DDW WRAP-UP 2012 CELIAC DISEASE

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OVERVIEW

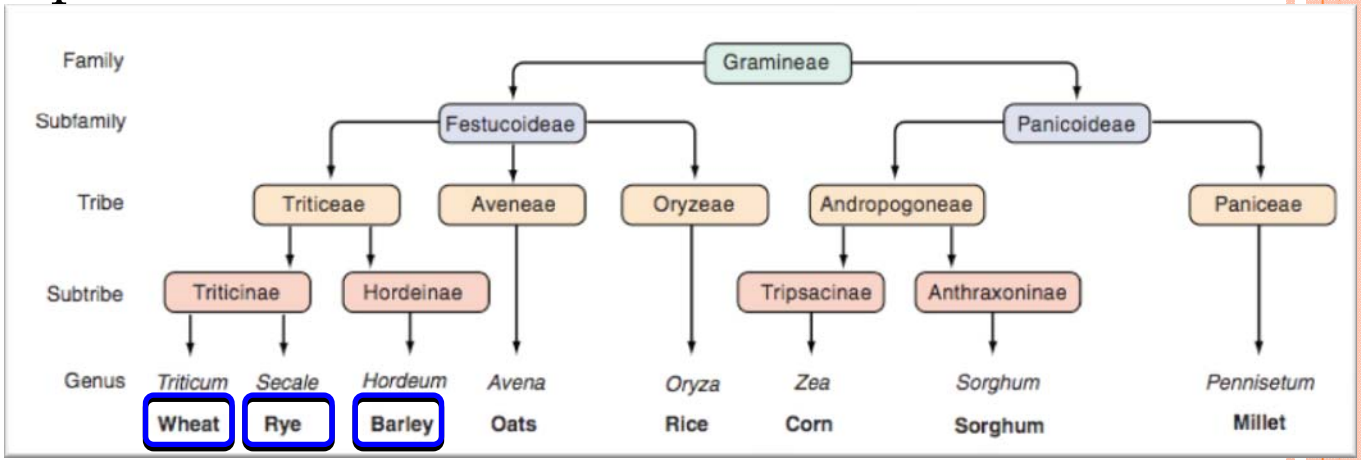
- Definition
- Susceptibility
- The Changing Clinical Presentation
- Medical Associations
- Diagnosis
- Treatment

DEFINITION

- Chronic small intestinal immune-mediated enteropathy precipitated by exposure to dietary gluten in genetically predisposed individuals
- AKA celiac sprue, gluten intolerance, and gluten-sensitive enteropathy
- Preferred term is “Celiac Disease” (CD)

WHY DOES IT DEVELOP?

- Cereal prolamines initiate immune-mediated response in predisposed individuals
  - Gliadin (wheat)
  - Secalin (rye)
  - Hordein (barley)



WHO IS SUSCEPTIBLE?

- 1:100 are genetically susceptible
- Genetic Factors
  - Increased frequency of HLA haplotypes
    - (DR3-DQ2, DR5/7, DR4-DQ8)
  - 70% concordance in twins
  - 10-15% prevalence in first-degree relatives
- Environmental Factors? Infectious Factors? (adenovirus, HP)

CLINICAL PRESENTATIONS

CLASSICAL DISEASE

- Failure to Thrive
- Weight Loss
- Protuberant Abdomen
- Bloating, Diarrhea, Steatorrhea
- Abdominal Pain
- Dramatic Response to Gluten-Free Diet (GFD)

- Less likely to see classical presentation
- Many non-classical presentations

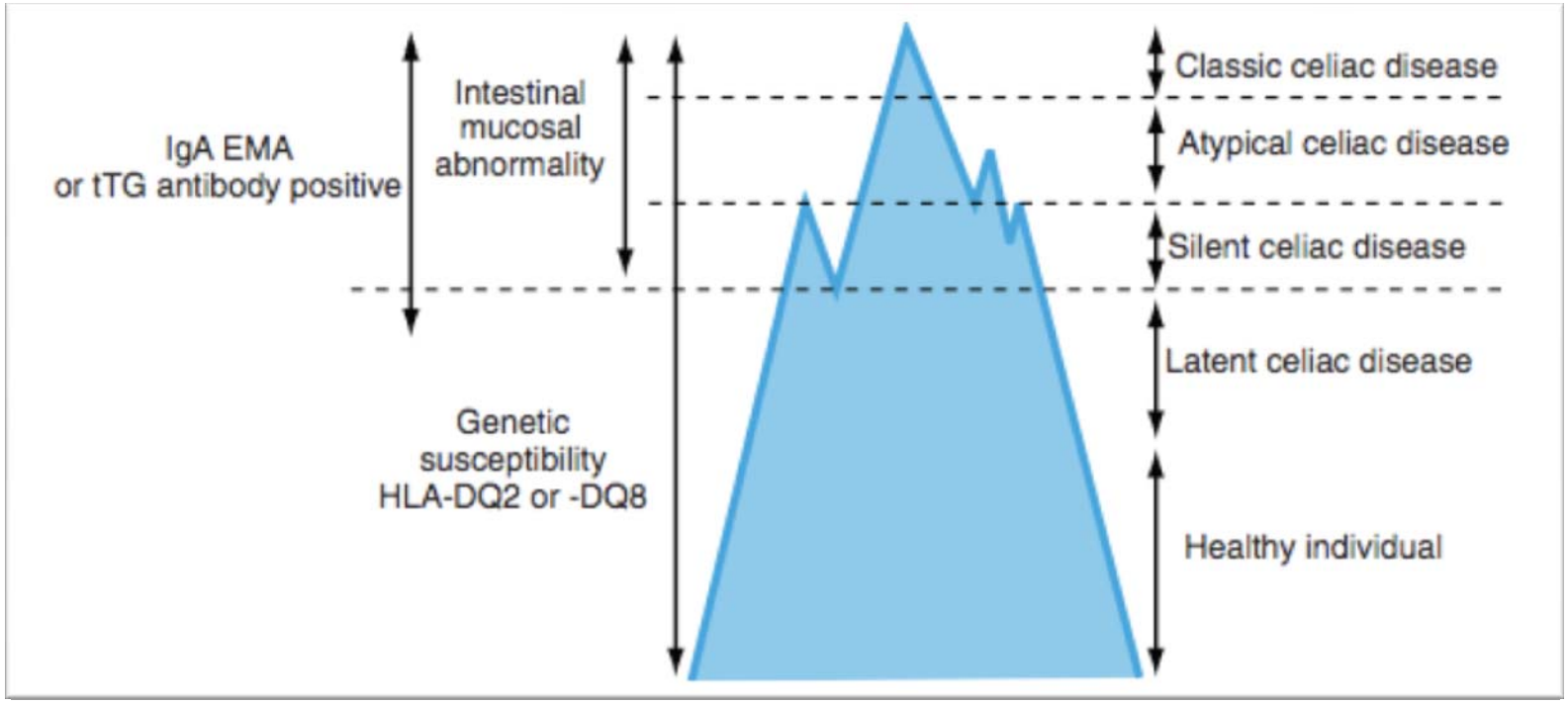
NON-CLASSICAL DISEASE

- Adults
- Constipation, Alternating C/D
- Dyspepsia
- Heartburn
- Non-GI Symptoms

CHANGING PRESENTATION OF CD

VARYING FORMS

- ~ Classical or Non-Classical Disease
- ~ Asymptomatic or Subclinical Disease
- ~ Potential Disease



CHANGING PICTURE OF DISEASE → MANY MYTHS

- Disease of Females
  - Women outnumber men 2-3:1 on diagnosis
  - M = F on frequency of positive serological testing
- Disease of Young People
  - Average age of diagnosis is in the 5th decade of life
- Disease of Caucasians
  - Higher prevalence in Western Ireland, other European countries, and the US
  - Affects people across the worlds, including Africans and Asians

MORE MYTHS. . .

- Disease of Thin People
  - Many are overweight or obese
  - "High Prevalence of Overweight and Obese Adult Celiac Disease Patients in the Midwestern United States."
    - Dr. Kupfer. Retrospective study by U of Chicago CD Center – 22-32% of CD pts with BMI> 25. Those with high BMIs were more likely to be older at age of diagnosis. (less severe disease, low clinical suspicion, later onset of disease?)

- Easy to Diagnose
  - Many are not tested, or are tested inappropriately
  - Confounding factors, including that many without CD respond to GFD

MYTHS CONTINUED. . .

- Easy to Treat
  - GFD is about 3-4x as expensive
    - Insurance companies do not help offset the cost
  - Only ingestion matters
    - Includes lipstick and makeup
    - Not cleaning products
  - "Celiac Disease Has Higher Treatment Burden than Common Medical Problems."
    - Dr. Shah – Harvard. Treatment burden is high, but pts view their overall health as well, do not see PCP/Specialists as often as other chronic diseases.

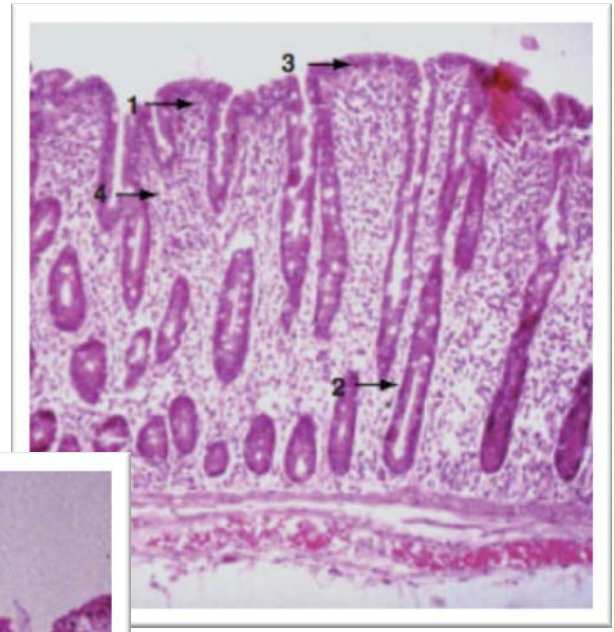
VARIOUS ASSOCIATIONS

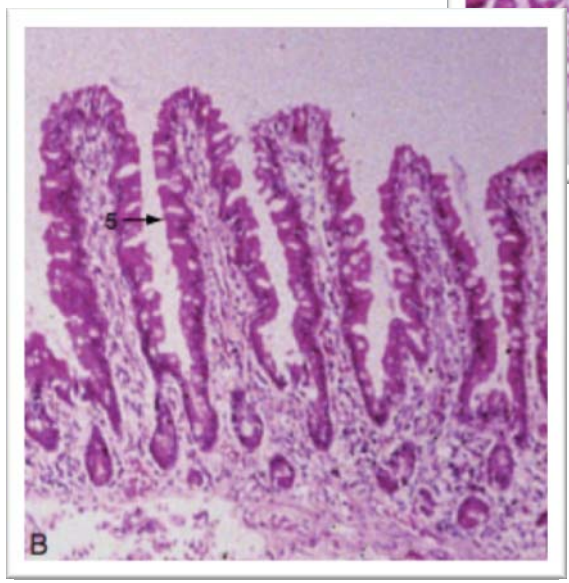
NEUROPSYCH	OB-GYN	HEPATOBILIARY	AUTOIMMUNE
HDAD	Delayed menarche	PBC	DM 1
Irritability	Earlier menopause	PSC	Thyroiditis
Cerebral Ca++	Secondary amenorrhea	Elevated LFTs	Adrenal D/O
Seizures	Infertility		Sjogren's
Ataxia	Higher miscarriage rate		RA
Autism	IUGR		SLE
Migraines	Lower birth weight		
Schizophrenia	Premature births		

DIAGNOSIS

tTG IgA
=
recommended serum test

- Clinical findings
- Serological testing
- Histological response to GFD
- Intestinal biopsies
  - Notching/scalloping folds, mucosal fissuring, flattened/absence of folds
  - False positive
    - Peptic duodenitis
    - SBBO
    - Enteric infections
  - False negative
    - Insufficient sample
    - Patchy disease
    - Subtle findings

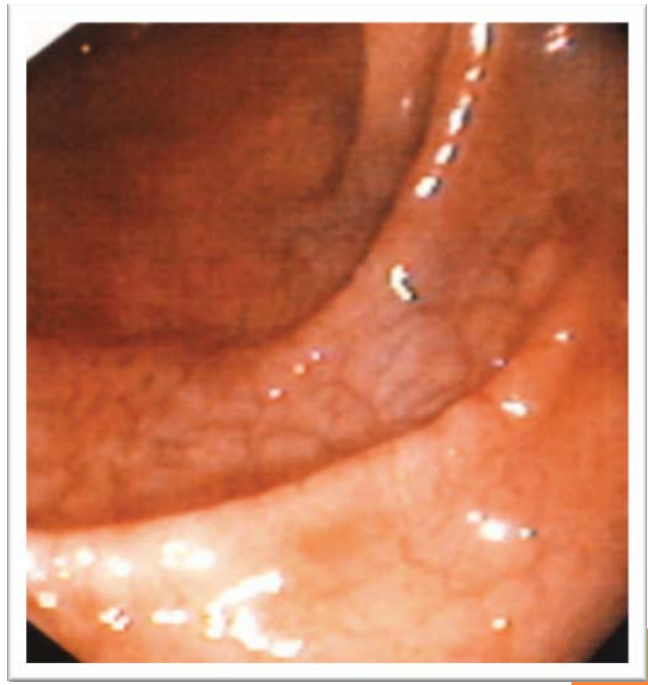




MISSING THE DIAGNOSIS

REMEMBER, 4-6 BIOPSIES, ONE FROM THE BULB

- "Prior Endoscopy in Patients with Newly Diagnosed CD; A Missed Opportunity."
  - Dr. Green from Columbia. Most endoscopists do not take enough biopsies (most take 2 or fewer). Review study of their patient population, most patients whose CD was missed did not have enough biopsies taken on prior EGD. Also their presenting sx were more likely to be dyspepsia/reflux.



PROPOSED NEW CRITERIA

4 out of 5 to Diagnose
Controversial

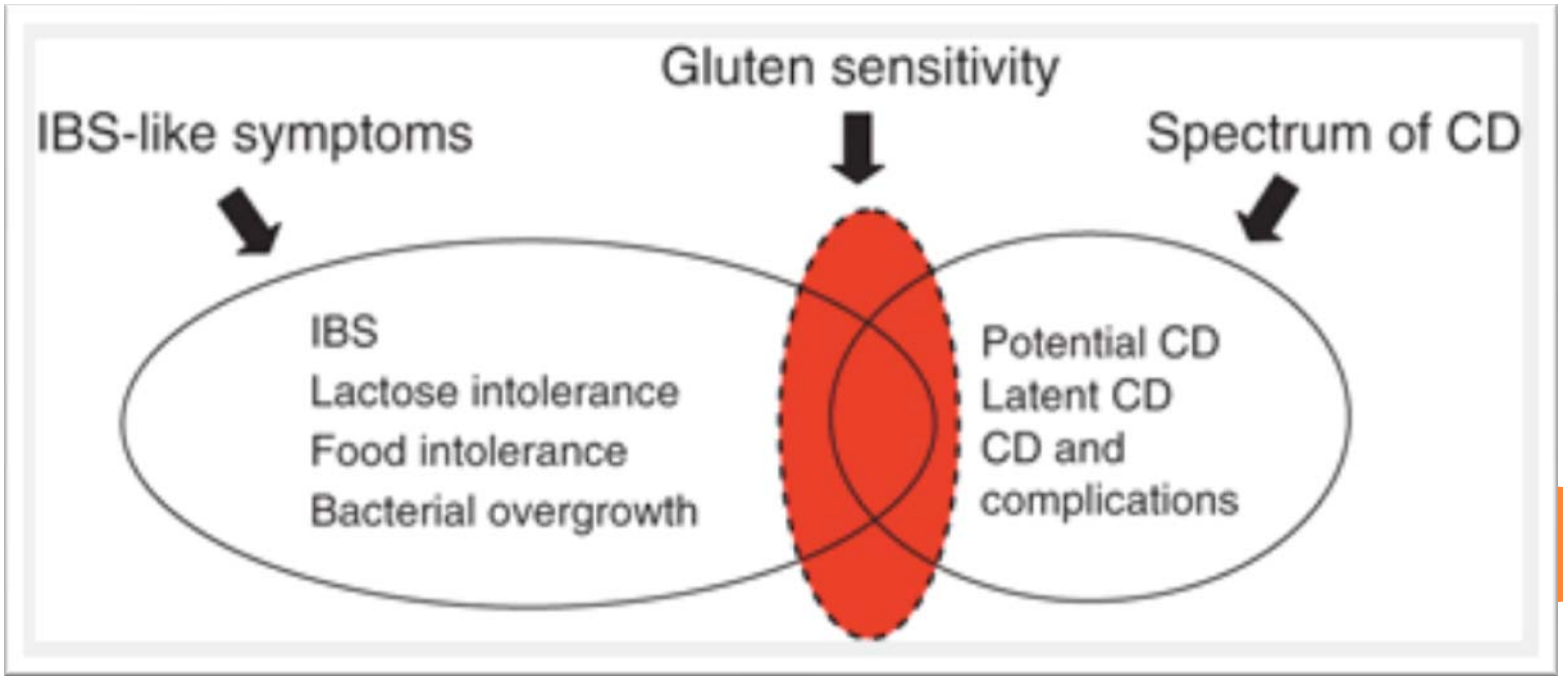
- Typical symptoms
- High titer of serum CD IgA class autoantibodies
- HLA DQ-2 and/or DQ-8 genotypes
  (necessary but not sufficient)
- Celiac enteropathy by small bowel bx
- Response to GFD
  (high placebo response)

GENETIC TESTING

- HOW
  - RNA PCR from cheek swab or blood sample
- WHO
  - Close relatives of pts with CD if they want to know if they are at risk and are willing to undergo treatment
  - Pts on GFD to confirm CD
  - Equivocal histology and serology findings in which a negative test would make CD unlikely
- HOW OFTEN
  - Once in a lifetime

CD/IBS/GLUTEN-SENSITIVITY

- Can be overlap of symptoms
- Placebo response to GFD in high
- Gluten can be hard to digest and increases stool volume



MANAGEMENT

- Return pts to healthy state and avoid complications of untreated disease
- Life-long GFD
- Nutrition supplements as necessary
- Refer to a knowledgeable nutritionist

TREATMENT

- Non-compliance
  - Intentional and non-intentional, overall <50%
- Unclear how much gluten is safe
  - New FDA guidelines suggest up to 10mg/day
- Benefits
  - Decreases cancer risk
  - Improves ob/gyn complications
  - Improves osteoporosis
  - Improves QOL
- Improvement
  - Clinical improvement: 2 weeks in 70%, 6 weeks in most.
  - Serological improvement: 4-6 weeks.
  - Histological improvement: up to 2 years or more.

FOLLOW-UP

- Follow tTG IgA until normal, then consider q1-2 yrs
- DEXA
- Consider repeat EGD with biopsies in some
- Drug treatment?
  - Larazotide acetate: to close tight junctions to block absorption of gluten

RESOURCES FOR PATIENTS

- Celiac Disease Foundation: www.celiac.org
- Gluten Intolerance Group of NA: www.gluten.net
- National Foundation of Celiac Awareness: www.celiaccentral.org
- Canadian Celiac Association: www.celiac.ca
- Celiac Sprue Association: www.csaceliacs.org
- Case, Shelley – The Gluten Free Diet 2010
- Blumer and Crowe – Celiac Disease for Dummies 2010
- Dennis, Leffler – Real Life with Celiac Disease: Troubleshooting and Thriving on a Gluten Free Diet. 2010.

DON'T ONLY TEST THIN GIRLS FROM IRELAND

(atypical presentations are now the norm)

AT LEAST 4-6 BIOPSIES, INCLUDING THE BULB

CONSIDER GENETIC TESTING

SEND TO CALIFORNIA, OR AN INFORMED NUTRITIONIST AND SUPPORT GROUPS

REFERENCES

- "Celiac Disease: Diagnosis, Management, and Complications" by Dr. Sheila Crowe UCSD – presented at DDW 2012
- Sleisenger and Fordtran "Celiac Disease and Refractory Celiac Disease."
- Verdu EF, Armstrong D, and Murray J. "Between Celiac Disease and Irritable Bowel Syndrome: The "No Man's Land" of Gluten Sensitivity. The American Journal of Gastroenterology 104, 1587-1594 (June 2009).