CELIAC DISEASE, 2008

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DIAGNOSIS OF CELIAC DISEASE

• Presence of consistent pathology and response to a gluten-free diet

• Serology and HLA supportive

• Celiac disease is a provisional diagnosis

• Classically a diarrheal illness of childhood
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) in adults  
  - childhood diagnosis associated with increased mortality in adulthood (accidents, suicide)

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  
  - USA adults & children (*Arch Int Med*, 2003) 1/133
WHY IS CELIAC DISEASE UNDERDIAGNOSED?

- Rate of diagnosis is low, varies country to country
- Finland 70%, Australia, Ireland, Italy 30%
- USA <5%

WHY
- Shift to silent form (due to breast feeding?)
- Failure of physician recognition
- Lack of pharmaceutical industry involvement
  - Medical research
  - Medical education

[Graph showing trends in CD and Type 1 DM prevalence]
PATHOGENESIS OF CELIAC DISEASE

GENETIC FACTORS

GLUTEN

EPITHELUM
Innate response
LAMINA PROPRIA
Adaptive response

ENVIRONMENTAL FACTORS

GASTROINTESTINAL AND SYSTEMIC MANIFESTATIONS

Autoantibodies (tTG, EMA)

Intraepithelial lymphocytosis + Villous atrophy

GENETIC FACTORS

• GENETICALLY DETERMINED
  Runs in families (10%)
  Twin occurrence rates (70%)

• What genes
  HLA DQ2 92% DQ8 8%
  These HLA genes are necessary
  HLA accounts for <50% genetic influence
  Other genes ?multiple
ENVIRONMENTAL FACTORS – THE SWEDISH EPIDEMIC

THE SWEDISH EPIDEMIC

- Cases per 100,000 person-years
- Year of diagnosis

Odds ratio

- Large amount of flour
- Small-medium amount of flour
- No. of infectious episodes

0-1.9 years
2-4.9 years
5-14.9 years
Evolution of Wheat

4,000,000,000 years BP* → Origins of life
400,000,000 years BP → Complex organisms living in the seas invade the land (B cells and T cells already present in sharks)
200,000,000 years BP → Flowering plants begin to evolve
100,000,000 years BP → Grasses begin to evolve
20,000,000 years BP → Divergence of the common line that gives rise to wheat and barley
500,000 years BP → Early man (*Homo sapiens*)
10,000 years BP → Diploid wheat domesticated by man

*BP = Before Present
THE SPREAD OF FERTILE CRESCENT CROPS ACROSS WESTERN EURASIA

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

**Gliadin peptide**

$\text{tTG}$

Deamidated gliadin peptide

**DQ2/DQ8**

**T cell receptor**

**CD4**

$\text{IFN-\gamma}$

PATHOGENESIS OF CELIAC DISEASE

**GENETIC FACTORS**
- HLA DQ2/8
- Unidentified genes

**EPITHELİUM**
- Innate immune response
- LAMINA PROPRIA
- Adaptive immune response

**ENVIRONMENTAL FACTORS**
- Breast feeding
- Timing of gluten ingestion
- Infections

**GLUTEN**

**TOXIC PEPTIDES**

**Autoantibodies**
- (tTG, EMA)

**GASTROINTESTINAL AND SYSTEMIC MANIFESTATIONS**
- Intraepithelial lymphocytosis
- Villous atrophy
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
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

N=232

BMI in Women

% Frequency

<18.5 18.5-24.9 25-29.9 >=30

15 68 13 4

BMI in Women NHANES

% Frequency

<18.5 18.5-24.9 25-29.9 >=30

3.6 37.7 29.6 29.1

N=232

NHANES
SILENT CELIAC DISEASE
NON-DIARRHEAL PRESENTATIONS

- Incidental at endoscopy
- Iron deficiency anemia
- Osteoporosis
- Screening  1. relatives
  2. other groups (TI DM, Down syndrome, PBC)

NOT ALL ARE ASYMPTOMATIC

- Others - neurological presentations
DERMATITIS HERPETIFORMIS

LESS COMMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
  - Dental enamel defects
  - Aplthous ulceration
Celiac children 22.7% (61/269) vs 7.1% (41/575) (p=<0.0001, OR 4.3; 95% CI 2.7-6.7).
71% (33/46) reported significant improvement on gluten-free diet, (p=0.0003)

Campisi, Dig Liver Dis. 2007

PRESENTATIONS OF SILENT CELIAC DISEASE

BLOOD TEST ABNORMALITIES
Abnormal LFTs, low ferritin
Hypocholesterolemia, Hyperamylasemia
Hypoalbuminemia
Hyposplenism
Elevated ESR, prolonged PT, vitamin deficiency
Hypocalcemia, secondary hyperparathyroidism
TOTAL CHOLESTEROL AT PRESENTATION (N=232)

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CLINICAL SPECTRUM OF CELIAC DISEASE

Asymptomatic with low cholesterol and large forehead and spots on teeth

IBS \[\rightarrow\] Diarrhea

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

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

Clinical Suspicion \(\rightarrow\) Positive Serologies \(\rightarrow\) Biopsy
\(\uparrow\)
Endoscopy for any Reason

Pathological Spectrum

Normal \(\leftrightarrow\) I \(\leftrightarrow\) II \(\leftrightarrow\) III \(\rightarrow\) IV
ROLE OF SEROLOGICAL TESTING IN CELIAC DISEASE

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

ANTIBODIES IN CELIAC DISEASE

• **Antigliadin** *(AGA IgA & IgG)*
  low specificity
• **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

1. PATHOLOGY NOT SPECIFIC
2. NEED RESPONSE TO A GLUTEN-FREE DIET
3. SEROLOGIC TESTS ARE VALUABLE BUT NOT ESSENTIAL
4. 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
AUTOIMMUNE DISEASES

IDDM, Sjogren’s syndrome
Liver disease (PBC, CAH,)
Thyroid disease
Neurologic (neuropathy, epilepsy, ataxia)
IgA nephropathy, Macroamylasemia
Cardiomyopathy, Addison’s disease
Alopecia, viteligo
Chronic autoimmune urticaria
PREVALENCE OF AUTOIMMUNE DISEASES (CUMC)

General Population | Celiac Patients (CPMC)

Prevalence of Autoimmune Disease in Celiac Disease

χ² for trend=63.45; p<0.001

Age at Diagnosis of Celiac Disease (Yr)

<2 | 2 to 4 | 4 to 12 | 12 to 20 | >20

Prevalence

0% | 10% | 20% | 30% | 40%
BURDEN OF DISEASE
IN CELIAC DISEASE

• Autoimmune diseases
  10X the general population

• Malignancy
  small intestinal carcinoma 33X
  esophageal carcinoma 11.6X
  non-Hodgkin’s lymphoma 9.1X
  melanoma 5X


  Papillary thyroid cancer 23X

MANAGEMENT

GLUTEN-FREE DIET

Sources
  Local support groups
  National support groups

Dietitian

Internet

Pitfalls
  restaurant foods, preprepared foods,
  fast foods, communion wafers,
  medications

DON'T ABANDON THE PATIENT!
Desserts

Baked cheesecake with raspberry coulis  €6.00
Chocolate truffle cake  €6.00
Mixed berry crumble  €6.00
Skelligs handmade Irish chocolates  €4.00

Our beef, lamb and pork are all organic reared on our family farm in the Burren, Co.Clare. Our cheeses, oysters, 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.
FUTURE

• More diagnosed
• Greater awareness
• Increased services
• NON-DIETARY THERAPIES
  permeability blocker
  enzymes
  DQ2 blockers
  tTG blockers