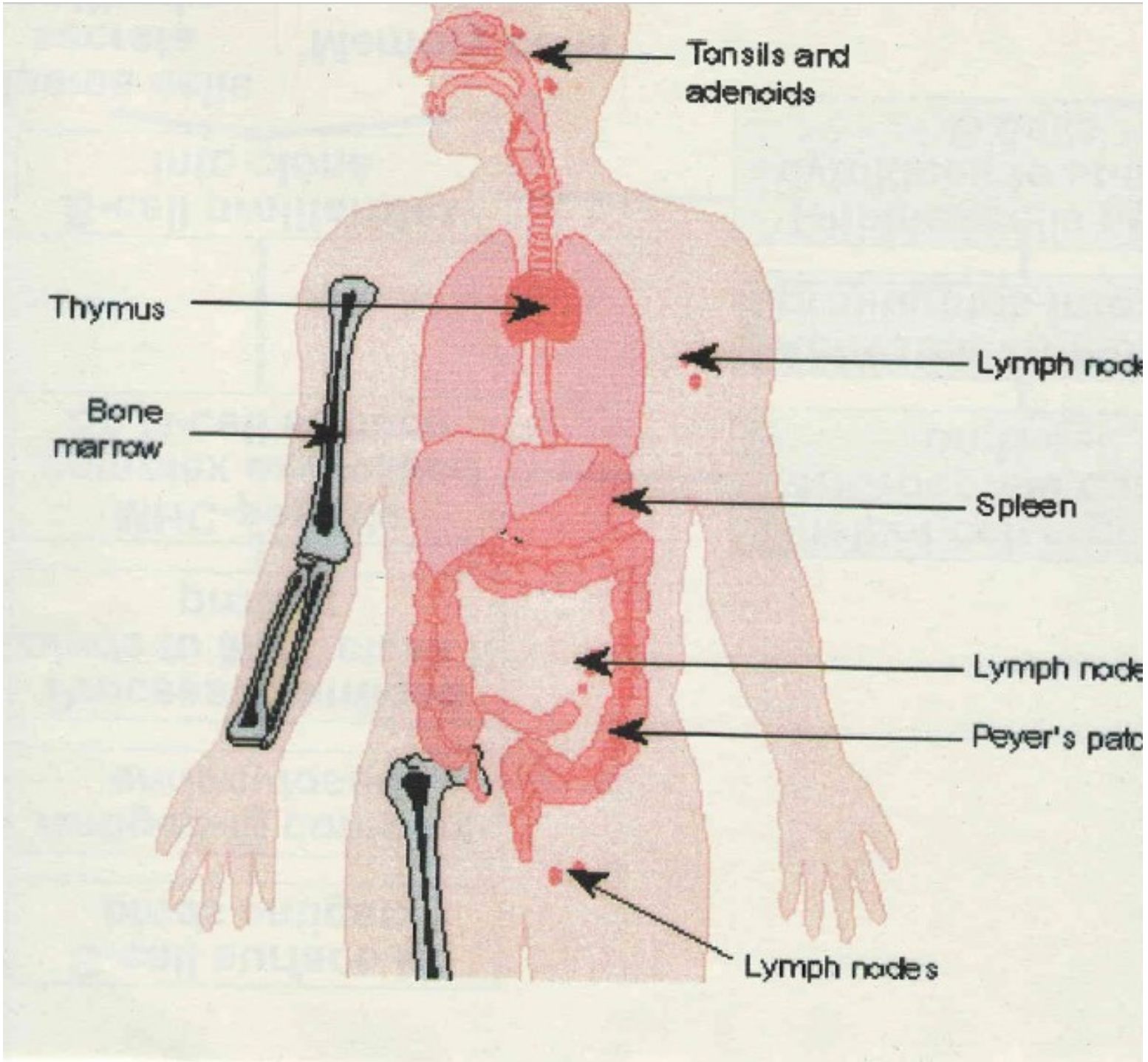
IMMUNE SYSTEM

It took 400 million years of evolution than our immune system developed into a highly complex and adaptable mechanism.

The role of the immune system is underestimated, it is very important and has its logic.

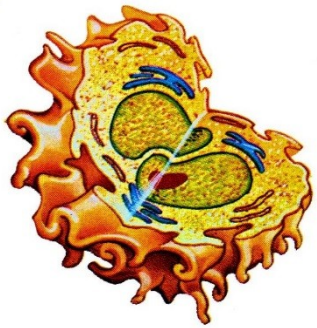

Tonsils and adenoids
Thymus
Bone marrow
Lymph node
Spleen
Lymph node
Peyer's patc
Lymph nodes

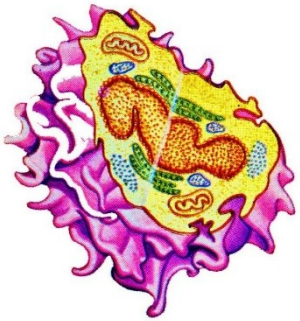
LEUKOCYTES

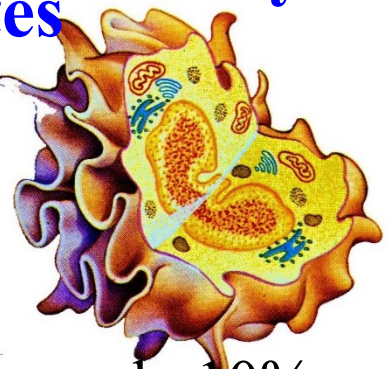
granulocytes

agranulocytes

neutrophils **basophils** **eosinophils** **lymphocytes** **monocytes**







60% do0,5% do 5% 20-50% do 10%

Basic dyes acidic dyes

lymphocytes lymphocytes lymphocytes

T **B** **NK**

70-80% 10-15% **Natural killer cells**

IMMUNITY

- the ability to recognize and tolerate the substances of the body
- to recognize a foreign body - to defeat the body against the attack (eliminate foreign matter)
- removal of non-functional or damaged cells of the organism
- supervision of the removal of body substances of their own but which have alienated the body = heterologous (eg tumor) cells

IMMUNITY

INNATE

(non-specific)

We are born with her - defensive responses are still the same, they hit at the same speed in the same way

ACQUIRED

(specific)

We obtaine it when meeting with various antigens; the system reacts for the first time slowly, but at a later meeting it is faster and more efficient

CELLULAR

HUMORAL

CELLULAR

HUMORAL

LYMFOID ORGANS

Central:

Thymus - - does not participate in immune reactions
- Provides a T cell maturing environment

Bone marrow

(Bursa Fabrici in birds, its equivalent in mammals – lymphoid tissue in GIT, appendix) – provides a B cell maturing environment

Peripheral:

Lymphatic nodes - a filter for foreign particles and tissue debris

Spleen

Lymphoidal tissue with mucosa - diffuse lymphoid tissue of mucosal surfaces (digestive tract, respiratory system, kidney system)

Tonsiles - located at the site with the greatest contact of the antigens, the deep crypts facilitate the capture of foreign particles, from where they are transported to the lymphoid follicles

ANTIGEN - the ability of the molecule to respond with products of obtained immunity - with antibodies - compounds may react with antibodies but may not induce an immune response

IMUNOGEN - a molecular or supramolecular structure that can cause an immune response in the recipient

- All ***immunogens are antigens***, but *not all antigens are immunogens*
- *PAMPs* - Pathogen Associated Molecular Patterns) - lipopolysacharides in bacterial membranes
- *PRR* - Pathogen Recognition Receptor – recognize PAMPs

- PAMPs – Pathogen Associated Molecular Patterns – they are not commonly found in the body (liposaccharide G bacteria, double strand RNA viruses, manan saccharide forming yeast wall)

- PRR – in our body, main function – recognise patogens

=Pathogen Recognition Receptor - recognise PAMPs - our body has its structure built into its genetic code, because co-existence with pathogens has taken a long time, and information about PAMPs has come to our DNA

Types of PRR

- PRR in circulation (solubile PRR) – e.g. manose binding lectin (MBL) - start of complement cascade
- PRR on cell membrane be able:
  - Initiate endocytosis (e.g. - scavenger receptors on macrophages - +Ag – starts phagocythosis
  - Activate intracelular cascade (e.g. TLR – toll like receptors + PAMPs – induce cells division, cell death, production ROS)
  - PRR intracelular

IMUNOGENITY depends on:

- Biochemical structure

proteins

complex sacharides+proteins (as glykoproteins)

lipids – complex: lipids + proteins – lipids +polysacharides

Nucleic acid – complex: nucleic acid + proteins

- Molecular weight

Ideal - 10 000

- dose

Ideal – optimal dose

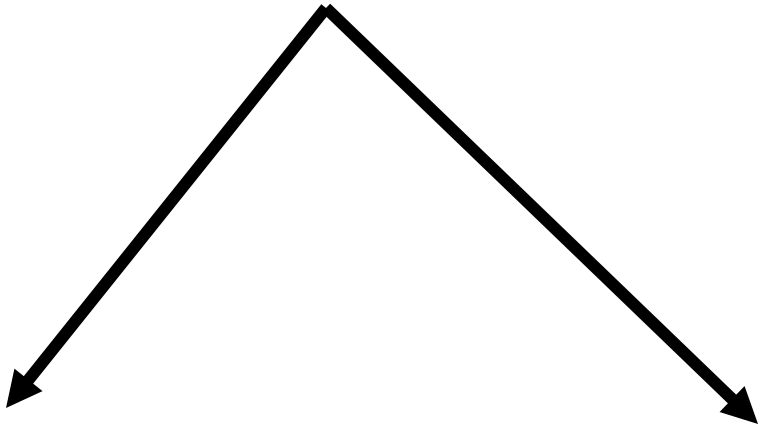
- Biological factor

As age, level of hormones, genetics

INNATE = NON-SPECIFIC IMMUNITY

- the ability of a „normal animal“ to survive in an environment without the damage resulting from infection by certain microorganisms
- not related to previous individual experience with pathogenic microorganisms

INNATE= NONSPECIFIC IMMUNITY



CELLS mediated

MONOCYTES / MACROPHAGES
GRANULOCYTES
-phagocytosis
NK (naturale killers) cells
- natural toxicity

HUMORAL

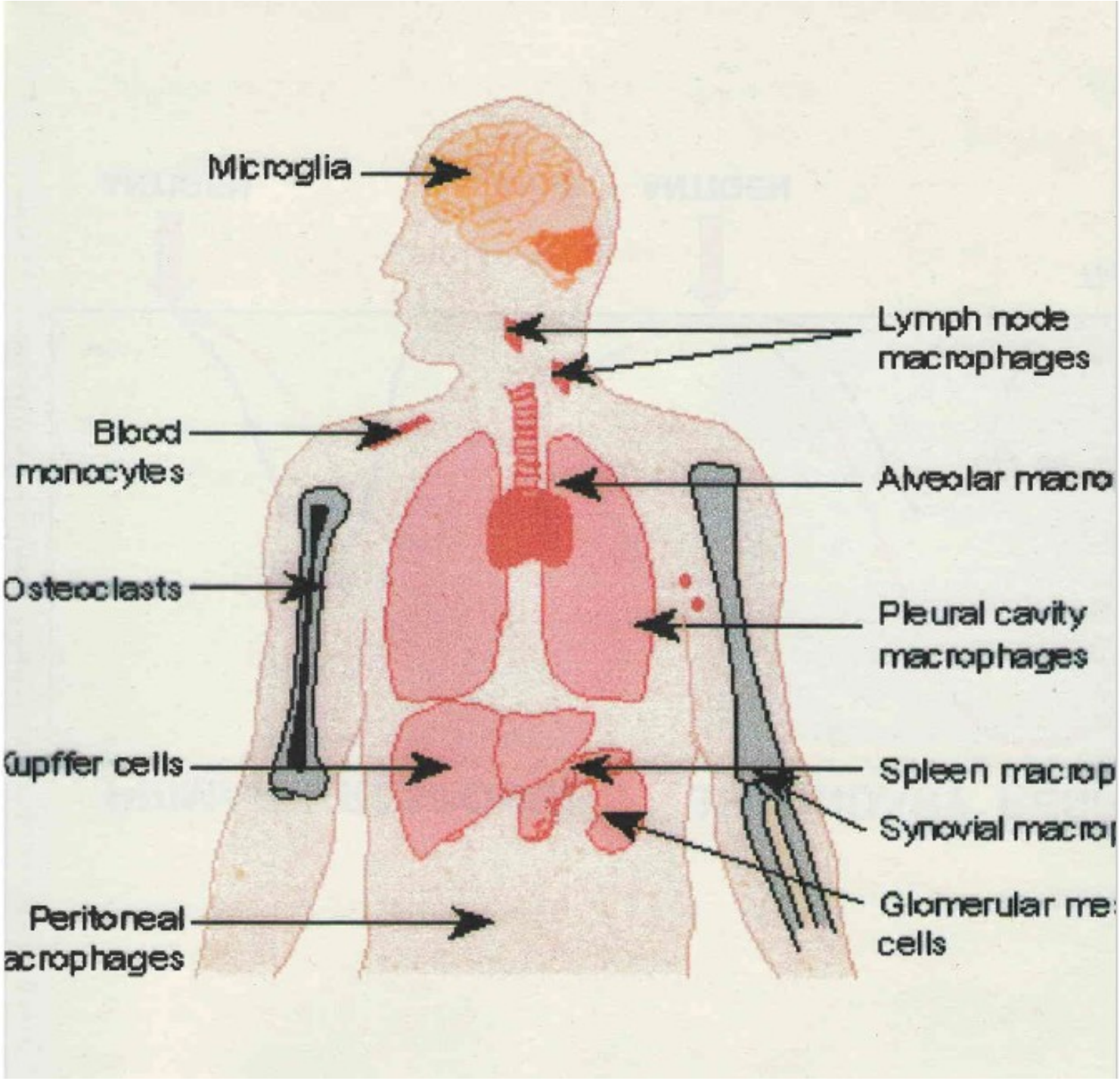
COMPLEMENT
-alternative way
LECTINES
-C reactive protein
INTERLEUKINES
INTERFERONES

MONOCYTES AND MACROPHAGES

A set of cells spread throughout the body gifted with the ability of phagocytosis

MONOCYTES- they circulate in the blood for several hours and then travel to the perivascular space where they develop into large MACROPHAGES (increase in volume: 20-40µm in diameter, increase in amount of lysosomes ... to be effective removers); from Greek-macro (as a large), phagein (as eat)- serves 2 functions: 1)the phagocytosis of pathogens or cellular debris +2) the presentation of antigens to lymphocytes

(Note: monocytes produce endogenous pyrogens - induction of prostaglandin E2 formation in the blood-brain barrier - mechanism of fever)

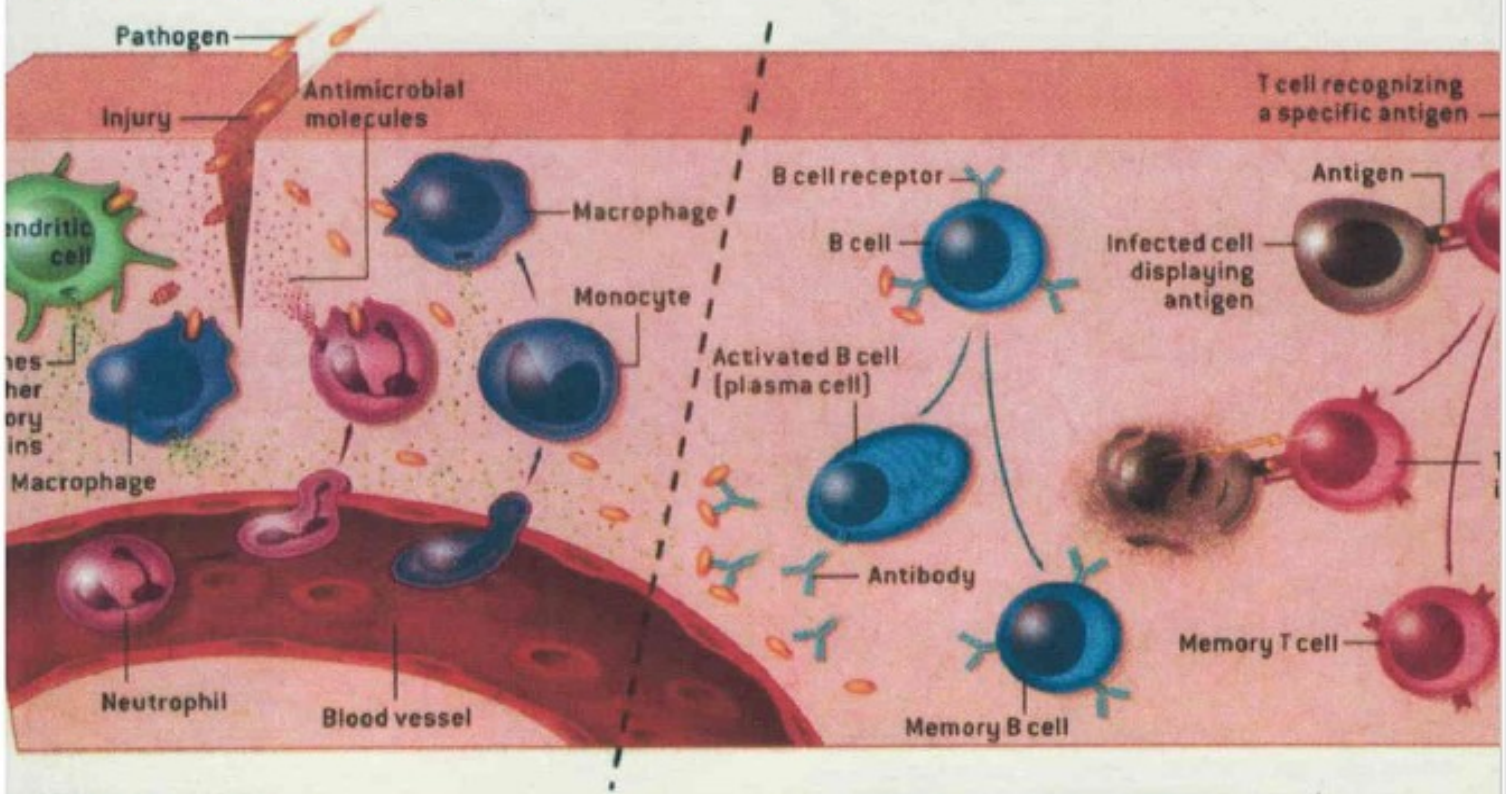

Microglia
Lymph node macrophages
Blood monocytes
Alveolar macro
Osteoclasts
Pleural cavity macrophages
Kupffer cells
Spleen macrop
Synovial macro
Glomerular me cells
Peritoneal acrophages

Nonactivated dendritic cells

- Langerhans´s cells of epidermis (from monocytes)
- Are in the skin and mucose
- Its dendrites penetrates to the skin layers or mucose
- = antigen presenting cells

THE DIVISIONS OF THE IMMUNE SYSTEM

nmalian immune system has two overarching
s. The innate part (*left side*) acts near entry points
body and is always at the ready. If it fails to
contain a pathogen, the adaptive division (*right sid*
mounting a later but highly targeted attack against
the specific invader.



E IMMUNE SYSTEM

tem includes, among other components, antimicrobial
es and various phagocytes (cells that ingest and destroy
ns). These cells, such as dendritic cells and macrophages,
ivate an inflammatory response, secreting proteins called
s that trigger an influx of defensive cells from the blood.
he recruits are more phagocytes—notably monocytes
an mature into macrophages) and neutrophils.

ADAPTIVE IMMUNE SYSTEM

This system "stars" B cells and T cells. Activated B cells se
antibody molecules that bind to antigens—specific compo
to a given invader—and destroy the invader directly or ma
attack by others. T cells recognize antigens displayed on
T cells help to activate B cells and other T cells (*not shown*
directly attack infected cells. T and B cells spawn "memor
promptly eliminate invaders encountered before.

PHAGOCYTOSIS

Migration - phagocytes travel towards the particles to be absorbed. When traveling from vessels, they adhere to the endothelium (adheresis) and stretch out between individual endothelial cells (diapedesis). ***Phagocytosis*** – the phages of a series of individual steps **recognize** the foreign particles, **adhere** it *(adheresis)* and **ingest it** *(ingestion)*. Then follows releases of granule content into phagocytic vacuoles (*degranulation)* and increseas of intensity its oxidative metabolism (*respiratory flare*).

- phagocytosis can be facilitated by binding "flavorings" - OPSONINS (antibodies or complement)

Nature Killer cells

- defense against viral infections and tumor cells without the need to recognize HLA on the target cell
- have no antigenic specificity, no immunological memory
- killing activity is activated by interleukins
- Easily kills cells "flavored" by the antibody

NEUTROPHILS - microphages

- body defense against penetrating microorganisms - against bacteria
- cytoplasmic granules include digestive enzymes (use for intracellular or extracellular killing and digestion of microorganisms – lysosomal enzymes, peroxidase, collagenase and other enzymes capable of digesting foreign material.

In the presence of chemotactic attractant, neutrophils approach foreign substances, such as bacteria, to phagocytose them within a phagocytic vacuole. By a proces known as degranulation, granules merge with the vacuole and empty their contents into the vacuole. Bacteria are destroyed within the vacuole by the action of hydrogen peroxide (H_2O_2) and the superoxid anion radical.

BASOPHILS (inducers of inflammation - the granules contain histamine = blood form of mast cells, histamine in the surrounding area causes vasodilatation and increases the permeability of blood vessels - makes the site of inflammation available to other cells)

EOSINOPHILS

– killing parasites: the granules contain major basic protein (MBP), which is toxic to parasites, as well as other enzymes. These cells are important in the response to parasites and viruses.

– secondary: also play a role in allergic reactions (e.g. asthma)

Inflammation

- It is the non-specific reaction of the organism to damage, which is macroscopically described by five so-called Celsi characters:
  - Rubor – redness
  - Calor – increase of temperature
  - Tumor – edema
  - Dolor – pain
  - Functio laesa – damage of function

Non specific humoral immunity

- **Bazic polypeptids** – spermin, defenzines
- **Acid substances** – lactat, HCl in
- **Lysozym** – enzym in saliva, on mucos membranes, in tears
- **Cytokines** – substances for communication between the cells

COMPLEMENT *complemented of effects of antibodies*

- a group of proteins in blood serum (C1-C9) activated by a special stimulus as a cascade-like way, normally inactive
  - complement + antigen in cell surface – this binding leads to irreversible cell damage – cytolysis
- **classic pathway** - complement je activated by complex antigen-antibody type IgG or IgM (on this imunocomplex then binds component C1, activates cascade C2-C4-C3-C5-C6-C7-C7-C8-C9; not completely straightforward, some components fall into two parts)
- **Basic 3 complement features:**

Opsonization (marking "this is alien" + „flavoring“ as a spices for better flavor)

Chemotaxe (lure of other cells)

Osmotic lysis of the microbe (disruption of the cell membrane and destruction of the enemy - C9 has the shape of a wedge, locks, damages the membrane, penetration of water or sodium into the cell, ionic dysbalance)

COMPLEMENT

Alternative way - complement is activated via surface bacterial polysacharides

Lectin way – helps to fight yeast infections (mannan is attached to the yeast surface by mann-binding lectin, which becomes part of the immunocomplex that activates the C3 complement

NON-SPECIFIC IMMUNITY

Cutaneous and mucosal barrier

SKIN - dry, contains bactericidal substances from sweat and sebum
- settlement by "foreign" bacteria is hampered by presence „own“ = symbiotic bacteria (microflora)

GASTROINTESTINAL TRACT

oral cavity - separation of superficial epithelial cells
- the presence of bactericidal (bacteria killing) substances in the saliva

stomach - the presence of hydrochloric acid (HCl)

intestine - effects bile acids
- mucus in the intestinal mucosa
- normal intestinal microflora
- fast-recovering intestinal mucosa
- submucosal phagocytes

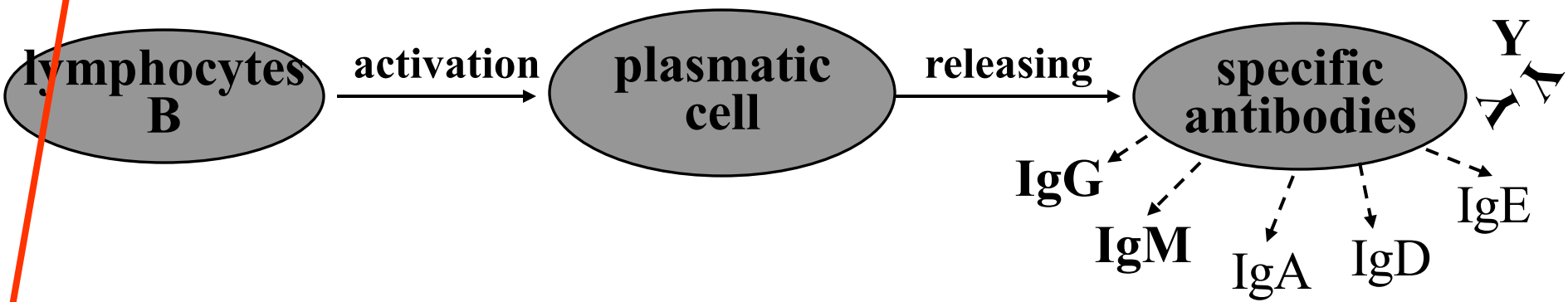
reflexes - vomiting

RESPIRATORY SYSTEM - ciliary epithelium removes mucus with entrapped bacteria and impurities into the pharynx, followed by swallowing and destruction of HCl in the stomach
- Antibodies and virus inhibitors are present in mucus
reflexes - sneezing, cough, bronchoconstriction (narrowing of the bronchi)

URINE TRACT - Fast urine flow; - mucus and slightly acidic secretions
FEMALE VAGINA - "Döderlein's" lactobacil - produces lactic acid that prevents the growth of other bacteria
EYE - blinking and washing with tears (bactericidal substances)

SPECIFIC IMMUNITY

HUMORAL – mediated B lymphocytes



CELL Mediated – mediated T lymphocytes

T lymphocytes which represents 70-80% of peripheral lymphocytes in blood; undergo maturation primarily in the thymus, where they train to recognize their own antigens and destroy foreign antigens

B-lymphocytes – represents 10-15%, undergo maturation on bone marrow and peripheral lymphoid tissue. When B lym integrate with antigen in the presence of T cells and macrophages, B cells can transform into plasma cells which abbundantly make and secrete antibodies that are directed against specific antigens

MAIN HISTOCOMPATIBILITY COMPLEX (MHC)

For the successful functioning of the immune system, this system must be able to distinguish „forigner" from "own". This distinction is achieved through MHC (main histocompatibility complex) molecules in the cell membrane. In humans, the system is found on leukocytes and is referred to as human leukocyte antigen (HLA)

Class I - present on all nuclear cells - presents a "foreign" molecule (viral, tumor) cytotoxic T lymphocytes (during transplantation, the class I molecule on recipient organs is directly recognized by recipient leukocytes - graft rejection)

Class II - on the surface of antigen presenting cells (APC)
(lymphocytes B, macrophages, T-cell activation, thyroid cells, endothelial cells)

- submits foreign molecules to helper T cells (in bone marrow transplantation, molecules of class II with linked unknown proteins in the donor cells elicit a donor leukocyte response - graft versus host

- Specific immunity is always directed against a single specific antigen-antigenic determinant-epitope
- Recognising in Tlymfocyts - Tcell receptor (TCR) , in Blymfocyts - Bcell receptor (BCR)
- For activation – antigen must be presented

IMMUNOGLOBULINS

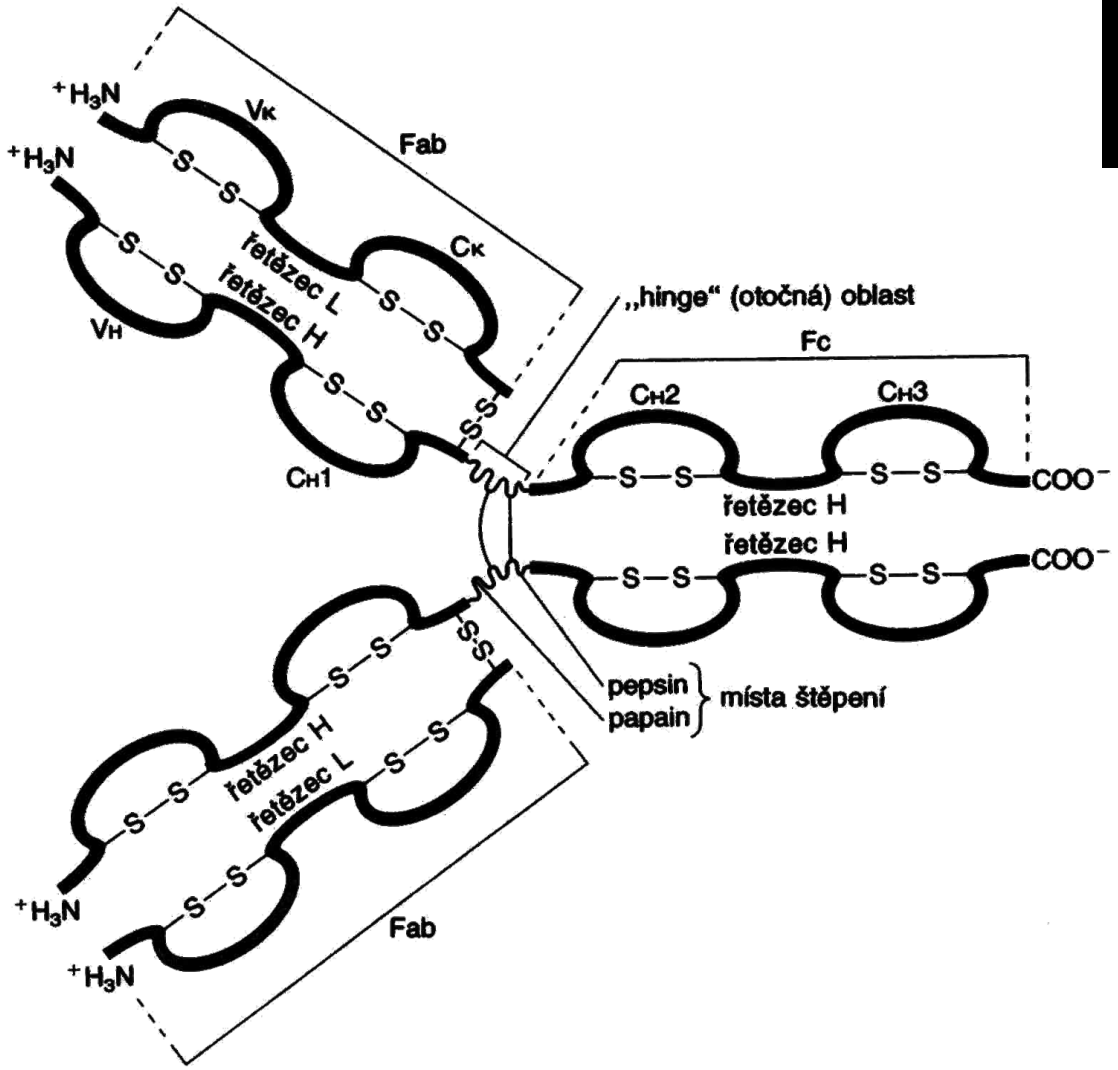
- proteins with antibody activity
  - bind to the antigen that caused their production
- **Ig G**–complement activation, passes through the placenta and provides for the defense of the newborn in the first few months of life, They are capable of OPSONIZATION - facilitate the absorption of bacteria by phage; anamnestic pt-we have already had a disease
- **IgA** (15%) - alpha chain, dimers pt on the mucous membranes - the dominant class of the mucosal immune system, neutralizes viruses and bacteria taken up by food - part of mucus of saliva, tears, breast milk

- **IgM** (10%) - the first antibody to early immune responses (macromolecular-large molecules, clustering bacteria / viruses in larger groups - well visible and phagocytable)

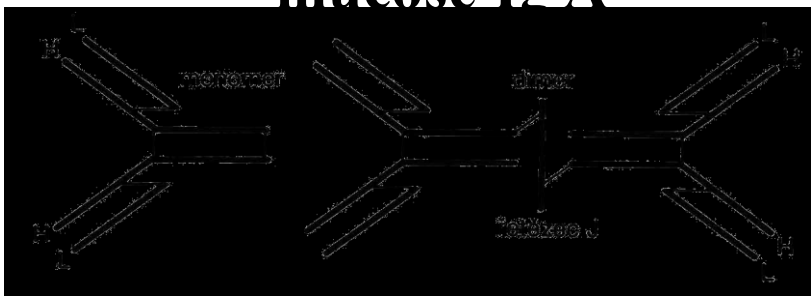
  IgD (0.2%) - delta-chain, monomers, structure identical to B cell receptors (BCR) - on B lymophocytes surface

  IgE (0.004%) - the eta chain; defense against parasitic bacteria
  - binding to mast cells causes release of histamine (allergy)

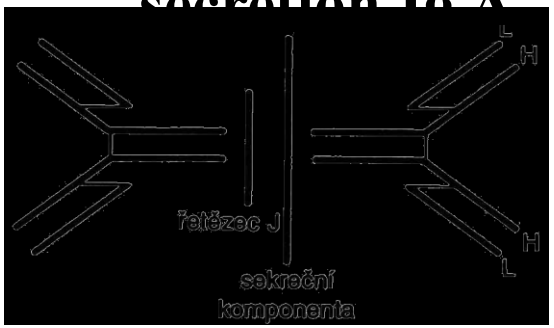
IMMUNOGLOBULINS structure

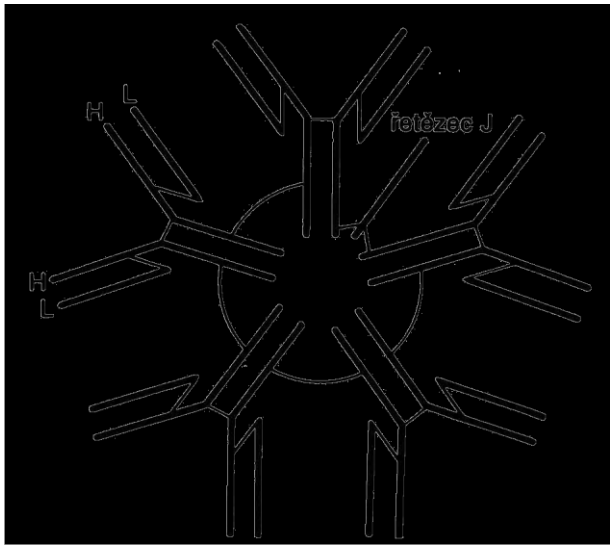


mucose Ig A



secretion Ig A





LYMPHOCYTES T

- bone marrow, maturation in thymus (take own Tcells Receptor)
- Started of immune answer
- Regulated function of any others leucocytes by special substances

classification according CD:

CD4+ - binding HLA II

CD8+ - binding HLA I

As co-receptors

Helper T cells (CD 4+)- increase odf answer B cells a cytotoxic T cells, production of interleukins

Cytotoxic T cells (CD 8+) – killer foreign cells (e.g. by vireus)

Supresor T cells (CD 8+)

How the cells of the immune system communicate together 1

- When an antigen gets into the body - it is presented through the APC to a specific immune system (if possible, the non-specific activated)
- If Ag is presented through HLA I (on all nuclear cells) - activation of CD8 lymphocytes - via cytotoxic mechanisms destroyed cells with antigen - fight with viruses + tumor cells, helper - NK cells

How the cells of the immune system communicate together 2

- If Ag is exposed via HLA II (found on APC) -activation of helper T lymphocytes (CD4)

  - Activation of TH1-Interferon gamma production - Increases cytotoxicity of macrophages and destroys the antigen - combating intracellular Ag

  - Activation of TH2-production of interleukins 4,5,6- promoted transformation of B lymphocytes into plasma cells - production of different classes of antibodies - those linked to Ag and destroying it + opsonizing it for nonspecific immunity (complement, granulocytes, NK) bacterial (parasitic) infections

CYTOKINES

- Large groups of chemical substances for regulation of immune cells

Interleukins (IL) – the main regulator of leukocyte development and activity (IL1-proinflammatory, main mediator of fever, IL2 produced by TH1, stimulates other T lymphocytes, IL4,5,6-produced TH2 - stimulate B lymphocytes to produce antibodies of different classes

Interferons – IFN alfa-beta – interfere with virus multiplication in the host cell, after infecting the cell with the virus-producing interferon-that diffuses to nearby cells; these cells slow down the proliferation; inhibit viral replication and propagation; give time for the immune system; IFN gamma - produced by TH1-lymphocytes, increased cytotoxicity of macrophages

Chemokins – stimulate the movement of the immune system cells towards the site of inflammation - mainly affecting granulocytes

IMMUNIZATION

Passive immunization - administration of specific antibodies (IgG)
- Immediate reaction with antigen, limited protection
- Your immune system is not activated
- no memory cells

Active immunization - administration of antigenic material (dead / attenuated viruses, bacteria or toxins)
- the need for administration long before contact with the antigen
- activation of the immune system
- memory cells are created - long-term immunity

IMMUNE DISORDERS

ALERGY - Exaggerated, disproportionate response of the immune system to a common external stimulus

AIDS (acquired immunodeficiency syndrome)
- Infectious disease, the HIV virus attacks the cells of the immune system
(T helper lymphocytes and macrophages), impaired defense ability

AUTOIMMUNITY DISEASE - disturbed ability to distinguish own cells from foreign ones, damage to their own tissues

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