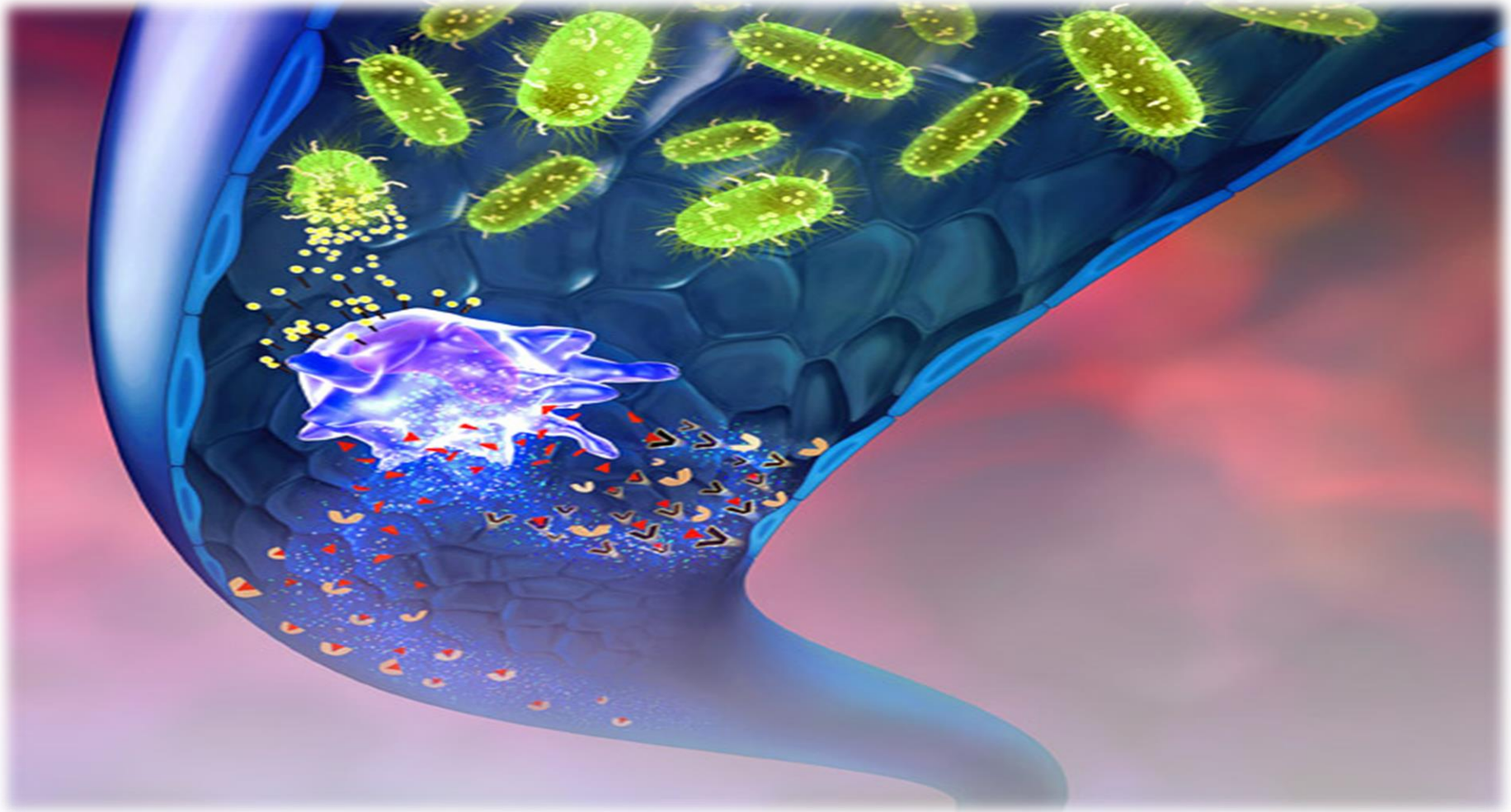


Sepsis.

Sepsis.

I. Microspecimens:

№ 101. Purulent embolic nephritis. *(H.E. stain).*

Indications:

1. Microbes emboli in the lumen of glomerular capillaries.
2. Focus of necrosis around the microbial embolus.
3. Clusters of leukocytes (abscess).
4. Unchanged glomerulus.

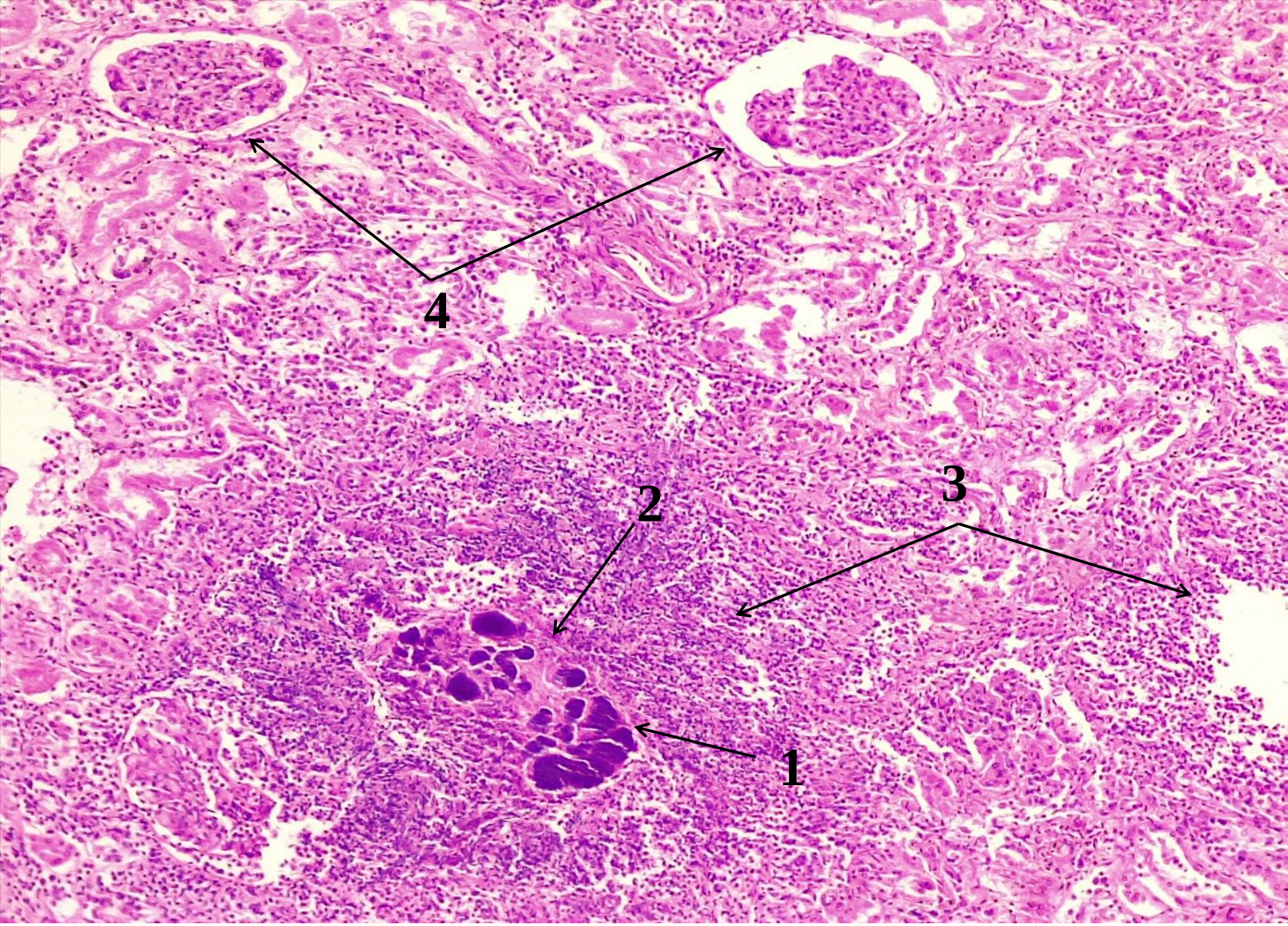
In some glomeruli there are agglomerations of microbes (microbial emboli), intensely stained basophilic, around which necrotic changes are determined (karyolysis) and agglomerations of neutrophilic leukocytes (metastatic abscesses); microbial emboli are also observed in the lumen of some afferent arterioles and in the veins; In some parts microbial masses are found in the lumen of the collecting tubes in the medullary layer of the kidney.

№ 100. Purulent embolic myocarditis. *(H.E. stain).*

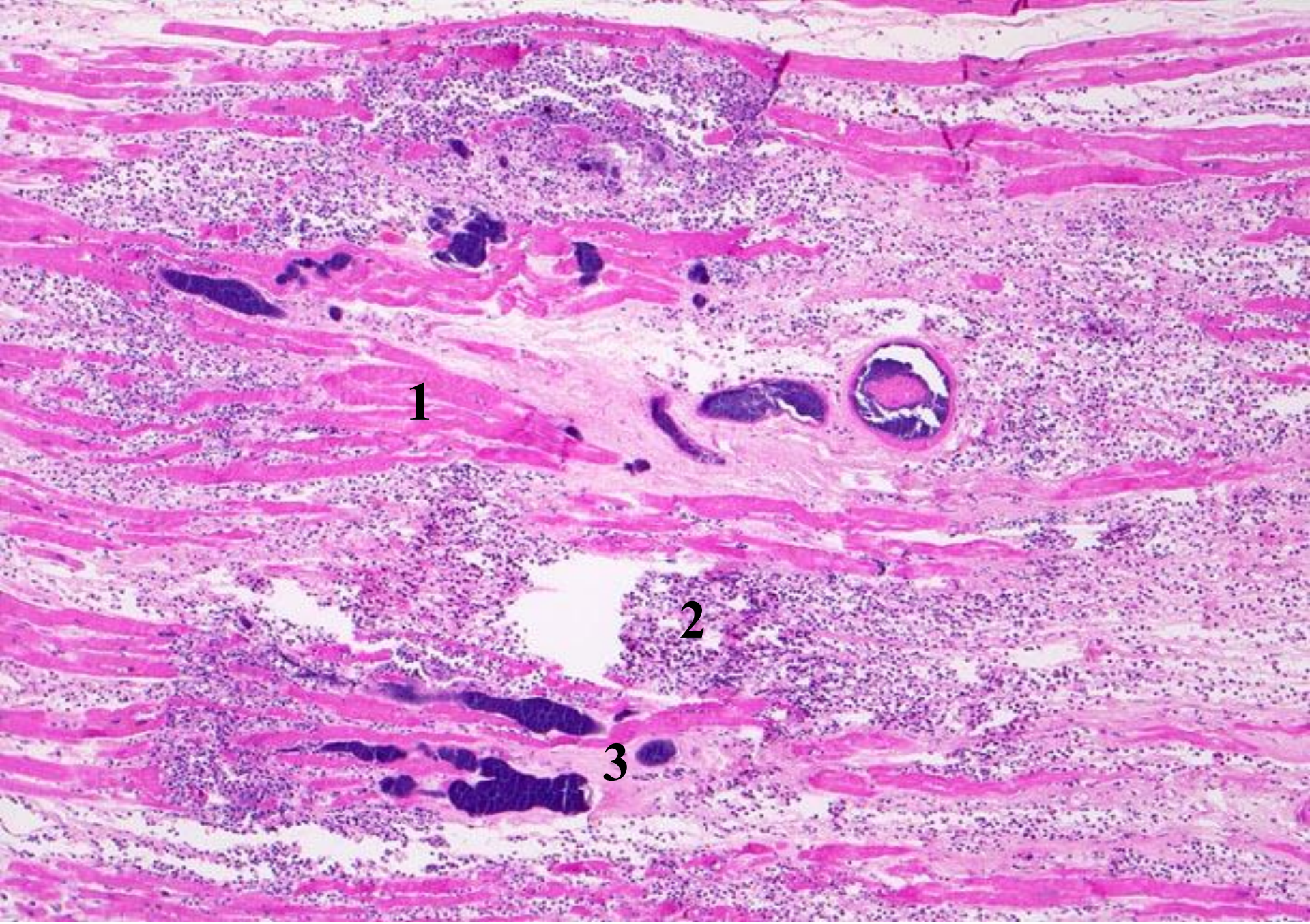
Indications:

1. Foci of myocardial necrosis.
2. Clusters of leukocytes (abscess).
3. Colonies of microbes in necrotic foci.

In the myocardium, in the lumen of vessels are revealed multiple microbial emboli and freely arranged microbial colonies, in some vessels are mixed thrombo-microbial emboli (septic thrombi), adjacent cardiomyocytes are necrotic, anucleated (caryolysis), some of them in the course of plasmo-cytorexis, this area is abundantly infiltrated with viable and disintegrated neutrophil leukocytes (abscess); in the adjacent myocardial tissue is present proteic dystrophy of cardiomyocytes, circulatory disorders.



№ 101. Purulent embolic nephritis. *(H.E. stain).*



№ 100. Purulent embolic myocarditis. *(H.E. stain).*

№ 103. Purulent embolic encephalitis. *(H.E. stain).*

Indications:

1. Microabscess in brain tissue.
2. Colonies of microbes.
3. Adjacent edematous cerebral tissue.

In the brain tissue there are multiple focal agglomerations of disintegrating neutrophil leukocytes, in the center of which are colonies of microbes in the lumen of blood vessels or located freely, adjacent brain tissue rarefied, with pronounced pericellular and perivascular edema, sometimes perivascular hemorrhages.

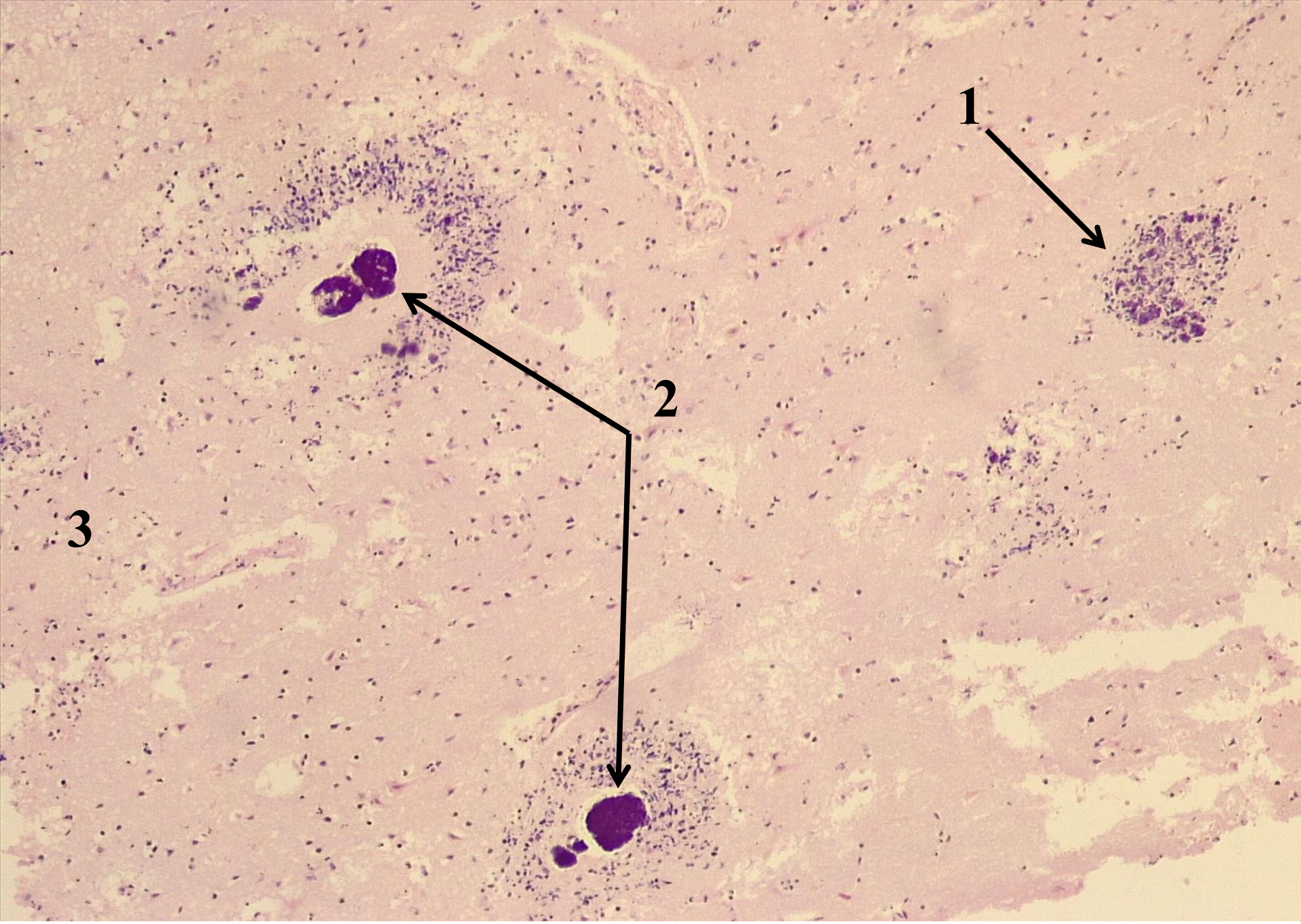
Purulent embolic nephritis, myocarditis and encephalitis are manifestations of sepsis - a form of sepsis with bacteremia, the presence of a primary septic outbreak at the entrance to the infection, in which there is purulent inflammation (abscess or phlegmon) involving lymph vessels (lymphangitis, lymphothrombosis and purulent lymphadenitis) and veins (phlebitis and purulent thrombophlebitis). Embolism develops with fragments of septic thrombi, which leads to metastatic or embolic abscesses, pyemic, more frequently in the lungs, brain, myocardium, kidneys, liver. Severe polyorganic insufficiency (MODS - multiple organ dysfunction syndrome) occurs in patients, disseminated intravascular coagulation syndrome (CID), septic shock is possible.

№ 116. Aortic valve in bacterial endocarditis. *(H.E. stain).*

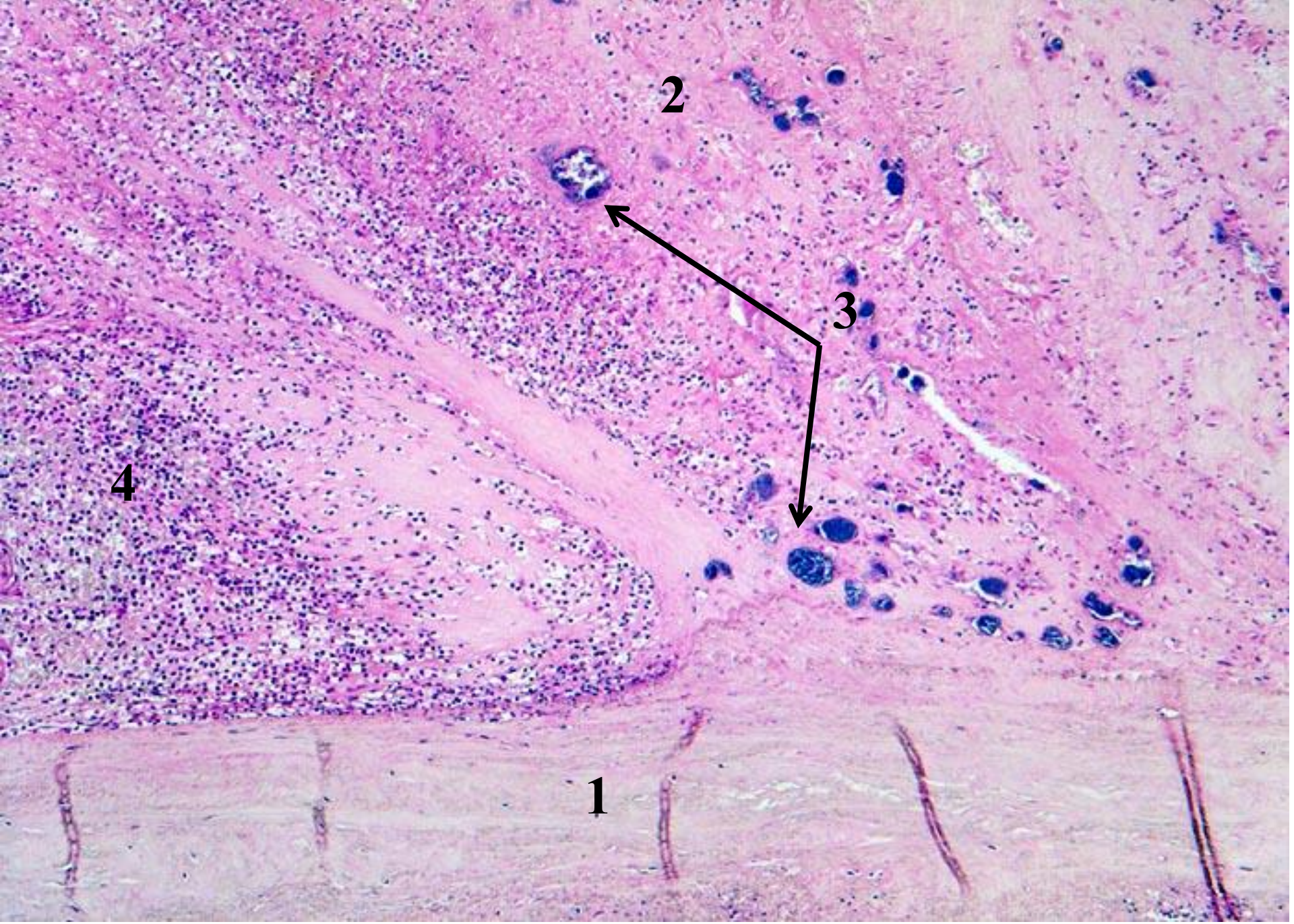
Indications:

1. Valvular tissue.
2. Thrombotic masses on the surface of the valve.
3. Colonies of microbes.
4. Lympho-histiocytic infiltration.

On the surface of the valve there are vegetation, consisting of fibrin and tissue debris colored eosinophilic, lympho-histiocytic inflammatory infiltration, colonies of microbes stained basophilic, granular-looking basophilic calcium deposits may be present.



№ 103. Purulent embolic encephalitis. *(H.E. stain).*



№ 116. Aortic valve in bacterial endocarditis. *(H.E. stain).*

II. Macrospecimens:

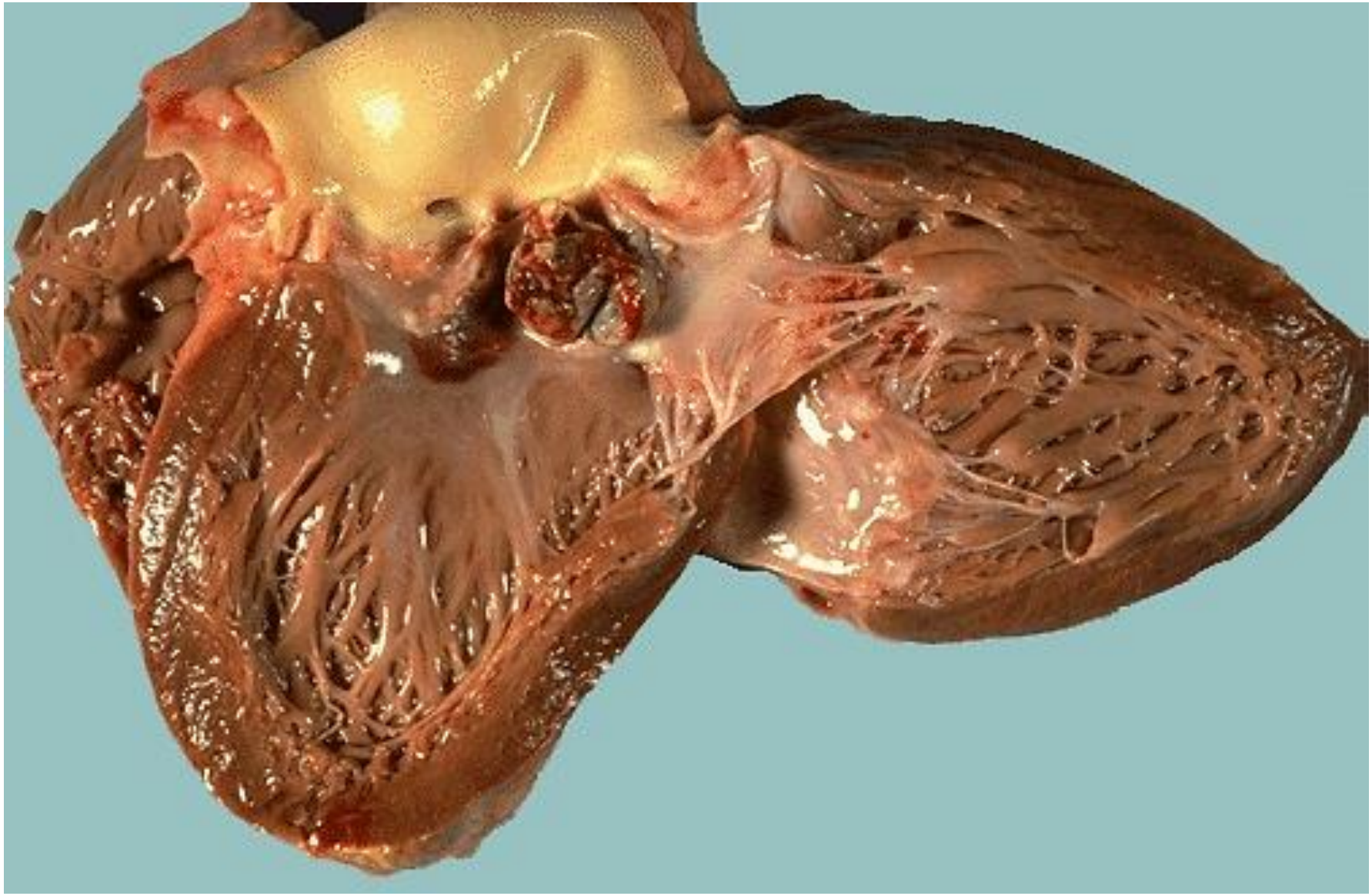
№ 17. Ulcerative-polypous endocarditis of aortic valve.

The aortic valve is deformed, covered with massive thrombotic vegetation of brown-gray color, friable, with polypoid appearance, the valves are thickened, sclerosed, on their surface may be ulcerative defects.

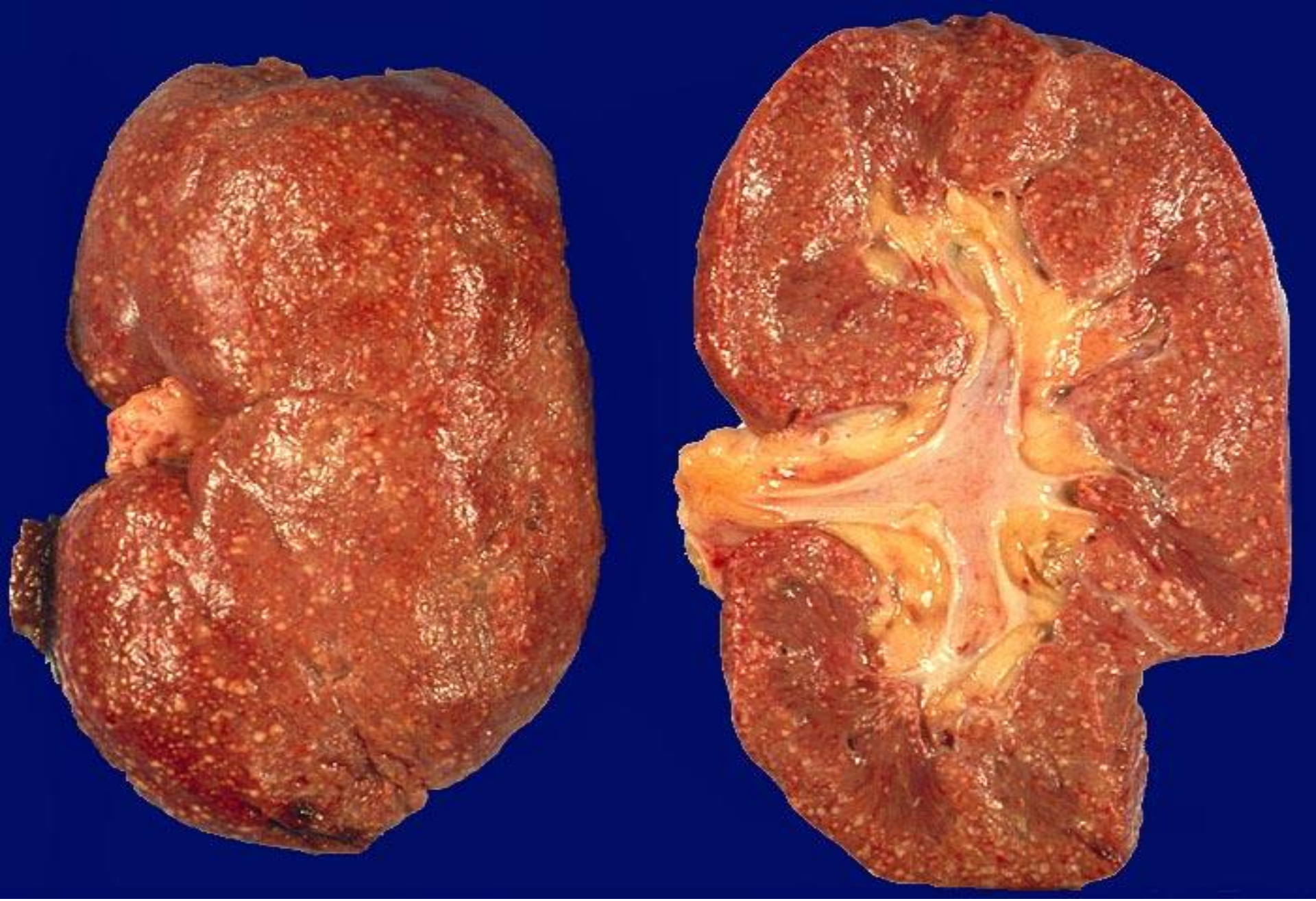
Infectious endocarditis develops as a result of damage to the valvular and/ or parietal endocardium by infectious agents present in blood circulation. More commonly affected are aortic and/ or mitral valves, both normal and damaged, vicious valves. Clinically, depending on the severity of the disease and the evolution over time, there are 2 variants of infectious endocarditis: acute and subacute or slow. infectious endocarditis. The acute variant develops in cases of infectious agents of high virulence and compromised immunity, more frequently on normal valves, and the subacute variant - in cases of infectious agents with low virulence, usually on sclerosed valves, with deformities and scars. Among the infectious factors in acute endocarditis predominates Staphylococcus aureus, and in the subacute - Streptococcus viridans. The gateway to infection can be varied. There are several factors predisposing to the development of infectious endocarditis, eg, rheumatic valvulopathy (50%), congenital heart abnormalities (20%), atherosclerotic valvulopathy, dental procedures, heart surgery, surgery on various organs, intravenous drug injection, immunodeficiency conditions, etc. It is characteristic the formation of voluminous, friable vegetation, which contains infectious agents, on the surface of the heart valves. Of all the valvular endocarditis, the most massive thrombotic deposits on the valves occur in the infectious one. Due to the friability of the vegetation, they detach, producing ulcerative defects on the surface of the valves, perforations, microaneurysms are possible. Embolism with fragments of infected vegetation leads to septic infarction in various organs, more commonly in the lungs, brain, liver, kidneys. Infectious endocarditis results in the installation of severe valvular insufficiency with progressive congestive heart failure. Valve failure is more severe in cases where the fibrous ring of the aortic valve is also affected.

№ 85. Purulent embolic nephritis.

The kidney is enlarged in size, under the capsule are observed multiple disseminated foci of purulent inflammation, yellowish in color, with a diameter of a few mm, which protrude on the surface of the organ - metastatic abscesses.

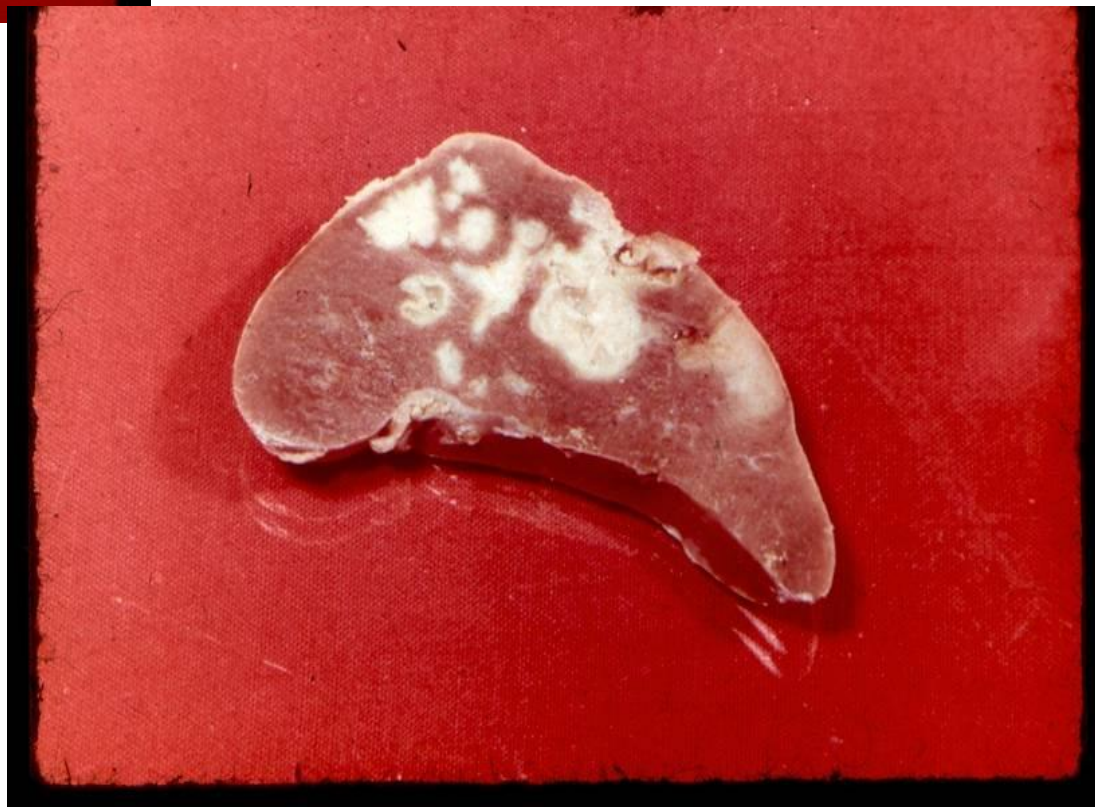


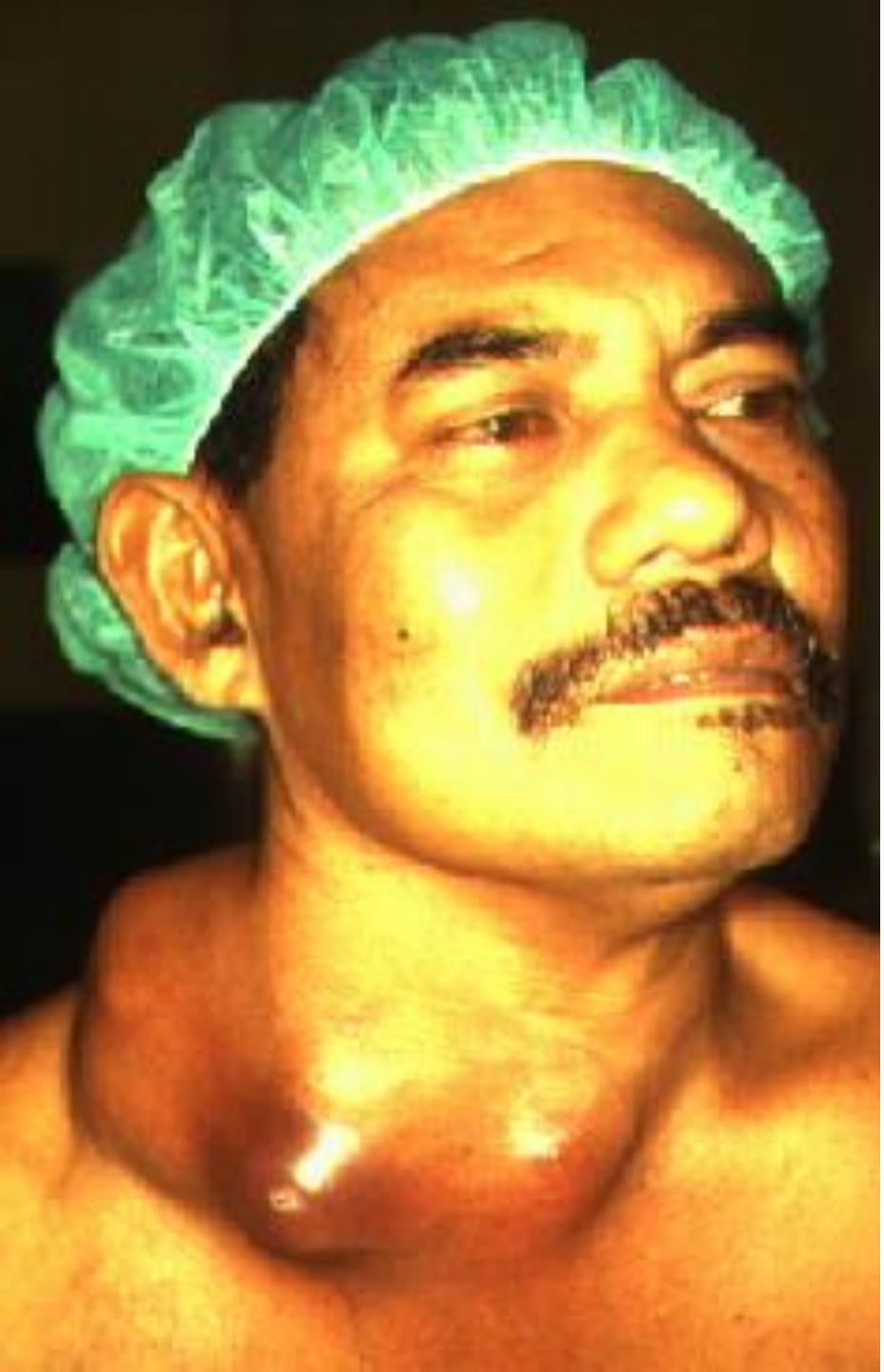
№ 17. Ulcerative-polypous endocarditis of aortic valve.

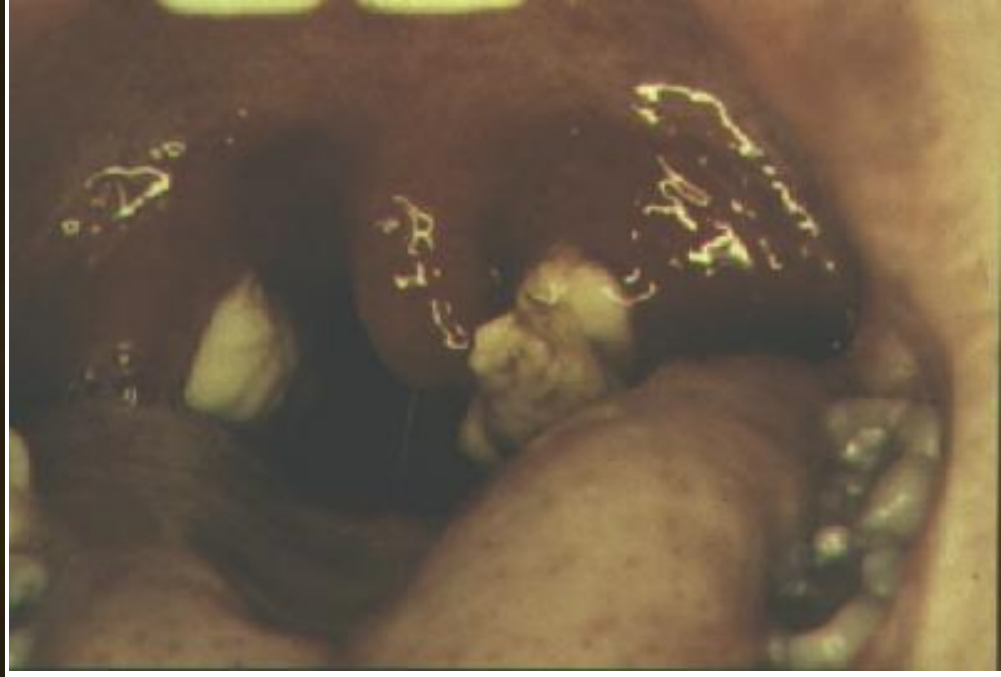


№ 85. Purulent embolic nephritis.

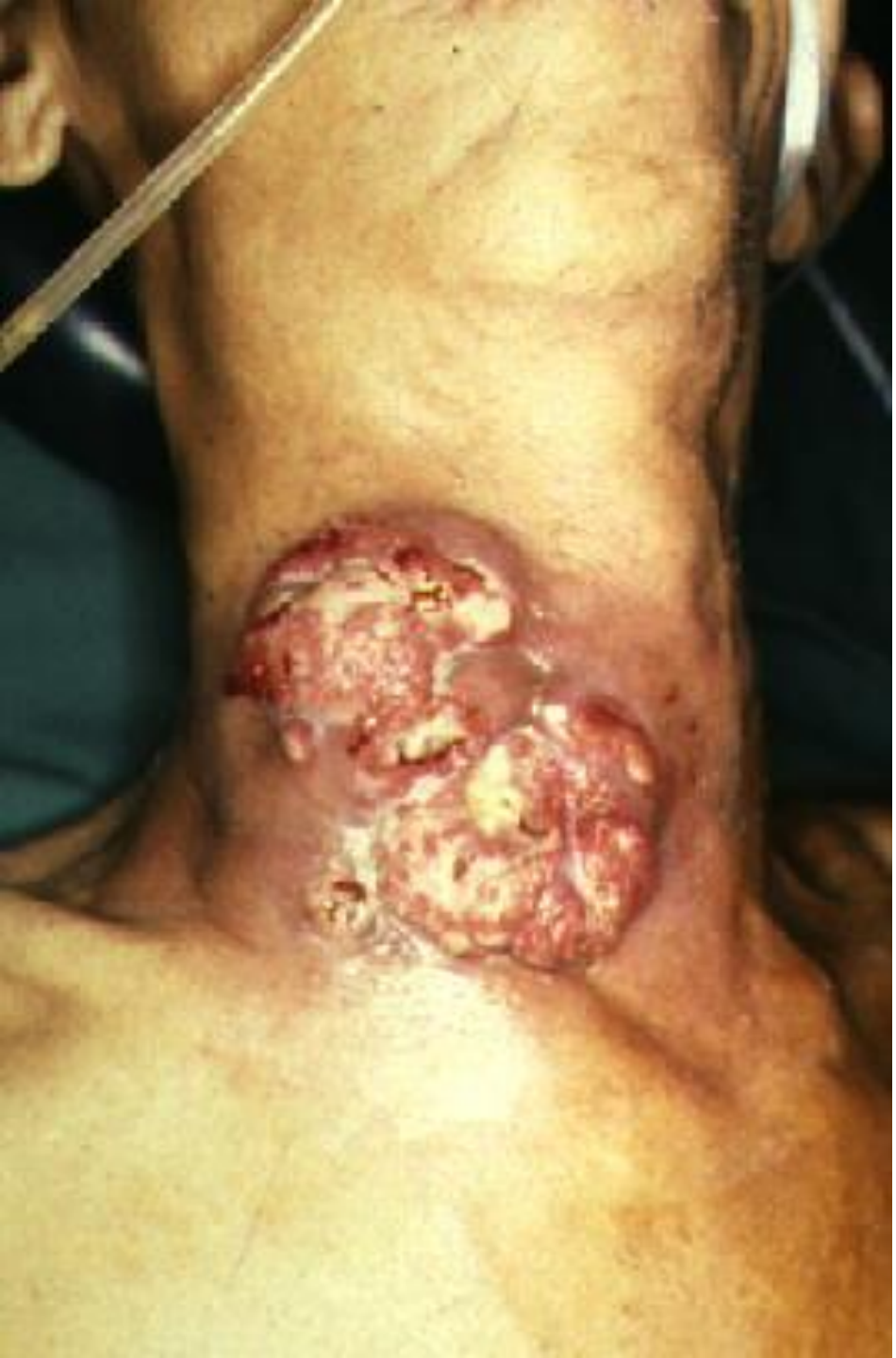
Umbilical sepsis.



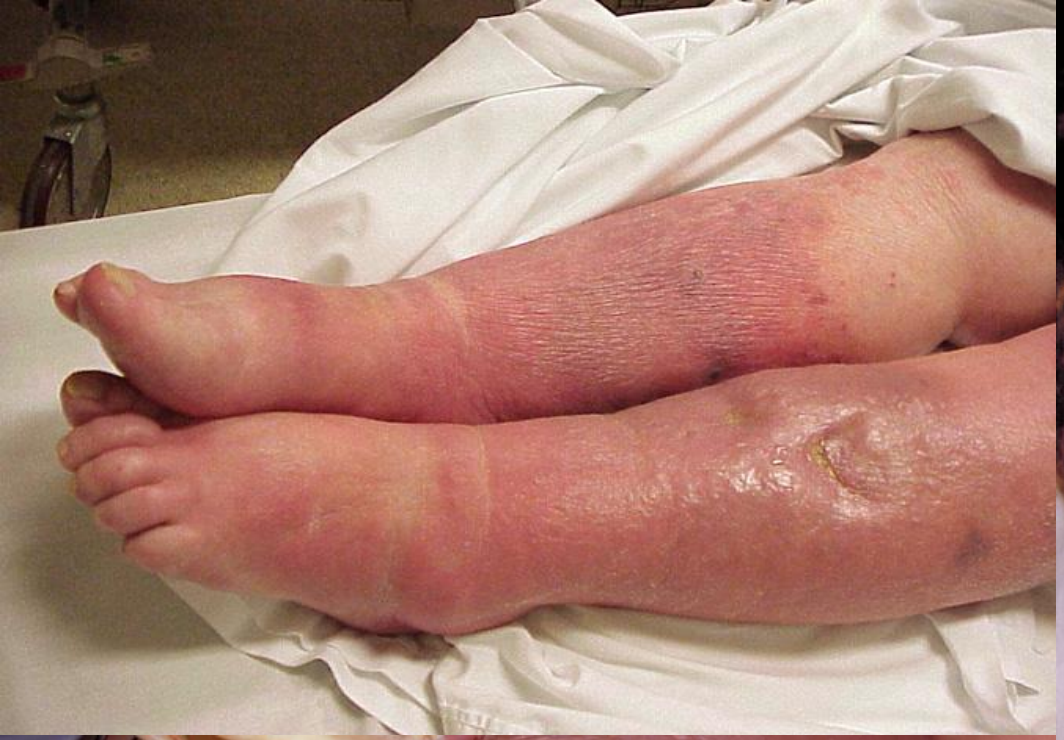


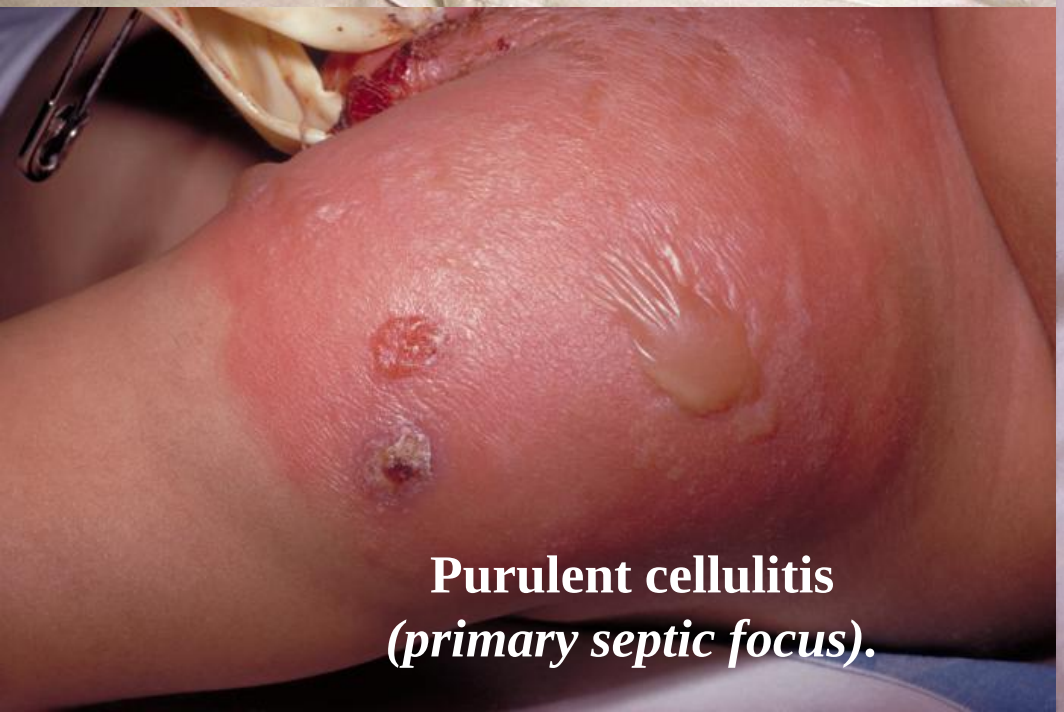


Cervical carbuncle.
Purulent tonsillitis.

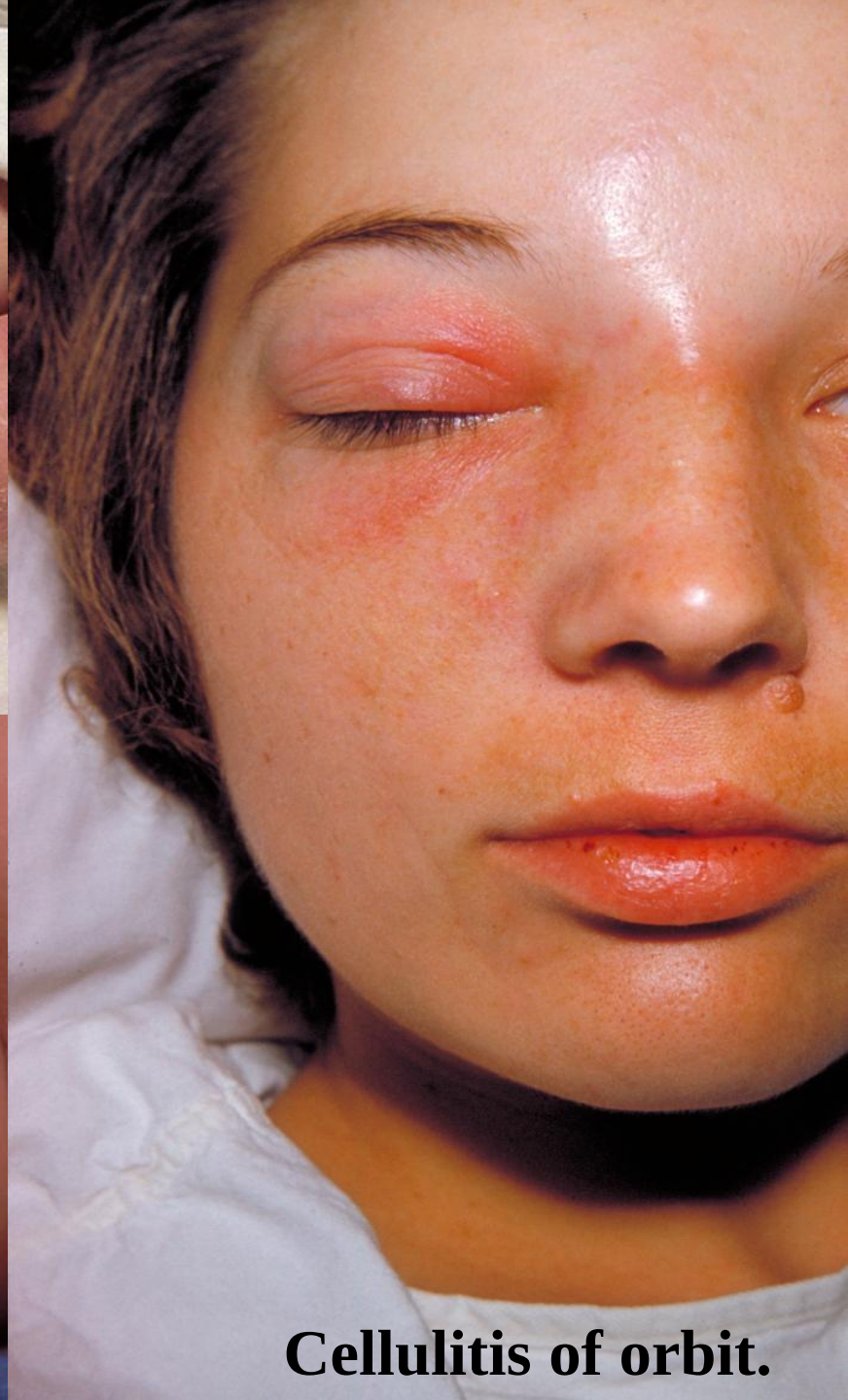


Cervical carbuncle

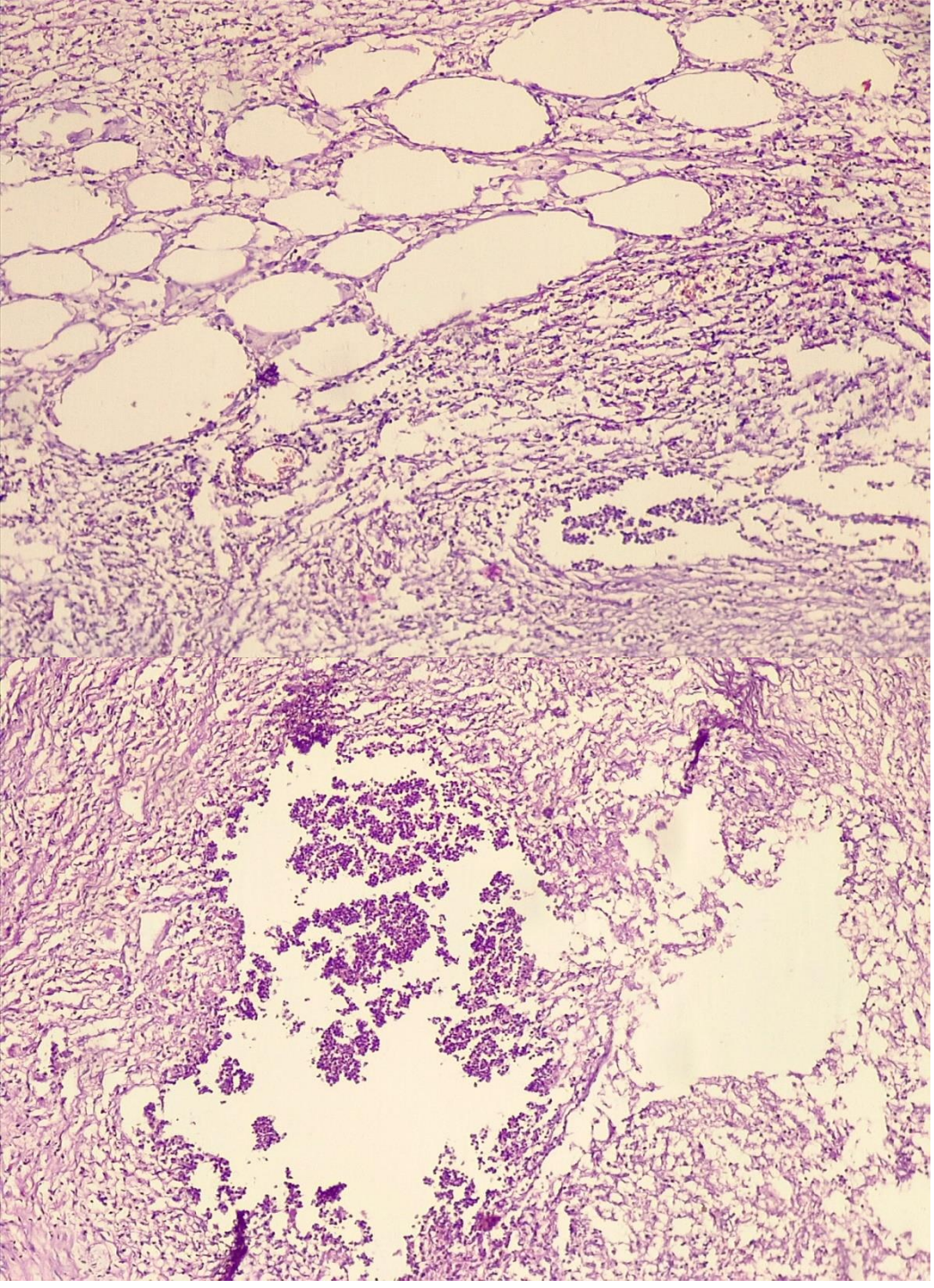




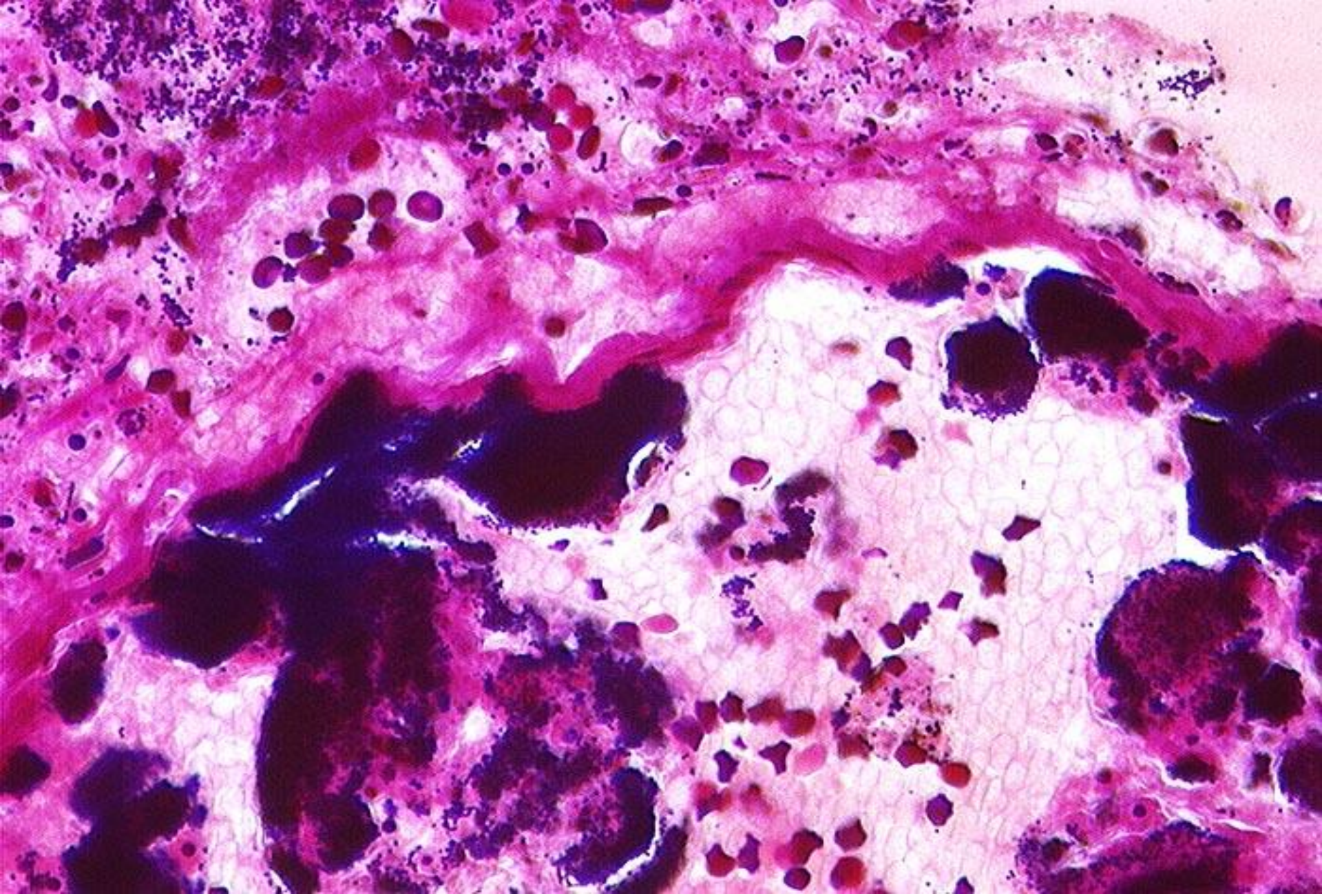
Purulent cellulitis
(primary septic focus).



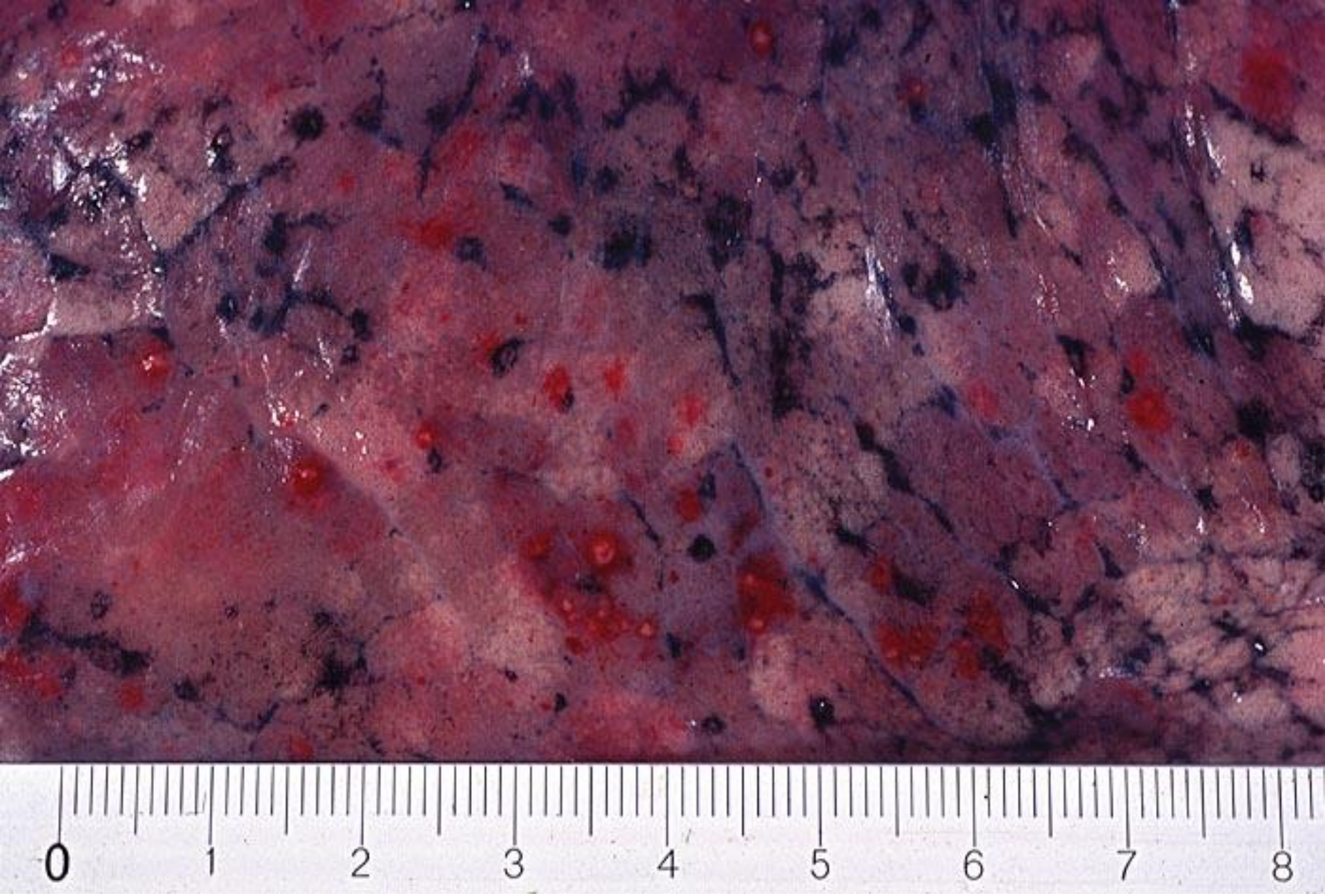
Cellulitis of orbit.



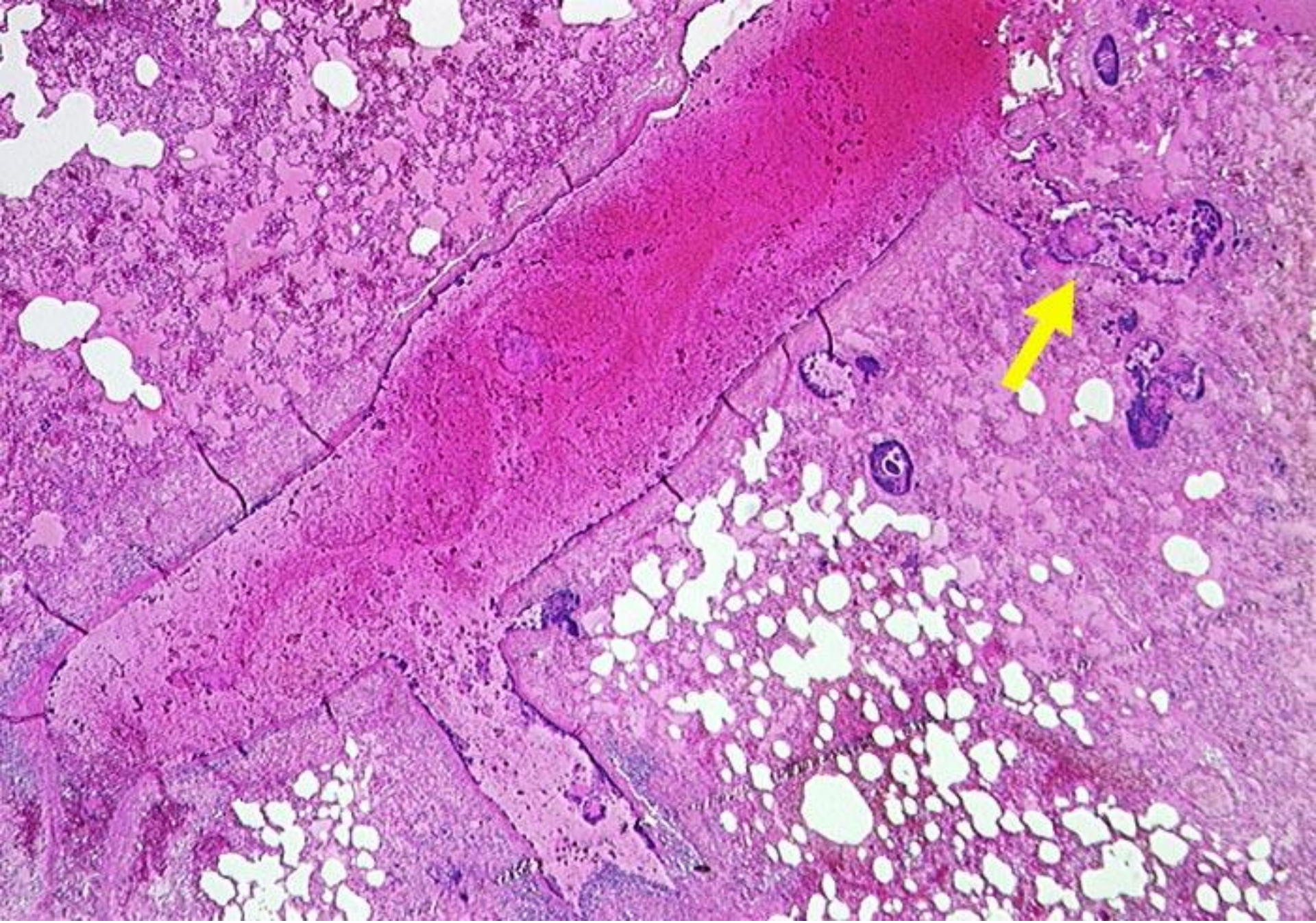
Purulent cellulitis in primary septic focus.



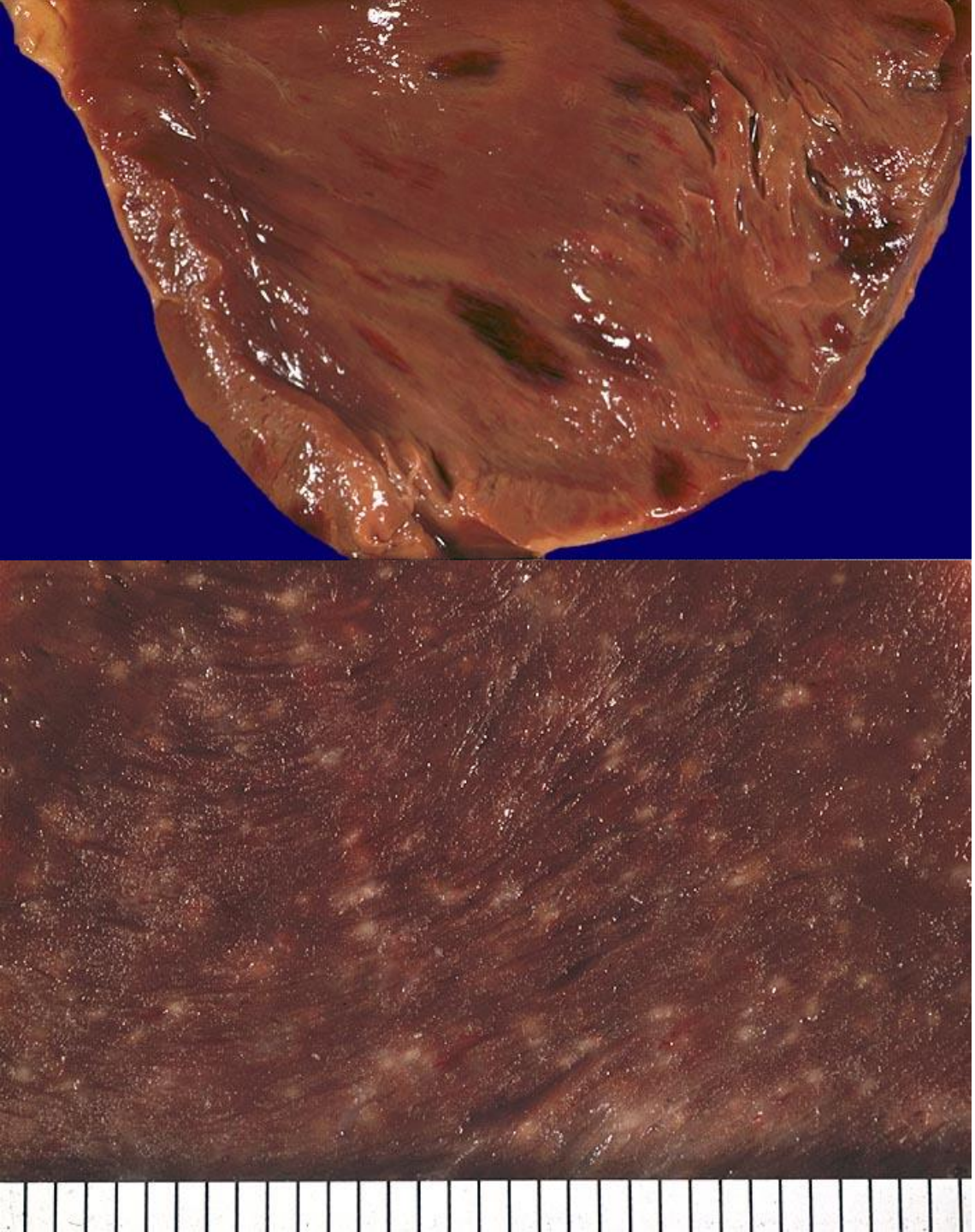
Septic embolism (*Staphylococcus aureus*).



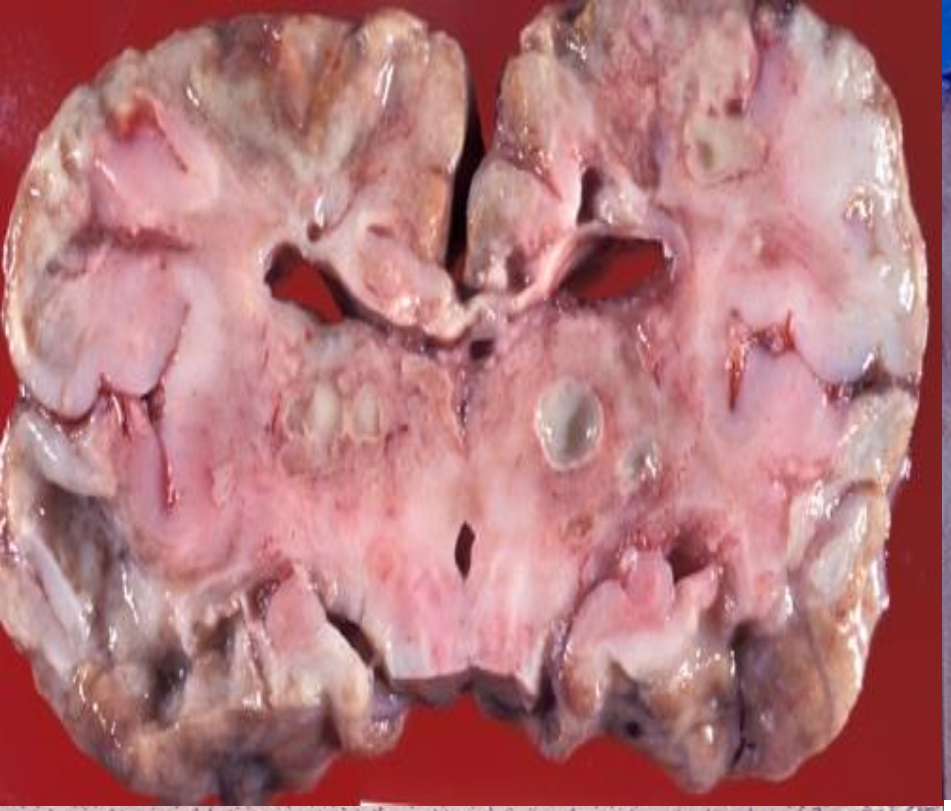
Metastatic abscesses in the lungs.

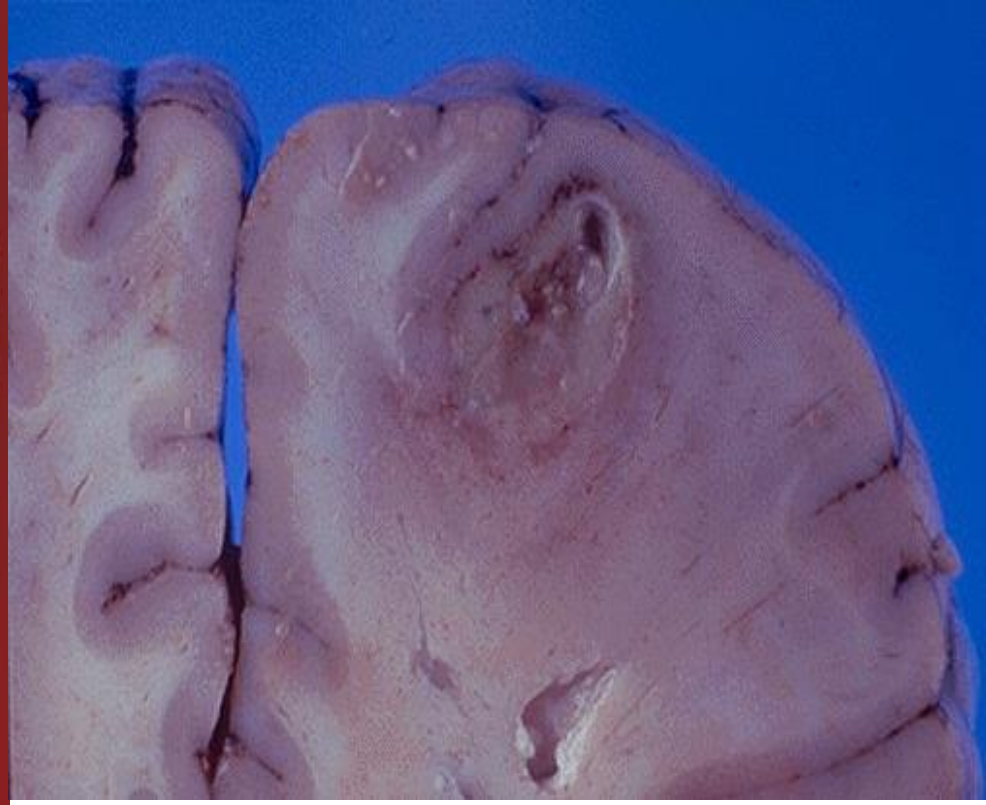


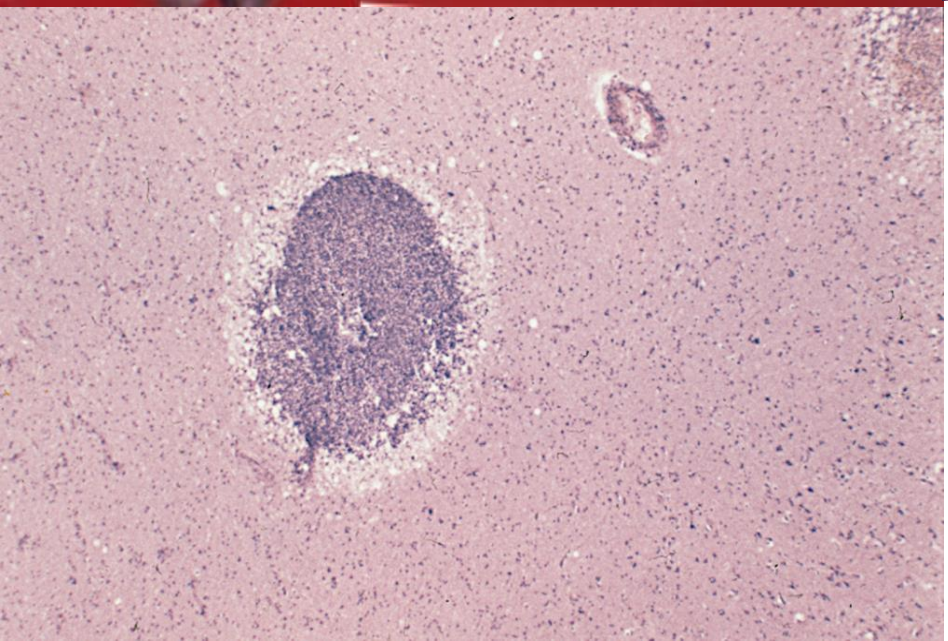
Septic embolism in the lungs.



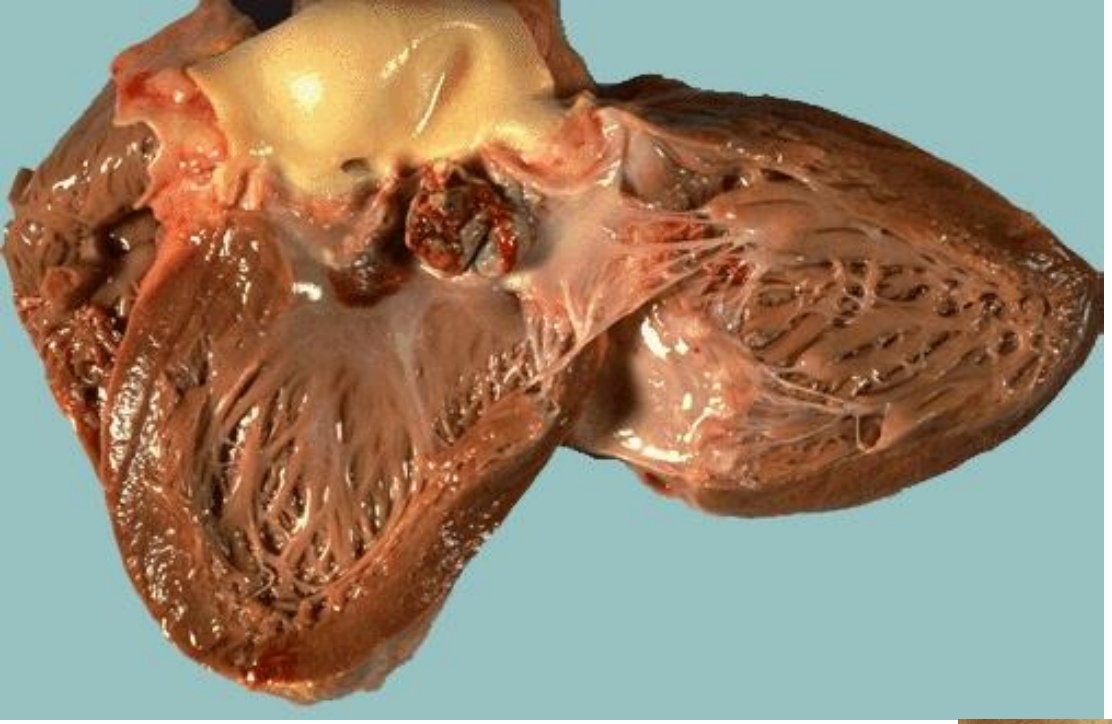
Metastatic abscesses in the myocardium.





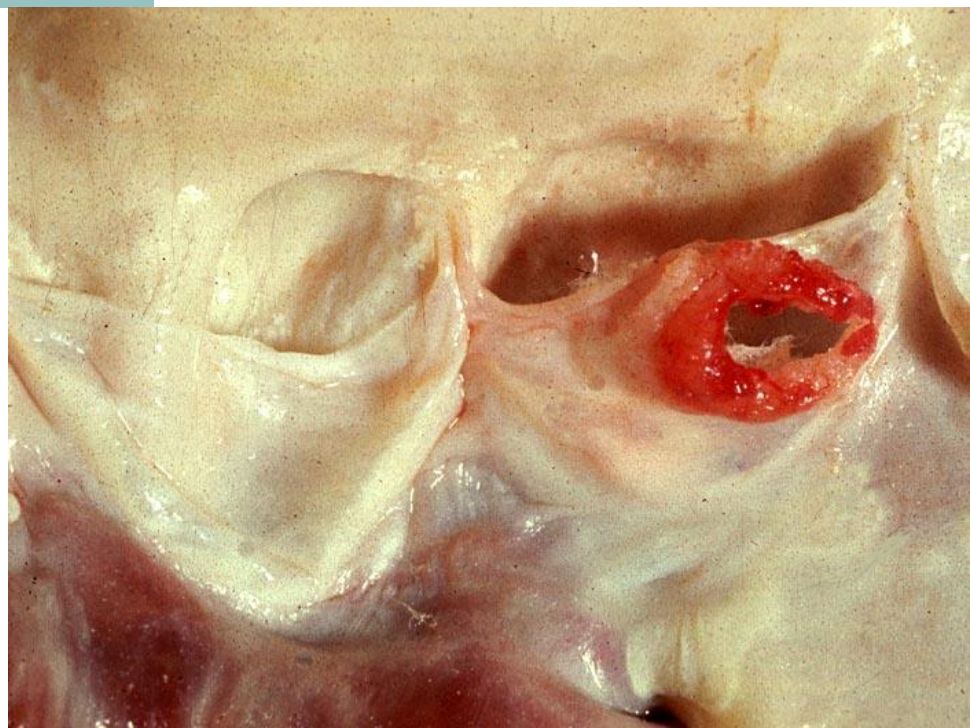


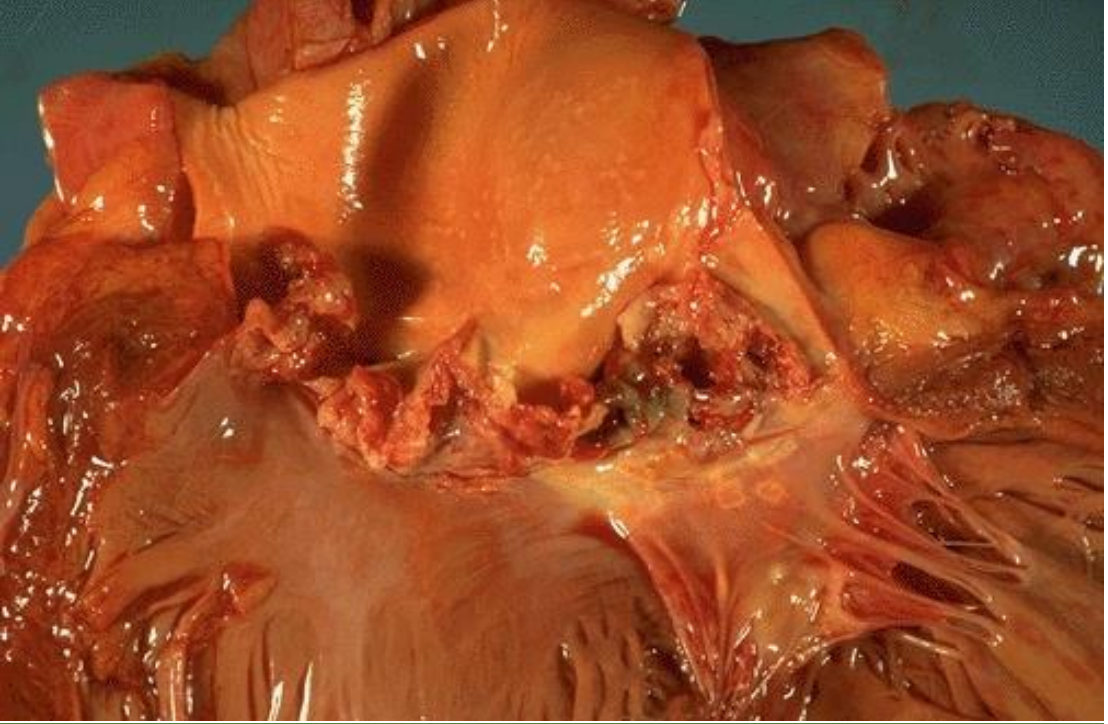
Metastatic abscesses in the brain.

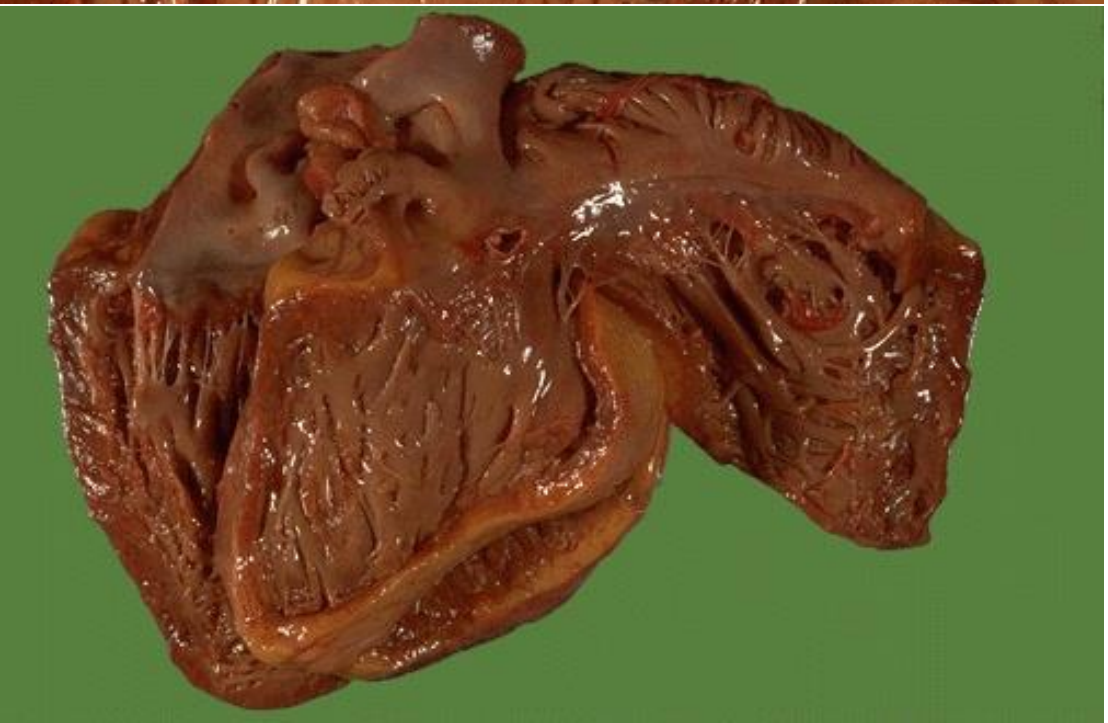


Aortic valve perforation.

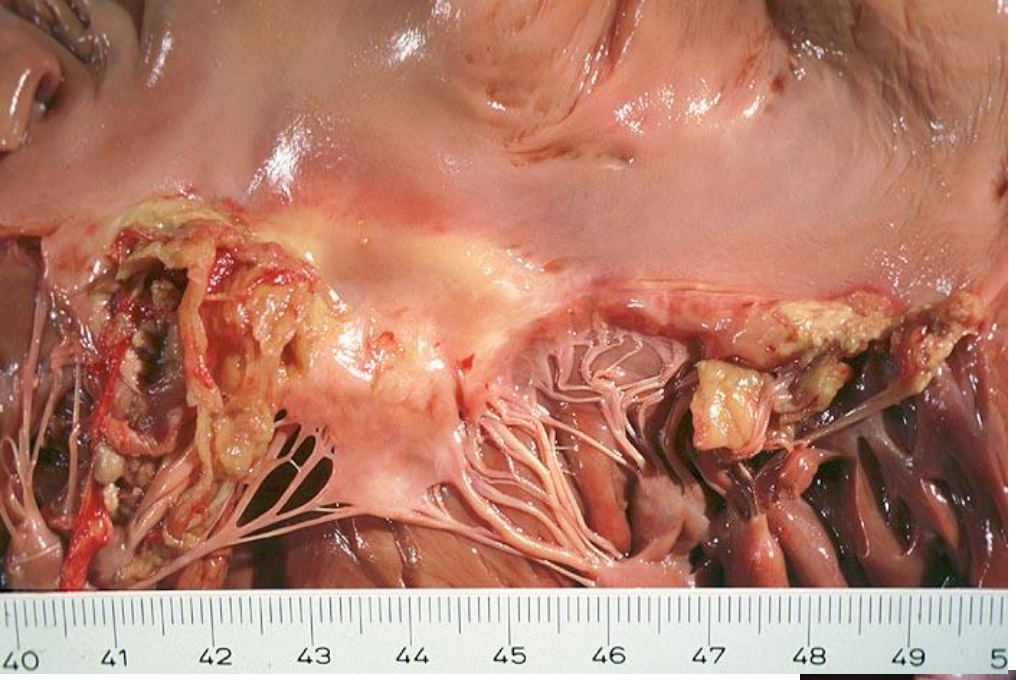
Verrucous infectious endocarditis of the aortic valve.



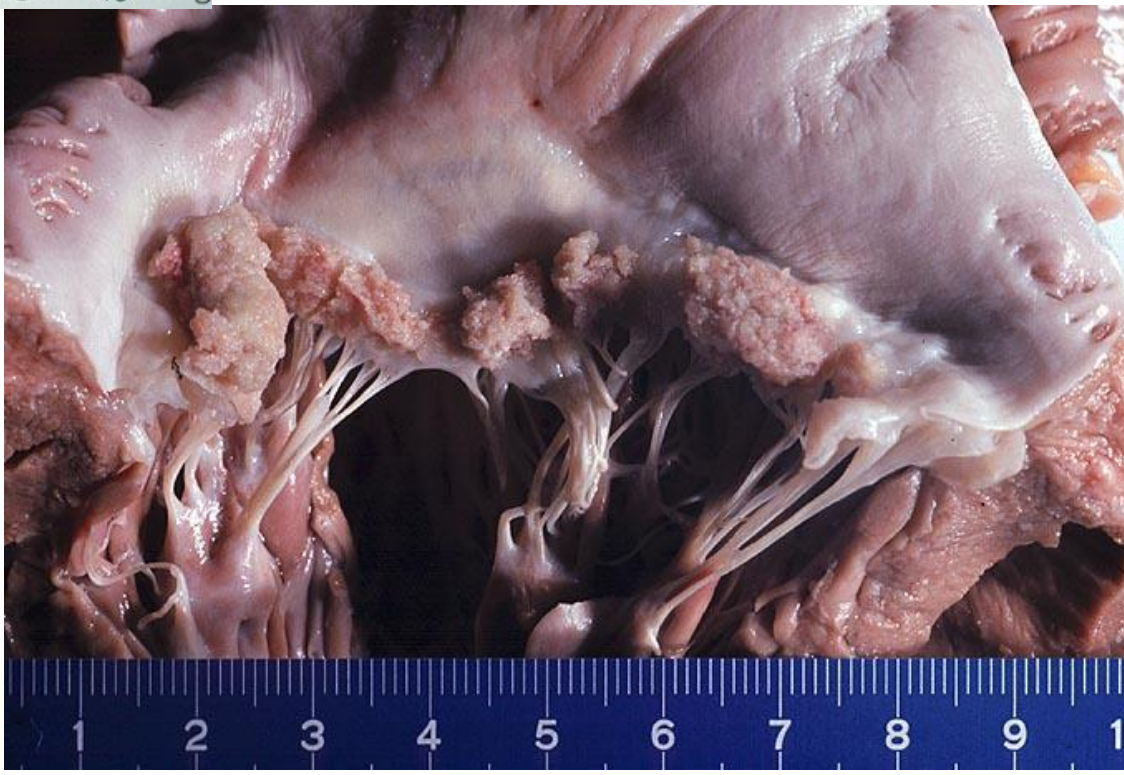


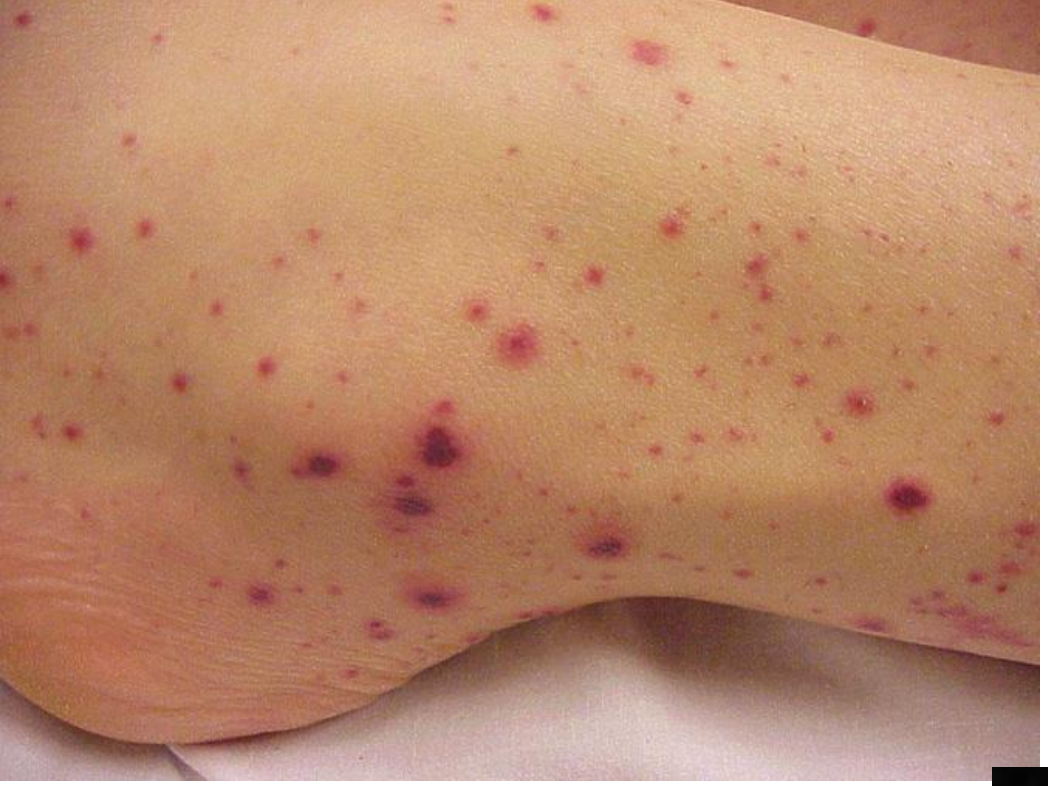


Verrucous infectious endocarditis with rupture of aortic valve, bottom - fistula in the interatrial septum.

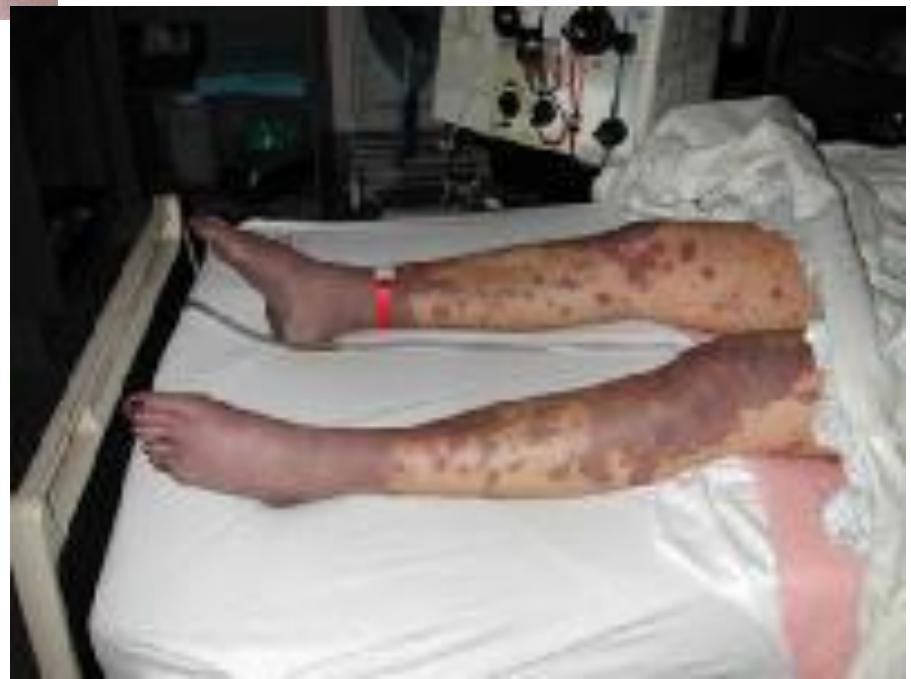


Polypous ulcerative endocarditis of the mitral valve.





Hemorrhagic rash in sepsis.



INFECTIOUS DISEASES

- VIRULENCE is termed extent of host damage by microorganisms.
- TOXICITY is termed ability for production and secretion of various toxins.
- INVASIVENESS is termed the microorganism ability to get over host barrier mechanisms,
  reproduce and spread ability.

INFECTIOUS DISEASES

- Reactions of macroorganism (host) in infectious diseases occur as follow:
- 1 adjustment reactions
- 2 compensative reactions
- 3 defense reactions

INFECTIOUS DISEASES

- 1 Adjustment reactions are conditioned by environment (external factors) when host can not change impaired living conditions.
- 2 compensative reactions are similar to adjustment reactions but connected with host changes.
- 3 defense reactions are an biologic defense of the host.

INFECTIOUS DISEASES

- Gnotobiotes are children with genetic inability to have Symbiosis with microorganisms.
- Gnotobiotes can not be in the atmosphere because they can not take an ordinary air,

  they die suddenly.
- They can take only sterile air without microorganisms. Microorganisms are killers for Gnotobiotes.

INFECTIOUS DISEASES

- Imbalance between host and microorganisms when microorganisms become pathogenic with decreasing of host reactivity, increasing of microorganism activity which take on pathogenic properties leads to infectious disease.

INFECTIOUS DISEASES

- Endogenic infection is termed the disease which developments with condition of immunity decreasing to own saprophytic microorganisms.

- Exogenic infection is termed the disease caused by pathogenic microorganism.

INFECTIOUS DISEASES

- 1 CLASSIFICATION
- According to etiology:
- 1viral
- 2 mycoplasmal
- 3 rickettsial
- 4 bacterial
- 5 fungal
- 6 protozoan
- 7 parasitic

INFECTIOUS DISEASES

CLASSIFICATION according to clinical morphological sign origin:

1 Infections with skin lesion predominance (pyoderma, erysipelas, smallpox, dermatomycoses);

2 Respiratory infections (influenza, bronchitis, tracheitis, pneumonias);

3 Digestive system infections (salmonellosis, typhoid fever, dysentery);

INFECTIOUS DISEASES

4 Nervous system infections (poliomyelitis, purulent leptominengitis, encephalitis);

5 Transmissive infections (malaria,

hemorrhagic fevers);

6 Cardio-vascular infection (syphilis,

brucellosis);

7 Urogenital system infections (gonorrhoea, pyelonephritis).

INFECTIOUS DISEASES

- Opportunistic or conditionally pathogenic infections are the infections caused by saprophytic microorganisms of host with diminished resistance.
- For example: HIV-infected persons;
- The opportunistic infections have no clinical-morphological differences.

Opportunistic infections

- Opportunistic or conditionally pathogenic infections develops within premature or debilitated infants; in severe somatic diseases with immunity decreasing; after large surgical operations; after depressant and antibiotic taking;

  That is why conditionally pathogenic infections are hospital- acquired or nosocomial infection.

Hyperergetic reaction with intoxication

- A) fatty dystrophy of the organs;
- B) stromal reactive serous of the organs;
- C) DIC- syndrome;
- D) bacterial shock;
- E) systemic inflammatory response syndrome;
- G) jaundice;
- J) anemia.

Immunity

- Immunity plays a significant role in infection diseases.
- Immune system takes information about antigens and immune reaction are beginning: humoral and cellular.
- Immunity has got its own morphology reflecting infect characteristics.

Clinical effects of dysregulation of innate immune responses

- Clinical sepsis
  - Fever
  - Hypoperfusion
  - Hypotension → Shock
  - Clotting → Disseminated intravascular coagulation
    - Renal failure
    - Cardiac depression
    - Central nervous system depression
    - Acute respiratory Distress syndrome

SEPSIS

- Sepsis is general severe infectious disease,

  caused by permanent or recurrent microorganism admission into blood from

  nidus of infection.

  Sepsis is a polyetiologic, non contagious disease characterized by generalized infection, acyclic clinical course, and special significance of changed reactivity.

SEPSIS

Difference from other infectious diseases:

1 polyetiologic causes: pyogenic bacteria, fungi;

2 non contagious,

3 non reproduce in experiment;

4 clinical course is stereotype, it is no depends on etiologic agent;

SEPSIS

5 the most common sign of generalized infection

is metastatic foci at a distance from primary focus;

6 cyclic course is absent;

7 incubation period is absent;

8 immunity is absent;

9 hyperergic reaction is predominance

Pathogenesis of SEPSIS

- Infective agent
- Entry of infection
- Initial focus state
- Organism reactivity
- Lymphogenic spread is lymphangitis and lymphadenitis
- Hematogenic spread is phlebitis and thrombophlebitis with bacterial thromboembolism

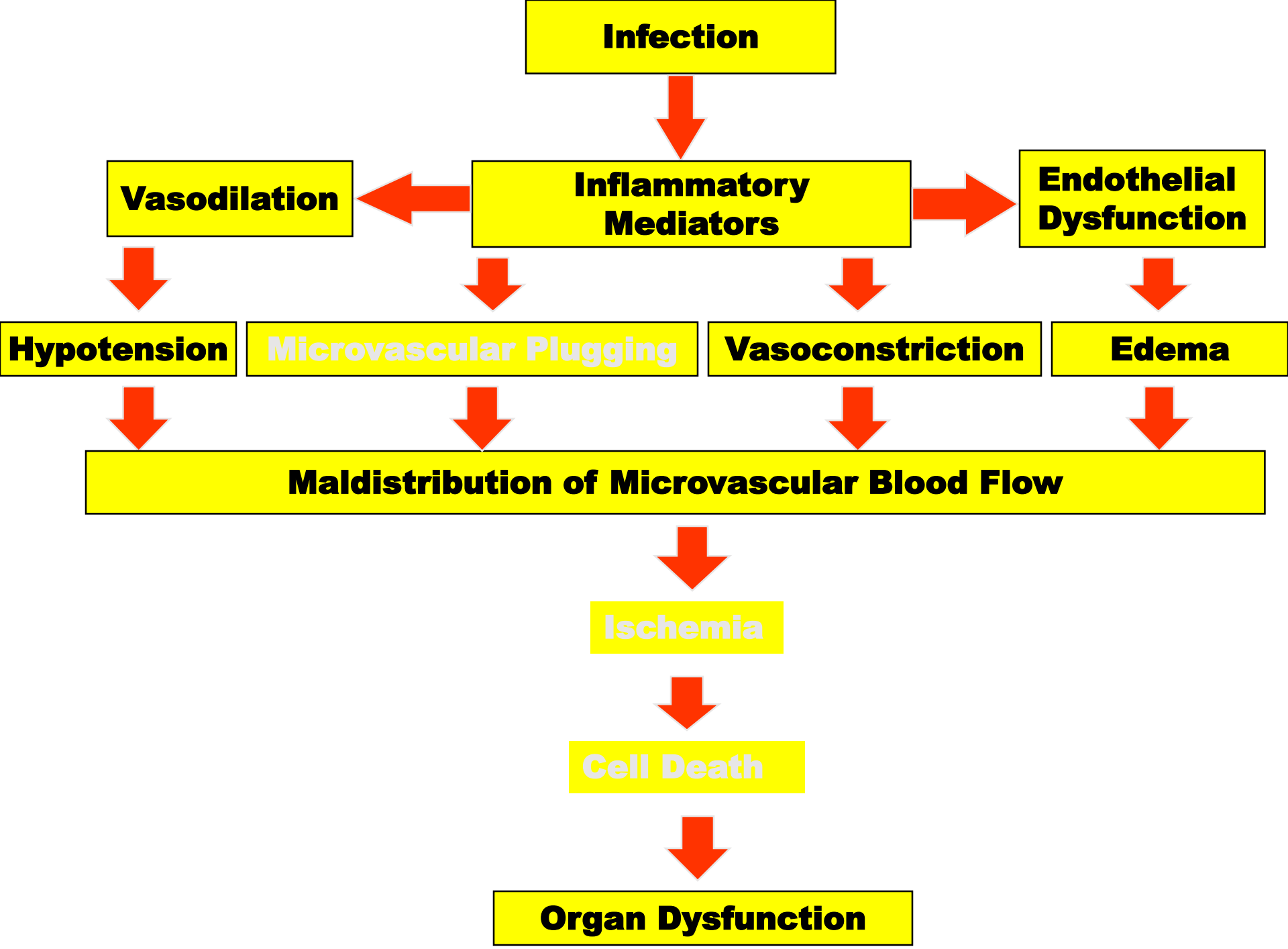
Pathophysiology of Sepsis-Induced Organ Injury

- **Multiple Organ Dysfunction (MODS) and Multiple Organ Failure (MOF) result from diffuse cell injury / death resulting in compromised organ function.**

- **Mechanisms of cell injury / death:**
  - **Cellular Necrosis (ischemic injury).**
  - **Apoptosis.**
  - **Leukocyte-mediated tissue injury.**
  - **Cytopathic Hypoxia**

Pathophysiology of Sepsis-Induced Ischemic Organ Injury

- **Cytokine production leads to massive production of endogenous vasodilators.**
- **Structural changes in the endothelium result in extravasation of intravascular fluid into interstitium and subsequent tissue edema.**
- **Plugging of select microvascular beds with neutrophils, fibrin aggregates, and microthrombi impair microvascular perfusion.**
- **Organ-specific vasoconstriction.**


Infection
Vasodilation
Inflammatory Mediators
Endothelial Dysfunction
Hypotension
Microvascular Plugging
Vasoconstriction
Edema
Maldistribution of Microvascular Blood Flow
Ischemia
Cell Death
Organ Dysfunction

Clinical morphological forms:

- 1 septicemia;
- 2 septicopyemia;
- 3 septic endocarditis;
- 4 chroniosepsis.

❑**Sepsis**

SIRS + infection

❑**Severe sepsis**

Sepsis with organ dysfunction, hypoperfusion or hypotension

❑**Septic Shock**

Sepsis with hypotension and perfusion abnormalities despite adequate volume replacement

SEPSIS

Clinical definition of sepsis is as follow:

- System inflammatory reaction syndrome
- (SIRS) is the response to invasion of difference microorganisms.
- It is characterized by two or more SIRS signs.
- Hyperthermia, Tachycardia, Tachypnoe,

  Leukocytosis.

Sepsis classification according to entry of infection

- 1 therapeutic ;
- 2 surgical;
- 3 gynecologic;
- 4 umbilical;
- 5 tonsilogenic;

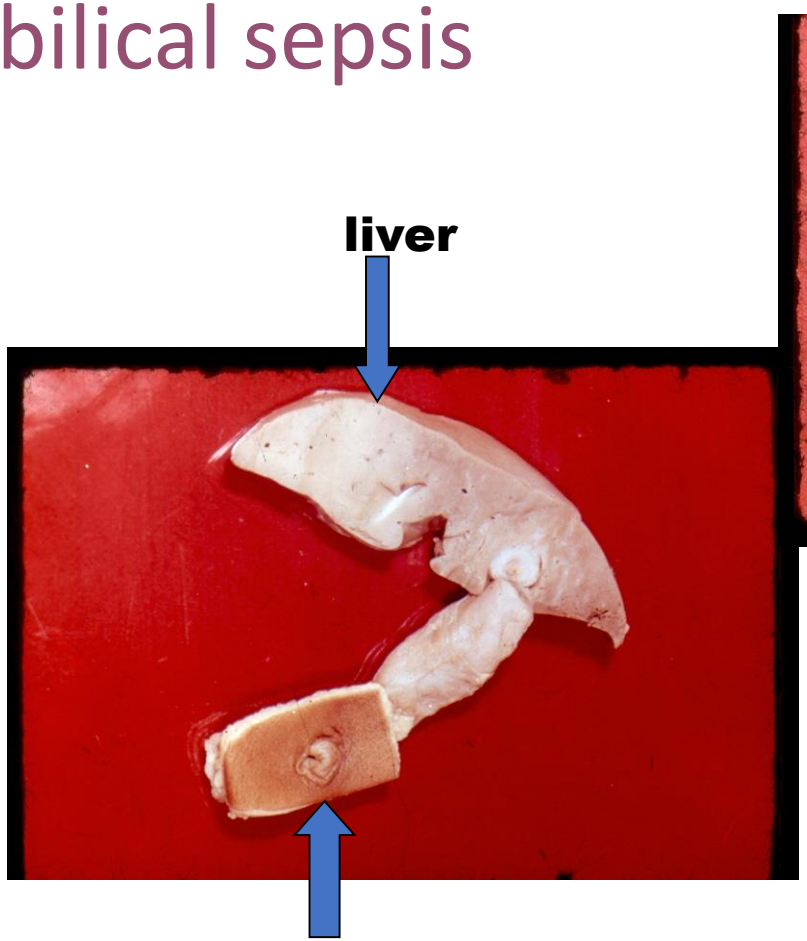
- **6 odontogenic;**
- **7 otogenic ;**
- **8 urogenic ;**
- **9 cryptogenic.**

Organ Dysfunction

• Lungs	➢ Adult Respiratory Distress Syndrome
• Kidneys	➢ Acute Tubular Necrosis
• CVS	➢ Shock
• CNS	➢ Metabolic encephalopathy
• PNS	➢ Critical Illness Polyneuropathy
• Coagulation	➢ Disseminated Intravascular Coagulopathy
• GI	➢ Gastroparesis and ileus
• Liver	➢ Cholestasis
• Endocrine	➢ Adrenal insufficiency
• Skeletal Muscle	➢ Rhabdomyolysis

SEPSIS

- umbilical sepsis



SEPTICEMIA

- Septicemia is very shot way to septicopyemia, but patient does not live so long.
- Septicemia is systemic inflammative reaction with general lesion of circulatory bed.
- Septicemia is disability of organism capability to produce leukocyte infiltration.
- Septicemia is sepsis without purulent metastases.

Septicopyemia

- Septicopyemia is the form of sepsis characterized by purulent inflammation
- (abscesses, phlegmon, interstitial purulent inflammation)
- In various organs and tissues due to
- Hematogenic spread of microbe emboli from primary septic focus.
- Septicopyemia is sepsis with purulent metastases.
- Septicemia is sepsis without purulent metastases.

Septic endocarditis

- Septic endocarditis or sepsis lenta
- entry of infection is cardiac valves
- 70% previous rheumatic valve disease
- 30% lesion of normal valves is named Tchernogubov’s disease
- Allergic reaction directs bacterial endocarditis course.

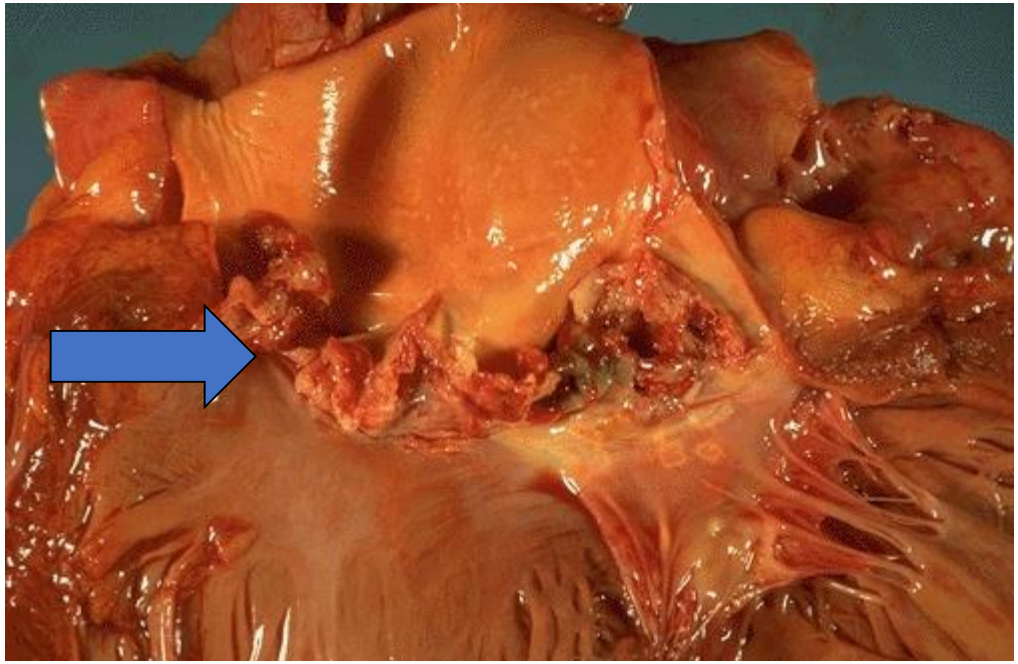
Septic endocarditis

- Acute endocarditis - 2 weeks
- Subacute one – 3 months
- Lingering or sepsis lenta one – years.

- Valvular inflammation consists of lymphocytes, macrophages and hystiocytes, no neutrophyles.

Septic endocarditis

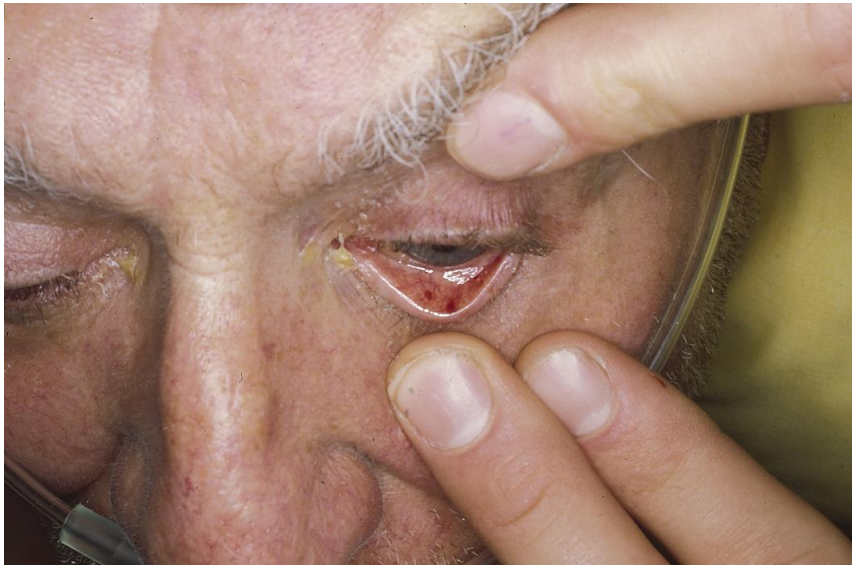
- Polypous ulcerous endocarditis

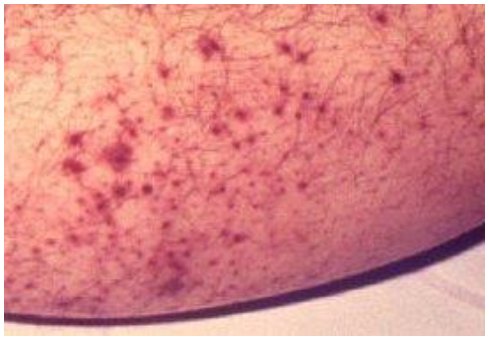


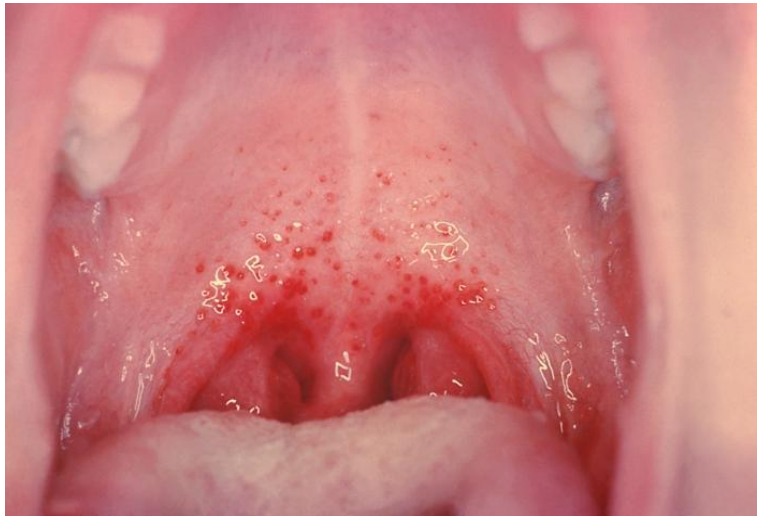
Aortic valve disease

Petechiae

1. Nonspecific
2. Often located on extremities or mucous membranes





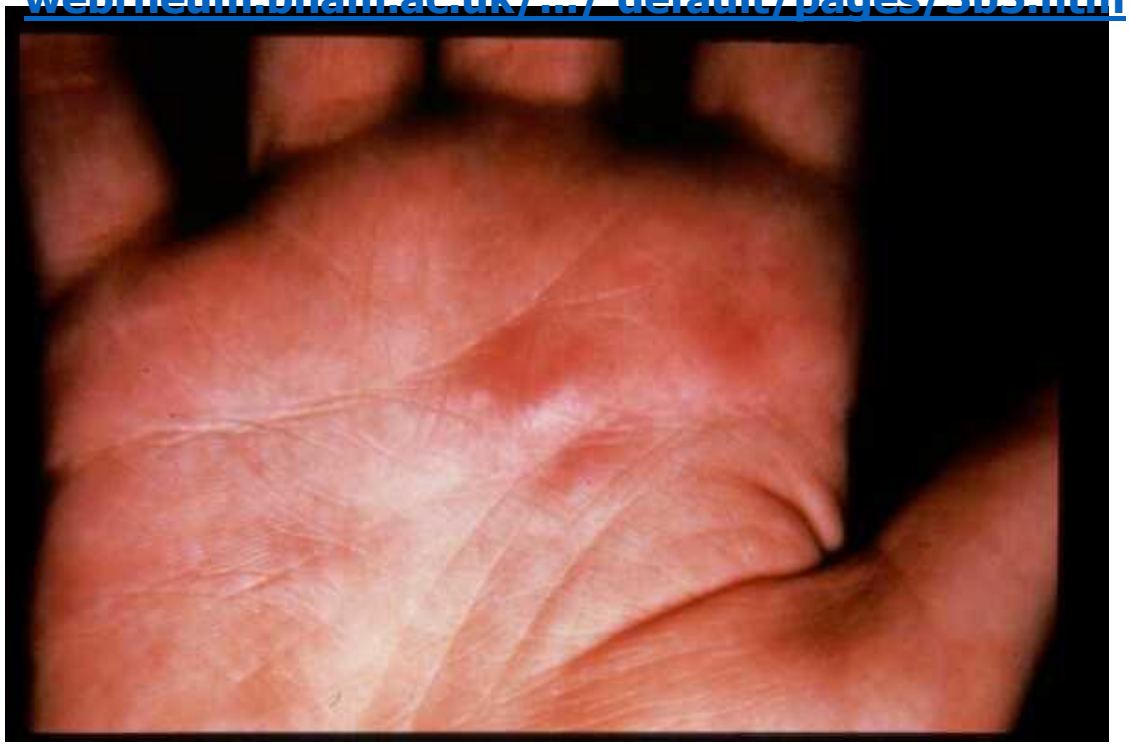


Splinter Hemorrhages

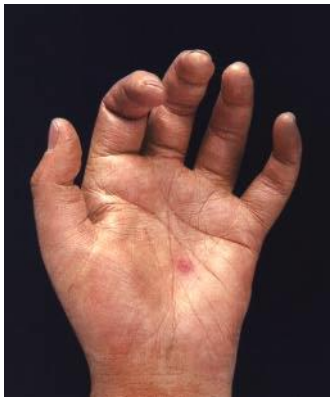
1. Nonspecific
2. Nonblanching
3. Linear reddish-brown lesions found under the nail bed
4. Usually do NOT extend the entire length of the nail

Osler's Nodes

American College of Rheumatology
webrheum.bham.ac.uk/.../ default/pages/3b5.htm

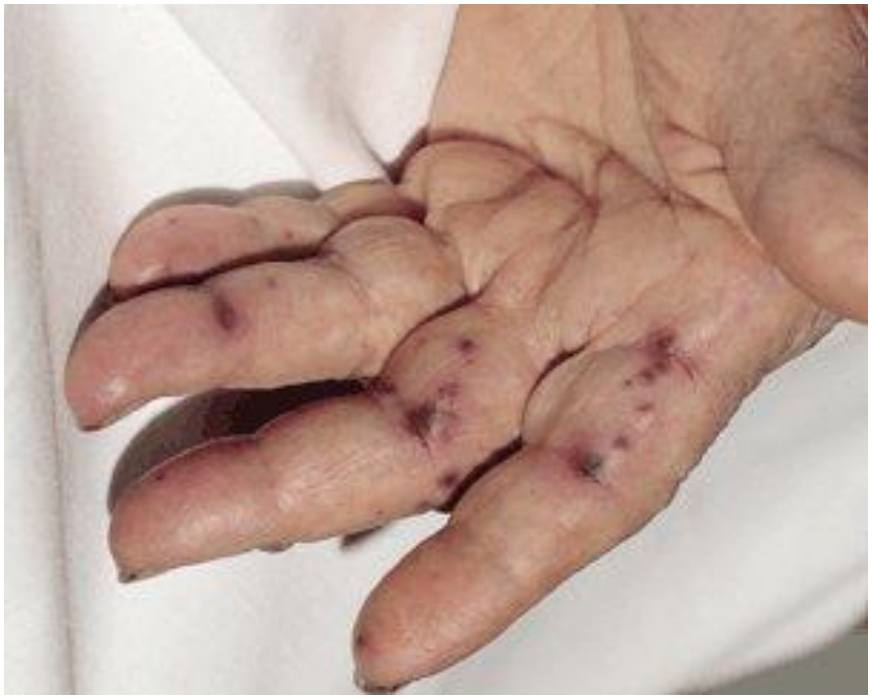


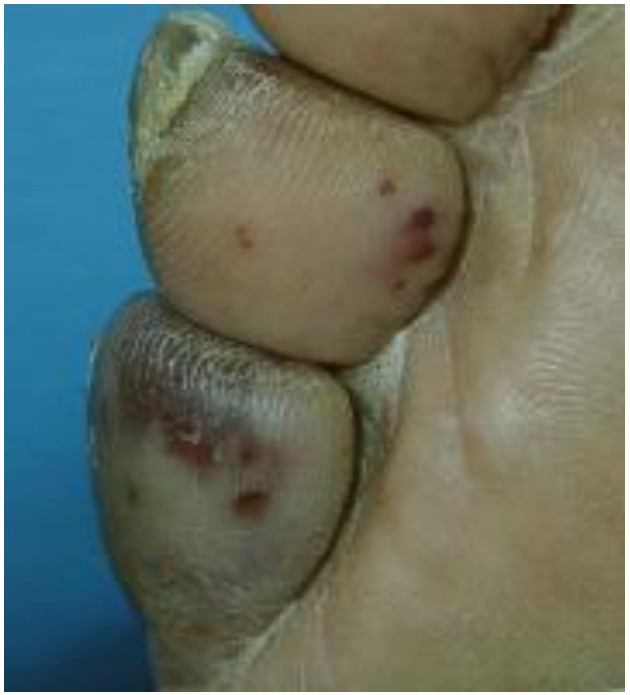
www.meddean.luc.edu/.../ Hand10/Hand10dx.html



1. More specific
2. Painful and erythematous nodules
3. Located on pulp of fingers and toes
4. More common in subacute IE

Janeway Lesions



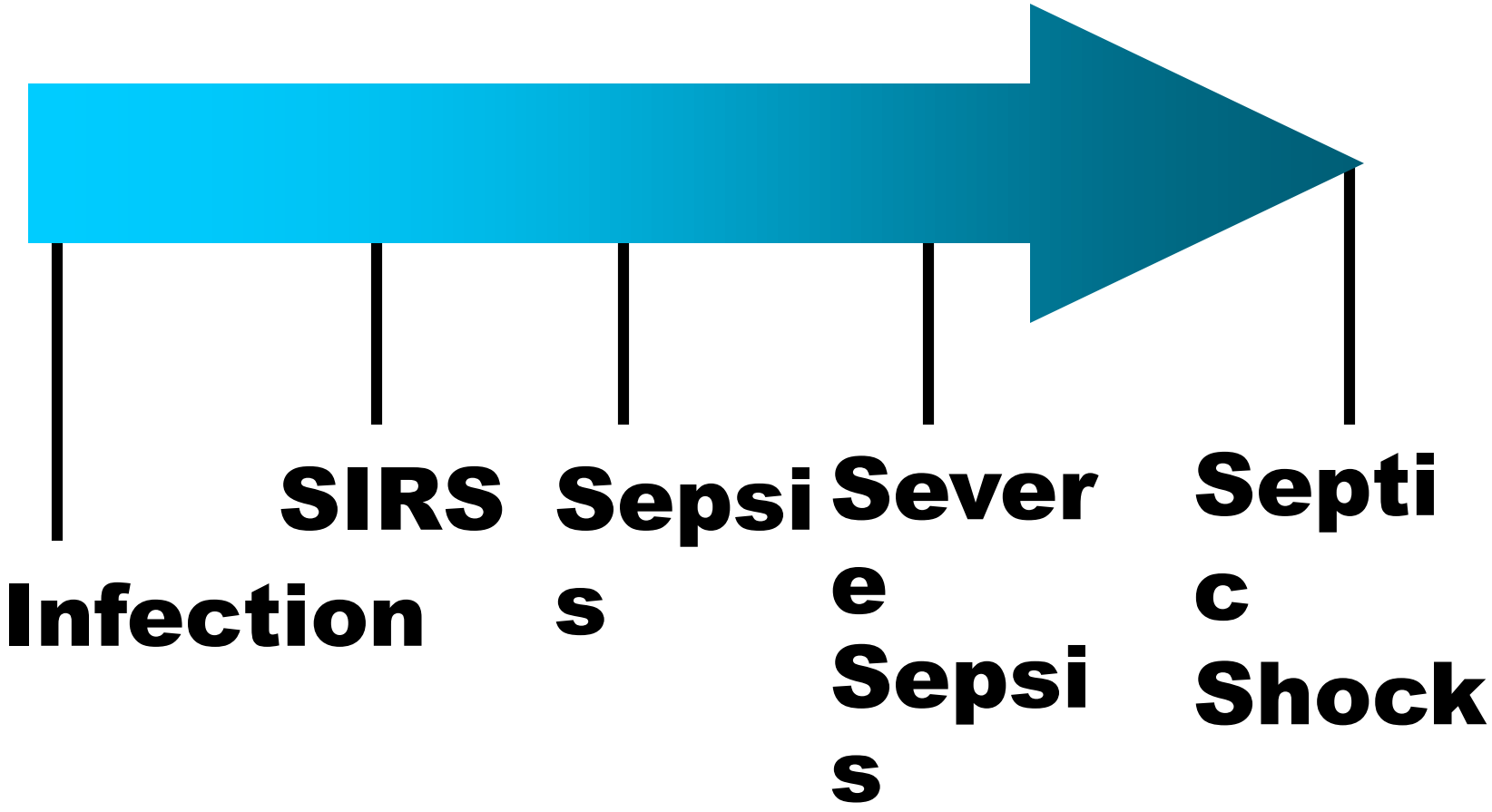


1. More specific
2. Erythematous, blanching macules
3. Nonpainful
4. Located on palms and soles

Chroniosepsis

- DIC-syndrome,
- Hemorrhagic syndrome,
- Dystrophy,
- Necrosis,
- Hyperplasia of the spleen, lymph nodes and red marrow
- Metaplasia fatty bone marrow into red marrow

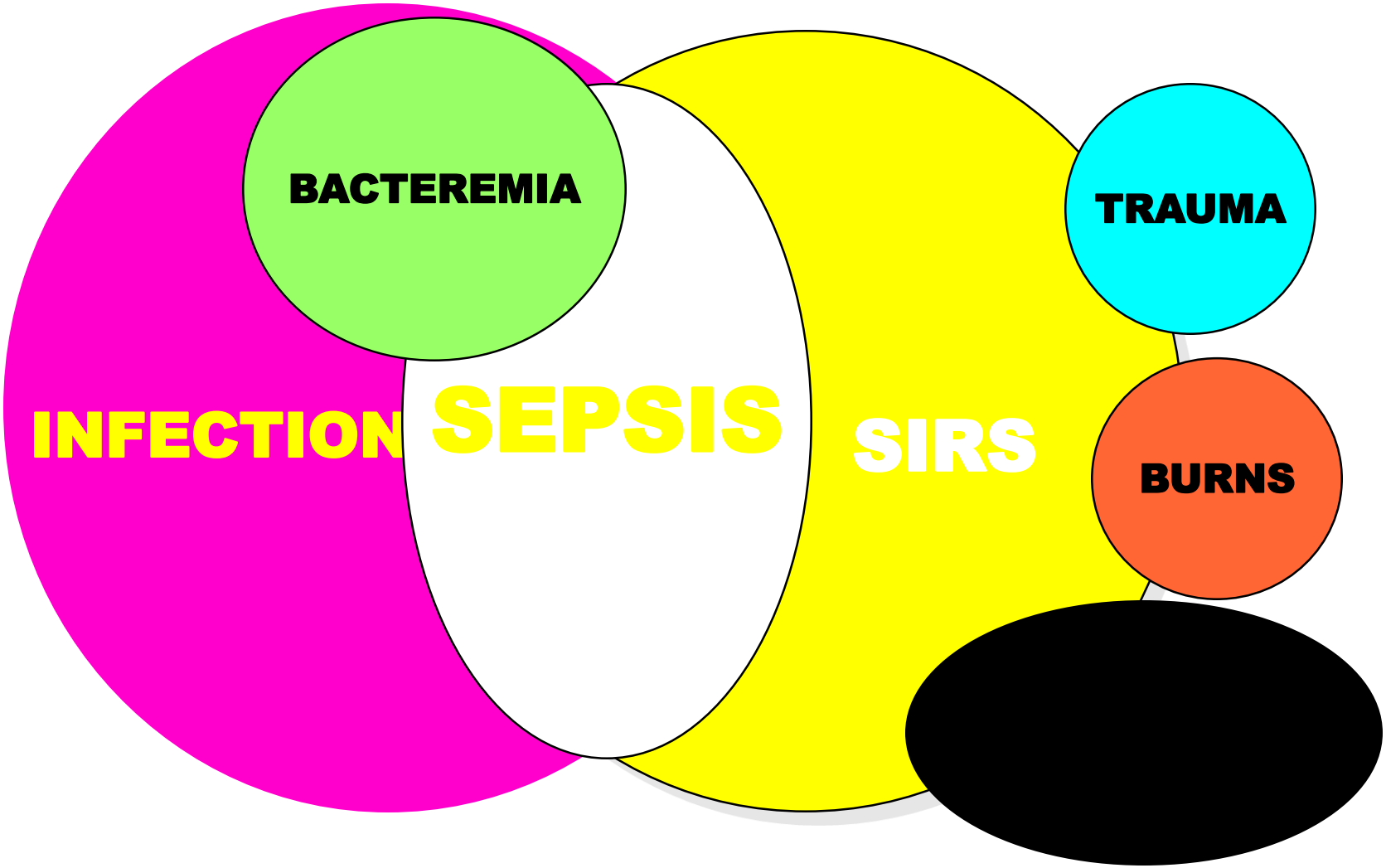
Definitions



Systemic Inflammatory Response Syndrome

- Systemic Inflammatory Response Syndrome (SIRS)
  - ≥ 2 of the following:
    - Temp > 38°C or < 36°C
    - Heart rate > 90 bpm
    - Respiratory rate > 20 bpm
    - WBC > 12,000, < 4,000 or bands > 10%

Relationship Between Sepsis and SIRS



Levels of Clinical Infection

- **Level I Locally Controlled.**
- **Level II Locally Controlled, Leukocytosis.**
- **Level III Systemic Hyperdynamic Response.**
- **Level IV Oxygen metabolism becomes uncoupled.**
- **Level V Shock, Organ Failure.**

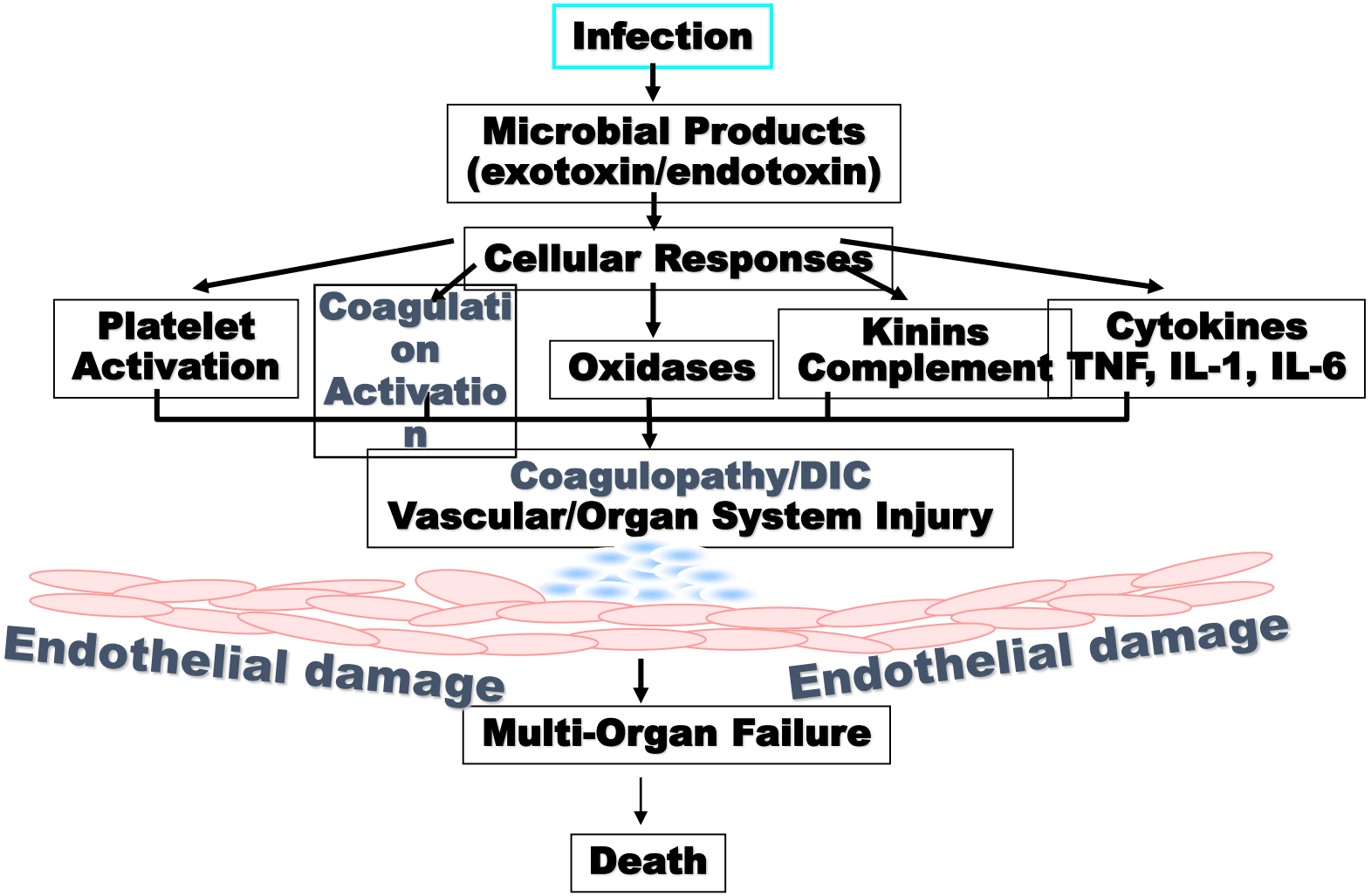
Stages In the Development of SIRS (Bone, 1996)

- **Stage 1. In response to injury / infection, the local environment produces cytokines.**
- **Stage 2. Small amounts of cytokines are released into the circulation:**
  - **Recruitment of inflammatory cells.**
  - **Acute Phase Response.**
  - **Normally kept in check by endogenous anti-inflammatory mediators (IL-10, PGE2, Antibodies, Cytokine receptor antagonists).**

Stages In the Development of SIRS

- **Stage 3. Failure to control inflammatory cascade:**
  - **Loss of capillary integrity.**
  - **Stimulation of Nitric Oxide Production.**
  - **Maldistribution of microvascular blood flow.**
  - **Organ injury and dysfunction.**

Pathogenesis of Severe Sepsis



Definitions (ACCP/SCCM):

- **Multiple Organ Dysfunction Syndrome (MODS): The presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.**

Definitions (ACCP/SCCM):

- **Septic Shock: Sepsis induced with hypotension despite adequate resuscitation along with the presence of perfusion abnormalities which may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.**

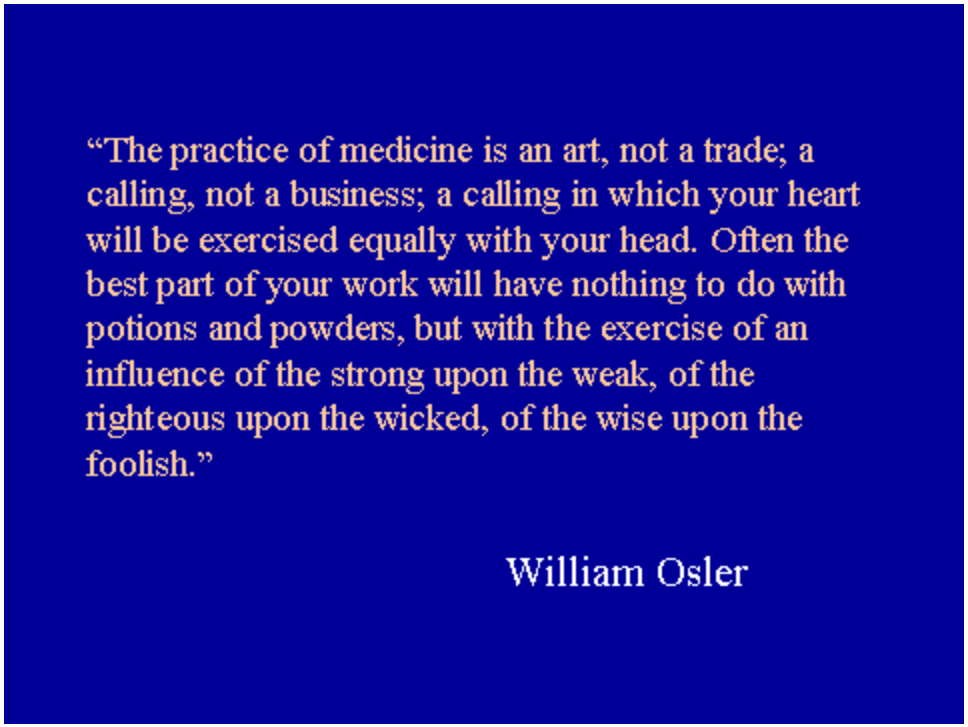
Clinical Signs of Septic Shock

- **Hemodynamic Alterations**
  - **Hyperdynamic State (“Warm Shock”)**
    - **Tachycardia.**
    - **Elevated or normal cardiac output.**
    - **Decreased systemic vascular resistance.**
  - **Hypodynamic State (“Cold Shock”)**
    - **Low cardiac output.**

Clinical Signs of Septic Shock

- **Myocardial Depression.**
- **Altered Vasculature.**
- **Altered Organ Perfusion.**
- **Imbalance of O2 delivery and Consumption.**
- **Metabolic (Lactic) Acidosis.**

The end


"The practice of medicine is an art, not a trade; a calling, not a business; a calling in which your heart will be exercised equally with your head. Often the best part of your work will have nothing to do with potions and powders, but with the exercise of an influence of the strong upon the weak, of the righteous upon the wicked, of the wise upon the foolish."
William Osler