MUNI
MED

Pathophysiology of chronic inflammation, ethiopathogenesis, consequences, systemic inflammation, SIRS, MODS

Julie Dobrovolná

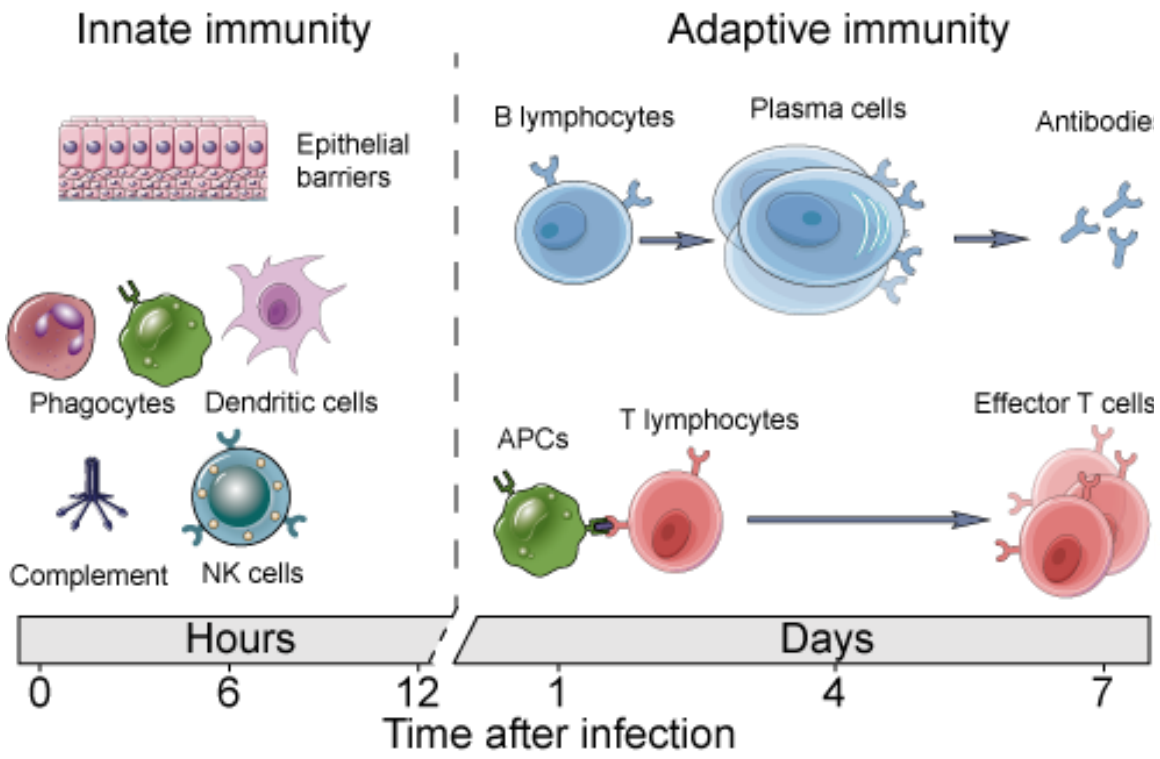
The types of immune response - revision

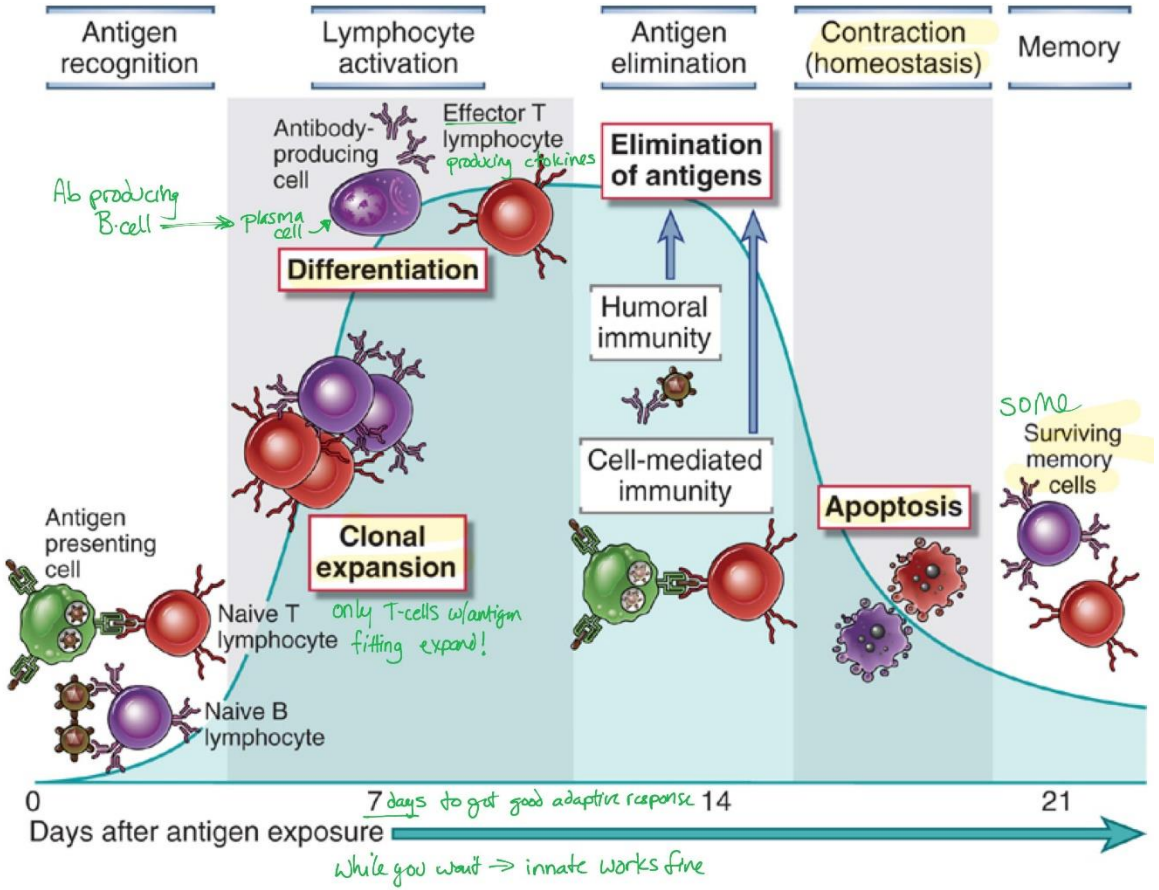
- **Innate (non-adaptive):** the first-line immune response relies on mechanisms that existed before infection

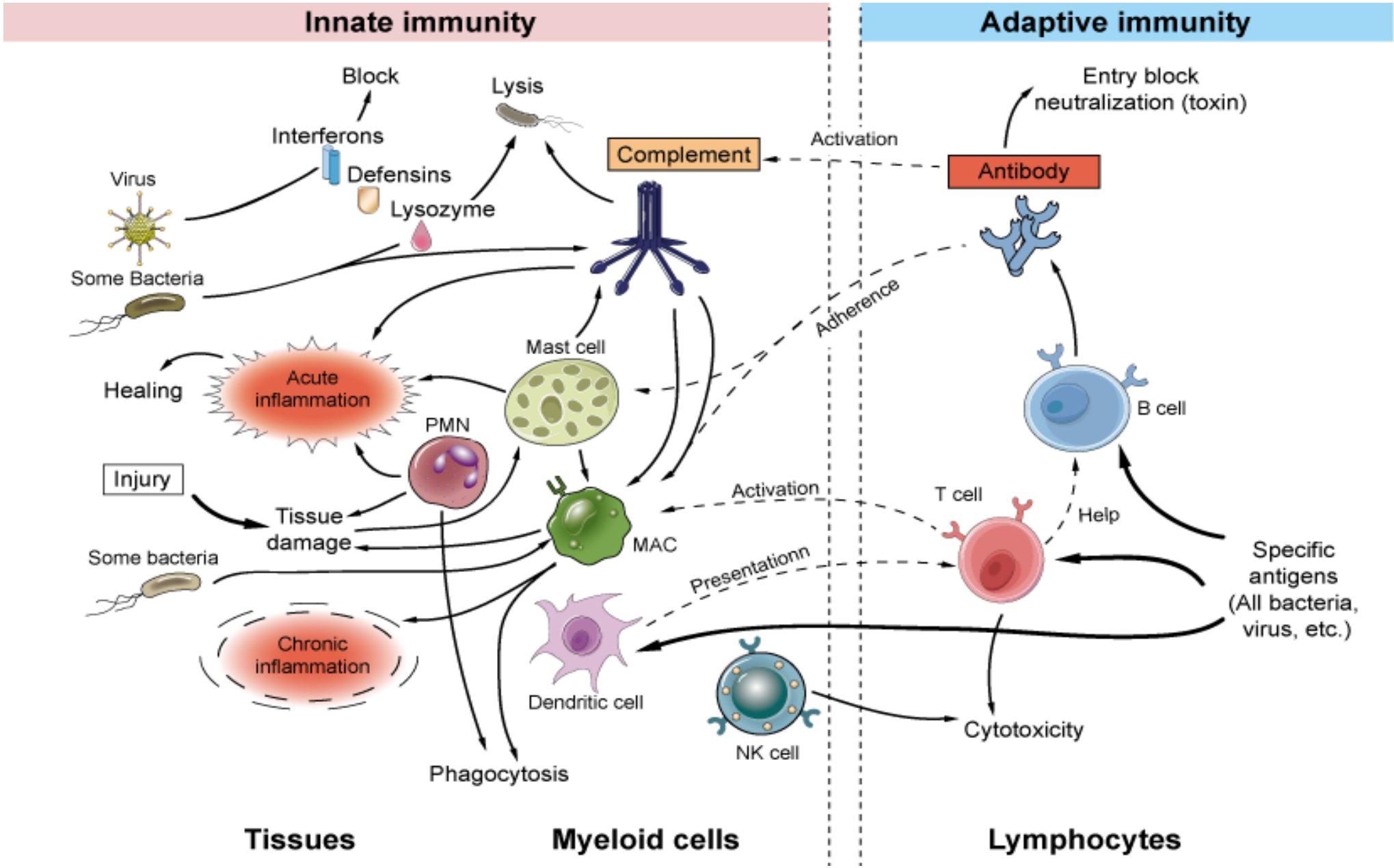
- **Acquired (adaptive) immunity:** The second line of response (if innate immunity fails) relies on mechanisms involving cellular memory of key T- and B-lymphocytes

MUNI
MED

Timeline


Innate immunity
Adaptive immunity
Epithelial barriers
B lymphocytes
Plasma cells
Antibodie
Phagocytes
Dendritic cells
APCs
T lymphocytes
Effector T cells
Complement
NK cells
Hours
Days
0
6
12
1
4
7
Time after infection

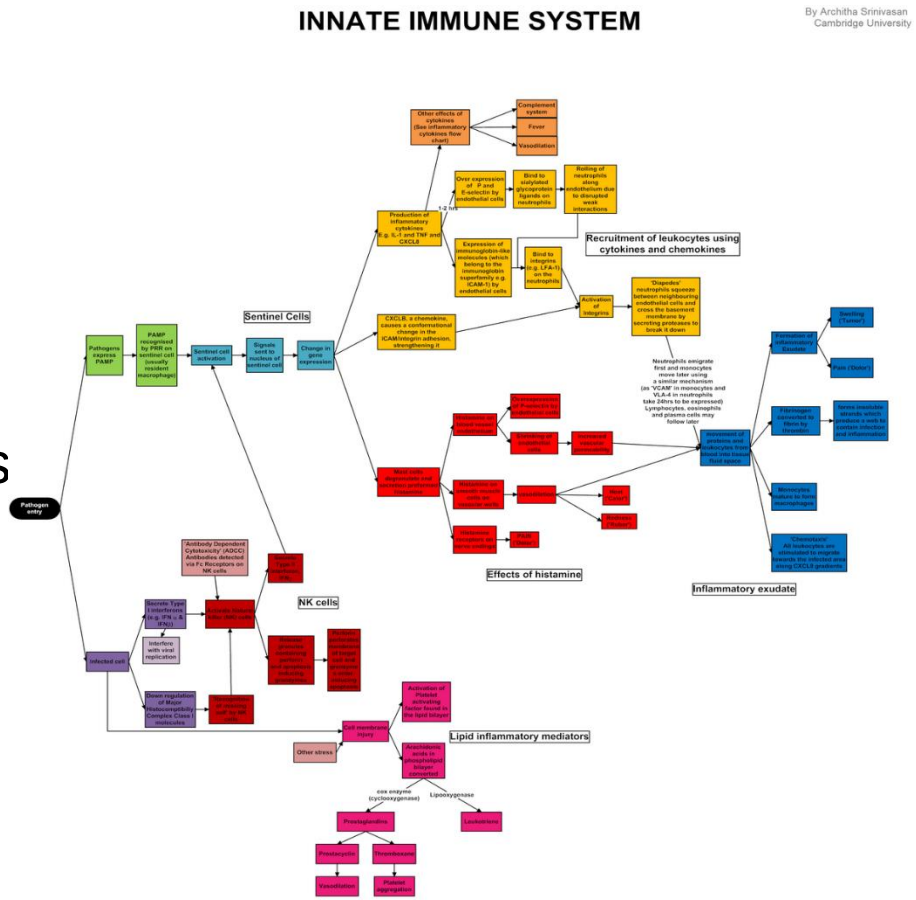

Antigen recognition
Lymphocyte activation
Antigen elimination
Contraction (homeostasis)
Memory
Antibody-producing cell
Effector T lymphocyte
Elimination of antigens
Differentiation
Humoral immunity
Cell-mediated immunity
Clonal expansion
Apoptosis
Surviving memory cells
Antigen presenting cell
Naive T lymphocyte
Naive B lymphocyte
0
14
21
Days after antigen exposure


Innate immunity
Adaptive immunity
Block
Lysis
Interferons
Defensins
Lysozyme
Virus
Some Bacteria
Complement
Activation
Entry block
neutralization (toxin)
Antibody
Adherence
Mast cell
Healing
Acute
inflammation
PMN
B cell
Injury
Tissue
damage
Activation
T cell
Help
MAC
Some bacteria
Presentationn
Specific
antigens
(All bacteria,
virus, etc.)
Chronic
inflammation
Dendritic cell
NK cell
Cytotoxicity
Phagocytosis
Tissues
Myeloid cells
Lymphocytes

MUNI MED

Innate immunity

- Based on genetic background
- Relies on existing system components
- Rapid response: within minutes of infection
- Not specific: the same molecules / cells respond to many pathogens
- No memory: the same response after repeated exposure
- Does not lead to clonal expansion



Innate immunity mechanisms

- Mechanical barriers / excretion on the skin surface, acidic pH in the stomach, cilia
- Humoral mechanisms
- Lysozymes, basic proteins, complement, interferons
- Mechanisms of cell defense by natural killers (NK cells) neutrophils, macrophages, mast cells, basophils, eosinophils

MUNI
MED

Adaptive immunity

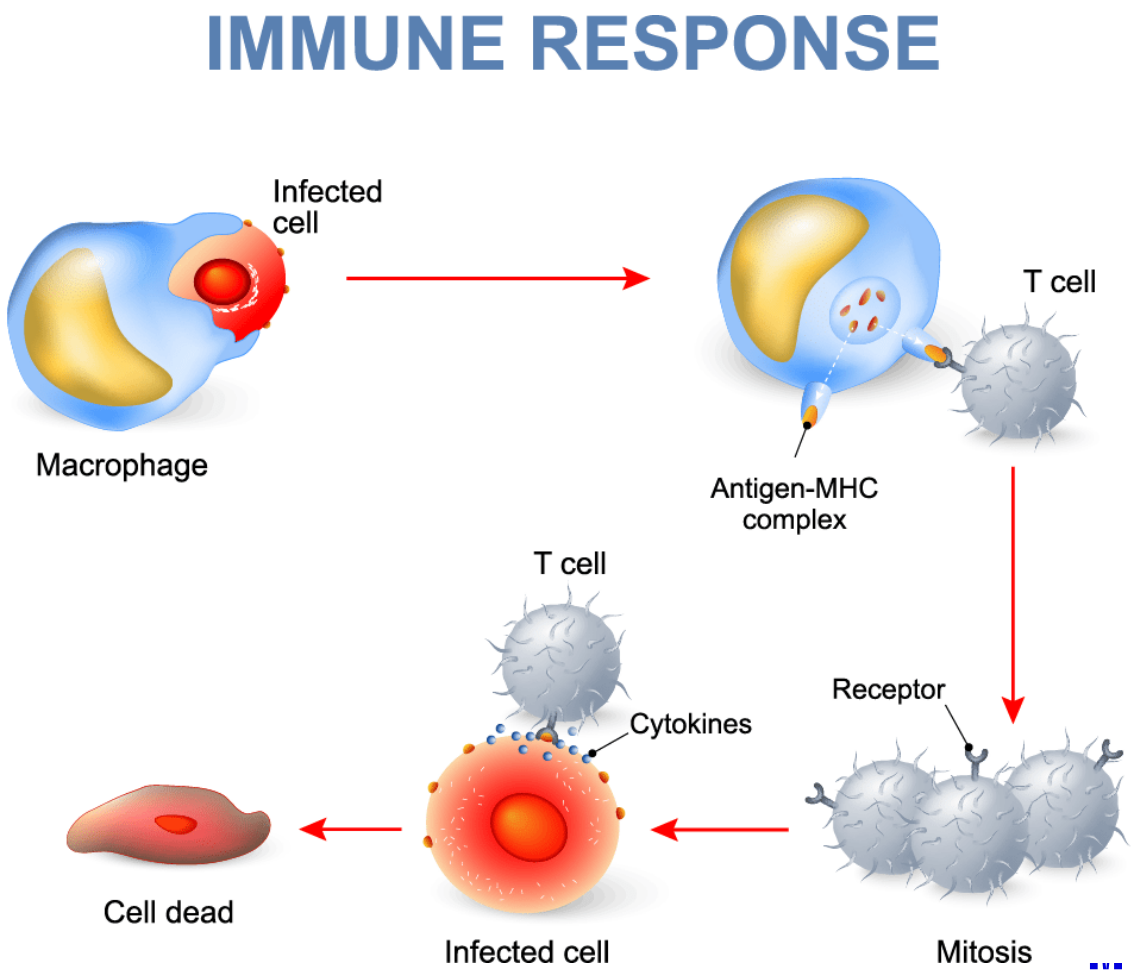
- Based on resistance acquired during life
- Relies on the genetic background of the individual and cell growth
- The reaction is slower, in a number of days
- It is specific
- Each cell responds to one epitope on the antigen
- It has anamnestic memory
- Repeated exposure leads to a faster and stronger reaction
- It leads to clonal expansion

MUNI
MED

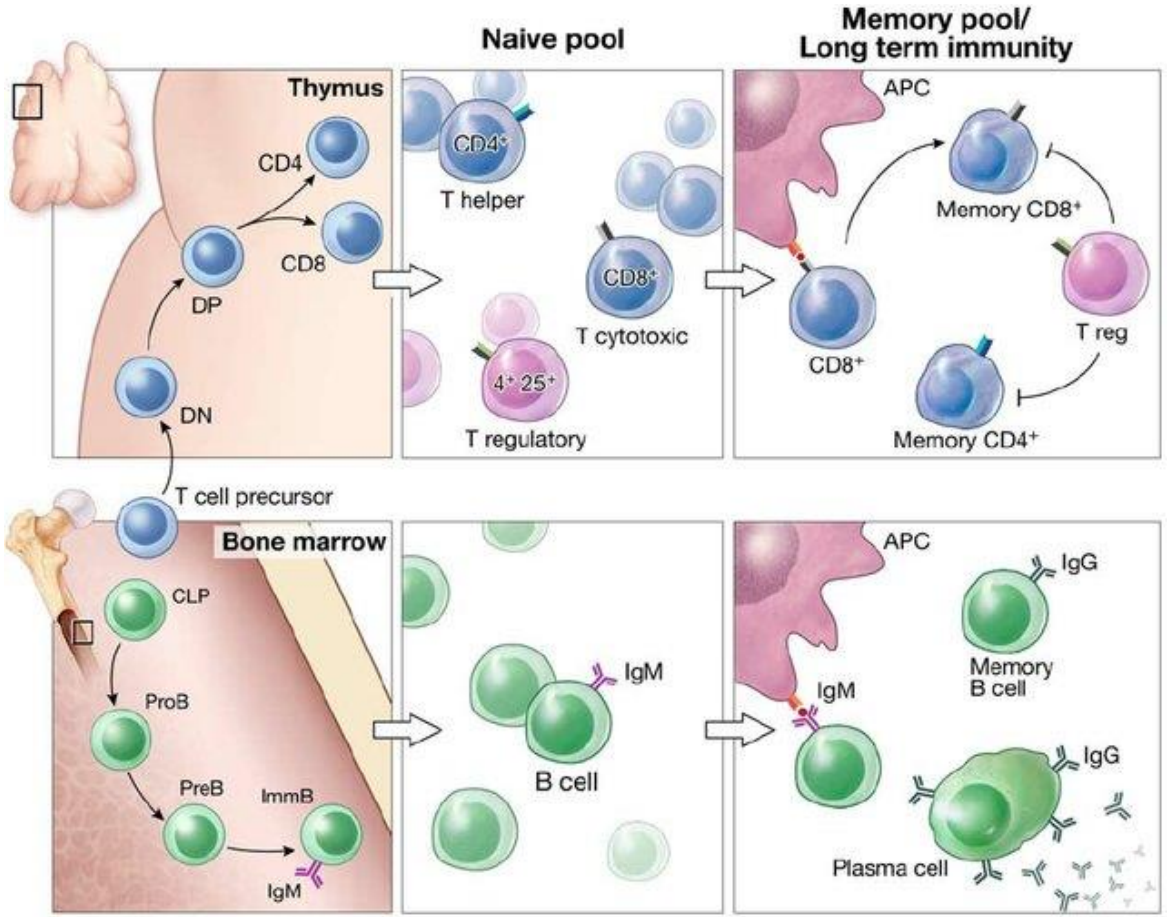
Adaptive immunity mechanisms

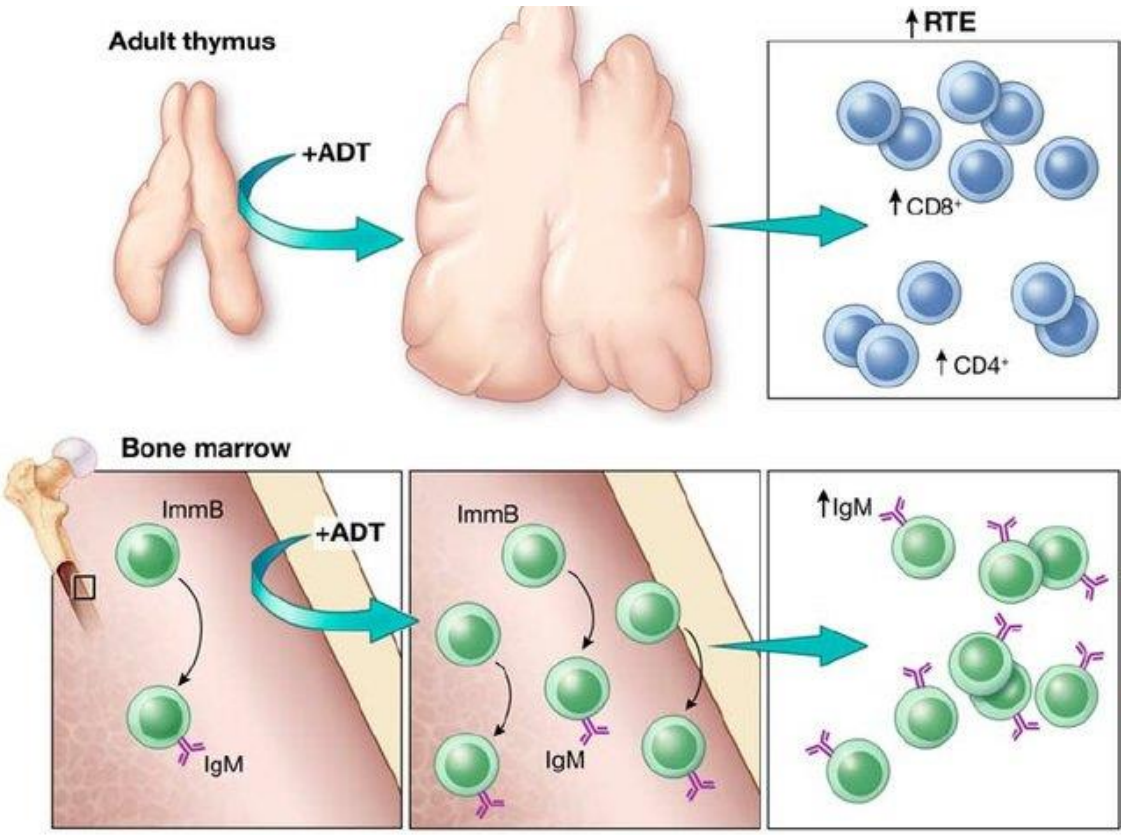
- **Cell-mediated immune response** (CMIR)
- T-lymphocytes
- Elimination of intracellular microbes that survive inside phagocytes or other infected cells

- **Humoral immune response (HIR)**
- B-lymphocytes
- antibody-mediated
- Elimination of intracellular microbes or their toxins



Adaptive immunity: mechanisms

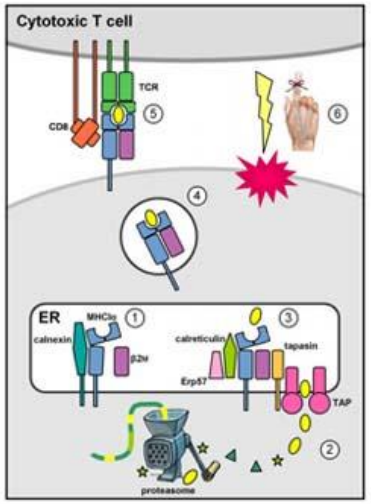


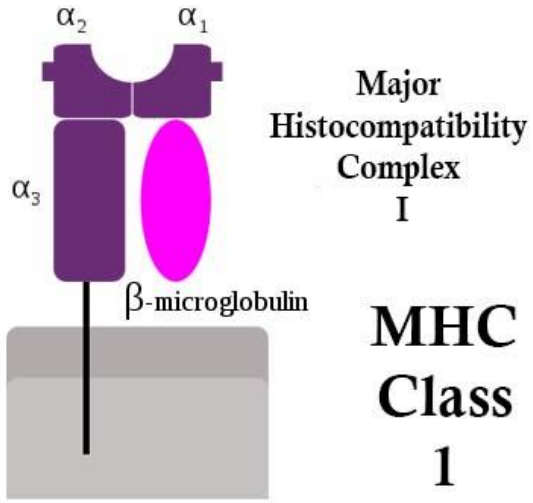


MUNI
MED

MHC

- **The major histocompatibility complex** (MHC) is part of the genome of all vertebrates that encode molecules important for immune recognition. In humans, MHC is a cluster of genes located on chromosome 6 that encode MHC proteins, also called **human leukocyte antigen** (HLA). MHC proteins are a set of proteins on the cell surface and within the adaptive part of the immune system they are necessary for the presentation of the antigen, which in turn determines its histocompatibility. **The main function of MHC molecules is to bind to peptide antigens and display them on the cell surface for recognition by appropriate T cells.** Of the many genes in human MHC, those that encode MHC class I, class II, and class III proteins are considered important.





MUNI MED

Mechanism of action of MHC I

- **MHC class I glycoproteins** are antigens of endogenous origin for CD8 + T-cell TCRs. Endogenous peptides are derived from the degradation of intracellular proteins, including viral or tumor antigens in infected or transformed cells, by the proteasome. The degradation products translocate from the cytoplasm to the endoplasmic reticulum (ER), where they are deposited on MHC class I molecules via a peptide-containing complex comprising an ER transporter associated with antigen processing (TAP1 / 2), tapasin, ERp57 oxidoreductase and calreticulin chaperone protein . The cellular components involved in the presentation of endogenous antigens, from proteasome subunits to the peptide-delivery complex, are collectively referred to as (APM). In addition to T-cell receptors (TCRs), CD8 + T cells express CD8 receptors. When the cytotoxic T cell receptor CD8 attaches to an MHC class I molecule and the TCR fits into an epitope in the MHC class I molecule, CD8 + T cells trigger apoptosis in the cell. This helps to mediate cellular immunity, which is the primary means of combating certain intracellular pathogens, such as viruses and some bacteria.

MUNI
MED

Function of MHCI

Antigen processing and presentation

A nuclear cell normally contains peptides, mostly intrinsic peptides derived from protein turnover and defective ribosomal products.

Also during viral infection, infection of intracellular microorganisms, or cancer transformation, such proteins degraded within the cell by the proteasome are also applied to MHC class I molecules and displayed on the cell surface.

Transplant rejection

During organ or stem cell transplantation, the MHC molecules themselves act as antigens and may elicit an immune response in the recipient causing transplant rejection.

Because the variation of MHC in the human population is high and no two individuals other than identical twins express the same MHC molecules, they can mediate transplant rejection.

MUNI
MED

Mechanism of action of MHC II

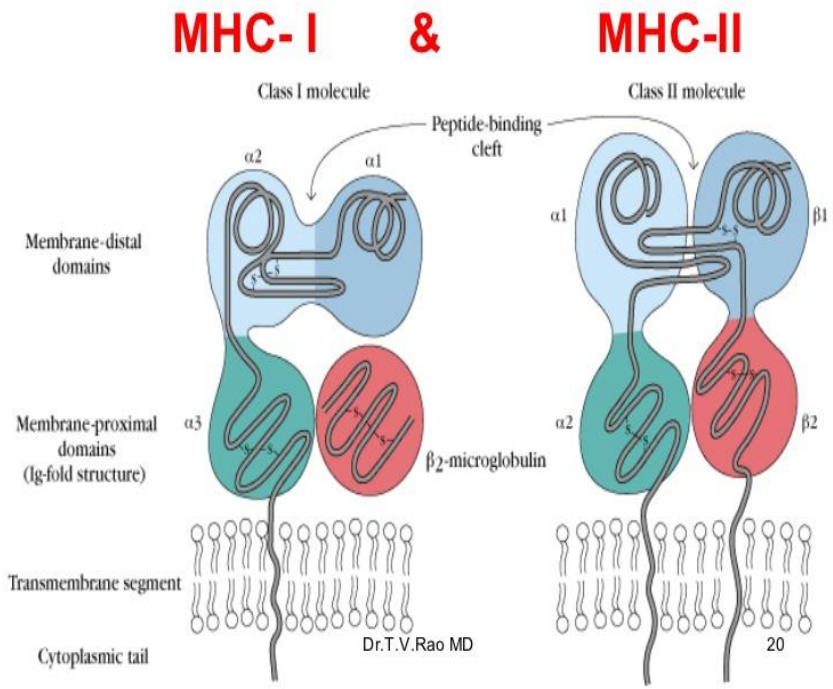
MHC class II molecules present antigen of exogenous origin to CD4 + T cells. Phagocytes, such as macrophages and immature dendritic cells, take pathogens by phagocytosis into phagosomes that fuse with lysosomes, and acidic enzymes cleave the captured protein into many different peptides. During the synthesis of MHC class II molecules, the molecules are transported from the endoplasmic reticulum (ER) via the Golgi to the endosomal compartments. The α and β chains produced are linked to a special polypeptide known as the invariant chain (Ii). II prevents endogenous peptides from binding to MHC class II molecules. After removal of II in the acidic endosomal compartments, the peptides are able to bind to MHC. The MHC class II molecules with the peptide are then transported to the membrane surface for antigen presentation. The peptide: MHC class II complex is then recognized by a related T cell helper T cell receptor (TCR).

.

MUNI
MED

Function of MHC II

- MHC class I proteins are encoded by the HLA-A, HLA-B and HLA-C genes encoding HLA-A, HLA-B and HLA-C molecules. Class I molecules are found on virtually all nuclear cells in the body, including platelets. Key exceptions are observed in retinal and brain cells and nuclear-free red blood cells. CD8 co-receptors are recognized by the MHC class I β2 subunit. These MHC class I molecules sample peptides generated in the cell and signal the physiological state of the cell to effector cells of the immune system, especially CD8 + T cells.
- .



Function of MHC II

Involvement of TCR-peptide: MHC class II is essential for the induction and regulation of adaptive immunity by selecting a mature repertoire of CD4 + T cells in the thymus and activating these lymphocytes in the periphery. Secure attachment to the MHC molecule by the presented peptide ensures stable binding of the peptide, which increases antigen recognition by T cells, T cell recruitment, and proper immune response. Because they harvest and present antigens from exogenous sources, MHC class II molecules are critical to initiating an antigen-specific immune response.

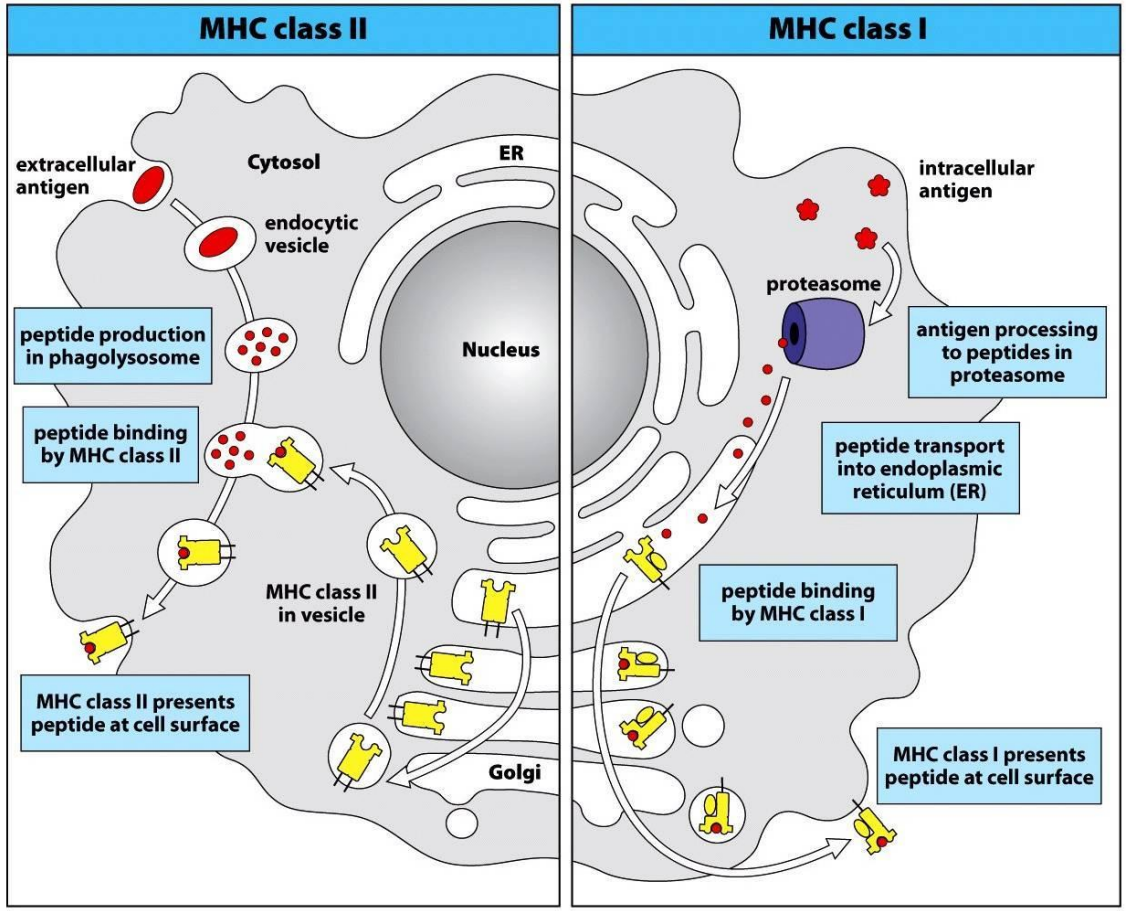


Figure 5.20 The Immune System, 3ed. (© Garland Science 2009)

MUNI MED

Inflammation definition I

Inflammation (from Latin: *inflammatio*) is part of the complex biological response of body tissues to harmful stimuli, such as pathogens, damaged cells, or irritants, and is a protective response involving immune cells, blood vessels, and molecular mediators. The function of inflammation is to eliminate the initial cause of cell injury, clear out necrotic cells and tissues damaged from the original insult and the inflammatory process, and initiate tissue repair.

Inflammation definition II

„Inflammation is generally defined as a response to stimulation by invading pathogens or endogenous signals such as damaged cells that results in tissue repair or sometimes pathology, when the response goes unchecked. However, understanding of the mechanisms, context and role of inflammation during physiological immune responses and pathology is constantly evolving. Recent advances have been driven by increased understanding of the commensal microbiota, immunometabolism and cancer and by technical advances such as single-cell analysis and high-throughput epigenetic, transcriptional and proteomic profiling of cells.“

https://www.nature.com/articles/ni.3798

Inflammation

The five cardinal signs are **heat, pain, redness, swelling**, and **loss of function** (Latin calor, dolor, rubor, tumor, and functio laesa).

Inflammation is a generic response, and therefore it is considered as a mechanism of innate immunity, as compared to adaptive immunity, which is specific for each pathogen.

Too little inflammation could lead to progressive tissue destruction by the harmful stimulus (e.g. bacteria) and compromise the survival of the organism.

In contrast, too much inflammation, in the form of chronic inflammation, is associated with various diseases, such as hay fever, periodontal disease, atherosclerosis, and osteoarthritis.

Inflammation - mechanisms

Inflammation is characterized by a multitude of interactions between leukocytes, endothelial cells, and platelets. Irrespective of its etiology, inflammation causes endothelial activation. Activated endothelial cells express cell adhesion molecules such as P- and E-selectin, which mediate leukocyte rolling, the first step in the adhesion cascade leading to leukocyte extravasation.1,2 Rolling leukocytes become activated by chemokines such as monocyte chemoattractant protein 1 (MCP-1) and RANTES (regulated upon activation, normal T cell expressed and presumably secreted), also presented by the endothelium. Subsequently, leukocytes, through their integrins, bind firmly to other endothelial adhesion molecules of the immunoglobulin superfamily, such as intercellular adhesion molecule-1 (ICAM-1) and vascular adhesion molecule-1 (VCAM-1). Following firm adhesion, leukocytes migrate across the endothelial barrier. The process of diapedesis (transmigration) involves various adhesion receptors expressed on both leukocytes and endothelial cells, such as platelet-endothelial cell adhesion molecule 1

Inflammation – systemic reaction

Inflammation may be **local** or it may be a **systemic** inflammatory response (SIRS - see below). However, even in the case of local inflammation, the organism responds to local changes with an overall response. Lymphokines released by lymphocytes and macrophages (eg IL 1, 6, prostacyclins and prostaglandins) act on the stress axis of HPA (CNS-CRH-ACTH-corticoids) and thus convert local inflammation into a whole-body general stress response. Inflammation is therefore a stressor. Fever is another symptom that occurs along with local signs of inflammation. Although fever is caused by many causes, the final pathway is always mediated by the release of endogenous pyrogens (especially from macrophages and neutrophilic granulocytes). These act on the thermoregulatory center in the hypothalamus, where the body's "thermostat" is set for higher heat production (fever). Fever is not only a symptom, but also a very effective defense mechanism that increases the number of peripheral leukocytes, phagocytosis performance, antibody production, cytotoxic effects of T-lymphocytes, etc.

Systemic symptomatology

- fever (irritation of centre of thermoregulation)
  - TNF, IL-1
  - IL-6 – high erythrocyte sedimentation rate
- leucocytosis - increased number of WBC
  - bacteria – neutrophils
  - parasites – eosinophils
  - viruses - lymphocytosis
- leucopenia - decreased " "
  - viral infections, salmonella infections, rickettsiosis
- immunologic reactions - increased level of some substances (C-reactive protein)

MUNI MED

Vascular changes

- vasodilation
  - increased permeability of vessels due to widened intercell. junctions and contraction of endothelial cells (histamin, VEGF, bradykinin)
- protein poor transudate (edema)
- protein rich exsudate

- leukocyte-dependent endothelial injury
  - proteolysis – protein leakage
- → platelet adhesion → thrombosis

MUNI
MED

Cellular events

- leukocytes margination → rolling → adhesion → transmigration
- emigration of:
  - neutrophils (1-2 days)
  - monocytes (2-3 days)
- chemotaxis
  - endogenous signaling molecules - lymphokines
  - exogenous - toxins
- phagocytosis - lysosomal enzymes, free radicals, oxidative burst
- passive emigration of RBC - no active role in inflamm. - hemorrhagic inflammation

MUNI MED

Phagocytosis

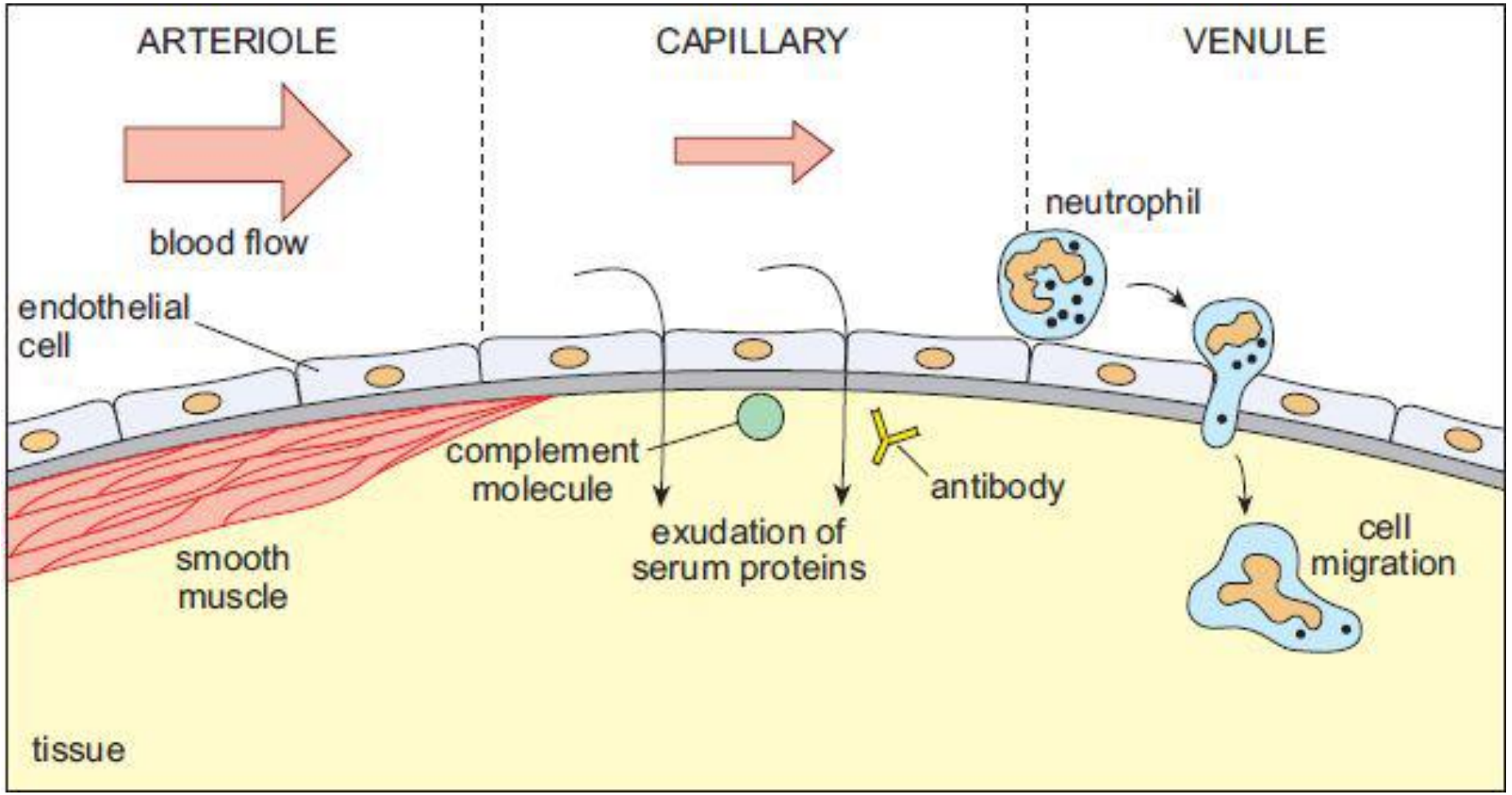
- adhesion and invagination into cytoplasm
- engulfment
- lysosomes - destruction
- in highly virulent microorganisms can die leucocyte and not the microbe
- in highly resistant microorganisms - persistence within macrophage - activation after many years

MUNI
MED

Stages of inflammation

1. **Stage of alteration** - hyperemia due to dilation of arterioles and overflow of capillary blood, the passing wall becomes permeable to non-cellular and cellular components of blood (see next stage)
2. **Stage of exudation and infiltration** - increased blood flow with intravascular fluid and cellular elements entering the interstitium
3. **Stage of proliferation (repair)** - it is mainly a matter of epithelium, endothelium, fibroblasts and their metabolic activities The purpose of proliferation is the restoration of damaged tissue components. But recovery is not always complete and effective. The result is, for example, the formation of granulomas, which are a sign of chronic inflammation. See also pathophysiology of wound healing.

Stages of inflammation



MUNI MED

SIRS = systemic inflammatory response syndrome

V případě SIRS není v těle žádné ložisko infekce. Provokující faktor zánětu je v organismu systémově. Pokud se ložisko infekce najde, nejedná se o SIRS, ale jde o sepsi.

SIRS: vysoké koncentrace mediátorů zánětu v krvi, v celém systému aktivován endotel spolu s makrofágy a neutrofily, generalizovaná dysfunkce endotelu

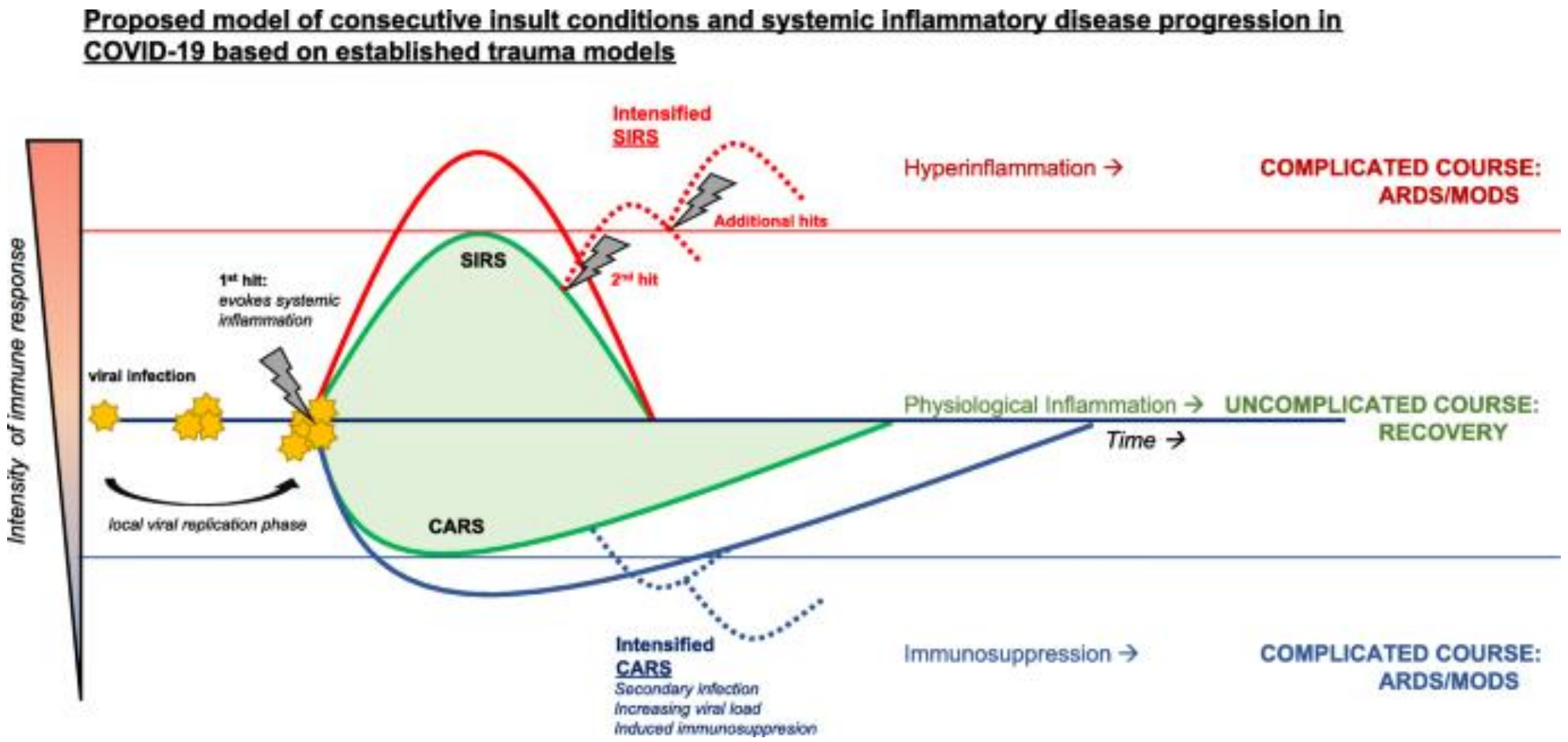
Příčinou může být těžké trauma, akutní pankreatitida, či stav po vyléčeném šoku.

Deregulovaný systémový zánět vyvolává nežádoucí hemodynamické změny: systémová vazodilatace, deprese myokardu, postižení mikrocirkulace s únikem tekutiny do intersticia a následně intersticiální otok, tvorba mikrotrombů

Klinické příznaky SIRS: tělesná teplota vyšší než 38 °C nebo nižší než 36 °C, tepová frekvence vyšší než 90 tepů/min, frekvence dýchání vyšší než 20/min, počet leukocytů více než 12 000/μl nebo méně než 4 000/μl krve

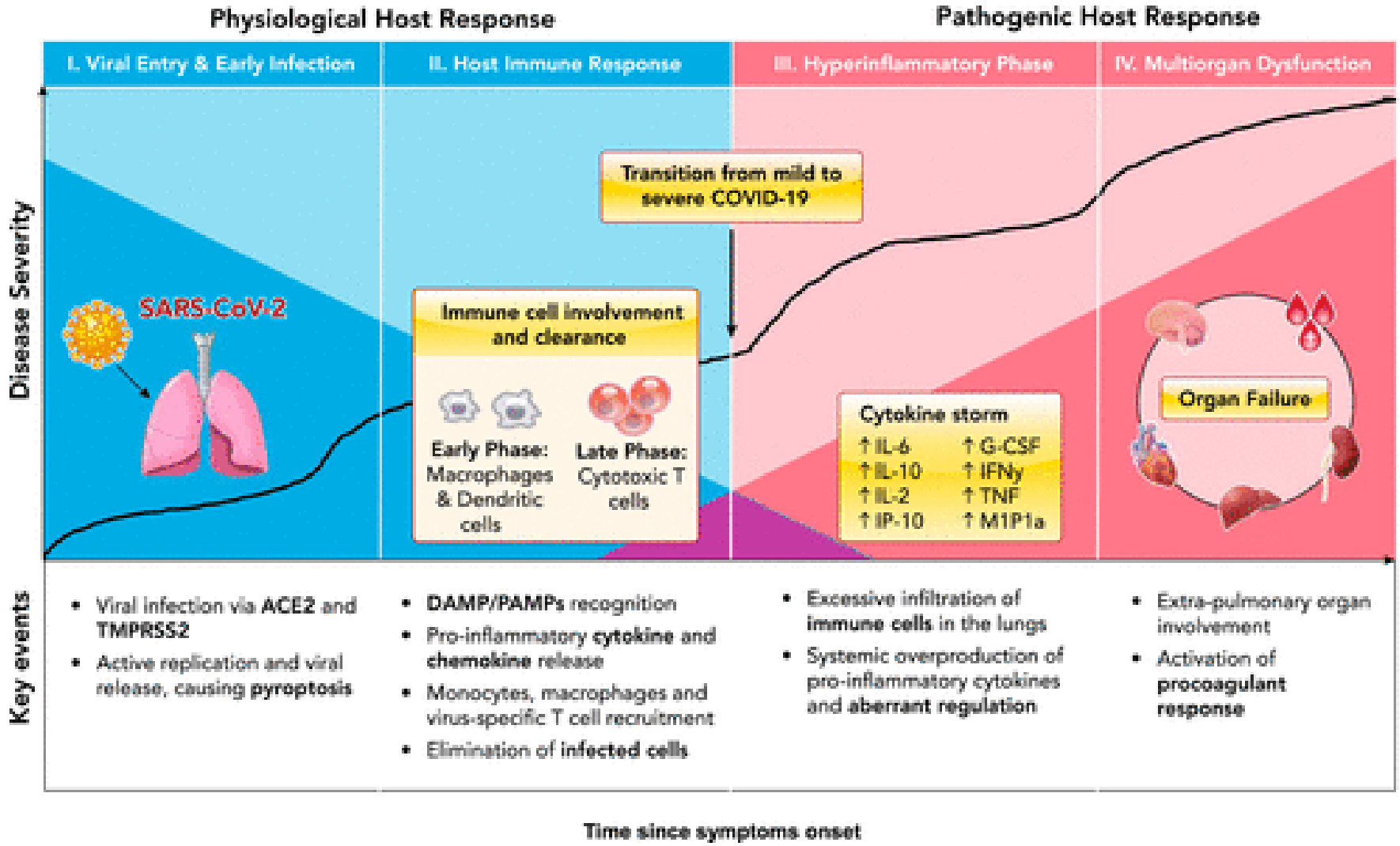
MUNI MED

SIRS a Covid-19



MUNI MED

Pathogenesis of covid-19



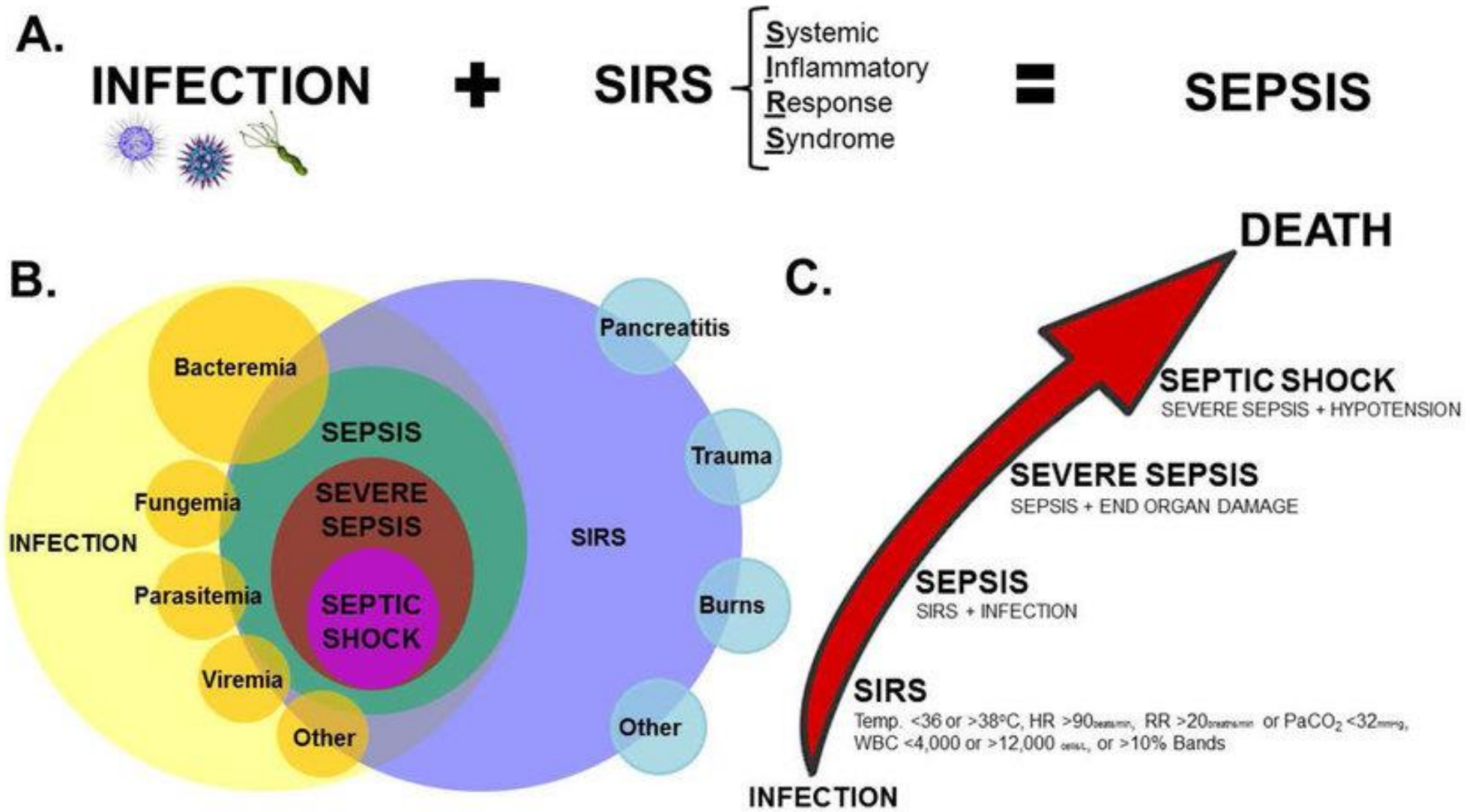
MUNI MED

SIRS

- Generalizovaný deregulovaný destruktivní proces
- Často spojen s devastací vzdálených orgánů
- U hypersenzitivních osob se SIRS může projevit i při působení velmi malého množství antigenu

- Klasifikace:
- 1) septický SIRS – spojený s infekcí
- 2) neseptický SIRS – po těžkém traumatu, hypoxémie, popáleniny, otravy, inkompatibilní transfuze

MUNI
MED


A.
INFECTION
SIRS
Systemic
Inflammatory
Response
Syndrome
SEPSIS
B.
Bacteremia
Fungemia
Parasitemia
Viremia
Other
INFECTION
SEPSIS
SEVERE SEPSIS
SEPTIC SHOCK
SIRS
Pancreatitis
Trauma
Burns
Other
C.
DEATH
SEPTIC SHOCK
SEVERE SEPSIS + HYPOTENSION
SEVERE SEPSIS
SEPSIS + END ORGAN DAMAGE
SEPSIS
SIRS + INFECTION
SIRS
Temp. <36 or >38°C, HR >90, RR >20 or PaCO2 <32,
WBC <4,000 or >12,000 , or >10% Bands
INFECTION

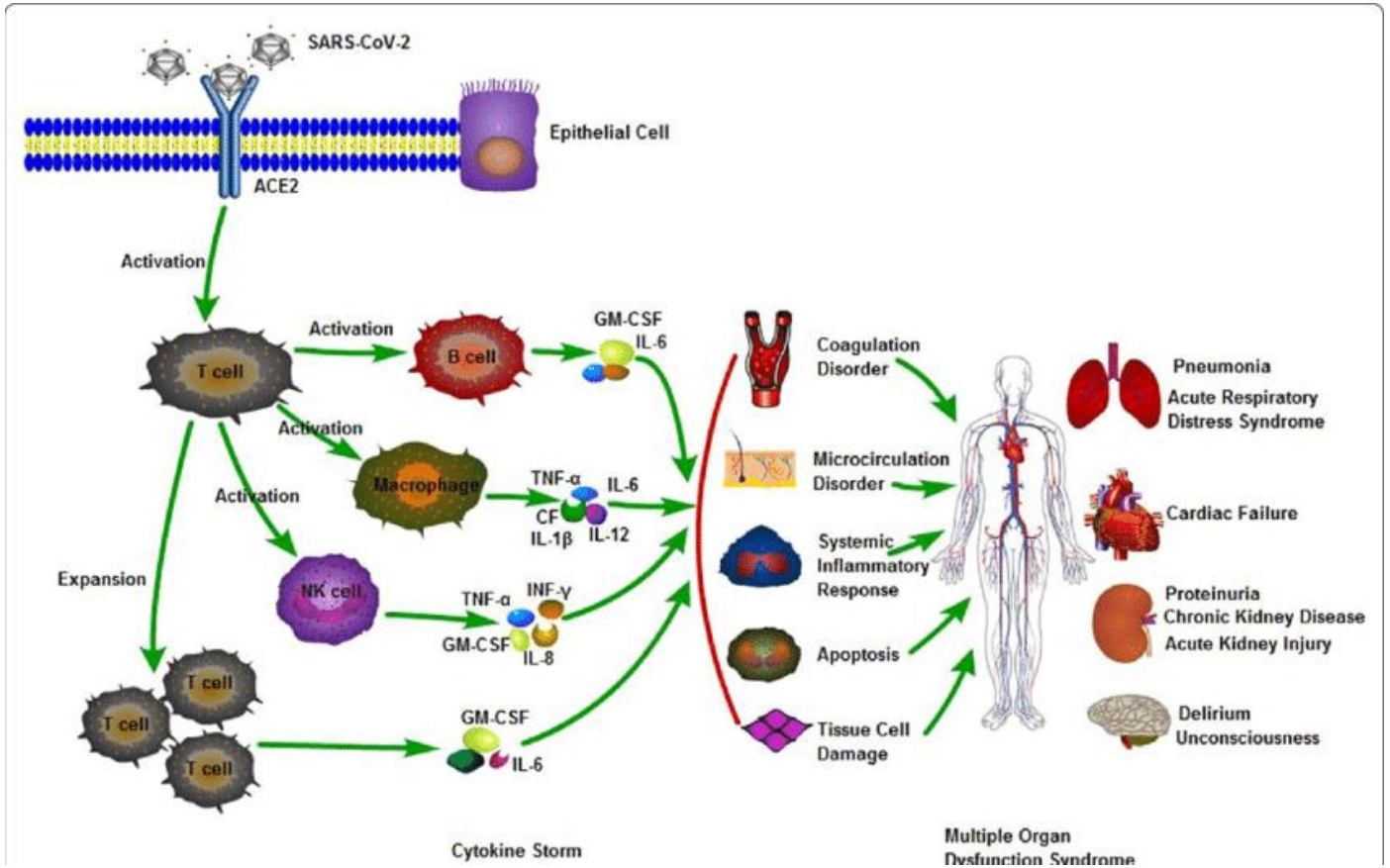
Septic SIRS

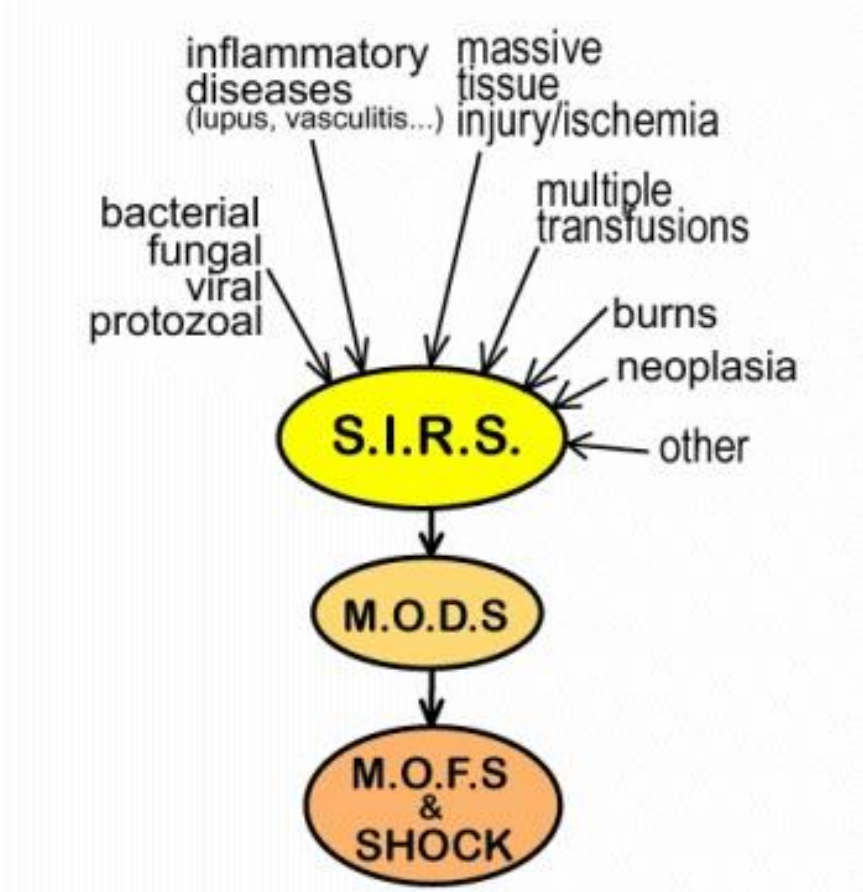
- Diseminovaná mikrobiální infekce
- 50 % - grampozitivní bakterie, 30 % - gramnegativní bakterie, 5 % - polymikrobiální infekty, 5 % kvasinky a plísně a 1 % anaeroby
- 1/3 postižených umírá

Primární SIRS
Sekundární SIRS

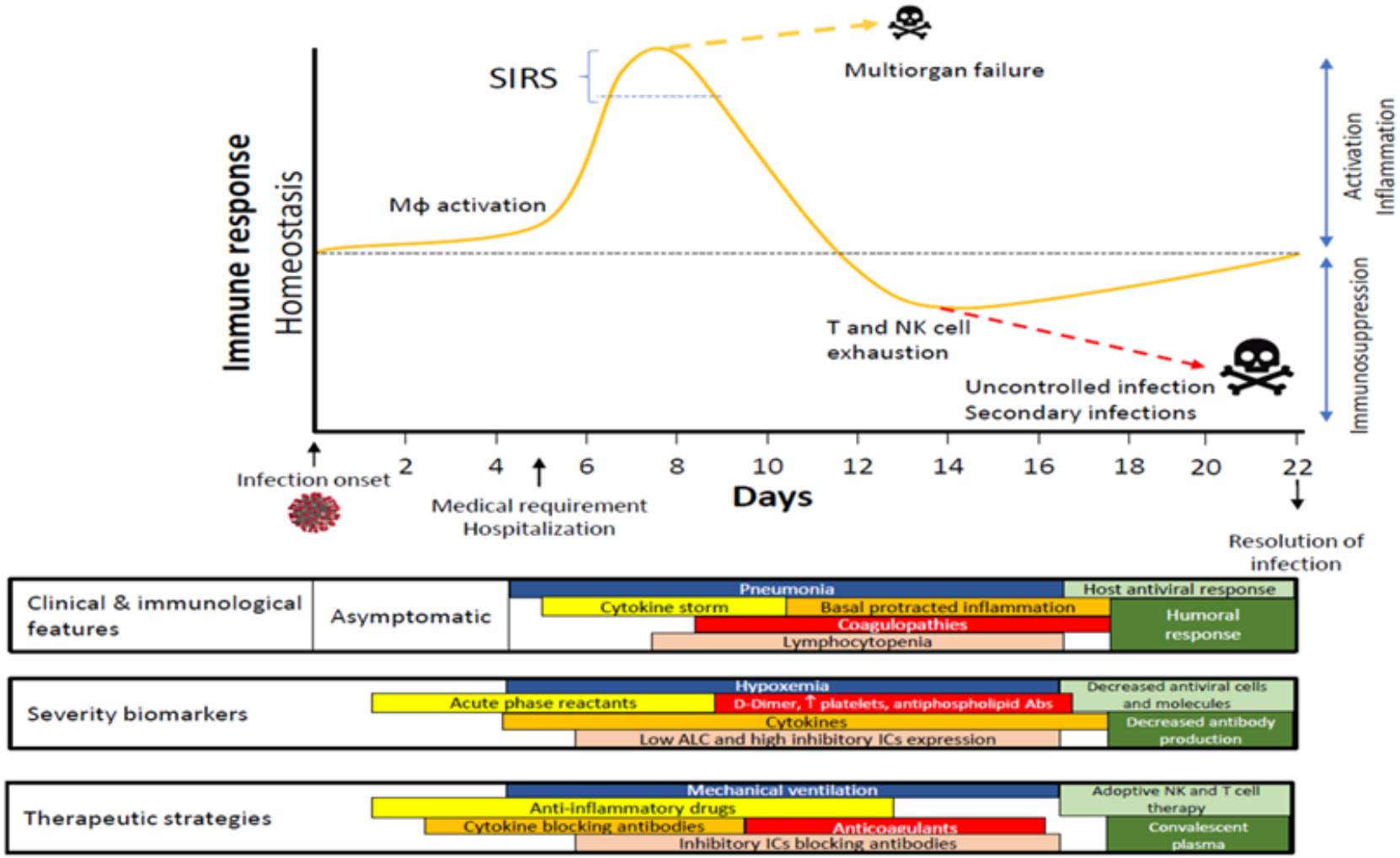
MUNI
MED

MODS

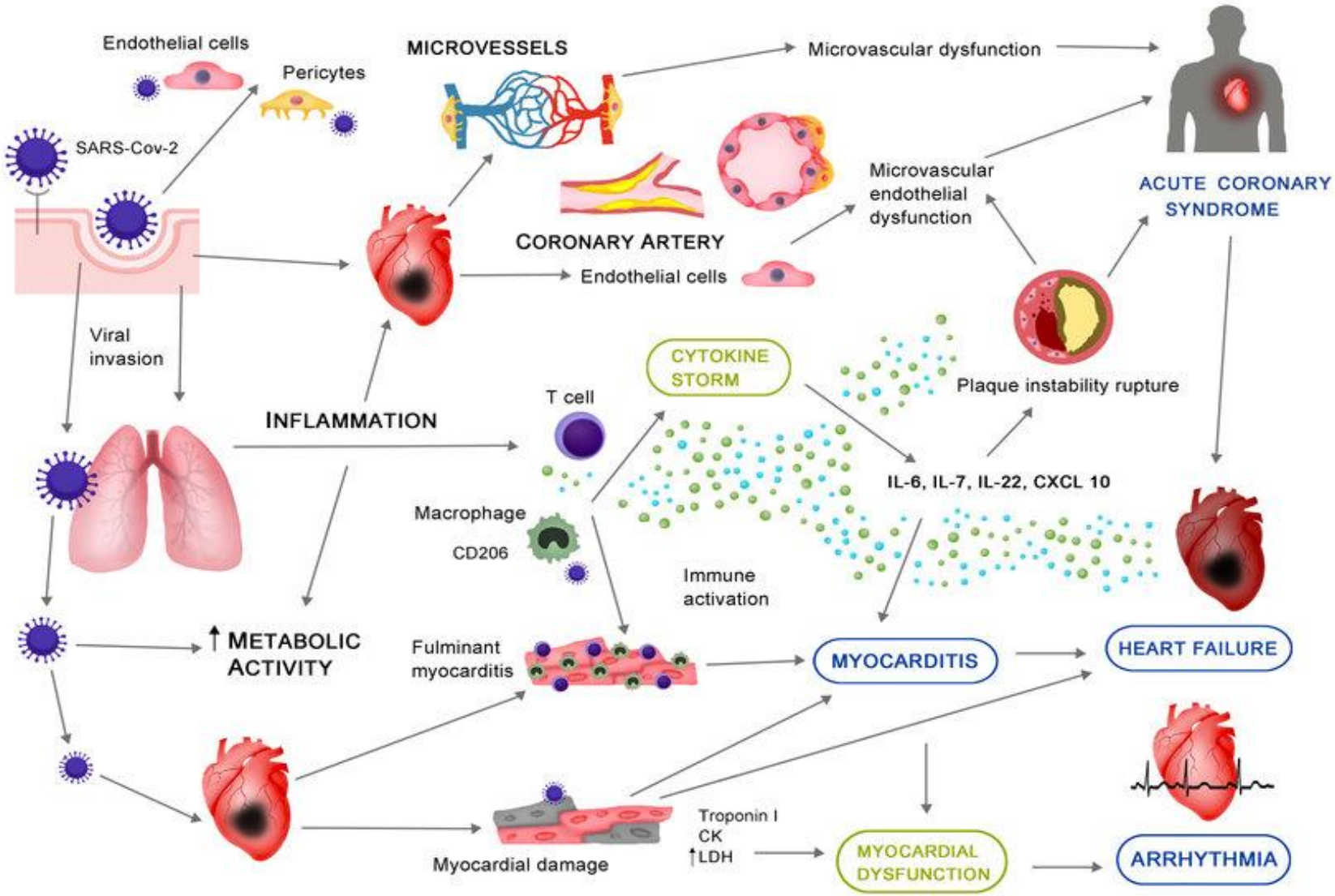

SARS-CoV-2
ACE2
Epithelial Cell
Activation
T cell
Activation
B cell
GM-CSF
IL-6
Activation
Macrophage
TNF-α
IL-6
CF
IL-1β
IL-12
Activation
NK cell
Expansion
TNF-α
INF-γ
GM-CSF
IL-8
T cell
T cell
T cell
GM-CSF
IL-6
Cytokine Storm
Coagulation Disorder
Microcirculation Disorder
Systemic Inflammatory Response
Apoptosis
Tissue Cell Damage
Pneumonia
Acute Respiratory Distress Syndrome
Cardiac Failure
Proteinuria
Chronic Kidney Disease
Acute Kidney Injury
Delirium
Unconsciousness
Multiple Organ Dysfunction Syndrome


inflammatory diseases (lupus, vasculitis...)
massive tissue injury/ischemia
bacterial
fungal
viral
protozoal
multiple transfusions
burns
neoplasia
other
S.I.R.S.
M.O.D.S
M.O.F.S & SHOCK

SIRS, MODS and Covid-19

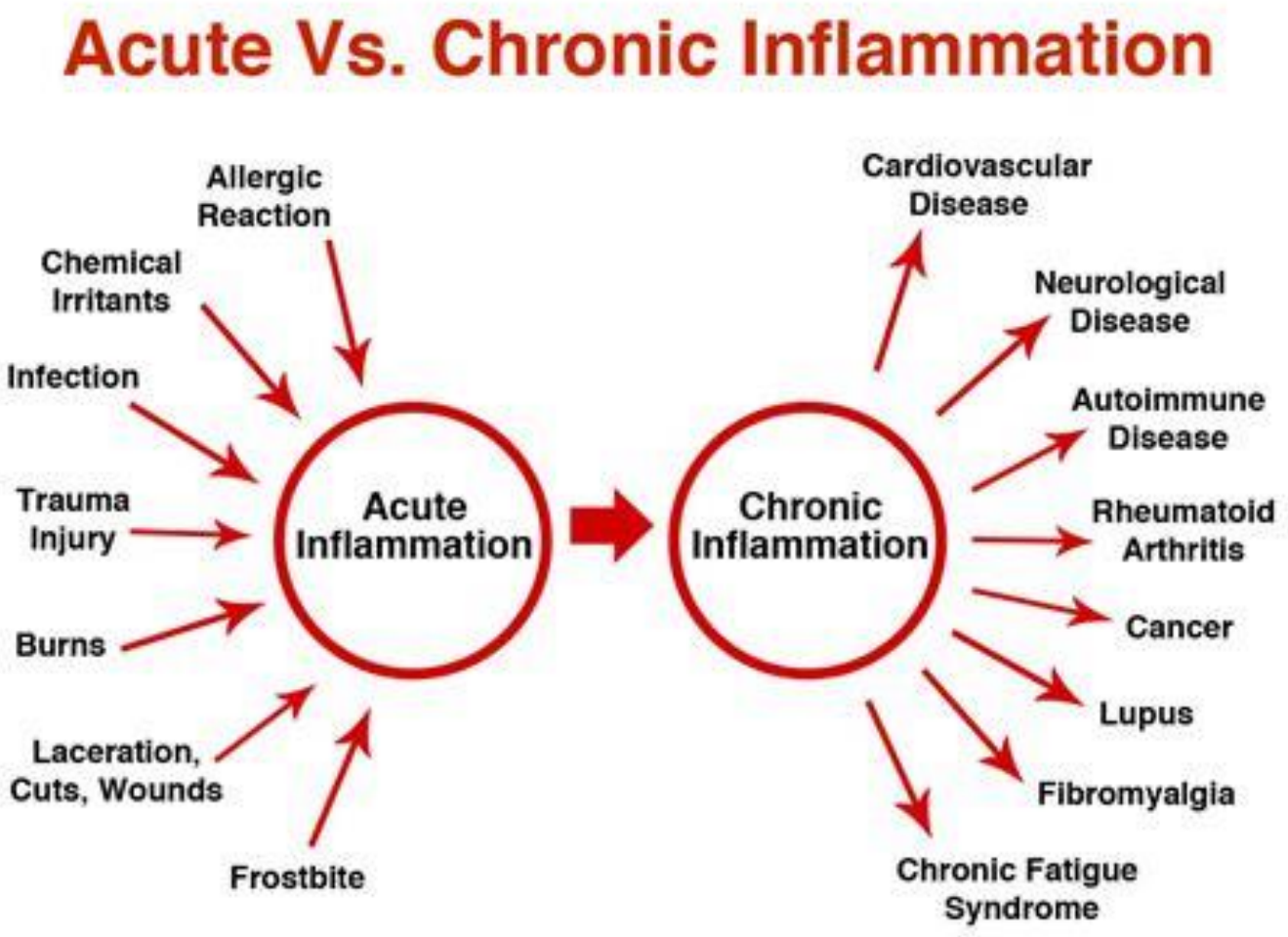


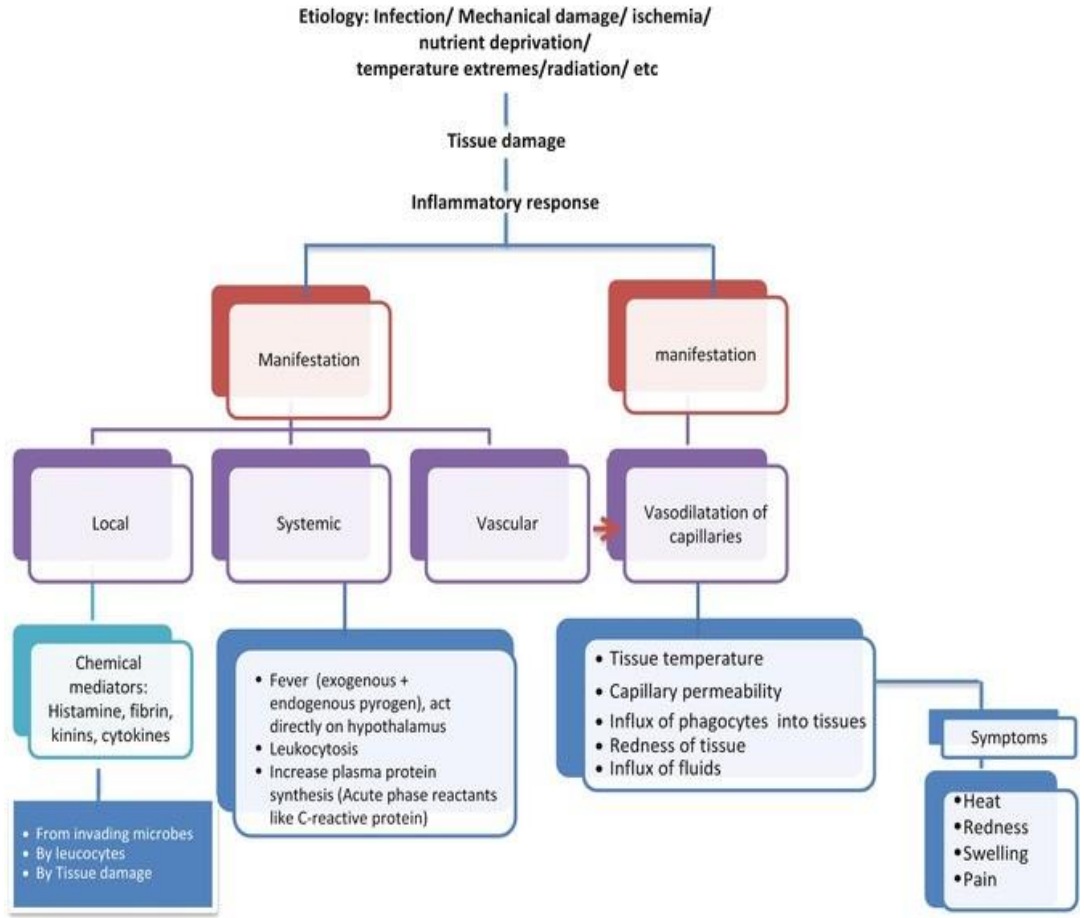
MUNI MED


Endothelial cells
Pericytes
MICROVESSELS
Microvascular dysfunction
SARS-Cov-2
CORONARY ARTERY
Endothelial cells
Microvascular endothelial dysfunction
ACUTE CORONARY SYNDROME
Viral invasion
CYTOKINE STORM
Plaque instability rupture
INFLAMMATION
T cell
IL-6, IL-7, IL-22, CXCL 10
Macrophage
CD206
Immune activation
METABOLIC ACTIVITY
Fulminant myocarditis
MYOCARDITIS
HEART FAILURE
Troponin I
CK
↑LDH
Myocardial damage
MYOCARDIAL DYSFUNCTION
ARRHYTHMIA

MUNI MED

Acute vs Chronic Inflammation





MUNI MED

Chronic inflammation

- reasons:
  - persisting infection or prolonged exposure to irritants (intracell. surviving of agents - TBC)
  - repeated acute inflamations (otitis, rhinitis)
  - primary chronic inflammation - low virulence, sterile inflammations (silicosis)
  - autoimmune reactions (rheumatoid arthritis, glomerulonephritis, multiple sclerosis)

Chronic inflammation

- chronic inflammatory cells ("round cell" infiltrate)
  - lymphocytes
  - plasma cells
  - monocytes/macrophages activation of macrophages by various mediators - fight against invaders
- lymphocytes → plasma cells, cytotoxic (NK) cells, coordination with other parts of immune system
- plasma cells - production of Ig
- monocytes-macrophages-specialized cells (siderophages, gitter cells, mucophages)

MUNI MED

Morphologic patterns of inflammation

- 1. alterative
- 2. exsudative
  - 2a. serous
  - 2b. fibrinous
  - 2c. suppurative
  - 2d. pseudomembranous
  - 2e. necrotizing, gangrenous
- 3. proliferative
  - primary (rare) x secondary (cholecystitis)

MUNI
MED

Morphologic patterns of inflammation

- 2a. serous - excessive accumulation of fluid, few proteins - skin blister, serous membranes - initial phases of inflamm.
- modification - catarrhal - accumulation of mucus

- 2b. fibrinous - higher vascular permeability - exsudation of fibrinogen -> fibrin - e.g. pericarditis (cor villosum, cor hirsutum - "hairy" heart
- fibrinolysis $\rightarrow$ resolution; organization $\rightarrow$ fibrosis $\rightarrow$ scar

MUNI
MED

- 2c. suppurative (purulent) - accumulation of neutrophillic leucocytes - formation of pus (pyogenic bacteria)
- interstitial
  - phlegmone – diffuse soft tissue
  - abscess - localized collection
    - acute – border – surrounding tissue
    - chronic – border - pyogenic membrane
    - Pseudoabscess – pus in lumen of hollow organ
- formation of suppurative fistule
- accumulation of pus in preformed cavities - empyema (gallbladder, thoracic)

MUNI MED

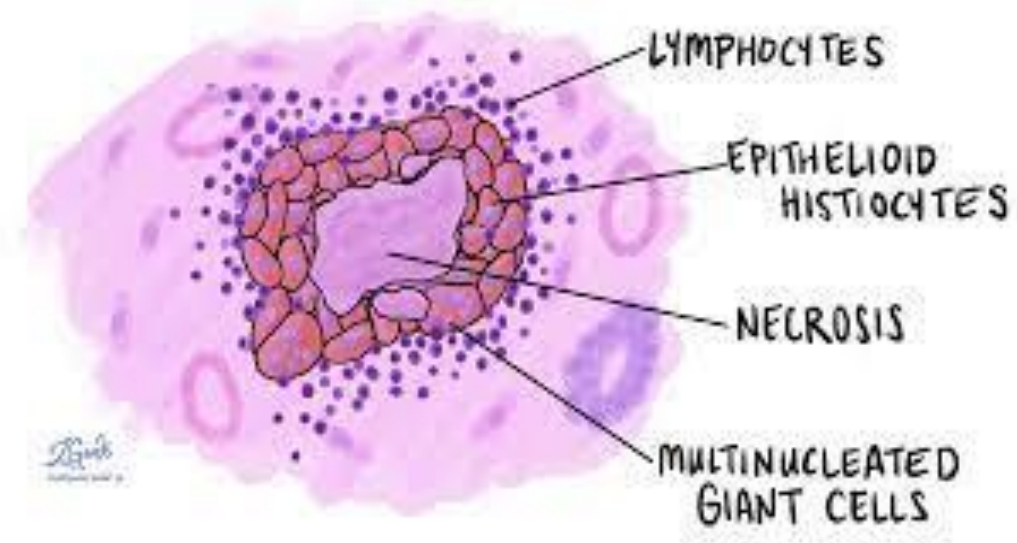
- complications of suppurative inflamm.:
- bacteremia (no clinical symptoms!; danger of formation of secondary foci of inflamm. (endocarditis, meningitis)
- sepsis (= massive bacteremia) - septic fever, activation of spleen, septic shock
- thrombophlebitis - secondary inflammation of wall of the vein with subsequent thrombosis - embolization - pyemia - hematogenous abscesses (infected infarctions)
- lymphangiitis, lymphadenitis

MUNI MED

- 2d. pseudomembranous - fibrinous pseudomembrane (diphtheria - Corynebacterium, dysentery - Shigella) - fibrin, necrotic mucosa, etiologic agens, leucocytes
- 2e. necrotizing - inflammatory necrosis of the surface - ulcer (skin, gastric)
  - gangrenous - secondary modification by bacteria - wet gangrene - apendicitis, cholecystitis - risk of perforation - peritonitis

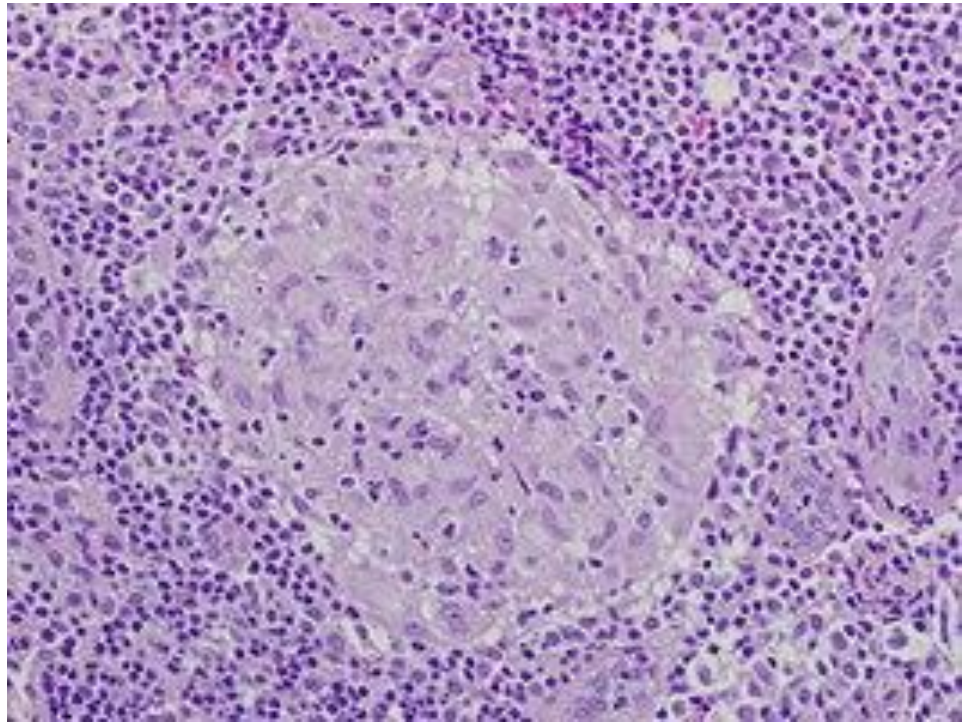
Granulomatous inflammation

- distinctive chronic inflammation type
- cell mediated immune reaction (delayed)
- aggregates of activated macrophages → epithelioid cell → multinucleated giant cells (of Langhans type x of foreign body type)
- NO agent elimination but walling off
- intracellulary agents (TBC)



Granulomatous inflammation

- 1. Bacteria
  - **TBC**
  - leprosy
  - syphilis (3rd stage)
- 2. Parasites + Fungi
- 3. Inorganic metals or dust
  - silicosis
  - berylliosis
- 4. Foreign body
  - suture (Schloffer „tumor“), breast prosthesis
- 5. Unknown - **sarcoidosis**



MUNI
MED

Tuberculosis – general pathology

- 1. TBC nodule – proliferative
- Gross: grayish, firm, 1-2 mm (milium) → central soft yellow necrosis (cheese-like – caseous) → calcification
- Mi: central caseous necrosis (amorphous homogenous + karyorrhectic powder) + macrophages → epithelioid cells → multinucleated giant cells of Langhans type + lymphocytic rim
- 2. TBC exsudate – sero-fibrinous exsudate (macrophages)

MUNI
MED

Leprosy

- ***M. leprae,*** Asia, Africa
- in dermal macrophages and Schwann cells
- air droplets + long contact
- rhinitis, eyelid destruction, facies leontina
- 1. lepromatous – infectious
  - skin lesion – foamy macrophages (Virchow cells) + viscera
- 2. tuberculoid – sterile
  - in peripheral nerves – tuberculoid granulomas - anesthesia
- death – secondary infections + amyloidosis

MUNI
MED

Syphilis

- ***Treponema pallidum*** (spichochete)
- STD + transplacental fetus infection
- acquired (3 stages) x congenital
- basic microspical appearance:
  - 1. proliferative endarteritis (endothelial hypertrophy → intimal fibrosis → local ischemia) + inflammation (plasma cells)
  - 2. gumma – central coagulative necrosis + specific granulation tissue + fibrous tissue

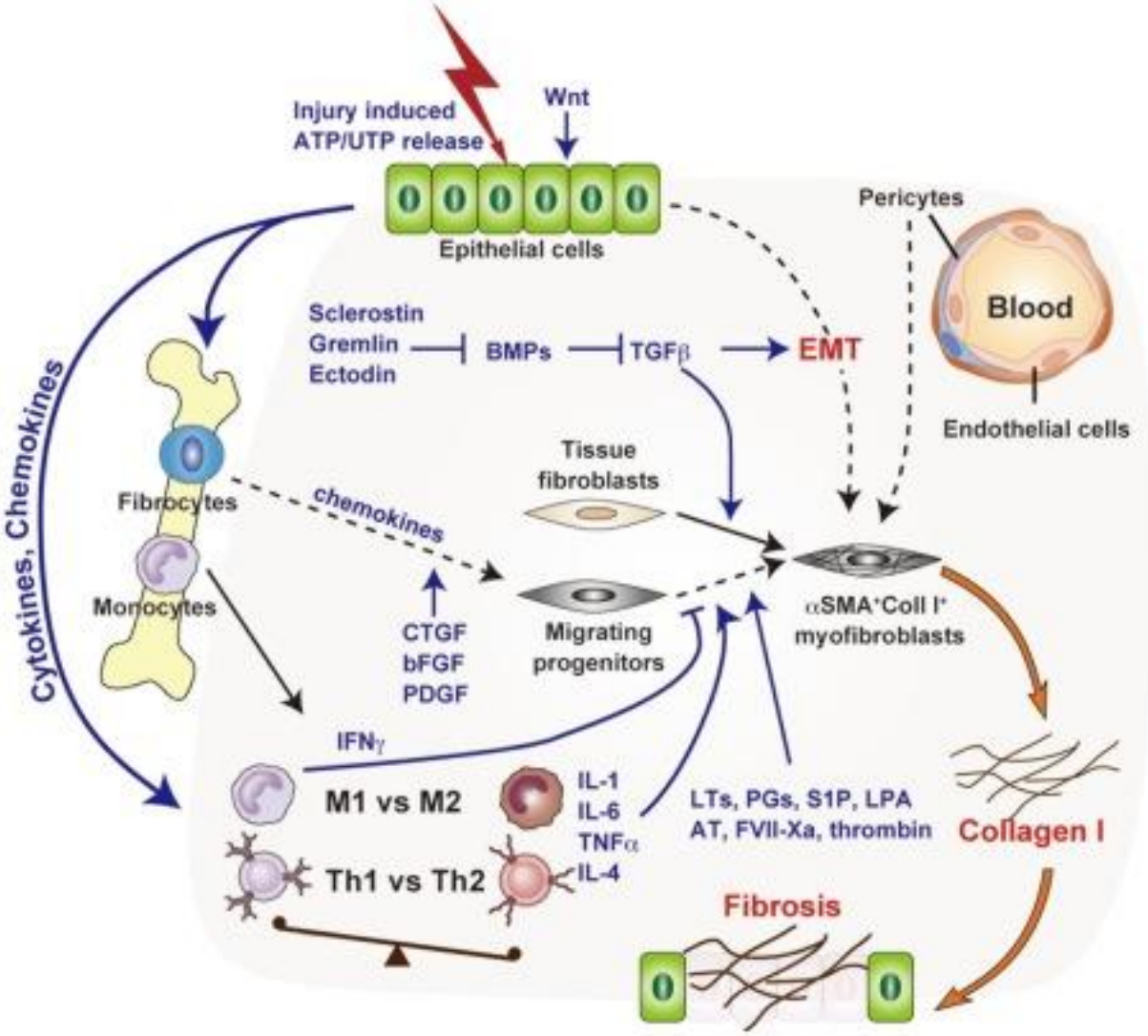
MUNI
MED

Syphilis

- 1. primary syphilis - contagious
- chancre (ulcus durum, hard chancre)
- M: penis x F: vagina, cervix
- painless, firm ulceration + regional painless lymphadenopathy
- spontaneous resolve (weeks) → scar

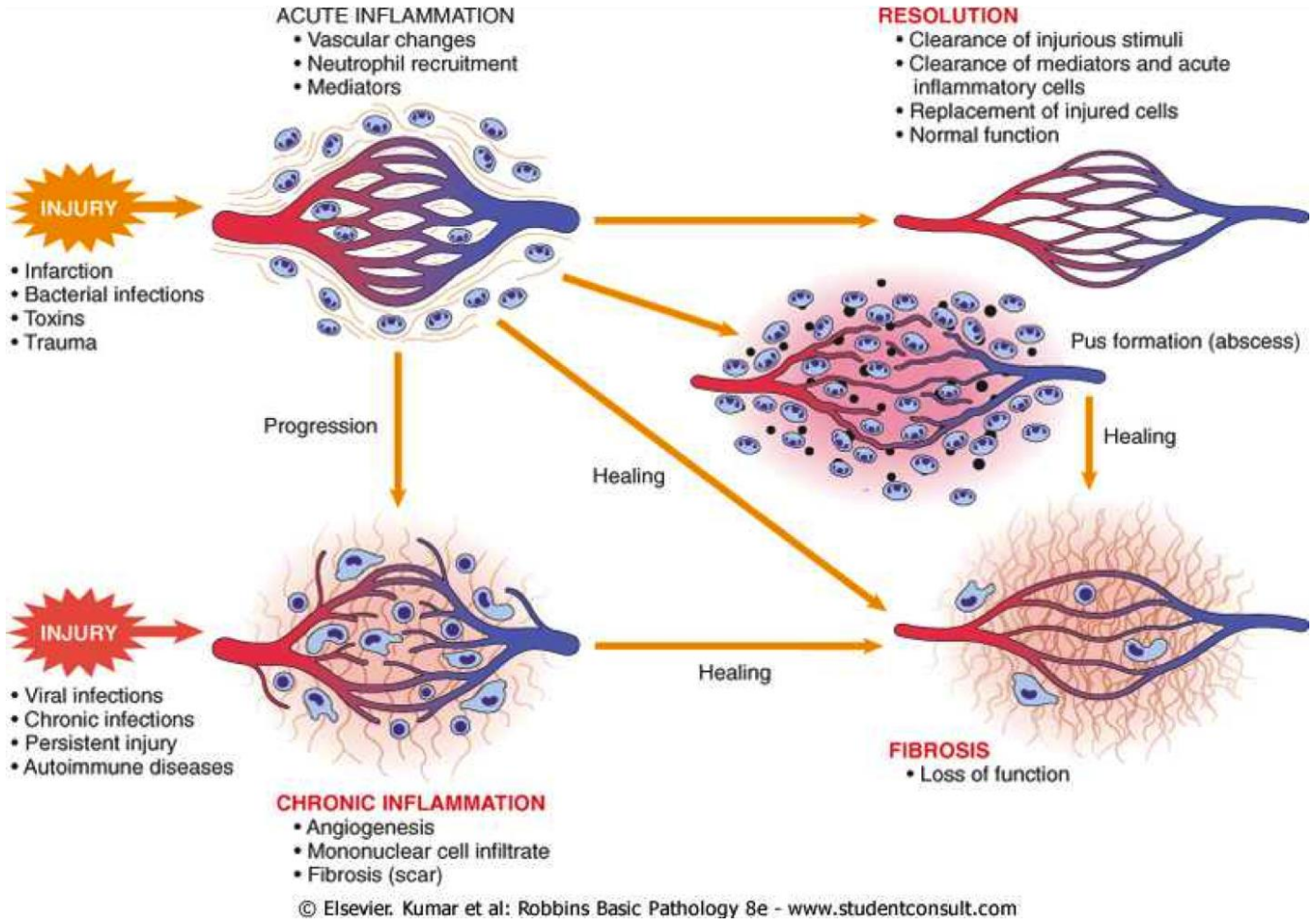
MUNI
MED

Mechanisms of chronic inflammation



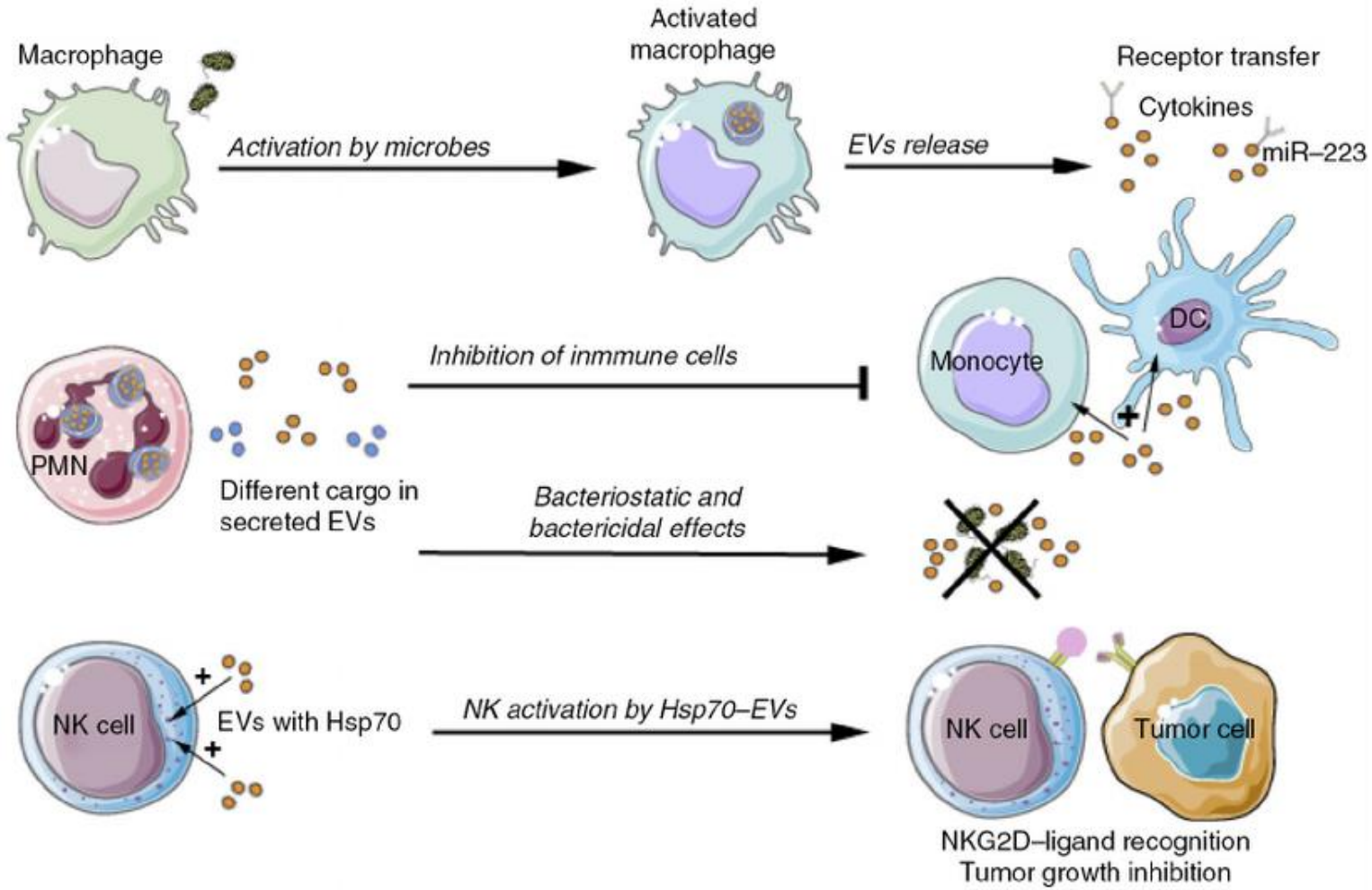
MUNI MED

Morphological features of chronic inflammation



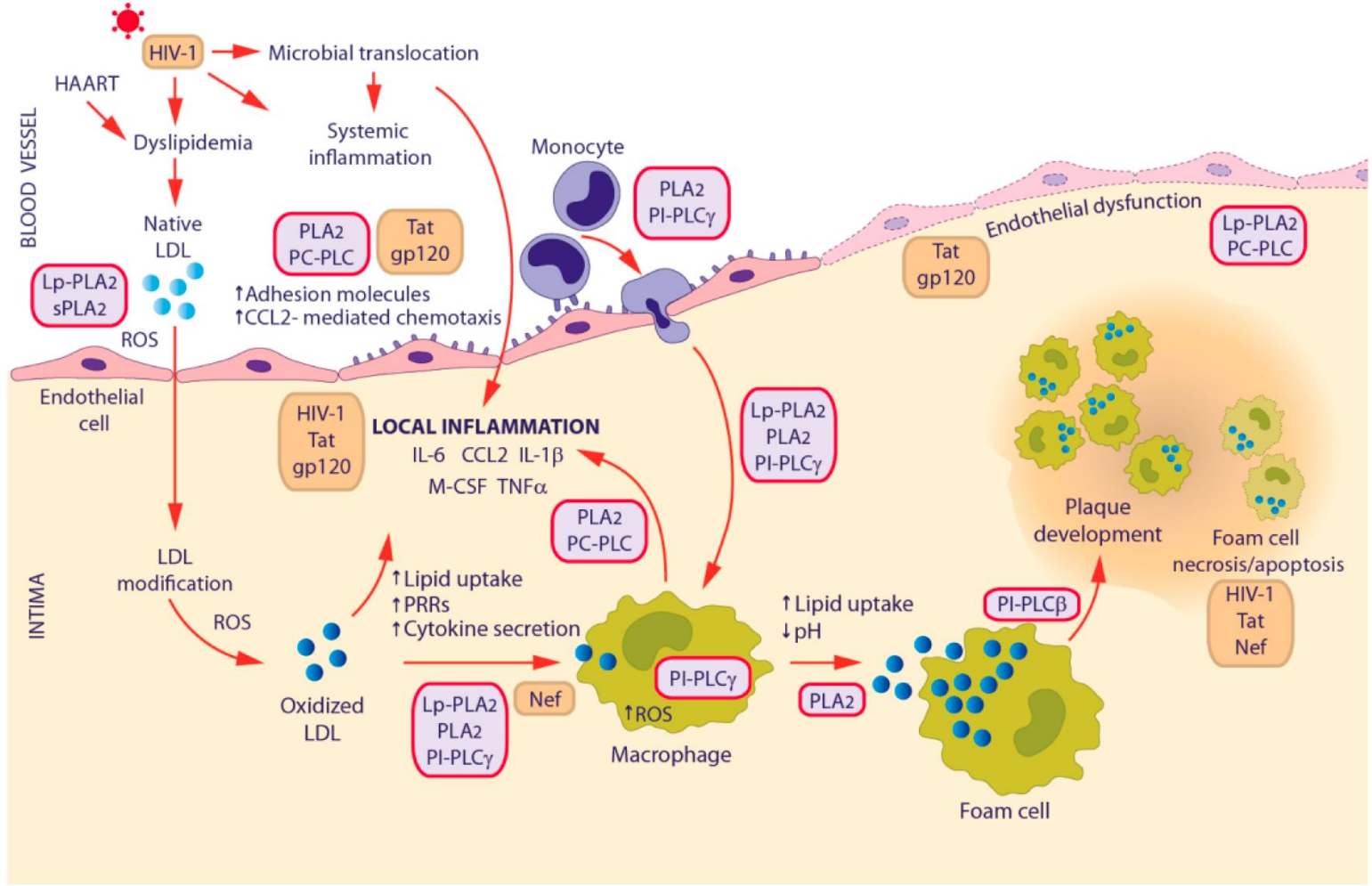
MUNI MED

The role of macrophages in chronic inflammation



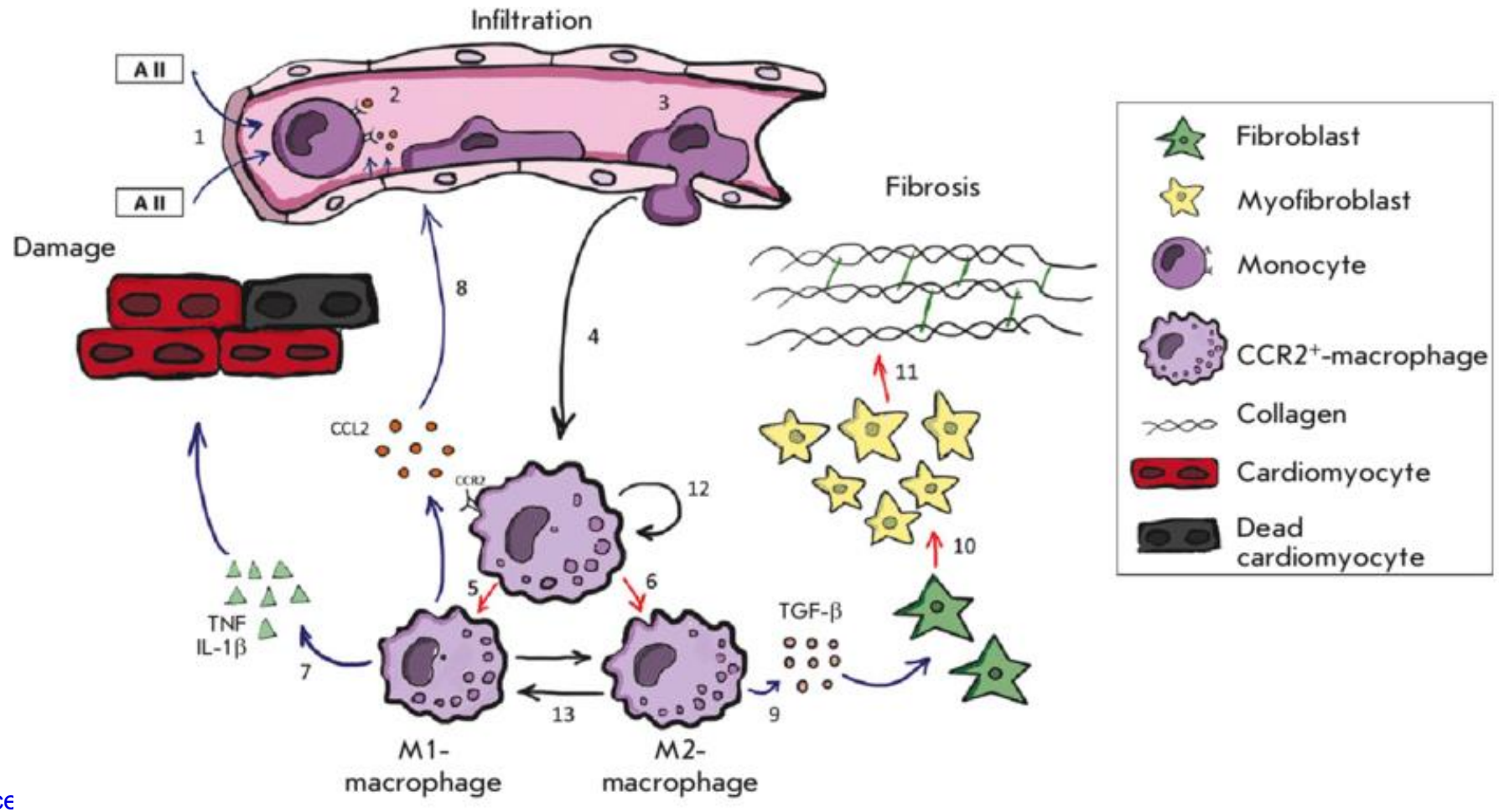
MUNI MED

The role of macrophages in chronic inflammation



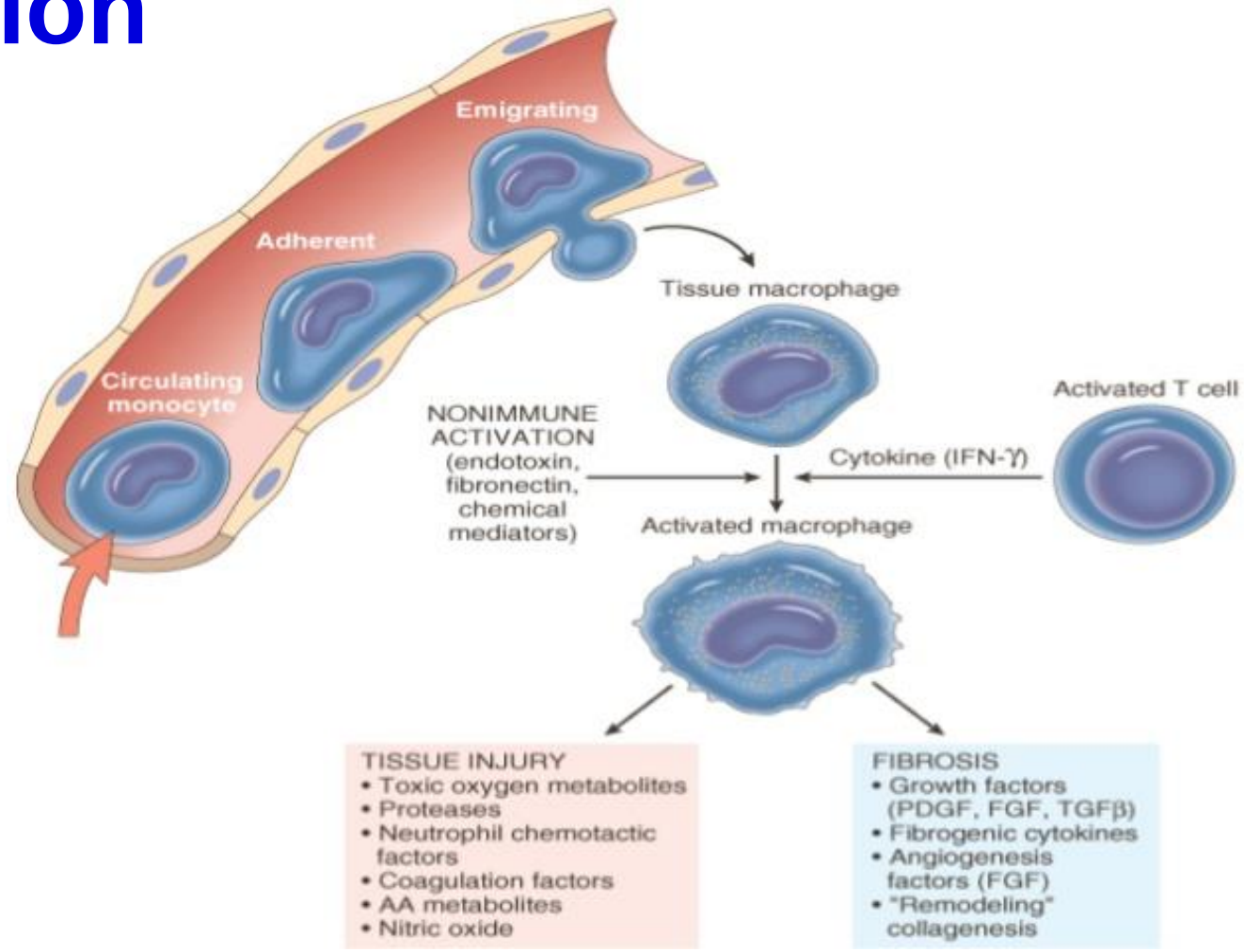
MUNI MED

The role of macrophages in chronic inflammation



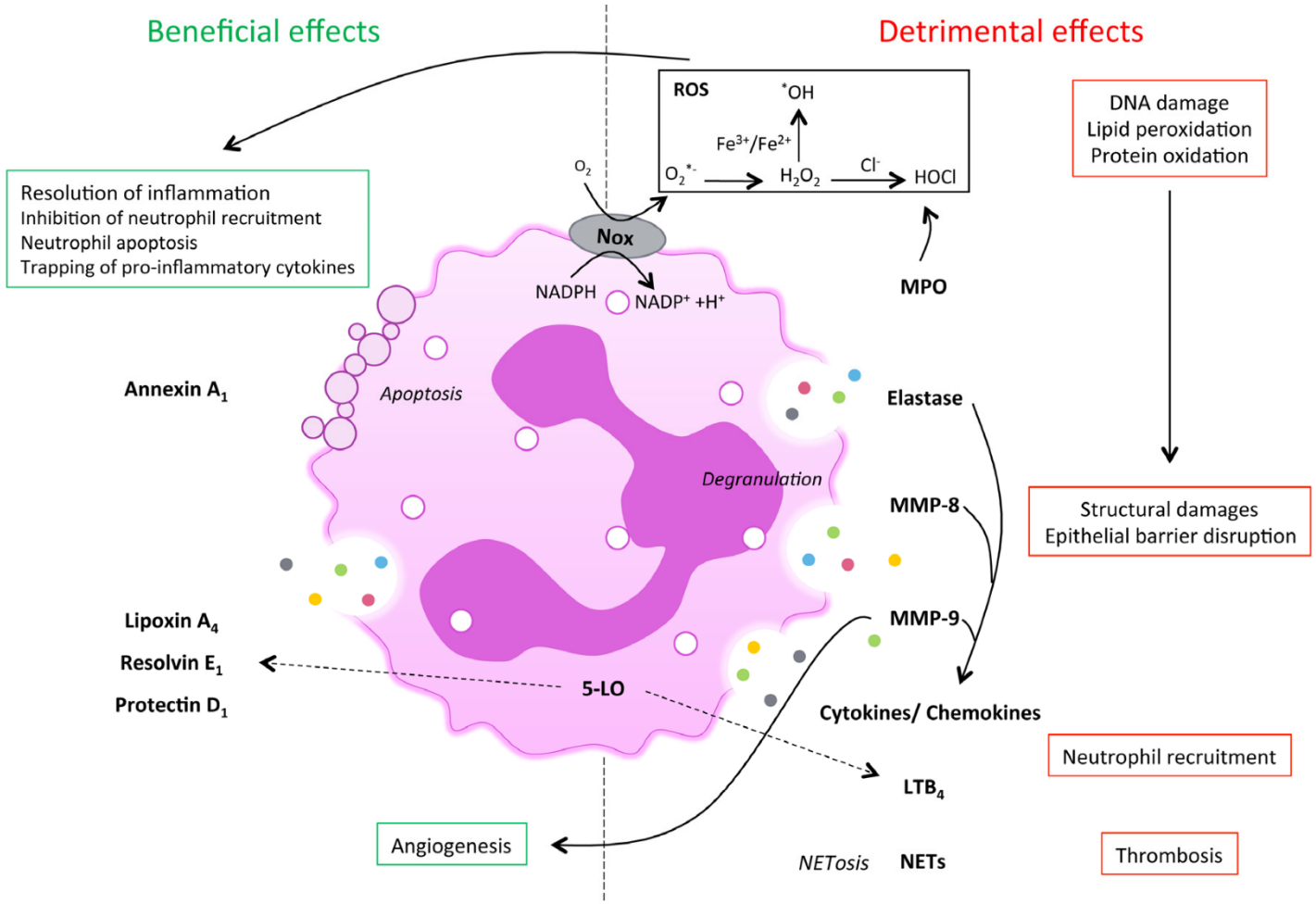
MUNI MED

The role of macrophages in chronic inflammation



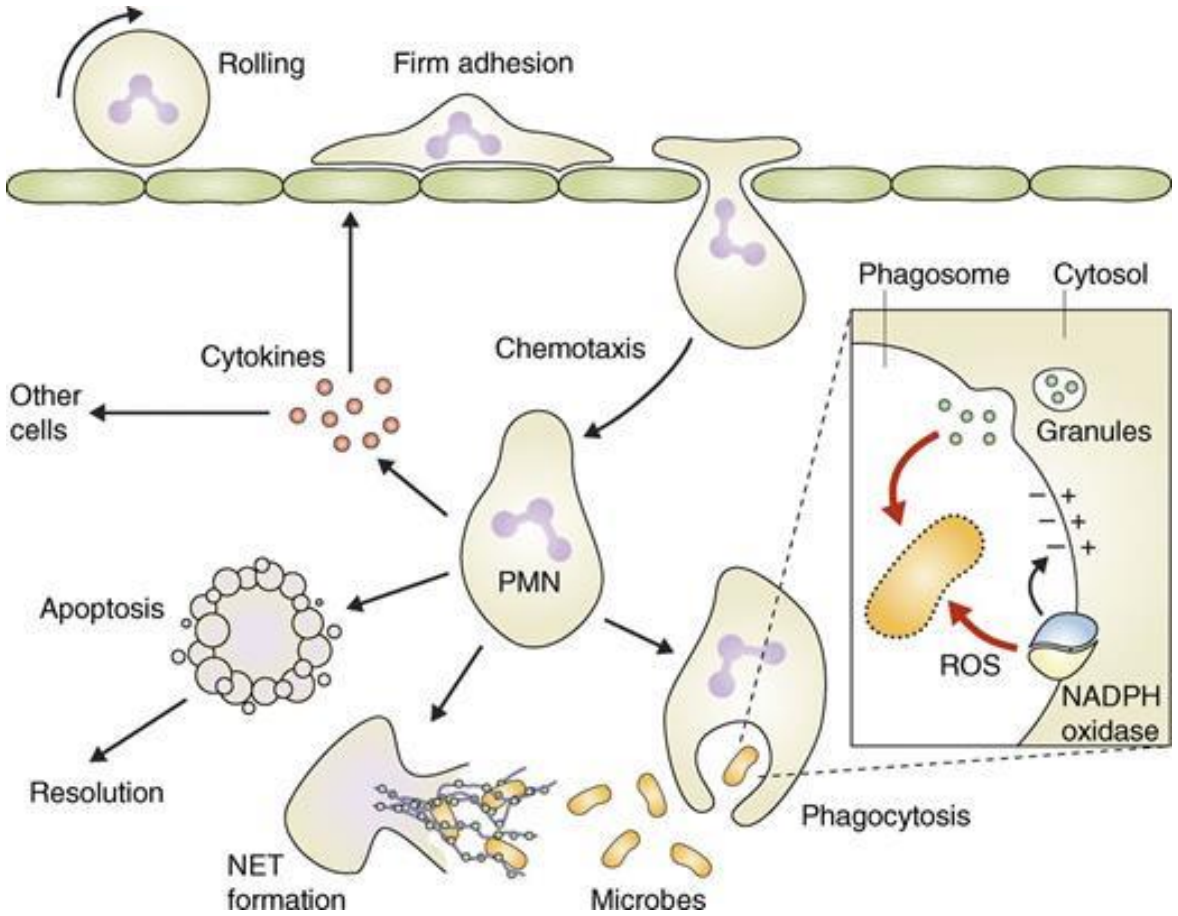
MUNI MED

The role of neutrophils in chronic inflammation



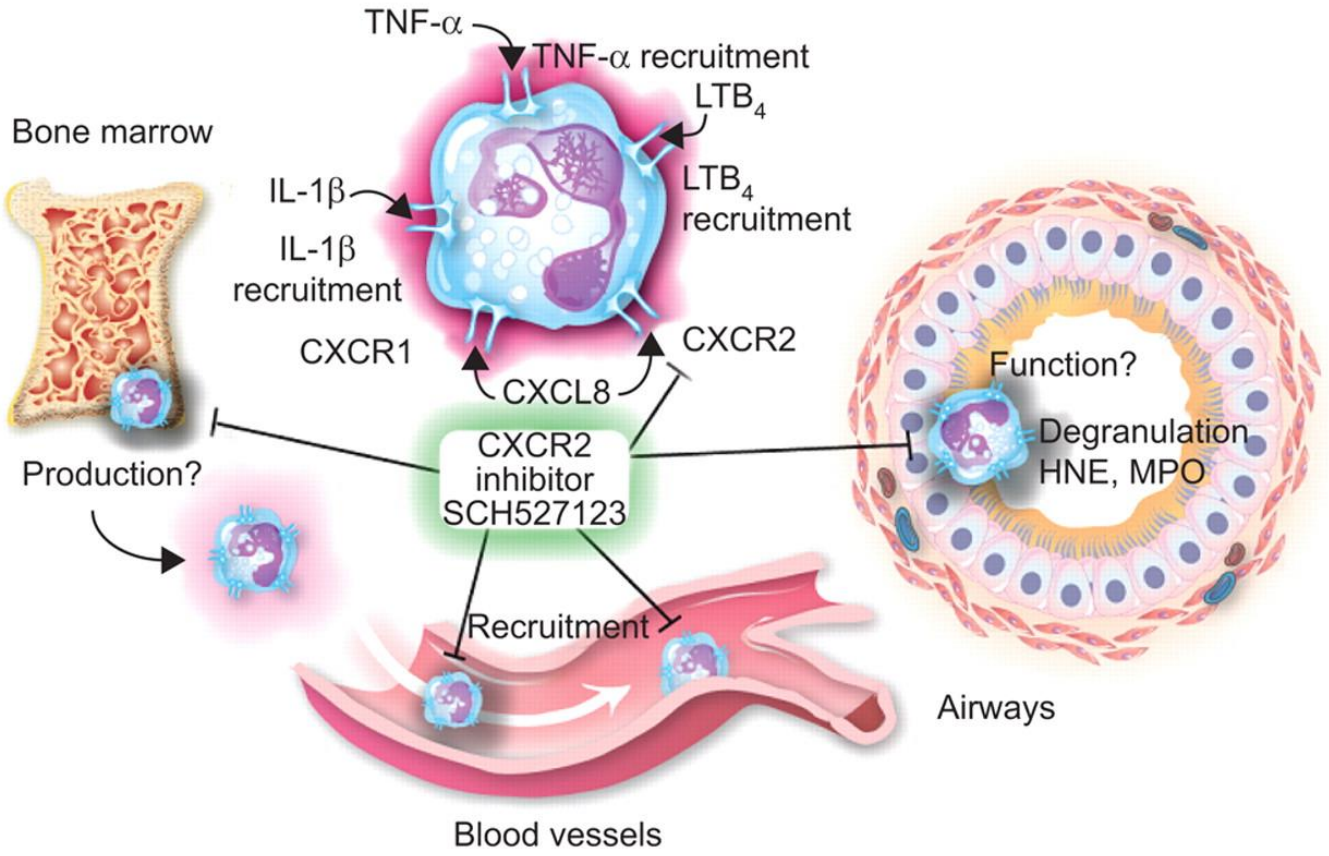
MUNI MED

The role of neutrophils in chronic inflammation



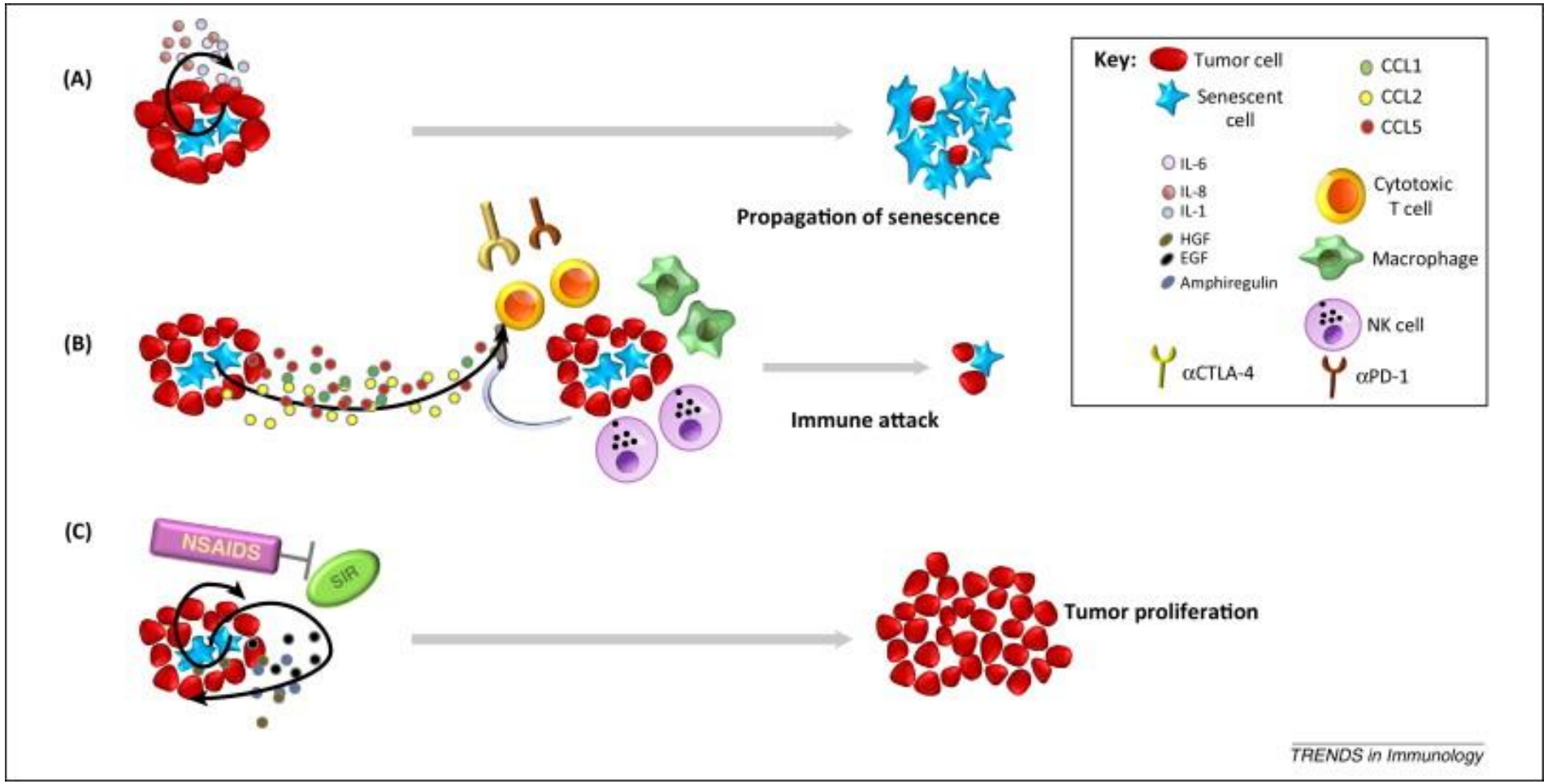
MUNI MED

The role of neutrophils in chronic inflammation



MUNI MED

Age-dependent consequences



MUNI MED

SIRS – systemic inflammatory response syndrome

- Generalized acute inflammatory reaction that spreads throughout the body
- Intense inflammatory response to primary local, multiple or otherwise complex damage
- In SIRS, subsequent inflammation is not limited to the area where the inflammation occurred, but spreads throughout the body
- Even common inflammation spreads throughout the body - the difference from SIRS is that in SIRS, the mechanisms of inflammation control stop working

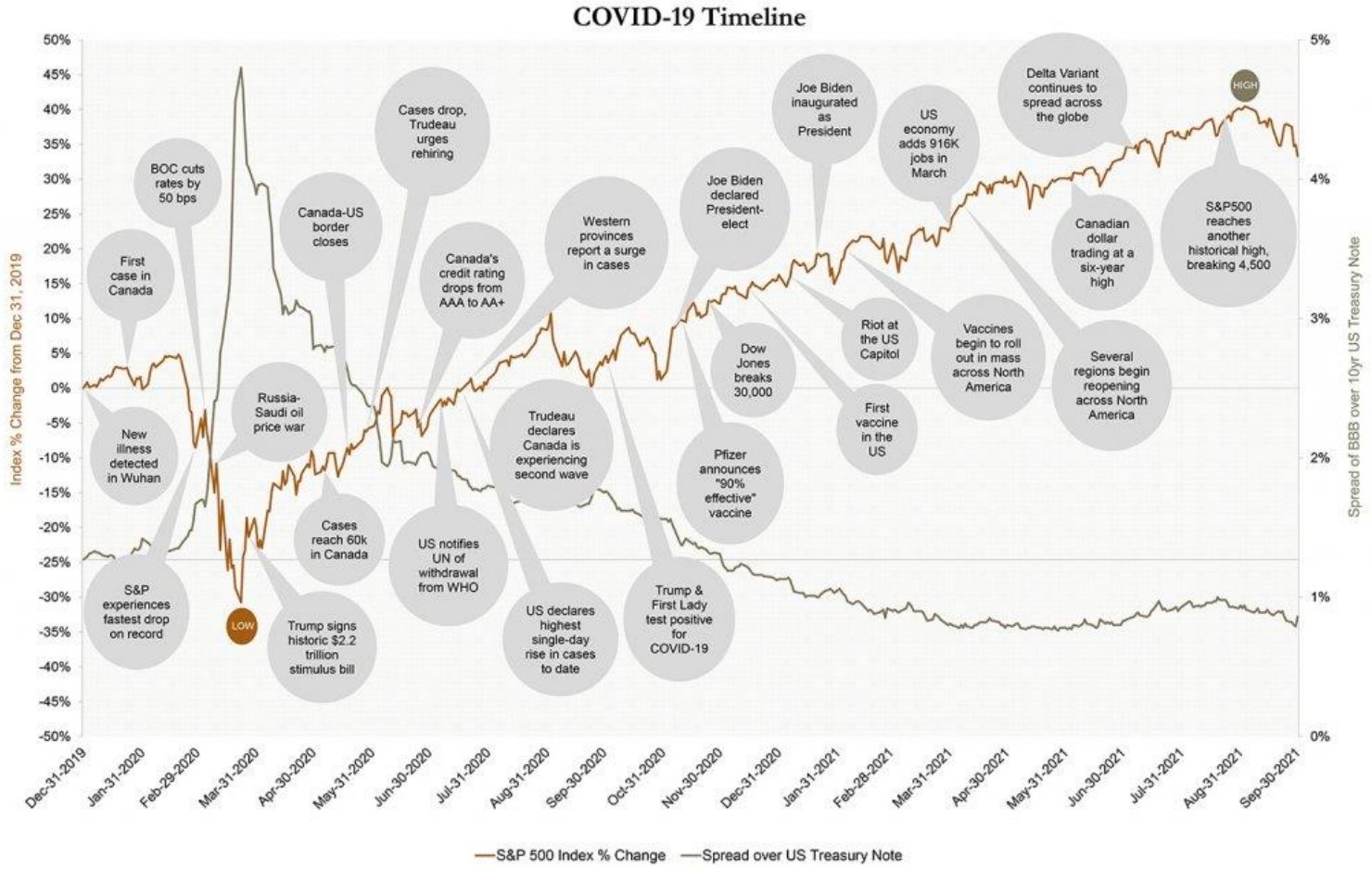
MUNI MED

Pathogenesis of Covid-19 disease

Coronaviruses belong to the Coronaviridae family in the Nidovirales order

Corona represents crown-like spikes on the outer surface of the virus; thus, it was named as a coronavirus

Coronaviruses are enveloped viruses, minute in size (65–125 nm in diameter) and contain a single-stranded RNA as a nucleic material, size ranging from 26 to 32kbs in length



Covid-19 facts

Globally, as of 4:30pm CET, 15 November 2021, there have been 253 163 330 confirmed cases of COVID-19, including 5 098 174 deaths, reported to WHO. As of 15 November 2021, a total of 7 307 892 664 vaccine doses have been administered. (who.int)

In Czechia, from 3 January 2020 to 4:30pm CET, 15 November 2021, there have been 1 896 075 confirmed cases of COVID-19 with 31 541 deaths, reported to WHO. As of 7 November 2021, a total of 12 154 562 vaccine doses have been administered.

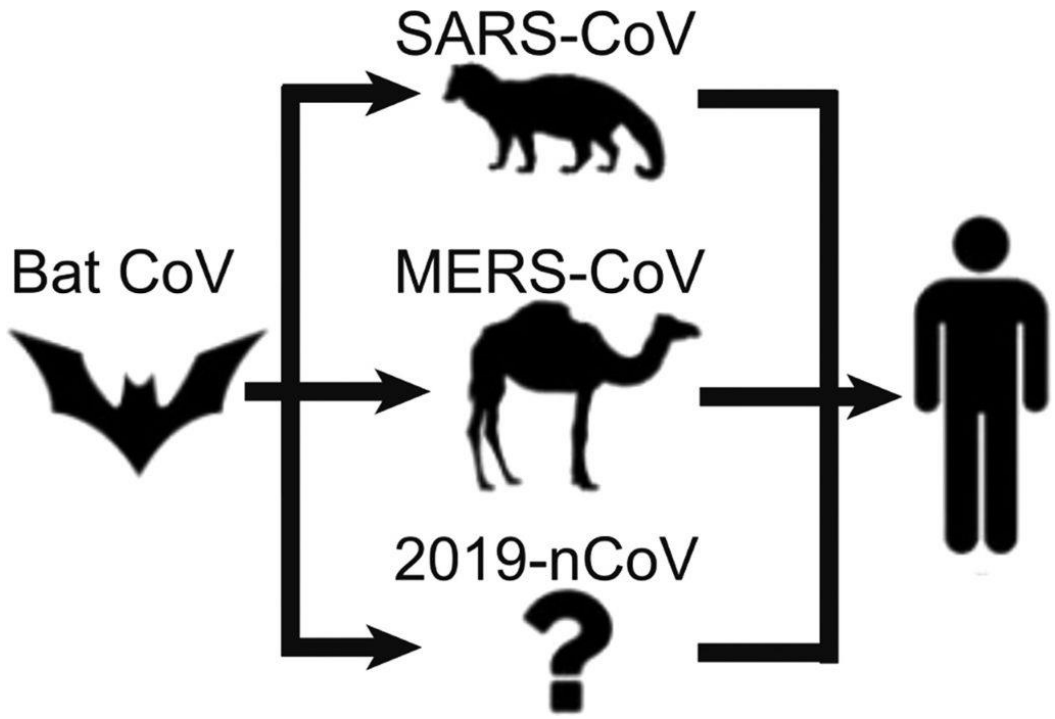
MUNI MED

Covid-19 facts

- SARS-CoV-2 is the official, scientific name of the virus, the germ that causes the disease COVID-19
- COVID-19 is the name of the disease – the fever, cough, chills and other symptoms that people have when they are infected with the virus SARS-CoV-2.

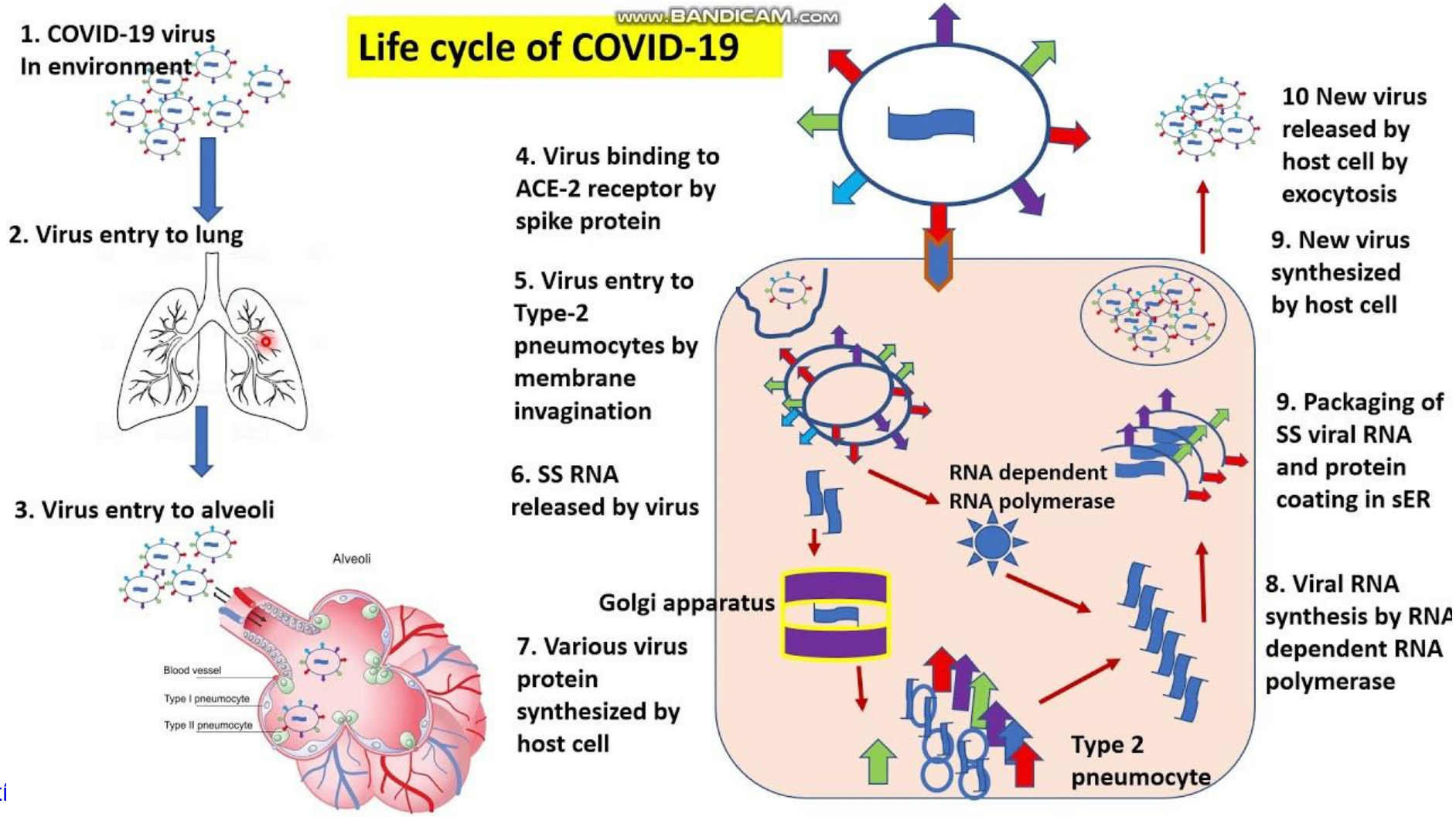
Human coronaviruses

- The most likely ecological reservoirs for coronaviruses are bats, but it is believed that the virus jumped the species barrier to humans from another intermediate animal host.
- This intermediate animal host could be a domestic food animal, a wild animal, or a domesticated wild animal which has not yet been identified.



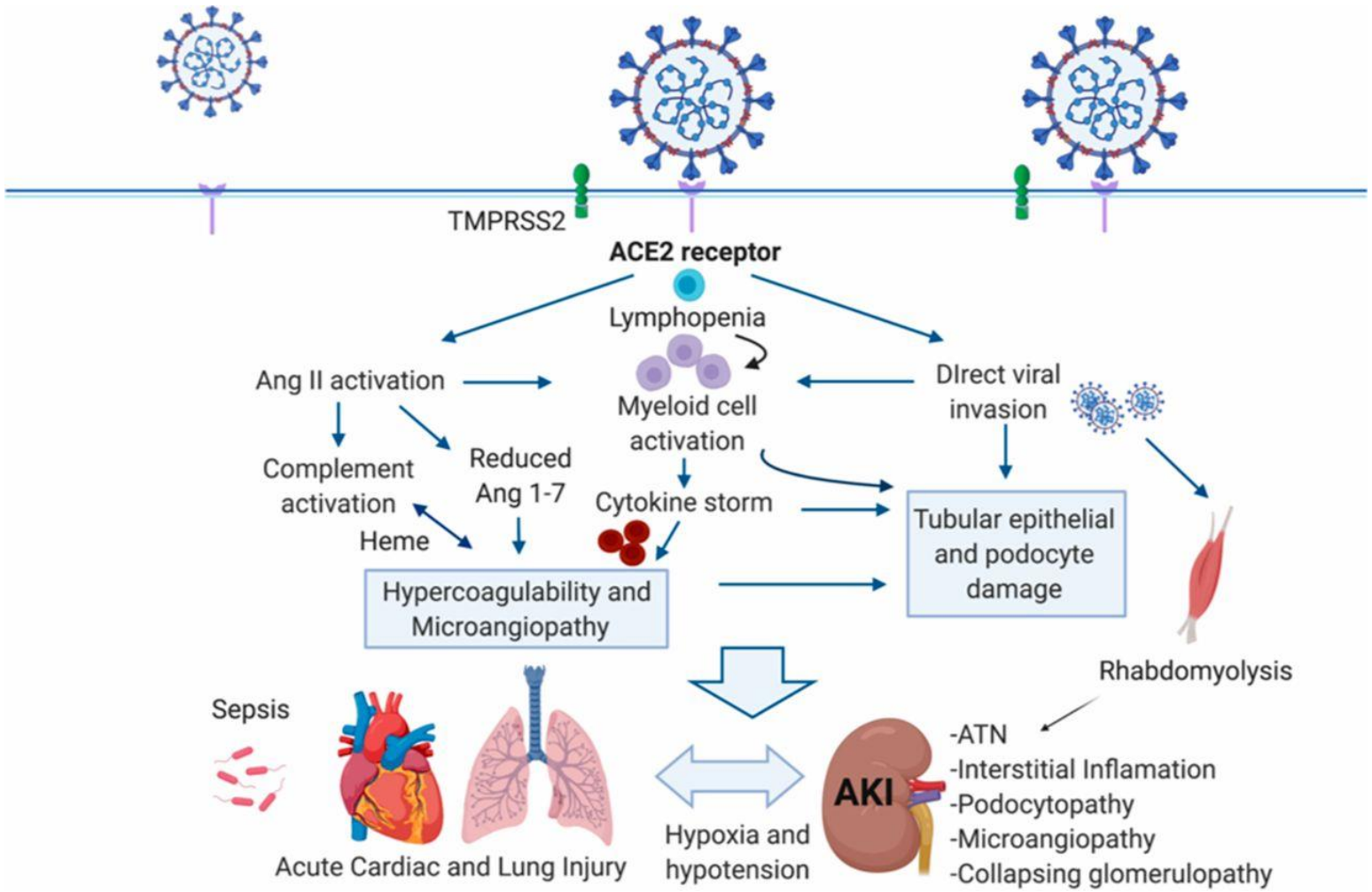
MUNI MED

Pathogenesis of Covid-19 disease



MUNI MED

Pathogenesis of Covid-19 disease

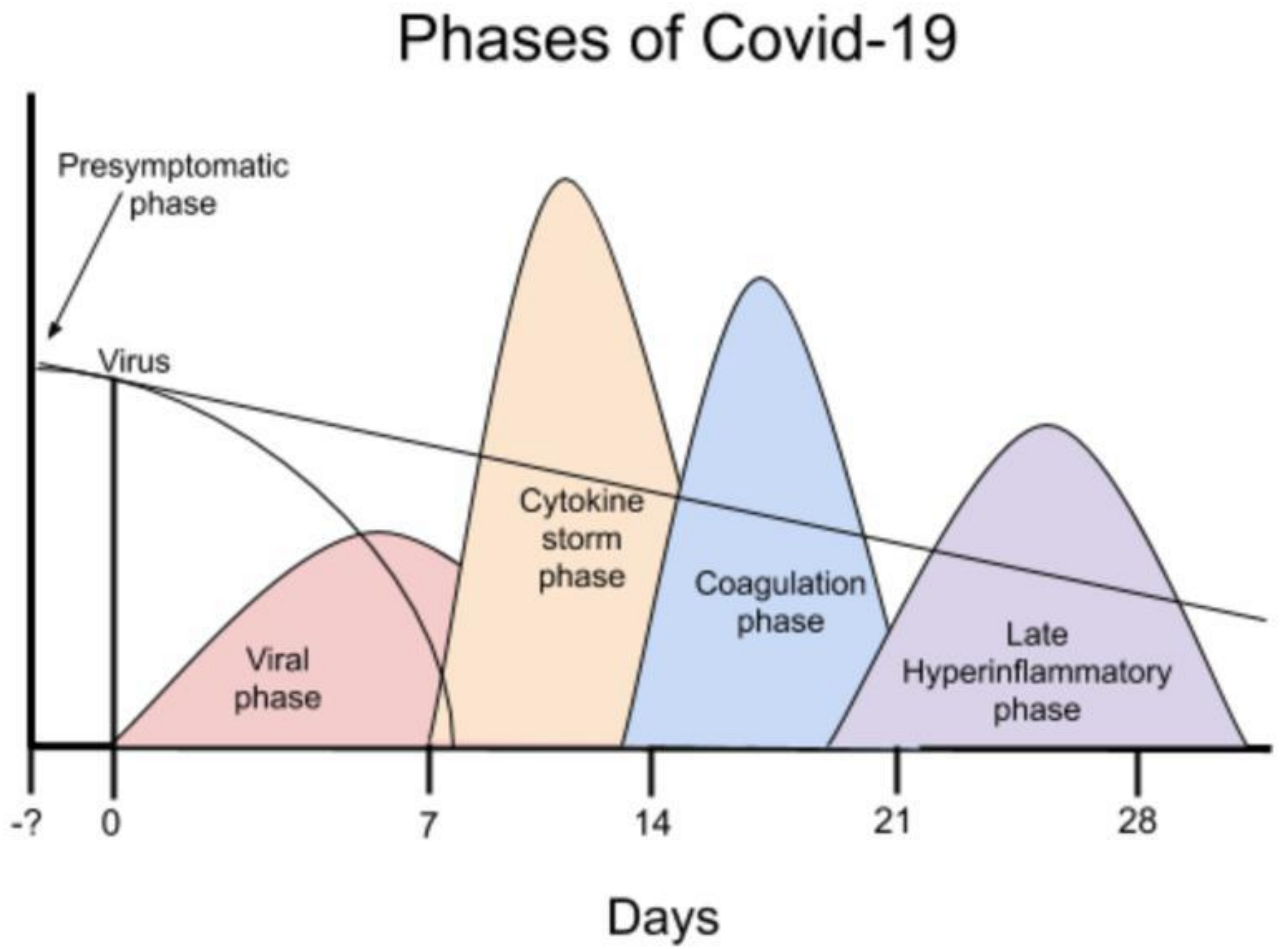


MUNI MED

Pathogenesis of Covid-19 disease

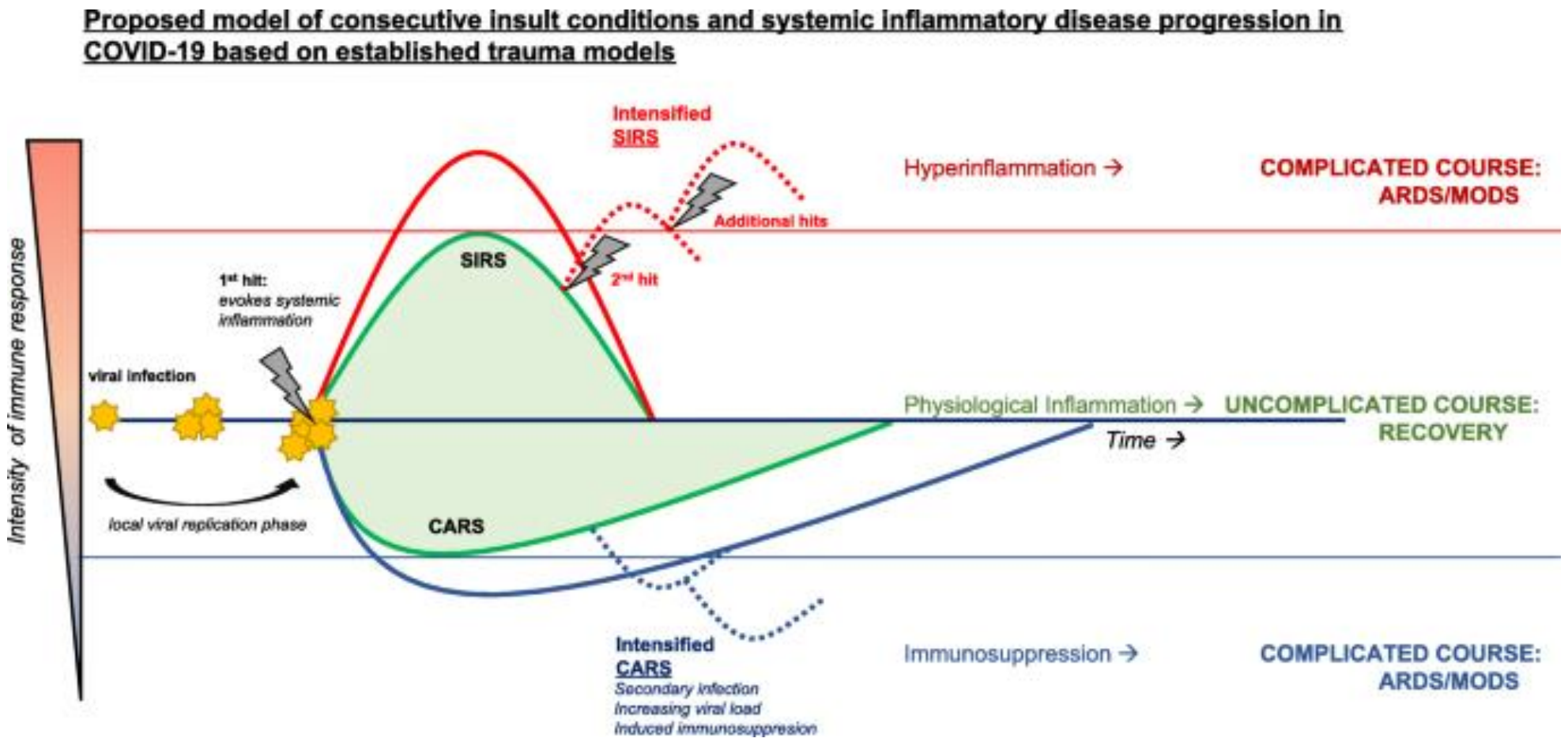
- Coronavirus is one of the major pathogens that primarily targets the human respiratory system. Previous outbreaks of coronaviruses (CoVs) include the severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV which have been previously characterized as agents that are a great public health threat. In late December 2019, a cluster of patients was admitted to hospitals with an initial diagnosis of pneumonia of an unknown etiology.

Pathogenesis of Covid-19 disease



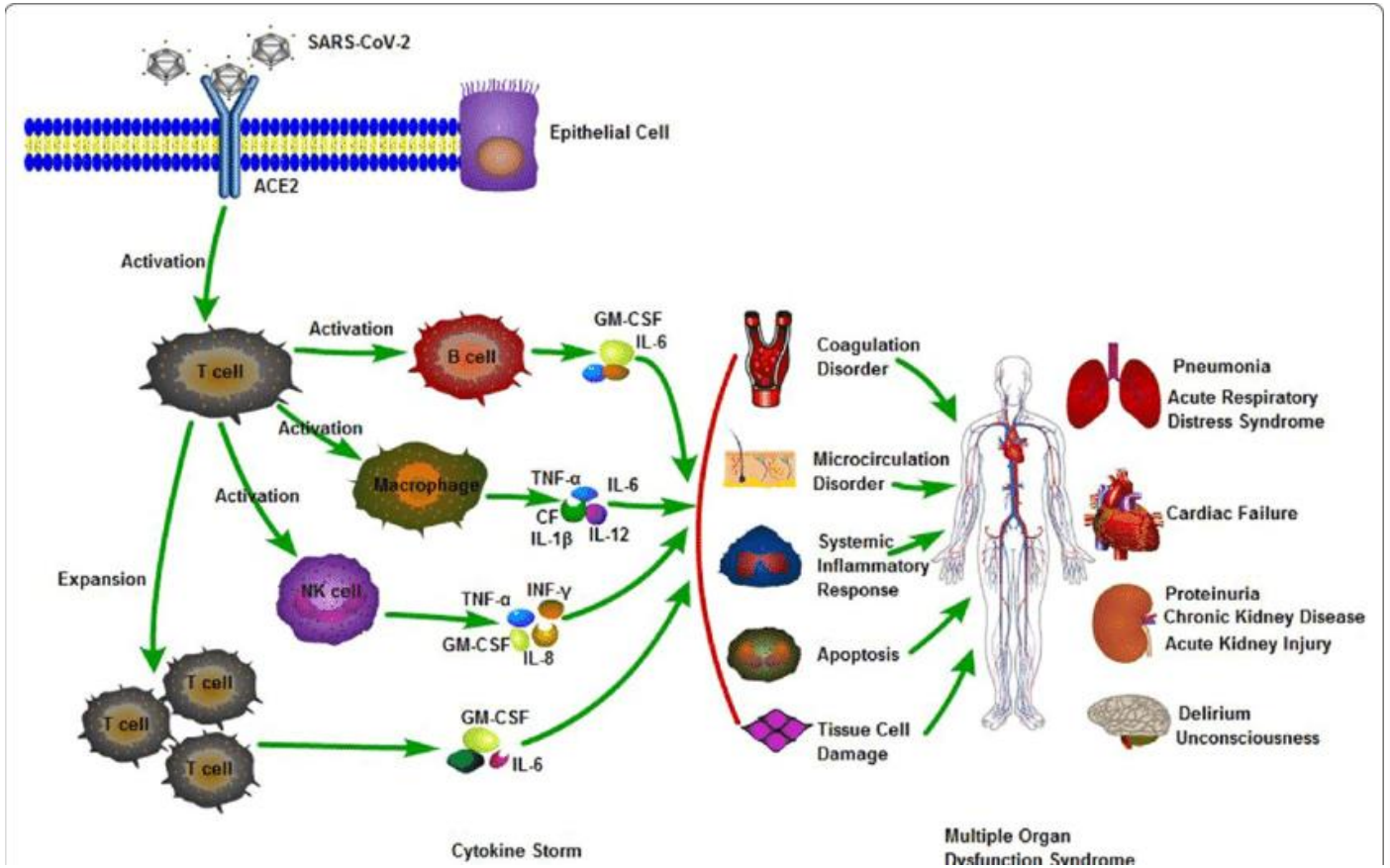
MUNI MED

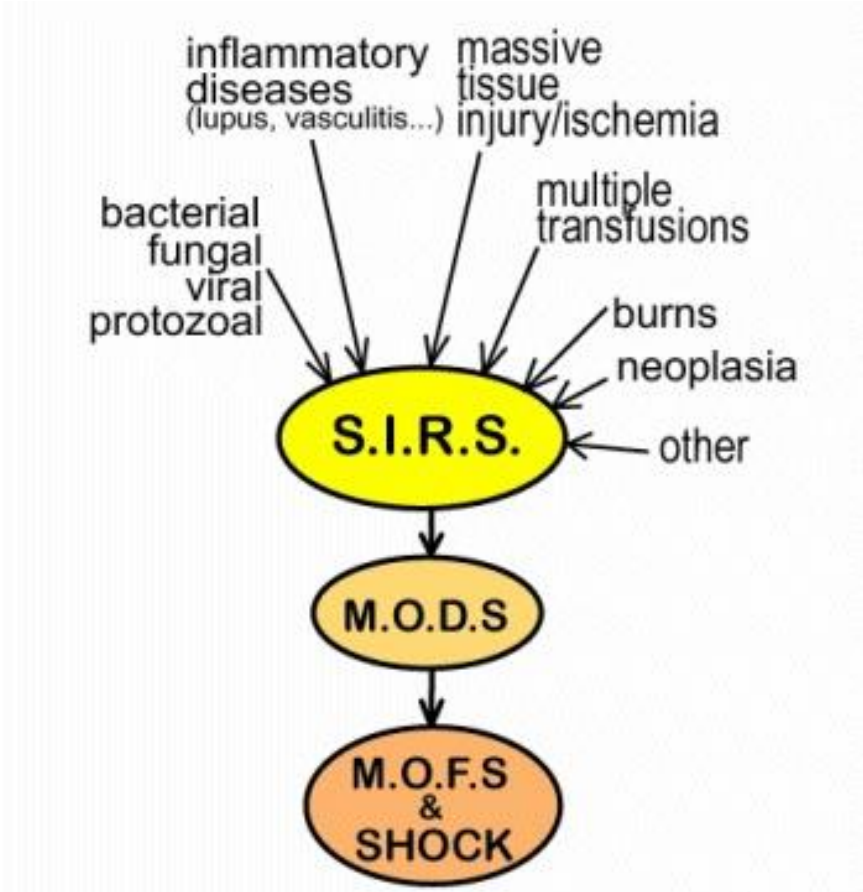
SIRS and Covid-19



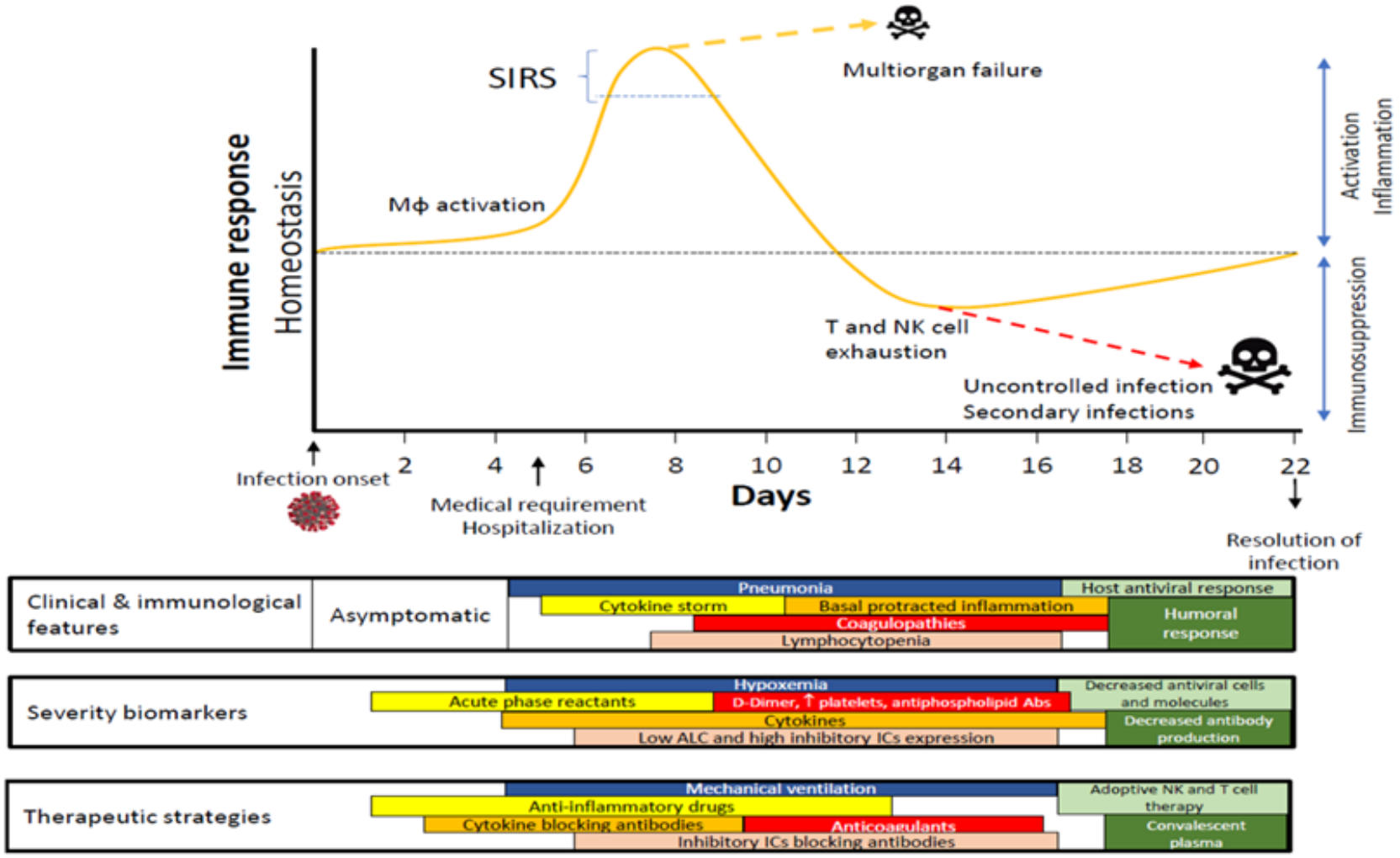
MUNI MED

MODS


SARS-CoV-2
ACE2
Epithelial Cell
Activation
T cell
Activation
B cell
GM-CSF
IL-6
Activation
Macrophage
TNF-α
IL-6
CF
IL-1β
IL-12
Activation
NK cell
Expansion
TNF-α
INF-γ
GM-CSF
IL-8
T cell
T cell
T cell
GM-CSF
IL-6
Cytokine Storm
Coagulation Disorder
Microcirculation Disorder
Systemic Inflammatory Response
Apoptosis
Tissue Cell Damage
Pneumonia
Acute Respiratory Distress Syndrome
Cardiac Failure
Proteinuria
Chronic Kidney Disease
Acute Kidney Injury
Delirium
Unconsciousness
Multiple Organ Dysfunction Syndrome

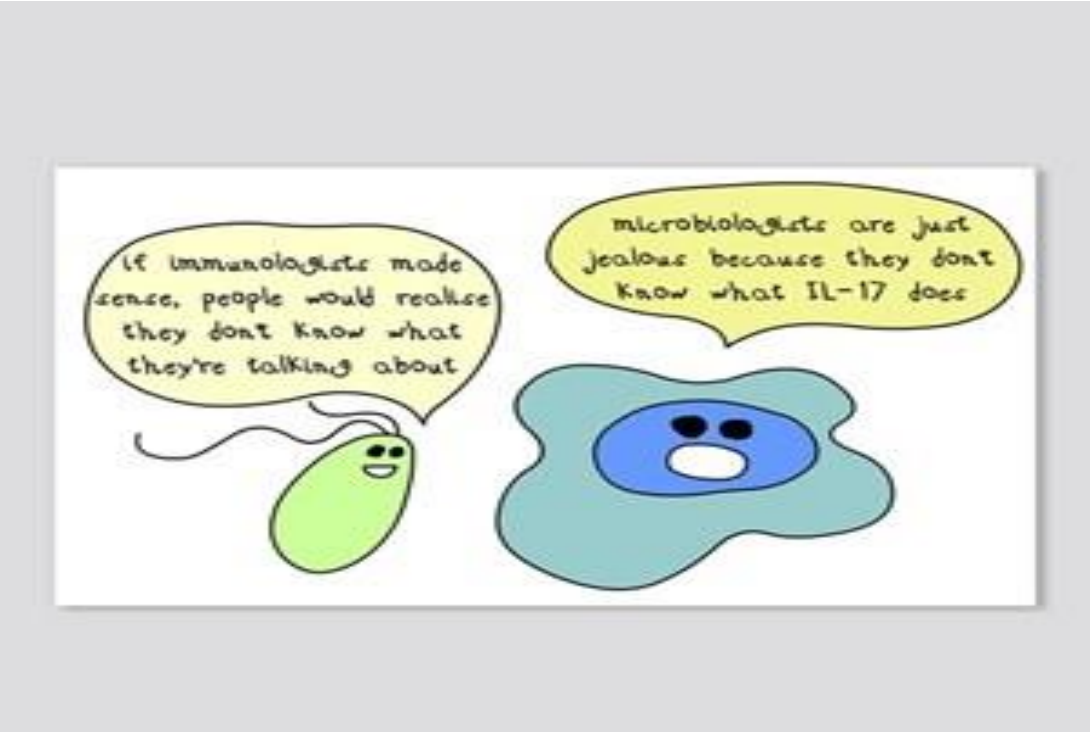

inflammatory diseases (lupus, vasculitis...)
massive tissue injury/ischemia
bacterial
fungal
viral
protozoal
multiple transfusions
burns
neoplasia
other
S.I.R.S.
M.O.D.S
M.O.F.S & SHOCK

SIRS, MODS and Covid-19



MUNI MED

Thank you for you attention



MUNI MED