

## Urticaria-Inducing Activity

Urticaria (hives) typically indicates an immune reaction to an allergen, such as foods, plants, or medications. Urticaria may also appear as a response to physical or emotional stress. The severity of the immune reaction varies, and urticaria is considered chronic if welts remain for longer than 6 weeks and recur often over weeks or months. Identifying the cause of recurrent urticaria may be difficult. Testing helps detect basophil-activating factors by inducing histamine release and CD203c upregulation in serum samples from individuals with suspected chronic urticaria.

## Typical Testing Strategy

Initial testing should rule out more common etiologies for urticaria:

- Complete blood count with eosinophil count
- Examination of stool for ova and parasites if appropriate travel history is present
- Vasculitis evaluation:
  - Antinuclear antibody (ANA), rheumatoid arthritis (RA)
  - Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
  - Skin biopsy may be necessary
- Cryoglobulinemia evaluation:
  - Hepatitis B and C testing
  - Serum cryoglobulin
  - Complement assays: C3, C4, C1-esterase

If initial testing is negative, proceed with:

- Chronic urticaria index testing
- TSH with autoimmune thyroid testing

## Disease Overview

### Prevalence

20% in general population

- Common and complex dermatological condition

### Symptoms

- Defined as hives lasting for >6 weeks
  - Wheal usually lasts for <24 hours
  - Pruritus may be intense
- Pigmentary changes if lesions last longer
- Associated with autoimmune thyroid disease (particularly Hashimoto thyroiditis)

### Pathophysiology

- Basophil activation results in:
  - Release of histamine
  - Upregulation of CD203c, a human basophil-specific lineage marker

## Tests to Consider

### Urticaria-Inducing Activity 2005413

**Method:** Semi-Quantitative Ex Vivo Challenge/Cell Culture/Quantitative Enzyme-Linked Immunosorbent Assay

Determine histamine release in suspected chronic urticaria if urticaria may be due to autoimmune antibodies to the basophil IgE receptor or to IgE

### Urticaria-Induced Basophil Activation 2005416

**Method:** Semi-Quantitative Flow Cytometry

Determine whether CD203c is upregulated in suspected chronic urticaria if urticaria may be due to autoimmune antibodies to the basophil IgE receptor or to IgE

### Urticaria-Inducing Activity with Thyroid Antibodies and Stimulating Hormone 2005415

**Method:** Semi-Quantitative Ex Vivo Challenge/Cell Culture/Quantitative Enzyme-Linked Immunosorbent Assay/Quantitative Chemiluminescent Immunoassay

Screen for possible thyroid autoimmunity in individuals with suspected chronic urticaria

- Pathogenesis of the disease is poorly understood:
  - No evidence for exogenous allergen as cause
  - IgG autoantibodies directed against basophil- or mast cell-associated autoantibodies cause disease in many individuals
  - High-affinity IgE-Fc receptor1: ~40%
  - IgE: ~5%
  - Unknown etiology in remaining

## Test Interpretation

### Results

- Positive: possible presence of basophil stimulating autoantibodies (or other serum factors)
  - Suggests autoimmune basis for urticaria
- Negative: no basophil stimulating autoantibodies detected
- Indeterminate: borderline basophil activation detected
  - May have autoimmune basis for urticaria

### Limitations

- Validated for serum only
- Does not identify specific basophil-stimulating serum factors
  - Factors are most likely antibodies that target the high-affinity IgE-Fc receptor or IgE

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Content Review November 2019 | Last Update May 2020