MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE

DEPARTMENT OF PEDIATRICS

Lecture № 15

ALLERGIC DISORDERS. ASTHMA

Assoc. Prof. N. Balgaranov

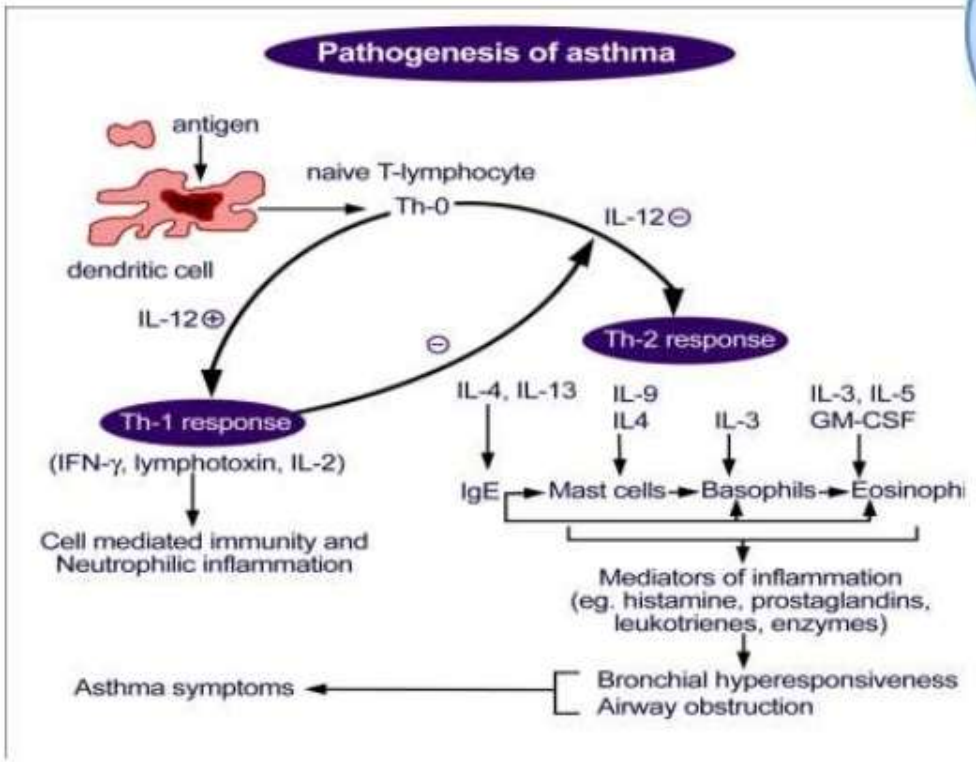
MU Pleven

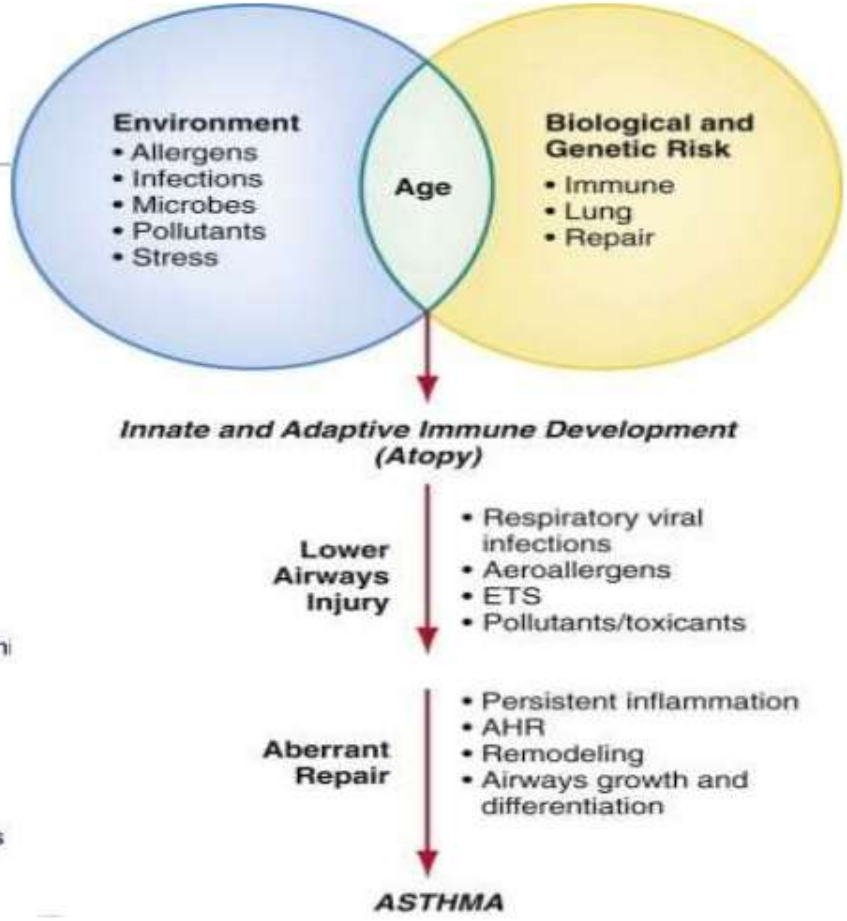
Definition of Asthma

- A chronic inflammatory disease of the airways with the following clinical features:
  - Episodic and/or chronic symptoms of airway obstruction
  - Bronchial hyperresponsiveness to triggers
  - Evidence of at least partial reversibility of the airway obstruction
  - Alternative diagnoses are excluded

Etiology

- Although the cause of childhood asthma has **not been determined**, contemporary research implicates a combination of
- **Environmental exposures and**
- **Inherent biologic and**
- **Genetic vulnerabilities .**





Epidemiology

- **Asthma** is a common chronic disease, causing considerable **morbidity**.
- In **2007**, 9.6 million children (13.1%) had been diagnosed with asthma in their lifetimes.
- Boys (14% vs 10% girls) and children in poor families (16% vs 10% not poor) are more likely to have asthma.
- Approximately **80**% of all asthmatic patients report disease onset prior to **6 yr of age**.

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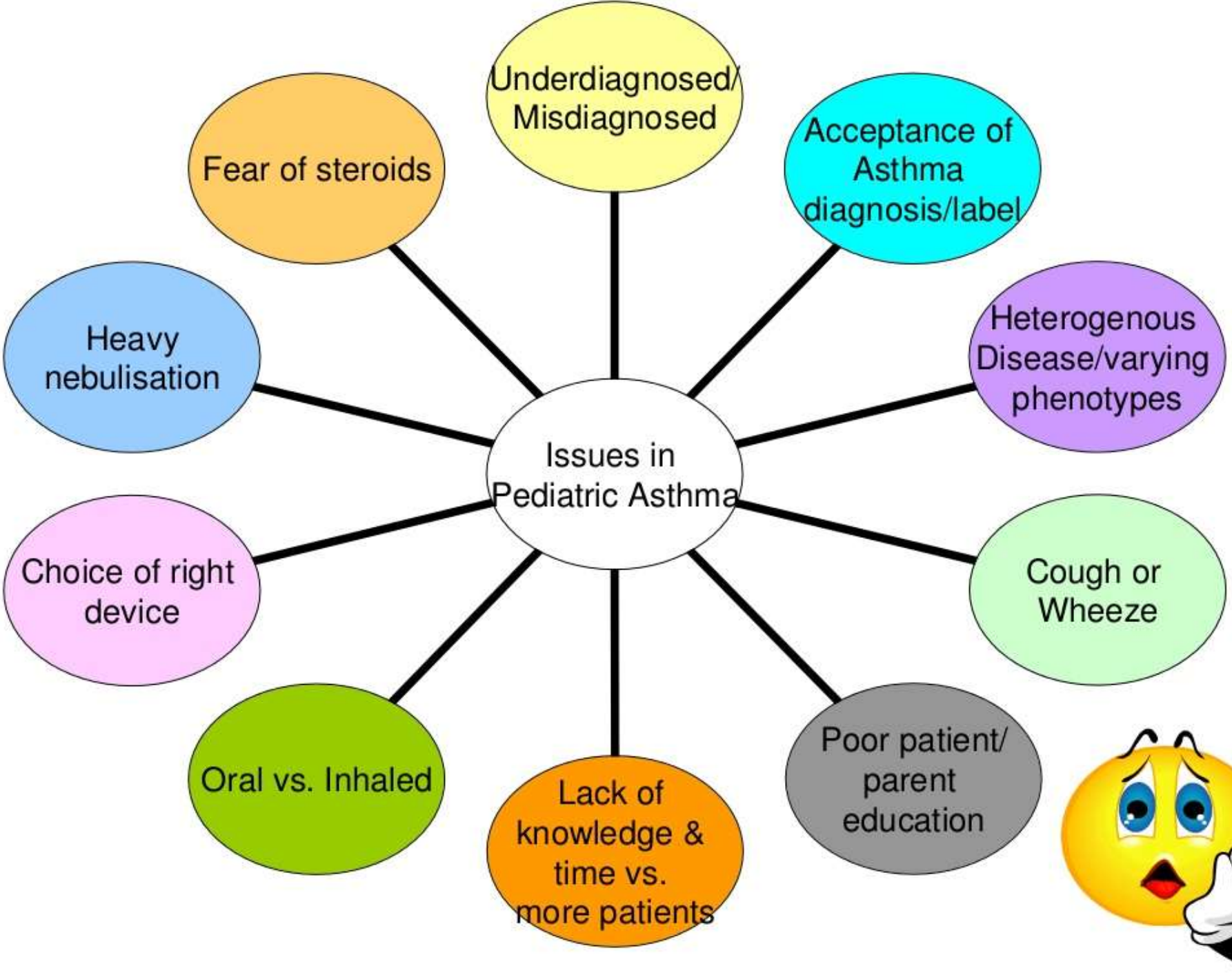
Issues in Pediatric Asthma
Underdiagnosed/ Misdiagnosed
Fear of steroids
Acceptance of Asthma diagnosis/label
Heavy nebulisation
Heterogenous Disease/varying phenotypes
Choice of right device
Cough or Wheeze
Oral vs. Inhaled
Lack of knowledge & time vs. more patients
Poor patient/ parent education

Types of Childhood Asthma

- There are 2 main types of childhood asthma:
- (1) **recurrent wheezing** in early childhood, primarily triggered by common viral infections of the respiratory tract, and
- **(2) chronic asthma** associated with allergy that persists into later childhood and often adulthood.
- A 3rd type of childhood asthma typically emerges in females who experience obesity and early-onset puberty (by 11 yr of age).

Pathogenesis

- **Airflow obstruction** in asthma is the result of numerous pathologic processes. bronchoconstriction of bronchiolar smooth muscular bands restricts or blocks airflow.
- A cellular **inflammatory** infiltrate and exudates distinguished by **eosinophils**,
- but also including other inflammatory cell types (neutrophils, monocytes, lymphocytes, mast cells, basophils),
- Helper T lymphocytes and
- other immune cells that produce proallergic, proinflammatory **cytokines** (IL-4, IL-5, IL-13),
- and **chemokines** (eotaxin) mediate this inflammatory process.

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Clinical Manifestations and Diagnosis

- Intermittent dry **coughing**
- expiratory **wheezing**
- **shortness of breath and chest tightness**
- Intermittent, nonfocal chest pain.
- Respiratory symptoms can be worse at **night**
- **Daytime symptoms**, often linked with physical activities or play.
- limitation of physical activities, general fatigue.

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Wheezing—Asthma?

- Wheezing with upper respiratory infections is very common in small children, but:
  - Many of these children will not develop asthma.
  - Asthma medications may benefit patients who wheeze whether or not they have asthma.

All that wheezes is not asthma.

Cough—Asthma?

- Consider asthma in children with:
  - Recurrent episodes of cough with or without wheezing
  - Nocturnal awakening because of cough
  - Cough that is associated with exercise/play

Cough may be the only symptom present in patients with asthma.

Goldsobel AB, Chipps BE. Cough in the pediatric population. *J Pediatr*. 2010;156(3):352–358

Typical features of Asthma

- Afebrile episodes
- Personal atopy (allergic rhinitis, allergic conjunctivitis, atopic dermatitis, food allergies),
- Family history of atopy or asthma
- Nocturnal Exacerbations.
- Exercise /Activity induced symptoms
- Trigger Induced Symptoms
- Seasonal exacerbations
- Relief with bronchodilators.

Asthma Predictive Index

- Identify high risk children (2 and 3 years of age):
  - ≥4 wheezing episodes in the past year

PLUS

- One major criterion
  - Parent with asthma
  - Atopic dermatitis
  - Aero-allergen sensitivity

OR

- Two minor criteria
  - Food sensitivity
  - Peripheral eosinophilia (≥4%)
  - Wheezing not related to infection

Modified from: Castro-Rodriguez JA, Holberg CJ, Wright AL, et al. A clinical index to define risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med*. 2000;162(4 Pt 1):1403–1406

On examination

- expiratory wheezing
- prolonged expiratory phase
- Decreased breath sounds in some of the lung fields.
- Crackles (or rales) and rhonchi.
- The combination of segmental crackles and poor breath sounds can indicate lung segmental atelectasis.
- In severe exacerbations, features of respiratory distress, with inspiratory and expiratory wheezing, increased prolongation of exhalation, poor air entry.
- In extremis, airflow may be so limited that wheezing cannot be heard .

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investigations

- Lung function tests can help to confirm the diagnosis of asthma and to determine disease severity.
- **Spirometry** is helpful as an objective measure of airflow limitation.usually feasible in **children > 6 yr of age.**

- **Peak expiratory flow (PEF) monitoring** devices provide simple and inexpensive home-use tools to measure airflow and can be helpful in a number of circumstances.
- **Radiology;** The findings of chest radiographs in children with asthma often appear to be normal, aside from subtle and nonspecific findings of hyperinflation (flattening of the diaphragms) and peribronchial thickening. Also complications and co morbidities can be looked.
- Other tests, such as allergy testing to assess sensitization to inhalant allergens, help with the management and prognosis of asthma.

Lung function tests in Asthma

Spirometry (in clinic):
Airflow limitation: •Low FEV_1 (relative to percentage of predicted norms) •FEV_1/FVC ratio <0.80
Bronchodilator response (to inhaled β-agonist): **○Improvement in FEV_1 ≥12% and ≥200 mL***
Exercise challenge: •Worsening in FEV_1 ≥15%*
Daily peak flow or FEV1 monitoring: day to day and/or am-to-pm variation ≥20%*

FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity.
* MAIN criteria consistent with asthma.

The Causes of Asthma exacerbations

- The causes or **inducers** of asthma is very different to what may **trigger** asthma.

Inducers

- **Inducers causes both of the airway to be inflamed and the airway hyper-responsive.**
- **The symptoms that cause induces often last longer.**
- A common form of inducers is allergens. Inhalant allergens are the most important inducer.
- Exposure to any allergen may cause inflammation after a **7-8 hours**.
- **Because inflammation occurs so slowly it is often impossible for the physician to identify the asthma attack.**

The common inhaled allergens are:
Pollen – from grass, tress and weeds
Animal – common household pets such as cats and dogs furs
Molds
Household dust and mites

Triggers

- **Triggers is when the airway become irritated and tightening and as a result causes bronchoconstriction.**
- **Triggers do not cause inflammation.**
- **The symptoms and bronchoconstriction caused by triggers then are immediate and short lived.**
- If inflammation is already present the airway will react more quickly to triggers.

The common triggers of bronchoconstriction include everyday stimuli such as:		
Smoke – from cigarette or factory	Cold Air	Exercise
Strong Fumes – from cars, truck or factory	Dust	Inhaled irritants
Chemicals in the air or in food	Viral infections, such as the common cold	Emotional upsets

Treatment

- **Management** of asthma should have the following components:
- (1) assessment and monitoring of disease activity;
- (2) education to enhance the patient's and family's knowledge and skills for self-management;
- (3) identification and management of precipitating factors and co-morbid conditions that may worsen asthma; and
- (4) appropriate selection of medications to address the patient's needs.
- The long-term goal of asthma management is attainment of optimal asthma control.

In general ???

❖ **There are two main types of drugs used for treating asthma.**

❑ Medications to reduce **bronchoconstrictions:**

- **Beta 2 Agonist**
- **Anticholinergics**
- **Theophylline**

❑ Medications to reduce inflammations:

- **Steroids (oral, Parenteral & Inhalers)**
- **Not steroids:**

- **Leukotriene modifiers (** montelukast is available worldwide; zafirlukast is mentioned only in NAEPP and pranlukast only in Japanese Guideline for Childhood Asthma, 2008 (JGCA).
- **Cromolyn & Nedocromil (**Reduction of mast cell degranulation)

Treatment

Farther more ???

- Long-term control medications:
  - **Corticosteroids (mainly ICS, occasionally OCS).**
  - **Long Acting Beta Agonists (LABA's)** including salmeterol and formoterol,
  - **Leukotriene Modifiers (LTM)**
  - **Cromolyn & Nedocromil**
  - **Methylxanthines: (Sustained-release theophylline)**

- Quick- relief medications:
  - **Short acting Beta Agonists (SABA's)**
  - **Systemic corticosteroids**
  - **Anticholinergics**

- **Classifying Asthma Severity** into intermittent, mild, moderate, or severe persistent asthma depending on symptoms of impairment and risk
- Once classified, use the **6 steps** depending on the severity to obtain asthma control with the lowest amount of medication
- **Controller medications** should be considered if:
- **>4 exacerbations/year,**
- **2 episodes of oral steroids in 6 months, or**
- **use of SABA's (salbutamol) more then twice a week**

FDA Approved Therapies

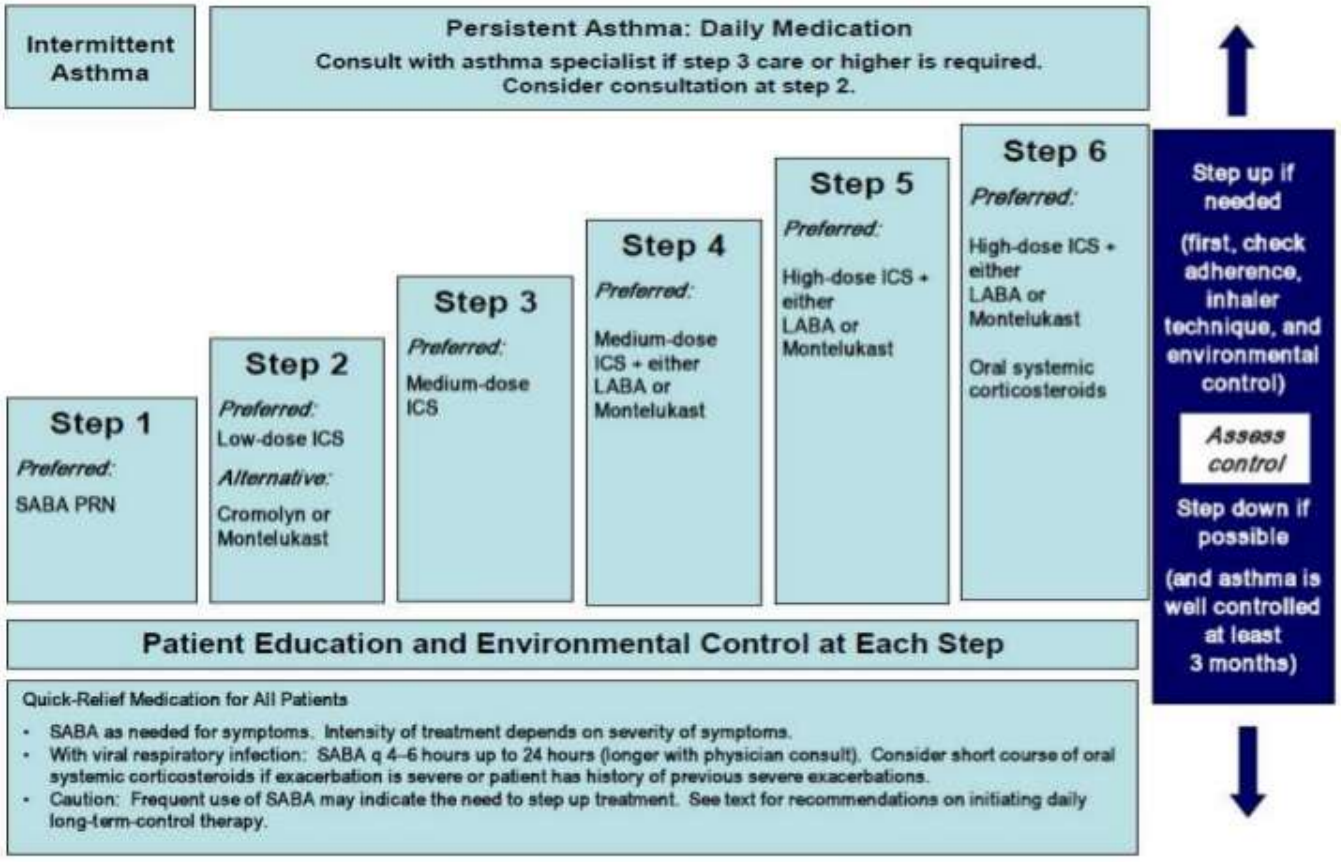
- ICS budesonide nebulizer solution (**1-8 years**)
- ICS fluticasone DPI (**4 years of age and older**)
- LABA and LABA/ICS combination DPI and MDI (**4 years of age and older**)
- Montelukast chewables (**2-4 years**), granules (**down to 1 year of age**)
- Cromolyn sodium nebulizer (**2 years and older**)

Classifying Asthma Severity and Initiating Treatment in Children 0 to 4 Years of Age

Components of Severity		Classification of Asthma Severity (0–4 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0	1–2x/month	3–4x/month	>1x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year	≥2 exacerbations in 6 months requiring oral systemic corticosteroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time. →			
		Exacerbations of any severity may occur in patients in any severity category.			
Recommended Step for Initiating Therapy (See figure 4–1a for treatment steps.)		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	
		In 2–6 weeks, depending on severity, evaluate level of asthma control that is achieved. If no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternative diagnoses.			

Adapted from: National Asthma Education and Prevention Program. *Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma*. US Department of Health and Human Services. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed July 5, 2012

Stepwise Approach for Managing Asthma in Children 0 to 4 Years of Age



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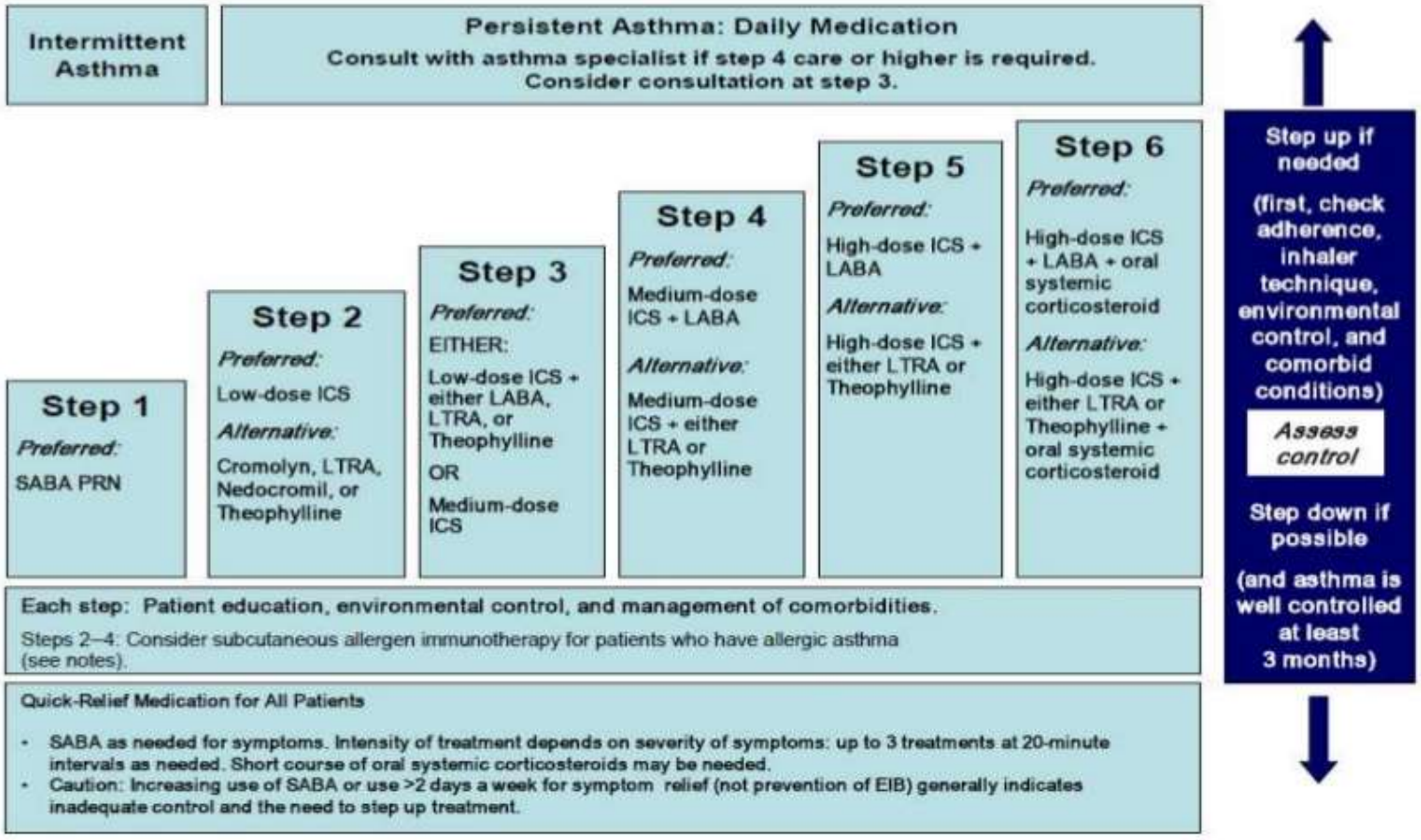
Classifying Asthma Severity and Initiating Treatment in Children 5 to 11 Years of Age

Components of Severity		Classification of Asthma Severity (5–11 years of age)			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC >85%	• FEV_1 = >80% predicted • FEV_1/FVC >80%	• FEV_1 = 60–80% predicted • FEV_1/FVC = 75–80%	• FEV_1 <60% predicted • FEV_1/FVC <75%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Therapy (See figure 4–1b for treatment steps.)		Step 1	Step 2	Step 3, medium-dose ICS option and consider short course of oral systemic corticosteroids	Step 3, medium-dose ICS option, or step 4 and consider short course of oral systemic corticosteroids
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.			

Stepwise Approach for Managing Asthma in Children 5 to 11 Years of Age

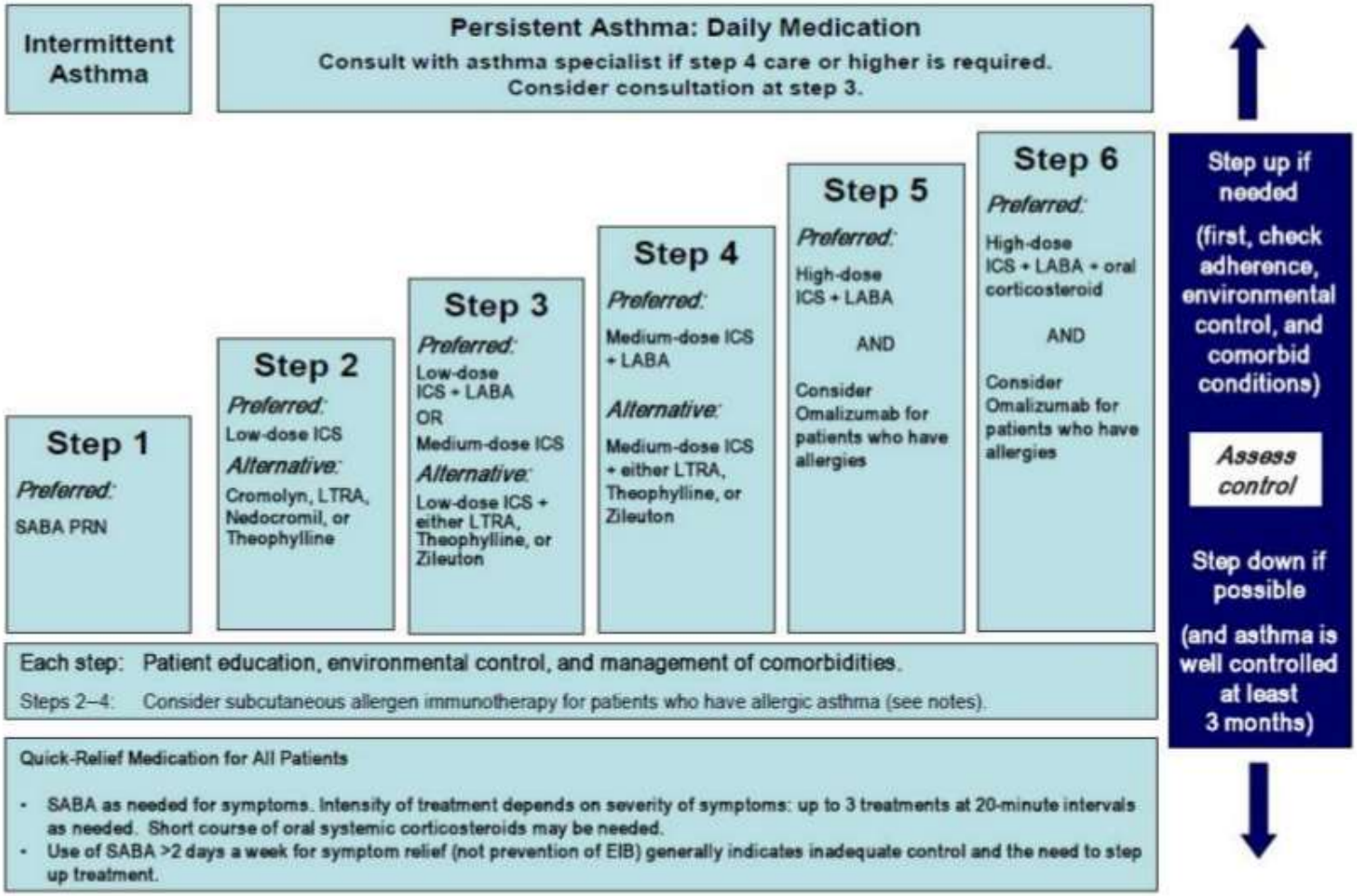


Adapted from: National Asthma Education and Prevention Program. *Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma*. US Department of Health and Human Services. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf. Accessed July 5, 2012

Classifying Asthma Severity and Initiating Treatment in Youth ≥12 Years of Age and Adults

Components of Severity		Classification of Asthma Severity ≥12 years of age			
			Persistent		
		Intermittent	Mild	Moderate	Severe
Impairment Normal FEV_1/FVC: 8–19 yr 85% 20–39 yr 80% 40–59 yr 75% 60–80 yr 70%	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily, and not more than 1x on any day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	• Normal FEV_1 between exacerbations • FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >80% predicted • FEV_1/FVC normal	• FEV_1 >60% but <80% predicted • FEV_1/FVC reduced 5%	• FEV_1 <60% predicted • FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		
		← Consider severity and interval since last exacerbation. → Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.			
Recommended Step for Initiating Treatment		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4 or 5
(See figure 4–5 for treatment steps.)		In 2–6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

Stepwise Approach for Managing Asthma in Children 12 Years of Age and Adults



Low, medium and high dose inhaled corticosteroids

Inhaled corticosteroid	Total daily dose (mcg)		
	Low	Medium	High
Beclometasone dipropionate (CFC)	100–200	>200–400	>400
Beclometasone dipropionate (HFA)	50–100	>100–200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide (HFA)	80	>80–160	>160
Fluticasone propionate (DPI)	100–200	>200–400	>400
Fluticasone propionate (HFA)	100–200	>200–500	>500
Mometasone furoate	110	≥220–<440	≥440
Triamcinolone acetonide	400–800	>800–1200	>1200

Reviewing response and adjusting treatment

- **How often should asthma be reviewed?**
  - 1-3 months after treatment started, then every 3-12 months
  - After an exacerbation, within 1 week
- **Stepping up asthma treatment**
  - *Sustained step-up*, for at least 2-3 months if asthma poorly controlled
    - Important: first check for common causes (symptoms not due to asthma, incorrect inhaler technique, poor adherence)
  - *Short-term step-up*, for 1-2 weeks, e.g. with viral infection or allergen
    - May be initiated by patient with written asthma action plan
- **Stepping down asthma treatment**
  - Consider step-down after good control maintained for 3 months
  - try to reduce therapy (usually by 25-50%)
  - Find each patient's minimum effective dose, that controls both symptoms and exacerbations.

Inhaled Medication deliveries

Inhaled medication delivery devices

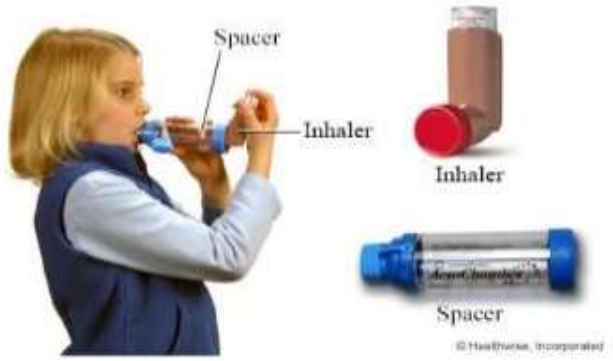
0 to ~5 years

pMDI with static-treated spacer and mask (or mouthpiece as soon as the child is capable of using)

>~5 years

Choice of: pMDI with static-treated spacer and mouthpiece, DPI (rinse or gargle after inhaling ICS), breath-actuated pMDI (depending on patient ability to use, preference)

Nebulizer: second choice at any age



Age specific recommendations for drug delivery devices

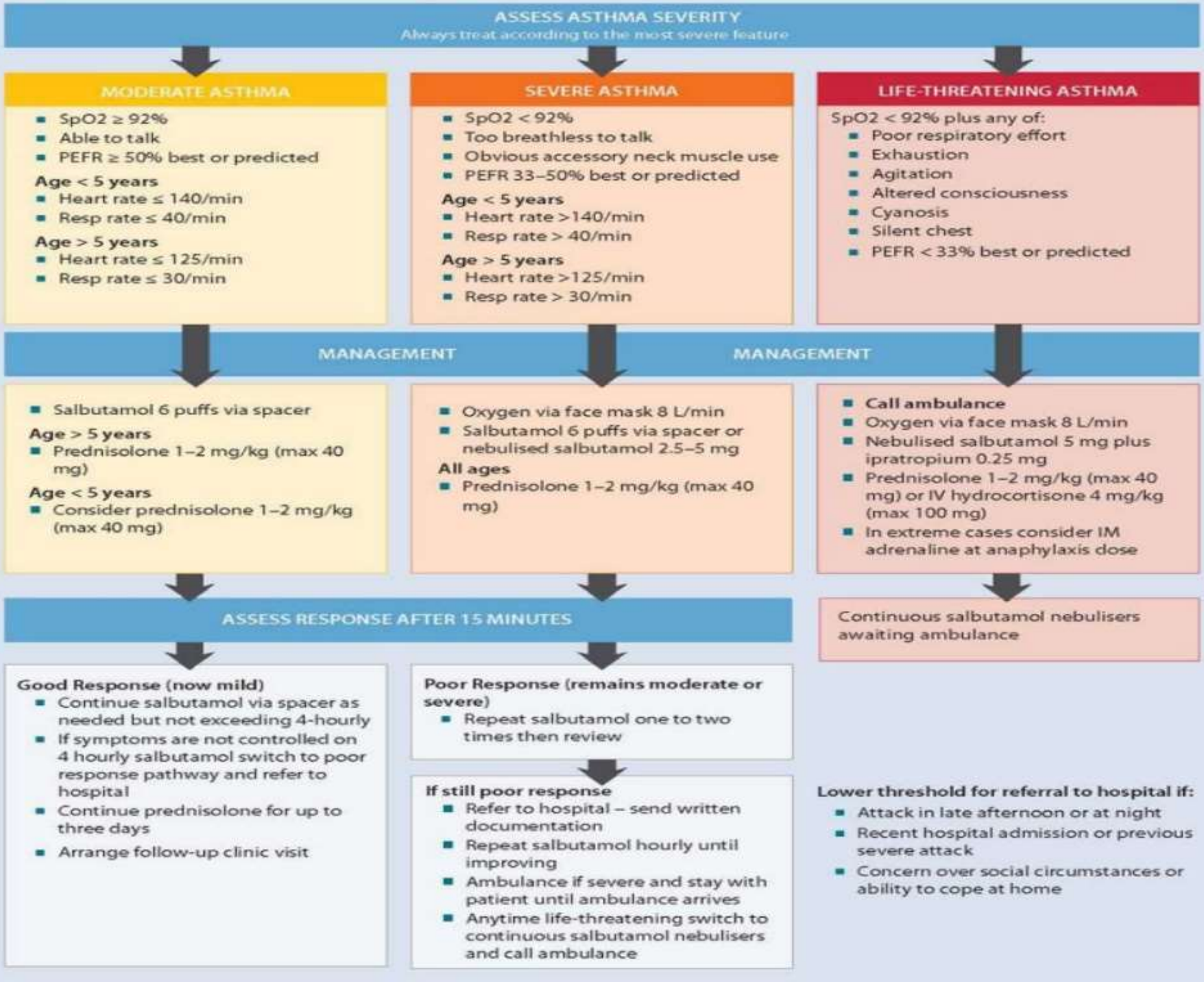
Table 1 Age specific recommendations for drug delivery devices

Age (years)	*First choice*	*Second choice*	*Comments*
0–2	MDI + spacer and facemask	Nebuliser	Ensure optimum spacer use Avoid "open vent" nebulisers
3–6	MDI + spacer	Nebuliser	Very few children at this age can use dry powder inhalers adequately
6–12 (bronchodilators)	MDI + spacer, breath actuated or dry powder inhaler	–	If using breath actuated or dry powder inhaler, also prescribe MDI + spacer for acute exacerbations
6–12 (steroids)	MDI + spacer	Dry powder inhaler	May need to adjust dose if switching between inhalers Advise mouth rinsing or gargling
12+ (bronchodilators)	Dry powder inhaler or breath actuated MDI	–	
12+ (steroids)	MDI + spacer	Dry powder inhaler or breath actuated MDI	May need to adjust dose if switching between inhalers Advise mouth rinsing or gargling
Acute asthma (all ages)	MDI + spacer	Nebuliser	Ensure optimum spacer use and appropriate dosing Nebulise for a set period of time Written instructions for what to do in acute asthma

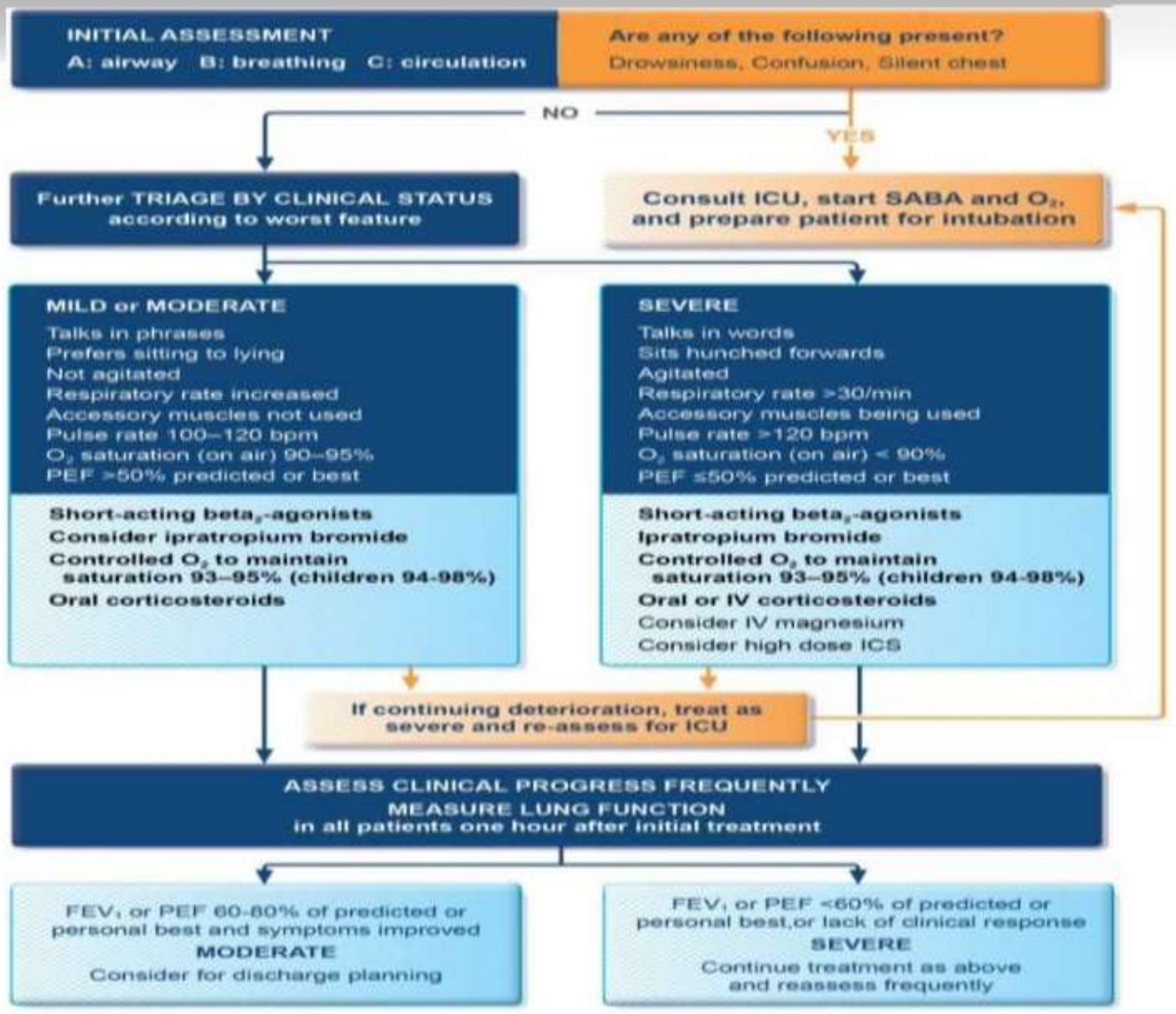
MDI, pressurised metered dose inhaler.

Assessment of exacerbation severity

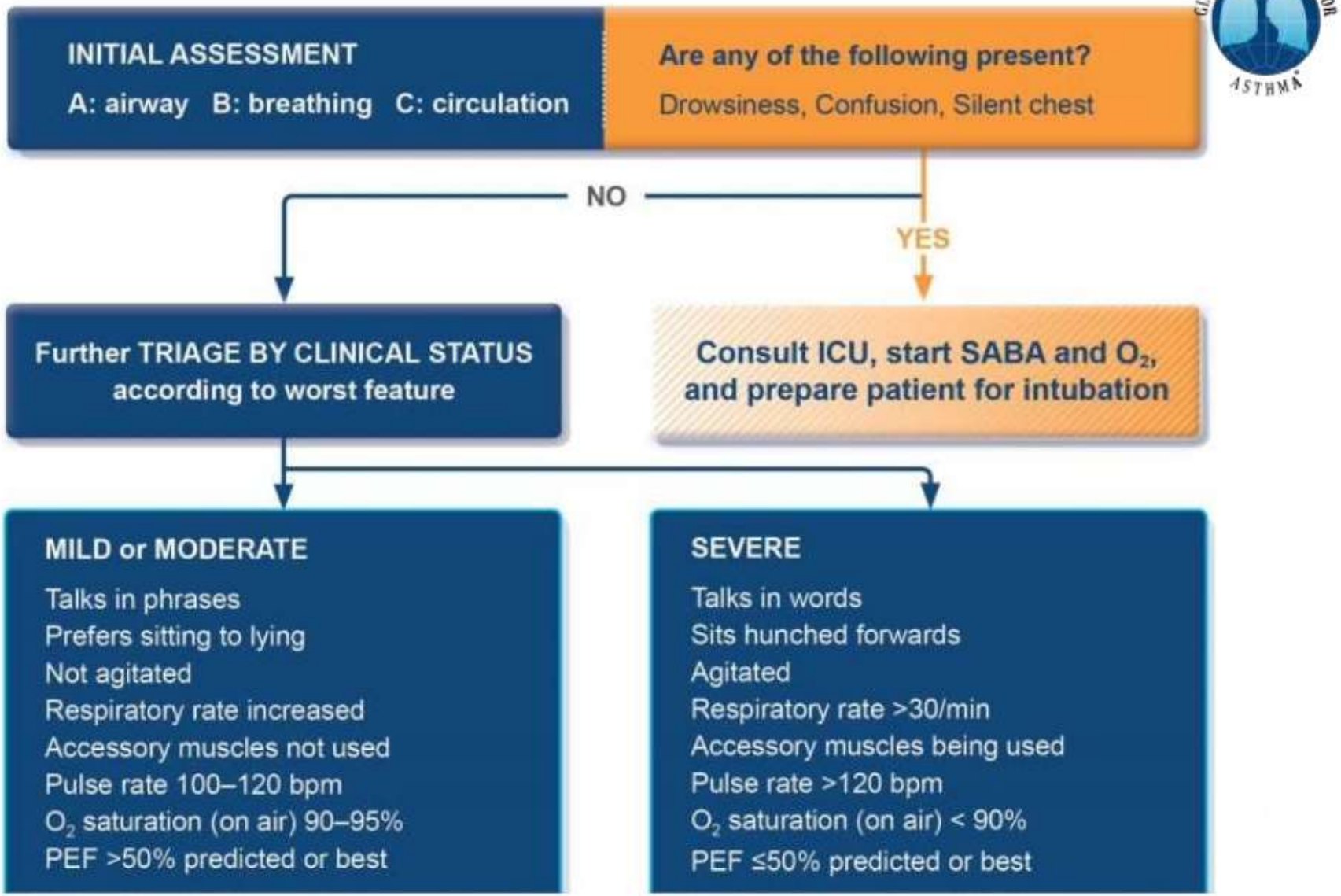
	Mild	Moderate	Severe	Very severe
Wheeze	Variable	Moderate to loud	Loud – on both inhalation and exhalation	Often quiet
Breathlessness	Walking	At rest	At rest/sits upright	
Speaks in	Sentences	Phrases	Words	Unable to speak
Accessory muscle use	No	Common	Marked	Paradoxical
Consciousness	Not affected	Not affected	Agitated, confused	
Respiratory rate	Slightly increased	Increased	Highly increased	Undetermined
Pulse	<100	<140 (depending on age)	>140	Bradycardia
PEF (% of predicted or personal best)	>60–70	40–70	<40	<25
SaO_2 (% on air)	>94–95	90–95	<90	
PCO_2 (mmHg)	<42	<42	≥42	


ASSESS ASTHMA SEVERITY
Always treat according to the most severe feature
MODERATE ASTHMA
SpO2 ≥ 92%
Able to talk
PEFR ≥ 50% best or predicted
Age < 5 years
Heart rate ≤ 140/min
Resp rate ≤ 40/min
Age > 5 years
Heart rate ≤ 125/min
Resp rate ≤ 30/min
SEVERE ASTHMA
SpO2 < 92%
Too breathless to talk
Obvious accessory neck muscle use
PEFR 33–50% best or predicted
Age < 5 years
Heart rate >140/min
Resp rate > 40/min
Age > 5 years
Heart rate >125/min
Resp rate > 30/min
LIFE-THREATENING ASTHMA
SpO2 < 92% plus any of:
Poor respiratory effort
Exhaustion
Agitation
Altered consciousness
Cyanosis
Silent chest
PEFR < 33% best or predicted
MANAGEMENT
MANAGEMENT
Salbutamol 6 puffs via spacer
Age > 5 years
Prednisolone 1–2 mg/kg (max 40 mg)
Age < 5 years
Consider prednisolone 1–2 mg/kg (max 40 mg)
Oxygen via face mask 8 L/min
Salbutamol 6 puffs via spacer or nebulised salbutamol 2.5–5 mg
All ages
Prednisolone 1–2 mg/kg (max 40 mg)
Call ambulance
Oxygen via face mask 8 L/min
Nebulised salbutamol 5 mg plus ipratropium 0.25 mg
Prednisolone 1–2 mg/kg (max 40 mg) or IV hydrocortisone 4 mg/kg (max 100 mg)
In extreme cases consider IM adrenaline at anaphylaxis dose
ASSESS RESPONSE AFTER 15 MINUTES
Continuous salbutamol nebulisers awaiting ambulance
Good Response (now mild)
Continue salbutamol via spacer as needed but not exceeding 4-hourly
If symptoms are not controlled on 4 hourly salbutamol switch to poor response pathway and refer to hospital
Continue prednisolone for up to three days
Arrange follow-up clinic visit
Poor Response (remains moderate or severe)
Repeat salbutamol one to two times then review
If still poor response
Refer to hospital – send written documentation
Repeat salbutamol hourly until improving
Ambulance if severe and stay with patient until ambulance arrives
Anytime life-threatening switch to continuous salbutamol nebulisers and call ambulance
Lower threshold for referral to hospital if:
Attack in late afternoon or at night
Recent hospital admission or previous severe attack
Concern over social circumstances or ability to cope at home

Managing exacerbations in acute care settings



NEW!



MILD or MODERATE

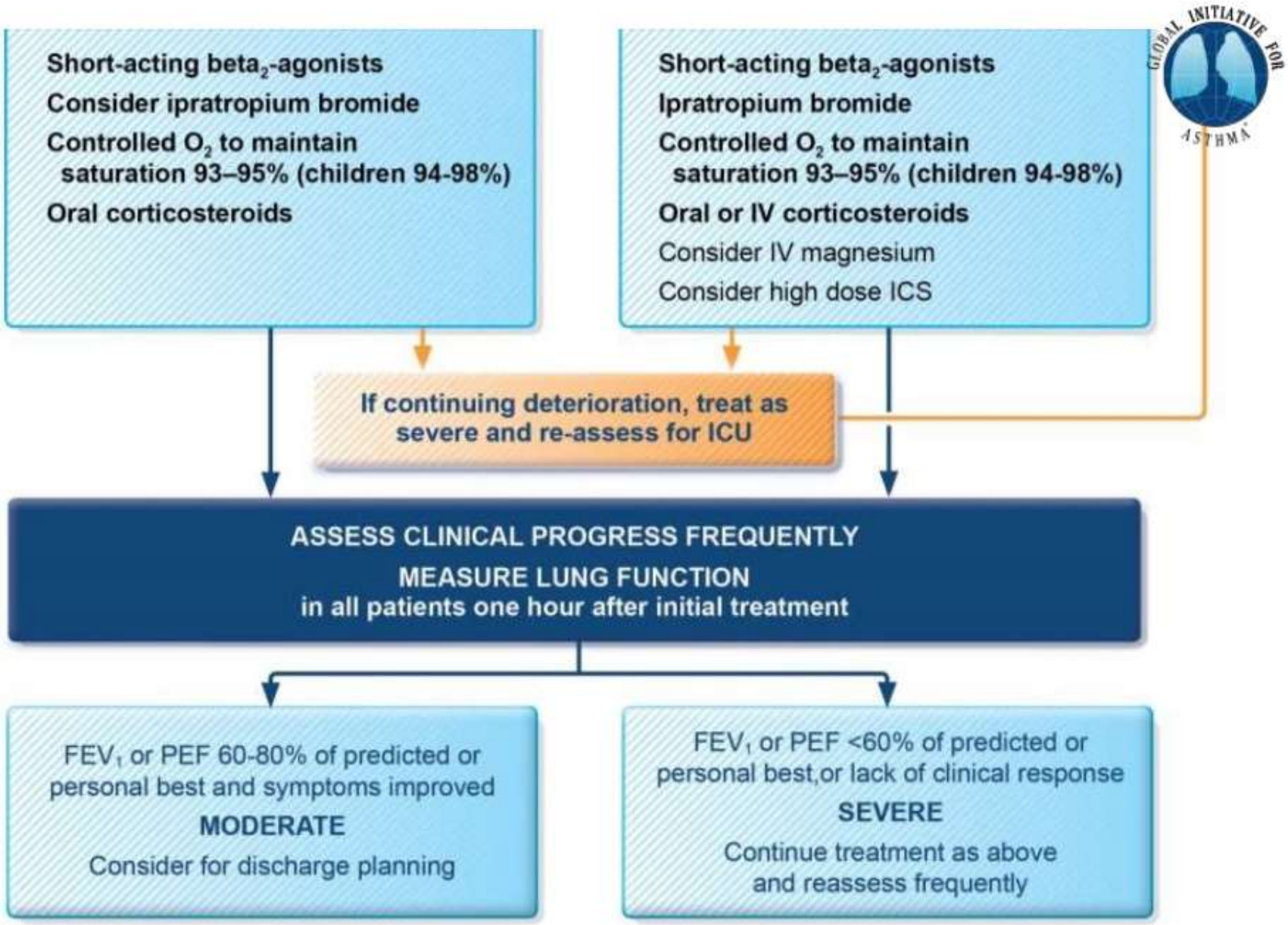
Talks in phrases
Prefers sitting to lying
Not agitated
Respiratory rate increased
Accessory muscles not used
Pulse rate 100–120 bpm
O_2 saturation (on air) 90–95%
PEF >50% predicted or best

Short-acting beta$_2$-agonists
Consider ipratropium bromide
Controlled O_2 to maintain saturation 93–95% (children 94-98%)
Oral corticosteroids

SEVERE

Talks in words
Sits hunched forwards
Agitated
Respiratory rate >30/min
Accessory muscles being used
Pulse rate >120 bpm
O_2 saturation (on air) < 90%
PEF ≤50% predicted or best

Short-acting beta$_2$-agonists
Ipratropium bromide
Controlled O_2 to maintain saturation 93–95% (children 94-98%)
Oral or IV corticosteroids
Consider IV magnesium
Consider high dose ICS



Prognosis

- Recurrent coughing and wheezing occurs in 35% of preschool-aged children.
- Of these, approximately one third continue to have persistent asthma into later childhood, and approximately two thirds improve on their own through their teen years.

Prognosis

- Asthma severity by the ages of 7-10 yr of age is predictive of asthma persistence in adulthood.
- Children with moderate to severe asthma and with lower lung function measures are likely to have persistent asthma as adults.
- Children with milder asthma and normal lung function are likely to improve over time, with some becoming periodically asthmatic (disease-free for months to years);
- **however, complete remission for 5 yr in childhood is uncommon.**

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Prevention

- Investigations into the environmental and lifestyle factors responsible for the lower prevalence of childhood asthma suggest that early immunomodulatory intervention might prevent asthma development.
- A **"hygiene hypothesis"** purports that naturally occurring microbial exposures in early life might drive early immune development away from allergic sensitization, persistent airways inflammation, and remodeling.

Prevention

- **Several nonpharmacotherapeutic measures with numerous positive health attributes—**

✓ avoidance of environmental tobacco smoke (beginning prenatally),

✓ prolonged breastfeeding (>4 mo),

✓ an active lifestyle, and a healthy diet—might reduce the likelihood of asthma development.

✓ Immunizations are currently not considered to increase the likelihood of development of asthma; therefore, all standard childhood immunizations are recommended for children with asthma, including varicella and annual influenza vaccines.

ALLEGIC RHINITIS IN CHILDREN

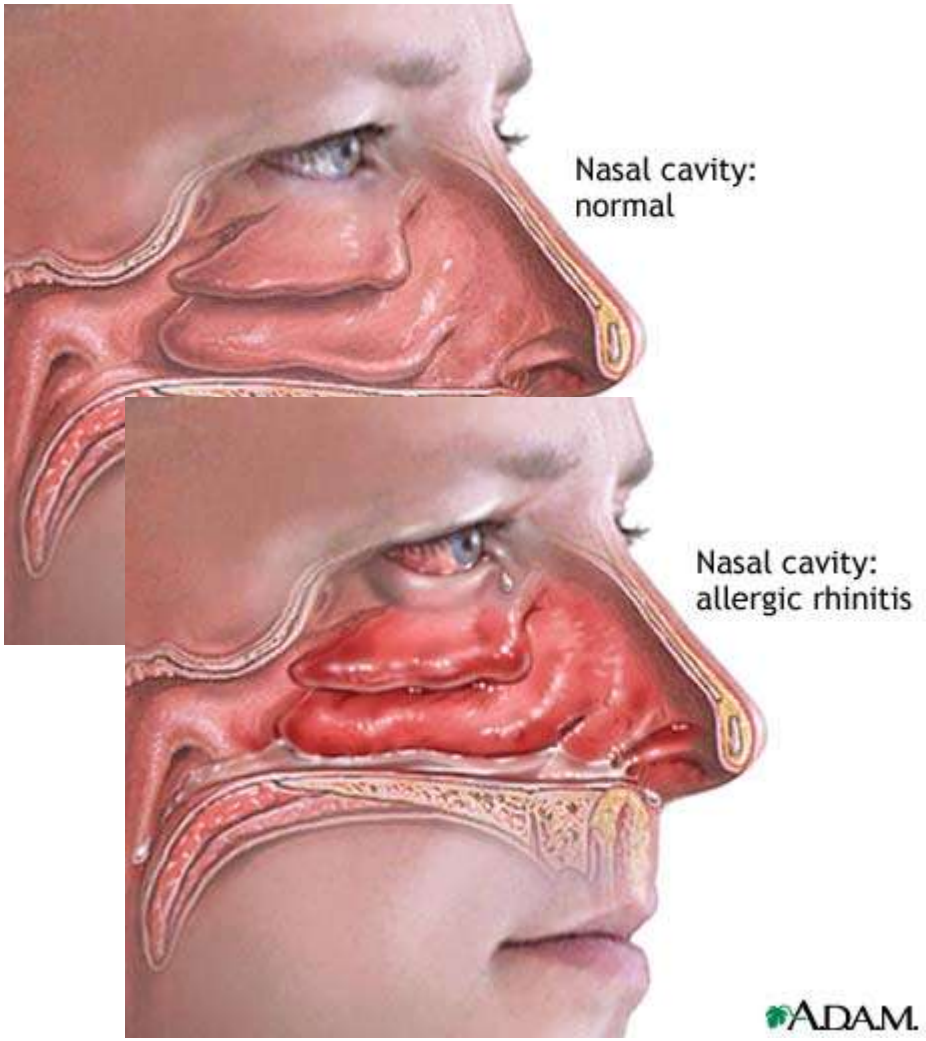
Assoc. Prof. N. Balgaranov
MU Pleven

Outline of Presentation

- What is allergic rhinitis?
- Epidemiology
- Pathophysiology
- Diagnosis and differential diagnosis
- Assessment and classification of AR
- Health effects of AR
- Management of AR

What is Allergic Rhinitis

- Allergic rhinitis involves inflammation of the mucous membranes of the nose, eyes, eustachian tubes, middle ear, sinuses, and pharynx.
- The nose invariably is involved, and the other organs are affected in certain individuals.
- Inflammation of the mucous membranes is characterized by a complex interaction of inflammatory mediators but ultimately is triggered by an immunoglobulin E (IgE)–mediated response to an extrinsic protein



- Rhinorhoea
- Nasal blockage
- Postnasal drip
- Itchiness
- Sneezing
- Associated health effects

!! **IgE mediated**

Pathophysiology

- The tendency to develop allergic, or IgE-mediated, reactions to extrinsic allergens has a genetic component.
- In susceptible individuals, exposure to certain foreign proteins leads to allergic sensitization, which is characterized by the production of specific IgE directed against these proteins.
- This specific IgE coats the surface of mast cells, which are present in the nasal mucosa.
- When the specific protein is inhaled into the nose, it can bind to the IgE on the mast cells, leading to immediate and delayed release of a number of mediators.

Pathophysiology

- The mediators that are immediately released include histamine, tryptase, chymase, kinins, and heparin.
- The mast cells quickly synthesize other mediators, including leukotrienes and prostaglandin D2.
- These mediators, via various interactions, ultimately lead to the symptoms of rhinorrhea (ie, nasal congestion, sneezing, itching, redness, tearing, swelling, ear pressure, postnasal drip).
- Mucous glands are stimulated, leading to increased secretions. Vascular permeability is increased, leading to plasma exudation.
- Vasodilation occurs, leading to congestion and pressure. Sensory nerves are stimulated, leading to sneezing and itching. All of these events can occur in minutes; hence, this reaction is called the early, or immediate, phase of the reaction

Pathophysiology

- Over 4-8 hours, these mediators, through a complex interplay of events, lead to the recruitment of other inflammatory cells to the mucosa, such as neutrophils, eosinophils, lymphocytes, and macrophages.
- This results in continued inflammation, termed the late-phase response.
- The symptoms of the late-phase response are similar to those of the early phase, but less sneezing and itching and more congestion and mucus production tend to occur.[13]
- The late phase may persist for hours or days.

Epidemiology

Frequency: Allergic rhinitis affects approximately 40 million people in the United States. Recent US figures suggest a 20% cumulative prevalence rate. Scandinavian studies have demonstrated a cumulative prevalence rate of 15% in men and 14% in women.[17] The prevalence of allergic rhinitis may vary within and among countries. This may be due to geographic differences in the types and potency of different allergens and the overall aeroallergen burden.

Mortality/Morbidity- While allergic rhinitis itself is not life-threatening (unless accompanied by severe asthma or anaphylaxis), morbidity from the condition can be significant. Allergic rhinitis often coexists with other disorders, such as asthma, and may be associated with asthma exacerbations.

Epidemiology

Race: Allergic rhinitis occurs in persons of all races. Prevalence of allergic rhinitis seems to vary among different populations and cultures, which may be due to genetic differences, geographic factors or environmental differences, or other population-based factors.

Sex: In childhood, allergic rhinitis is more common in boys than in girls, but in adulthood, the prevalence is approximately equal between men and women.

Age: Onset of allergic rhinitis is common in childhood, adolescence, and early adult years, with a mean age of onset 8-11 years, but allergic rhinitis may occur in persons of any age. In 80% of cases, allergic rhinitis develops by age 20 years.

Diagnosis of Allergic Rhinitis

1. History & symptoms of recurrent or persistent rhinitis and/or associated health effects
2. Signs of atopy and recurrent or persistent rhinitis
3. Demonstration of IgE allergy
4. Exclusion of other causes of rhinitis

Diagnosis of Allergic Rhinitis

1. History & clinical symptoms of recurrent or persistent rhinitis and/or associated health effects
   - Rhinorhoea
   - Nasal blockage
   - Postnasal drip
   - Itchiness
   - Sneezing
   - Others: conjunctivitis, eczema, asthma, chronic rhinosinusitis, otitis media with effusion, sleep obstruction…

History

Important elements in history include an evaluation of the nature, duration, and time course of symptoms; possible triggers for symptoms; response to medications; comorbid conditions; family history of allergic diseases; environmental exposures; occupational exposures; and effects on quality of life.

- Symptoms that can be associated with allergic rhinitis include sneezing, itching (of nose, eyes, ears, palate), rhinorrhea, postnasal drip, congestion, headache, earache, tearing, red eyes, eye swelling, fatigue, drowsiness, and malaise.

Symptoms and chronicity

- Determine the age of onset of symptoms and whether symptoms have been present continuously since onset.
- Determine the time pattern of symptoms and whether symptoms occur at a consistent level throughout the year (ie, perennial rhinitis), only occur in specific seasons (ie, seasonal rhinitis), or a combination of the two.
- During periods of exacerbation, determine whether symptoms occur on a daily basis or only on an episodic basis. Determine whether the symptoms are present all day or only at specific times during the day.
- Determine which organ systems are affected and the specific symptoms.

Trigger factors

- Determine whether symptoms are related temporally to specific trigger factors. This might include exposure to pollens outdoors, mold spores, specific animals, or dust while cleaning the house.
- Irritant triggers such as smoke, pollution, and strong smells can aggravate symptoms in a patient with allergic rhinitis. These are also common triggers of vasomotor rhinitis.
- Other patients may describe year-round symptoms that do not appear to be associated with specific triggers. This could be consistent with nonallergic rhinitis, but perennial allergens, such as dust mite or animal exposure, should also be considered in this situation.

Co-morbid conditions

- Patients with allergic rhinitis may have other atopic conditions such as asthma or atopic dermatitis.
- Look for conditions that can occur as complications of allergic rhinitis. Sinusitis occurs quite frequently
- Other possible complications include otitis media, sleep disturbance or apnea, dental problems (overbite), and palatal abnormalities.
- Nasal polyps occur in association with allergic rhinitis, although whether allergic rhinitis actually causes polyps remains unclear.
- Investigate past medical history, including other current medical conditions. Diseases such as hypothyroidism or sarcoidosis can cause nonallergic rhinitis.

Family history

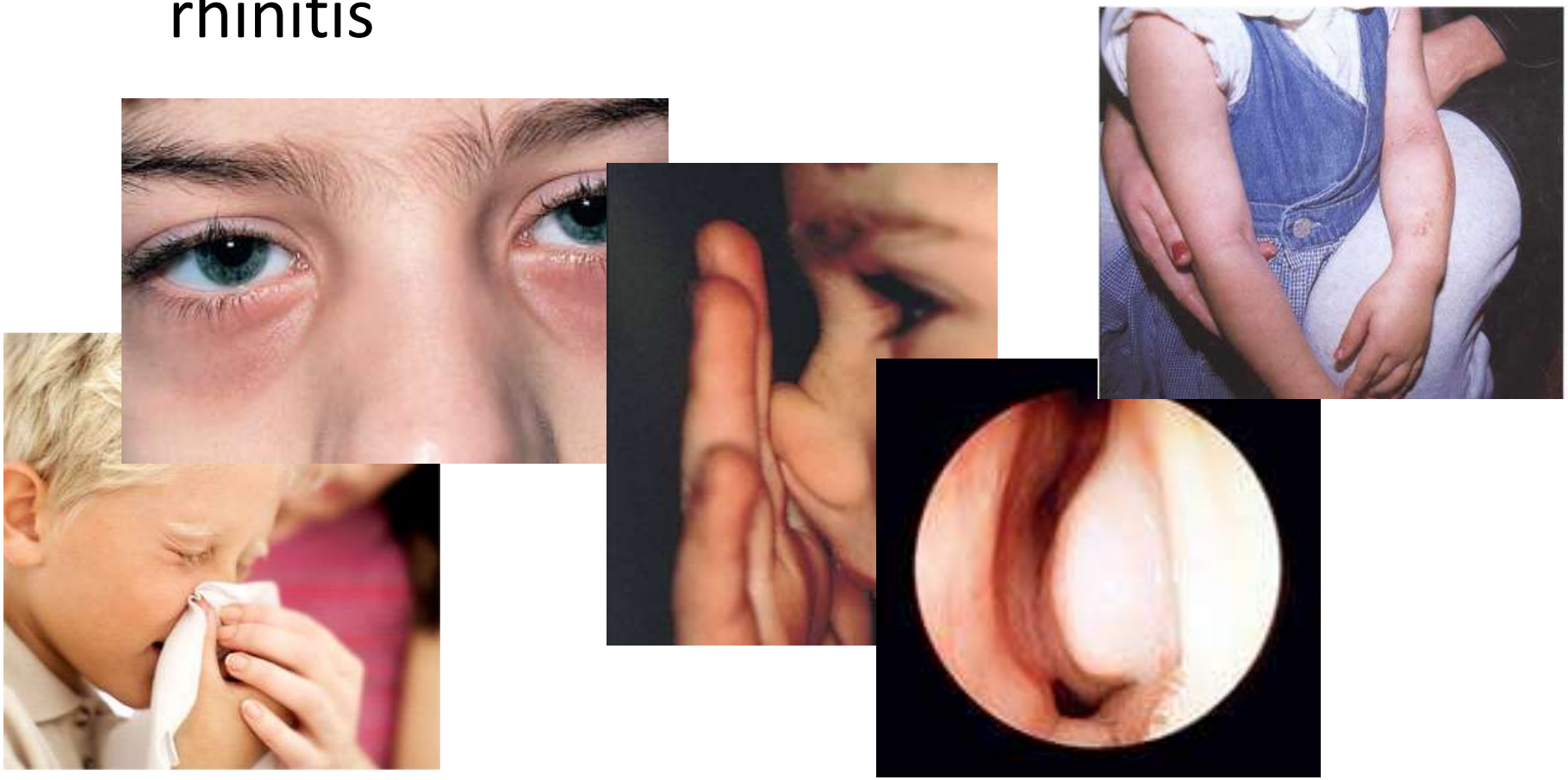
- Because allergic rhinitis has a significant genetic component, a positive family history for atopy makes the diagnosis more likely.
- A greater risk of allergic rhinitis exists if both parents are atopic than if one parent is atopic.
- However, the cause of allergic rhinitis appears to be multifactorial, and a person with no family history of allergic rhinitis can develop allergic rhinitis.

Environmental exposure

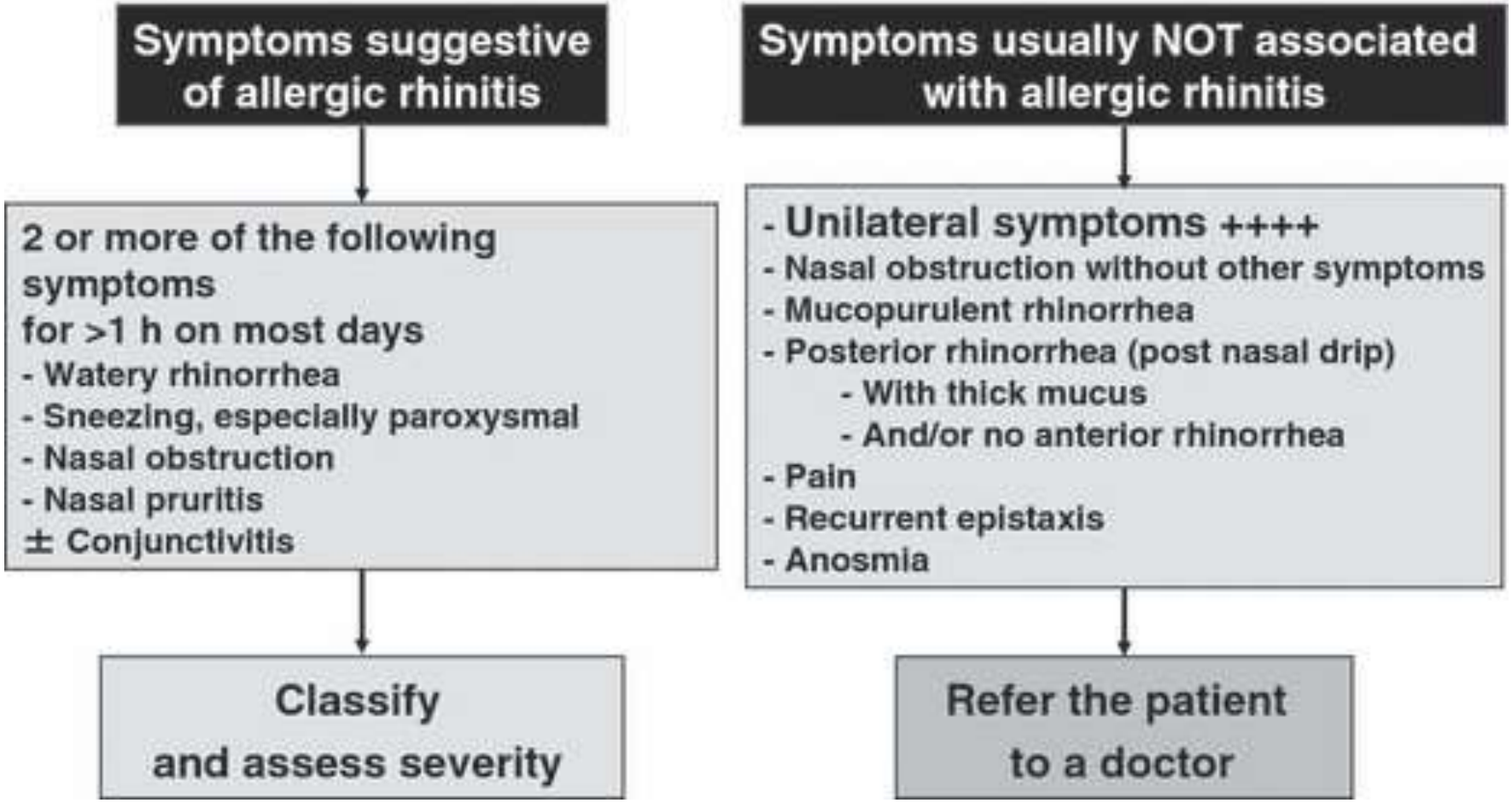
- A thorough history of environmental exposures helps to identify specific allergic triggers.
- This should include investigation of risk factors for exposure to perennial allergens (eg, dust mites, mold, pets).
- Risk factors for dust mite exposure include carpeting, heat, humidity, and bedding that does not have dust mite–proof covers.
- Chronic dampness is a risk factor for mold exposure.
- A history of hobbies and recreational activities helps determine risk and a time pattern of pollen exposure.

Diagnosis of Allergic Rhinitis

2. Signs of atopy and recurrent or persistent rhinitis

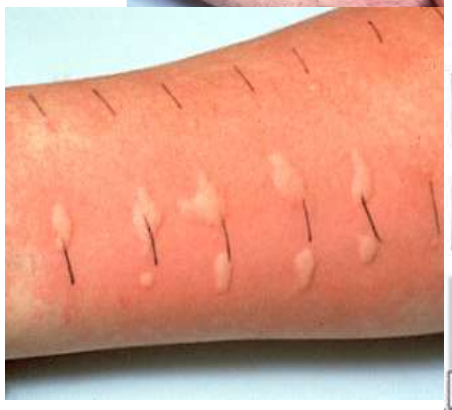


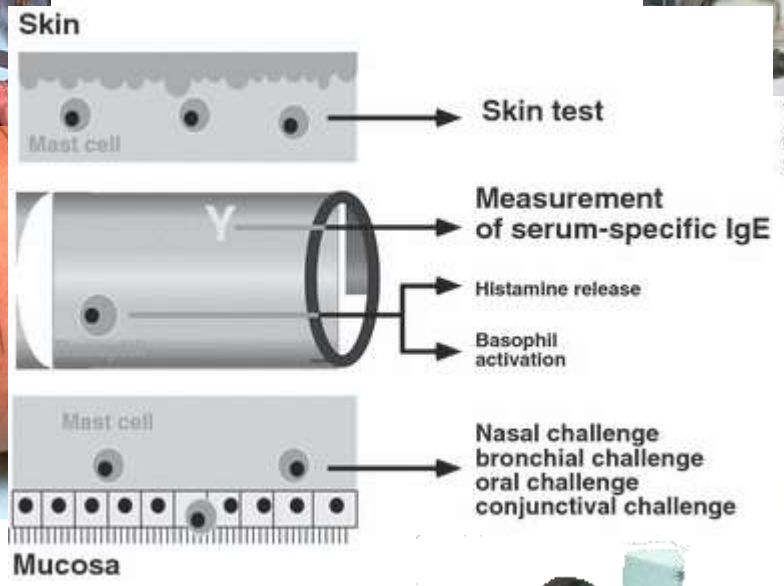
Diagnosis in Primary Care Setting



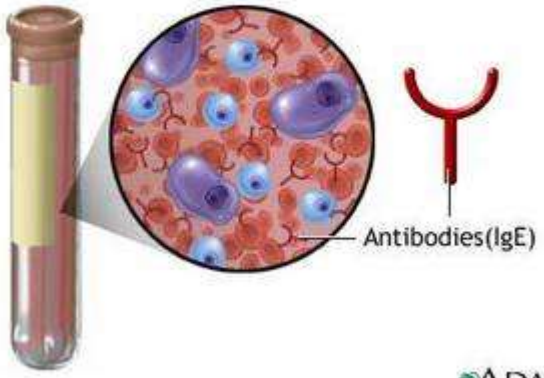
Diagnosis of Allergic Rhinitis

3. Demonstration of IgE allergy





The blood test measures the levels of allergy antibody, or IgE, produced when your blood is mixed with a series of allergens in a laboratory



Immunoassay vs Skin Test for Diagnosis of Allergy

Immunoassay

- Not influenced by medication
- Not influenced by skin disease
- Does not require expertise
- Quality control possible
- Expensive

Skin test

- Higher sensitivity
- Immediate results
- Requires expertise
- Cheaper

Other Causes of Rhinitis in Children

- Infection
  - Viral, bacterial,
  - Rhinosinusitis
- Foreign body in the nose
- Rhinitis associated with physical or chemical factors
- Drug, food induced rhinitis
- NARES, aspirin sensitivity
- Vasomotor rhinitis

Health Effects of Allergic Rhinitis

- Social inconvenience
- Sleep disturbances/obstruction
- Learning difficulties
- Impaired maxillary growth
- Dental problems
- Infection: nose and sinuses
- Co-morbidities: conjunctivitis, asthma, rhinosinusitis, otitis media

Link Between Allergic Rhinitis and Other Chronic Disorders

Comorbidities[1,2]

Asthma

Allergic rhinoconjunctivitis

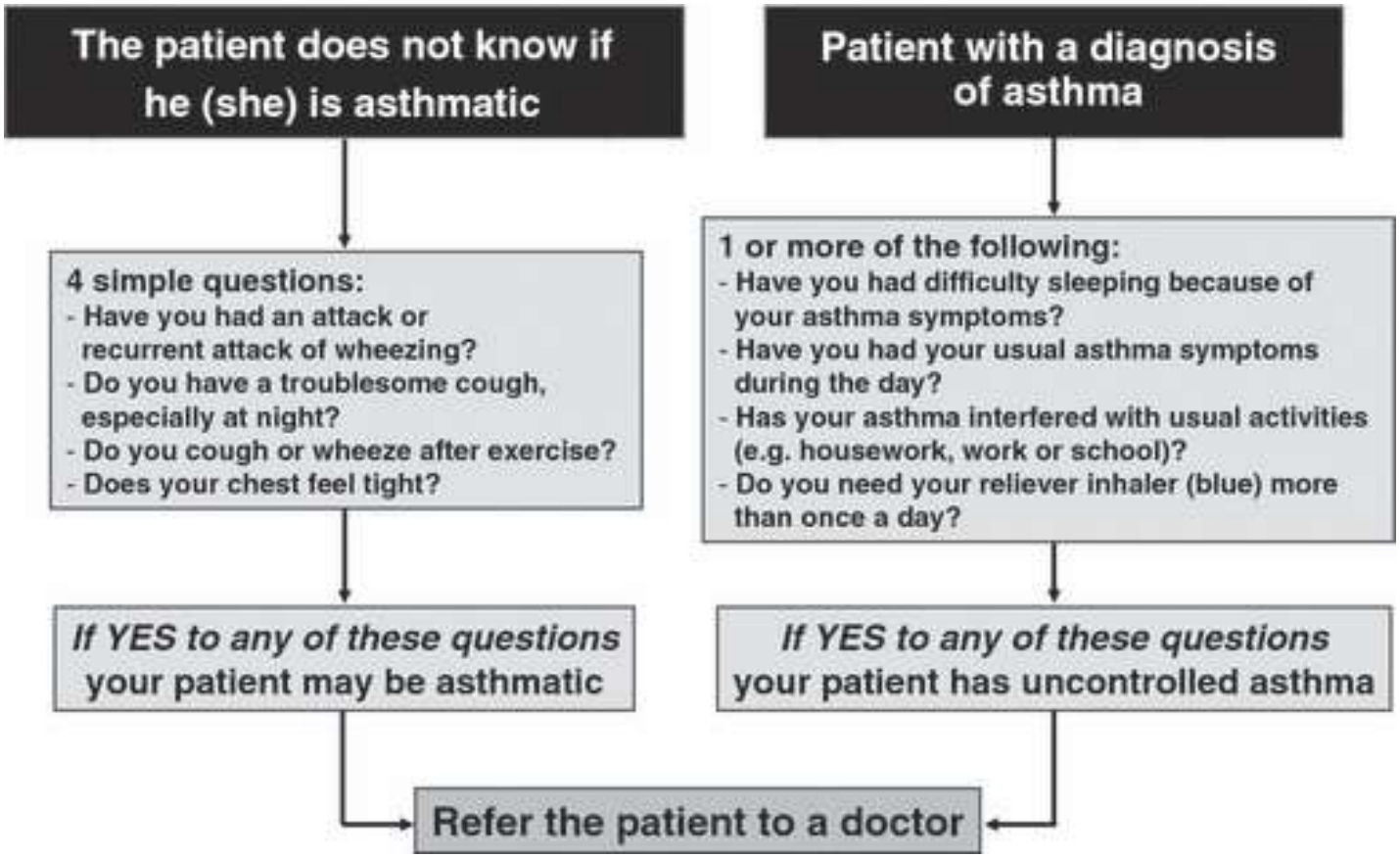
Sinusitis

Otitis media

Complications[1,3]

1. Spector SL, et al. *J Allergy Clin Immunol.* 1997;99:S773-S780.
2. O'Connell EJ. *Allergy.* 2004;78:7-11.
3. Rachelefsky GR. *Ann Allergy Asthma Immunol* 1998;82:1-10.

Looking for asthma…



In Patients with Rhinitis:

- Routinely ask for symptoms suggestive of asthma
- Perform chest examination
- Consider lung function testing
- Consider tests for bronchial hyperresponsiveness in selected cases

AR Classification

Intermittent

. < 4 days per week

. or < 4 weeks

Persistent

. > 4 days per week

. and > 4 weeks

Mild

normal sleep

& no impairment of daily activities, sport, leisure

& normal work and school

& no troublesome symptoms

Moderate-severe

one or more items

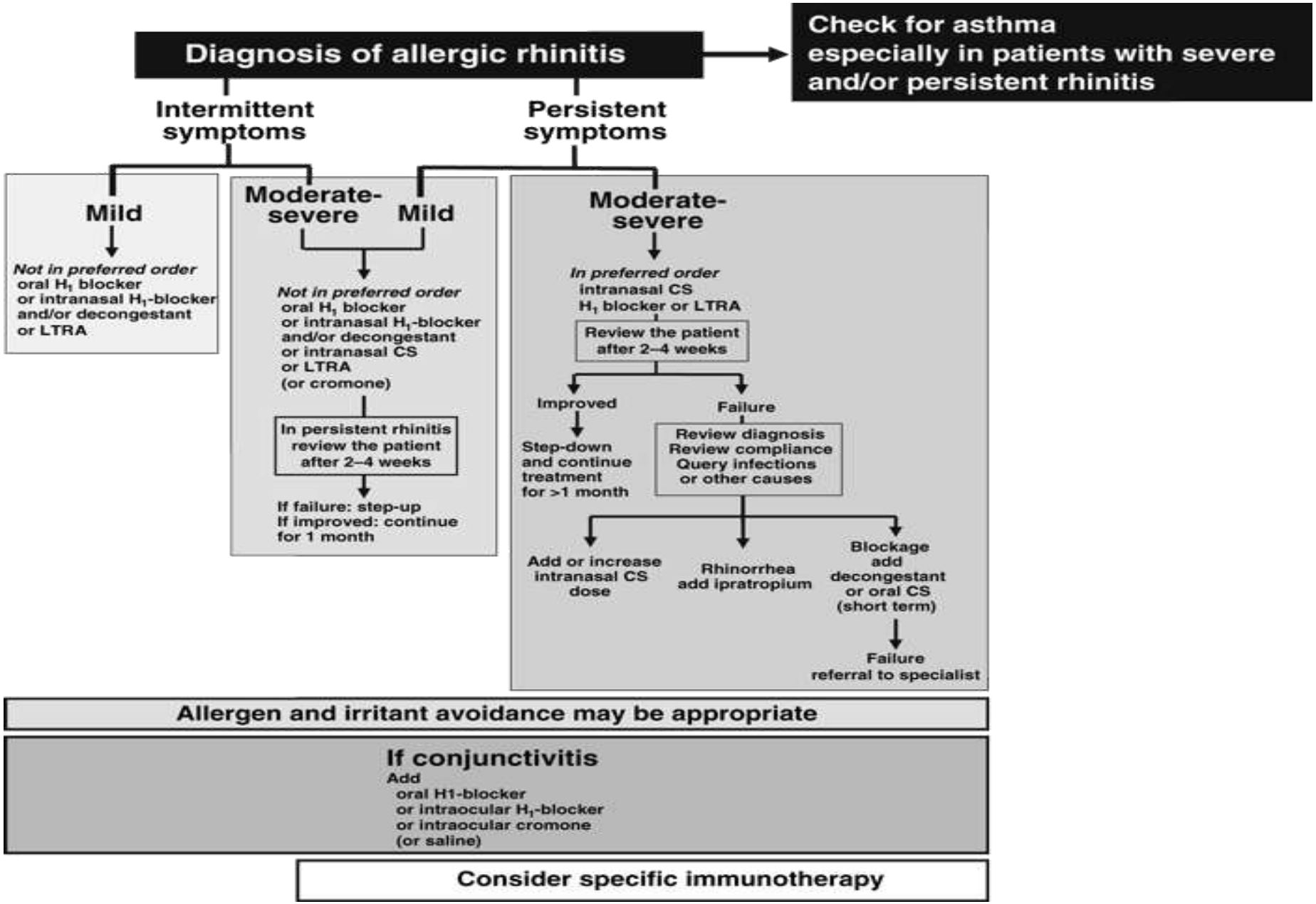
. abnormal sleep

. impairment of daily activities, sport, leisure

. abnormal work and school

. troublesome symptoms

in untreated patients


Diagnosis of allergic rhinitis
Check for asthma especially in patients with severe and/or persistent rhinitis
Intermittent symptoms
Persistent symptoms
Mild
Not in preferred order
oral H1 blocker
or intranasal H1-blocker
and/or decongestant
or LTRA
Moderate-severe
Mild
Not in preferred order
oral H1 blocker
or intranasal H1-blocker
and/or decongestant
or intranasal CS
or LTRA
(or cromone)
In persistent rhinitis review the patient after 2–4 weeks
If failure: step-up
If improved: continue for 1 month
Moderate-severe
In preferred order
intranasal CS
H1 blocker or LTRA
Review the patient after 2–4 weeks
Improved
Step-down and continue treatment for >1 month
Failure
Review diagnosis
Review compliance
Query infections
or other causes
Add or increase intranasal CS dose
Rhinorrhea add ipratropium
Blockage add decongestant or oral CS (short term)
Failure referral to specialist
Allergen and irritant avoidance may be appropriate
If conjunctivitis
Add
oral H1-blocker
or intraocular H1-blocker
or intraocular cromone
(or saline)
Consider specific immunotherapy

Management of allergic rhinitis

The management of allergic rhinitis involves the following components:

- Allergen avoidance
- Pharmacotherapy.
- Allergen immunotherapy. Of note, immunotherapy helps prevent the development of asthma in children with allergic rhinitis, and thus should be given special consideration in the pediatric population.

Medications for Allergic Rhinitis - ARIA

	sneezing eye symptoms	rhinorrhea	nasal obstruction	nasal itch	
H1-antihistamines					
oral	+++	+++	0 to +	+++	++
intranasal	++	+++	+	++	0
intraocular	0	0	0	0	+++
Corticosteroids	+++	+++	++	++	+
Cromones					
intranasal	+	+	+	+	0
intraocular	0	0	0	0	++
Decongestants					
intranasal	0	0	++	0	0
oral	0	0	+	0	0
Anti-cholinergics	0	+++	0	0	0
Anti-leukotrienes	0	+	++	0	++

Oral Antihistamines

- **First generation agents**

  Chlorpheniramine

  Brompheniramine

  Diphenydramine

  Promethazine

  Tripolidine

  Hydroxyzine

  Azatadine

- **Newer agents**

  Acrivastine

  Azelastine

  Cetirizine

  Desloratadine Fexofenadine

  Levocetirizine Loratadine

  Mizolastine

Nasal Antihistamines

- Azelastine
- Levocabastine
- Olopatadine

Newer Generation Oral Antihistamines

- First line treatment for mild allergic rhinitis
- Effective for
  - Rhinorrhea
  - Nasal pruritus
  - Sneezing
- Less effective for
  - Nasal blockage
- Possible additional anti-allergic and anti-inflammatory effect
    - In-vitro effect > in-vivo effect
- Minimal or no sedative effects
- Once daily administration
- Rapid onset and 24 hour duration of action

Decongestants: Alpha-2 Adrenergic Agonists

- Oral

  Pseudoephedrine

- Nasal

  Phenylephrine

  Oxymetazoline

  Xylometazoline

Decongestants

EFFICACY:

- Oral decongestants: moderate
- Nasal decongestants: high

ADVERSE EFFECTS:

- Oral decongestants: insomnia, tachycardia, hyperkinesia tremor, increased blood pressure, stroke (?)
- Nasal decongestants: tachyphylaxis, rebound congestion, nasal hyperresponsiveness, rhinitis medicamentosa

Anti-Leukotriene Treatment in Allergic Rhinitis

Efficacy

- Equipotent to H1 receptor antagonists but with onset of action after 2 days
- Reduce nasal and systemic eosinophilia
- May be used for simultaneous treatment of allergic rhinitis and asthma

Safety

- Dyspepsia (approx. 2%)

Nasal Corticosteroids

Beclomethasone dipropionate

Budesonide

Ciclesonide

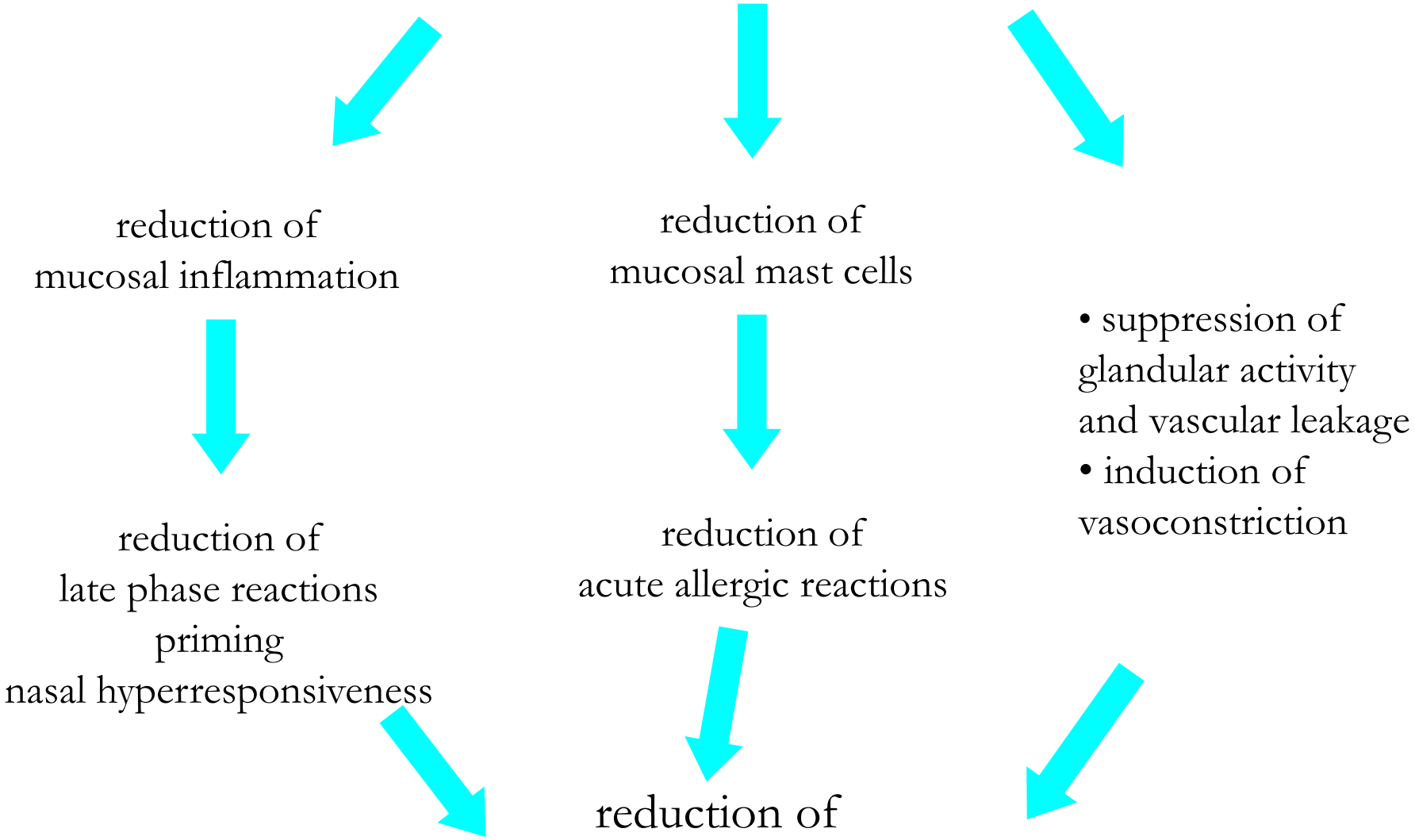
Flunisolide

Fluticasone propionate

Mometasone furoate

Triamcinolone acetonide

Nasal Corticosteroids



Nasal Corticosteroids

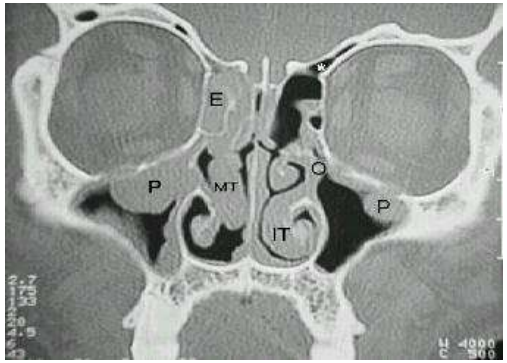
- Most potent anti-inflammatory agents
- Effective in treatment of all nasal symptoms including obstruction
- Superior to anti-histamines and anti-leukotienes
- First line pharmacotherapy for persistent allergic rhinitis

Nasal Corticosteroids

- Overall safe to use
- Adverse Effects
  - Nasal irritation
  - Epistaxis
  - Septal perforation (extremely rare)
  - HPA axis suppression
  - Suppressed growth

Other Management Aspects

- Manage other co-morbidities:
  - Allergic conjunctivitis
  - Asthma
  - Sinusitis…
- Environmental manipulations:
  - allergen avoidance
  - Pollution treatment
- Nutritional support
- Activities and sports



Environmental Control

1. **Allergens**
   - House dust mites
   - Pets
   - Cockroaches
   - Molds
   - Pollen

2. **Pollutants and Irritants**

House dust mite allergen avoidance

- Provide adequate ventilation to decrease humidity
- Wash bedding regularly at 60˚C
- Encase pillow, mattress and quilt in allergen impermeable covers
- Use vacuum cleaner with HEPA filter
- Dispose of feather bedding
- Remove carpets
- Remove curtains, pets and stuffed toys from bedroom

Allergen Avoidance

- **Pets**
  - Remove pets from bedrooms and, even better, from the entire home
  - Vacuum carpets, mattresses and upholstery regularly
  - Wash pets regularly (±)
- **Molds**
  - Ensure dry indoor conditions
  - Use ammonia to remove mold from bathrooms and other wet spaces
- **Cockroaches**

  Eradicate cockroaches with appropriate gel-type, non-volatile, insecticides

  Eliminate dampness, cracks in floors, ceilings, cover food; wash surfaces, fabrics to remove allergen
- **Pollen**
  - Remain indoors with windows closed at peak pollen times
  - Wear sunglasses
  - Use air-conditioning, where possible
  - Install car pollen filter

To Conclude…

- Allergic rhinitis is very common and causes considerable morbidity
- Adequate and appropriate treatment leads to significant improvement in quality of life
- Co-morbid conditions are common and warrants special attention and treatment for optimal results
- Environmental manipulations is also important in the control of disease

ATOPIC DERMATITIS IN CHILDREN

Assoc. Prof. N. Balgaranov
MU Pleven

What is Eczema

- **Eczema** is a general term, often used interchangeably with dermatitis.
- Eczema is a chronic, inflammatory skin condition that is characterised by
  - **Dryness**
  - **Deep-seated itch**
  - **Redness and inflammation**
  - **Sometimes areas can be weepy or oozing**

Incidence

- One of the most common skin disorders of childhood.
- The incidence of eczema has increased steadily in westernised countries, over the past 40 years
- It is believed that up to 1 in 4 children may be affected

❑ **It affects around :**

- **30% of preschool-age children,**
- **15% of school-age children and**
- **9% of adolescents**

❑ **60 % of the children will have onset before the age of 1 year.**

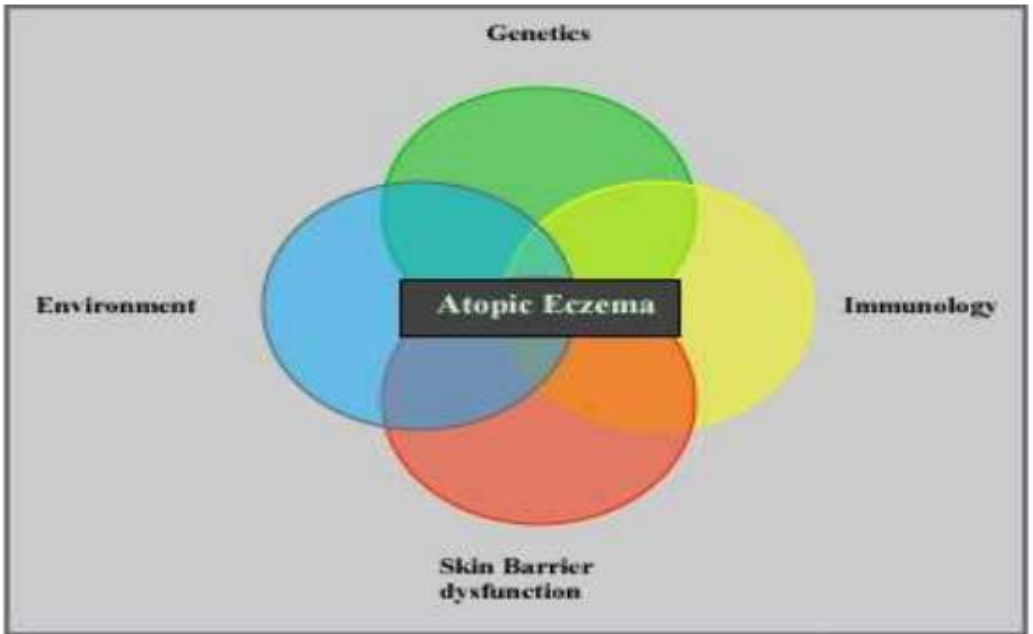
Name Confusion?

- The word '**atopy**' comes from the Greek word meaning 'without place, unusual.' Described by Coca and Cooke in **1923**
- Eczema has been historically thought of as an allergic disease
- Atopic Dermatitis (**inflammation of the skin due to allergies**)
- However, more recently it has been suggested that we should be dividing the condition of '**eczema**' into 2 terms.

- **Atopic** - having allergic tendencies (extrinsic)
- **Non atopic** – not having allergic tendencies (intrinsic)

Pathogenesis

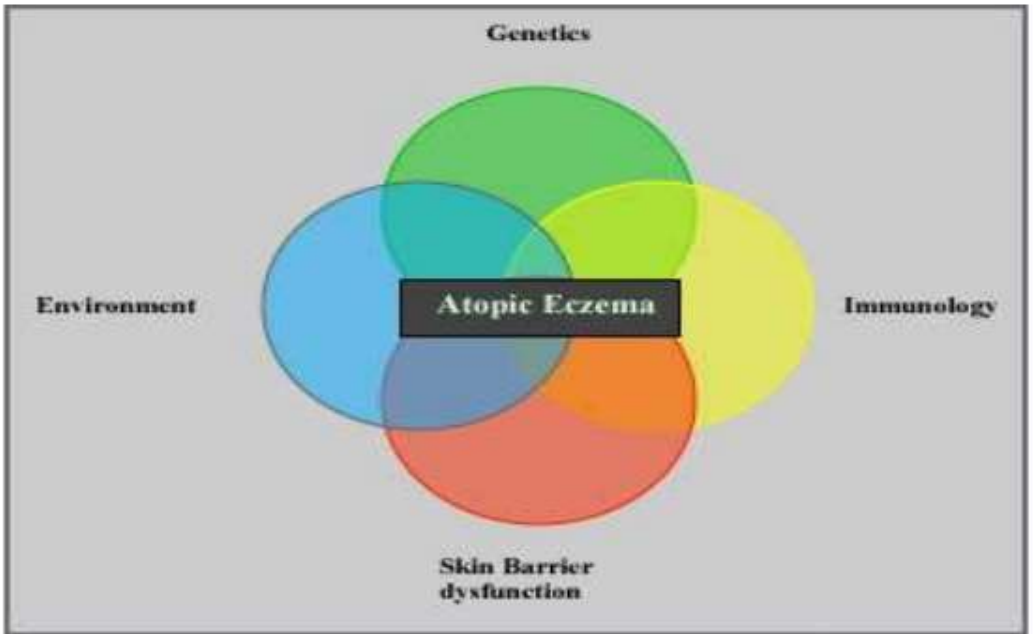
- **Etiology is multifactorial**
  - Clinical factors
  - Molecular factors- Immunological factors
  - Genetic link



Factors contributing to the pathogenesis of atopic dermatitis.

Pathogenesis

- **Etiology is multifactorial**
  - Clinical factors
  - Molecular factors- Immunological factors
  - Genetic link



Factors contributing to the pathogenesis of atopic dermatitis.

Functions of the skin

Skin cells (keratinocytes) divide at the bottom of the epidermis to make a new supply of skin cells

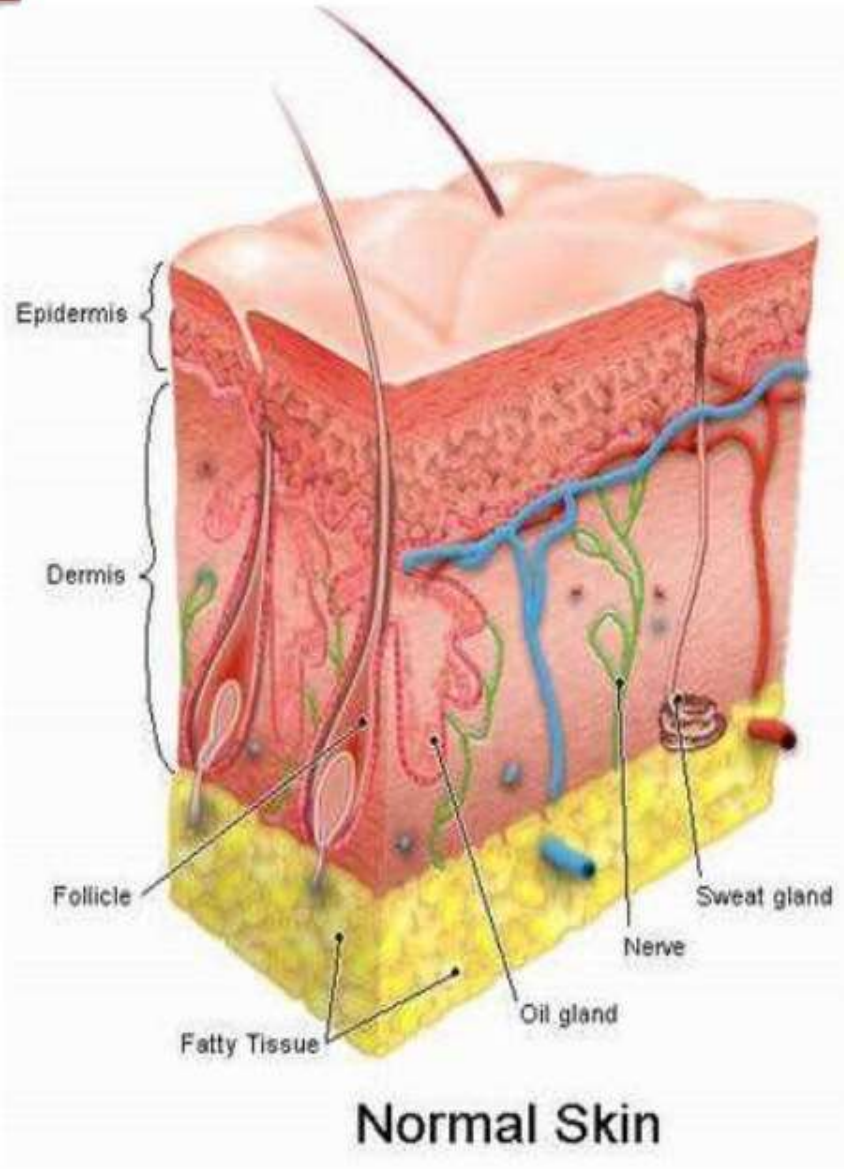
The new cells mature as they move up through the skin

At the top of the skin, the skin barrier (stratum corneum) is formed

The barrier protects the body from the environment and prevents the penetration of irritants and allergens

The skin cells in the stratum corneum are locked together by structures call corneodesmosomes and the skin cells are surrounded by lipid bi-layers.

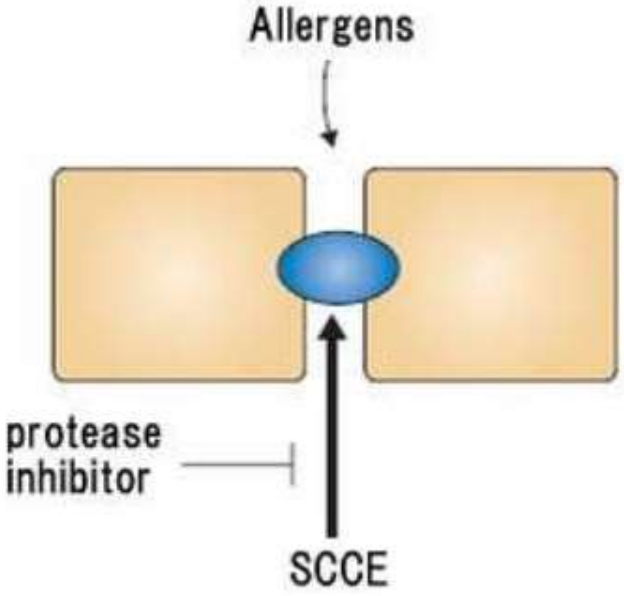
(Cork et al, Exchange, NES 2006)



Genetic link

- Inherited disorder, presumably **autosomal dominant**
- Often associated with either a family or a personal history of other 'allergic' conditions (e.g. asthma or allergic rhinitis)
- If a child has one parent with atopic eczema – **20%**
- If both parents have (or had) atopic eczema – 50%

Genes associated with strength of skin barrier



- Chemicals called proteases break down the corneodesmosomes
- Normal skin has low levels of proteases so skin barrier is thick
- **allergic eczema : change in the gene which produces higher levels of protease**
- Leads to premature break down of the corneodesmosomes.

Molecular factors

1. Keratinocytes primed to react to antigenic stimuli by producing preformed interleukin (IL)-1, followed by more IL-1 produced by endothelial cells and macrophages

2. Secondary cytokines (tumor necrosis factor (TNF)-α, IL-6, IL-8) are then produced

3. T lymphocytes bind to endothelial cells and migrate into the dermis and epidermis, producing damage to the epidermal barrier

4. Imbalance of Th2 > Th1 lymphocytes
a. Th1 cells produce interferon-α, IL-1, IL-2, TNF-β
b. Th2 cells produce IL-4, IL-5, IL-6, IL-10

5. Cytokines of Th2 cells are self-amplifying and inhibit Th1 responses

6. T cells in atopic dermatitis are responsive to IL-4, which suppresses IFN-γ, with subsequent promotion of B-cell proliferation and increased IgE production

7. IL-4 stimulates mast cells to release histamine

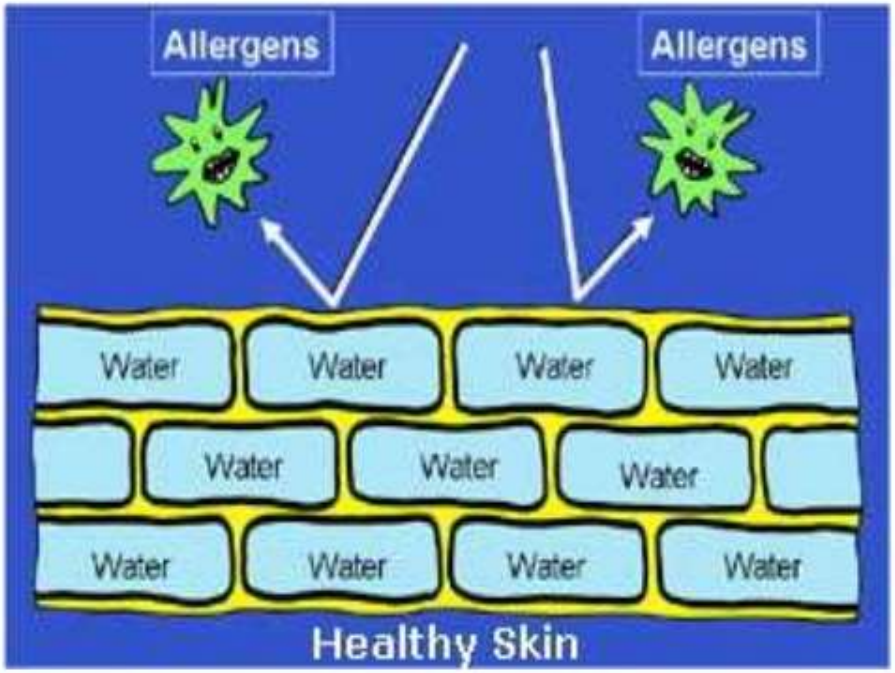
8. Vicious cycle caused by repeated stimulation, abnormal responses and cytokine release

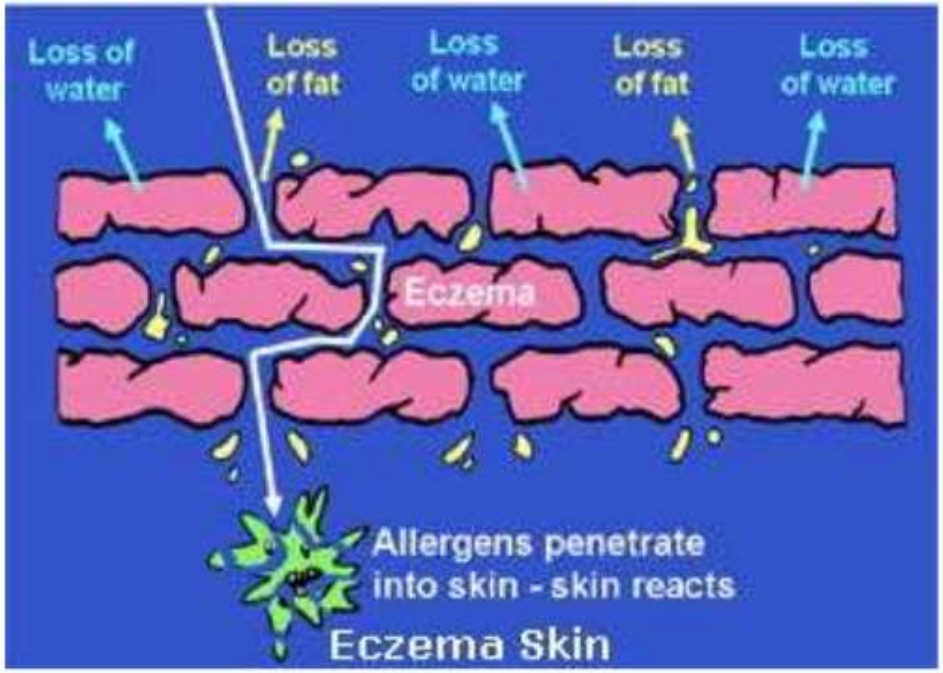
Why has the prevalence increased?

- The **genes** that predispose us to eczema has not changed, but our environment has
- **One theory** - we are exposing our skin to more **soaps** and surfactants such as bubble baths to wash babies
- Soap and surfactants shown to decrease the stratum corneum by **40%**

(Cork et al Dermatol in Practice, 2002)

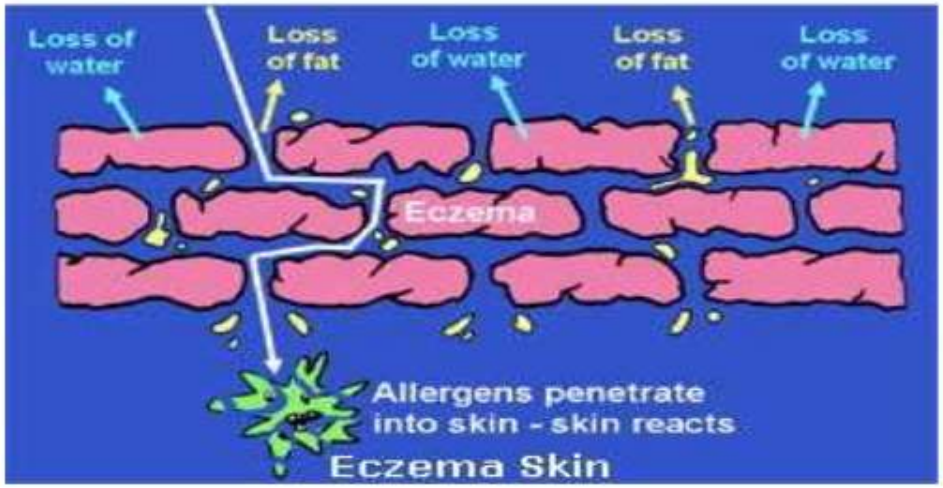
- Normal **pH** of the skin is **5.5**
- Exposure to soap and surfactants **↑ 7.5 or higher**
- **50%** increase in protease activity
- greater breakdown of the skin barrier
- Increase penetration of irritants and allergens.


Allergens
Allergens
Water
Water
Water
Water
Water
Water
Water
Water
Water
Water
Water
Water
Healthy Skin

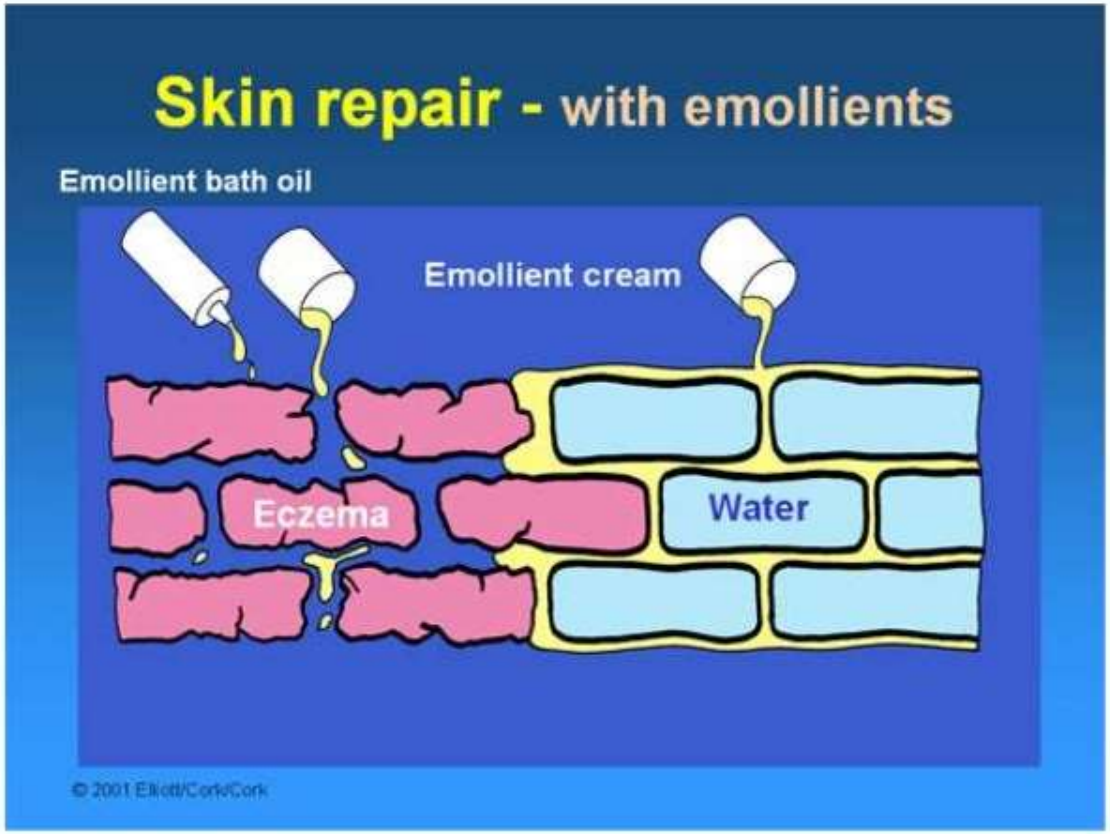

Loss of water
Loss of fat
Loss of water
Loss of fat
Loss of water
Eczema
Allergens penetrate into skin - skin reacts
Eczema Skin

Clinical factors

- **Xerosis (dry skin), is caused by**
- reduced water content of the stratum corneum,
- decreased secretion of sebum and sweat
- **Dry & Sensitivity**: result in loss of epidermal barrier and a higher incidence of irritation from certain stimuli such as wool clothing, soaps, etc

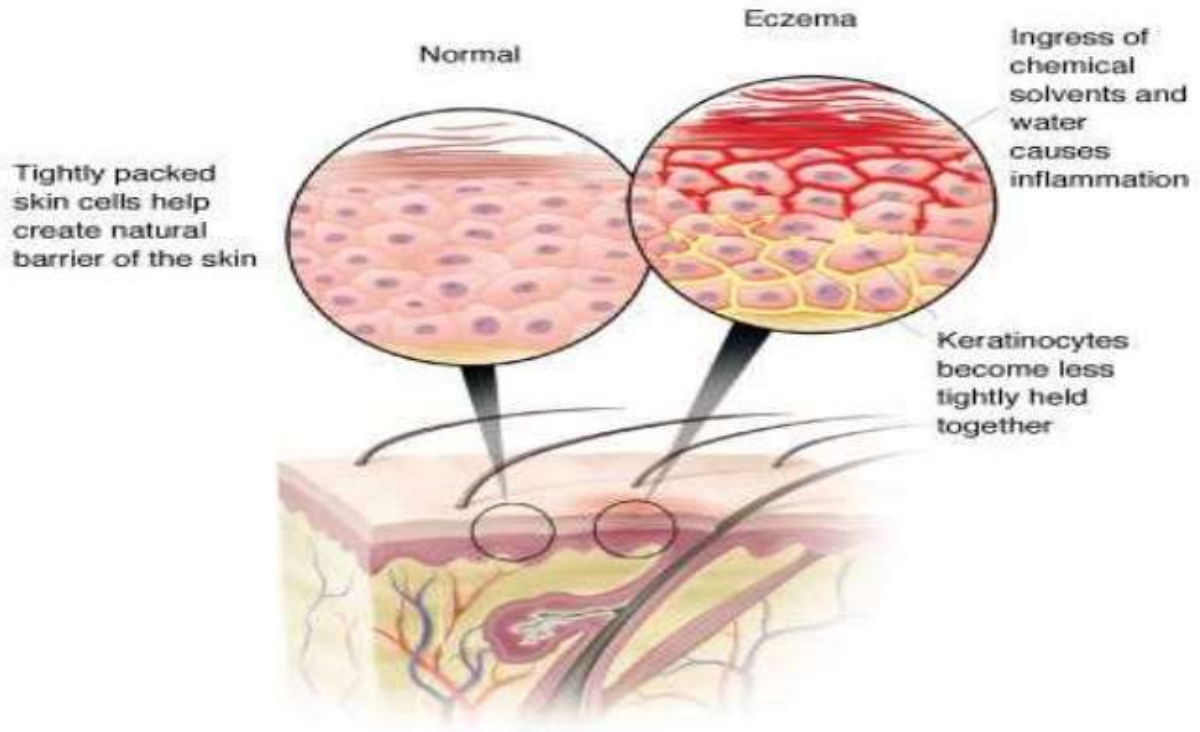


Management includes repairing the skin barrier with moisturisers (more discussion later)



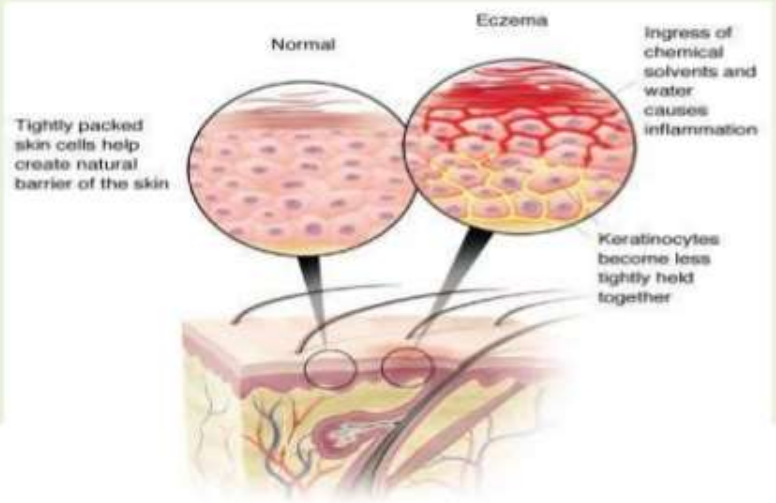
However.....

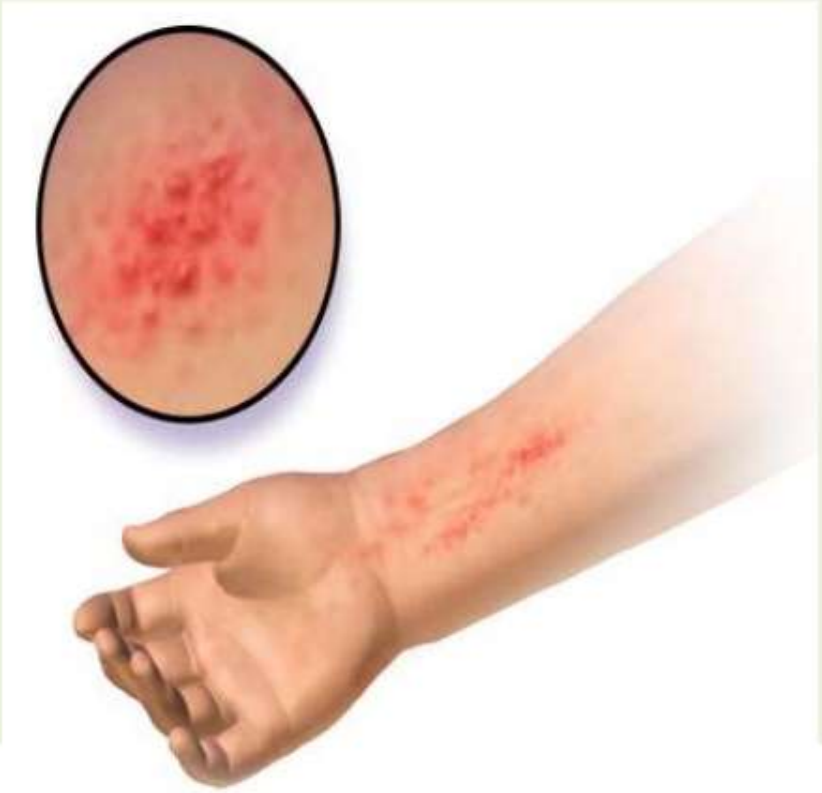
Regardless of the classification, it is thought that the primary problem is the **skin barrier**



Diagnosis

- **Clinical diagnosis**
- **Laboratory**
- **Histology**





Criteria for the diagnosis of atopic dermatitis in children (Hanifin & Rajka)

Major features (must have three)

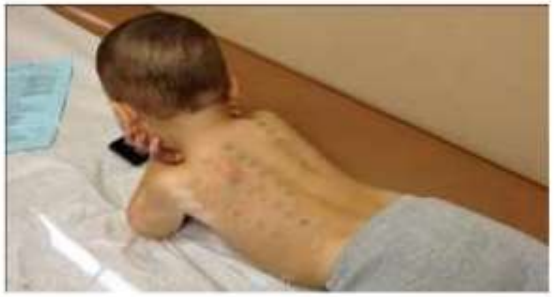
- 1. Pruritus
- 2. Typical morphology and distribution
  - Facial and extensor involvement during infancy and early childhood
  - Flexural lichenification in childhood or adolescence
- 3. Chronic or chronically relapsing dermatitis
- 4. Personal or family history of atopy

Minor or less specific features

- Xerosis
- Periauricular fissures
- Ichthyosis/ Hyperlinear palms/ Keratosis pilaris
- IgE reactivity (increased serum IgE, RAST, or prick test positivity)
- Hand or foot dermatitis
- Scalp dermatitis
- Susceptibility to cutaneous infections (especially *Staphylococcus aureus and herpes simplex)*
- Perifollicular accentuation (especially in darkly pigmented races)

- **Trigger** (things that irritate) factors include:
  - infections/bacterial, viral, fungal
  - Irritants: Soap based products, body wash chemicals
  - Extremes of weathers
  - Stress and anxiety
  - rough clothes.
  - Allergen:
    - Certain food chemicals or colourings: eggs, peanuts, milk, fish, wheat
    - Aeroallergens: dust, mite, pollen, animal dander & molds.

❑ Laboratory: no specific laboratory criteria



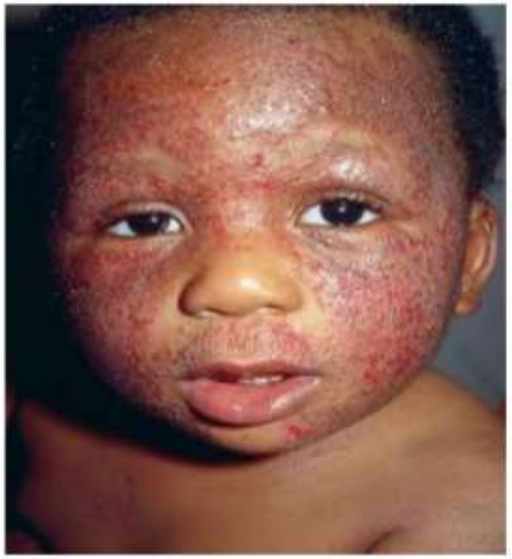
- **1. Allergy testing (prick tests)**
  - a. Food allergies in minority of patients
  - b. Inhalant allergies in some patients
- **2. Blood tests**
  - a. Complete blood count – may see increase in numbers of eosinophils
  - b. Serum IgE may be slightly or markedly elevated
  - c. Radioallergosorbent test (RAST) may help define some allergies

❑ Histology:

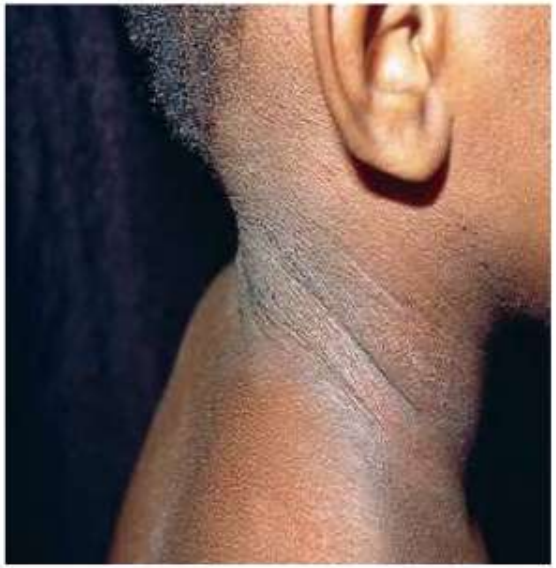
variable lymphocytic infiltration of the upper dermis and epidermis; hyperkeratosis; thick-walled blood vessels in papillary dermis

Diagnosis

Types of eczema

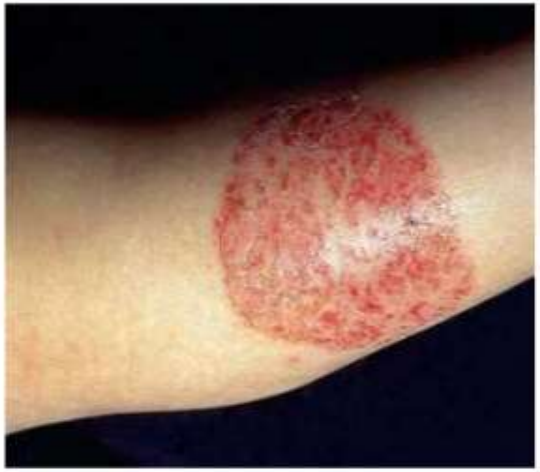


Infantile eczema

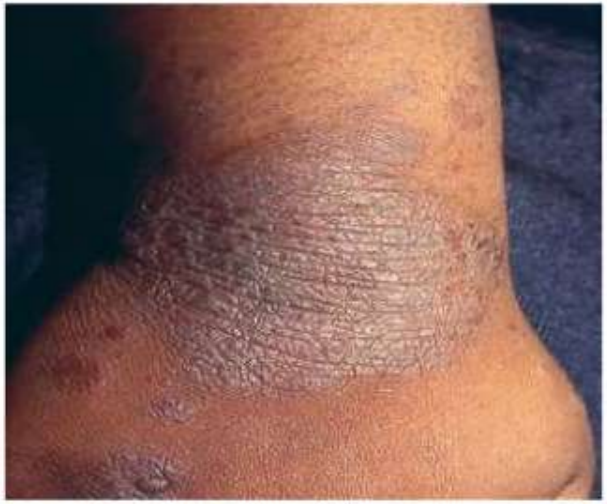


Childhood eczema

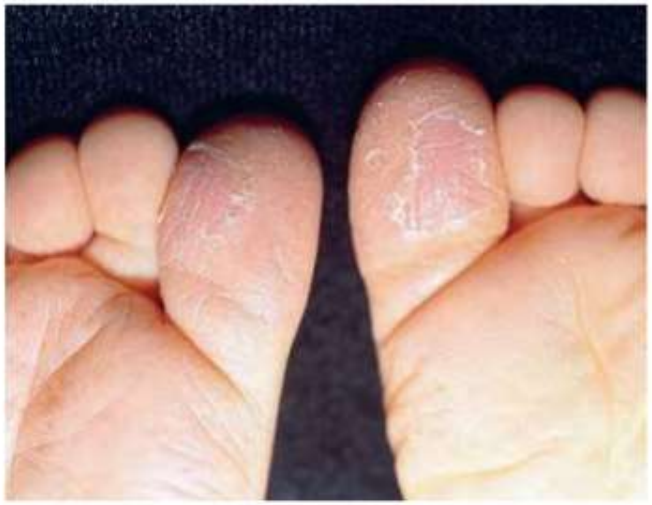
Adult/teenage eczema



Nummular eczema



lichenification eczema



Juvenile plantar dermatitis

Differential diagnosis

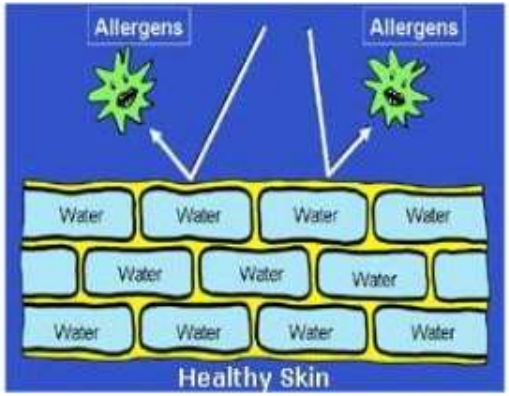
- Scabies
- Seborrheic dermatitis
- Immunodeficiences
- Langerhans cell histiocytosis
- Acrodermatitis enteropathica
- Psoriasis
- Contact dermatitis
- Phenyketonuria

Management

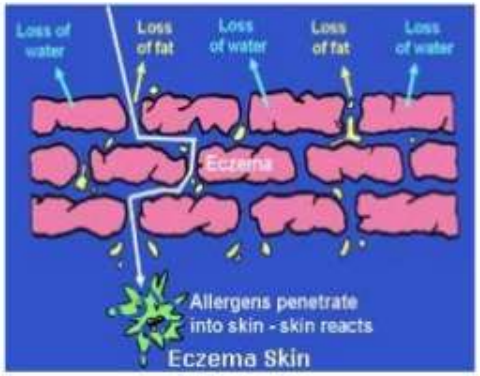
- Goal of therapy is control of skin inflammation, pruritus and secondary infections.
- at present there is no 100% life-long cure for Atopic dermatitis.
- Management compromise combining adjuvant basic therapy, anti-inflammatory measurements and identification & avoidance of triggering factors.
- Major factor in successful management is compliance & proper communication between doctor and patient.

Which leads us to the treatments

Our increasing knowledge and understanding of how the skin barrier breaks down, reinforces the importance of skin-barrier maintenance and repair



first-line treatment



Complete emollient (moisturiser) regimes

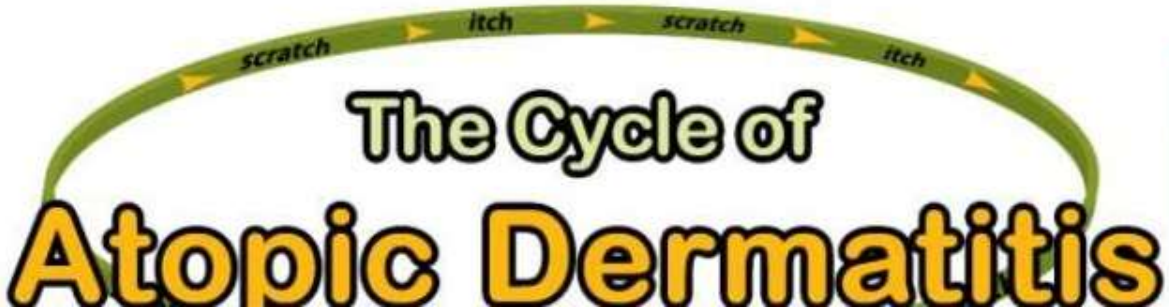
2nd line of treatment

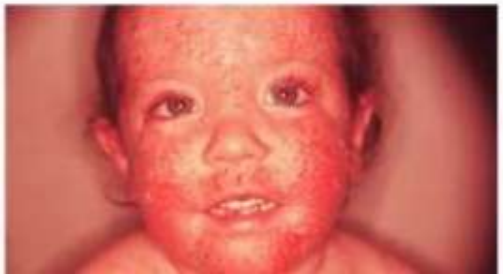
Identification and avoidance of irritants and allergens

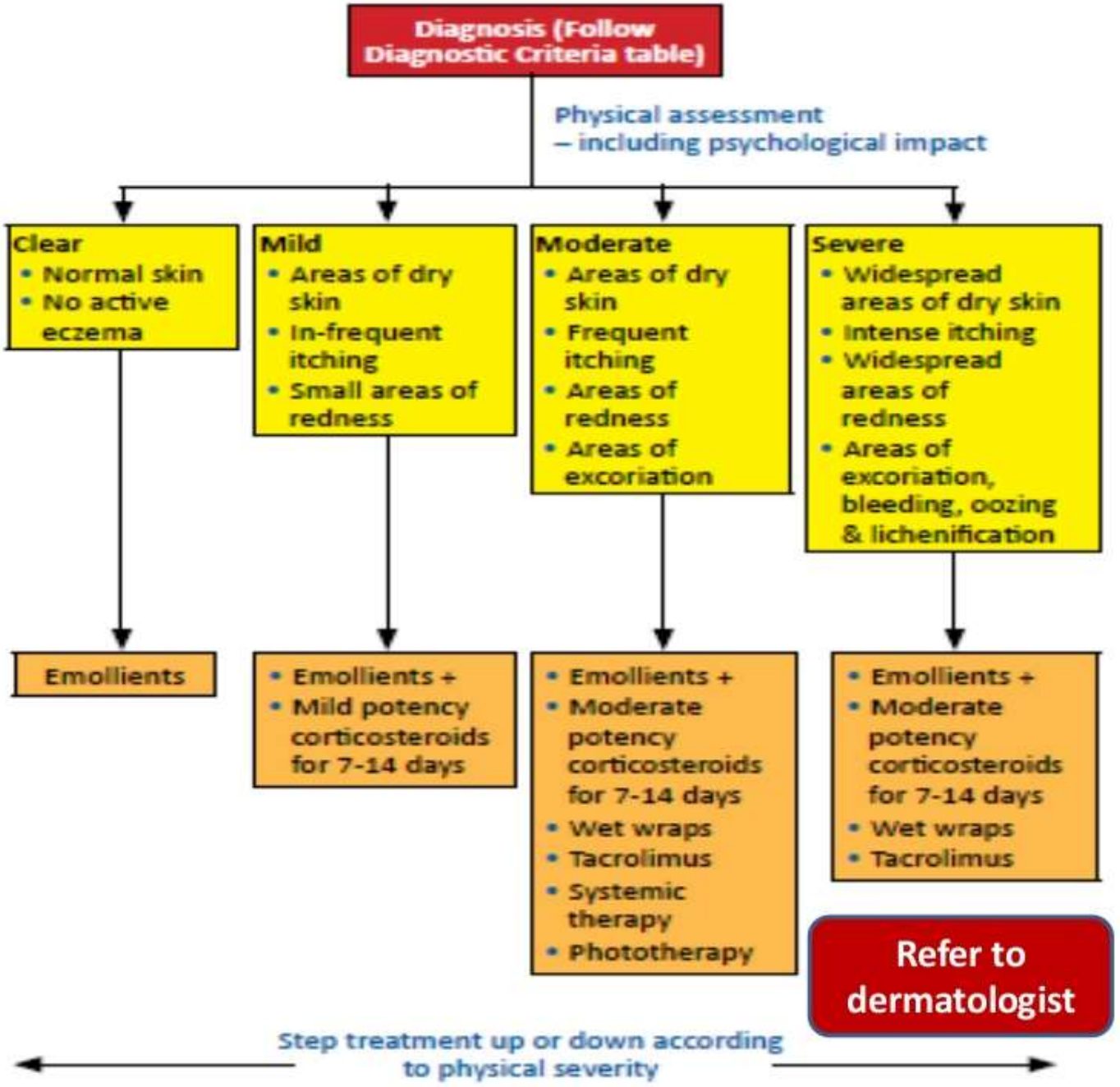
3rd line of treatment

Treatment of flares

The more attention paid to the first two steps, the less often flares will occur






Diagnosis (Follow Diagnostic Criteria table)
Physical assessment – including psychological impact
Clear
• Normal skin
• No active eczema
Mild
• Areas of dry skin
• In-frequent itching
• Small areas of redness
Moderate
• Areas of dry skin
• Frequent itching
• Areas of redness
• Areas of excoriation
Severe
• Widespread areas of dry skin
• Intense itching
• Widespread areas of redness
• Areas of excoriation, bleeding, oozing & lichenification
Emollients
• Emollients +
• Mild potency corticosteroids for 7-14 days
• Emollients +
• Moderate potency corticosteroids for 7-14 days
• Wet wraps
• Tacrolimus
• Systemic therapy
• Phototherapy
• Emollients +
• Moderate potency corticosteroids for 7-14 days
• Wet wraps
• Tacrolimus
Refer to dermatologist
Step treatment up or down according to physical severity

Treatment measures

- Avoid Aggravating Factors.
- Avoid coarse or irritating clothing (e.g. wool)
- Avoid both extreme f temperatures.
- Bath & Emollients
- Topical corticosteroid
- Relief of pruritus,
- Treatment of secondary infection.
- Treatment of refractory cases

Bath & Emollients

- ✓ **Bathing** can be performed once daily, but excessive bathing causes increased dryness
- ✓ baths are helpful in soothing itching and removing crusting. They should be lukewarm and limited to 10 minutes duration.
- ✓ Reduce use of detergent & **soaps**; Soap should be kept to a minimum, and applied only to excessively dirty areas
- **Emollients** are best applied after bath.
- They should be applied to normal and abnormal skin.
- They should be applied at least twice a day and more frequently in severe cases.

Topical Corticosteroids

- Topical corticosteroid is an anti -inflammatory agent and the mainstay of treatment for atopic eczema.
- Topical steroid are often prescribed intermitently for short term reactive treatment of acute flares and supplemented by emollients.
- choice depends on a balance between efficacy and side-effects

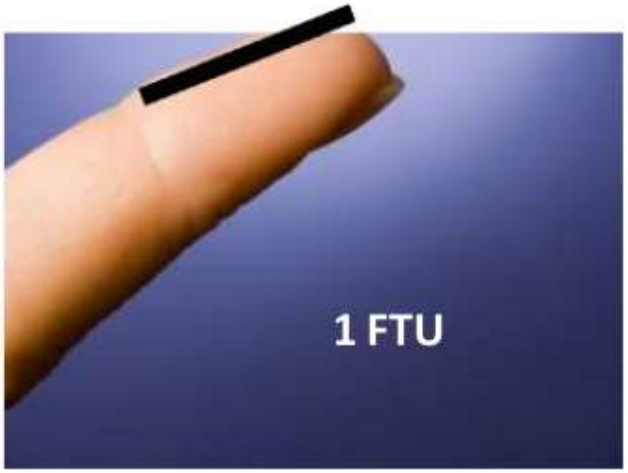
- apply steroid cream twice daily
- use milder steroids for face, flexures and scalp.
- Ointments (oil-based) are more effective than creams, although creams and lotions (water-based) are useful when the skin is inflamed
- Educate parents/patients that side effects are related to the potency of the steroid, the amount used and site of application

Topical Corticosteroids

Dosing of Topical Medications

- **Amount of topical steroid to be used** – the finger tip Units (FTU) is convenient way of indicating to patients how much of a topical steroid should be applied to skin at any one site.
- 1 FTU is the amount of steroid expressed from the tube to cover the length of the flexor aspect of the terminal phalanx of the patient's index finger.
- FTU (Finger tip unit) = ½ gm ---- 2 FTUs = 1 gram

Area	the finger tip (FTU)
1 hand / foot / face	1 FTU
1 arm	3 FTU
1 leg	6 FTU
Front and back of trunk	14 FTU



Amount of steroid to apply (in Finger Tip Units) by body site and age

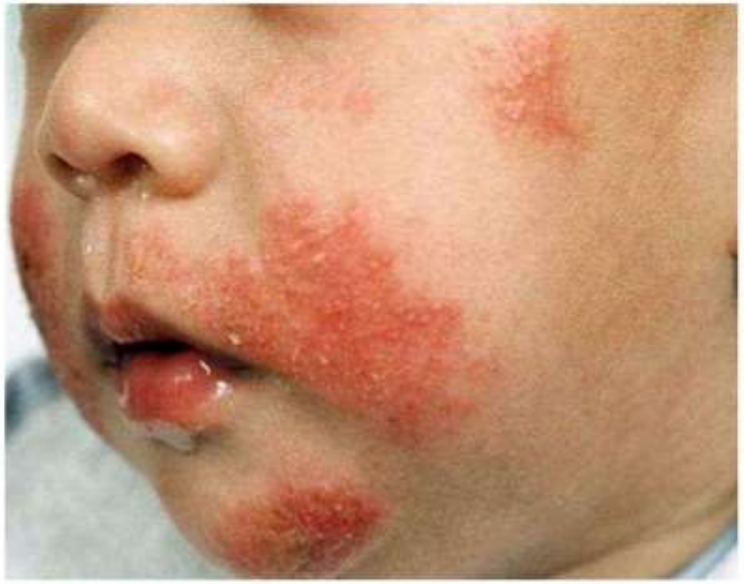
Age	*Face and neck*	*Arm and hand*	*Leg and foot*	*Ant trunk*	*Post trunk*
3 to 6 m	1	1	1.5	1	1.5
1 to 2 y	1.5	1.5	2	2	3
3 to 5 y	1.5	2	3	3	3.5
6 to 10 y	2	2.5	4.5	3.5	5

- **Adverse effect** results from prolonged use of potent topical steroids.
- **Local effects :** include skin atrophy, telangiectasia, purpura, striae, acne, hirsutism and secondary infectioons.
- **Systemic effects :** are adrenal axis suppression, Cushing syndrome.

Steroid Potency	
Potency of topical steroid	**Topical steroid**
Mild	Hydrocortisone cream/ointment 1%
Moderate	Bethametasone 0.025% (1:4dilution)
	Eumovate (clobetasone butyrate)
Potent	Bethametasona 0.050%
	Elomet (mometasone furoate)
Super potent	Dermovate (clobetasone propionate)

Systemic Therapy Consists of :

- relief of pruritus,
- treatment of secondary infection, and
- treatment of refractory cases



Relief of Pruritus (Antihistamines)

- Do not routinely use oral antihistamines.
- Offer a 1-month trial of a non-sedating antihistamine to:
  - Children with severe atopic eczema
  - Children with mild or moderate atopic eczema where there is severe itching or urticaria.
- Offer a 7–14 day trial of a **sedating** antihistamine to children over 6 months during acute flares if sleep disturbance has a significant impact.

Treatment of Secondary Infection:

- Secondary bacterial skin infection is common and may cause acute exacerbation of eczema.
- Systemic antibiotics are necessary when there is evidence of extensive infection.
- Commonly *Staphyloccus aureus.*
- Choice: Oral cloxacillin 15mg/kg/day 6 hourly for 7-14 days, *or* Oral Erythromycin

- Secondary infection can arise from Herpes simplex virus causing *Eczema Herpeticum.*
- *Treatment using antiviral e.g. Acyclovir may be necessary.*

Refractory cases

- Refractory cases do not response to conventional topical therapy and have extensive eczema.
- Refer such cases to the Dermatologist for treatment and monitoring:
- **systemic steroid**
- **cyclosporin**
- **interferon**
- **azathioprine**
- **phototherapy**

For Relapse

- Check compliance.
- Suspect secondary infection – send for skin swab; start antibiotics.
- Exclude scabies
- For severe eczema, emollient and topical steroid can be applied under occlusion with 'wet wrap'. This involves the use of a layer of wet, followed by a layer of dry Tubifast to the affected areas i.e. limbs and trunk.
- The benefits are probably due to cooling by evaporation, relieving pruritus, enhanced absorption of the topical steroid and physical protection of the excoriation.

WET WRAP THERAPY
for Atopic Dermatitis (Eczema)

1 in 5 Children
Suffer with Eczema

*Use under the advice of your child's physician and for suggested length of treatment

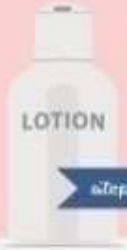
step 1
Soak wraps in warm water

Wet wraps have a cooling anti-itch effect.

step 2
Bathe child in warm (not hot) water for 15-20 minutes and use a gentle cleanser

step 3
Lightly pat child's skin dry with a towel

Apply lotion or prescribed cream within 3 minutes!



step 4

step 5
Wring out excess water from wrap and immediately dress child in damp wrap to seal in moisture

Wet wrap therapy relieves eczema by adding needed moisture to the skin.

step 6
Apply a dry layer of clothing on top.

Smile.

Studies of WET WRAP THERAPY show an average reduction of symptoms of 71%.

ref: Wet Wrap Therapy in Children with Moderate to Severe Atopic Dermatitis as in a Multidisciplinary Treatment Program

AD RescueWear, LLC September 2014. Order wet wrap therapy products from www.ADRescueWear.com.

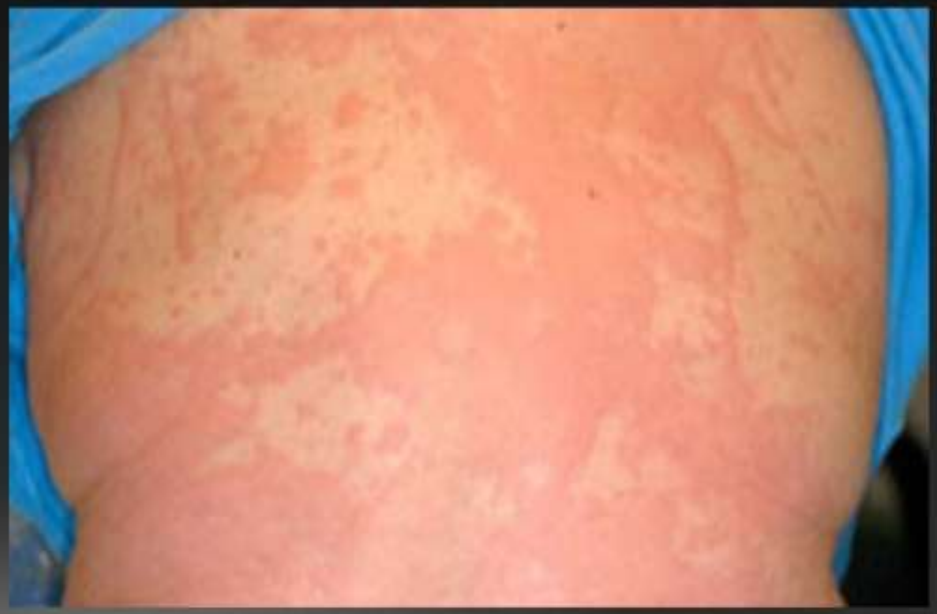
Prognosis

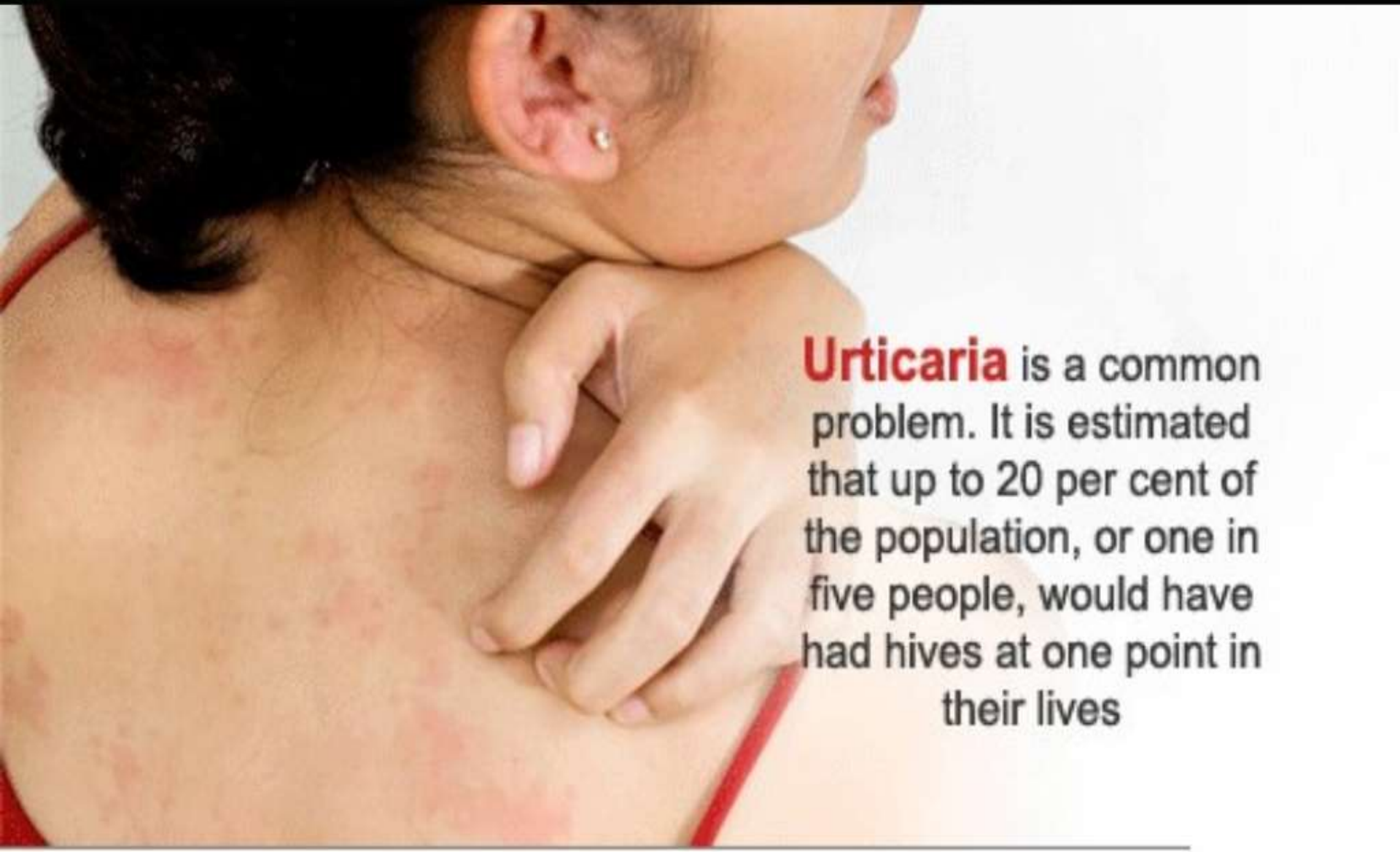
- tendency towards improvement throughout childhood
- Half of the cases of typical atopic dermatitis improve by 2 years of age
- Most improve by teenage years
- Less than 10% of patient have lifelong problem

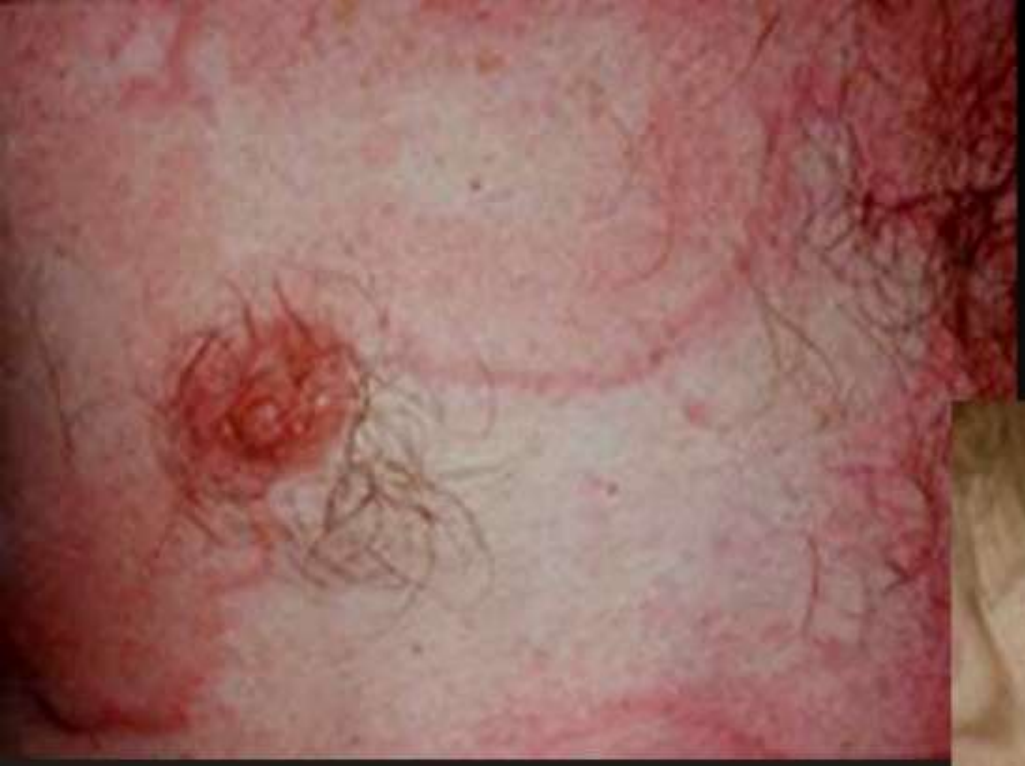
URTICARIA IN CHILDREN

Assoc. Prof. N. Balgaranov
MU Pleven

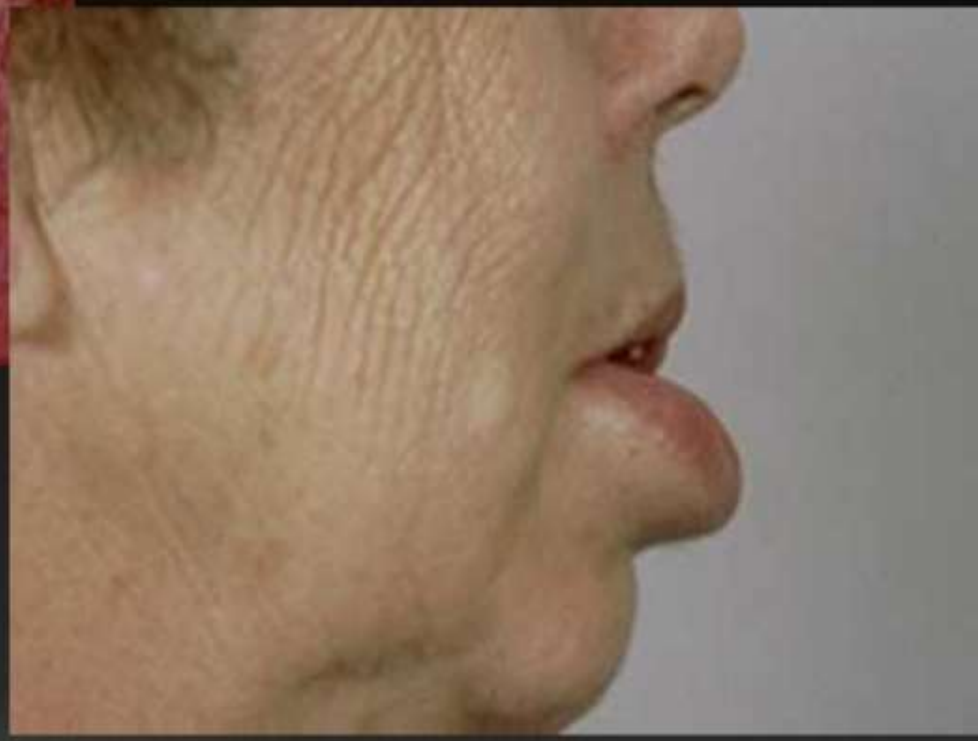
- **Urticaria** (from the ***urtica*, "nettle"** from ***urere*, "to burn"**) commonly referred to as **hives**, is a kind of skin rash notable for pale red, raised, itchy bumps.




Urticaria is a common problem. It is estimated that up to 20 per cent of the population, or one in five people, would have had hives at one point in their lives

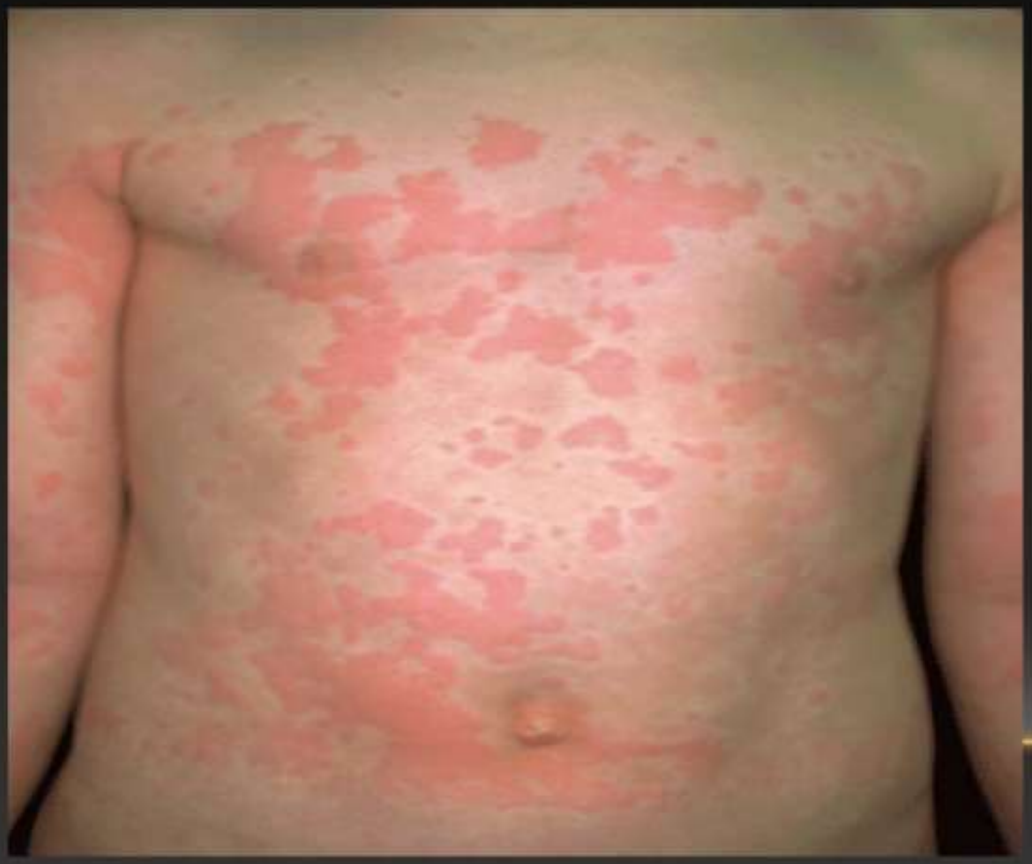


Urticaria



Angioedema

Urticaria, is characterized by transient, itchy, elevated edematous wheals or red papules.

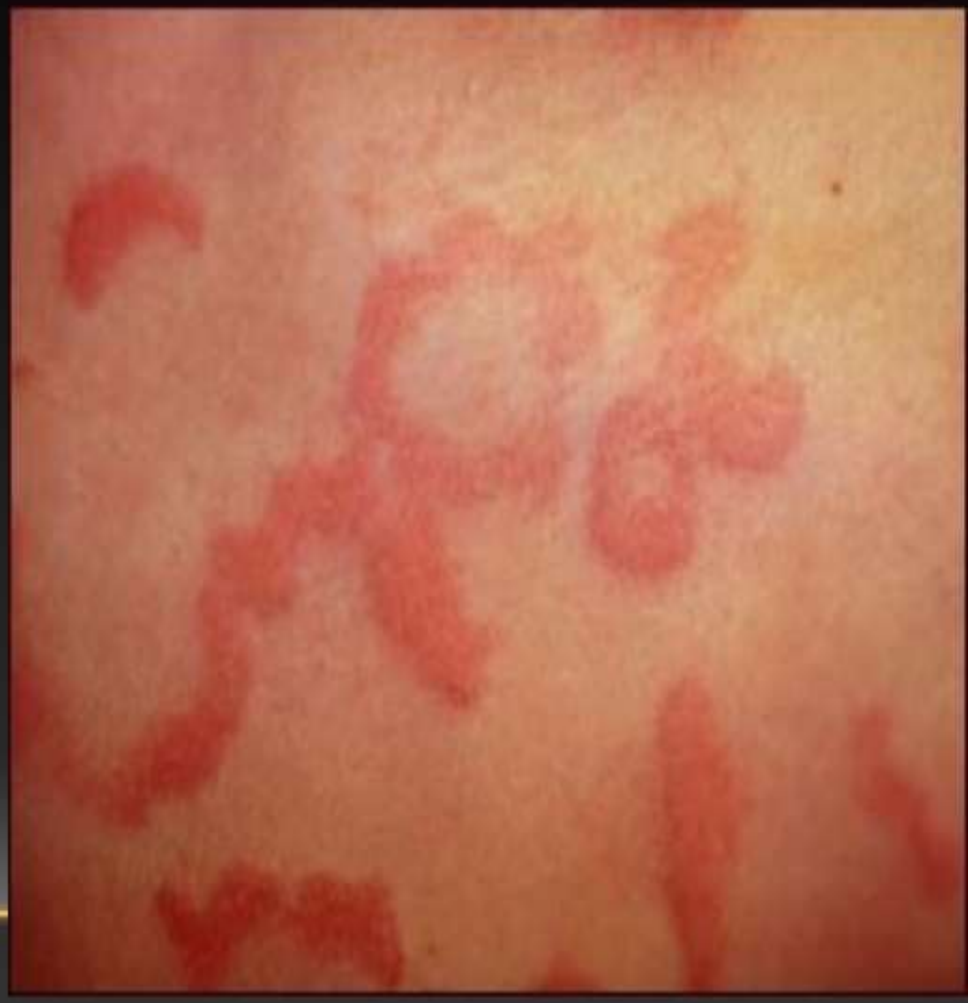


Wheal

A central swelling, surrounded by erythema.

Itching or burning sensations

The wheal disappear usually within 1-24 h.



Angioedema

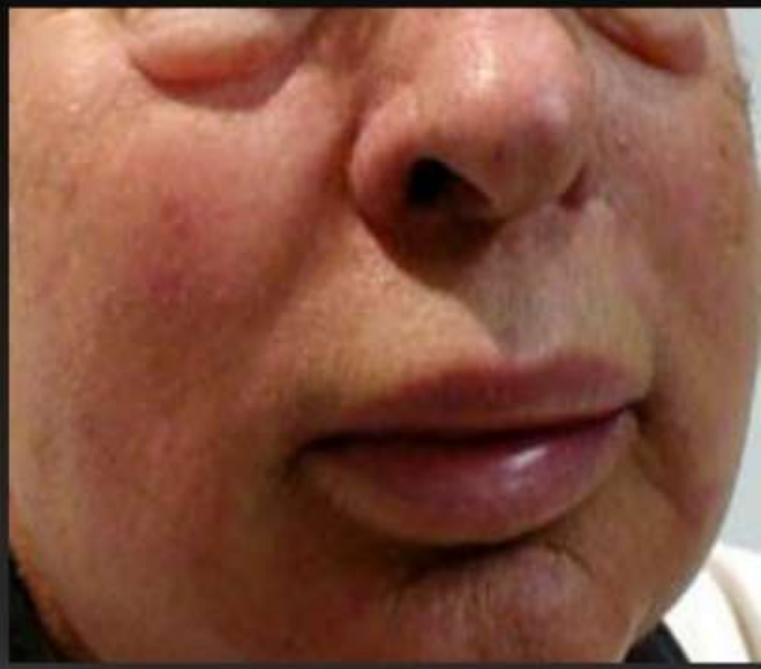
Pronounced swelling of the lower dermis and subcutis.

Most often found in the lips, eyelids or genitalia.

Itching and sometimes pain.

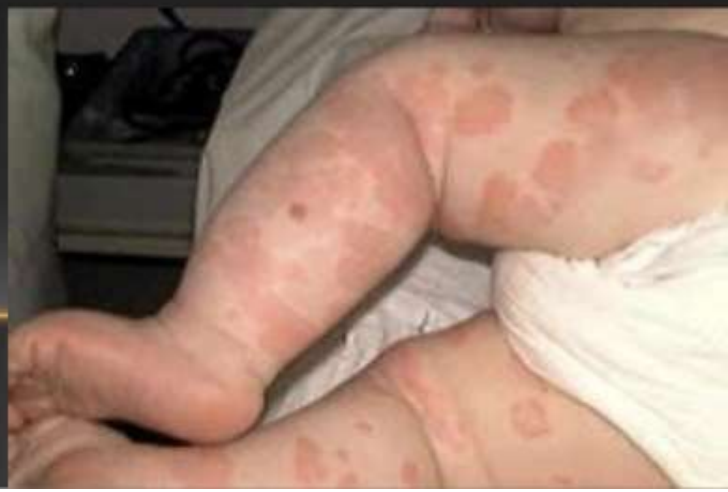
Resolution can take up to 72h.

It is associated with urticaria in about 40% of cases.



CLASSIFICATION

- Ordinary urticaria- acute , chronic, episodic.
- Physical urticaria
- Angioedema
- Contact urticaria
- Urticarial vasculitis



Causes: at a glance

- Drug reactions (medications, vaccines, insulin, etc.)
- Food, food additive or preservative reactions
- Inhaled/ingested allergens which often come in contact with the skin
- Transfusion reactions
- Infections: bacterial, fungal, viral, parasitic
- Insect bites/stings (e.g. papular urticaria)
- Collagen vascular diseases (e.g. systemic lupus erythematosis)
- Cutaneous vasculitis, serum sickness
- Hereditary diseases
- Physical triggers (heat, cold, light, pressure, etc.)

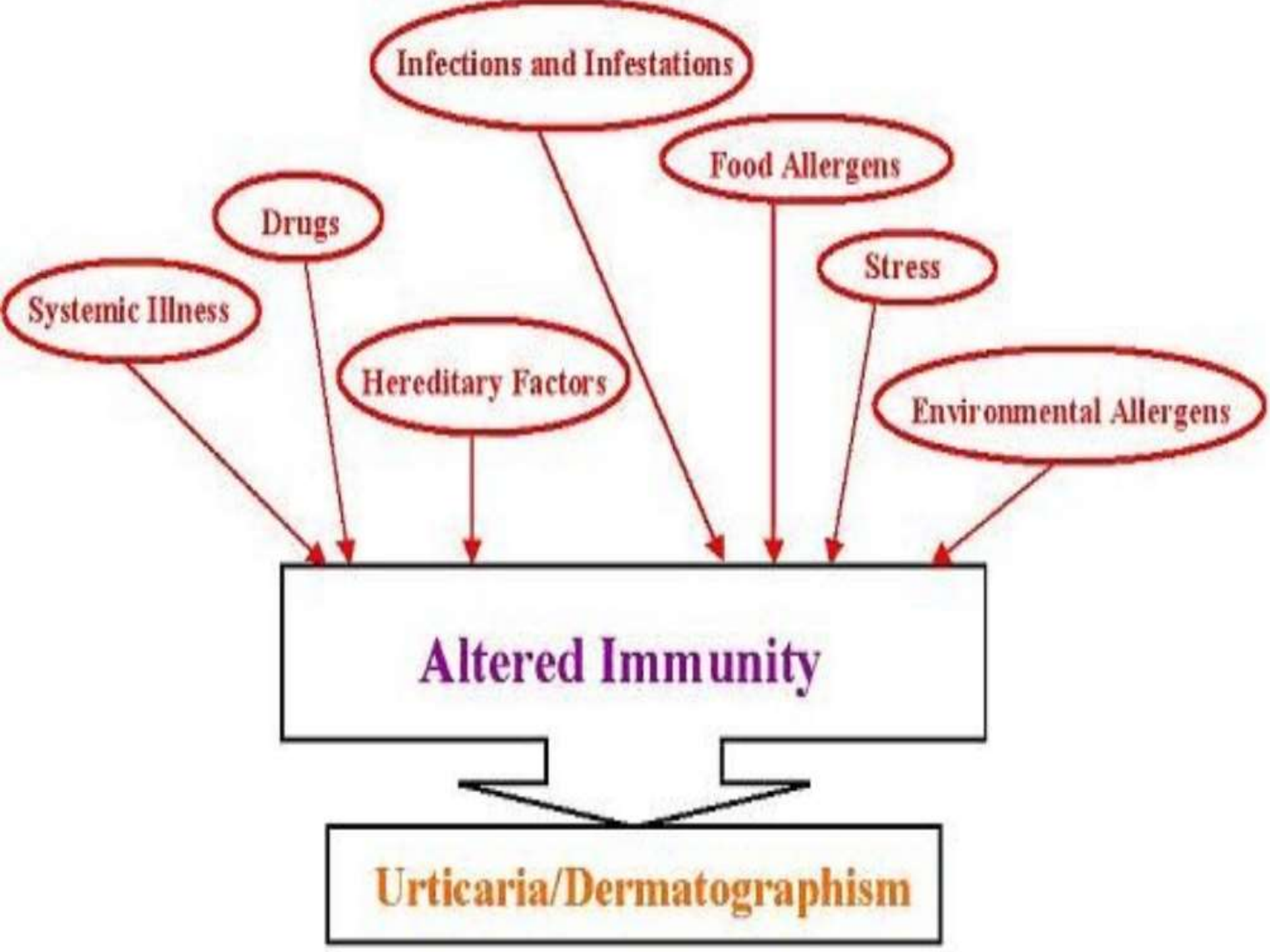
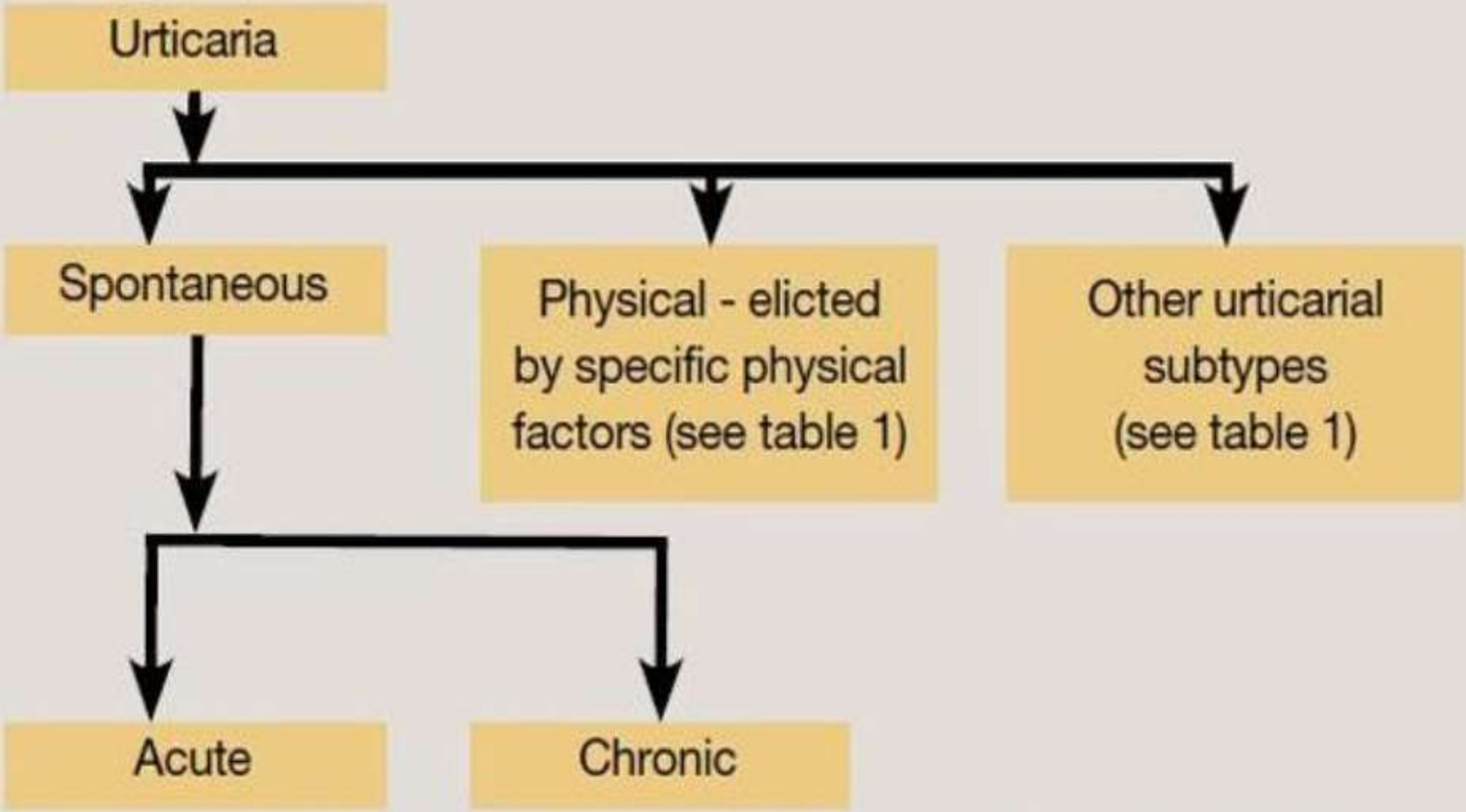

Infections and Infestations
Food Allergens
Drugs
Stress
Systemic Illness
Hereditary Factors
Environmental Allergens
Altered Immunity
Urticaria/Dermatographism

Table 2 – Causes and forms of angioedema

- IgE-mediated allergic reactions (eg, foods, medications, environmental allergens)
- Non–IgE-mediated drug-induced causes (eg, ACE inhibitors, opioid analgesics, ASA/NSAID-induced alteration in arachidonic acid metabolism)
- Autoimmune
- Idiopathic
- Hereditary
- Acquired

ACE, angiotensin-converting enzyme; ASA, acetylsalicylic acid.

Figure 1: Classification of urticaria.



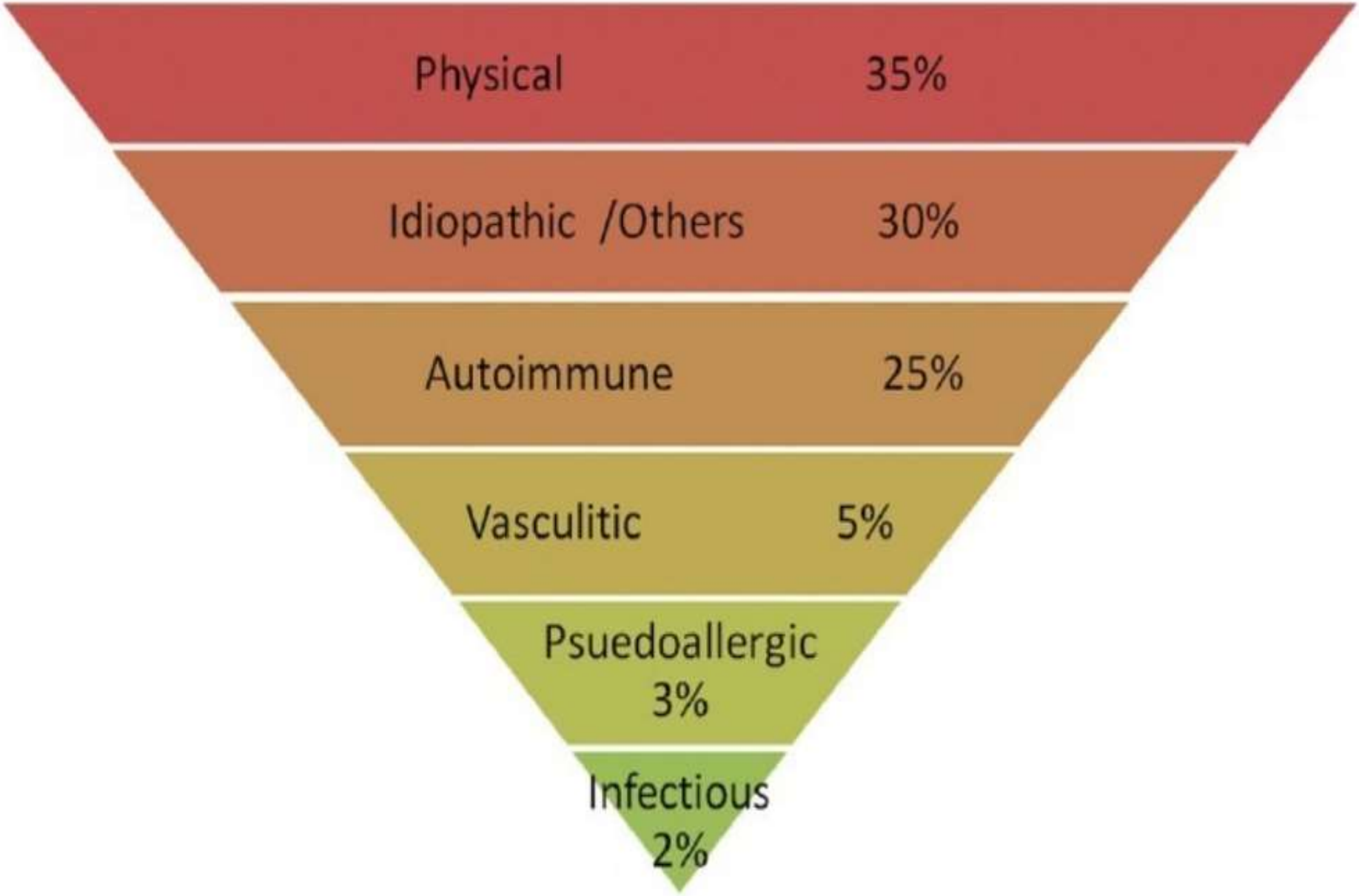
Chronic urticaria has a peak prevalence in the middle-aged population, especially females (with a female to male ratio of 4:1).[5]

ALLERGIC TRIGGERS

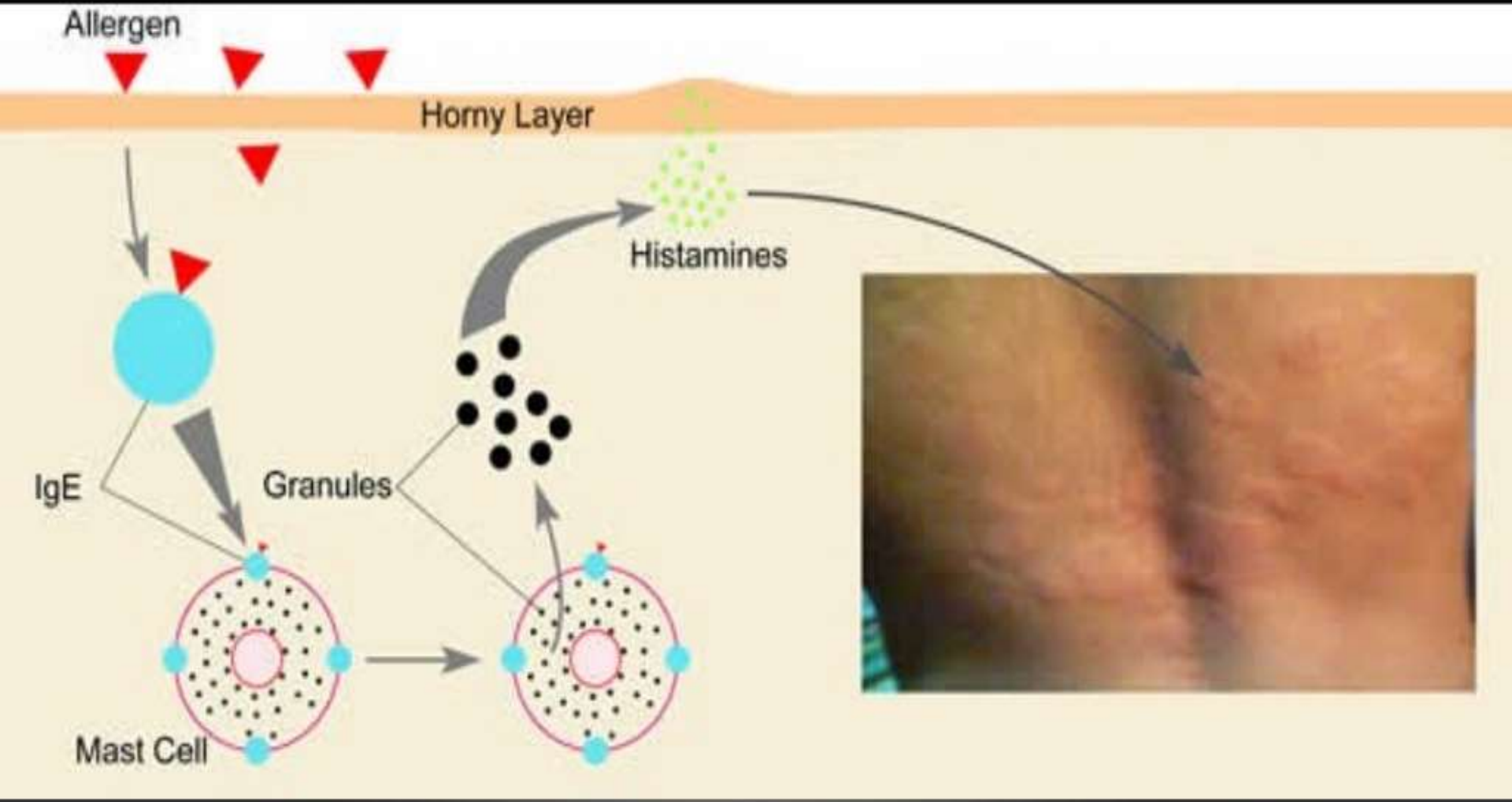
- **Acute Urticaria**
  - Drugs - β-lactam antibiotics, sulfonamides, aspirin
  - Foods - milk, eggs, peanuts, sesame, soy wheat, shellfish, fish
  - Food additives
  - Infections
  - Insect bites and stings
  - Contactants and inhalants (includes animal dander and latex)

Chronic Urticaria

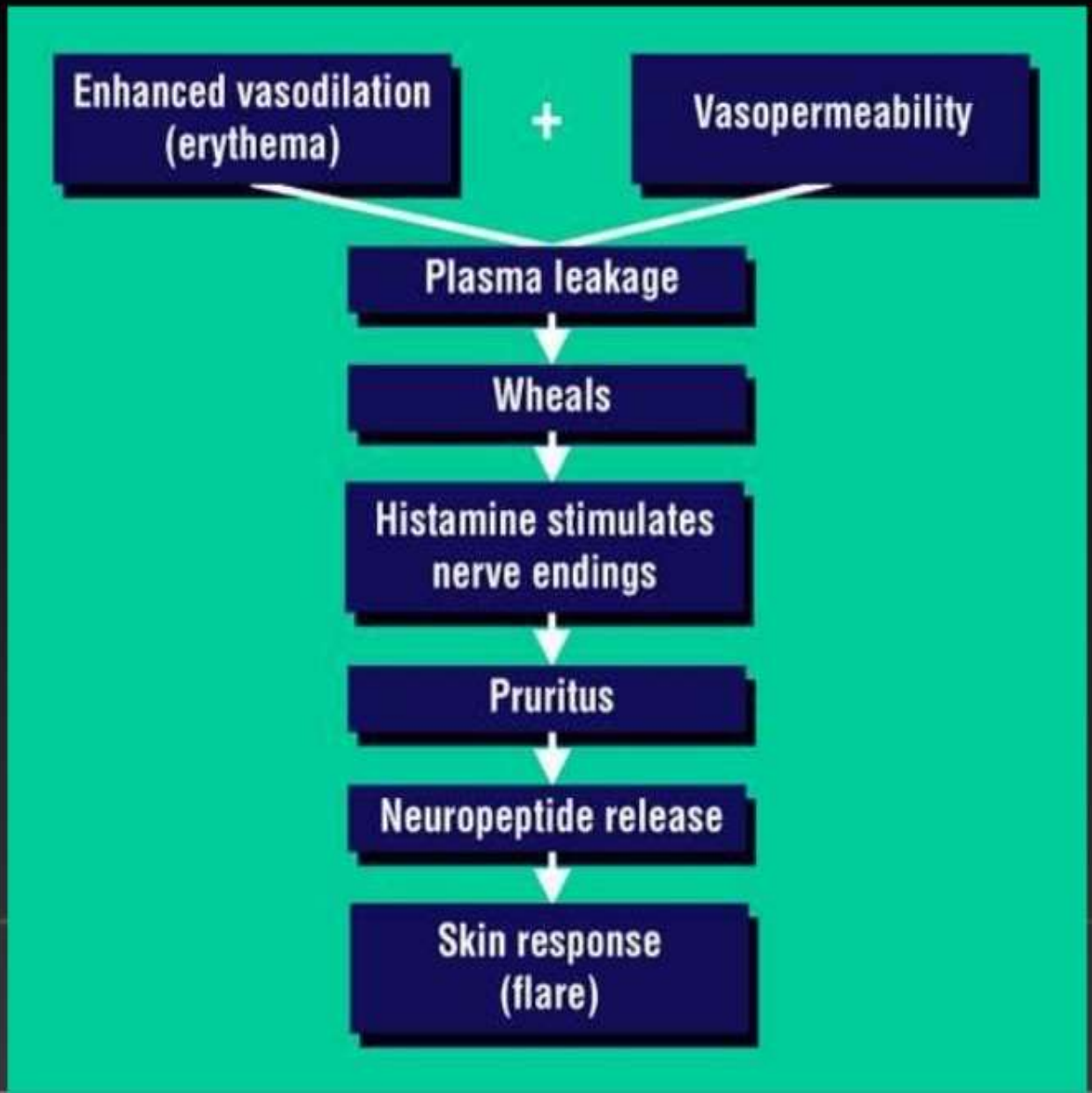
- Physical factors
  - –cold
  - –heat
  - –dermatographic
  - –pressure
  - –solar
- Idiopathic



CHRONIC URTICARIA – COMMON CAUSES


Allergen
Horny Layer
Histamines
IgE
Granules
Mast Cell

HISTAMINE AS A MAST CELL MEDIATOR



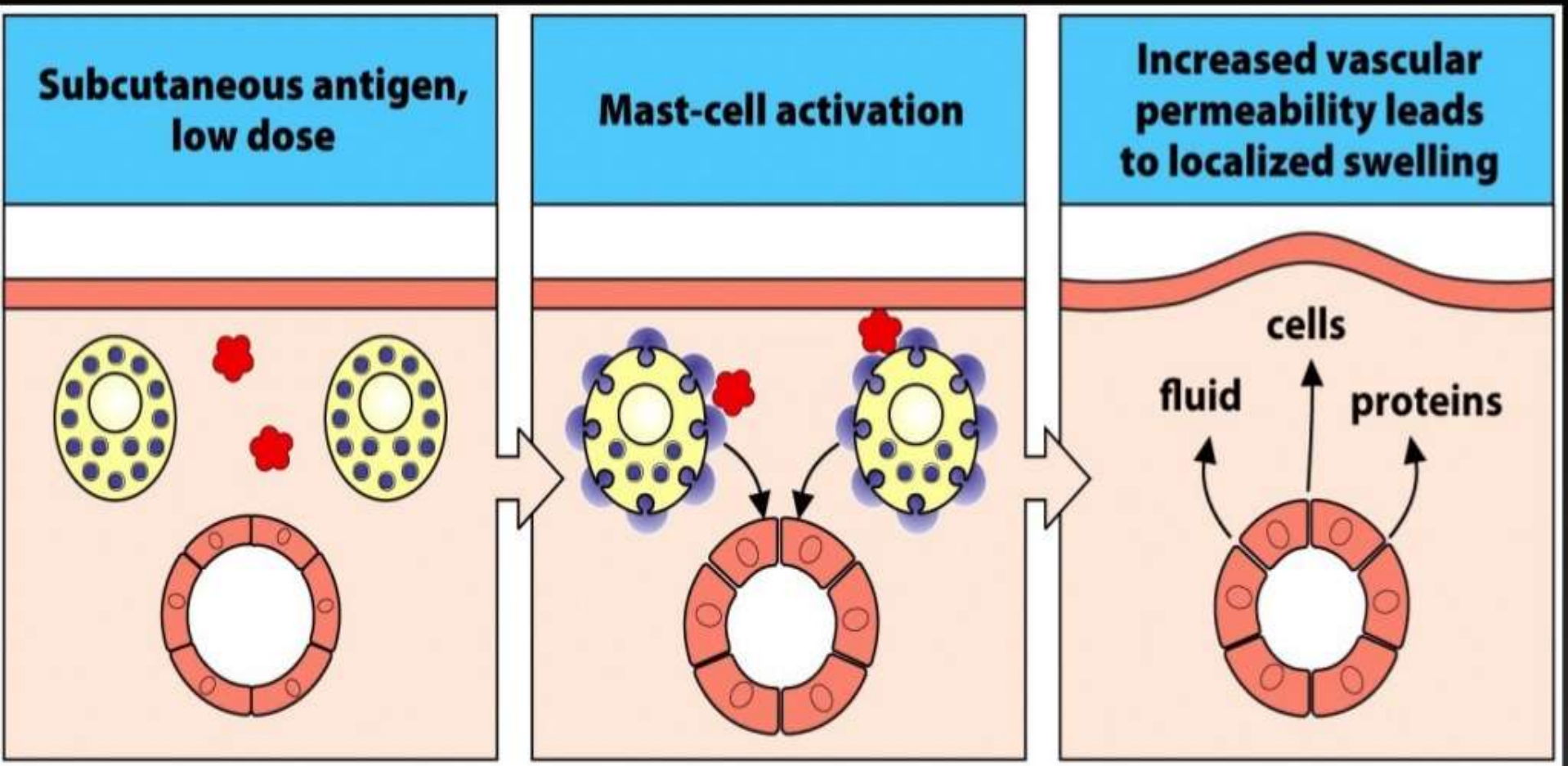


Figure 12.24 part 1 of 2 The Immune System, 3ed. (© Garland Science 2009)

INFECTIONS

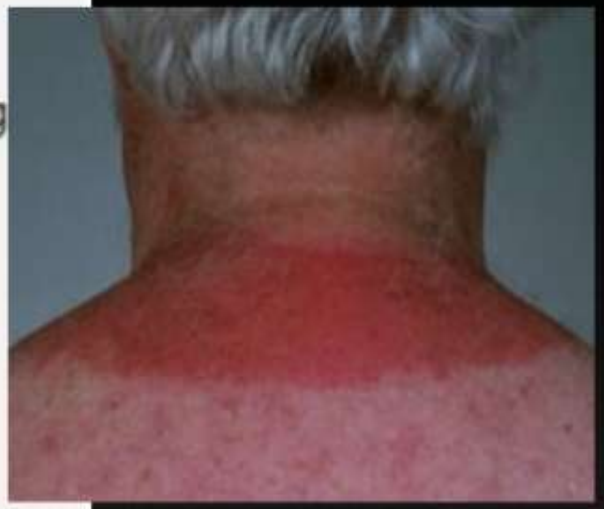
- **viral** : herpes simplex, hepatitis B,

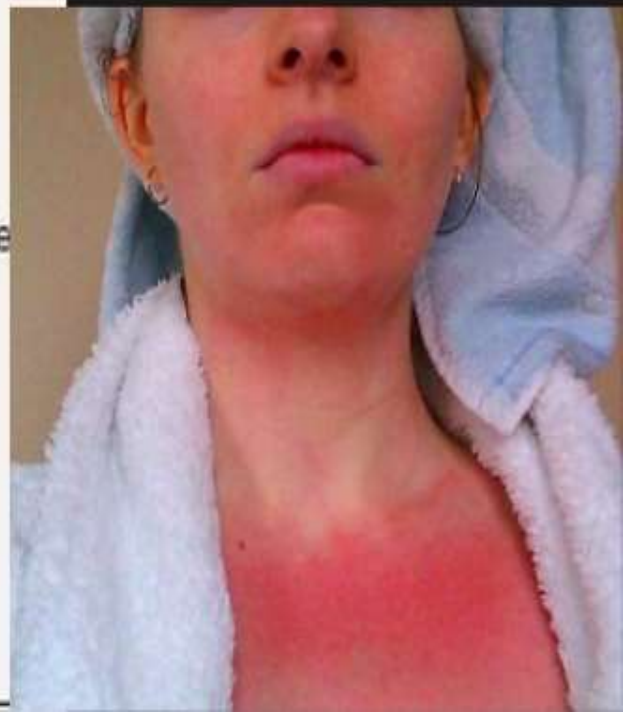
  coxsackie A and B, upper respiratory infections.
- **Bacterial** - associated with certain infectious foci: dental caries/abscesses, pharyngitis /tonsillitis, otitis media, occult abscesses, UTI.
- **Parasitic** : ascaris, strongyloides, echinococcus, toxocara, fasciola, filaria, schistosoma.
- **Fungal? :** candida

Table 1 – Classification of urticaria

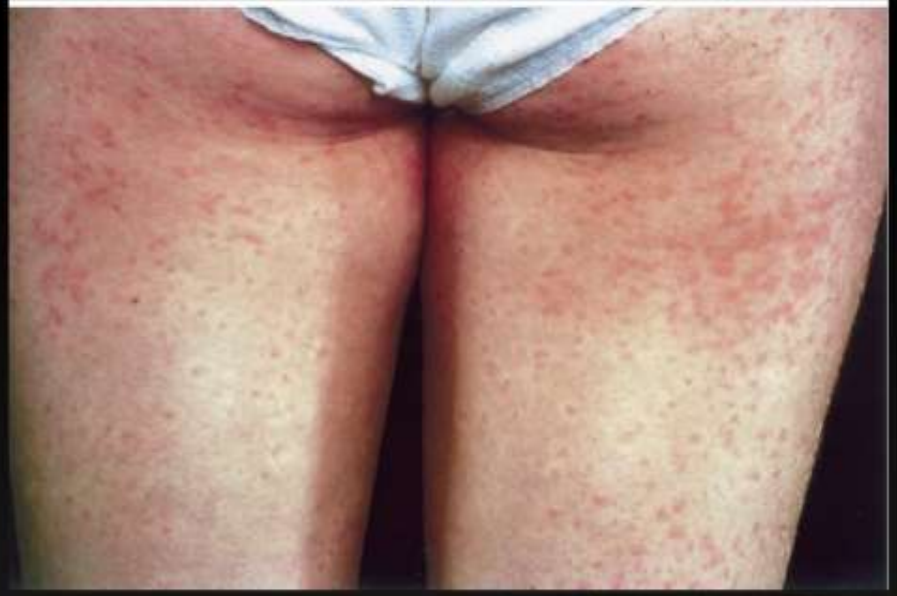
	Acute	Chronic
Time course	< 6 wk	> 6 wk
Causes	Immunological reactions to medications, foods, contact allergens, and insect venoms; viral infections; idiopathic	Idiopathic; autoimmune; drug-induced; complement-mediated, secondary to a systemic disorder; rarely, caused by foods or other environmental triggers
Natural history	Typically self-limited	Chronic, with episodic exacerbations
Treatment	Symptom control with antihistamines	Symptom control with antihistamines; for severe refractory urticaria, consider addition of second-line treatment (eg, leukotriene modifiers, hydroxychloroquine, cyclosporine[5])

	Subtypes	Triggering factor
Physical urticaria	*Due to mechanical stress*	
	Dermatographism	Mechanical (scratching/rubbing etc)
	Delayed pressure urticaria	Constant pressure on skin
	Vibratory urticaria	Any vibrating force
	Contact urticaria	Urticariogenic substance
	Due to temperature changes	
	Cold contact urticaria	Cold objects/weather
	Heat contact urticaria	Localised heat source
	Due to sweating or stress	
	Cholinergic urticaria	Increased core body temperature
	Adrenergic urticaria	Stress
	Exercise-induced urticaria	Physical exercise
	Due to other causes	
	Solar urticaria	UV or visible light
	Aquagenic urticaria	Contact with water



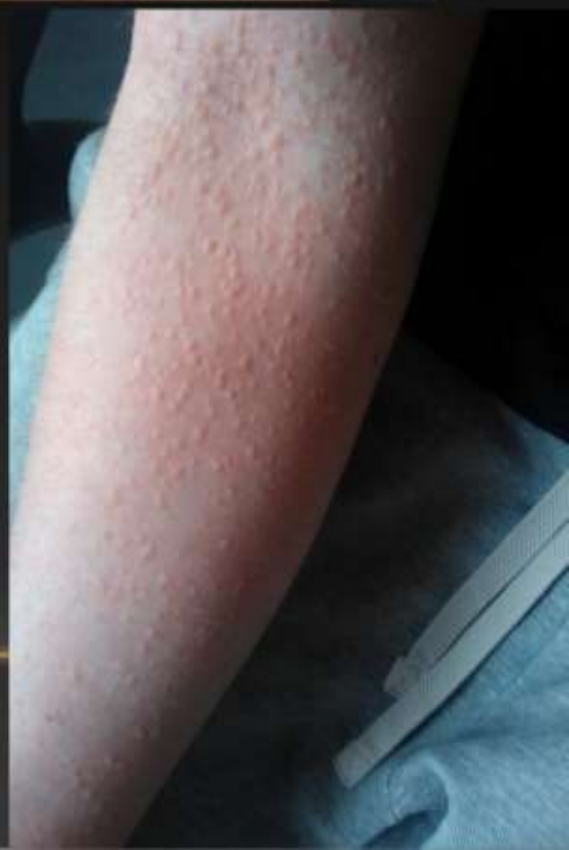


Physical urticaria – cholinergic (STRESS)



Itchy, monomorphic pale or pink wheals on trunk, neck, and limbs – after exercise or a hot shower, spicy food, under too many covers.

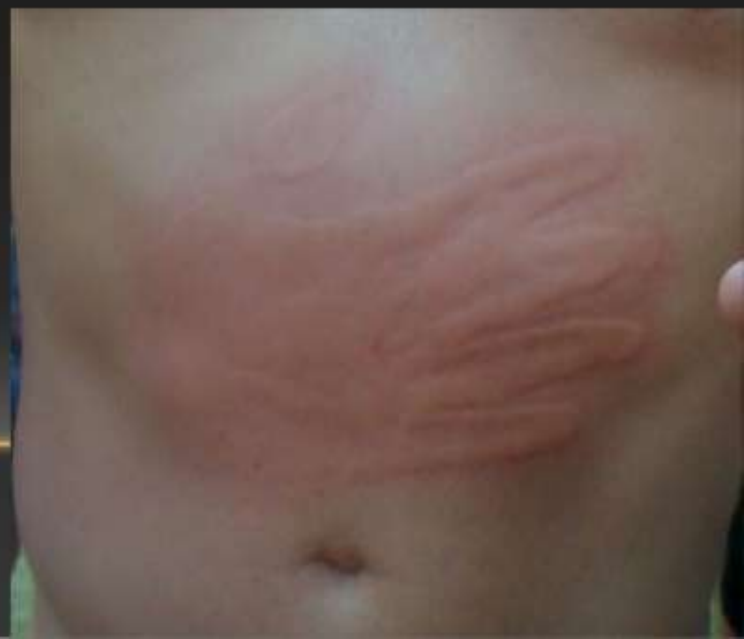
Anything that raises internal body temperature



Prevalence of 11% in the age group of 16-35 years.

Physical urticaria-pressure

Large painful or itchy red swelling at sites of pressure (soles, palms, or waist) lasting 24 hours or more - application of pressure perpendicular to skin produces red swelling after a latent period of 1 to 4 hours.



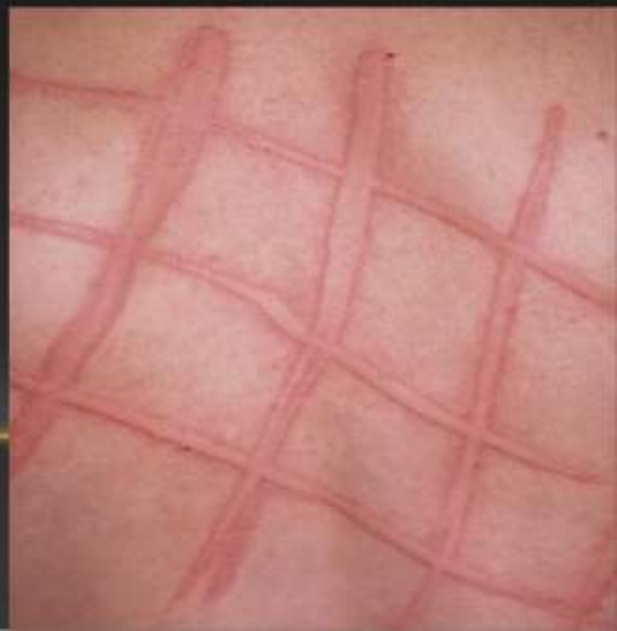
Physical urticaria - Dermographic urticaria

Itchy, linear wheals with surrounding bright-red flare at sites of scratching or rubbing.

The most frequent form of physical urticaria.

Affecting mainly young adults

Mean duration 6.5 years

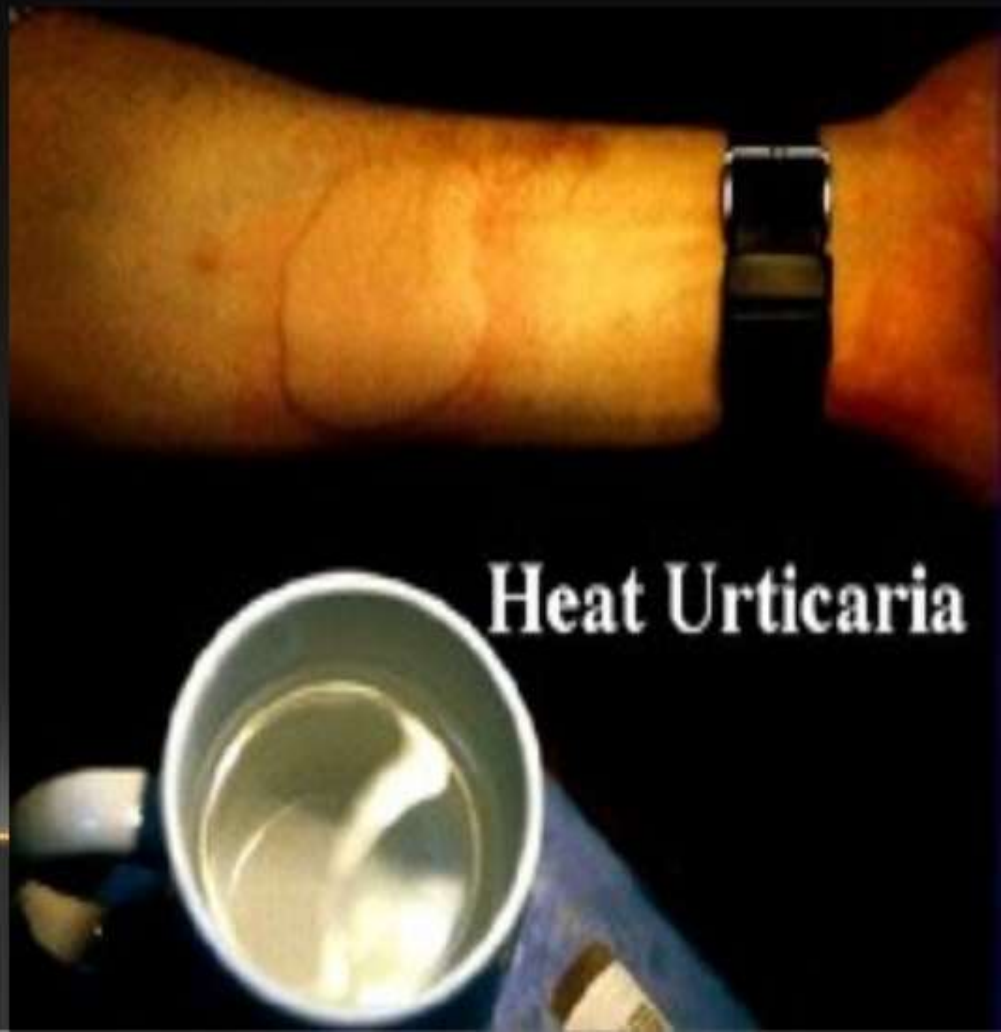


Physical urticaria - Heat

- A rare form of urticaria.

- Induced by direct contact of the skin with warm objects or warm air.

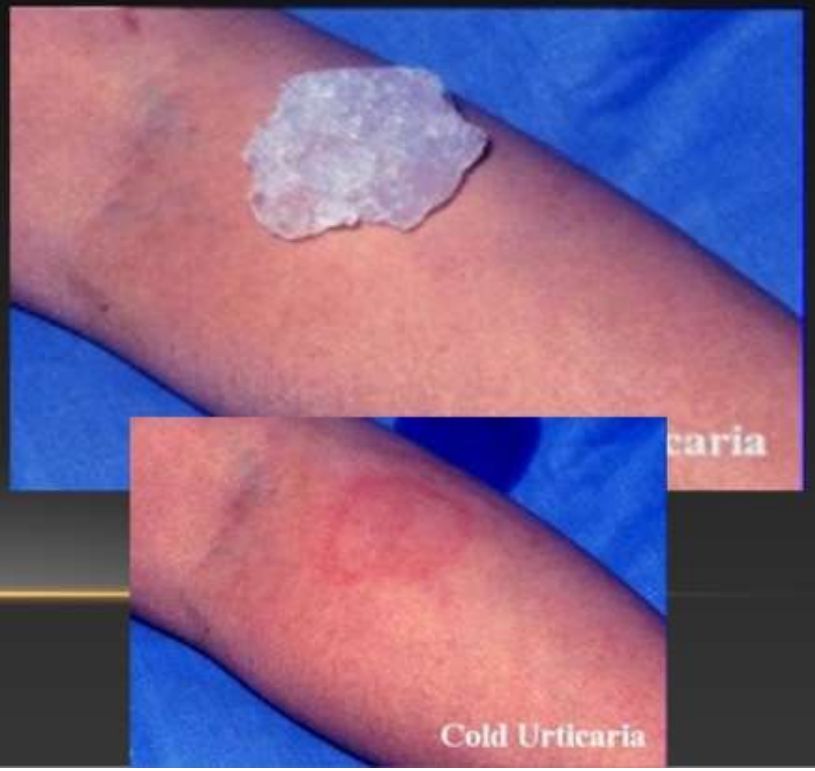
- The eliciting temperature ranges from 38° C to more than 50 ° C .

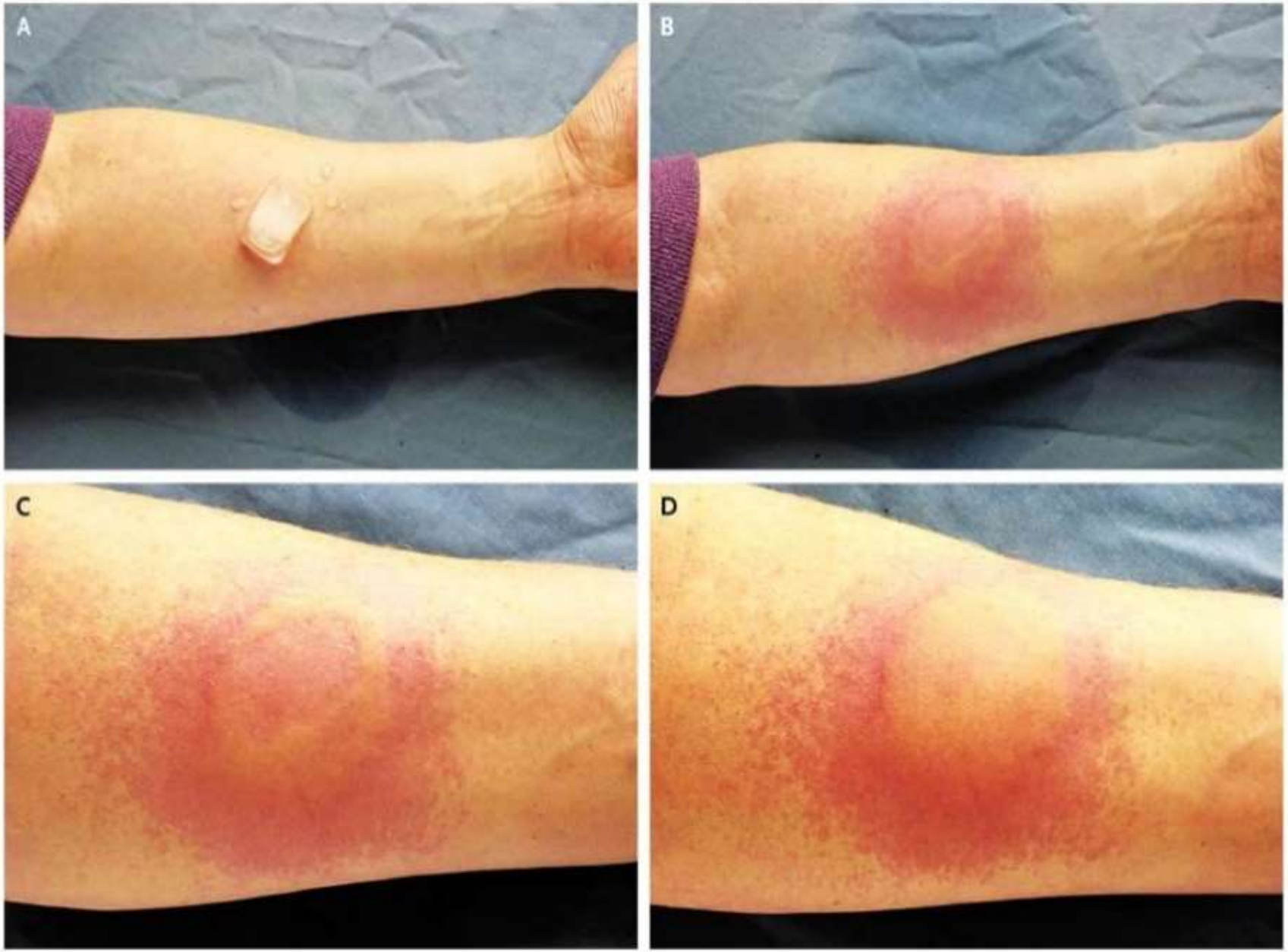


PHYSICAL URTICARIA- COLD

Itchy pale or red swelling at sites of contact with cold surfaces or fluids- ten minutes application of an ice pack causes a wheal within five minutes of the removal of ice.

ICE CUBE TEST



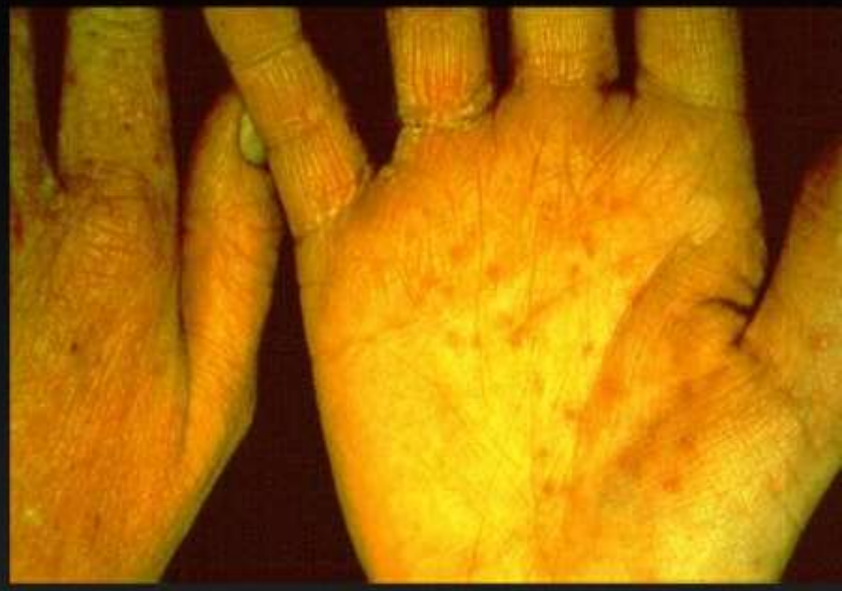

A
B
C
D

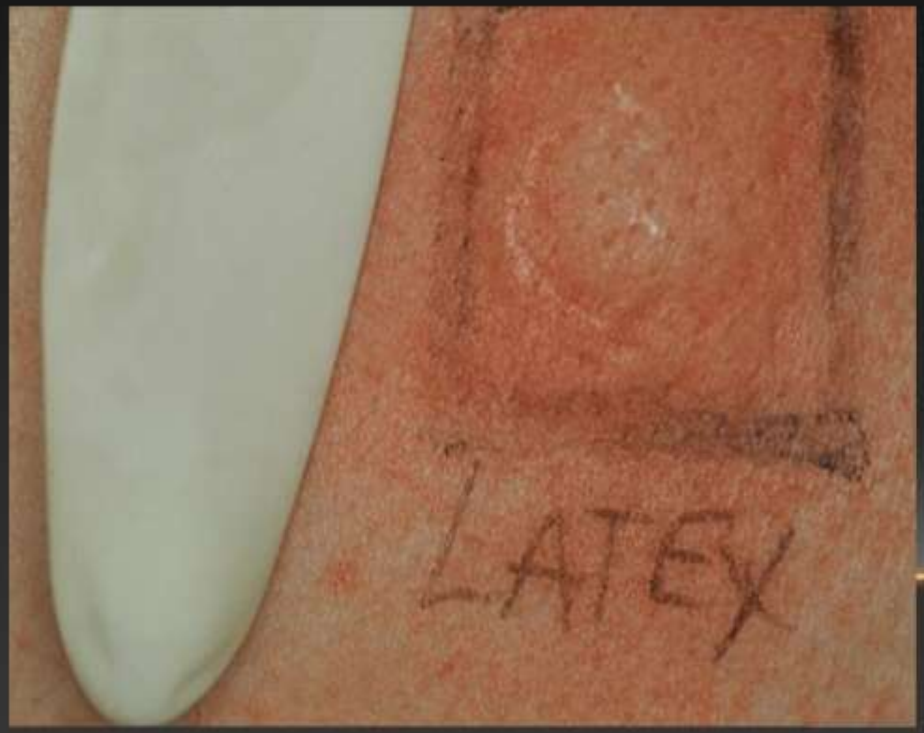
Lukewarm water immersion of forearm for Aquagenic urticaria

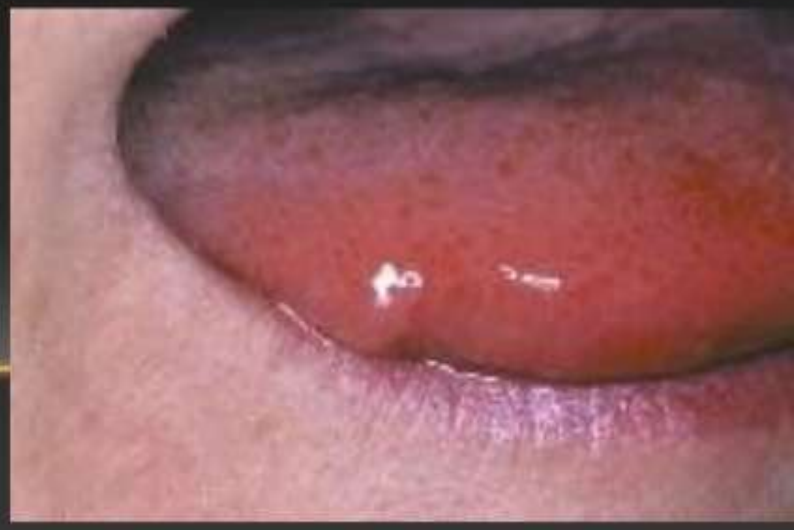
urtication in aquagenic urticaria; should not be performed in patients with a history of aquagenic angioedema or anaphylaxis

CONTACT URTICARIA

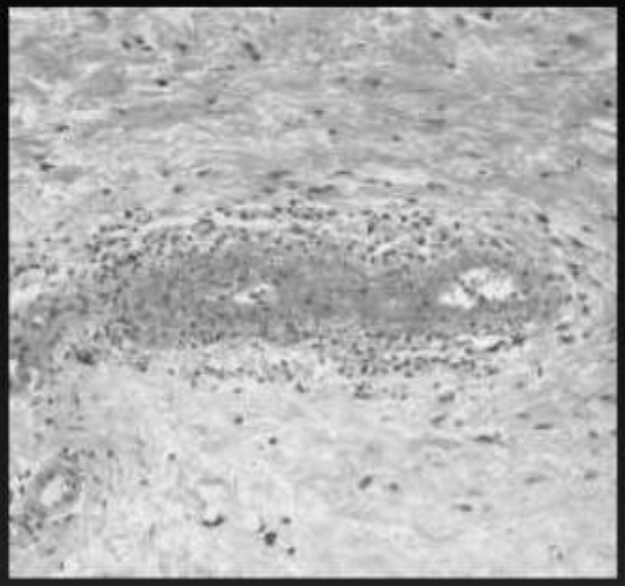
Contact urticaria is an important manifestation of natural rubber latex allergy.

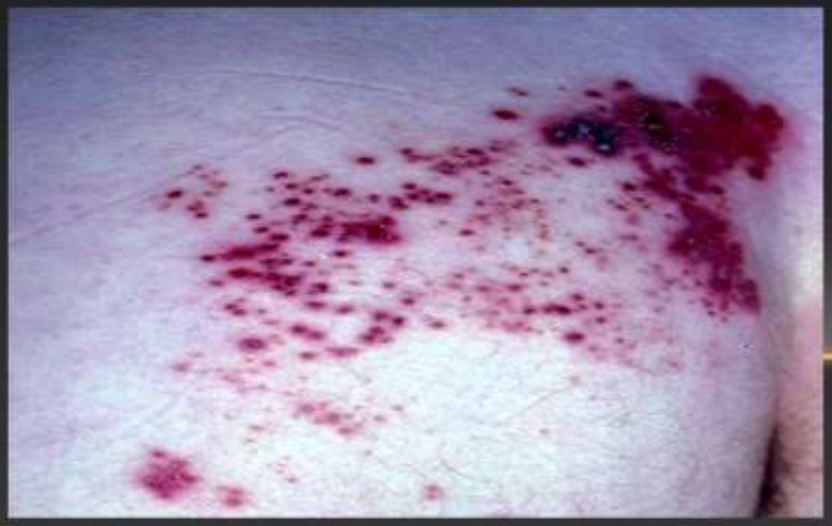


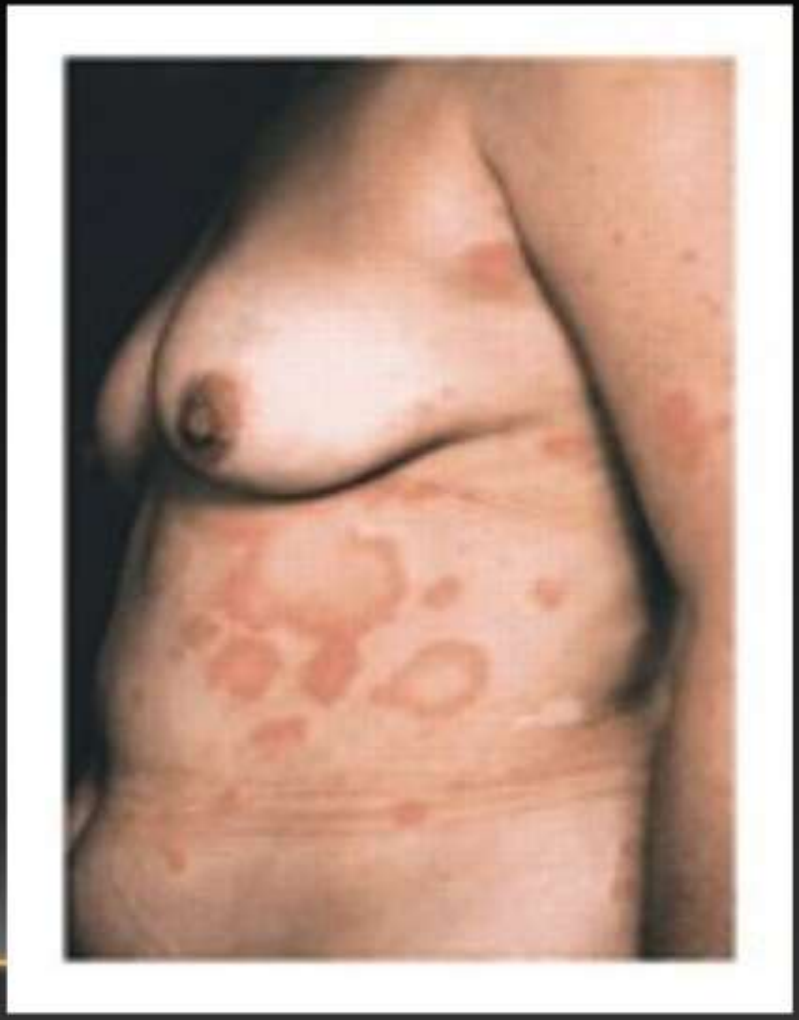




Urticarial Vasculitis







Feature	Chronic Urticaria	Urticarial Vasculitis
Characteristics of wheals		
Duration (hr)	<24	>24
Purpura*	No	Yes
Pain	No	Yes
Itch	Yes	Maybe
Hyperpigmentation	No	Yes
Systemic signs		
Arthralgia	Maybe	Yes
Fever*	No	Yes
Abdominal pain	Maybe	Yes
Nephritis*	No	Yes
Obstructive airways disease	No	Yes
Laboratory findings		
Elevated erythrocyte sedimentation rate	Maybe	Yes
Increased acute-phase proteins	Maybe	Yes
Reduced serum C3*	No	Maybe
Serum immune complexes*	No	Maybe
Histologic features of skin		
Venular endothelial-cell swelling	Maybe	Yes
Leukocyte invasion of venular endothelium	Maybe	Yes
Extravasation of red cells*	No	Yes
Leukocytoclasia*†	No	Yes
Fibrin deposition	Maybe	Yes
Findings on direct immunofluorescence		
C3	No	Yes
Immunoglobulin	Maybe	Yes
Fibrin	Maybe	Yes
Response to treatment with antihistamines	Yes	Maybe

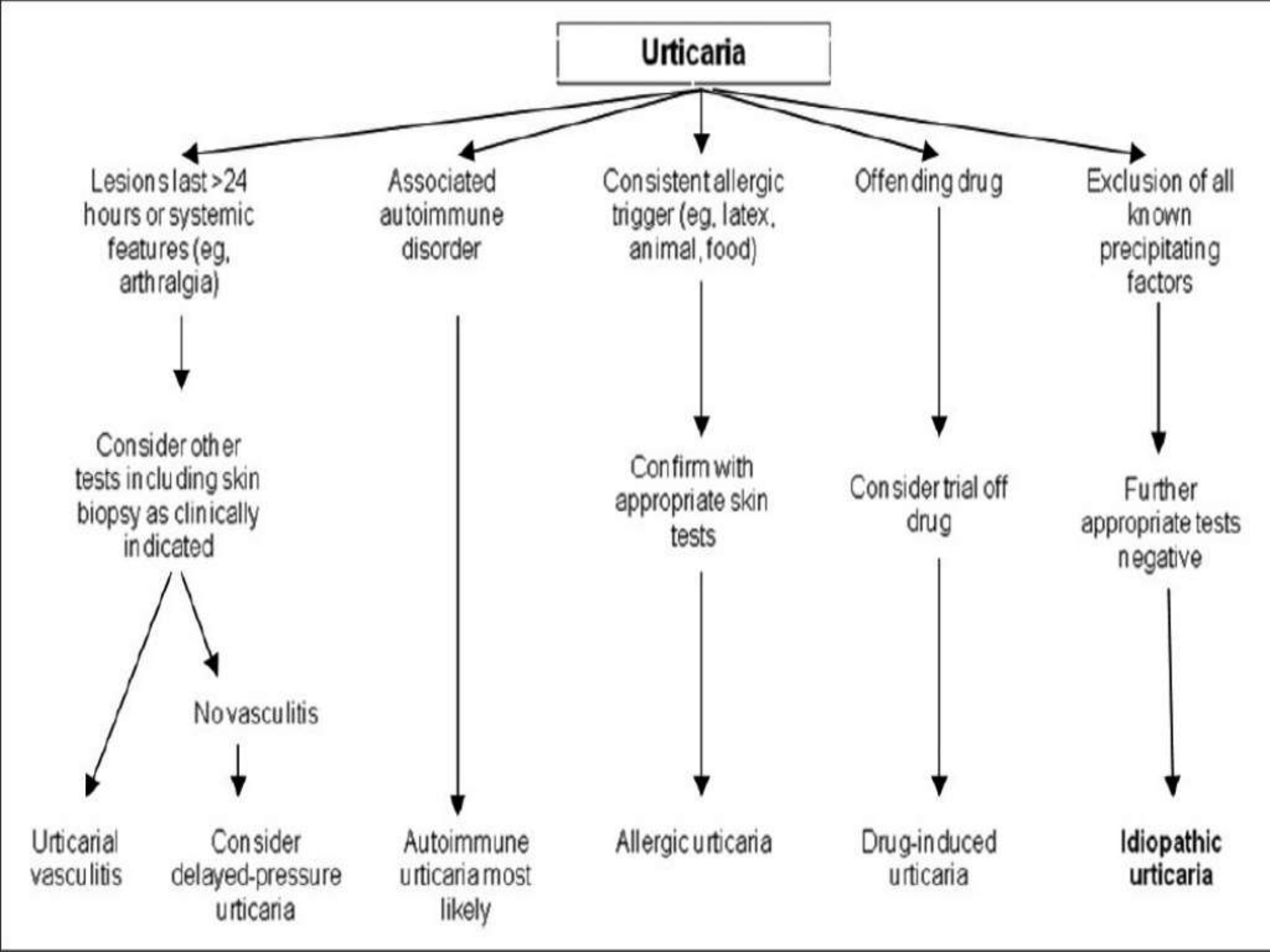
LABORATORY ASSESSMENT

Initial tests

- **CBC with differential**
- **Erythrocyte sedimentation rate**
- **Urinalysis**

- Possible tests for selected patients
  - Stool examination for ova and parasites
  - Blood chemistry profile
  - Antinuclear antibody titer (ANA)
  - Hepatitis B and C
  - Skin tests for IgE-mediated reactions

- **RAST for specific IgE**
- **Complement studies: CH_{50}**
- **Cryoproteins**
- **Thyroid microsomal antibody**
- **Antithyroglobulin**
- **Thyroid stimulating hormone (TSH)**


Urticaria
Lesions last >24 hours or systemic features (eg, arthralgia)
Associated autoimmune disorder
Consistent allergic trigger (eg, latex, animal, food)
Offending drug
Exclusion of all known precipitating factors
Consider other tests including skin biopsy as clinically indicated
No vasculitis
Confirm with appropriate skin tests
Consider trial off drug
Further appropriate tests negative
Urticarial vasculitis
Consider delayed-pressure urticaria
Autoimmune urticaria most likely
Allergic urticaria
Drug-induced urticaria
Idiopathic urticaria

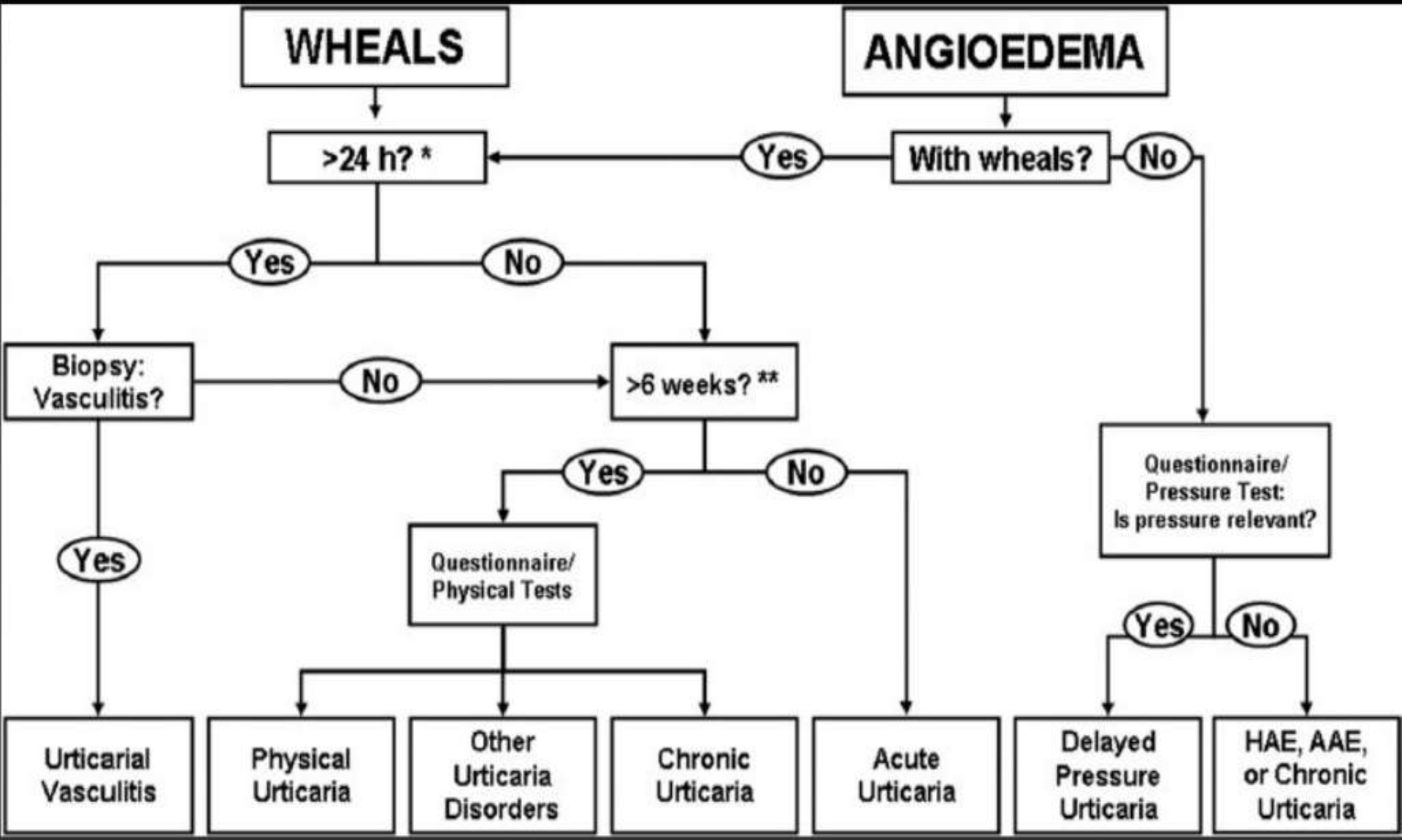
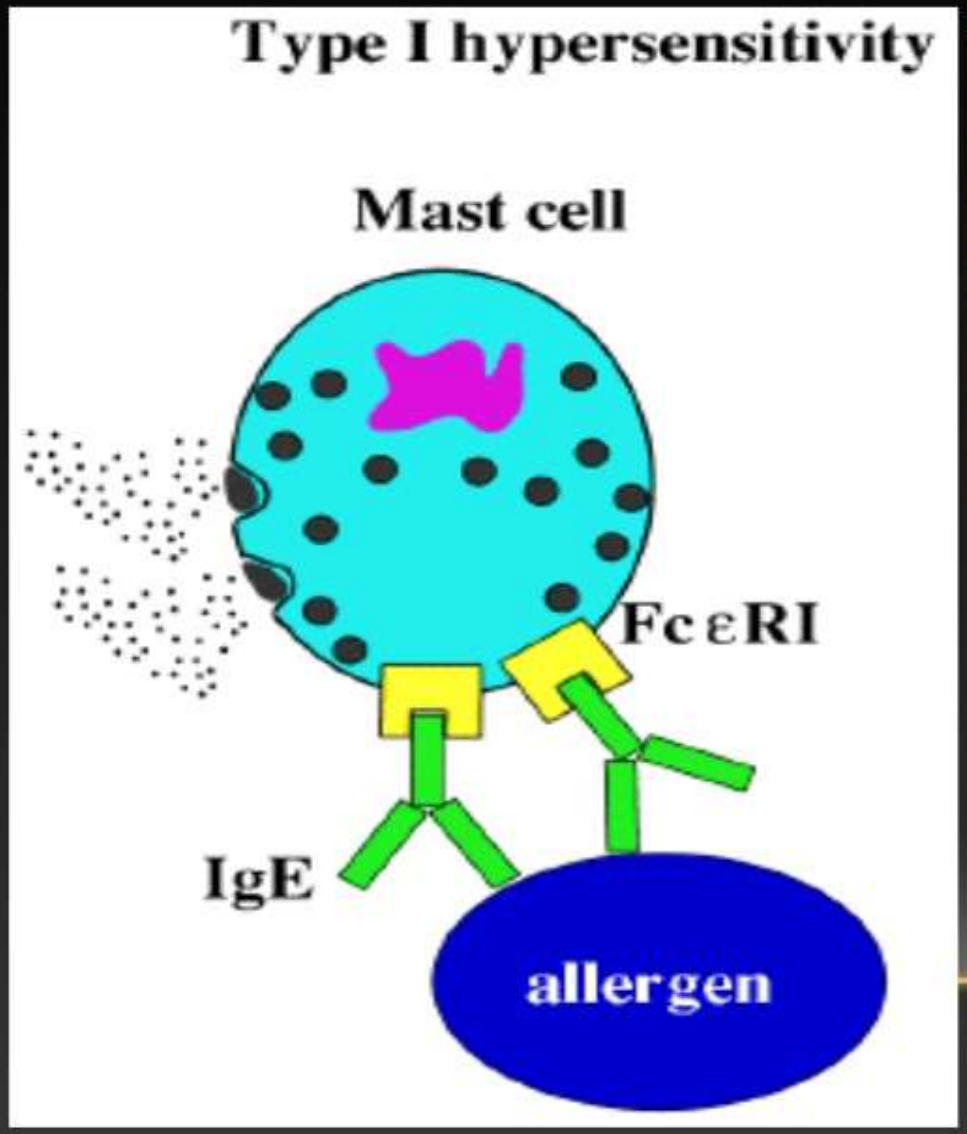

WHEALS
ANGIOEDEMA
>24 h? *
Yes
With wheals?
No
Yes
No
Biopsy: Vasculitis?
No
>6 weeks? **
Yes
No
Questionnaire/ Pressure Test: Is pressure relevant?
Yes
Questionnaire/ Physical Tests
Yes
No
Urticarial Vasculitis
Physical Urticaria
Other Urticaria Disorders
Chronic Urticaria
Acute Urticaria
Delayed Pressure Urticaria
HAE, AAE, or Chronic Urticaria

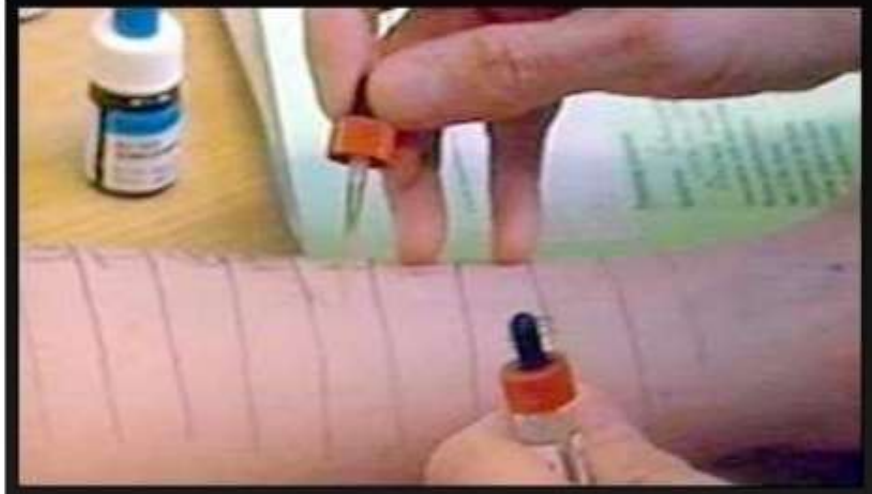
Table 2 Assessment of disease activity in urticaria patients

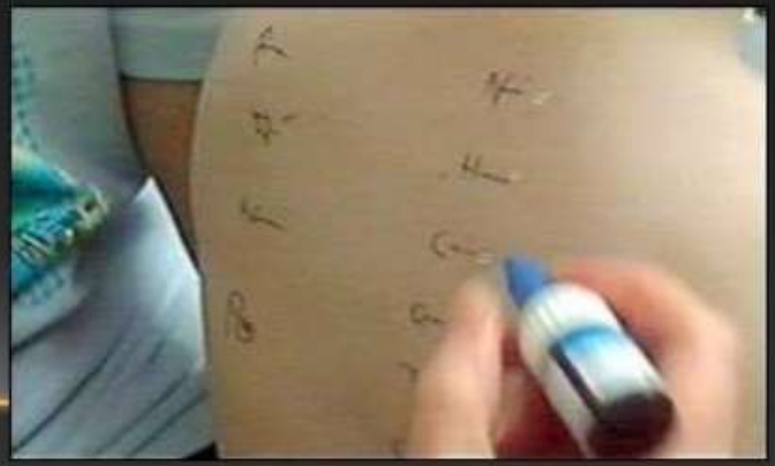
Score	Wheals	Pruritus
0	None	None
1	Mild (<20 wheals/24 h)	Mild (present but not annoying or troublesome)
2	Moderate (20–50 wheals/24 h)	Moderate (troublesome but does not interfere with normal daily activity or sleep)
3	Intense (>50 wheals/24 h or large confluent areas of wheals)	Intense (severe pruritus, which is sufficiently troublesome to interfere with normal daily activity or sleep)

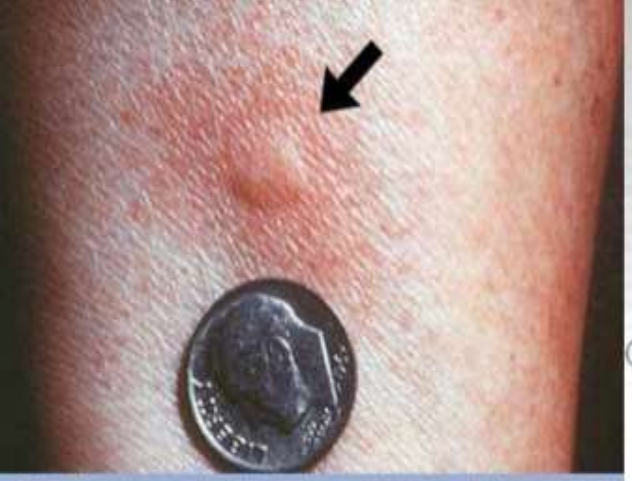
Sum of score: 0–6

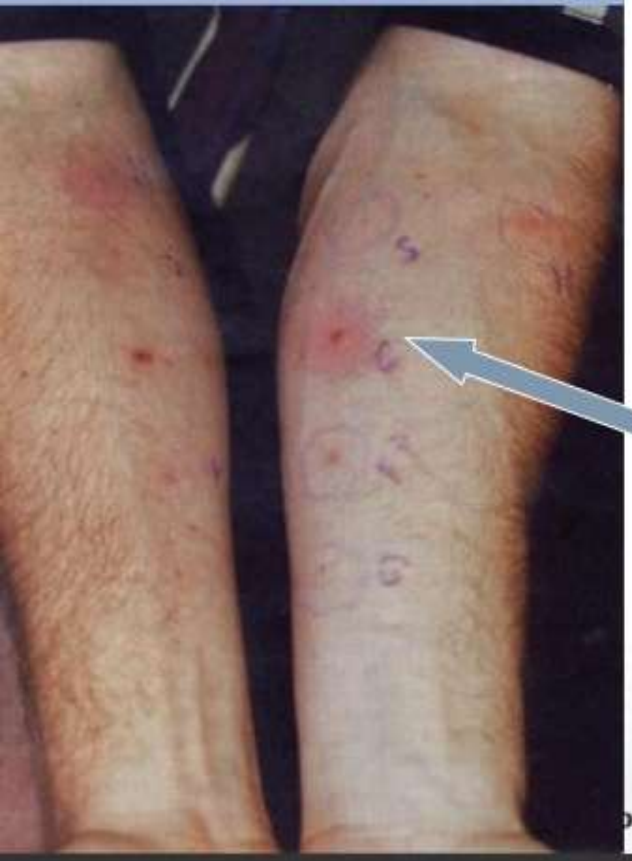
Skin Prick Test (SPT)







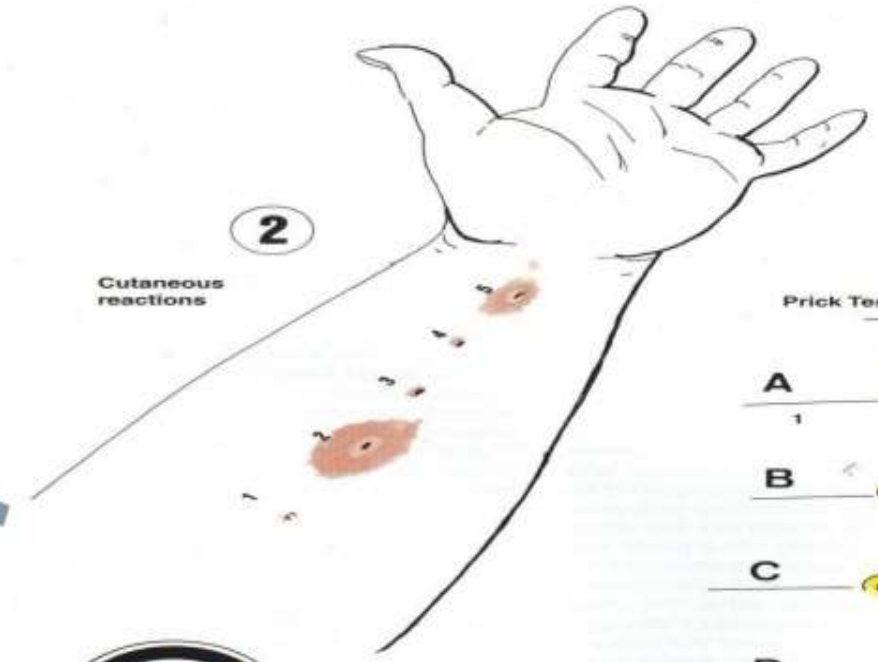




SKIN TESTS IN ALLERGY

1

Allergens for tests with known concentrations

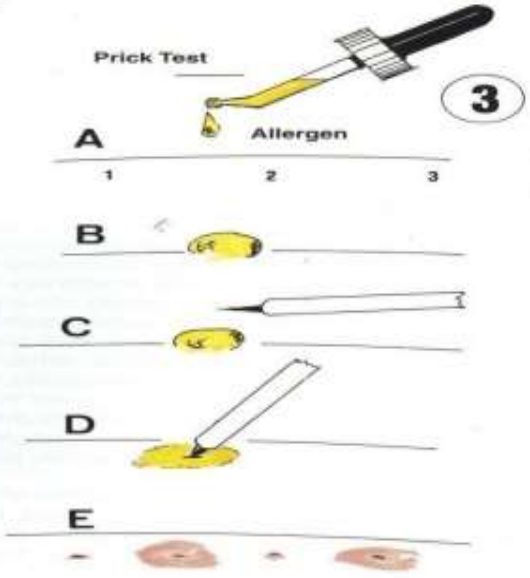


2

Cutaneous reactions

Reading of the tests after 20'

4



THERAPY FOR URTICARIA

- Search for triggers
  - treat the treatable causes
- Anti-histamines
  - Short-acting (Benadryl, Atarax)
  - Long-acting (Claritin, Reactine)
- Corticosteroids
  - start around 1 mg/kg/day (single or divided doses)

ASSOCIATED WITH OTHER CONDITIONS

- Collagen vascular disease (eg, systemic lupus erythematosus)
- Complement deficiency, viral infections (including hepatitis B and C), serum sickness, and allergic drug eruptions
- Chronic tinea pedis
- Pruritic urticarial papules and plaques of pregnancy (PUPPP)
- Schnitzler's syndrome

Table 2: Differential diagnoses of urticaria[2,3]

Condition	Distinguishing features
Urticaria pigmentosa(mastocytosis)	Brown patches; urticariate on pressure
Urticarial vasculitis	Lasts >24 hours, leaves bruising/ purpura
SLE	Longer lasting; sun exposed areas
Non-histaminergic angioedema • Hereditary angioedema • Acquired angioedema with C1 inhibitor deficiency	Facial and/or genital areas
Cryoglobulinemia	Usually worse in extremities; purpura
Polymorphic eruption of pregnancy	Pregnant females
Associated syndromes	**Associated features**
Cryopyrin-associated periodic syndrome • Muckle–Wells syndrome • Familial cold urticaria	Development of wheals early in life that are resistant to antihistamine treatment; unprovoked attacks of fever, rashes, musculoskeletal and neurologic manifestations
Hypereosinophilic syndromes • Well's syndrome	Pruritic cellulitis-like eruption occurs, followed by reticular pigmentation/ scarring alopecia. Flame figures on biopsy
Schnitzler syndrome	Nonpruritic urticarial rash with recurrent fever, bone pain, joint pain, organomegaly, and monoclonal IgM gammopathy