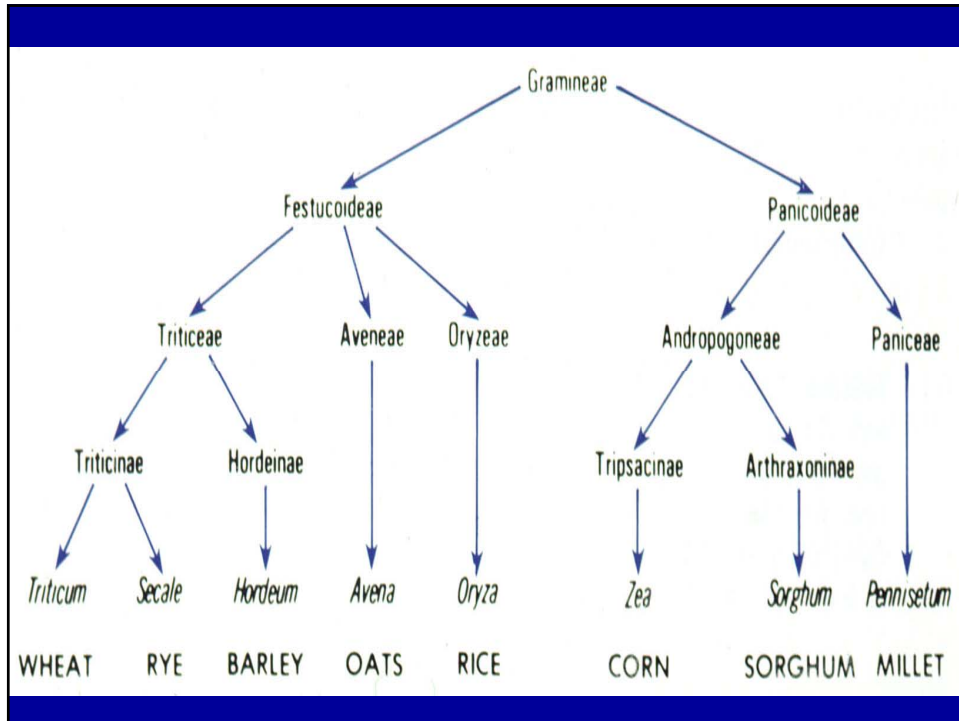


CELIAC DISEASE, 2006

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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

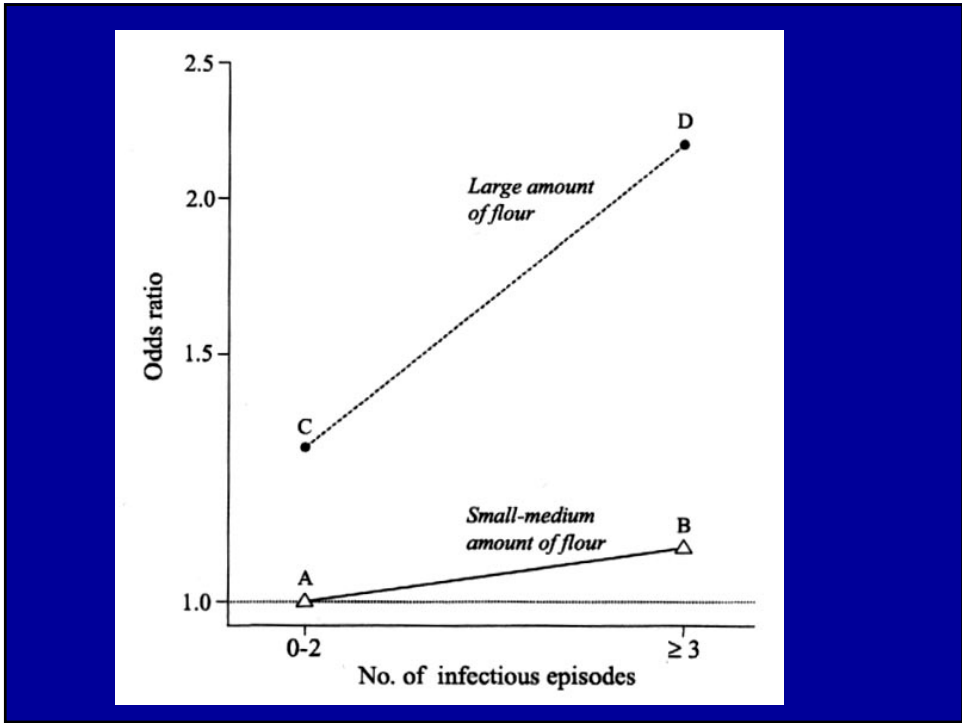
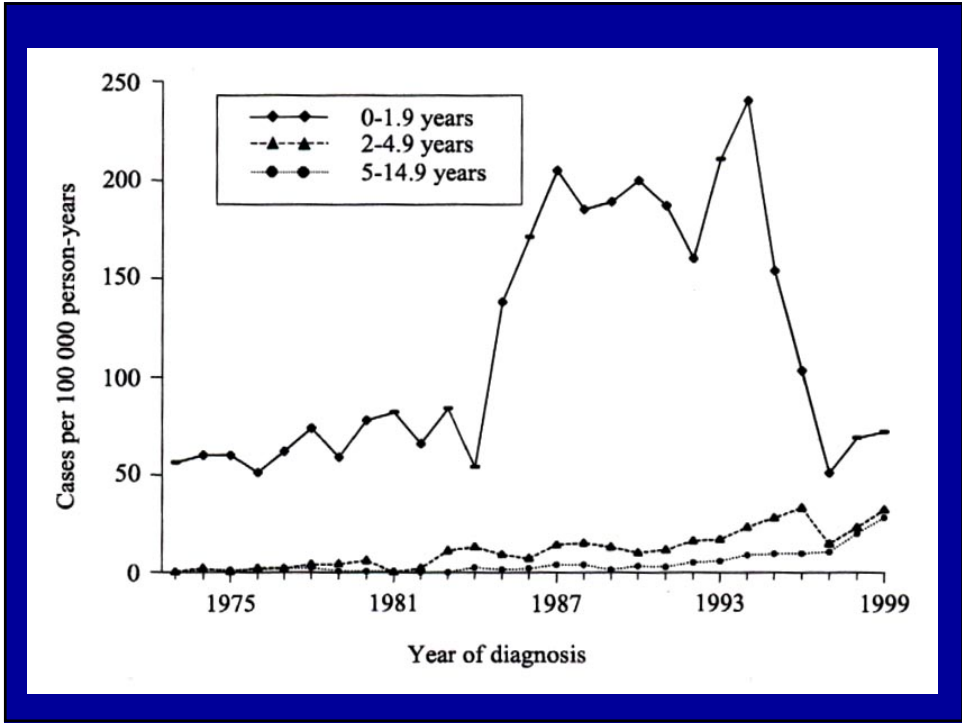
+

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 (<i>Gut</i> , 2003)	1/100
UK children (<i>BMJ</i> , 2004)	1/100
Finland children (<i>NEJM</i> , 2003)	1/99
Turkey children (<i>J Clin Gastroenterol</i> , 2005)	1/115
Turkey adults (<i>J Clin Gastroenterol</i> , 2005)	1/99
North Africa children (<i>Lancet</i> , 1999)	1/18
USA adults & children (<i>Arch Int Med</i> , 2003)	1/133

WHY IS CELIAC DISEASE UNDERDIAGNOSED IN USA?

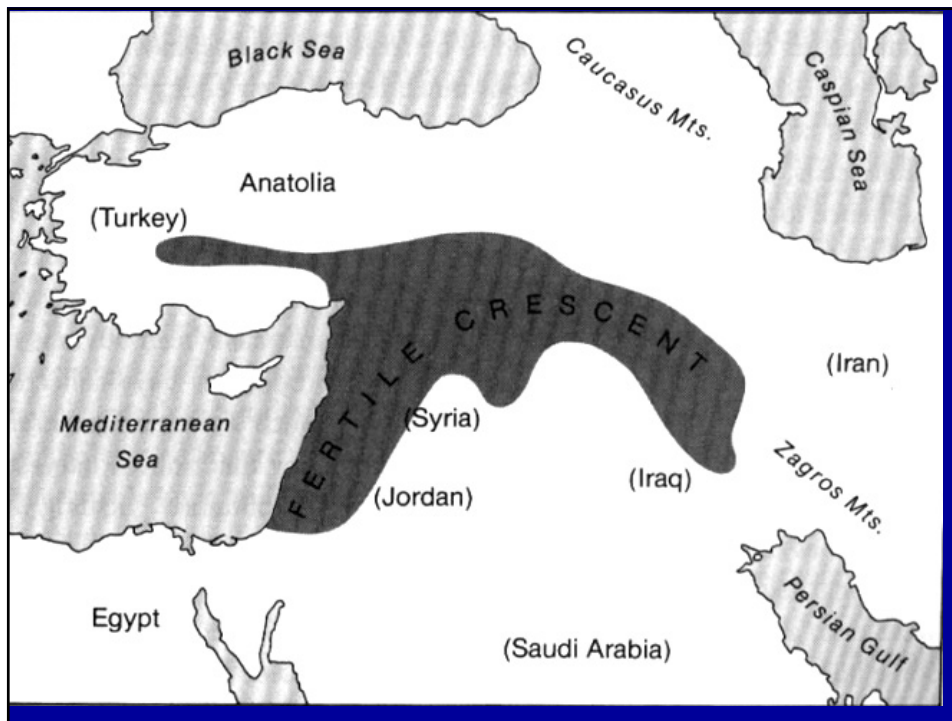
- Shift to silent form (due to breast feeding?)
- Failure of physician recognition
- Diagnoses “stick” (eg IBS)
- Lack of pharmaceutical support
 - Medical research
 - Medical education

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

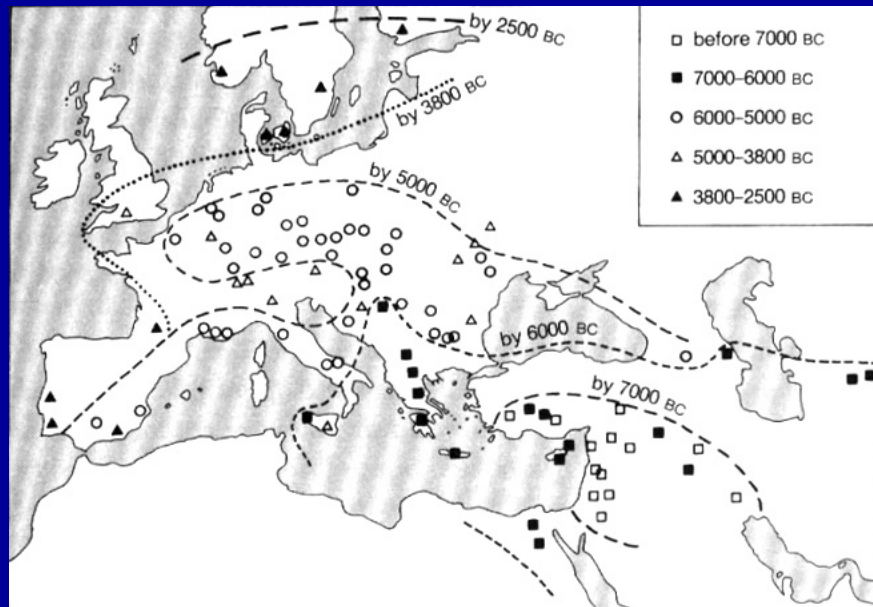
Evolution of Wheat

- 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



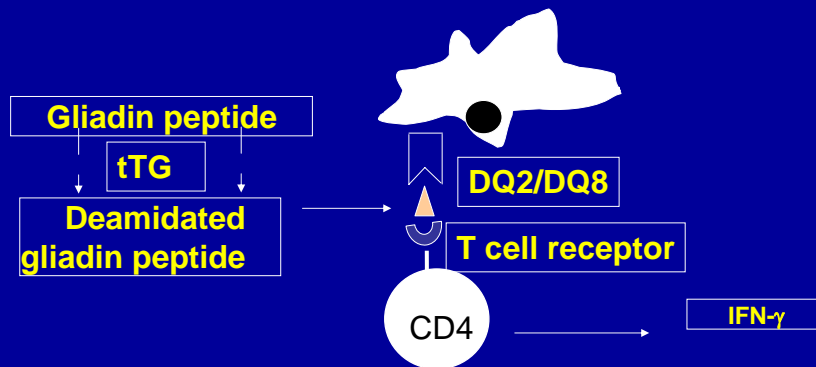
PATHOPHYSIOLOGY OF CELIAC DISEASE

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

IMMUNOLOGIC MECHANISM OF GLIADIN INDUCING VILLOUS ATROPHY LAMINA PROPRIA

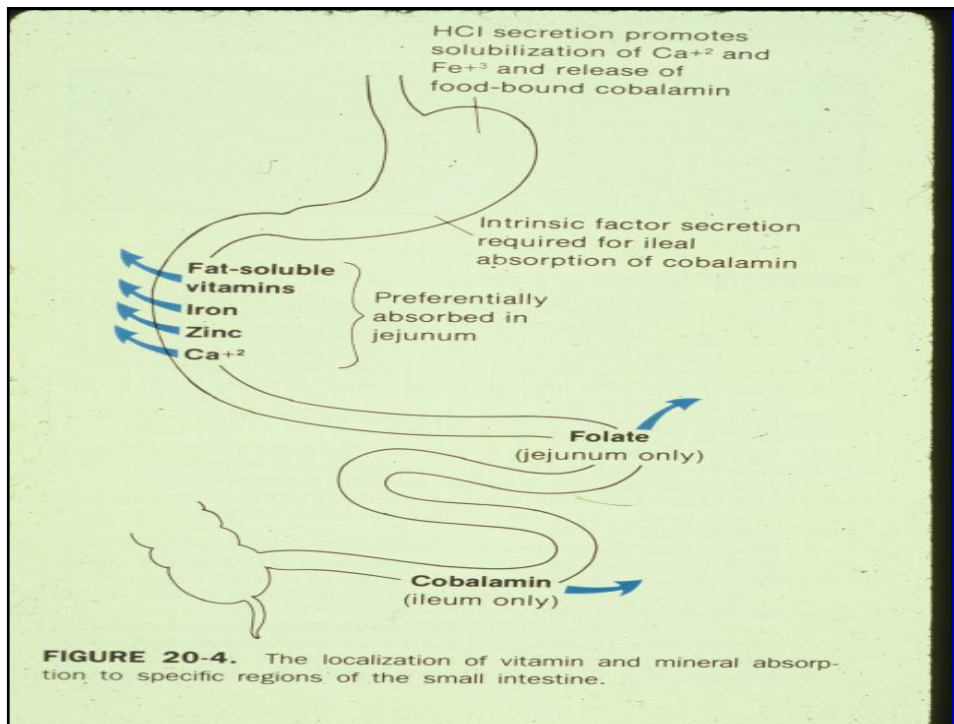


Celiac Disease

Traditionally a pediatric disease

Originally Dickie described the association with wheat ingestion after WW II

Classical presentation is with steatorrhea, malabsorption and weight loss

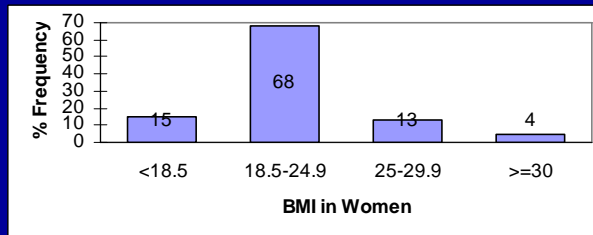


CLINICAL PRESENTATION OF CELIAC DISEASE

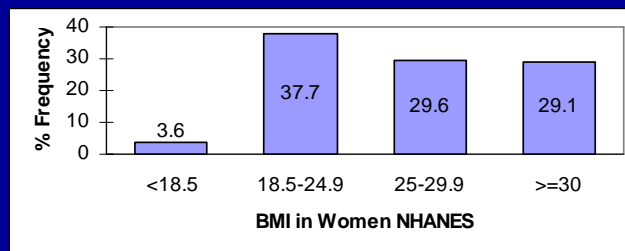
- **CLASSICAL** diarrhea predominant
 +/- malabsorption
 may be severe
- **SILENT** atypical
 complications
 associated diseases
 asymptomatic

BMI (WOMEN) CELIAC DISEASE Vs US NATIONAL DATA

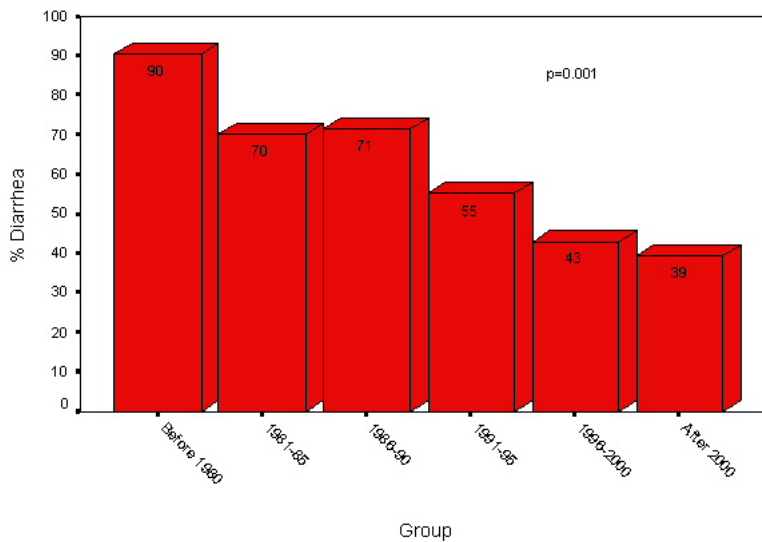
N=232



NHANES



Diarrhea as a Presenting Symptom of CD from 1952-2002



SILENT CELIAC DISEASE NON-DIARRHEAL PRESENTATIONS

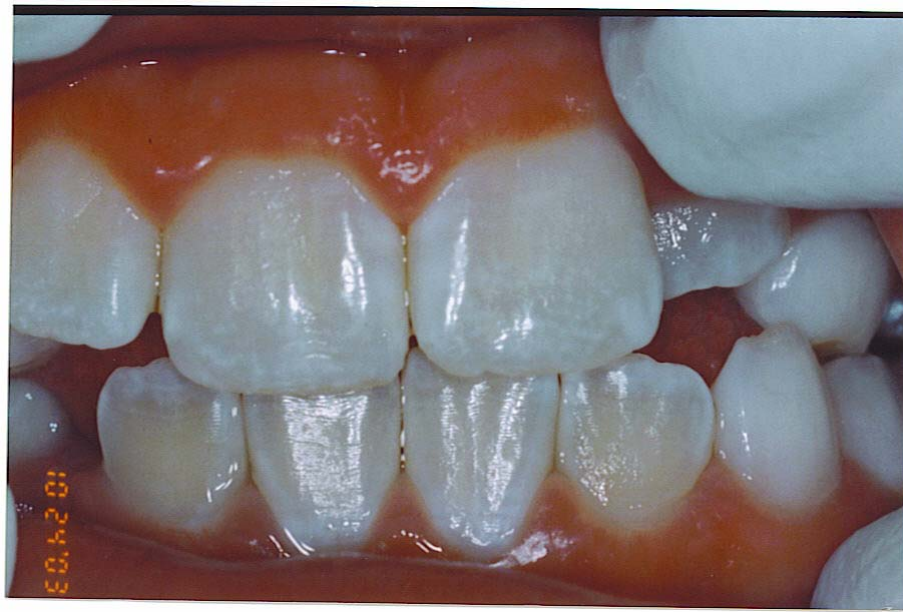
- Incidental at endoscopy
- Iron deficiency anemia
- Osteoporosis
- Screening
 1. relatives
 2. other groups (diabetics)

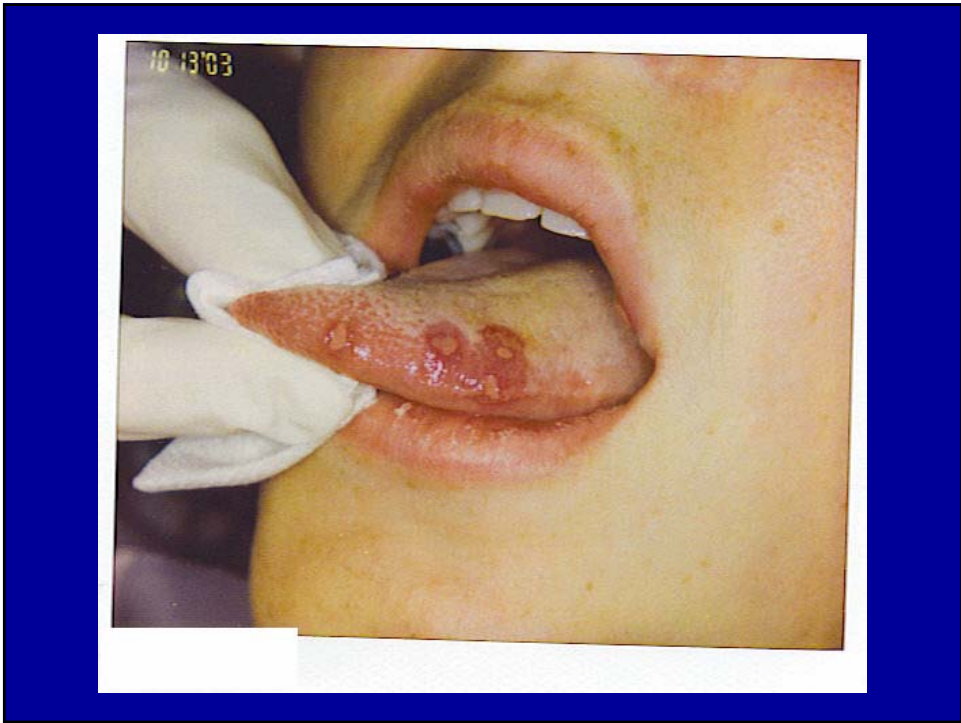
NOT ALL ARE ASYMPTOMATIC
- Others - neurological presentations



LESS COMMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
 - Dental enamel defects
 - Apthous ulceration

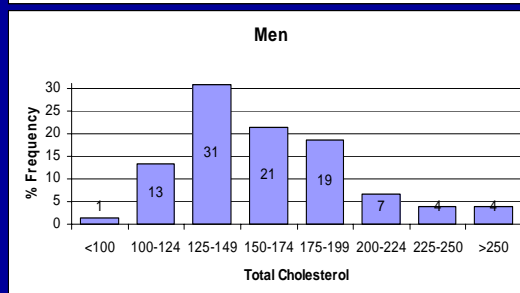
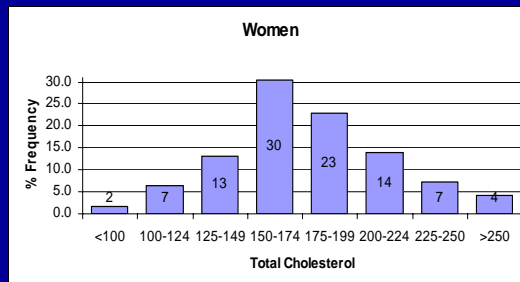


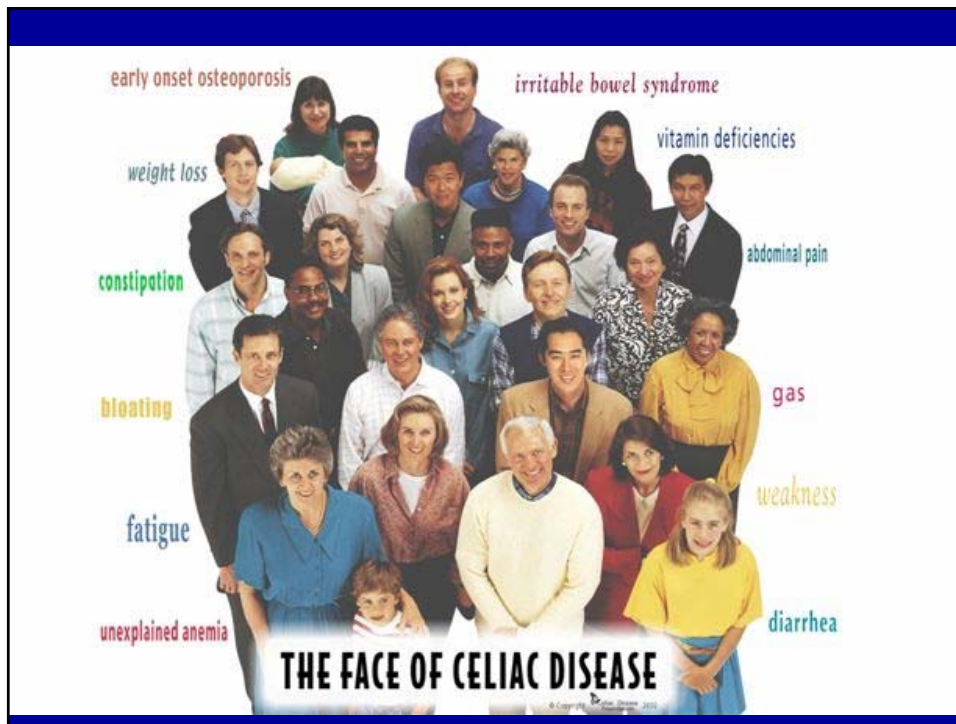


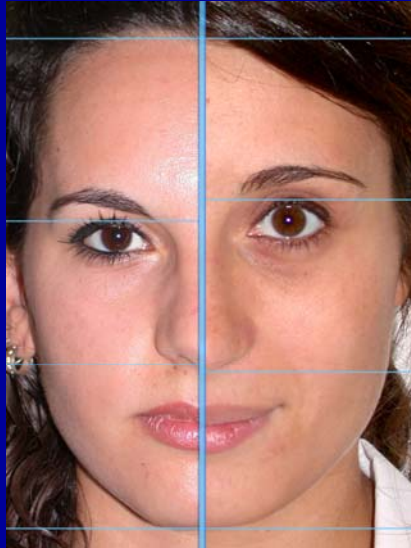
LESS COMMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
 - Dental enamel defects
 - Apthous 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

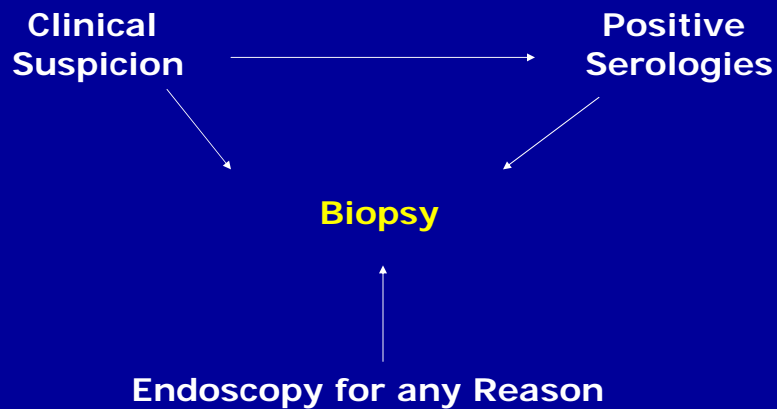


Diarrhea

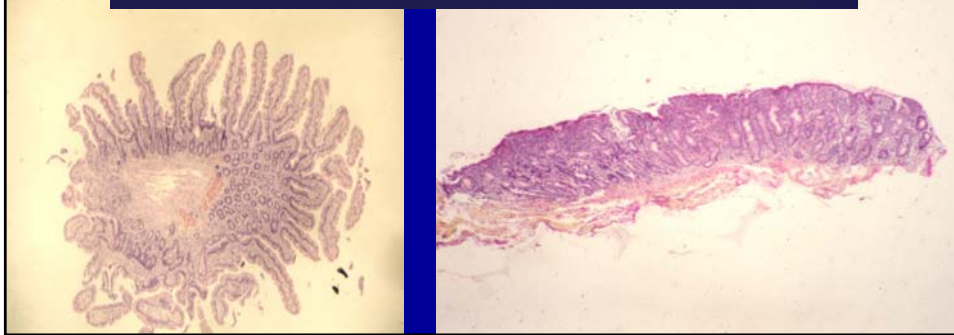
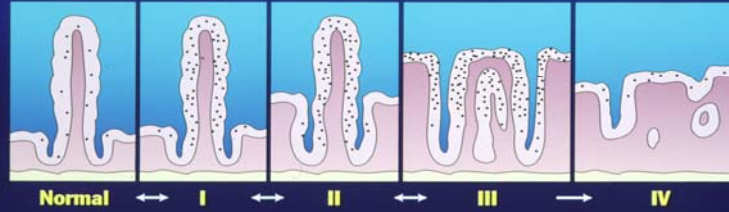
Severe autoimmune disease
Life threatening illness
Critically ill with RS, EATL

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

DIAGNOSIS OF CELIAC DISEASE



Pathological Spectrum



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

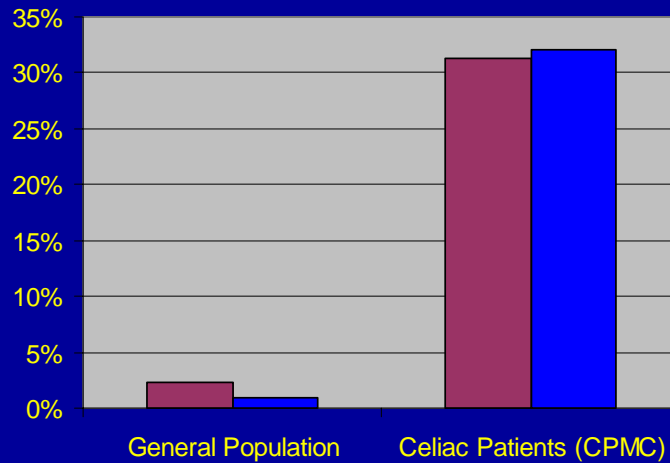
PATHOLOGY NOT SPECIFIC
NEED RESPONSE TO A GLUTEN-FREE
DIET
SEROLOGIC TESTS ARE VALUABLE
BUT NOT ESSENTIAL
HLA MAY BE SUPPORTIVE

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

PREVALENCE OF AUTOIMMUNE DISEASES (CUMC)



MANAGEMENT

GLUTEN-FREE DIET

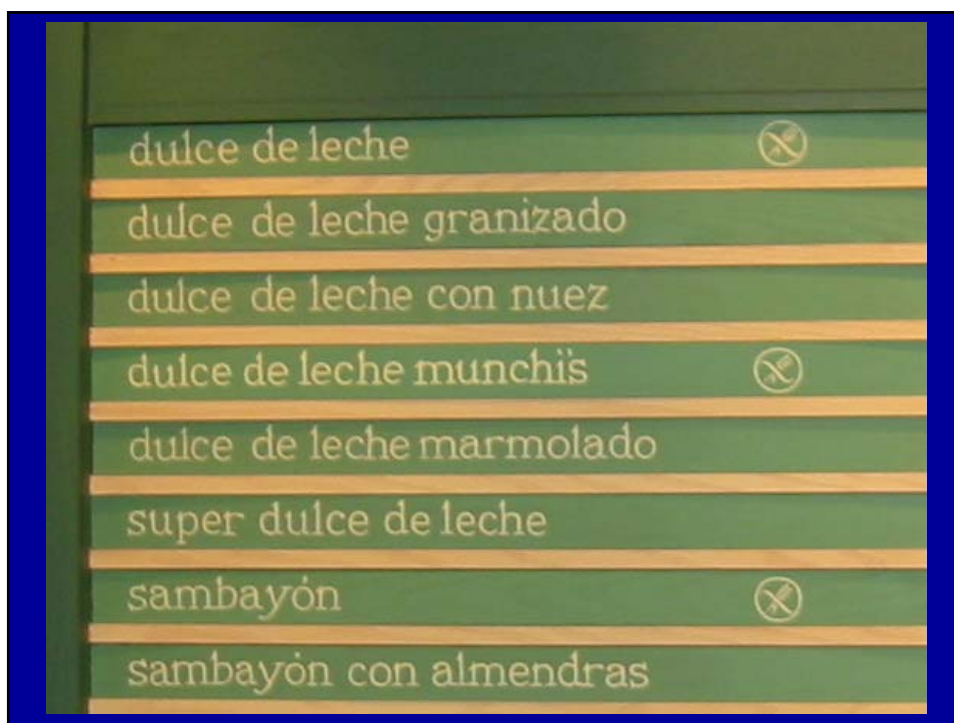
Sources Local support groups
National support groups
(CDF, GIG, CSA/USA)

Dietician

Internet

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

DON'T ABANDON THE PATIENT!



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

