Urticaria

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Learning outcomes

- At the end of lecture, the student should be able to tell
  - Classification, clinical features and management of urticaria
  - Clinical features and classification of bullous disorders

Definition Urticaria

- Short-lived swellings of the epidermis and dermis due to plasma leakage
- Characterized by very pruritic wheals
- Wheals disappear within 24 hours

Core Concepts

Definition Angio-oedema

- Condition in which swellings affect the deeper dermal, subcutaneous and submucosal tissues.
- usually painful rather than itchy
- Presents as ill defined areas of non pitting edema

Core Concepts

Urticaria. Clinical classification

- Ordinary/ Spontaneous urticaria
  - Acute **(<6 weeks)**
  - Episodic (acute and chronic intermittent)
  - Chronic **(>6 weeks)**
- Inducible urticaria
  - Mechanical/ dermographism
  - Thermal (cold/heat contact)
  - Cholinergic
  - Contact urticaria
  - Solar urticaria
  - Aquagenic urticaria

Core Concepts

Aetiology of spontaneous urticaria

Acute urticaria

- **Idiopathic**
- **Infectious**
  - Upper respiratory tract infection
  - Streptococcal infection
  - Hepatitis B infection
- **Allergy** (immediate hypersensitivity)
  - Foods
  - Drugs
  - Inhalants
    - Grass pollens, mould spores, animal danders and house dust mite
- **Non-allergic**
  - Histamine liberators (e.g. codeine, atracurium)
  - Pseudoallergens
    - Aspirin and other non-steroidal anti-inflammatories

Chronic urticaria

- **Idiopathic**
- **Autoimmunity**
  - Functional autoantibodies
- **Pseudoallergy**
  - Salicylates
  - Food colours, preservatives, antioxidants and flavour enhancers
- **Infection**
  - Bowel parasites
  - ? *Helicobacter pylori*
  - ? Candidiasis of the bowel
  - ? Chronic sepsis (e.g. dental abscess)

Associations with chronic ordinary urticaria

- **Autoimmune disease**
  - Thyroiditis
  - Other organ-specific autoimmunity
    - (e.g. vitiligo, pernicious anaemia)
  - Systemic lupus erythematosus
  - ? Coeliac disease
- **Infection**
  - *Helicobacter pylori gastritis*
- **? Malignancy**
  - Anecdotes only

Vertical Integration

Pathophysiology

- Local increase in permeability of capillaries and venules
  - due to activation of cutaneous mast cells
    - immunological
    - non-immunological

Vertical Integration

Pathogenesis

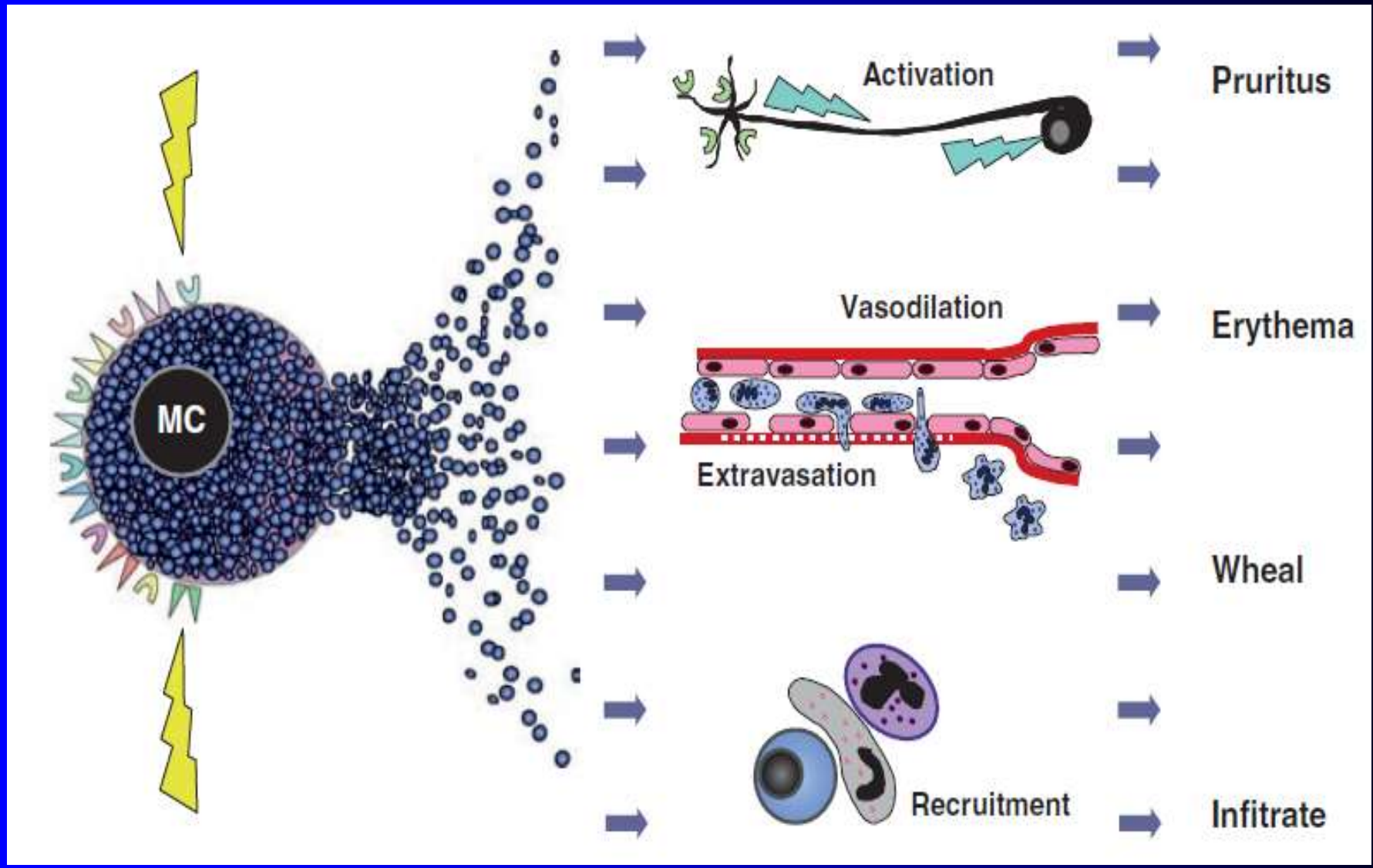
Immunologic

- **Type I allergy**
  - most common
  - commoner in atopics
- **Type II allergy**
- **Type III allergy**

Nonimmunologic

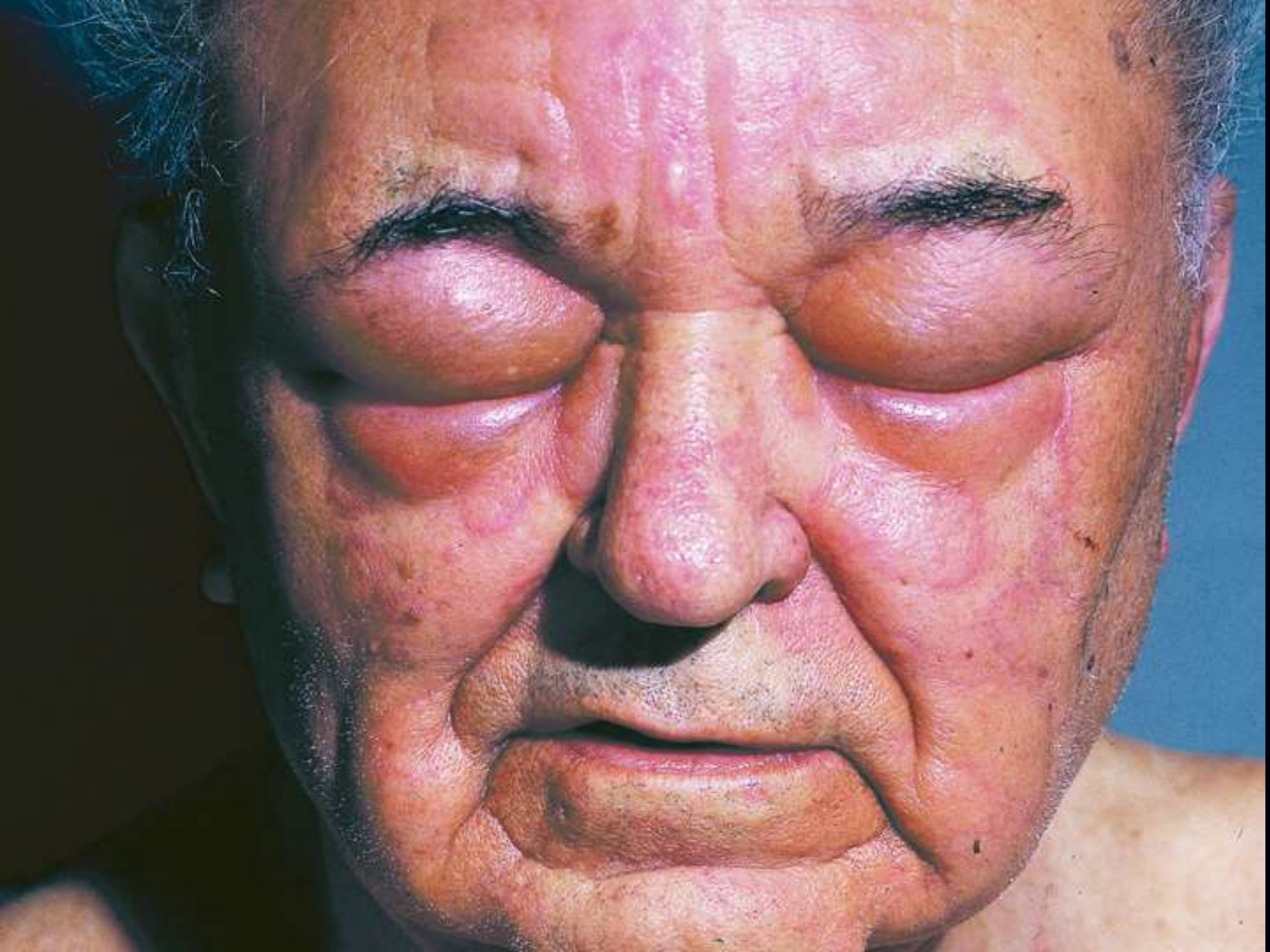
- **Histamine releaser : aspirin**

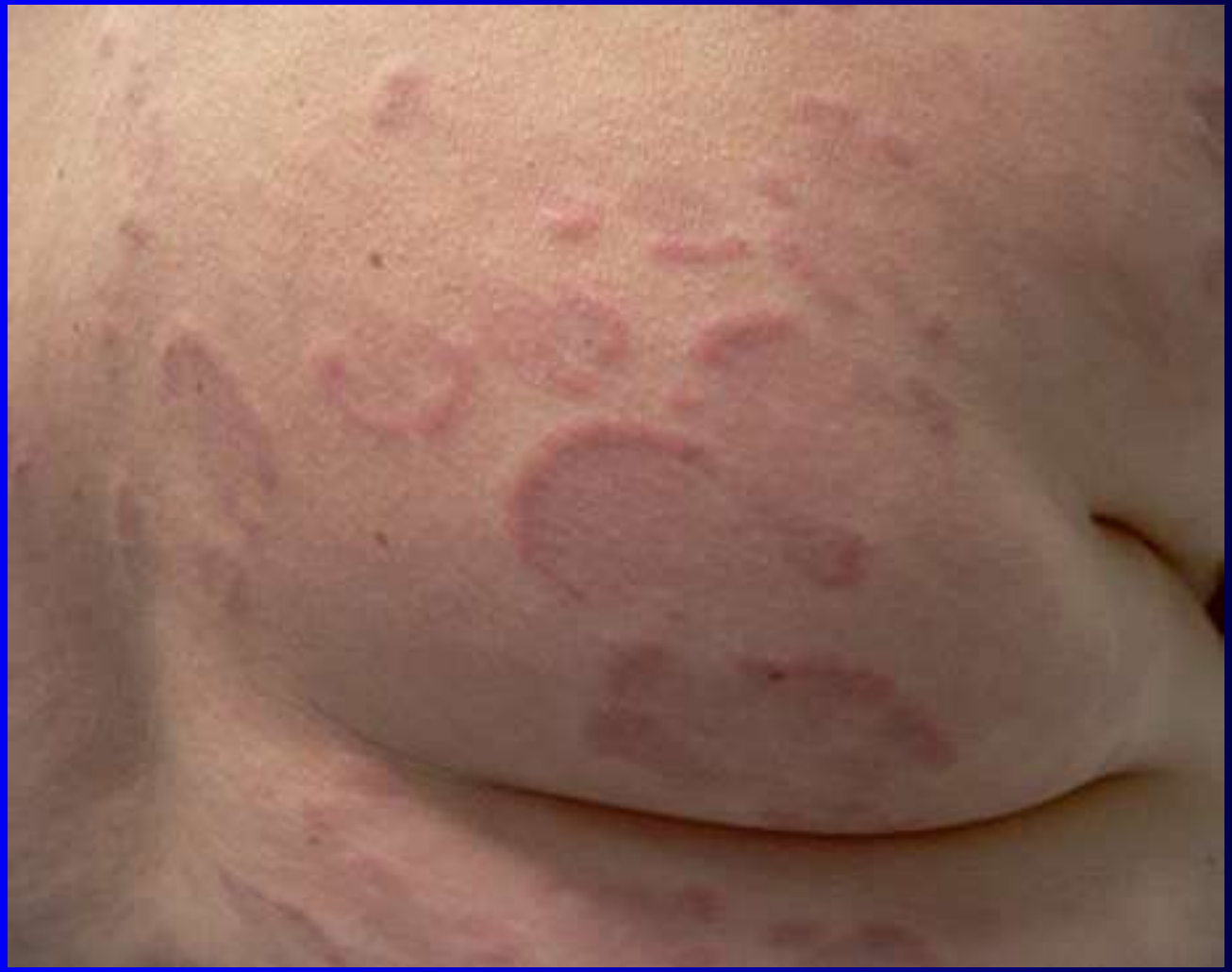
Mast cell degranulation and its effects



Ordinary urticaria Clinical features

- **Itching erythematous macules develop into weals**
  - last a few hours and resolve within 24 h
  - occur anywhere on the body
  - very itchy
  - varying shapes including rounded, annular, serpiginous and bizarre patterns
- **Associated angio-oedema** 50%
- **mucosal surfaces involvement**
  - **respiratory distress, abdominal pain and hoarseness.**
- **Systemic symptoms**
  - Vomiting, malaise, loss of concentration, low mood, feeling hot and cold, headache, abdominal pain, diarrhea, arthralgia, dizziness and syncope, anaphylaxis





Anular wheals in chronic urticaria

Core Concepts

classification of physical urticarias

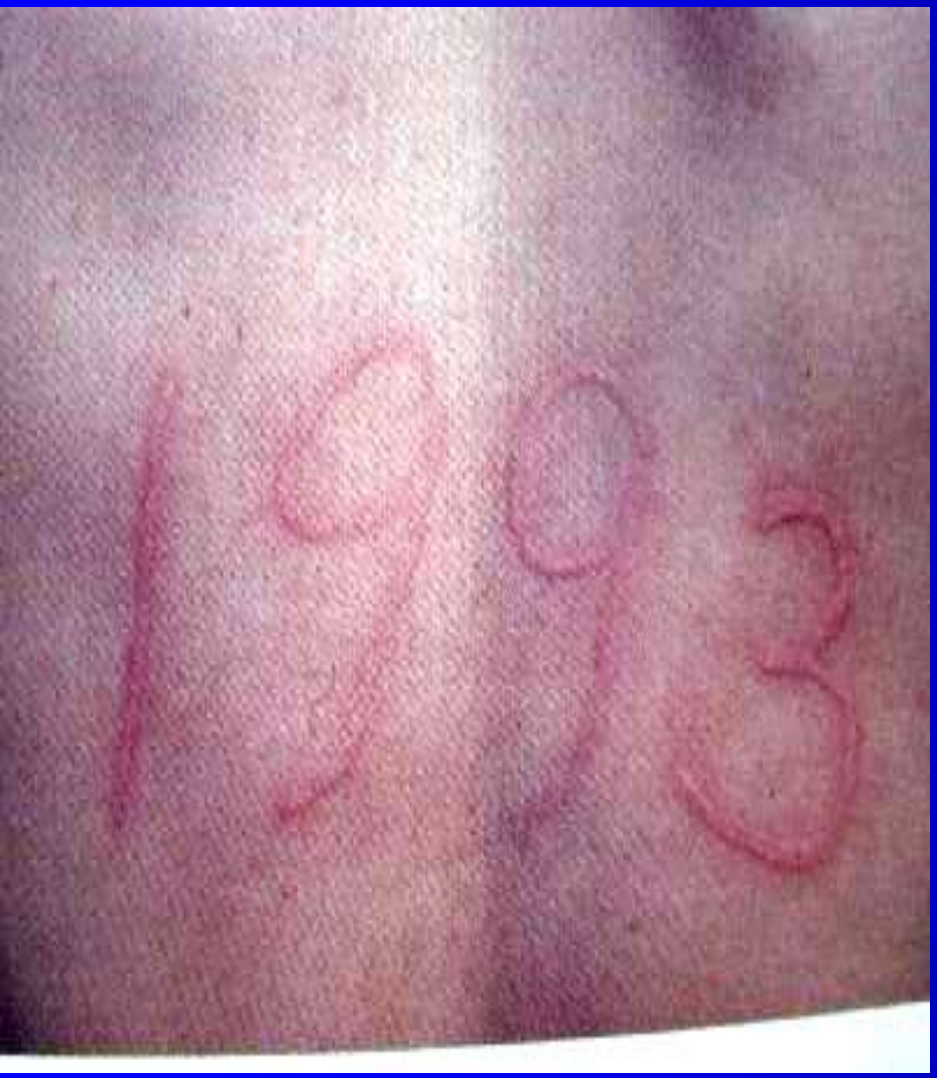
- *Due to mechanical force*
- *Due to heat*
- *Due to cold*
- *Others*
  - Solar urticaria
  - Aquagenic urticaria

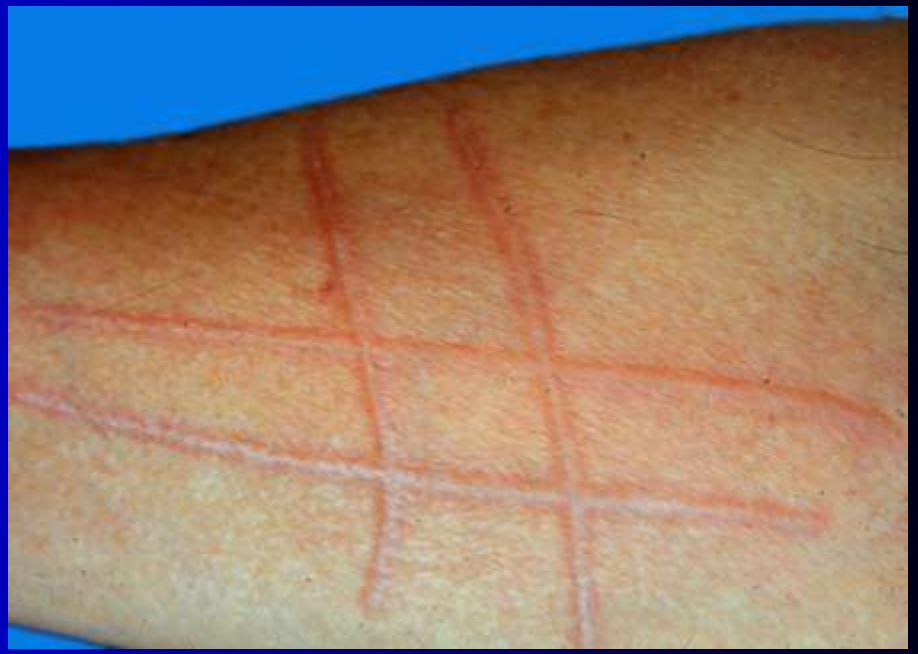
Core Concepts

Dermographism

- Firm stroking of the skin causes triple response
  - ***local erythema*** *due to* capillary vasodilatation
  - followed by ***oedema*** *and a* ***surrounding flare*** *due to axon reflex-induced dilatation of arterioles*

  This reaction is physiological
- **Simple dermographism**
  - sufficiently **exaggerated** physiological response
- **Symptomatic dermographism**
  - response accompanied symptomatically by **itching**





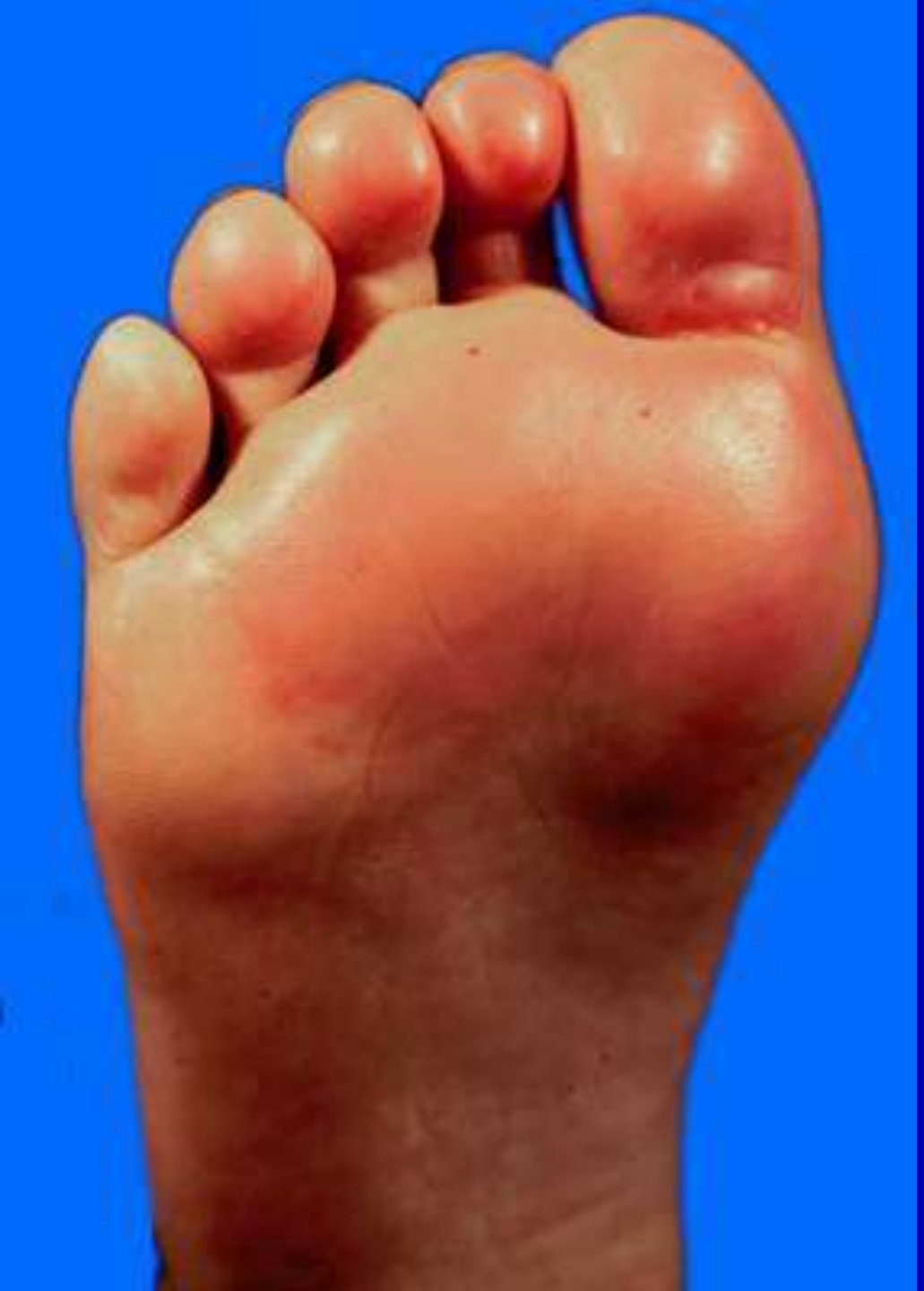
Core Concepts

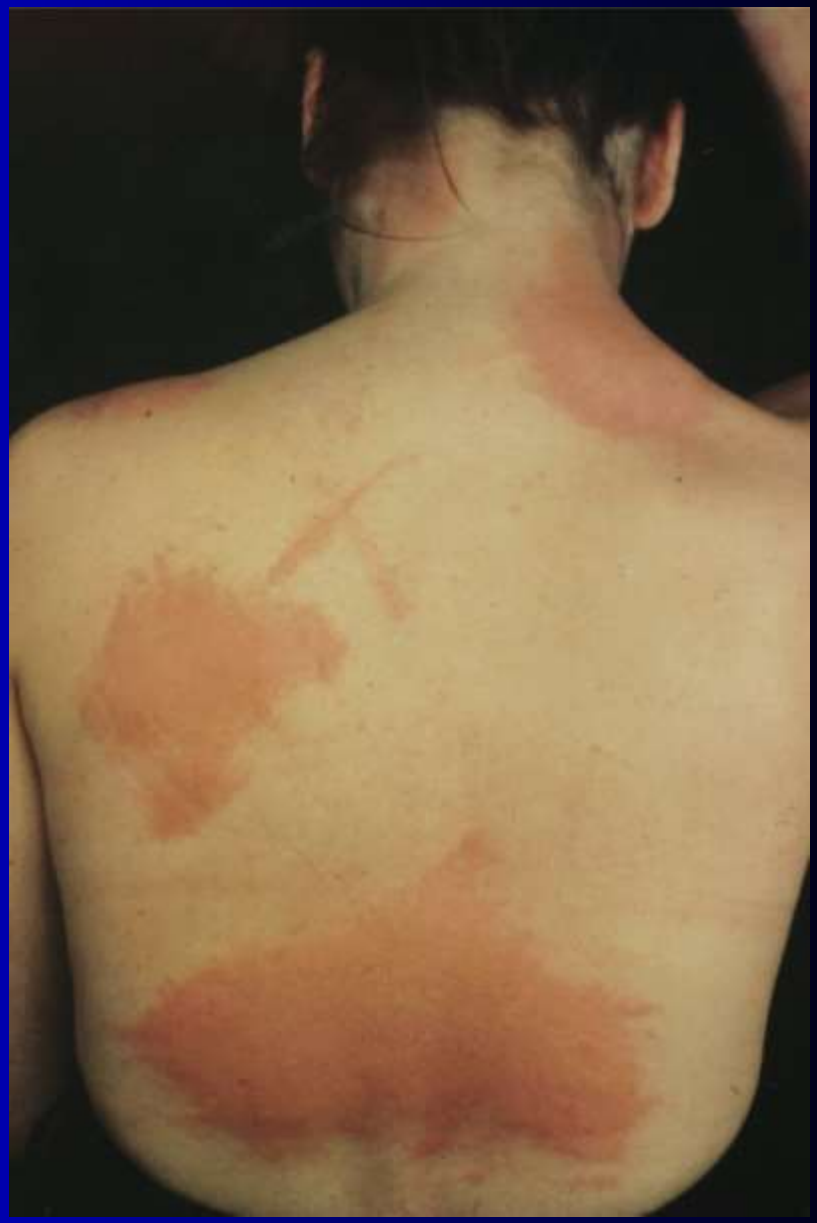
Physical urticarias Due to mechanical force

Delayed pressure urticaria

- Wealing occurs at sites of sustained pressure applied to the skin after a delay of 30 min to 9 h, but usually 4–8 h, and lasts 12–72 h
  - under tight clothing
  - on the hands after manual work
  - on the buttocks and lower back after sitting
  - feet after walking
- usually occurs in patients with chronic ordinary urticaria

Pressure urticaria





Delayed pressure urticaria

- **Symptoms**
  - LOCAL
    - Lesions often tender or painful, particularly on the soles and scalp
    - may be itchy
  - SYSTEMIC
    - malaise, flu-like symptoms, arthralgia, myalgia and leukocytosis

Core Concepts

Physical urticarias *due to heat*

- **Generalized heating**
  - **Cholinergic urticaria**
    - Variants
      - Cholinergic pruritus
      - Persistent cholinergic erythema
  - **Cholinergic dermographism**
    - Exercise-induced anaphylaxis
- **Localized heating**
  - Heat contact urticaria

Core Concepts

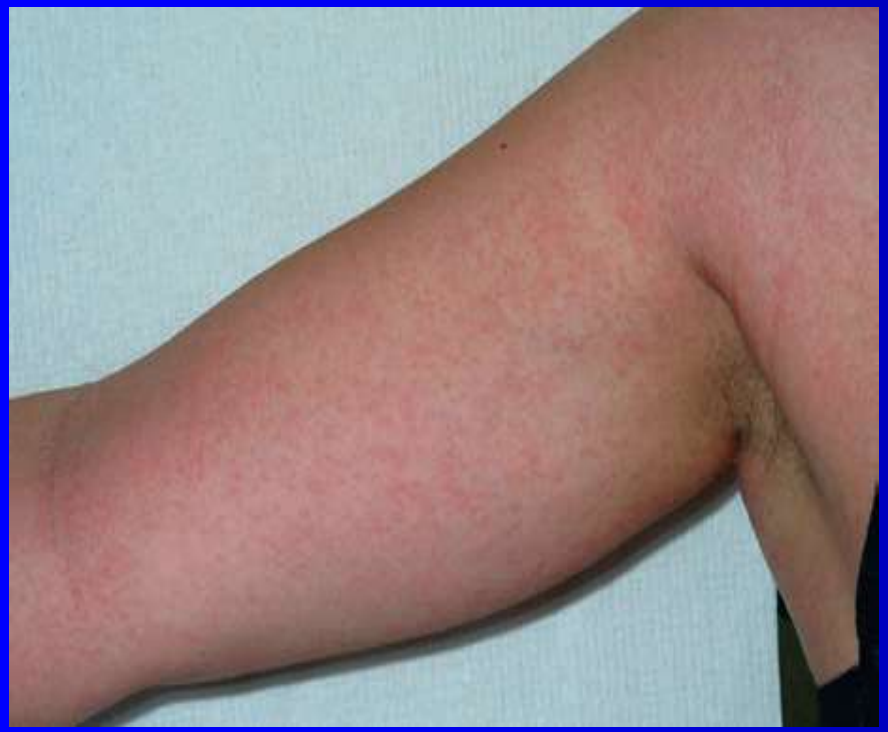
Physical urticarias *due to heat*

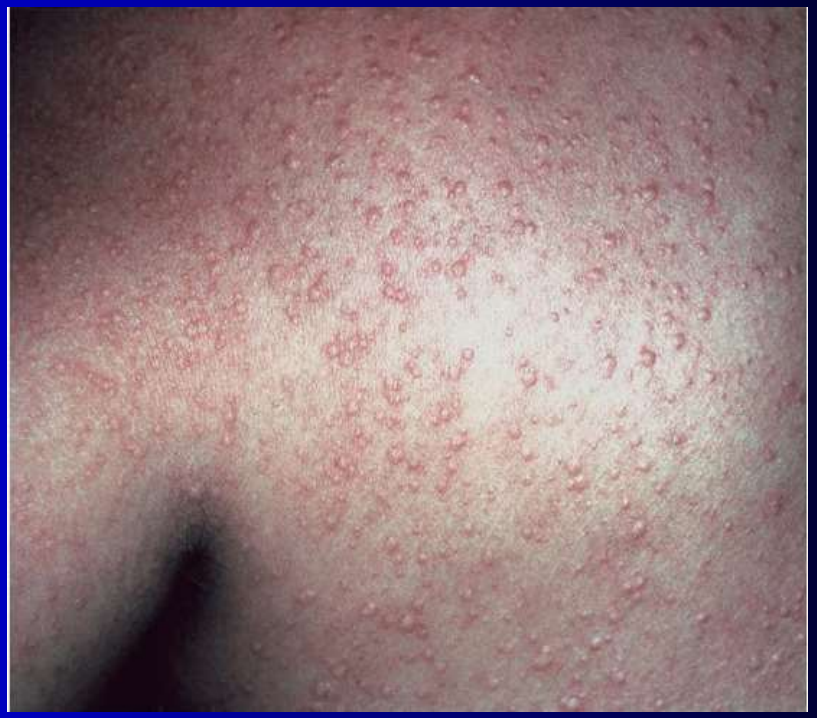
Cholinergic urticaria

- Characteristic small weals appear on sweating
  - rise in core temperature
  - emotion
  - gustatory stimuli
- Pathogenesis
  - stimulation of the **cholinergic postganglionic sympathetic nerve supply** to the sweat glands

Ordinary urticaria not precipitated by heat may be associated

Cholinergic urticaria





- multiple small typical wheals
- lesions persist for a few minutes to an hour or two

Core Concepts

Physical urticarias due to cold

- **Acquired**
  - **Primary (idiopathic)**
    - **Localized cooling**
      - Immediate cold contact urticaria (commonest)
      - Delayed cold contact urticaria
      - Localized cold contact urticaria
      - Cold erythema
    - **Generalized**
      - Generalized reflex cold urticaria
      - Cold-dependent cholinergic urticaria
  - **Secondary**

    (to serum cryoproteins)
- **Inherited**

Core Concepts

Immediate cold contact urticaria

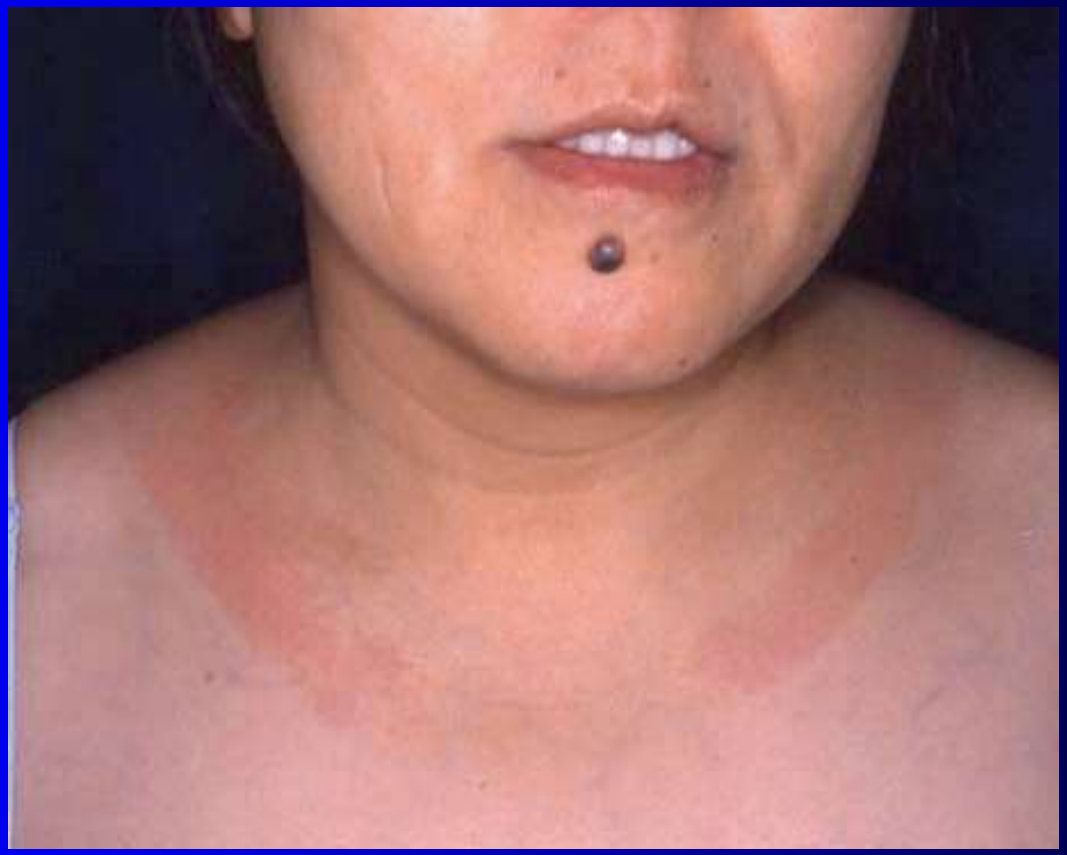
- **Itching and wealing of the skin occur on cold exposure within minutes and last up to 1 h**
- **Stimuli**
  - Cold winds
  - cold rain
  - drinking cold liquids (mouth & pharynx may swelling)
- **Systemic symptoms**
  - flushing, palpitations, headache, wheezing and loss of consciousness
- **Testing**
  - Application of a melting ice cube in a thin plastic bag for up to 20 min
  - results in an itching weal at the site within minutes of removal

Core Concepts

Solar urticaria

- Weals develop at the site of exposure within minutes of visible or UV light and usually fade within 2 h
- **Cause**
  - usually idiopathic
  - rarely secondary to porphyrias, drugs, chemicals
- **Treatment**
  - Avoiding sun exposure, antihistamines, and irradiation of UV range light

solar urticaria



Note that whealing is not observed in the pigmenting area including face and neck where the skin was frequently exposed to the sunlight **(hardening effect)**

Core Concepts

Aquagenic urticaria

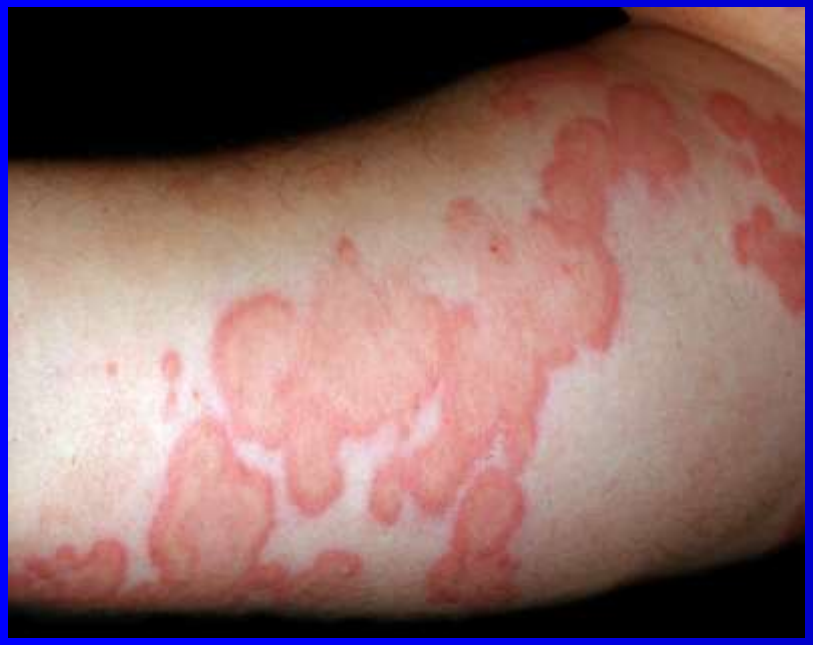
- Contact with water at any temperature induces an eruption resembling cholinergic urticaria
- **D/D**
  - **Other urticarias induced by water**
    - cold urticaria, cholinergic urticaria and dermographism
  - **Aquagenic pruritus**
    - water induced itching but no wealing
- **TREATMENT**
  - Prophylactic H1 antihistamines

Core Concepts

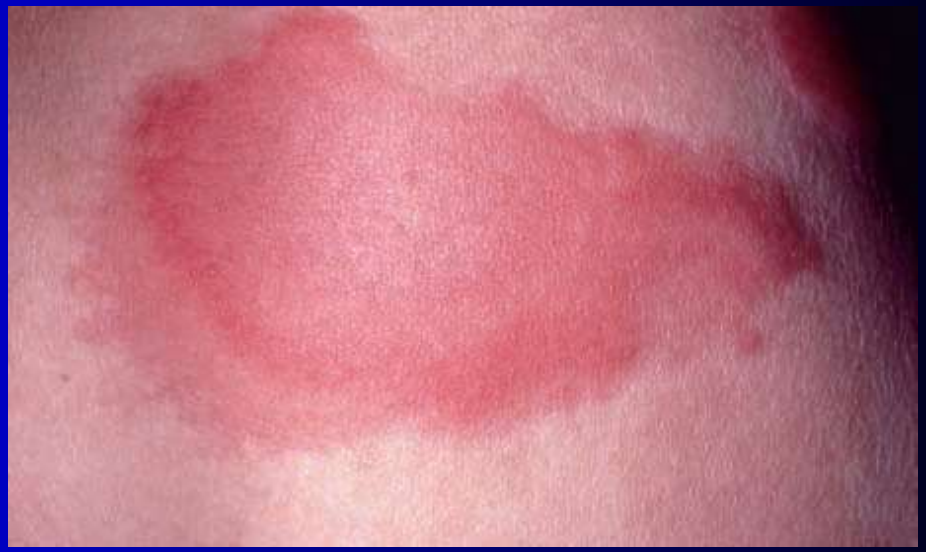
Urticarial vasculitis

- Lesions differ from those of simple urticaria
  - lesions **persist for more than 24 h**
  - often demonstrate **purpura**
  - symptoms of **burning** (rather than itch)
  - **post-inflammatory pigmentation**
  - **Biopsy- vasculitis**

Urticarial vasculitis



lesions persisting for more than 24 h



Contact urticaria

Urticaria resulting from skin or mucosal contact with the provoking substance

Allergic (immunological)

- Cow's milk
- Cod
- Kiwi fruit
- Peanuts
- Sesame seeds
- Spices
- Celery

•Type I hypersensitivity
•result in an immediate, localized weal and flare
•resolving within 2 h
•Investigation
•*CAP fluoroimmunassay* (RAST)

Non-allergic (non-immunological)

- Balsam of Peru
- Cinnamic aldehyde
- Methyl salicylate
- Benzoic acid
- Sorbic acid
- Witch hazel
- Jellyfi sh
- Nettles

•PGD2 formation
•take up to 45 min to develop
•Investigation
•*Prick test or patch test*

Core Concepts

Angioedema

- acute circumscribed edema that usually affects the most distensible deeper dermal, subcutaneous tissues or mucous membranes
- usually painful rather than itchy

Horizontal Integration

Investigations of urticaria

- **Acute urticaria**
  - **Usually none, except where suggested by the history**
  - Specific IgE tests
    - CAP fluoroimmunassay or
    - skin-prick tests
  - Tests for upper respiratory viral or bacterial infection
- **Episodic urticaria**
  - Pseudoallergy challenge capsules (if available)
    - **Food additives**
    - **NSAIDs**

- Tartrazine
- aspirin
- sodium benzoate
- 4hydroxybenzoate

Horizontal Integration

Investigations Ch urticaria

- Physical challenge provocation tests

  (where suggested by the history)

- Blood tests

  (ordinary urticaria, unresponsive to H1-antihistamines)

  - FBC, ESR

eosinophilia

parasitic disease

Raised ESR

- LE
- urticarial vasculitis
- macroglobulinaemia

Other Investigations Ch urticaria

- Thyroid antibodies, thyroid function tests
- C4 complement
  - angio-oedema without weals
  - urticaria vasculitis
- Autologous serum skin test (ASST)
  - screening test for autoantibodies in chronic idiopathic urticaria
  - pink weal when Sera injected intradermally into the patient's own skin
  - results need to be interpreted with caution
- Basophil histamine release assay
  - Functional autoantibodies

Horizontal Integration

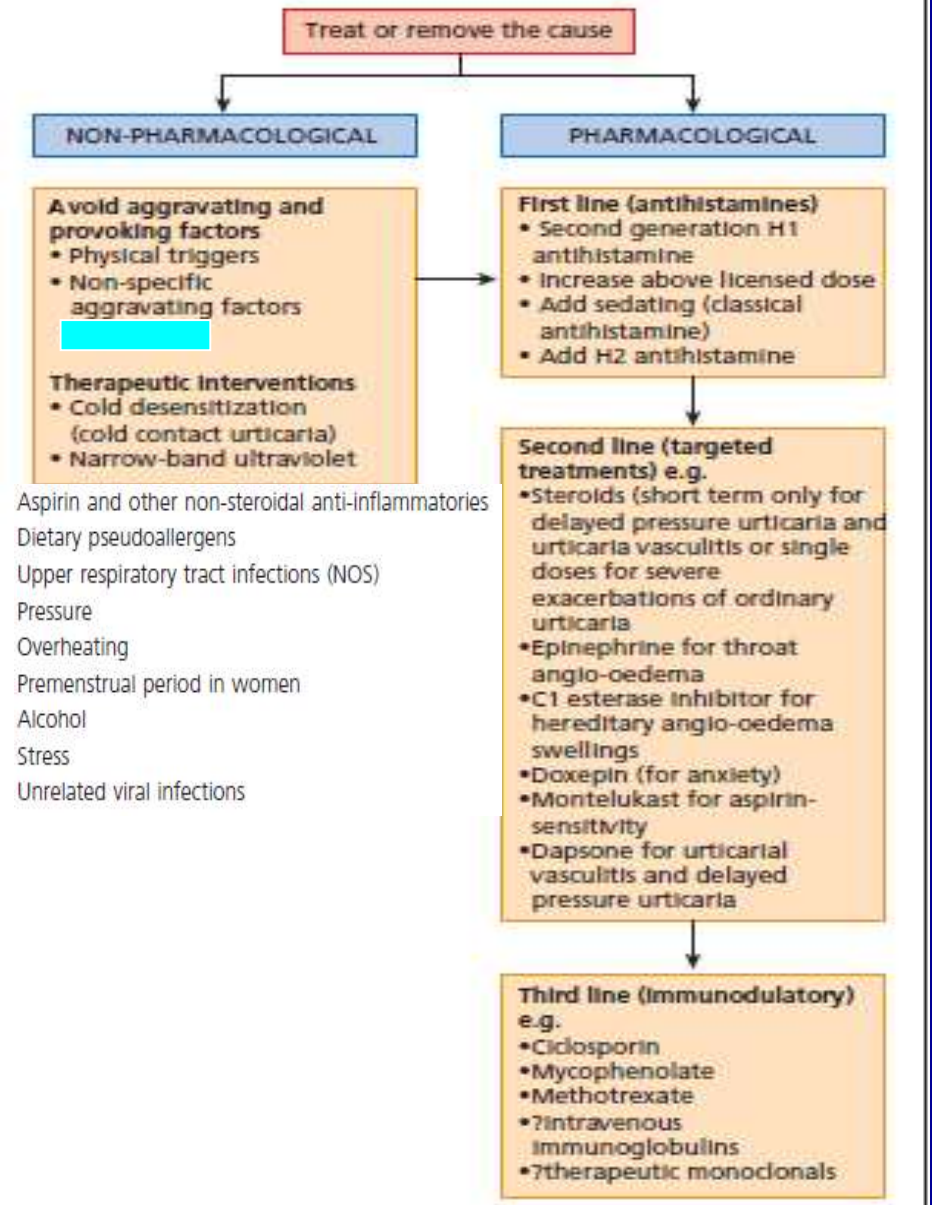
Other Investigations Ch urticaria

as *determined by the history and physical examination*

- Skin biopsy
  - if urticarial vasculitis suspected
  - 12–16 h old lesions
- Stool examination for parasites
  - if infection suspected
- Testing for *Helicobacter pylori infection*
  - *if peptic ulcer symptoms*
- Testing for coeliac disease
  - primarily symptomatic children
- Imaging
  - none routinely

Horizontal Integration

Management of urticaria



- **0.5-1.0 ml of 1 in 1000 I/M or SC**
- **Can be repeated 5-15 minute**
- **Can be given by I/V infusion**
- **Never give I/V bolus dose**

- Cyclophosphamide
- Tacrolimus
- omalizumab (anti-IgE)

Vertical Integration

New Generation Antihistamines

Product	Dose
Cetirizine	10 mg daily
Loratadine	10 mg daily
Desloratadine	5 mg daily
Fexofenadine	60 mg twice daily
Levocetrizine	5 mg daily

- reduces dermal eosinophil accumulation
- poorly metabolized in liver
- Excreted in urine
- sedation

metabolized in the liver
by cytochrome P450

Recent advances in treatment of Ch. Urticaria

New treatments for chronic urticaria

Pavel Kolkhir [1], Sabine Altrichter [2], Melba Munoz [2], Tomasz Hawro [2], Marcus Maurer [3]

Affiliations + expand

PMID: 31446134 DOI: 10.1016/j.anai.2019.08.014

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PMID: 35090671 No abstract available.

Abstract

Objective: Chronic urticaria (CU) is a common, heterogeneous, and debilitating disease. Antihistamines and omalizumab are the mainstay therapies of CU. Additional treatment options are needed. Here, we review the off and beyond label use of licensed drugs, novel treatments that are currently under development, and promising new targets.

Data sources: MEDLINE was searched for recent reports of the successful use of treatments in CU and promising targets for the development of novel treatment options. We also searched ClinicalTrials.gov for recent and ongoing randomized clinical trials in CU.

Study selections: Relevant articles were selected and reviewed.

Results: Omalizumab, the treatment of choice in patients with antihistamine-resistant chronic spontaneous urticaria (CSU), should be explored for use in chronic inducible urticaria in children