CELIAC DISEASE

• Gluten sensitive enteropathy

• Traditionally a malabsorption syndrome

• Currently resembles a multisystem disease
CELIAC 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
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
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 NHANES

Diarrhea as a Presenting Symptom of CD from 1952-2002
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
  Apthous ulceration
LESS COMMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
  - Dental enamel defects
  - Aphthous ulceration
- BLOOD TEST ABNORMALITIES
  - Hypocholesterolemia

TOTAL CHOLESTEROL AT PRESENTATION (N=232)
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?

DIAGNOSIS OF CELIAC DISEASE

- Clinical Suspicion
- Positive Serologies
- Biopsy
- Endoscopy for any Reason
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
- **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
AUTOIMMUNE DISEASES

IDDM, 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
PREVALENCE OF AUTOIMMUNE DISEASES (CUMC)

![Graph showing prevalence comparison between General Population and Celiac Patients (CPMC)]

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!
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.
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

ALTERNATE THERAPIES IN CELIAC DISEASE

- Endopeptidases
- Digest gliadin
- Gliadin peptide
- tTG
- Deamidated gliadin peptide
- DQ2/DQ8
- T cell receptor
- CD4
- IFN-γ