Reactivity and Resistance

Allergy and hypersensitivity

Immunodeficiency states

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Reactivity

- **Species** (primary, genetically coded)
- **Group** (populational)
  - Gender
  - Age
- **Individual**
  - Physiologic
  - Pathologic

Non-specific
Specific
Types of reactivity

- Normergic (normergia)
- Hypergic (hypergia)
- Hyperergic (hyperergia)
- Anergic (anergia)
  - Positive (effective defense mechanisms)
  - Negative (undeveloped or "exhausted" defense mechanisms)

Modulating factors

- External (environmental)
  - Physical, chemical, biological
  - Society

- Constitutional (internal)
  - Gender
  - Age
  - Type of neural system
  - Profile of autonomic nervous system
  - Endocrine status
Resistance

- **Natural** (unreceptiveness)
- **Acquired** (in postnatal period)
  - Artificially
    - Active (vaccinations)
    - Passive (serotherapy, blood transfusion)
  - Naturally
    - Active (disease)
    - Passive (AB through placenta or mother’s milk)

Immunologic resistance

- Complex mechanism of defensive and adaptive reactions
- Highly specific response
- Aimed against
  - *external* (bacteria, viruses, etc.) *and*
  - *internal* (functionally inefficient and mutated cells) factors.
Immune response - phases

1. Processing and presenting of the antigen

2. Recognition of the complex MHC *- antigen with activation of $T_H$ lymphocyte

3. Activation of B-cells and/or T-cytotoxic lymphocytes

4. Elimination of the antigen

* MHC = Major histocompatibility complex

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Immune response - mechanism
Stimulation of $T_H$ lymphocyte

$T_H^1$ and $T_H^2$ immune reactions
Immunological memory

Allergies in the past

- In 4 b.c. the Greek physician Hippocrates (460BC-370 BC) noticed that particular foods, although harmless for some people, cause disease in others.

- Galen (AD 131-201) also wrote about allergic reactions to some plants, but he proposed no explanation for that phenomenon.
Anaphylaxis

- 1902 г. Charles Richet, together with Paul Portier - **Anaphylaxis**
- 1913 г. Charles Richet received a Nobel prize for his contribution in the field of anaphylactic reactions

Allergy

- 1906 *Clemens Peter von Pirquet* and Bela Schick – **аллергия** (greek *Allos* – other и *ergon* – reaction)

- **Pirquet** reaction – skin tuberculin scarification test, upon which Mantoux in 1907 introduced a test for diagnosis of tuberculosis.
Definition

Pirquet, 1906 – Allergy is altered reactivity to a distinct antigen (allergen).

Gell & Coombs, 1968 – Hypersensitivity due to which immunologically induced tissue destruction develops.

General characteristics

- Allergic reactions are typical only for homeothermic animals and men
- Allergies are usually preceded by sensibilization and underlying genetic predisposition
- Allergies are immunologically mediated diseases
Allergens and routes of administration

- Pollens
- House dust mites
- Goose down, wool, furs
- Foods
- Animal products
- Cosmetics, dyes, plastics
- Medicines

- Inhalant allergens
- Ingestant allergens
- Contactant allergens
- Injected allergens

Pollens
Reproductive structures of anemophilous plants

- Grass
- Hey
- Weed
- Poplar
- Birch
- Molds
Foods
The most common food allergens are:

- Milk
- Eggs
- Peanuts
- Fish
- Clam shells
- Soy, sesame
- Wheat

House dust mite
Dermatophagoides pteronyssinus (D. Farinae)

- Parasite in the upper layer of the human skin
- Their feces contain a protein (enzyme) which appears to be common allergen
Medicines

- Antibiotics
  - Penicillin
  - Tetracycline
  - Sulphonamides
- NSAIDs*
  - Salicilate
  - Opiates
- Local anesthetics
- Antiepileptic drugs

*NSAID – non-steroid anti-inflammatory drug

Allergic reactions
Hypersensitivity - types

- **Humoral type**
  - Anaphylaxis
  - Cytotoxic reactions
  - Immune complexes

- **Cell-mediated type**
  - Mixed

### Classification of Gell & Coombs (1963)

<table>
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<tr>
<th>Type</th>
<th>Alternative names</th>
<th>Often mentioned disorders</th>
<th>Mediators</th>
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</table>
| I          | Allergy (immediate) | - Atopy  
- Anaphylaxis  
- Asthma | IgE |
| II         | Cytotoxic, antibody-dependent | - Autoimmune hemolytic anemia  
- Thrombocytopenia  
- Erythroblastosis fetalis  
- Goodpasture's syndrome | IgM or IgG  
(Complement) |
| III        | Immune complex disease | - Serum sickness  
- Arthus reaction  
- Systemic lupus erythematosus (SLE) | IgG  
(Complement) |
| IV         | Delayed-type hypersensitivity (DTH), cell-mediated immune memory response, antibody-independent | - Contact dermatitis  
- Mantoux test  
- Chronic transplant rejection  
- Multiple sclerosis | T-cells |
Type I – cytotropic type

- Explosive response - within minutes of contact with the allergen
- Mediated mainly by IgE
- Mediators of anaphylaxis
  - Preformed
    - Histamin
    - Serotonin
  - Newly created
    - Metabolites of arachidonic acid
    - Cytokines
- Atopic diseases – bronchial asthma, allergic rhinitis, urticaria etc.
Type I – clinical signs

Signs and symptoms in a patient with acute asthma attack
Type II – Cytotoxic Antibody Reaction

- Mediated by IgG and IgM to specific antigens
- Endogenous or exogenous (haptens) allergens

Examples
- Transfusion Reaction
- Rhesus Incompatibility (Rh Incompatibility)
- Mycoplasma pneumoniae related cold agglutinins
- Hashimoto's Thyroiditis
- Good pasture’s Syndrome
- Delayed transplant graft rejection

Type II – mechanism

A. Complement-dependent
- Target cell
- + Ab
- + Complement
- C3b
- C5b-9
- Membrane attack complex
- C3b
- Macrophage
- Phagocytosis
- lyse

B. ADCC
- Target cell
- + Ab
- + Complement
- C3b
- T cell
- Fc receptor
Type III: Immune Complex Reaction

- Antigen-antibody complexes deposit in tissue
- Reaction within 1-3 weeks after exposure

Examples
- Systemic Lupus Erythematosus
- Erythema Nodosum
- Polyarteritis nodosa
- Arthus Reaction (e.g. Farmer's Lung)
- Rheumatoid Arthritis
- Elephantiasis (Wuchereria bancrofti reaction)
- Jarisch-Herxheimer Reaction
- Serum Sickness

Localized or generalized vasculitis

Type III – mechanism
Type IV: Delayed-Type Hypersensitivity

- Mediated by T-Lymphocytes to specific antigens
  - Involves major histocompatibility complex (MHC)
  - Reaction within 2-7 days after exposure
- Examples
  - Mantoux Test (PPD)
  - Allergic Contact Dermatitis (e.g. Nickel allergy)

Type IV – mechanism

1. Antigen is introduced into subcutaneous tissue and processed by local antigen-presenting cells
2. A T\(_\text{H}1\) effector cell recognizes antigen and releases cytokines which act on vascular endothelium
3. Recruitment of T cells, phagocytes, fluid, and protein to site of antigen injection causes visible lesion

24-72 hours
Contact allergies

Diagnostic tests I

Skin tests are carried out with small quantities purified allergens

- **Skin prick test:** drop of the allergen is placed on the skin and a small quantity is introduced into the skin.

- **Intradermal test:** allergen is injected intradermally
Skin prick testing

- Scarification testing: the skin is scratched and then a drop of the allergen is placed upon.

- Testing with adhesive tape containing known allergens (eczema, contact dermatitis)

Diagnostic tests II
Antiallergic therapy

- Allergen avoidance
- Immunotherapy
  - Specific hyposensibilization
- Drug therapy
  - Antihistamines,
  - $\beta_2$ mimetics,
  - Corticosteroids,
  - Adrenaline

Allergen avoidance
Thank you!