

The lymphatic system and body defenses

Innate body defenses

Anita Spanjer – van Dijk (SPAI)
a.i.r.spanjer-van.dijk@pl.hanze.nl



Regel 1/ Regel 2/ Regels worden wél goed toegepast

Twee regels van het immuunsysteem:

1. Herken en vernietig de vreemde (het **NIET-ZELF**)
2. Herken en spaar het eigen individu (het **ZELF**)

Organisation of the immune system

- 3 Lines of defense
- 2 of those lines of defense are not specific
 - Non-specific defense: all “foreigners” are removed in a similar fashion
 - Specific defense: immune system adapts the immune response to the “foreigner”

The Immune System		
Innate (nonspecific) defense mechanisms		Adaptive (specific) defense mechanisms
First line of defense	Second line of defense	Third line of defense
<ul style="list-style-type: none">• Skin• Mucous membranes• Secretions of skin and mucous membranes	<ul style="list-style-type: none">• Phagocytic cells• Antimicrobial proteins• The inflammatory response	<ul style="list-style-type: none">• Lymphocytes• Antibodies• Macrophages

Table 12.1**Summary of Innate (Nonspecific) Body Defenses****Category and associated elements****Protective mechanism*****Surface Membrane Barriers—First Line of Defense***

Intact skin (epidermis)

Forms mechanical barrier that prevents entry of pathogens and other harmful substances into body.

- Acid mantle
- Keratin

Skin secretions make epidermal surface acidic, which inhibits bacterial growth; sebum also contains bacteria-killing chemicals.

Provides resistance against acids, alkalis, and bacterial enzymes.

Intact mucous membranes

Form mechanical barrier that prevents entry of pathogens.

- Mucus
- Nasal hairs
- Cilia
- Gastric juice

Traps microorganisms in respiratory and digestive tracts.

Filter and trap microorganisms in nasal passages.

Propel debris-laden mucus away from lower respiratory passages.

Contains concentrated hydrochloric acid and protein-digesting enzymes that destroy pathogens in stomach.

- Acid mantle of vagina
- Lacrimal secretion (tears); saliva

Inhibits growth of bacteria and fungi in female reproductive tract.

Continuously lubricate and cleanse eyes (tears) and oral cavity (saliva); contain lysozyme, an enzyme that destroys microorganisms.

Table 12.1**Summary of Innate (Nonspecific) Body Defenses****Category and associated elements****Protective mechanism*****Cellular and Chemical Defenses—Second Line of Defense***

Phagocytes

Engulf and destroy pathogens that breach surface membrane barriers; macrophages also contribute to immune response.

Natural killer cells

Promote cell lysis by direct cell attack against virus-infected or cancerous body cells; do not depend on specific antigen recognition.

Inflammatory response

Prevents spread of injurious agents to adjacent tissues, disposes of pathogens and dead tissue cells, and promotes tissue repair; releases chemical mediators that attract phagocytes (and immune cells) to the area.

Antimicrobial chemicals

- Complement
- Interferons
- Fluids with acid pH

Group of plasma proteins that lyses microorganisms, enhances phagocytosis by opsonization, and intensifies inflammatory response.

Proteins released by virus-infected cells that protect uninfected tissue cells from viral takeover; mobilize immune system.

Normally acid pH inhibits bacterial growth; urine cleanses the lower urinary tract as it flushes from the body.

Fever

Systemic response triggered by pyrogens; high body temperature inhibits multiplication of bacteria and enhances body repair processes.

Second line of defense

Cells:

- Phagocytes
- Natural Killer cells

Chemicals:

- Antibacterial chemicals
- Chemicals that stimulate tissue repair
- Chemicals that attract and activate immune cells

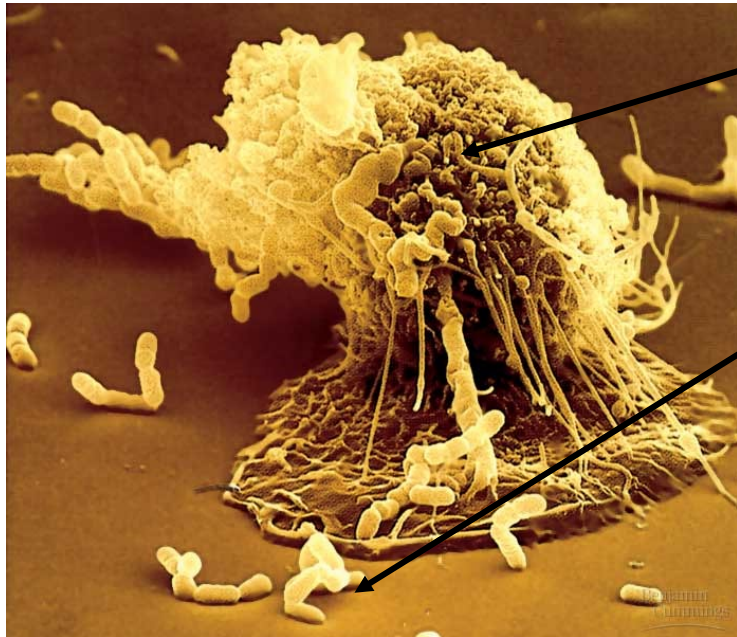
Other protective responses:

- Temperature (fever)

Second line of defense

- Phagocytic white blood cells
- Antimicrobial proteins
- The inflammatory response

Second line of defense: phagocytes



Macrophages:

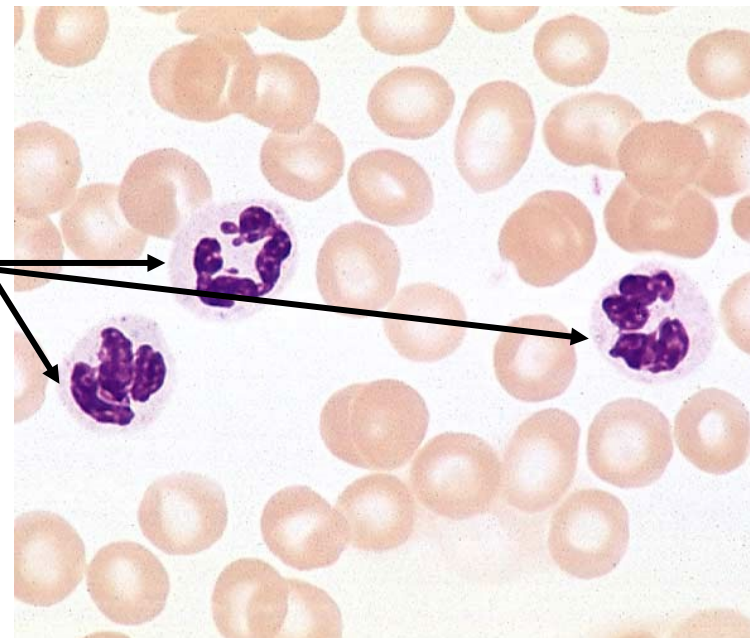
- “Eats” (Phagocytose) bacteria
- Is present in many tissues

Second line of defense

- **Phagocytic white blood cells**
- **Antimicrobial proteins**
- **The inflammatory response**

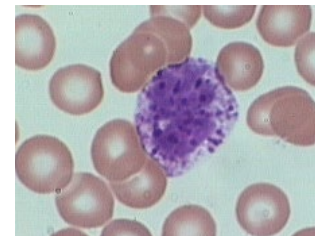
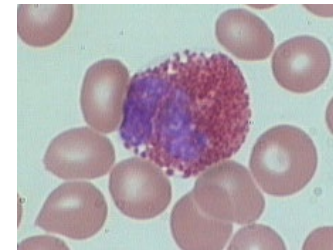
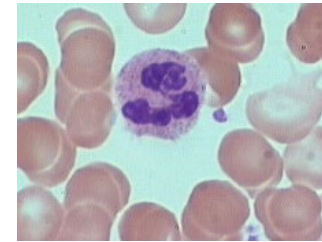
Neutrophilic granulocytes (neutrophils):

- Similar to macrophages (phagocytosis), but smaller
- Present in blood and drawn to the site of infection

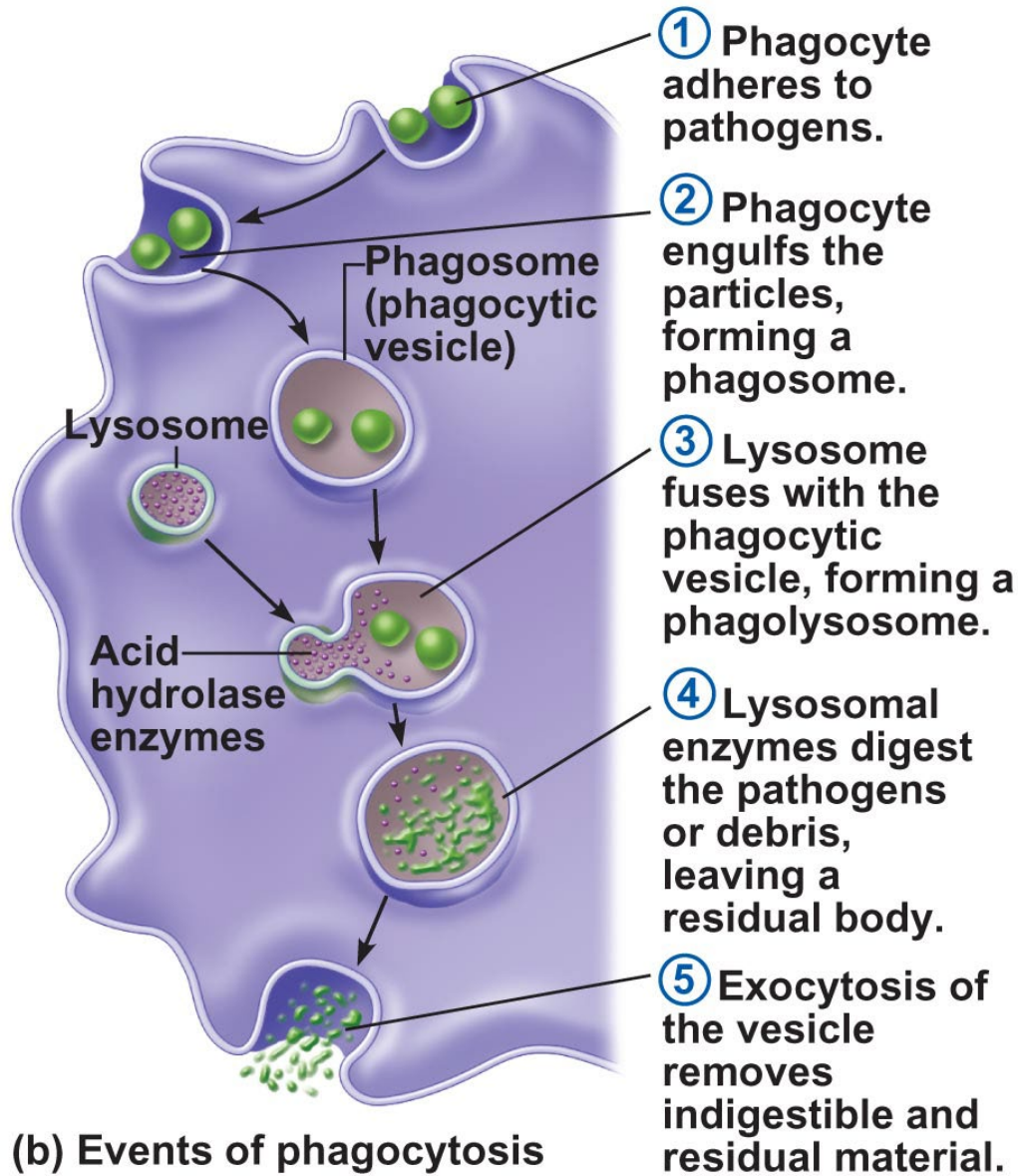


Neutrophils are not the only granulocytes

- Also called Polymorphic Nuclear Cells (PMNs) due to the irregular shape of their nucleus
- Granulocytes contain many granules!
- **Neutrophils**
 - Nucleus has 4 lobes
 - Both acidophilic and basophilic granules
 - Excellent phagocytes
- Eosinophils
 - Nucleus has 2 lobes
 - Acidophilic granules (pink in HE staining!)
 - Able to phagocytose
 - Role against parasites and also in allergy
- Basophils
 - Basophilic granules (histamine! Blue in HE staining)
 - Role against parasites and also in allergy
 - Important during the start of inflammation
 - Unable to phagocytose



Phagocytosis



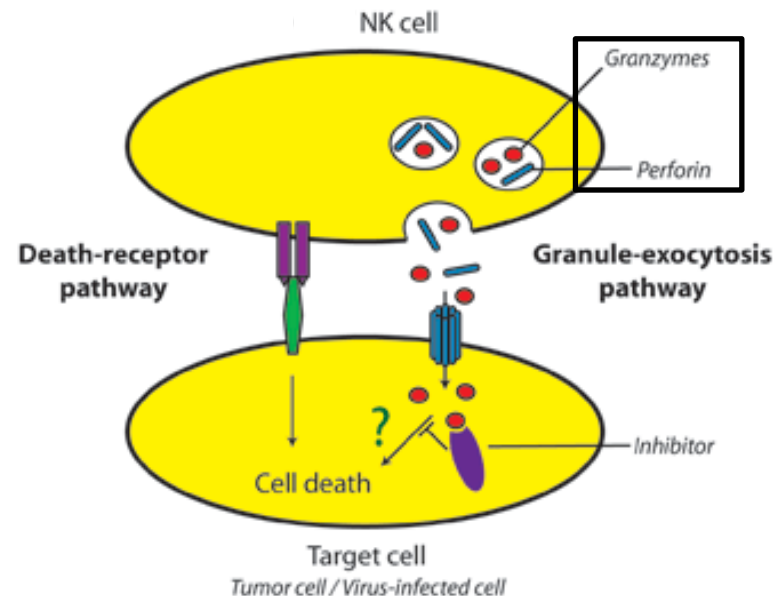
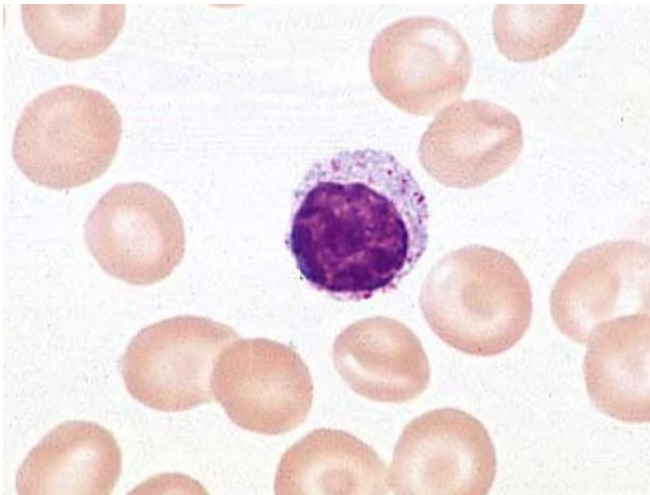
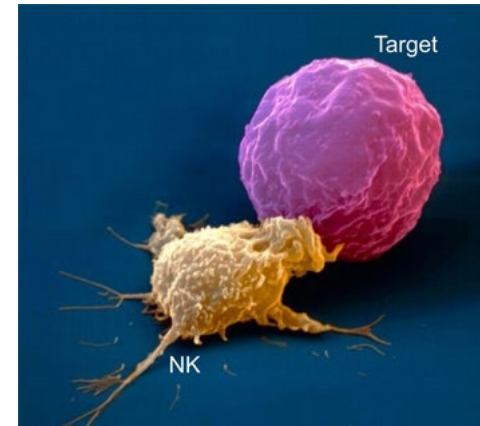
Movie "the process of phagocytosis"

Movie "neutrophil eating bacteria"

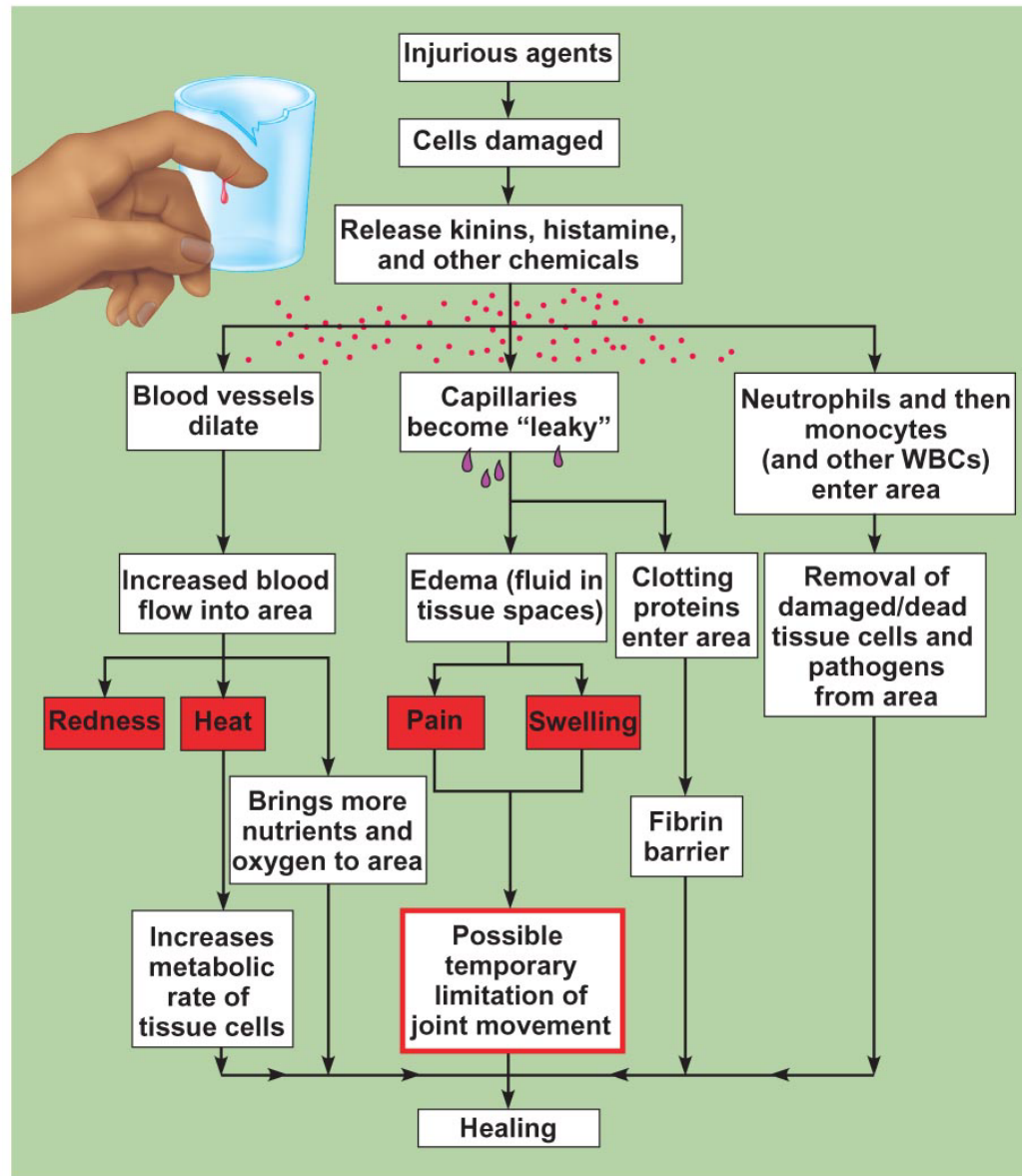
Phagocytosis provides protection against infections outside the cell, for instance bacterial infections (extracellular infections)!

Natural Killer cells

- Look like lymphocytes (3rd line of defense: adaptive immune system), but are not specific
- Part of the second line of defense: innate immune system
- **Not able** to phagocytose
- Are able to lyse virus-infected cells and cancer cells
- Provides protection against intracellular infection (virus)



The inflammatory response



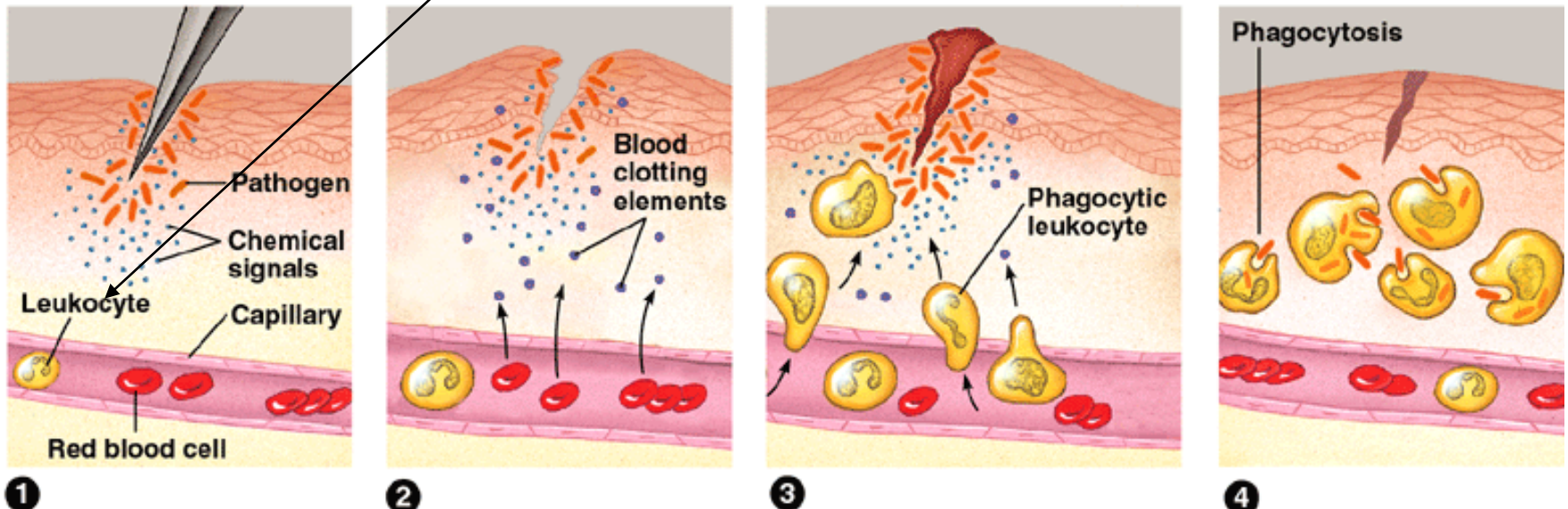
The inflammatory response

- When the first line of defense fails and an infection occurs, the cells of the innate immune system (2nd line of defense) come into action
- At the site of infection an inflammatory response is generated, which clears the infection
- If the infection is not cleared, the adaptive immune system (3rd line of defense) is activated

Second line of defense

- Phagocytic white blood cells
- Antimicrobial proteins
- The inflammatory response

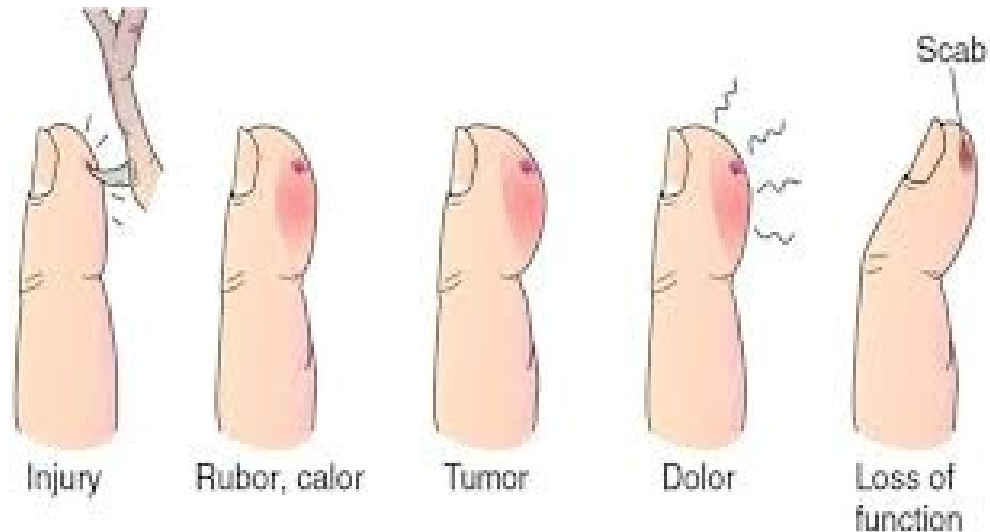
Leukocyte = white blood cell



White blood cells [especially phagocytes] leave the bloodstream to clear the infection. Chemical signals play an important role in this reaction!

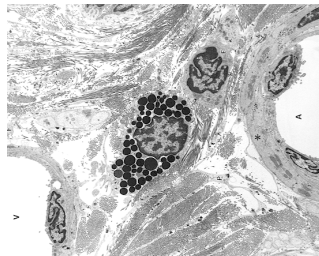
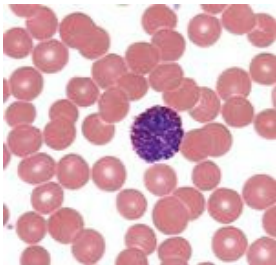
The 5 characteristics of inflammation

- **Rubor**: redness caused by vasodilation
- **Calor**: heat caused by vasodilation
- **Tumor**: swelling caused by increased vascular permeability; fluid leaks into the tissue
- **Dolor**: pain caused by chemical signals (kinine, ...) that stimulate painreceptors (nervous tissue)
- (**Functio laesa**: loss of function, for example in an inflamed joint)

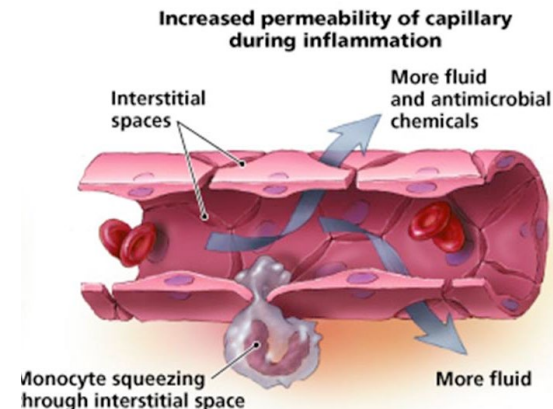
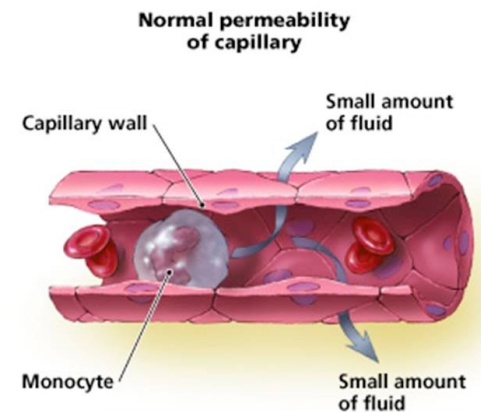


Chemical signals: Histamine and Kinine

- Many different chemical signals are involved in the inflammatory response, which work together to show immune cells the site of infection and to activate them
- Histamine:
 - Causes vasodilation and increased vascular permeability (leading to rubor, calor, and tumor. (Also chemotaxis, slide 24)
 - Produced by basophils, mast cells, platelets
- Kinine:
 - Causes pain by stimulating nerve endings
 - Naturally present in blood plasma

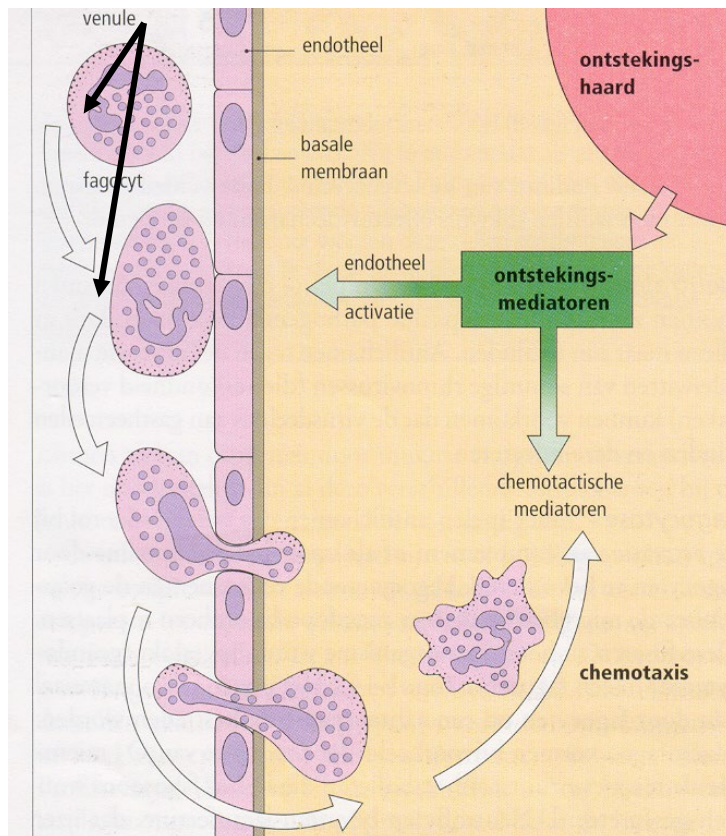


Basophils are present in blood (LM) Mast cells are present in tissues (EM)

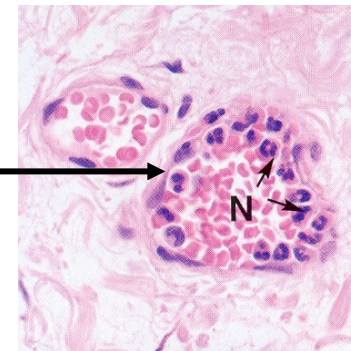


How do immune cells reach the tissue?

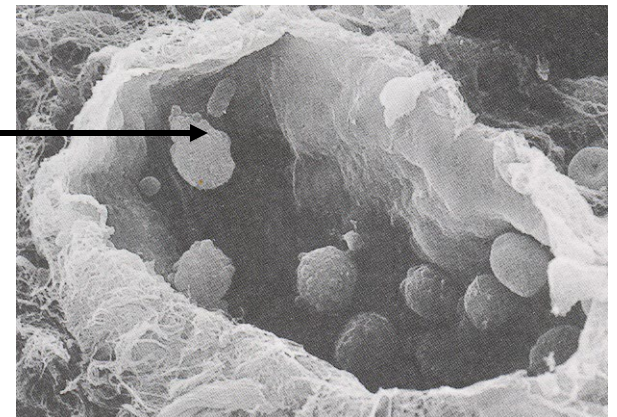
- Chemicals 'show' the immune cells where the infection is
- Margination: circulating leukocytes attach to the endothelial cells of the vascular wall (endothelium is the epithelium of blood vessels)



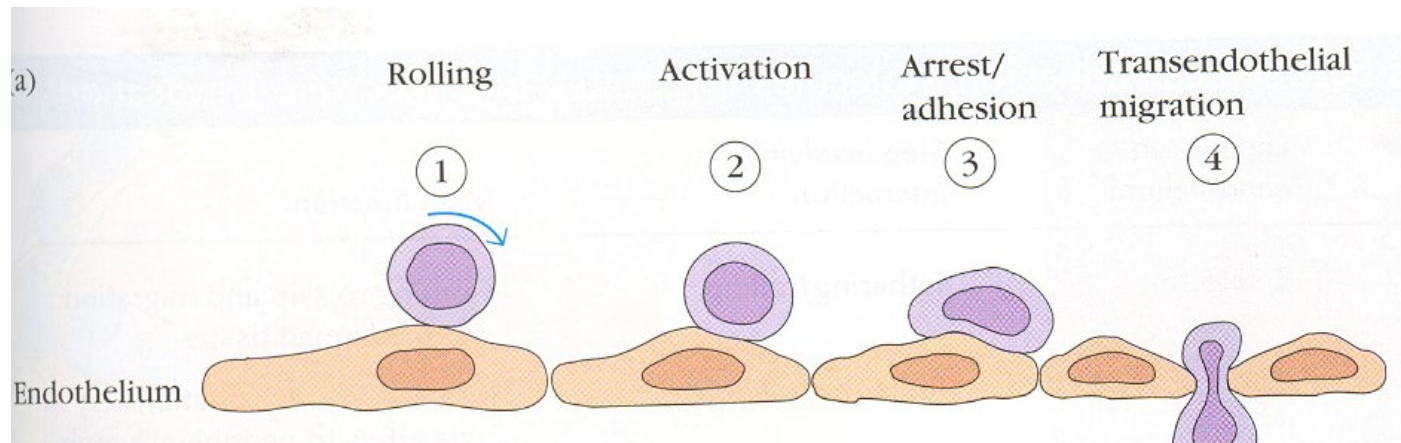
Margination
(light microscopy)



Margination
(scanning-EM)



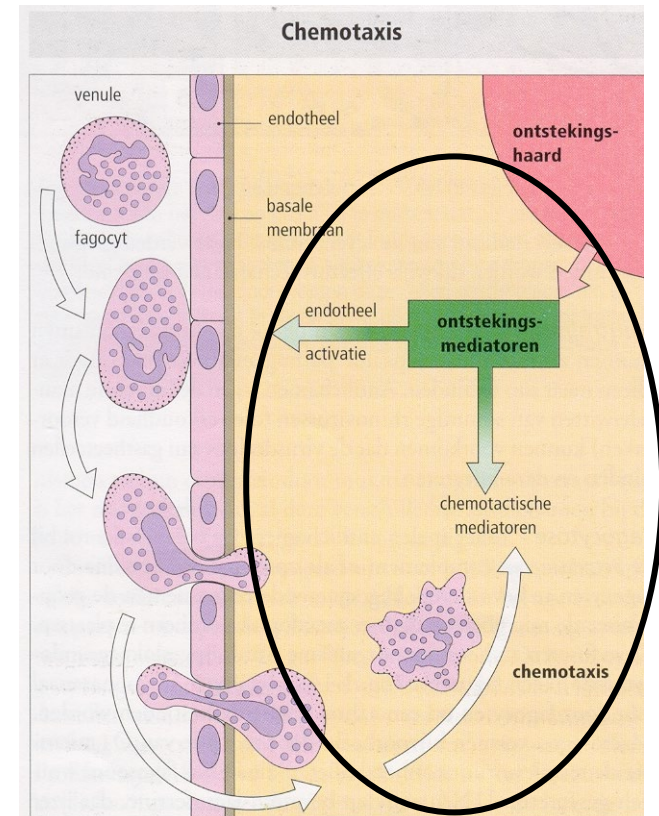
Immune cells squeeze through the vessel wall



- After margination the cells roll over the endothelium
- Rolling activates the immune cells, which allows them to 'grab' the endothelial cells (adhesion)
- The immune cells squeeze through the endothelial lining (called diapedesis, transendothelial migration, or extravasation)

Chemical signals that attract white blood cells

- Chemical produced at the site of infection attract immune cells
- These chemicals may be produced by the infection itself, by macrophages that encountered the infection (chemokines), or by activated complement (C5a & C3a) (Slide 27&28&30)
- Movement of cells towards a chemical stimulus is called (positive) **chemotaxis** (away is negative)



Antimicrobial proteins

- Complement proteins:
 - Able to lyse bacteria
- Interferons:
 - Inhibit viral replication

Second line of defense

- Phagocytic white blood cells
- Antimicrobial proteins
- The inflammatory response

Complement

- Group of 30 different proteins

Functions of complement proteins:

- Some of these proteins are able to damage cells (bacteria) by forming a membrane-attack-complex (MAC)
- Some of these proteins provide opsonisation, which enhances phagocytosis
- Some of these proteins enhance the inflammatory response (chemotaxis and activation)

Hier gaan we één van de volgende lessen dieper op in. Hoofdstuk 5 gaat helemaal over het complement systeem

Interferons

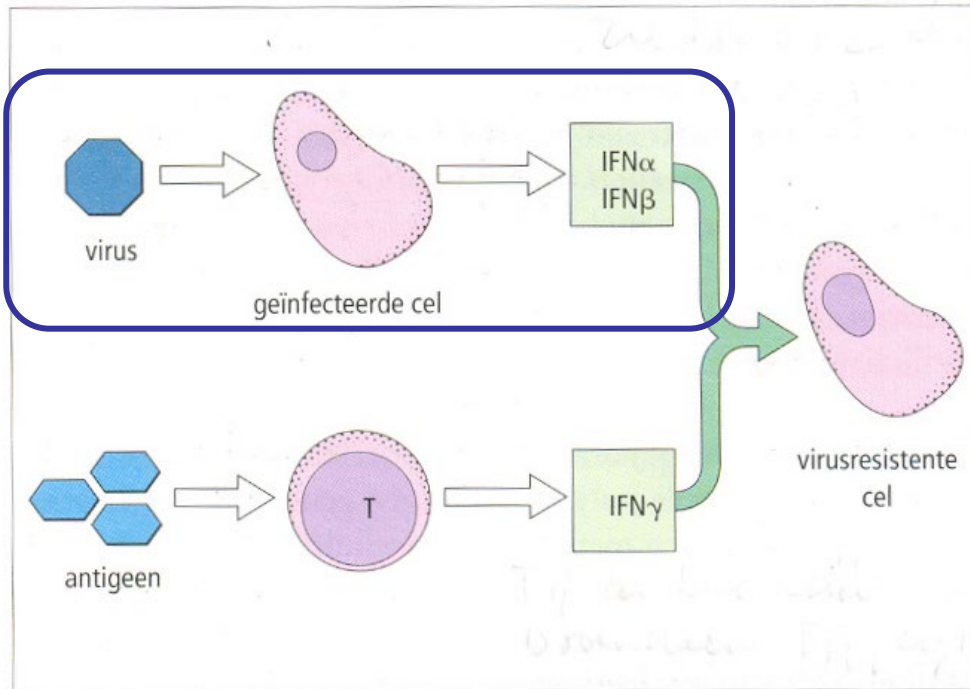


Fig. 1-8 Nadat gastheercellen geïnfecteerd zijn door virus kunnen ze interferon produceren. Verschillende cellen produceren interferon- α (IFN α) of interferon- β (IFN β); interferon- γ wordt door sommige T-lymfocyten geproduceerd na antigeenactivatie. Interferonen wekken bij gastheercellen weerstand op tegen virale infectie. IFN γ heeft bovendien nog andere effecten.

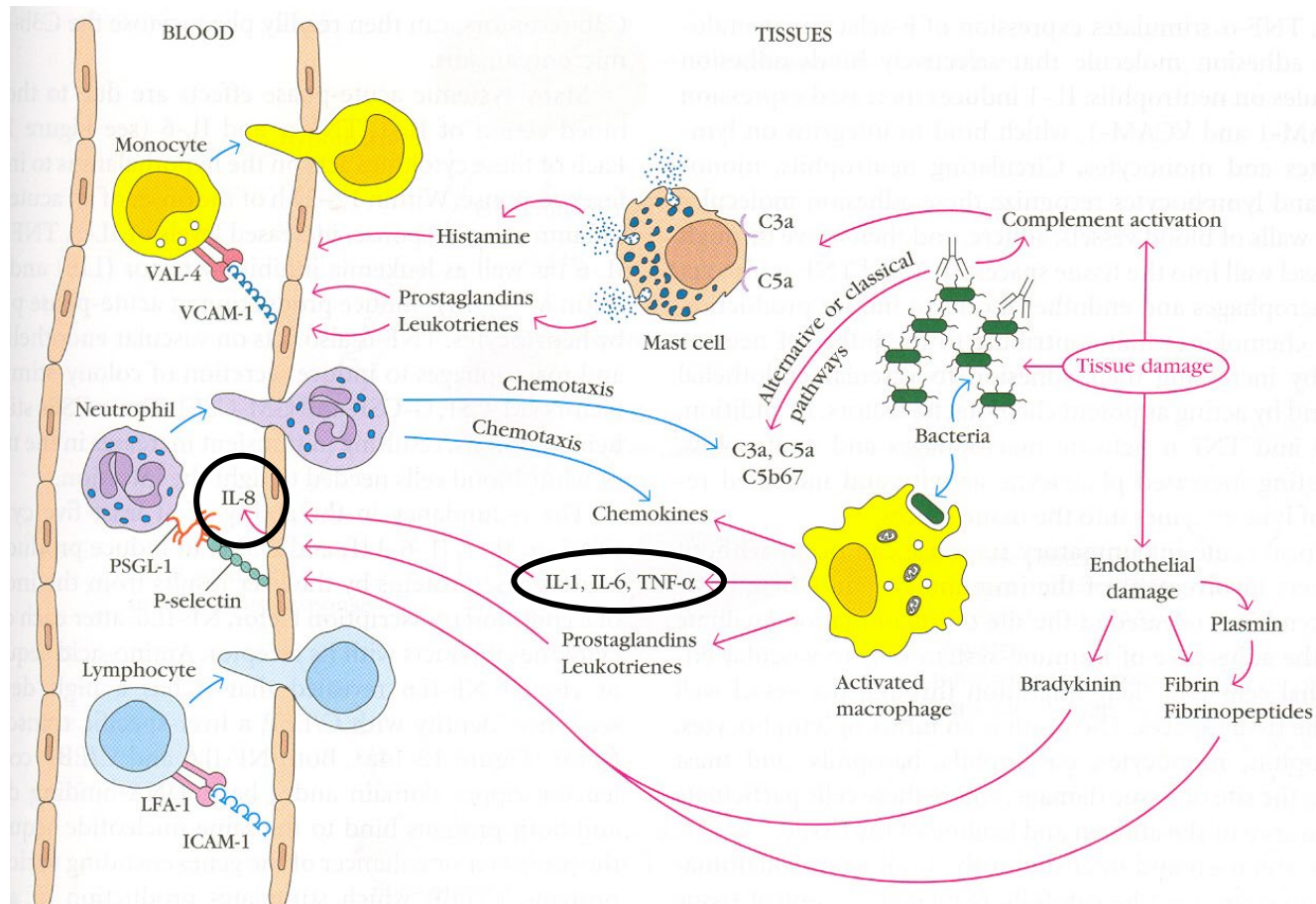
Second line of defense

- Phagocytic white blood cells
- Antimicrobial proteins
- The inflammatory response

- 3 types of interferons
- Interferon- α and interferon- β are produced by virus-infected cells
- All interferons inhibit viral replication

De volgende slide bevat een immuunreactie compleet met alle cytokines en chemokines (boodschappers) en de verschillende cellen. Dit nemen we als uitgangspunt voor de volgende colleges en we gaan steeds een stukje verder uitleggen.

Chemokines and Cytokines



- Activated immune cells produce cytokines, which are chemicals that attract (chemokines) and activate other immune cells
- Verklaar de therapie bij reumapatiënten, waarbij antilichamen tegen TNF gegeven worden