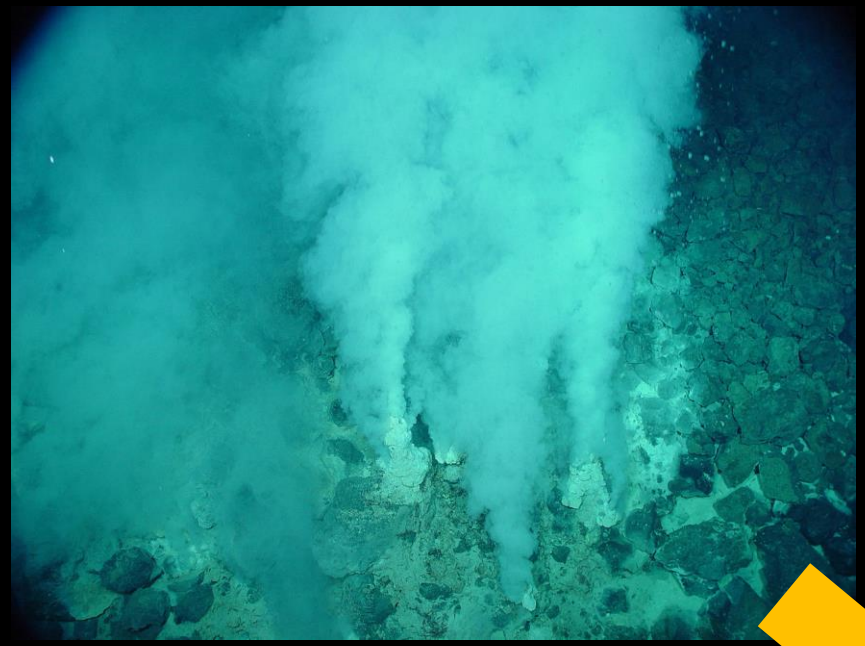
Inflammation



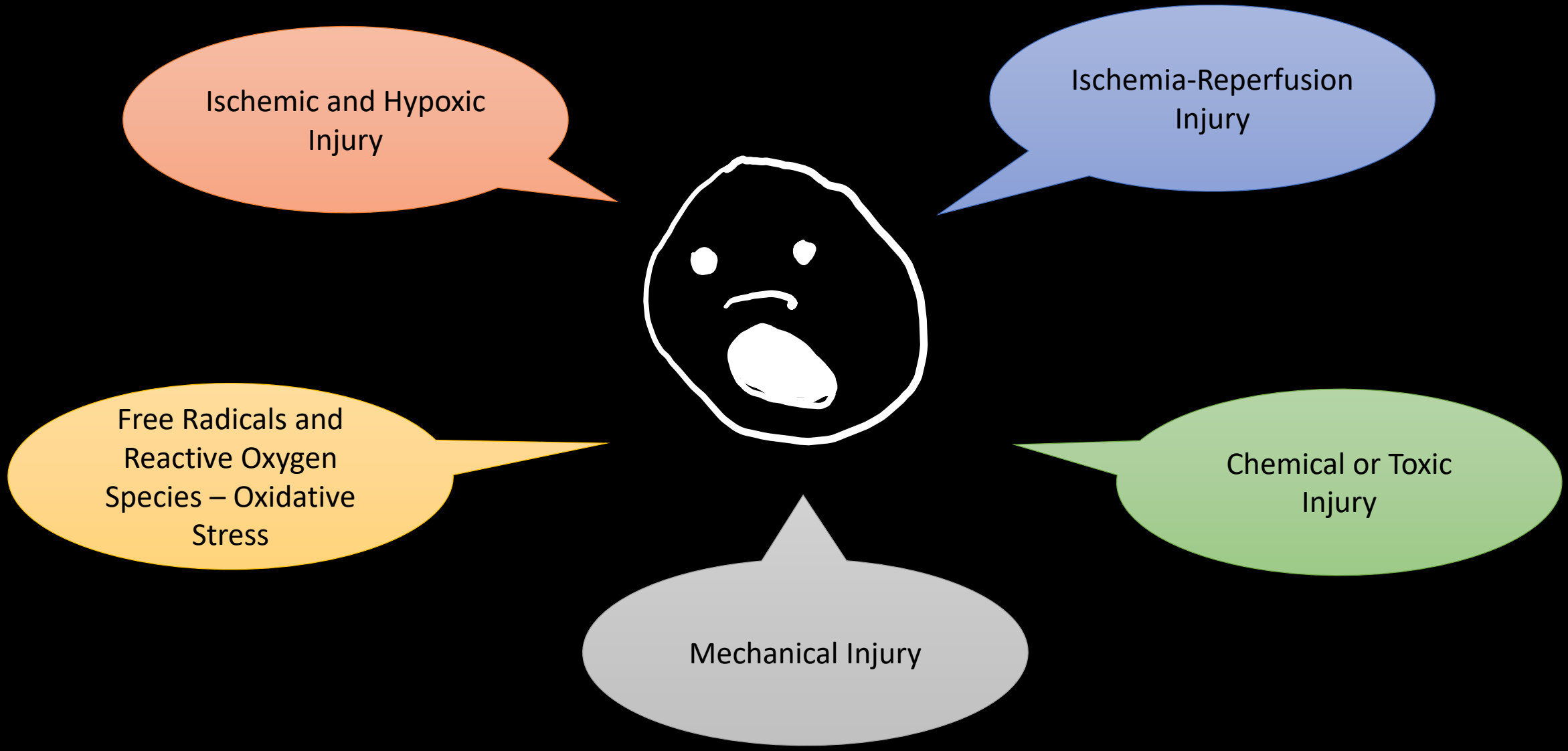
LUCA

4.5 billion years

multicellular organism

[21]

Forms of Cellular Damage



Inflammation

Definition:	• the organism **protective response** against a harmful agent
Aim:	• **to confine** the extent of damage, **kill** microorganisms, **remove** cellular debris and activate **healing**

Inflammation

- complex non-specific reaction of vascularized tissue
  - *Inflammation in avascular tissue is modified.*
- **non-specific**, **normal** *(physiological mechanism)*, **necessary**
- also part of the healing process
- every defense reaction includes a component that damages its own tissues and whether positive or destructive components prevail depends on the regulation
- during acute inflammation, in the first phase mainly components of non-specific immunity are activated, in the second phase specific immunity is activated

Causes of Inflammation

microorganisms

- bacteria, viruses, fungi, protozoas

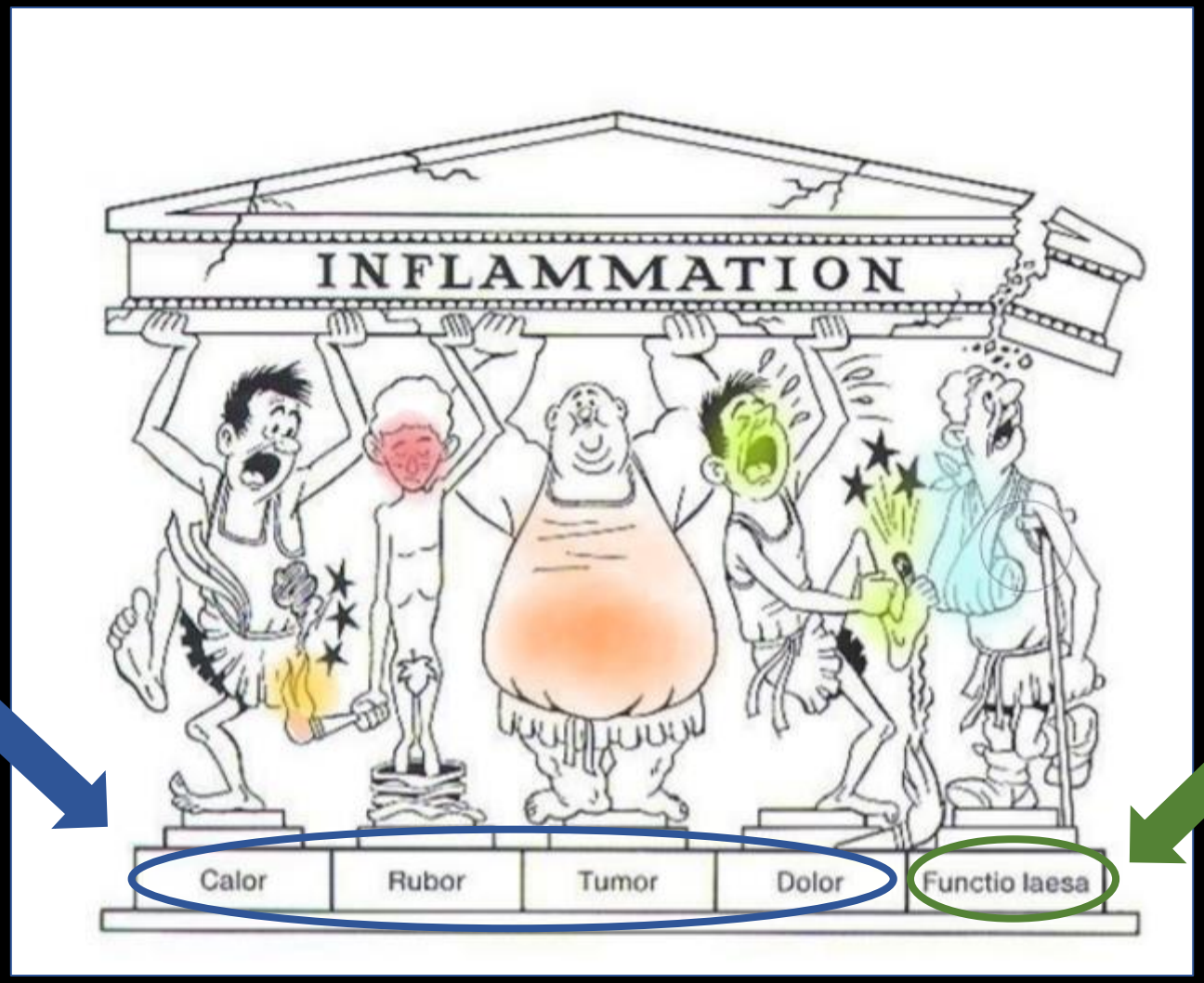
chemical agents

- exogenous proteins (pollen), asbestos or silicate crystals

damage

- mechanical, chemical, thermal injury, radiation, endogenous harmful substances (urate, phosphate and oxalacetate crystals, cholesterol), immunological (decaying cancer cells, extravascular blood, AI reaction, cholesterol)

25 BC – 50 AD



129 – 199 AD

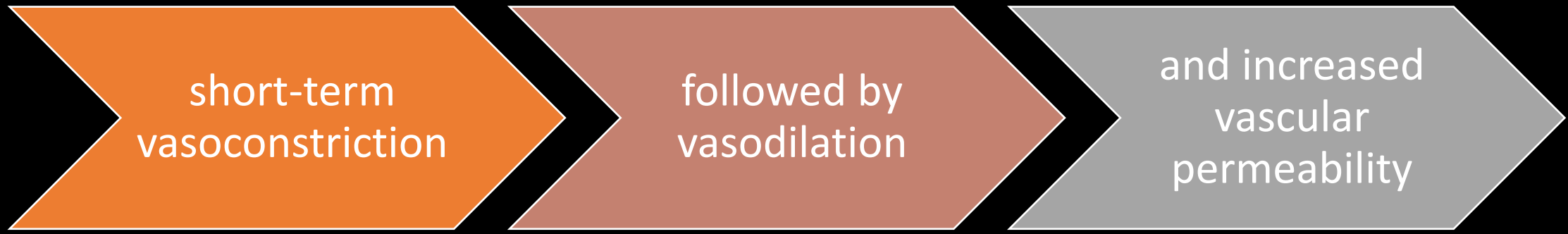
Components of Inflammation

Vascular response

Plasma protein system

Cells and vascular tissue

1st Vascular Response



Vascular Response (seconds - minutes)

Short-lived vasoconstriction

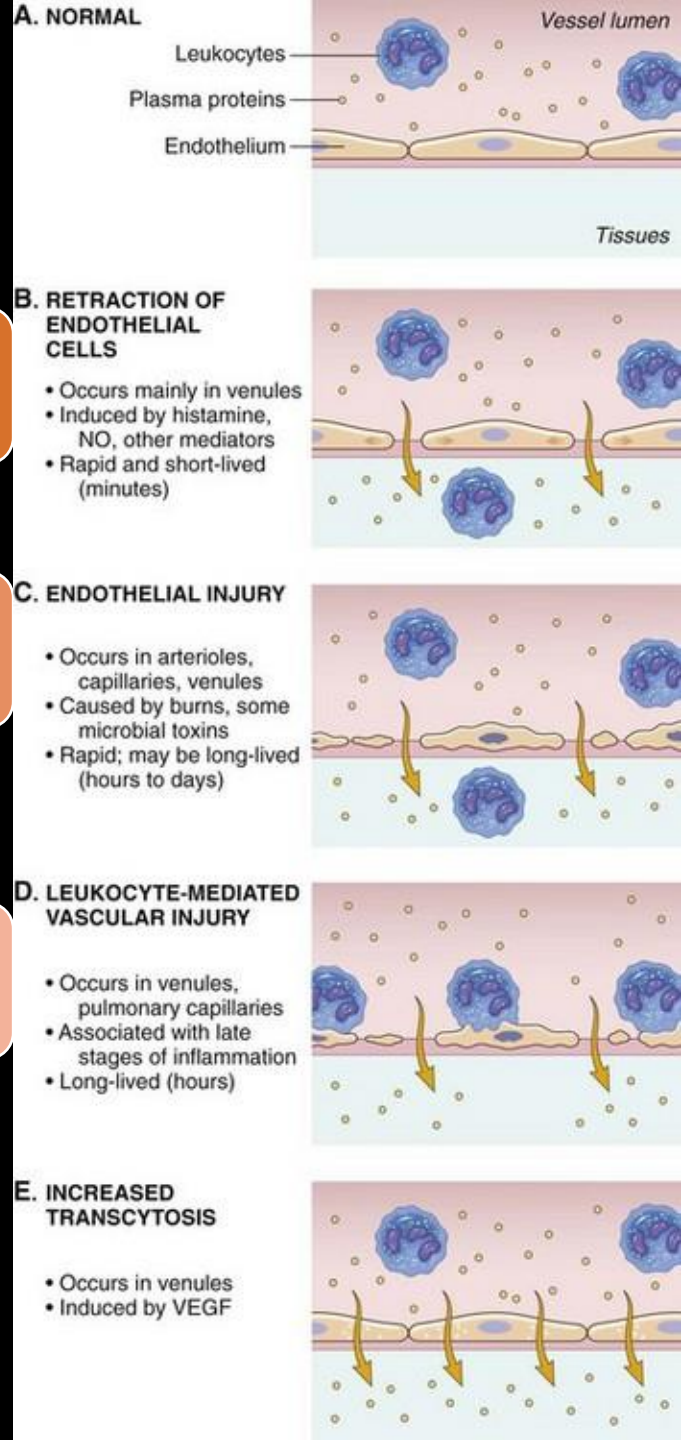
- limiting bleeding, but worsening of ischemia

Followed by vasodilatation

- ← NO production by the endothelium
- → ↑ perfusion of inflamed tissue, slowing of blood flow

Retraction of endothelial cells

- ← reaction to mechanical and chemical irritation
- → ↑ permeability → transfer of plasma, including proteins to interstitium



Principal mechanisms of increased vascular permeability in inflammation and their features and underlying causes.*NO,* Nitric oxide; *VEGF,* vascular endothelial growth factor.

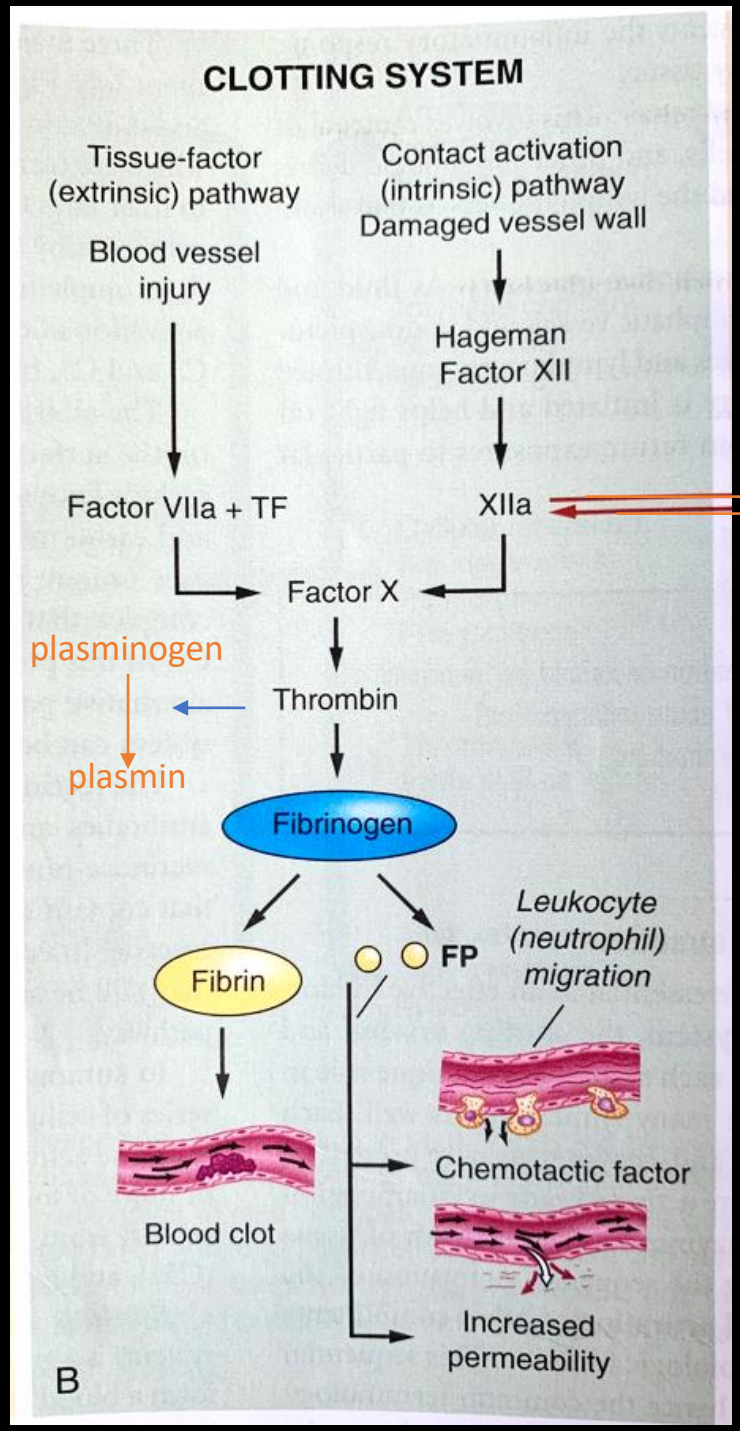
[34]

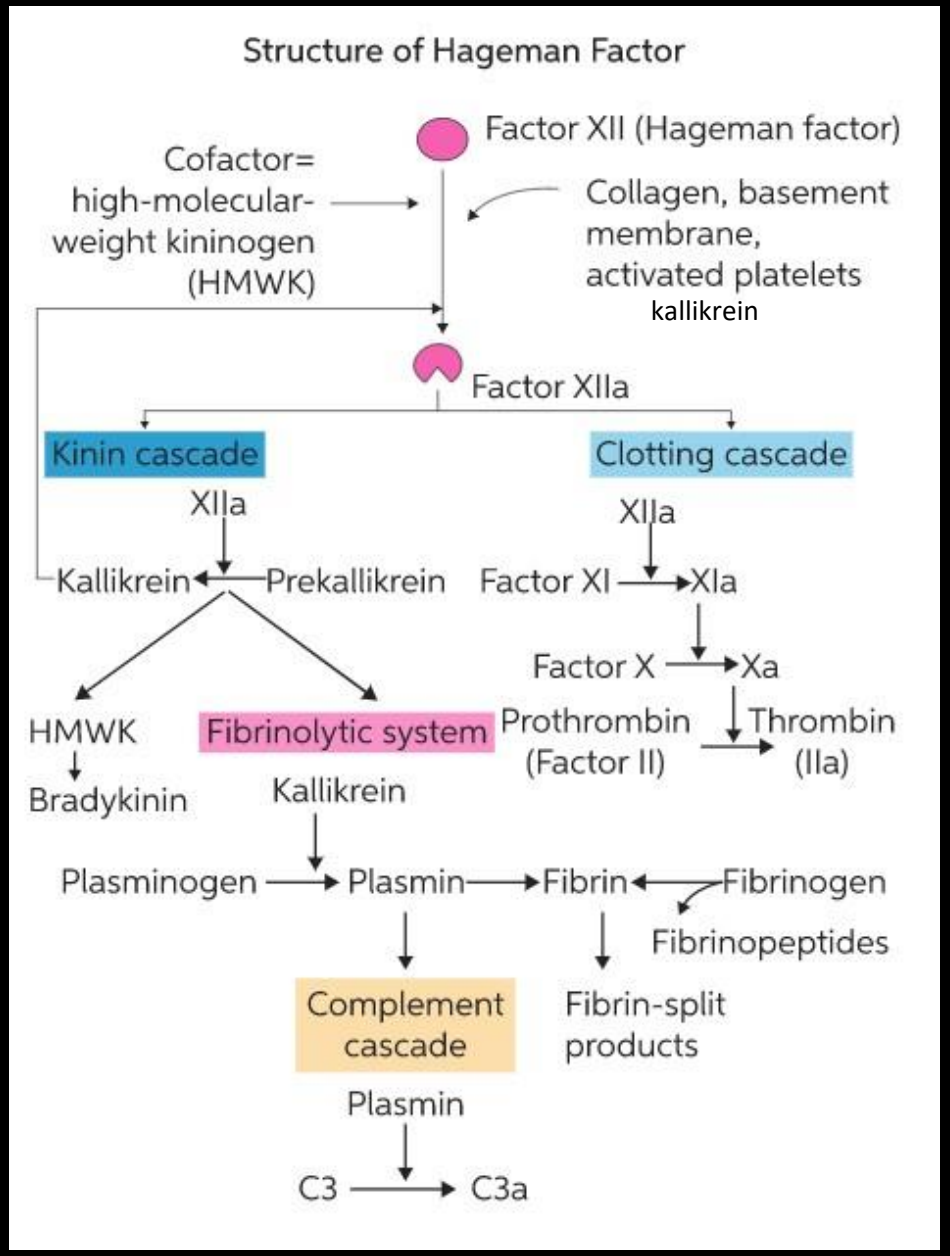
2nd Plasma Protein System

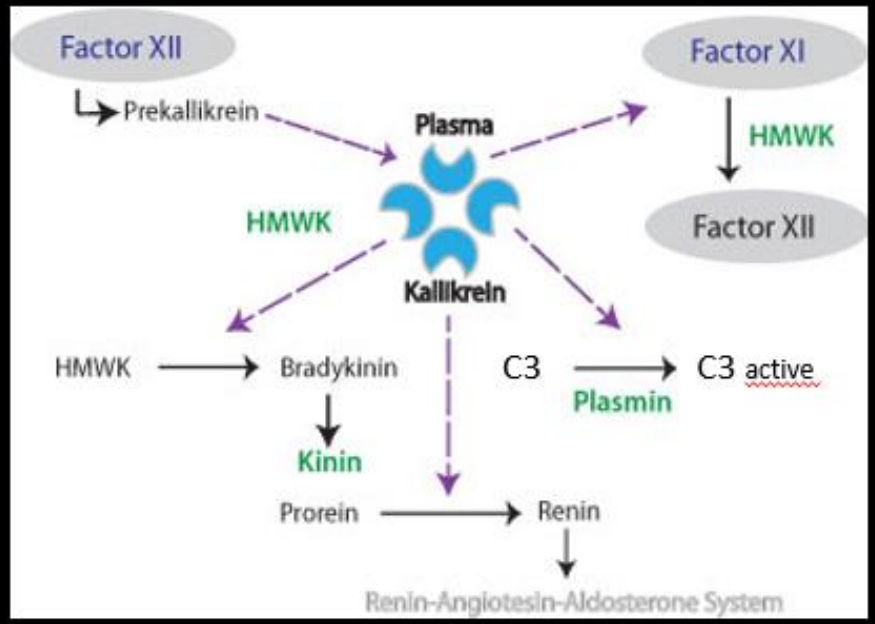
- Clotting system
- Complement
- Kinin system
- (regulation of the above systems)

Clotting System

- bounding of inflammation, limitation of spread
- (network) for future healing
- activated Hageman factor (XII) activates complement and the kallikrein-kinin system
- **simultaneous activation of the fibrinolytic system** as a defence against thrombus forming in blood vessels and the possibility of mild, further spread under local ↑ pressure




Structure of Hageman Factor
Factor XII (Hageman factor)
Cofactor= high-molecular-weight kininogen (HMWK)
Collagen, basement membrane, activated platelets
kallikrein
Factor XIIa
Kinin cascade
Clotting cascade
XIIa
Kallikrein
Prekallikrein
XIIa
Factor XI
XIa
Factor X
Xa
HMWK
Fibrinolytic system
Prothrombin (Factor II)
Thrombin (IIa)
Bradykinin
Kallikrein
Plasminogen
Plasmin
Fibrin
Fibrinogen
Fibrinopeptides
Complement cascade
Fibrin-split products
Plasmin
C3
C3a


Factor XII
Prekallikrein
Plasma
Factor XI
HMWK
HMWK
Factor XII
Kallikrein
HMWK
Bradykinin
C3
C3 active
Plasmin
Kinin
Prorein
Renin
Renin-Angiotesin-Aldosterone System

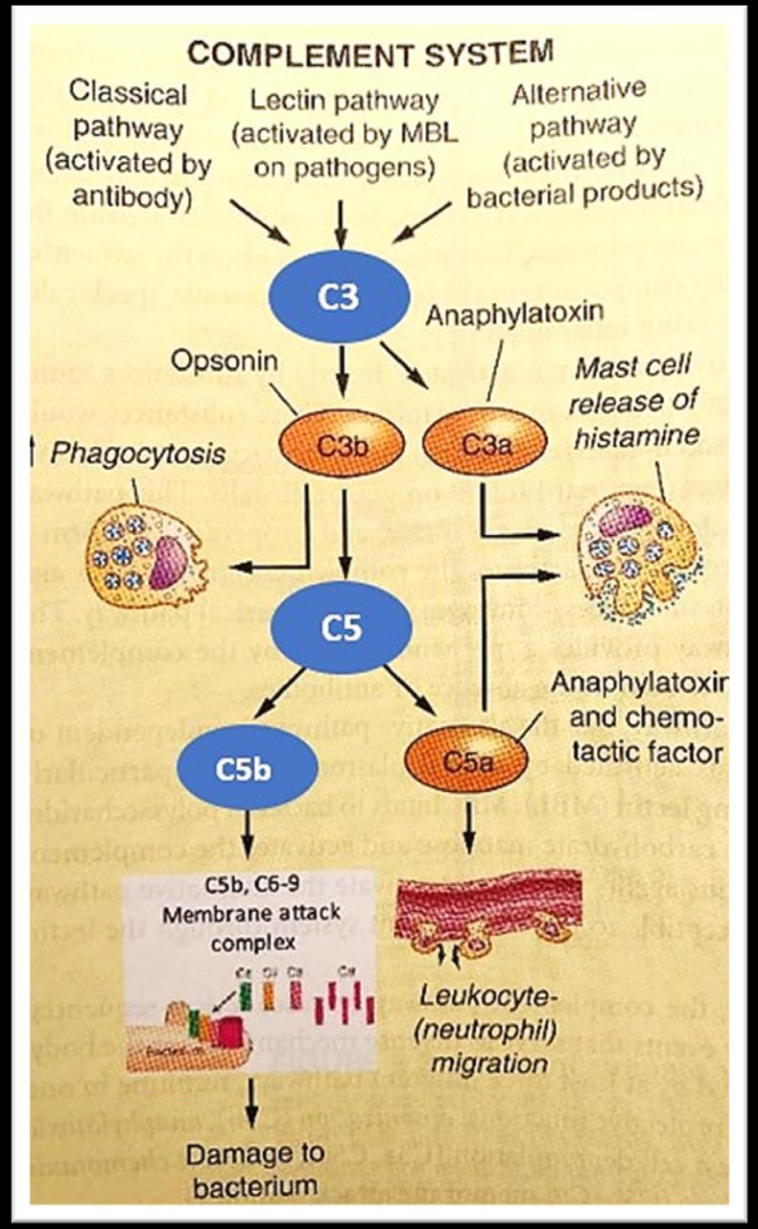
Hageman Factor Deficiency

https://encrypted-tbn0.gstatic.com/images?q=tbn:ANd9GcTDwPJJTe7LP689xipCpgAc3zQNpYUMztjtMQXj1f_TurbmHTGP4Z0sRok5GBxo-8k7IhY&usqp=CAU

https://onlinelibrary.wiley.com/doi/full/10.1046/j.1365-2141.2003.04459.x

Complement System

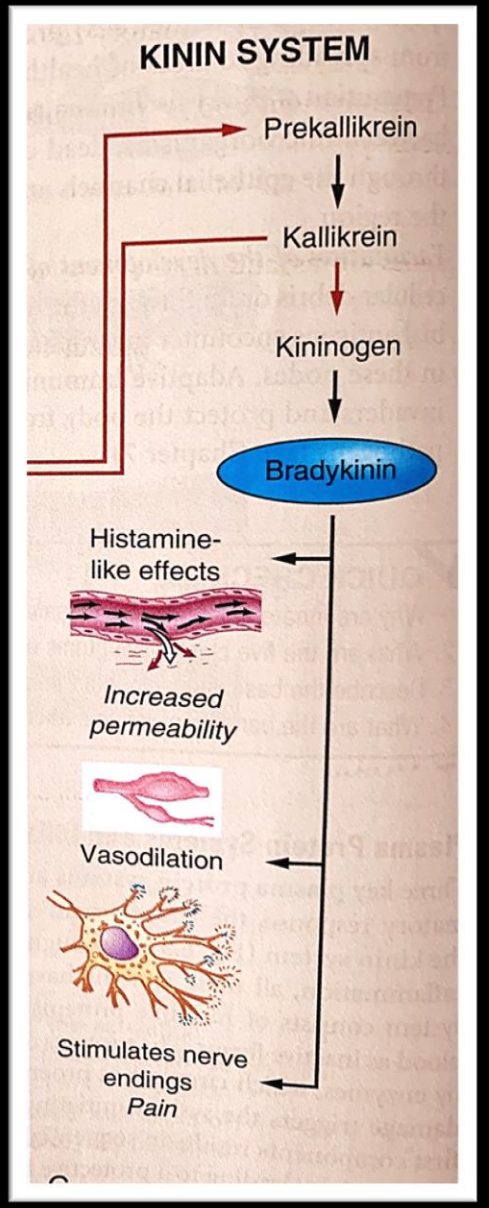
- mast cells activation (C3a, C5a)
- chemotaxes (C5a), opsonization (C3b)
- cytolytic effect (C5b, C6-9)
- neutralization



Kallikrein-kinin System

- through bradykinin :
  - vasodilatation
  - ↑ vascular permeability
  - irritation of free nerve endings

XIIa



HMWK

kallikrein

+

ACE

-

bradykinin

ACE

+

C1 inhibitor

+

inactive metabolites

contraction of non-vascular smooth muscle cells

- bronchoconstriction
- (dry cough accompanying ACEi use)

increased vascular permeability

- oedema
- (in C1 inhibitor deficiency angioedema)

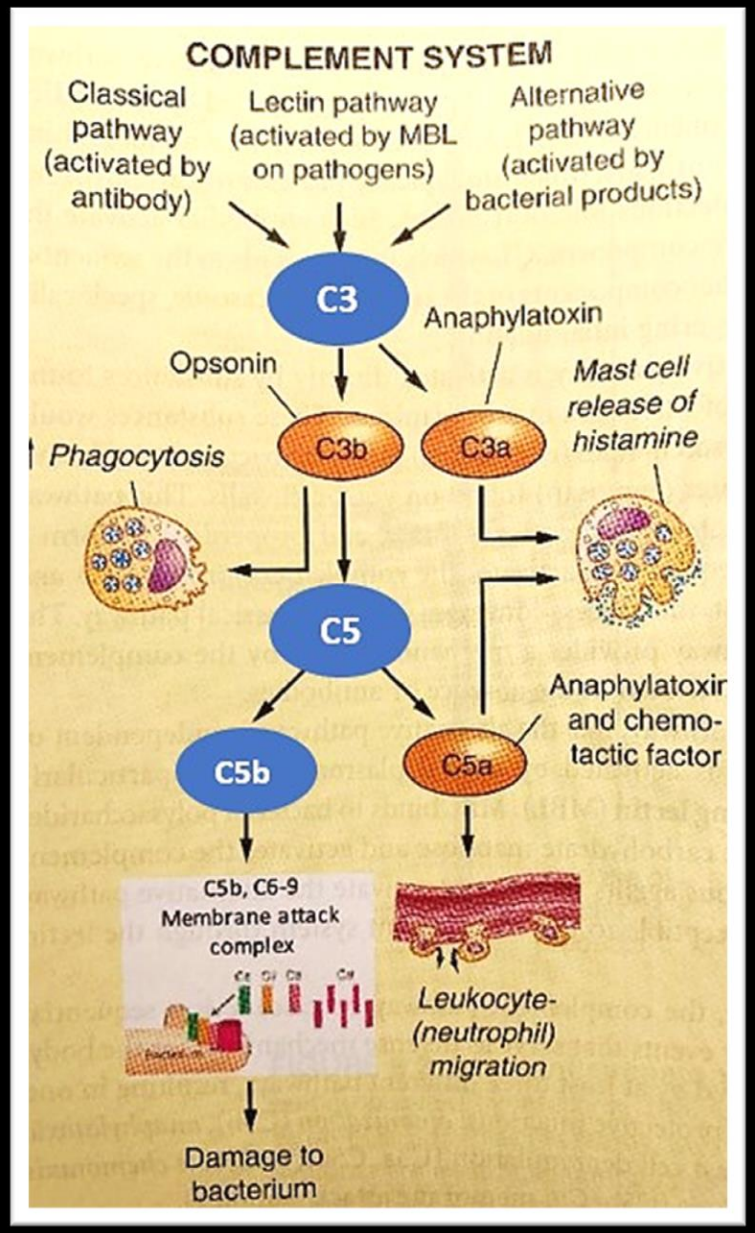
pain

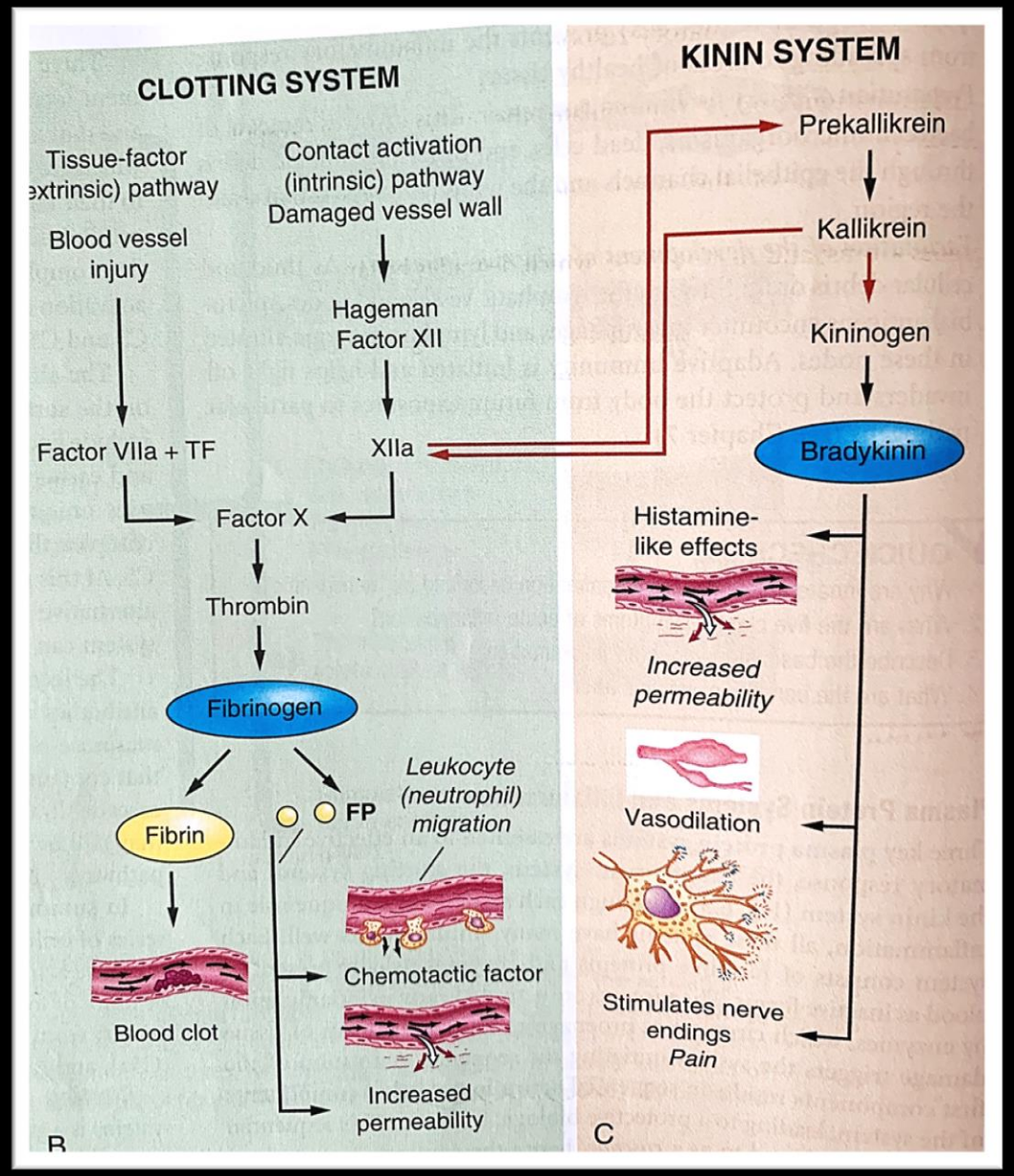
- chronic pain accompanying chronic inflammation

vasodilatation and natriuresis

- hypotension

https://www.priznaky-projevy.cz/images/priznaky_projevy/angioedem-angioneuroticky-quinckeho-edem-priznaky-projevy-symptomy-3.jpg


COMPLEMENT SYSTEM
Classical pathway (activated by antibody)
Lectin pathway (activated by MBL on pathogens)
Alternative pathway (activated by bacterial products)
C3
Anaphylatoxin
Opsonin
Mast cell release of histamine
Phagocytosis
C3b
C3a
C5
Anaphylatoxin and chemo-tactic factor
C5b
C5a
C5b, C6-9 Membrane attack complex
Leukocyte-(neutrophil) migration
Damage to bacterium


CLOTTING SYSTEM
Tissue-factor (extrinsic) pathway
Contact activation (intrinsic) pathway
Damaged vessel wall
Blood vessel injury
Hageman Factor XII
Factor VIIa + TF
XIIa
Factor X
Thrombin
Fibrinogen
Fibrin
FP
Leukocyte (neutrophil) migration
Chemotactic factor
Blood clot
Increased permeability
B
KININ SYSTEM
Prekallikrein
Kallikrein
Kininogen
Bradykinin
Histamine-like effects
Increased permeability
Vasodilation
Stimulates nerve endings
Pain
C

[4]

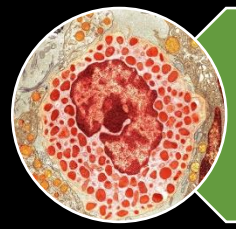
Regulation of the Plasma Protein System

- all 3 described plasma systems interact with each other and activation of one leads to activation of the other
- the successful course of inflammation depends on the effective activation of these systems
- activated inflammatory mediators are also potentially harmful - therefore their activity must be strictly regulated
  - restriction to the site of infection
  - penetration of plasma proteins that destroy mediators of inflammation:
    - protease inhibitors - **C1 inhibitor**, **carboxypeptidase** (x C3a and C5a)
    - **kininases** *(x kinins)*
    - **histaminases**
    - **fibrinolytic system** (plasmin)

Cellular Component and Vascular Tissue

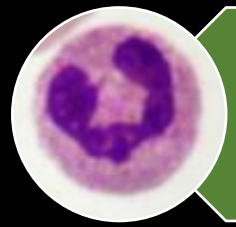
- local – dendritic cells (fixed macrophages), mast cells (mastocyte) and their “chemical weapons “
- chemotactically attracted – neutrophils and monocytes → macrophages
- chemotaxis and phagocytosis
- cellular receptors: PRRs and antigens: PAMPs and DAMPs
- cellular mediator and products

Cellular Components of Inflammation



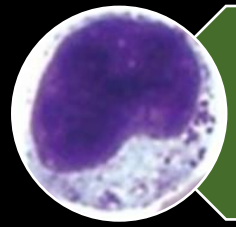
1st line

- **tissue macrophages**, **dendritic cells**, **mast cells**, activation within minutes



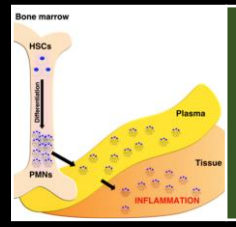
2nd line

- **neutrophil granulocytes**, activation in a few minutes, in the tissue in 6 – 12 h



3rd line

- **monocytes**, activation within 8 hours, in the tissue the first in 24 h



4th line

- activated bone marrow, activation within 3 – 4 days

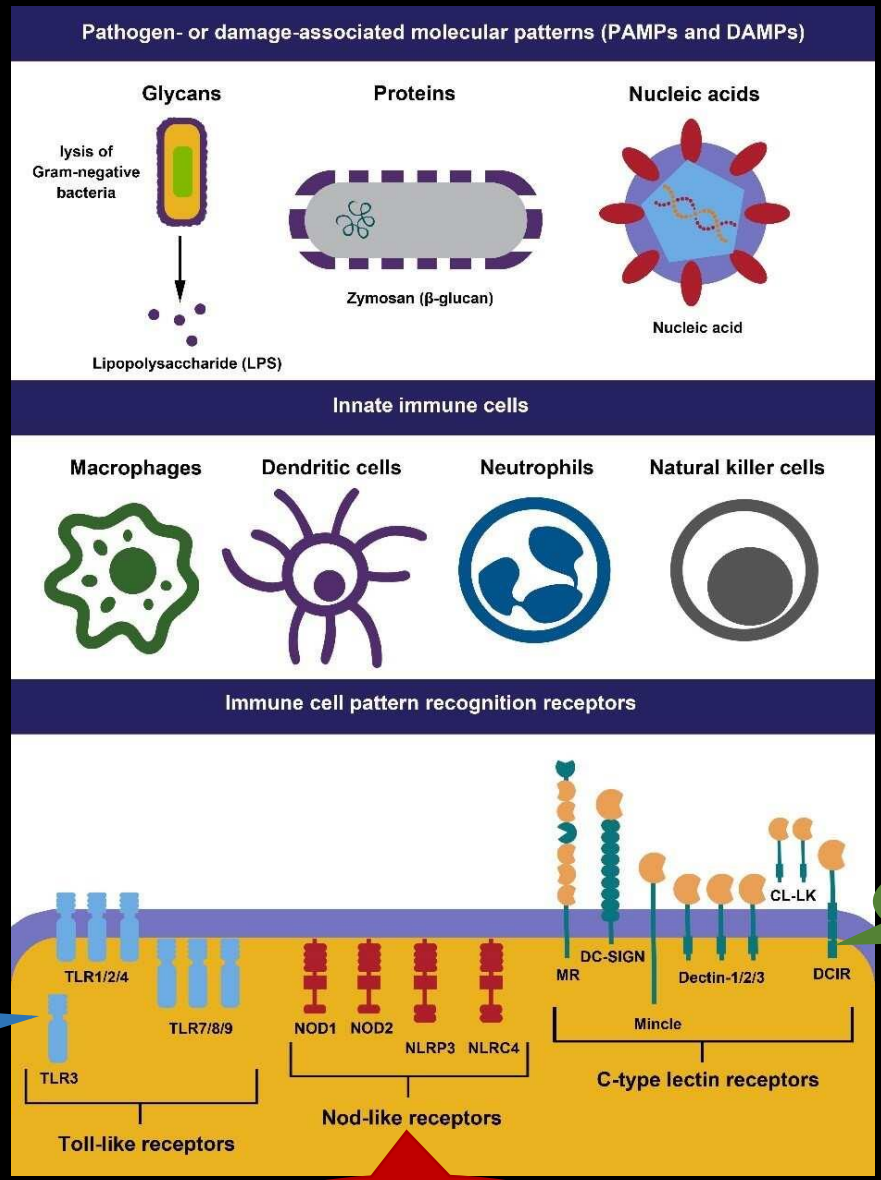
[38]

How do the cells of non-specific immunity recognize "their enemy" (foreign element)?

PRRs	PAMPs	DAMPs
• Pattern Recognition Receptors	• **Pathogen**-Associated Molecular Patterns	• **Damage**-Associated Molecular Patterns

PRRs
PAMPs
DAMPs

- *PRR are found on the surface of non-specific immunity cells and on cells near the body surface*
- *over 100 different PRRs*
- *allow differentiation of more than 1000 molecules*



membrane

membrane

cytoplasmic

[5]

Overview of PRR

Toll-like receptors (TLRs)

- outer membrane – mucous epithelial cells, mastocytes, neutroneutrophils, macrophages, dendritic cells, lymphocytes
- distinguish different PAMPs – lipopolysaccharides, flagellin, peptidoglycans, lipoproteins, zymosan, viral and bacterial NA, virus coat proteins and DAMPs

C-typ lectin receptors

- outer membrane of phagocytes
- distinguish PAMPs (especially fungal) and DAMPs

NLR, NOD-like receptors

- cytoplasm – innate immune cells and lymphocytes

Complement receptors (C3a, C5a, C3b)

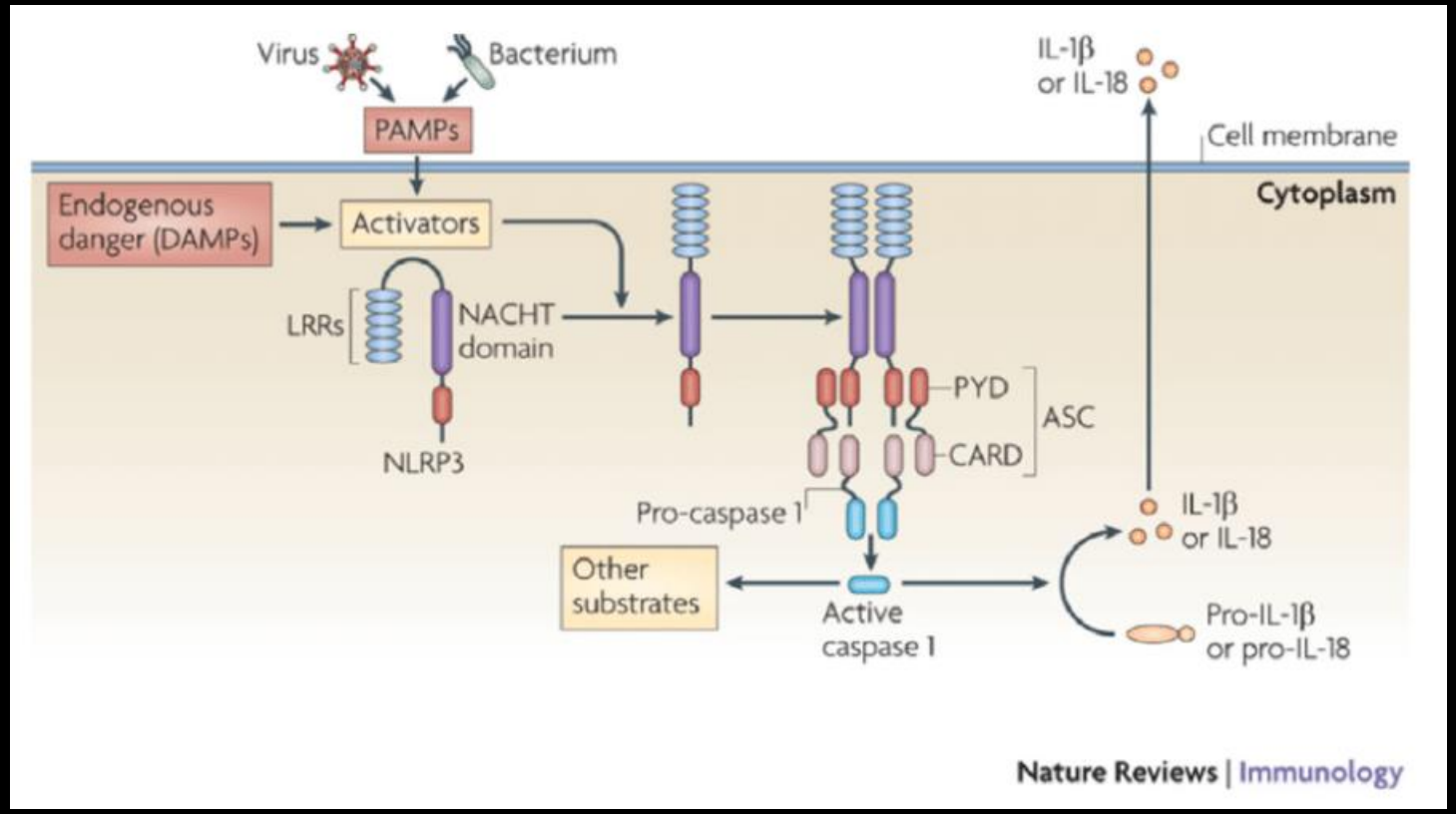
- outer membrane of innate immune cells, platelets, endothelial cells, vascular smooth muscle cells

Scavenger receptors

- outer membrane of macrophages
- differentiation of membrane phospholipids, phagocytosis of LDL, HDL, oxLDL

inflammasome creation → proinflammatory cytokines production → acute inflammation activation

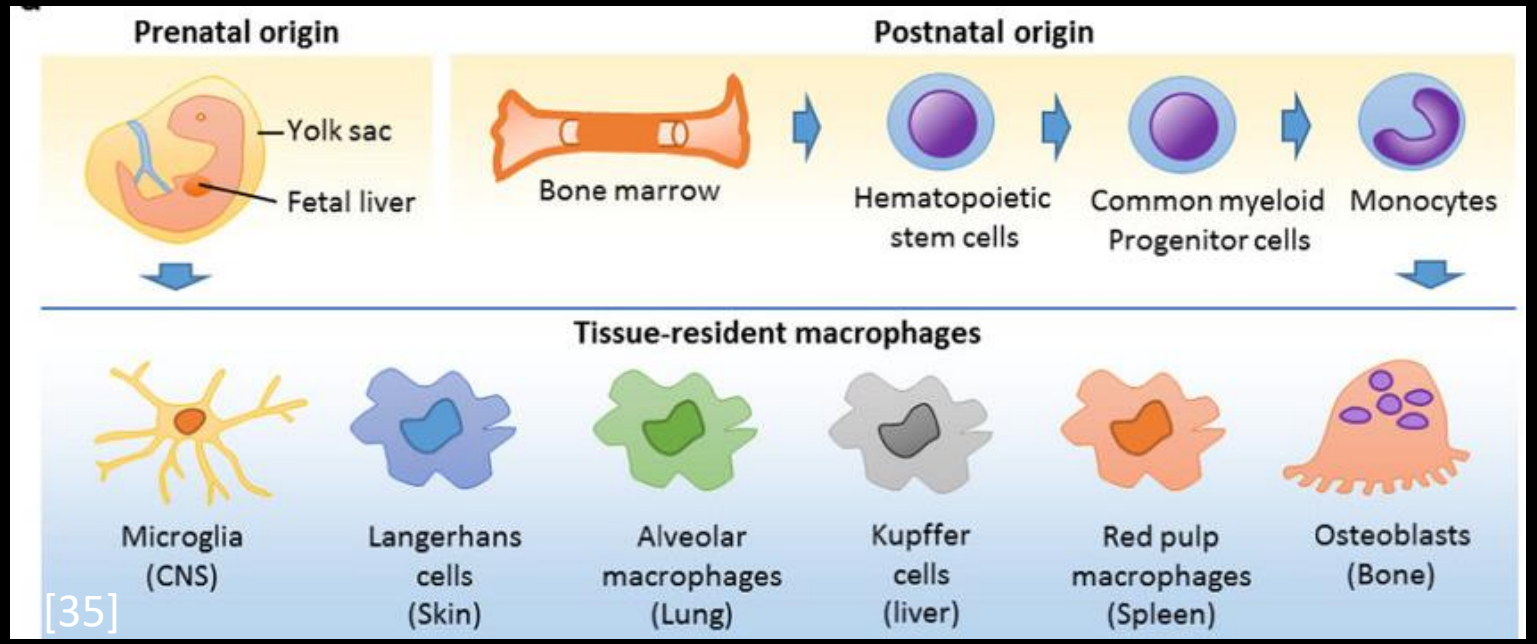
Inflammasome *= protein complex created in cytosol after PPR activation*



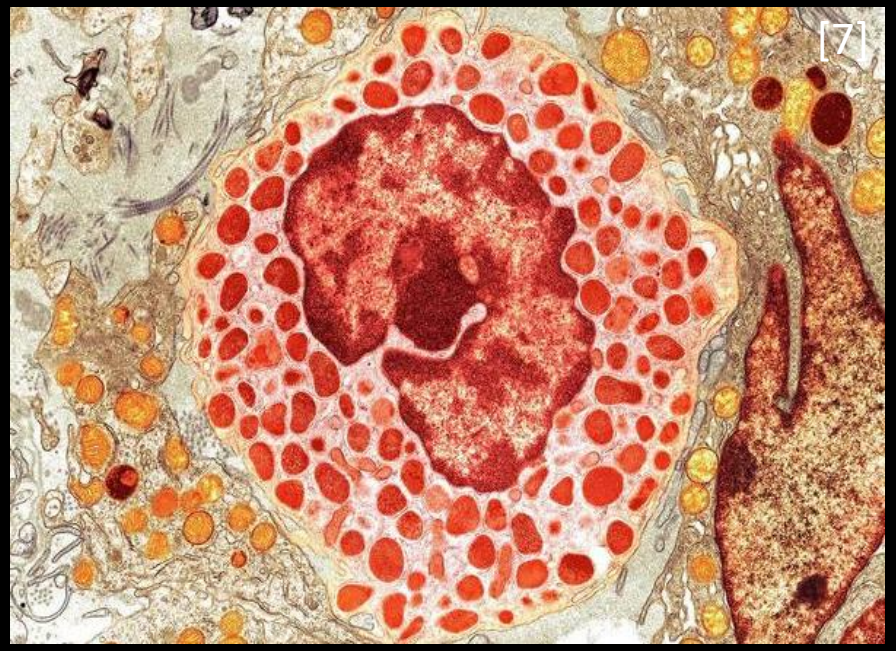
[6]

https://www.researchgate.net/figure/NLRP3-inflammasome-activation-Under-healthy-conditions-NOD-like-receptor-family-pyrin_fig1_305423876


[36]



[35]

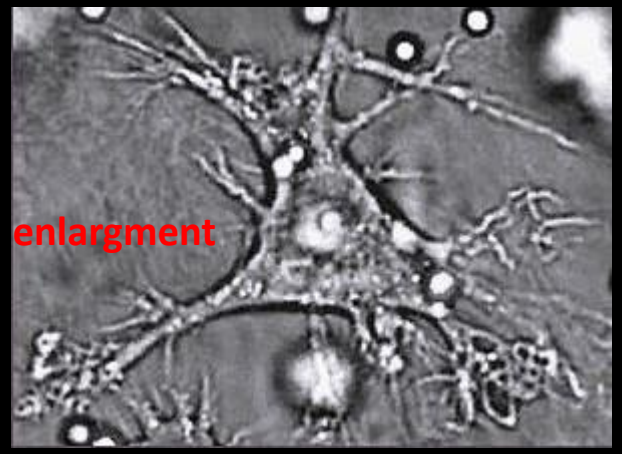

[7]

1st Line of Cellular Defence

https://blog.ernste.net/wp-content/uploads/2016/01/buckguardawp.jpg

Tissue Macrophages, Dendritic Cells

tissue injury



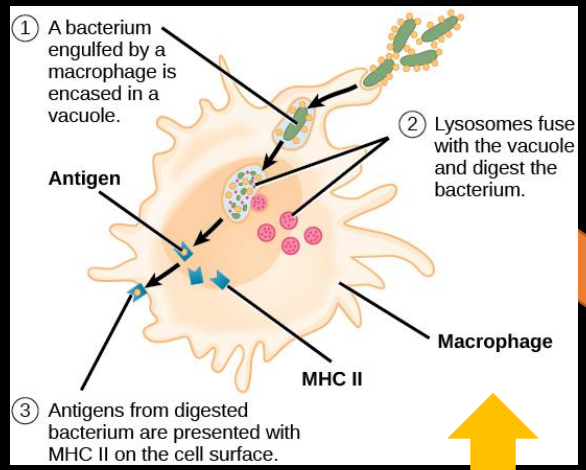
cytokines, IL production

phagocytosis

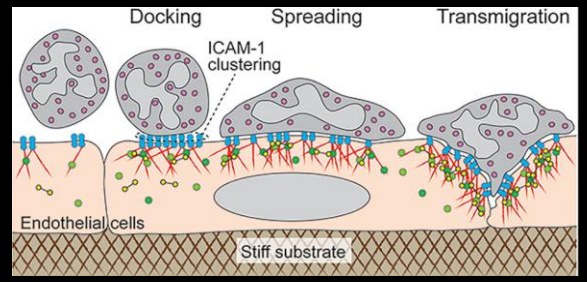
↑ mobility

managements of processes on the inflammatory site

endothelial cell activation – adhesive molecules expression



[44]



[41]

- part travel to **lymph nodes**

alien **antigen presentation**

Mastocyte

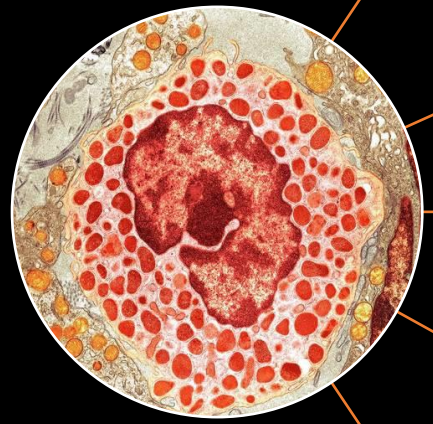
PAMPs

DAMPs

+

complement

IgE



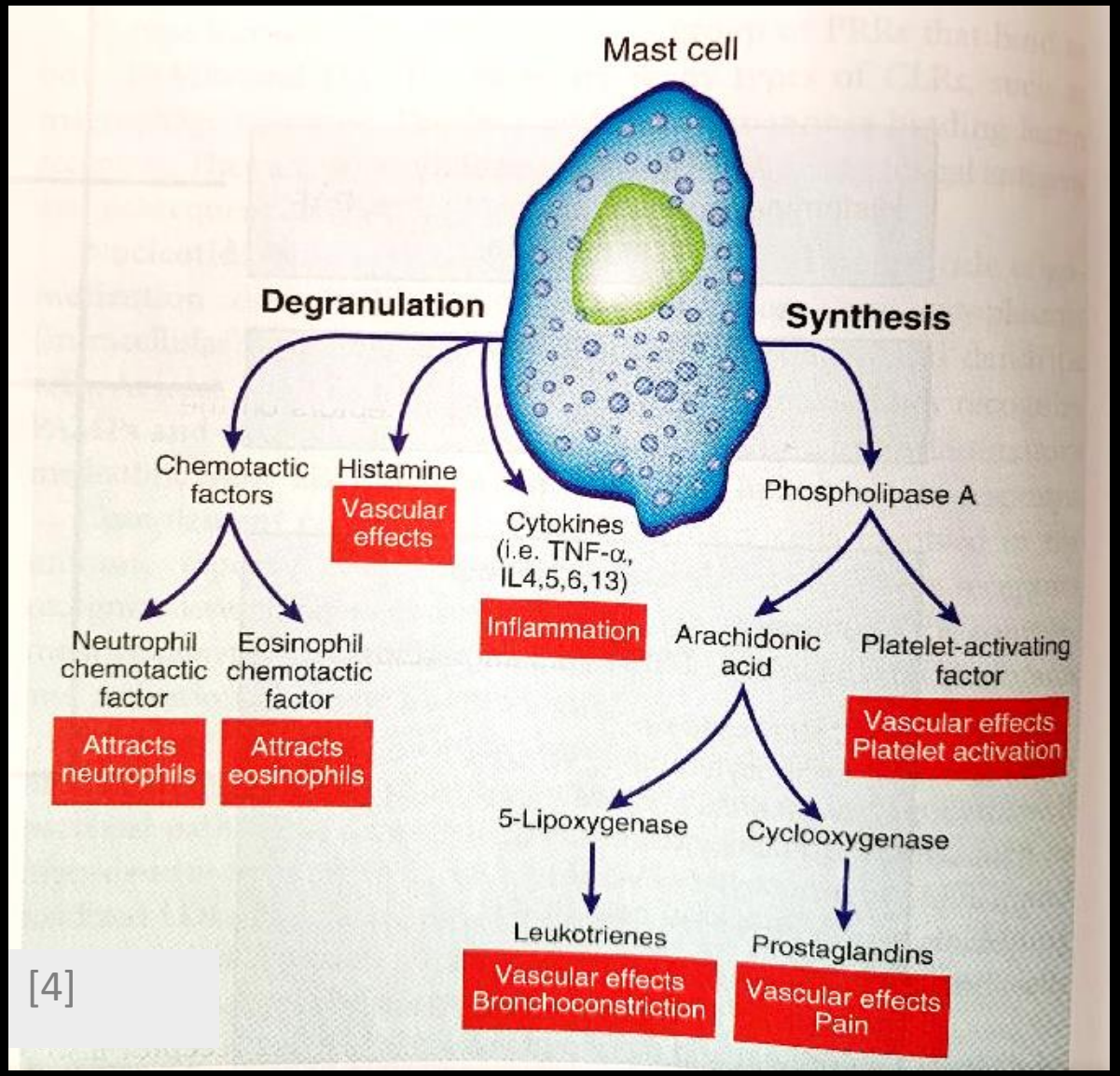
heparin
- anticoagulation
- inflammation spreading

histamin
- vasodilatation
- ↑ vascular permeability
- chemotaxis

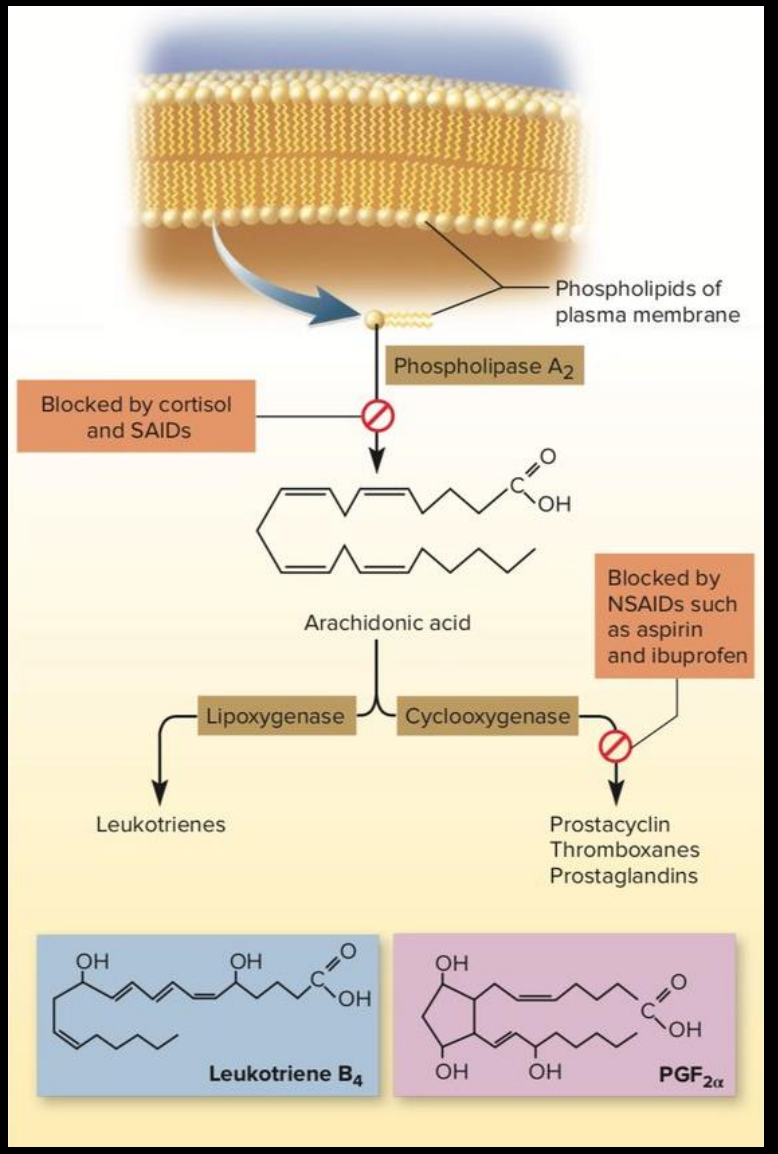
TNFα, IL-6
- pro-inflammatory effects, including systemic

LT a PG
- vasodilatation
- irritation of free nerve endings

PAF
- platelet activation


Mast cell
Degranulation
Synthesis
Chemotactic factors
Histamine
Vascular effects
Cytokines (i.e. TNF-α, IL4,5,6,13)
Inflammation
Phospholipase A
Neutrophil chemotactic factor
Eosinophil chemotactic factor
Attracts neutrophils
Attracts eosinophils
Arachidonic acid
Platelet-activating factor
Vascular effects Platelet activation
5-Lipoxygenase
Cyclooxygenase
Leukotrienes
Vascular effects Bronchoconstriction
Prostaglandins
Vascular effects Pain

[4]

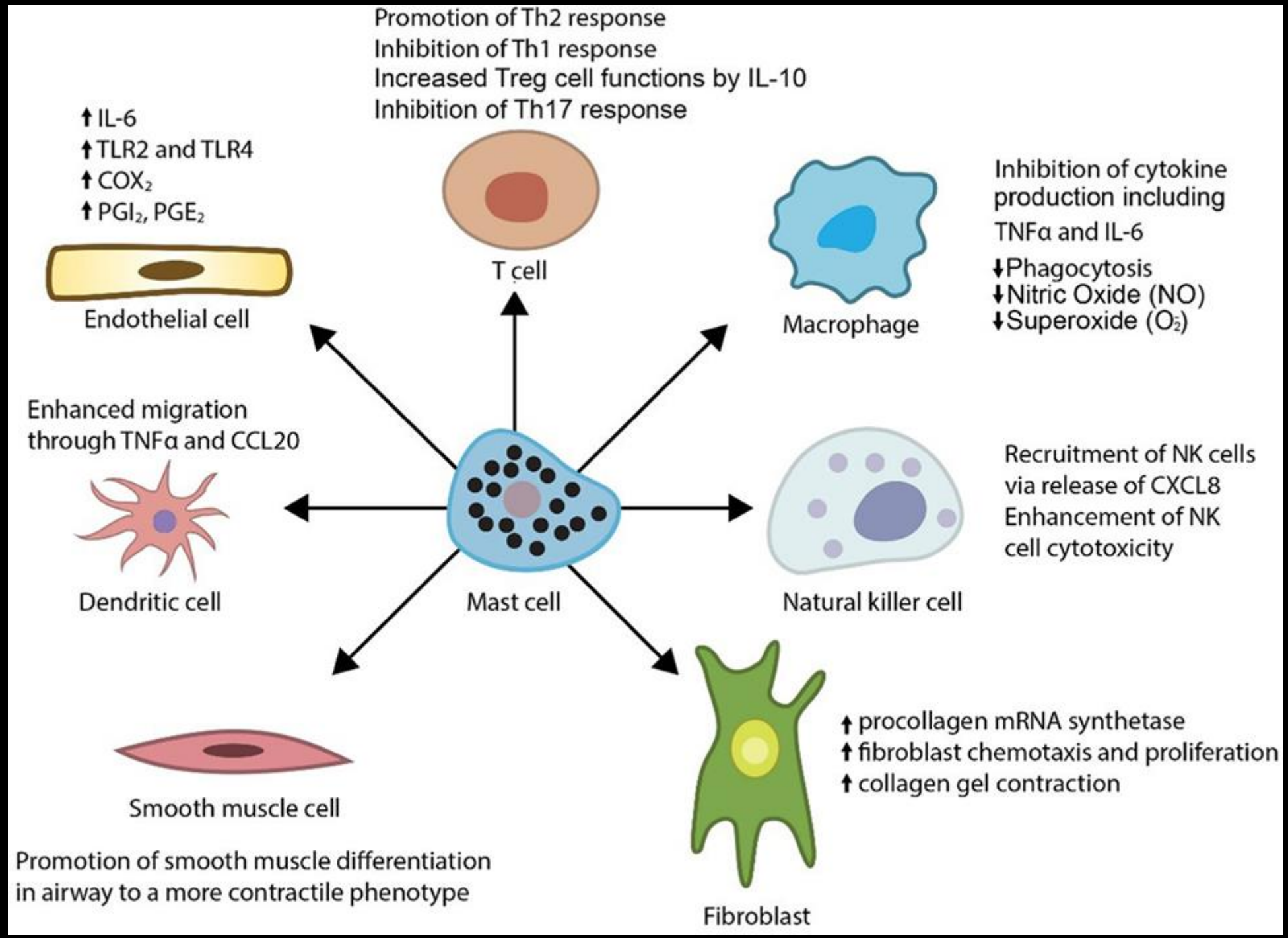

Phospholipids of plasma membrane
Phospholipase A_2
Blocked by cortisol and SAIDs
Arachidonic acid
Blocked by NSAIDs such as aspirin and ibuprofen
Lipoxygenase
Cyclooxygenase
Leukotrienes
Prostacyclin
Thromboxanes
Prostaglandins
Leukotriene B_4
$PGF_{2\alpha}$


ASPIRIN

[3]

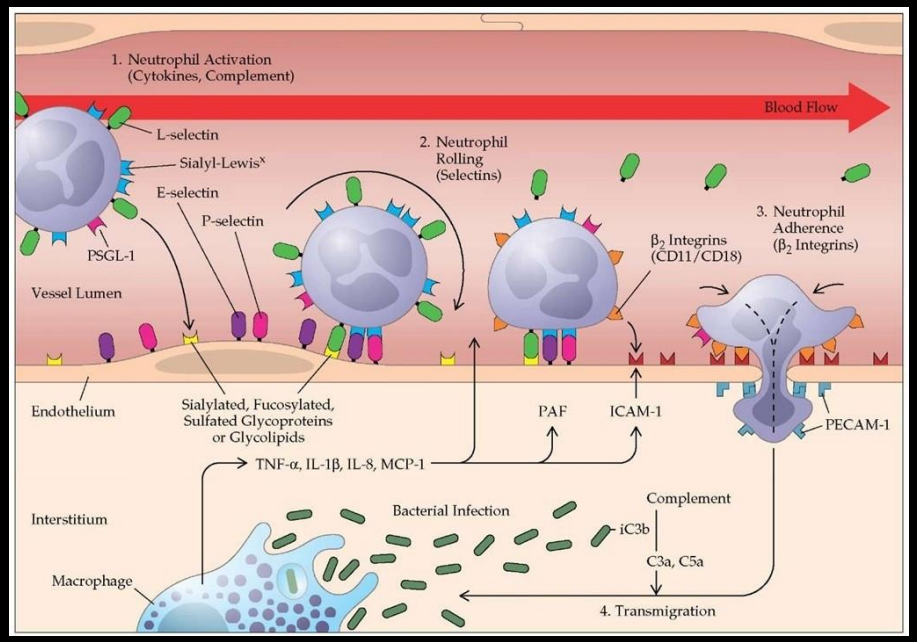
Effects of inflammatory mediators released by the mast cell (revision)

histamine	•through H1R pro-inflammatory effects - VD, ↑ vascular permeability, neutrophil chemotaxis, ↑ leukocyte adherence, bronchoconstriction •anti-inflammatory effects via H2 receptors - suppression of leukocyte function, HCl secretion
heparin	•anti-clotting effect, spread of inflammation
proteases	•spread of inflammation
leukotrienes	•↑ vascular permeability, important in late phase of inflammation, bronchoconstriction
prostaglandins	•↑ vascular permeability, neutrophil chemotaxis, pain
PAF - platelet activating factor	•↑ vascular permeability and leukocyte adhesion, platelet and mast cell activation •also produced by phagocytes, endothelia and platelets
eosinophil and neutrophil chemotactic factors	•neutrophil and eosinophil chemotaxis
TNFα, IL 4, 5, 6, 13	•pro-inflammatory and systemic effects


Promotion of Th2 response
Inhibition of Th1 response
Increased Treg cell functions by IL-10
Inhibition of Th17 response
↑IL-6
↑TLR2 and TLR4
↑COX_2
↑PGI_2, PGE_2
Endothelial cell
T cell
Macrophage
Inhibition of cytokine production including TNFα and IL-6
↓Phagocytosis
↓Nitric Oxide (NO)
↓Superoxide (O_2^-)
Enhanced migration through TNFα and CCL20
Dendritic cell
Mast cell
Natural killer cell
Recruitment of NK cells via release of CXCL8
Enhancement of NK cell cytotoxicity
Smooth muscle cell
Promotion of smooth muscle differentiation in airway to a more contractile phenotype
Fibroblast
↑procollagen mRNA synthetase
↑fibroblast chemotaxis and proliferation
↑collagen gel contraction

[6]

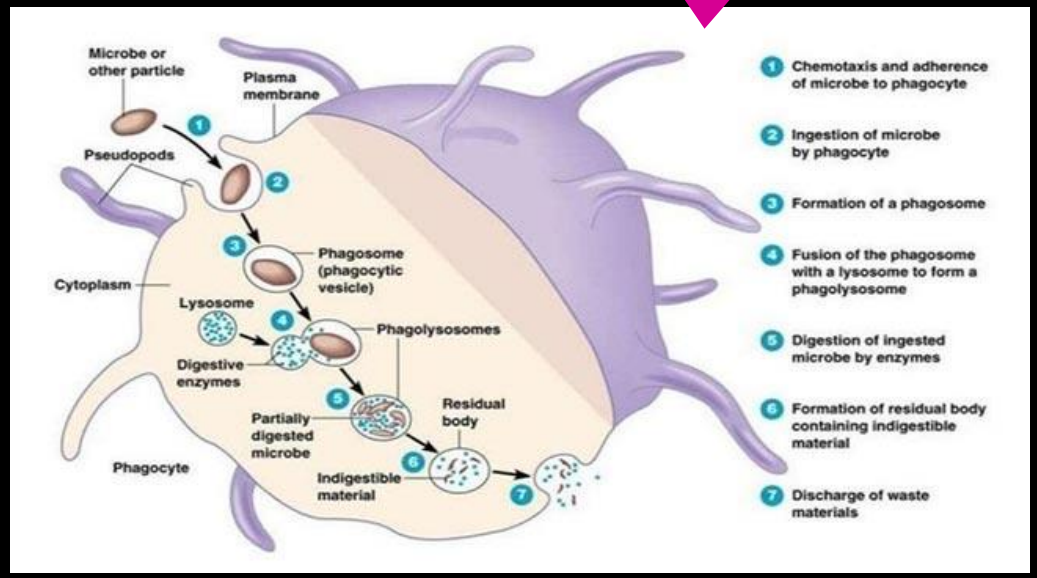
2nd Line of Cell Defence - Neutrophils



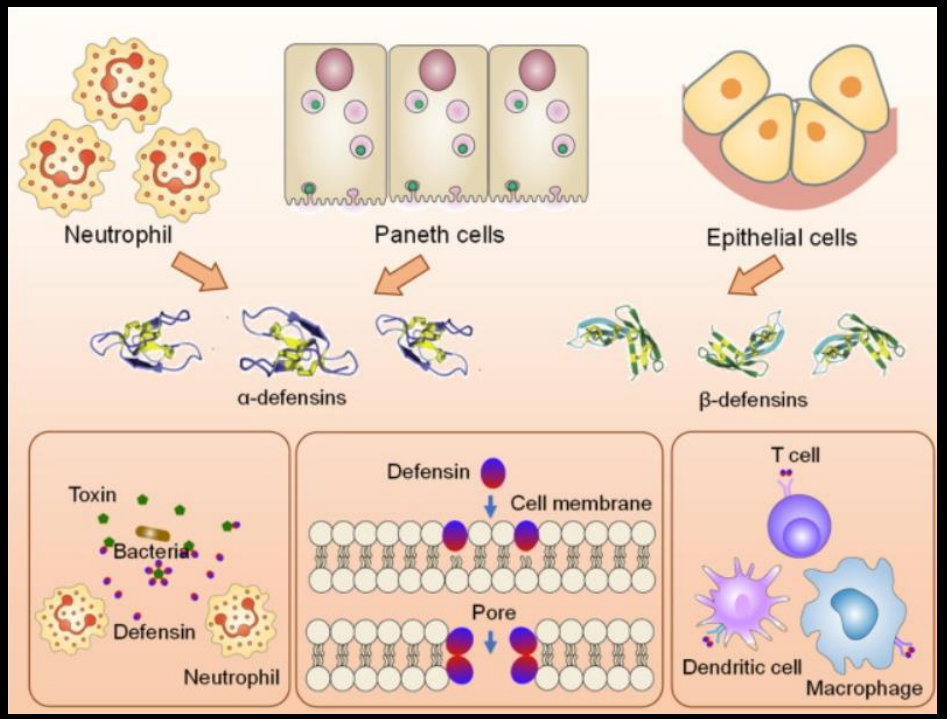
[42]

During their life, which lasts about **a week**, they **phagocytose up to 10 particles**.

- equipment of neutrophil **azurophilic granules**:
  - defensins
  - proteolytic enzymes
  - lysozyme
  - myeloperoxidases

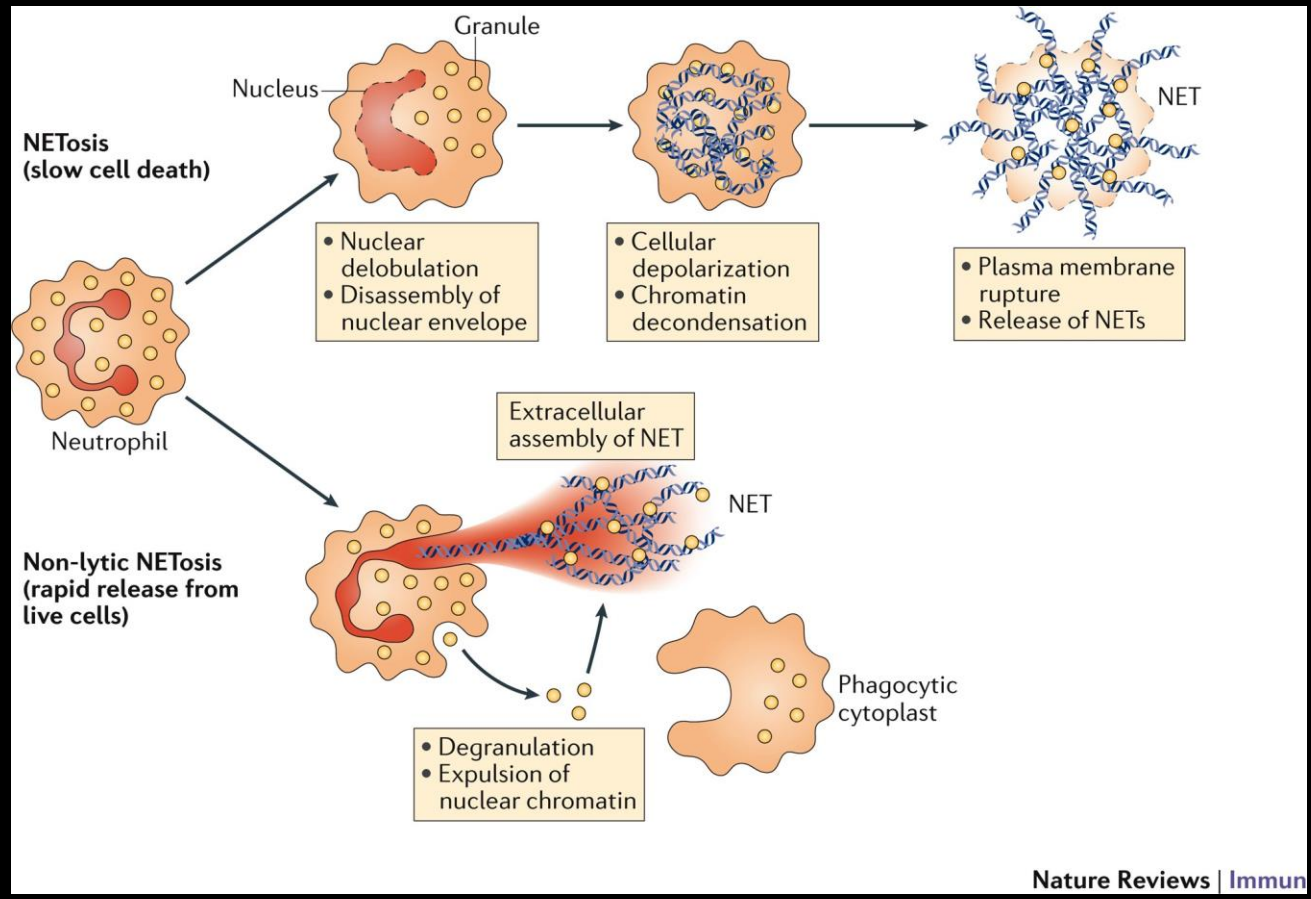


[40] [43]

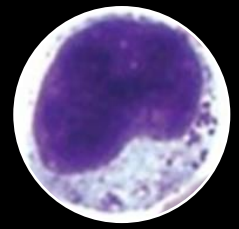


NETs – Extracellular Neutrophil Networks

- "traps for microorganisms"
- formation from neutrophils by NETosis
- composed of filaments of nuclear chromatin, with granular and cytoplasmic proteins (enzymes)
- stimulus to trigger formation: bacteria and their components, viruses, protozoa, fungi, cholesterol crystals, urate crystals

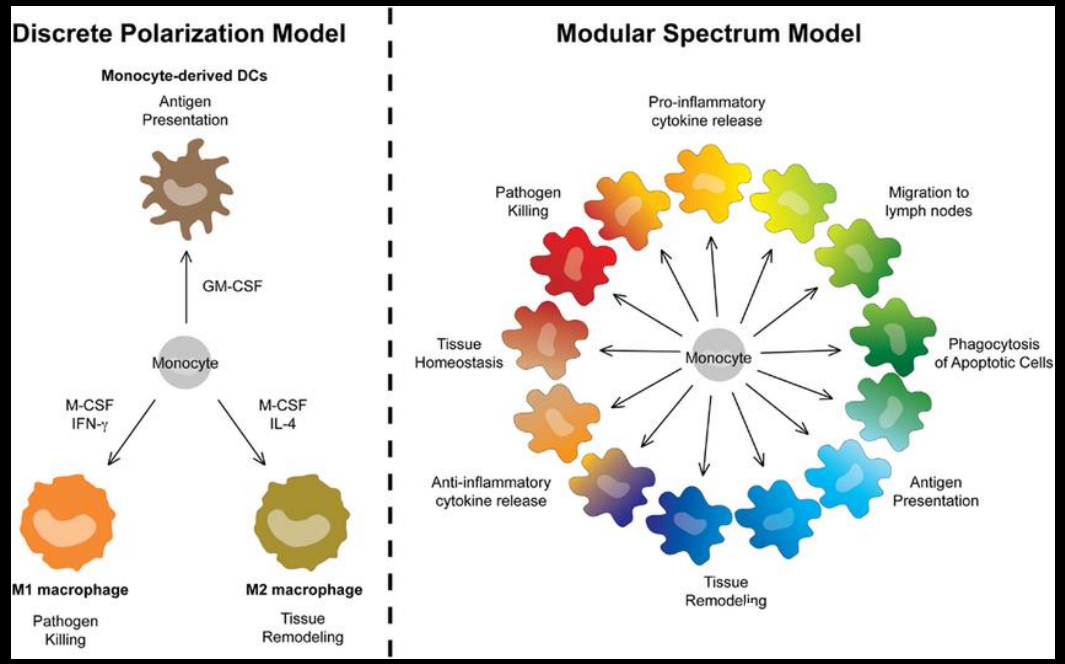


3rd Line of Cell Defense– Monocytes



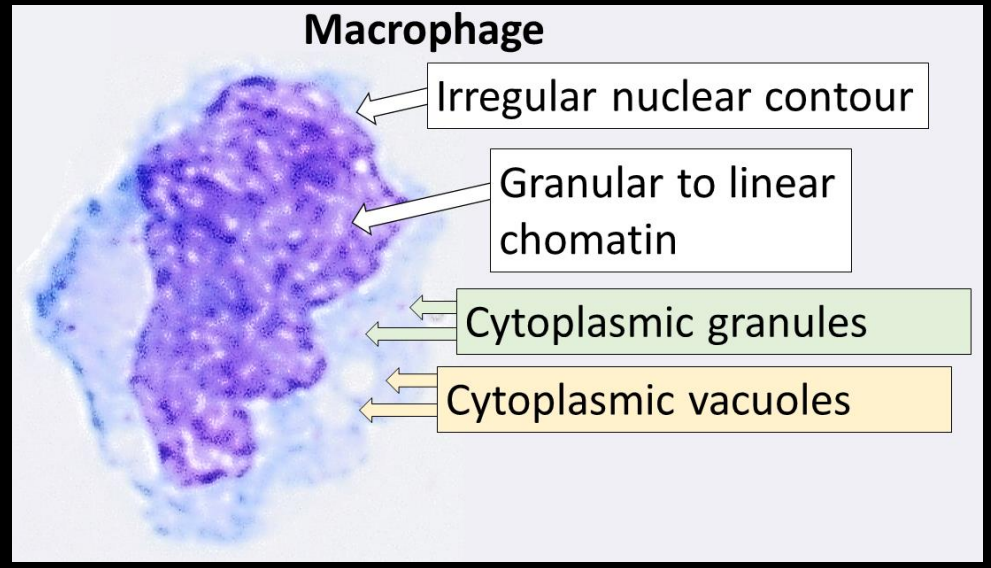
- → activation within 8 - 12 hours → macrophages
- long-lasting, efficient phagocytic and Ag presenting cells
- production of 100 various substances
  - IL-1, IL-6, IL-8, TNF-α, PG, clottings factors

adaptive immunity activation

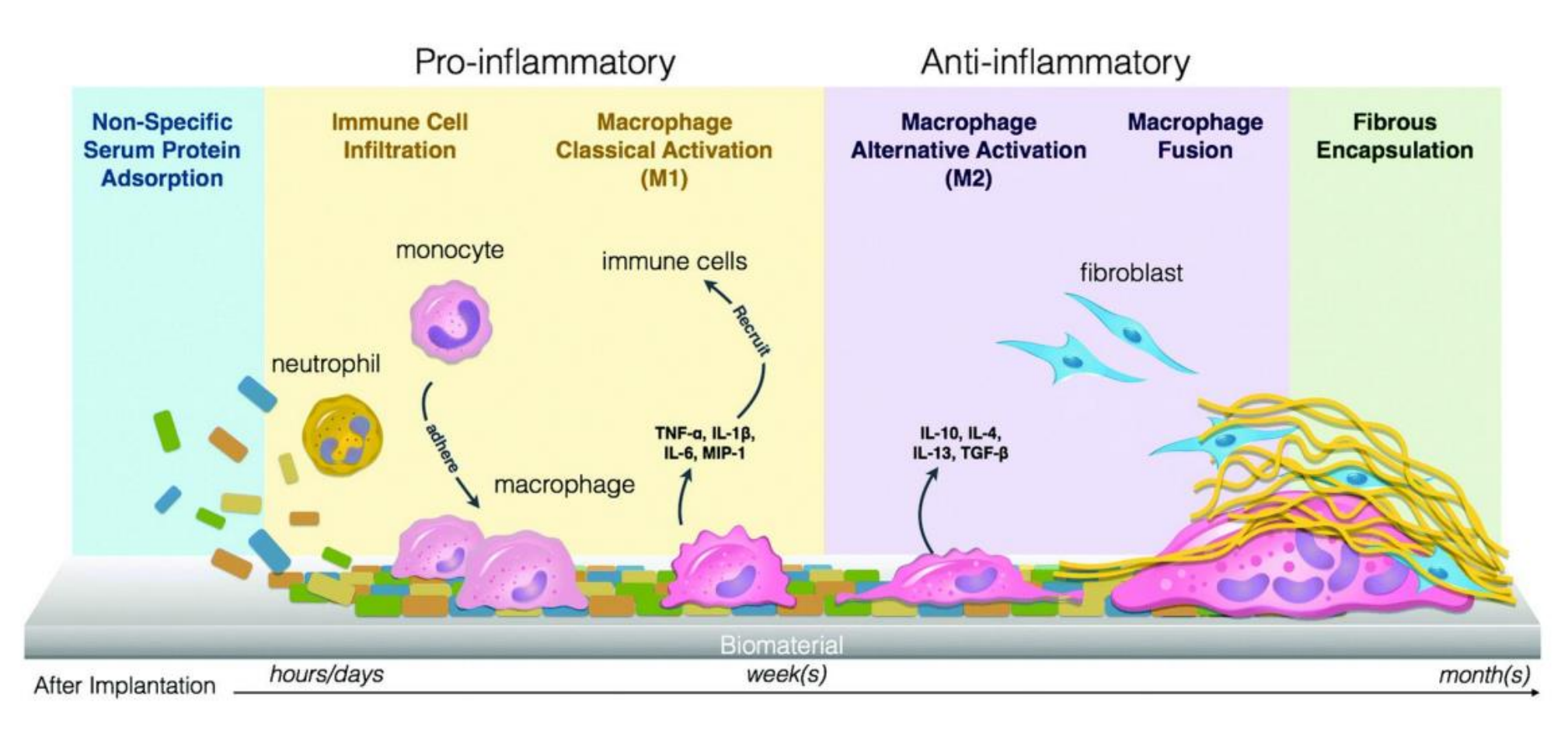


Monocytes → Macrophages

- largest leukocytes
- migrate to sites of inflammation and transform into macrophages (become even larger)
- appear a day later behind neutrophils at the site of inflammation; arrive in larger numbers after 3-7 days
- attracted by chemotactic factors
- able to survive, proliferate and phagocytose in acidic environments
- activate in 2 subpopulations
  - “pro-inflammatory" M1
  - "healing" M2
- essential role in:
  - removal of tissue detritus
  - healing - production of RF, promotion of angiogenesis
- bacteria resistant to destruction inside macrophages:
  - mycobacterium tuberculosis
  - mycobacterium leprae
  - salmonela typhi
  - brucella abortus
  - listeria monocytogenes



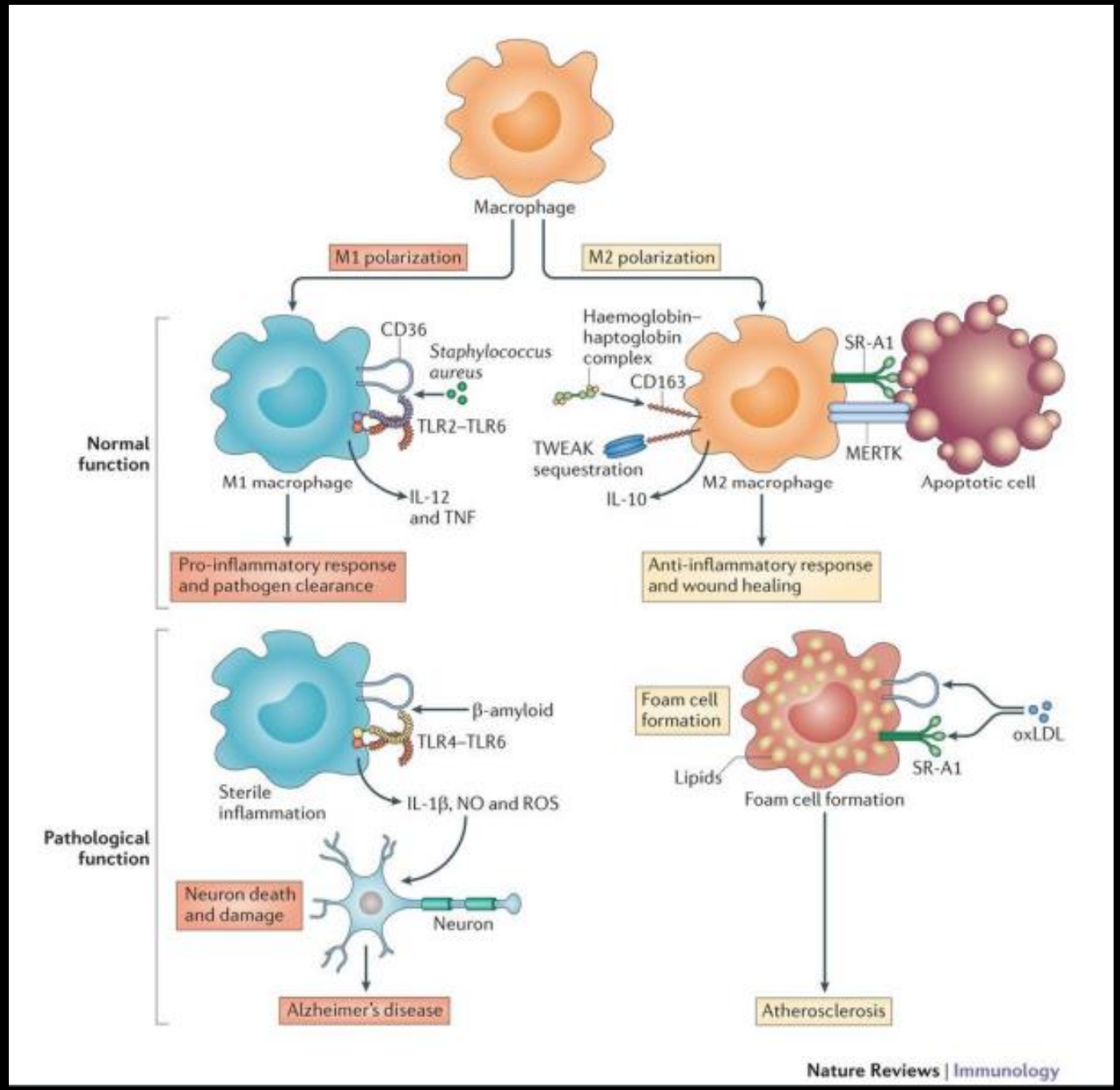
The Role of Phagocytes in the Inflammatory Process



Polarization of Macrophages –
notes to the previous slide

- Macrophages play a **key role in the regulation of healing**. During inflammation, their phenotype changes to provide the needs of the healing process.
- **Pro-inflammatory macrophages M1**
  - activated by TLR-ligands and IFNγ
  - produce NO, ROS, IL1, IL6, TNFα and MMP2 and 9 (creating space for infiltration by inflammatory cells)
- **Anti-inflammatory M2 macrophages**
  - activated by IL-4 and IL-13L
  - produce GF - PDGF, ILG1, VEGF, TGFβ-1 - help with proliferation, granulation, angiogenesis
  - also produce inhibitors of metalloproteinases
  - produce IL-10 to suppress inflammation
  - restore homeostasis, minimize fibrosis by apoptosis of myofibroblasts, suppress T-cell proliferation, maintain balance of metalloproteinases and their inhibitors

Role of M1 and M2 Macrophages in Pathophysiology



[14]

Inflammatory Mediators

- Prostaglandins
- Vasoactive substances
- Cytokines
  - soluble intercellular signaling molecules
  - pro and anti-inflammatory effect, systemic effects
  - IL - interleukins - produced mainly by lymphocytes and macrophages
  - **Importance:**
    - expression of **adhesion** molecules CAMs
    - **chemotaxis**
    - **proliferation** and **maturation of leukocytes**
    - **enhancement or suppression of nonspecific and specific immune responses**

[3]

Proinflammatory Cytokines

TNFα

- from activated macrophages, mast cells, neutrophils and lymphocytes
- chemotaxis, leukocyte adherence, stimulation of phagocytosis, leukocyte proliferation
- **systemic effects**: fever, RAF synthesis, muscle atrophy, prothrombogenic

the most important mediator of inflammation and sepsis - discovered in the 1970s while studying anticancer mechanisms

IL - 1

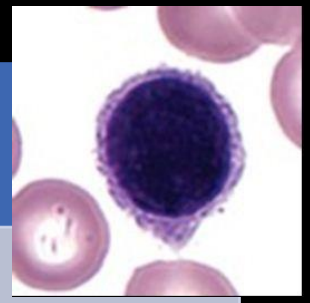
- from macrophages
- activates monocytes, macrophages, lymphocytes
- endogenous pyrogen
- GF
- enhances specific and non-specific immunity

IL - 6

- from monocytes, lymphocytes, fibroblasts
- bone marrow activation
- stimulation of fibroblast growth

Antiinflammatory Cytokines

IL 10



- from lymphocytes
- suppression of other lymphocytes activity and proliferation
- inhibits the production of pro-inflammatory cytokines by macrophages

TGF β

- transforming growth factor β
- from many cells
- suppresses lymphocyte activity
- inhibits cytokine production by macrophages
- stimulation of fibroblasts

Interferons

IFN α a β

- produced by cells infected with the virus
- activation of defence mechanisms in surrounding healthy cells

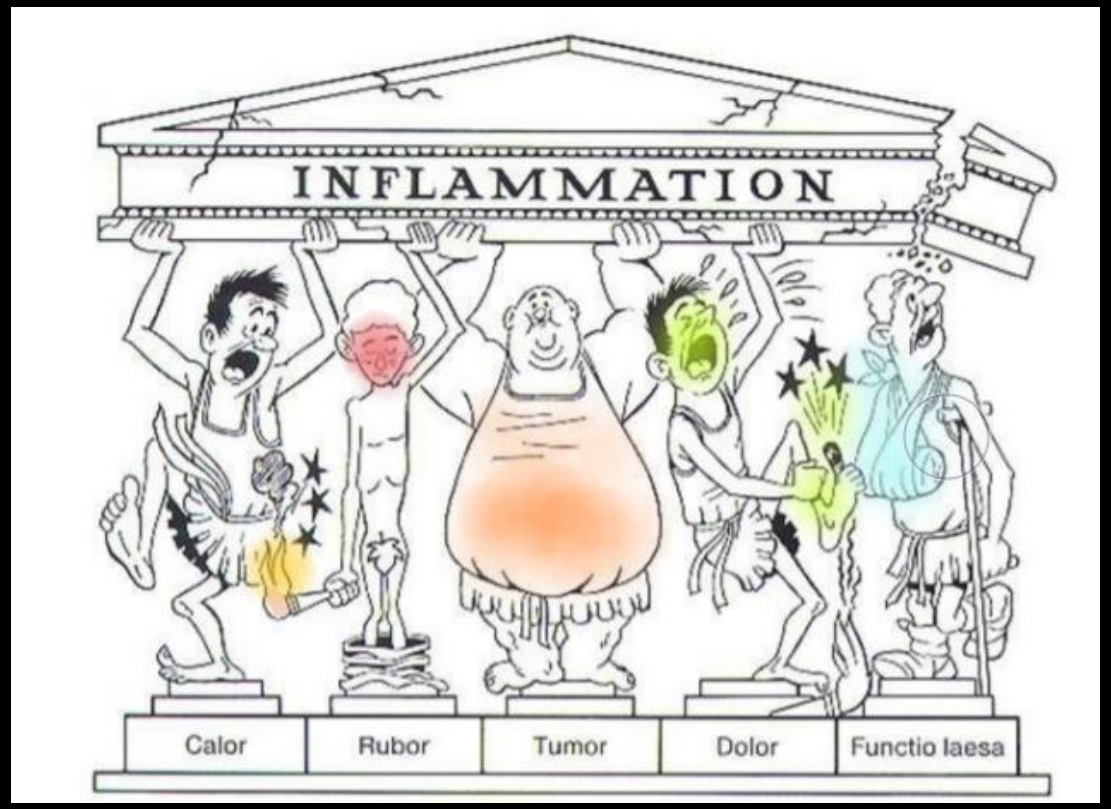
IFN γ

- from lymphocytes
- activation of macrophages

Symptoms of Inflammation

inflammatory focus

↑↑↑ cytokines production
(IL-1, IL-6, TNFα)



- fever
- lethargy, malasy
- drowsiness
- weakness
- anorexia
- leukocytosis
- ↑FW
- acute-phase reactant production

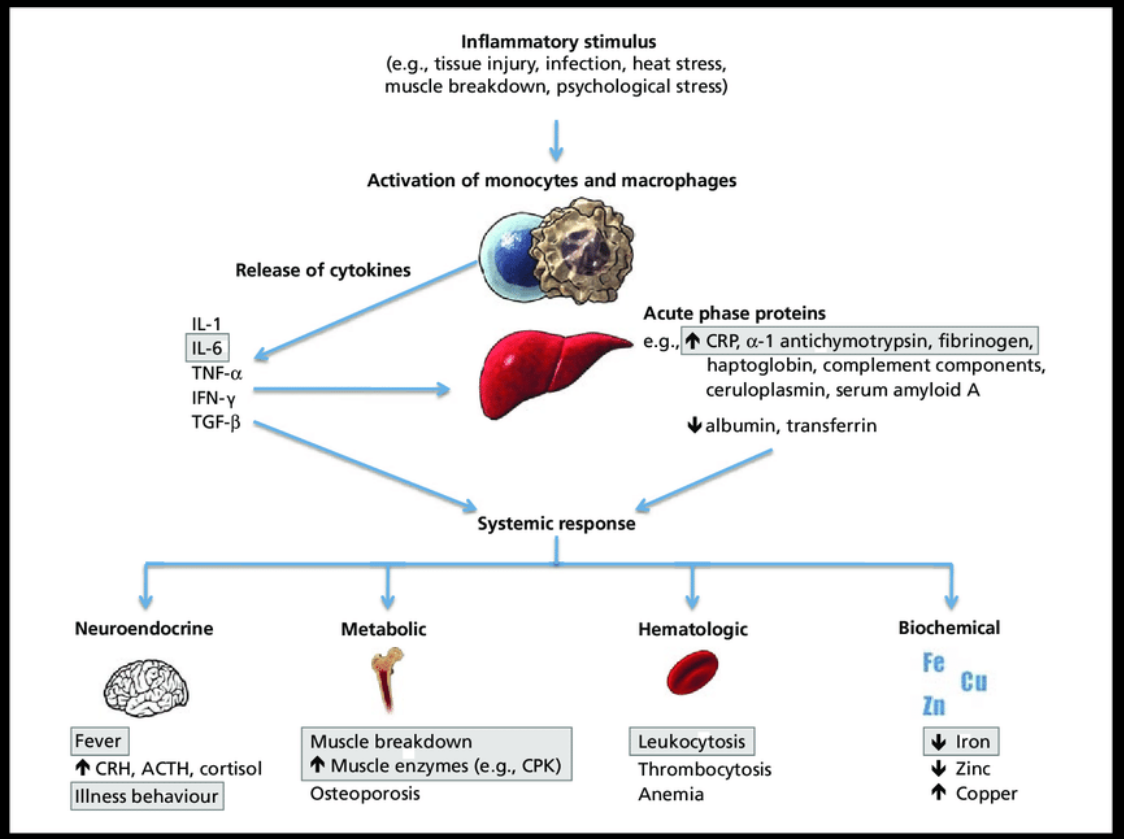
local

general

General Symptoms of Inflammation

caused by action of cytokines on

- **liver** → **acute-phase reactants** production
  - **CRP**
    - innate immunity stimulation
    - production proportional to the severity of inflammation
    - determination of plasma level replaces FW
  - **fibrinogen**
    - helping to limit inflammation
  - **antiproteases**
    - inhibition of enzymes from desintegrated phagocytes
    - α1-antitrypsin, α1-chymotrypsin
  - **hepcidin**
    - reduces the absorption of Fe from enterocytes and locks already absorbed Fe into macrophages
    - responsible for anemia of chronic disease
  - **ceruloplazmin**
    - oxidation Fe^{++} → Fe^{+++}
  - **haptoglobin**
    - binding of hemoglobin



↓availability Fe^{++} to bacteria
→ ↓ bacterial multiplication

Father Thomas Ganz Vilém (more like William at the time the picture was taken) Ganz (left) and Jeremy Swan pose with the Swan-Ganz catheter for measuring blood pressure and flow in the pulmonary artery, which they developed in the early 1970s.

Otec Tomáše Ganze Vilém (v době pořízení snímku už spíše William) Ganz (vlevo) a Jeremy Swan pózují u Swanova-Ganzova katétru pro měření krevního tlaku a průtoku v plicnici, který vyvinuli počátkem sedmdesátých let.
Snímek archiv Tomáše Ganze

V roce 2014 ocenila Americká hematologická společnost Tomáše Ganze cenou E. Donnalla Thomase za jeho průkopnický výzkum v oblasti homeostázy železa, včetně objevu hepcidinu.
Snímek archiv Tomáše Ganze

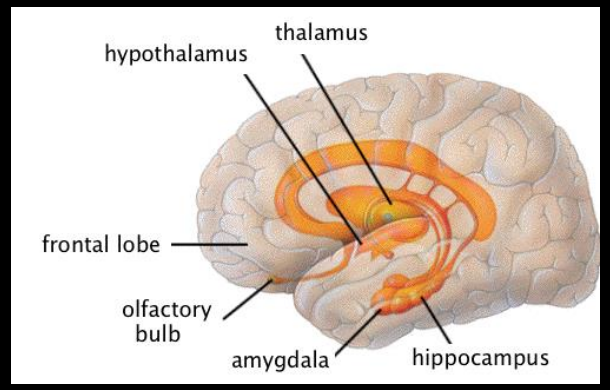
In 2014, the American Society of Hematology awarded Tomáš Ganz the E. Donnall Thomas Award for his pioneering research on iron homeostasis, including the discovery of hepcidin.

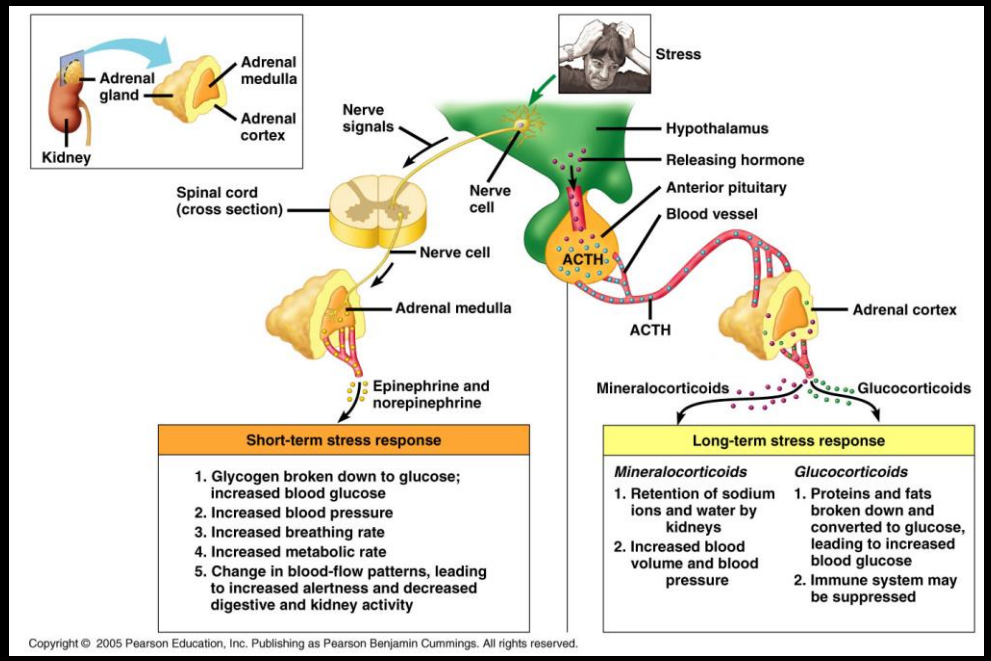
https://vesmir.cz/cz/casopis/archiv-casopisu/2022/cislo-2/muz-se-zeleznou-laskou.html

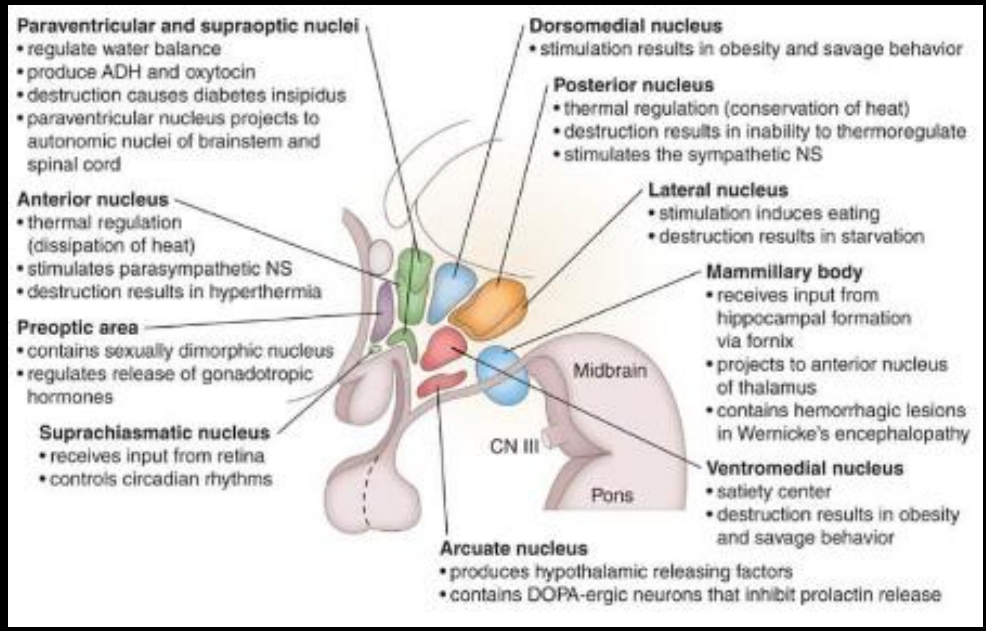
General Symptoms of Inflammation

caused by action of cytokines on:

- amygdala
  - ➢ malasy, drowsiness
- hypothalamus:
  - ➢ fewer
  - ➢ anorexia
  - ➢ triggering the stress response
    - ➢ sympathetic activation → leucocytosis

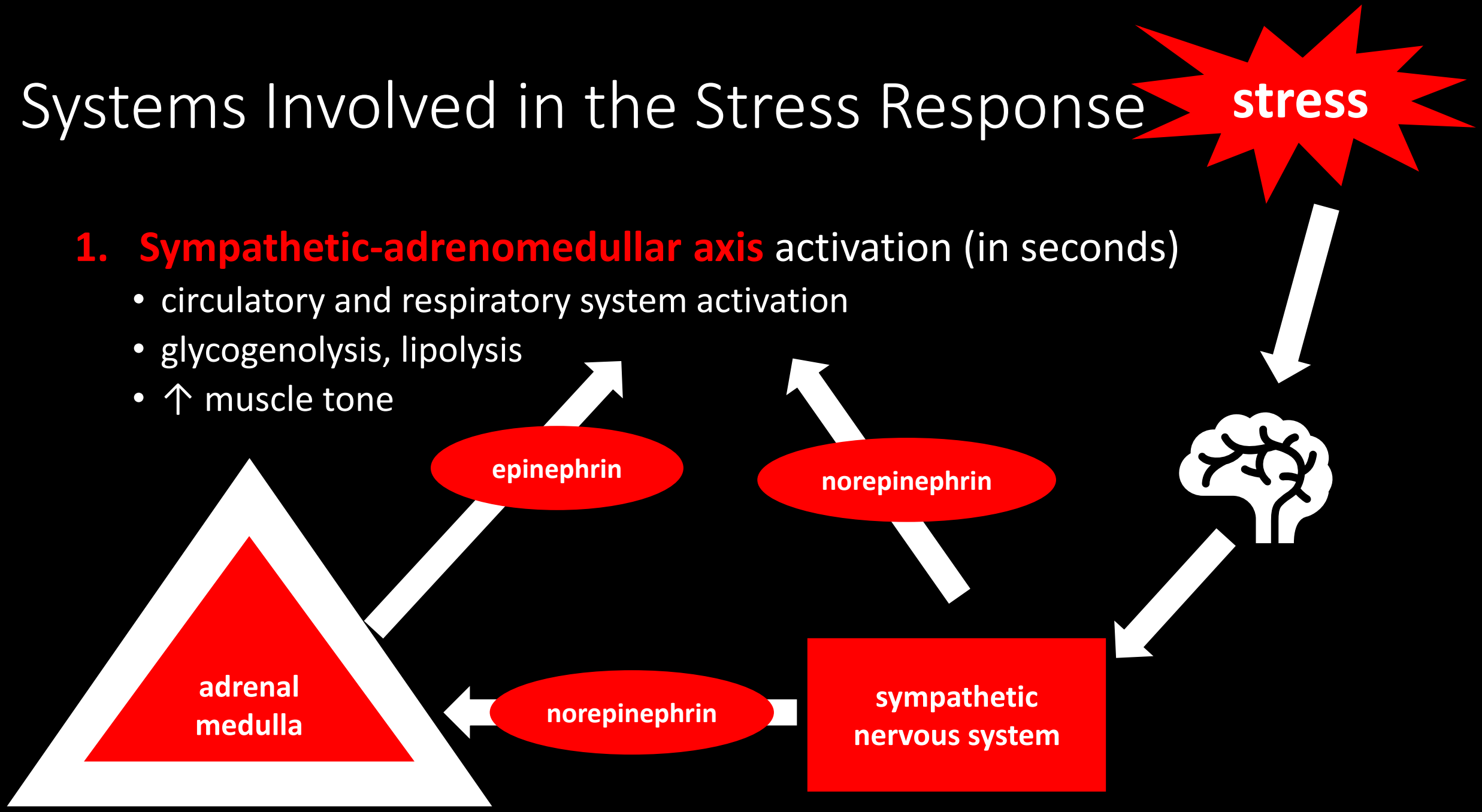






[49]

Systems Involved in the Stress Response

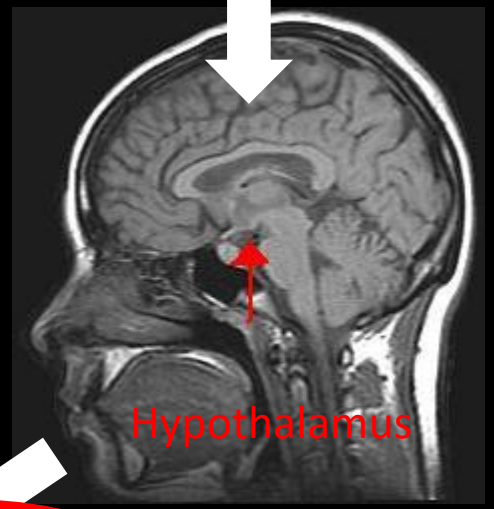


1. **Sympathetic-adrenomedullar axis** activation (in seconds)
   - circulatory and respiratory system activation
   - glycogenolysis, lipolysis
   - ↑ muscle tone

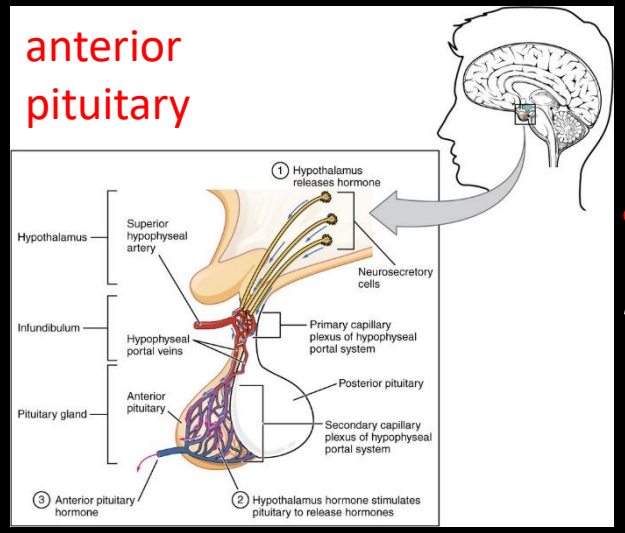
Systems Involved in the Stress Response

stres

2. **Hypothalamic-Pituitary-Adrenal** (HPA) axis activation
   - metabolic sources provision (gluconeogenesis, glycogenolysis, lipolysis)
   - anti-inlflammatory and immunosuppressive effects



CRH



ACTH

cortisol

adrenal cortex

[48]

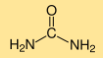
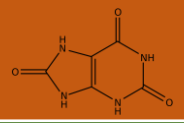
Systems Involved in the Stress Response - Hormones

3. **Endorphines**
   - a by-product of ACTH formation in the adenohypophysis
4. **Oxytocin**
   - modulation of social behaviour (tend and befriend)
5. **Aldosteron**
   - from the adrenal cortex, production also stimulated by the HPA axis
   - increases blood pressure (**retains sodium cation** in plasma, defense against salt loss)
6. **ADH**
   - produced by hypothalamus, released by neurohypophysis
   - increases blood pressure (**retains water** in the body, defense against water loss)
7. **STH**
   - produced by adenohypophysis
   - provides energy sources (glycogenolytic and lipolytic effect) and at the same time protects the muscles (proteoanabolic)

Systems Involved in Stress Response - Neurotransmitter

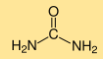
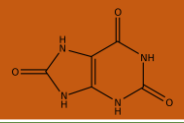
8. **Dopamin**
   - faster decision making
9. **Serotonin**
   - lowering fear
10. **Acetylcholin, Noradrenalin**
   - improving the ability to concentrate

Metabolic Consequences of Inflammation

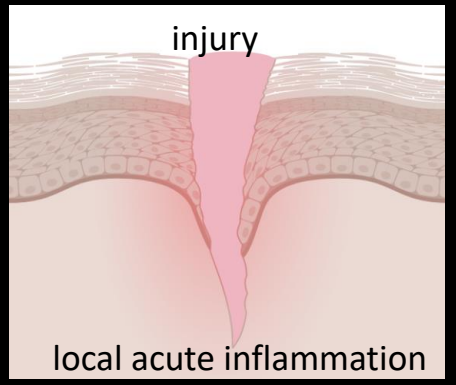
Change +/-	↑↓	Cause
Glycaemia		
Insulin receptors sensitivity		
Kalemia ($_{pl.}K^+$)		
Uremia ($_{pl.}$urea) 		
Uricemia ($_{pl.}$uric acid) 		
Acid-base balance		
Total body H_2O		
Urine volume		
Na^+ retention		
K^+ secretion into urine		

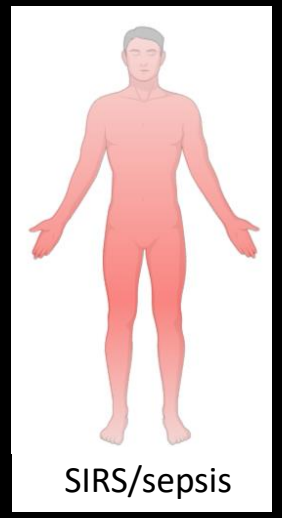
?

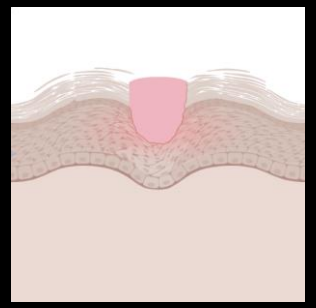
Metabolic Consequences of Inflammation

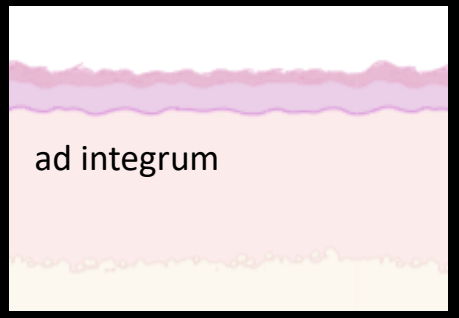
Change +/-	↑↓	Cause
Glycaemia	↑	← cortizol + glukagon + epinephrin + STH ← energy needs of brain
Insulin receptors sensitivity	↓	← cortisol, adrenalin
Kalemia ($_{pl.}K^+$)	↑	← cell lysis ← ↓ renal perfusion→ oliguria
Uremia ($_{pl.}$urea) 	↑	← protein degradation ← oligurie, ADH
Uricemia ($_{pl.}$uric acid) 	↑	← cell breakdown, from DNA ← oliguria
Acid-base balance	↑/↓ (due to nature of injury)	• ischemia, ↑ lactate, ↑ ketones → MAC • hyperventilation → RAL • aldosteron (→ H^+ excretion) → MAL
Total body H_2O	retention effort	↑ ADH, ↑ aldosteron
Urine volume	↓	← ↑ ADH, ↑ aldosteron
Na^+ retention	↑	← ↑ aldosteron
K^+ secretion into urine	↑	← ↑ aldosteron

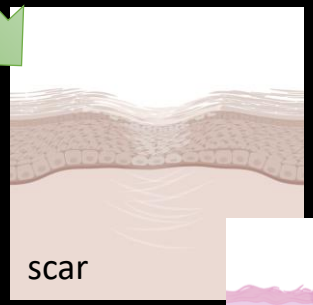
Further Progression of Local Inflammation

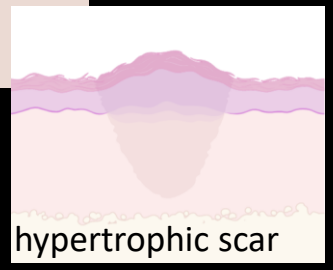


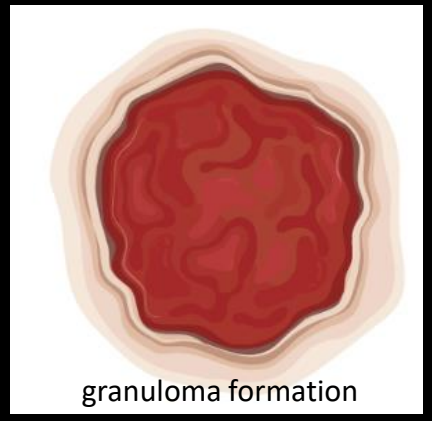




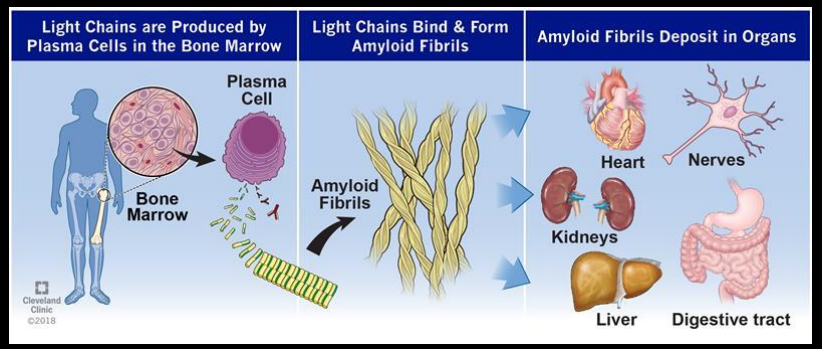




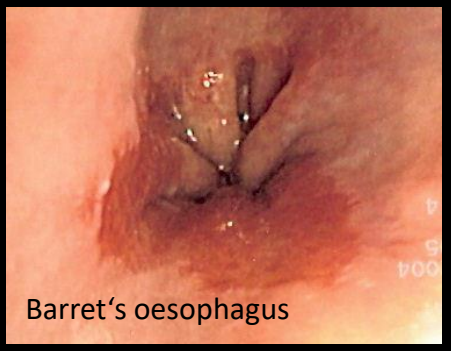




Chronic Inflammation



[66]



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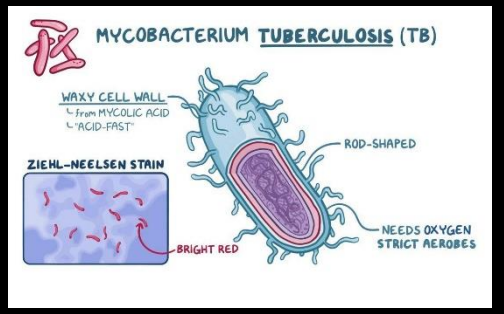


[67]

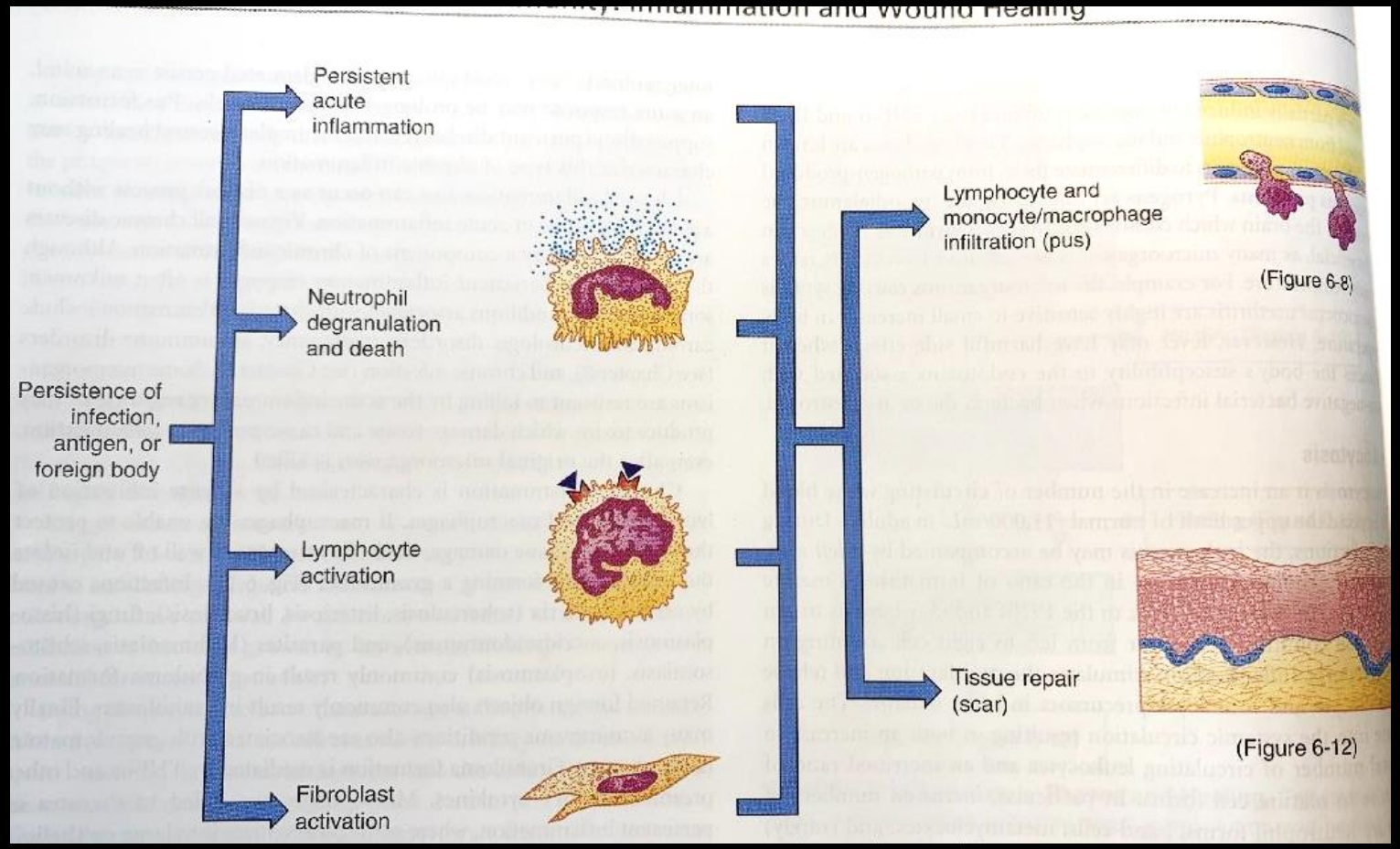
- duration > **6** weeks
- burdening, damaging, exhausting
- causes:
  - unhealed acute inflammation
  - repetitive tissue irritation
  - the causative pathogen resistant to immune mechanisms (mycobacterium tuberculosis)
- **adaptive immunity** activation
- possibly hidden local symptoms
- general symptomps maintained by cytokines (fatigue, anorexia, ↑ FW, ↑ leu, ↑ BM)
- possible **further damage to the affected organ** (tumor formation)
- possible **systemic changes** (amyloidosis in bone marrow inflammation)

Acute x Chronic Inflammation

Inflammation	Acute	Chronic
Causes	pathogenes, tissue injury	persisting acute inflammation and healing also, autoimunne reaction
Mechanisms, Immune Cells	prevailance of **innate** immunity, neutrophils, monocytes, macrophages	prevailance of **acquired** immunity , monocytes, macrophages, lymphocytes
Duration	several days	month - years
Consequences	healling, absces, chronic inflammation	tissue destruction, fibrotization, tumors, system amyloidosis

podle: ROKYTA, Richard. *Fyziologie a patologická fyziologie: pro klinickou praxi*. Praha: Grada Publishing, 2015. ISBN 978-80-247-4867-2.

Chronic Inflammation

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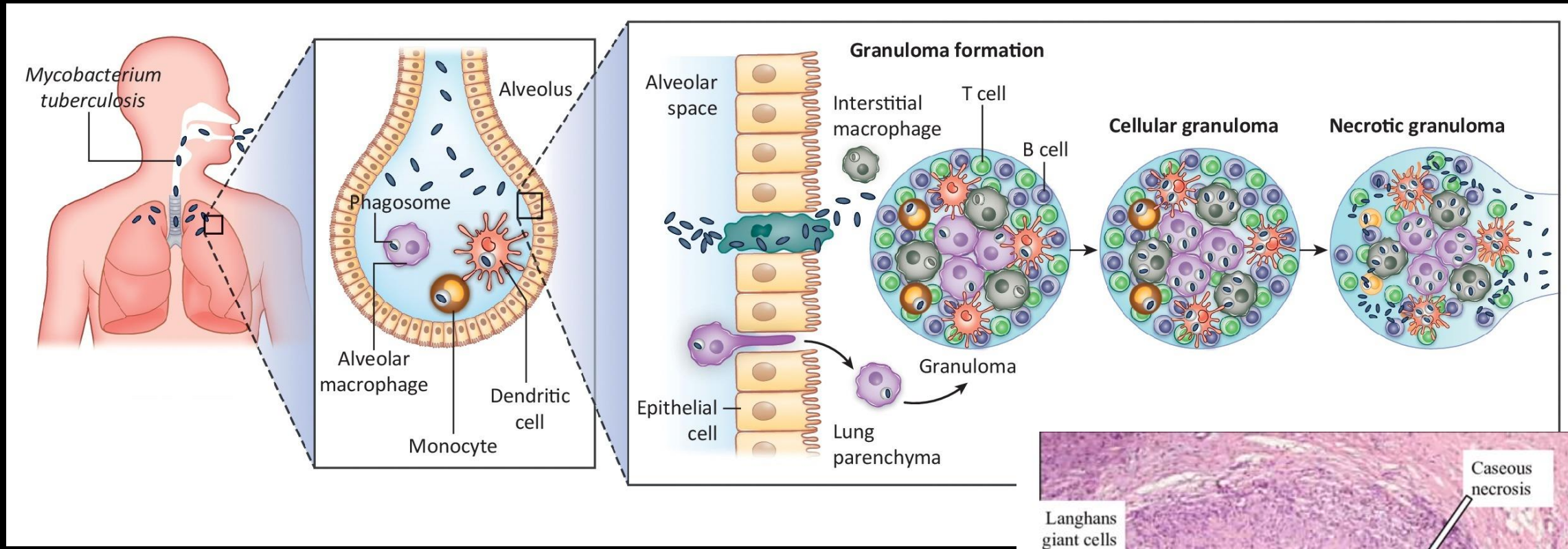
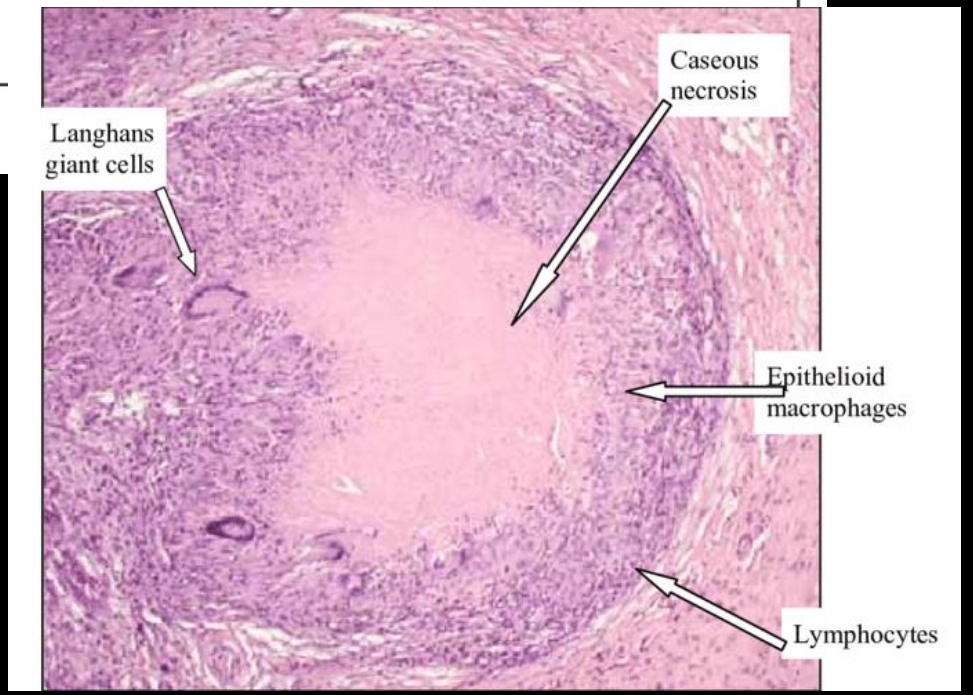


Granuloma

- attempt to isolate damaged tissue when the phagocytic function of macrophages fails
- foreign material, congenital disorders of phagocytic function, bacteria resisting phagocytosis
- formation stimulated by TNF-α and pro-inflammatory cytokines

[20]



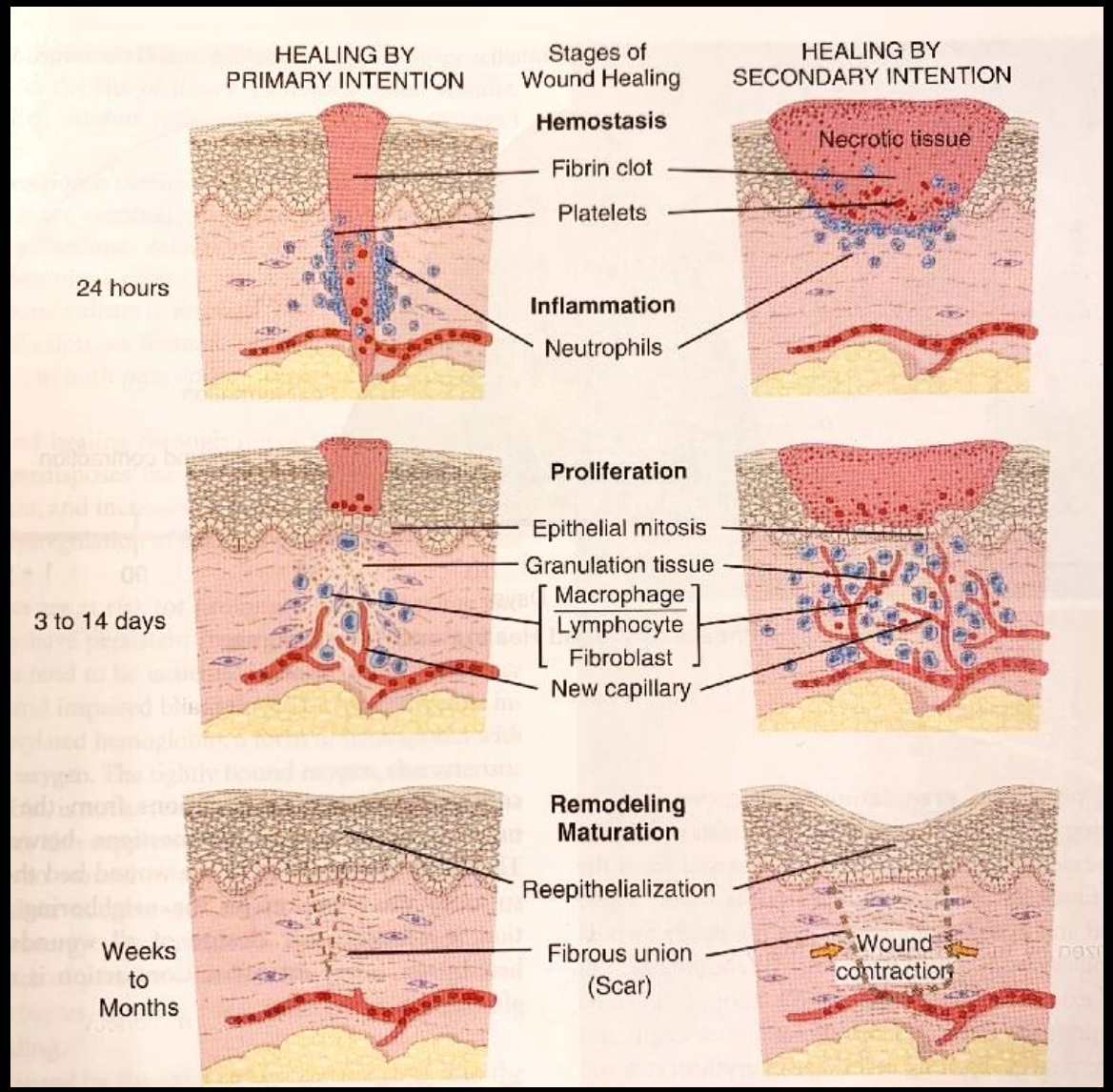
The Role of Chronic Inflammation in the Development of Civilization Diseases

atherosclerosis	• the inflammatory immune response generally accelerates processes in the vessel wall leading to plaque formation
diabetes mellitus type II	• inflammation in the visceral fat of the obese → pro-inflammatory cytokines→ ↑ CRP → direct damage to endothelium, hepatocytes, pancreatic β-cells and insulin resistance development • vicious circle (alteration of cells by glycation promotes inflammation)
Alzheimer disease	• the resulting βamyloid plaques are considered by the immune system as damaged tissue suitable for removal

https://kraje.rsd.cz/plzensky/wp-content/uploads/sites/12/2022/08/A15.jpg

4 Stages of Healing

- Hemostasis
- Inflammation
- Proliferation with new tissue formation
- Remodeling and maturation



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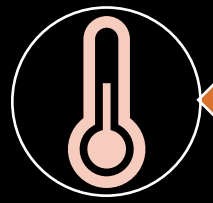
SIRS = Systemic Inflammatory Response Syndrom

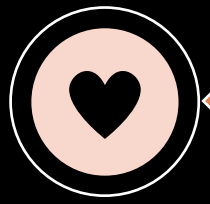
- generalized acute inflammatory reaction, acute phase reaction RAF
- inflammation that has become delocalized, deregulated, and autoaggressive
- → lost its original (defensive) meaning
- strength proportional to the extent and intensity of the damage inflicted
- 2 basic forms:
  - septic SIRS = sepsis
    - if the precipitating cause is infection
  - aseptic SIRS
    - response to non-infectious tissue damage
    - may become septic secondarily

Clinical Signs Defining SIRS

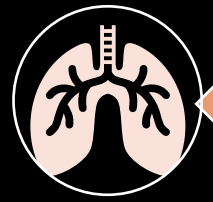
positivity of 2 or more of the listed symptoms = SIRS



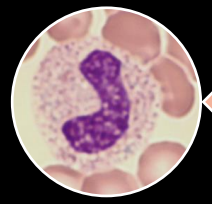
temperature > 38°C or < 36°C



heart rate > 90 min^{-1}



respiratory rate > 20 min^{-1}, or
hyperventilation with p_aCO_2 < 32 mm Hg



leucocytes > 12 x 10^9/l or < 4 x 10^9/l or > 10 % bands

[58]

Použité obrázky

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- [7] https://fineartamerica.com/shop/prints/mastocytes
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- [10] https://www.researchgate.net/publication/331693914/figure/tbl2/AS:735807753170944@1552441647137/P-I-R-O-sepsis-patient-staging-system.png
- [11] https://www.researchgate.net/publication/358807947/figure/fig2/AS:1133132740870144@1647171306405/Comparison-of-old-and-new-sepsis-definitions-The-first-definition-of-sepsis-and.png
- [12] https://images.slideplayer.cz/42/11424462/slides/slide_3.jpg
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