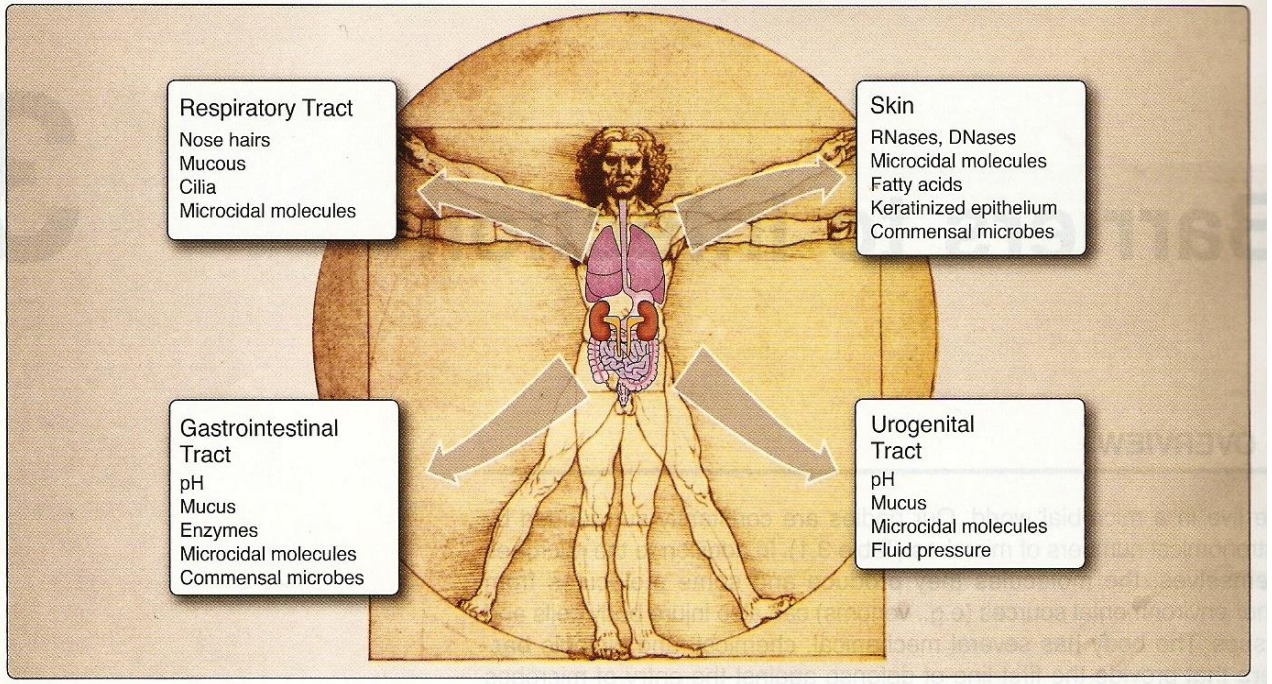
Immunology 2

Barriers

Cells

Nonspecific innate immune mechanisms

- innate
- prepared to react at once
- steady during the reaction
- same during the life
- the same type of reactions against any invader
- without memory
- same intensity
- always as for the first time



1st defensive line

- against microbes and substances they produce, against venon and mechanical dirties
- mechanical, biological and chemical barriers
- interfers with enter of invading microbes to the steril tissues

Barriers

- Skin – physical, chemical, microbes
- Mucous membrane GIT- physical, chemical, microbes
- Respiratory tract – physical, chemical, microbes
- Urogenital tract – physical, chemical, microbes

differently important

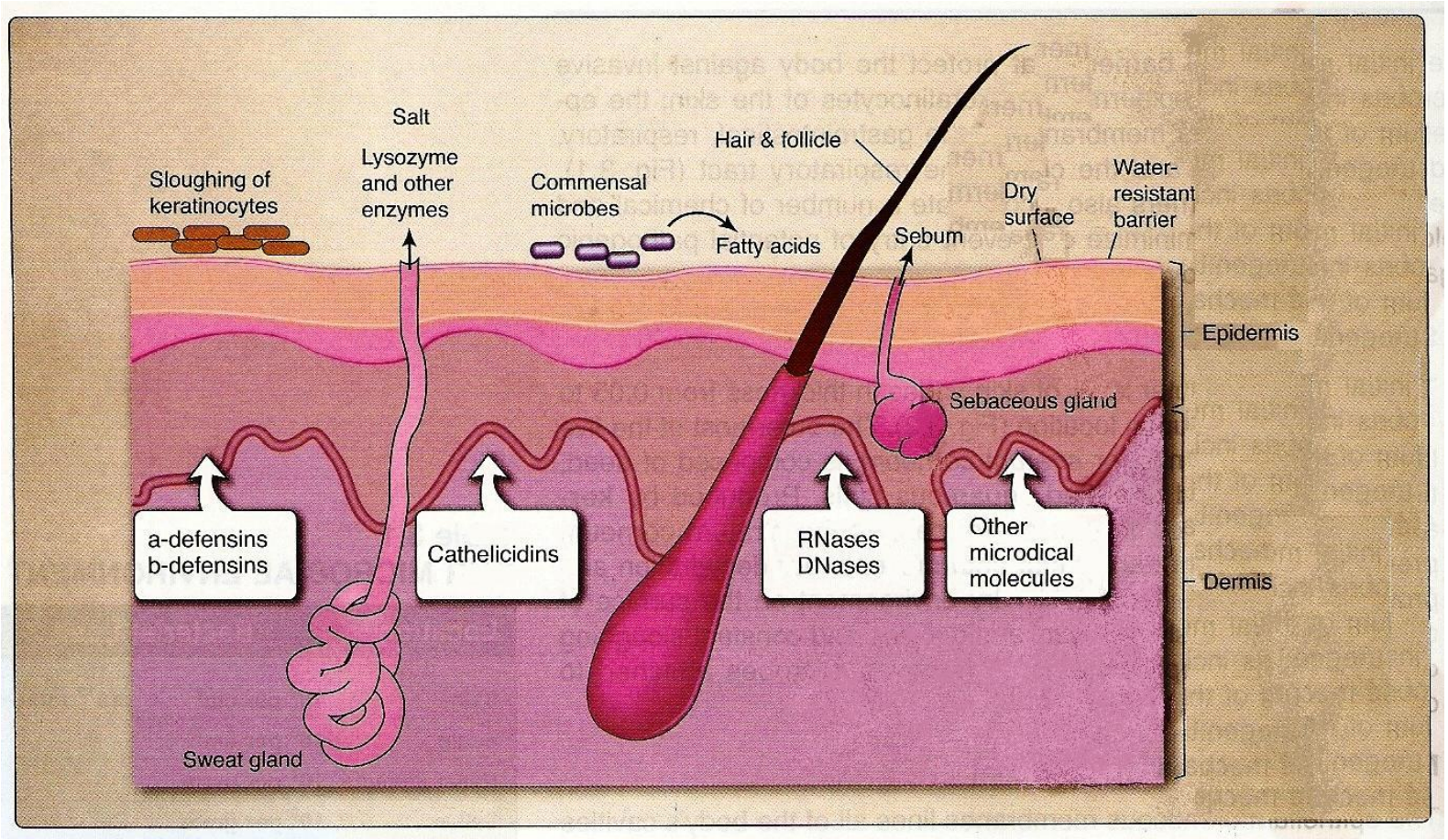
Physical barriers

- **Skin**

– different thickness

- 5 layers – 4 layers with differently mature keratinocytes – dividing sa :
- **stratum corneum** – outermost layer of dead cells, desquamating together with adhered microbes
- waterproof, interfere with dehydratation, unfavorable environment for microbes dry, salty
- (cooperation with *chemical and biological barriers – sweat, sebaceous glands, physiological microflora*)

Obranné mechanizmy kože

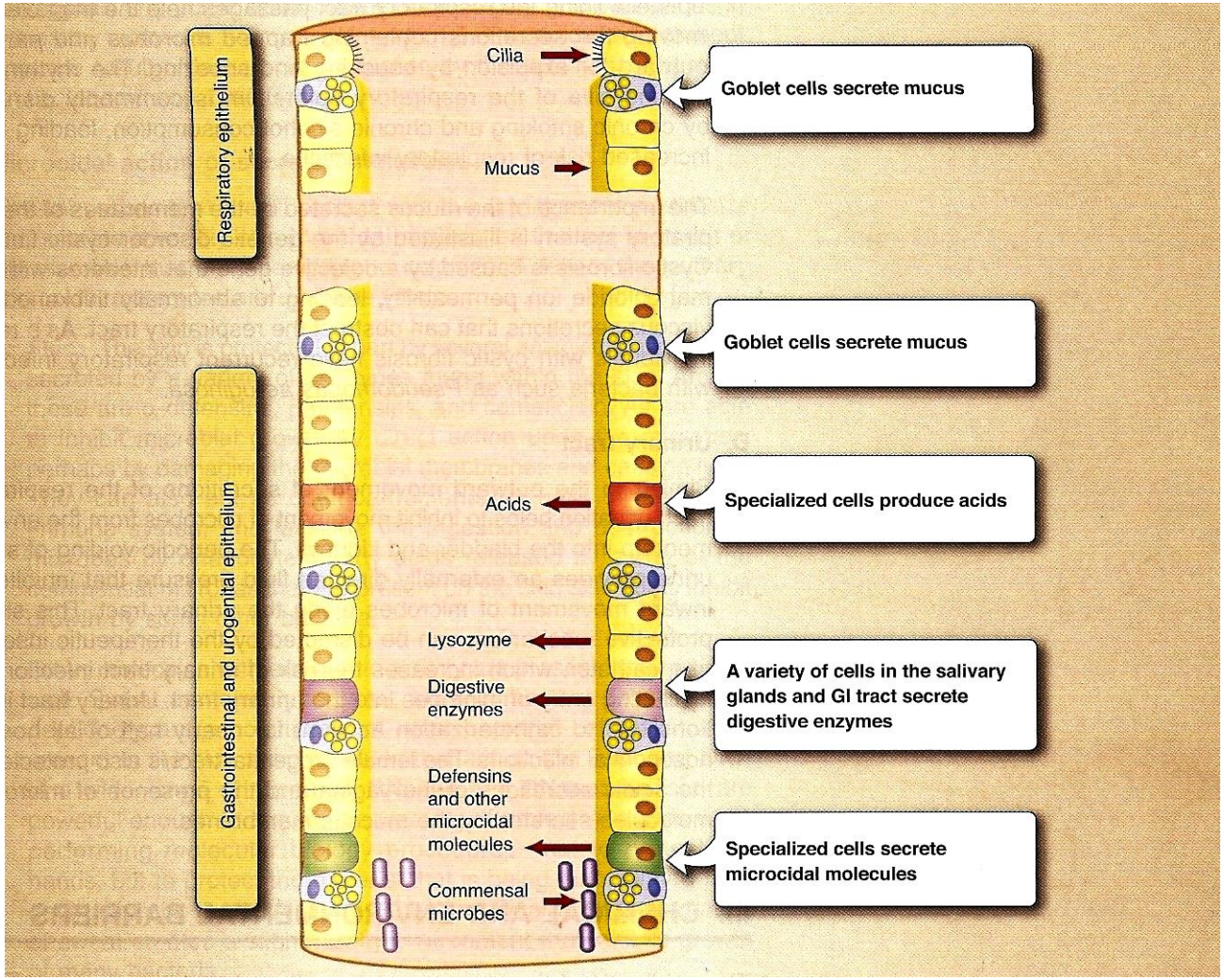


Physical barriers

- **Mucous membranes** – epitel cells overlying the body organs and are in contact with outside environment
- Changes of molecules and ions, interference with invaders, desquamation of superficial layers with microbes
- Epitel contain goblet cells, that secrete mucous (4 litres daily in GIT - reabsorbation)
- **Mucous** – mechanically catches microobes and dirties (respiration tract)

  - protection of tissue against digestive ensyms (GIT)

Obranné mechanizmy slizníc



Respiratory tract

- movement of tiny hairs in nostrils – mechanical capture of dirties (10μm)
- fimbriae of epitel cells – move dirties outwards – nasal secretion
- coughing and sneezing
- movement of fimbriae is disrupted by smoking and chronical consumption of alcool
- role of epitel and mucous – genetically based disease of permeability of chlorid ions **- Cystic fibrosis** – viscosity = repeating infections (*Pseudomonas aeruginosa*)

Urogenital tract

- Mechanical barriers
- Urination –interference of spread of bacteria to bladder, and upwards
  - exclusion of bacteria

Disease

- Firm adherention of microbes – fimbriae enable to adher on epitel (gonococcus, *E.coli*)
- Anatomical changes, strictures, stones – interfer with regular and strong flow of urine
- Cathetrisation – most common cause of infection in hospitalised patients

Chemical barriers

- pH – skin, sebaceous glands, vagina
- mikrobicidal substances – on skin, in sweat, tears, GIT, respiratory tract,
- lysosyne, RNáza, DNáza, HCl,

pH

medically important bacteria are neutrofil, pH < 6,0 inhibits their growth

Skin – sebaceous and sweat glands – slightly acid – pH kože 5,5., +lipids,

Stomac – few bacteria, pH 1,0 **-** 3,0 interfers colonisation

Vagina – pH 4,4 – 4,6 is the result of lactic acid production by metabolical activity of *Lactobacilli spp*. in glycogen containig environment

Microbicidal substances

- Different tissues, that are in contact with outside environment can secrete them – molecules inhibit or kill microbes, that are trying to colonise mucous membrane

Skin

antimicrobial peptids produced by cells in skin
– α,β – defensins, cathelicidin
– inhibits microbial growths directly or by disrupting membranes, or enabling ingestion

- chemoattractants for cells of innate nonspecific immunity

fatty acids – released by some commensals, inhibit growths of other bakcteria

Sweat

- **lysosyme** – ensyme disrupting peptidoglycans (part of bacterial cell wall)
- **RNáza a DNáza** – present on skin (very strong for causing denaturation of molecules in genetic tests)
- **Evaporation of sweat** produces salty environment, that inhibits growth of many bacteria

Mucous membrane

- **Respiratory tract** – microbicidal molecules – β-defensins. Make microbes more prepared for ingestion and destruction by phagocytosis
- **GIT** – mikrobicidal molecules – α-defensins., 22 digestive ensyms in saliva, stomach juice and intestin.
- Lysosyme in saliva – digestion and destruction of pathogens

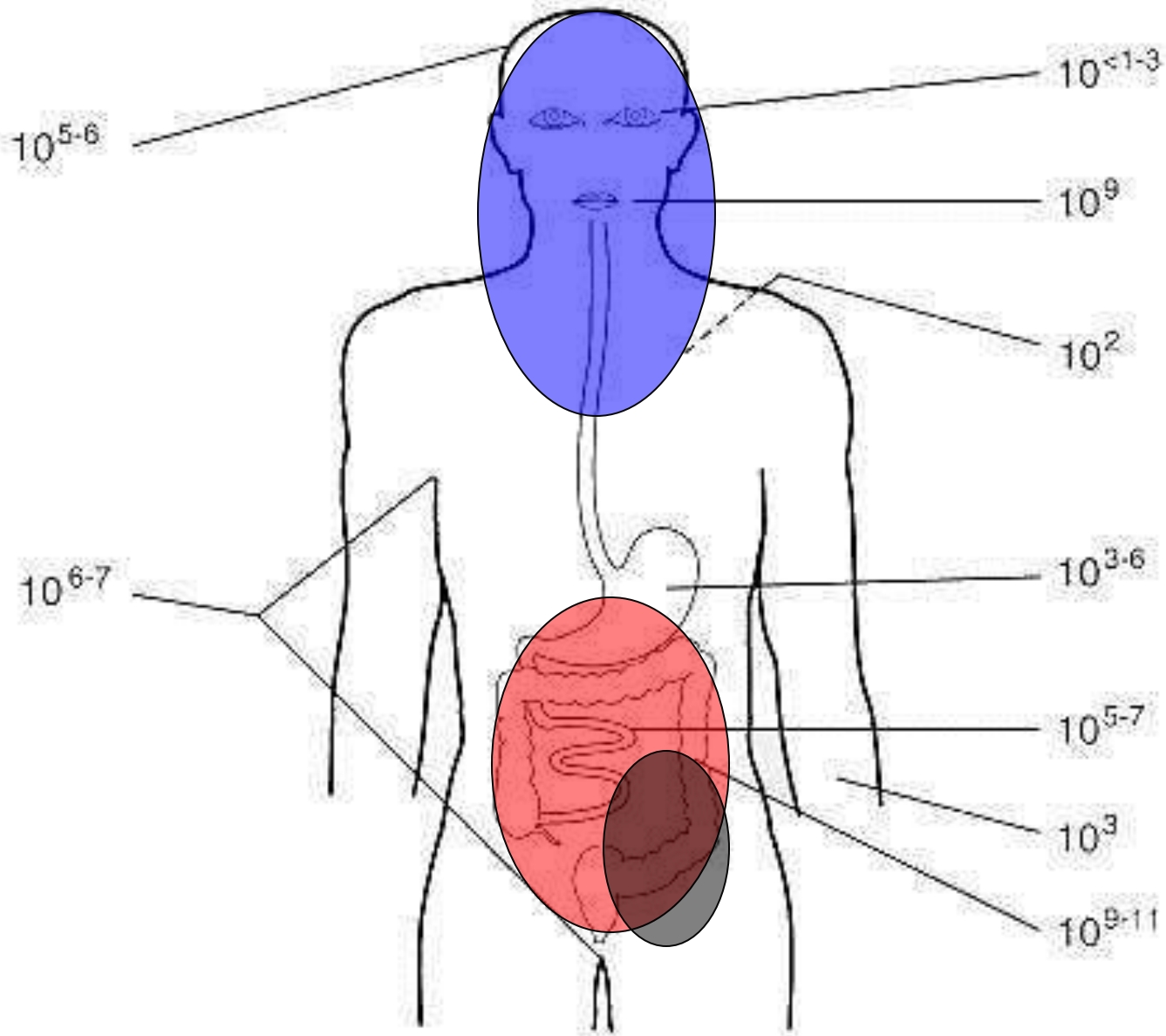
Tears

- Lysosym – antimicrobial activity – 1,4 glycosidic bound within peptidoglycan

Biological barriers- physiological flora

Microbial environment

- Skin 10^{12}
- Hairs $10^{6}/cm^{2}$
- Nasal secrets $10^{7}/g$
- Saliva $10^{8}/g$
- Mouth 10^{12}
- Stool $10^{8}/g$
- GIT $10^{14}/g$


10^{5-6}
$10^{<1-3}$
10^{9}
10^{2}
10^{6-7}
10^{3-6}
10^{5-7}
10^{3}
10^{9-11}

Benefits from IF

- Mutual control of composition based on:
  -the supervision of colonisation and implantation of pathogens (*Bifidobacteria* in colon of breast feeded child interfers with colonisation by enteric pathogens, *streptococcus viridans* - blocs colonisation by Candida in mouth
- producton of viatmins (K,B) - avitaminis in atb therapy
- competion for sources of energy
- immunostimulation

Possible risks from IF

- Facultative pathogens - in immunosupression
- Endotoxin- producing bacteria- constant intoxication
- Bacteroides - mutagen production - Ca of colon
- PNC-ase producing Staphylococci can interfere with therapy (PNC in eradication of gonococci)
- Streptococci in mouth - oral cavity - active role in dental carries forming

- IF is physiological only in defined environment
- when microbes are inoculated in other place with other composition of IF or in place physiologically sterile - it can cause the disease - is pathogenic (*Escherichia coli* - IF in colon - patogen in urinary tract)

Colon

- Number of bacteria is increasing in downward direction 10^{10}/g of feces
- In breast feeding - lactobacilus
- In mixed food - E. coli, Bacteroides, Clostridia, Enterococcus
- Streptococcus mitis, Enterococcus faecalis,Lactobacillus sp., Escherichia coli, Pseudomonas aeruginosa, Bacteroides sp., Mycoplasma sp., Candida albicans, Bifidobacterium bifidum, anaerobe micrococci, Streptococcus salivarius, Clostridium sp., Alcaligenes faecalis, Klebsiella aerogenes, Fusobacterium sp., Eubacterium sp, Citrobacter sp., Proteus sp.

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External genitals

- Staphylococcus epidermidis, Enterococcus faecalis, Eschoerichia coli, Bacteroides sp., Mycobacterioum smegmatis, Fusobacterium sp., Corynebacterium sp. - diphteroids, Streptococcus sp., anaerobe streptococci, Spirilium sp, Treponema dentium, Candida albicans, Mycoplasma sp.,

Vagina

- Anaerobe micrococci, Neisseria sp., Haemophilus sp., Treponema dentium, Lactobacillus vaginalis, Streptococcus viridans, Corynebacterium sp.,
- colonisation with lactobacilli soon after birth + staphylococcus, enterococcus, diphteroids
- with onset of puberty - lactobacilli are evidently responsible for acidity of vaginal secretions in child bearing age via chemical changes of glycogen
- postmenopausa - like in prepuberty

Urinary tract

- Lower third of uretra can be contaminated by phsiological flora from adjacent skin or external genitals
- Significant bacteriuria - the quantity of bacteria in 1ml that is very significant for infection (10^5 of bacteria in 1 ml of urine)

Changes in IF

- Dysmicrobia - changes in delicate equillibrumin composition of microflora - broadspectrum of atb
- overfrowth of on species from IF
- colonisation by pathogens in distinct environment (*Staf. aureus* in hospital, *Neisseria meningitidis* in military crowds)

Sites steril in physiological conditions

- Respiratory tract downward from pharynx
- GIT from oesofagus - (transiently microbes present in food or saliva) - down to colon
- Urinary tract - (sledom IF in low third of uretra)
- Internal genitals
- Inner ear
- Inner tissues
- Structures of nervous systems
- Blood

Sampling materials normally without bacteria

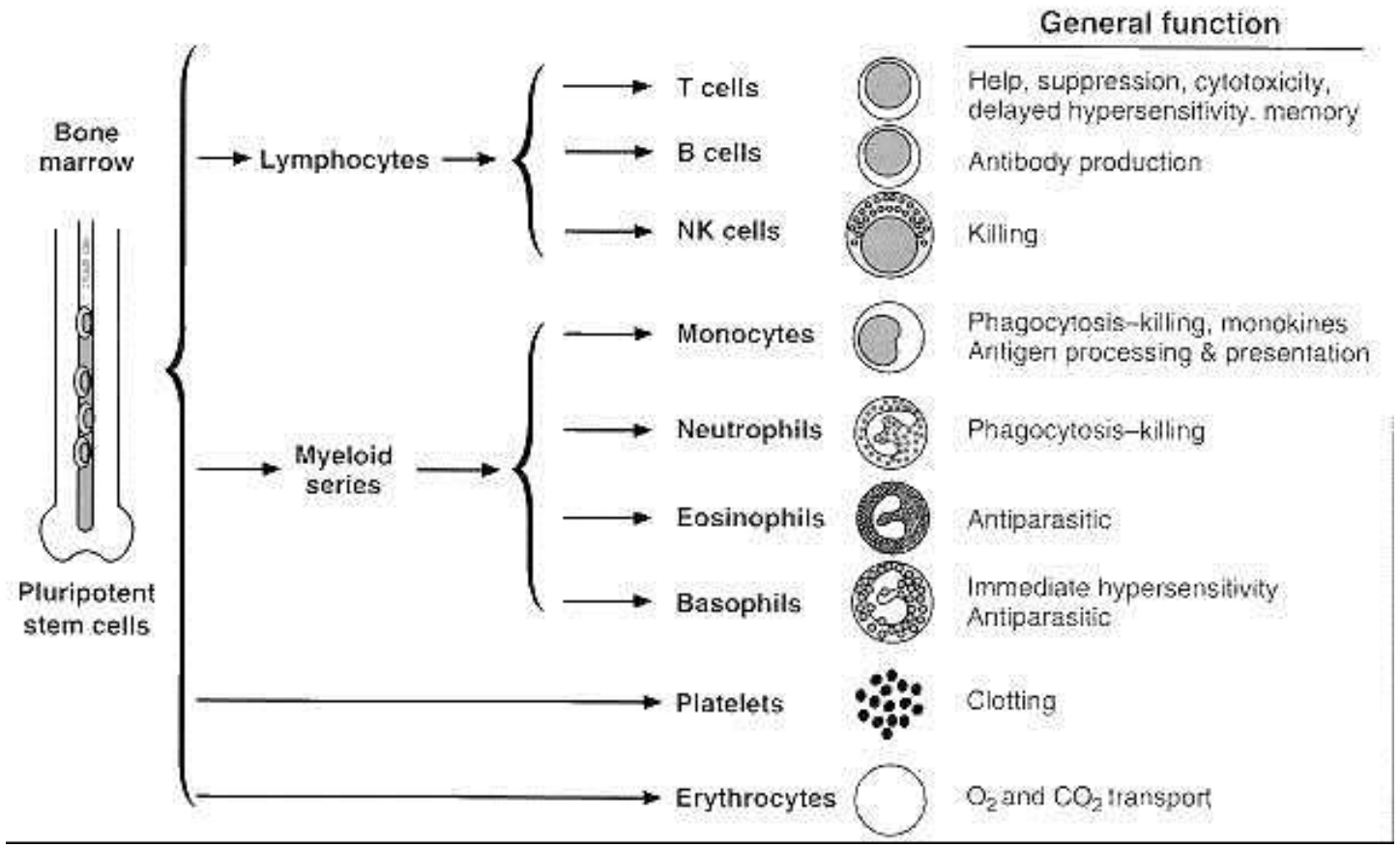
- Punctures - paranasal sinuses, soft tissues, joins, pleural, pericardial
- sputum, aspiration from pulmon, middle ear aspirates
- CSF
- Blood
- Urine
- Samples from endoscopy

Interpretation of findings

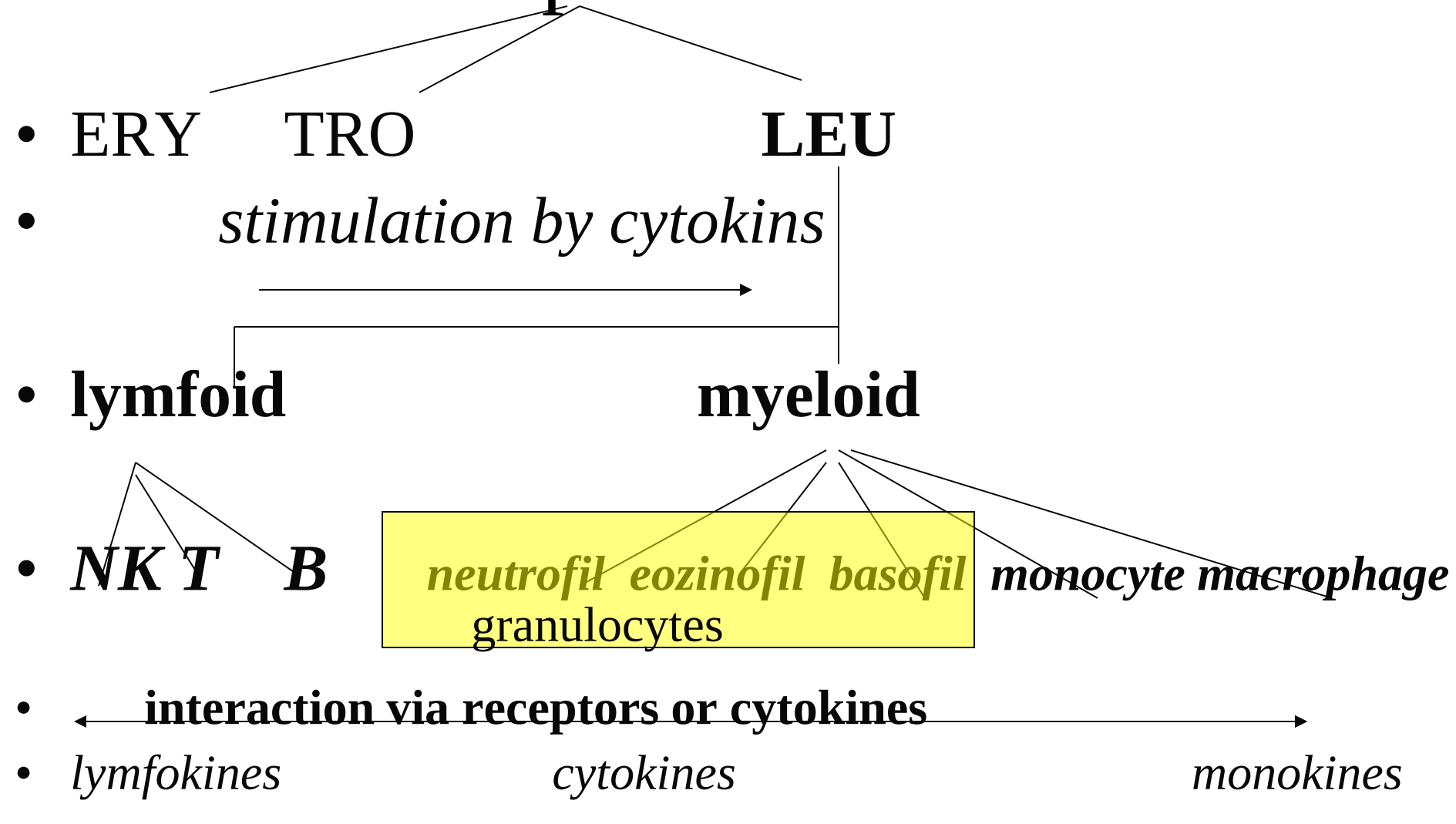
- Isolation of nonpathogens consistent with IF *(Str. viridans* in mouth)
- Isolation of facultative pathogens consistent with IF (*Haemophilus influenzae* from nasopharynx)
- Isolation of nonpathogens not consistent with IF *(E. coli* from nose or lower third of uretra)
- Isolation of any bacteria from sites physiologically sterile (! Contamination)

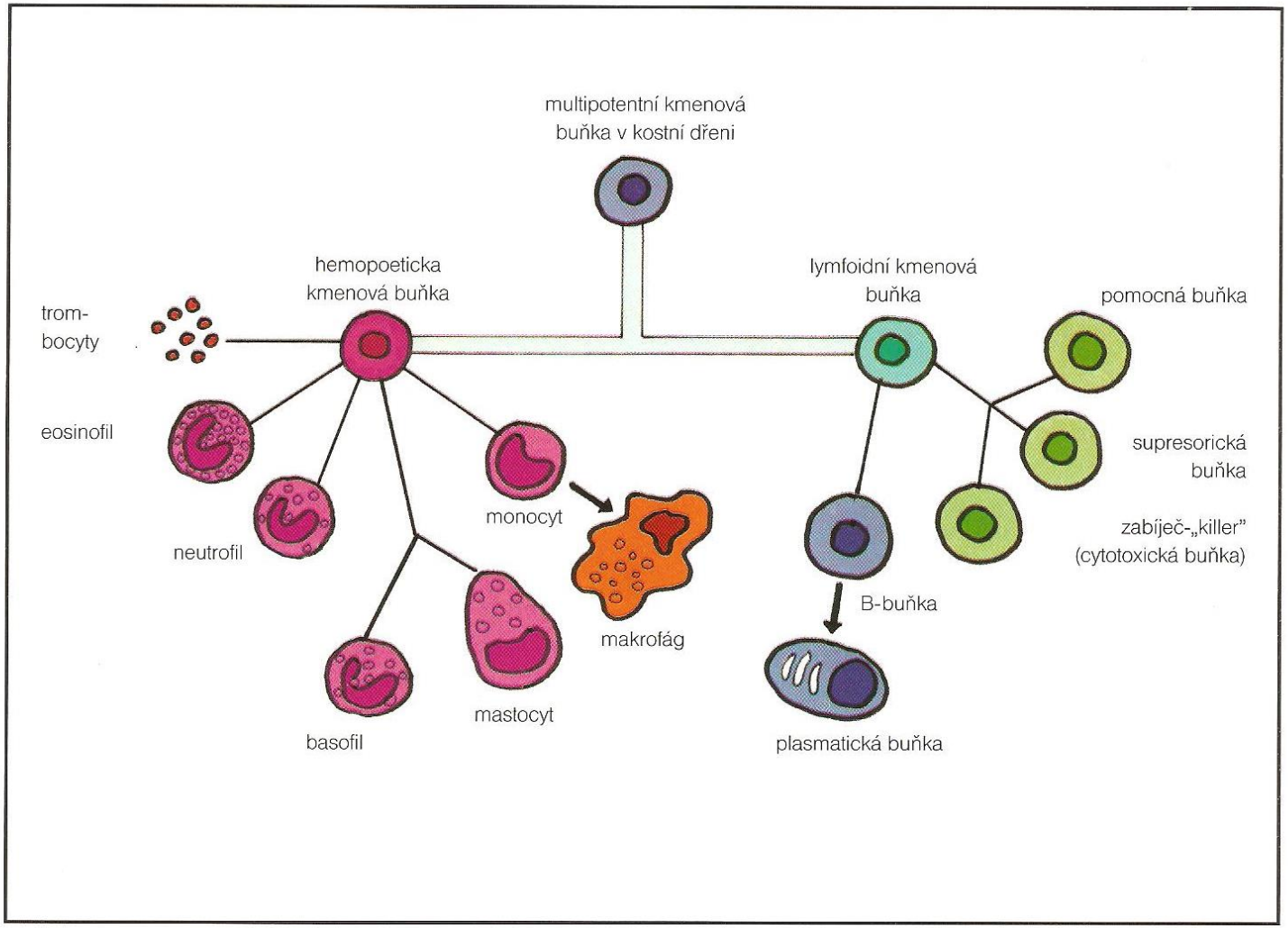
Cells of innate immune mechanisms

- Leucocytes – defense and patrolling cells
- Watch tissues and organs by circulationg in blood and lymphatic ways
- Classified acc.to morphology, number of nucleus lobes, presence of granules
- Acting directly and by production of soluble molecules


General function
Bone marrow
Pluripotent stem cells
Lymphocytes
Myeloid series
T cells
B cells
NK cells
Monocytes
Neutrophils
Eosinophils
Basophils
Platelets
Erythrocytes
Help, suppression, cytotoxicity, delayed hypersensitivity, memory
Antibody production
Killing
Phagocytosis–killing, monokines Antigen processing & presentation
Phagocytosis–killing
Antiparasitic
Immediate hypersensitivity Antiparasitic
Clotting
O_2 and CO_2 transport

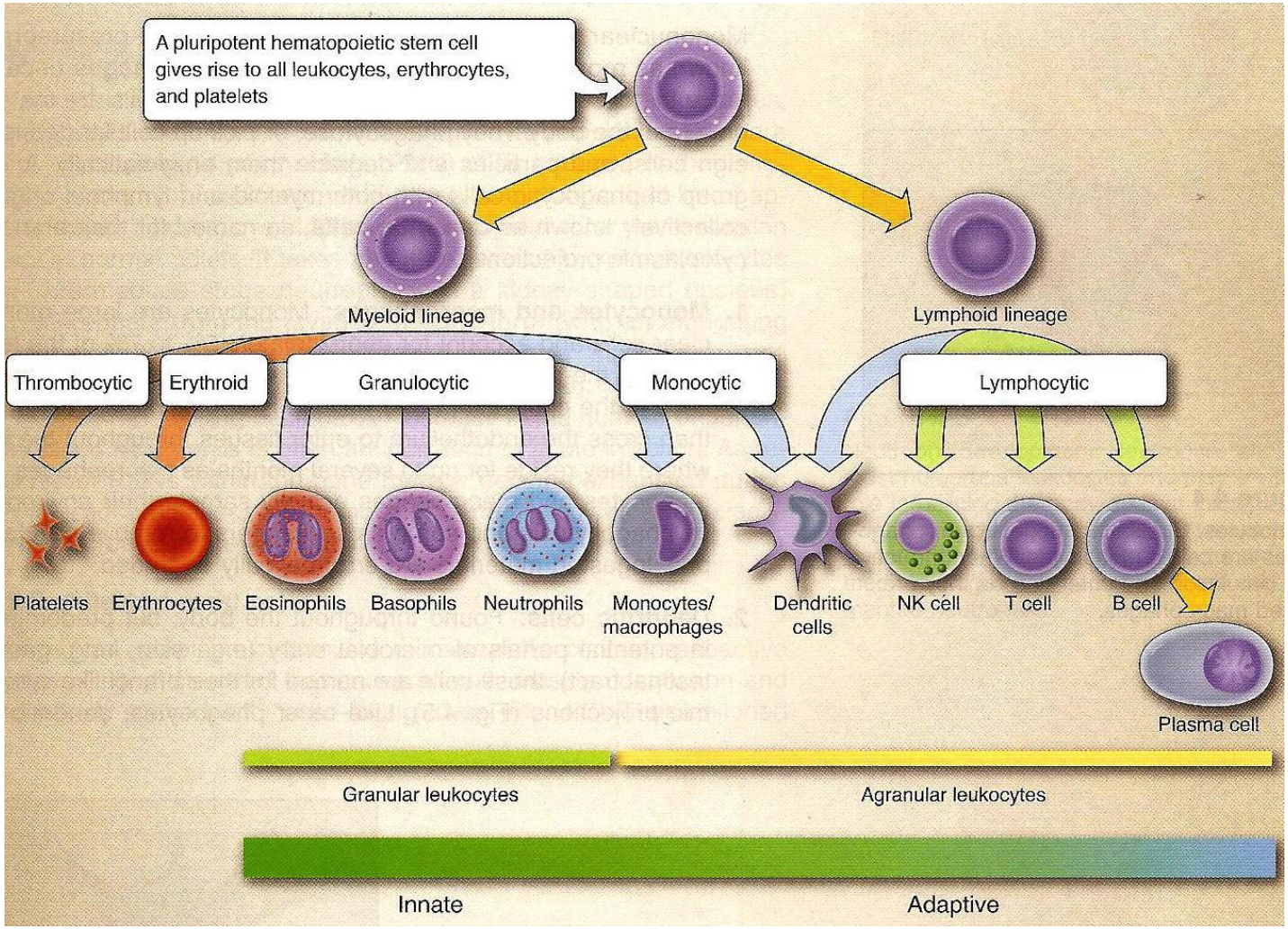
Pluripotent stem cell





Obr. 16: Schematické znázornění buněk imunitního systému.

Hematopoetic line



Pluripotent hematopoetic cell

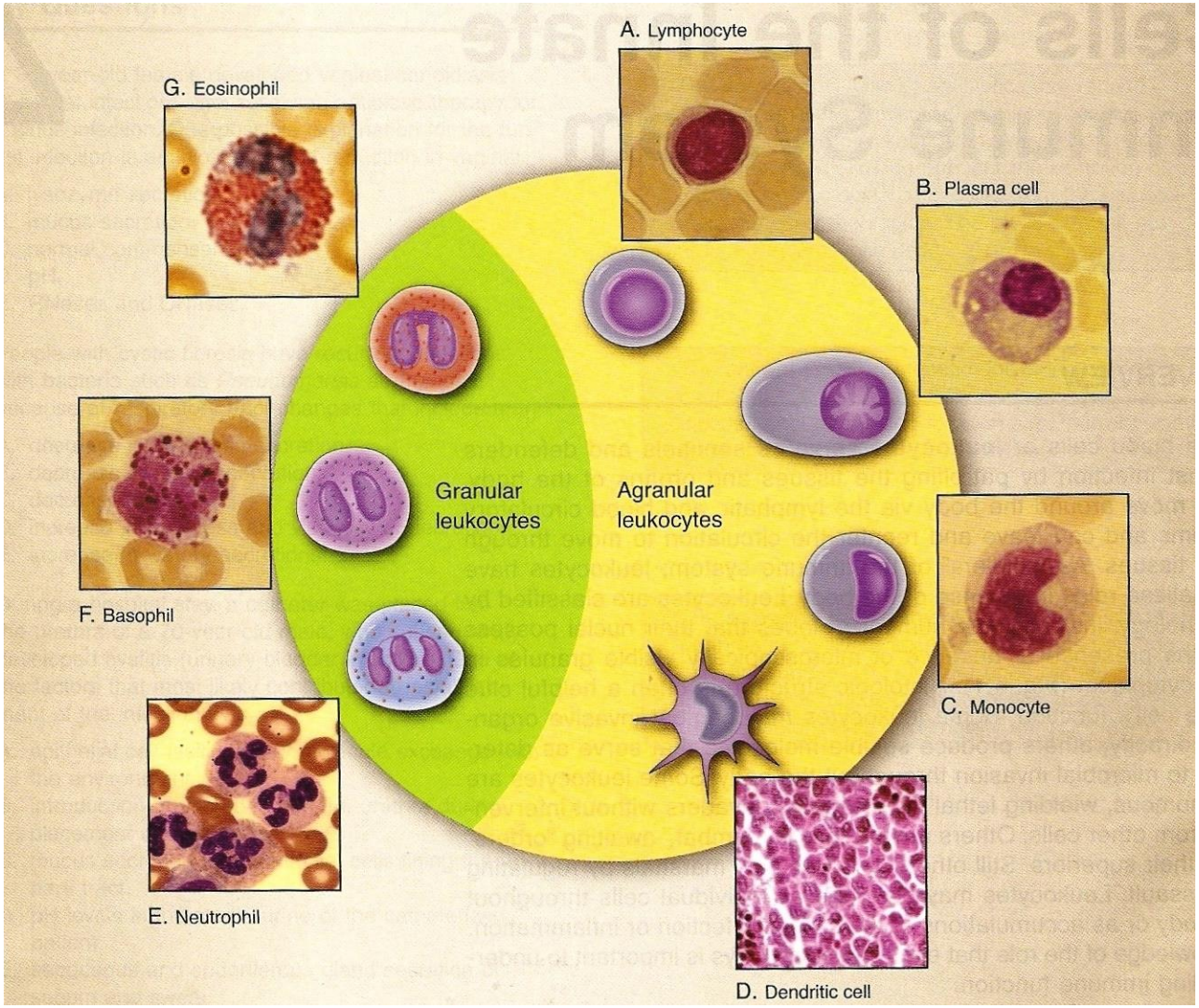
- all immunocompetent cells are derived from it
- stem cell – any type of leucocytes, erytrocytes or trombocytes can develop from them

Leukocyty

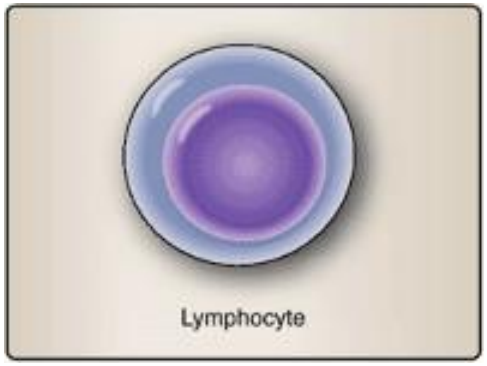
- **Biele krvinky** – s viaclaločnatým jadrom a obsahujúce veľké množstvo cytoplazmatických granúl – granulocyty

-- s uniformným jadrom a cytoplazmou bez granúl alebo len s malým počtom granúl – agranulocyty (35% - 38%) odvodené od prekurzora
– lymfoidnej línie

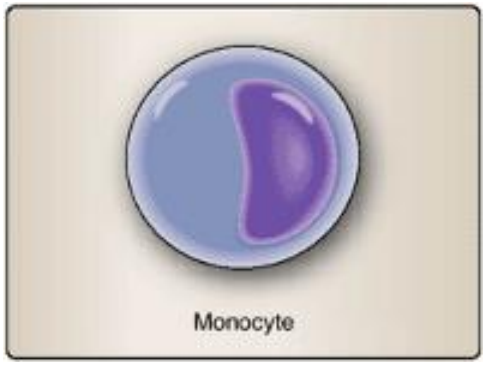
-- myeloidnej línie


A. Lymphocyte
G. Eosinophil
B. Plasma cell
Granular leukocytes
Agranular leukocytes
F. Basophil
C. Monocyte
E. Neutrophil
D. Dendritic cell

Agranulocytes lymphoid line



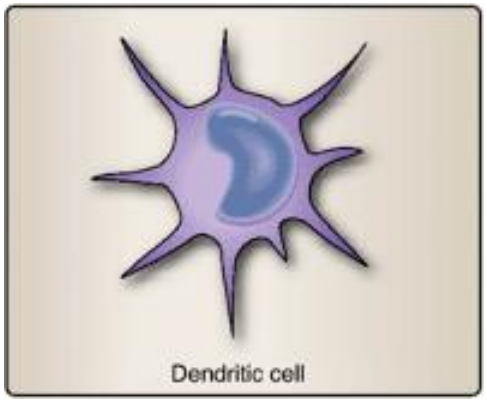
- Lymphocytes 4.3
  - B cells – resid in bone marrow, able to differentiate to plasma cells and synthetise molecules of immunoglobulins
  - T cells – origin from bone marrow, then touched by thymus leave it to enter circulation
  - NK cells – different from T and B cells – large non phagocyting granular leucocytes. Killing abnormal (infected or cancer) host cells (10% of lymphocytes)



Myeloid line monocytes and macrophages

- **Mononucleare** cells differenciating from myeloid precursors
  - monocytes in circulation – 1-2 days in circulation then spreading to tissues, where present for several mnths
  - macrophages in tissues

  (5%-7% leucocytes) – looking for debrits of cells, foreign cells – degradation of them
- **Dendritic cells** –active fagocyting cells (phagocytosis, macropinocytosis) mostly in the site of enter of microbes they have myeloid or lymfoid origin

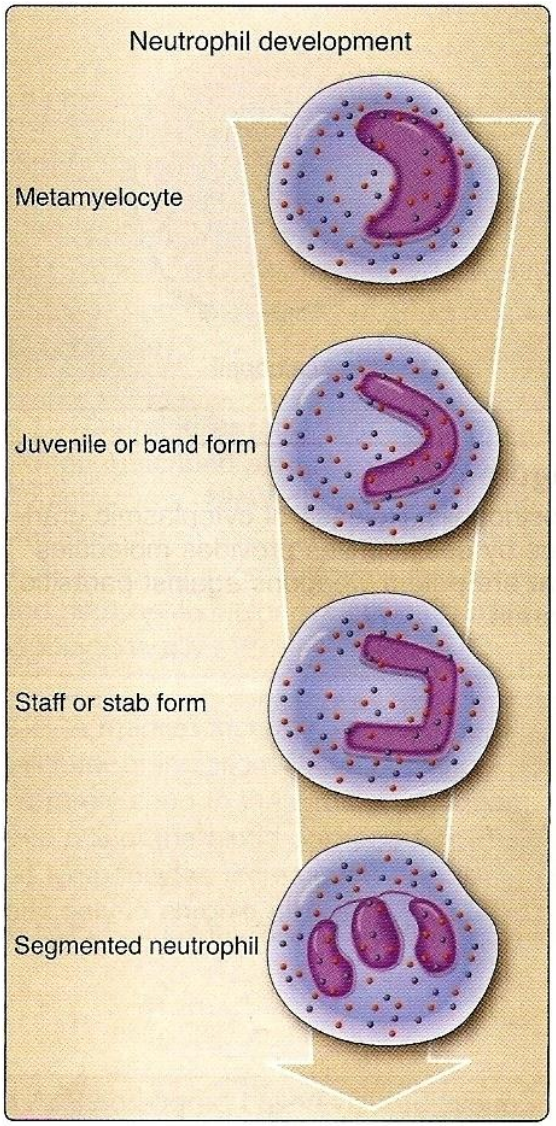


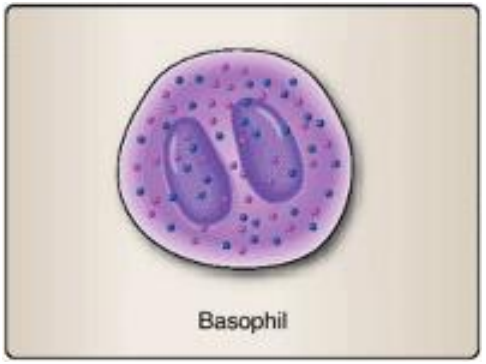
Granular leukocytes

- Multilobular nucleus, cytoplasmatic granules contain
  - amins – stainable basic stains
  - basic proteins – stainable by acid – loving acidophil or eosinophil stains
- Neutrophils
- Basophils and mastocytes
- Eosinophils

Neutrophils

- 60% periferal leucocytes PMNL **polymorphonuclear leucocytes**
  - different number of nucleus segments (2-5)
  - halftime – 7 hrs
  - 100 000 of new/daily
  - differenciation (2 weaks): metamyelocyte – kidneyshape nc. juvenil band forme segmented leucocyte
- Effectively killing bacteria
- Present in acute infection



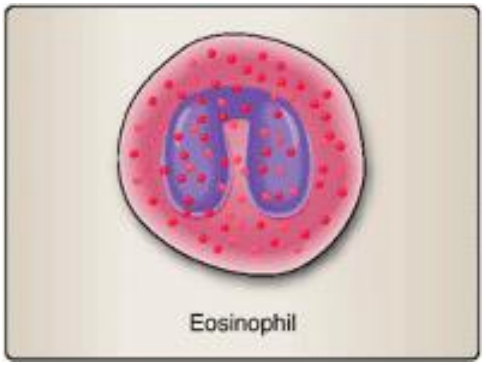


Basofils and mastocytes

Role in alergic reaction

Containing acidophil granules with vasoactive amines (histamin) – contraction of smooth musles,
- stainable by basic stains

- **Basophily** – 0% -1% in circulation
- **Mastocytes** – in tissues



Eosinophils

0% - 5% of periferal blood leucocytes

- Bilobar granulocytes
- Eosinophil granules – basic proteins
- Active role in innate and adaptive immune mechanisms against parasitic worm infections