



Diagnostic Testing Algorithms for Celiac Disease

HOT TOPIC / 2018

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Disclosures

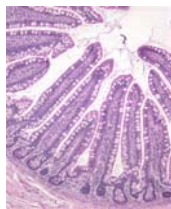
- Member of Strategic Advisory Committee for Inova Diagnostics

Utilization Message

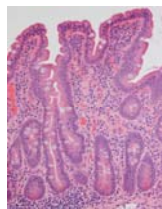
- As you view this presentation, consider the following important points regarding testing:
 - How is the test going to be used in your practice?
 - When should the tests be used?
 - How will results impact patient management?

Introduction to Celiac Disease

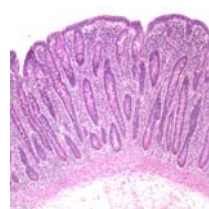
- Chronic inflammatory disease targeting the small intestine
 - Associated with production of autoantibodies
- Pro-inflammatory immune reaction within small intestine leads to damage and atrophy of intestinal villi



Normal small intestine



Partial villous atrophy



Total villous atrophy

Clinical Manifestations of Celiac Disease

- | | | |
|--|--|---|
| <ul style="list-style-type: none"> • Gastrointestinal <ul style="list-style-type: none"> • Diarrhea • Weight loss • Steatorrhea • Abdominal pain • Bloating • Constipation • Nausea | <ul style="list-style-type: none"> • Malabsorption <ul style="list-style-type: none"> • Fe-deficient anemia • B12 deficiency • Folate deficiency • Hypoproteinemia • Hypocalcemia | <ul style="list-style-type: none"> • Extra-GI <ul style="list-style-type: none"> • Ataxia • Infertility • Arthralgias • Dermatitis herpetiformis • Hyposplenism • Other autoimmune conditions |
|--|--|---|

Factors Associated with Development of Celiac Disease

- Genetic component
 - Increased risk for family members
 - Prevalence of 10% in first-degree relatives
 - Known genetic association
 - HLA-DQ2
 - HLA-DQ8
- Environmental component
 - Ingestion of cereal grain proteins
 - Wheat
 - Barley
 - Rye
 - Collectively referred to as gluten


Diagnosis of Celiac Disease

- Initial diagnosis
 - Positive antibody serology
 - Intestinal biopsy with characteristics of villous atrophy
- Definitive diagnosis
 - Resolution of clinical symptoms after initiation of gluten-free diet
 - Generally accompanied by conversion to negative serology and reconstitution of intestinal villi

Diagnosis of Celiac Disease

- Serologic tests
 - Endomysial antibodies
 - Tissue transglutaminase antibodies
 - Gliadin antibodies
 - Unmodified gliadin antigen
 - Deamidated gliadin antigen
- Genetic tests
 - HLA-DQ2 and HLA-DQ8

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- 

Caveats of Serology Testing for Celiac Disease

- Selective IgA deficiency
 - Defined as absence of IgA in presence of normal IgG and IgM production
 - More common in patients with celiac disease compared to general population
 - IgA isotype for celiac-specific serologies more sensitive and specific compared to IgG isotype
- Effect of gluten-free diet
 - Downregulation of inflammatory immune response
 - Reduction in autoantibody production

Caveats of Genetic Testing for Celiac Disease

- | | |
|--|---|
| <ul style="list-style-type: none"> • HLA-DQ2 <ul style="list-style-type: none"> • Present in 90% to 95% of patients with celiac disease | <ul style="list-style-type: none"> • HLA-DQ8 <ul style="list-style-type: none"> • Present in 5% to 10% of patients with celiac disease |
|--|---|

Caveats of Genetic Testing for Celiac Disease

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Combined frequency of 30%-40% in most US and European populations

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**Negative for
HLA-DQ2 and DQ8**
Exclude celiac disease
as a possible diagnosis

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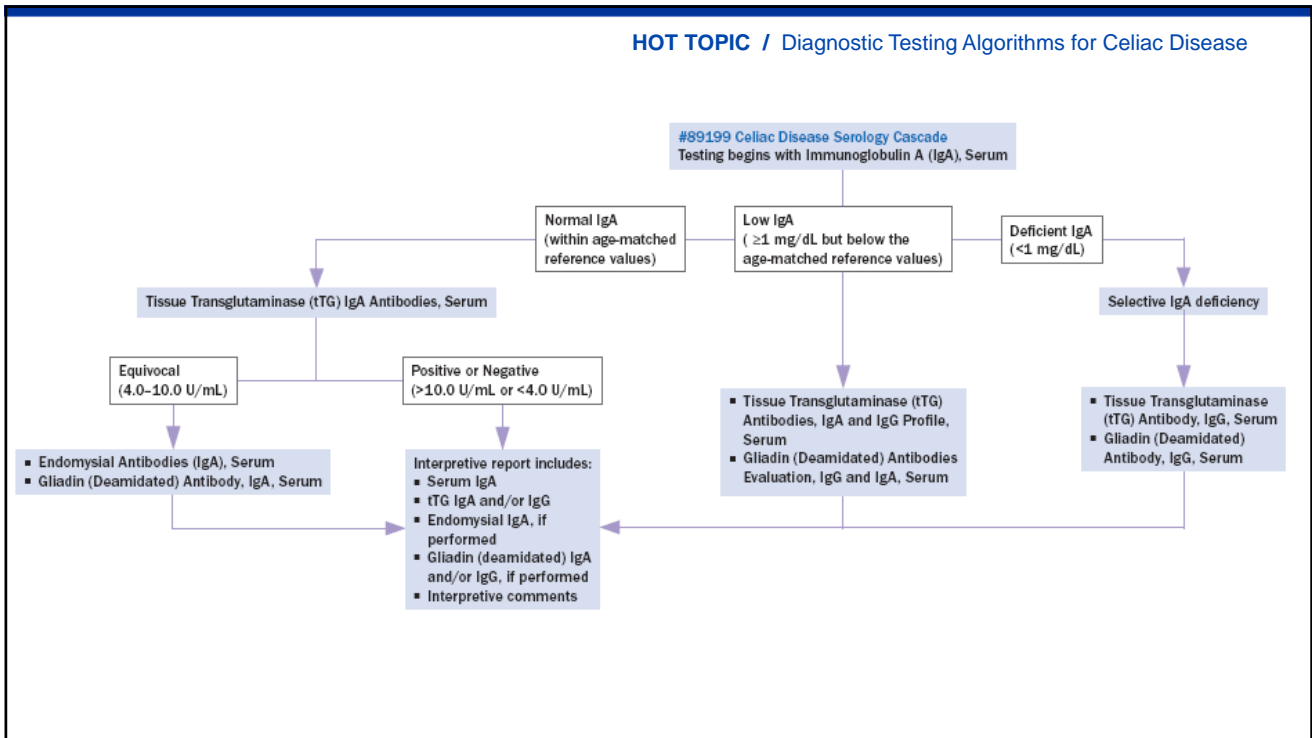
Positive for HLA-DQ2 and/or DQ8
Consistent with possible diagnosis of celiac disease

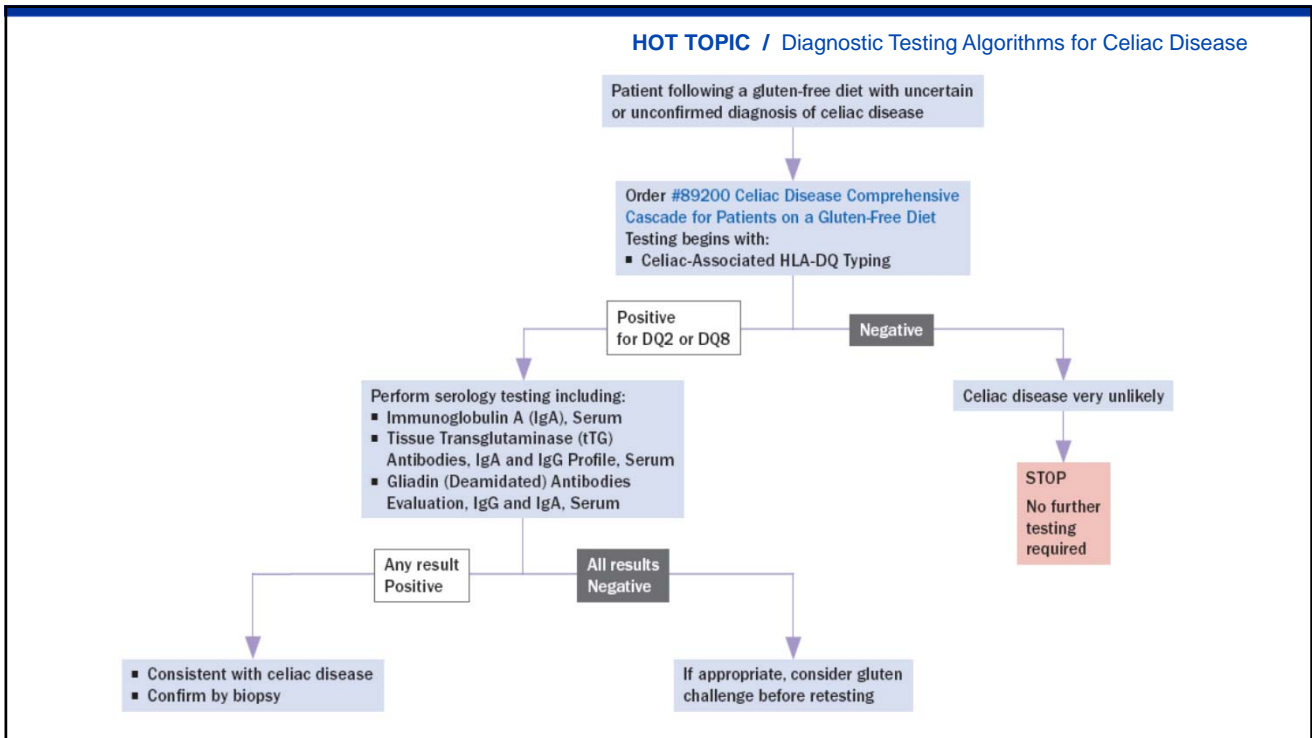
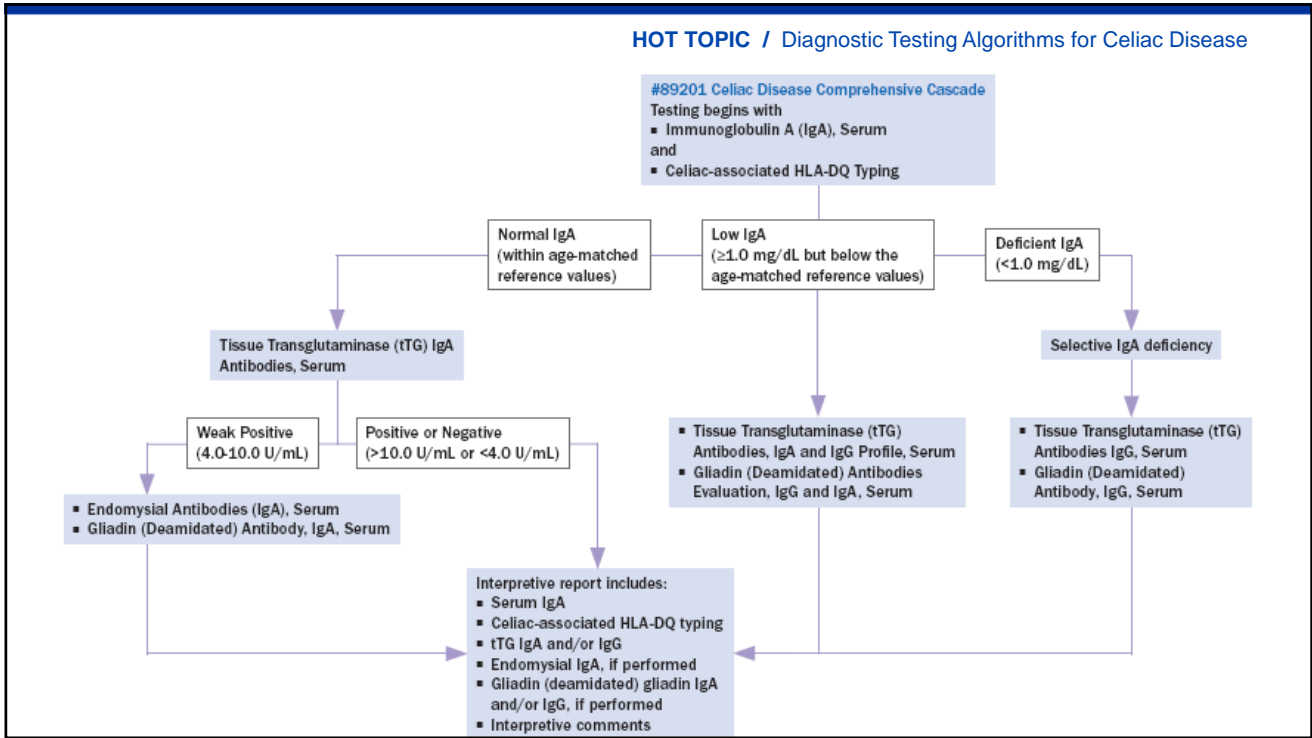
Test Performance and Utility

- TTG and deamidated gliadin IgA
 - Best combination of sensitivity and specificity
- EMA IgA
 - Excellent specificity
 - Analytical challenges
- TTG and deamidated gliadin IgG
 - Most appropriate in context of IgA deficiency
- HLA-DQ2 and HLA-DQ8
 - Useful as rule-out test

Laboratory Testing Algorithms

- Celiac Disease Serology Cascade
 - CDSP
 - Serologic testing only
- Celiac Disease Comprehensive Cascade
 - CDCOM
 - Serologic and genetic testing
- Celiac Disease Comprehensive Cascade for Patients on a Gluten-Free Diet
 - CDGF
 - Perform serology only for individuals with HLA-DQ2 and/or HLA-DQ8 alleles





Summary

- Laboratory diagnostic testing algorithms
 - Celiac Disease Serology Cascade (CDSP)
 - Celiac Disease Comprehensive Cascade (CDCOM)
 - Celiac Disease Comprehensive Cascade for Patients on a Gluten-Free Diet (CDGF)
- Individual test options
 - Most appropriate for monitoring patients on a gluten-free diet

Questions or requests...

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For more information...

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