CELIAC DISEASE, 2006

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CELIAC DISEASE

• Gluten sensitive enteropathy
• Traditionally a malabsorption syndrome
• Currently resembles a multisystem disease

• GENETICALLY DETERMINED
  Sib and twin occurrence rates
  HLA 92% DQ2, 8% DQ8
• Environmental precipitant (s)
  Gluten
  Breast feeding
  GI infections
  Smoking
  ?

MORBIDITY & MORTALITY IN CELIAC DISEASE

• Morbidity - classical presentation,
  - silent CD-anemia, bone
  - chronic liver disease
• Mortality increased 1.9-3.8 X
  - due to malignancy (lymphoma)

CELIAC DISEASE

Genetic factors
HLA + ? Genes
  +
  Gluten
  +
Other factors
breast feeding, amount and timing of gluten introduction,
GI infections, smoking, etc
PREVALENCE OF CELIAC DISEASE

- Common, affects ~1% of the population
- Evidence from serologic screening studies
  - UK adults (Gut, 2003) 1/100
  - UK children (BMJ, 2004) 1/100
  - Finland children (NEJM, 2003) 1/99
  - Turkey children (J Clin Gastroenterol, 2005) 1/115
  - Turkey adults (J Clin Gastroenterol, 2005) 1/99
  - North Africa children (Lancet, 1999) 1/18
  - USA adults & children (Arch Int Med, 2003) 1/133

WHY IS CELIAC DISEASE UNDERDIAGNOSED IN USA?

- Shift to silent form (due to breast feeding?)
- Failure of physician recognition
- Diagnoses “stick” (eg IBS)
- Lack of pharmaceutical support
  - Medical research
  - Medical education

Where are they? Osteoporosis, IBS, infertility, neurology, oncology or rheumatology clinics

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THE SPREAD OF FERTILE CRESCENT CROPS ACROSS WESTERN EURASIA

Celiac Disease
Traditionally a pediatric disease
Originally Dickie described the association with wheat ingestion after WW II
Classical presentation is with steatorrhea, malabsorption and weight loss

PATHOPHYSIOLOGY OF CELIAC DISEASE
Gluten has toxic epitopes
Gluten is poorly digested by gastric, duodenal and pancreatic secretions leaving toxic epitopes, especially a 33 mer
Gliadin (somehow) enters the mucosa

IMMUNOLOGIC MECHANISM OF GLIADIN INDUCING VILLOUS ATROPHY LAMINA PROPRIA

CLINICAL PRESENTATION OF CELIAC DISEASE
- CLASSICAL diarrhea predominant +/- malabsorption may be severe
- SILENT atypical complications associated diseases asymptomatic
BMI (WOMEN)
CELIAC DISEASE Vs US NATIONAL DATA

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>% Frequency</th>
</tr>
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<tbody>
<tr>
<td>&lt;18.5</td>
<td>3.6</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>37.7</td>
</tr>
<tr>
<td>25-29.9</td>
<td>29.6</td>
</tr>
<tr>
<td>&gt;=30</td>
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</tbody>
</table>

BMI in Women NHANES

N=232

LES S COMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
  - Dental enamel defects
  - Aphthous ulceration

SILENT CELIAC DISEASE
NON-DIARRHEAL PRESENTATIONS

- Incidental at endoscopy
- Iron deficiency anemia
- Osteoporosis
- Screening
  1. relatives
  2. other groups (diabetics)

NOT ALL ARE ASYMPTOMATIC

- Others - neurological presentations
LESS COMMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
  - Dental enamel defects
  - Aphthous ulceration
- BLOOD TEST ABNORMALITIES
  - Hypocholesterolemia
  - Hyperamylasemia
  - Hypoalbuminemia
  - Hyposplenism
  - Elevated ESR
CLINICAL SPECTRUM OF CELIAC DISEASE
Asymptomatic with low cholesterol and large forehead and spots on teeth

IBS                  Diarrhea

Severe autoimmune disease
Life threatening illness
Critically ill with RS, EATL

WHAT IS RESPONSIBLE FOR THE VARIED CLINICAL SPECTRUM IN CELIAC DISEASE?

ROLE OF SEROLOGICAL TESTING IN CELIAC DISEASE

- Triage patients for biopsy
- Monitoring adherence to diet
- Screening high risk groups

CLINICAL SPECTRUM OF CELIAC DISEASE
DIAGNOSIS OF CELIAC DISEASE

Endoscopy for any Reason

Positive Serologies

Biopsy

Clinical Suspicion

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Antibodies in Celiac Disease

- Antigliadin (AGA IgA & IgG)
  low specificity
- Antireticulin
- Endomysial (EMA IgA)
  specificity ~100%
  sensitivity ? 80-95%
- Tissue transglutaminase (tTG IgA)
  specificity > 90%
  sensitivity > 90%

Role of Genetic Testing

HLA DQ2/DQ8

- DQ2/DQ8
  celiac disease 100%
  general population 40%

Role
  1. assessing relatives
  2. questionable diagnoses
  3. already on gluten-free diet

Value is in the 100% negative predictive value

Celiac Disease
A Pathologic Diagnosis

Pathology not specific
Need response to a gluten-free diet
Serologic tests are valuable but not essential
HLA may be supportive
AUTO-IMMUNE DISEASES
LIVER DISEASE
MALIGNANCIES
REDUCED BONE DENSITY
INFERTILITY
NEUROLOGICAL DISEASES
CARDIOMYOPATHY

MECANISM OF BONE DISEASE
• Malabsorption of calcium and vitamin D
• Secondary hyperparathyroidism
• Failure to obtain maximum bone density
• Magnesium deficiency
• Circulating cytokines
• Auto-immune
• Premature menopause
• Reduced gonadal function in men
• Primary hyperparathyroidism

PREVALENCE OF AUTOIMMUNE DISEASES (CUMC)

MANAGEMENT
GLUTEN-FREE DIET
Sources
Local support groups
National support groups (CDF, GIG, CSA/USA)
Dietician
Internet
Pitfalls
restaurant foods, preprepared foods, fast foods, communion wafers, medications
DON’T ABANDON THE PATIENT!

AUTOIMMUNE DISEASES
IDD dm, sjogren’s syndrome
Liver disease (PBC, CAH, autoimmune cholangitis)
Thyroid disease
Neurologic (neuropathy, epilepsy, ataxia)
IgA nephropathy, Macroamylasemia
Cardiomyopathy, Addison’s disease
Alopecia, viteligo
Chronic autoimmune urticaria

General Population  Celiac Patients (CPMC)
ALTERNATIVE THERAPIES TO A GLUTEN FREE DIET

- Why? Patients want it
  Biopsies do not normalize
  Persistent risk of NHL

- How? Genetically modify wheat
  Induce tolerance to gluten
  Oral peptidases
  Block tTG
  Block binding to the DQ groove
  Block cytokines

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Desserts
- Baked cheesecake with raspberry coulis
- Chocolate truffle cake
- Mixed berry crumble
- Skelligs handmade Irish chocolates

Our beef, lamb and pork are all organic reared on our family farm in the Burren, Co. Clare. Our sauces, syrups, seafood and handmade chocolates are all sourced locally from suppliers who share our hands on approach.

There is no service charge, except on parties of six or more, where 12.5% service will applied.

*suitable for coeliacs

Some dishes may contain traces of nuts.