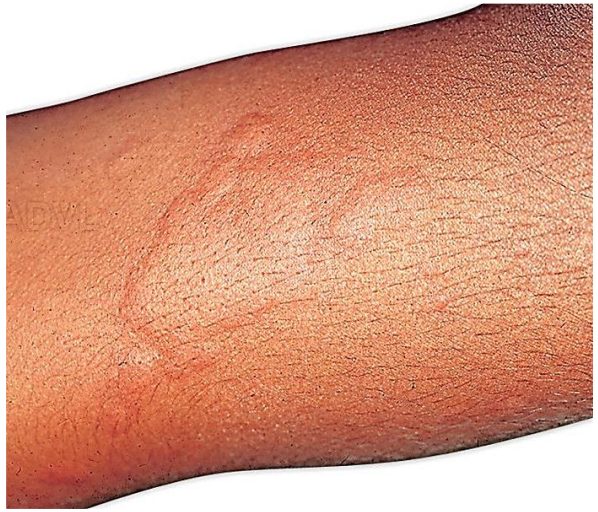
Urticaria

Urticaria

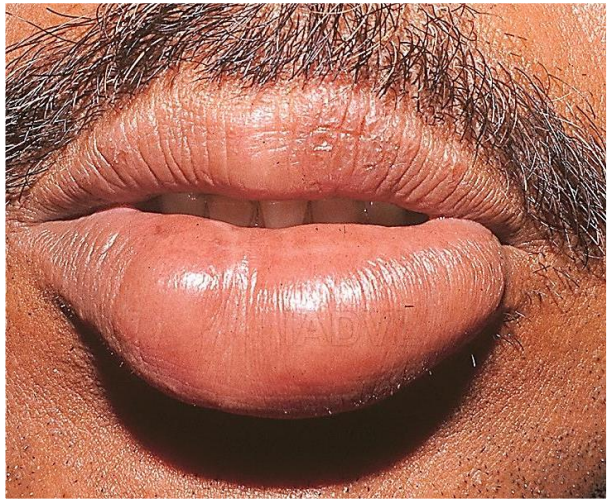
- Urticaria is derived from Latin word “Urtica” meaning stinging nettle.
- It is a cutaneous reaction pattern consisting of transient, dermal swellings in form of **wheals or angioedema**.

Urticaria

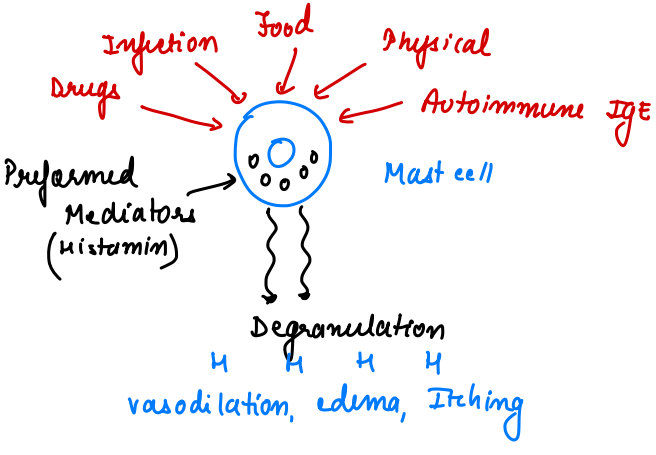
- **Individual wheals are pruritic , pink or pale swellings of superficial dermis that have red flare around them and usually subside within 24 hours.**



Angioedema



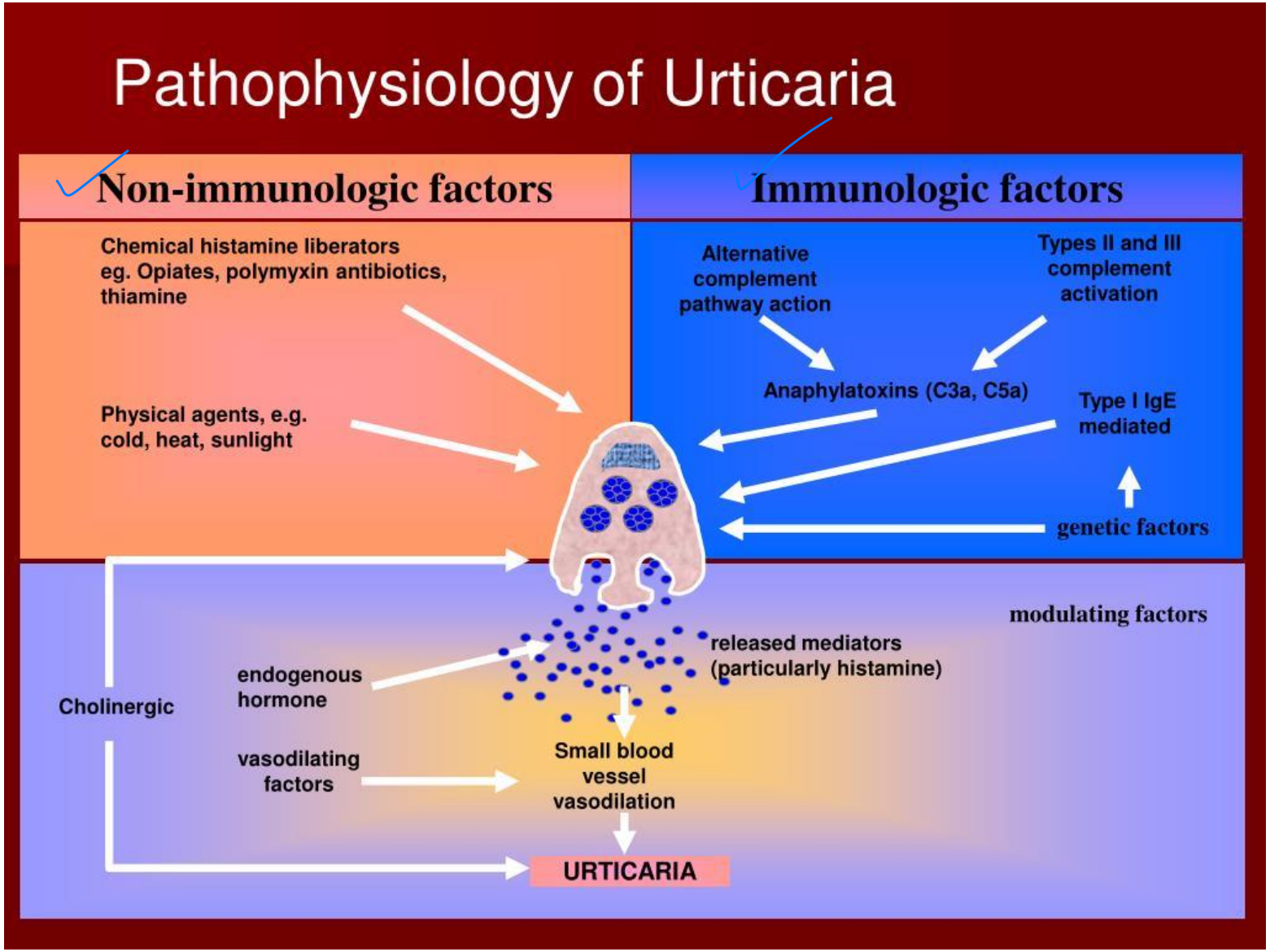
- Deeper
- Less well defined
- Painful rather than itchy
- Less erythematous
- Involves deeper tissues such as hypodermis and submucosa and
- Takes longer than 24 hours to resolve


Infection
Food
Physical
Drugs
Autoimmune IgE
Preformed
Mediators
(Histamin)
Mast cell
Degranulation
H H H H
vasodilation, edema, Itching

Pathogenesis

- For urticaria / angioedema to happen, **vasodilatation and plasma leakage is required**.
- Most commonly, this is brought about by **histamine (usually released by mast cells)**.
- But many other chemicals like **sorbic acid, benzoic acid and bradykinin can also cause it (not released by mast cells)**.

Pathophysiology of Urticaria



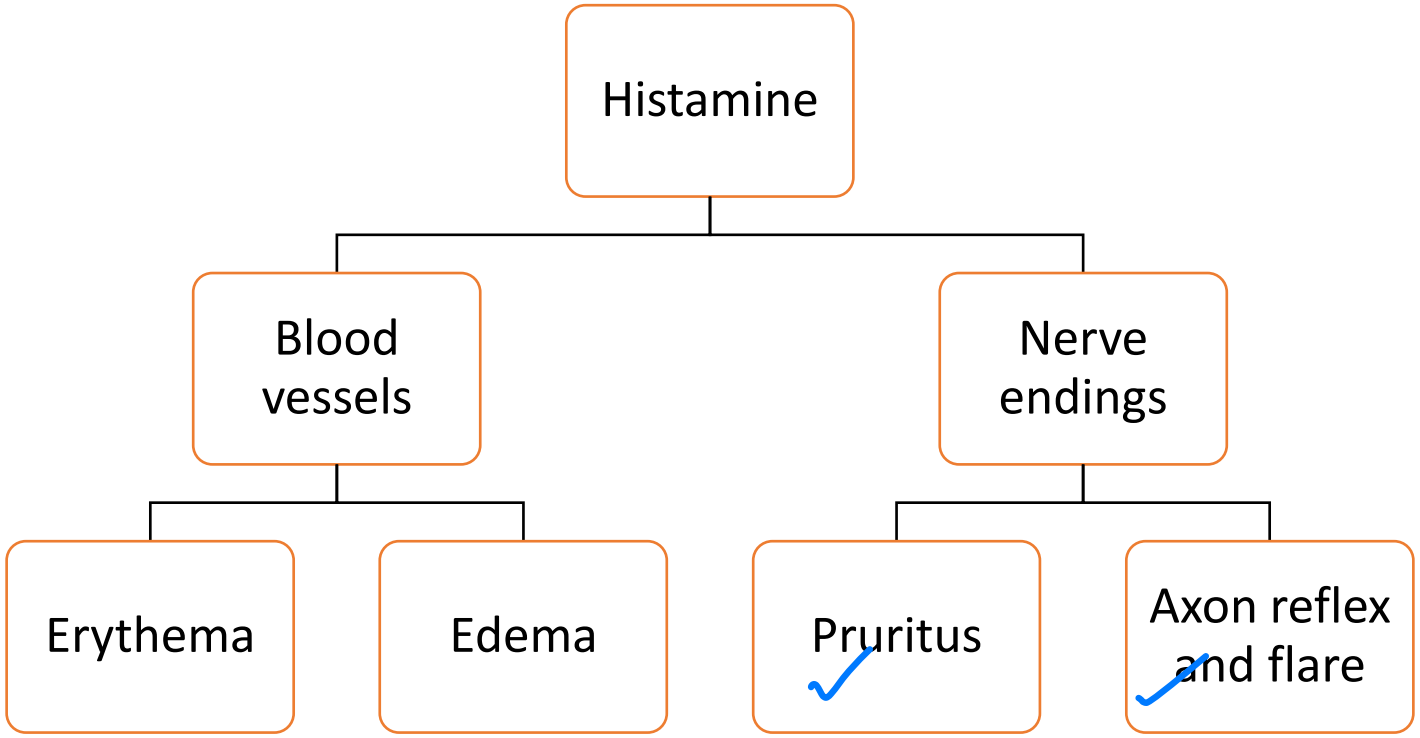
Mediators released by human dermal mast cell degranulation

Preformed mediators

- Histamine
- Heparin
- Proteases like tryptase

New synthesis of mediators

- Prostaglandin D2
- Leukotrienes C4, D4, E4
- Platelet activating factor



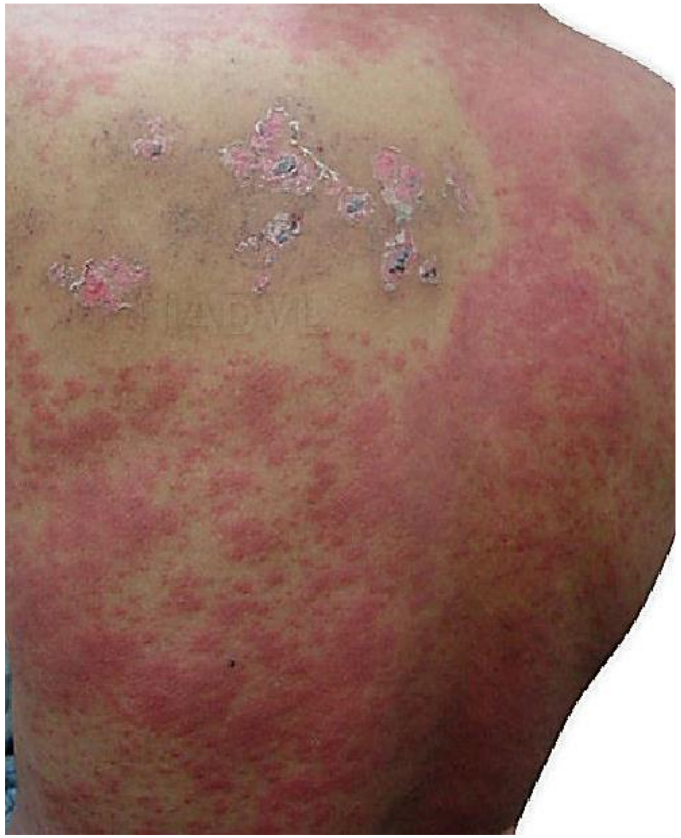
Lewis triple response – erythema, flare and wheal.

Classification and causes of urticaria

Acute urticaria	Chronic urticaria
Duration less than 6 weeks. ▪ Infections (40%) ▪ Drugs(9%) ▪ Food items (1%) ▪ Idiopathic (50%)	Daily or almost daily for more than 6 weeks. ▪ Chronic spontaneous urticaria (autoimmune, pseudoallergic, infection and idiopathic) (65%) ▪ Physical/ inducible urticaria (35%) ▪ Urticarial vasculitis (5%)

Causes

- **Exogenous (Allergens and Pseudoallergens)**
  - **Inhalants :** pollens, house dust, fungi, dander.
  - **Ingestants** : fish, egg, brinjal , soy, milk, chocolate, nuts, (pseudoallergens - food additives, dyes, preservatives, flavors).
  - **Drugs :** NSAIDs, Polymyxin, Vancomycin, Morphine, codeine, Penicillins, Cephalosporins



Drug induced urticaria

Endogenous

- **Infections :**
  - Gastrointestinal, respiratory, urinary tract infections
  - Bacterial, protozoal, helminthic, viral (CMV, EBV, HSV)
- **Systemic diseases :**
  - Hashimoto’s thyroiditis
  - Systemic lupus erythematosus
  - Chronic active hepatitis
  - Malignancies

Physical urticaria

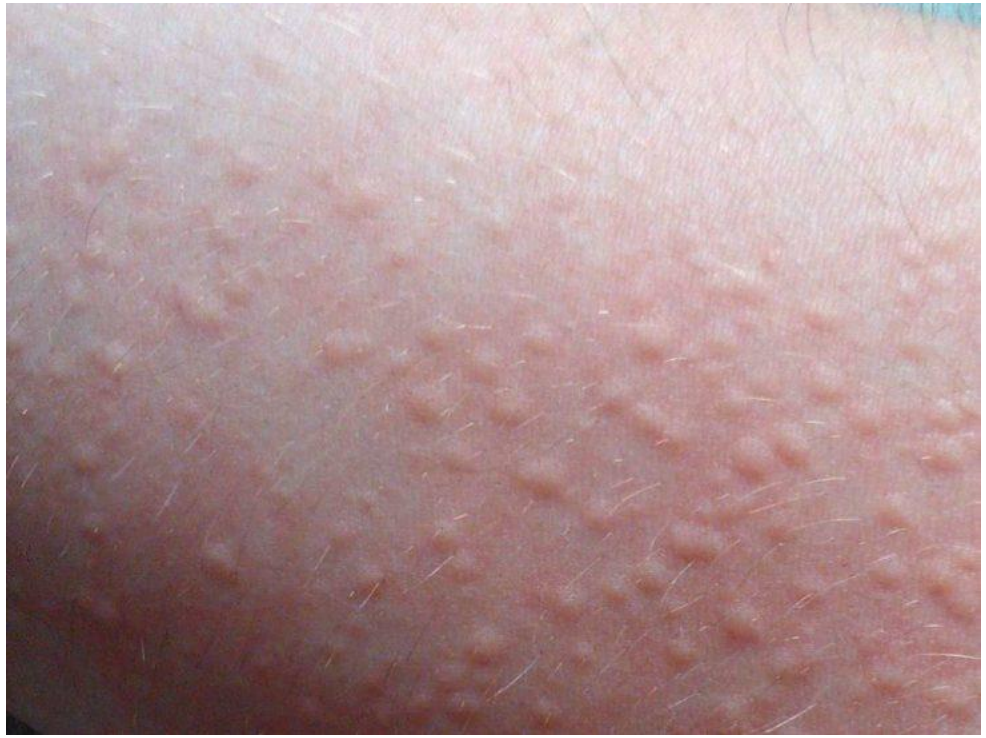
Urticaria factitia / dermographism (most common type, red, itchy, linear wheal appearing immediately after light stroking of the skin)	Eliciting factor : mechanical sheering forces (weals arising within 1-5 minutes)
Cold contact urticaria	Eliciting factor : cold objects, air, fluids, wind
Heat contact urticaria	Eliciting factor : localized heat
Solar urticaria	Eliciting factor : UV and / or visible light.
Delayed pressure urticaria (appear at site of pressure on the skin , painful rather than itchy last for more than 24 hrs, poor prognosis)	Eliciting factor : vertical pressure (weals arising with 3 - 12 hrs. latency)

Physical urticaria

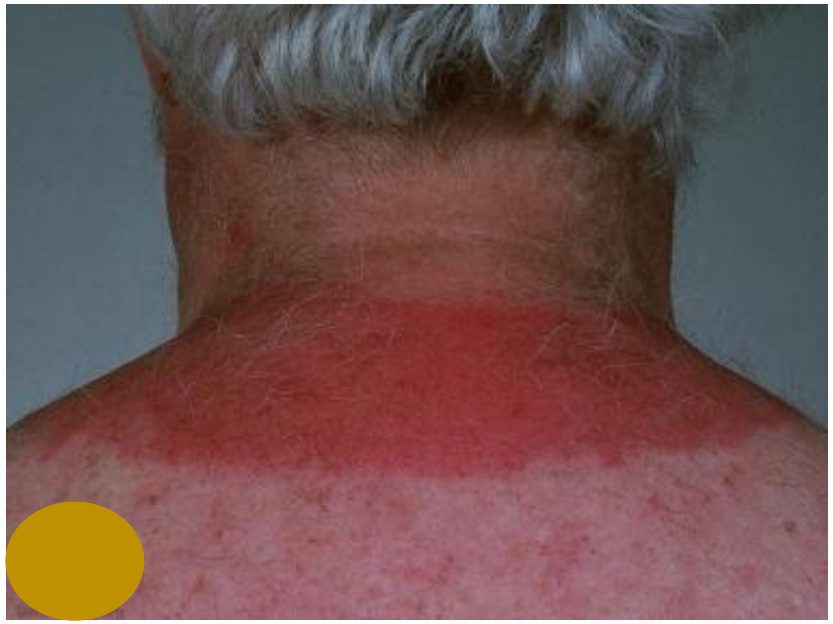
Vibratory urticaria / angioedema	Eliciting factor : vibratory forces
Aquagenic urticaria	Eliciting factor : water
Cholinergic urticaria (small (2-4mm) erythematous papules surrounded by a pink flare, most commonly on trunk and proximal limbs)	Eliciting factor : increase in core body temperature, by exercise or spicy food.
Contact urticaria [Can be IgE dependent or independent (immunologic or non-immunologic)]	Eliciting factor : contact with urticariogenic substance
Exercise induced urticaria / anaphylaxis	Eliciting factor : physical exercise

Dermographism

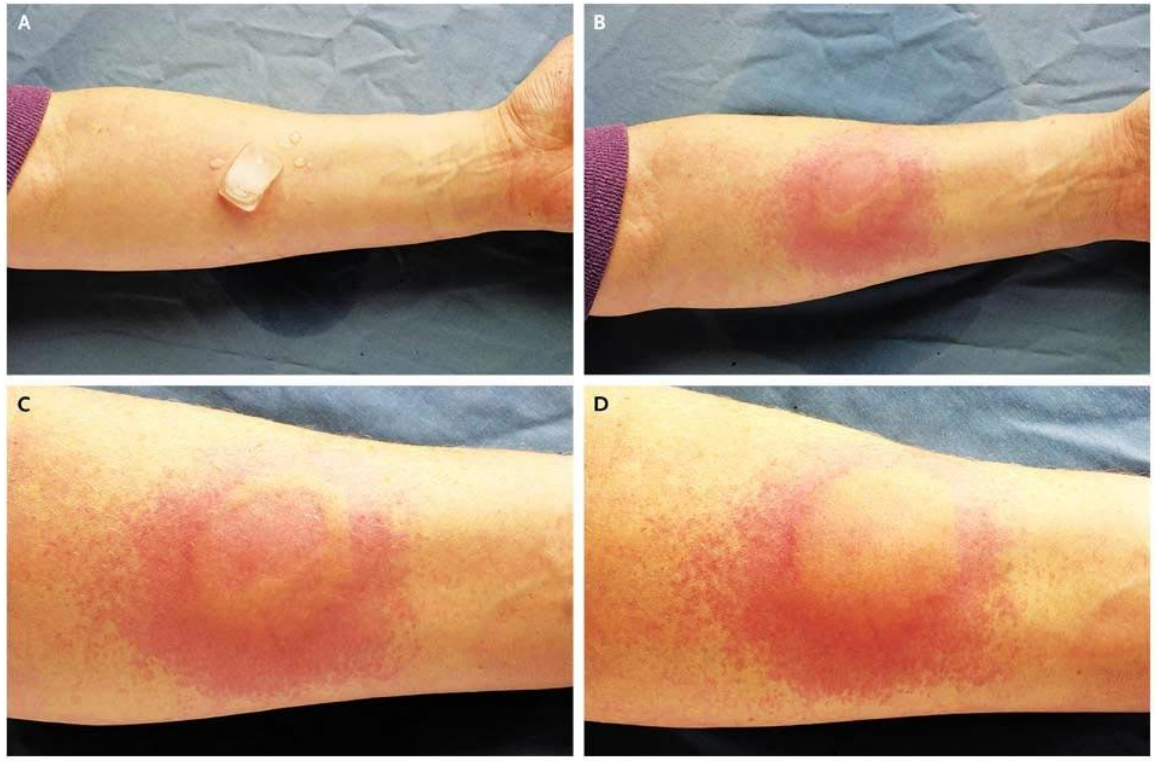
Cholinergic urticaria



Solar urticaria



Cold urticaria



Clinical features and differentials

- **Symptoms :**
  - Pruritus
- **Signs :**
  - Pale pink well defined swellings (Hives or wheals) Spreads with scratching and coalesce to form large lesions.
- **Course of Lesions :**
  - Lesions last 90 minutes to 24 hours

Difference between urticaria and urticarial vasculitis

Urticaria	Urticarial vasculitis
▪ Generalized body involvement ▪ Individual lesions last less than 24 hours ▪ Itchy ▪ Don’t leave post inflammatory pigmentation ▪ Rare systemic symptoms ▪ Biopsy does not reveal vasculitis	▪ Trunk and proximal limbs ▪ Individual lesion last more than 24 hours ▪ Associated with burning and pain ▪ Have purpuric centre and leave post inflammatory pigmentation ▪ Systemic symptoms, fever, arthralgia present

Workup in a patient of urticaria

Careful History

- Travel and work history
- Ingestion of foods, medications, herbals, vitamins
- Recent infection
- Known allergies / atopy
- Family History of allergy or thyroid disease

Provocation tests for physical urticaria

Dermographism	Stroking of skin by blunt object
Delayed pressure urticaria	Locally applied weight for 20 min.
Cold urticaria	Cold contact (ice cube for 20 min.)
Cholinergic urticaria	Physical exercise/hot bath
Aquagenic urticaria	Contact with water of any temperature
Exercise anaphylaxis	Supervised exercise (shortly after meal)
Solar urticaria	Phototesting

Hereditary angioedema

- Recurrent laryngeal edema or colicky abdominal pain, skin swellings especially on distal limbs.
- May be preceded by reticular erythema.
- Family history present (autosomal dominant).
- Trauma and estrogens are triggers.
- These individuals lack C1 esterase/C1 inhibitor and over-activity of C1 results in generation of kallikrein, which converts kininogen to bradykinin.
- Bradykinin acts on vasculature and results in angioedema attacks.
- Attacks can be life threatening and are associated with arthralgia too.

Diagnosis of hereditary angioedema

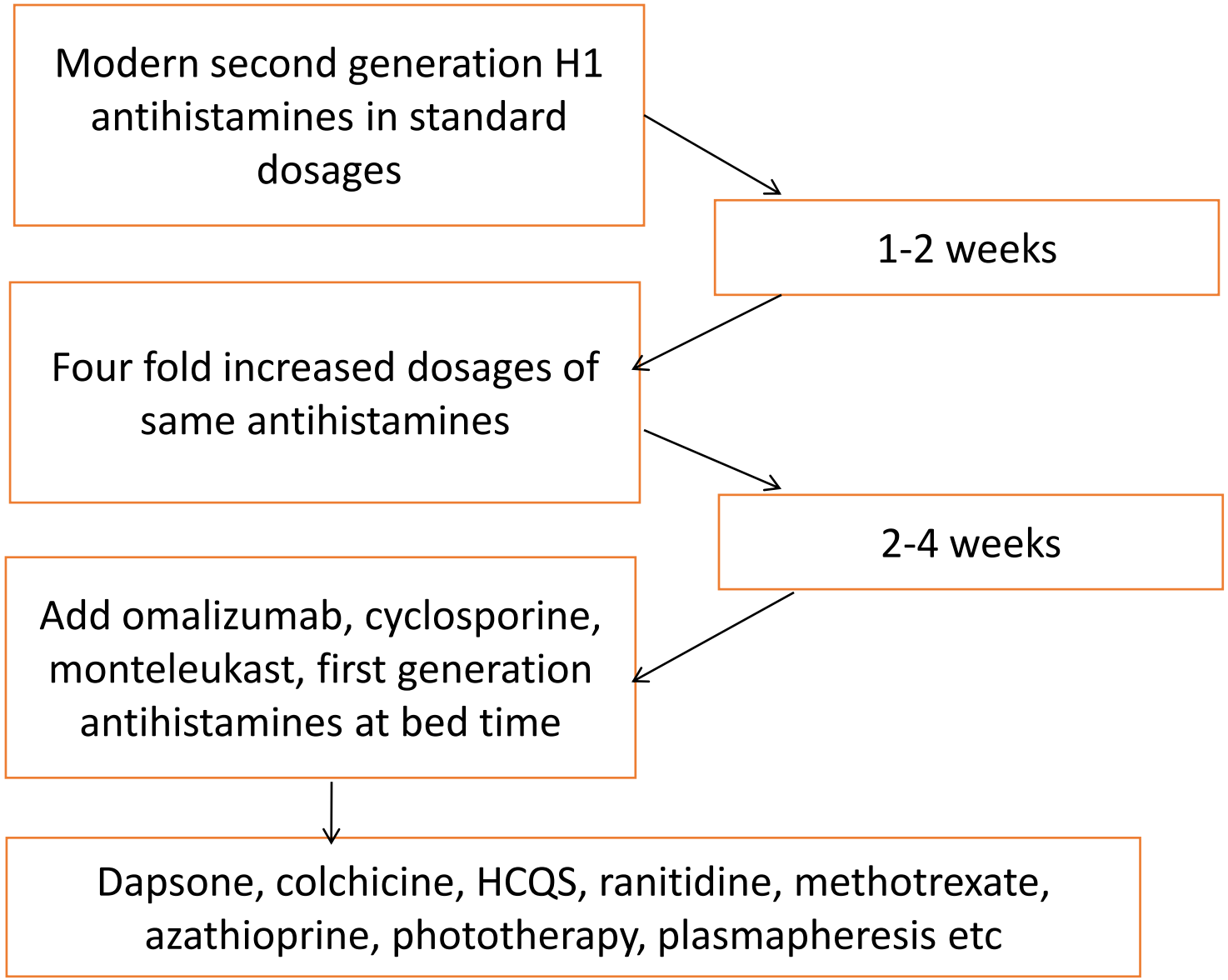
- Detection of **low serum level of C4** is very sensitive, but non specific screening test.

- Acquired angioedema due to lymphomas and SLE etc. has **low C1q** levels along with low C4 levels.

Treatment

- General
  - **Rule out Anaphylaxis**
  - Discontinue offending drugs, food, or behavior
  - Offer Reassurance

Discuss idiopathic nature of chronic urticaria and possibility of inability to identify a specific cause.


Modern second generation H1 antihistamines in standard dosages
1-2 weeks
Four fold increased dosages of same antihistamines
2-4 weeks
Add omalizumab, cyclosporine, monteleukast, first generation antihistamines at bed time
Dapsone, colchicine, HCQS, ranitidine, methotrexate, azathioprine, phototherapy, plasmapheresis etc

Oral steroids

- **Oral corticosteroids (short courses for 10 days) are** useful in
  - Acute severe exacerbations of chronic urticaria
  - Severe angioedema
  - Delayed pressure urticaria
  - Urticarial vasculitis

Omalizumab

- **Omalizumab** is humanized monoclonal antibody against IgE approved by US-FDA in 2014 for the treatment of patients 12 years of age and older with Chronic urticaria that is not controlled with H1 antihistamine therapy.
- Dose recommended is 300 mg monthly given subcutaneously.

Therapy for physical urticaria

Symptomatic dermographism	H1 receptor antagonists
Delayed pressure urticaria	Systemic corticosteroids, NSAIDs, sulfasalazine, dapsone, monteleukast
Cholinergic urticaria	H1 receptor antagonists, danazol
Cold urticaria	H1 receptor antagonists, ketotifen, cyproheptadine, Systemic corticosteroids, epinephrine
Solar urticaria	Induction of tolerance by UVB/PUVA, sunscreens, hydroxychloroquine

J Allergy Clin Immunol 2014; 2:73-88.

- **Three months of good control is recommended prior to tapering therapies, and it can be longer for patients with one or more of the following characteristics :**
  - Symptoms that were present for years.
  - Very severe and difficult to control symptoms.
  - Concomitant physical urticaria.

Therapy for hereditary angioedema

- Danazol for maintenance therapy
- For acute attacks, fresh frozen plasma is the treatment of choice.
- New drugs available :
  - Berinert (nano-filtered C1 concentrate)
  - Ruconest (recombinant C1 inhibitor)
  - Icatibant (bradykinin antagonist)
  - Ecallantide (kallikrein inhibitor)

Q) A 5 yr old male child has multiple hyperpigmented macules over the trunk. On rubbing the lesion with the rounded end of a pen, he developed an urticaria wheal confined to the border of the lesion. Most likely diagnosis is?

1.Fixed drug eruptions

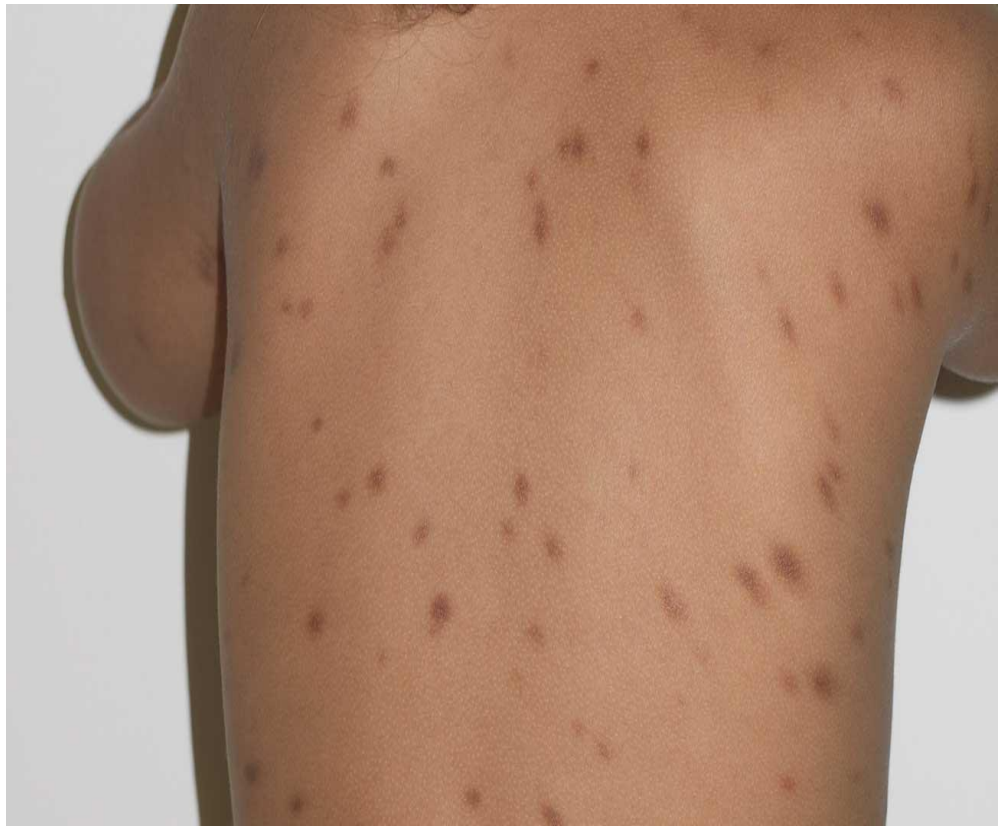
2.Lichen planus

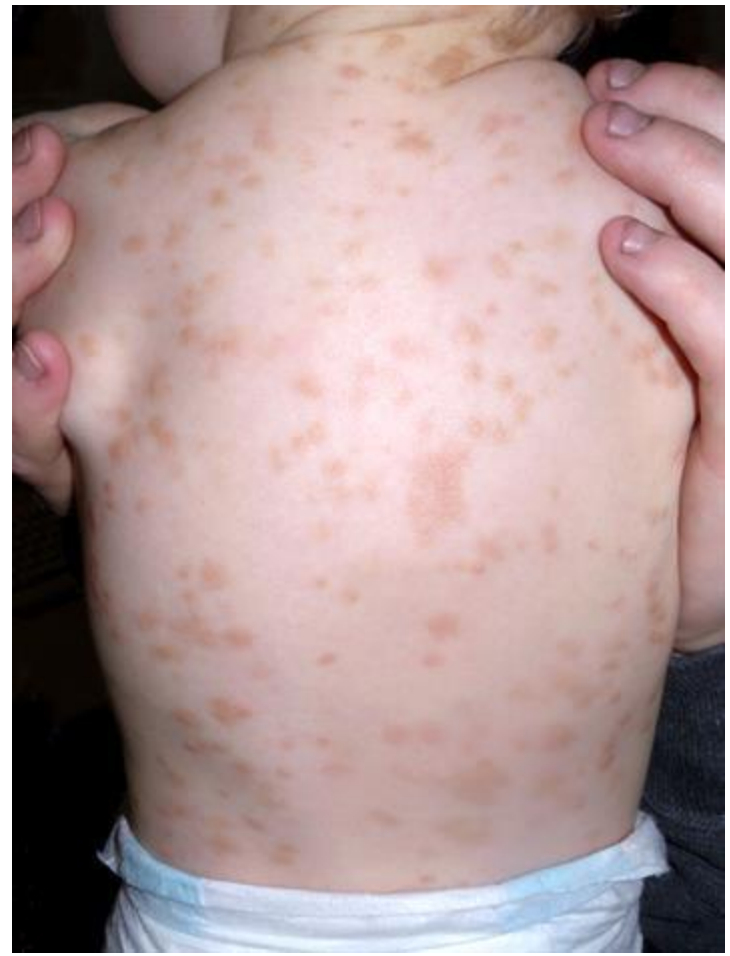
3.Urticaria pigmentosum

4.Urticarial vasculitis

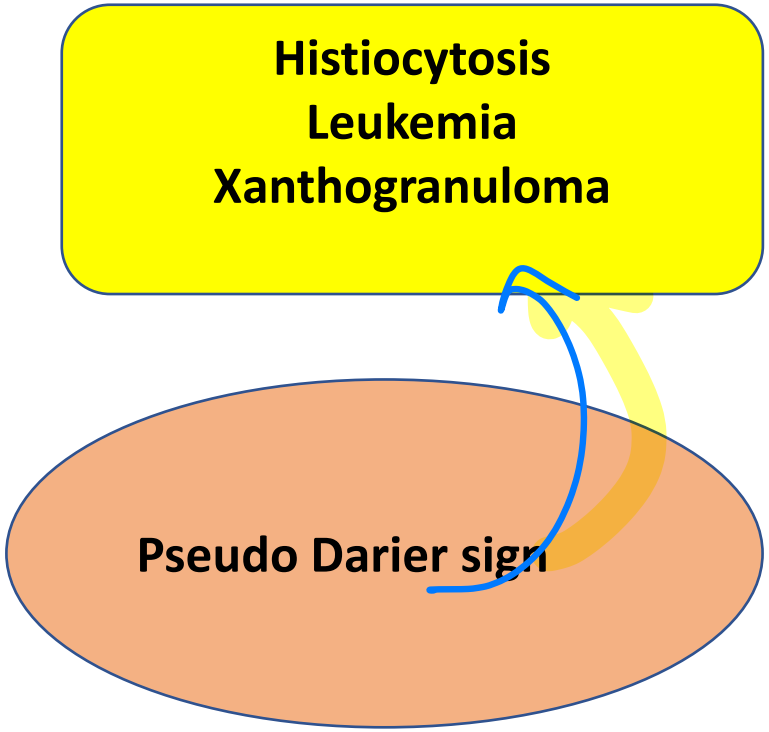
Mastocytosis

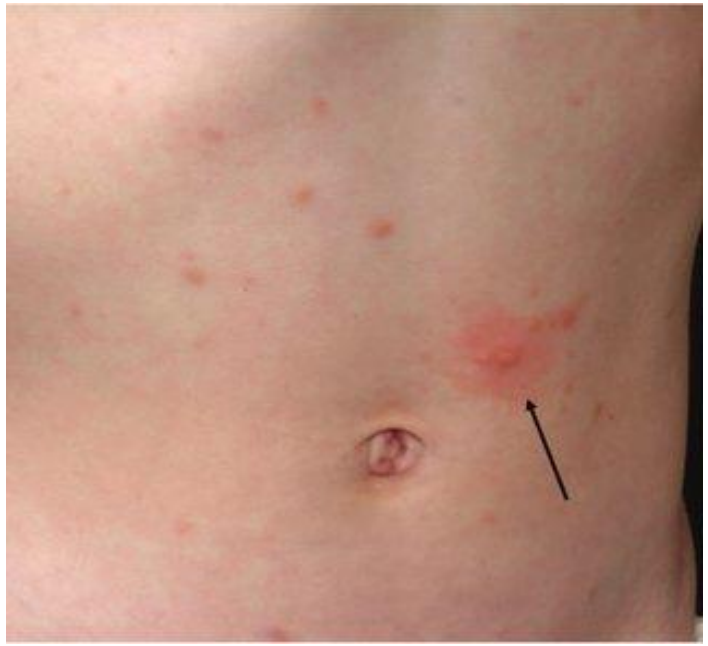
- Accumulation of mast cells in the tissue- Skin or systemic organs or both
- Mutation: c-KIT gene
- In children most common type of Mastocytosis is Urticaria Pigmentosa
- UP- cutaneous deposits of numerous Mast cells





Darier sign


Histiocytosis
Leukemia
Xanthogranuloma
Pseudo Darier sign



Q.2) What is the screening test of choice for Hereditary angioedema?

A. High C3 levels
B. High C4 levels
C. High C1 levels
D. Low C4 levels

Q.3) Chronic urticaria is defined as duration of disease more than :

A. 2 weeks
B. 4weeks
C. 6 weeks
D. 8 weeks

Q.6) Omalizumab is

A. Anti IgA antibody
B. Fully human anti IgE antibody
C. Humanized anti IgE antibody
D. Third generation antihistamine

Thank You!