

Allergic disease

Katalin Molnár MD

Contents

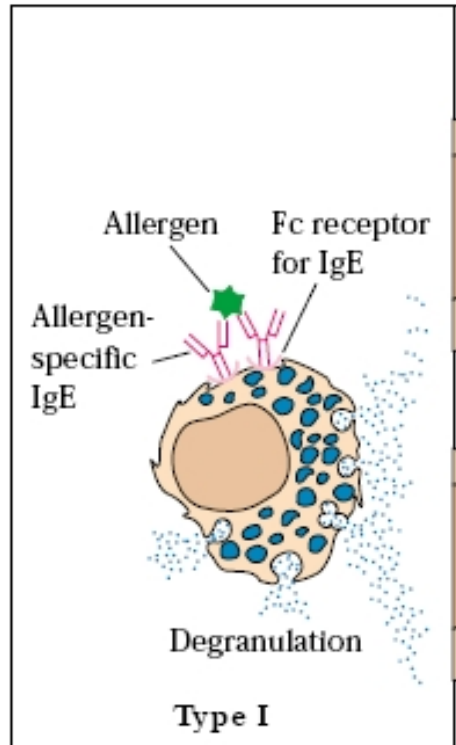
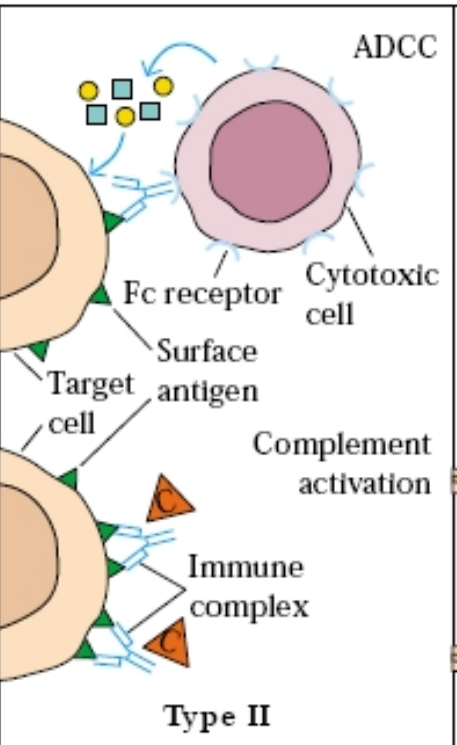
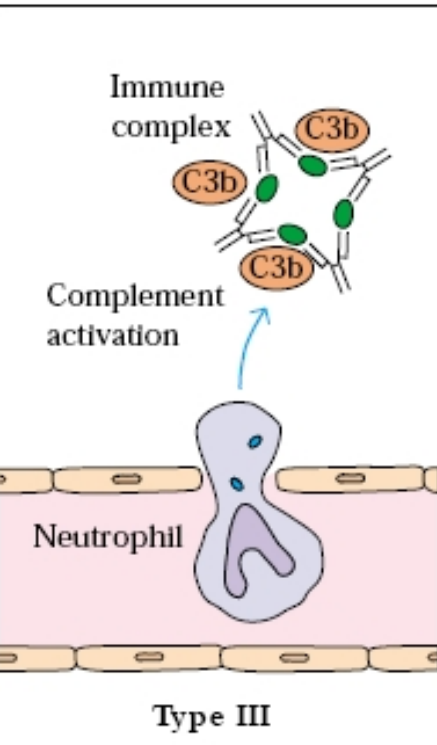
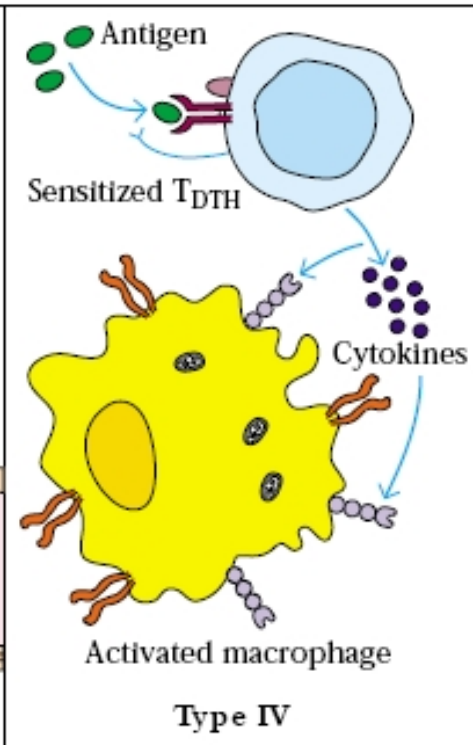
- Atopy, Allergy, Hypersensitivity reactions
- Pathomechanism
- Allergic disease:
 - Allergic and non allergic rhinitis
 - Food allergy
 - Urticaria, angioedema (+hereditary angioedema)
 - Anaphylaxis
 - Drug allergy
 - Sting insect allergy

Atopy

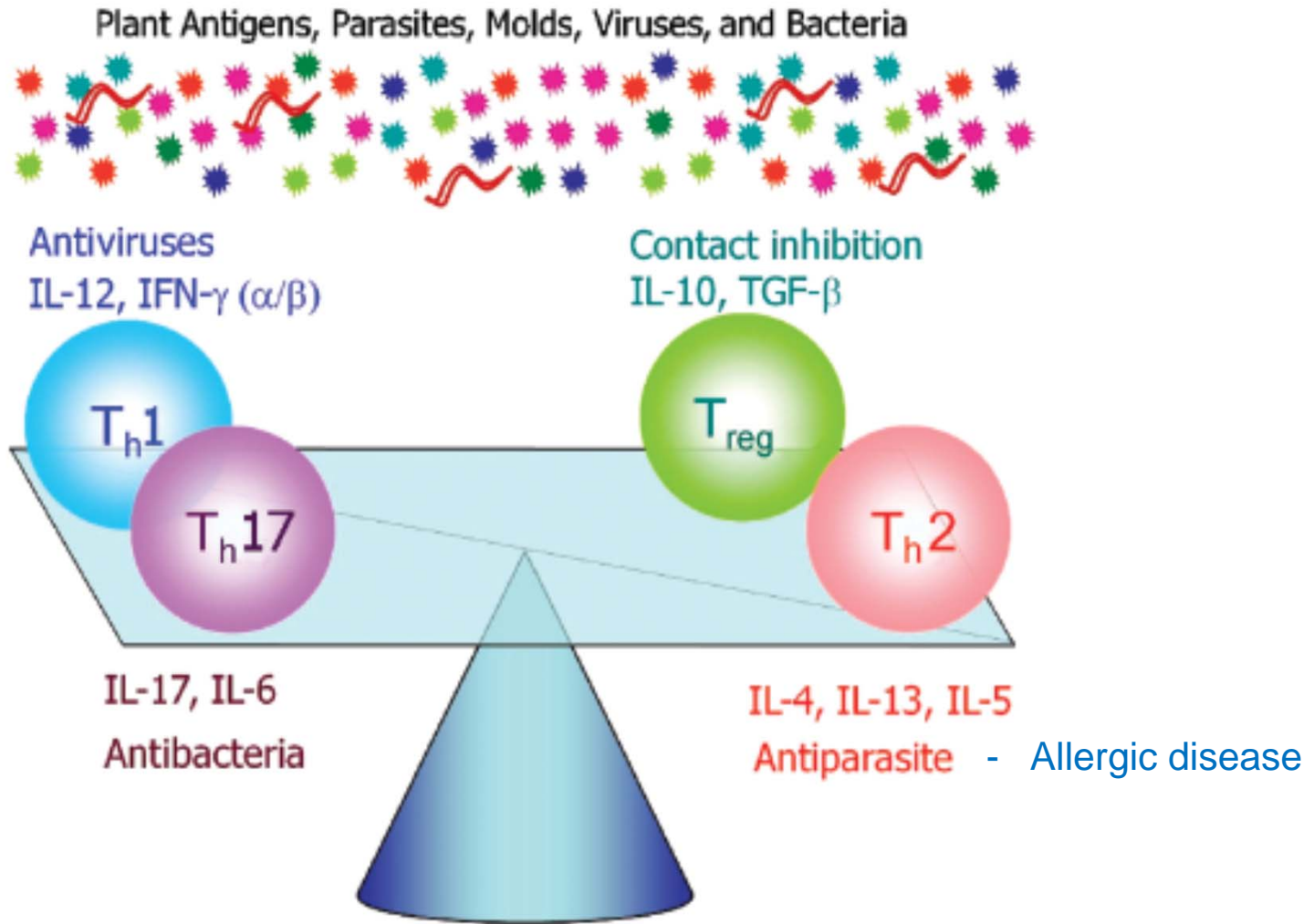
- **The genetic predisposition** to produce high quantities of Immunoglobulin (IgE)
- **Etiology** is unknown but there is strong evidence for a complex of genes with a variable degree of expression encoding protein factors.
- **Involved cells:** Mast cells, basophils, eosinophils, Th2 cells
- **Allergic rhinitis, allergic asthma, atopic dermatitis** are the most common manifestation of **atopy**.
- Allergic gastroenteropathy is rare. These manifestation may coexist in the same patients at different times.
- Atopy can be asymptomatic.

Allergy

- Allergic reaction is an exaggerated or inappropriate immune reaction and causes damage to the host.
- Allergic Disease is mostly mediated by IgE.
- First described by Prausnitz & Kustner in 1921.
- Proposed the existence of “atopic reagin” in serum of allergic subjects.
- 45 years later Ishizaka described a new class of immunoglobulin – IgE.
- Seen in 30-35% of the population.

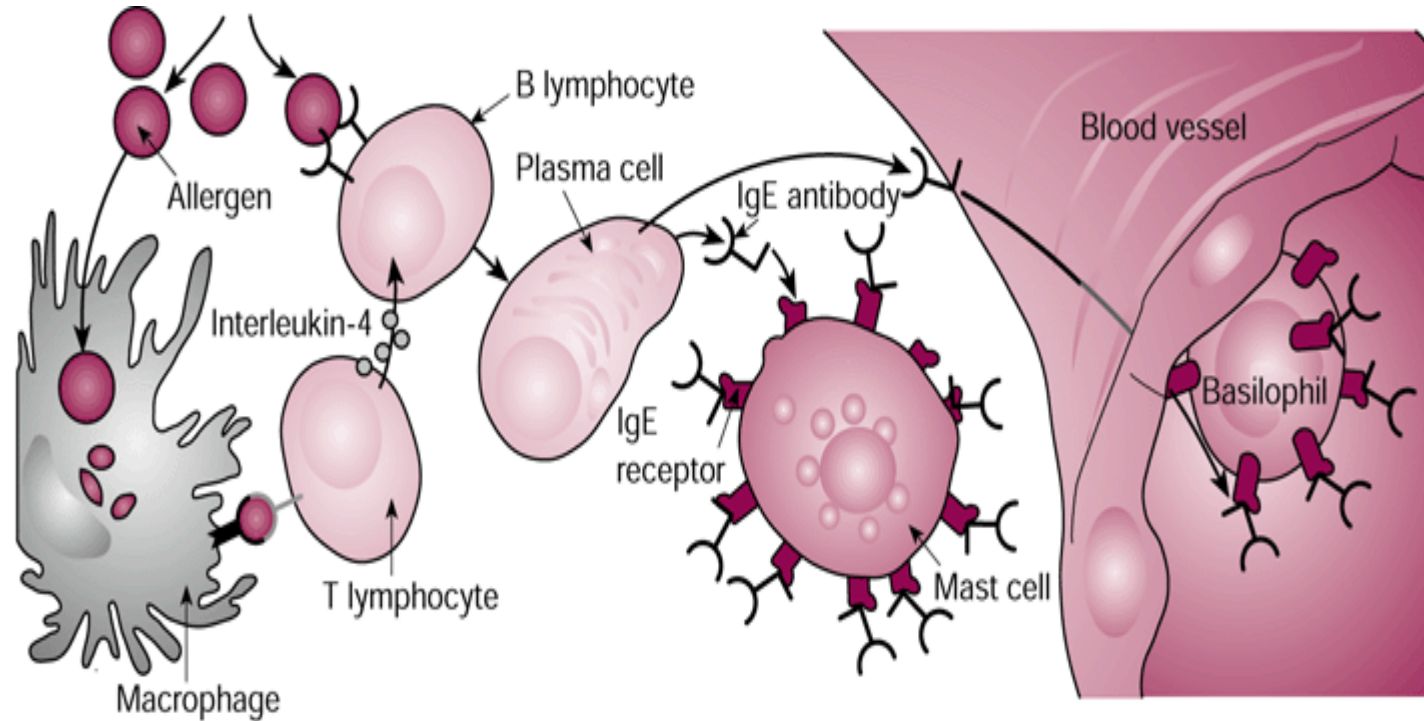
			
IgE-Mediated Hypersensitivity	IgG-Mediated Cytotoxic Hypersensitivity	Immune Complex-Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces crosslinking of IgE bound to mast cells and basophils with release of vasoactive mediators	Ab directed against cell surface antigens mediates cell destruction via complement activation or ADCC	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils	Sensitized T _H 1 cells release cytokines that activate macrophages or T _C cells which mediate direct cellular damage
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus	Typical manifestations include contact dermatitis, tubercular lesions and graft rejection

Roles of T cells



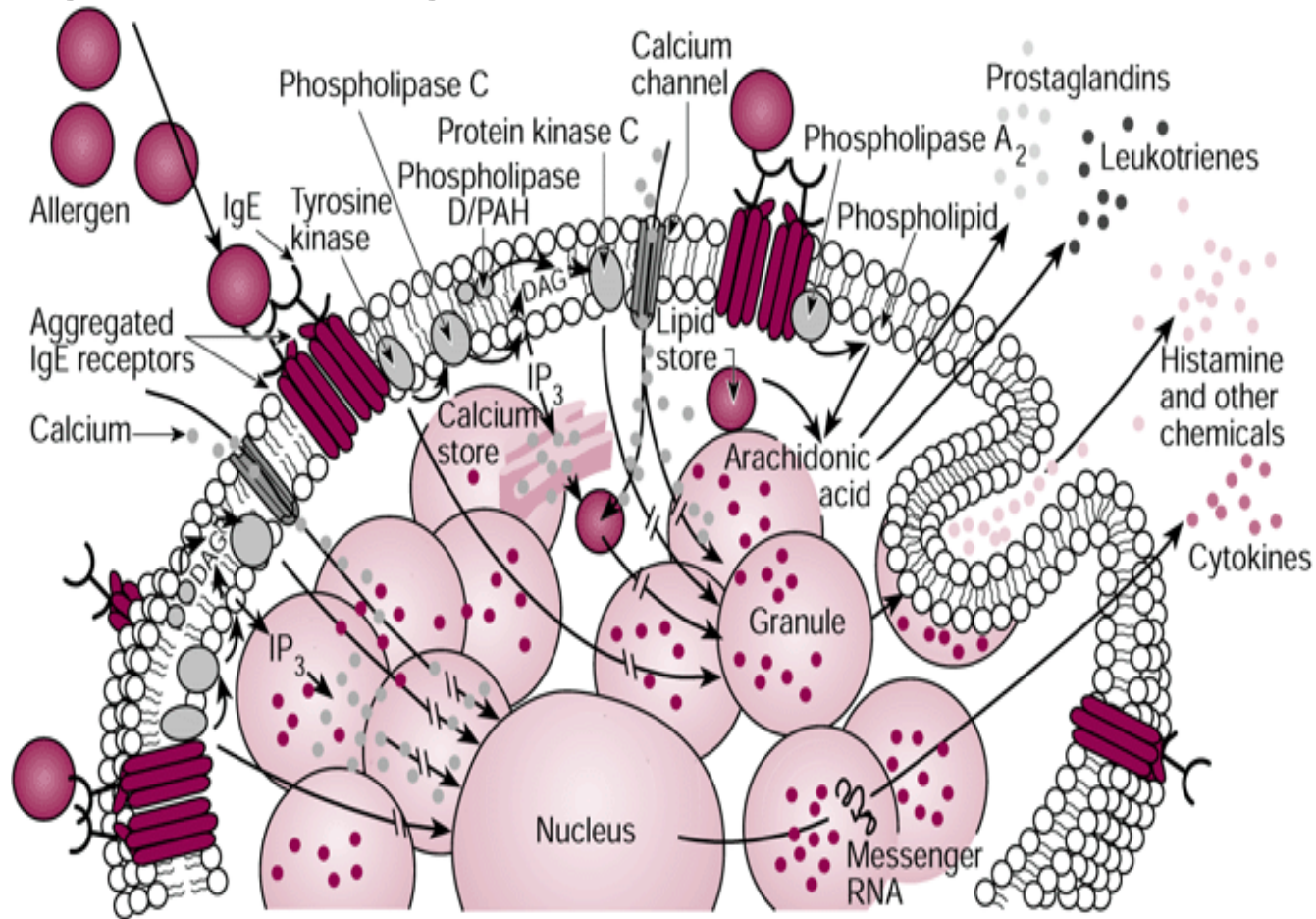
Stages of an allergic reaction

1: Sensitization



The **initial meeting** of an allergen and the immune system yields **no symptoms**; it may prepare the body to react promptly to future encounters with the substance. The sensitization process begins when **macrophages degrade the allergen and display the resulting fragments to T lymphocytes**. Following this, in a process involving secretion of **interleukin 4** by T cells, **B lymphocytes mature into plasma cells** able to secrete allergen-specific molecules known as **IgE antibodies**. **These antibodies attach** to receptors on mast cells in tissue and on basophils circulating in blood.

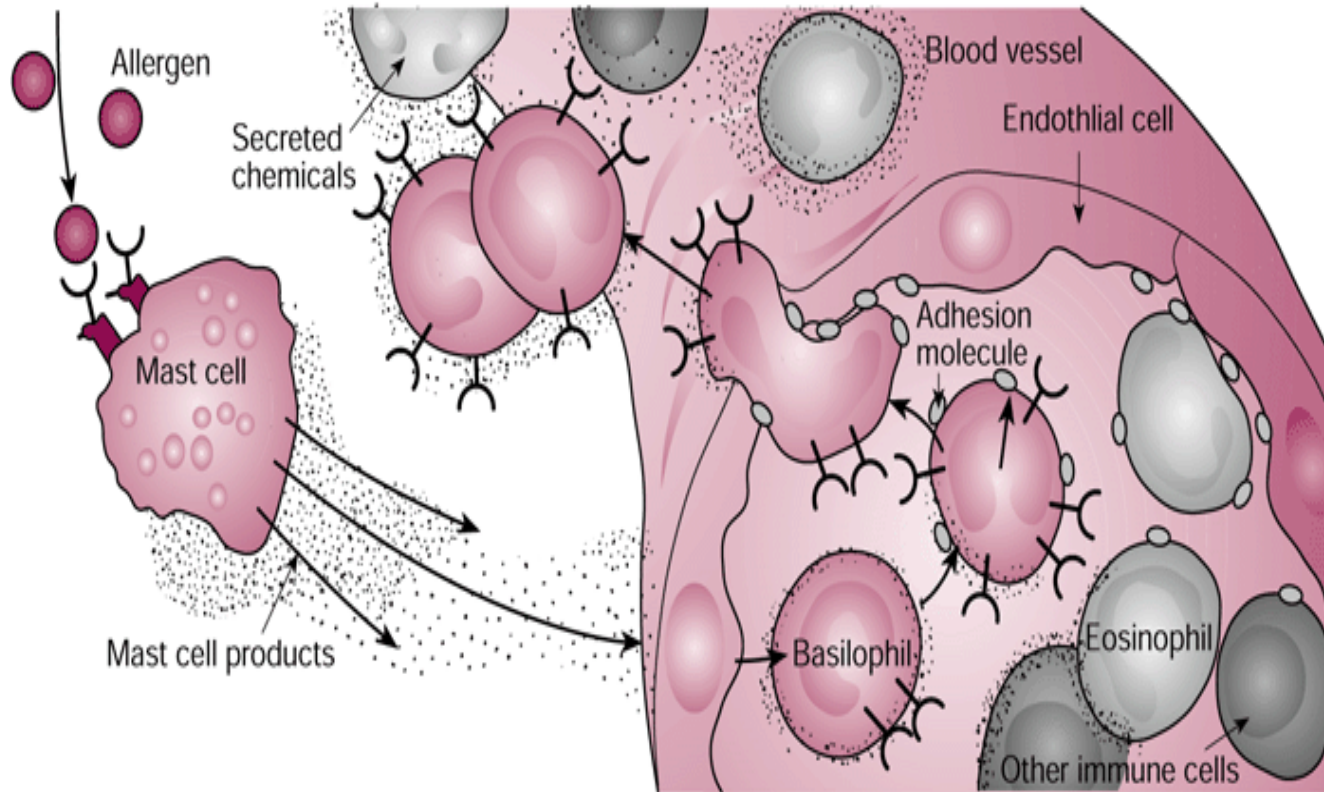
Stages of an allergic reaction 2: Activation of mast cells.



On further exposure between the allergen and the immune system, **allergen molecules bind to IgE antibodies** on mast cells. When one such molecule connects with two IgE molecules on the cell surface, **it draws together the attached IgE receptors, thereby directly or indirectly activating various enzymes in the cell membrane.** Cascades of chemicals and enzymes are released from intracellular granules. **These cascades also appear to promote the synthesis and release of chemicals known as cytokines.** The various **chemicals released by mast cells** are responsible for many **allergic symptoms.**

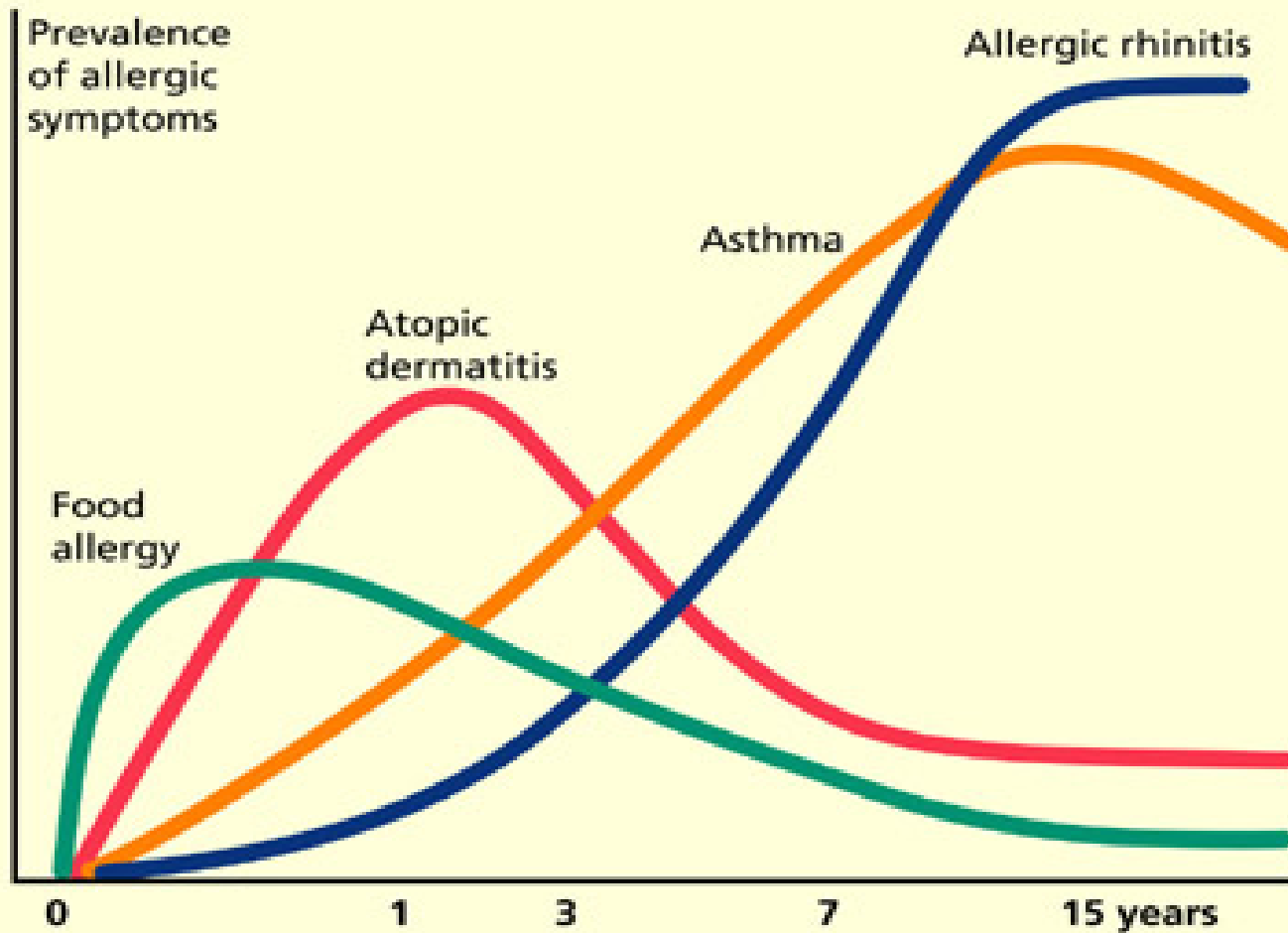
Stages of an allergic reaction

3: Prolonged immune activity.



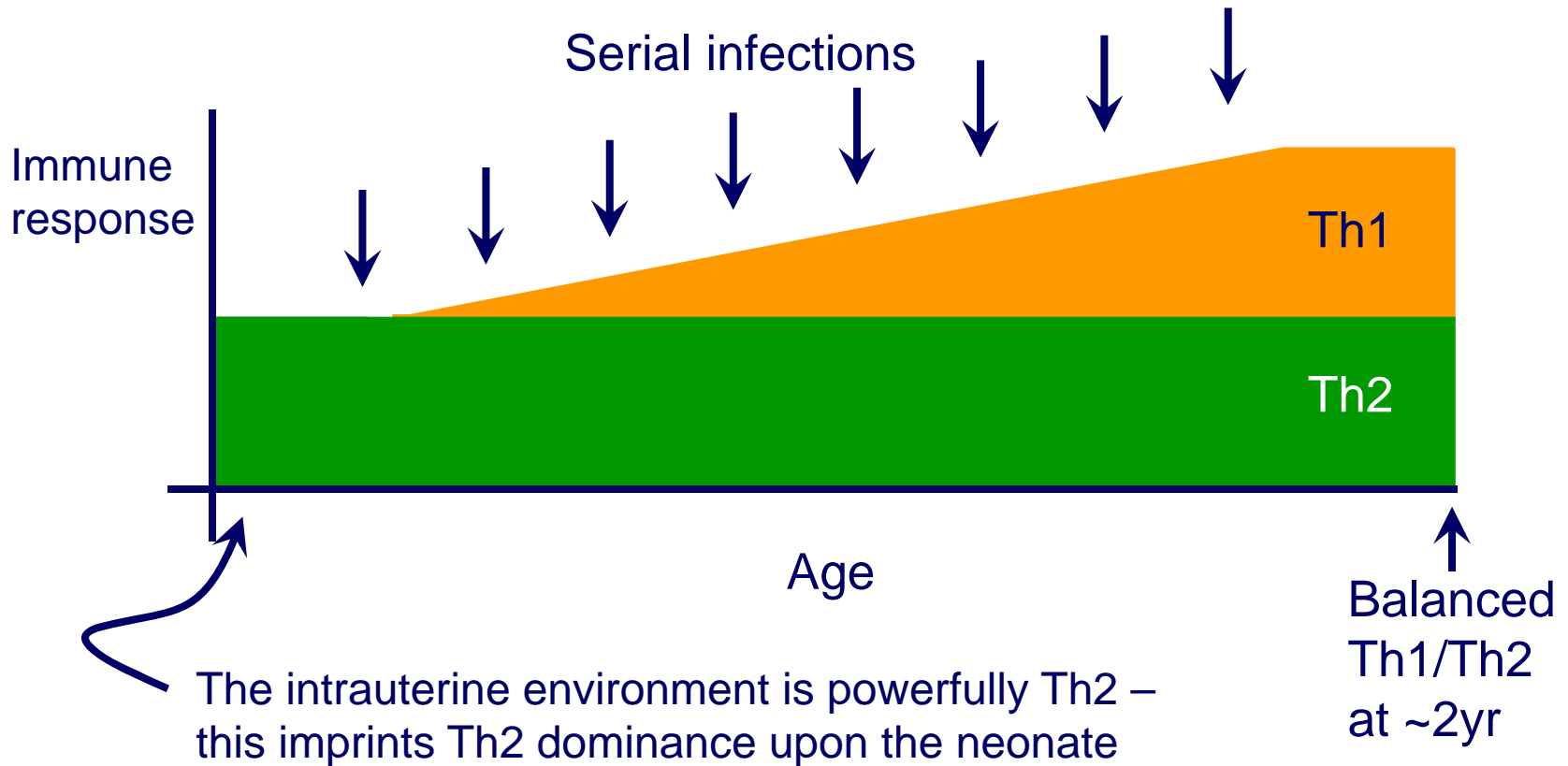
Chemicals emitted by activated mast cells and their neighbours in tissue may induce basophils, eosinophils, and other cells flowing through blood vessels to migrate into that tissue. The chemicals facilitate migration by promoting the expression and activity of adhesion molecules on the circulating cells and on vascular endothelial cells. The circulating cells then attach to the endothelial cells, roll along them, and eventually, cross between them into the surrounding matrix. These recruited cells secrete chemicals of their own, which can sustain immune activity and damage tissue.

Typical evolution of allergic diseases

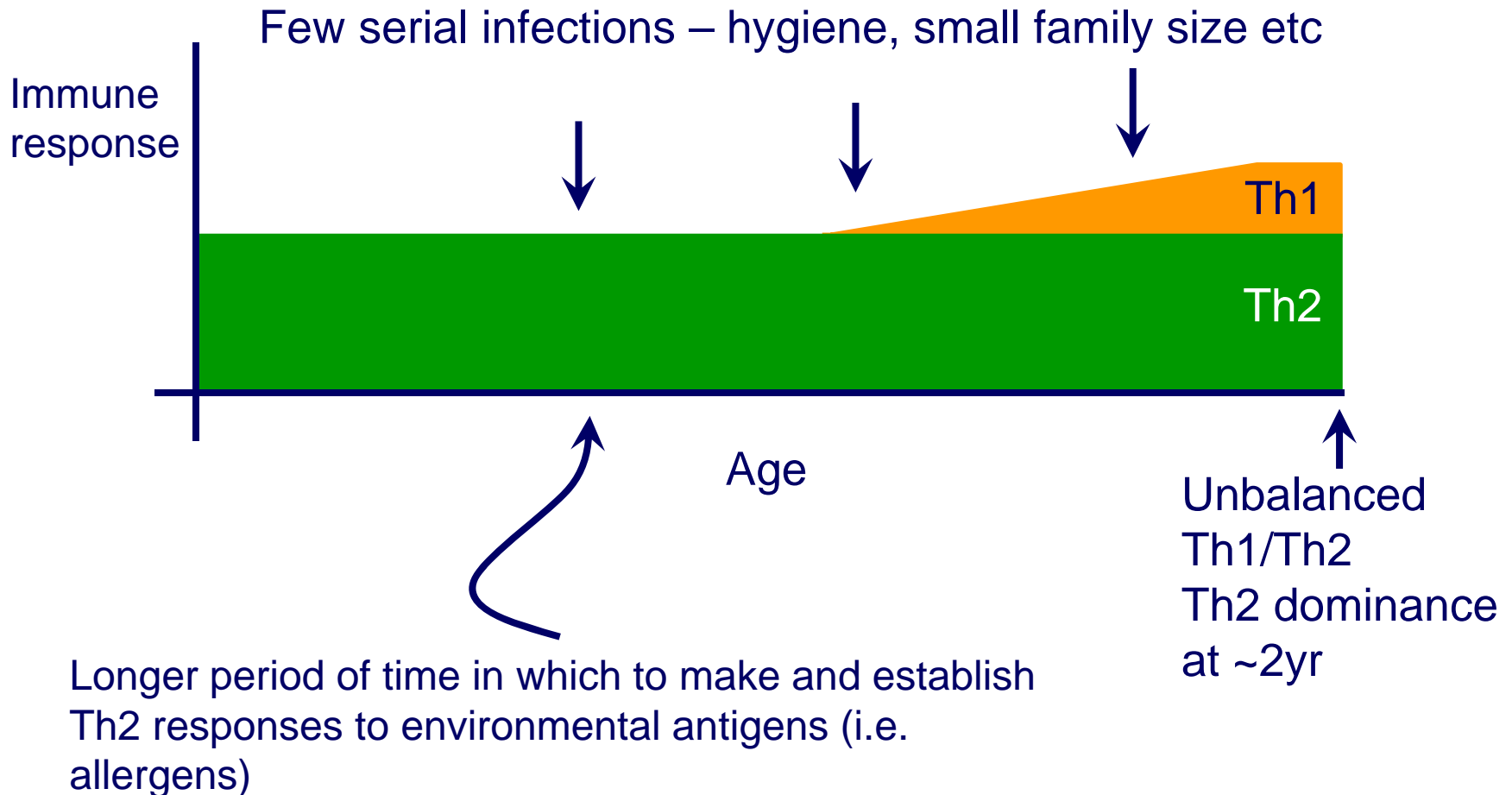


Adapted from Holgate S, Church MK, eds. Allergy. London: Gower Medical Publishing, 1993

Neonatal & infant immune systems



Delayed maturation of Th1 capacity



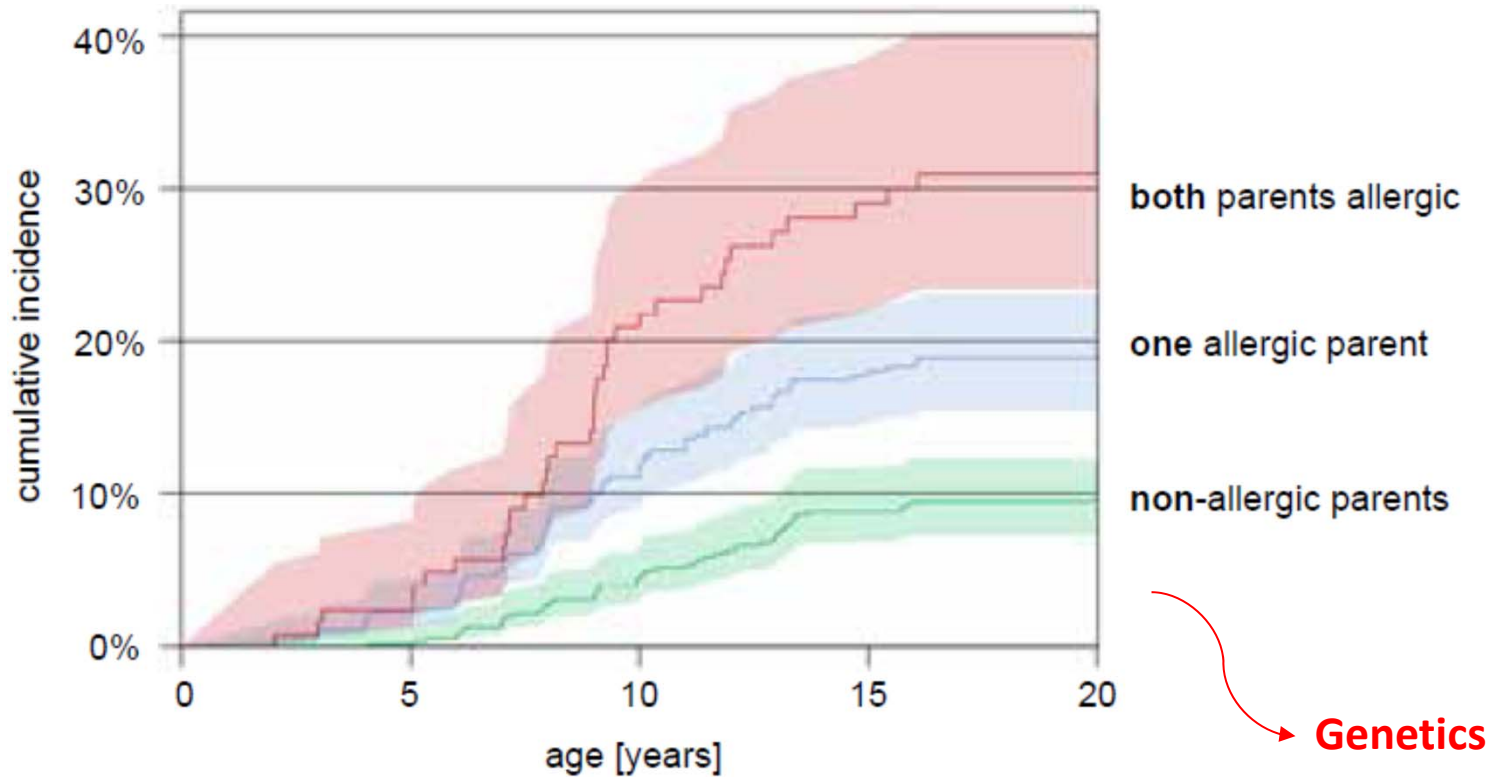
The hygiene hypothesis (Strachan, 1989)

Based upon the epidemiology of hay fever

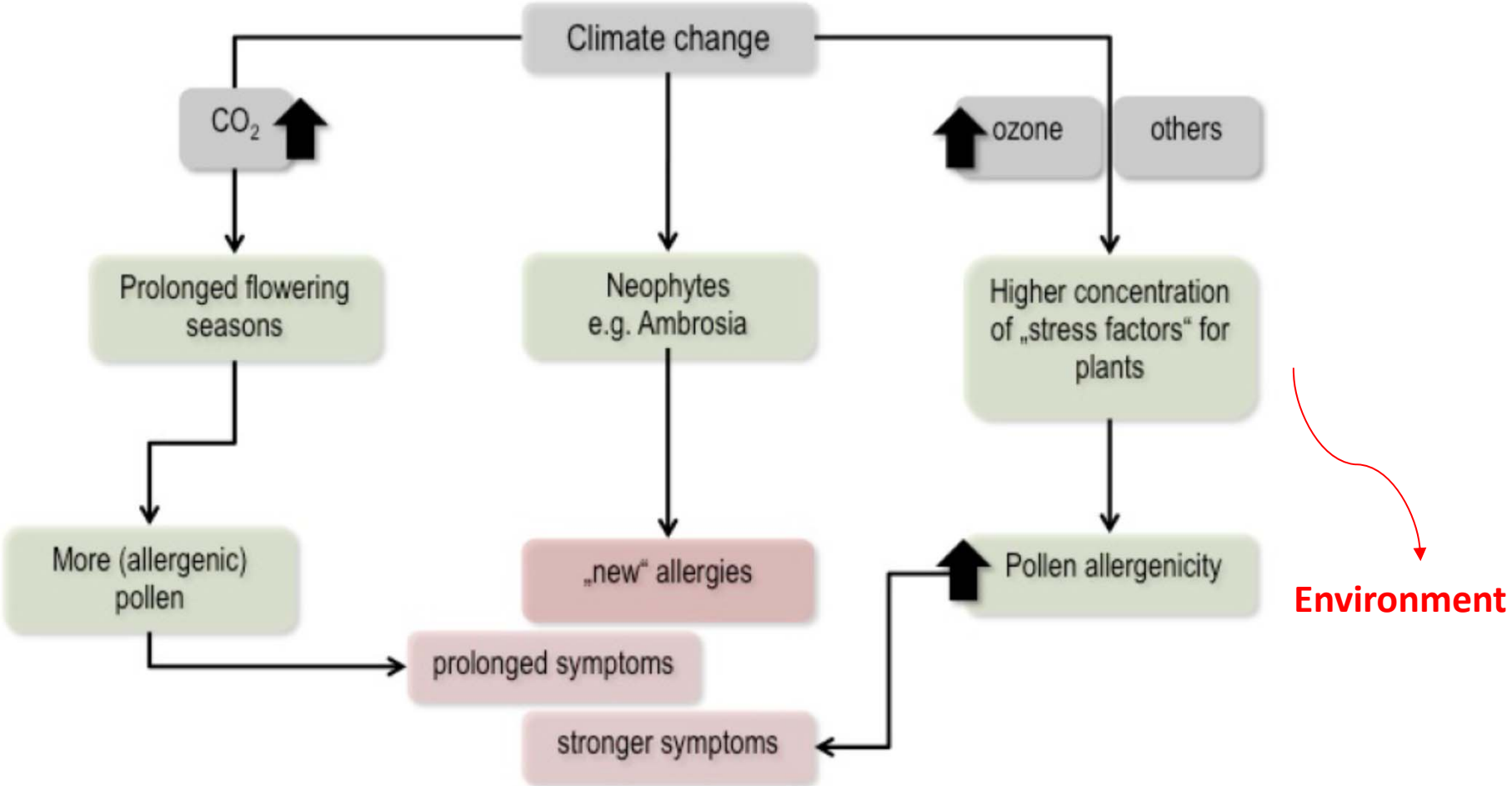
“Declining family size, improved household amenities, and higher standards of personal cleanliness have reduced the opportunities for cross-infection in young families. This may have resulted in more widespread clinical expression of atopic disease”

It can be interpreted in terms of a failure to microbially modulate default Th2 responses in childhood

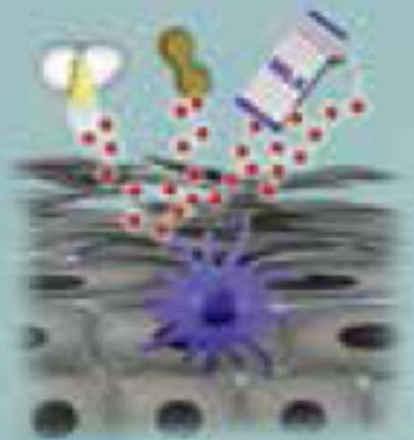
Family history for asthma and cumulative incidence of allergic diseases in offspring.



Climate change impact on the ecosystem of pollen-producing plants



CUTANEOUS EXPOSURE



Skin



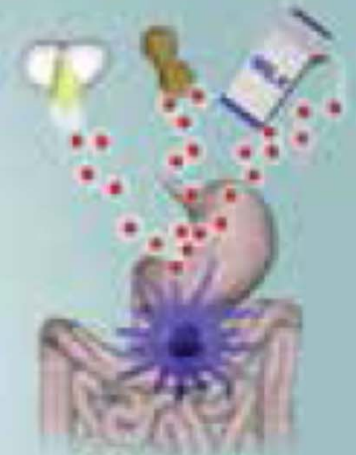
Skin-draining lymph nodes

IL-4
IL-5
IL-13

Th2 memory

ALLERGY

ORAL EXPOSURE



GI Track

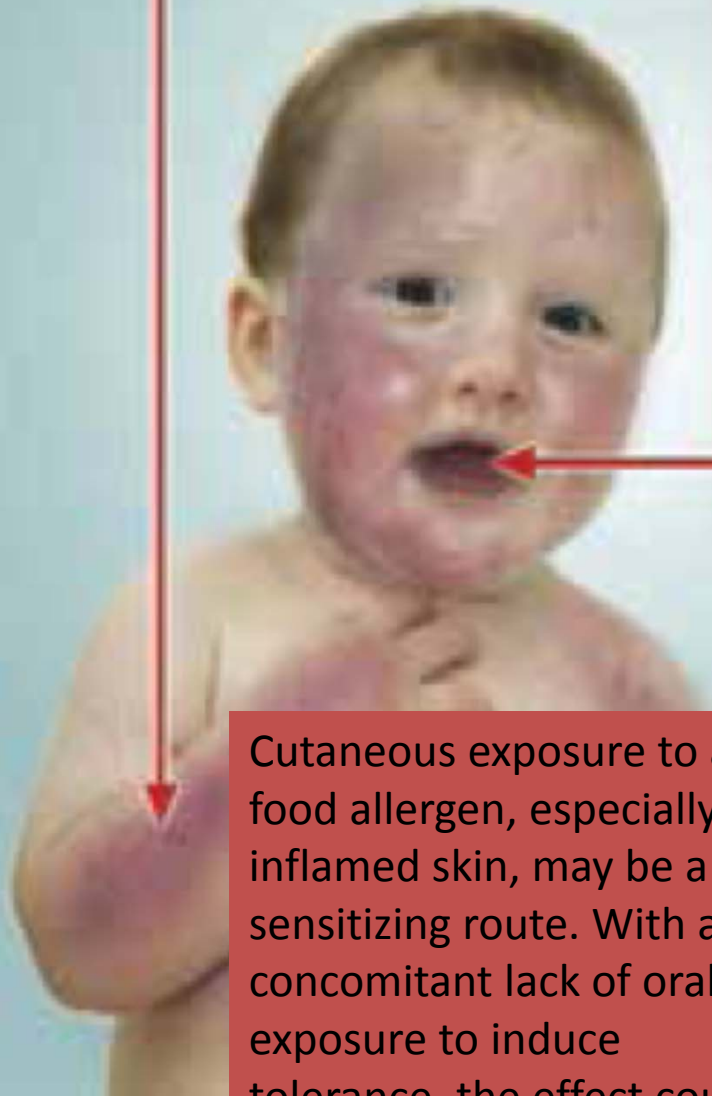


Mesenteric lymph nodes

IFN γ
TNF α IL-10
TGFB

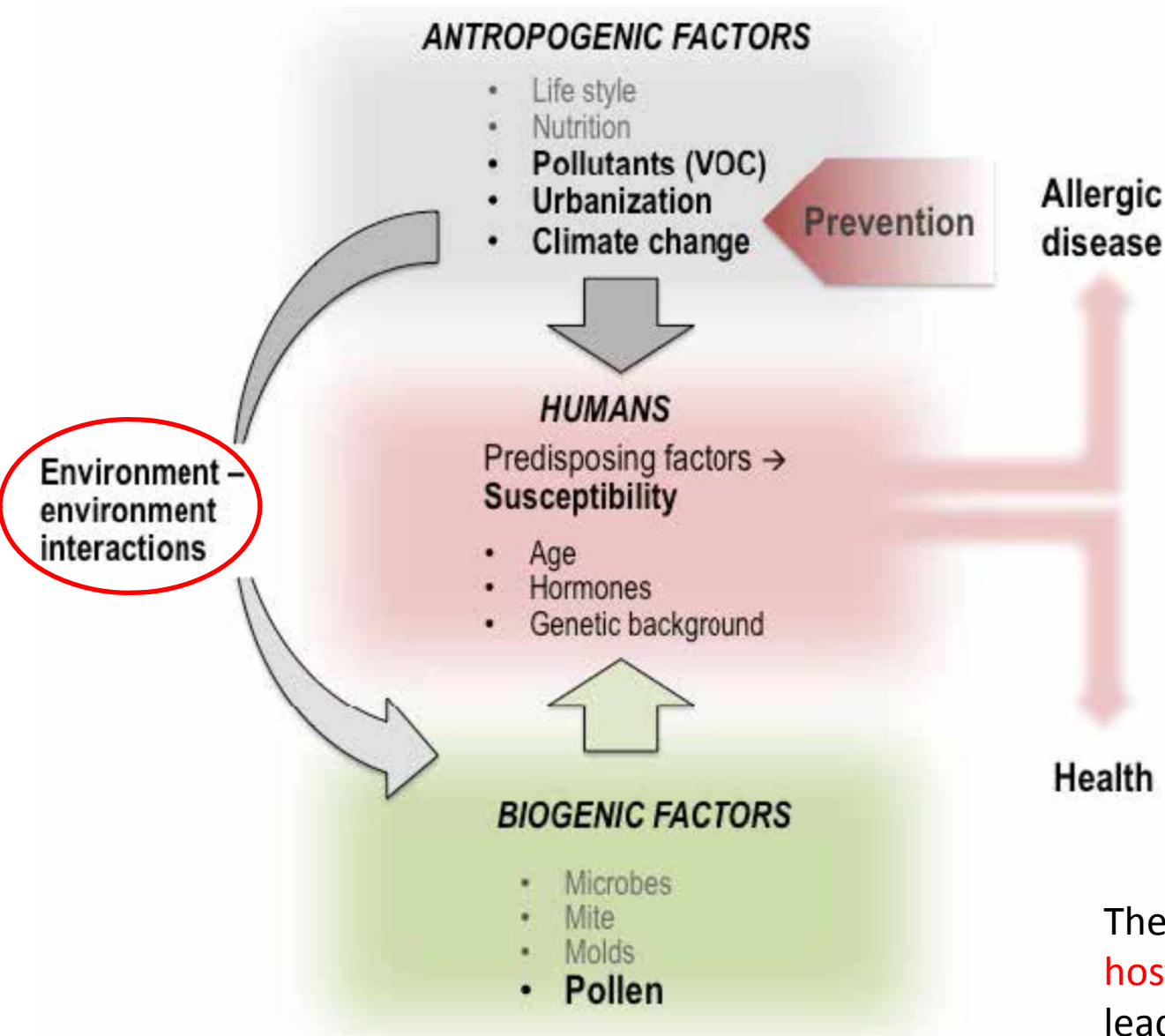
Th1 memory Treg memory

TOLERANCE



Cutaneous exposure to a food allergen, especially to inflamed skin, may be a sensitizing route. With a concomitant lack of oral exposure to induce tolerance, the effect could be promoting food allergy

Nutrition



The complex interplay between **host and environmental factors** leading to allergic diseases

Allergic Rhinitis



- **Rhinitis** - definition: Inflammation of the membranes lining the nose
- Characterized by nasal congestion, rhinorrhea, sneezing, itching of the nose, and/ or post nasal drainage, dry cough, ocular symptoms
- **Allergic rhinitis** - definition: Rhinitis that is caused by an IgE-mediated reaction to an aeroallergen.

Allergic Rhinitis

- Most common atopic disorder
- 10-25% of population affected
- 80% develop symptoms before age 20
- Impairs quality of life, affects school and work performance
- Cost greater than \$5 billion annually

Allergic Rhinitis

Allergens (aeroallergens)

- Seasonal:
 - Tree, grass, weed pollens, molds
- Perennial:
 - Indoor allergens: dust mite, cat, dog, cockroach, mold
- Occupational:
 - Latex, lab animals

Allergic Rhinitis

Diagnosis

- History — timing, triggers, season, FH
- Exam — eyes, nose, ears, pharynx
- Mucosa- pale, boggy, clear secretions
- Pharynx — post nasal drip
- Identification of specific IgE
- Skin test — Prick, Intradermal
- RAST= Radioallergosorbent test

Allergic Rhinitis

Differential diagnosis of rhinitis

- Infection: viral, bacterial, other
- Drug induced: aspirin, antihypertensive
- Hormonal: pregnancy, puberty,
- Other Irritants: food,
- NARES (nonallergic rhinitic eosinophilic syndrome), polyps, emotional, atrophic, foreign body, CSF
- Non-allergic, non infectious

Allergic Rhinitis

Treatment

- Avoidance - environmental control
- Antihistamines:
 - Block H1R: sec. gener. loratadine, desloratadine, cetirizine, levocetirizine, fexofenadine
 - Decrease rhinorrhoea, pruritus, sneezing, but not very effective for congestion
- Nasal steroid sprays:
 - Antiinflammatory: shrink nasal mucosa, effective on rhinorrhea and congestion
 - More effective than any monotherapy , helpful in patients with nasal polyps, slower onset; daily use required,
 - Side effects: epistaxis, headache, dry nasal mucosa

Allergic Rhinitis

Treatment

- Anti-leukotrienes:
 - Montelukast, zafirlukast
 - Combination with antihistamine better than alone
 - Effective in allergic rhinitis and asthma
- Decongestants: oxymethazolin, naphazolin, tramazolin
- Immunotherapy:
 - Allergen specific therapy, most effective for pollens
 - Only form of treatment that can alter the immune response
 - Potential long-term cure of disease
 - Time commitment of 3-5 years
 - Risk of anaphylaxis

Allergic Conjunctivitis

- Allergic conjunctivitis (seasonal/perennial)
- Often accompanies allergic rhinitis
- Due to pollens, pet allergens, dust mite
- Symptoms include ocular itching, redness, increased lacrimation, white stringy exudate,
- Up to 30% of patients only have ocular symptoms

Allergic Conjunctivitis



Treatment

- Ocular antihistamines: Olopatadine
- Ocular mast cell stabilizers: Lodoxamine
- Ocular antihistamine/decongestant:
Naphazoline

Allergic Rhinitis

Oral Allergy Syndrome

- Occurs in 30-70% of patients with pollen allergy
- Symptoms occur after oral mucosa contacts certain foods (fruits, celery)
- Symptoms are itching of palate, throat, lips; may lead to angioedema in minority
- Due to cross-reactivity between pollens and substances in certain foods

Allergic Rhinitis

Oral allergy syndrome - examples

- Ragweed — banana, melons, watermelon
- Birch pollen — apple, cherry, peach, celery, hazelnut, pear

Treatment

- Avoidance of offending food

OAS



Food Allergy

Overall prevalence of food allergy

- Children: 4-8%
- Adults: 1-2%
- Higher in select population: Atopic dermatitis → Up to 35% have food allergy

Food Allergy

Most common food allergens

- Children: Cow's milk, wheat, soy, egg, and peanut
- Account for 90% of reactions
- Adults: Peanuts, tree nuts, fish and shellfish, egg, fruits and vegetable

Food Allergy

Cutaneous symptoms: Diffuse pruritis, Acute Urticaria +/- Angioedema

- Exacerbations of atopic dermatitis
- Implicated in 35% with moderate to severe atopic dermatitis
- Common offenders — egg, peanut, milk, soy, wheat, fish

Food Allergy

Respiratory symptoms

- Rhinoconjunctivitis
- Asthma
- Respiratory symptoms alone are rare
- Usually part of systemic anaphylaxis

Cardiac-GI:

- hypotension/arrhythmias/vascular collapse
- nausea/vomiting/abdominal cramping/diarrhea

Food Allergy

Diagnosis

- Careful history with emphasis on reaction
- Selective skin testing or RAST if suspect IgE-mediated (Useful if skin tests contraindicated, Dermatographism, Severe dermatitis, Inability to stop antihistamines, High risk of anaphylaxis)
- Appropriate exclusion diet
- Blinded provocation

Food Allergy

Treatment

- Strict elimination of offending agent
- Emergency care plan
- Written anaphylaxis action plan
- Injectable epinephrine
- Medic Alert bracelet
- Annual flu with Allergist

Urticaria and Angioedema

- Overview
- Definitions / epidemiology
- Pathogenesis
- Differential diagnosis
- Evaluation
- Treatment
- Natural history

Urticaria - Definition

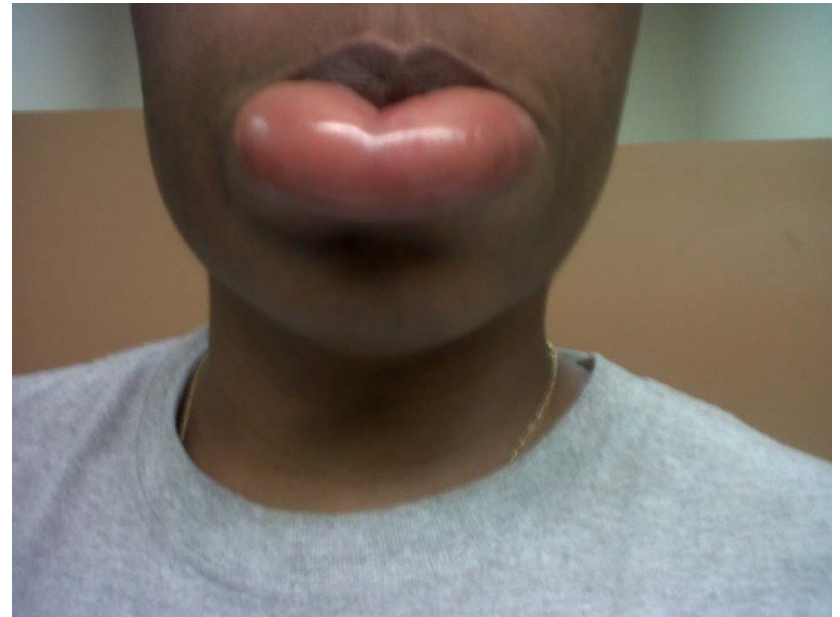
- Pruritic, erythematous elevations that blanch with pressure
- Wax and wane over time
- Capillary dilatation in superficial dermis
- Dermal edema
- Mild perivascular infiltrate of lymphocytes, eosinophils and neutrophils.
- Common name: Hives

Urticaria



Angioedema - Definition

- Well-demarcated swelling of deep skin structures
- Predilection for face, tongue, extremities, and genitalia
- May be painful or burning
- Little or no pruritus
- Nonerythematous
- Asymmetric distribution



Urticaria/Angioedema Treatment

- Removal of stimulus
- Avoidance of precipitators
- Antihistamine prophylaxis
- For severe or life threatening symptoms
- Administration of 0.3 to 0.5 mL of 1:1000 (1.0 mg/mL) **Epinephrine** SC or IM
- Steroids
- Medic Alert bracelet

Hereditary Angioedema

- Autosomal dominant
- 85% reduced C1-esterase inhibitor (C1-INH)
- 15% abnormal C1-INH function
- Baseline low C4 (best screen)
- Decreased C2 during attacks



Hereditary Angioedema

Treatment for acute events or short term prophylaxis

- C1-esterase inhibitor concentrate
- Bradykinin receptor antagonist (icatibant)
- Kallikrein inhibitor (ecallantide)
- FFP

Long-term management of recurrent attacks

- Androgen derivatives: Danazol or Stanozolol
- Anti-fibrinolytic: tranexamic-acid

Anaphylaxis

- Anaphylaxis is a life-threatening allergic reaction to a foreign antigen
- Mediated by IgE antibody located on membranes of mast cells and basophils
- Resulting in the release of preformed mediators which cause the systemic reaction

Anaphylaxis

Non-IgE-mediated = "anaphylactoid"

- Complement mediated (Immune complex => anaphylatoxins)
- Antibody mediated mismatched blood transfusions
- IV gammaglobulin

Anaphylaxis

Non-IgE-mediated (continued)

- Non-immunologic mast cell activators also called "pseudo-allergic reaction"
- Opiates/narcotics, RCM, dextrans, neuromuscular blockers, Vancomycin (Red Man Syndrome)



Anaphylaxis

Examples:

- Food
- Hymenoptera
- Drugs
- Latex
- Exercise
- Idiopathic
- Immunotherapy

Anaphylaxis

- Incidence and prevalence data limited
- Most common causes are antibiotics (PCN) and radiocontrast agents
- Penicillin (PCN) accounts for 75% of deaths in U.S. due to anaphylaxis
- 1 reaction per 5000 exposures
- Account for the majority of deaths
- < 10% of reactions are fatal

Anaphylaxis



Management: General principles

- **Rapid recognition of anaphylaxis** and assessment of severity
- **Epinephrine** (# 1 treatment; Do first!): Delay in epinephrine risk factor for death
 - Adults 0.3 - 0.5 ml IM (1:1000) → repeat in 5-20 min if needed
 - Children 0.01mg/kg IM
- **Establish and maintain airway**: Airway obstruction is the most common cause of death.
- **Fluid resuscitation**,
- **Secondary medication**: antihistamin, corticosteroid (?), B2 agonist (bronchoconstriction), vasopressors and volume expanders (severe hypotension)
- If on beta blocker, consider glucagon (1 mg bolus with continuous infusion of 1 - 5 mg/hour)
- Identification of inciting agent: Prevention and avoidance

Epipen (ALK-Abelló) auto-injector



1. Remove device from carton
2. Remove grey safety cap
3. Place black tip against thigh at 90°
4. Press hard into thigh until auto-injector mechanism functions (should click)
5. Hold for 10 seconds
6. Massage area for several seconds
7. Discard device safely

Anapen (Colltech) auto-injector



1. Remove black needle cap
2. Remove black safety cap from red firing button
3. Place against thigh at 90°
4. Press red firing button
5. Hold for 10 seconds
6. Massage area for several seconds
7. Discard device safely

Drug Allergy

- Adverse reactions to drugs are common
- "Allergy" or hypersensitivity to a drug is defined as "any immunologic response to a drug or its metabolites that results in an adverse reaction"
- Most allergic reactions require previous sensitization
- Exception when drugs share antigenic determinants

Drug Allergy

Generally drug reactions are classified into 2 broad categories:

- **Type A:**

- Common and predictable reactions that can occur in any patient,
- dose-dependent,
- account for 80% of adverse drug reactions,
- produced from pharmacologic action of drug,
- *toxicity, side effects, teratogenic effects, drug-drug interactions*

Drug Allergy

- **Type B:**
 - Uncommon and unpredictable reactions occurring in only susceptible patients, the minority of drug reactions
 - Not related to the drug's pharmacologic actions and not dose-dependent
 - Labeled *intolerance, idiosyncratic reactions, allergic and "pseudoallergic" reactions*
 - Idiosyncratic reactions may be difficult to distinguish from allergic reactions.
 - Intolerance — tinnitus due to aspirin
 - Idiosyncratic — Coumadin® induced skin-necrosis in pt with protein C def.
 - Allergic — penicillin (IgE-mediated)
 - Pseudoallergic — radiocontrast media (direct mast cell degranulation)

Urticaria, Quincke-edema



Immunkomplex vasculitis



Delayed hypersensitivity mediated by T-cells

Contact dermatitis by Nickel



IV.a Th1/ γ IFN monocyte

IV.b Th2/IL-5 eosinophil

Drug Reaction/rash with Eosinophilia and Systemic Symptoms

IV.d IL-8/GM-CSF neutrophil

IV.c CD8+ FasL/perforin/granzim B cytotoxicity



Toxic epidermal necrolysis



Acute generalized exanthematous pustulosis

Stinging Insect Allergy

- Local reactions: 85%
- Large local reactions: 10 - 15%
- Systemic reactions: 0.5 - 5%
- 0.4 - 0.8% of children; 3% of adults
- 40 - 150 deaths/ year in U.S.
- 5% of fatalities < age 20
- 80% of fatalities > age 40
- 40% of fatalities had NO history of prior sting reaction

Stinging Insect Allergy

- 9 -32% of general population have venom-specific IgE
- Presence of IgE venom antibody not necessarily predictive of clinical sensitivity
- Skin testing not indicated for asymptomatic persons

Stinging Insect Allergy

The Culprits:

- Yellow Jacket



- Hornet



- Wasp



- Honeybee



- Fire Ant



Stinging Insect Allergy

Reactions: Local/ Large local

- Most stings cause local reactions
- Pain, swelling, erythema at site of sting
- May be accompanied by itching
- Last from hours to a few days
- No specific treatment required
- Ice, antihistamine, analgesics help

Stinging Insect Allergy

Anaphylaxis

- Usually occurs within 20 min; reports up to 72 hrs
- Same symptoms as other anaphylaxis
- 50-60 % chance of recurrence with subsequent stings
- Skin testing and immunotherapy indicated

Stinging Insect Allergy

Toxic

- Due to multiple stings
- Myalgias
- Fever / chills
- Serum sickness (7-14 days following sting)
- Neuritis, glomerulonephritis, encephalitis
- Vasculitis (1-2 days following sting)
- Guillan Barré

Stinging Insect Allergy

Management: Avoidance

- Kill or relocate the offending insects
- Don't dress or smell like a flower
- Cover exposed skin
- Wear shoes, socks, long pants, long sleeved shirt, gloves
- Self injectable epinephrine
- Refer for evaluation for Immunotherapy (IT) - systemic reaction risk 1 to 2-3%

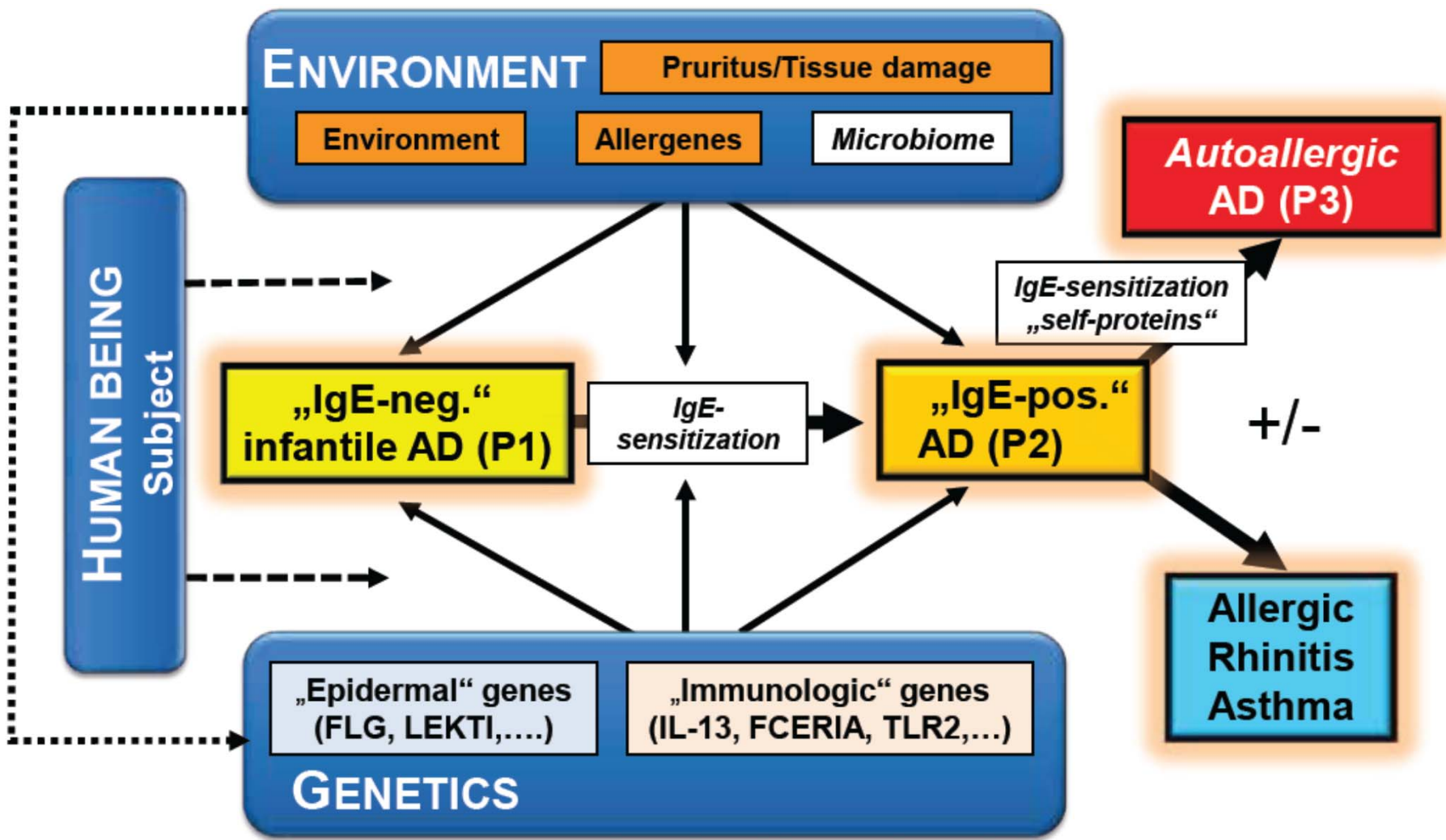
Thank you for your attention



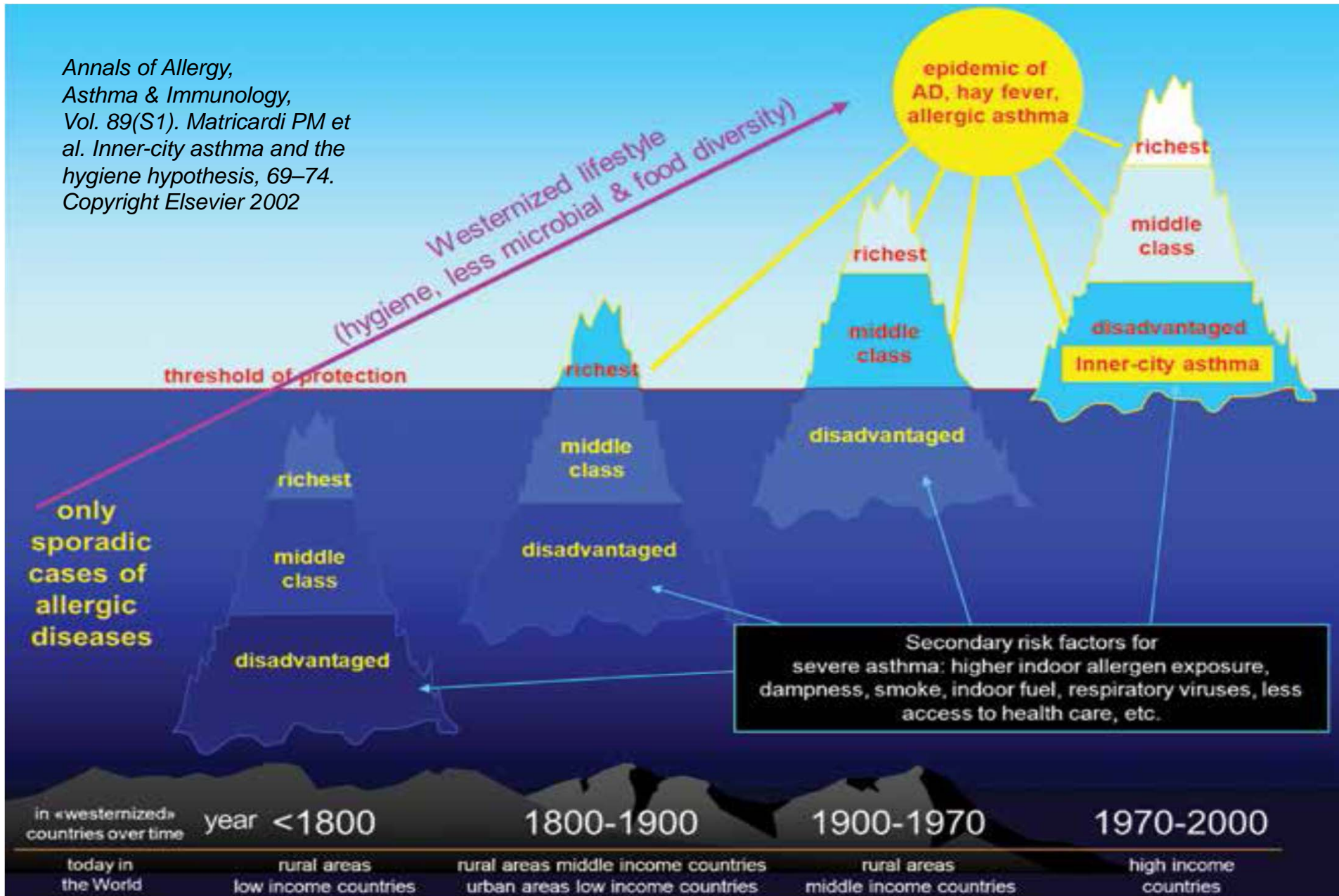
Additional slides

POLLEN
ATTACK!

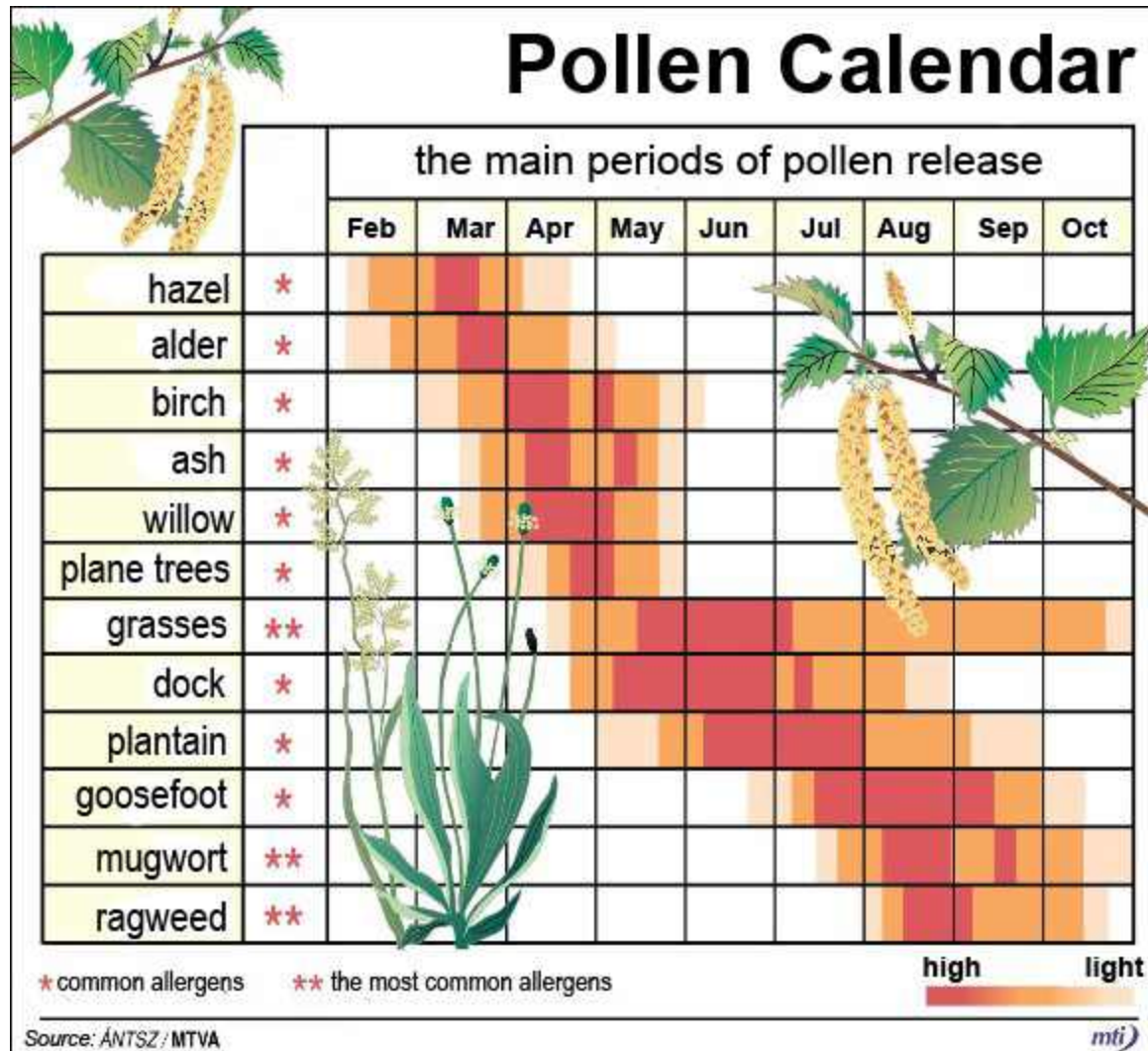
Epigenetic regulation



*Annals of Allergy,
Asthma & Immunology,
Vol. 89(S1). Matricardi PM et
al. Inner-city asthma and the
hygiene hypothesis, 69–74.
Copyright Elsevier 2002*



The Pollen Calendar of ÁNTSZ (National Public Health and Medical Officer Service)



Food Allergy

Adverse food reaction - any aberrant reaction after ingestion of a food or food additive

- Toxic reactions — due to toxin (bacterial, other) present in a food
- Nontoxic reactions - depends on individual susceptibilities
- Immune - allergy or hypersensitivity (Type I)
- Nonimmune – intolerances: Due to pharmacological properties of the food (caffeine or tyramine), Unique susceptibility of the host (lactase deficiency), E.g.: Chinese restaurant syndrome

Angioödéma



Urticaria/Angioedema

Definitions

Acute urticaria/angioedema

- < 6 weeks in duration
- Children and young adults
- Increased incidence in atopics
- Most common identifiable cause is viral infection » meds, idiopathic, foods

Urticaria/Angioedema

Definitions

Chronic urticaria/angioedema

- >6 weeks in duration
- 80-90% idiopathic
- Up to 20% physical urticaria
- M:F = 1:2 (middle-aged females)
- <2% related to food allergens in adults
- 50% urticaria and angioedema, 40% urticaria alone, 10% angioedema alone
- *Rarely* IgE mediated

Classification of urticaria and/or angioedema

1. IgE-dependent
 - a. Specific antigen sensitivity (pollens, foods, drugs, fungi, molds, Hymenoptera venom, helminths)
 - b. Physical: dermographism, cold, solar
 - c. Autoimmune
2. Bradykinin-mediated
 - a. Hereditary angioedema: C1 inhibitor deficiency: null (type 1) and dysfunctional (type 2)
 - b. Acquired angioedema: C1 inhibitor deficiency: anti-idiotypic and anti-C1 inhibitor
 - c. Angiotensin-converting enzyme inhibitors
3. Complement-mediated
 - a. Necrotizing vasculitis
 - b. Serum sickness
 - c. Reactions to blood products
4. Nonimmunologic
 - a. Direct mast cell-releasing agents (opiates, antibiotics, curare, D-tubocurarine, radiocontrast media)
 - b. Agents that alter arachidonic acid metabolism (aspirin and nonsteroidal anti-inflammatory agents, azo dyes, and benzoates)
5. Idiopathic

Hereditary Angioedema

- Recurrent attacks
- No urticaria or pruritus
- May be precipitated by trauma
- Duration of hours to days
- Facial, glossal, laryngeal (potentially life-threatening), or GI involvement

Anaphylaxis

- Hymenoptera stings are next most common
- 25% of population may be at risk - tens of thousands of reactions
- Less than 100 deaths per year

Anaphylaxis

Risk of recurrent reaction with reexposure

- PCN 10-20%
- Radiocontrast media 20-40%
- Insect stings 40-60%

Anaphylaxis

- Rapid onset (seconds-minutes)
- May be biphasic (i.e. late phase response)
- Cutaneous: flushing, pruritus, urticaria, AE
- Respiratory: OBSTRUCTION → DEATH
 - Upper: stridor, hoarseness, dysphonia from laryngeal edema
 - Lower: dyspnea, wheezing, chest tightness, coughing
- Cardiovascular: lightheadedness, tachycardia, shock
- GI: cramping pain, dysphagia
- GU: Uterin cramping
- Neur: confusion, loss of consciousness, seizures
- ENT: nasoocular symptoms
- Other: fear of impending doom and metallic taste

Anaphylaxis

Differential Diagnosis

- Vasovagal reactions
- Hereditary angioedema
- Serum sickness
- Carcinoid syndrome
- Systemic mastocytosis
- Pheochromocytoma
- May measure tryptase levels in difficult cases

Anaphylaxis

Risk factors for poor response to therapy

- Asthma
- Beta blockers
- Blocks the B1, B2 anti-anaphylactic actions of epinephrine
- Unopposed alpha blockage may cause constriction of coronary arteries, elevation of blood pressure
- Elderly patients with cardiovascular disease

Anaphylaxis

Prevention:

- Avoidance of causative agents
- Avoid beta-blockers in high risk patients
- Preventative protocols
- Pretreatment for IV dye loads in pt with dye allergy
- Wash blood products in IgA deficient patients

Drug Allergy

- Immunologically-mediated reactions represent up to 10% of observed adverse drug reactions in inpatients
- Individual risk of allergic reaction to a drug is 1-3%
- Drug associated fatalities reported in 0.1% of medical inpatients
- Fatal drug reactions often have allergic features

Drug Allergy

Allergic drug reactions - characteristics

- High molecular weight drugs (insulin, antisera); low molecular wt drugs (PCN)
- Proteins allergens
- Inflammation already present (adjuvant which enhances immunologic response)
- Prolonged or repeated therapies
- Certain genetic HLA phenotypes or predisposed individuals (atopic)

Drug Allergy

***Allergic or hypersensitivity* drug reactions are immunologically-mediated and share the following characteristics:**

- Occur in small numbers of patients
- Require previous sensitization
- Develop rapidly after re-exposure
- Produce clinical syndromes associated with immunologic reactions

Drug Allergy

Gell and Coombs Type I:

- IgE-mediated mast cell degranulation and newly formed mediators causing anaphylactic reactions usually within 30 min after drug administration (urticaria/angioedema, wheezing)
- Diagnosis: history, skin testing, IgE, RAST
- Treatment with avoidance vs. desensitization

Drug Allergy

Type II:

- Cytotoxic reactions mediated by binding IgG, IgM to cell bound antigens, leading to activation of complement destroying cell to which antigen is bound
- Diagnosis by clinical syndrome, *in vitro* demonstration of antibody
- Treat by removing offending agent/steroids

Drug Allergy

Type III:

- Immune-complex mediated by antigens binding to antibodies (IgG and IgM, subsequent tissue deposition and complement activation)
- Serum sickness is a classic example (skin eruptions [urticarial/morbilliform], fever, arthralgias, GN, vasculitis)
- Serum sickness usually 7-21 days after drug started
- Treatment: Remove offending agent/steroids. Future administration of agent is relative contraindication.

Drug Allergy

Type IV:

- Delayed hypersensitivity mediated by T-cells, cell mediated immunity
- Examples: some forms of AIN, contact dermatitis, drug fever and drug-induced vasculitis
- Diagnosis by clinical syndrome, patch test (for topical substances), *in vitro*
- Treatment: Removal of offending agent (relative contraindication) and steroids

Drug Allergy

Erythema Multiforme/Stevens-Johnson Syndrome

- Erythematous, polymorphic eruption caused by drugs in 10-20% cases
- Includes target lesions, maculopapular rash, urticaria, vesicles — typically symmetric and on extremities
- Stop offending agent immediately! Avoid in future

Drug Allergy

Stevens-Johnson Syndrome (EM Major)

- Severe form of EM with mucosal and conjunctival involvement
- Epidermal loss <10% of BSA
- 50% of cases associated with drugs (NSAIDs, sulfonamides, anticonvulsants, allopurinol)
- Visceral involvement associated with poor prognosis
- Treatment: stop offending agent immediately!
Avoid in future! Steroids (1mg/kg/day) may prevent visceral involvement and decrease duration and severity of clinical findings

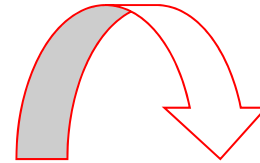
Drug Allergy

Toxic Epidermal Necrolysis (TEN):

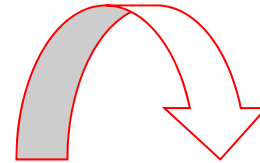
- Acute illness characterized by fever, epidermal loss >30% of BSA
- Visceral involvement with high mortality (30-40%)
- May be difficult to distinguish from SJS (?spectrum of disease) with many of the same drugs causing both
- Re-administration of drug likely to cause TEN and therefore is an **ABSOLUTE CONTRAINDICATION!**
Steroids are not helpful. Contraindicated in TEN!



Erythaema exudativum multiforme



Stevens-Johnson syndroma



Lyell syndroma/TEN



Drug Allergy

Morbilliform/maculopapular exanthem

- Most common drug induced skin reaction
- Usually symmetric, confluent macules or papules that spare the palms, soles
- Predilection for dependent areas in hospitalized patients Common drugs: PCN, NSAIDs, β -lactams, sulfa, anticonvulsants, Allopurinol
- Removal, or future avoidance of offending agent recommended. Can consider continuation if no evidence of other findings (EM, SJS, serum sickness, hypersensitivity vasculitis)



Drug Allergy

Allergy to Specific Drugs:

- Detecting drug-specific IgE can help assess risk for future reactions
- Testing includes skin testing, RAST
- Skin testing/RAST not helpful or indicated for non-IgE-mediated types of reactions
- Desensitization indicated when no available substitute for offending drug

Drug Allergy

- Most common cause of allergic drug reactions
- 400-800 fatalities per year in US
- Skin test reactivity decreases by 10% annually
- 95% of PCN metabolized to major determinant (penicilloyl)
- Minor determinants = remaining 5%
- Allergy to minor determinants associated with severe anaphylaxis

Stinging Insect Allergy

Large local reactions

- Occur in 10-15% of adults
- Swelling >10cm or crossing a joint
- Peaks at 24-48 hrs, lasts 5-7 days
- Subsequent stings usually also large local RXN (90-95%)
- Does NOT tend to progress to anaphylaxis (5-10%)
- Skin testing and immunotherapy is NOT indicated

Prevention

- **Avoid triggers** that have caused an allergic reaction, even a mild one. This includes detailed questioning about ingredients when eating away from home. Ingredient labels should also be carefully examined.
- A **medical ID tag** should be worn by people who know that they have serious allergic reaction.
- If any history of a serious allergic reactions, **carry emergency medications** (such as diphenhydramine and injectable epinephrine).
- **Do not use** your injectable epinephrine **on anyone else**. They may have a condition (such as a heart problem) that could be affected by this drug.