Epidemiology
Epidemiology

The “old” Celiac Disease Epidemiology:

• A rare disorder typical of infancy
• Wide incidence fluctuates in space (1/400 Ireland to 1/10000 Denmark) and in time
• A disease of essentially European origin
Celiac Disease in London, Year 1938
The Changing Celiac Epidemiology

The availability of sensitive serological markers made it possible to discover Celiac Disease even when the clinical suspicion was low.

<table>
<thead>
<tr>
<th>Year</th>
<th>AGA</th>
<th>EMA</th>
<th>TTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td></td>
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</tbody>
</table>
“Mines” of Celiac Disease Were Found Among:

- Relatives
  - Patients with short stature, anaemia, fatigue, hypertransaminasemia
  - Associated diseases: autoimmune disorders, Down’s, IgA deficiency, neuropathies, osteoporosis, infertility

- “Healthy” groups: blood donors, students, general population
The First Picture of the Celiac Iceberg

Coeliac disease in the year 2000: exploring the iceberg

C Catassi, I M Rizzello, E Fabiani, M Rassau, P Borricchia, F Candela, G V Doppia, P I Giorgi

Summary
It is now generally believed that coeliac disease is common in the general population. In our unselected screening for this disorder in a school population in central Italy, screening was divided into three levels: first, IgA and IgG antigliadin antibody (AGA) assay on capillary blood returned by finger prick; second, AGA plus IgA antiendomysium antibody (AEA) test and measurement of serum immunoglobulin concentrations; and third, intestinal biopsy. Of the 7855 students (66% of the eligible population, aged 11–15 years, and attending one school) screened, 31 (2%) were selected because of AGA positivity. Of these subjects, 18 were selected to undergo second-level screening and undergo intestinal biopsy. Coeliac disease was diagnosed in 11 subjects, most of whom had no serious symptoms. Selective IgA deficiency was found in 4 subjects. Of those who had coeliac disease, the prevalence of subclinical coeliac disease in the study group was 3.9 per 1000.

Coeliac disease screening is feasible and involves only slight discomfort in the general population. Second-level screening can detect large numbers of cases of coeliac disease, which can be treated with a gluten-free diet. Many subclinical cases of coeliac disease would not be detected by screening only a selected group of at-risk patients.

Introduction
It has become apparent over the past few years that clinically manifest cases of coeliac disease represent only a small proportion of the total population with this disorder. There are many patients who are free of major symptoms but who have typical damage to the small intestine on intestinal histology (clinical or "silent" coeliac disease). These patients are not treated. They risk complications such as anaemia, infertility, and malignancy disorders; they may die prematurely. Early dietary management of these complications seems to protect coeliac disease patients from the development of malignancy disorders.

The serum antigliadin antibody (AGA) assay is a widespread and simple screening test for coeliac disease and is especially informative when AGA of both IgA and IgG classes is measured. We undertook a pilot study on subclinical coeliac disease screening in a general school population. The first step was IgA AGA and IgG AGA assays on blood obtained from finger pricks. Our aim was to characterize and quantify the prevalence of subclinical coeliac disease in the general population.

Patients and methods

CDHNE NASPESAN

6
Celiac Disease Epidemiological Study in USA

Projected number of celiacs in the U.S.A.: 2,115,954
Actual number of known celiacs in the U.S.A.: 40,000
For each known celiac there are 53 undiagnosed patients.

# Celiac Disease Prevalence Data

<table>
<thead>
<tr>
<th>Geographic Area</th>
<th>Prevalence on clinical diagnosis*</th>
<th>Prevalence on screening data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brasil</td>
<td>?</td>
<td>1:400</td>
</tr>
<tr>
<td>Denmark</td>
<td>1:10,000</td>
<td>1:500</td>
</tr>
<tr>
<td>Finland</td>
<td>1:1,000</td>
<td>1:130</td>
</tr>
<tr>
<td>Germany</td>
<td>1:2,300</td>
<td>1:500</td>
</tr>
<tr>
<td>Italy</td>
<td>1:1,000</td>
<td>1:184</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1:4,500</td>
<td>1:198</td>
</tr>
<tr>
<td>Norway</td>
<td>1:675</td>
<td>1:250</td>
</tr>
<tr>
<td>Sahara</td>
<td>?</td>
<td>1:70</td>
</tr>
<tr>
<td>Slovenia</td>
<td>?</td>
<td>1:550</td>
</tr>
<tr>
<td>Sweden</td>
<td>1:330</td>
<td>1:190</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1:300</td>
<td>1:112</td>
</tr>
<tr>
<td>USA</td>
<td>1:10,000</td>
<td>1:133</td>
</tr>
<tr>
<td>Worldwide (average)</td>
<td>1:3,345</td>
<td>1:266</td>
</tr>
</tbody>
</table>

*based on classical, clinical presentation

# Celiac Societies Data in Europe and USA
(approximate estimates)

<table>
<thead>
<tr>
<th>Country</th>
<th>Celiac Society members (n)</th>
<th>Population</th>
<th>Frequency of CD membership</th>
</tr>
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<tbody>
<tr>
<td>United Kingdom</td>
<td>48,000</td>
<td>55,500,000</td>
<td>1:1146</td>
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<tr>
<td>Italy</td>
<td>25,000</td>
<td>57,000,000</td>
<td>1:2280</td>
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<tr>
<td>Sweden</td>
<td>18,000</td>
<td>8,700,000</td>
<td>1:483</td>
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<tr>
<td>Germany</td>
<td>15,000</td>
<td>80,000,000</td>
<td>1:5333</td>
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<tr>
<td>Finland</td>
<td>11,000</td>
<td>5,100,000</td>
<td>1:464</td>
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<tr>
<td>Spain</td>
<td>8,000</td>
<td>38,500,000</td>
<td>1:4812</td>
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<td>Norway</td>
<td>6,000</td>
<td>4,300,000</td>
<td>1:716</td>
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<tr>
<td>Netherlands</td>
<td>4,500</td>
<td>15,100,000</td>
<td>1:3355</td>
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<tr>
<td>France</td>
<td>3,700</td>
<td>57,000,000</td>
<td>1:15405</td>
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<td>Belgium</td>
<td>1,800</td>
<td>10,000,000</td>
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<td>Austria</td>
<td>2,400</td>
<td>7,800,000</td>
<td>1:3250</td>
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<tr>
<td>Switzerland</td>
<td>2,300</td>
<td>6,900,000</td>
<td>1:3000</td>
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<td>Ireland</td>
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<td>Denmark</td>
<td>1,100</td>
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<td>Europe</td>
<td>149,200</td>
<td>354,600,000</td>
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<tr>
<td>USA</td>
<td>40,000</td>
<td>281,421,906</td>
<td>1:7035</td>
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Celiac Disease Icebergs

Overall
Diagnosed

Ireland               Italy Netherlands Sweden USA
In Italy the Celiac Case-Finding is Increasingly Efficient

Incidence of CD on 1000 newborns in the March (Middle Italy)
The Size of the Submerged Iceberg is Decreasing in Many Countries Due to Active Case-Finding

Even an intensive policy of Celiac Disease case-finding will leave at least 50% of celiacs without a diagnosis.
Natural History Of Celiac Disease At Glance

- **Genetically predisposed subject**
- **Development of celiac enteropathy**
  - **Clinically overt CD**
  - **Silent CD**
  - **Persistently Silent CD**

**ENVIRONMENTAL TRIGGERS**
- Gluten “load”
- Intestinal infections
- Pregnancy
- Cancer

**THE PROPORTION OF SYMPTOMATIC CASES INCREASES WITH AGE**
Where Have The Aging Celiacs Gone?

CD Prevalence (%)

0.6 0.4 0.2 0.0

0 - 19 20 - 39 40 - 59 > 60

Years
Increased Overall Mortality In Adult Life

Causes of Death in Patients With Celiac Disease in a Population-Based Swedish Cohort

Mortality in patients with coeliac disease and their relatives: a cohort study

Giovanni Canone, Gino Roberto Corazza, Viviana Bigiardi, Silviana Busco, Carolina Ciaud, Maria Cotone, Corin Sergio Guglielmi, Paolo Ciofi, Pietro Casori, Maria Antonietta Prati, Silvio Luperto, Umberto Iona, Antonio Castoro, Maria Certo, for the CDHM and Tertiary Study Group
Risk Factors

The Grains

The Genes

HLA DR3 Frequency (%)
Spreading of Agriculture and Celiac Disease

1. Cereals domestication started 10,000 years ago in the Fertile Crescent...

2. Catalhuyuc, The first town in the world was built 9,000 y ago

3. Catalhöyük, Excavations of a Neolithic Anatolian Neolithic

4. CD genes confer disadvantage in areas of high cereal consumption

INVERSE RELATIONSHIP BETWEEN CD FREQUENCY AND LENGTH OF TIME SINCE THE INTRODUCTION OF AGRICULTURE?
Celiac Disease in the Saharawis

• 1:18 children are affected with Celiac Disease
• Diarrhea, stunting, anemia
• EMA pos, typical jejunal damage
• High frequency of DR3/DR3 and DR3/DR4
• High mortality (especially in summer)
Celiac Disease in Iran

• The prevalence of Celiac Disease among 2000 Iranian blood donors is one of the highest in the world (1:166).
• Celiac Disease is a common finding among patients labelled as irritable bowel syndrome (11%).
• The theory on the East-West increasing gradient of Celiac Disease prevalence does not hold.
Celiac Disease in India

- Common cause of chronic diarrhea both in children and in adults
- Long diagnostic delay
- “Hypertypical” clinical presentation
- Strong association with DQ2 heterodimer and with DR3 Asian haplotypes (A26-B8-DR3)
Celiac Disease in Developing Countries

- Worldwide circulation of gluten-containing food could cause epidemics of Celiac Disease
- Largely underestimated (e.g. along the “silk road”)
- Typical symptoms and stunting (nutritional dwarfism)
- Celiac Disease serological markers still reliable
- Formidable treatment difficulties
The Global Village of Celiac Disease

- In many areas of the world Celiac Disease is one of the commonest, lifelong disorders affecting around 1% of the general population.
- Most cases escape diagnosis and are exposed to the risk of complications.
- Active Celiac Disease case-finding is needed but mass screening should be considered.
- The impact of Celiac Disease in the developing world needs further evaluation.