Inflammation •
L3•

ILO: K1
objectives of lecture

1- granulomatous inflammation (T.B granuloma)

2- systemic effects of inflammation - fever

-acute phase proteins

- leukocytosis

- septic shock

Granulomatous inflammation

- is a distinctive pattern of chronic inflammation characterized by aggregates of activated macrophages that assume an epithelioid appearance, Granulomas are encountered in certain specific pathologic states; consequently, recognition of the granulomatous pattern is important because of the limited number of conditions (some life-threatening) that cause it.

- Granulomas can form in the setting of persistent T-cell responses to certain microbes (such as Mycobacterium tuberculosis, T. pallidum, or fungi), where T-cell-derived cytokines are responsible for chronic macrophage activation.

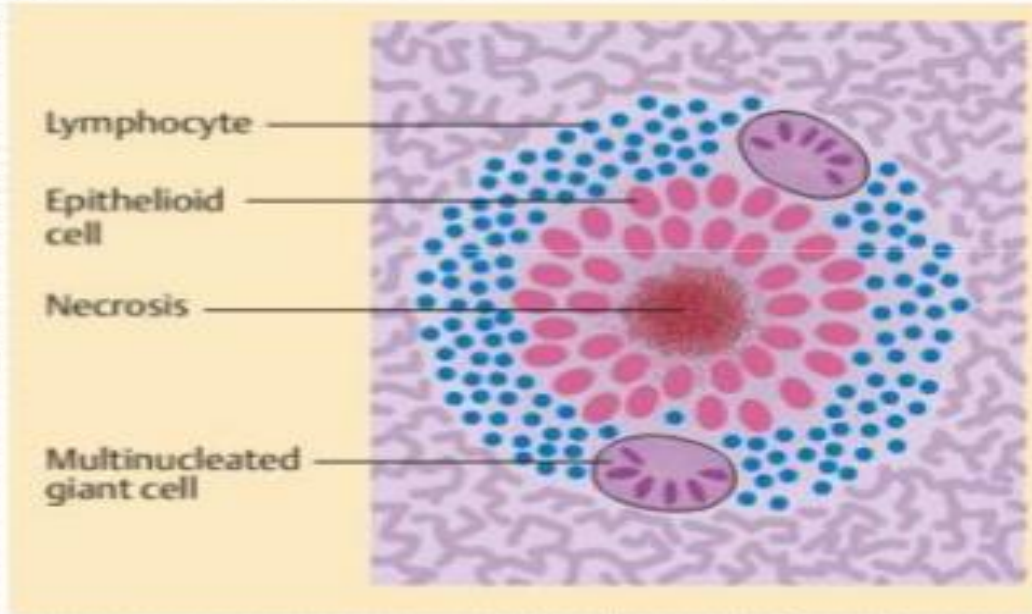
- Tuberculosis is the prototype of a granulomatous disease caused by infection and should always be excluded as the cause when granulomas are identified.
- Granulomas may also develop in response to relatively inert foreign bodies (e.g., suture or splinter), forming so-called foreign body granulomas.
- The formation of a granuloma effectively "walls off" the offending agent and is therefore a useful defense mechanism.
- However, granuloma formation does not always lead to eradication of the causal agent, which is frequently resistant to killing or degradation, and granulomatous inflammation with subsequent fibrosis may even be the major cause of organ dysfunction in some diseases, such as tuberculosis.

Recognition of granuloma in biopsy specimen is important because it

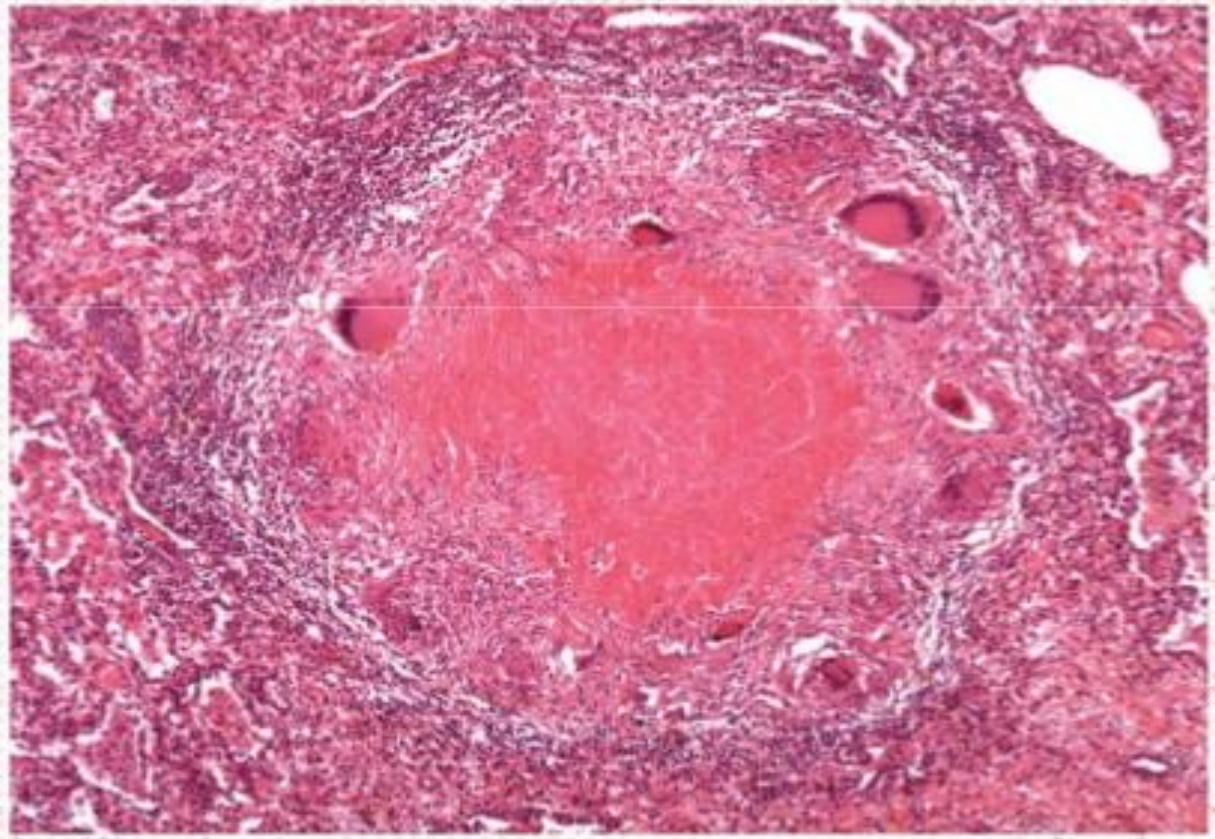
- shorten the list of differential diagnosis, granuloma is a focus of chronic inflammation consist of aggregation of macrophages that are transformed into epithelioid cells surrounded by a collar of mononuclear leukocytes principally lymphocytes and occasionally plasma cells, older granulomas develop an enclosing rim of fibroblasts and connective tissue .frequently , epithelioid cells fuse to form multinucleated giant cells in periphery or sometime in the center of the granuloma, they have 20 or more small nuclei arranged either peripherally (Langhans-type giant cell) or haphazardly (foreign body –type giant cell)

COMPOSITION OF GRANULOMA

- Following structural components
  - Epitheloid cells
  - Multinucleate giant cells
  - **Lymphoid cells** - cell mediated immune reaction
  - Necrosis & Fibrosis.



Histological features



SYSTEMIC EFFECTS OF INFLAMMATION

- the systemic effects of inflammation, collectively called the acute-phase reaction, or the systemic inflammatory response syndrome. The cytokines TNF, IL-1, and IL-6 are the most important mediators of the acute-phase reaction.
- The acute-phase response consists of several clinical and pathologic changes:

1. Fever : •

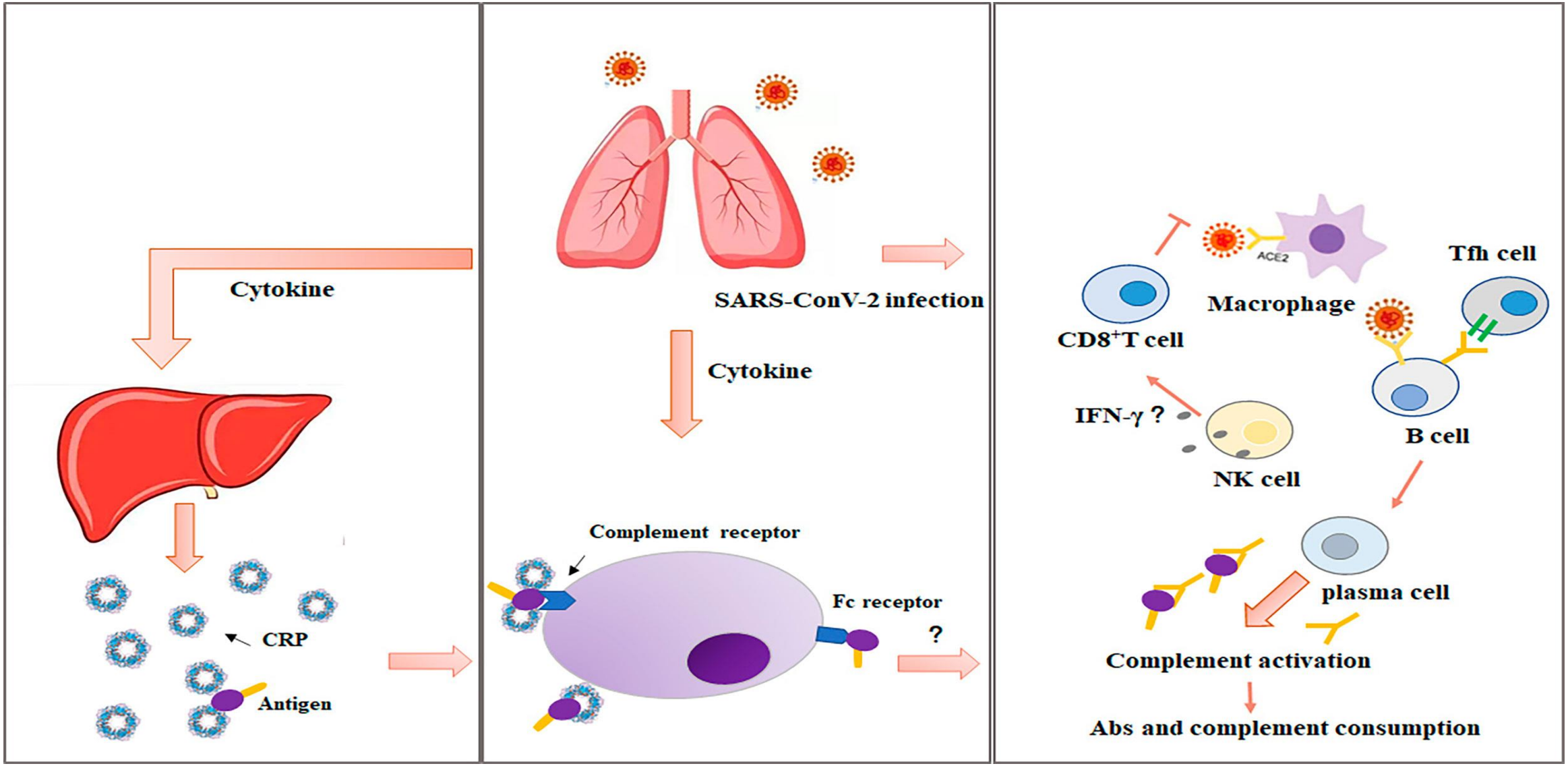
is produced in response to substances called pyrogens that act by • stimulating prostaglandin (PG) synthesis in the vascular and perivascular cells of the hypothalamus.

2. Acute-phase proteins: •

which are plasma proteins, mostly synthesized in the liver, whose • concentrations may increase several 100-fold as part of the response to inflammatory stimuli Three of the best-known of these proteins are C-reactive protein (CRP), fibrinogen, and serum amyloid A (SAA) protein .

CRP and SAA, bind to microbial cell walls, and they may act as opsonins and fix • complement, thus promoting the elimination of the microbes. Fibrinogen binds to erythrocytes and causes them to form stacks (rouleaux) that sediment more rapidly at unit gravity than do individual erythrocytes.

The role of CRP in covid-19 infection



3- Leukocytosis

- is a common feature of inflammatory reactions, especially those induced by bacterial infection. The leukocyte count usually climbs to 15,000 or 20,000 cells/μL, but sometimes it may reach extraordinarily high levels, as high as 40,000 to 100,000 cells/μL.
- The leukocytosis occurs initially because of accelerated release of cells from the bone marrow post-mitotic reserve pool (caused by cytokines, including TNF and IL-1)

Prolonged infection also stimulates production of colony-stimulating factors (CSFs), leading to increased bone marrow output of leukocytes, which compensates for the loss of these cells in the inflammatory reaction. Most bacterial infections induce an increase in the blood neutrophil count, called neutrophilia. Viral infections are associated with increased numbers of lymphocytes (lymphocytosis)

- Other manifestations of the acute-phase response include increased heart rate and blood pressure; decreased sweating, mainly because of redirection of blood flow from cutaneous to deep vascular beds, to minimize heat loss through the skin; and rigors (shivering), chills (perception of being cold as the hypothalamus resets the body temperature), anorexia, and malaise, probably because of the actions of cytokines on brain cells. Chronic inflammation is associated with a wasting syndrome called cachexia, which is mainly the result of TNF-mediated appetite suppression and mobilization of fat stores

5. In severe bacterial infections (sepsis), the large amounts of organisms and LPS (lipopolysaccharide) in the blood or extravascular tissue stimulate the production of enormous quantities of several cytokines, notably TNF, as well as IL-12 and IL-1. As a result, circulating levels of these cytokines increase, and the nature of the host response changes. High levels of TNF cause disseminated intravascular coagulation (DIC), hypoglycemia, and hypotensive shock. This clinical triad is described as septic shock.

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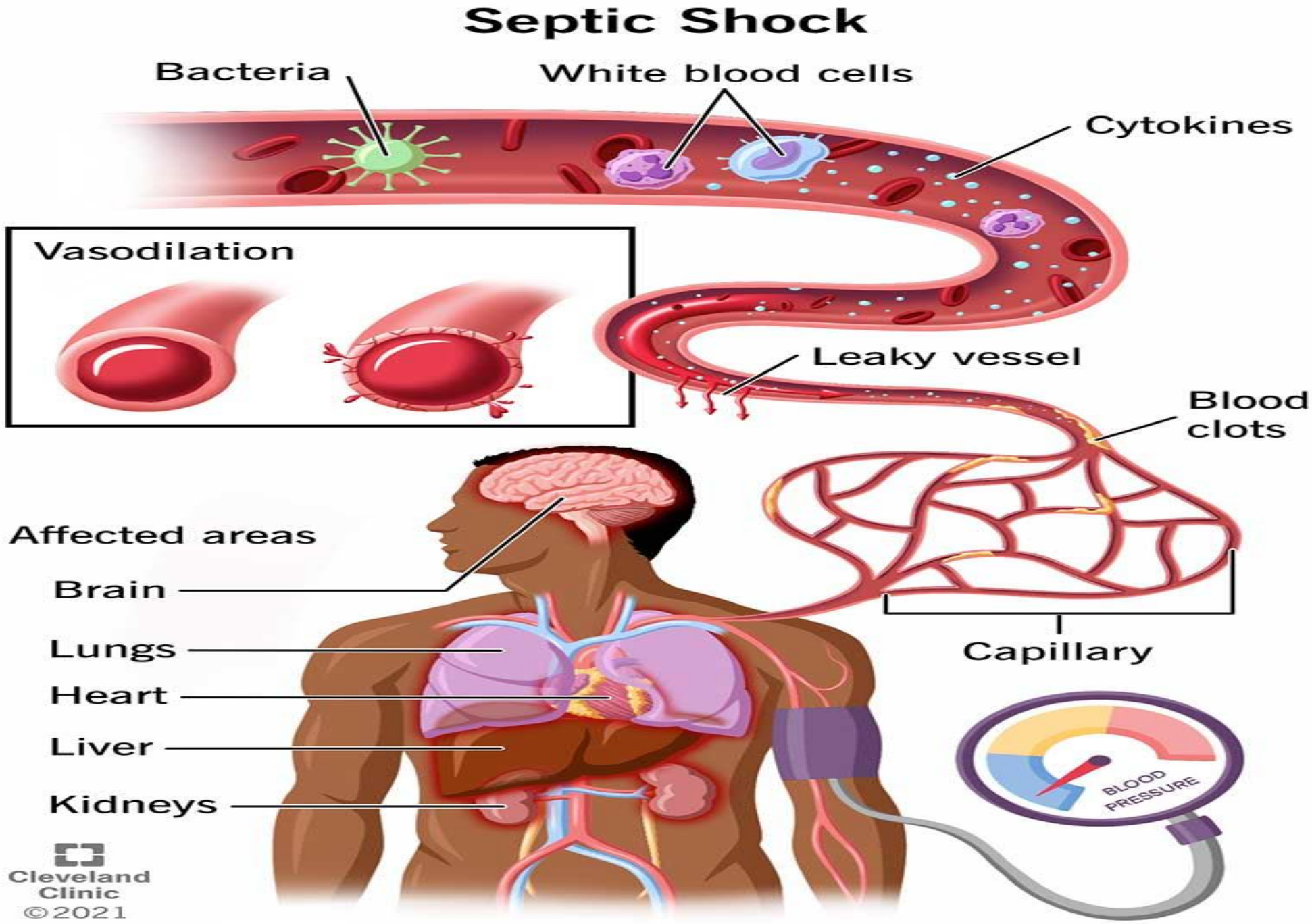
Septic Shock
Bacteria
White blood cells
Cytokines
Vasodilation
Leaky vessel
Blood clots
Affected areas
Brain
Lungs
Heart
Liver
Kidneys
Capillary
BLOOD PRESSURE
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