CD** (n=15, p=0.22)
- **VILLOUS ATROPHY** (n=26, p=0.02)
- **FINAL DIAGNOSIS CD** (n=52, p<0.01)
• One bite per pass of biopsy forceps yields more diagnostic specimens
CELIAC DISEASE
CELIAC DISEASE
VILLOUS ATROPHY, NEGATIVE SEROLOGIES
BENICAR
VILLOUS ATROPHY, NEGATIVE SEROLOGIES
CD4+LYMPHOMA
Villous Atrophy and Negative Celiac Serology: A Diagnostic and Therapeutic Dilemma

Marisa DeGaetani, MD1,2, Christina A. Tennyson, MD1,2, Benjamin Lebwohl, MD, MS1,2, Suzanne K. Lewis, MD1,2, Hussein Abu Daya, MD1, Carolina Arguelles-Grande, MD1, Govind Bhagat, MBBS3 and Peter H.R. Green, MD1,2

Number of patients
(N = 72)
Interest in a Medication

Biopsy Proven CD (n=339)

- A great deal: 55%
- Quite a bit: 16%
- Moderately: 11%
- Slightly: 11%
- Not at all: 8%

Tennyson Ther Adv Gastro 2013
ALV003 and AN-PEP: Endopeptidases that break up gluten into less-immunogenic peptides

LARAZOTIDE (AT-1001): Reduces paracellular transport of gluten peptides by regulating intercellular Tight Junctions

NECATOR AMERICANUS: Infection with this parasite would inhibit the immune response against gluten

CCX282B: Antagonist of the CCR9 receptor on T-cells which would prevent their migration to the intestinal lamina propria

NEXVAX2: Vaccine that uses 3 gluten peptides to induce T cell immune tolerance in HLA DQ2 positive coeliac patients
Gluten peptides from the diet

Transcellular  Paracellular

**ALV003 and AN-PEP:** Endopeptidases that break up gluten into less-immunogenic peptides

**LARAZOTIDE (AT-1001):** Reduces paracellular transport of gluten peptides by regulating intercellular Tight Junctions

Intestinal lumen

Intestinal epithelium

Basal membrane

Lamina propria

IEL

IEL

IEL

IEL

**NECATOR AMERICANUS:** Infection with this parasite would inhibit the immune response against gluten

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