Urticaria/Hives : Variants, Symptoms and treatment

Urticaria, commonly known as hives, is the most frequent dermatologic disorder characterized by sudden onset of raised, well-circumscribed erythematous (red) and edematous (swollen) plaques or wheals affecting the dermis and epidermis. These lesions are intensely pruritic (itchy).

Classification

- **Acute urticaria:** Duration < 6 weeks
- **Chronic urticaria:** Duration > 6 weeks

Variants of Urticaria

- **Acute IgE-mediated urticaria** (allergic)
- **Chemical-induced (non-IgE-mediated)**
- **Autoimmune urticaria**
- **Cholinergic urticaria** (triggered by heat/sweating)
- **Cold urticaria**
- **Mastocytosis / Urticaria pigmentosa** (mast cell proliferation)
- **Physical urticarias:** pressure, vibration, solar, etc.
- **Periodic fever syndromes:** Muckle-Wells syndrome
- **Others:** adrenergic urticaria, contact urticaria, papular urticaria (insect bites), urticarial vasculitis

Epidemiology and Pathophysiology

- Affects **10–20%** of the population at some point.
- **Mast cells** are central; histamine is the primary mediator causing vasodilation and increased vascular permeability.
- Mast cell activation may be triggered by:
    - IgE-dependent mechanisms
    - Direct non-IgE stimuli (drugs, complement fragments C3a, C5a)
    - Autoantibodies against IgE or its receptor (Fc?RI) in some chronic cases
    - Acetylcholine sensitivity in cholinergic urticaria

Causes

Acute Urticaria

- Often due to **exogenous allergens** or acute infections.
- Food, drugs, insect stings, infections.

Chronic Urticaria

- Mostly **idiopathic (75%)**
- Autoimmune mechanisms in some cases
- Physical triggers (cold, pressure, heat)
- Infections (Helicobacter pylori, Lyme disease)
- Autoimmune diseases (SLE, thyroid disorders)
- Stress
- Rare syndromes (Muckle-Wells, mastocytosis)
- Nutritional deficiencies (iron, B12, folate)

Differential Diagnosis

- Atopic dermatitis (eczema)
- Maculopapular drug eruptions
- Contact dermatitis
- Insect bites
- Erythema multiforme
- Pityriasis rosea
- Urticarial vasculitis (painful, often systemic symptoms)

Diagnosis

- **History and physical examination** are crucial.
- Identification of triggering factors and lesion characteristics.
- **Dermographism** test (stroking skin causes wheal).
- Physical urticaria can be reproduced:
    - **Pressure test**
    - **Ice cube test** for cold urticaria
- Blood tests:
    - CBC, ESR/CRP
    - Thyroid function tests
    - Autoantibodies if autoimmune suspected (ANA, ENA, dsDNA, RhF)
    - Cryoglobulins in cold urticaria
- Skin biopsy if vasculitis suspected.

Treatment

First-line: Antihistamines

- Use **non-sedating H1-antihistamines** at standard or increased doses (up to 4x normal dose if needed).
- Examples: fexofenadine, cetirizine, levocetirizine.
- Acute attacks: short-acting antihistamines like acrivastine may be used.
- H2-blockers (ranitidine, cimetidine) can be added but evidence is limited.

Second-line and Adjunctive Therapies

- **Doxepin:** antidepressant with H1 and H2 blocking properties
- **Ketotifen:** mast cell stabilizer with antihistamine effects

- **Mirtazapine:** useful for sedative and antihistaminic properties
- **Calcium-channel blockers:** stabilize mast cells (nimodipine preferred)
- **Leukotriene antagonists**
- **Colchicine:** for delayed pressure urticaria
- **Immunosuppressants:**
  - Methotrexate
  - Cyclosporine or tacrolimus (reserved for severe cases)
  - Mycophenolate mofetil
- **Others:** terbutaline (?2-agonist), phosphodiesterase inhibitors, pentoxifylline

Special considerations

- **Steroids:** for short-term use only due to side effects; may worsen upon withdrawal
- **High-dose IVIg:** used in resistant cases with variable success
- **Cold urticaria:** antihistamines often ineffective; NSAIDs may help in familial cases

Monitoring and Prognosis

- Chronic urticaria may spontaneously remit after 1–2 years.
- Regularly reassess need for treatment to avoid unnecessary long-term medication.
- Avoid known triggers where possible.