Prevention of Celiac Disease

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Prevention of celiac disease

- **Primary:** Prevent disease occurrence
- **Secondary:** Early diagnosis
- **Tertiary:** Avoid complications
3y prevention
optimize dietary treatment

CAUSES
TRASGRESSIONS (VOLUNTARY or INADVERTENT)
GLUTEN TRACES

POSSIBLE CONSEQUENCES
OSTEOPOROSIS
REFRACTORY CD
EATL

INTERVENTION
NUTRITIONAL EDUCATION
IMPROVE FOOD PROCESSING AND LABELLING
CD PATIENTS ARE A VULNERABLE GROUP

Lanzini et al, 2009

Bar chart:
- Normalization Responsive: (8%)
- Remission: (65%)
- No change: (26%)
- Deterioration: (1%)

Lanzini et al, 2009
### 2y prevention: early diagnosis
Mass screening vs Case-finding

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<th>Pros</th>
<th>Cons</th>
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<td><strong>MS</strong></td>
<td>• Very sensitive</td>
<td>• The burden of treatment can be heavier than benefits in a proportion of cases</td>
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<td>• Could impact CD-related morbidity and mortality</td>
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<td><strong>CF</strong></td>
<td>• Ethically sound</td>
<td>• At least 50 % of cases remain undiagnosed</td>
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<td>• Cheap</td>
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<td>• Efficient</td>
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Even by intensive case-finding the celiac iceberg remains hidden.
CD primary prevention
Environmental factors are responsible for short-term CD prevalence changes

Catassi C et al, Ann Med 2010
The Swedish epidemics of CD

Olsson et al, Pediatrics 2009
Components of environmental pressure on CD

- Quantity and quality of ingested gluten
- Dough fermentation
- Nutrition during the first year of life
- Intestinal infection
- Intestinal microbioma/metaboloma
Proof of Concept of Microbiome-Metabolome Analysis and Delayed Gluten Exposure on Celiac Disease Autoimmunity in Genetically At-Risk Infants

Maria Sellitto, Guoyun Bai, Gloria Serena, W. Florian Fricke, Craig Sturgeon, Pawel Gajer, James R. White, Sara S. Koenig, Joyce Sakamoto, Dustin Boothe, Rachel Gicquelais, Deborah Kryszak, Elaine Puppa, Carlo Catassi, Jacques Ravel, Alessio Fasano

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Controls

CD at-risk babies
Components of environmental pressure on CD

- Quantity and quality of ingested gluten
- Dough fermentation
- Nutrition during the first year of life
- Intestinal infection
- Intestinal microbioma/metaboloma
Breast feeding has a primary preventive role on CD development

Akobeng et al, Arch Dis Child 2005
When the first gluten?

- ESPGHAN suggests gluten introduction at 6 months.
- Could small amount of gluten (100 mg/day) between 4 and 6 months induce tolerance to gluten (PreventCD study)?
- Could delayed gluten introduction reduce the risk of gluten sensitization due to development of intestinal barrier?
729 infants at familial risk of CD
*Enrolment from 2003 to 2009 in 20 Italian centers*

**Group A**
- Gluten introduction at 4-6 months
- GFD from 0 to 4 – 6 months

**Group B**
- Gluten introduction at 12 months

12 months: diet with gluten

Positive for serology:
- a) TTG > 20 U.I. and EMA pos;
- b) AGA IgG in IgA deficit;
- c) AGA IgA and IgG in <2 yrs

HLA-DQ2/DQ8 + IgA tot
AGA, EMA and TTG at 15 months

AGA, EMA, and TTG at 24 and 36 months and 5 years
The study-group

1. 729 infants [365 F (50%)]

2. 397 enrolled in group A (54.5%) and 332 in group B (45.5%)

3. Type of kinship:
   a) Sibling 58.2%
   b) Mother 39.5%
   c) Father 8%
   d) Two relatives 8.1%

4. Gluten consumption at 15m:
   a) >6 gr/die 95.1%
   b) 3-6 gr/die 4.1%
   c) <3 gr/die 0.8%
The Italian Baby Study: development of CD autoimmunity at 0-3 yrs
Potential vs overt CD

Percentage of CD

101 positives (5 refused biopsy), 96 had the procedure

F 13 (50%); median age 2.1 years (range 1-5)
14 Marsh 0, 10 Marsh 1
23 TTG and EMA pos (1 a-DPG IgG pos)

All but one symptomless
Normal nutritional parameters
No other autoimmune diseases

23 out of 24 children with potential CD became antibody negative after a 2-years follow up

Lionetti et al, submitted
Decision tree analysis of factors associated with potential (instead than overt) CD development

- Symptoms at diagnosis
  - Asymptomatic
  - Typical or Atypical

- tTG Level
  - ≤ 11 x
  - > 11 x
    - Age at diagnosis
      - ≤ 24 months
        - Potential CD (22/6)
      - > 24 months
        - Overt CD (15/2)

- tTG level
  - ≤ 4.5 x
  - > 4.5 x
    - Breastfeeding duration
      - ≤ 8 months
        - Overt CD (5/2)
      - > 8 months
        - Potential CD (3/0)

Lionetti et al 2012 (submitted)
Prevention of Celiac Disease
Take home messages

• Secondary and tertiary prevention strategies may reduce the burden of CD-associated complications and mortality
• The role of the environmental component of CD is complex and still poorly understood
• Promotion of prolonged breast feeding is currently the most effective measure for reducing the CD risk
• The game of tolerance/intolerance to gluten is largely played during the first three years of life
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