

## 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

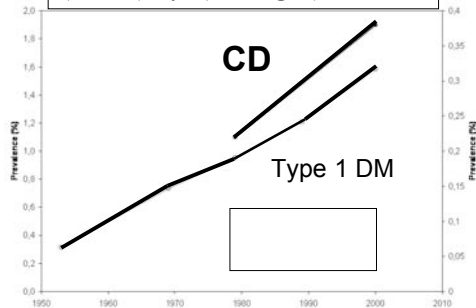
- **Morbidity** - classical presentation,
  - silent CD-anemia, bone
  - chronic liver disease
- **Mortality** increased 1.9-3.8 X
  - due to malignancy (lymphoma) in adults
  - childhood diagnosis associated with increased mortality in adulthood (accidents, suicide)

## PREVALENCE OF CELIAC DISEASE

- Common, affects ~1% of the population
- Evidence from serologic screening studies

UK adults ( <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

## FINLAND: NATIONAL DATA



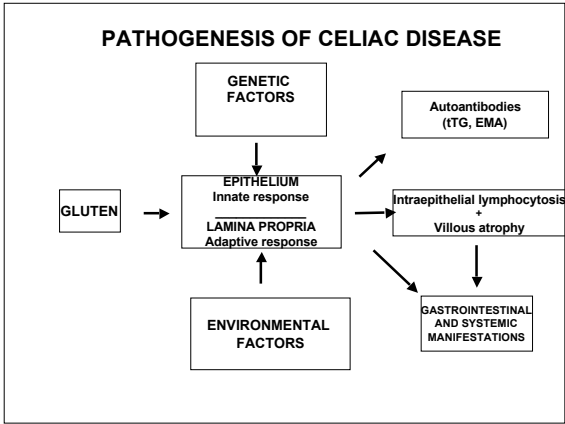
Lohi S et al., CDS 2006

## WHY IS CELIAC DISEASE UNDERDIAGNOSED?

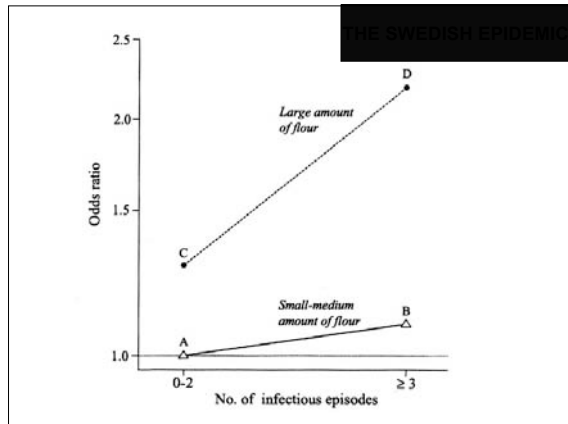
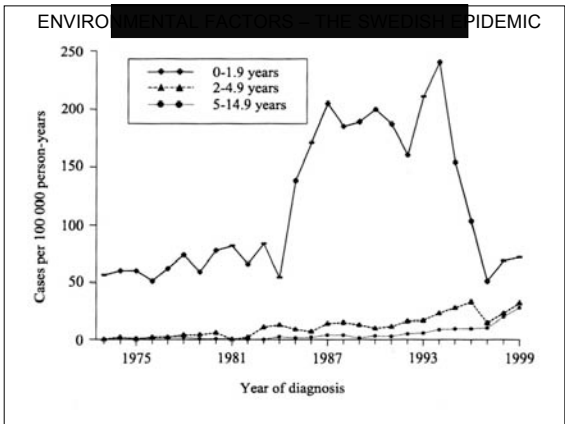
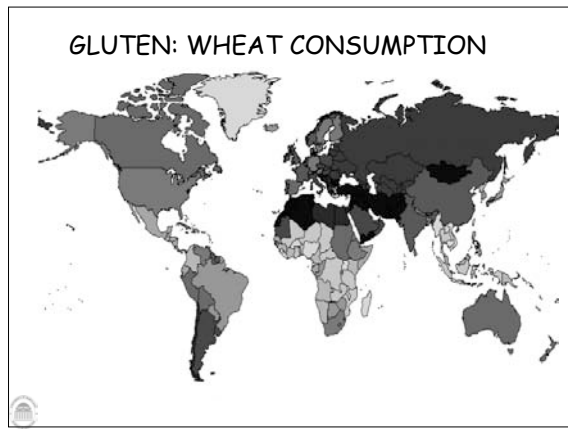
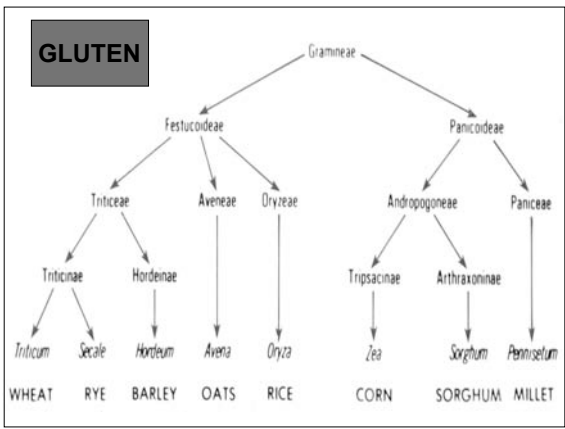
- Rate of diagnosis is low, varies country to country
- Finland 70%, Australia, Ireland, Italy 30%
- USA <5%

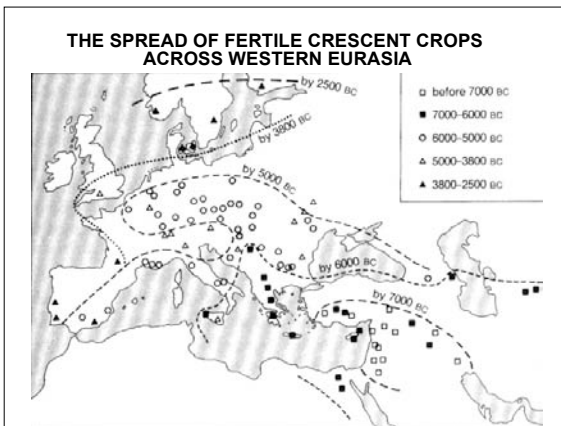
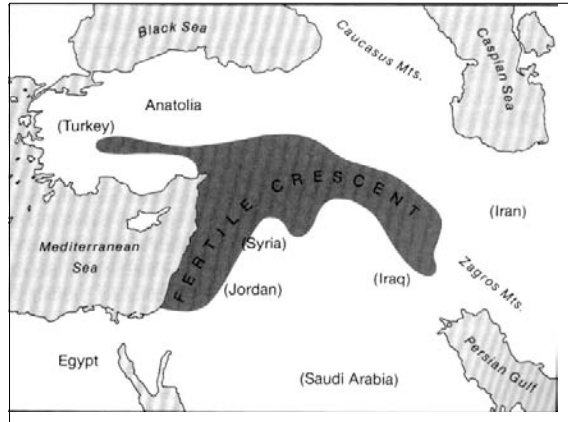
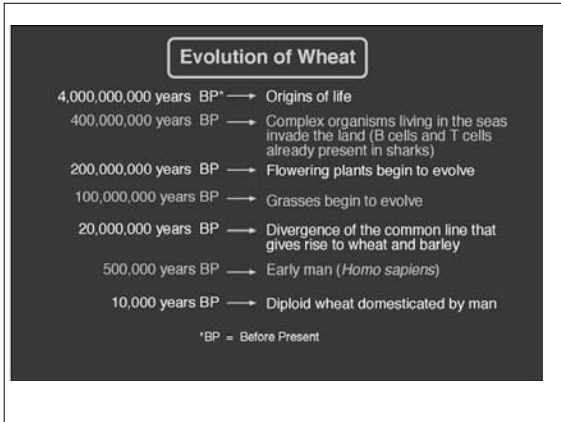
### WHY

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



- ### 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



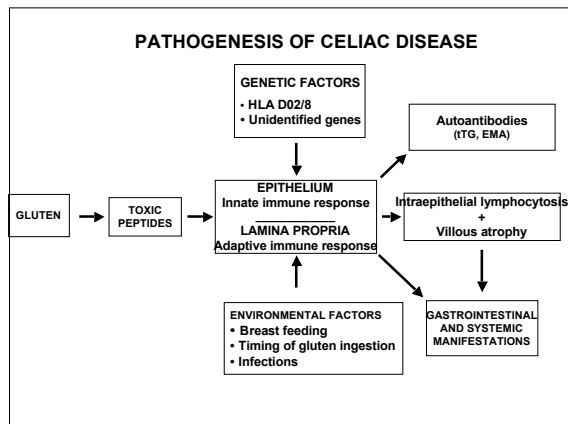
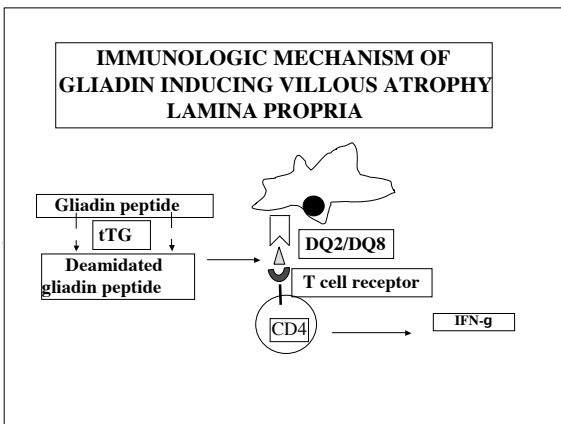


## PATHOPHYSIOLOGY OF CELIAC DISEASE

Gluten has toxic epitopes

Gluten is poorly digested by gastric, duodenal and pancreatic secretions leaving toxic epitopes, especially a 33 mer

Glialin (somehow) enters the mucosa

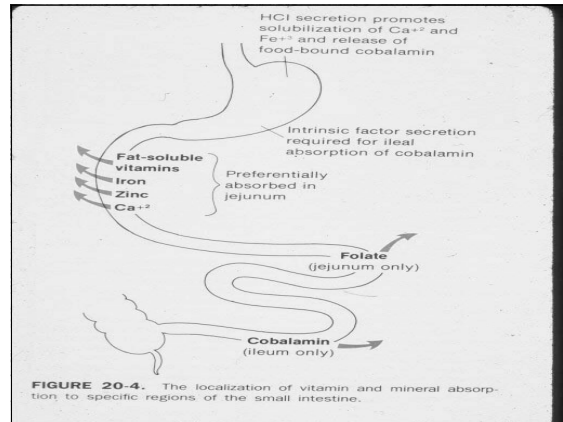


## CELIAC DISEASE

Traditionally a pediatric disease

Originally Dickie described the association with wheat ingestion after WW II

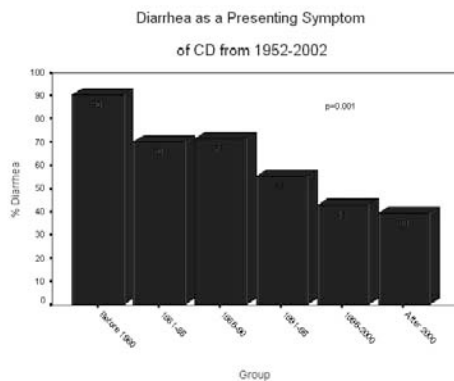
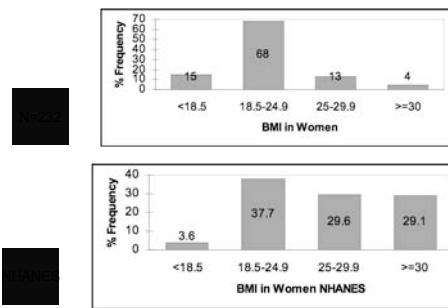
Classical presentation is with steatorrhea, malabsorption and weight loss



## CLINICAL PRESENTATION OF CELIAC DISEASE

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

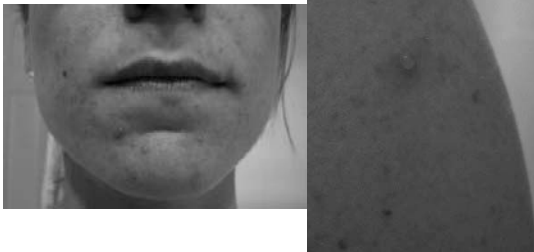
## BMI (WOMEN) CELIAC DISEASE Vs US NATIONAL DATA



## SILENT CELIAC DISEASE NON-DIARRHEAL PRESENTATIONS

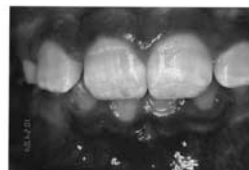
- Incidental at endoscopy
  - Iron deficiency anemia
  - Osteoporosis
  - Screening
    1. relatives
    2. other groups (TI DM, Down syndrome, PBC)
- NOT ALL ARE ASYMPTOMATIC
- Others - neurological presentations

DERMATITIS HERPETIFORMIS



## LESS COMMON PRESENTATIONS OF SILENT CELIAC DISEASE

- Oral presentations
  - Dental enamel defects
  - Apthous ulceration



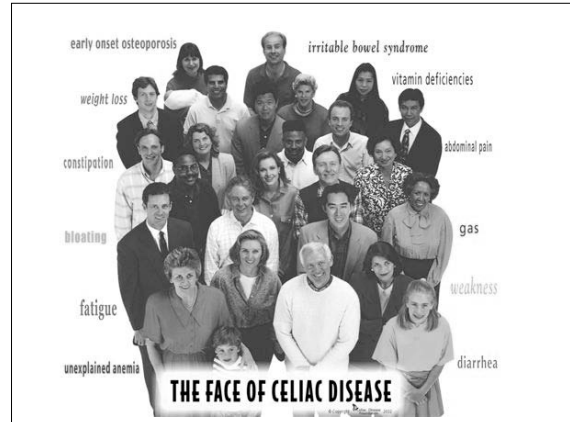
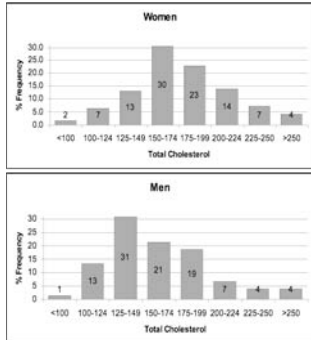
Celiac children 22.7% (61/268) vs 7.1% (4/570)  
( $p=0.0001$ , OR 4.3, 95% CI 2.7-6.7)  
7.1% (33/46) reported significant improvement on  
gluten-free diet. ( $p=0.0003$ )

## 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)



### 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

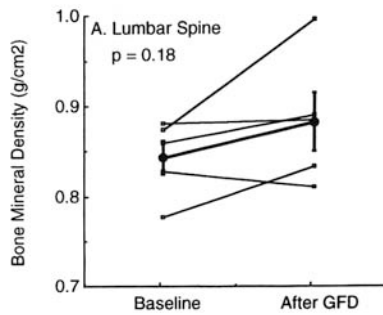
WHAT IS RESPONSIBLE FOR THE VARIED CLINICAL SPECTRUM IN CELIAC DISEASE?



AUTO-IMMUNE DISEASES  
 LIVER DISEASE  
 MALIGNANCIES  
 REDUCED BONE DENSITY  
 INFERTILITY  
 NEUROLOGICAL DISEASES  
 CARDIOMYOPATHY

MECANISM OF BONE DISEASE

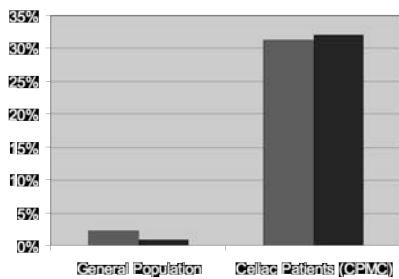
- Malabsorption of calcium and vitamin D
- Secondary hyperparathyroidism
- Failure to obtain maximum bone density
- Magnesium deficiency
- Circulating cytokines
- Auto-immune
- Premature menopause
- Reduced gonadal function in men
- Primary hyperparathyroidism



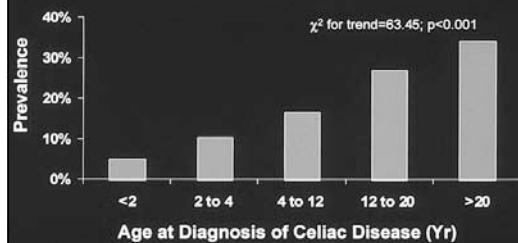
AUTOIMMUNE DISEASES

- 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)



Prevalence of Autoimmune Disease in Celiac Disease





## 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
- Green, Am J Med. 2003;115:191.*
- Papillary thyroid cancer 23X

## MANAGEMENT

### GLUTEN-FREE DIET

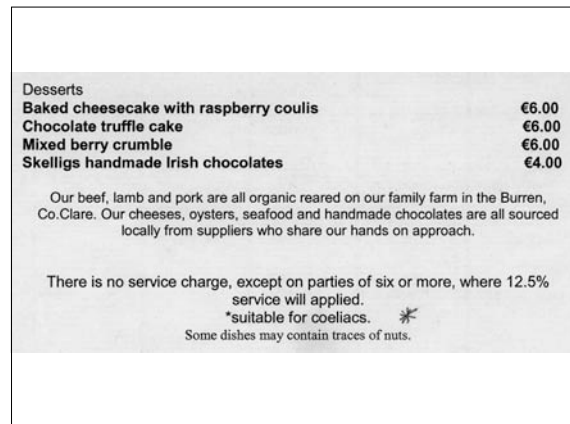
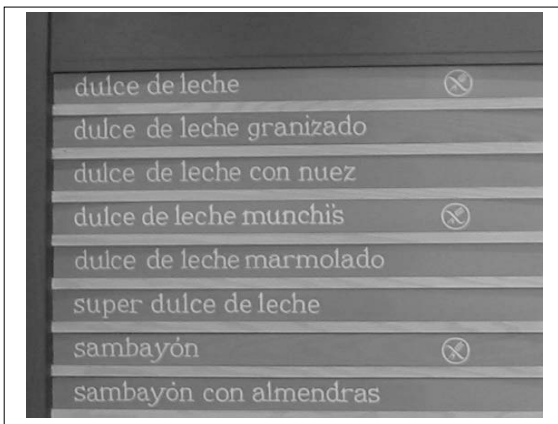
**Sources** Local support groups  
National support groups

**Dietitian**

**Internet**

**Pitfalls** restaurant foods, prepared foods,  
fast foods, communion wafers,  
medications

**DON'T ABANDON THE PATIENT!**



## FUTURE

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