

Monitoring and Managing Celiac Disease



Presented by B Kerzner

What we know

- Trigger



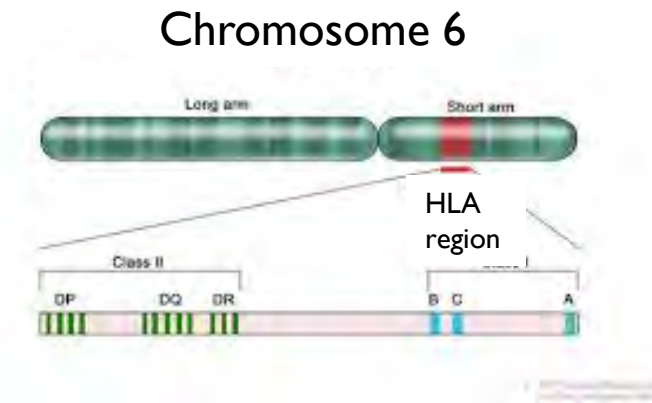
Willen-Karel Dicke 1952

What we know

- Trigger
- Prevalence
 - US - 1% (overall)
 - Finland - 2%
 - Sahrawis on African West Coast - 5.6%
 - Incidence is rising

What we know

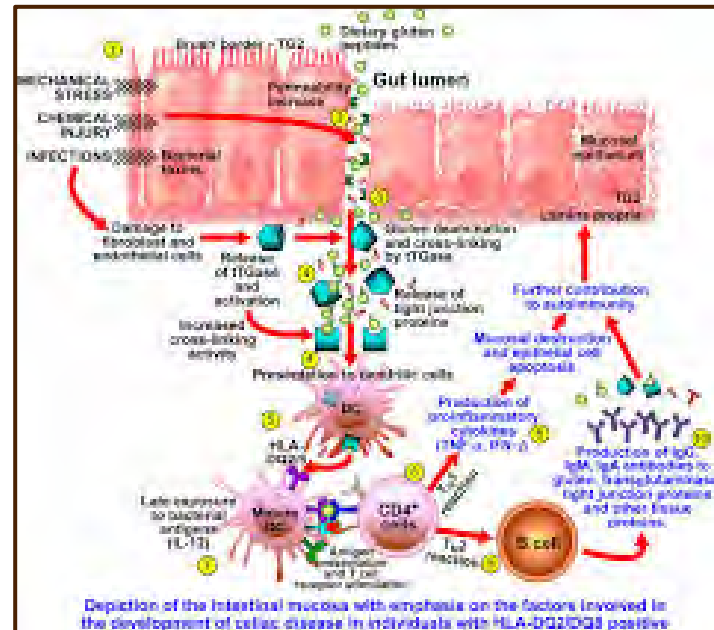
- Trigger
- Prevalence
- **Genetics**



HLA-DQ2 and 8 bind gluten peptide fragments more strongly and can trigger an immune response more readily

What we know

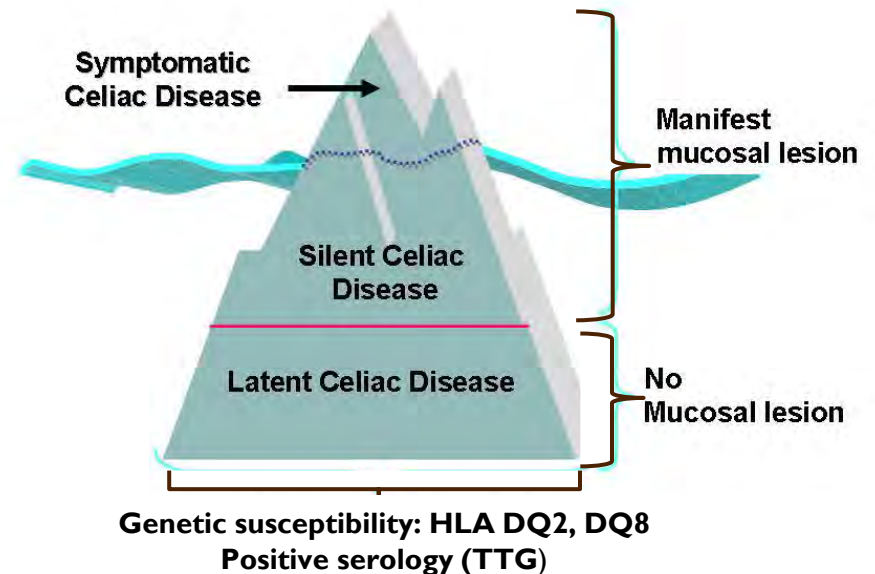
- Trigger
- Prevalence
- Genetics
- Immune mechanism



What we know

- Trigger
- Prevalence
- Genetics
- Immune mechanism
- **Diagnostic criteria**

The Celiac Iceberg



What we know

- Trigger
- Prevalence
- Genetics
- Immune mechanism
- Diagnostic criteria
- **However, we had no uniform approach to monitoring**

***Therefore a
Best Practices Conference of Experts
Funded by our Celiac Program
Directed by Dr. Snyder was undertaken***



PEDIATRICS

August 2016

Evidence-Informed Expert Recommendations for the Management of Celiac Disease in Children

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Alessio Fasano, Stefano Guandalini, Edwin Liu,
Kimberly P. Newton*

Method for reaching consensus regarding a 'Best Practice'

	Apply at the initial evaluation	Apply at subsequent evaluation(s)	Grade* of Evidence	Strength** of Statement
Routinely draw initial total IgA and IgA anti-TG antibody	Yes or No Yes	Yes or No -	High, Moderate, Low, or Very low High	Strong or Weak Strong

* **Grade** refers to the quality of the evidence

- noting that double blind control studies are strongest,
- case reports the weakest


** **Strength** relates to the balance between

- benefits versus harm



Methodology used to evolve the “Best Practices”

- Six acknowledged experts for six areas of interest
 1. Bone disease
 2. Endocrine problems,
 3. Hematologic issues,
 4. Liver issues,
 5. Nutritional problems,
 6. Tests to Diagnose and Monitor CD
- Review thoroughly related literature
 - 600 original articles, 172 included
- Established options for optimal management
- Anonymous vote to adopt these “Best Practices”.



Consensus on Best Practices for Testing

Summary of testing to diagnose and manage CD

IgA-anti Tissue Transglutaminase

- Drawn at first visit for diagnosis
 - *Highly recommended and strongly supported*
- Subsequently to monitor compliance
 - *Recommended but efficacy has not been very convincingly confirmed by concurrent biopsy evaluation*
- Can be misleading
 - Cant definitively exclude CD
 - *~ 10% of CD have a negative IgA-tTG in some studies*
 - False +ves are possible
 - *with other autoimmune diseases e.g. T1DM and Immune hepatitis*
 - Laboratory techniques are not standardized


Background - Testing and Monitoring - Serology



It's a simple stress test – I send your blood to different labs and get back very different results

Summary of testing to diagnose and manage CD

- Anti Endomysial antibodies –
 - More specific and less sensitive
 - Indicated when other autoimmune phenomena could cause a false positive Anti TTG
- HLA typing
 - Strongly recommended for diagnostic dilemmas
 - Notably those on GFD without a prior biopsy
 - Patients at risk for CD who have negative serology

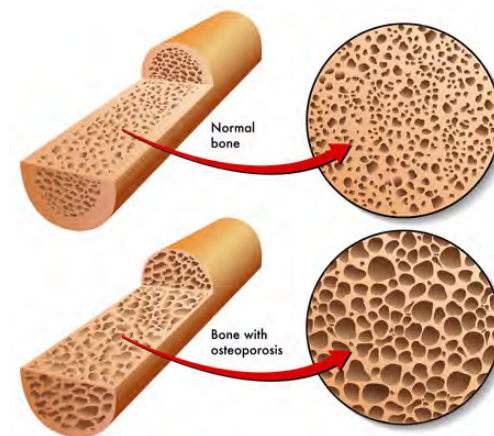


Consensus on Best Practice for Bone Health

Bone Health Information

- Findings

- Bone pain and Tetany
- Growth failure
- Fractures with minimal trauma
- Rickets
- Osteoporosis



- Rare at presentation except ↓ bone density by DEXA
- A Gluten Free Diet rapidly restores bone mass in young children and some adolescents.
- Most of the bone symptoms relate to bone density

Proposed Best Practice for Bone Health

Should bone density imaging to evaluate bone health be done routinely for all children and adolescents with CD when they are seen at 1-year follow-up?

The answer is **No**

- *Discussion*
 - *Young children (short duration) recover rapidly and completely*
 - *Repeat studies - not required or cost-effective.*
 - *Adolescents - more data needed.*
 - *Abnormal bone density is likely and test of choice with:
severe malabsorption
prolonged delay in diagnosis
presentations with bone pain and fractures*
 - *If abnormal, follow-up every 1-2 yrs until normal especially in adolescents with slower recovery and difficult diet compliance*

Best Practice for Bone Health

Bone density studies should be done routinely for selected patients who do not adhere to a GFD

The answer is **Yes**

Discussion

- *Maximum bone density is accrued in adolescence, late teens and early adulthood when adherence to a GFD is most difficult.*
- *Reduction of bone density can then increase fracture risk and early onset of osteoporosis.*
- *If bone density abnormalities are identified, healthcare providers can*
 - explain the increased risk of bone disease*
 - provide dietary counseling.*


Best practices for bone health

Strongly recommended

- Dietitian counseling:
supplemental Ca and Vit D (take geographic location into account)
at diagnosis and follow-up
- Assess bone density:
if not following the gluten-free diet

Weaker recommendations

- Vit D at diagnosis and follow-up if previously abnormal.
- Routine screening for bone health if
 - severe malabsorption
 - prolonged delay in diagnosis
 - overt bone disease symptoms at diagnosisFollow-up at one year if previously abnormal.
- Bone density at one year if previously abnormal.



Consensus on Best Practices for Endocrine Conditions

Background on Endocrine Associated Disorders

- Frequently associated d/t shared genetic predisposition (HLA and non-HLA) to autoimmune phenomena
 - Autoimmune thyroid disease - 7%
 - Type 1 diabetes mellitus (T1DM) - 3 to 12%
 - Addison disease - rare
 - Parathyroid disorders - rare
 - Growth hormone deficiency - rare
- Pediatric GI societies recommend that in:
 - Pts with T1DM and
 - Autoimmune Thyroid disease } screen for CD but not the reverse

Proposed 'best practices' for Diabetes

1. Routine counseling regarding the risk and clinical features of Diabetes

Answer is **Yes**

- *Recommendation based on the limited risk of counseling.*
- *Evidence for the effectiveness of counseling on preventing morbidity or mortality is not available*

2. Routine screening for Type I Diabetes with islet cell auto-antibodies

Answer is **No**

- *Insufficient data to establish risk of diabetes*
- *No preventative strategies exist*

Proposed 'best practices' for Thyroid disease

1. Routine screening at diagnosis (TSH) - **YES**


- *Increased risk of autoimmune thyroiditis, especially Hashimoto's*
- *TSH levels are accurate and widely available*
- *Effective therapies for thyroid disease are available.*

2. Routine screening at follow up (TSH) - **YES**

- Thyroid disease is a coexisting condition
- Prevalence of thyroid disease has not been determined

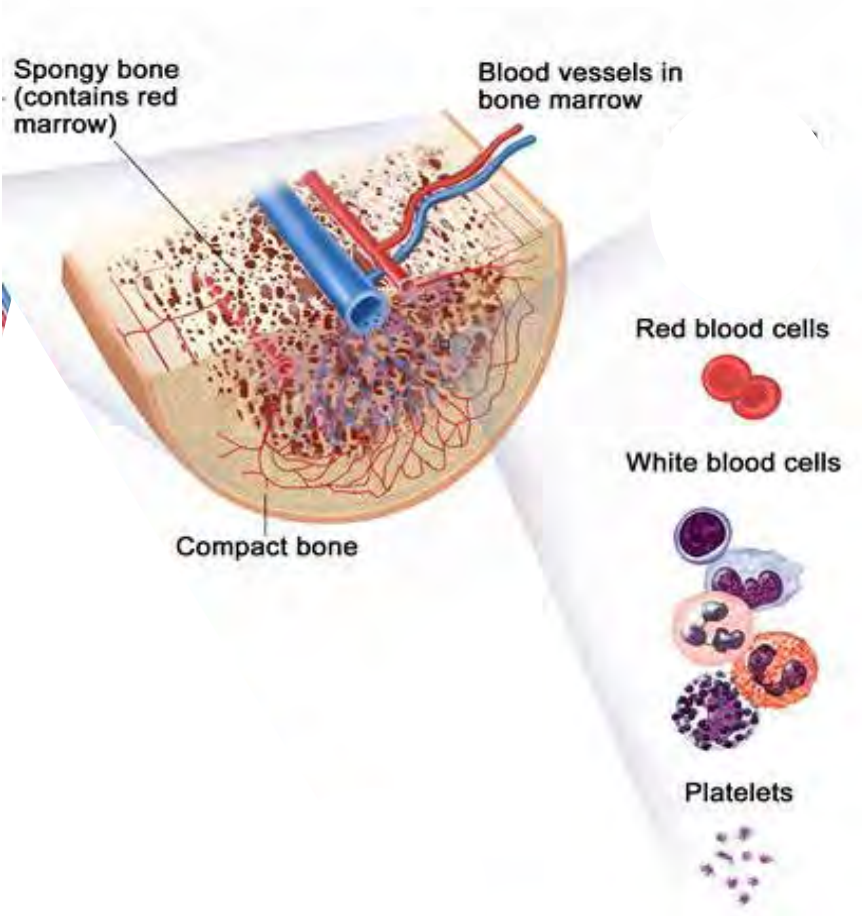
3. Screening thyroid with anti-thyroid antibodies - **NO**

- Natural history of thyroid autoimmunity and relationship to the development of clinical thyroid disease has not been determined



Consensus on Best Practices for Hematologic Issues

Described effects



Anemia

Iron

Folate

Vitamin B12

Vitamin B6

Chronic illness

Hypersplenism

Iron deficiency

- By far the most

**Less common
Suspected in
advanced cases.**

Immune issues

IgA


Vaccination (Hep B antibody)

Coagulation

Bleeding and Bruising

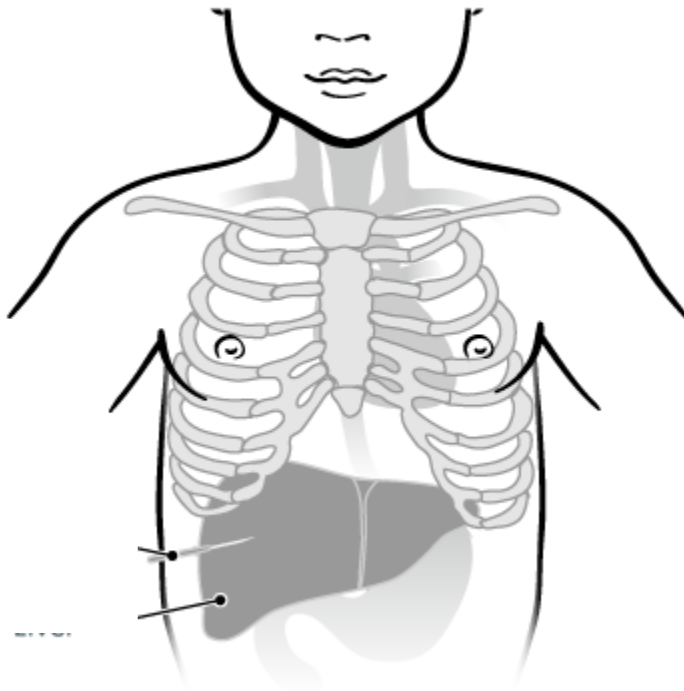
Three best practices were put to the vote

- Routine initial screen for anemia (CBC, Ferritin, Iron, TIBC) was strongly recommended.
 - *Anemia is very common and iron deficiency may precede it.*
- Routine follow up CBC is recommended
 - *Evidence for it is less well supported*
- Routine folate measurement was not supported
 - *Deficiency of it and other hematinics is described but should correct with a Gluten Free Diet, routine vitamin supplementation and an appropriate nutritious diet*



Consensus on Best Practice for Liver Issues

Consensus on Best Practices for Liver Issues

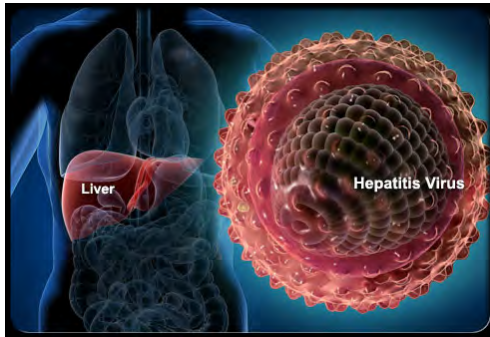


- Transaminitis is a frequent occurrence
- Injury is generally mild and reversible
- If not, be aware of Autoimmune liver disease

Best practice strongly recommended:
Routine screening for ALT and AST.
Track it to ensure it resolves

Consensus on Best Practice for Liver Issues

- 30% to 70% of patients with Celiac disease are nonresponsive to hepatitis B vaccine before treatment



Best practice fairly strongly recommended:
Screen for hepatitis B immunization
status at initial encounter and repeat
if after a booster on a GFD

Consensus on Best Practice for Nutrition Issues





Background on Nutrition Associated Problems

- The only treatment is a strict GFD
- Problems preceding diagnosis are replaced by those of the diet
- Close monitoring of growth in response to the diet is essential

Best Practices for Nutrition

Two are strongly endorsed

1. Routine assessment of anthropometric measures from the outset
2. *Sequential visits with access to an experienced dietitian*

Whereas

3. Routine screening for zinc and other trace elements (besides iron) at the time of diagnosis was positively discouraged.

However

4. *Multivitamins at the time of diagnosis are encouraged despite the supporting literature being relatively weak. The risk benefit ratio is acceptable*



At the first visit

- General counseling
 - Age-appropriate intake of calcium and vitamin D supplementation by a dietitian
- Physical examination
 - Routine assessment of anthropometric measures
- Instruction
 - Routine vitamin supplementation

At the first visit

- Testing

- Routine total quantitative IgA and IgA anti-tTG antibody
- IgA antiendomysial antibody if comorbidities that increase the chance of false-positive IgA tTG antibodies
- HLA typing for children at risk who have negative serology
- HLA typing for patients with diagnostic dilemmas

At the first visit

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- Routine 25-OH vitamin D level
- Ca, PO₄, alk phos etc. and DEXA for overt bone issues

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- Routine 25-OH vitamin D level
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- Routine (CBC, evaluation of mean cell volume, ferritin, iron, total iron-binding capacity)

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- **Routine screening for thyroid disease (TSH)**



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- **Testing**

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- Routine (CBC, evaluation of mean cell volume, ferritin, iron, total iron-binding capacity)
- Routine screening for thyroid disease (TSH)
- **Routine ALT and AST**
- **Screen for hepatitis B virus immunization status**

At Subsequent Visits

- History and Physical examination
 - Routine assessment of anthropometric measures
 - Are there clinical features of celiac disease.
Malaise, nausea, vomiting , distention, diarrhea, constipation
Additional features: anxiety , headaches, poor school performance
- Counseling with access to a dietician
 - Compliance with the GFD
 - Age-appropriate intake of calcium and vitamin D
 - Routine vitamin supplementation

At Subsequent Visits

- Blood work

- Quantitative IgA anti-tTG antibody
- IgA antiendomysial antibody if at risk for false +ve IgA tTG

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• Blood work

- Quantitative IgA anti-tTG antibody
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- Ca, PO₄, alk Phos, 25-OH vitamin D if previously abnormal.
- Bone density – if previously abnormal or not adhering to a GF diet



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- Bone density – if previously abnormal or not adhering to a GF diet
- CBC routinely, and if previously abnormal Zn and other trace elements
- Screen for thyroid disease(TSH)
- ALT and AST if previously abnormal
- Hepatitis B virus immunization status if previously abnormal

Members of our Multidisciplinary Team



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