



Epidemiology of allergies, laboratory diagnostic methods

Allergology 2018/II week
Timea Berki

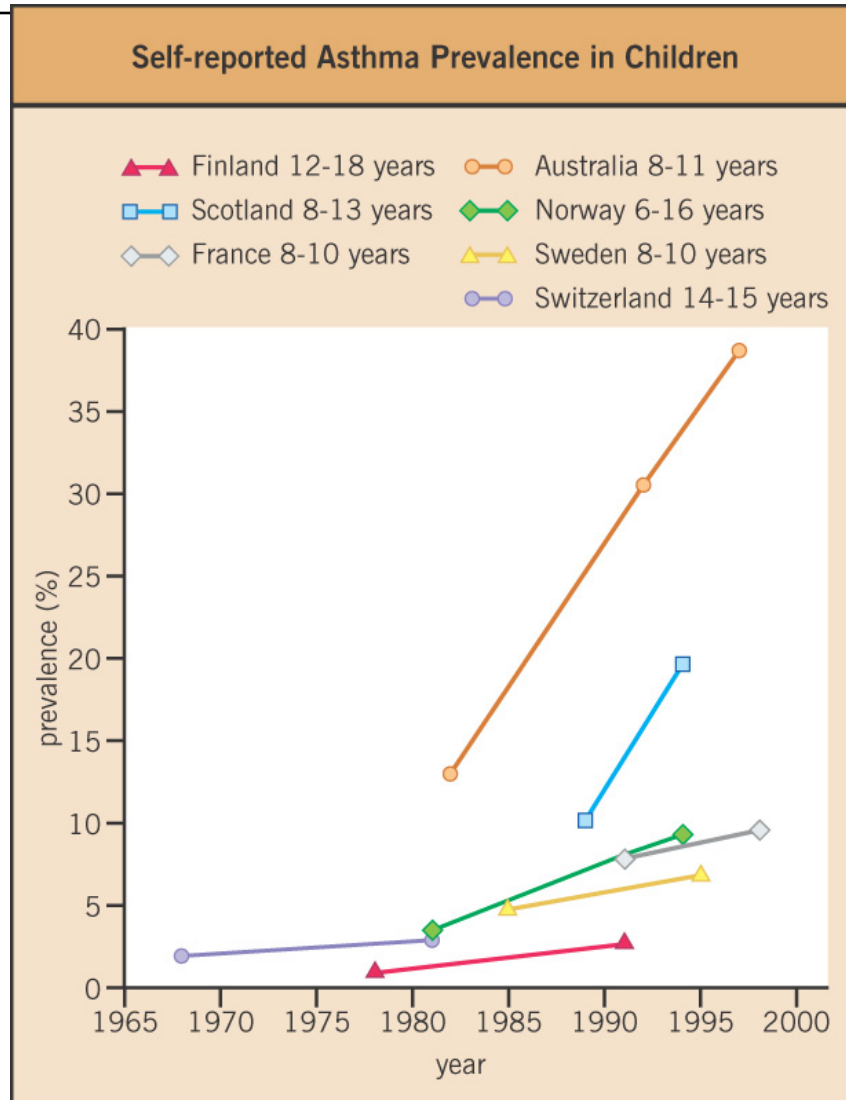
Atopy-allergy

- **Atopy**: The European Academy of Allergology and Clinical Immunology (EAACI) defines atopy as “a personal or familial tendency (genetic predisposition) to produce IgE antibodies in response to low doses of allergens, usually proteins, otherwise harmless environmental substances
- The term 'atopy' (Greek *atopos* meaning out of place)
- Atopic individuals may or may not have symptoms of allergy, but are genetically predisposed to develop one or more ADs (i.e., allergic rhinitis [AR], hayfever, asthma, atopic eczema and certain food allergies) and have a strong familial basis.
- Positive skin test without symptoms
- **Allergy**: as a consequence, to develop typical symptoms such as asthma, rhinoconjunctivitis or the atopic eczema/dermatitis syndrome (AEDS).

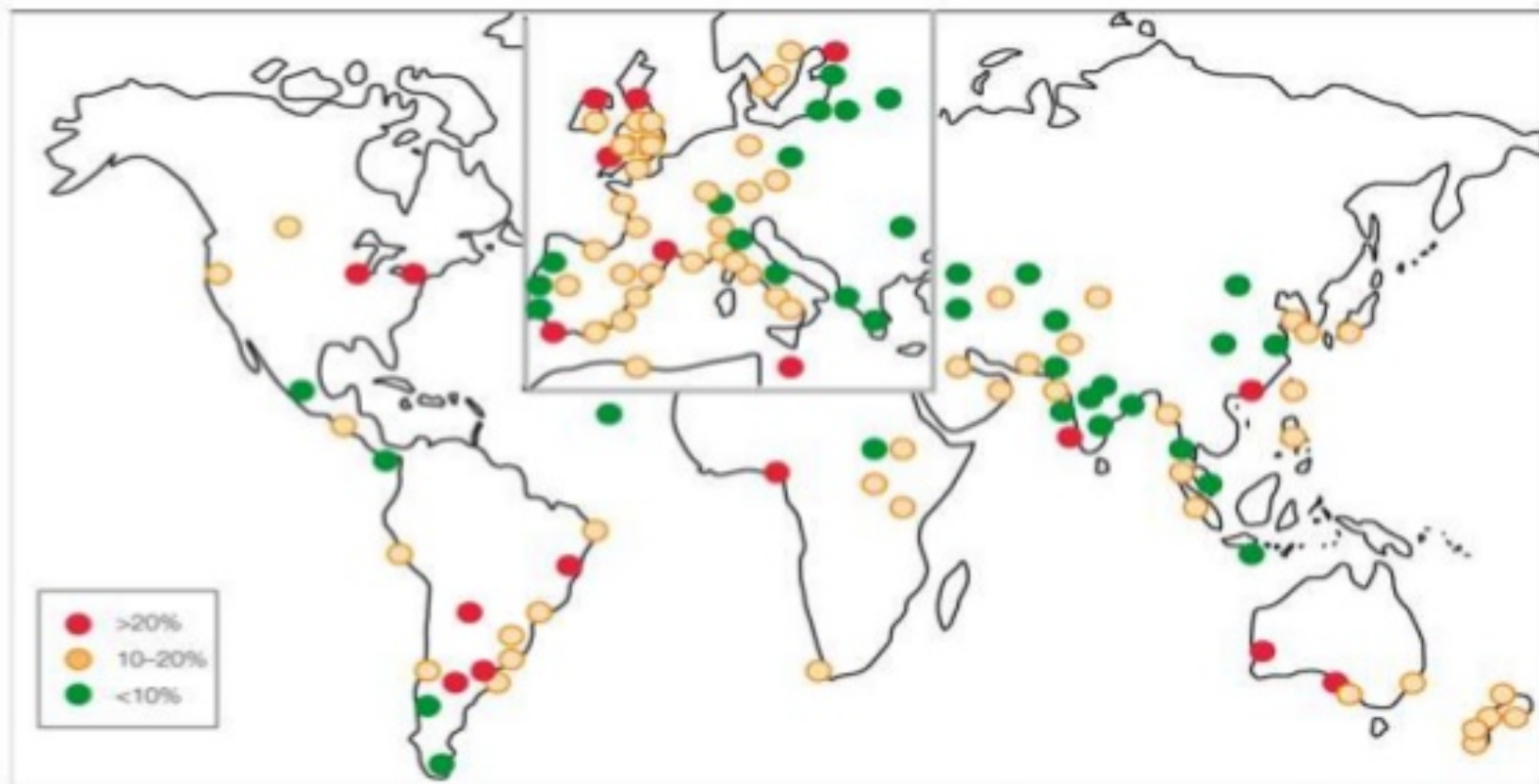
Prevalence of allergy

- According to recent data, worldwide prevalence of allergy ranges from 30 to 40%.
- In Europe and the USA, approximately half of the population is said to be either suffering from allergy or already sensitized to one or more allergens.^[5,6]
- ADs are more prevalent in children as compared with adults.
- According to the ISAAC Phase III study, every third child (<18 years of age) is allergic to one or other allergens.^[7]
- The prevalence of AD in developed societies has doubled in the past two decades and is increasing rapidly in developing countries (e.g., India), which were previously considered low endemic zones for allergy.

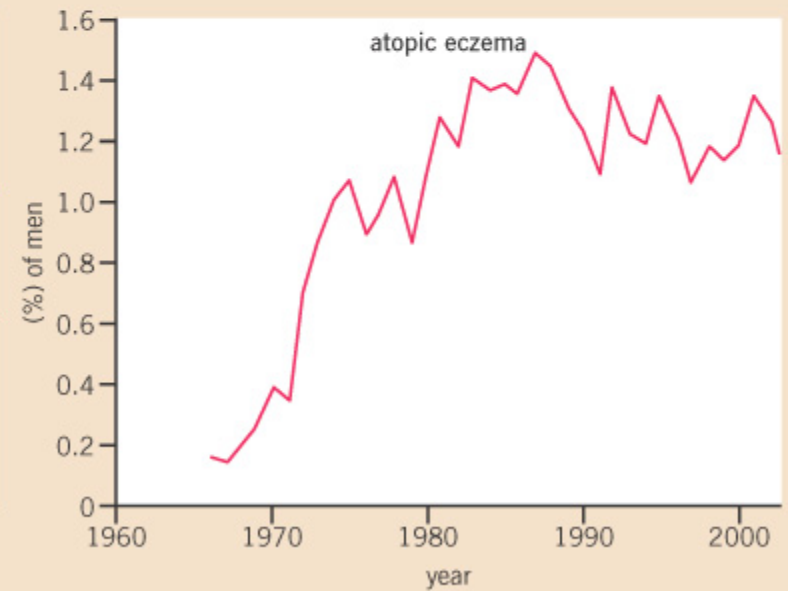
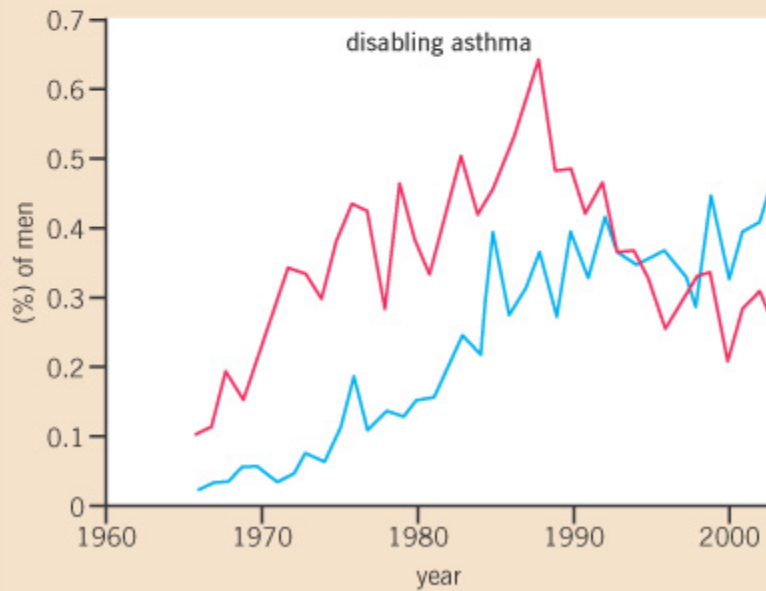
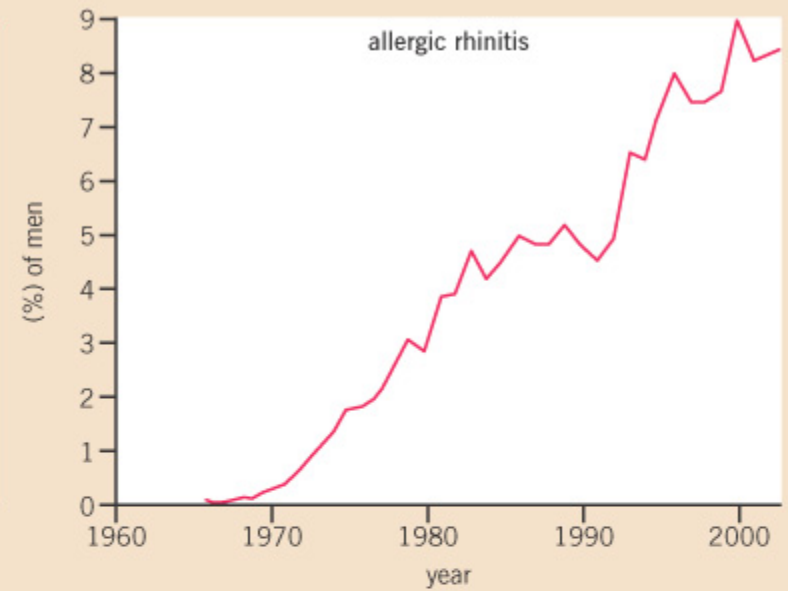
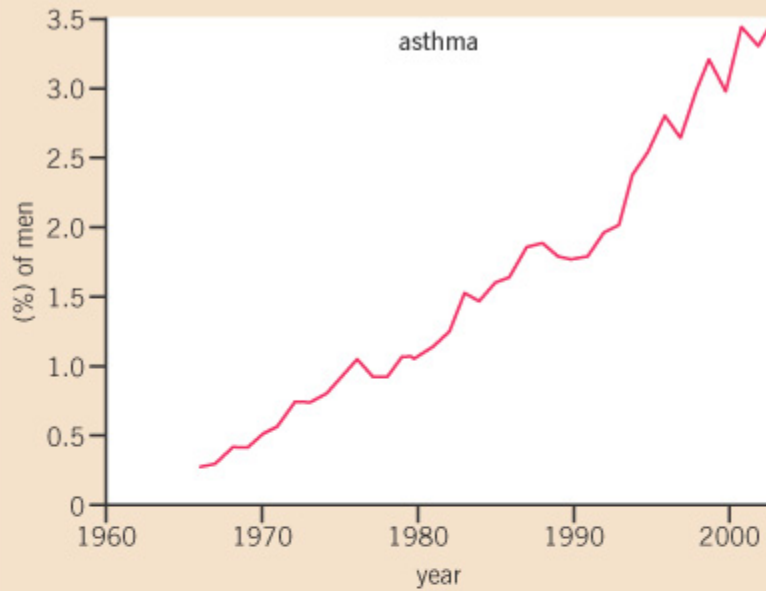
Increasing tendency of allergic diseases in the last 50 years



The International Study of Asthma and Allergies in Childhood noted the prevalence of rhinitis with itchy watery eyes, in six to seven year olds as 0.8 to 14.9 percent and in 13-14 year olds from 1.4 to 39.7 %.



Prevalence of Asthma and Allergic Disease in Finnish Men



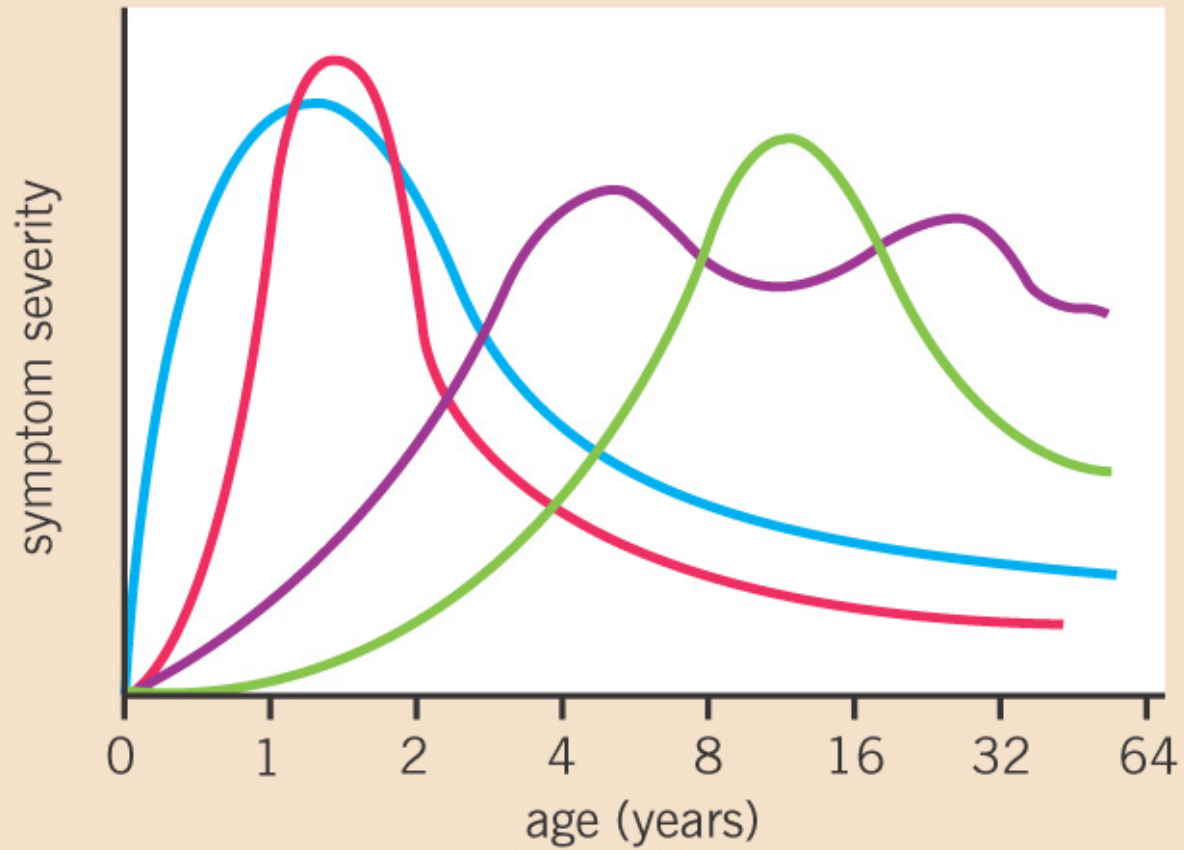
— at call-up
— during service



Age and the development of the different type of allergies

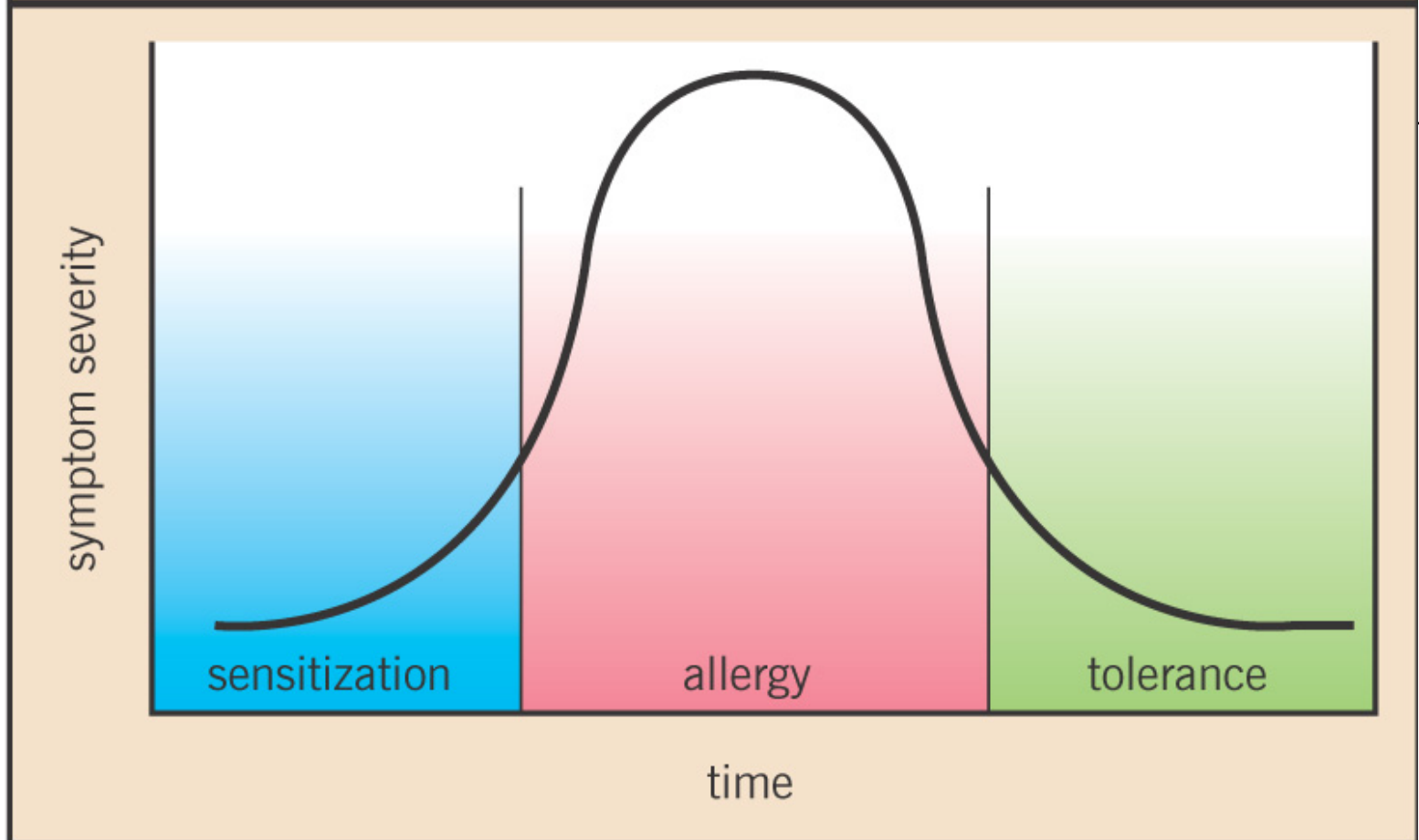
- Food allergy and eczema: early childhood
- Asthma is biphasic: childhood and the thirties
- Rhinitis between 10-30 years

Symptom Severity Versus Age



— eczema — food allergy — asthma — rhinitis

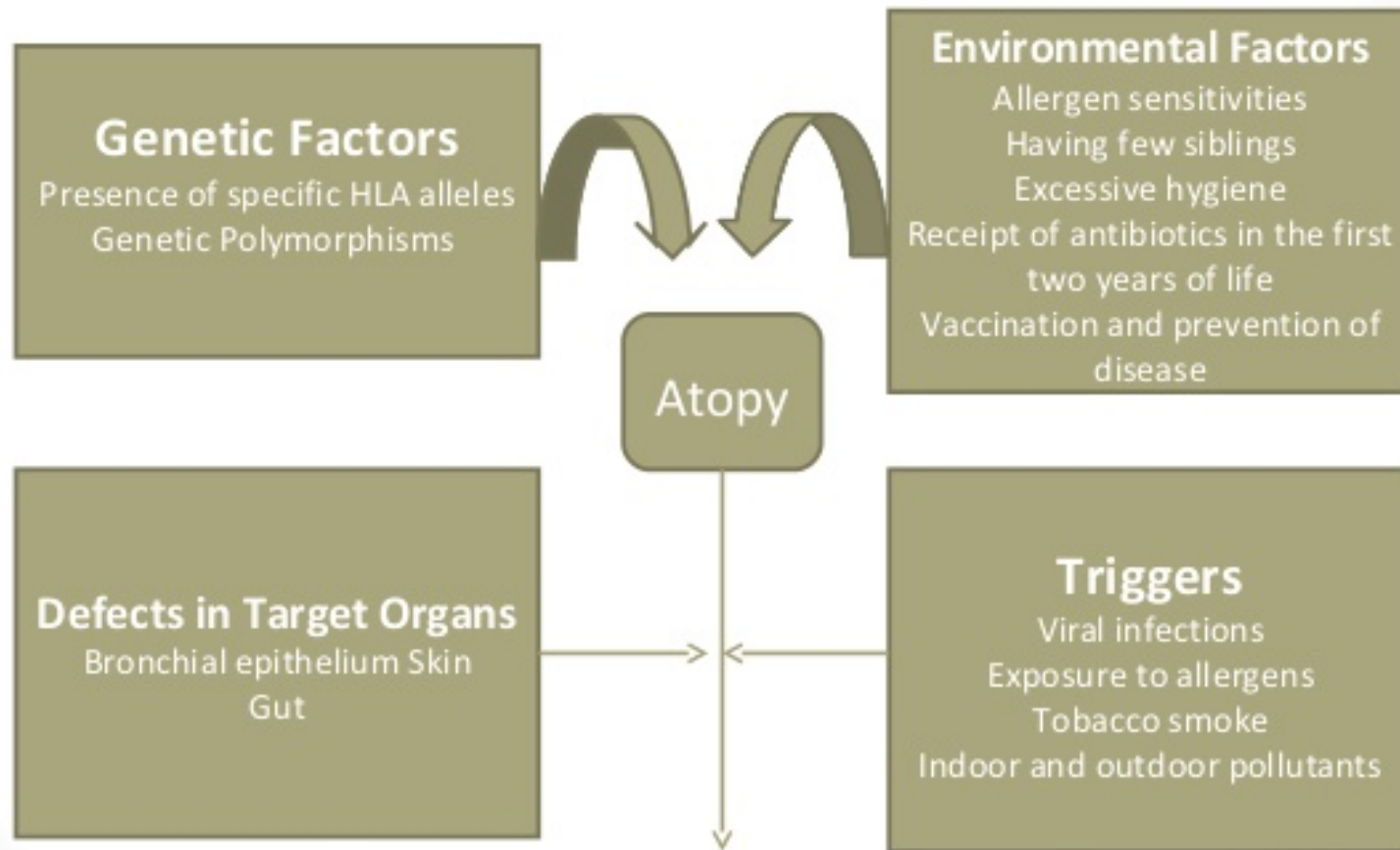
Symptom Severity Versus Time



Holgate, Church and Lichtenstein: Allergy 3rd edition © 2006 Elsevier Ltd

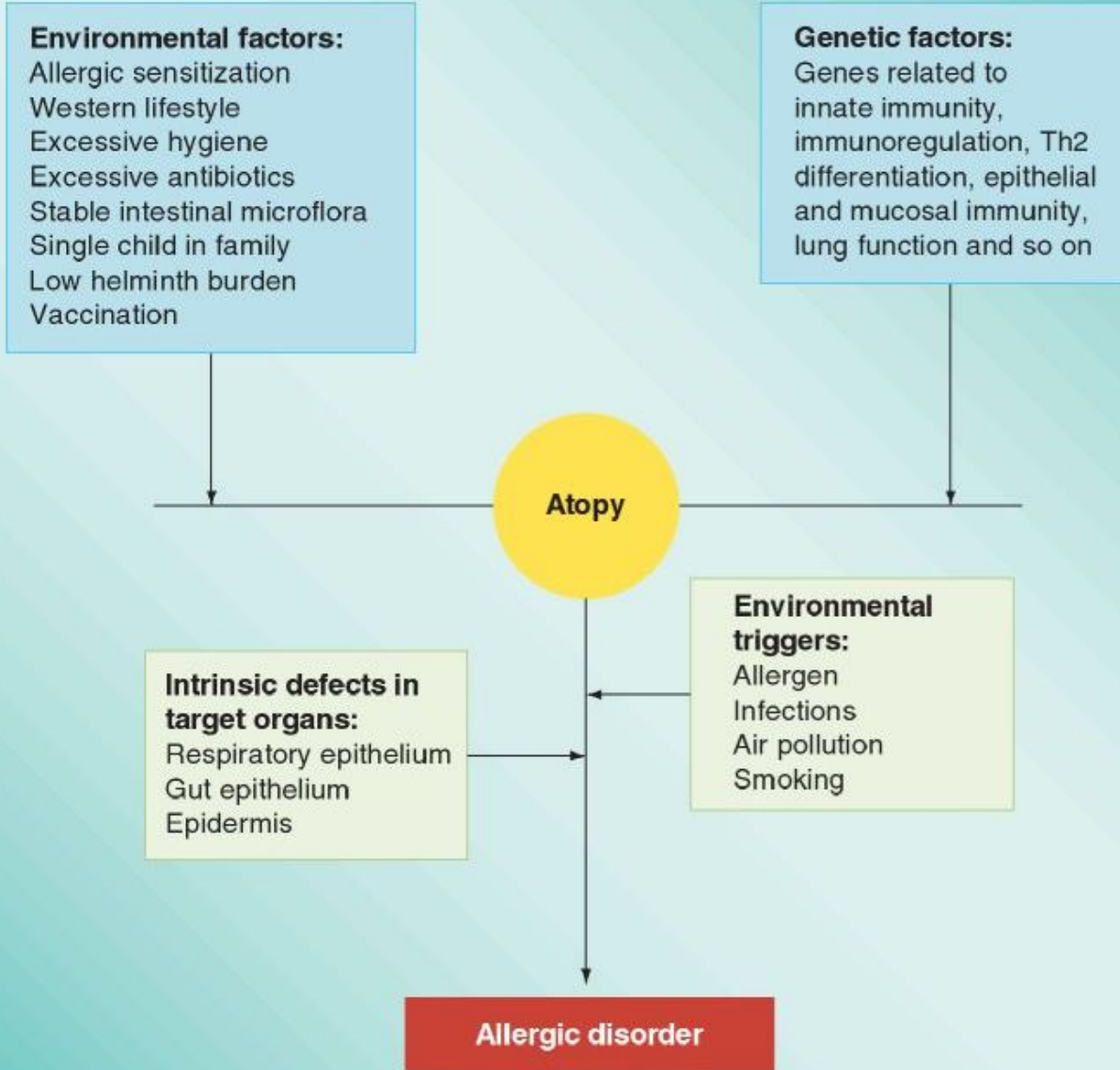
ADs are believed to be caused by a combination of both environmental and genetic factors, each accounting for approximately 50% of risk of susceptibility.^[4]

Causes of Allergy



Factors predisposing allergy

Medscape



Risk factors

Genetics and family history

- The best established risk factor for allergic rhinitis is a family history of allergy, especially of allergic rhinitis.
- Genes which appear to be involved in atopy include an area on the 5q chromosome.
- Other possible susceptibility loci exist on chromosome 11q, chromosome 13 in the Japanese population and chromosome 12q.

Environment-

Lifestyle changes, increased exposure to allergen, pollution and irritants, dietary modifications leading to a reduction in Th 1-type immune response and stress.

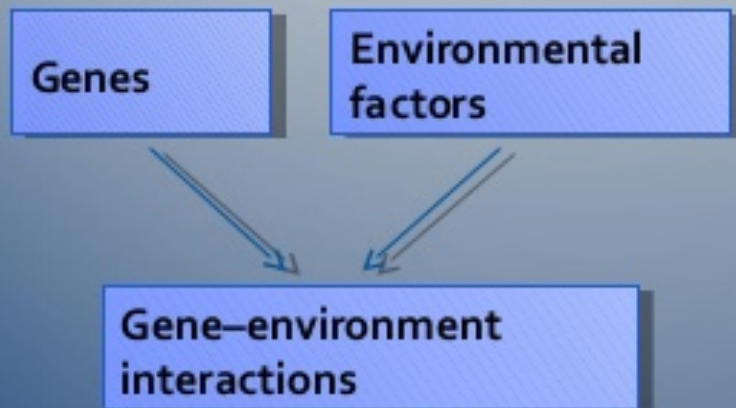
- Pollution increases symptomatic rhinitis.
- Living in developed countries, pollution, climate interaction and good hygiene all seem to be risk factors.

Co-morbidities-

Conditions associated with allergic rhinitis are asthma, sinusitis, otitis media, sleep disorders, LRTI & dental occlusion.

Risk Factors for Allergic Rhinitis

- Development of allergic diseases in atopic individuals is due to



- Family history of allergy is single most important factor predisposing a child to development of allergic disease
 - 50% with one parent having atopy
 - 66% with both parents having atopy
 - 85% have similar allergy like parents
- Other Risk Factors
 - small family size
 - early use of antibiotics
 - western lifestyle
 - dietary factors
 - passive smoke exposure
 - Atopic dermatitis
 - High serum IgE levels at 6 years of age

Risk factors

1. Genetic susceptibility:

2. Family history of atopy: e.g. asthma,eczema,hay fever,urticaria

(Genes involved in atopy - loci on 5q,11q and 12q chromosomes)

3. Environmental factors:

- Pollution-climate interaction

- **Irritants**

eg. fumes, tobacco smoke, diesel exhaust, mosquito repellents, perfumes, scented sticks, domestic sprays, bleaches

4. Exposure to **allergens**:

- Seasonal : Pollen, Fungus

- Perennial: Dust mite, domestic pets, cockroaches



EARLY CHILDHOOD RISK FACTORS FOR PERSISTENT ASTHMA

1. Parental asthma (single-20%, both-60%)
2. Allergy
 - Atopic dermatitis (eczema)
 - Allergic rhinitis
 - Food allergy
 - Inhalant allergen sensitization
3. Severe lower respiratory tract infections requiring hospitalization
 - Pneumonia
 - Bronchiolitis
4. Wheezing apart from colds
5. Male gender
6. Low birth weight
7. Environmental tobacco smoke exposure
8. Possible use of acetaminophen (paracetamol)
9. Exposure to chlorinated swimming pools
10. Reduced lung function at birth
11. Eosinophilia (>4%)

Allergic Rhinitis - Causes

Seasonal/ Intermittant

Pollen from trees,
grasses, and weeds

Perennial/ Persistent

House dust, mites
Mold and fungus spores
Cockroaches
Animal danders
Food
chemicals



Gastrointestinal Allergens

○ Food:

Cow milk

Nuts

Wheats

Fruits

Egg

Meat

Fish

Fruit di mare

○ Non-food

Bacterial antigens

Virus antigens

Fungal antigens

Helminths

Airway antigens

Chemicals

Drugs



Characteristics of allergens

- Hydrolytic enzymes – proteases, carbohydrase, ribonuclease (dust mite, fungi, pollen)
- Pectin lyase, enolase, aldolase, alcohol dehydrogenase activity
- Enzyme inhibitor activity
- Homology with transport proteins
- Homology with regulator proteins

Factors influencing allergenicity

Intrinsic

- Molecular weight
- Concentration
- Solubility
- Stability
- Foreignness
- Biochemical activity
- Indigestible
- Heat stable

Extrinsic

- Air pollution
- Cigarette smoke
- Virus infection
- Genetics
- Season of birth
- Hygiene

Causes of occupational asthma

Allergy agent

- Laboratory animals
- Flour
- Biological enzymes
enzimek
- Wood dust
- Latex rubber gloves
- Hair dyes
- Isocyanates
- Colophony (solder
fumes)

At-risk employment

- Scientific, animal house
work
- Baking
- Soap powder industry
work
- Saw milling, furniture
manufacturing
- Health workers
- Hairdresser
- Painting industry
- Electronic industry

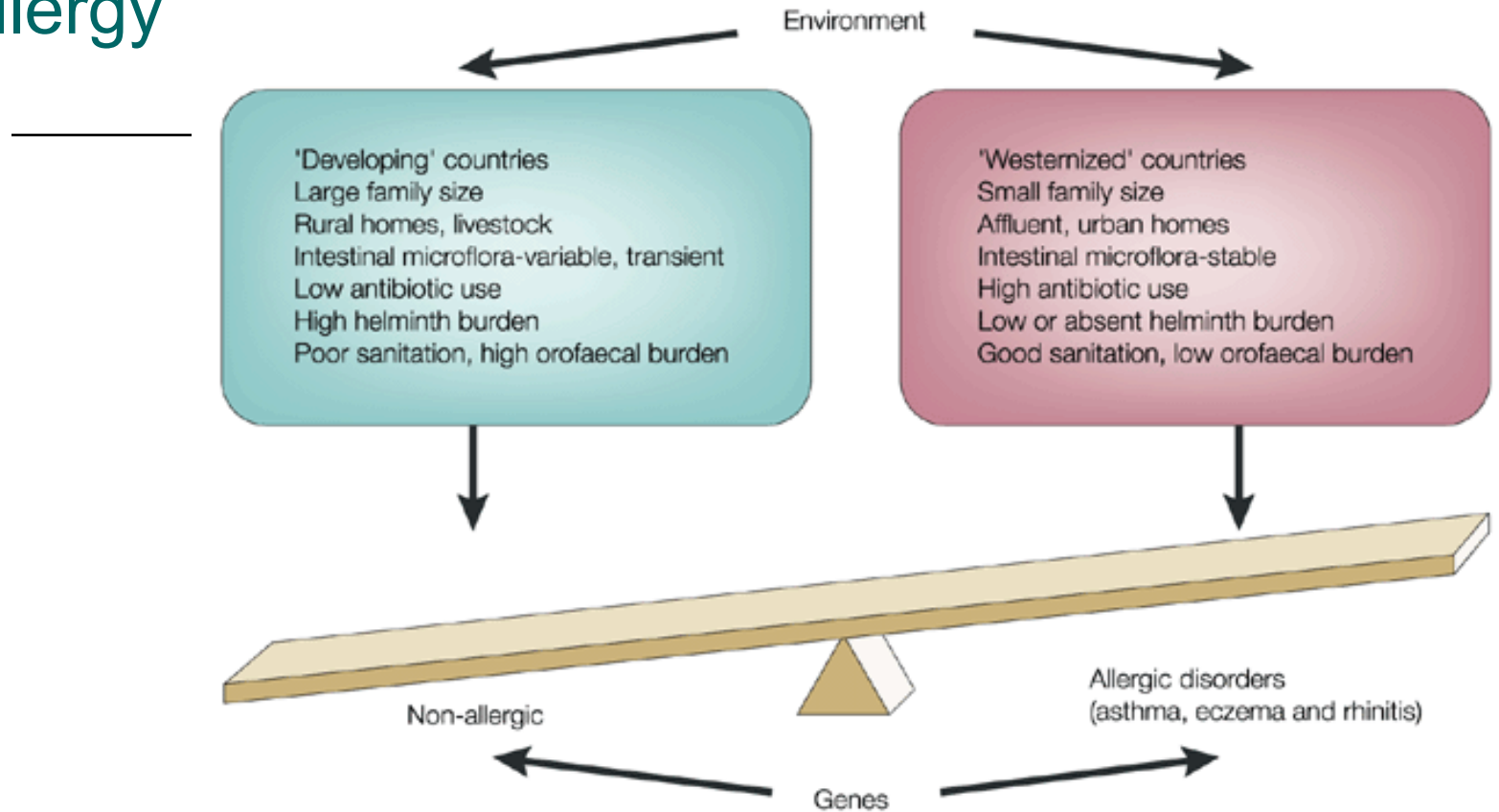
Examples of allergic contact eczema

- Nickel - Coins, watches, jewellery
- Cobalt - Metal-plated objects, wet cement
- Fragrances - Cosmetics
- Lanolin - Cosmetics, moisturizing creams
- P-Phenylendiamin - Hair dye, fur dye
- Epoxi resins - Adhesive

Cross-reactions between Inhalant Allergens and Food „Oral allergy syndrome”

- Birch pollen
 - Hazelnut, apple, pear, stone fruits (peaches, plums, cherries)
- Grasses
 - Melon, tomato, orange, cherries, potato
- Ragweed pollen
 - Melon, bananas
- House dust mite
 - Snails
- Latex
 - Banana, chestnut, avocado, kiwi fruit

Environmental conditions influence the prevalence of allergy



Increases in allergy prevalence have occurred primarily in 'westernized' societies over the past few decades. Although both genetic and environmental factors influence the aetiology of asthma, changes in the genetic make-up of stable populations does not occur in this time frame. The recent rise in the prevalence of allergies and asthma is therefore thought to be primarily due to changes that have taken place in the environment in developed countries as a result of modernization. A comparison of environmental conditions in developed and underdeveloped countries has provided insight into possible causes.

Factors favoring the Th1 phenotype

Presence of older siblings
Early exposure to day care
Tuberculosis, measles,
or hepatitis A infection
Rural environment



Protective
immunity

Factors favoring the Th2 phenotype

Widespread use of antibiotics
Western lifestyle
Urban environment
Diet
Sensitization to
house-dust mites
and cockroaches



Allergic diseases
including asthma

Cytokine
balance

The interaction of genes and environmental factors determine the risk of allergic sensitization

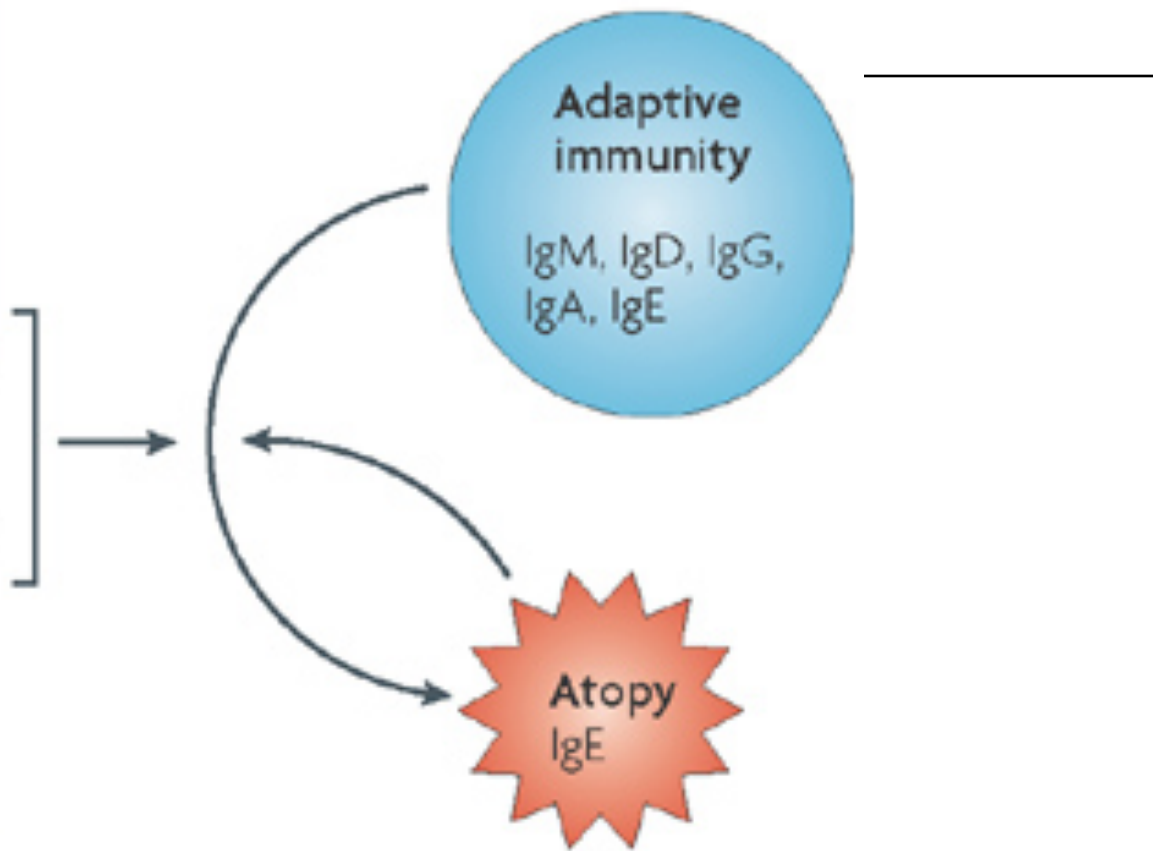
- By early 2006, six genes had been identified by positional cloning and over 100 by candidate gene association.
- Polymorphisms in some of the genes are directly involved in the synthesis or effector functions of IgE.
- Environmental factors associated with allergy:
 1. level of exposure to allergens¹⁰⁰;
 2. The way in which food is processed^{101, 102}; elevated pH of the stomach contents of the fetus and young babies, or caused by antacid medications in adults¹⁰³;
 3. atmospheric pollution¹
 4. Respiratory syncytial virus and rhinovirus infections during infancy
 5. Staphylococcal aureus infections, which generate superallergenic enterotoxins^{107, 108}; and the activity of autoantibodies^{109, 110}.

Once sensitization occurs, these factors continue to operate, and atopy is exacerbated by the resulting inflammation, persistent IgE synthesis and epitope spreading

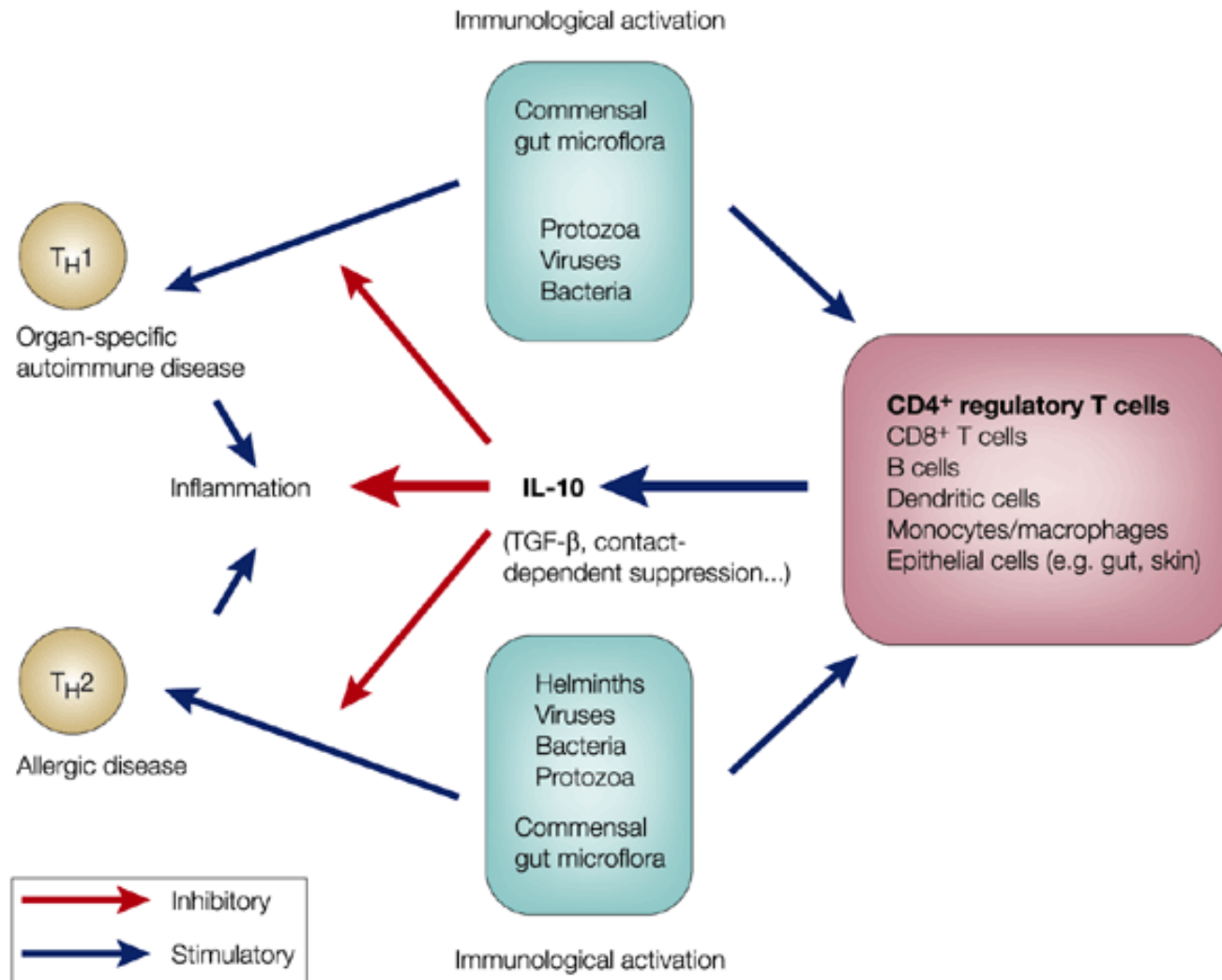
Environment
Maternal IgE
Allergens
Gut pH
Pollutants
Infections
Superallergens
Autoantibodies



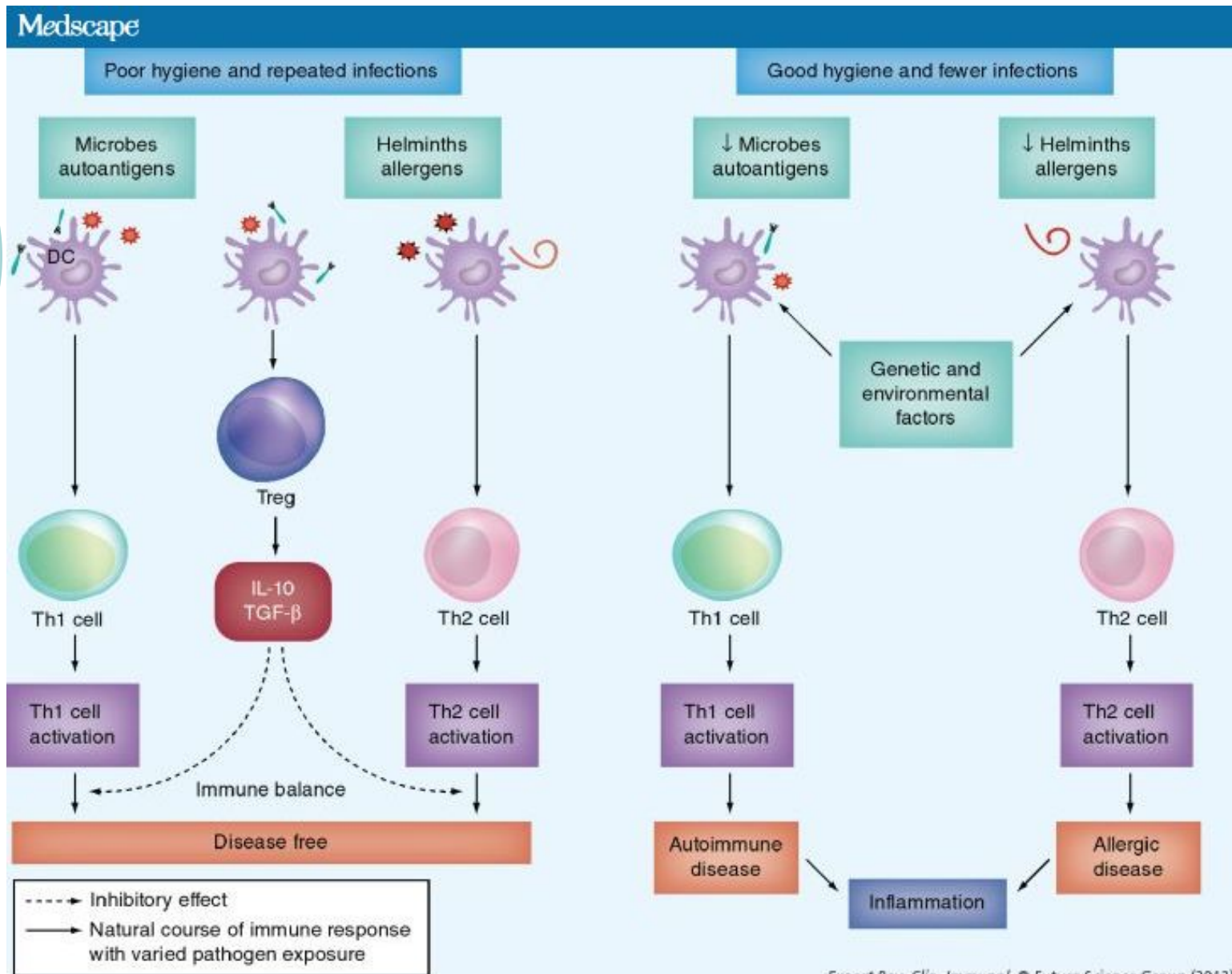
Genes
IL4 and *IL13*
IL4RA and *IL12RB*
TBET
STAT6
FCER1B
CD23
CD61 (integrin- β_3)



Schematic view of the counter-regulation hypothesis.

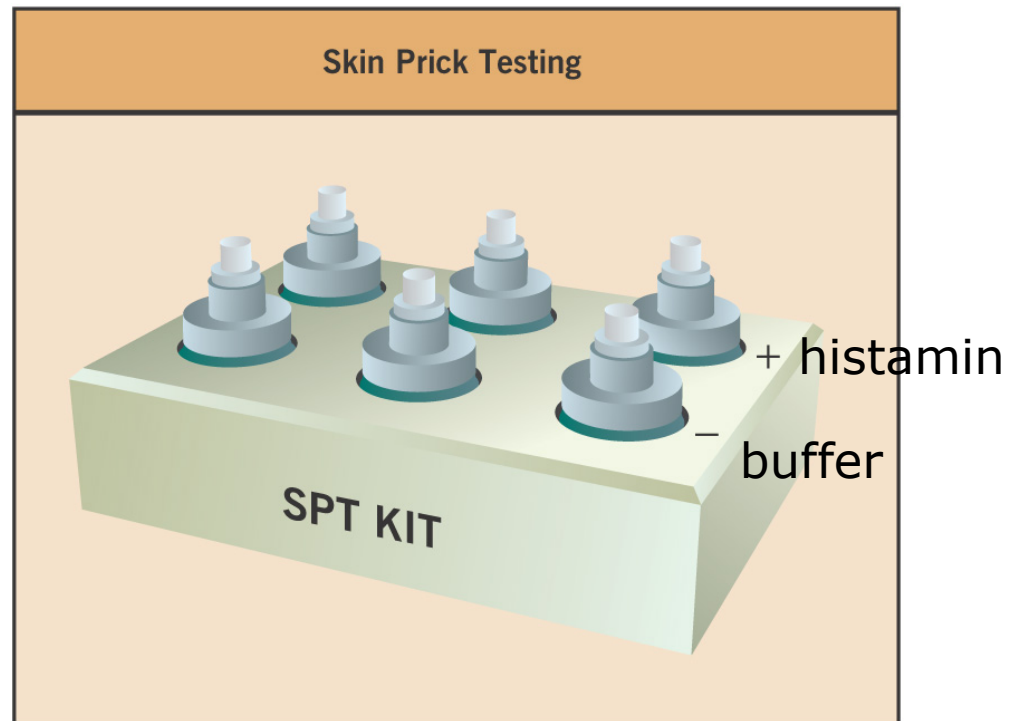
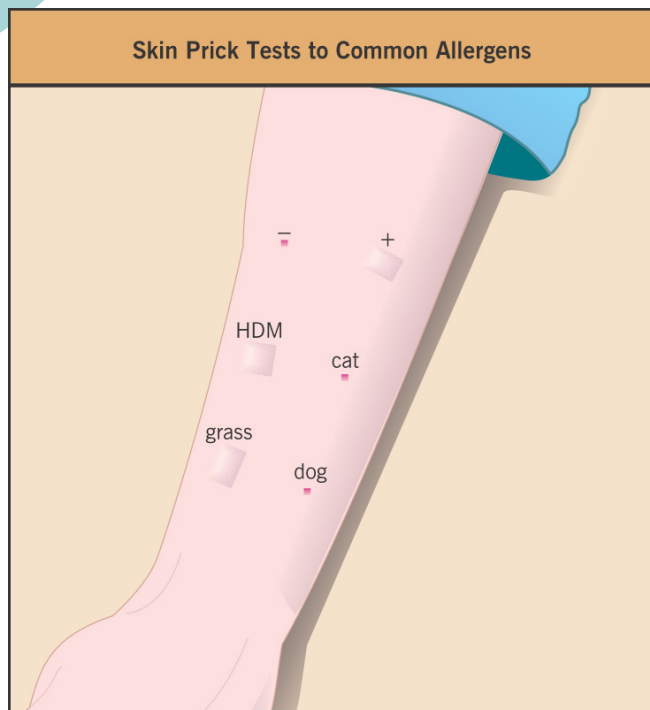


Hygiene hypothesis and counter-regulation theory for allergy.

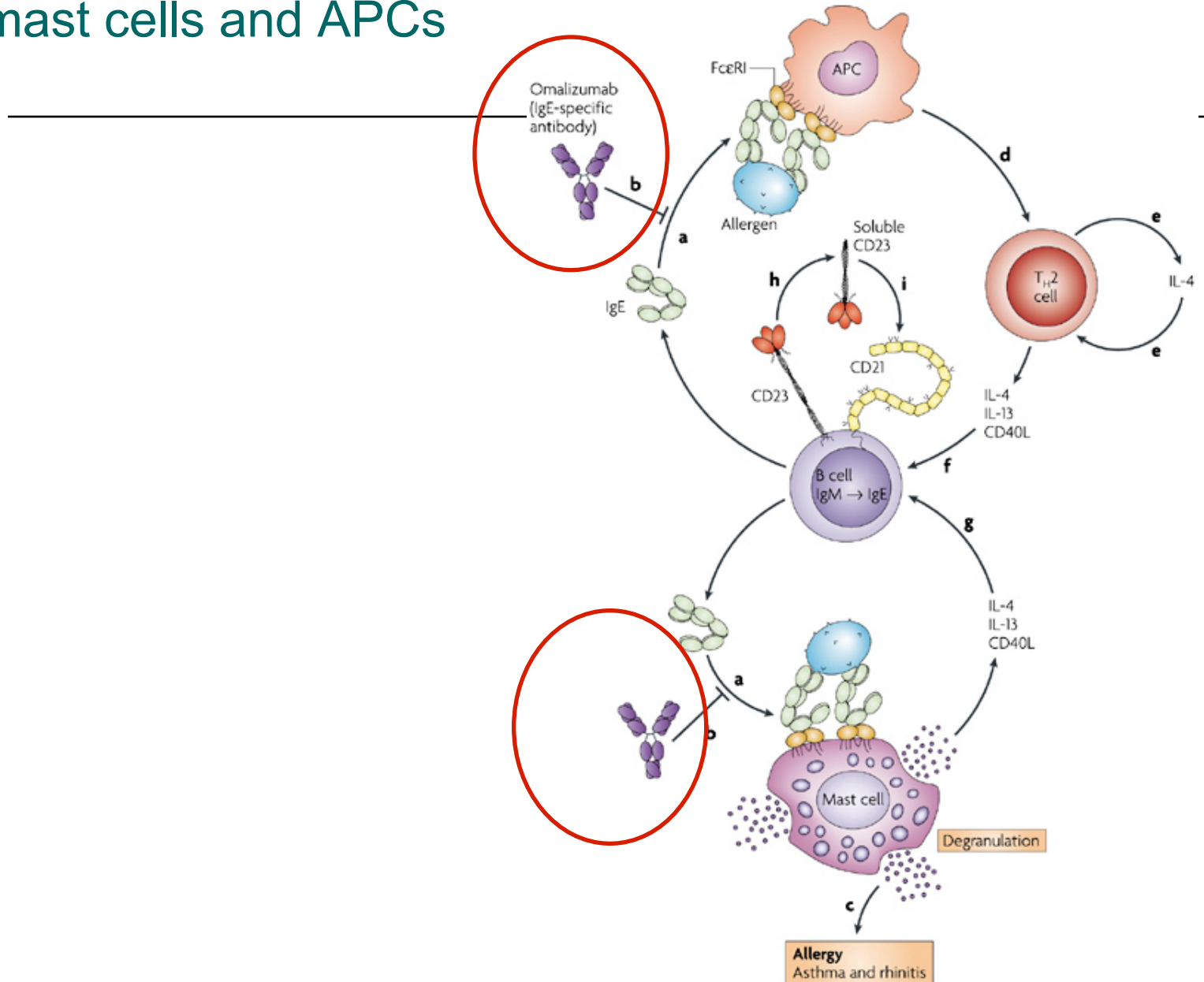


Skin prick test (SPT)= in vivo allergen skin test

- More sensitive but less specific than allergen specific IgE detection
- UK allergen groups: dog, cat, house dust, mite, grasses



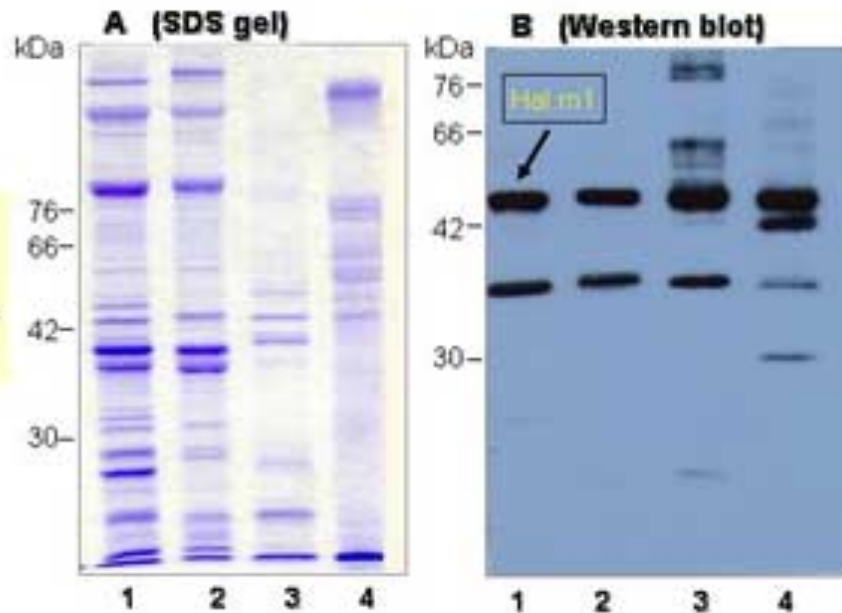
Omalizumad inhibits the binding of IgE to FcεR of mast cells and APCs



In vitro tests: – 1: total IgE

- Serum IgE 10 000x less than IgG
- Normal < 200ng/ml
- Allergy: 300-600 ng/ml

- 1. *H. midae*
- 2. *H. rubra*
- 3. Cooked *H. midae*
- 4. Dried *H. midae*



Tertiary structure of Parvalbumin, the major allergen found in most fish species

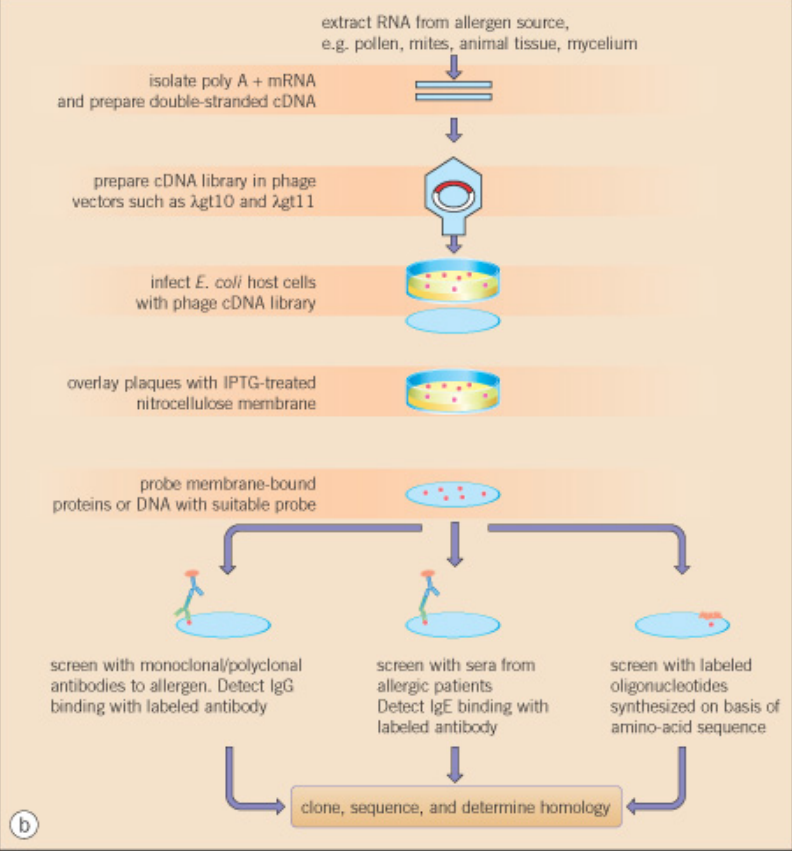
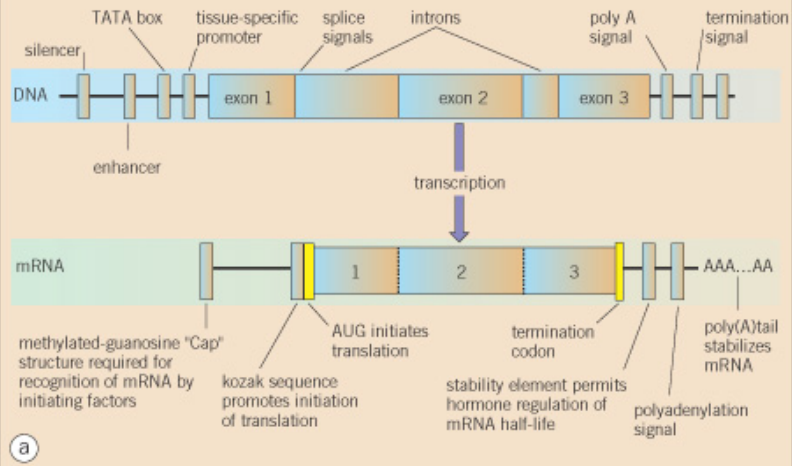
Novel allergens identified in *Haliotis midae* (abalone)



Isolation of allergens

- From the original allergen with water extraction, followed by chromatography
- Affinity chromatography with allergen specific monoclonal antibody
- DNA technique: cloning the allergen

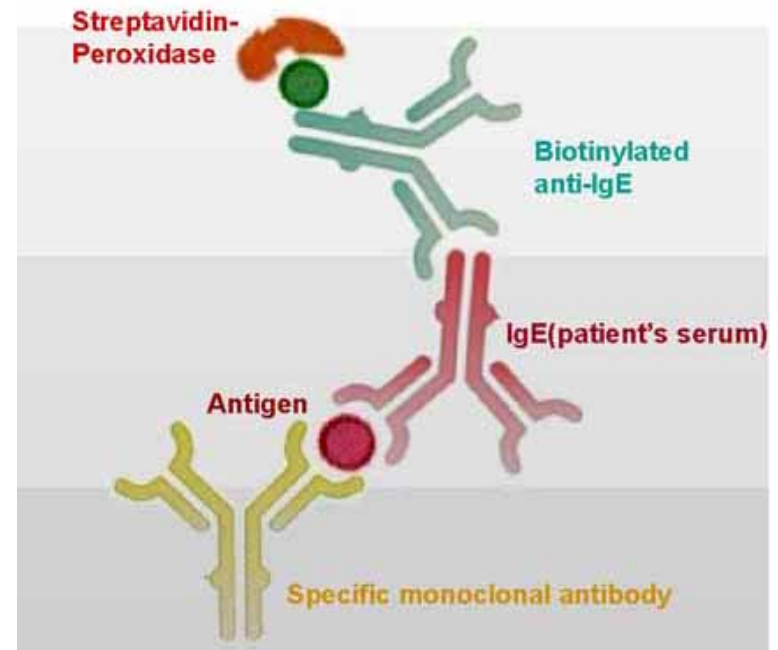
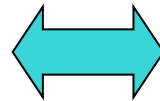
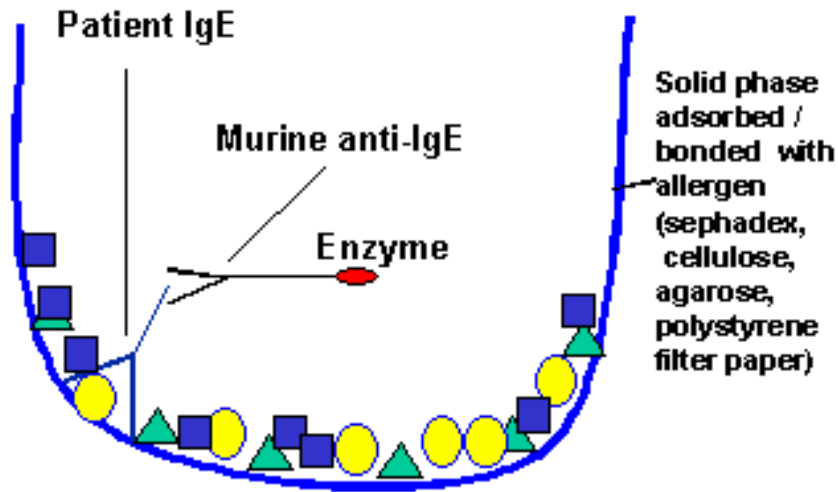
Cloning of Allergens



In vitro tests: – 2: allergén specifikus IgE

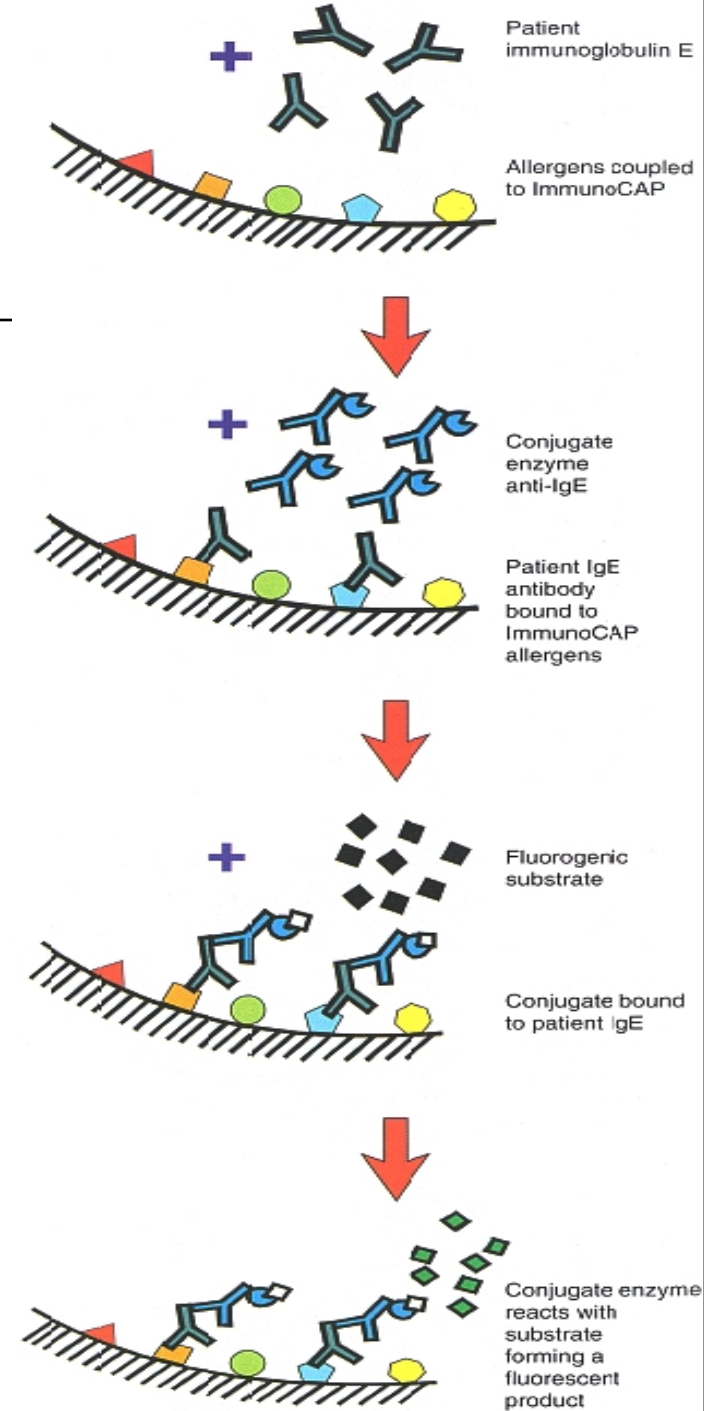
- RIA
- ELISA
- Chemiluminescent methods
- Western blot - Immunoblot

Allergen specific IgE ELISA sreen test



allergen specific mAb

ELISA

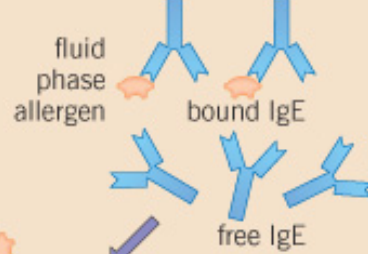


Allergosorbent Assays

EAST/RAST



EAST/RAST-inhibition



incubate with
solid phase
allergen

wash and
add labeled anti-IgE

wash and
determine response

a

RAST

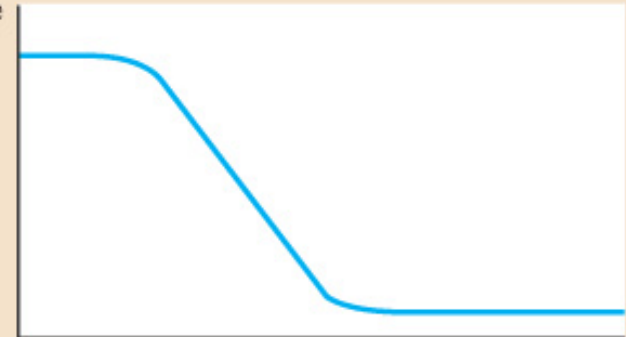
response



allergen or allergic serum

RAST-inhibition

response



allergen

b