Allergic diseases.
Classification, clinical examples.

Lecturer: Professor Vladimir Babadzhan

The Classification of the Hypersensitivity

	Type I	Type II	Type III	Type IV a	Type IV b	Type IV c	Type IV d
Immune reactant	IgE	IgG	IgG	IFNγ, TNFα (TH_1 cells)	IL-5, IL-4/IL-13 (TH_2 cells)	Perforin/ GranzymeB (CTL)	CXCL-8 GM-CSF (T-cells)
Antigen	Soluble antigen	Cell-or matrix-associated antigen	Soluble antigen	Soluble antigen presented by cells or direct T cell stimulation	Soluble antigen presented by cells or direct T cell stimulation	Cell-associated antigen or direct T cell stimulation	Soluble antigen presented by cells or direct T cell stimulation
Effector cells	Mast-cell activation	FcR+ cells (phagocytes NK cells)	FcR+ cells Complement immune complex	Macrophage activation	Eosinophils	T cells	Neutrophils
Example of hypersensitivity reaction	Allergic rhinitis, asthma, systemic anaphylaxis	Hemolytic anemia, thrombocytopenia	Serum sickness, Arthus reaction	Tuberculin reaction, contact dermatitis (with IVc)	Chronic asthma, chronic allergic rhinitis, maculopapular exanthema with eosinophilia	Contact dermatitis, maculopapular and bullous exanthema, hepatitis	AGEP Behcet disease

TYPE 1 HYPERSENSITIVITY REACTION

SYNONYMS:

- ALLERGY, ATOPY
- IgE-MEDIATED TYPE HYPERSENSITIVITY REACTIONS
- IMMEDIATE TYPE HYPERSENSITIVITY (EARLY PHASE)

TYPE 1 HYPERSENSITIVITY REACTION:

THE SUSCEPTIBILITY OF CERTAIN INDIVIDUALS TO BE ALLERGENIC TO ENVIRONMENTAL ALLERGENS

PREDISPOSING FACTORS IN THE PATHOGENESIS OF ALLERGIC DISEASES

IMMUNOLOGICAL/GENETICAL (Athopy)

- ↓ IgA
- Th1:Th2 imbalance

  ↓ IFNg, ↑IL4

  ↑IgE

ENVIRONMENTAL FACTORS ALSO PLAY A ROLE

- ALLERGY CAUSED BY ENVIRONMENTAL FACTORS
- SEASONAL NATURE OF ALLERGIES
- CHILDREN, RAISED IN HOMES OF SMOKERS, AT INCREASED RISK TO HAVE ASTHMA
- INCREASED RISK OF ALLERGIES IN DEVELOPED COUNTRIES

ABOUT ALLERGENS

- THEY ARE ANTIGENS THAT EVOKE $CD4^{+}TH_2$ CELLS THAT DRIVE AN IgE RESPONSE

- INHALED ALLERGENS ARE SMALL, HIGHLY SOLUBLE PROTEINS,
  CARRIED ON PARTICLES

- ALLERGENS ARE PRESENTED TO IMMUNE SYSTEM AT VERY LOW DOSES

TYPES OF ALLERGENS

Exogenous Allergens	Endogenous allergens	
Inhalant	Heteroallergens (Neoantigens)	Autoallergens
	1. Non-infectious	Normal intact self antigens characteristic of young healthy normal cells that commonly provoke autotolerance
Contact-type	Induced by alteration	
Ingestant	Atypical (senescent cell, tumor, embryonic)	
Injected	2. Infectious	
Infectious	-virus-induced	
Drug	-microorganism-induced	

Types of exogenous allergens:

Drugs (penicilline, etc)

Inhalative allergens: pollens (ragweed, mugwort, etc)

animal epithelium (cat, dog,etc)

mites

fungi (mucor, aspergillus, etc)

textile/cotton

Insects bee, wasp

Nutritive allergens: milk, egg, soybeen, etc.

Atopy: **pathologic hypersensitivity to allergic reactions. It is a diathesis.**
Anaphylaxy: **a lifethretening state when enormously high amouts of the inflammatory mediators get into the circulation, skin, lung and gastrintestinal truct**

a.) IgE mediated

b.) not IgE mediated forms (mediated by complement and other factors)

HOUSE DUST MITE

Type I. allergic reaction

The reaction is mediated by allegen specific IgE

The reaction is of immediate type (the symtoms of inflammation appear within 4 hours after the allergen challange)

The symptomes are elicited by mediator substances released from mast cells, basophils, eosinophils, macrophages or platelets.

Mediators of	***mast cells/basophils***	***eosinophils***	***macrophages***	***platelets***
	histamine, triptase	ECP	proteases	serotonine
	PGD2, LTC4	MBP	PGD2, PGE2	histamine
	PAF	ROS	TxA2, LTB4	TxA2
	IL-1, IL-4, IL-5	LTC4, PAF	LTC4, PAF	ROS
	TNFα, IFNγ	IL-5	IL-1, TNF	
			ROS	

ALLERGIC CONDITIONS

ALLERGIC RHINITIS

ALLERGIC ASTHMA

ATOPIC DERMATITIS

FOOD ALLERGY

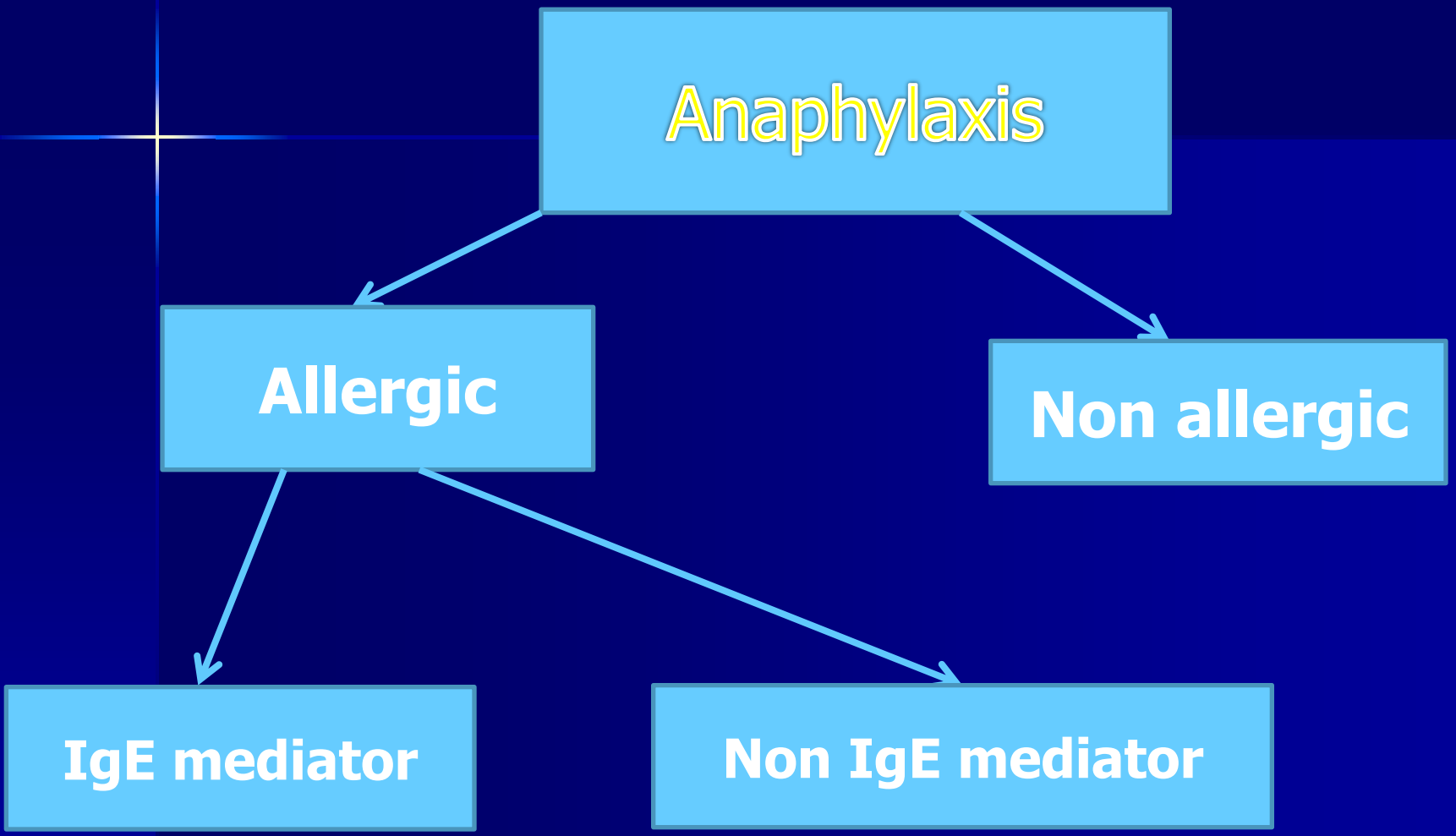
SYSTEMIC ANAPHYLAXIS

URTICARIA

Definition of anaphylaxis

- Ana (without) phyalxis (protection / guard)
- Is an sever life-treating generalized Or systemic hypersensitivity reaction .
- Its commonly ,but not always mediated by an
  - allergic mechanism , usually by IgE
  - Allergic Non IgE mediator anaphylaxis
  - Non allergic anaphylactic reaction formerly called anaphylactoid Or pseudo- allergic reaction

Revised momenclatued for anaphylaxis



Cell & combos classification of hypersensitivity

Anaphilaxis

- type 1 > Immediate hypersensitivity < 60 mim
- Type 2 > cytotoxic reaction < 72 hour
- Type 3 > immune complex reaction 1-3 weeks

Type 4 > delayed hypersensitivity > 48

Non allergic anaphslaxis

- Anaphylactic reaction are case by activation of mast cell and release of the same mediator , but without the involvement of IgE antibodies
- Management is similar to anaphylaxis

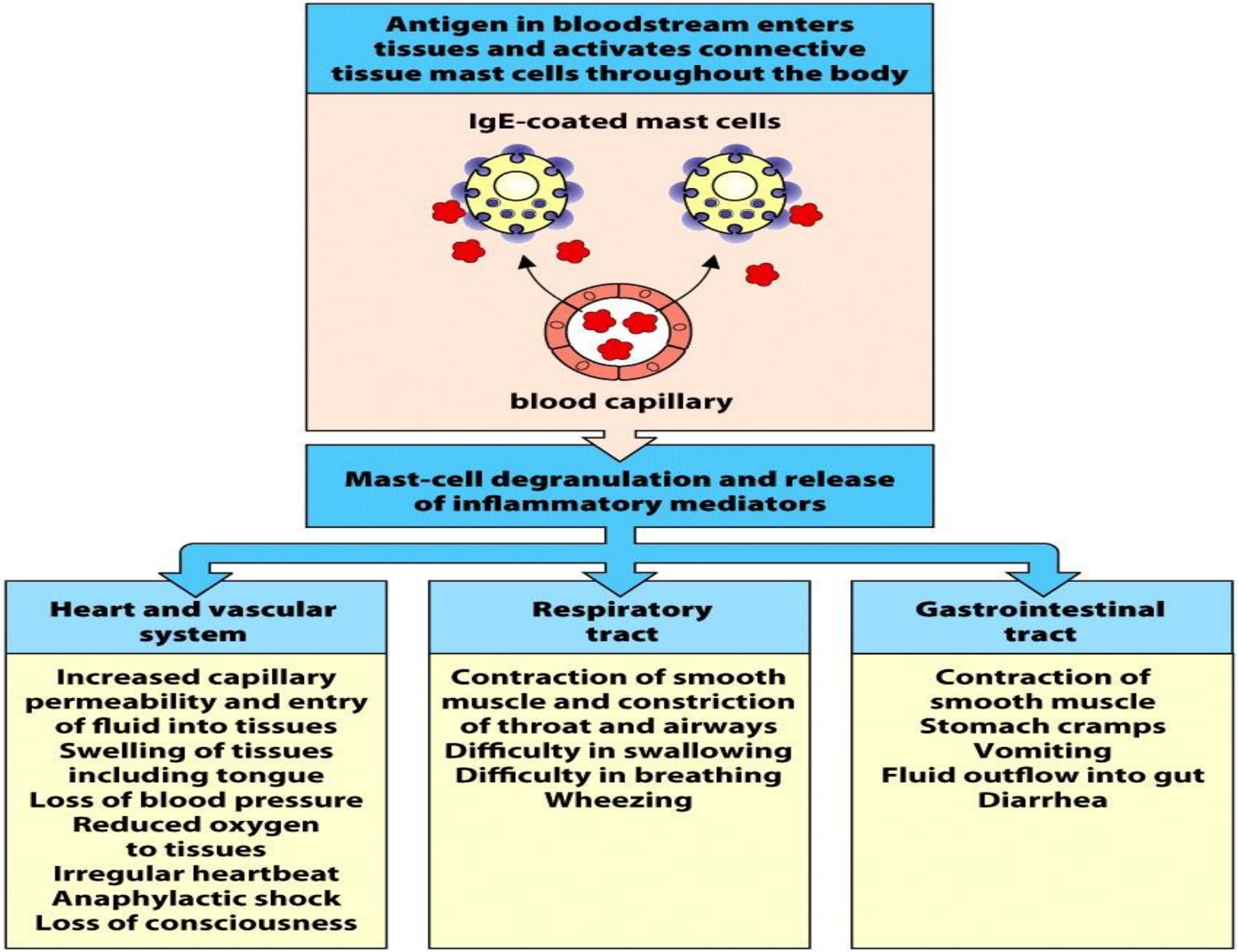


Figure 12.19 The Immune System, 3ed. (© Garland Science 2009)

Anaphylactic shock

- Anaphylaxis associated with systemic vasodilatation (hypotension , fainting , collapse) and bronco constriction (respiratory compromise)

Agent that cause anaphylaxis IgE –dependent

- Food (peanut, tree nut , seafood)
- Medication (bet-lactam ,antibiotic)
- Venoms
- Latex rubber

Cause of anaphylaxis

- Direct activation of mast cell
  - Opiates ,tubocurare , radiocontrast dyes
  - mediators of arachidonic acid metabolism
  - Aspirin
  - Non steroid anti-inflammatory drugs (NsAIDs)
  - Mechanism unknown
  - Sulphites
- other causes of anaphylaxis
  - ✓ Exercise – induced
  - ✓ Cold – induced
  - ✓ Idiopathic


Severe Reactions !
(Requires Immediate Treatment)
• Very low B/P
• Cardiac or respiratory arrest
• Loss of consciousness
• Convulsions
• Laryngeal edema
• Cyanosis
• Difficulty in breathing
• Profound shock
Copyright ©2001 Mosby, Inc.

Primary symptoms of anaphylaxis

- Skin
  - flushing , itching , urticaria , angioedema
- Gastro intestinal
  - Nausea , vomiting , bloating , cramping , diarrhea
- Other
  - Felling of impending doom , metallic taste
- Respiratory
  - dysphonia , cough , wheezing , dyspnea ,chest tightness ,asphyxiation , death
- cardiovascular :
  - Tachycardia , hypotension , dizziness ,collapse ,death

Pattern of anaphylaxis

- Uniphasic
  - Symptoms resolve within hour of treatment
- Biphasic
  - Symptoms resolve after treatment but return between 1 to 72 hour later (usually 1-3 hour)
- Protracted
  - Symptoms do not resolve with treatment and may last >24 hour

Medical clinical treatment of anaphylaxis

- Epinephrine
  - Up to 35% of patient mat need second dose
- Antihistamines
- Corticosteroids
- oxygen
- Impair further absorption
  - local epinephrine ,tourniquet
- Supine , elevate legs
- ER, ICU monitor /support fluid

1.Drugs for anaphylaxis

Epinephrine

Put the patient in supine position and elevate his /her leg maintain airway (endotracheal tube or cricothyrotomy)

Epinephrine

Adult – 1:1000 0,3-0.5ml q 5minutes (or less) PRN IM in lateral thigh

Child – 0.01 mg /kg ,max 0.3 ml q5minute (or less) PRN IM in lateral thigh

2. Drug : oxygen

- Optimally with all patient with anaphylaxis
- Any patient with hypotension or respiratory distress
- Any patient with 02 sat<95%
- Any patient requiring more than one epinephrine injection
- Face mask recommended over nasal prongs
- Start with 6-8 liter/ minute

Drugs : iv fluids

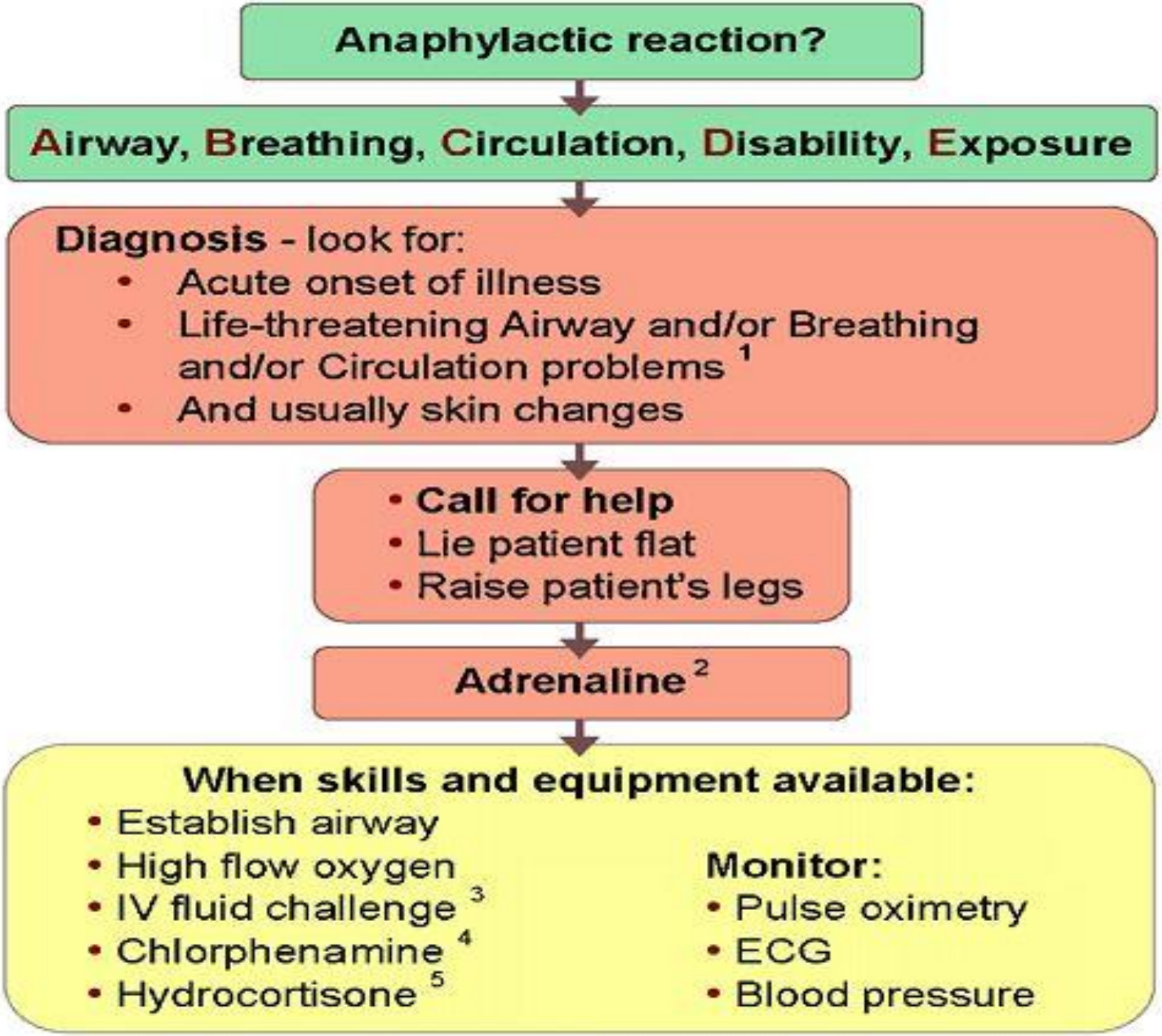
- For hypotension (systolic <100) or any one who has no responded to first IM epinephrine
- When there is shock in spite of increase vascular resistance
- 10% sever anaphylaxis not reversible with epinephrine
- select IV Fluids
- 0.9 % NaCl (isotonic crystalloid)
- Hydroxyethyl starch (hespan) (colloid) if saline not effective

iv fluids

- Once IV established
- 500_1000ml IV bolus in adult
- 20ml/kg bolus in child
- Monitor response – give further bolus as necessary
- Colloid or crystalloid
- 0.9% sodium chloride or Hartmann's
- Avoid colloid ,if colloid thought to have caused reaction .


EPIPEN 2-PAK®
(Epinephrine) Auto-Injectors 0.3 mg
OPEN IMMEDIATELY
EPIPEN Jr 2-PAK®
(Epinephrine) Auto-Injectors 0.15mg
OPEN IMMEDIATELY


EXP SEP 05
EPIPEN®
0.3mg EPINEPHRINE AUTO-INJECTOR
For Allergic Emergencies (Anaphylaxis)


Anaphylactic reaction?
Airway, Breathing, Circulation, Disability, Exposure
Diagnosis - look for:
• Acute onset of illness
• Life-threatening Airway and/or Breathing and/or Circulation problems [1]
• And usually skin changes
• Call for help
• Lie patient flat
• Raise patient's legs
Adrenaline [2]
When skills and equipment available:
• Establish airway
• High flow oxygen
• IV fluid challenge [3]
• Chlorphenamine [4]
• Hydrocortisone [5]
Monitor:
• Pulse oximetry
• ECG
• Blood pressure

Urticaria

Common Causes of Acute Urticaria

- Idiopathic
- Immune-mediated (IgE)
  - foods (shellfish, nuts)
  - drugs
- Nonimmune-mediated
  - opiates
- Nonspecific
  - viral infections (influenza)
  - bacterial infections (occult abscess, mycoplasma)

Etiology of Urticarial Reactions: Allergic Triggers

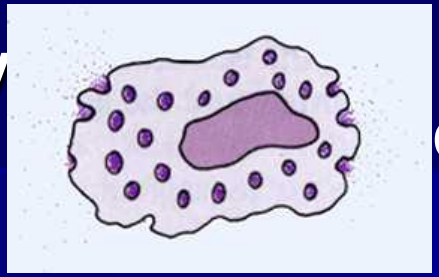
- Acute Urticaria
  - Drugs
  - Foods
  - Food additives
  - Viral infections
    - hepatitis A, B, C
    - Epstein-Barr virus
  - Insect bites and stings
  - Contactants and inhalants (includes animal dander and latex)

Chronic Urticaria

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

Role of Mast Cells in Chronic Urticaria: Lower Threshold for Histamine Release

- Release threshold decreased by
  - Cytokines & chemokines in the cutaneous microenvironment
  - Antigen exposure
  - Histamine-releasing factor
  - Autoantibody
  - Psychological factors

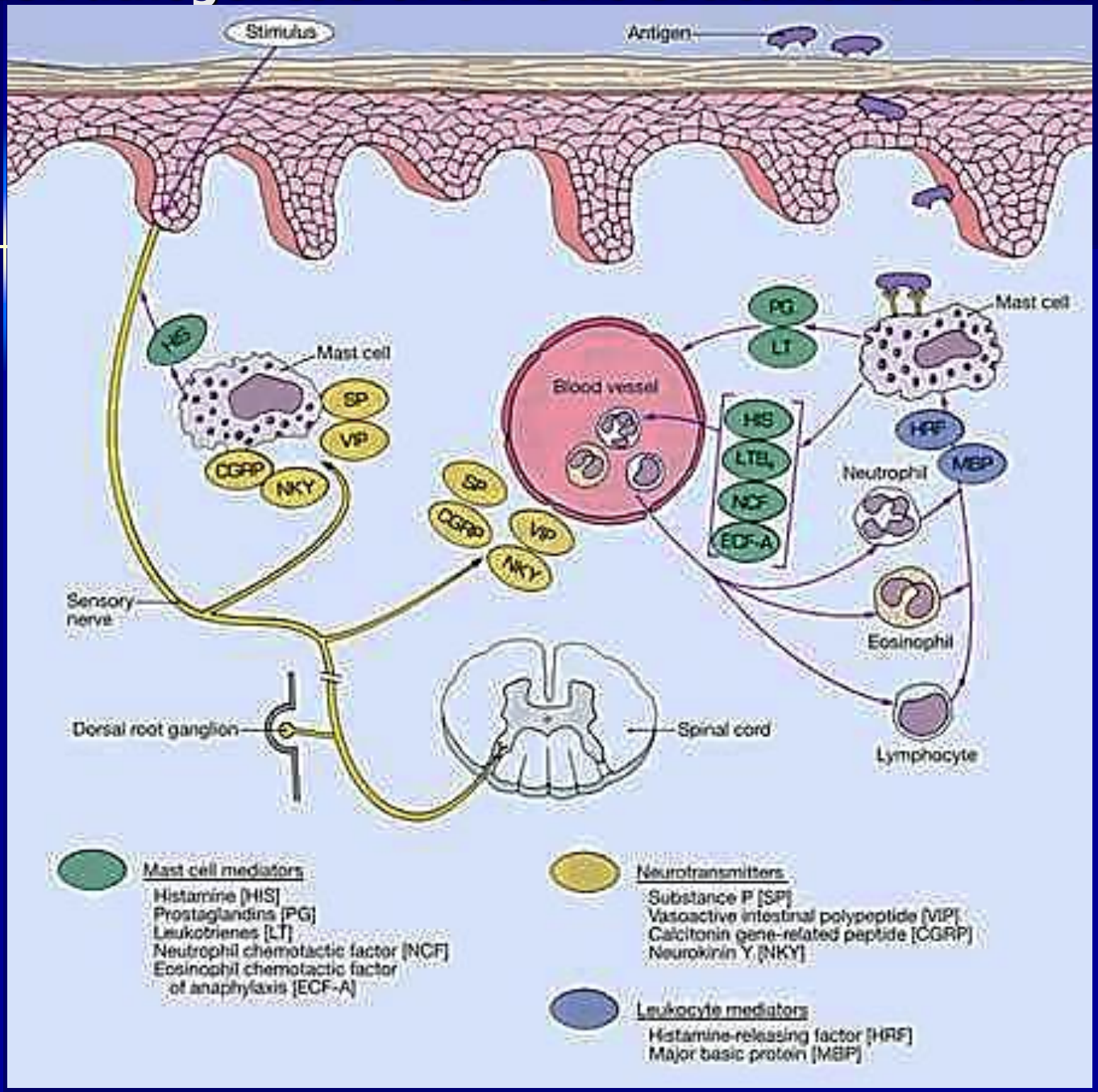


Cutaneous mass cell

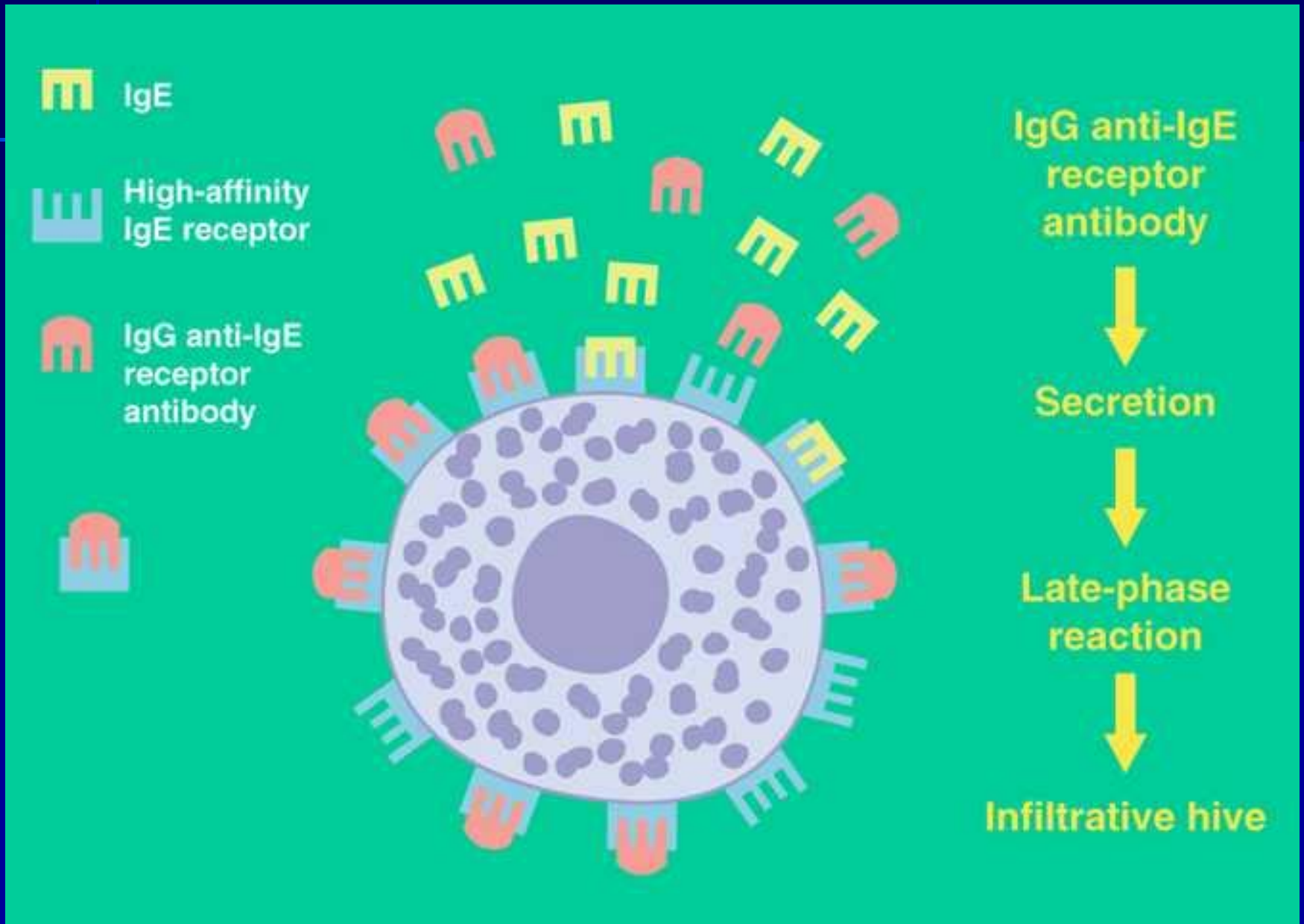
Release threshold increased by:

- Corticosteroids
- Antihistamines
- Cromolyn (in vitro)

The Pathogenesis of Chronic Urticaria: Cellular Mediators



An Autoimmune Basis for Chronic Idiopathic Urticaria: Antibodies to IgE



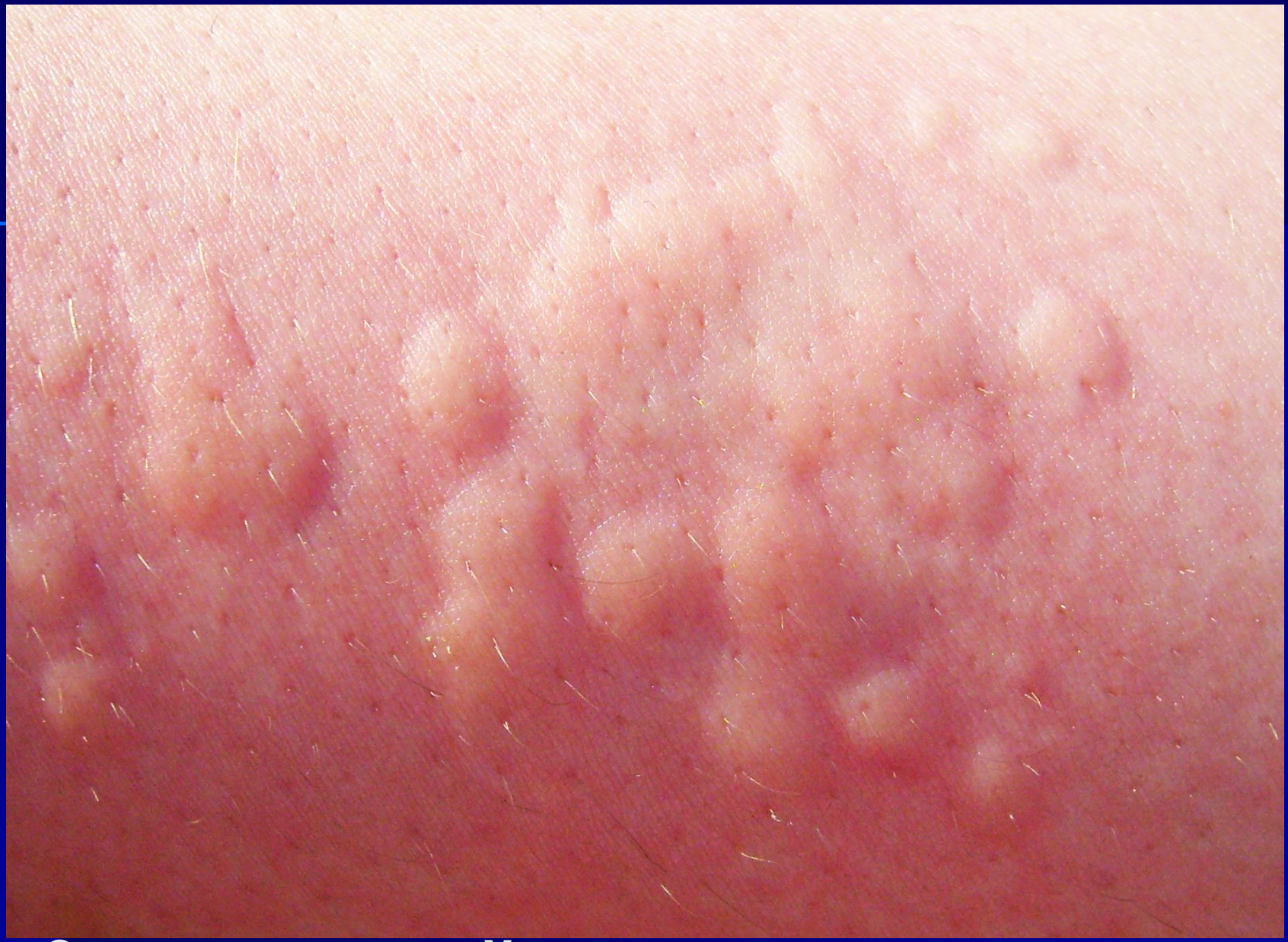
Initial Workup of Urticaria

- Patient history
  - Sinusitis
  - Arthritis
  - Thyroid disease
  - Cutaneous fungal infections
  - Urinary tract symptoms
  - Upper respiratory tract infection (particularly important in children)
  - Travel history (parasitic infection)
  - Sore throat
  - Epstein-Barr virus, infectious mononucleosis
  - Insect stings
  - Foods
  - Recent transfusions with blood products (hepatitis)
  - Recent initiation of drugs

Physical exam

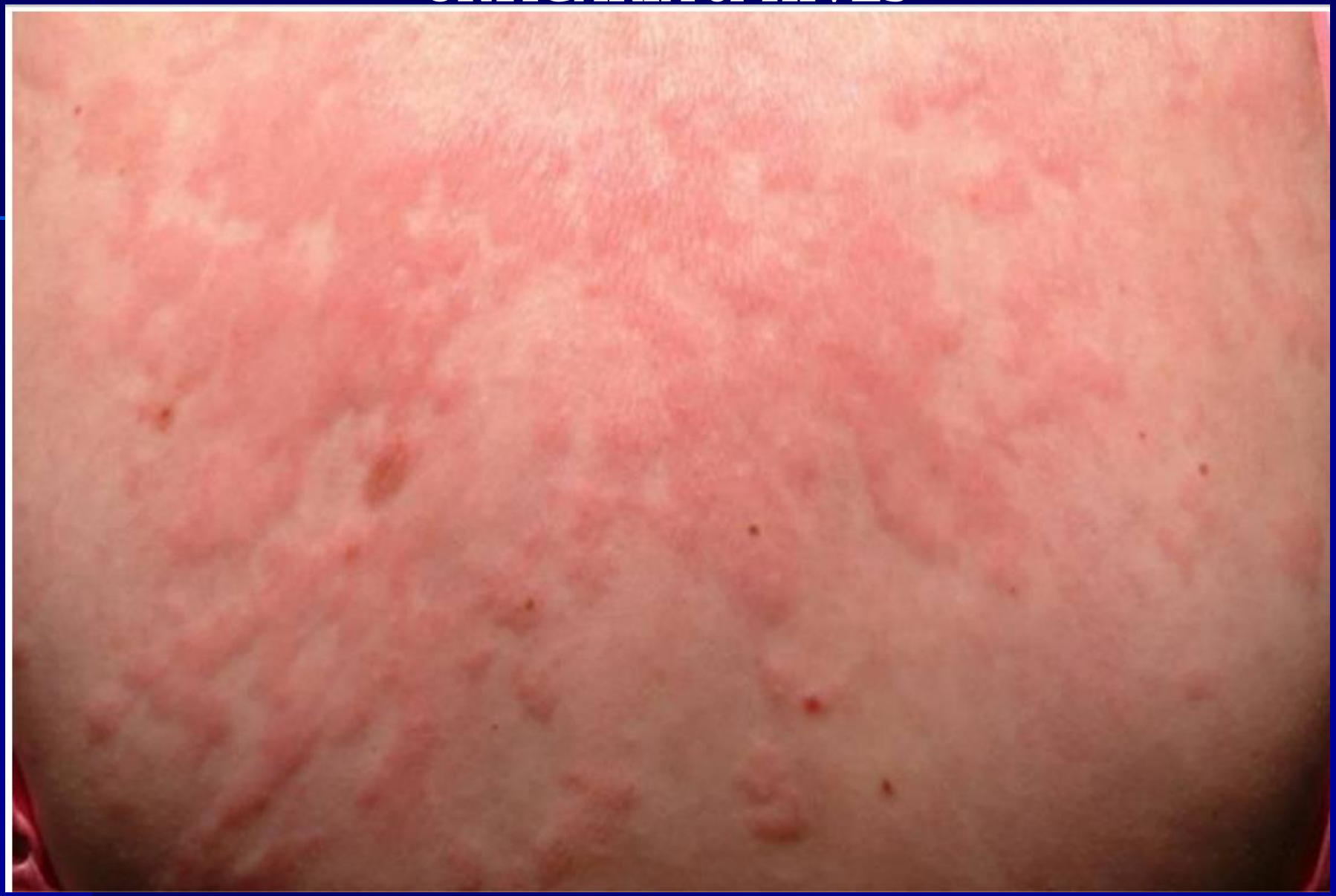
- **Skin**
- **Eyes**
- **Ears**
- **Throat**
- **Lymph nodes**
- **Feet**
- **Lungs**
- **Joints**
- **Abdomen**

URTICARIA or HIVES



Острая крапивница. Уртикарные высыпания, первые часы.

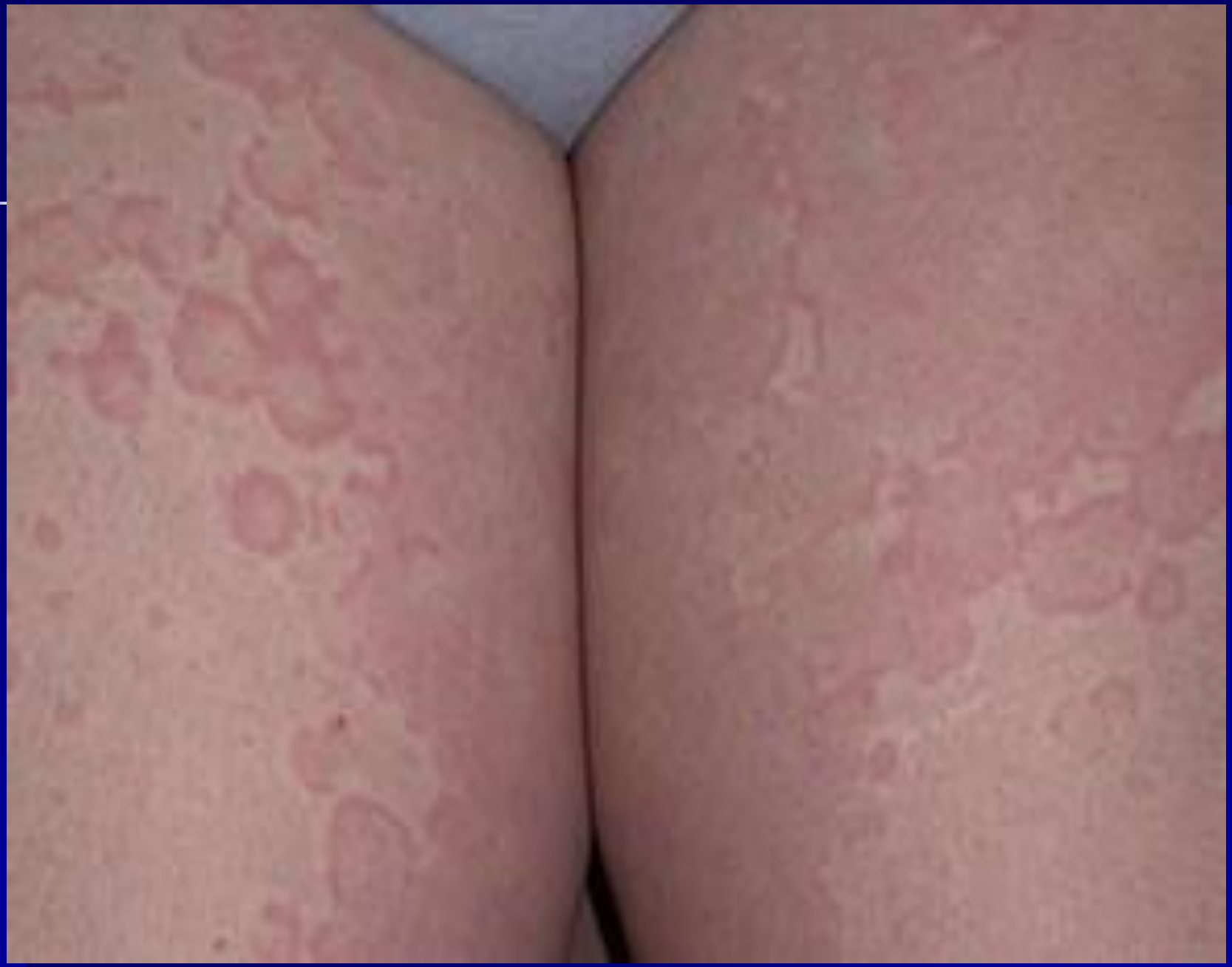
URTICARIA or HIVES



Острая крапивница. Уртикарные высыпания с элементами гиперемии на коже спины.

URTICARIA or HIVES

URTICARIA or HIVES



Laboratory Assessment for Chronic Urticaria

- 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

Initial tests

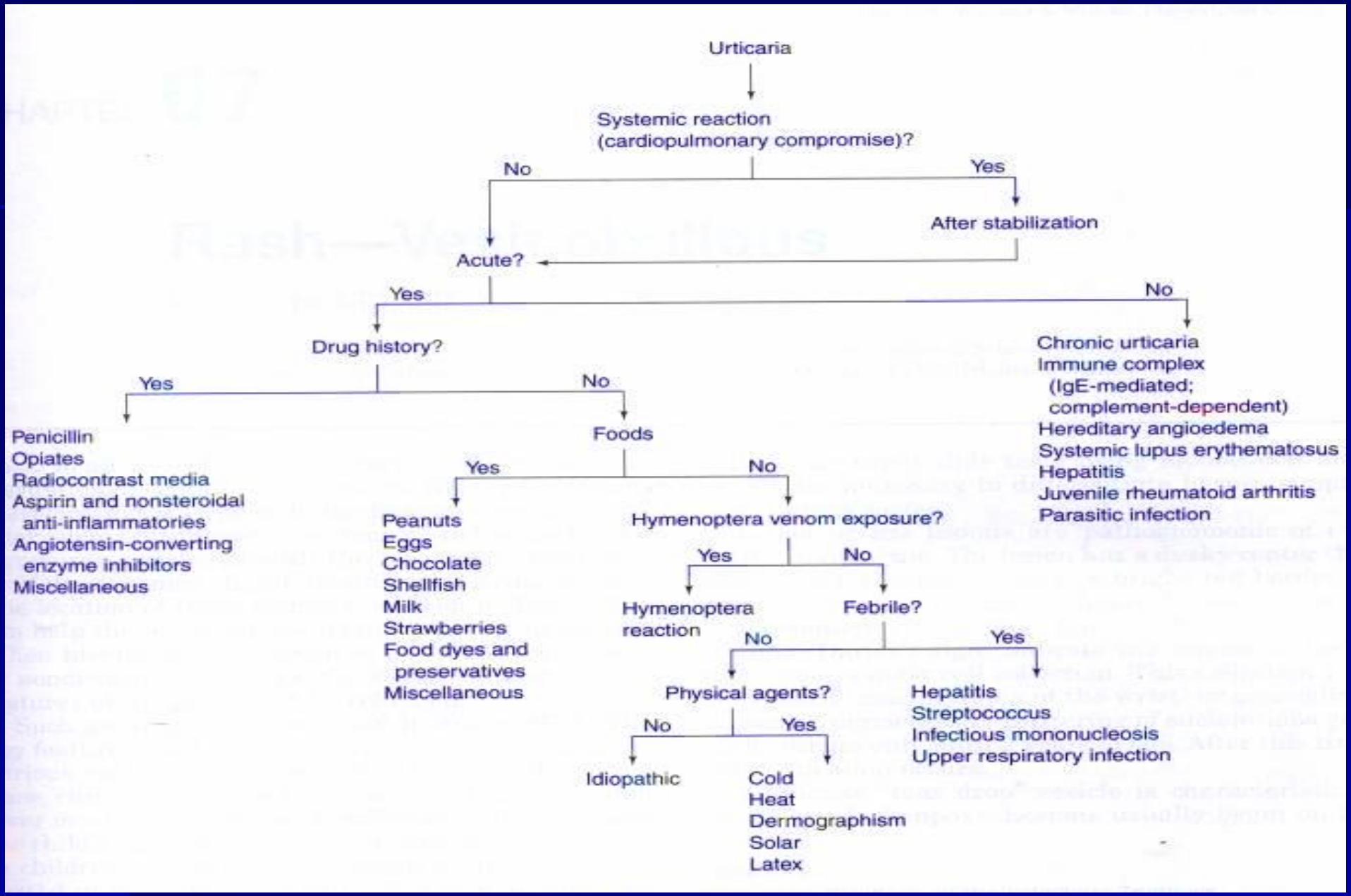
- **CBC with differential**
- **Erythrocyte sedimentation rate**
- **Urinalysis**

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

Urticaria 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** is characterized by chronic, nonpruritic urticaria in association with recurrent fever, bone pain, arthralgia or arthritis, and a monoclonal immunoglobulin M (IgM) gammopathy in a concentration of usually less than 10 g/L.

Algoritm for the evaluation of urticaria



Therapy for Urticaria

- Abbreviated search for triggers
  - treat the treatable causes
- Anti-histamines
  - Short-acting (Clemastine)
  - Long-acting (Loratadine, Cetirizine)
- Corticosteroids
  - start around 1 mg/kg/day (single or divided doses)

Treatment of Urticaria: Pharmacologic Options

- Antihistamines, others
  - First-generation H_1
  - Second-generation H_1
  - Antihistamine/decongestant combinations
  - Tricyclic antidepressants (eg, doxepin)
  - Combined H_1 and H_2 agents
- Beta-adrenergic agonists
  - Epinephrine for acute urticaria (rapid but short-lived response)
  - Terbutaline

Corticosteroids

- Severe acute urticaria
  - avoid long-term use
  - use alternate-day regimen when possible
- Avoid in chronic urticaria (lowest dose plus antihistamines might be necessary)

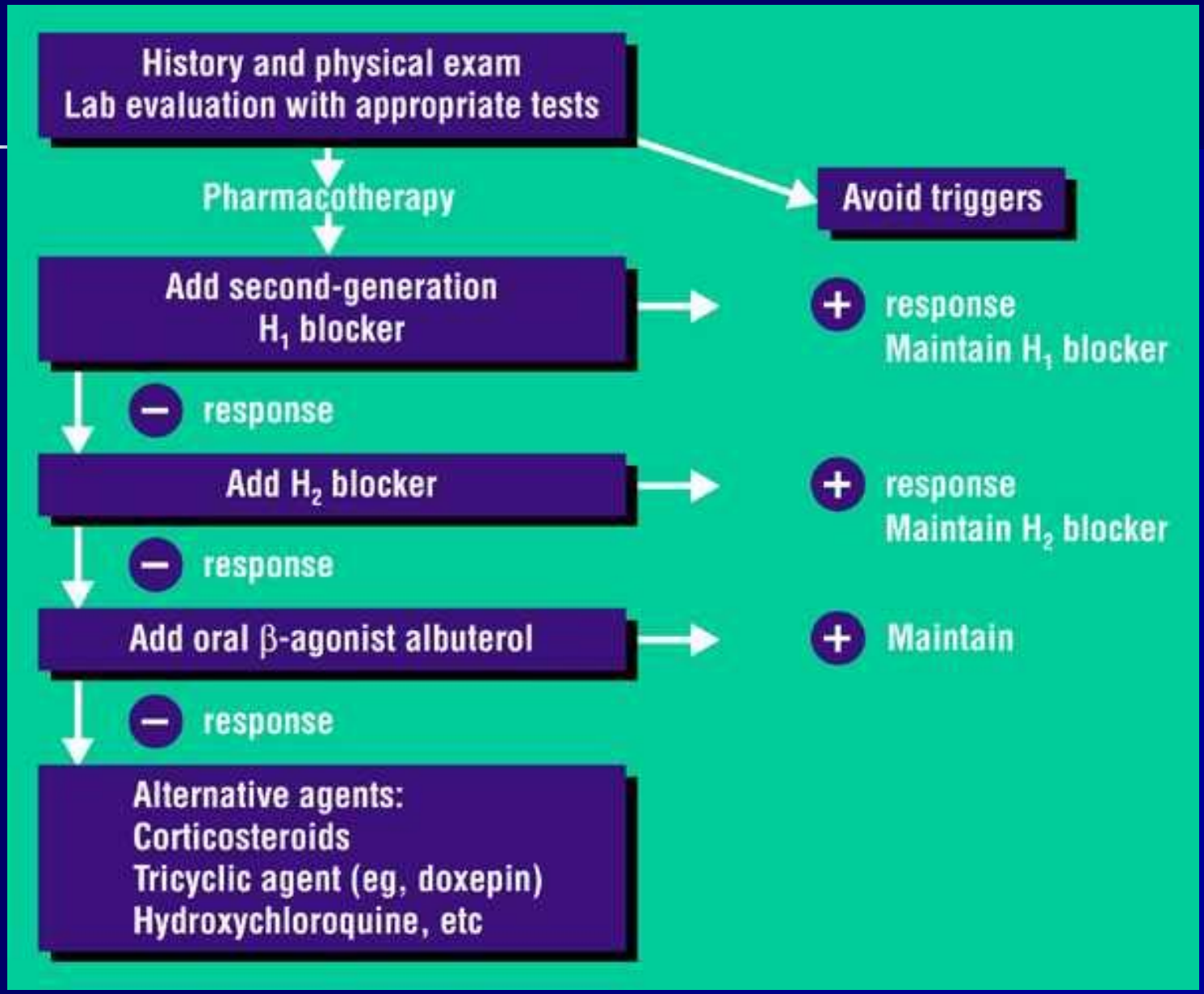
Miscellaneous

- PUVA
- Hydroxychloroquine
- Thyroxine

H_1-Receptor Antagonists: Pros and Cons for Urticaria and Angioedema

- First-generation antihistamines (diphenhydramine and hydroxyzine)
  - Advantages: Rapid onset of action, relatively inexpensive
  - Disadvantages: Sedating, anticholinergic
- Second-generation antihistamines (cetirizine, loratadine)
  - Advantages: No sedation (except cetirizine); no adverse anticholinergic effects; bid and qd dosing
  - Disadvantages: Prolongation of QT interval; ventricular tachycardia (astemizole only) in a patient subgroup
- Third-generation antihistamines (levocetirizine, fexofenadine, desloratadine)

An Approach to the Treatment of Chronic Urticaria



Angioedema Characteristics

- Similar process to urticaria
- Occurs deeper in subcutaneous tissue
- "Swelling" due to extravastation of fluid into tissues from vasodilators
- Typically seen in areas with little connective tissue such as lips, face, mouth, uvula and genitalia
- Can occur in bowel wall which manifests as colicky abdominal pain

Characteristics (cont)

- Rapid onset (typically minutes to hours)
- Often asymmetric in distribution
- Often in non-gravitationally dependent areas such as lips, mouth, face, tongue
- Can be associated with urticaria, sometimes with allergic reaction or part of anaphylaxis, or may occur in isolation

**Can be life-threatening if associated with airway compromise*

Classification of Angioedema

- **Mast cell-related angioedema**

– Can begin within minutes of exposure of trigger like food, drug, sting

– May occur with other allergic type symptoms such as urticaria

– Usually resolves within 24-48 hours

- **Bradykinin-induced angioedema**

– Develops more gradually

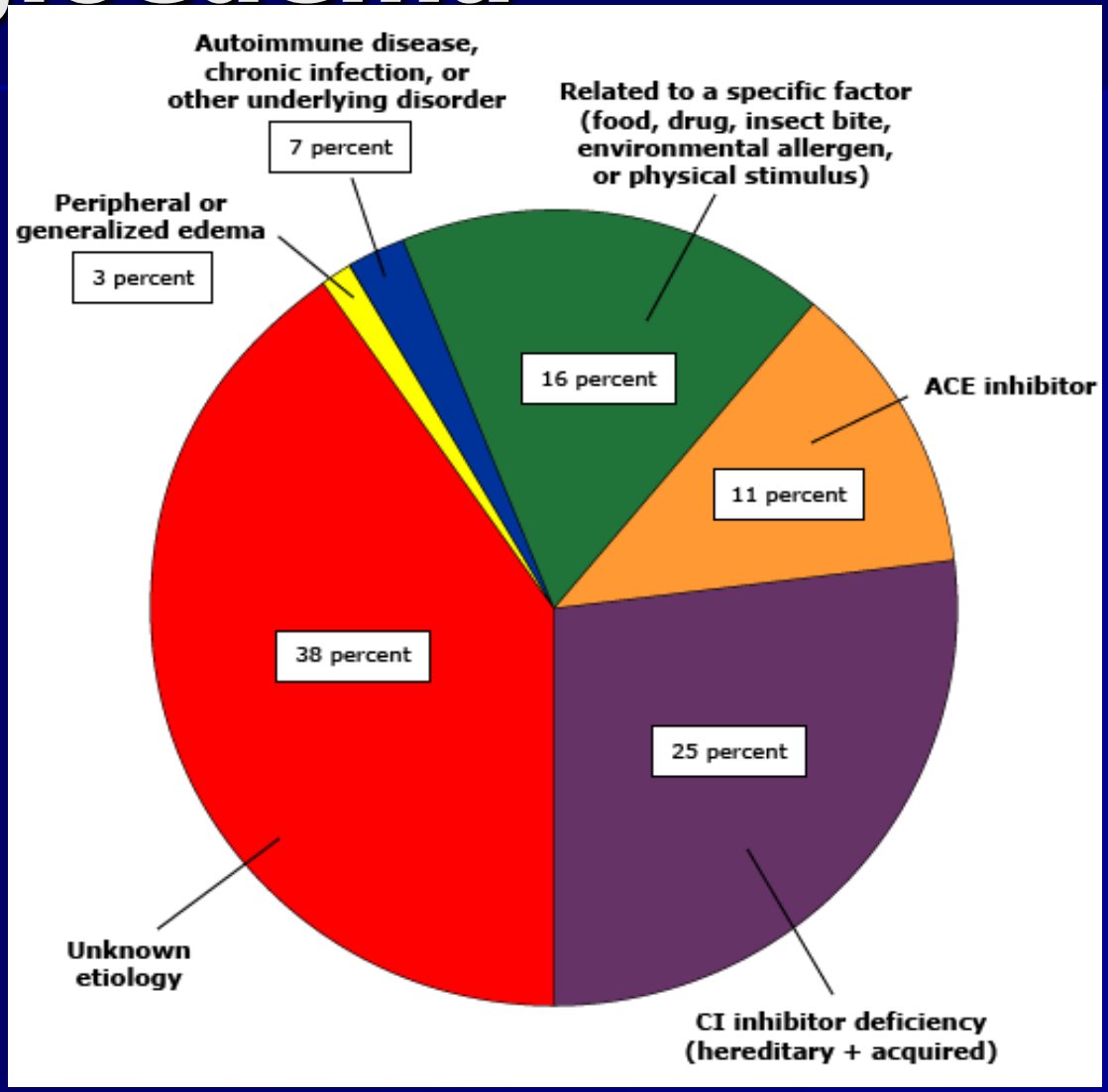
– Often longer to resolve 2-4 days

– Example: ACE induced angioedema

Medications Associated with Angioedema

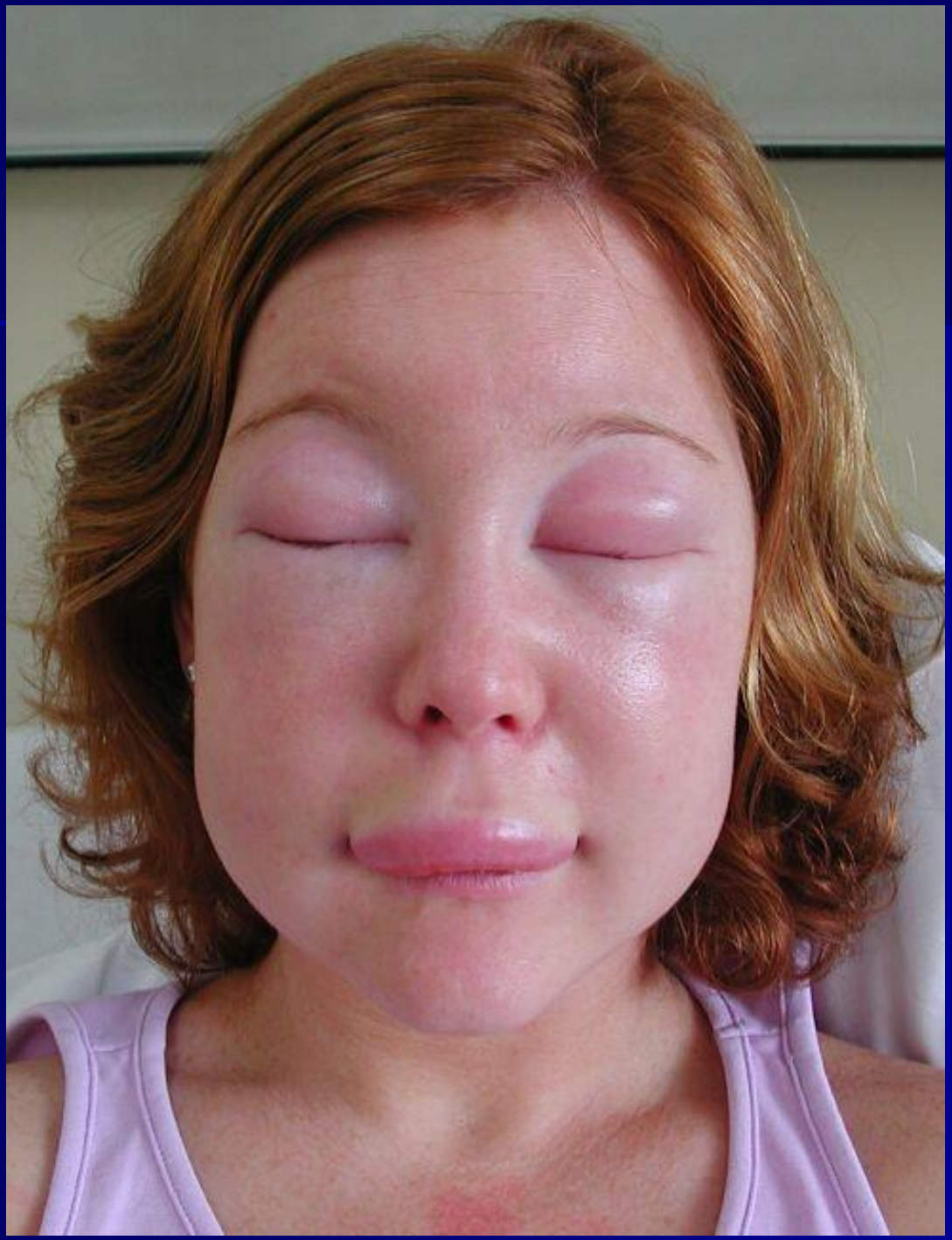
- ACE Inhibitors
- ARBs
- Ca^{2+} Channel Blockers
- Estrogens
- Fibrinolytics

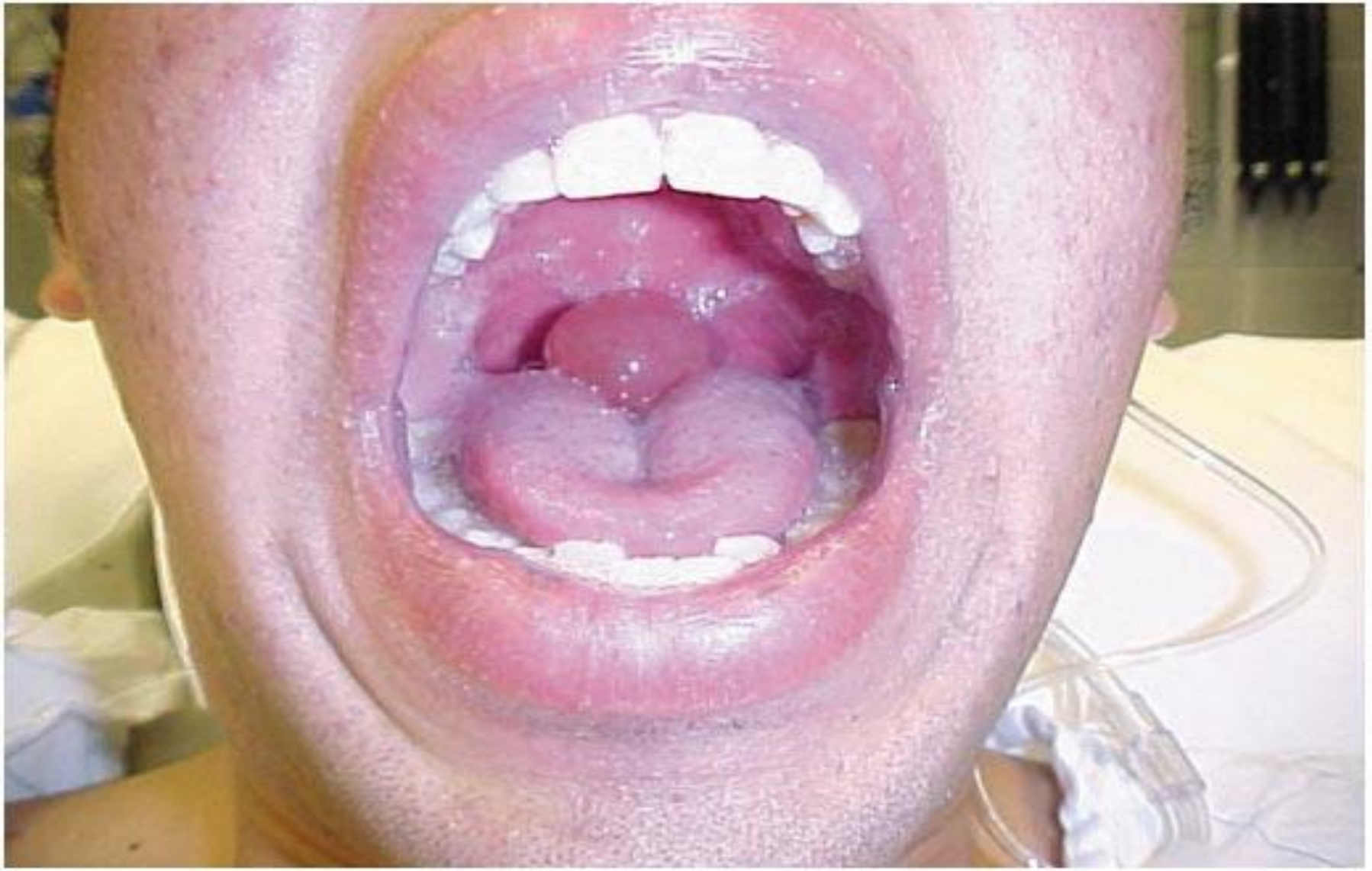
Epidemiology of Angioedema



Uptodate. Angioedema

Angioedema of eyelid





Hereditary Angioedema

- Usually presents in second decade of life

– May be seen in younger children or even into 30's

- Edema can be present in different organs and can alter presentation:

– Tongue – most serious as can cause obstruction

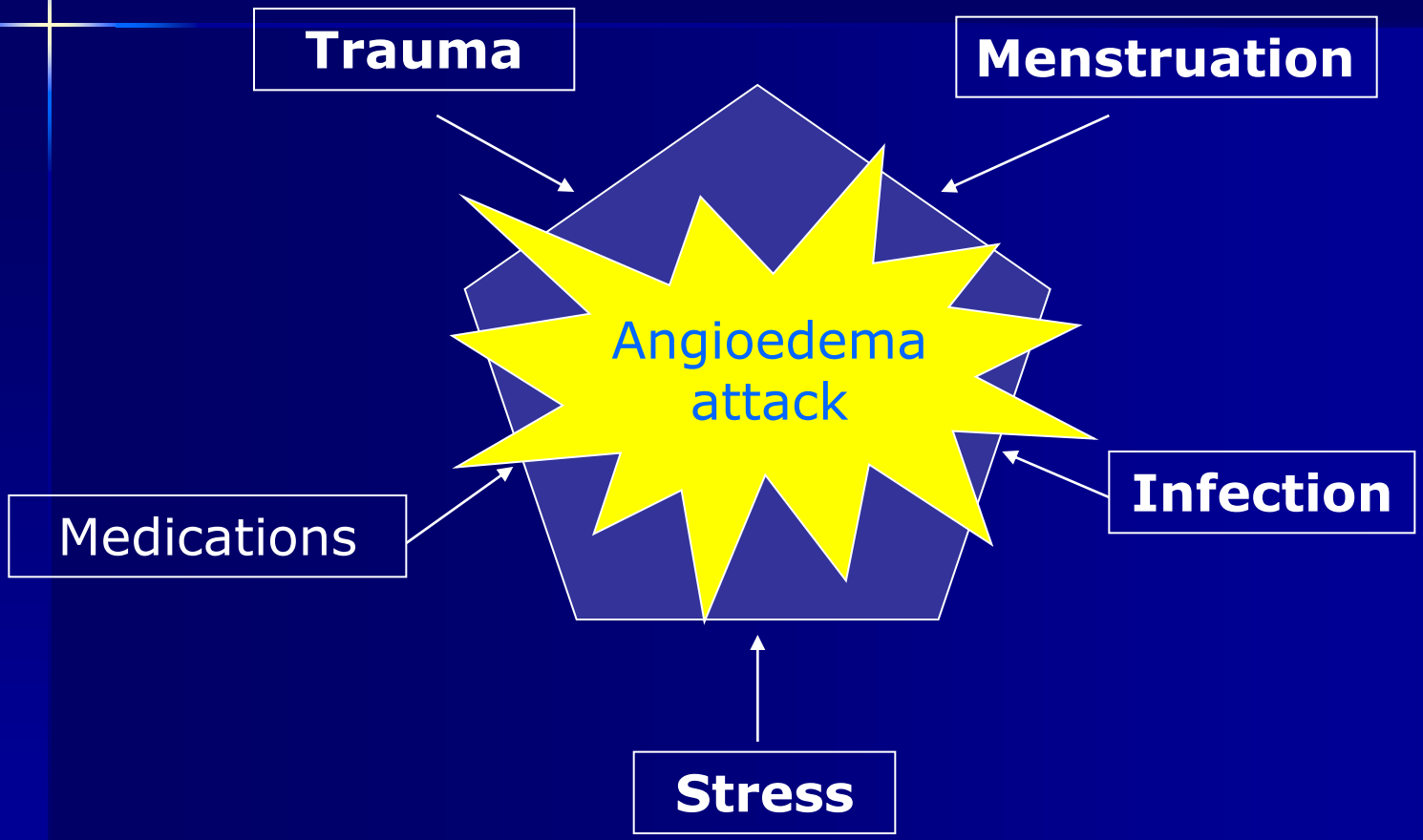
- Face
- Trunk
- Genitals

– GI track – can resemble SBO and have pt go for emergent surgery

– Extremities

- Attacks usually last 2-5 days

Common triggers of hereditary angioedema attacks



Aleena Banerji, MD. Overview of Hereditary and Acquired Angioedema. 2010.

Recurrent Angioedema - Familial

HAE due to ↓ C1 inhibitor def	Type I	Functional def – bradykinin mediated
	Type II	Functional def – Bradykinin mediated
HAE w/normal C1 inhibitor	Factor XII Mutation (prev Type III)	Assoc w/Factor XII mutation, likely bradykinin mediated
	Unknown cause	Mutation unknown, likely bradykinin mediated

Recurrent Angioedema - Sporadic

Acquired C1 inhibitor deficientis		Assoc w/underlying malignancy or anti C1 inhibitor antibodies likely bradykinin mediated
ACE - I Related		Decreased catabolism of bradykinin – likely bradykinin mediated
Allergic		Mast Cell degranulation

Laboratory Evaluation (cont)

- When you refer, we may order
  - Tryptase where anaphylaxis might be present
  - Immunocap testing to particular trigger
  - C1 inhibitor antigen and function

Medical Management HAE

- C1 inhibitor concentrates - direct C1-esterase inhibitors that decrease bradykinin production
  - Berinert
    - 20 units/kg intravenous infusion
    - Half life Berinert: 22 hours
    - Time to peak: ~4 hours
      - FDA approved 2009
  - Cinryze
    - 1000 units/patient BID weekly dosing for prophylaxis
    - Half life Cinryze: 56 hours
    - Time to peak: ~4 hours
      - FDA approved 2008

Medical Management of HAE

- Firazyr (Icatibant)
  - 30mg SC q6h for max of 3 doses
  - Bradykinin B2 receptor antagonist therefore stopping bradykinin action
  - Adverse Reactions:
    - >10%: Local: Injection site reaction
    - 1% to 10%: Central nervous system: Pyrexia, dizziness Hepatic: Transaminase increased
    - <1% Anti-icatibant antibody production, headache, nausea, rash
  - Pregnancy Class: C

Medical Management of HAE

- Kalbitor (Ecallantide)
  - 30mg SC
  - Reversibly inhibits plasma kallikrein therefore decreasing bradykinin levels
  - Adverse Reactions:
    - >10%: Central nervous system: Headache, fatigue; Gastrointestinal: Nausea, diarrhea
    - 1% to 10%: Central nervous system: Fever; Dermatologic: Pruritus, rash, urticaria; Gastrointestinal: Vomiting, upper abdominal pain; Local: Injection site reactions; Respiratory: Upper respiratory infection, nasopharyngitis; Miscellaneous: Antibody formation, anaphylaxis
    - <1% Hypersensitivity

Medical Management of HAE

- Lysteda (Tranexamic acid)
  - Oral, I.V.: 25 mg/kg/dose every 3-4 hours (maximum: 75 mg/kg/day)
  - 1000 mg 4 times/day for 48 hours
  - Displaces plasminogen from fibrin irreversibly to cause a decrease in fibrinolysis; also inhibits proteolytic activity of plasmin
  - Pregnancy category: B
  - Adverse Reactions:
    - IV Form: Cardiovascular: Hypotension (with rapid I.V. injection) Central nervous system: Giddiness; Dermatologic: Allergic dermatitis; Endocrine & metabolic: Unusual menstrual discomfort; Gastrointestinal: Diarrhea, nausea, vomiting; Ocular: Blurred vision
    - OralForm: >10%: Central nervous system: Headache; Gastrointestinal: Abdominal pain; Neuromuscular & skeletal: Back pain, muscle pain; Respiratory: Nasal/sinus symptoms; 1% to 10%

DISTINCTION BETWEEN TYPES OF ASTHMA

ALLERGIC ASTHMA

- FAMILY HISTORY OF ATOPY (ALLERGY)
- GENERALLY DEVELOP DISEASE EARLY IN LIFE (USUALLY IN INFANCY & CHILDHOOD)
- HIGH CIRCULATING IgE
- POSITIVE SKIN TEST
- SEASONAL OR EPISODIC NATURE

NON-ALLERGIC ASTHMA

- NOT ASSOCIATED WITH ATOPY
- A FAMILY HISTORY OF ASTHMA ONLY)
- GENERALLY OCCUR IN ADULT LIFE
- NORMAL LEVELS OF IgE

CHARACTERISTICS OF TYPE 1 HYPERSENSITIVITY

2 PHASES:

EARLY PHASE:

- WITHIN MINUTES
- INITIATED BY IgE STIMULATION OF MAST CELLS,BASOPHILS

LATE PHASE

- WITHIN 6-24 HOURS
- INFLUX OF Th2, EOSINOPHILS

LATE PHASE

INFLAMMATORY RESPONSE WITH:

- ↑ Th2 lymphocytes
- ↑ Eosinophils

ENZYMES DAMAGE AIRWAY EPITHELIUM

LEUKOTRIENES, PROSTAGLANDINS EFFECTS (Previous Slide)

FOODS THAT CAUSE ALLERGIES

TRUE FOOD ALLERGIES PRESENT IN:

1-4% OF GENERAL POPULATION
6% IN CHILDREN

NON-ALLERGIC FOOD INTOLERANCE

TOXICITY, FOOD ADDITIVES

↓

CHEMICAL REACTIONS, NOT TRUE ALLERGIC REACTIONS

HAPTENS

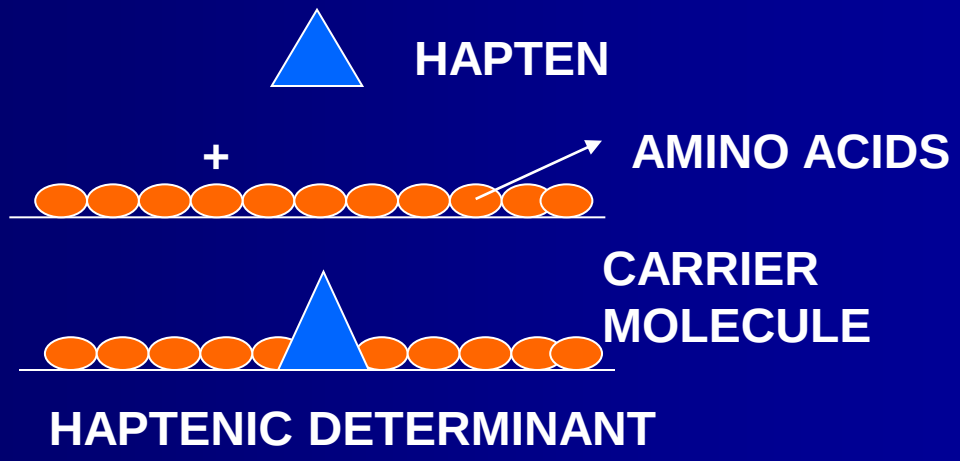
MOLECULAR MASS <1000: NOT TRUE AGs (ALLERGENS)

•BIND TO LARGER MOLECULE

(CARRIER MOLECULE)

↓

IMMUNOGENIC/ALLERGENIC



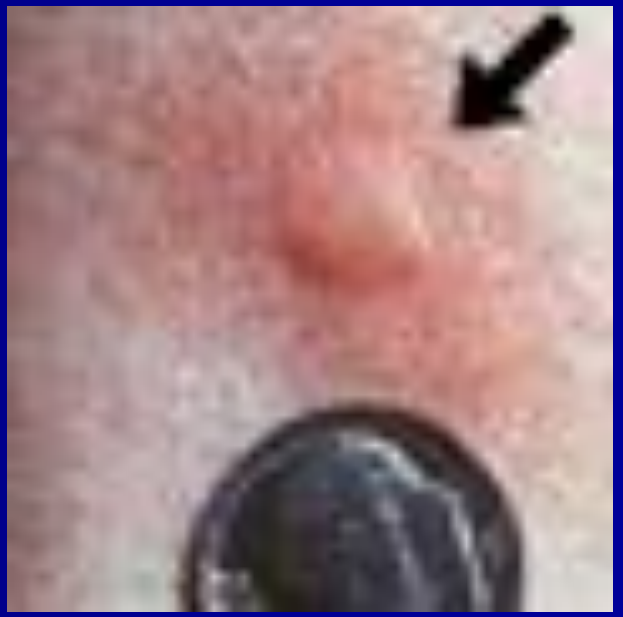
LOCALISED ALLERGIC REACTIONS

AREA	CONDITION	ALLERGEN
LUNG	Allergic bronchial asthma	Grass, house dust, animal hair, pollen, fungal AG's, foodstuffs
NOSE	Allergic rhinitis(hayfever)	Same
EYES	Conjunctivitis (hayfever)	Same
SKIN	Atopic dermatitis, urticaria	Foodstuffs, drugs, bee venom, chemicals
GIT	Vomiting, cramps, diarrhoea	Food Allergens

DIAGNOSIS OF ALLERGIC CONDITION 1

- SKIN TEST SENSITIVITY

POSITIVE SKIN TEST



WHEAL & FLARE REACTION

Laboratory diagnosis:

Determination of serum total IgE (nephelometry, turbidimetry)

Determination of allergen specific IgE (ELISA, FIA, dot-blot, ImmunoCAP)

Determination of activity markers: increased levels of eosinophil cationic protein (ECP) and tryptase

Determination of blood film: eosinophylia

PENICILIN ALLERGY

(HAPTEN= not an AG)

TRANSFORMED IN VIVO AND BIND TO PROTEINS TO BECOME ALLERGENIC:

PENICILIN

PENICILLENIC ACID (haptenic form)

PENICILIOIC ACID (haptenic form)

REACTS WITH FREE NH2-GROUPS ON PROTEINS TO FORM A HAPTENIC DETERMINANT

EVOKE ALLERGY

TESTS FOR PENICILIN SENSITIVITY

SKIN TEST
IMMUNOCAP TEST (specific IgE determent)

NB: PREPARATION USED IS SYNTHETIC HAPTENIC DETERMINANT FORM:

Penisilloyl:polylysine

PHARMACOLOGICAL TREATMENT

- Anti-histamine
- β-adrenergic stimulants
- cAMP-phosphodiesterase inhibitors
- Chromoglycates
- Corticosteroids
- Leukotriene receptor antagonists
- Anti-IgE monoclonal antibodies

HYPOSENSITISATION

- CONTROLLED INJECTION OF INCREASING AMOUNTS OF CAUSATIVE ALLERGEN FOR MONTHS->YEARS.

- THIS DIVERTS IgE RESPONSE DRIVEN BY Th2 →Th1 → DOWN REGULATION OF IgE

- PURIFIED MIXTURES OF ALLERGEN USED

WHO CAN BE DESENSITISED?

INDICATIONS

ALLERGIC RHINITIS
BEE-STING ANAPHYLAXIS

CONTRA-INDICATIONS

BRONCHIAL ASTHMA
ATOPIC DERMATITIS
FOOD ALLERGIES

SLIT (SUB LINGUAL IMMUNOTHERAPY
(ALLERGEN DROPS UNDER TONGUE)

USED IN CERTAIN PARTS OF THE WORLD.

THEY CLAIM THAT SLIT CAN BE USED FOR:

CHILDREN

HIGHLY REACTIVE PATIENTS

ASTHMATICS

THOSE WITH FOOD ALLERGIES

Type II. allergic reaction

Mechanism: **cytolytic and cytotoxic reactions induced by IgG and IgM, causing tissue damages:**

- **complement mediated cytolysis (classic pathway)**
- **stimulation of PMN, Eo cells and monocytes/macrophages by activated C3**
- **IgG bindig to effector cells: killer cells, PMN, Eo cells and monocytes/macrophages**

Allergens: **drugs: chinine, furosemide, gold salt, indomethacine, sulphonamides, salicylate, chloramphenicole**

Laboratory diagnosis:

measurement of complement activity
demonstration of the activation of PMN, Eo, monocytes/macrophages
ADCC

EXAMPLES OF ONLY TYPE II

- AUTO-IMMUNE HAEMOLYTIC ANAEMIA
- GOOD PASTURE SYNDROME
- DRUG-INDUCED HAEMOLYTIC ANAEMIA

THE TISSUE DAMAGE IN OTHER AUTO-IMMUNE DISEASES IS CAUSED BY COMBINATIONS OF TYPES II, III & IV

AUTO-IMMUNE HAEMOLYTIC ANAEMIA

COLD & WARM VARIANTS OF AIHA

↓ ↓

I ANTIGEN **Rh ANTIGEN**

ON SURFACE OF RBC

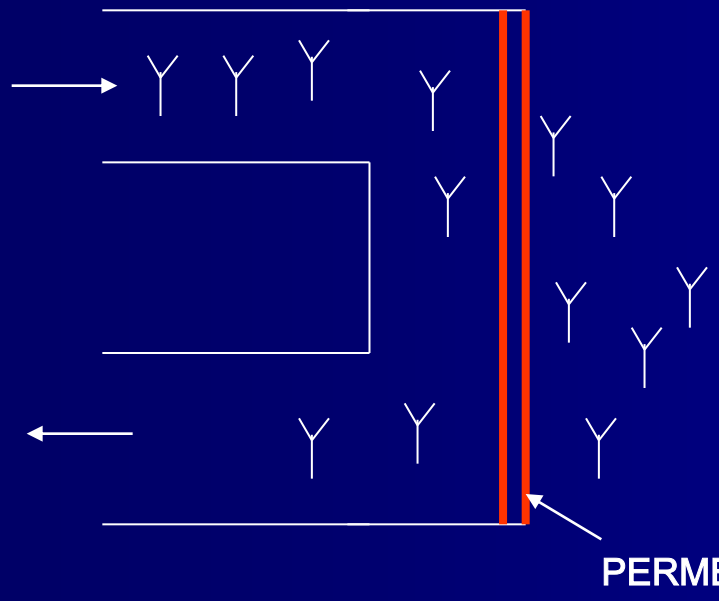
↓

LYSIS OF RED BLOOD CELLS

TREATMENT OF TYPE II

- PHARMACOLOGICAL: IMMUNOSUPPRESSIVE AGENTS: CORTICOSTEROIDS & CYTOTOXIC AGENTS
  ↓
  INHIBIT AB PRODUCTION
- PLASMA PHERESIS
- DRUG-INDUCED: STOP USING DRUG

PLASMAPHERESIS



BLOOD PUMPED AGAINST PERMEABLE MEMBRANE WHICH ALLOW Ig TO MOVE THROUGH

TYPE III TYPE HYPERSENSITIVITY

SYNONYM; IMMUNE COMPLEX-MEDIATED REACTIONS

Type III. allergic reaction

Mechanism: **tissue damages caused by immunocomplexes**

sedimentation of IC in circulation

sedimentation of IC in tissues

Allergens: **drugs, antibiotics, benzotiazine, hidantoine,**

bacteria: streptococcus, etc

viruses: hepatitis B,C, etc.

Laboratory diagnosis:

Measurement of IC level in serum

Measurement of complement factor activity in serum

Histology: microscopic IC verification

FAILING IF IC REMOVAL→ IMMUNE COMPLEX DEPOSITION

CHRONIC PRODUCTION OF IC
DURING AUTO-IMMUNE DISEASES
(INSOLUBLE COMPLEXES)

↓

EXHAUSTION OF MONOCYTE/
MACROPHAGE SYSTEM

ACUTE & EXCESSIVE PRODUCTION OF
IC DURING INFECTIONS & SERUM SICKNESS
(SOLUBLE IC WITH AG EXCESS

↓

POOR PHAGOCYTOSIS

ACCUMULATION OF IC IN THE BLOOD VESSELS & ORGANS,
PARTICULARLY KIDNEY

EXAMPLES OF TYPE III CONDITION

VASCULITIS-BLOOD VESSEL

ALVEOLITIS- LUNG

GLOMERULONEPHRITIS- KIDNEY

ARTHRITIS-JOINTS

SERUM SICKNESS

DEVELOP AFTER INJECTION OF LARGE QUANTITIES OF FOREIGN SERUM

(EG PASSIVE IMMUNISATION WITH HYPERIMMUNE SERUM)

↓

RECIPIENT PRODUCES AB’s TO AG IN SERUM

↓

IC FORMATION

↓

SPREADING & DEPOSITION OF IC THROUGHOUT THE BODY

(BLOOD VESSELS, SKIN, KIDNEY, JOINTS)

↓

GENERAL REACTION

CLINICAL PICTURE OF SERUM SICKNESS

- RAISED TEMPERATURE
- ENLARGED LYMPH GLANDS
- ARTHRITIS
- URTICARIA
- ↓ COMPLEMENT LEVELS

TREATMENT

- CORTICOSTEROIDS
- CYTOSTATIC AGENTS
- PLASMAPHERESIS

Type IV. allergic reaction

SYNONYM:

CELL MEDIATED HYPERSENSITIVITY REACTIONS

DELAYED TUPE HYPERSENSITIVITY REACTION

Mechanism: **„delayed type" hypersensitivity induced by the cytokines of Th1 cells. The symptoms appear within 12-24 hours after the allergen challange.**

Forms:

a.) Contact sensitivity

Hapten-carreir complexes processed by Langerhans cells to Th1 lymphocytes: cytokine release

antigens: nickel, gutta percha, oils, Hg salts, stains, drugs, cosmetics

EXAMPLES OF TYPE IV HYPERSENSITIVITY-MEDIATED TISSUE DAMAGE

- GRANULOMATOUS LESIONS: LEPROSY, TB
- CAVITATION & CASEATION (IN LUNG) IN TB
- TISSUE DAMAGE ASSOCIATED WITH FUNGAL & PARASITIC INFECTIONS
- REJECTION OF TRANSPLANTED ORGANS
- DESTRUCTION OF HOST TISSUE'S IN AUTO-IMMUNE DISEASES
- SKIN DAMAGE IN CONTACT DERMATITIS (DYES, MINERALS, CHEMICALS)
- BRONCHIAL OBSTRUCTION IN ASTHMATIC INDIVIDUALS

CONTACT HYPERSENSITIVITY REACTION

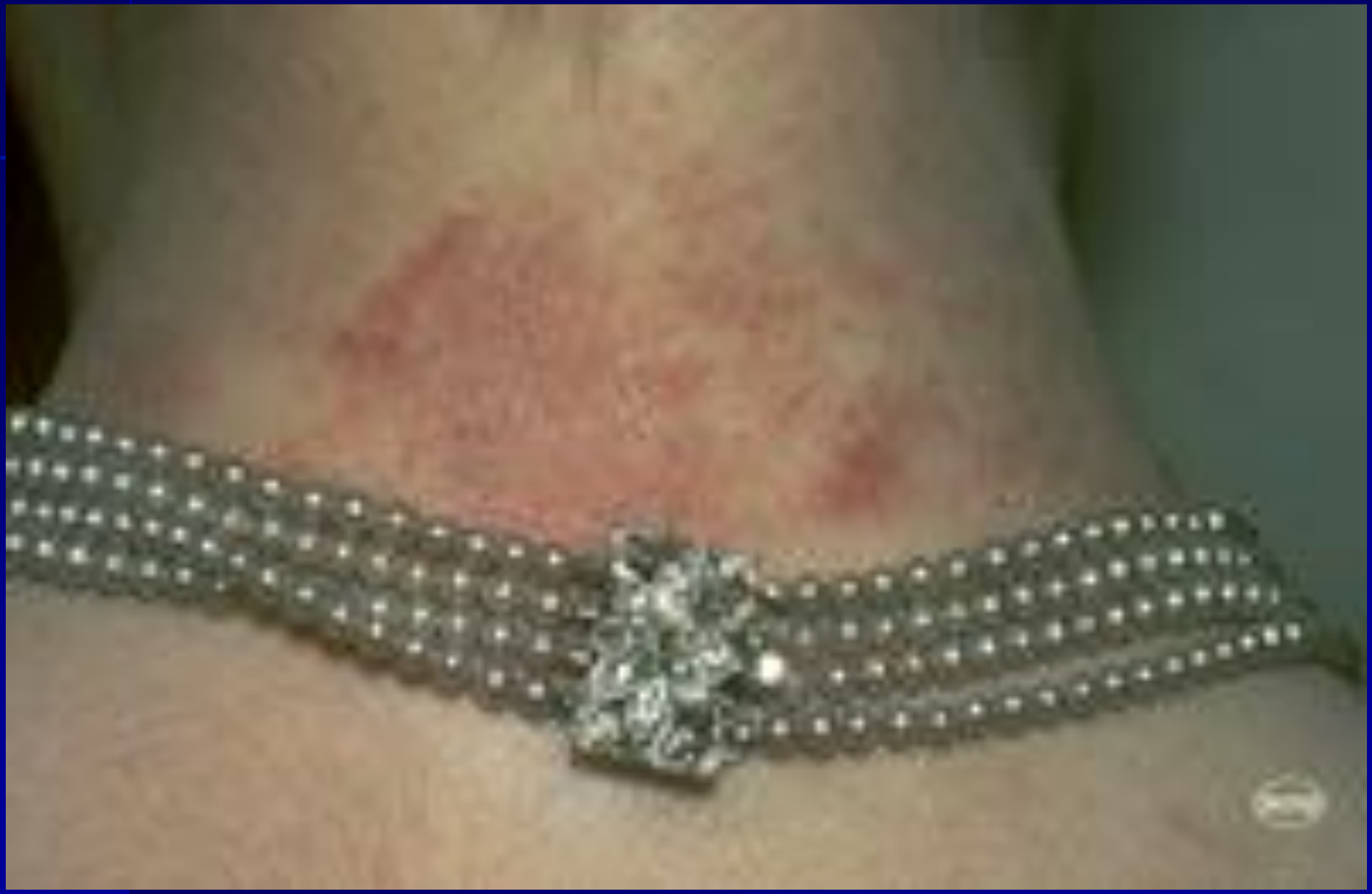
(CONTACT DERMATITIS)

IMMUNE RESPONSE BY CD4+Th1 OR CD8+ T LYMPHOCYTES, DEPENDING ON THE ROUTE OF AG PROCESSING.

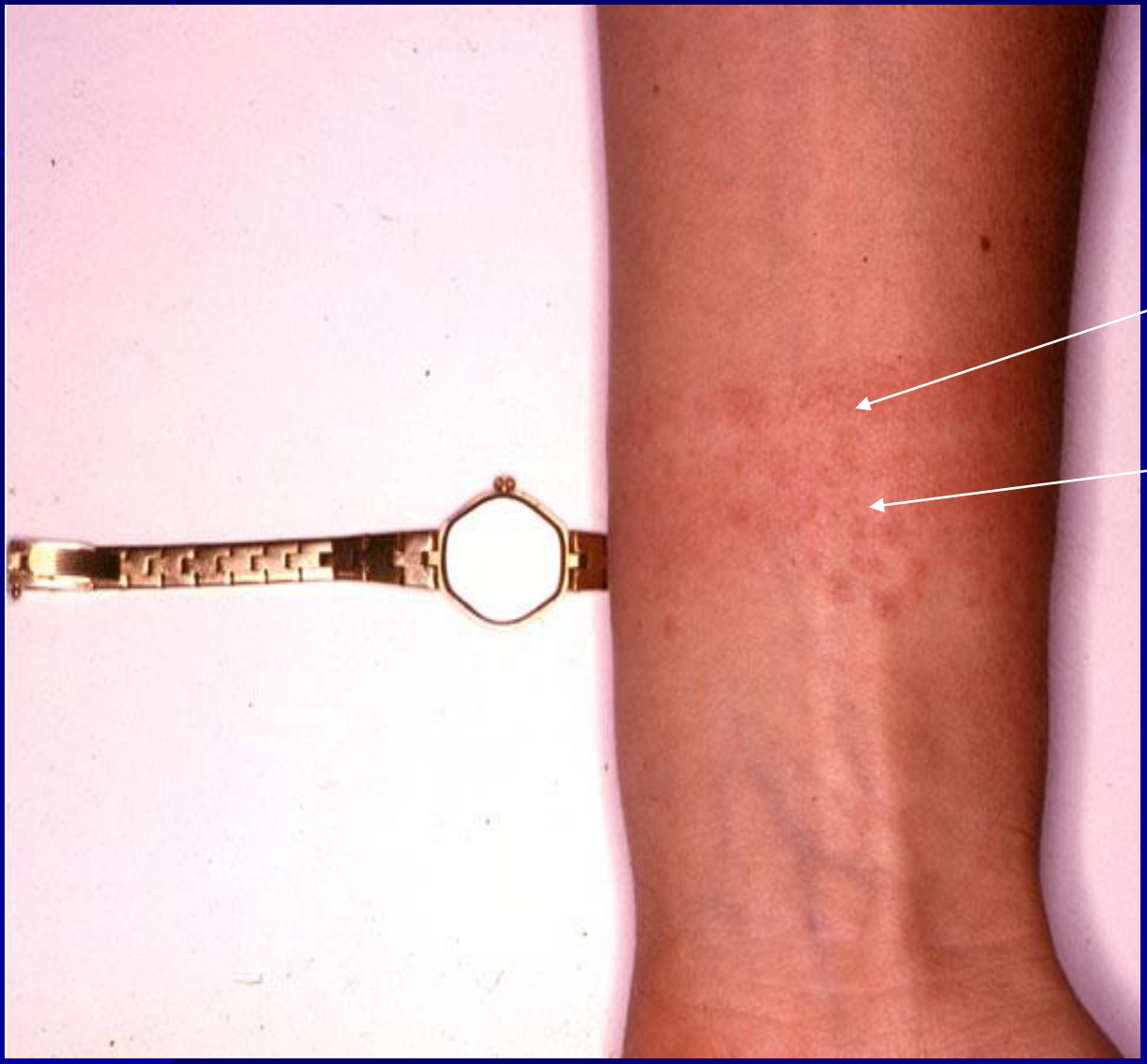
ANTIGENS ARE HIGLY REACTIVE SMALL MOLECULES THAT EASILY PENETRATE SKIN,
ESPECIALLY IF ITCHING CAUSE SCRATCHING.

AG IS A HAPTEN THAT BIND TO CARRIER PROTEIN MOLECULES IN SKIN.
EXAMPLES:
METALS , CHROMATE& NICKEL
CHEMICALS
POISON PLANTS

NICKEL ALLERGY



Contact Dermatitis



- Contact dermatitis with Nickel.
- Reddish marking and itching will occur.

TREATMENT OF SERIOUS TYPE IV REACTIONS

TREATMENT BASED ON INHIBITION OF

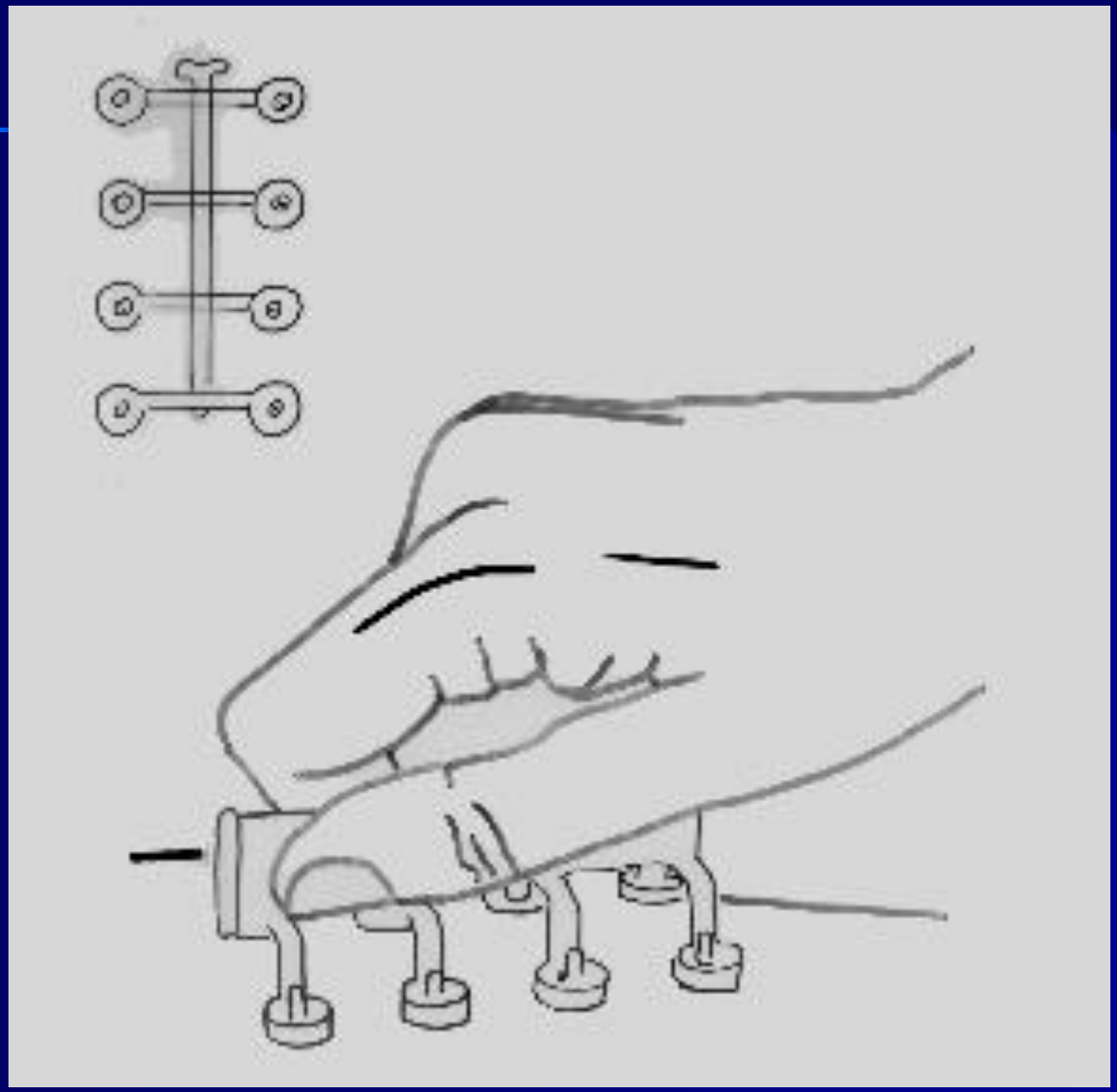
- **PHAGOCYTE ACCUMULATION**
- **RELEASE OF HIGHLY REACTIVE OXIDANTS AND PROTEOLYTIC ENZYMES**
- **PROLIFERATION OF CD4+ & CD8+ T-LYMPHOCYTES**

CORTICOSTEROIDS general and local

CYTOSTATIC DRUGS

CLINICAL APPLICATIONS OF TYPE IV SKIN TEST.

MULTITEST CMI



MULTITEST-CMI

USED TO TEST GENERAL STATUS OF THE CMI IN INDIVIDUALS WITH SUSPECTED ACQUIRED OR CONGENITAL ABNORMALITIES OF CMI.

APPARATUS CONTAINS 7 ANTIGENS + CONTROL

INJECTED INTO SKIN

TETANUS TOXOID, DIPHTHERIA TOXOID, STREPTOCOCCAL AG, PPD,

CANDIDA ALBICANS

TRICHOPHYTON MENTAGROPHYTES

PROTEUS MIRABILIS

IF POSITIVE TO AT LEAST 4 AG'S, CMI INTACT.

THANK YOU FOR LISTENING