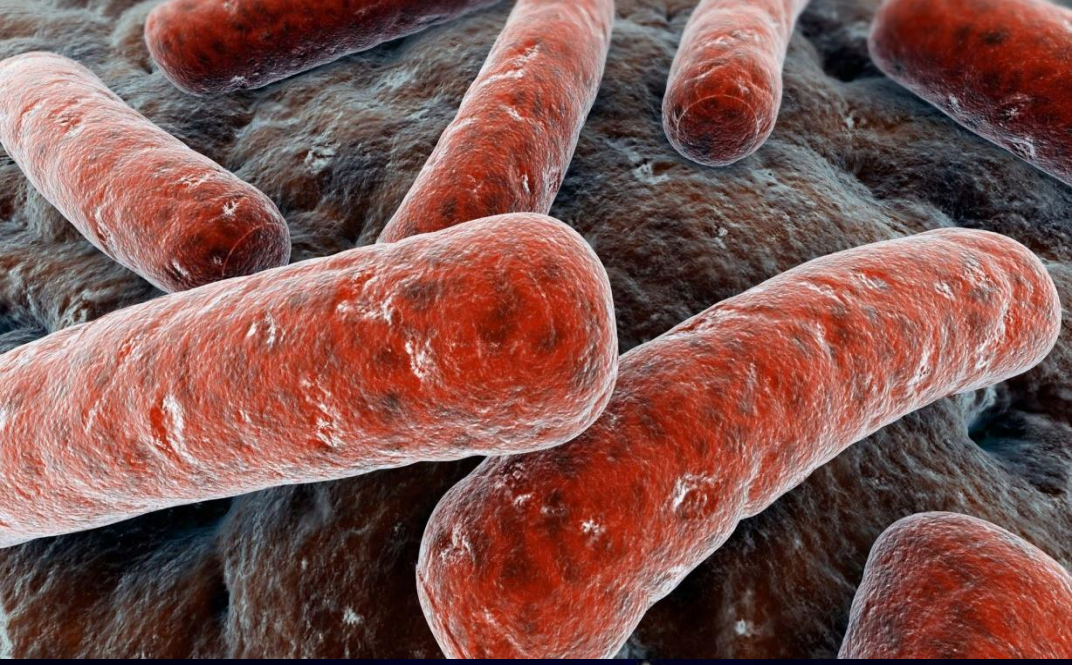
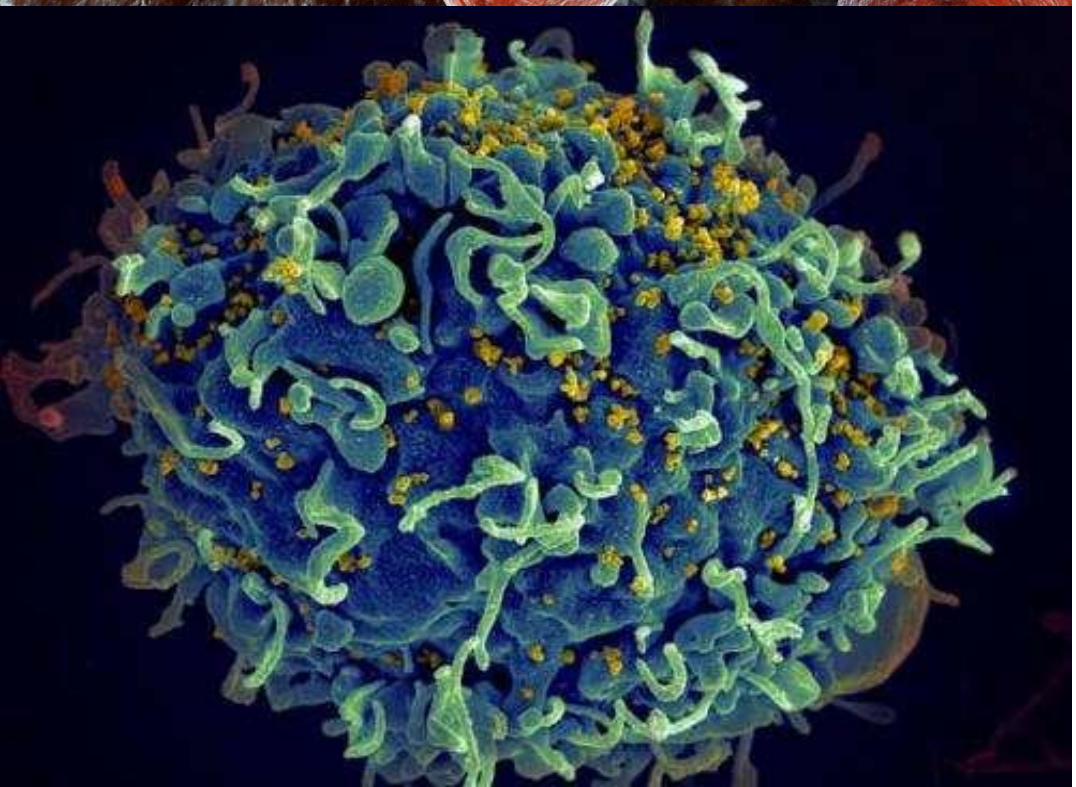




Infectious diseases. Aerogenic infections. Tuberculosis.

Infectious diseases.
Aerogenic infections. Tuberculosis.

I. Microspecimens:

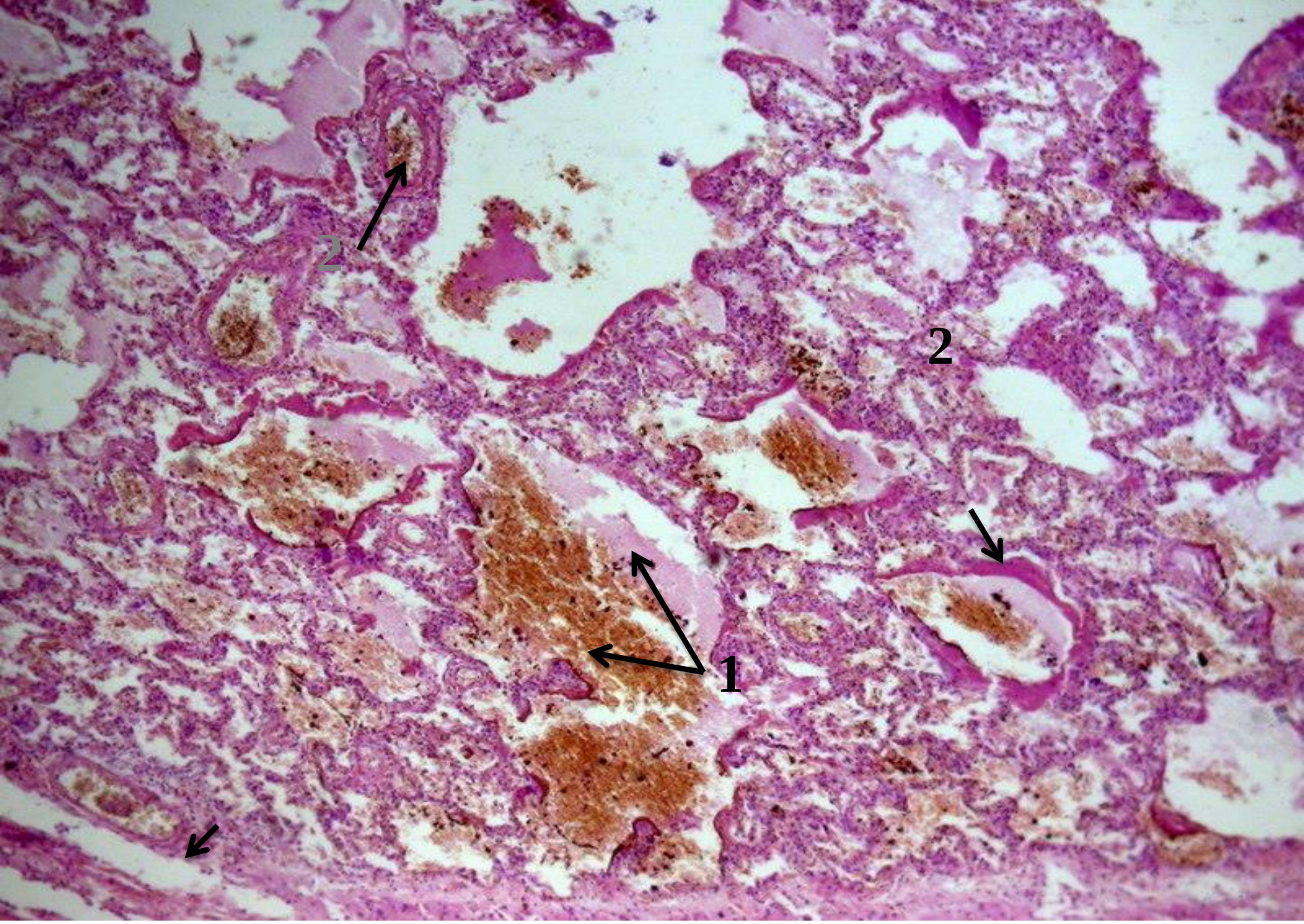
№ 106. Hemorrhagic pneumonia in influenza. *(H-E stain).*

Indications:

1. Inflammatory exudate into lumen of alveoli:
    a. erythrocytes;
    b. serous fluid.
2. Adjacent lung tissue with hyperemic vessels.

In the alveoli is present exudate, consisting of eosinophilic colored serous fluid and erythrocytes, in some alveoli the serous fluid predominates, in others - erythrocytes; in many alveoli the walls are covered with a homogeneous, eosinophilic membrane, consisting of fibrin and coagulated plasma proteins (hyaline membranes); the blood vessels are dilated and hyperemic.

Pneumonia develops in severe forms of the flu. The influenza virus exerts a cytopathic (cytolytic) action on the airway epithelium, causing degeneration, necrosis and desquamation, as well as vasopathic and vasoparalytic action with severe circulatory disorders (hyperemia, stasis, and hemorrhage). These peculiarities of the virus condition the sero-hemorrhagic character of influenza pneumonias. The alternation of foci of pneumonia with foci of compensatory emphysema and atelectasis gives the lung a mottled appearance, hence the name "big mottled lung in flu". The virus also has a pronounced immunosuppressive effect, which determines the association of the secondary infection. Possible complications: pulmonary edema, acute respiratory failure and abscesses development.



№ 106. Hemorrhagic pneumonia in influenza. *(H-E stain).*

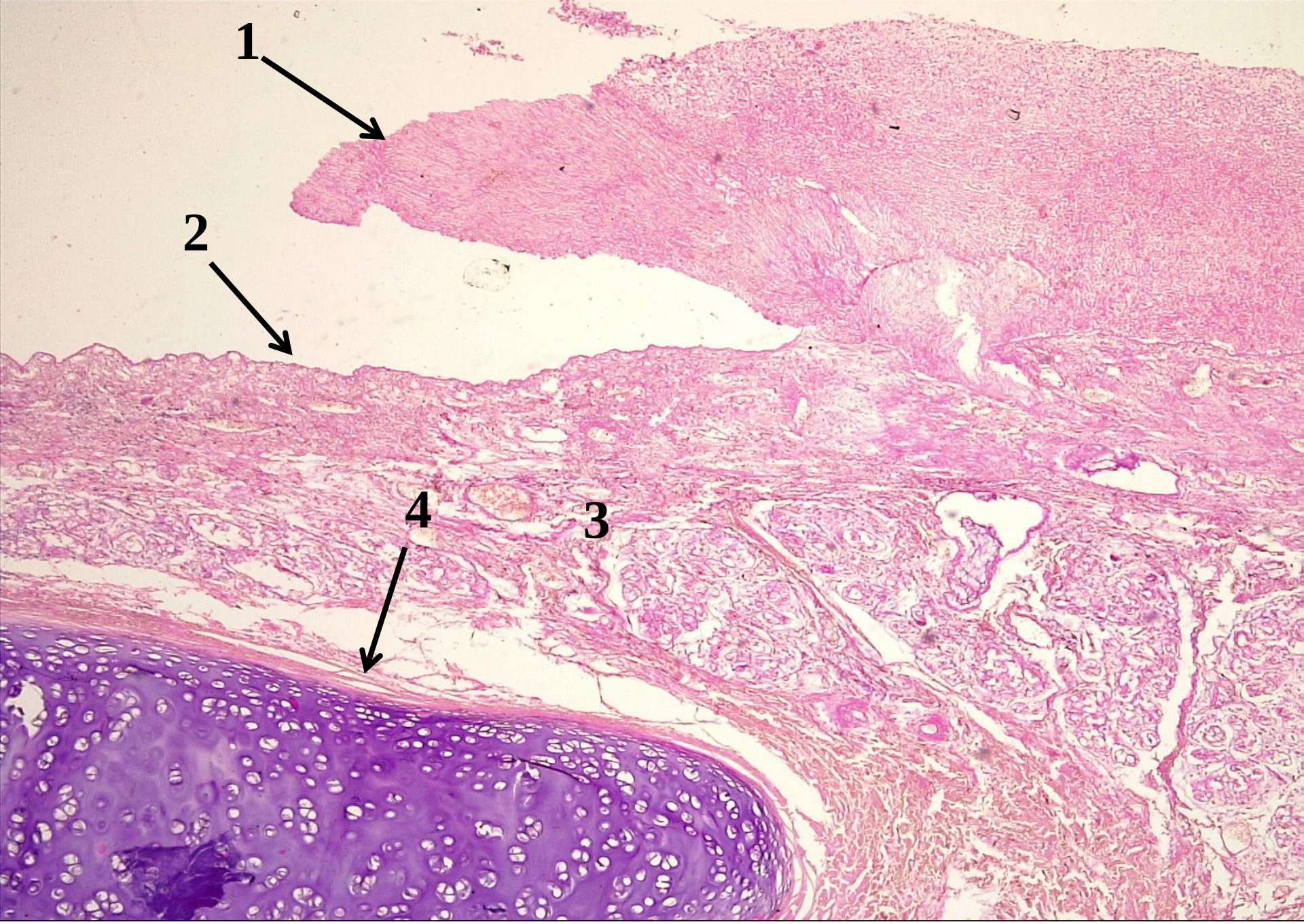
№ 99. Croupous tracheitis in diphtheria. *(H-E stain).*

Indications:

1. Fibrin deposits on the mucosa of the trachea.
2. Ulceration of the mucosa.
3. Edema and hemorrhage in submucosal layer.
4. Cartilaginous rings of the trachea.

The tracheal mucosa and submucosa are edematous, hyperemic, hemorrhagic foci are observed, the epithelium is sometimes necrotic and desquamated, forming ulcerative defects, covered with a layer of fibrin with a mixture of neutrophilic leukocytes and necrotic masses, which form a pseudomembrane.

Diphtheria is an acute infectious disease caused by the diphtheria bacillus - Corynebacterium diphtheriae, which eliminates exotoxin. The local effect of exotoxin consists of epithelial necrosis, extravasation of fibrinogen and the formation of pseudomembranes, consisting of fibrin and necrotic masses with a mixture of leukocytes, which macroscopically have a whitish-yellow color. Because the tracheal mucosa adheres loosely to the underlying connective tissue, the pseudomembranes are easily removed and expectorated by sputum (croupous fibrinous inflammation). Due to this fact in diphtheria, which affects the larynx, trachea and bronchi, no general intoxication is observed. There may be complications associated with the removal of pseudomembranes: laryngospasm, airway obstruction, pneumonia.



№ 99. Croupous tracheitis in diphtheria. *(H-E stain).*

№ 79. Pulmonary miliary tuberculosis. *(H-E. stain).*

Indications:

1. Tuberculous granuloma:
   a. caseous necrosis in the center of granuloma;
   b. layer of epithelioid cells;
   c. giant cells Langhans;
   d. lymphoid cell layer.
2. Adjacent lung tissue.

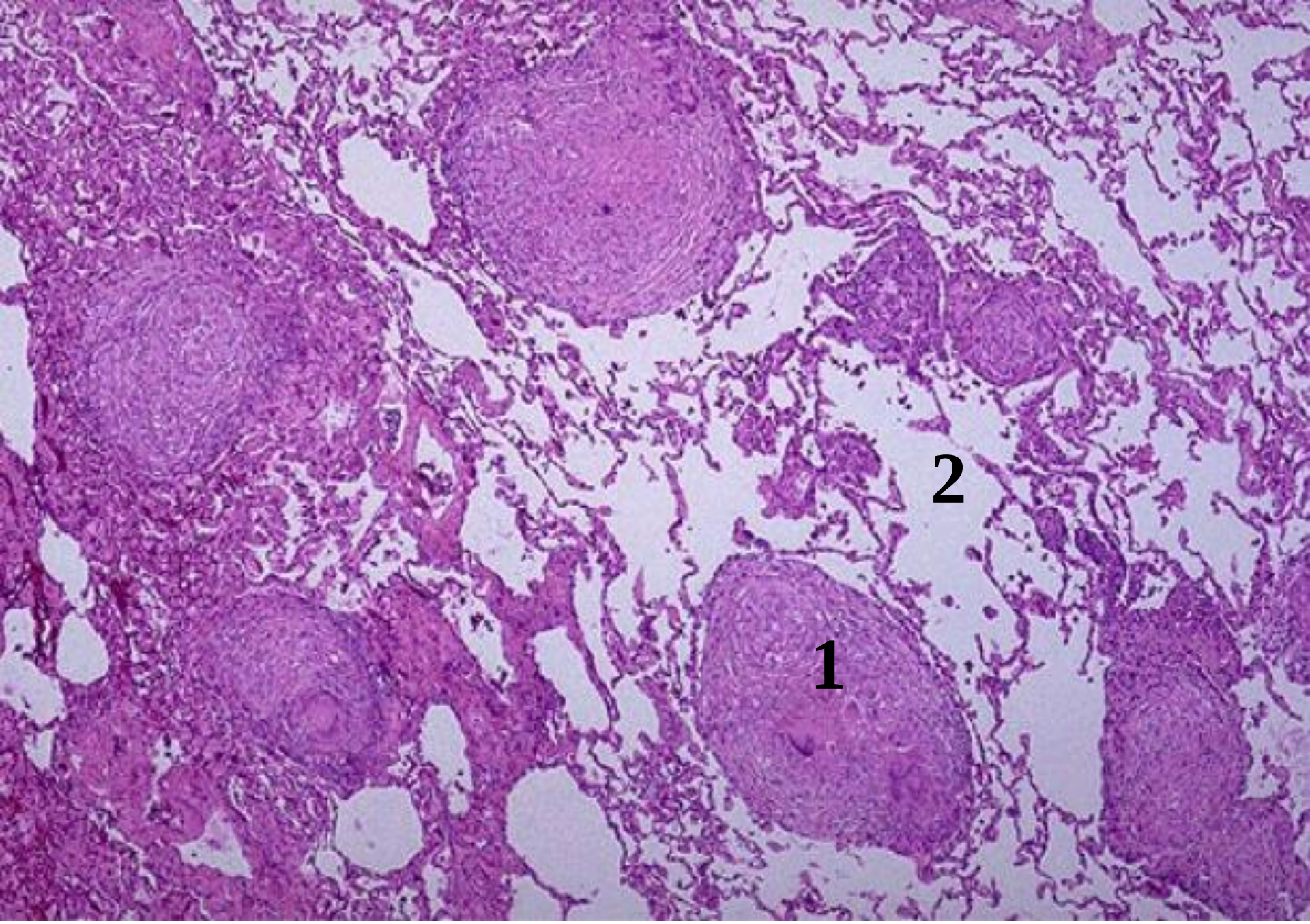
In the lung tissue there are multiple tuberculous granulomas at different stages of development, some with caseous necrosis in the center, which is intensely colored eosinophilic, surrounded by a cell cord, consisting of epithelioid cells with elongated, pale nuclei, arranged radially, "in the palisade "; among them are giant polynuclear cells Langhans with eosinophilic cytoplasm and nuclei placed in the shape of a horseshoe, circular along the membrane or 2 poles of the cell, and at the periphery - a layer of small lymphocytes, compactly placed, with round nucleus, hyperchrome and poor cytoplasm, which may include macrophages and plasma cells; around some granulomas are collagen fibers; other granulomas are in the fibrosis stage (replacement with fibrous connective tissue); In the lung parenchyma between granulomas, foci of emphysema are observed, some interalveolar septa are thickened, sclerosed.

№ 85. Caseous pneumonia. *(H-E. stain).*

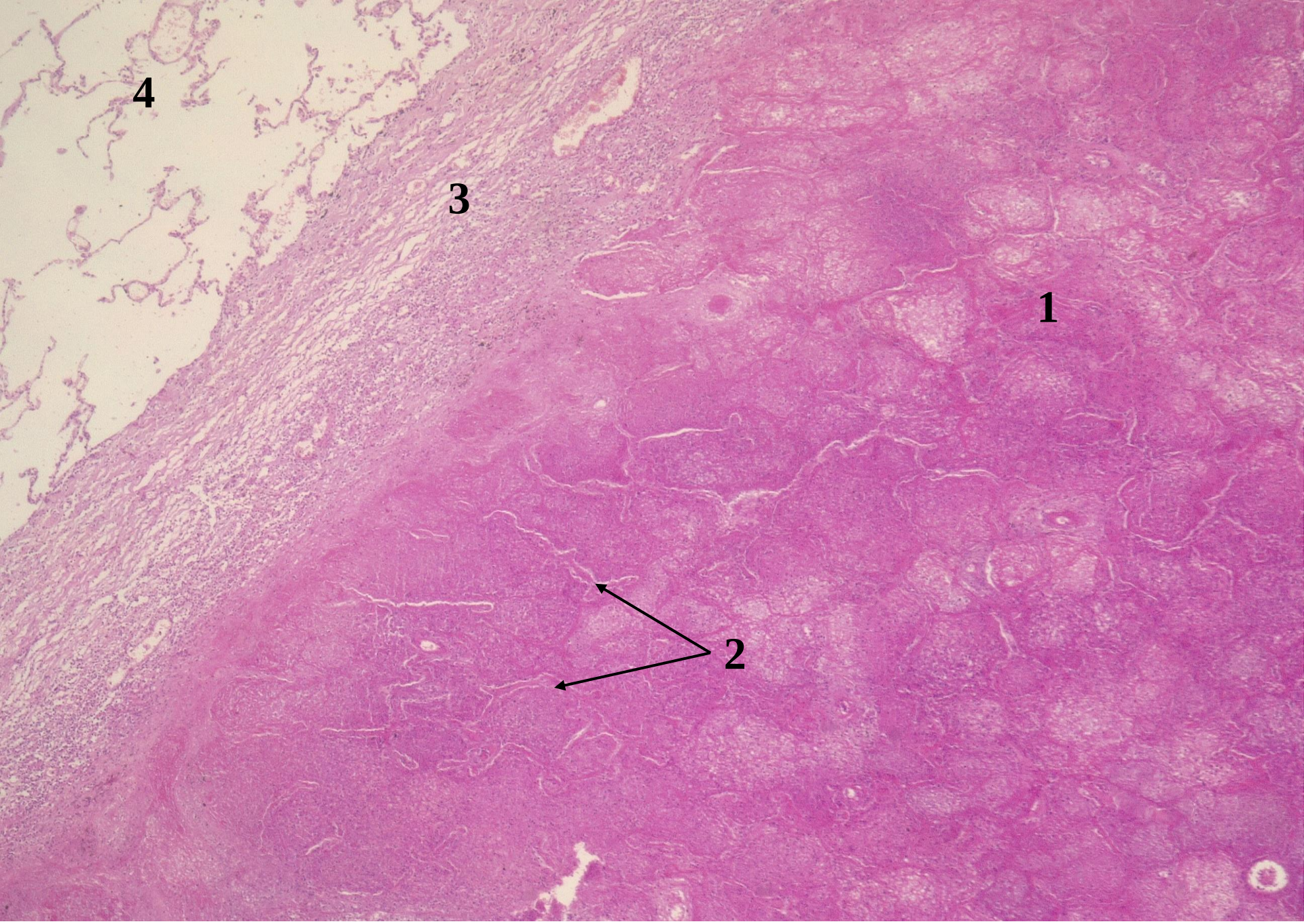
Indications:

1. Caseous necrosis area.
2. Interalveolar septa without nuclei (karyolysis).
3. Connective tissue infiltrated by lymphoid cells.
4. Adjacent emphysematous pulmonary tissue.

In the microspecimen there is an extensive area of necrosis of lung tissue, unventilated, the alveolar lumen contains intensely colored necrotic masses eosinophilic, fibrin, neutrophilic leukocytes, monocytes, disintegrated nucleus remains, necrotic interalveolar septa, devoid of nuclei with moderate lymphoid infiltration; in the adjacent lung tissue signs of emphysema.



№ 79. Pulmonary miliary tuberculosis. *(H-E. stain).*



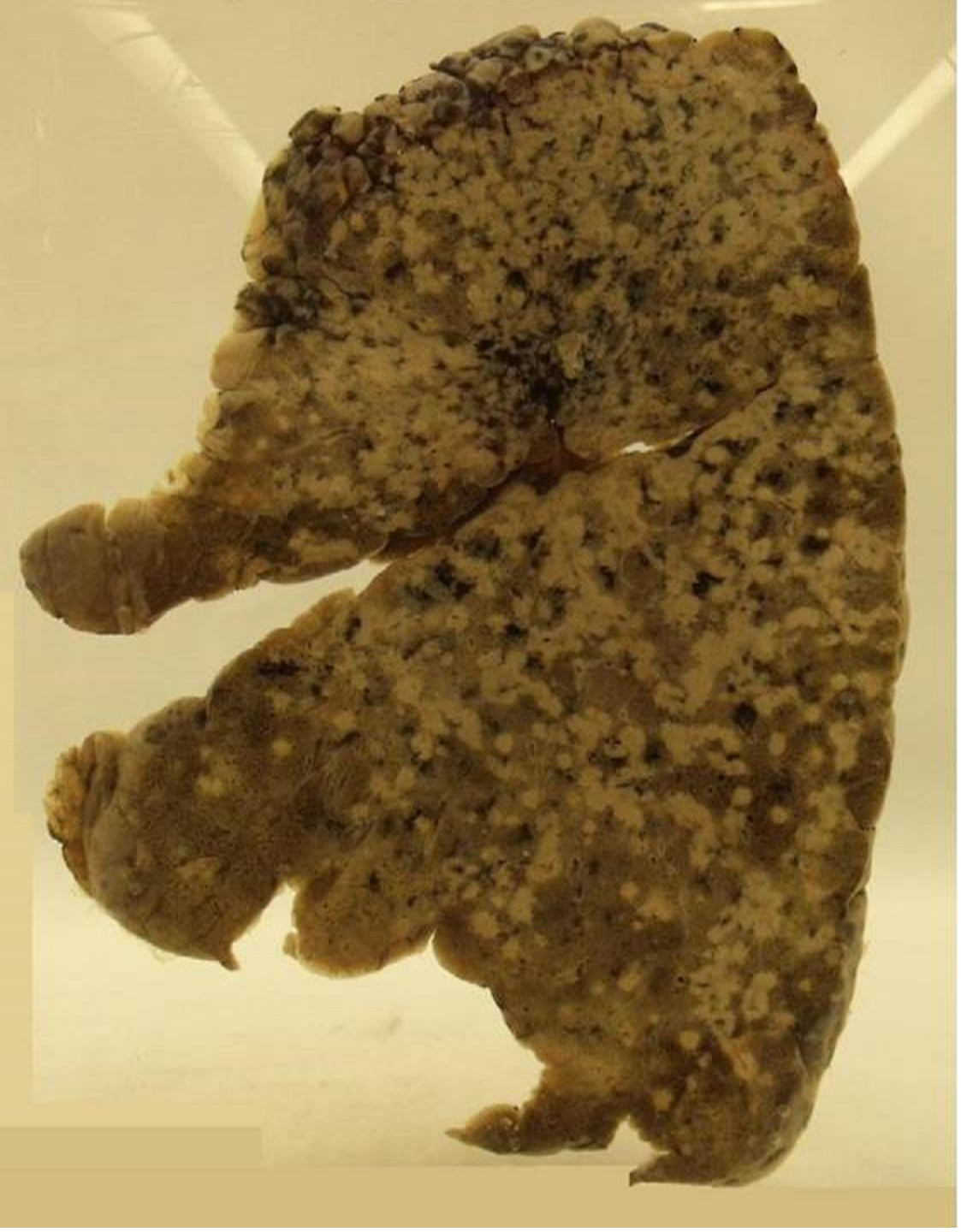
№ 85. Caseous pneumonia. *(H-E. stain).*

II. Macrospecimens:

№ 43. Caseous pneumonia.

In the lung there are multiple foci of caseous necrosis, unventilated, of different sizes, white-yellow color, the necrotic masses have a friable, crumbly appearance, it resembles dry cow's cheese (lat. Caseum - cheese).

Caseous pneumonia is found in secondary tuberculosis, but can also be in primary tuberculosis. Initially, acinar, lobular caseous outbreaks appear, which can extend to the level of a segment or even of an entire lobe - lobar caseous pneumonia. It develops in patients with low immunity, malnourished. There are deposits of fibrin in the pleura. The curd masses can be subjected to purulent lysis and liquefaction with the appearance of decomposition cavities - caverns (cavernous tuberculosis).

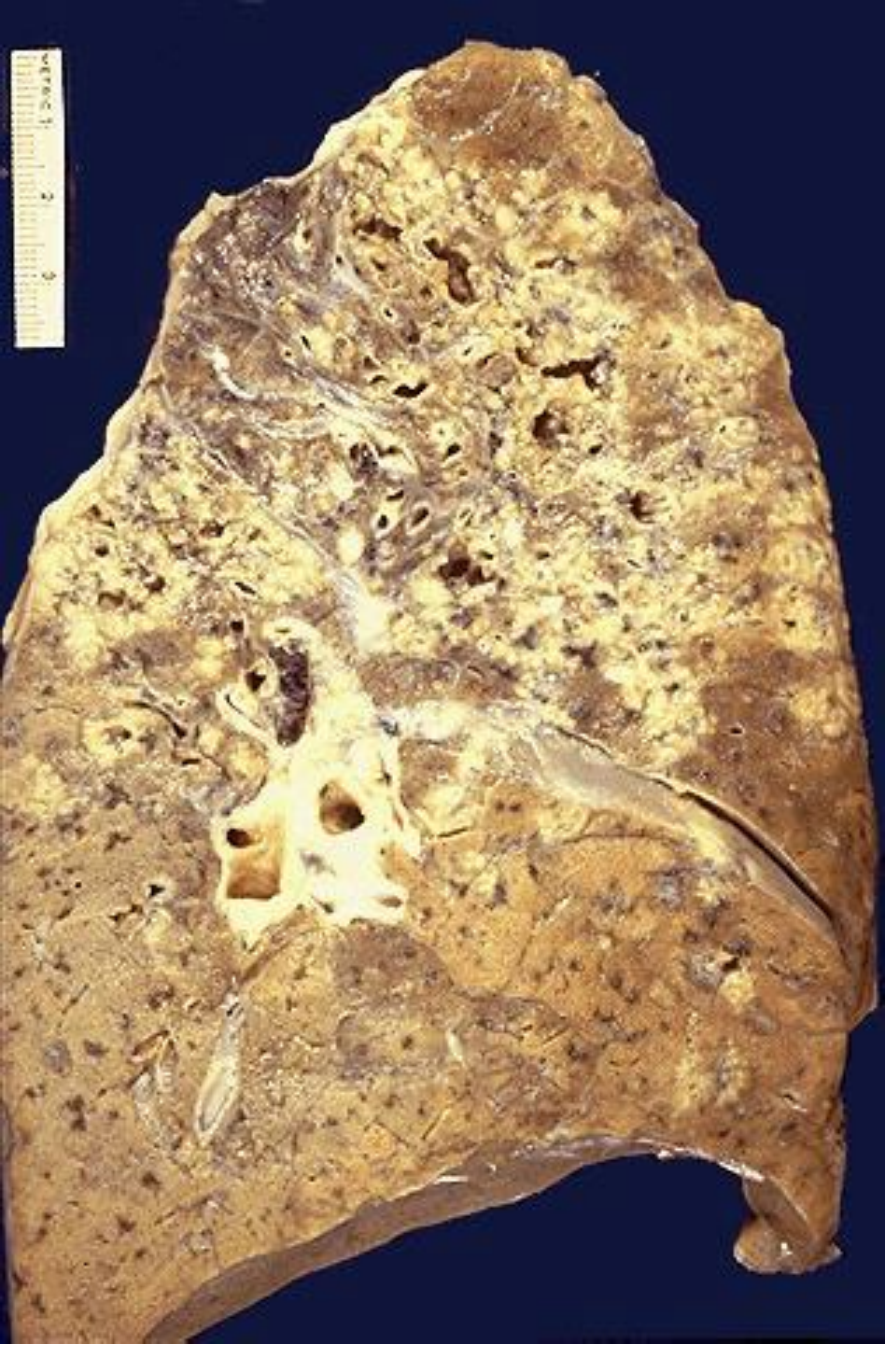


№ 43. Caseous pneumonia.

№ 44. Fibrocavitary tuberculosis.

The lung is deformed, on the section are observed multiple cavities of destruction - caverns of irregularly shaped, different sizes with thickened, sclerosed walls, rough internal surface, covered with necrotic masses; in the adjacent lung tissue unventilated white-yellow areas of caseous necrosis, pneumosclerosis, thickened bronchial walls may be seen.

Fibro-cavitary tuberculosis is a form of secondary pulmonary tuberculosis. In general, caverns are much more common in secondary tuberculosis than in primary tuberculosis. The formation of cavities for the destruction of lung tissue begins in the apical areas of the right lung and extends in the apico-caudal direction through direct contact and bronchogenic in the middle and lower lobes. The apical caverns are older than the distal ones. They have different sizes, irregular shape, walls consisting of 3 layers: caseous necrotic masses infiltrated with neutrophilic leukocytes, tuberculous granulation tissue, mature connective tissue. If the cavern is drained and communicates with the bronchi, the curd contents extend bronchially into the contralateral lung. At the same time, endobronchial, endotracheal, laryngeal and intestinal tuberculosis can develop by ingesting sputum containing tuberculous bacilli. In cases, when the contents of the cavern are evacuated bronchially, it collapses and heals. Possible complications: respiratory failure, pulmonary hemorrhage, pulmonary heart, secondary amyloidosis; in patients with compromised immunity, lymphatic and hematogenous dissemination may occur with the development of miliary tuberculosis.

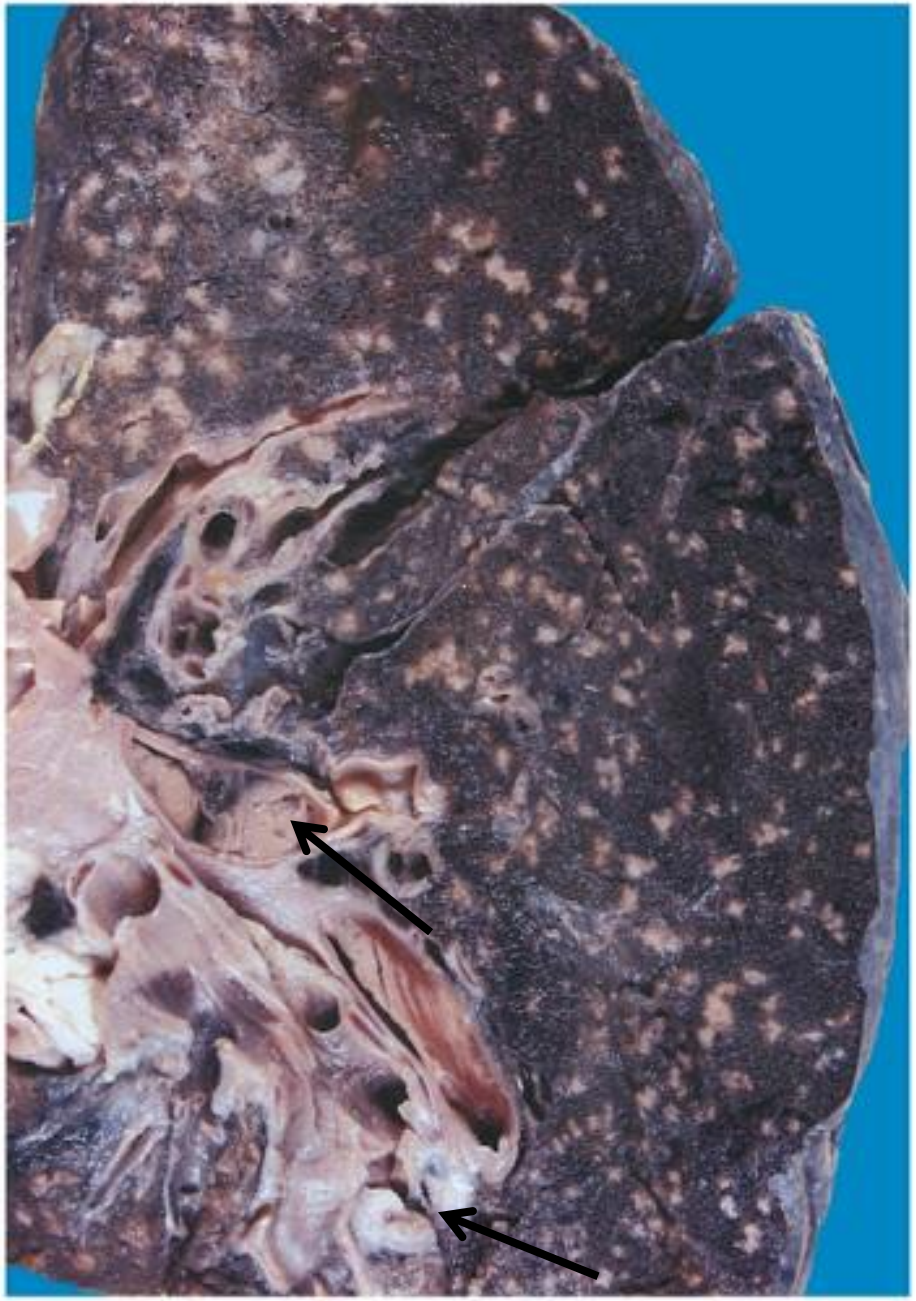


№ 44. Fibrocavitary tuberculosis.

№ 144. Tuberculosis of peribronchial lymph nodes.

The peribronchial lymph nodes are enlarged in size, dense, adhere closely to each other, forming bundles, conglomerates, on the section white-yellow color, dry cheese appearance.

Impaired lymph nodes are the most common manifestation of pulmonary tuberculosis. It is found primarily in primary tuberculosis as a component part of the primary tuberculous complex or the Gohn complex (primary affect, lymphangitis and lymphadenitis). In primary pulmonary tuberculosis, the hilar and bronchopulmonary nodules are affected, and in primary intestinal tuberculosis - mesenteric lymph nodes. In the initial period of secondary pulmonary tuberculosis, regional lymph nodes are much less affected due to the location of the tuberculous process in the apical areas of the lungs. Enlarged lymph nodes compress the nerves, blood vessels, neighboring organs, causing certain clinical manifestations. Viable tubercle bacilli may persist in the lymph nodes for several years, with the potential to reactivate the infection and develop secondary tuberculosis under conditions of decreased immunity.



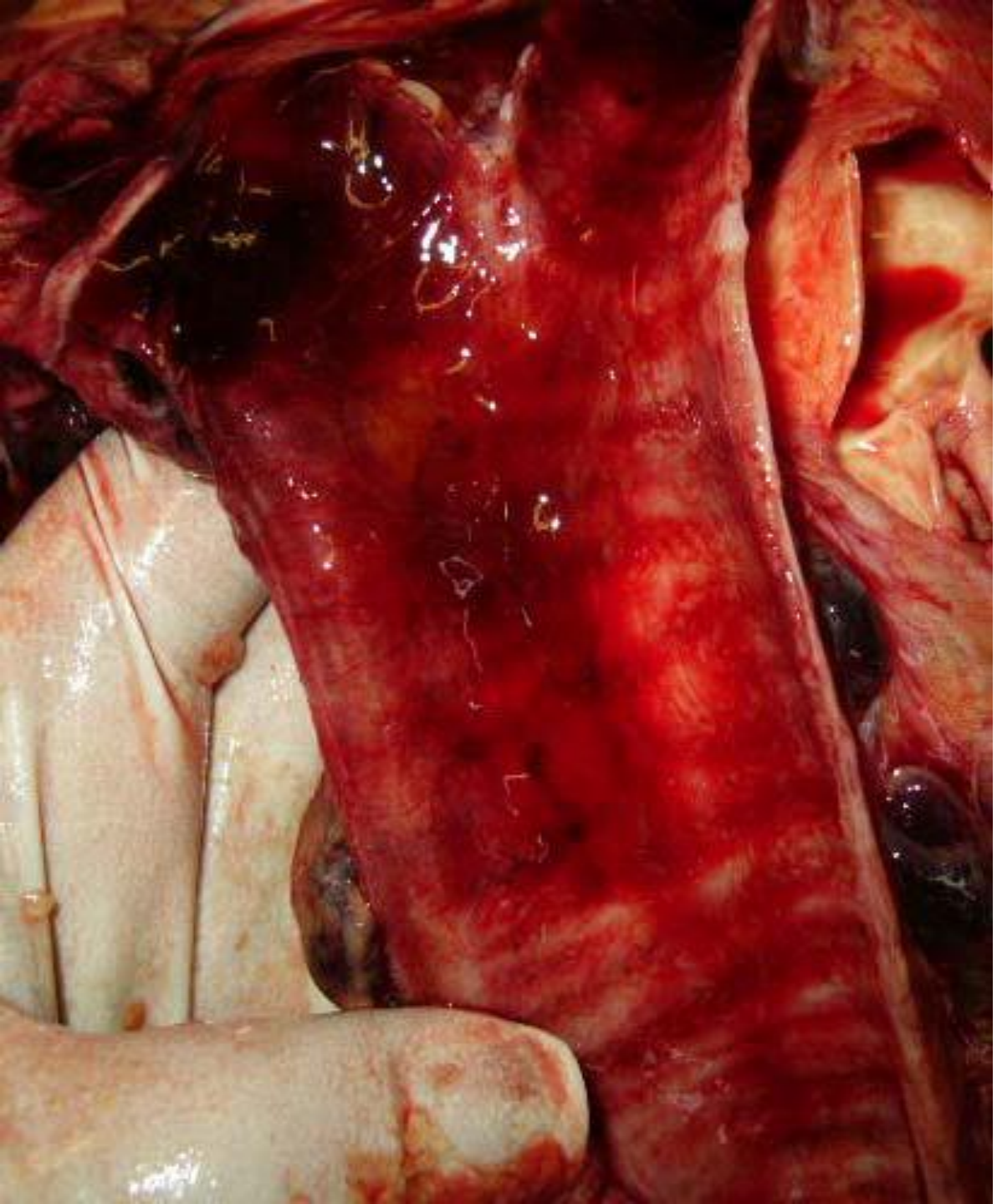
№ 144. Tuberculosis of peribronchial lymph nodes.

№ 153. Tuberculous spondylitis.

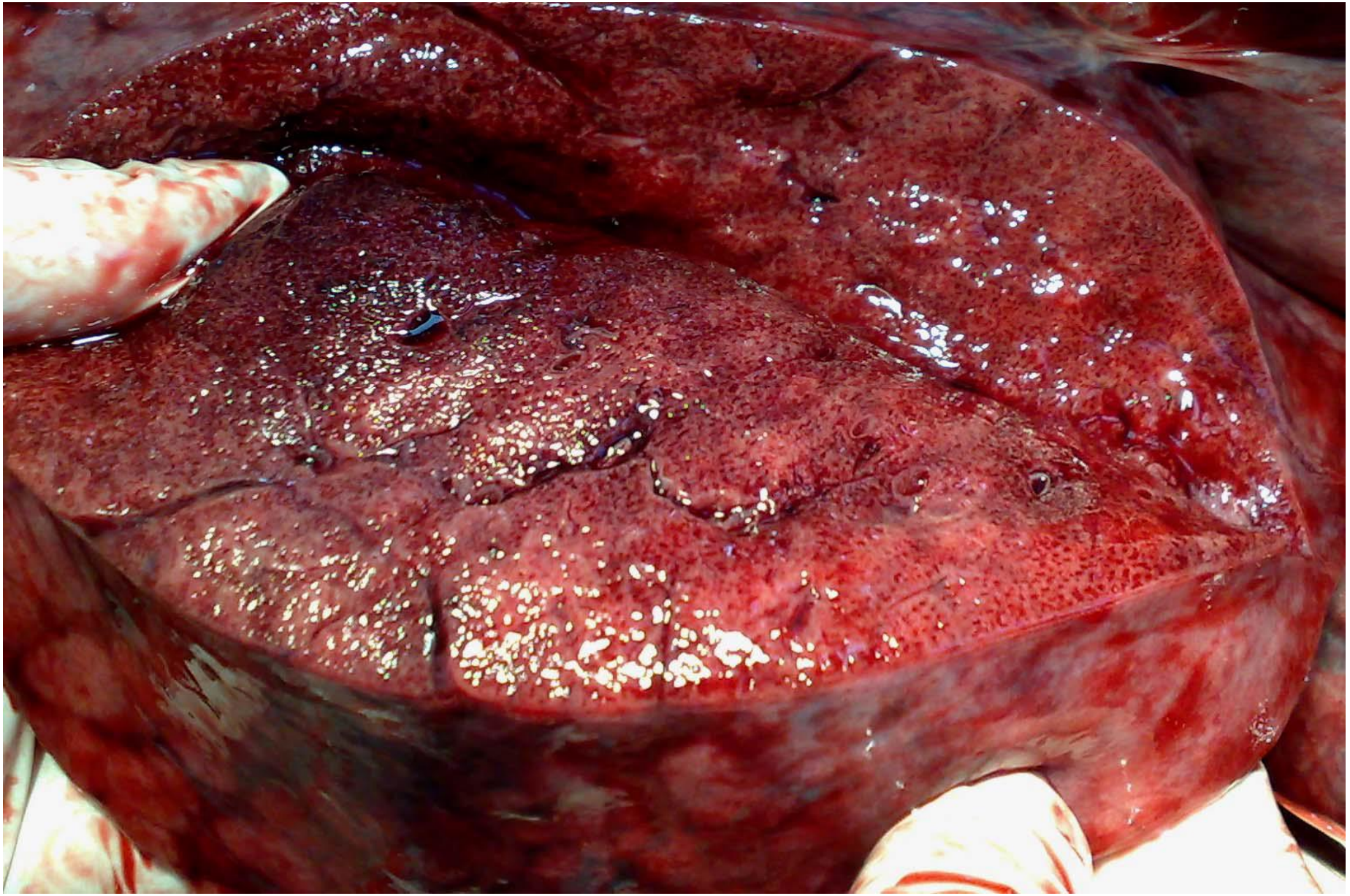
In the macrospecimen, there is a segment of the spine, the lumbar region, the deformation of the spine is observed, on the section the bodies of some vertebrae are destroyed, the apophyses are preserved, a cavity of destruction is outlined, the vertebrae are grown together.

Spinal cord injury in tuberculosis (tuberculous spondylitis or Pott's disease) is found in miliary tuberculosis following the hematogenous spread of tuberculosis mycobacteria. It is more common in children and adolescents. It affects the bodies of the vertebrae, in which tuberculous osteomyelitis with caseous necrosis occurs, destruction of bone tissue and intervertebral discs, seizures are formed, filled with necrotic and purulent masses and consequently deformity of the spine occurs with the appearance of a convex curve in the region chest (kyphosis). Necro-purulent masses can spread to the soft paraspinal tissues forming "cold" abscesses, which can fistulate the skin by removing the contents of the abscesses. Chronic tuberculosis spondylitis can be complicated by secondary amyloidosis. At the same time, it can affect the coxo-femoral joint (tuberculous coxitis) and the knee (tuberculous gonitis).

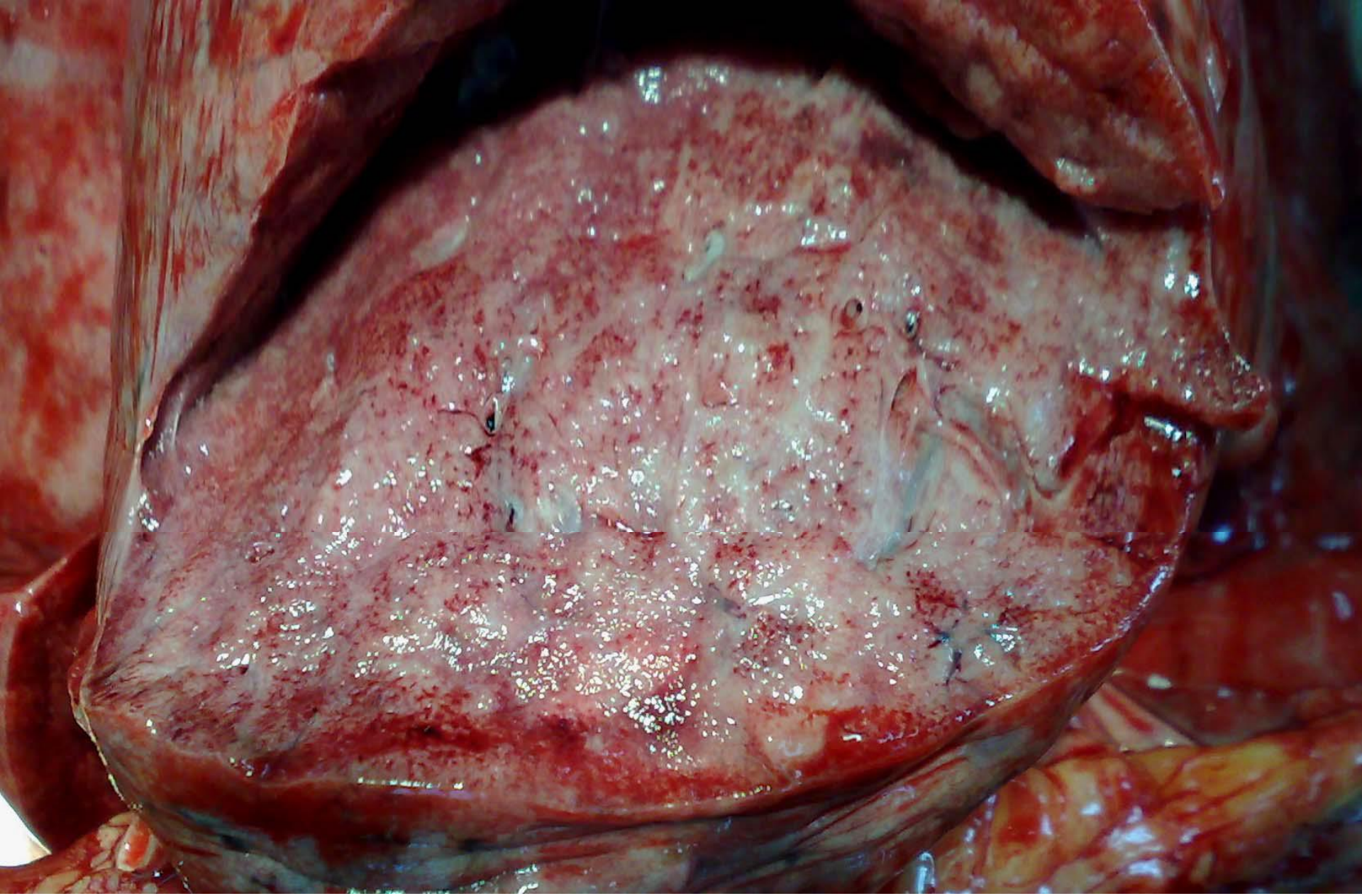
№ 153. Tuberculous spondylitis.
(Pott disease).



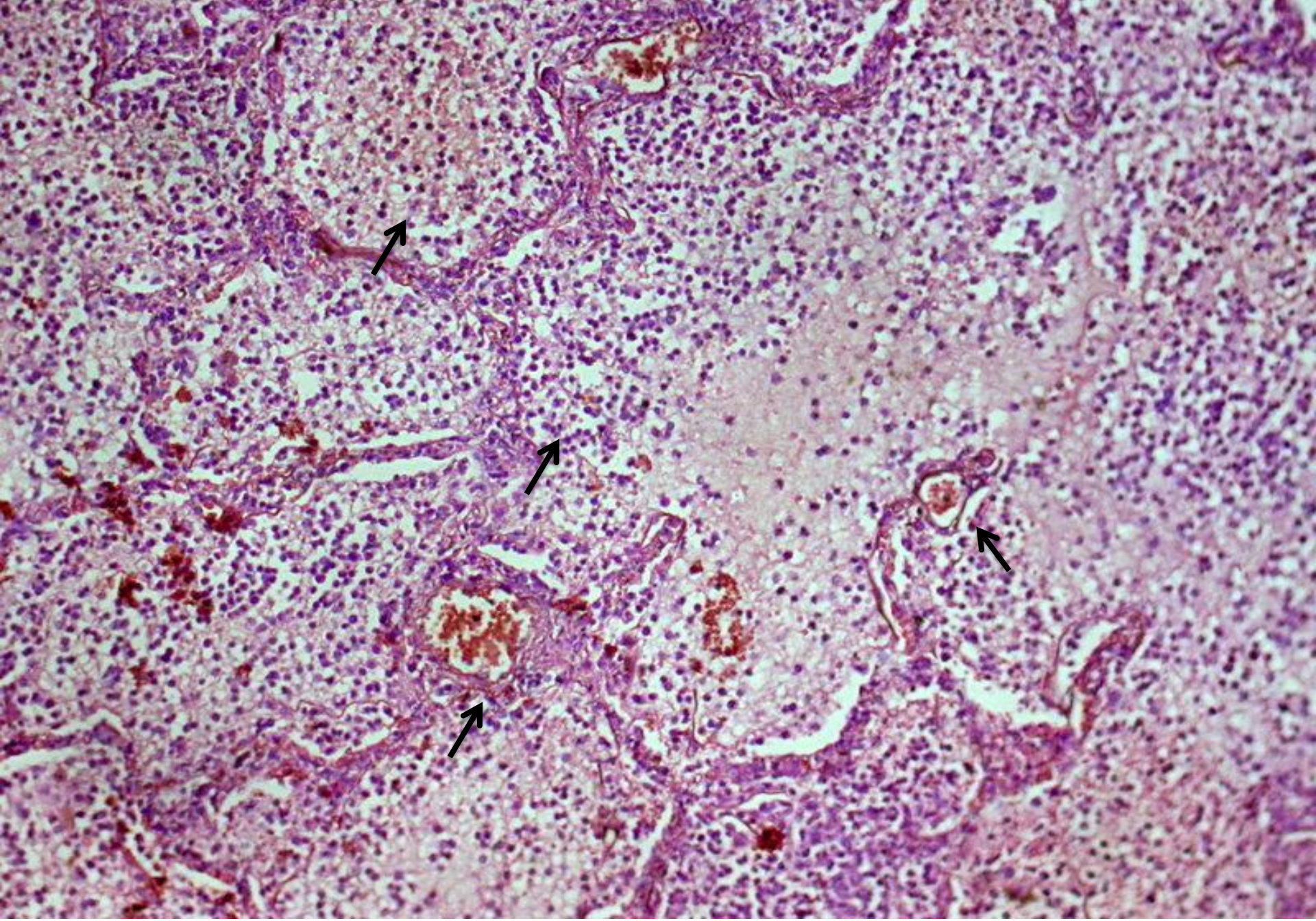
Influenza hemorrhagic tracheobronchitis.



Big mottled lung in influenza.

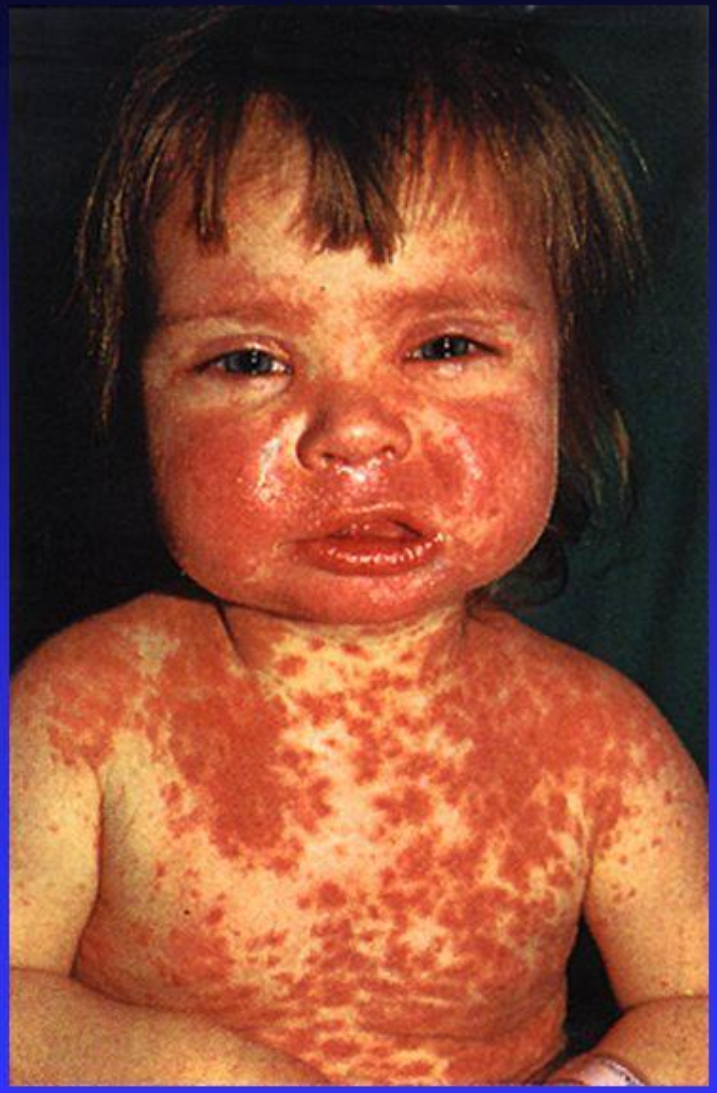


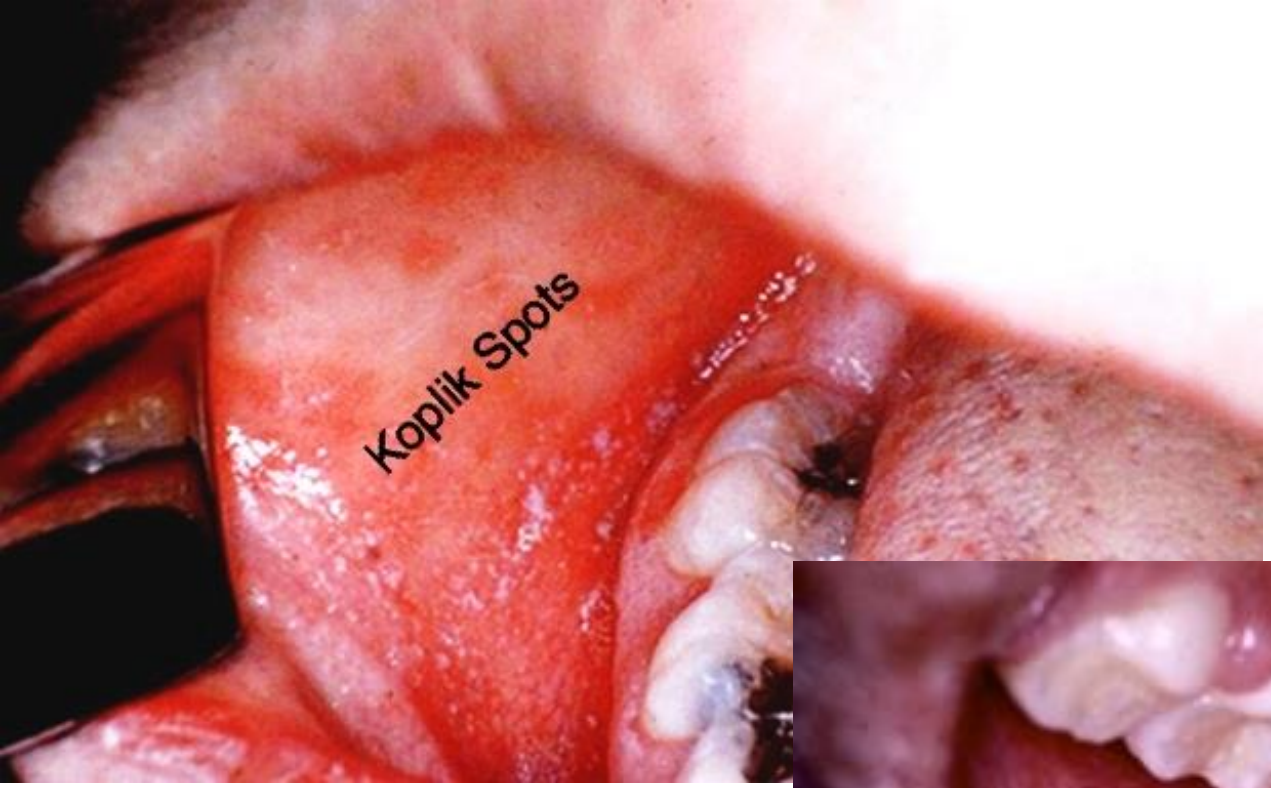
Lung in the proliferative stage of the diffuse alveolar lesion in influenza.

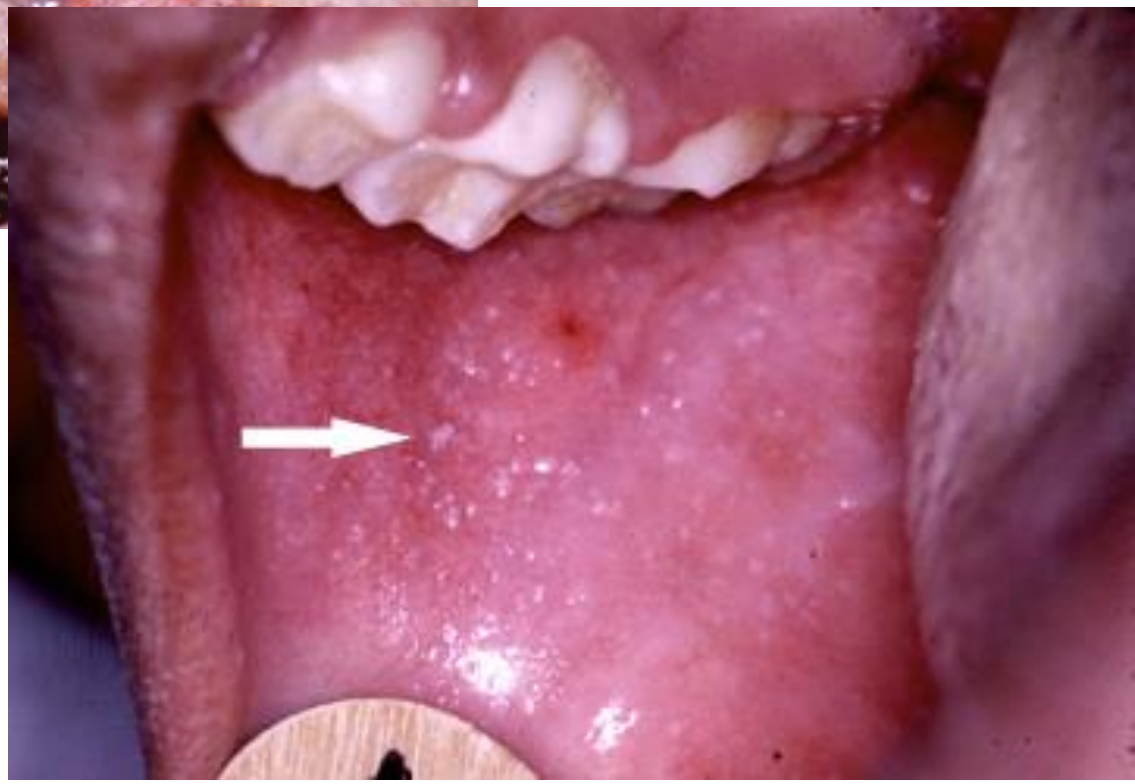


Influenza pneumonia associated with secondary infection.

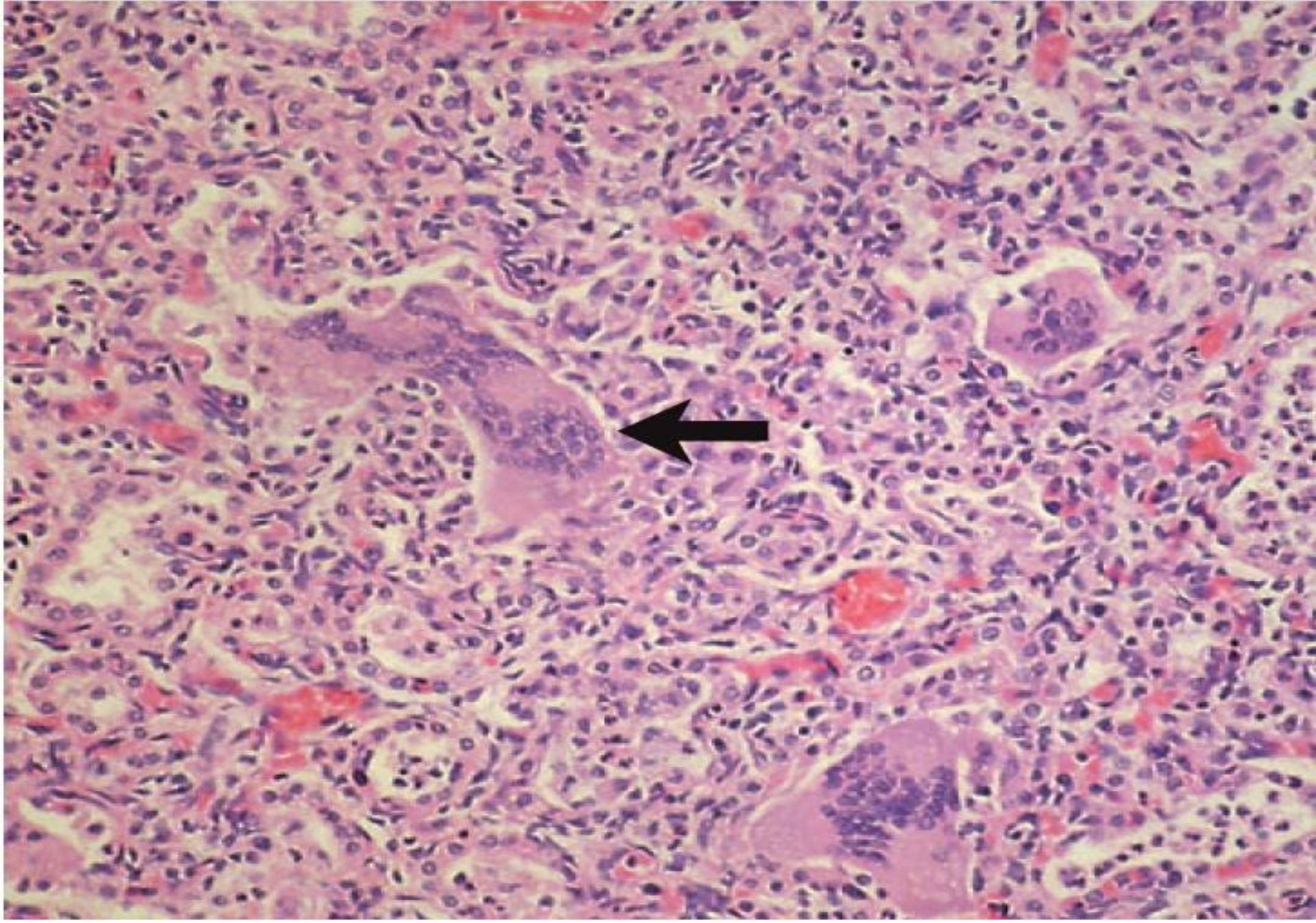
Measles: Rash, conjunctivitis, and rhinitis





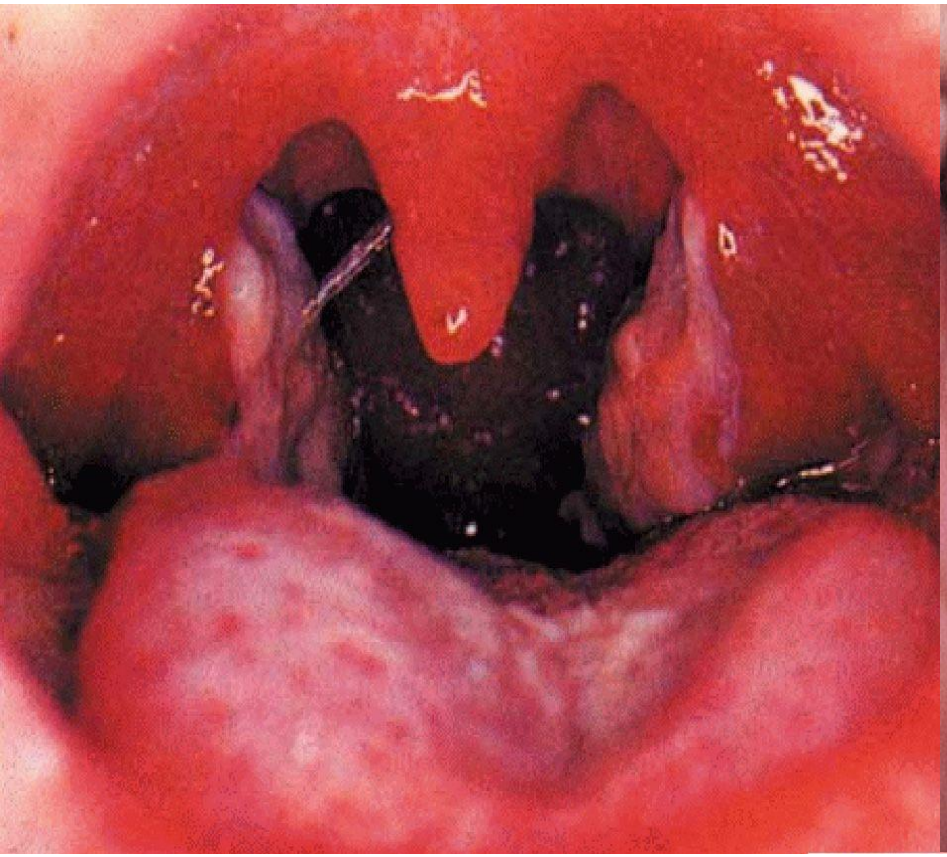


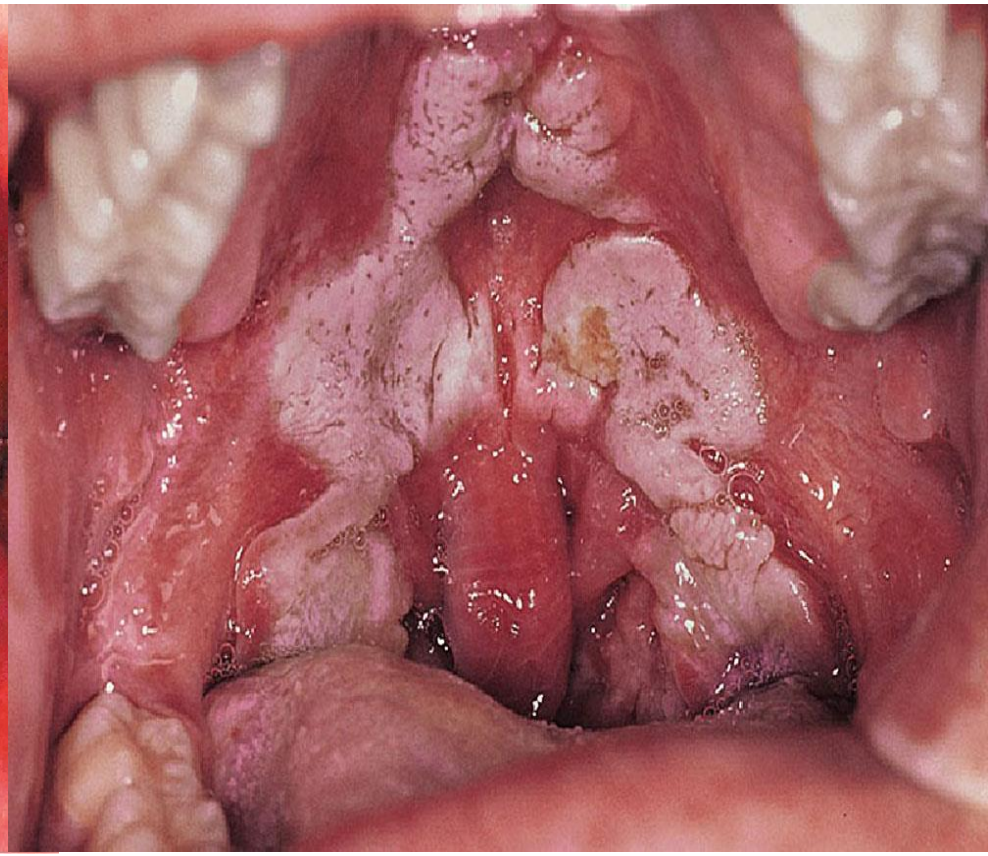
Measles enanthem **(whitish spots on the mucosa of the oral cavity).**



Giant cells pneumonia in measles. *(H-E stain).*

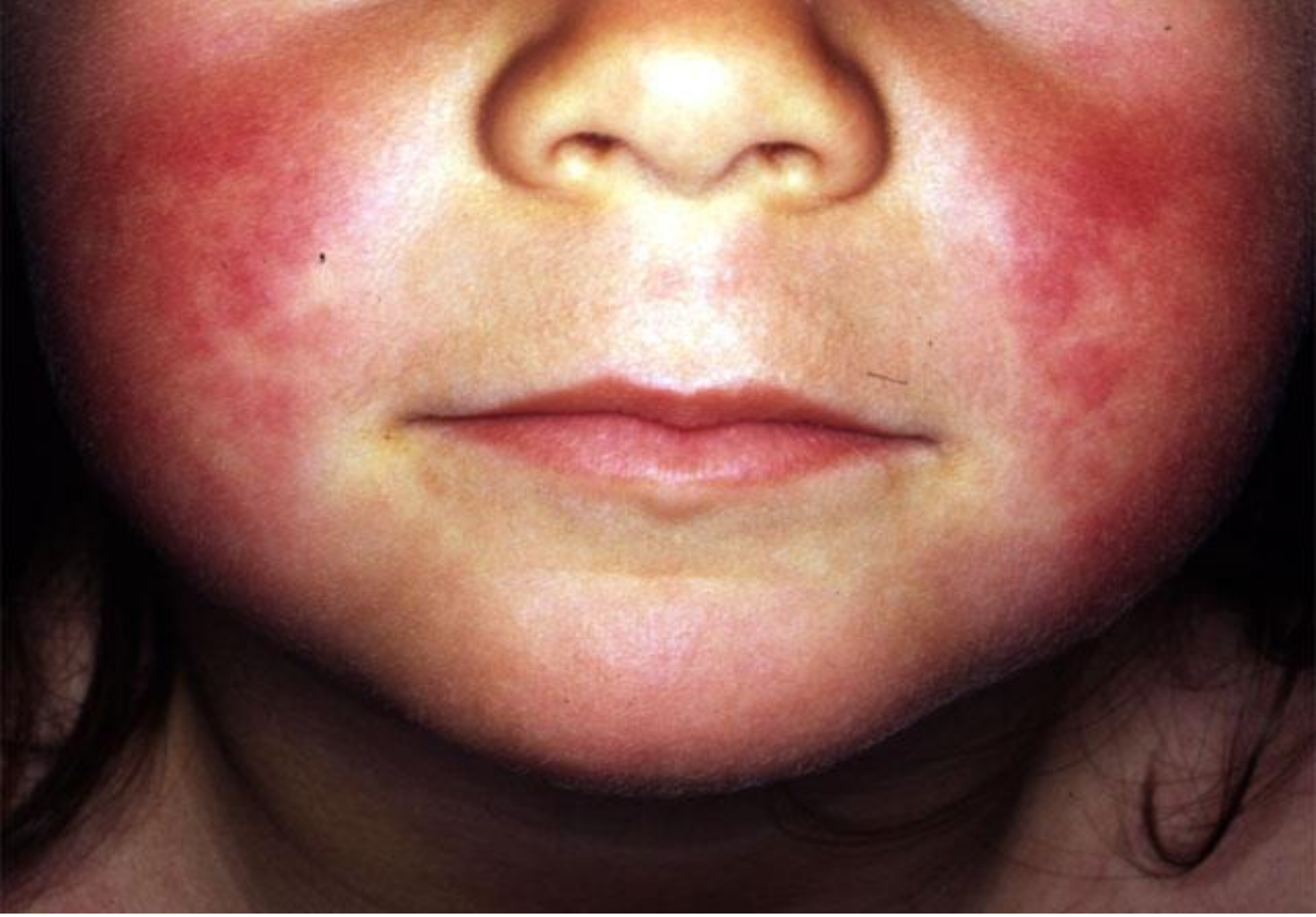
Diphtheritic (croupous) tracheitis.



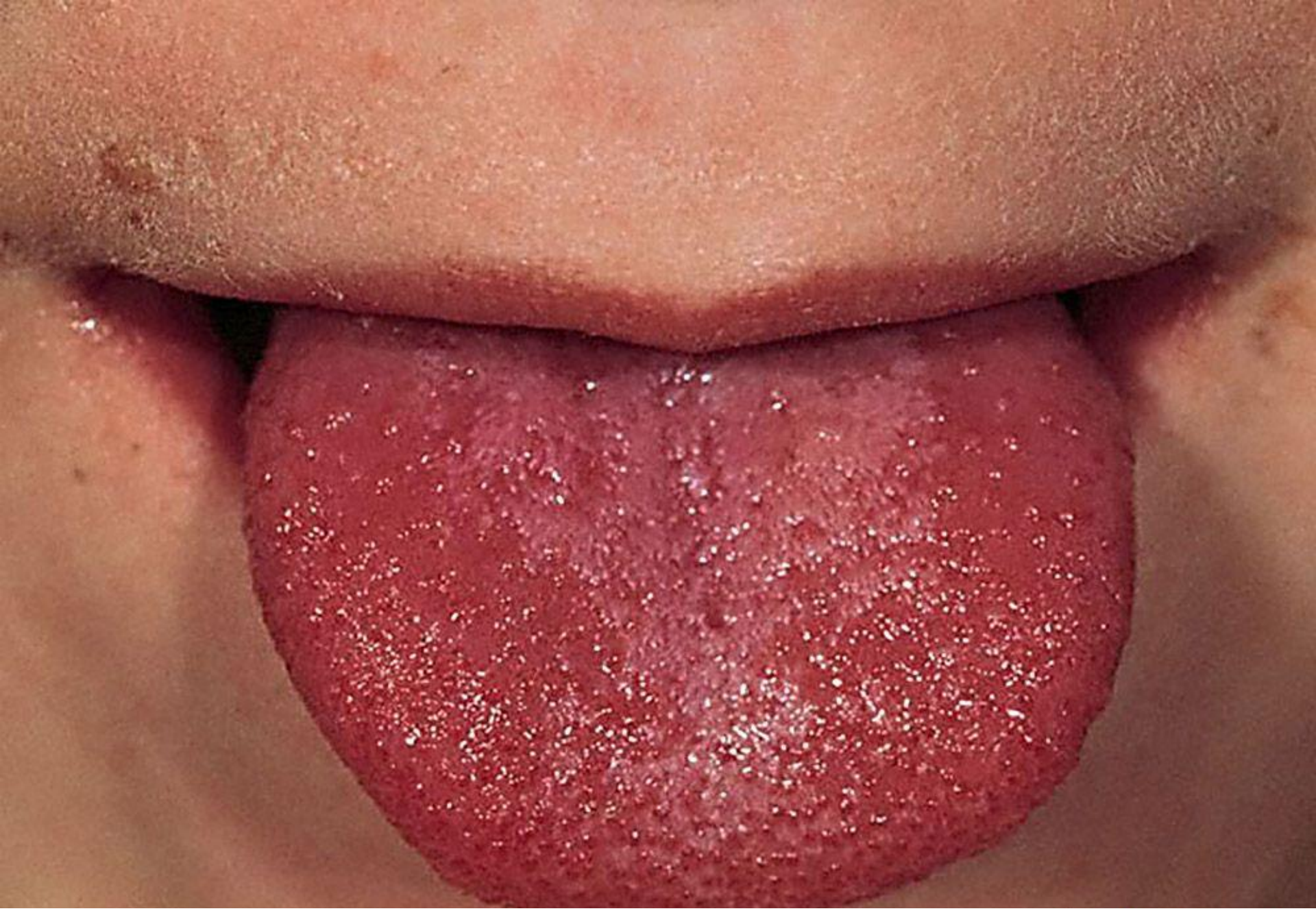


1 2

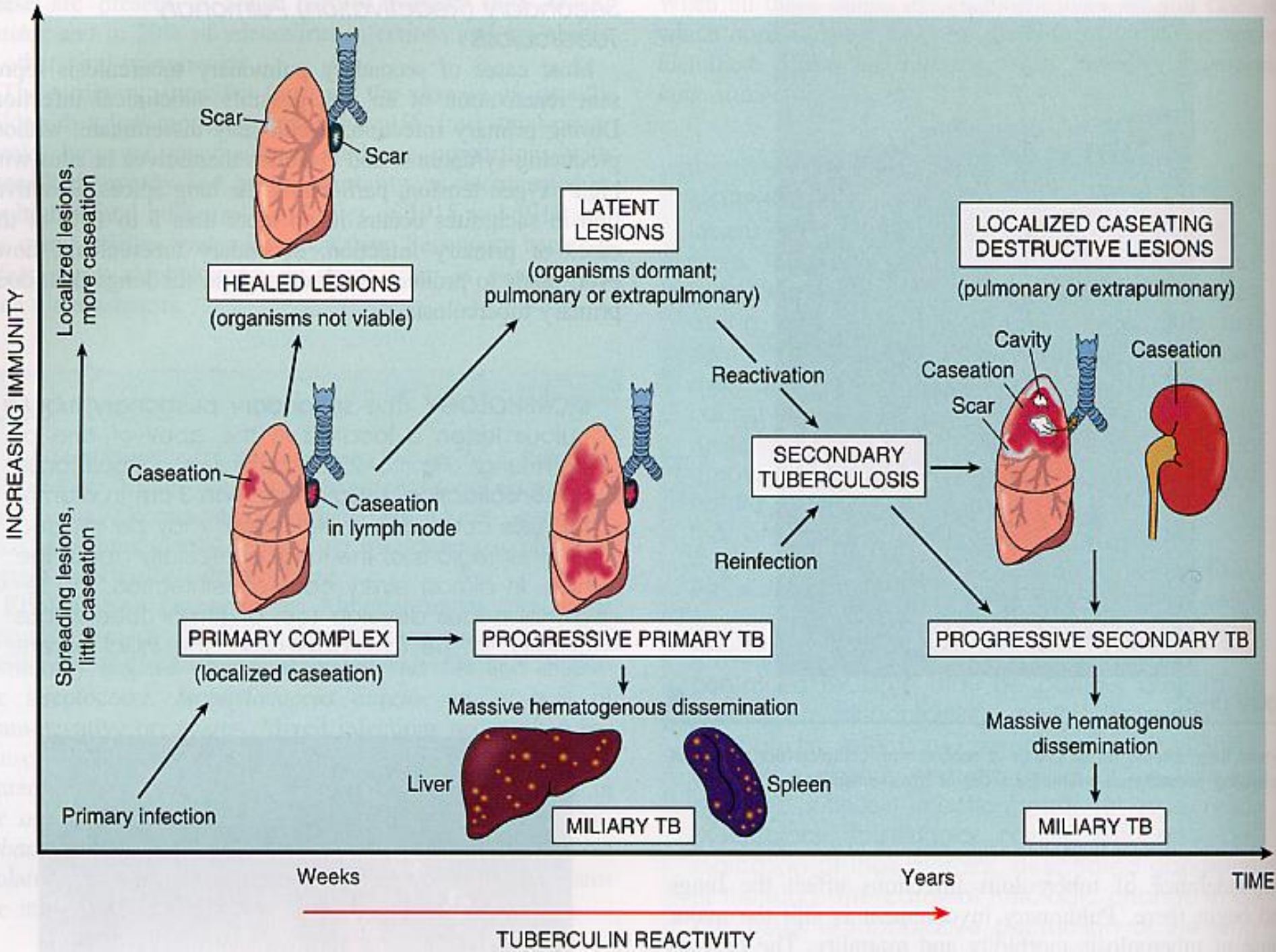
Pharyngeal diphtheria ***(1- localized form, 2 - toxic form)***

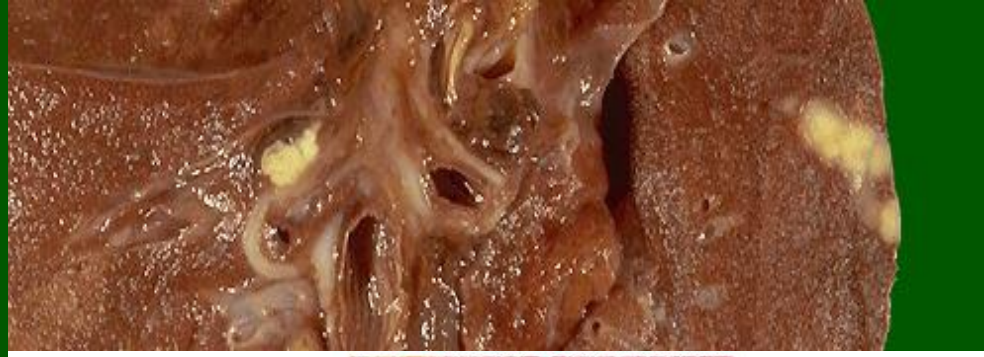


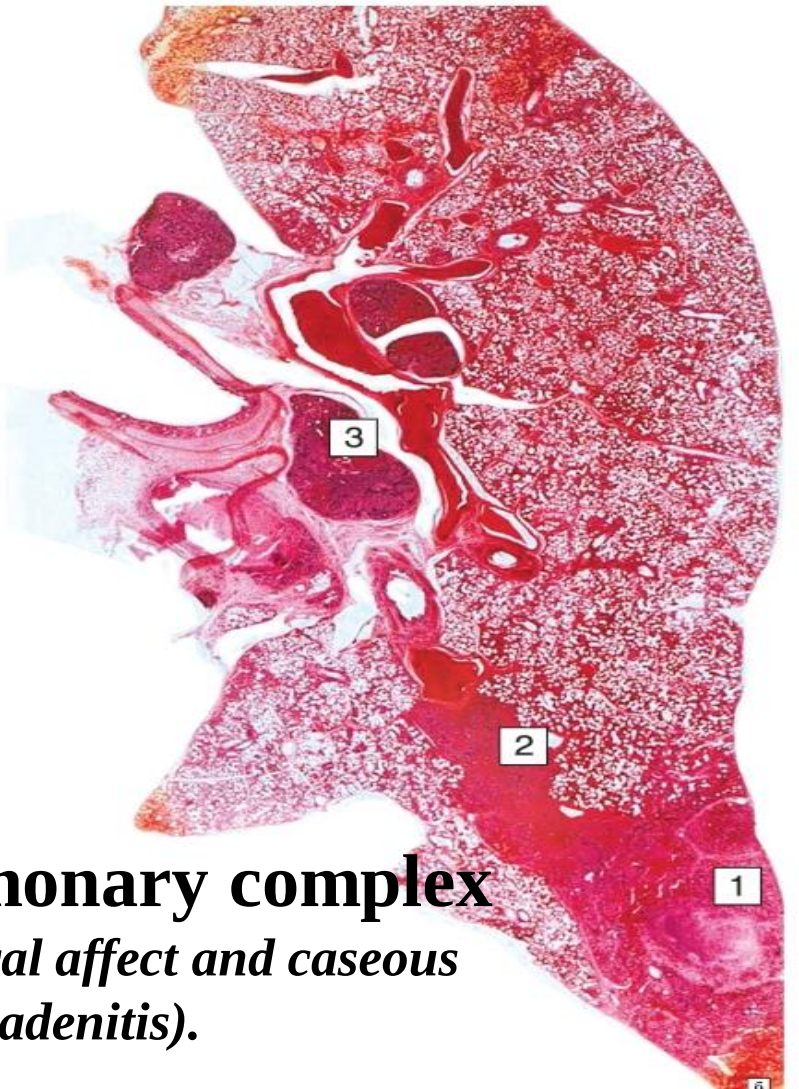
Scarlet fever, absence of rash around the lips.



Strawberry tongue in scarlet fever.

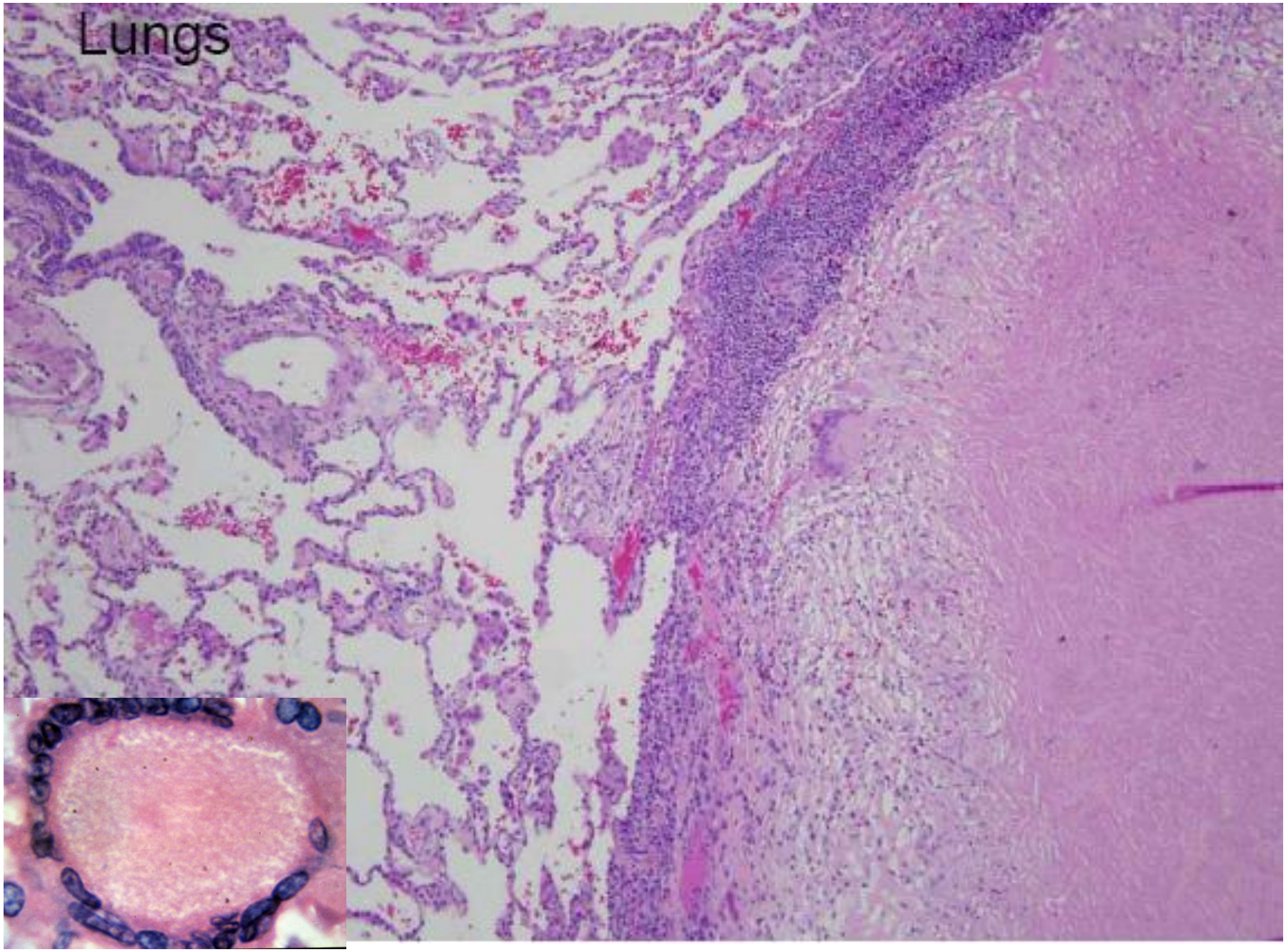

INCREASING IMMUNITY
Localized lesions, more caseation
Spreading lesions, little caseation
Scar
Scar
HEALED LESIONS
(organisms not viable)
LATENT LESIONS
(organisms dormant; pulmonary or extrapulmonary)
LOCALIZED CASEATING DESTRUCTIVE LESIONS
(pulmonary or extrapulmonary)
Reactivation
Cavity
Caseation
Caseation
Scar
Caseation
Caseation in lymph node
SECONDARY TUBERCULOSIS
Reinfection
PRIMARY COMPLEX
(localized caseation)
PROGRESSIVE PRIMARY TB
PROGRESSIVE SECONDARY TB
Massive hematogenous dissemination
Massive hematogenous dissemination
Liver
Spleen
MILIARY TB
MILIARY TB
Primary infection
Weeks
Years
TIME
TUBERCULIN REACTIVITY



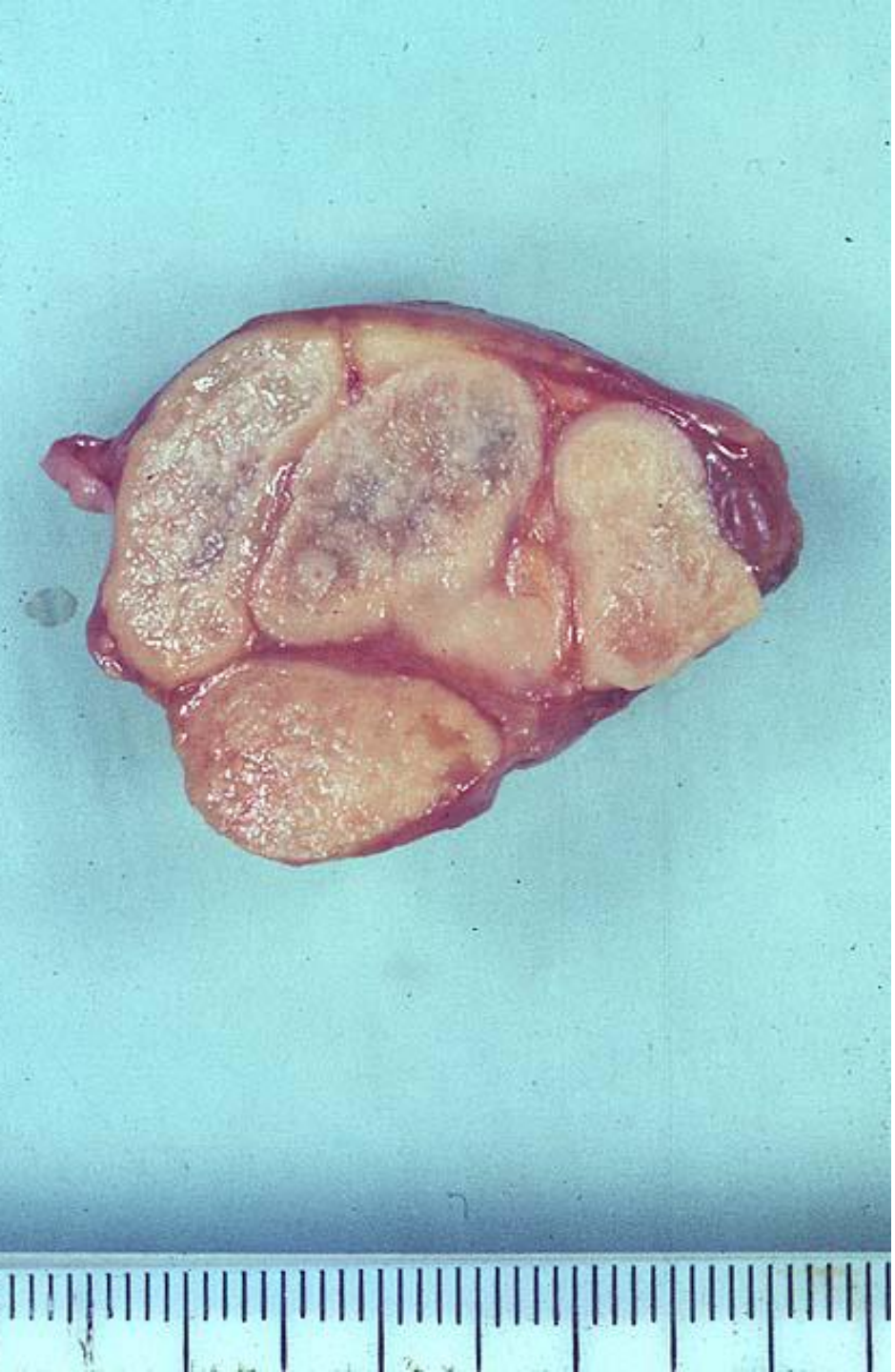


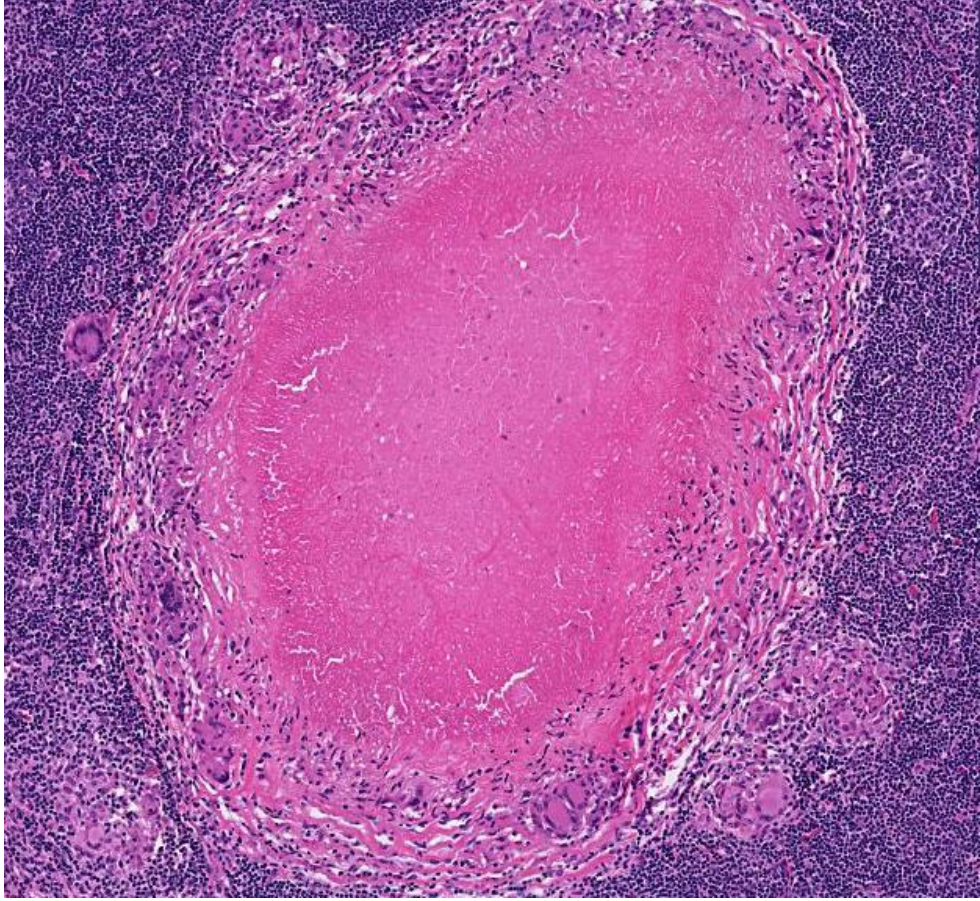
Primary pulmonary complex

(primary subpleural affect and caseous lymphadenitis).



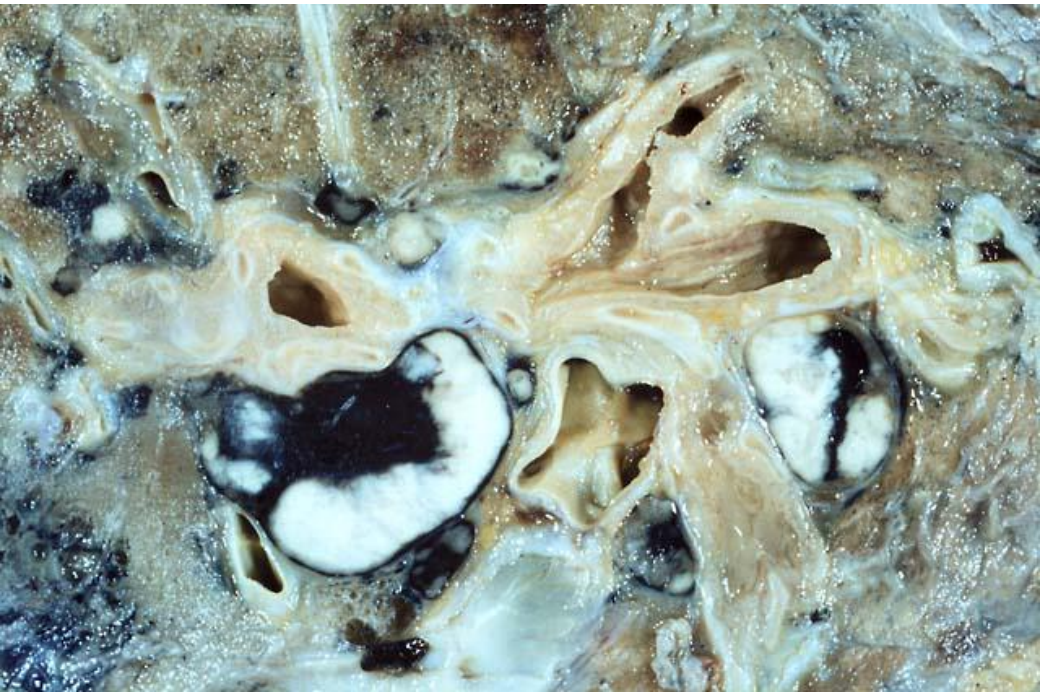
Primary pulmonary affect.



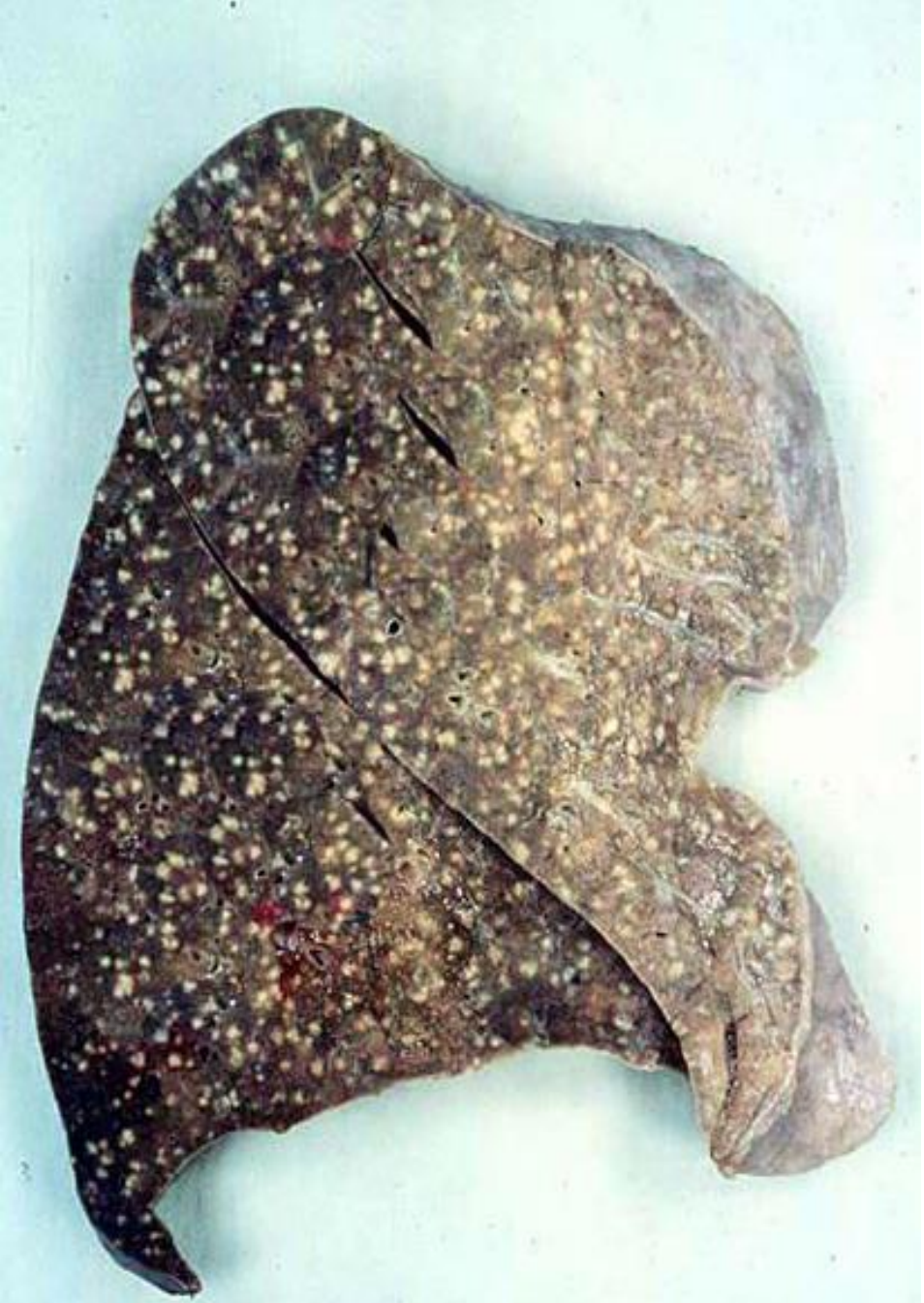


Tuberculous lymphadenitis.

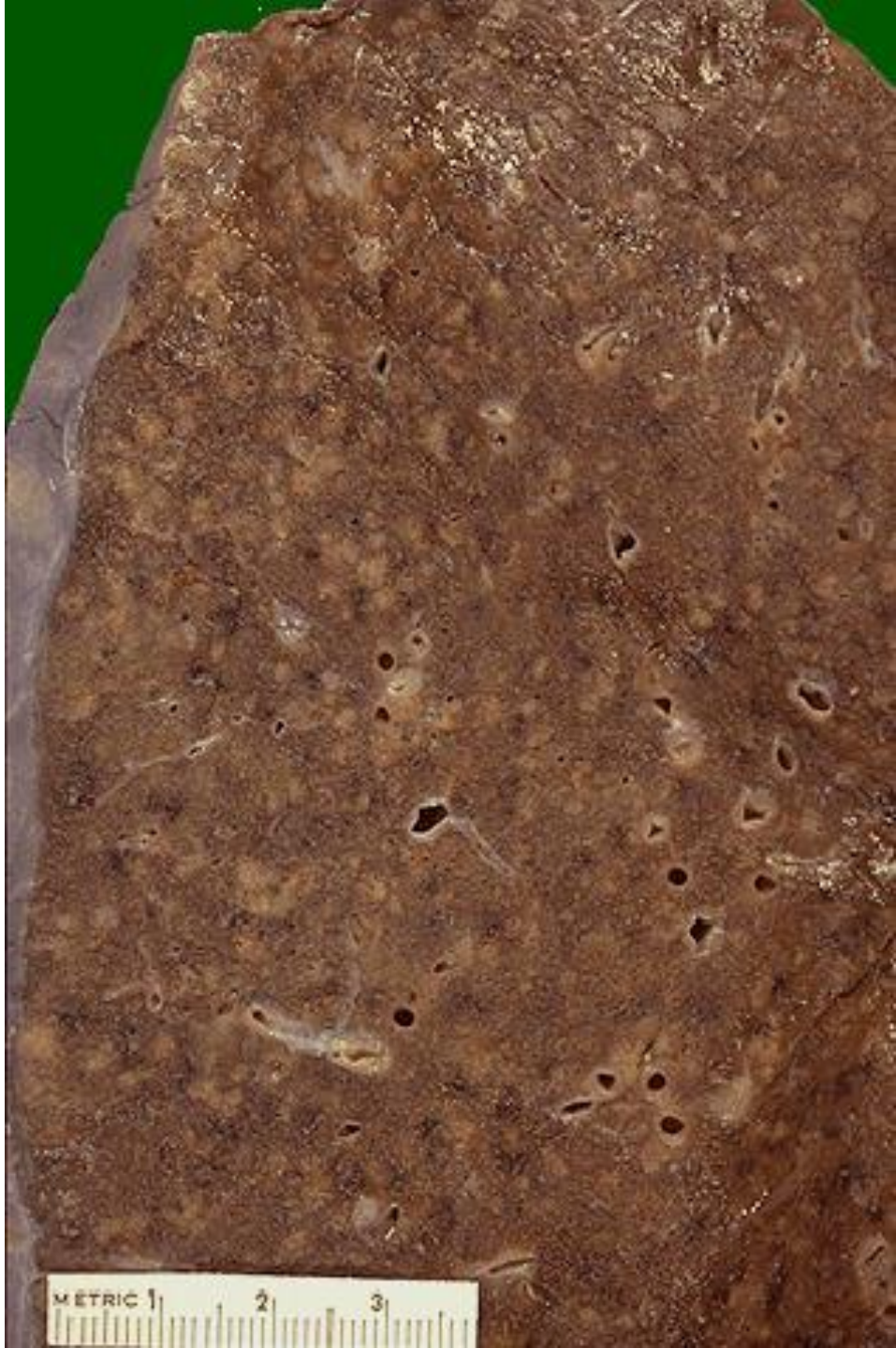
Primary intestinal complex.

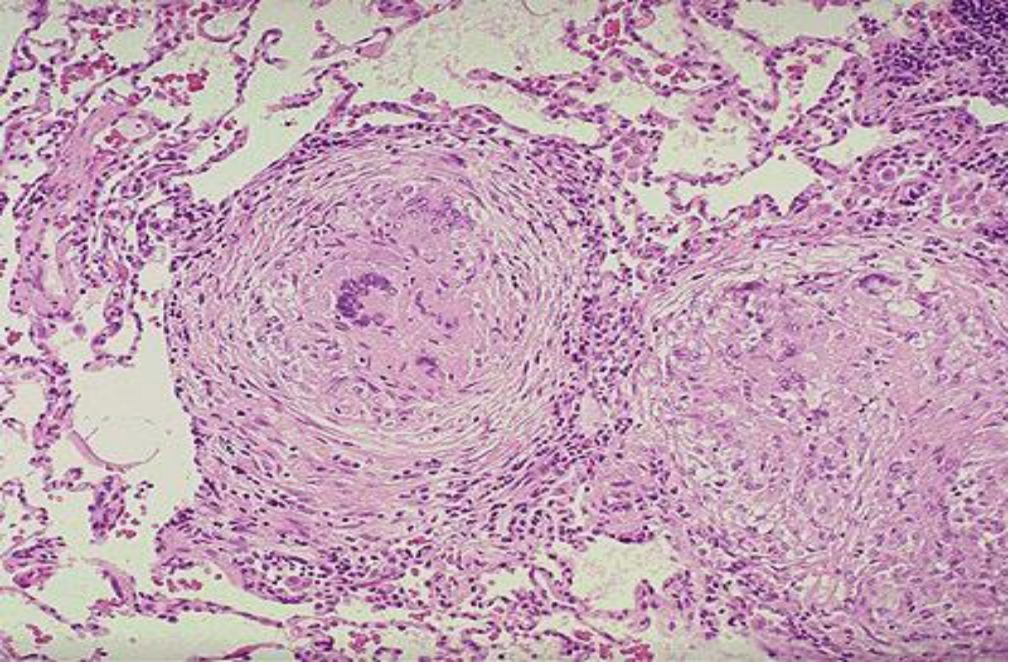


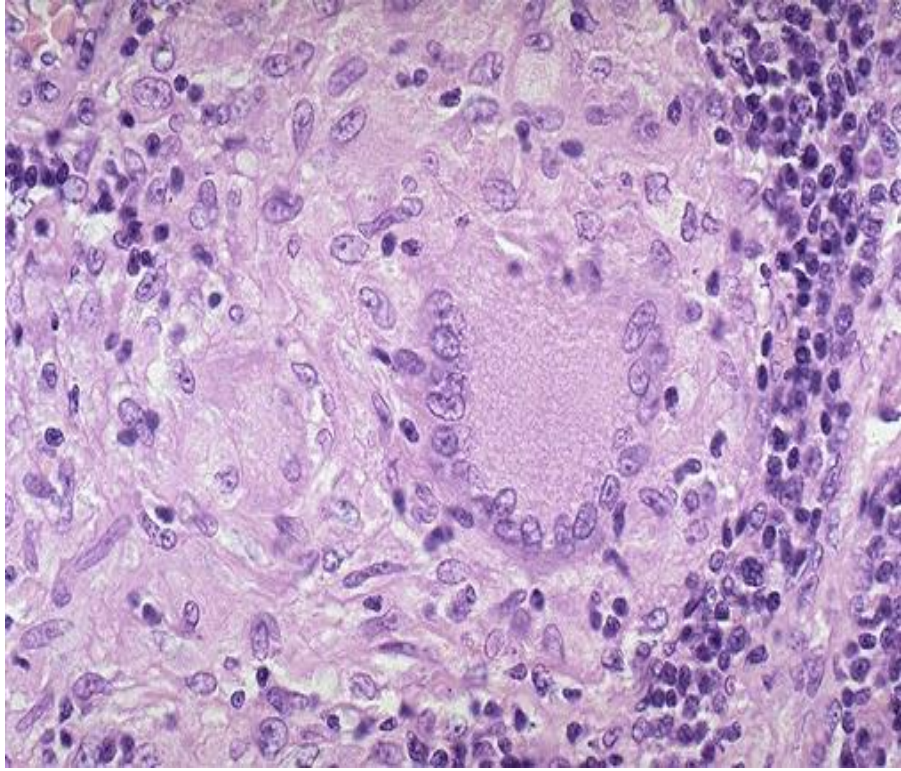
Healed primary complex *(sclerosis of the primary affect and calcinosis of lymph nodes).*

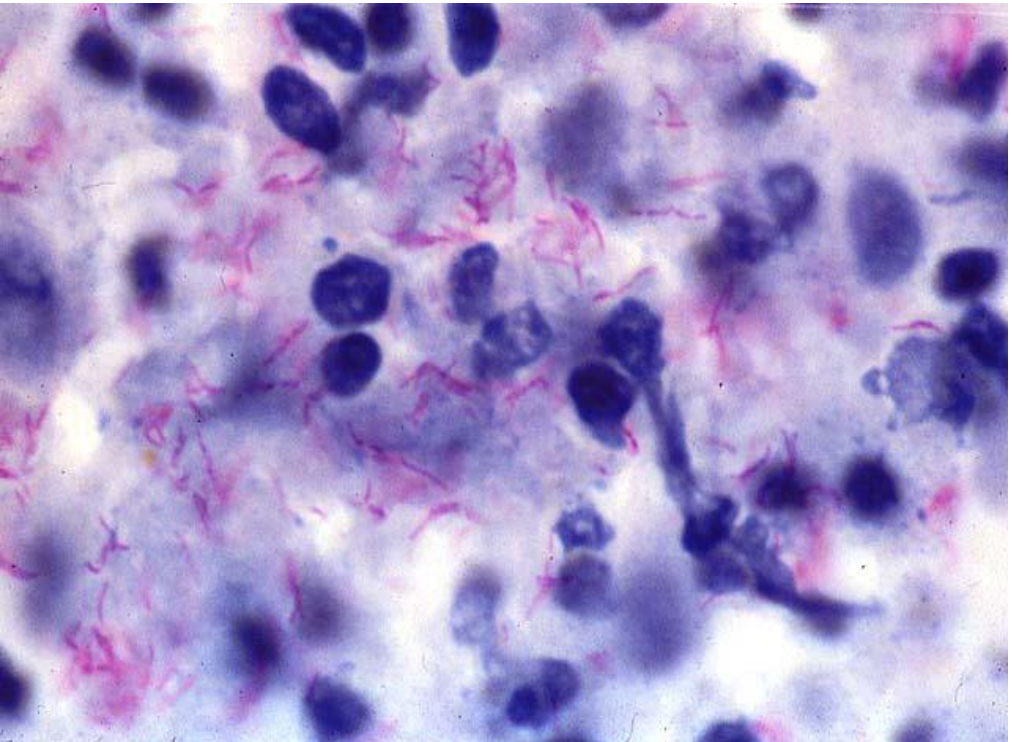


Pulmonary miliary tuberculosis.

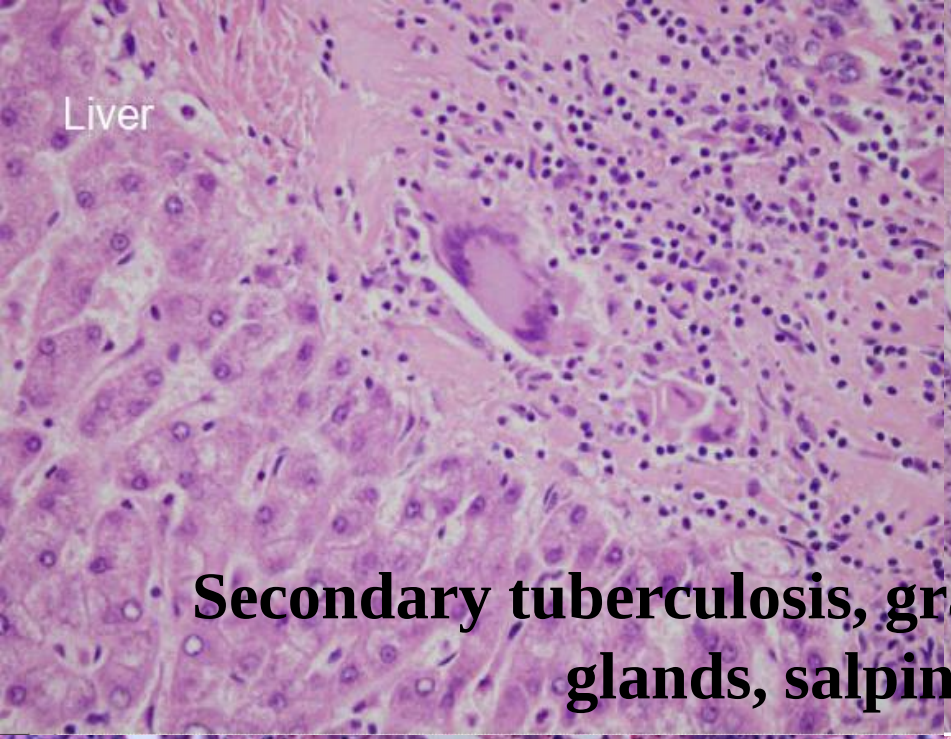


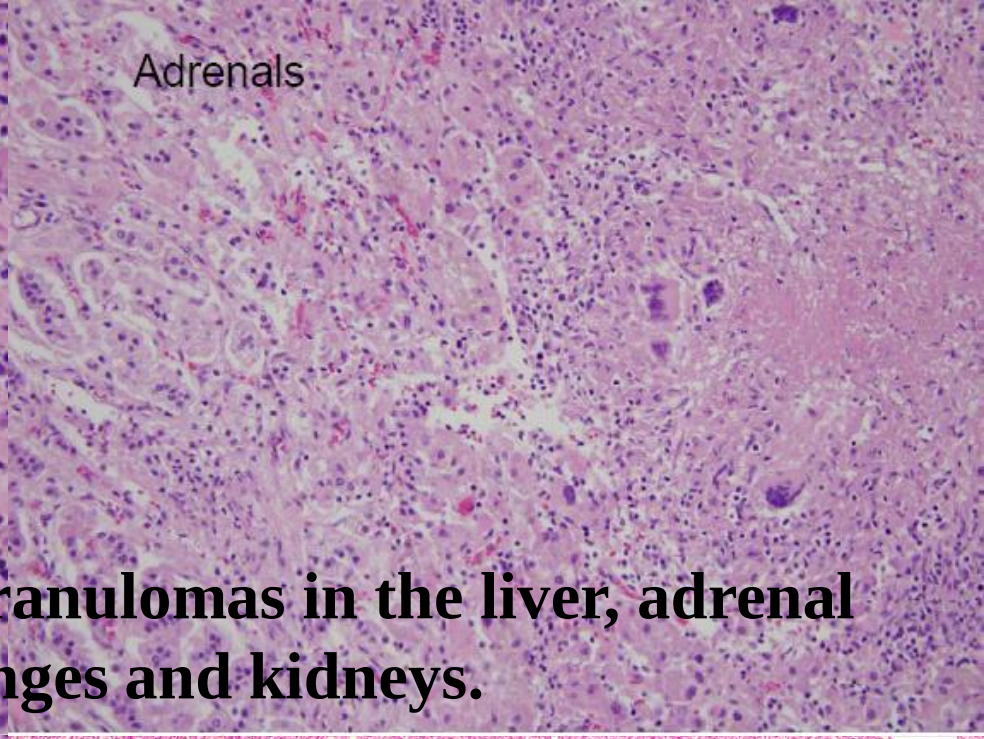




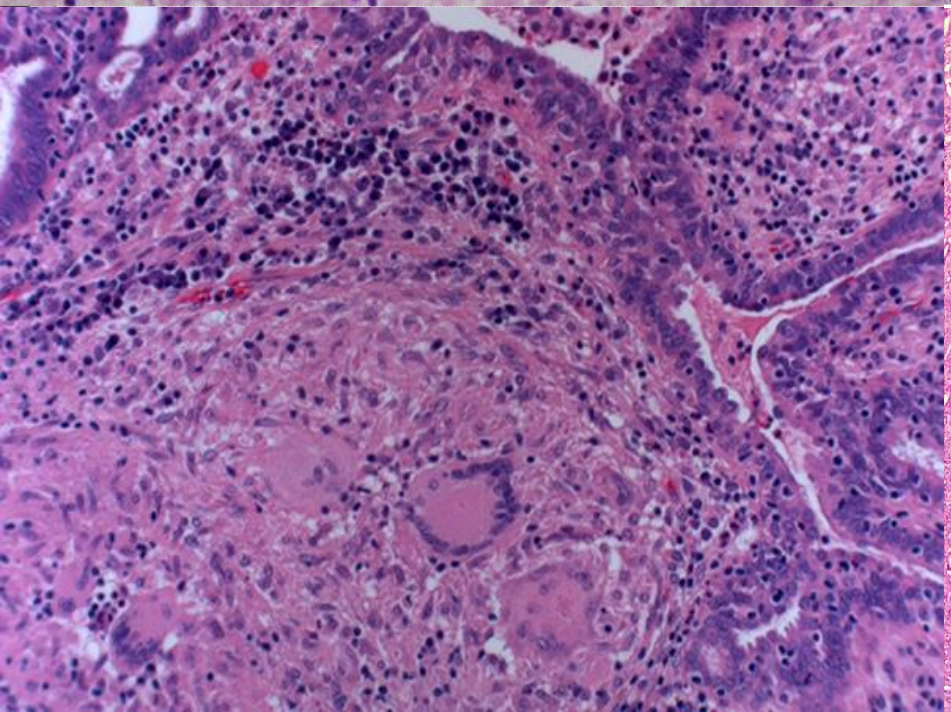


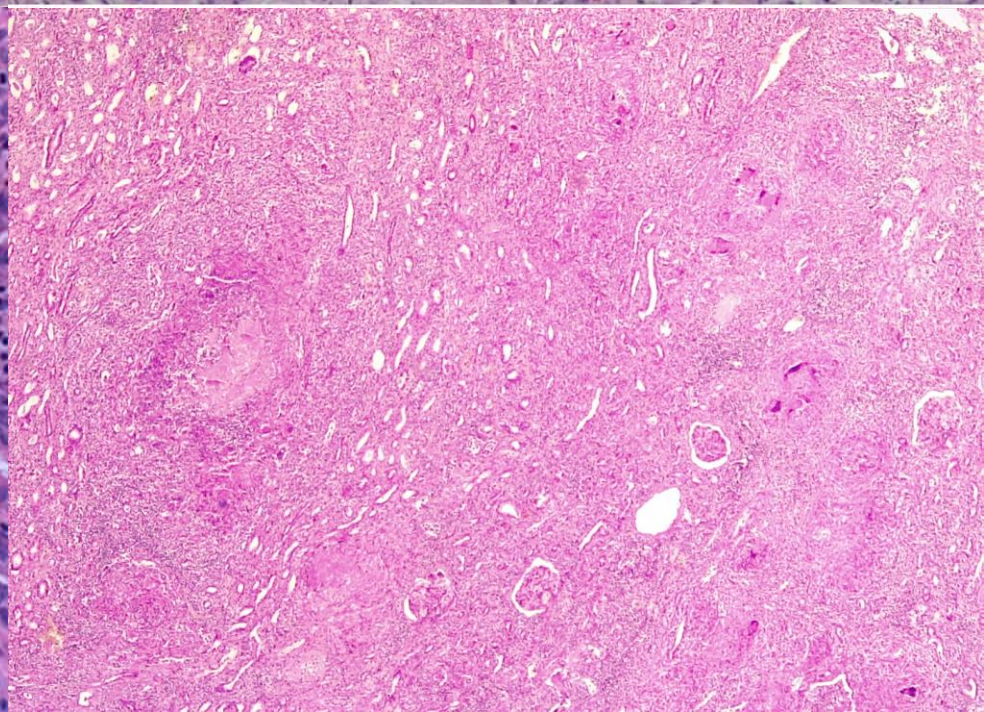
Tuberculous granulomas with giant Langhans cells, mycobacteria.
(Ziehl-Nielsen stain).

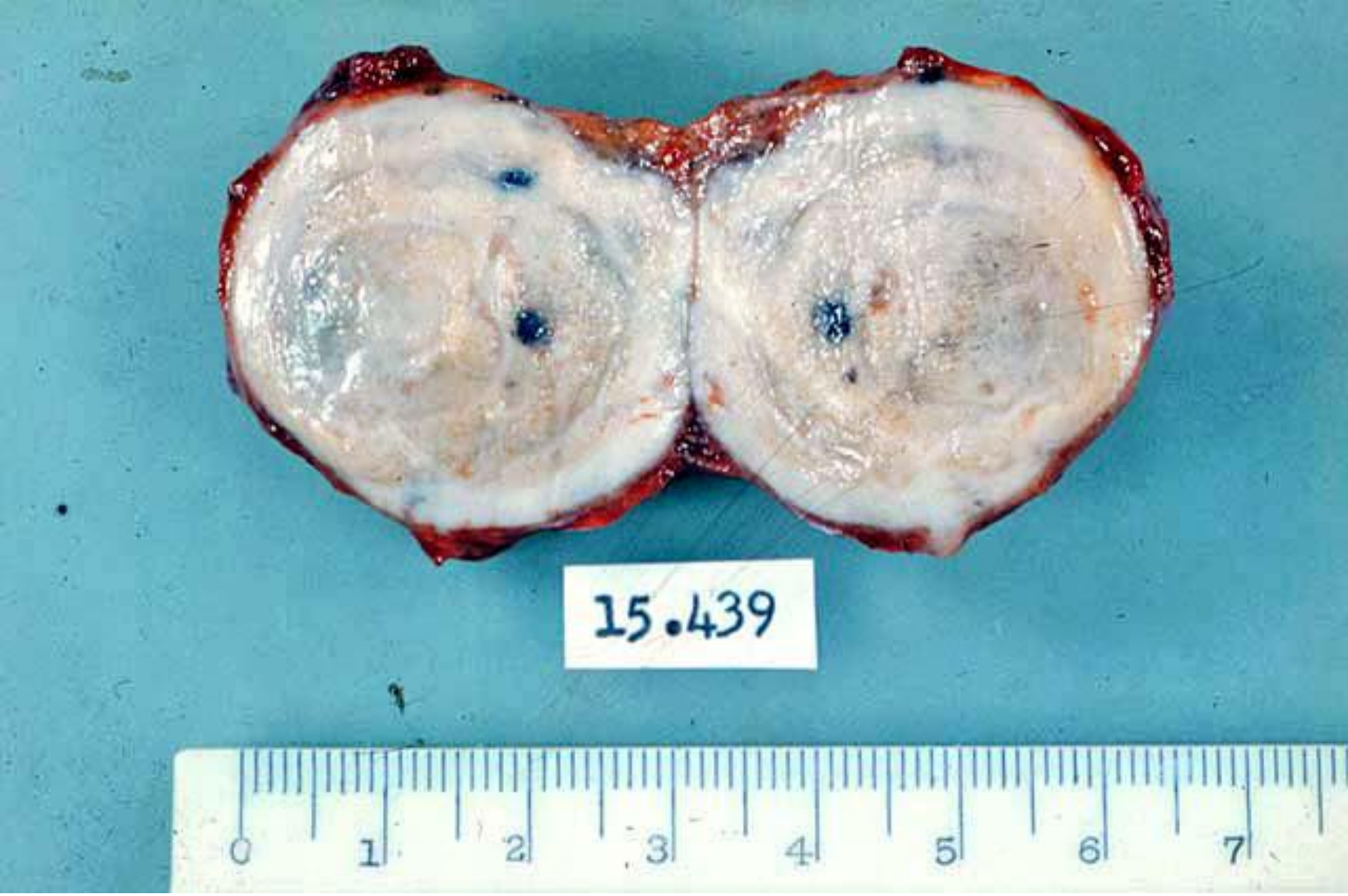




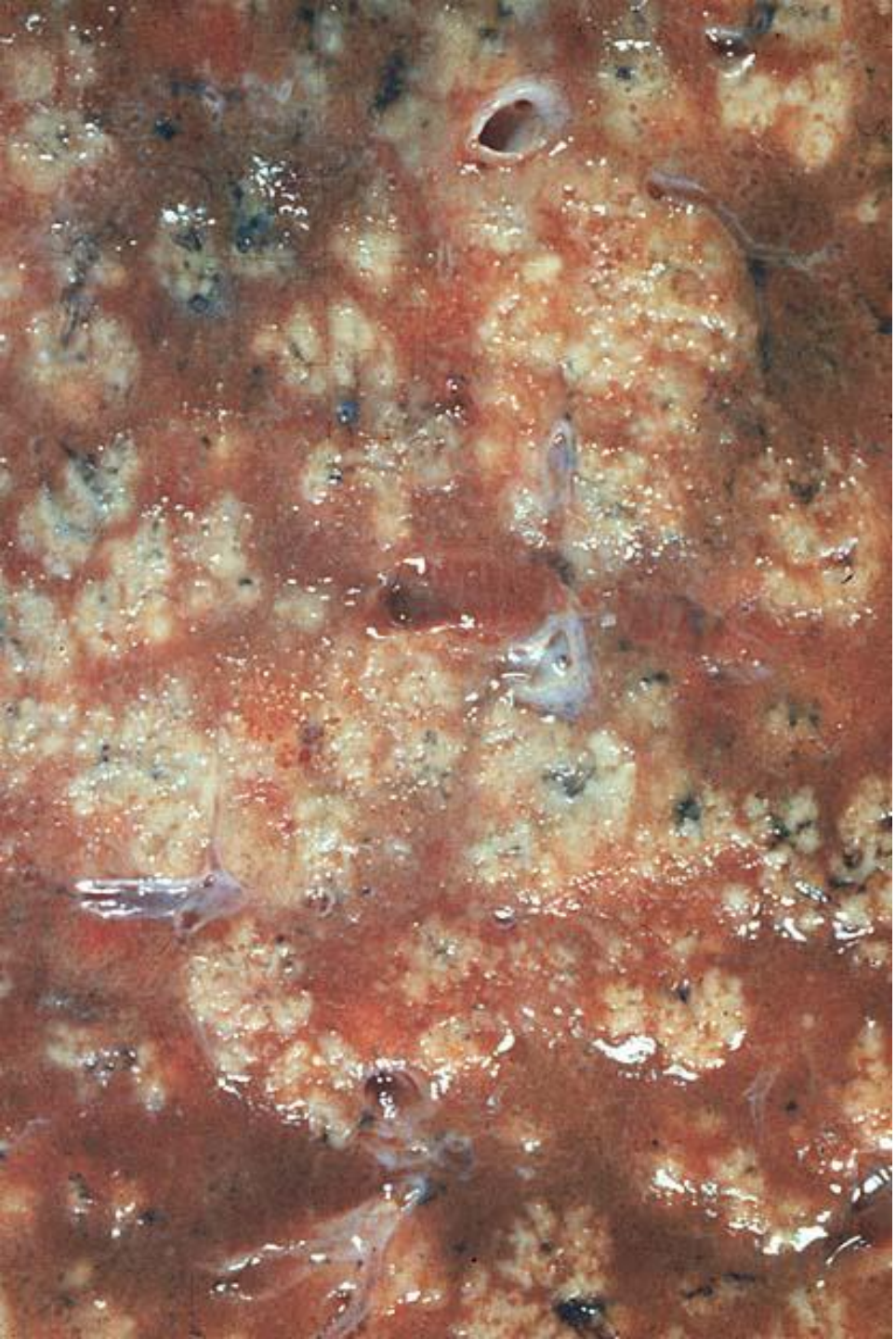
Secondary tuberculosis, granulomas in the liver, adrenal glands, salpinges and kidneys.

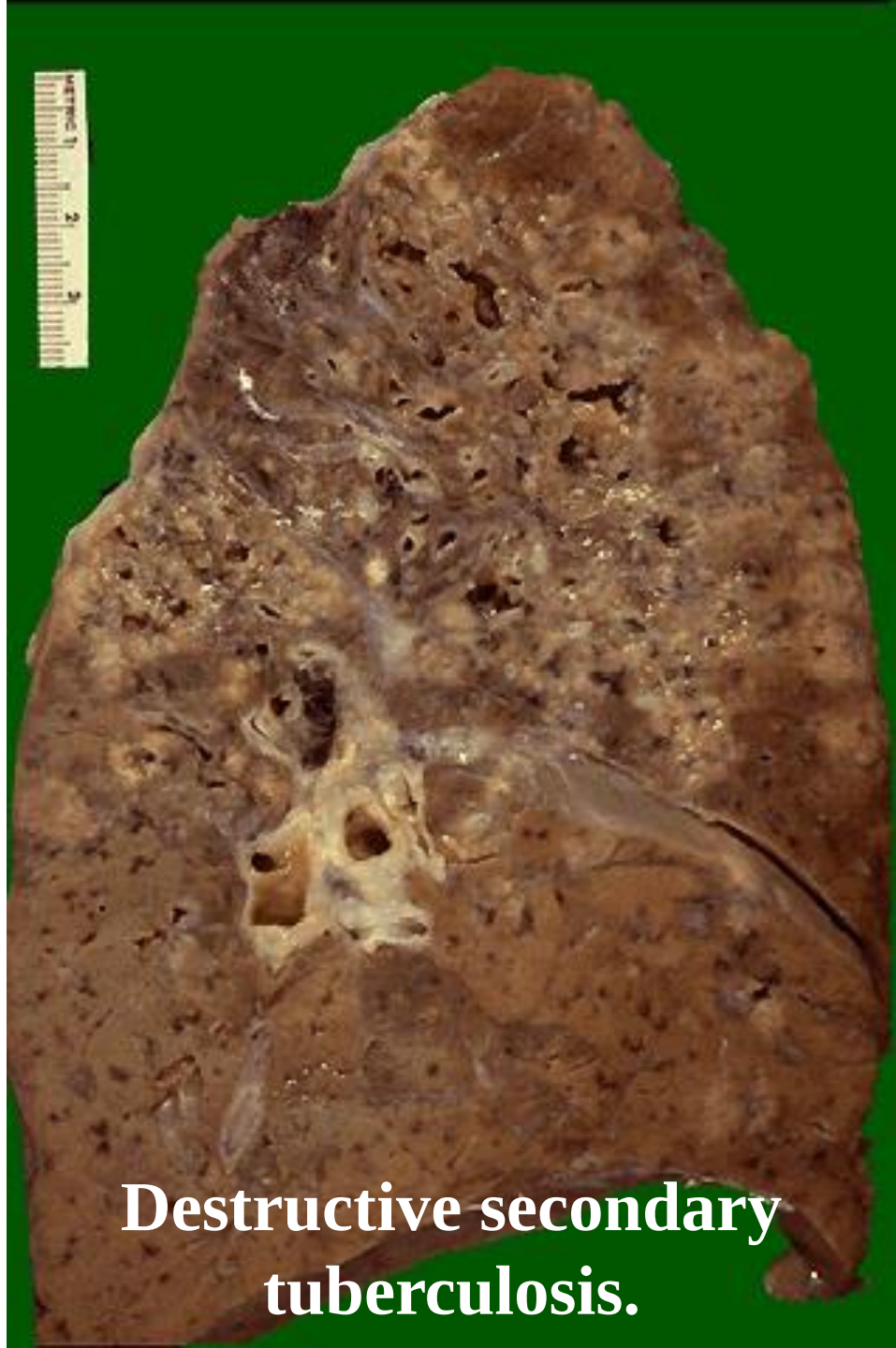




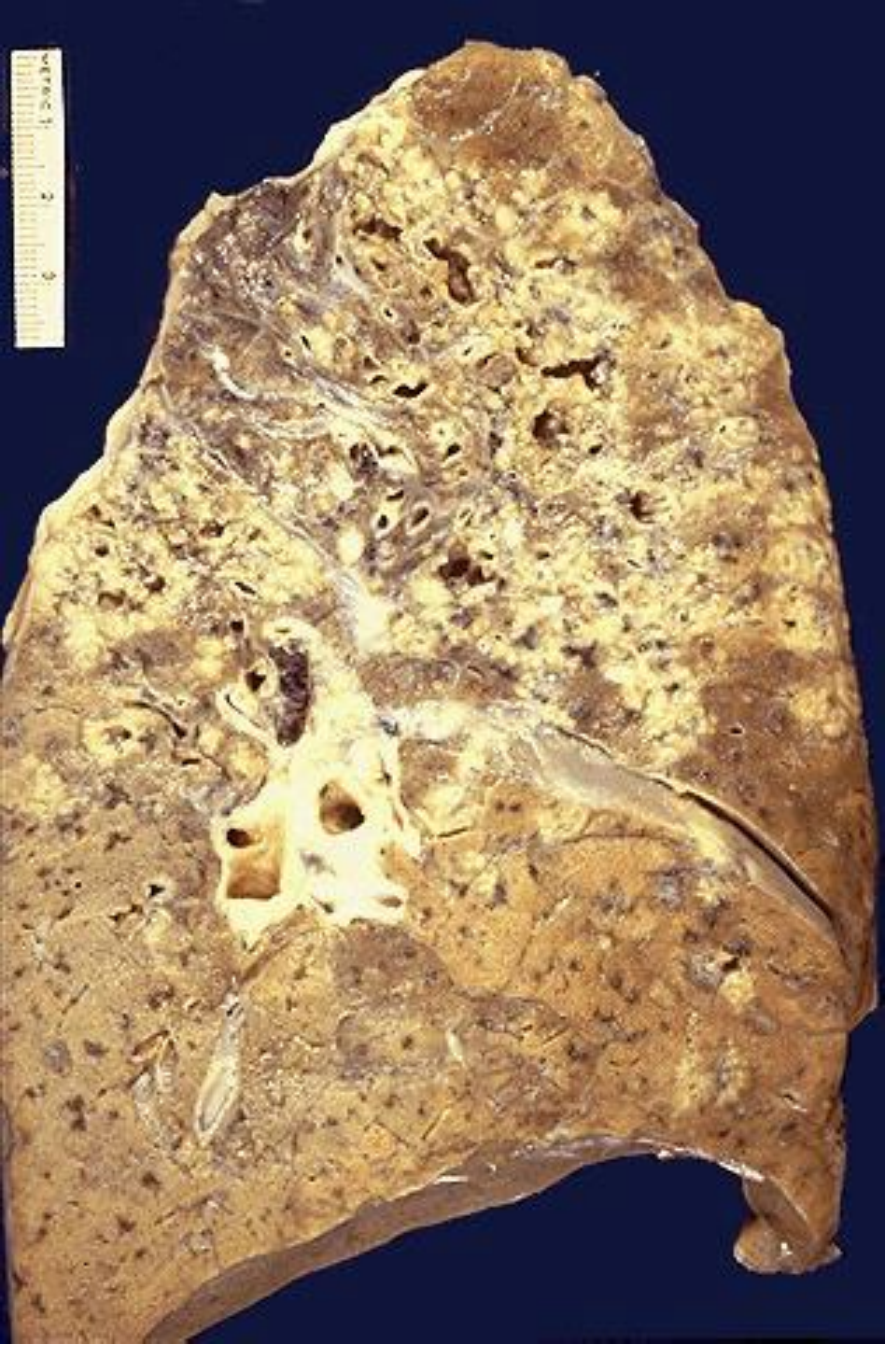


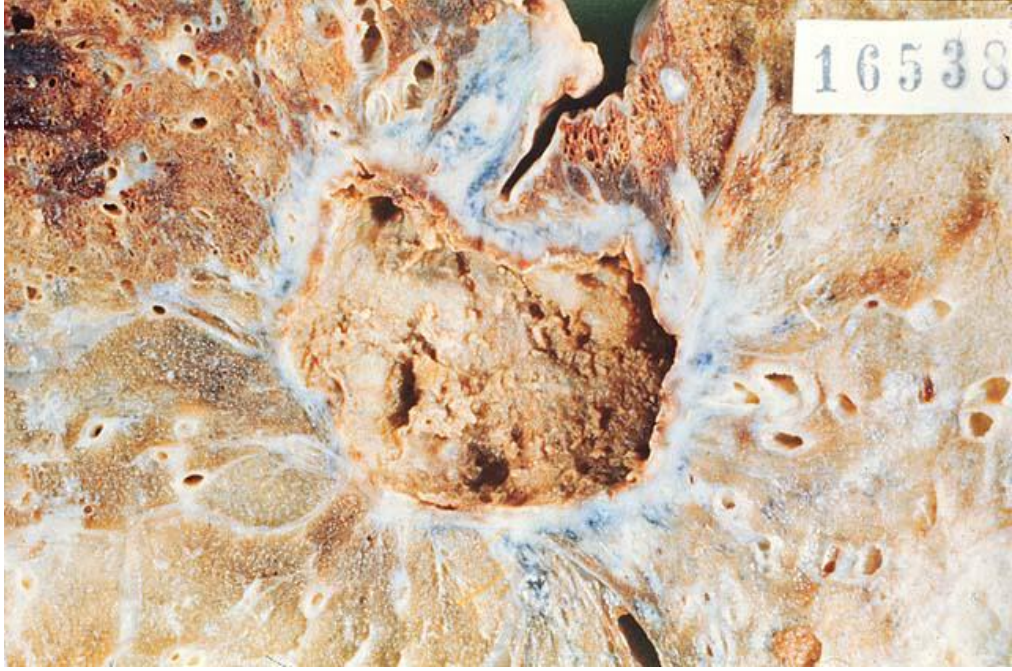
Encapsulated pulmonary tuberculoma.

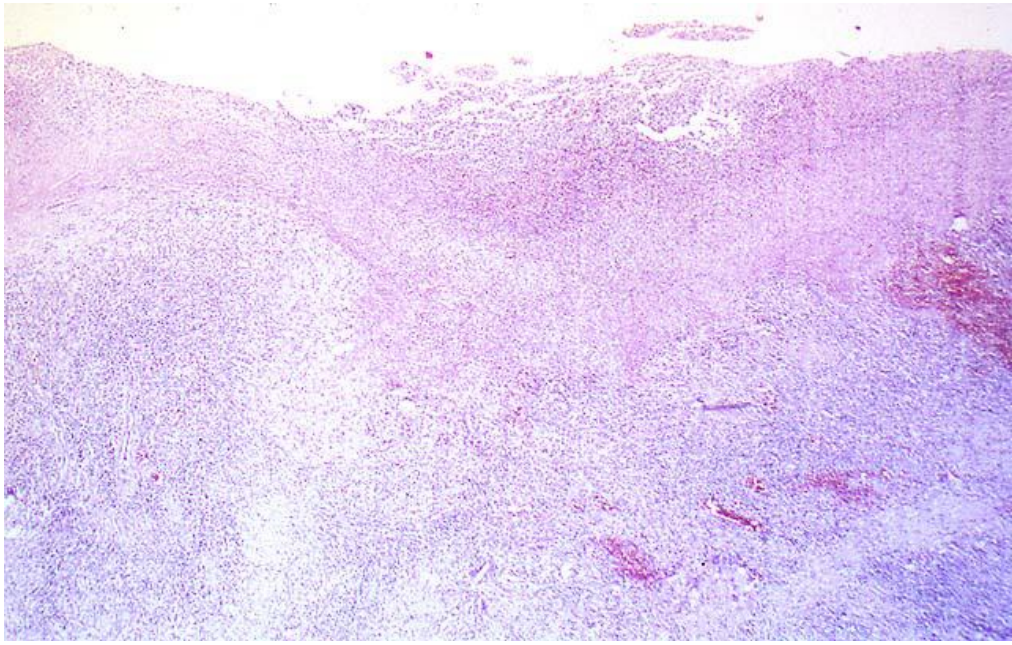




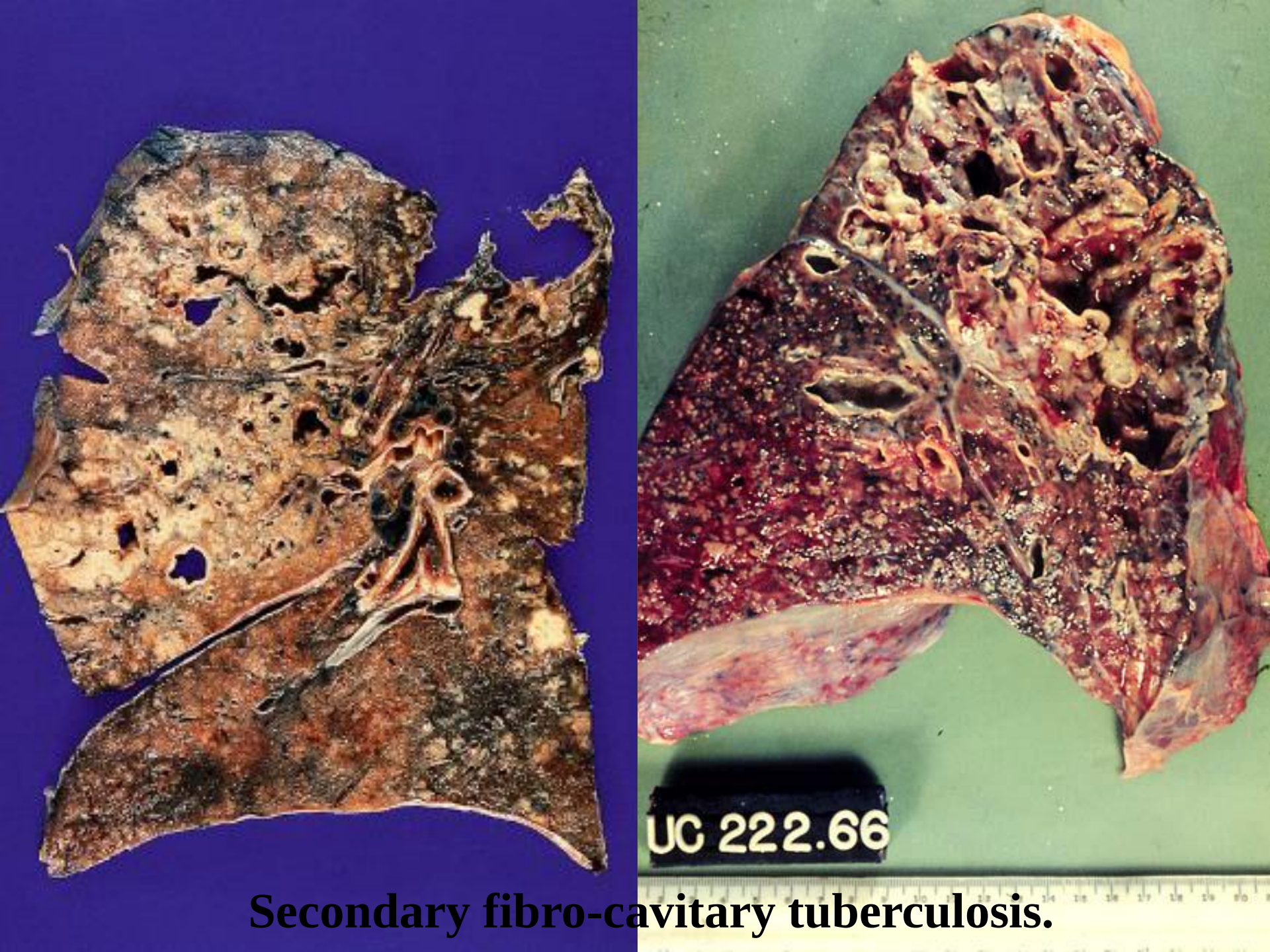
Destructive secondary tuberculosis.



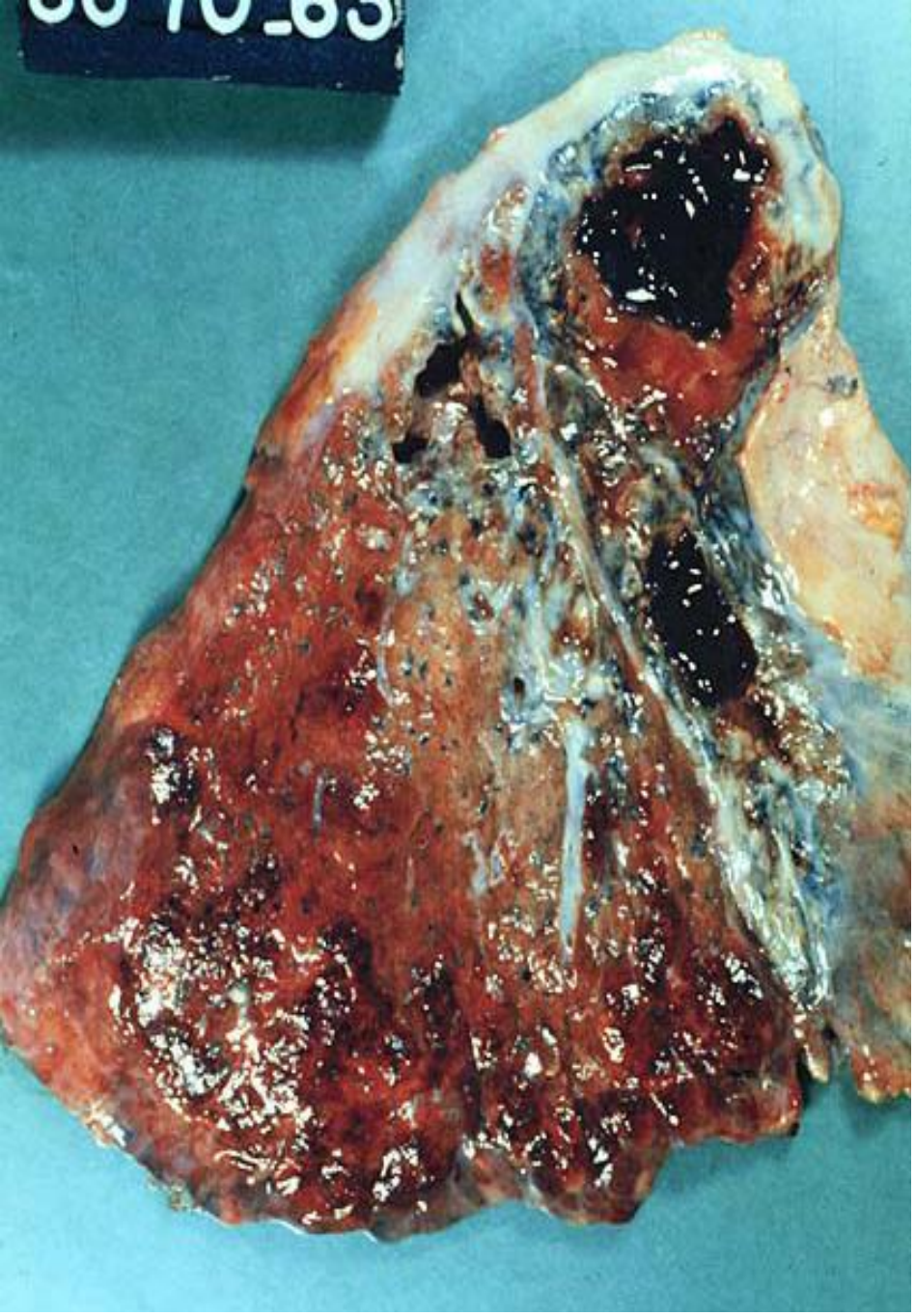


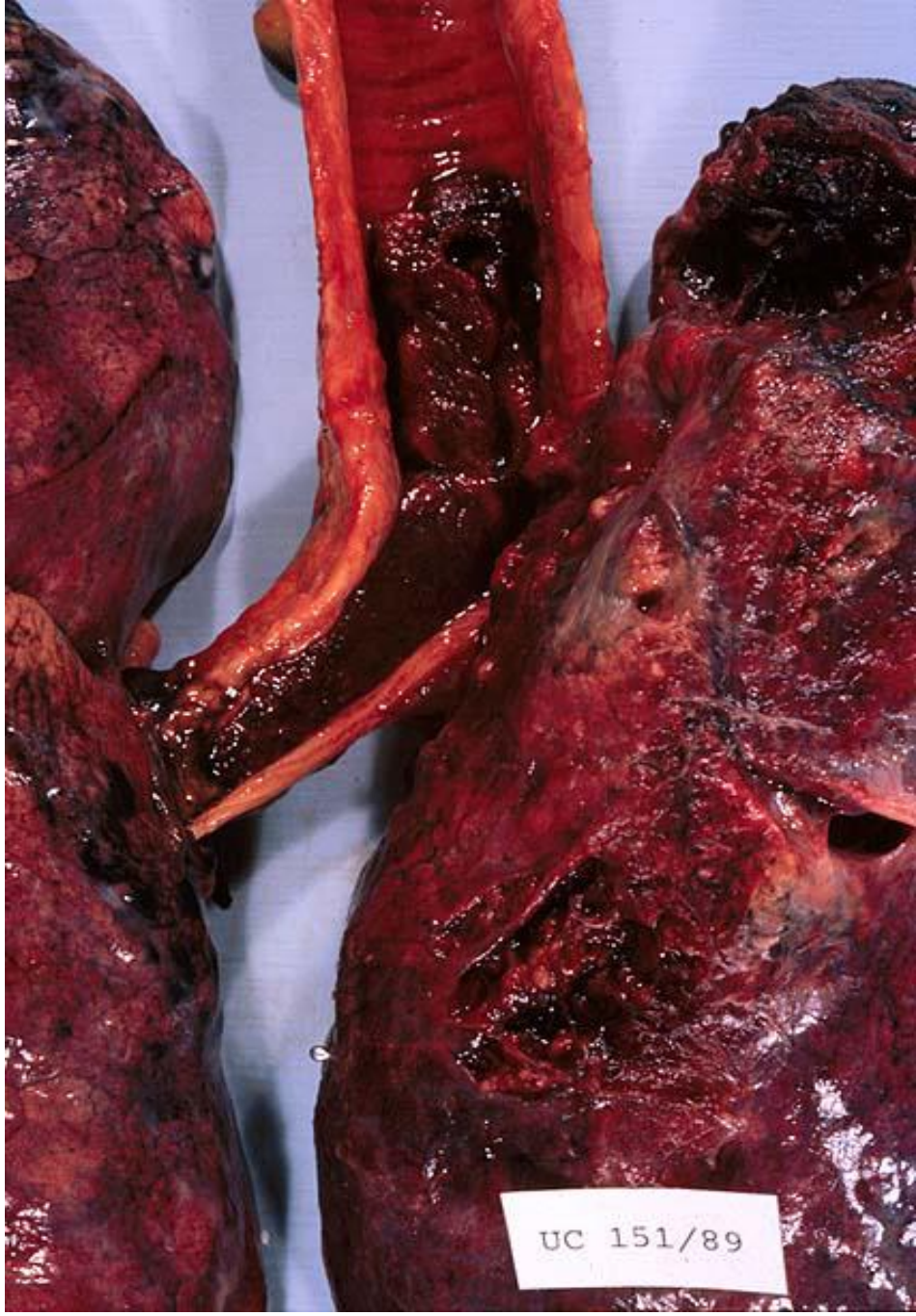


Secondary fibro-cavitary tuberculosis, cavity wall.

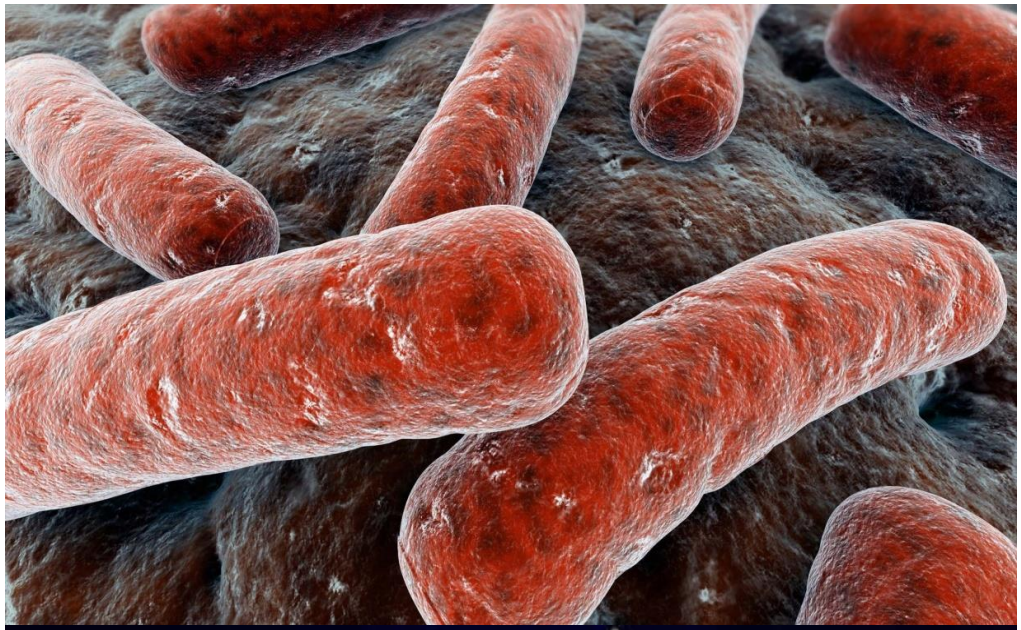


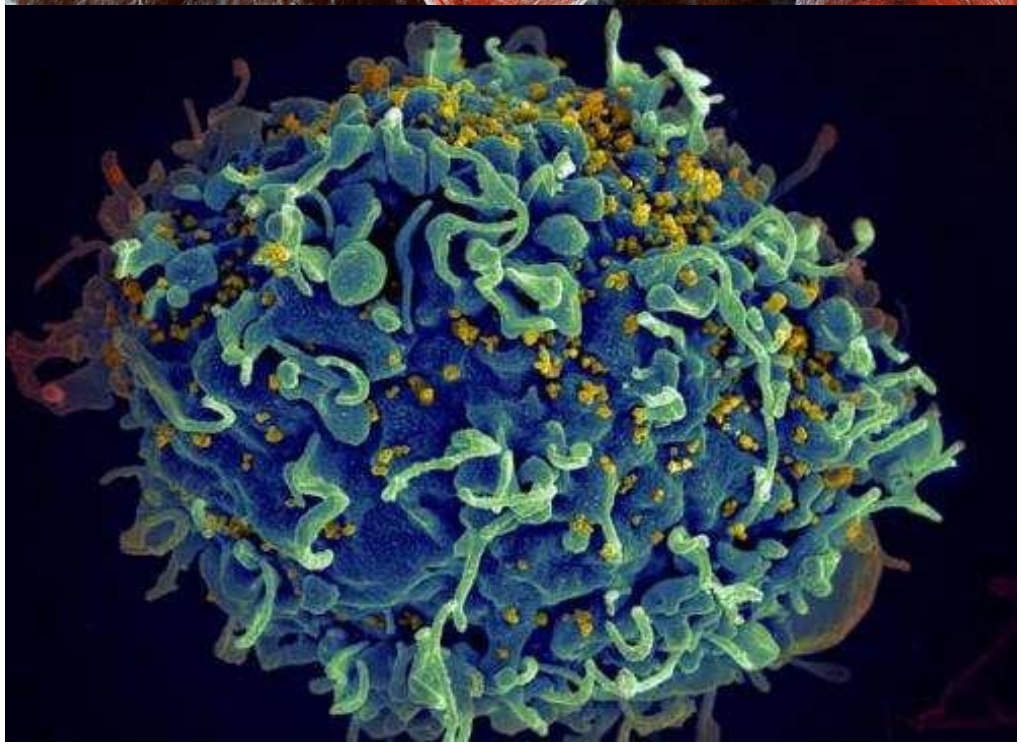
Secondary fibro-cavitary tuberculosis.





Pulmonary fibro-cavitary tuberculosis with hemorrhage.





Tuberculosis.
AIDS.
Aerogenic infections.

Introduction :

- Infects 1/3 to ½ of world population..!
- 3 million deaths due to TB every year
- Under privileged population -
  - Crowding, Poverty, malnutrition.
- Since 1985 incidence is increasing in west
  - AIDS, Diabetes, Immunosuppressed patients, Drug resistance.

- Tuberculosis (TB) remains the leading cause of death worldwide from a single infectious disease agent. Indeed up to ***1/2 of the world's population*** is infected with TB. The registered number of new cases of TB worldwide roughly correlates with economic conditions: the highest incidences are seen in those countries of Africa, Asia, and Latin America with the lowest gross national products. WHO estimates that eight million people get TB every year, of whom 95% live in developing countries. An estimated 2 million people die from TB every year.

- It is estimated that between 2000 and 2021, nearly **one billion** people will be newly infected, 200 million people will get sick, and **35 million will die** from TB - if control is not further strengthened. The mechanisms, pathogenesis, and prophylaxis knowledge is minimal. After a century of decline TB is increasing and there are strains emerging which are resistant to antibiotics. This excess of cases is attributable to the changes in the social structure in cities, the human immunodeficiency virus epidemic, and failure of most cities to improve public health programs, and the economic cost of treating.

- With the increased incidence of AIDS, TB has become more a problem in the U.S., and the world.
- It is currently estimated that 1/2 of the world's population (3.1 billion) is infected with *Mycobacterium tuberculosis*. *Mycobacterium avium* complex is associated with AIDS related TB.

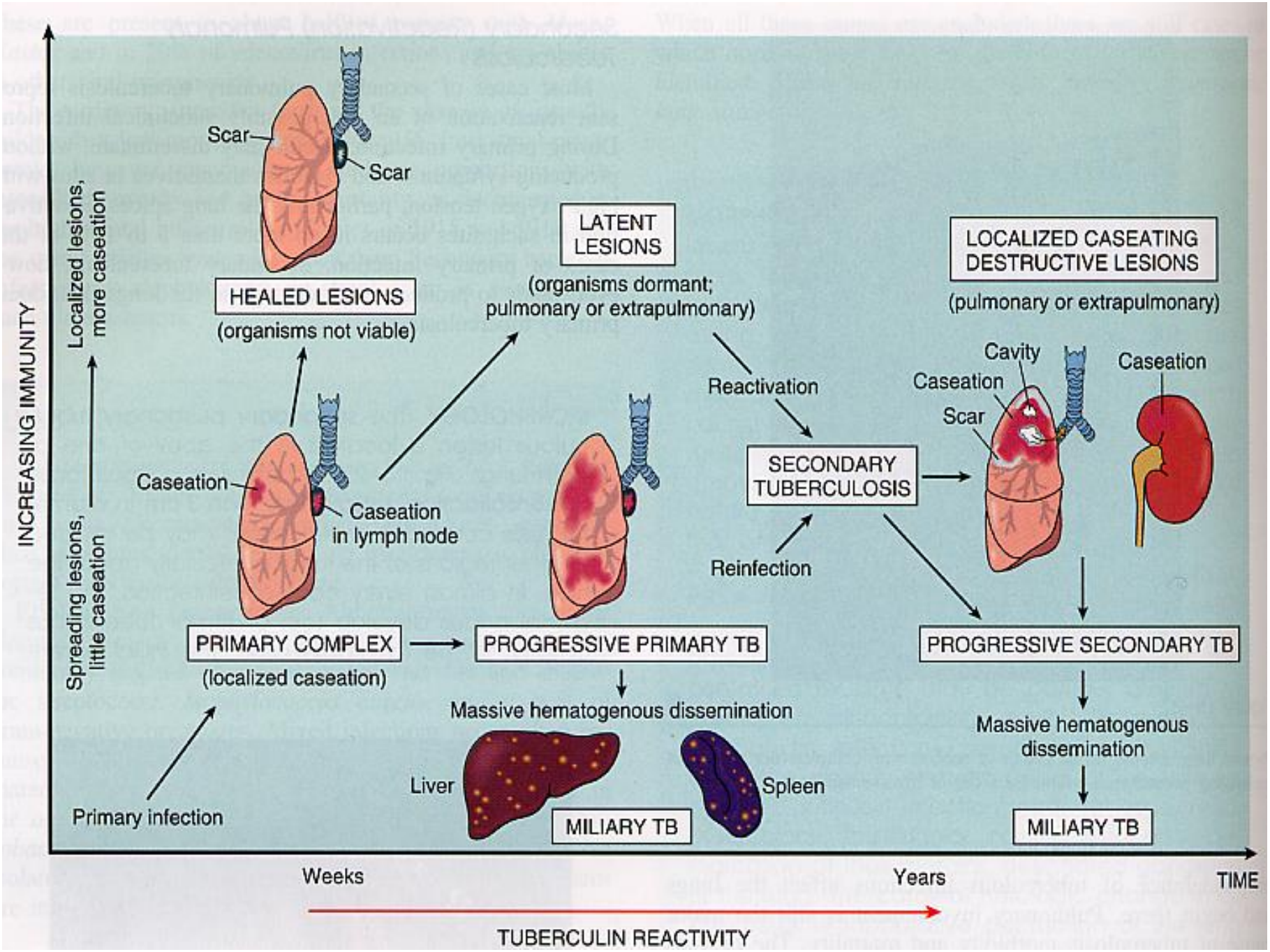
- TB is an ancient infectious disease caused by *Mycobacterium tuberculosis*. It has been known since 1000 B.C., so it not a new disease. Since TB is a disease of respiratory transmission, optimal conditions for transmission include:
  - overcrowding
  - poor personal hygiene
  - poor public hygiene

Transmission

- Pulmonary tuberculosis is a disease of respiratory transmission, Patients with the active disease (bacilli) expel them into the air by:
  - coughing,
  - sneezing,
  - shouting,
  - or any other way that will expel bacilli into the air

- Once inhaled by a tuberculin free person, the bacilli multiply 4 -6 weeks and spreads throughout the body. The bacilli implant in areas of high partial pressure of oxygen:
- lung
- renal cortex
- reticuloendothelial system

- This is known as the **primary infection.** The patient will heal and a scar will appear in the infected loci. There will also be a few viable bacilli/spores may remain in these areas (particularly in the lung). The bacteria at this time goes into a dormant state, as long as the person's immune system remains active and functions normally this person isn't bothered by the dormant bacillus.
- When a person's immune system is depressed., a secondary reactivation occurs. 85-90% of the cases seen which are of secondary reactivation type occurs in the lungs.


INCREASING IMMUNITY
Localized lesions, more caseation
Spreading lesions, little caseation
Scar
Scar
HEALED LESIONS
(organisms not viable)
LATENT LESIONS
(organisms dormant; pulmonary or extrapulmonary)
LOCALIZED CASEATING DESTRUCTIVE LESIONS
(pulmonary or extrapulmonary)
Caseation
Caseation in lymph node
Reactivation
Reinfection
Cavity
Caseation
Scar
Caseation
SECONDARY TUBERCULOSIS
PRIMARY COMPLEX
(localized caseation)
PROGRESSIVE PRIMARY TB
PROGRESSIVE SECONDARY TB
Massive hematogenous dissemination
Massive hematogenous dissemination
Liver
Spleen
Primary infection
MILIARY TB
MILIARY TB
Weeks
Years
TIME
TUBERCULIN REACTIVITY

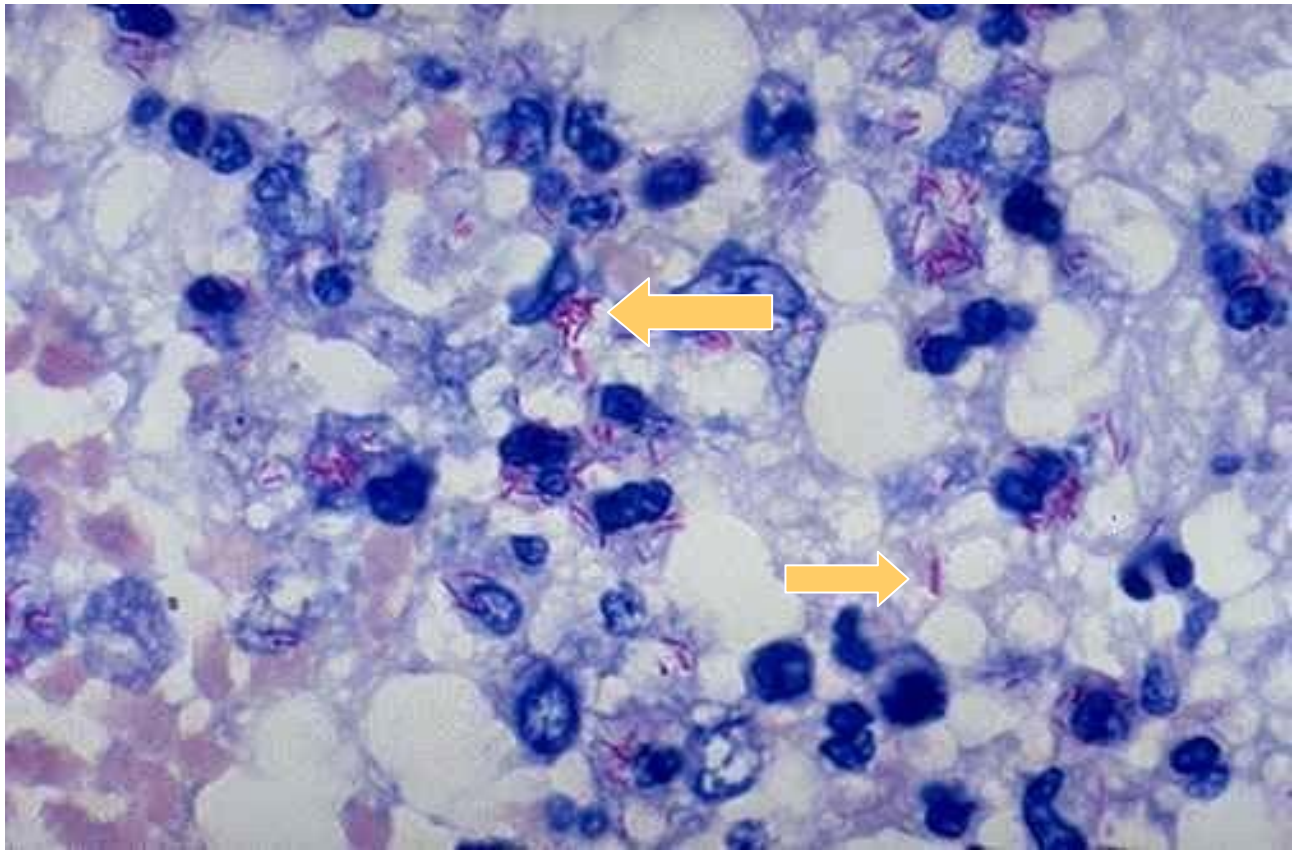
Pathogenesis of TB:

- Type IV hypersensitivity – T cells – Macrophages → Granuloma
- Activated macrophages – epithelioid cells.
- Remain viable inside macrophages
- Self destruction by lysosomal enzymes.

Microbiology of TB:

- Mycobacteria – ‘fungus like..
- Bacilli, Aerobic, no toxins, no spore.
- M. tuberculosis & M. bovis
- M. avium, M.intracellulare in AIDS - Atypical TB

AFB - Ziehl-Nielson stain



Classification of TB

1. Primary Pulmonary TB
2. Miliary TB
3. Secondary TB
   (invasive, carvitary, caseation ,
   Tuberculous Granulomas …)
4. Tuberculous Pleuritis
5. Extra-pulmonary TB
   (bone, joints, renal, adrenal,skin…)

Primary tuberculosis

- In a non immunized individual – children* adult*
- Deep inhalation of airborne droplet ~ 3 microns.
- Bacilli locate in the subpleural mid zone of lung
- Localized "atypical" pneumonia
- Brief acute inflammation – neutrophils.
- 5-6 days invoke granuloma formation.
- 2 to 8 weeks – healing – single round -Ghon focus.
- If lymph node is also involved → Ghon complex.

Primary or Ghon's Complex

- Primary tuberculosis is the pattern seen with initial infection with tuberculosis in children.
- Reactivation, or secondary tuberculosis, is more typically seen in adults.

Primary Tuberculosis

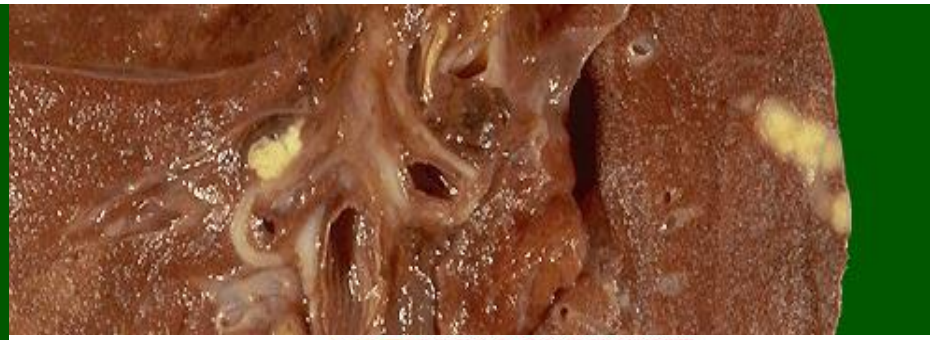
- In Non Immunized individuals (Children)

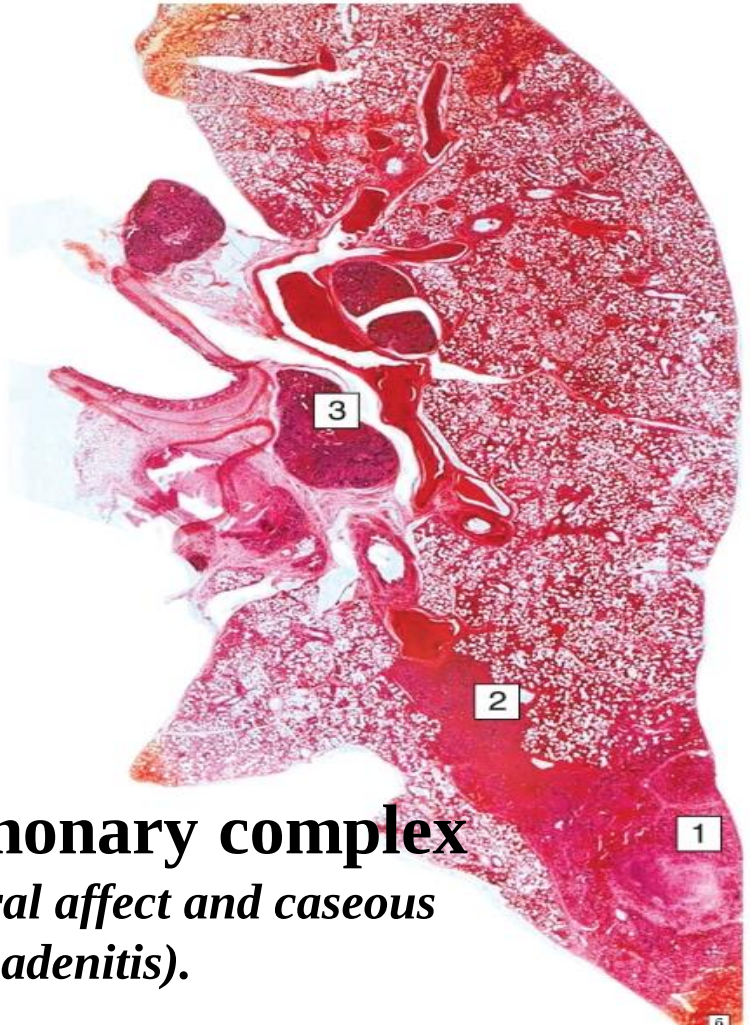
➢ Primary Tuberculosis:

- Self Limited disease
- Ghons focus, complex or Primary complex.

➢ Primary Progressive TB (in US.)

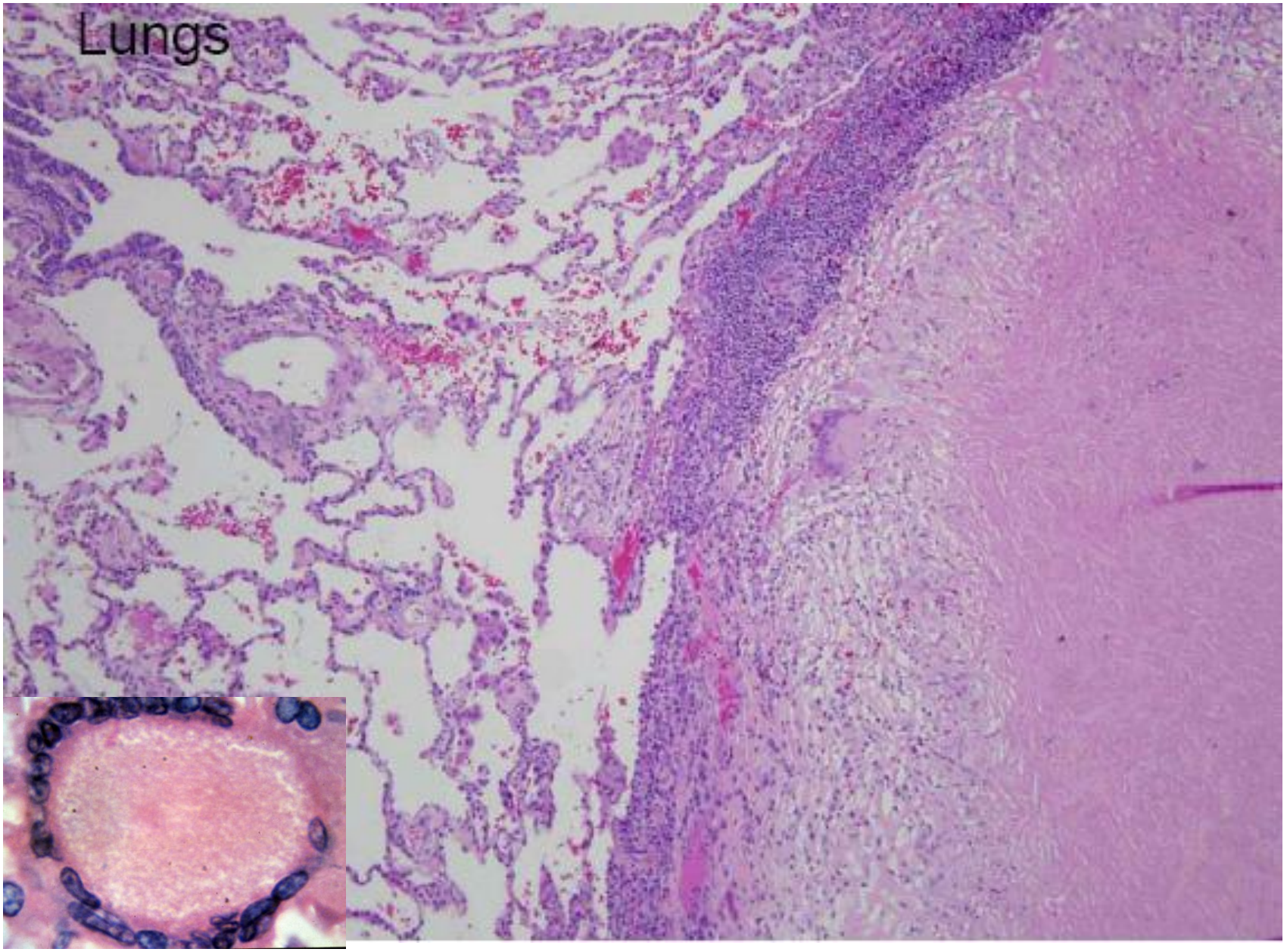
- Miliary TB and TB Meningitis.
- Common in malnourished children
- 10% of adults, Immuno-suppressed individuals



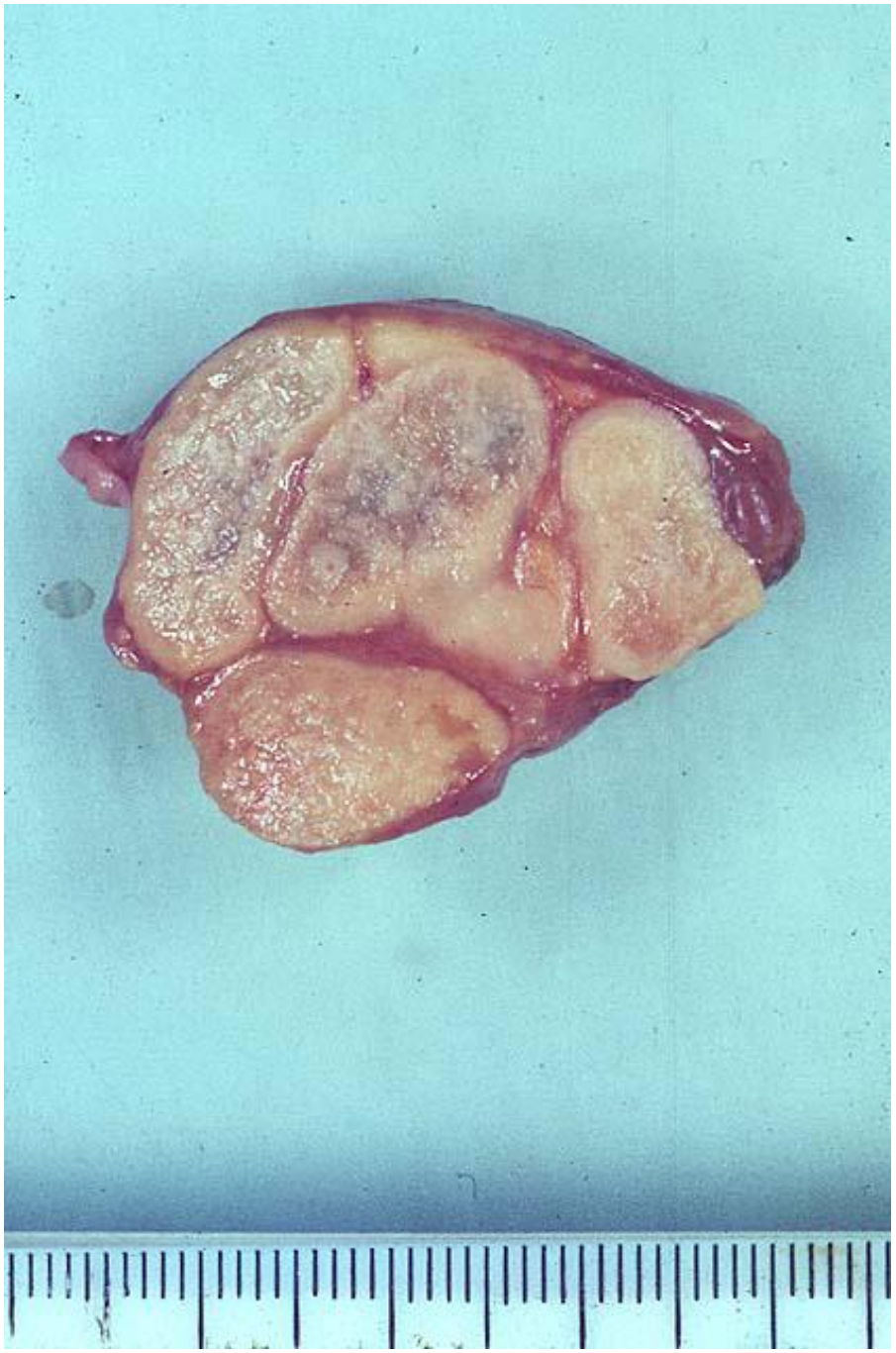


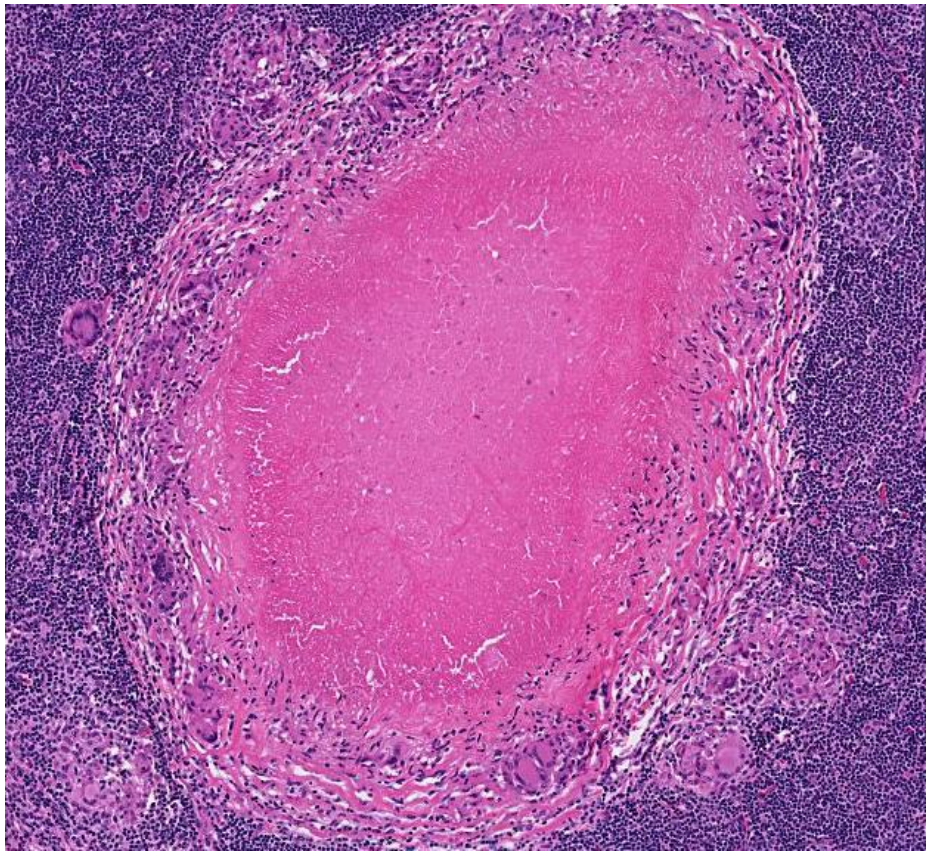
Primary pulmonary complex

(primary subpleural affect and caseous lymphadenitis).

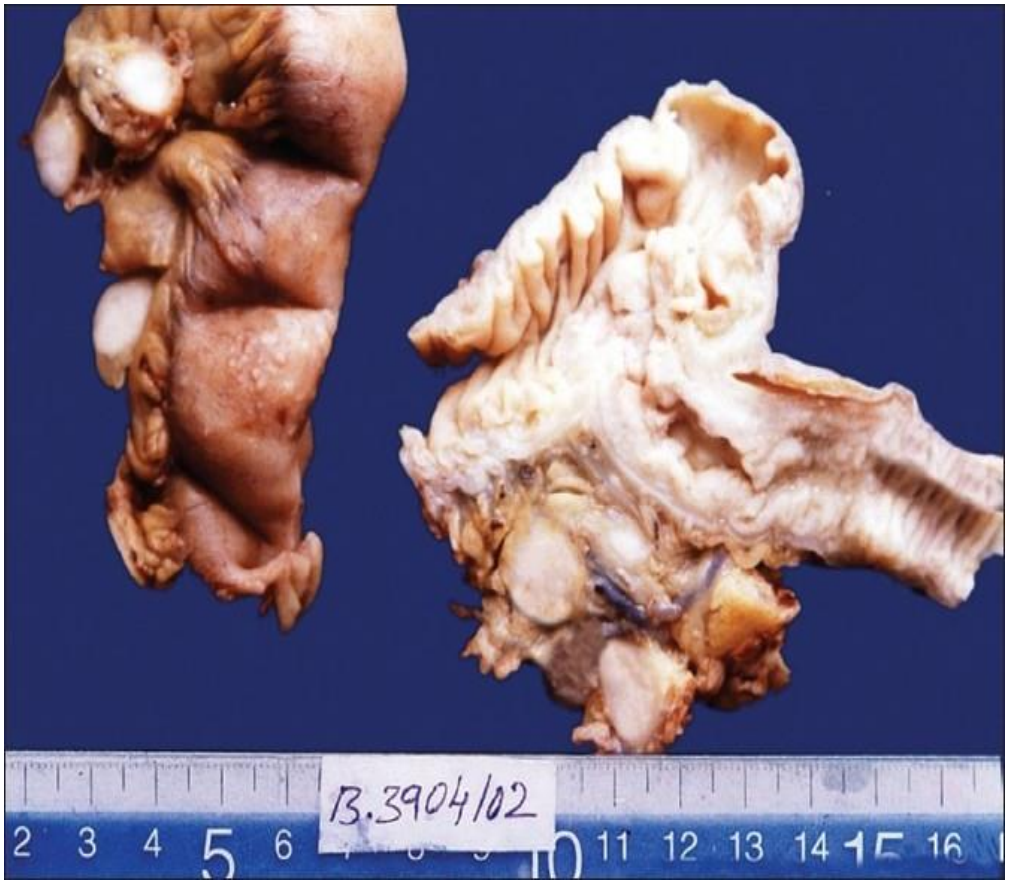


Primary pulmonary affect.

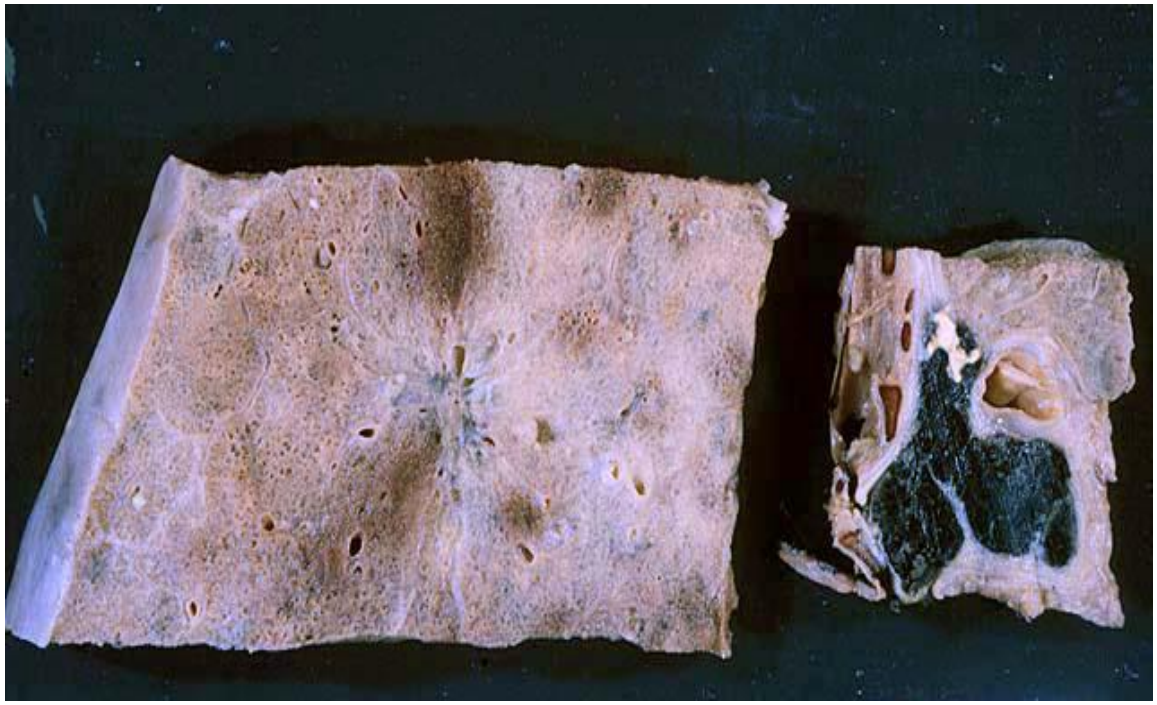


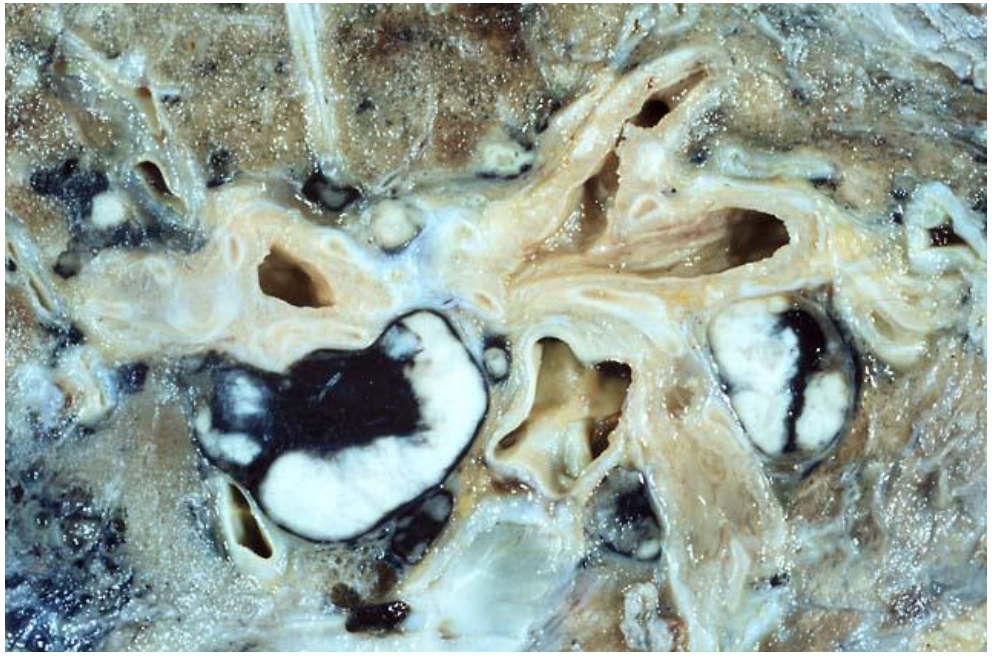


Tuberculous lymphadenitis.



Primary intestinal complex.





Healed primary complex *(sclerosis of the primary affect and calcinosis of lymph nodes).*

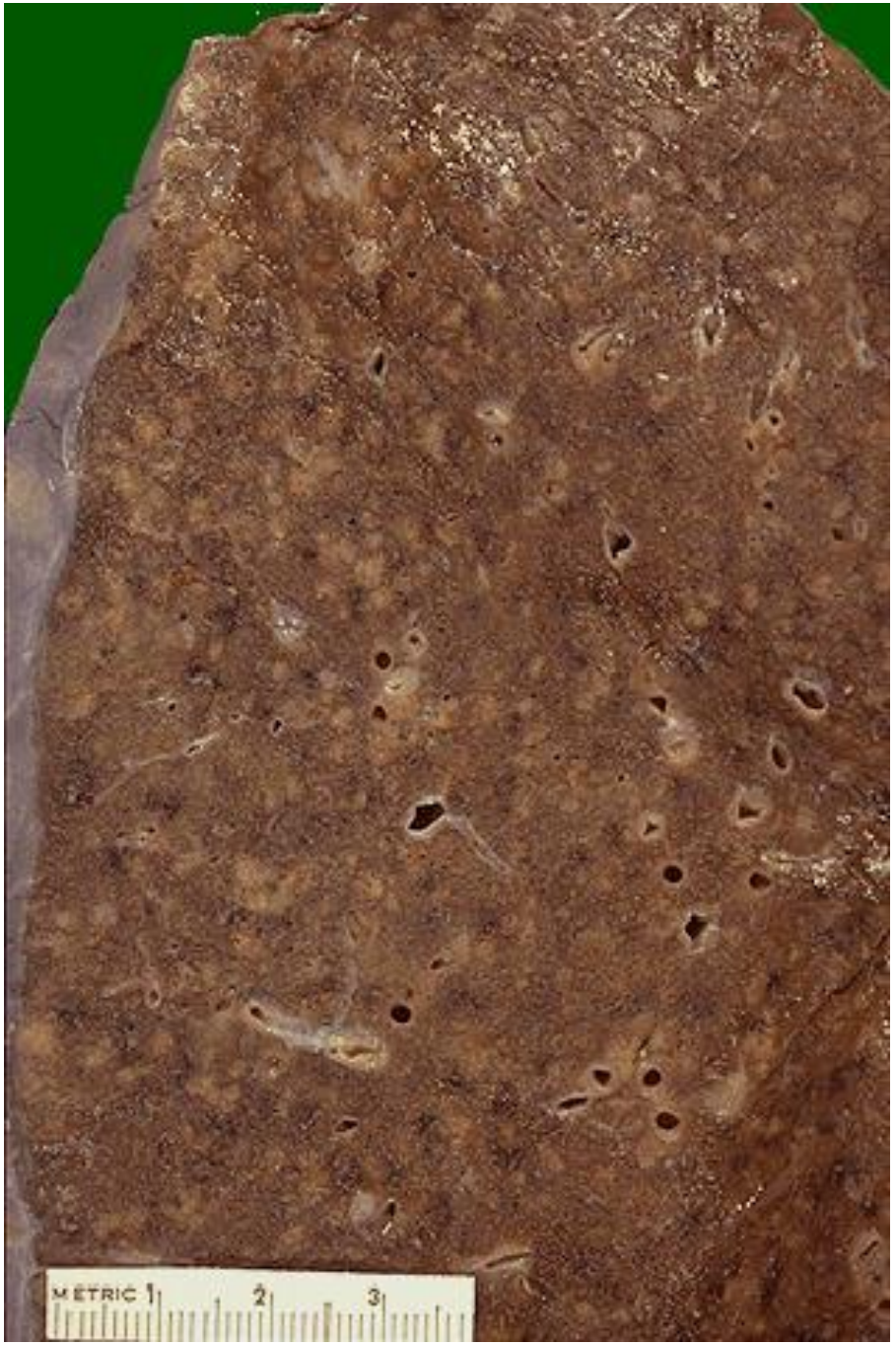
Secondary Tuberculosis:

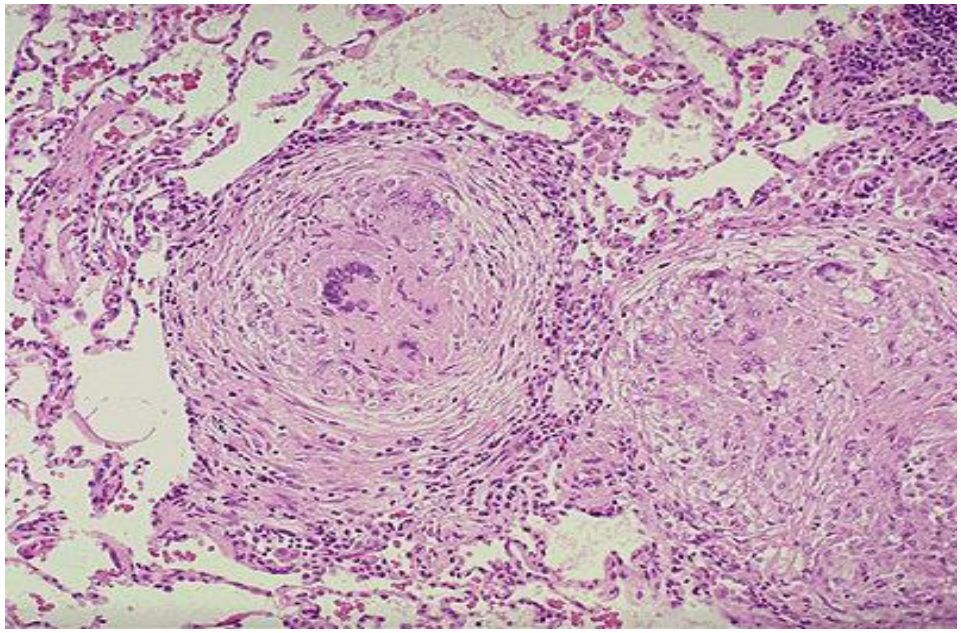
- Post Primary in immunized individuals.
- Cavitary Granulomatous response.
- Reactivation or Reinfection
- Apical lobes or upper part of lower lobes – O_2
- Caseation, cavity - soft granuloma
- Pulmonary or extra-pulmonary
- Local or systemic spread / Miliary
  - Vein – via left ventricle to whole body
  - Artery – miliary spread within the lung

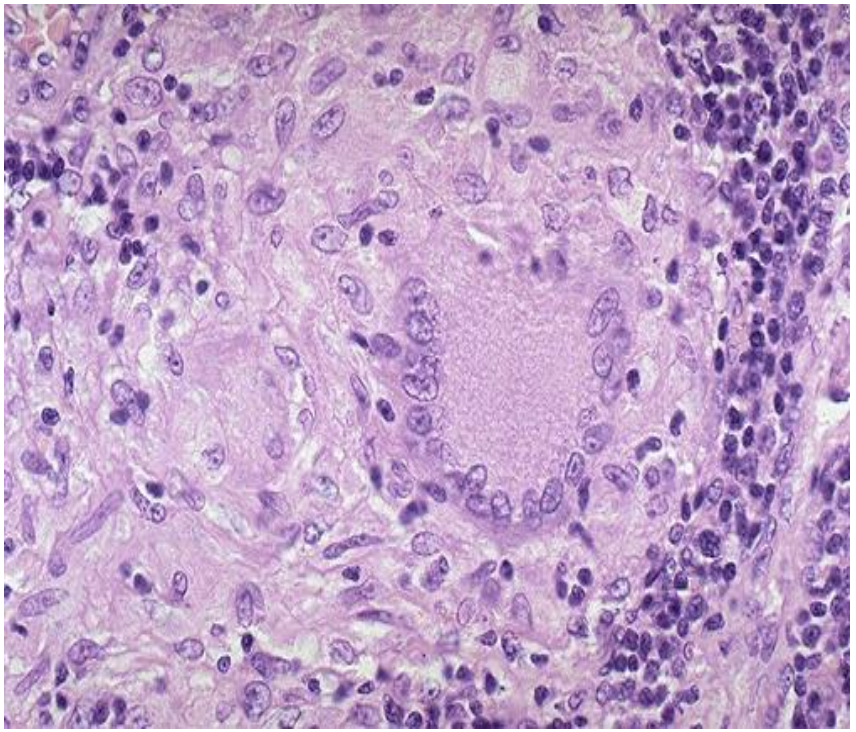
Secondary Tuberculosis:

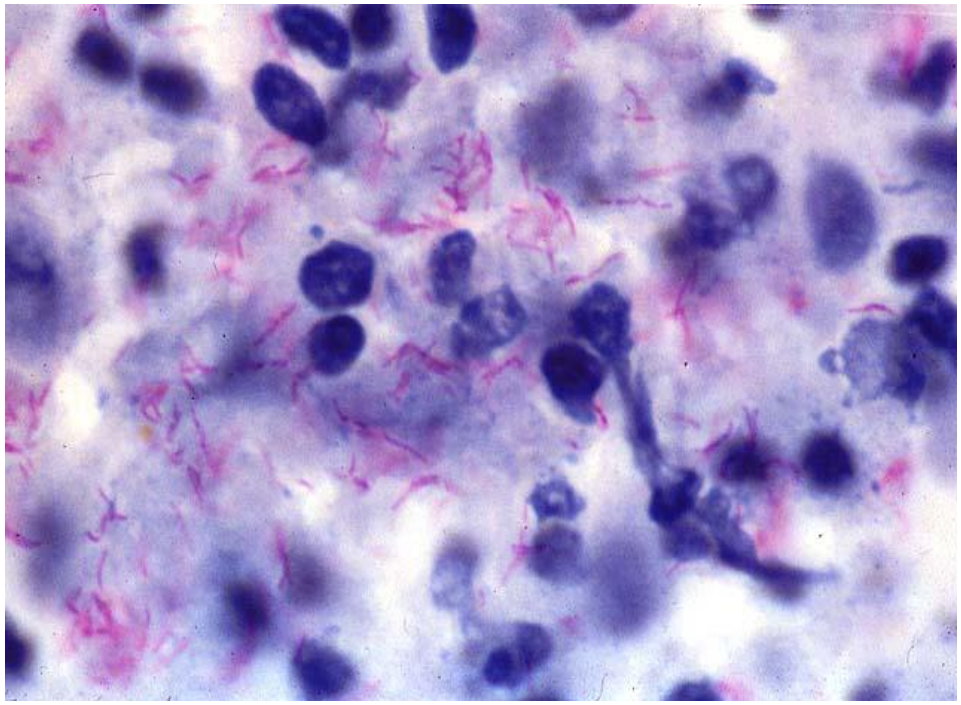
- Reactivation occurs in 10-15% of patients.
- Most commonly males 30-50 y
- Slowly Progressive (several months)
- Cough, sputum, Low grade fever, night sweats, fatigue and weight loss.
- Hemoptysis or pleuritic pain = severe disease

Pulmonary miliary tuberculosis.





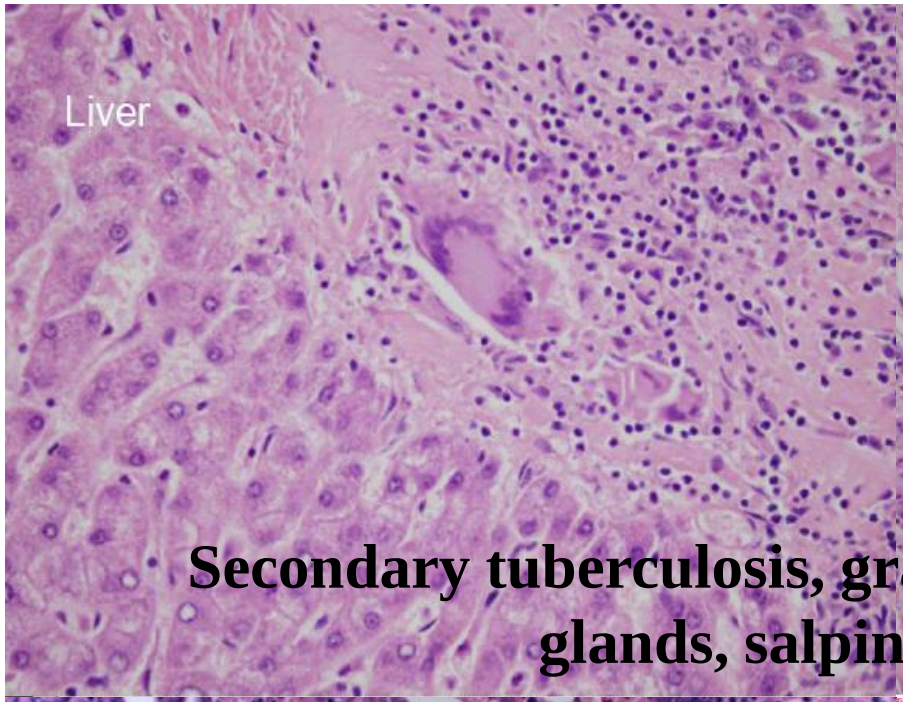


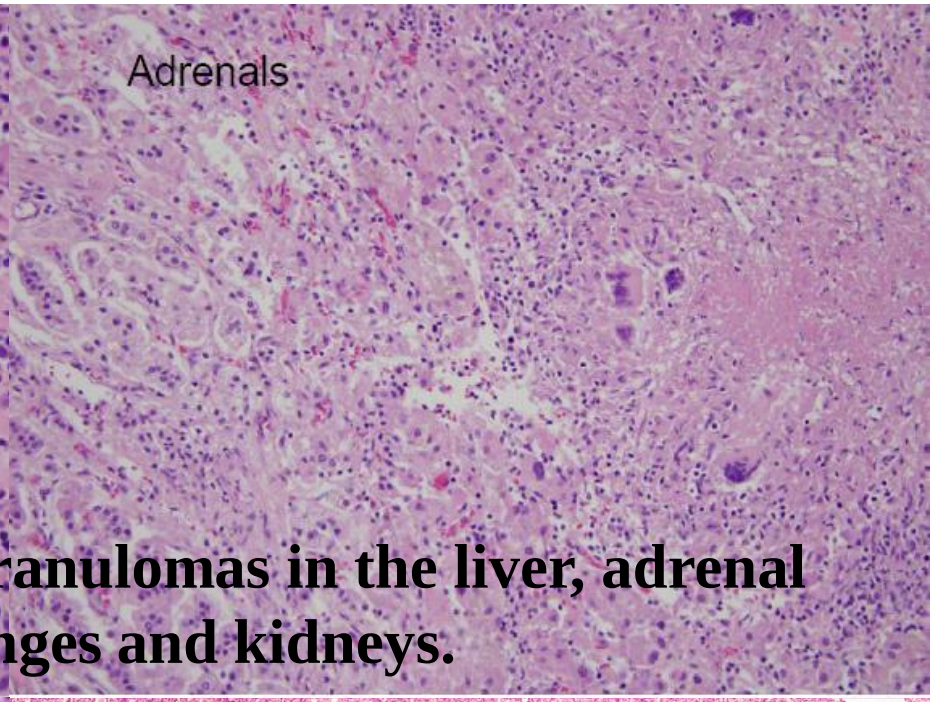


Tuberculous granulomas with giant Langhans cells, mycobacteria.
(Ziehl-Nielsen stain).

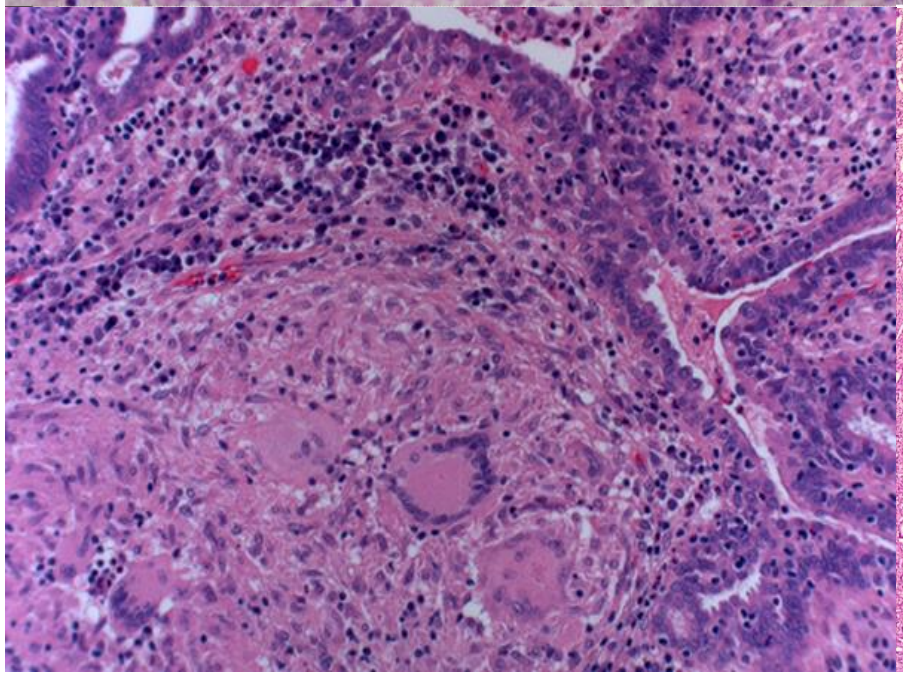
Morphology of Granuloma

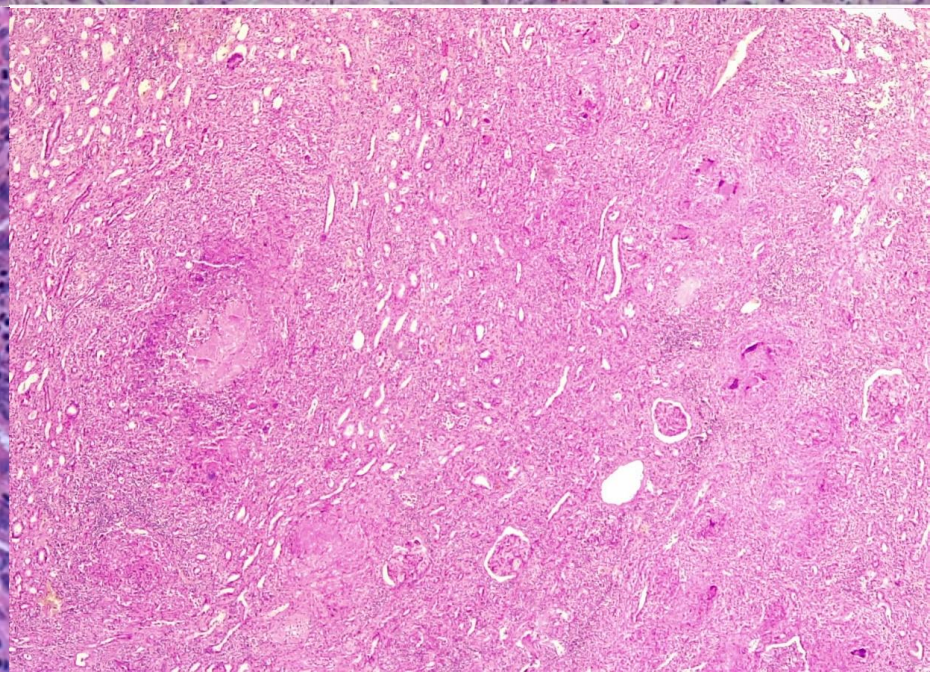
1. Rounded tight collection of chronic inflammatory cells.
2. Central Caseous necrosis.
3. Active macrophages - epithelioid cells.
4. Outer layer of lymphocytes, plasma cells & fibroblasts.
5. Langhans giant cells – joined epithelioid cells.



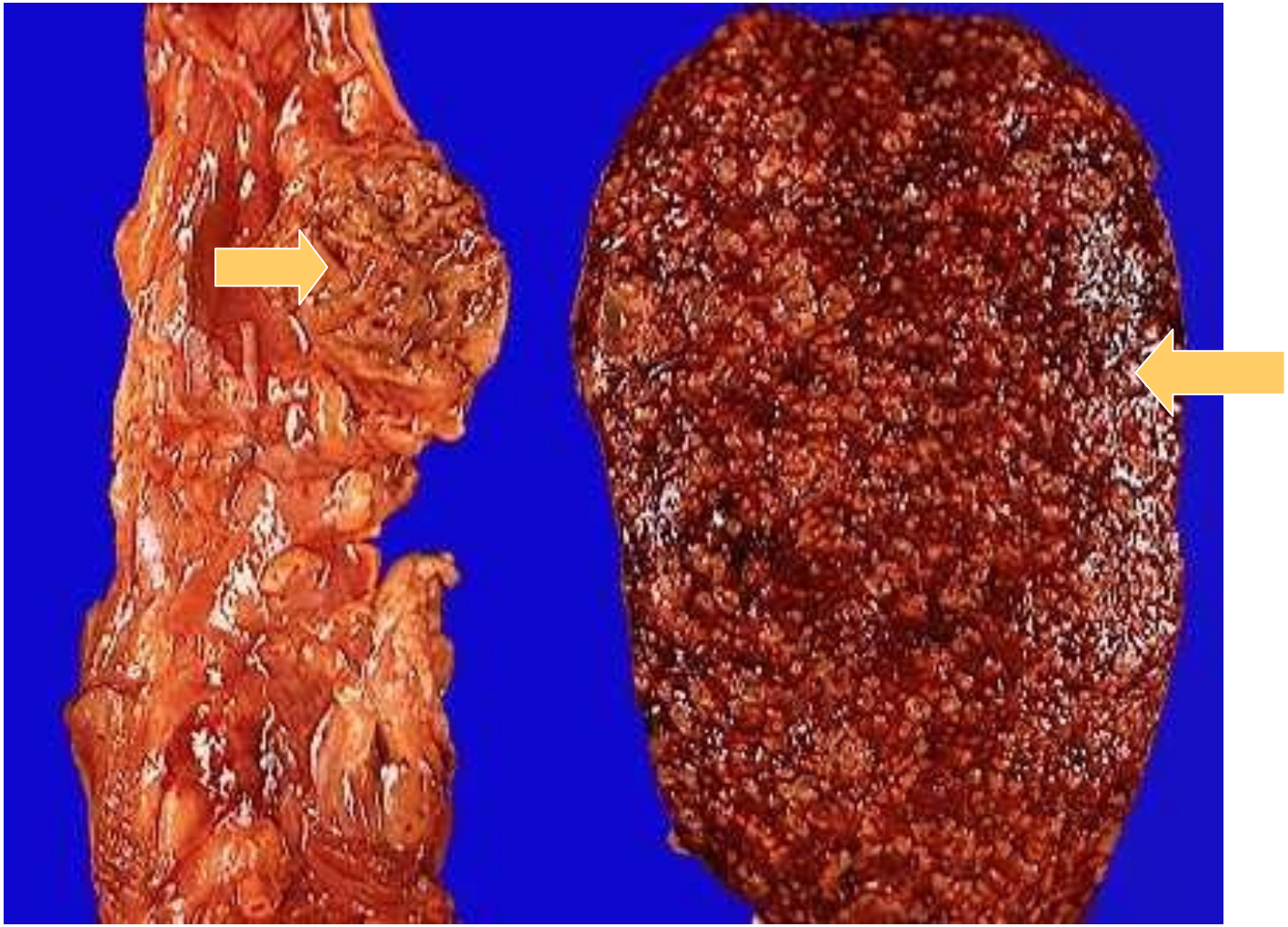


Secondary tuberculosis, granulomas in the liver, adrenal glands, salpinges and kidneys.



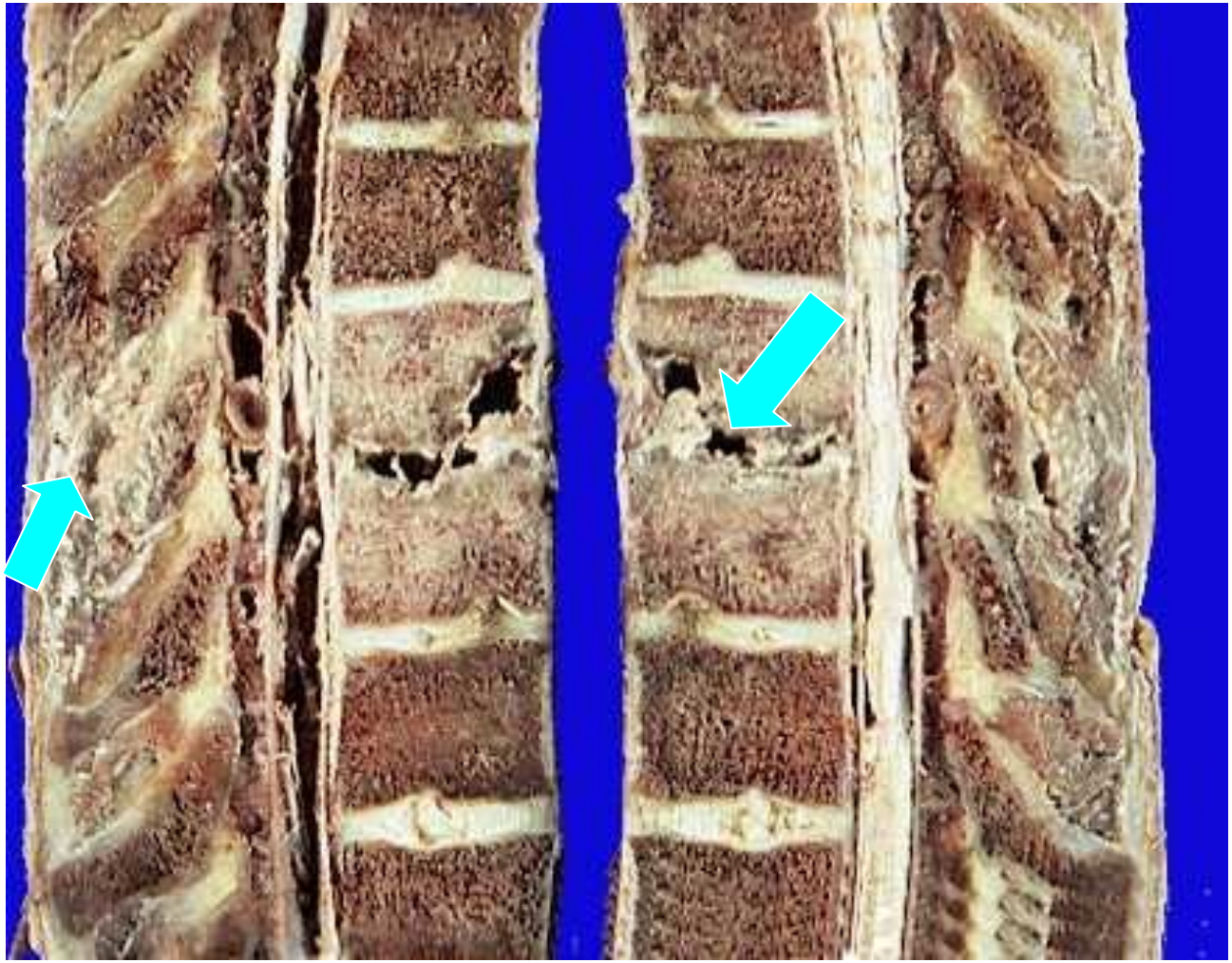


Systemic Miliary TB

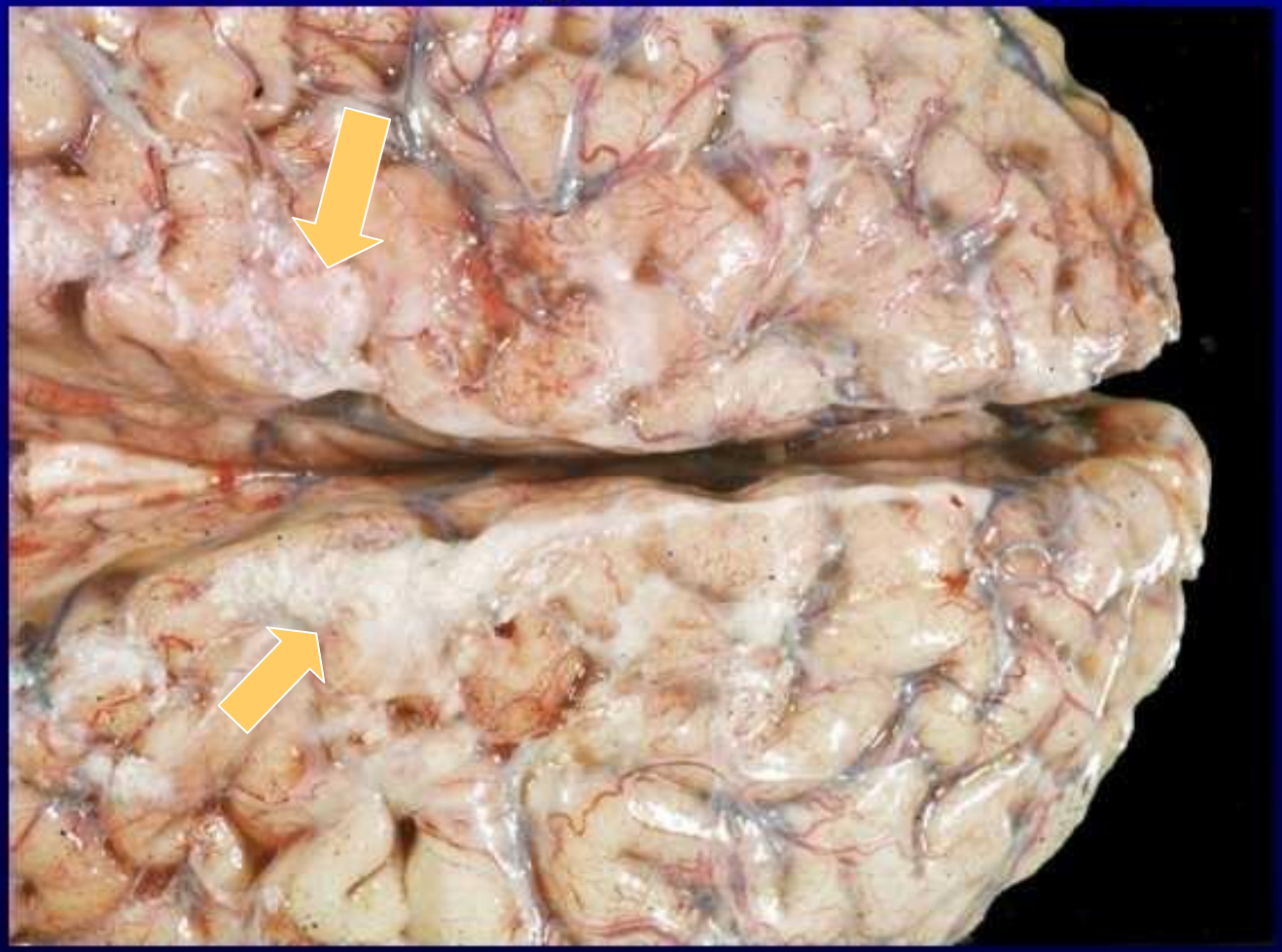


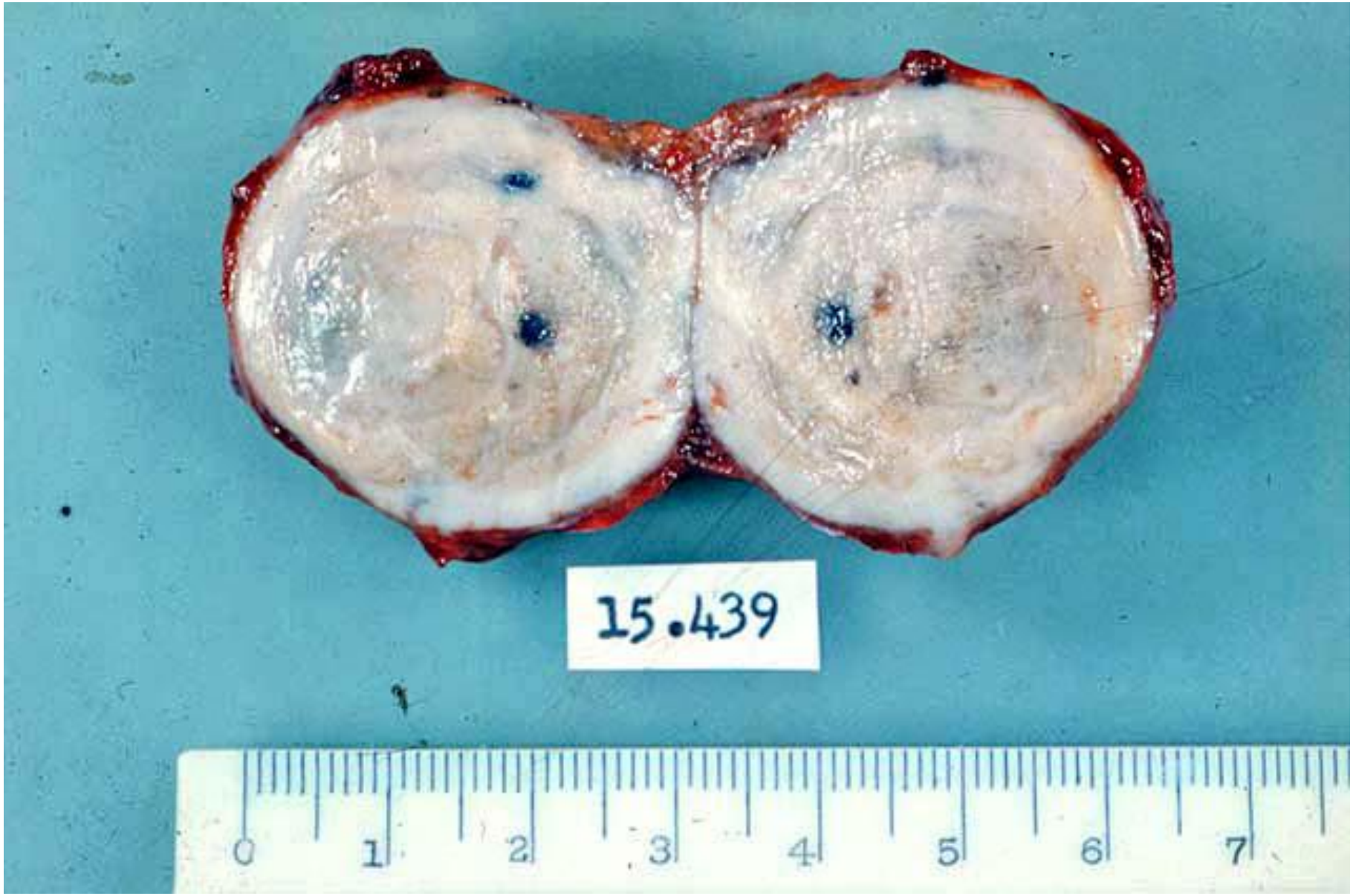
Adrenal TB - Addison Disease

Spinal TB - Potts Disease

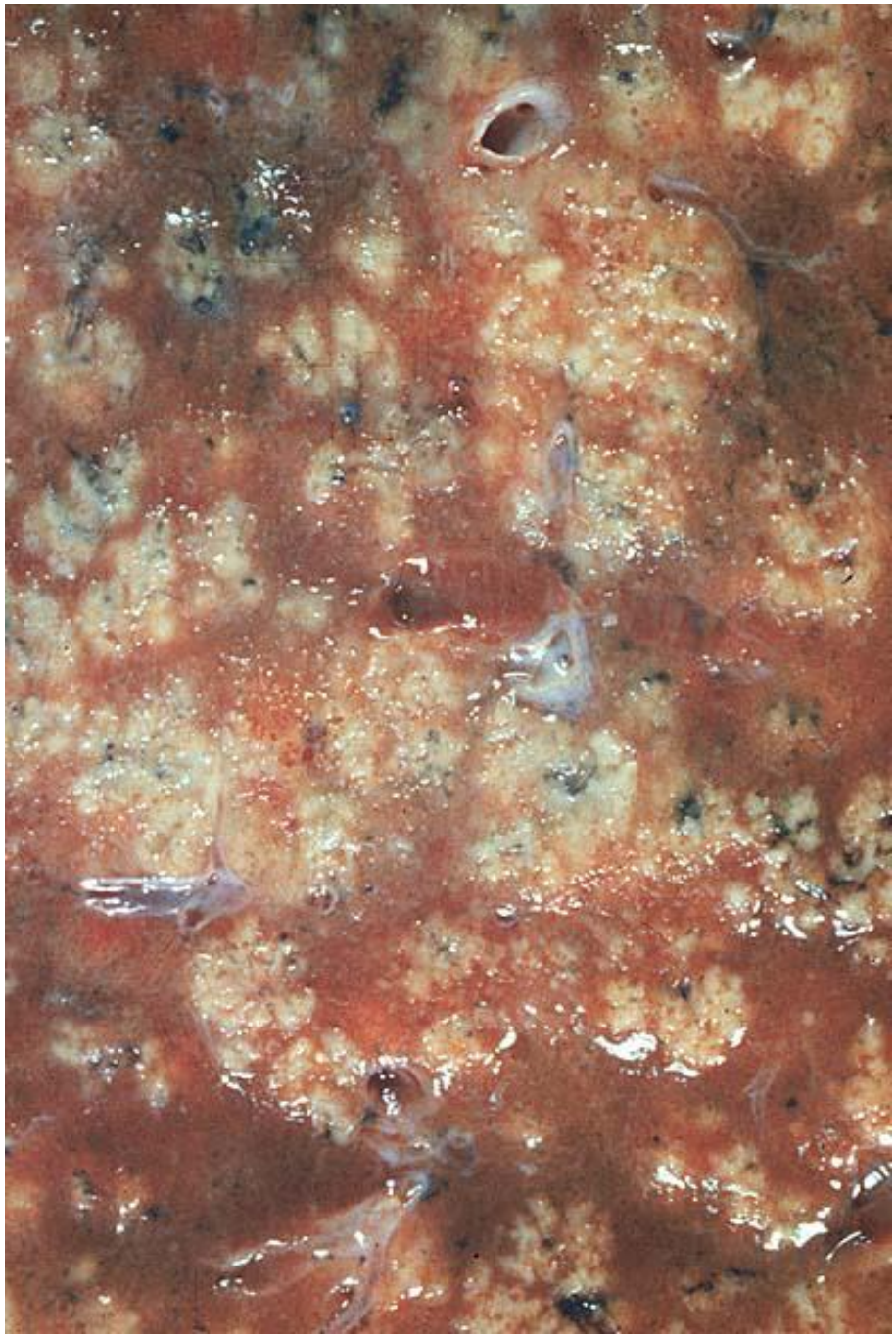


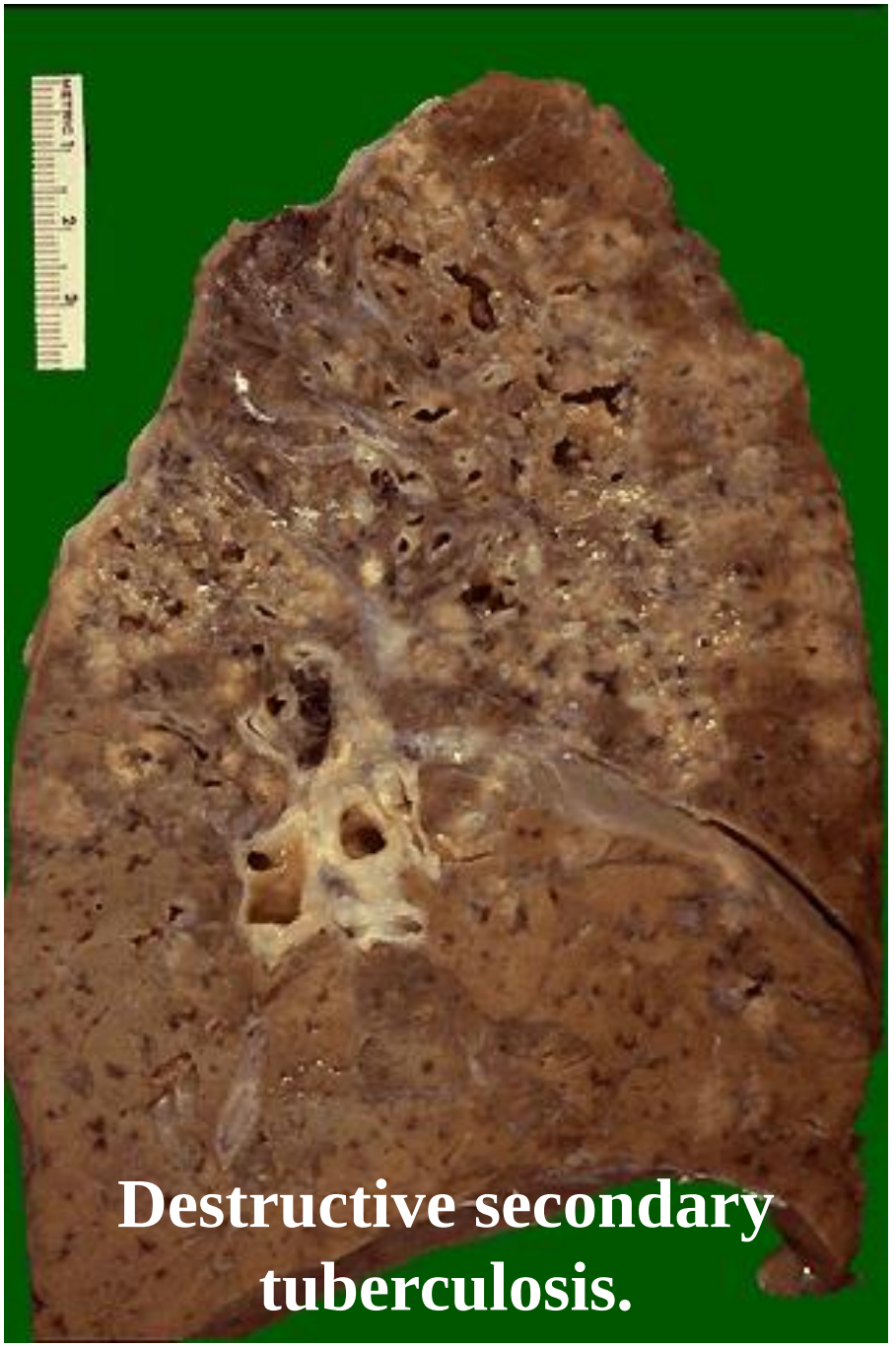
TB Meningitis Gross Brain



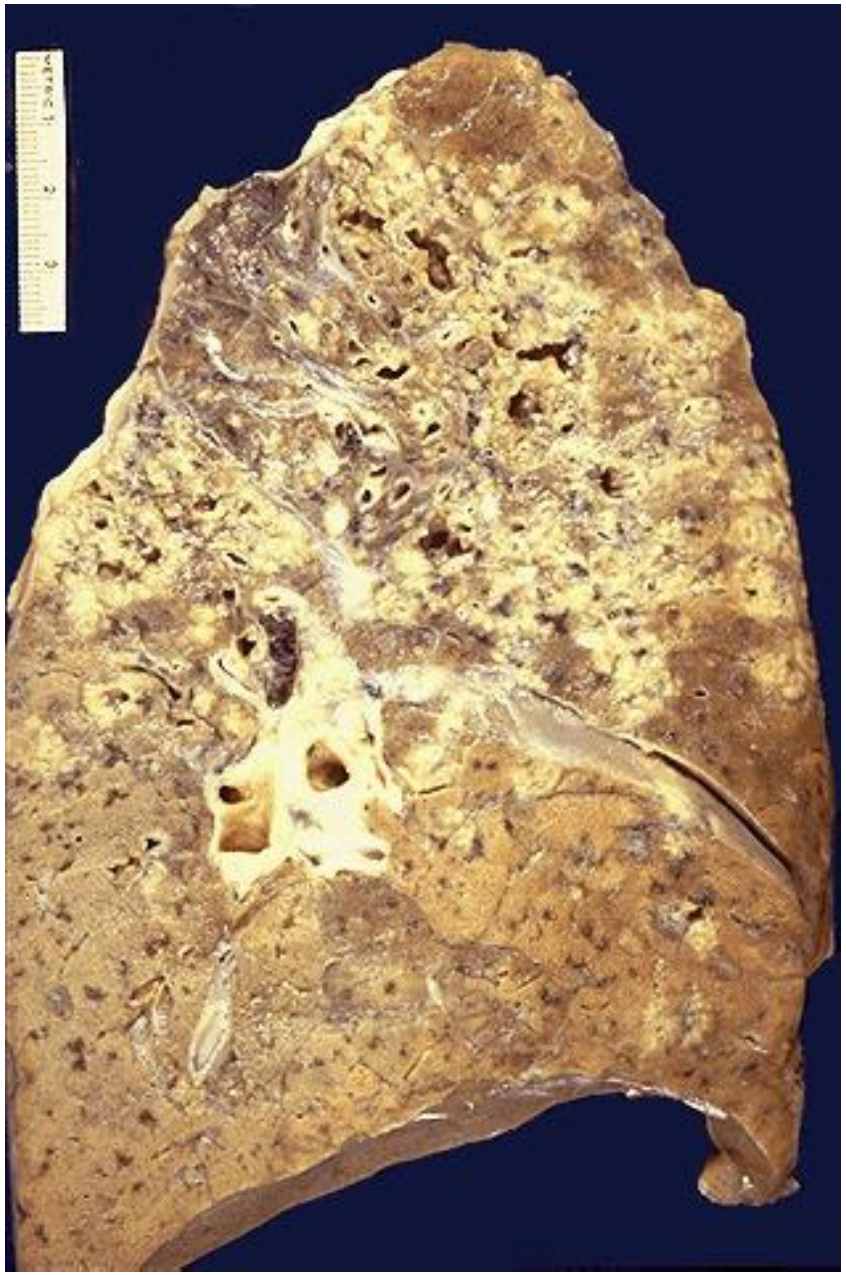


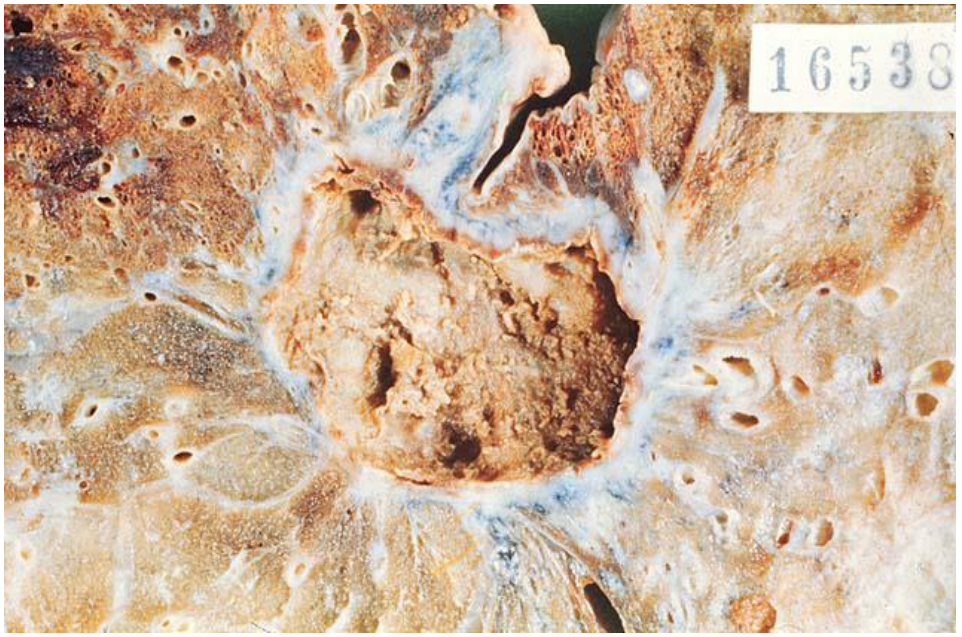
Encapsulated pulmonary tuberculoma.

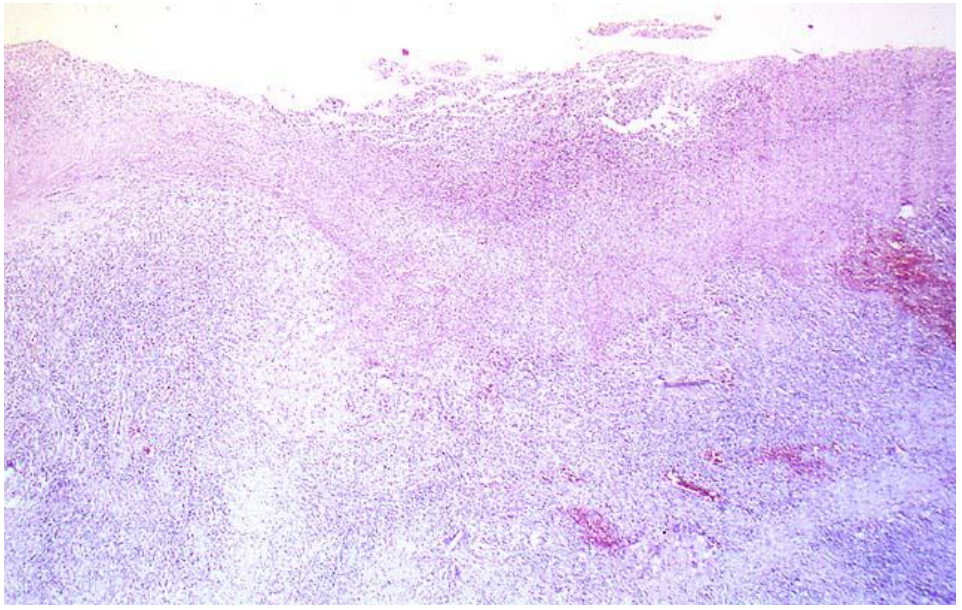




Destructive secondary tuberculosis.



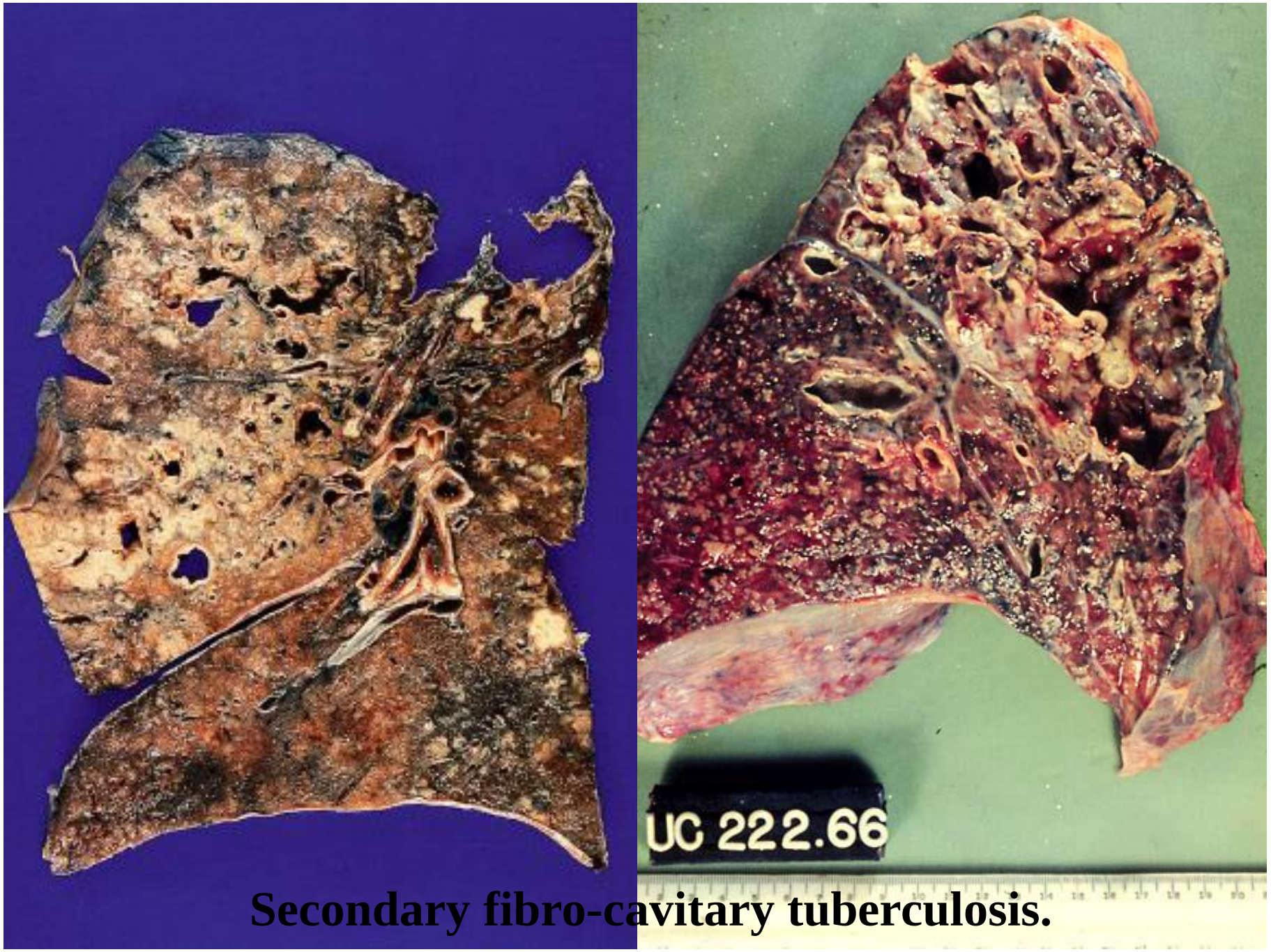




Secondary fibro-cavitary tuberculosis, cavity wall.

Cavitary Tuberculosis

- When necrotic tissue is coughed up → cavity.
- Cavitation is typical for large granulomas.
- Cavitation is more common in the secondary reactivation tuberculosis - upper lobes.



Secondary fibro-cavitary tuberculosis.

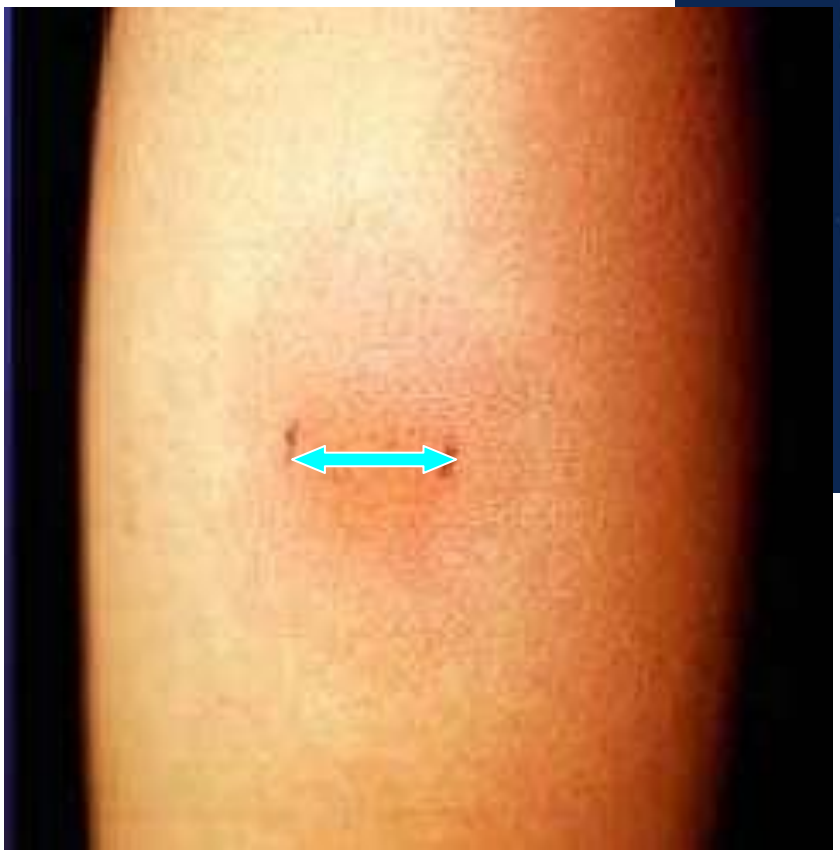
Diagnosis of TB

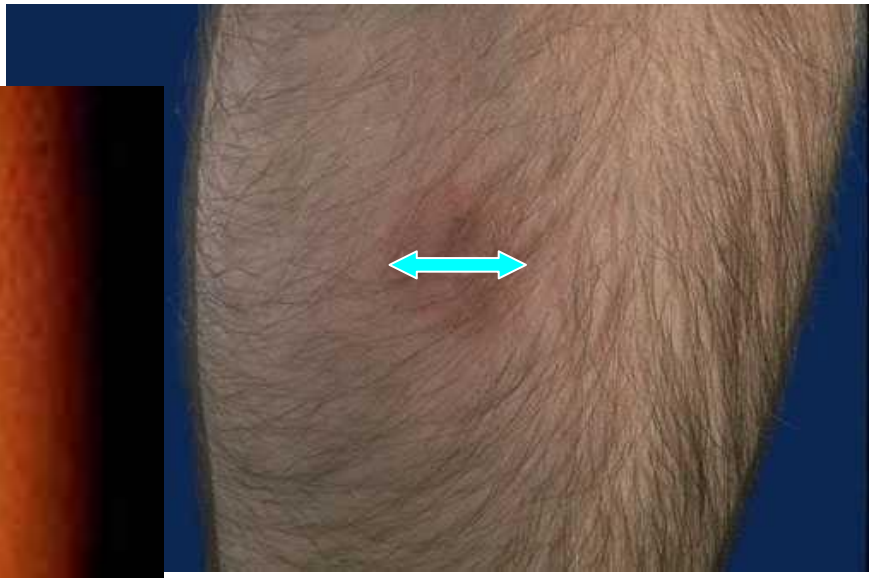
- Clinical features are not confirmatory.
- Zeil Nielson Stain - $1x10^4$/ml, 60% sensitivity
- Release of acid-fast bacilli from cavities intermittent.
- 3 negative smears to assure low infectivity*
- Culture most sensitive and specific test.
  - Conventional Lowenstein Jensen media 3-6 wks.
  - Automated techniques within 9-16 days
- PCR is available, but should only be performed by experienced laboratories
- PPD for clinical activity / exposure sometime in life.

PPD Tuberculin Testing

- Sub cutaneous
- Weal formation
- Itching – no scratch.
- Read after 72 hours.
- Induration size.
- 5-10-15mm (non-ende)
- < 72 hour is not diag*
- +ve after 2-4 weeks.
- BCG gives + result.

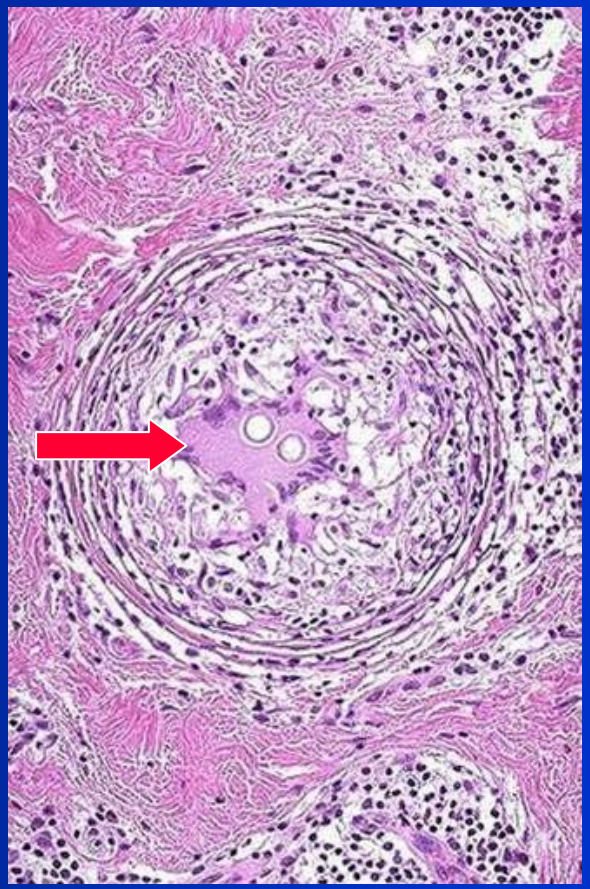
PPD Testing





Granuloma is not pathagnomonic of TB…!

- Foreign body granuloma.
- Fat necrosis.
- Fungal infections.
- Sarcoidosis.
- Crohns disease.

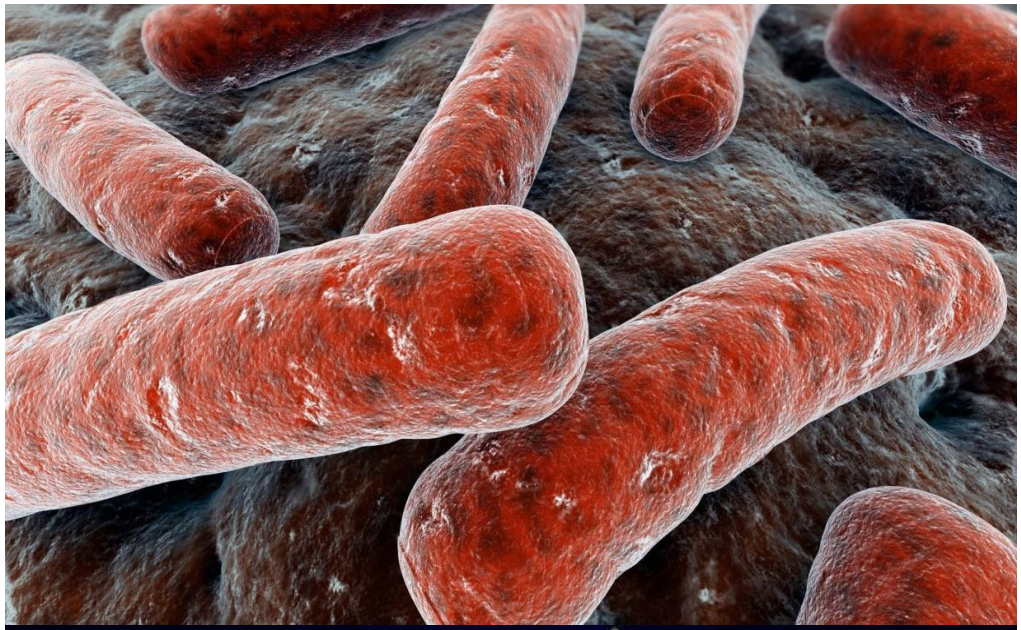


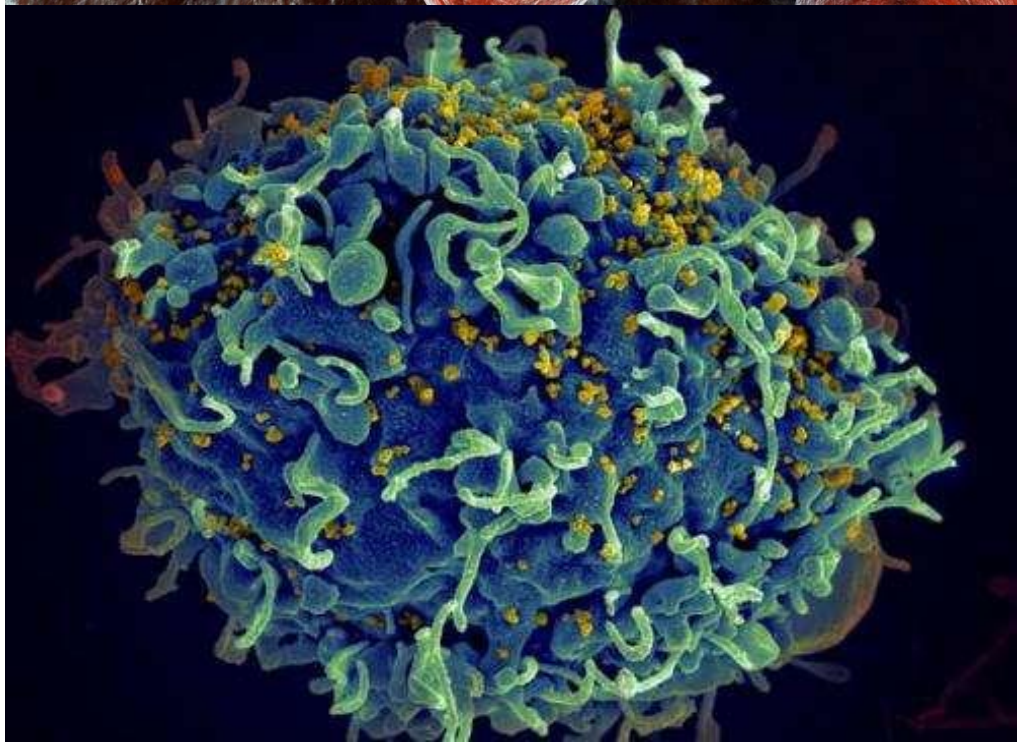
Conclusions:

- A chronic, common, infectious disease - Weight loss, fever, night sweats, lung damage.
- Commonest fatal infectious disease in the world.
- AIDS, Diabetes, malnutrition (poverty), crowding.
- Pulmonary,miliary,invasive,pleuritis,extrapulmonary,.
- Prevention depends on PPD & INH prophylaxis

What is New…?

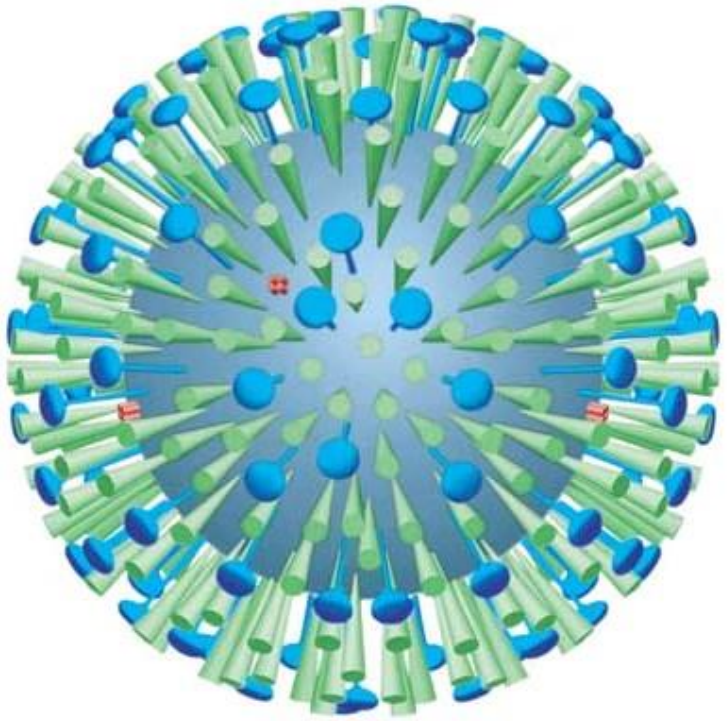
- 14-30% of TB patients also HIV infected.
- New drugs - Rifapentine, Interferons, Thalidomide.
- Immune therapy : Killed M. vaccine stimulates CD8 cells (increased INF and IL-12).
- The genome of TB has been identified (~4000 genes) potential to develop new vaccines and tests.





Tuberculosis.
AIDS.
Aerogenic infections.

Influenza



Influenza Virus belong to Myxovirus

- Enveloped RNA virus
- Absorb to mucoprotein receptors
- Many viruses are included in this group

Influenza

Mumps

Measles.

Newcastle disease

Parainluenza virus

INFLUENZA

- Cause of the infection of the respiratory tract.

- Occurs as

  Sporadic

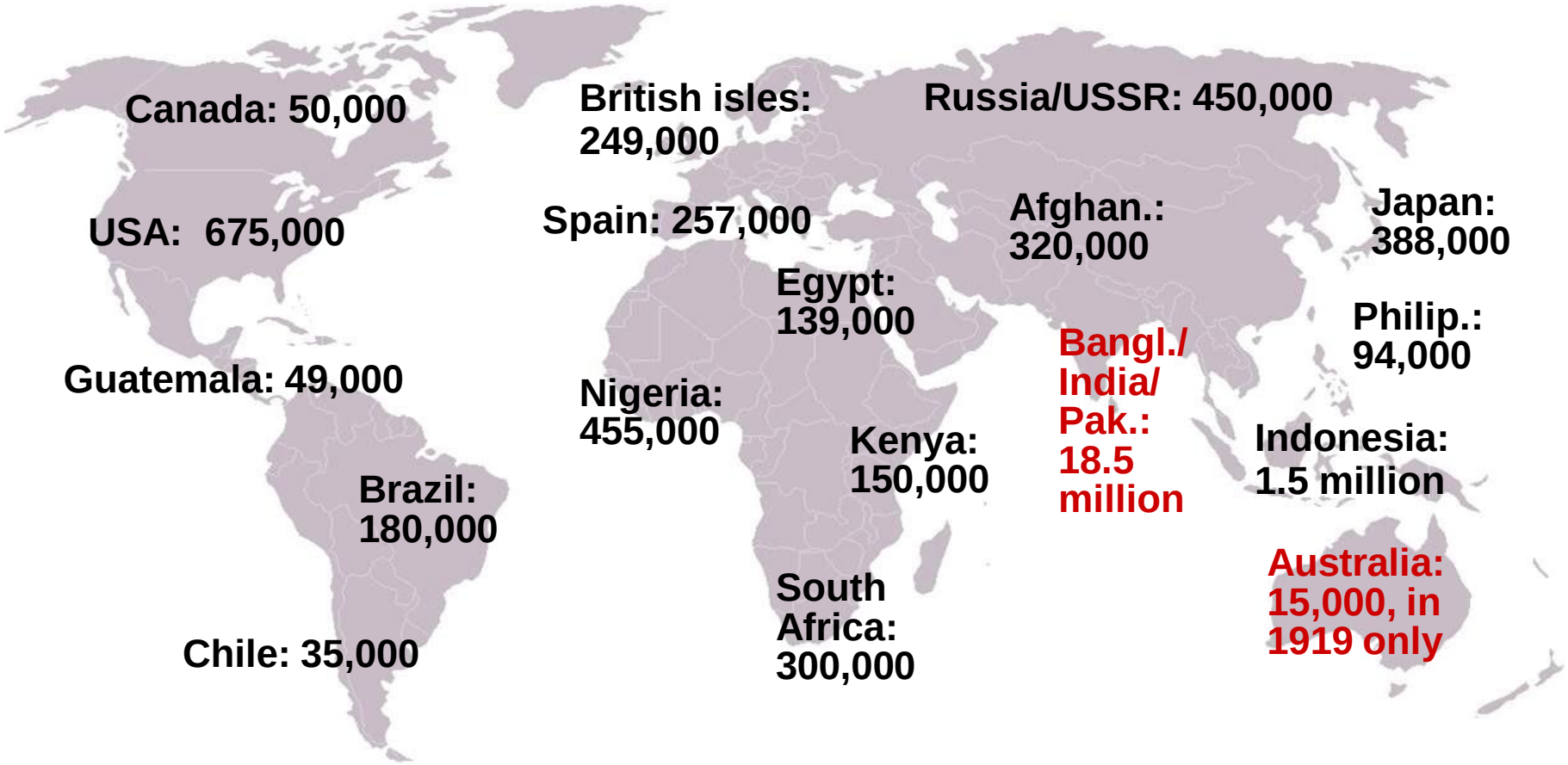
  Epidemic

  Pandemic

Major pandemic in 1918 – 1919

Published Pandemic Mortality Estimates for Selected Countries

(Johnson NPAS & Mueller J. Bulletin of the History of Medicine (2002) 76:105-15)
(**1918: 28% of current global population**. http://birdfluexposed.com/resources/NIALL105.pdf)



Global Total:
50 – 100 million
(WHO: 40 million +)

Definition: Influenza is an acute, febrile, generalized viral infection that affects the upper and lower respiratory tract.

Etiology: *myxovirus influenzae,* which has 3 major antigenic types (A, B, C). Influenza virus (especially A) is characterized by high antigenic variability. Genes encoding surface proteins (hemagglutinin and neuraminidase) are constantly changing, resulting in new subtypes and antigenic variants, against which the population is not immunized.

Classification of Influenza virus

What are A B C

Classification on the basis of Ribonucleoprotein Antigen and Matrix

Influenza virus

Hosts of influenza viruses

- *Influenza virus A :*
  - *humans, birds, pigs, horses, aquatic mammals*
  - *the most common cause of the flu*
  - *produces the most severe diseases*
- *Influenza virus B:*
  - *mostly in humans*
- *Influenza virus C:*
  - *mostly in humans, pigs*
  - *usually subclinical infections*

Nomenclature of influenza viruses

- type A, B, C
- origin of the host, if not human
- geographical location: city, country
- sample / strain number
- year
- subtypes H and N

Name of influenza viruses

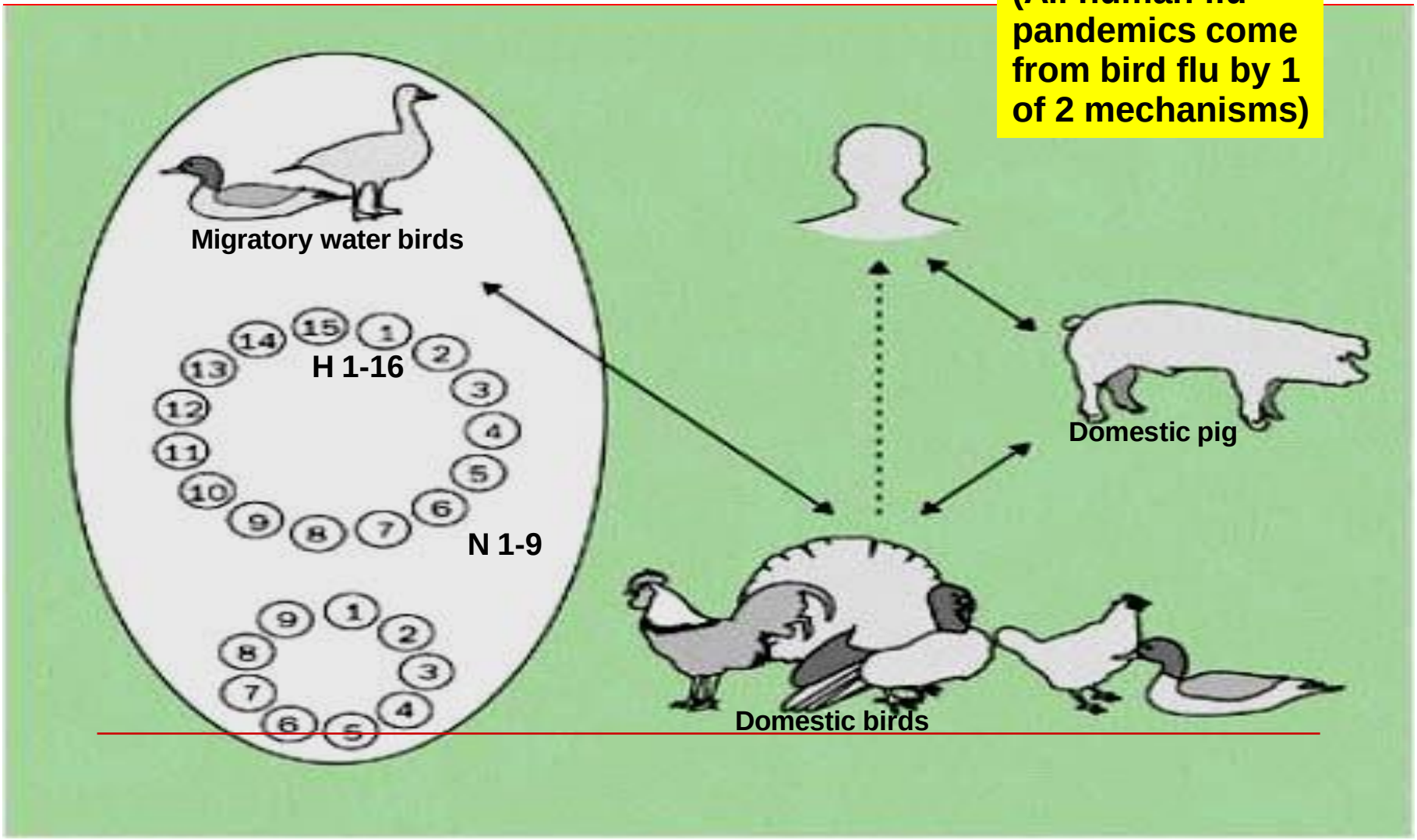
- A/swine/California/04/2009 (H1N1)
- A/Bangkok/1/1979 (H3N2)
- A/Thailand/1(KAN-1)/2004 (H5N1)

Natural hosts of influenza viruses (type A)

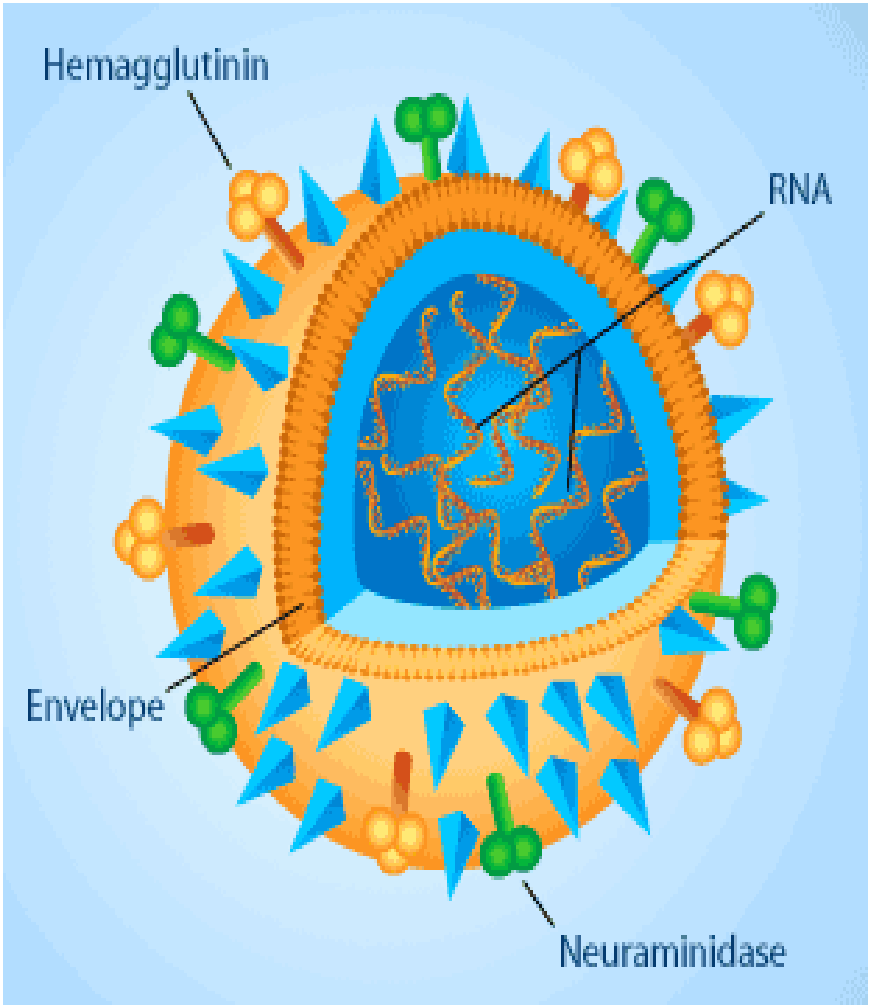
Haemagglutinin subtype					Neuraminidase subtype				
H1					N1				
H2					N2				
H3					N3				
H4					N4				
H5					N5				
H6					N6				
H7					N7				
H8					N8				
H9					N9				
H10									
H11									
H12									
H13									
H14									
H15									
H16				XXXXXX					

Origin of Pandemics Influenza

(All human flu pandemics come from bird flu by 1 of 2 mechanisms)



Viral structure



- Virus contains RNA in Helical symmetry
- **A negative sense Single stranded RNA genome is segmented into 8 segments**

Antigenic Structure Influenza virus

- Contains
  - Internal antigens
  - Surface antigens

Internal RNP antigen – Ribonucleic protein

It is a soluble antigen

Can be detected, complex fixation test and Immuno precipitation tests..

Anti RNP antibodies develop after natural infection, but not by killed vaccines

Surface Antigens

- antigens of virus present on surface

- antigens are two types
  Hemagglutinins
  Neuraminidases

Hemagglutinins are of two polypeptides
HA 1 and HA 2

Haemagglutinnins responsible for

Hemagglutination and Hem adsorption

Allows to absorb to mucoproteins on respiratory epithelium

Antihemagglutinin antibodies are produced following infection or Immunization

Types of Haemagglutinnins

- Hemagglutination is strain specific
- Great variation
- HA there are 15 subtypes H 1 to H15 in avian influenza
- But only three subtypes of hemagglutinin (H1, H2, and H3) have caused sustained epidemics in the human population.

Neuraminidases

- Neuraminidase are glycoprotein's
- Destroys cell receptors by hydrolysis cleavage
- Anti neuraminidase antibodies are produced following infection and immunization
- Not protective as Antihemagglutinin antibodies
- Strain specific exhibit variation, There are *nine different subtypes N 1 – N9*

  But only two subtypes of hemagglutinin (N1 and N2) have caused sustained epidemics in the human population.

Antigenic Variation

- Unique feature of this virus lies with antigenic variation.
- High in type A virus
- Less in type B virus
- Not in type C virus
- RNP and Matrix proteins are stable
- Hemagglutination and Neuraminidase are independ of the variations.

Influenza prominent Antigenic Changes

- Antigenic Shift
  - major change, new subtype
  - caused by exchange of gene segments
  - may result in pandemic
- Example of antigenic shift
  - H2N2 virus circulated in 1957-1967
  - H3N2 virus appeared in 1968 and completely replaced H2N2 virus

Antigenic Shift

- It is abrupt and Drastic
- Discontinuous variation in structure in antigens
- Results in novel virus and unrelated to previous strains causing infections
- Involves – Hemagglutinins, Neuraminidase or both
- Subtypes depends only on antigenic shifts, occurs on Hemagglutinins

Influenza Antigenic Changes

- Antigenic Drift
  - minor change, same subtype
  - caused by point mutations in gene
  - may result in epidemic
- Example of antigenic drift
  - in 2002-2003, A/Panama/2007/99 (H3N2) virus was dominant
  - A/Fujian/411/2002 (H3N2) appeared in late 2003 and caused widespread illness in 2003-2004

Pathogenesis

- Infects the respiratory tract
- Even 3 or few viral particles can infect
- Neuraminidase facilitates infection reducing the viscosity of Mucous
- Ciliated cells are infected in the Respiratory tract - site of viral infection
- When superficial layers are damaged exposes the basal layers
- And exposure of the basal layer causes the bacterial infections.

Pathogenesis – Viral Pneumonia

- Thickening of the Alveolar cells
- Intestinal infiltration with leucocytes with capillary thrombosis of Leucocytic exudates
- Hyaline membrane is formed occupying alveolar ducts and alveoli
- In late stages infiltration with Macrophages

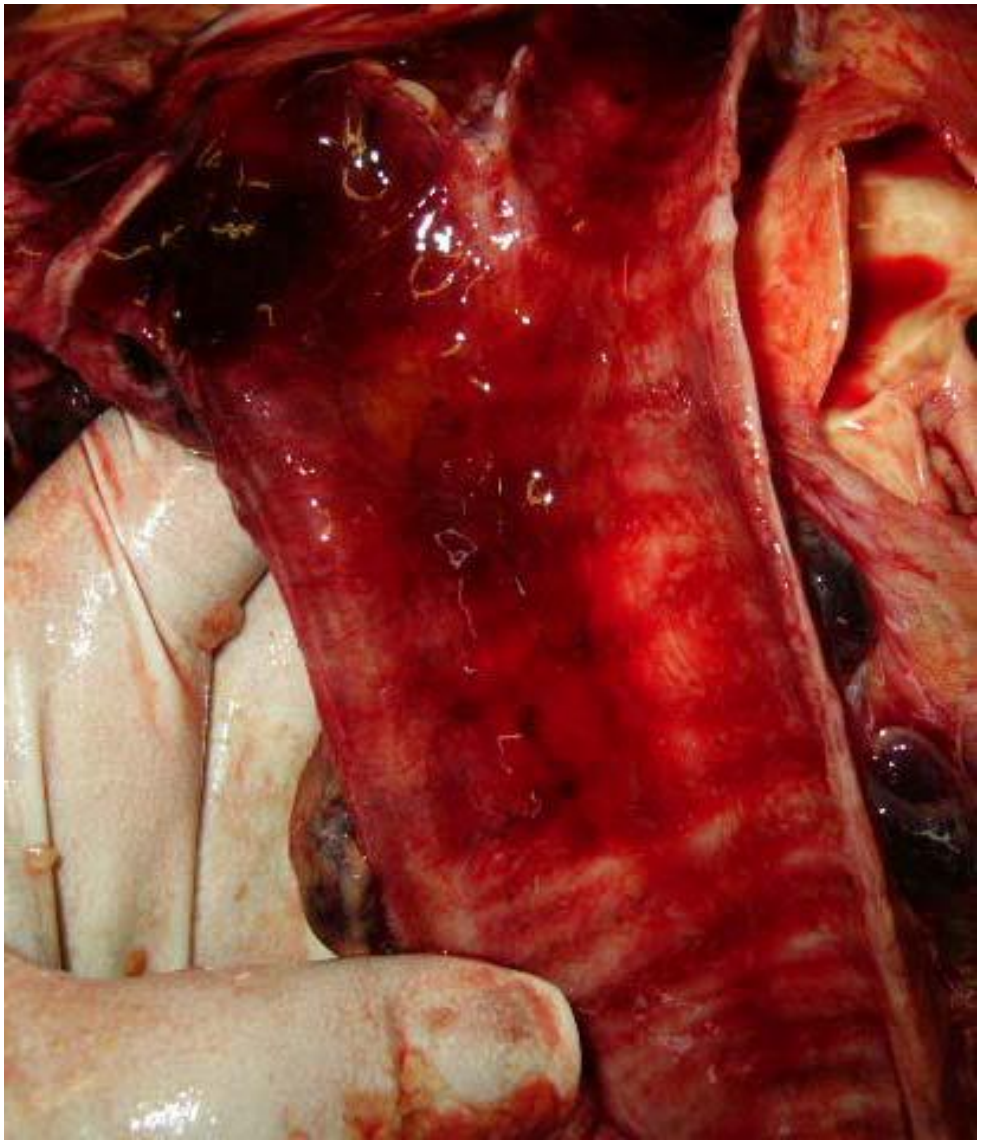
Clinical features

- Incubation 1 to 3 days
- Present with mild cold lead to fulminating rapidly fatal Pneumonia
- Can abruptly present with head ache

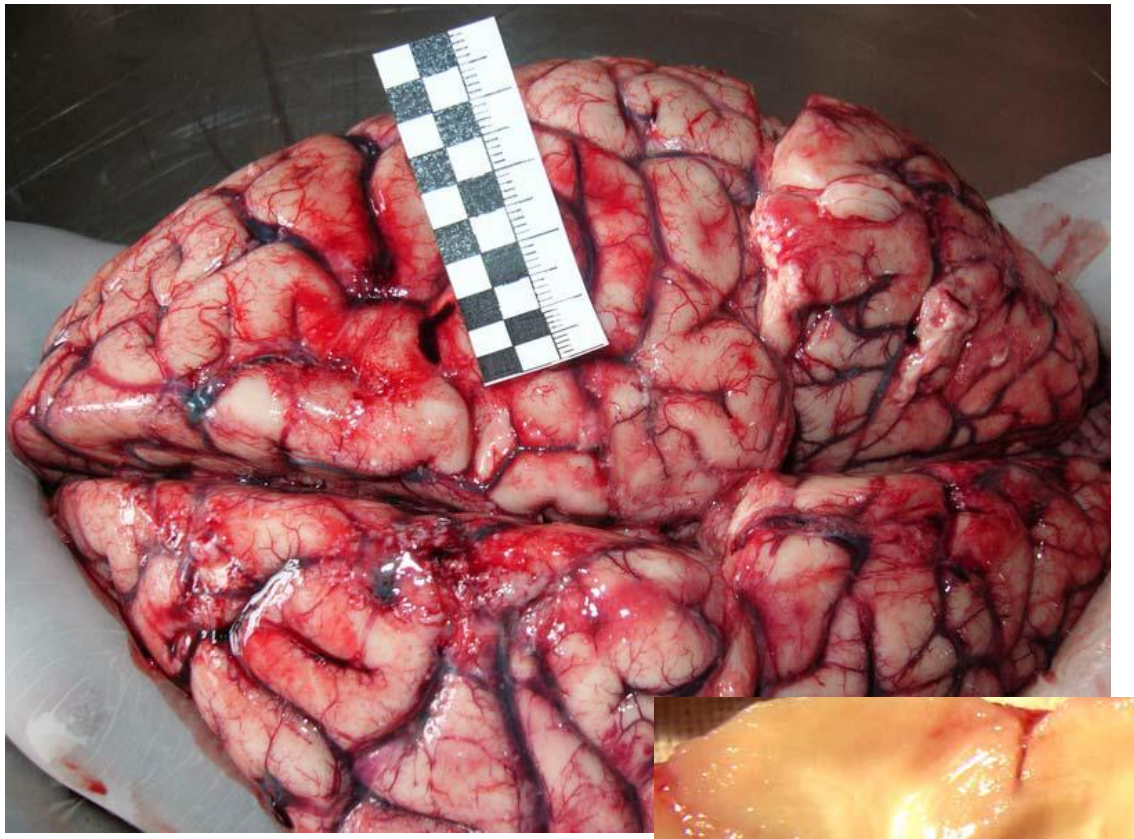
- Can also present with abdominal pain with type B in children
- Bacteria superinfect

Complication in Influenza

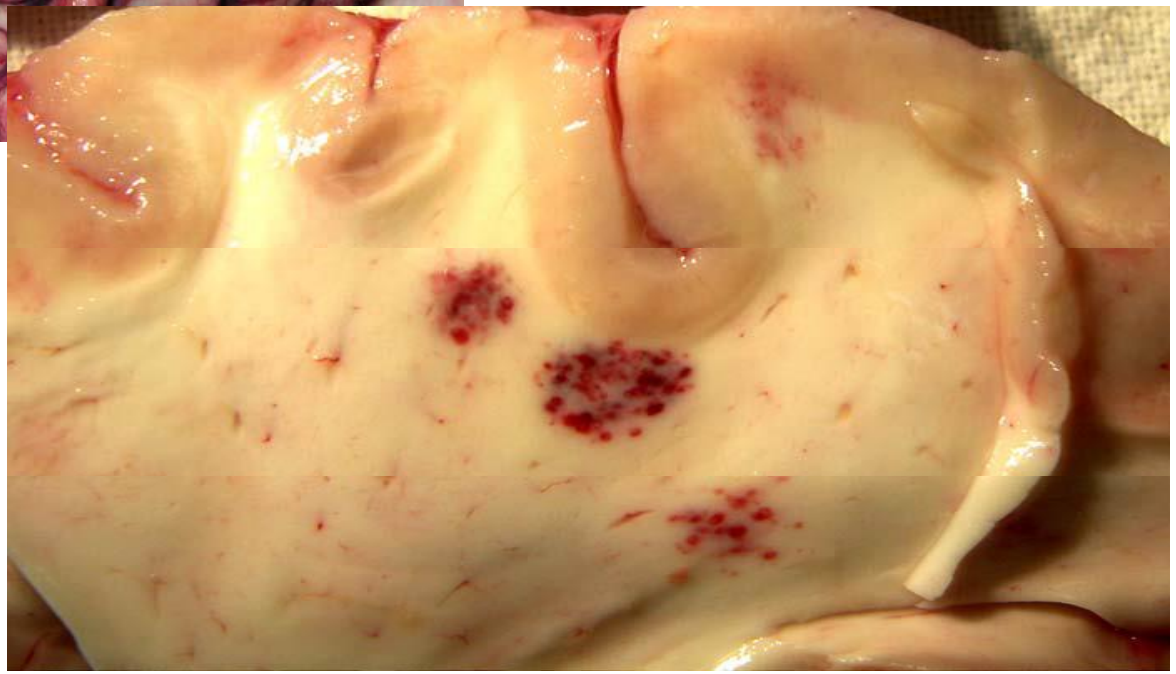
- Pneumonia
  - secondary bacterial
  - primary influenza viral
- Reye's syndrome
- Myocarditis
- Death 0.5-1 per 1,000 cases

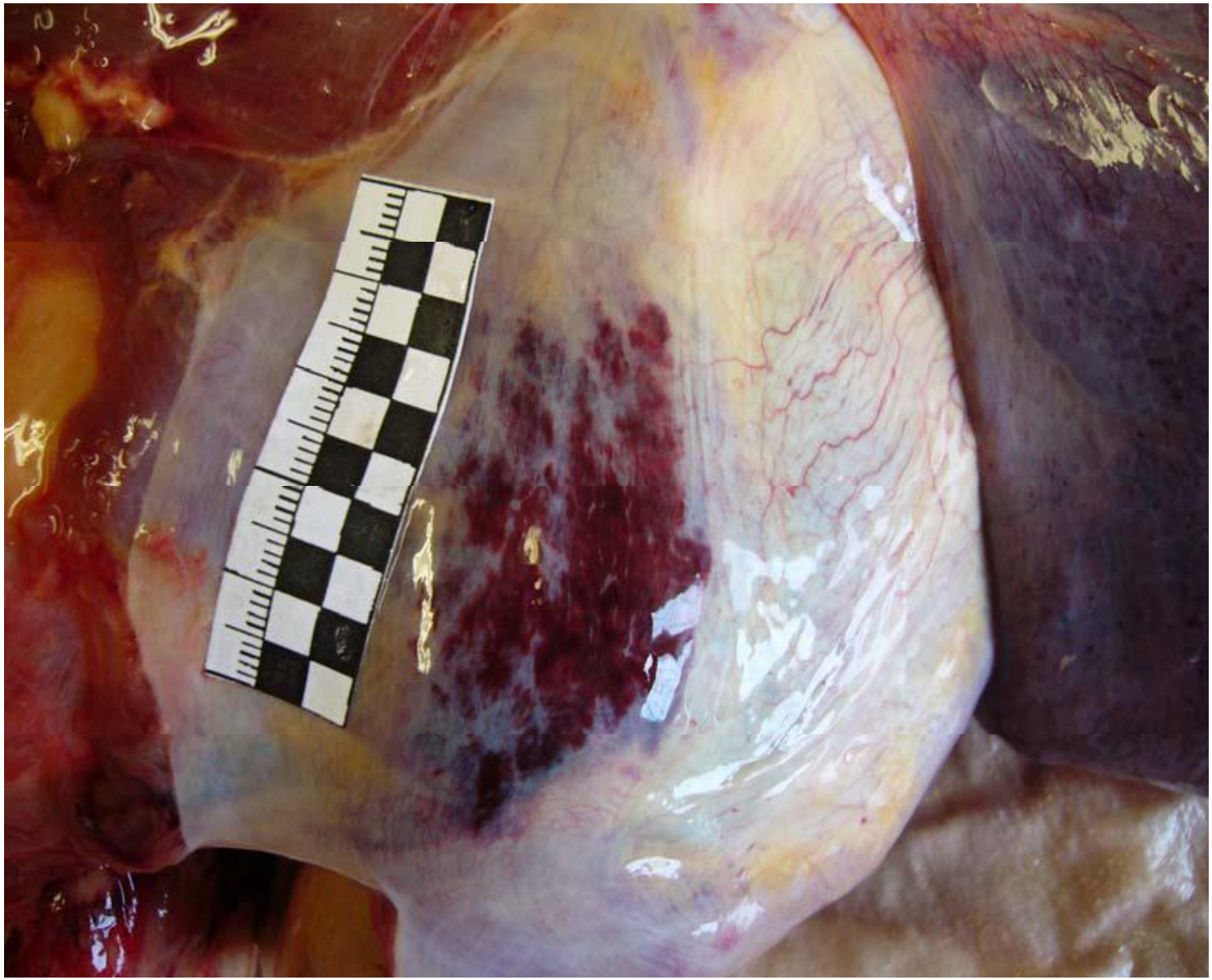


Hemorrhagic tracheobronchitis (day 9)

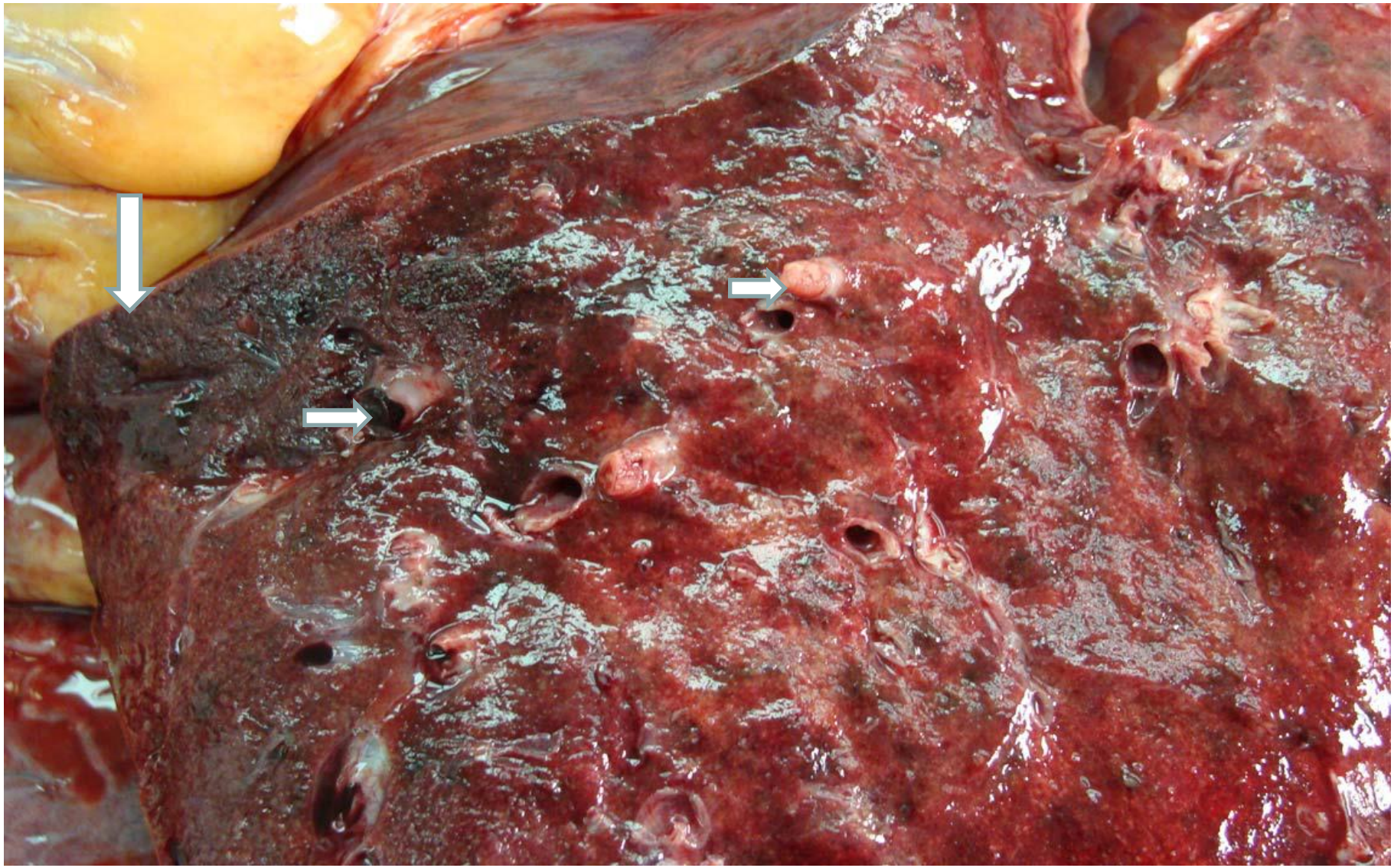


Subarchnoid hemorrhage and through diapedesis in the white matter of the brain (9 days)

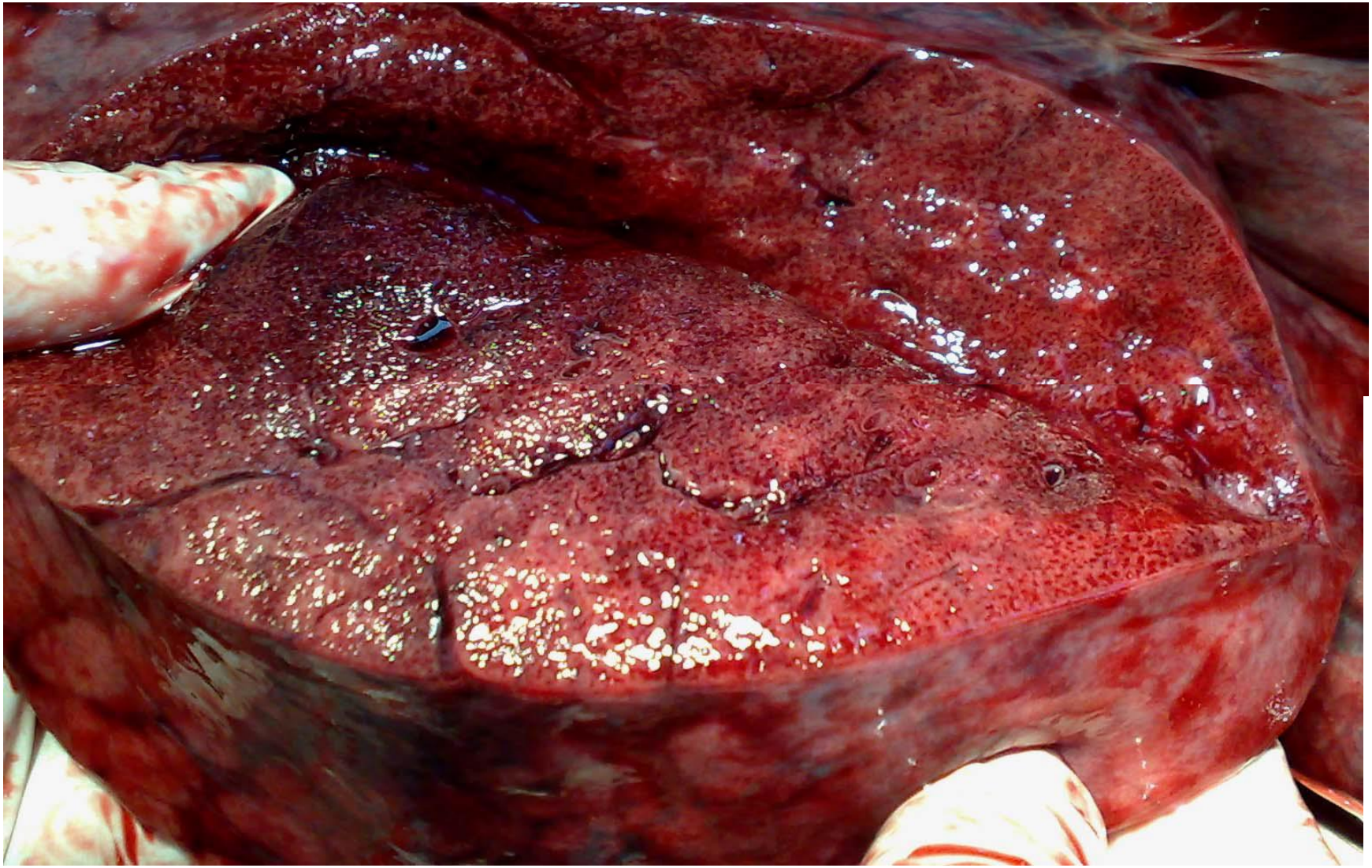




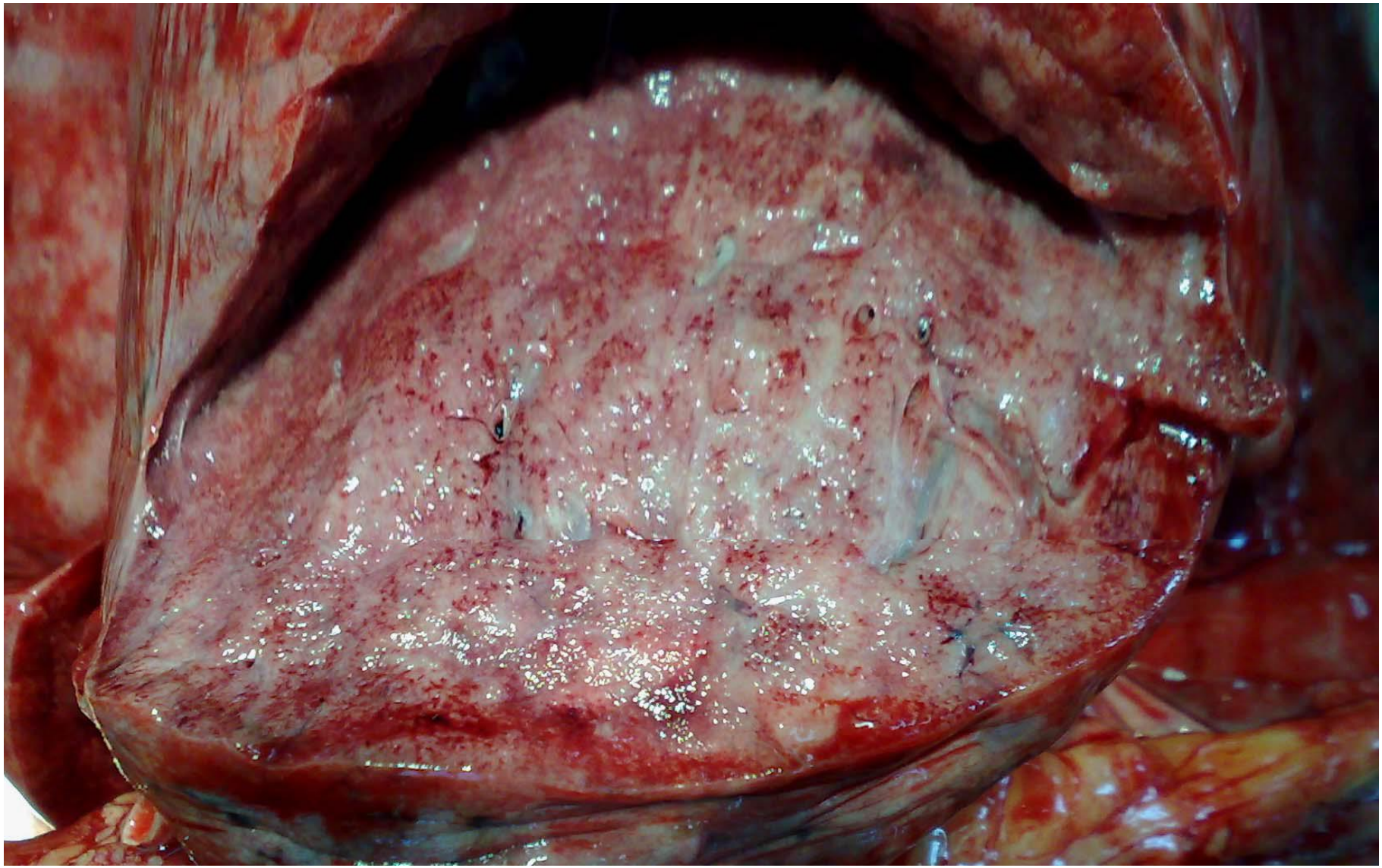
Hemorrhages in diaphragm (9 days)



White and red thrombi in pulmonary arteries and vein.
Pulmonary hemorrhagic infarction (day 16)

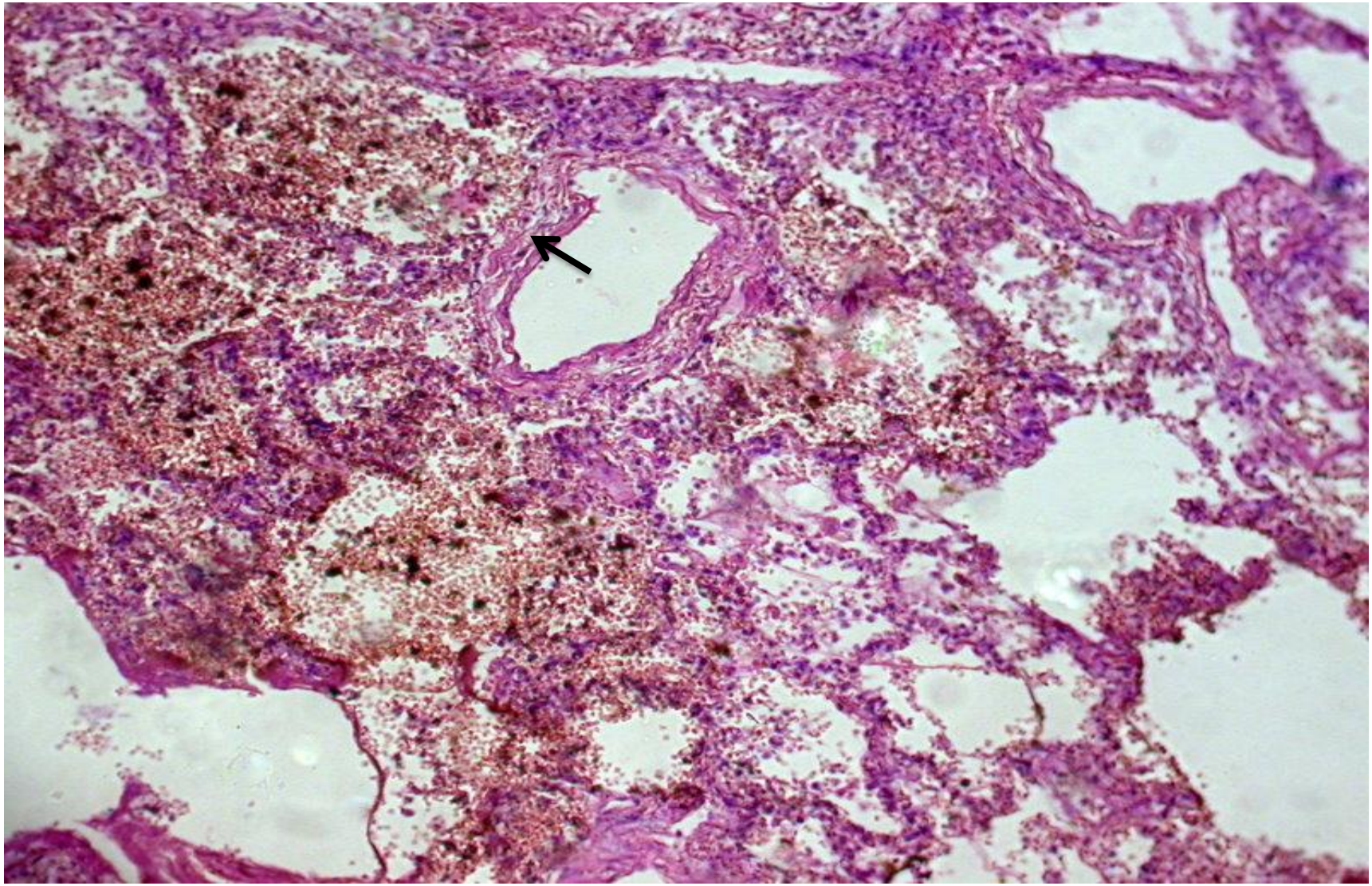


Obvious hyperemia, with alternating of whitish areas.
Big mottled lung (19 days)

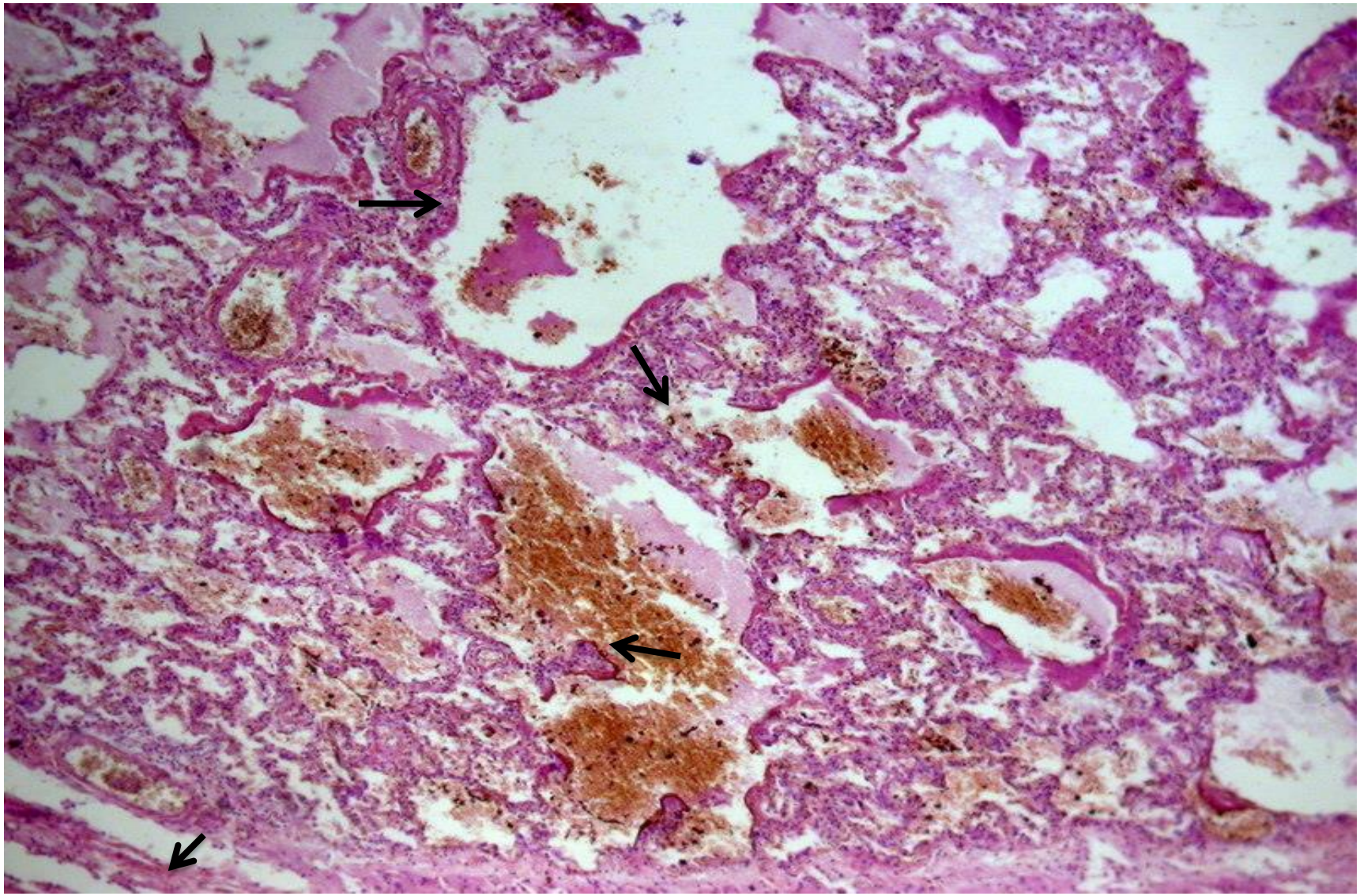


Proliferative stage of diffuse alveolar lesion (20 days)

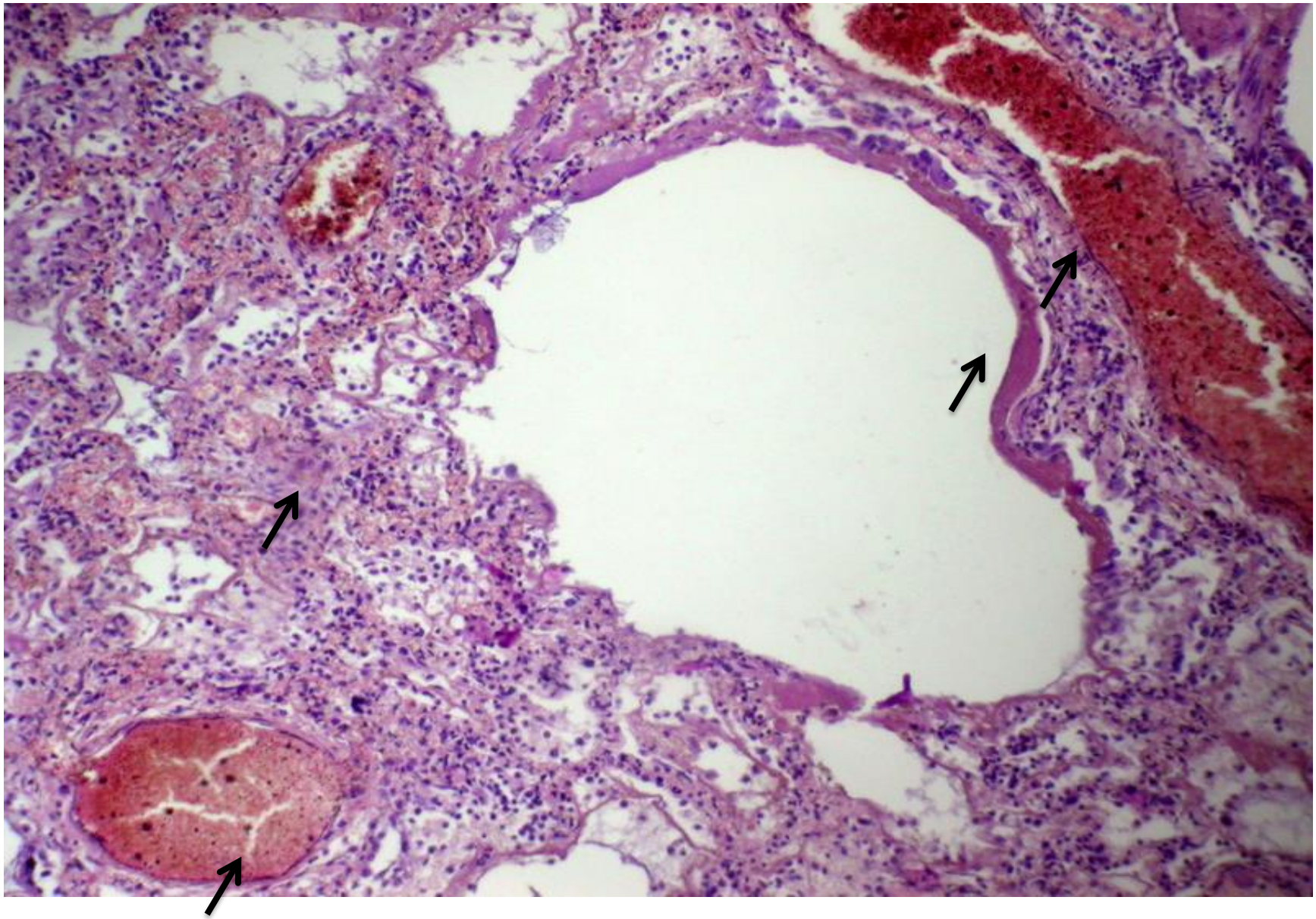
Influenza pneumonia with hemorrhagic component



Influenza pneumonia with hemorrhagic component

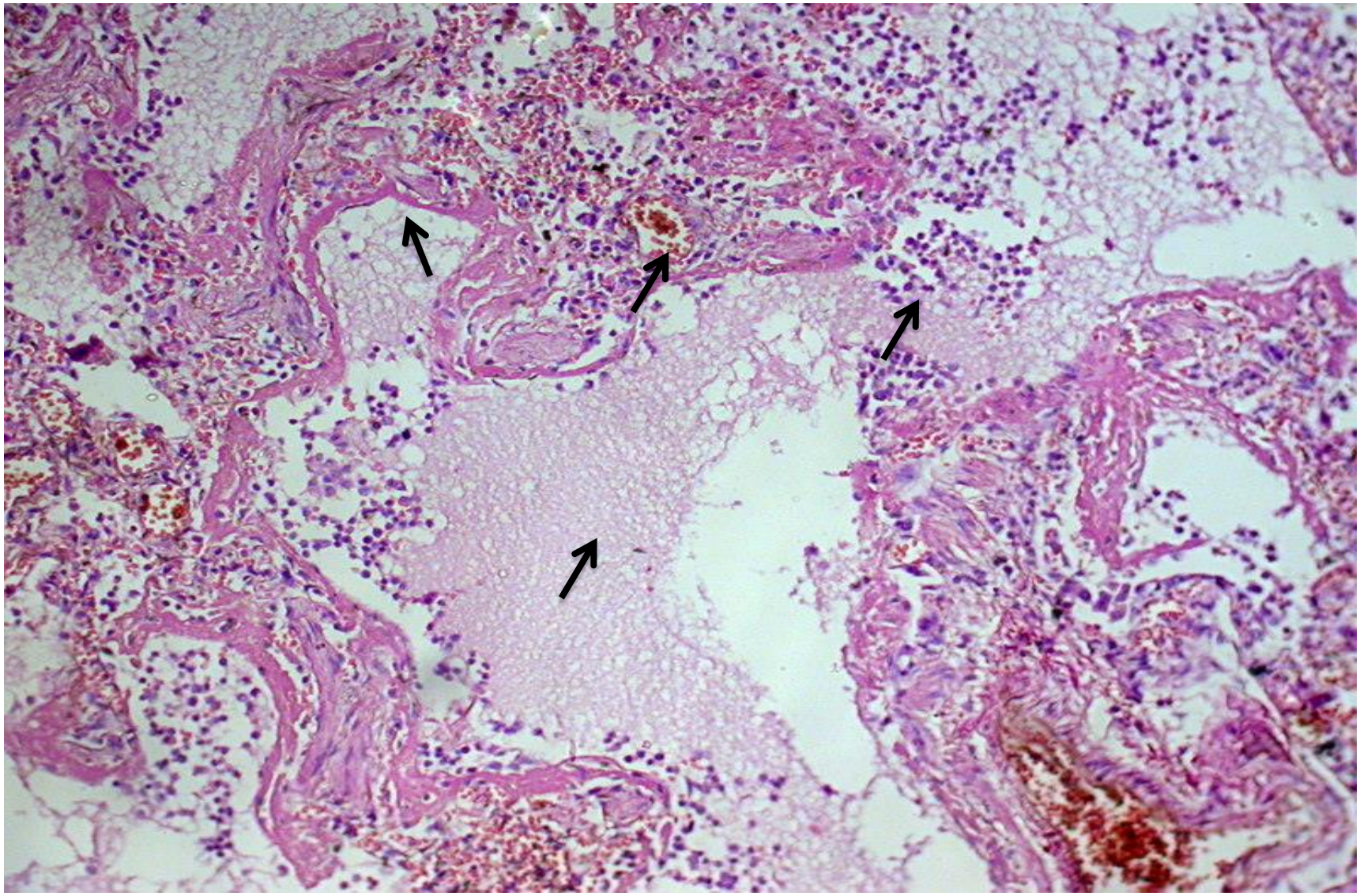


1) Hemorrhagic exudate, 2) Thickening of septa with lymphoid infiltration, 3) Hyperimic vessels.



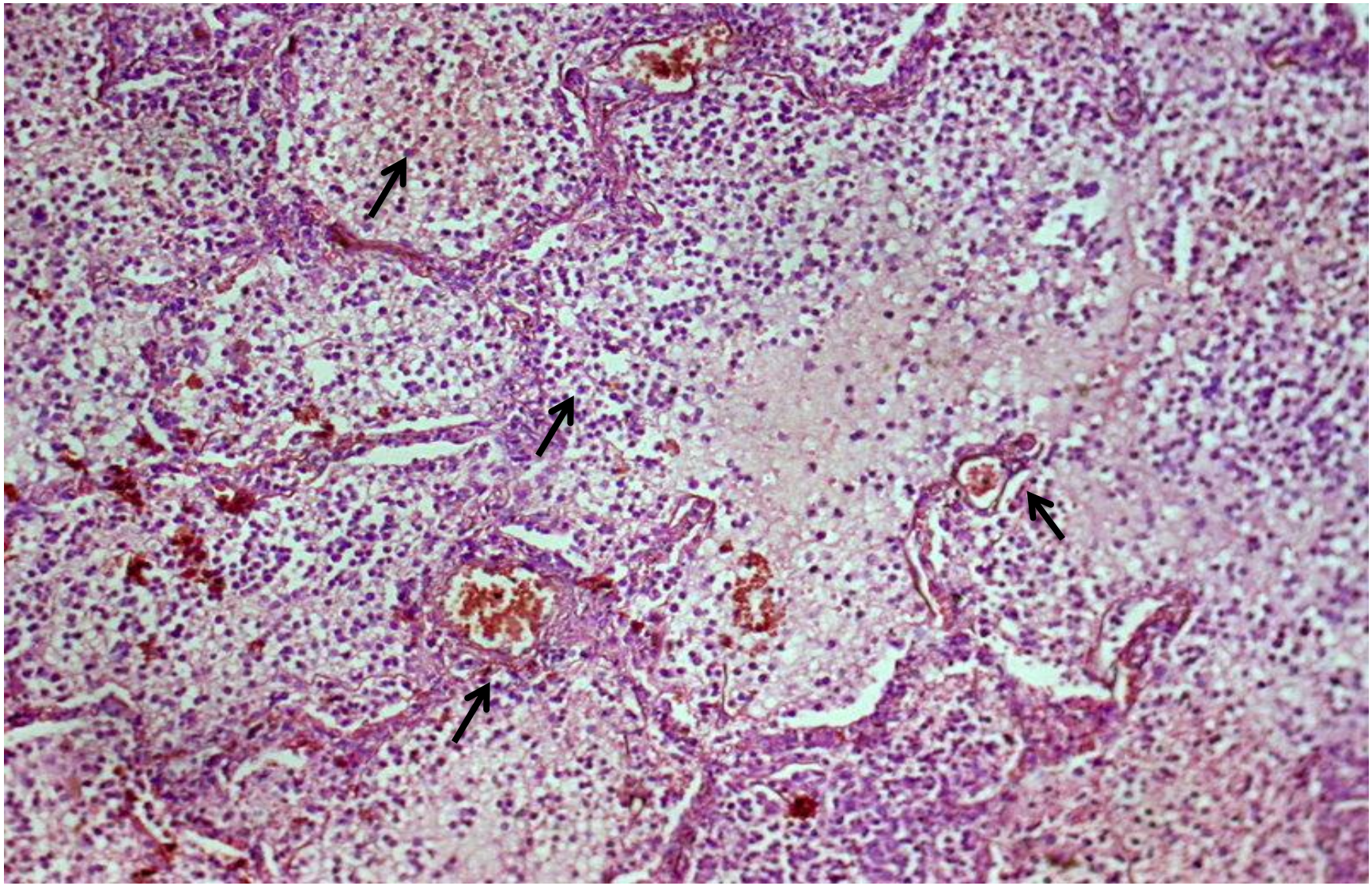
1. Thickened septa, with lymphoid infiltration, 2. Congested vessels 3. Alveolus with hyaline membranes

Diffuse alveolar lesion

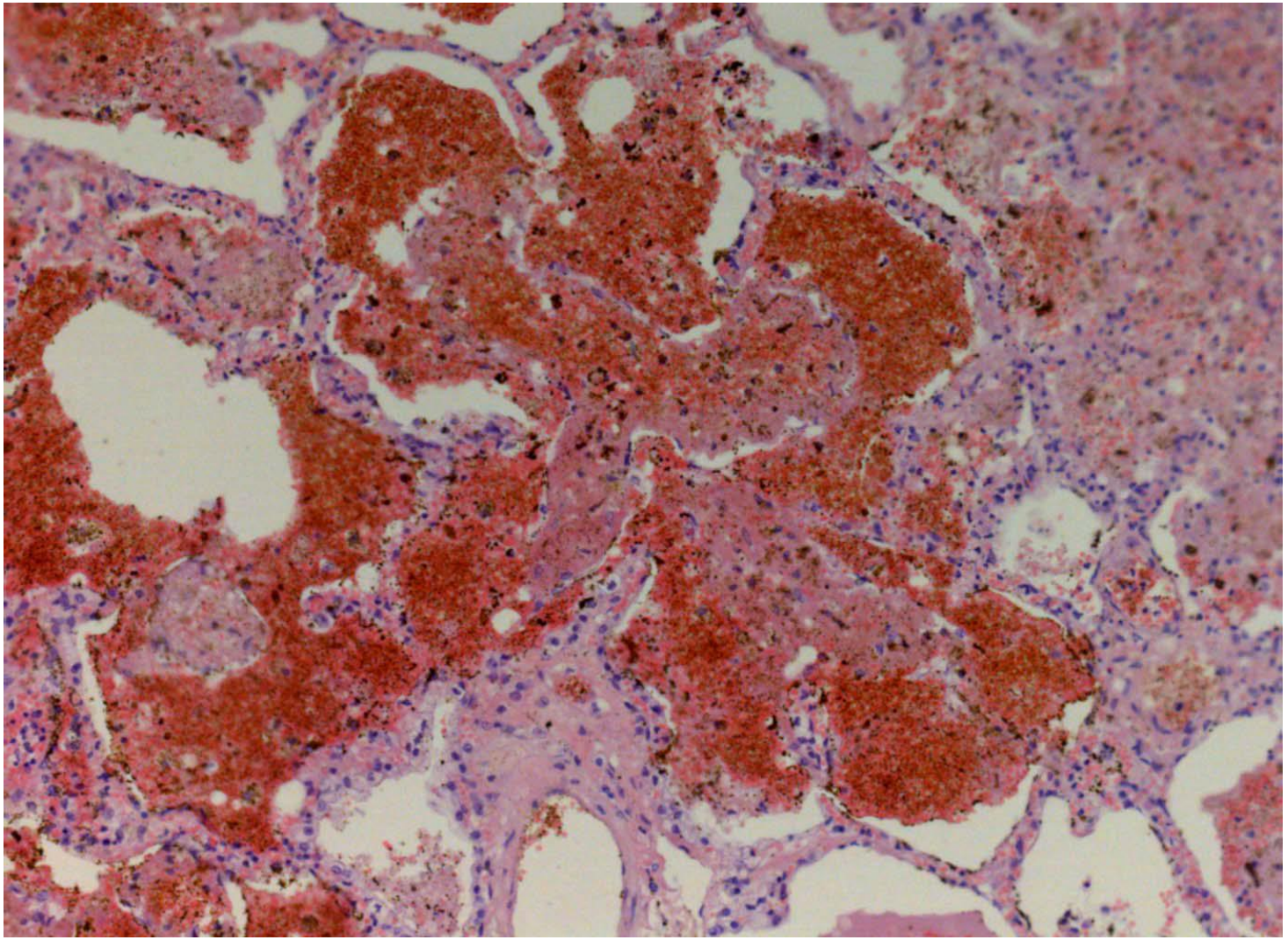


1) Hyaline membranes 2) Thickening of interalveolar septa 3) Lymphoid infiltration in septa and alveolar lumen 4) Hyperimic vessels 5) Serous exudate

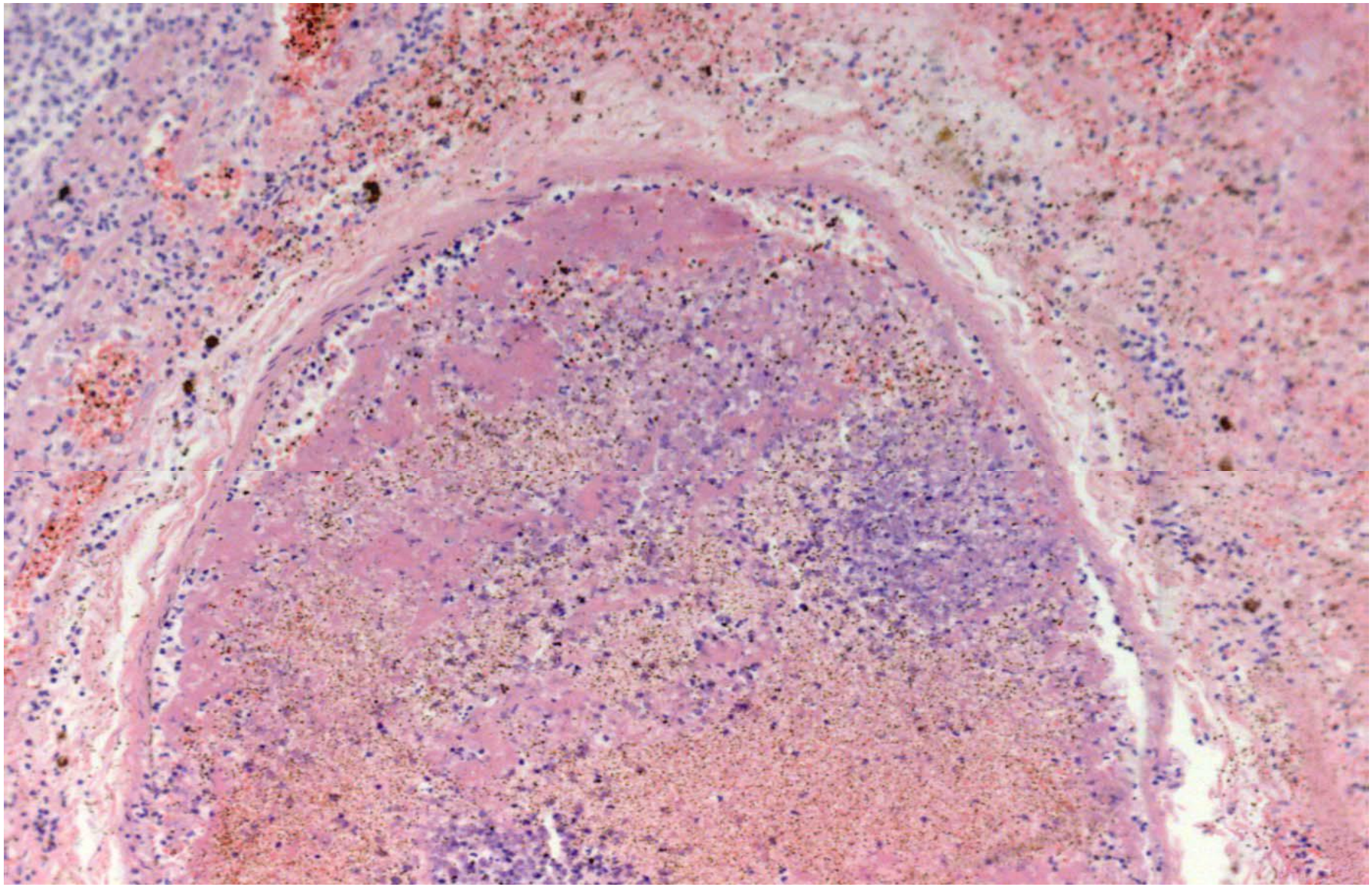
Influenza pneumonia associated with secondary infection



1) Hemorrhagic exudate, 2) Neutrophil exudate, 3) Congested vessels, 4) Destruction of interalveolar septa

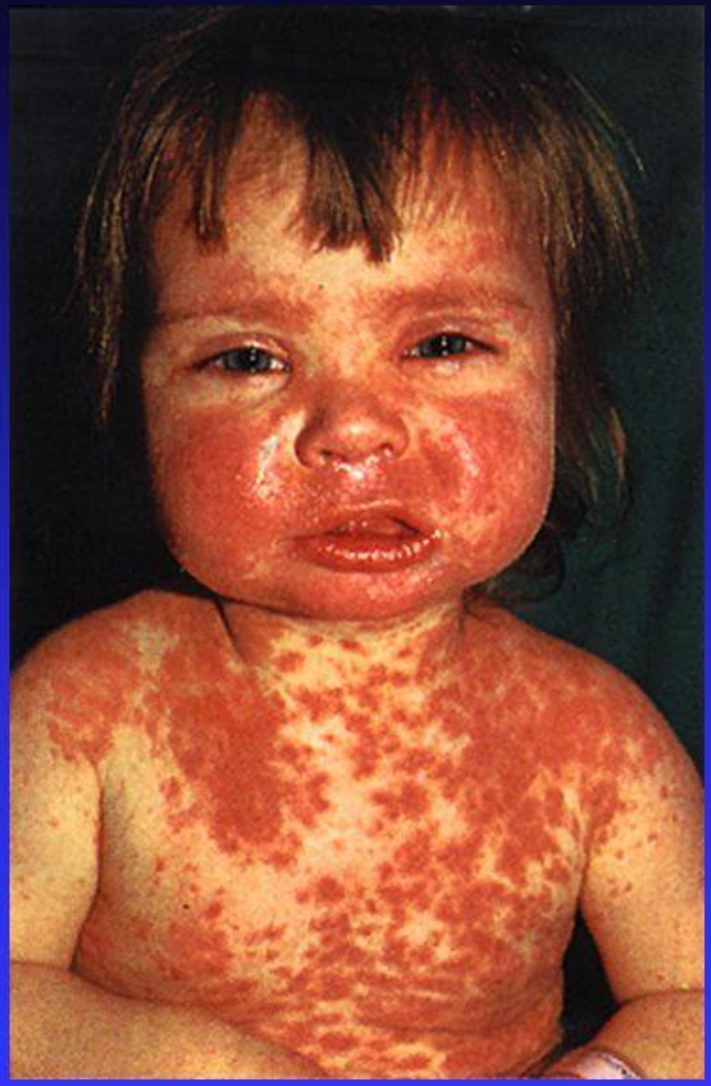


Erythrocytes in the alveoli -
pulmonary infraction



Thrombus in course of organization in the branches of the pulmonary artery.

Measles: Rash, conjunctivitis, and rhinitis



Measles (Rubeola)

It is an acute viral infection characterized by a final stage with a maculopapular rash erupting successively over the neck and face, trunk, arms, and legs, and accompanied by a high fever.

Etiology

- Measles virus, the cause of measles, is an RNA virus of the genus Morbillivirus in the family Paramyxoviridae.
- Only one serotype is known

Epidemiology

- Measles is endemic throughout the world.
- In the past, epidemics tended to occur irregularly, appearing in the spring in large cities at 2-4-yr intervals as new groups of susceptible children were exposed.

Epidemiology

(Cont.)

- It is rarely subclinical.
- Prior to the use of measles vaccine, the peak incidence was among children 5-10 yr of age.

Individuals born before 1957 are considered to have had natural infection and to be immune

TRANSMISSION

- Measles is highly contagious; approximately 90% of susceptible household contacts acquire the disease.
- Maximal dissemination of virus occurs by droplet spray during the prodromal period (catarrhal stage).

Pathology

- The essential lesion of measles is found in the skin, conjunctivae, and the mucous membranes of the nasopharynx, bronchi, and intestinal tract.
- Serous exudate and proliferation of mononuclear cells and a few polymorphonuclear cells occur around the capillaries.

Pathology (cont.)

- **Koplik spots** consist of serous exudate and proliferation of endothelial cells similar to those in the skin lesions.
- •A general inflammatory reaction of the buccal and pharyngeal mucosa extends into the lymphoid tissue and the tracheobronchial mucous membrane.

Pathology(cont.)

- Interstitial pneumonitis resulting from measles virus takes the form of **giant cell pneumonia**.
- Bronchopneumonia may occur from secondary bacterial infection.

Pathology (cont.)

- In fatal cases of encephalomyelitis, perivascular demyelinization occurs in areas of the brain and spinal cord.
- In subacute sclerosing panencephalitis (SSPE), there may be degeneration of the cortex and white matter with intranuclear and intracytoplasmic inclusion bodies

Clinical Manifestations

- Measles has three clinical stages:

1. an incubation stage
2. a prodromal stage with an enanthem (Koplik spots) and mild symptoms
3. a final stage with a maculopapular rash accompanied by high fever.

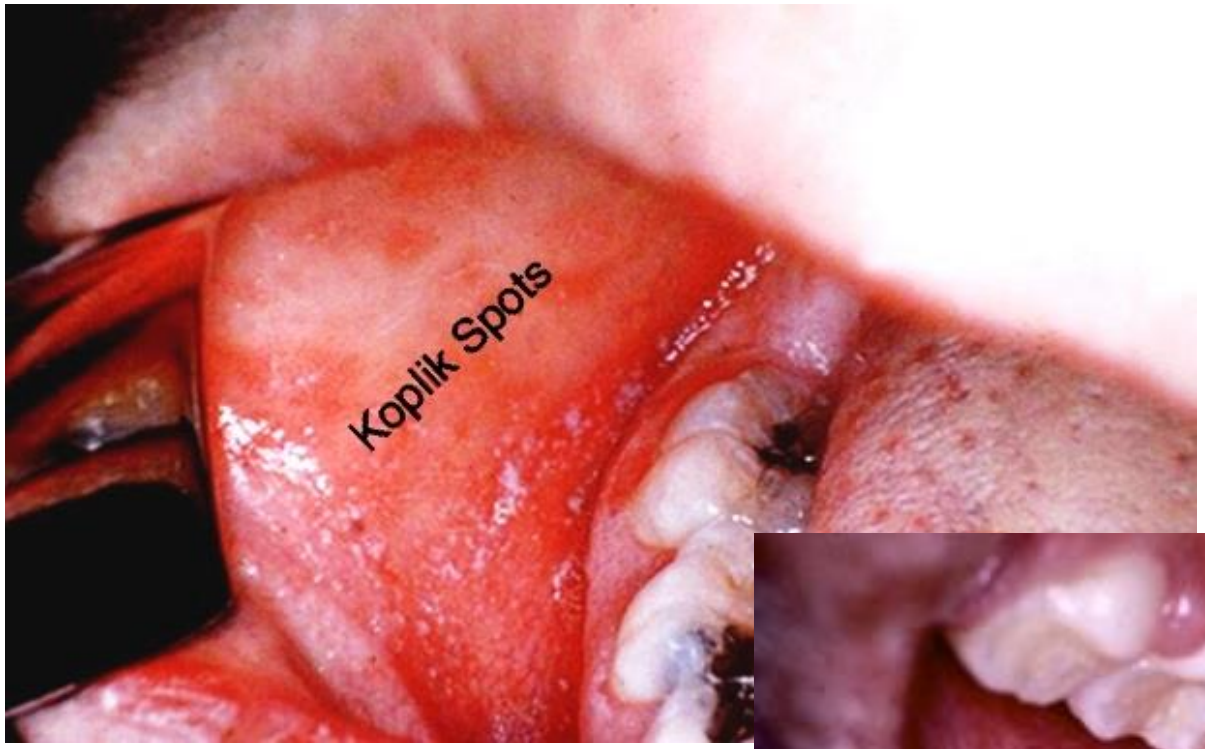
Koplik spots

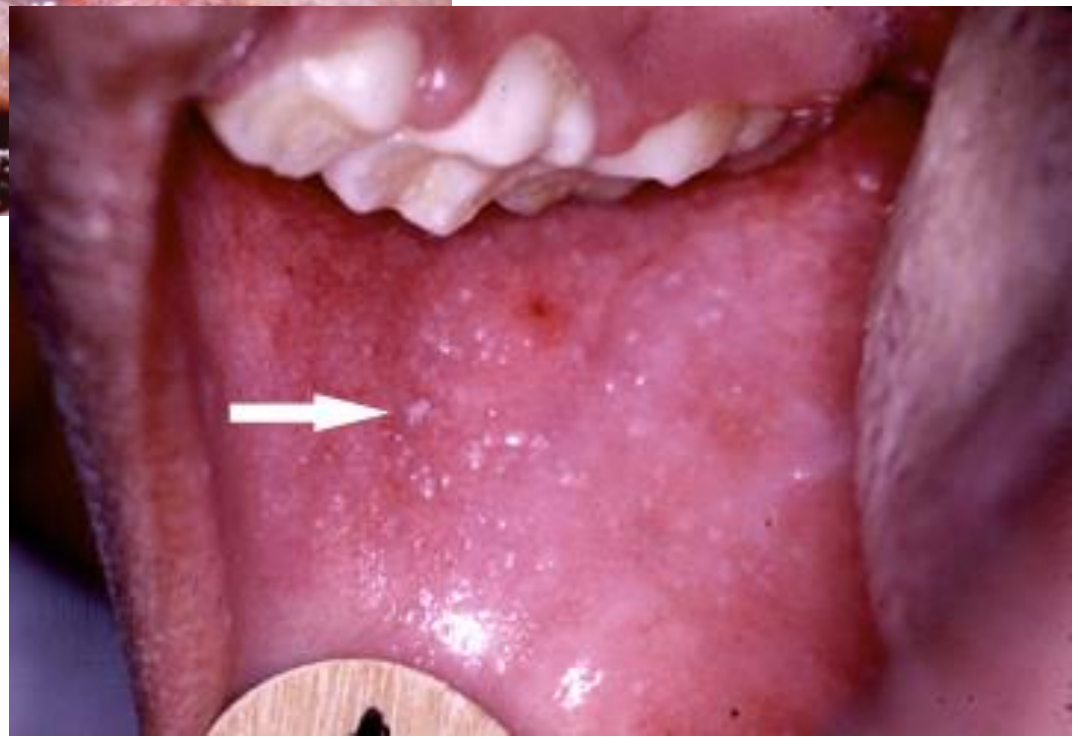
- An enanthem or red mottling is usually present on the hard and soft palates
- the pathognomonic sign of measles:

Koplik spots (cont.)

- • are grayish white dots, usually as small as grains of sand, that have slight, reddish areolae; occasionally they are hemorrhagic.

  • tend to occur opposite the lower molars but may spread irregularly over the rest of the buccal mucosa.


Koplik Spots



The rash

- usually starts as faint macules on the:
  * upper lateral parts of the neck
  * behind the ears
  * along the hairline
  * posterior parts of the cheek.

The rash

(cont.)

- The individual lesions become increasingly maculopapular as the rash spreads rapidly over the:
  * entire face
  * neck
  * upper arms
  * upper part of the chest

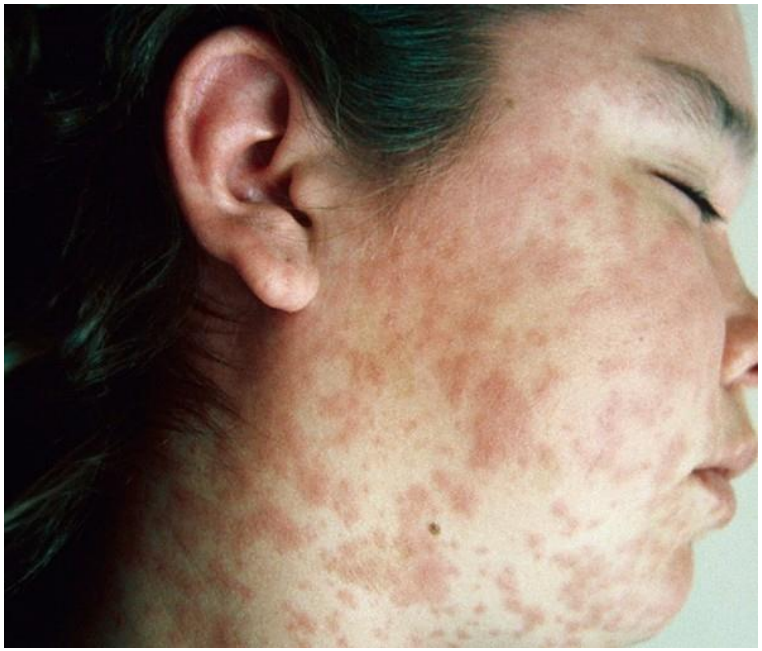
  within approximately the first 24 hr

The rash

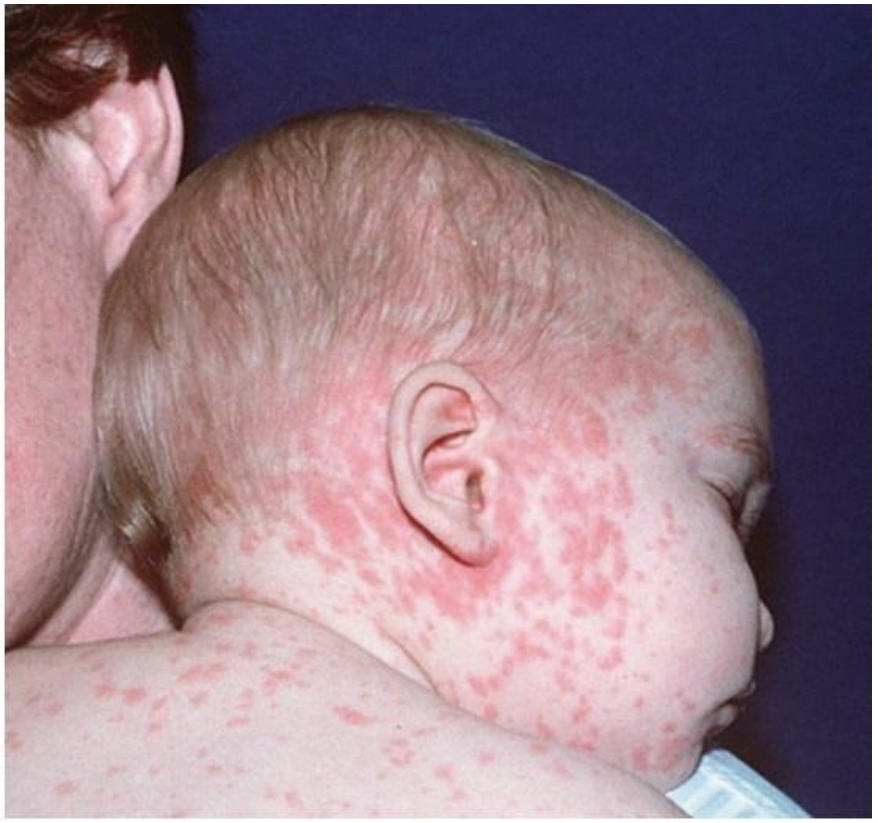
(cont.)

- During the succeeding 24 hr the rash spreads over the back, abdomen, entire arm, and thighs.
- As it finally reaches the feet on the 2nd-3rd day, it begins to fade on the face.

Typical rash on day 2–3 of measles



Rash on day 5 of measles showing typical confluence and density on head with scattered lesions on the trunk.



The prodromal phase

- Otitis media
- bronchopneumonia
- gastrointestinal symptoms such as diarrhea and vomiting

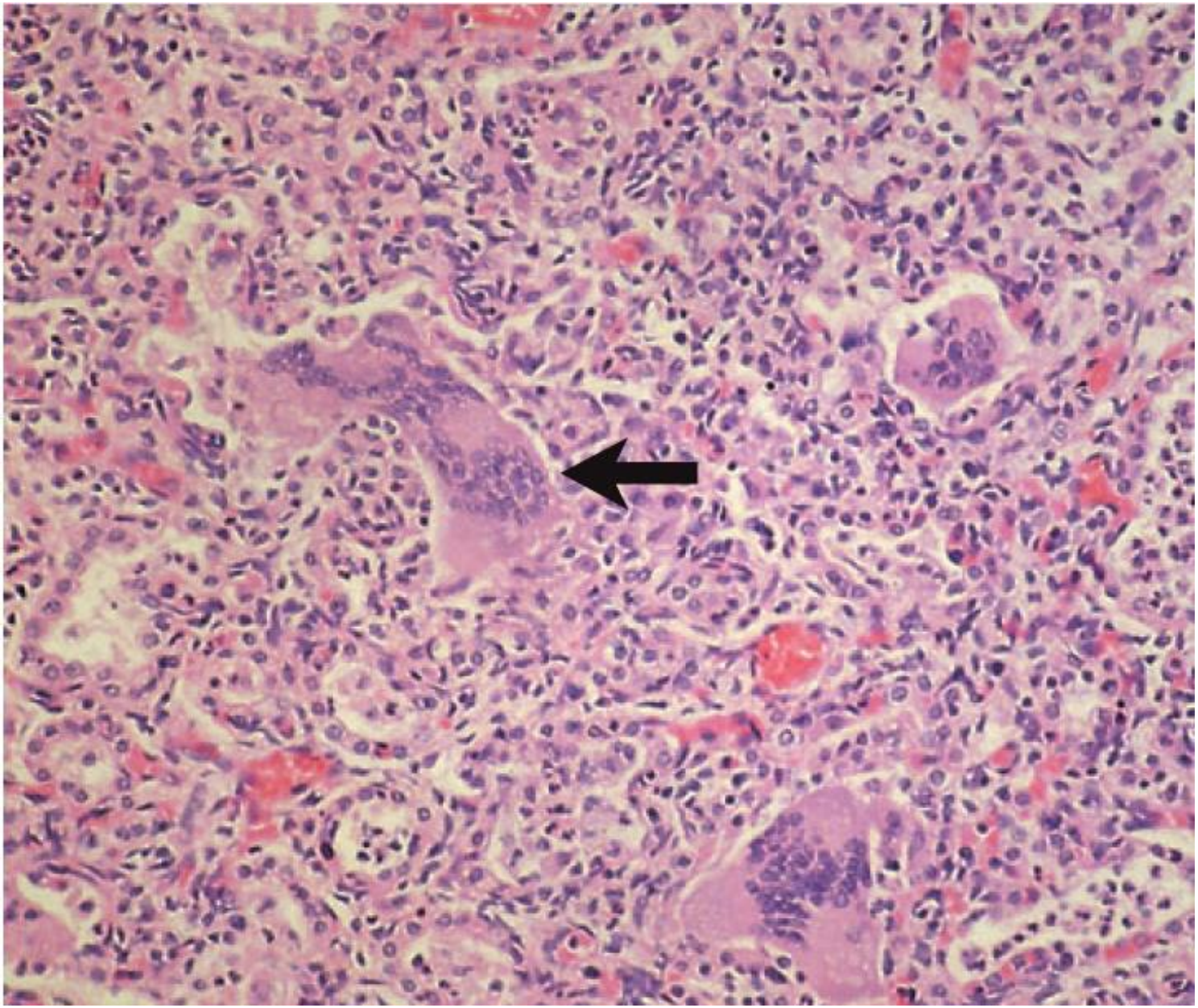
Are more common in infants and small children (especially if they are malnourished) than in older children.

Complications

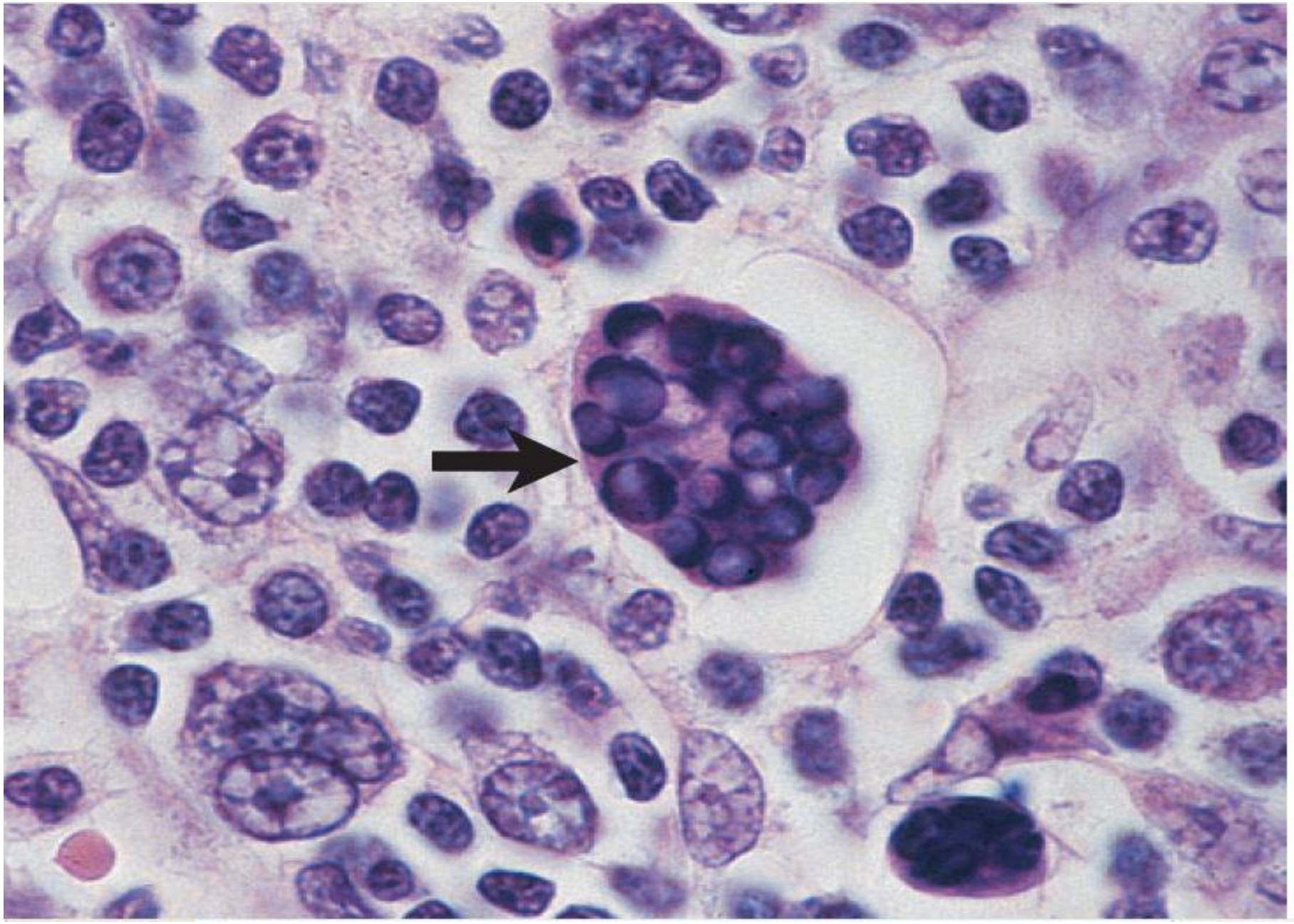
- The chief complications of measles are:
  - otitis media
  - pneumonia
  - encephalitis.

Respiratory tract complications

- Interstitial pneumonia may be caused by the measles virus (giant cell pneumonia).
- Bacterial superinfection and bronchopneumonia are more frequent, however, usually with pneumococcus, group A Streptococcus, Staphylococcus aureus, and Haemophilus influenzae type b.
- Laryngitis, tracheitis, and bronchitis are common and may be due to the virus alone



Interstitial pneumonia



Giant Warthin-Finkeldey cell in measles. H-E

DIPHTHERIA

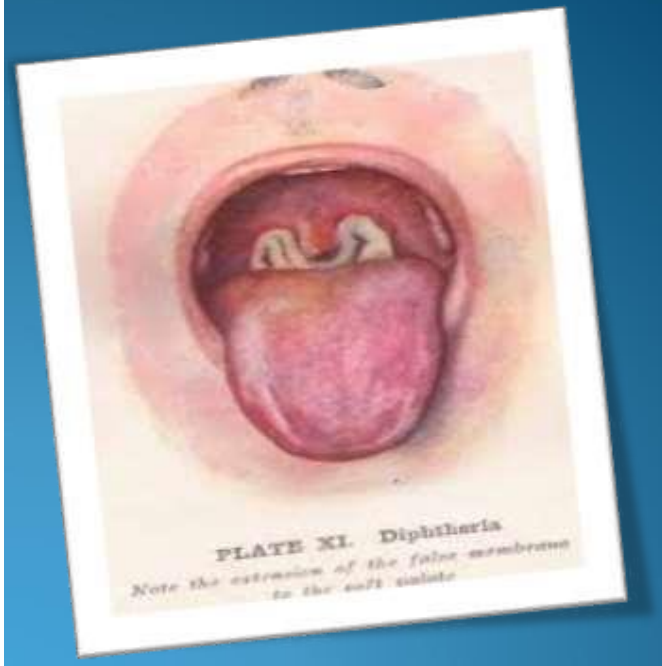
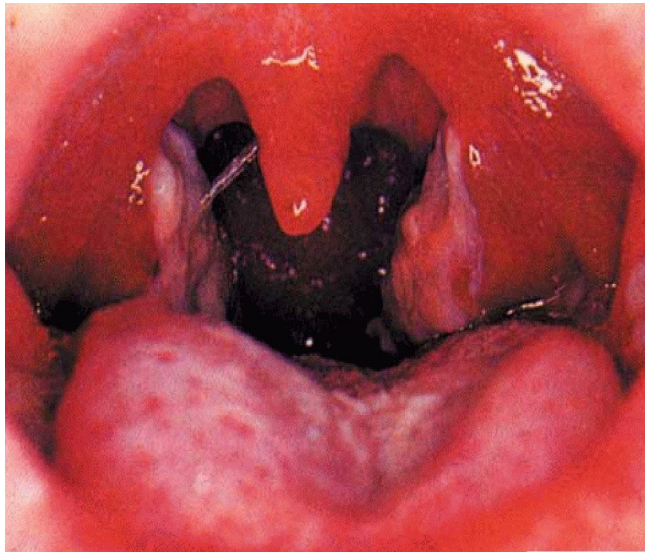


PLATE XI. Diphtheria
Note the extension of the false membrane to the soft palate

INTRODUCTION

- Acute infectious disease caused by toxigenic strains of **Coryne bacterium diphtheriae**.
- Bacilli multiply locally in throat and produce powerful exotoxin.
- Exotoxin inhibits the biosynthesis of respiratory cycle ferments, paralyzing tissue respiration.



HISTORY

- Took its name from greek word “diphthera” meaning leather.
- Named in 1826 by French physician Pierre Bretonneau.
- In the past, disease was called as general disease or killer disease because there was no treatment and was the cause of high mortality in children.
- It was said that the disease killed as many as 80% of the children below 10 yrs.

AGENT

Agent → *Corynebacterium diphtheria*

- Gram positive motile organism
- No invasive power but produce powerful exotoxin after multiplication locally in the throat responsible for:

1. Formation of false membrane over tonsils, pharynx or larynx, with well defined edges and membrane cannot be wiped away.
2. Marked congestion, edema, local tissue destruction
3. Enlargement of lymph nodes
4. Toxaemic signs and symptoms

MODE OF TRANSMISSION

- Droplet infections
- Can also be transmitted directly to susceptible persons from infected cutaneous lesions.
- Transmission by objects contaminated by naso-pharyngeal secretions of patients is also possible.

PORTAL OF ENTRY

- Respiratory route- respiratory tract

- Non-respiratory route-

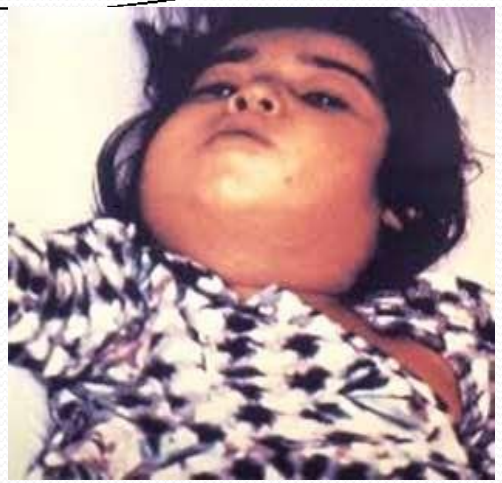
  - Portal of entry may be skin where cuts, ulcers and wounds not properly attended to or through umbilicus of new born.
  - Site of implantation may be eyes, genitalia or middle ear.

CLINICAL FEATURES

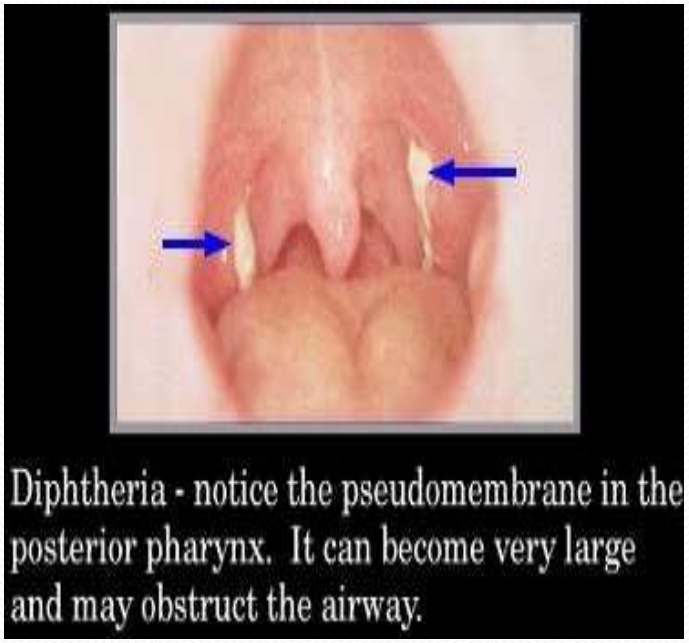
- Respiratory tract forms of diphtheria-

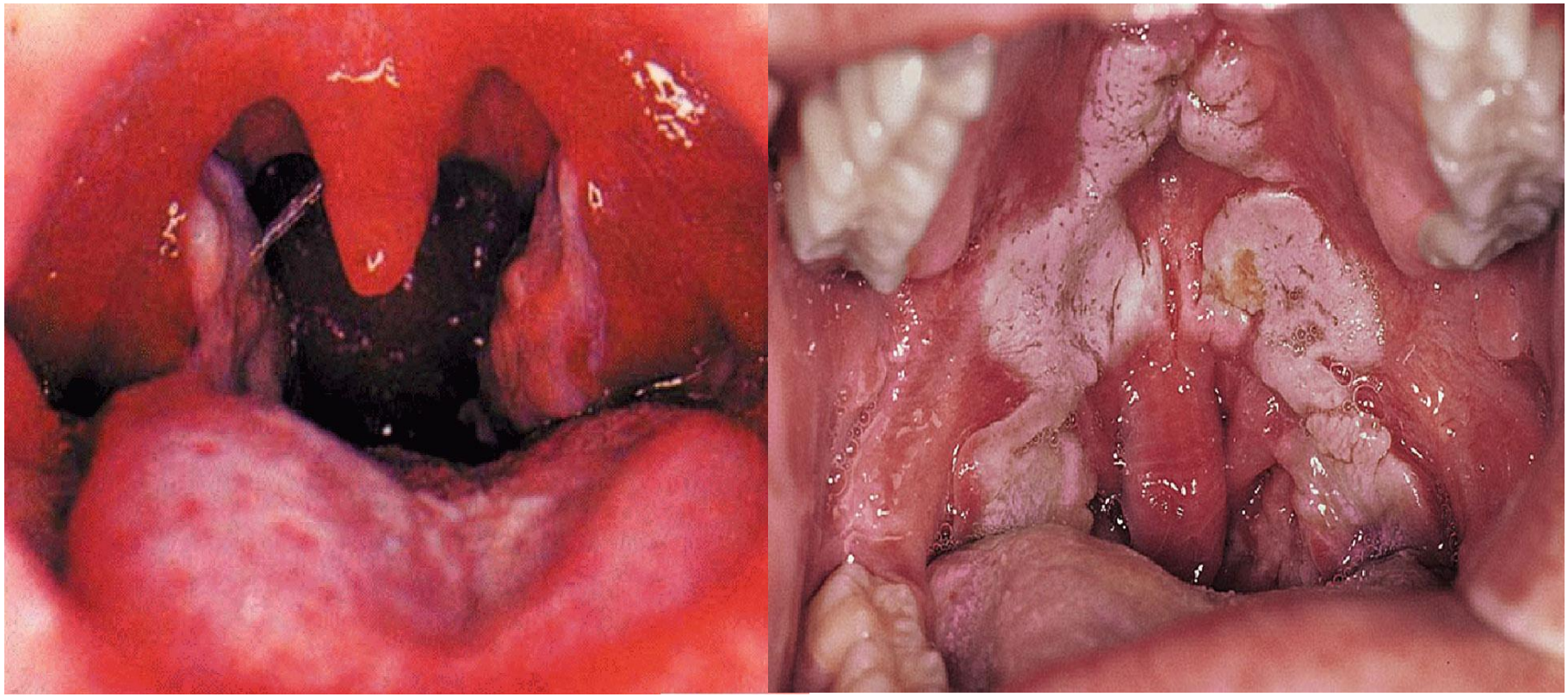
  pharyngo-tonsillar
  laryngo tracheal
  nasal
  combinations

Pharyngo-tonsillar diphtheria



- Sore throat
- Difficulty in swallowing
- Low grade fever at presentation
- Presence of pseudo membrane over tonsils
- Oedema in sub mandibular region
- Bull necked appearance



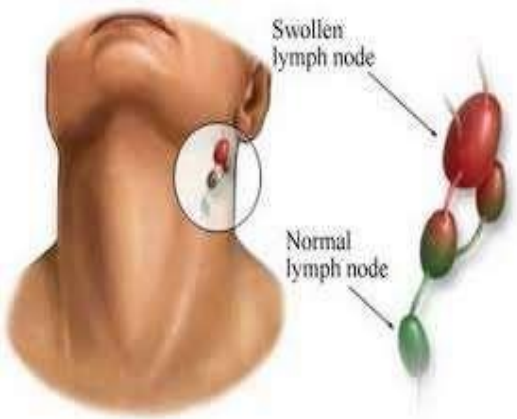


1 2

Pharyngeal vestibule diphtheria (1 - localized form, 2 - toxic form)

Laryngo-tracheal diphtheria

- Preceeded by pharyngo tonsillar diphtheria
- Fever, hoarseness and croupy cough
- Dyspnoea



Toxin damage

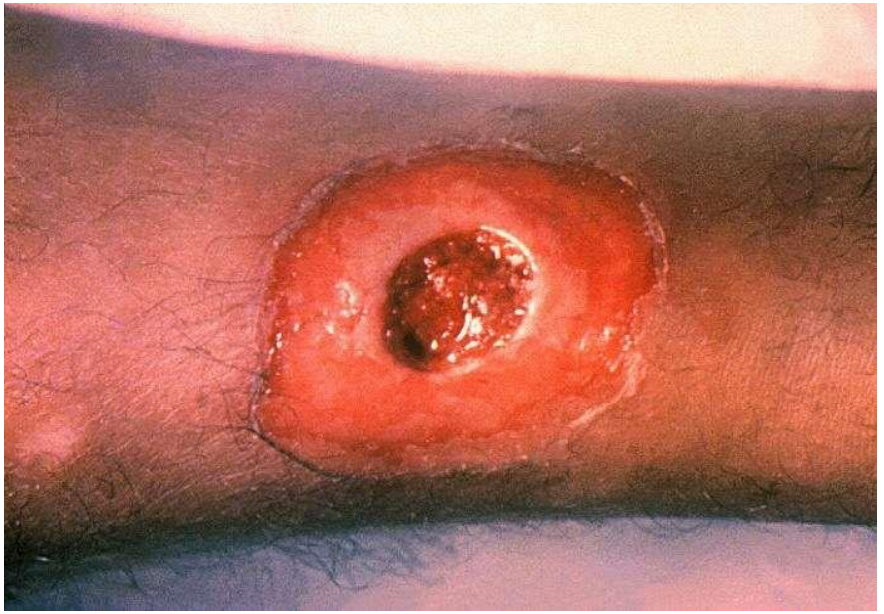
- parenchymatous degeneration
- necrosis in heart muscles, liver, kidneys and adrenals
- vision difficulties, speech, swallowing or movements of arms or legs
- paralysis of soft palate, eye muscle or extremities

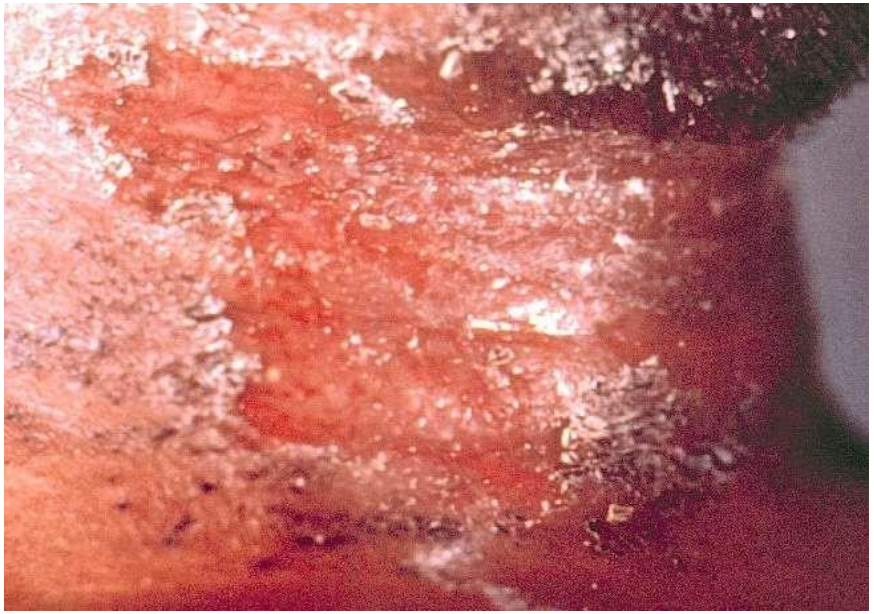
Nasal diphtheria

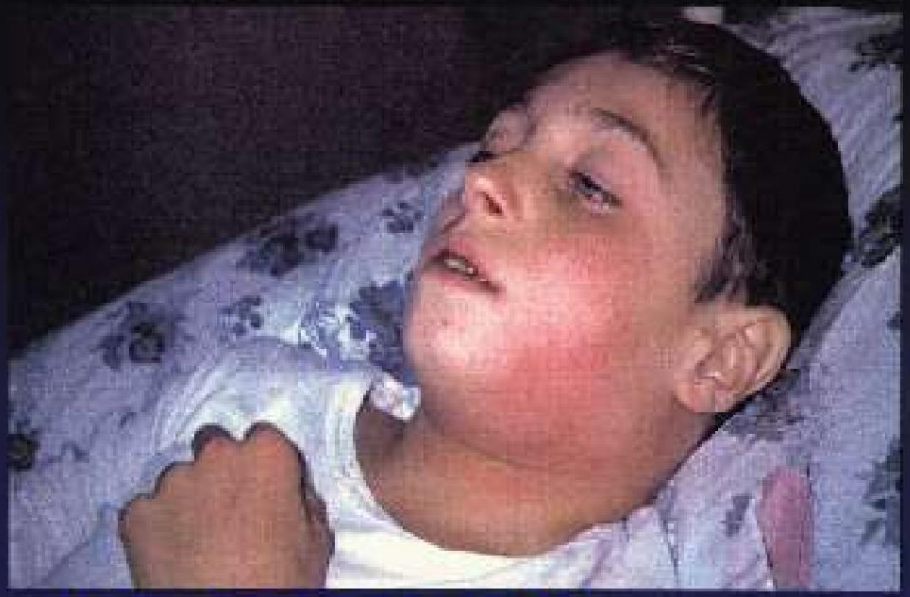
- Mildest form
- Localized in septum or turbinates of one side of nose
- Conjunctiva and genitals also sources of infection
- Membrane extends to pharynx.

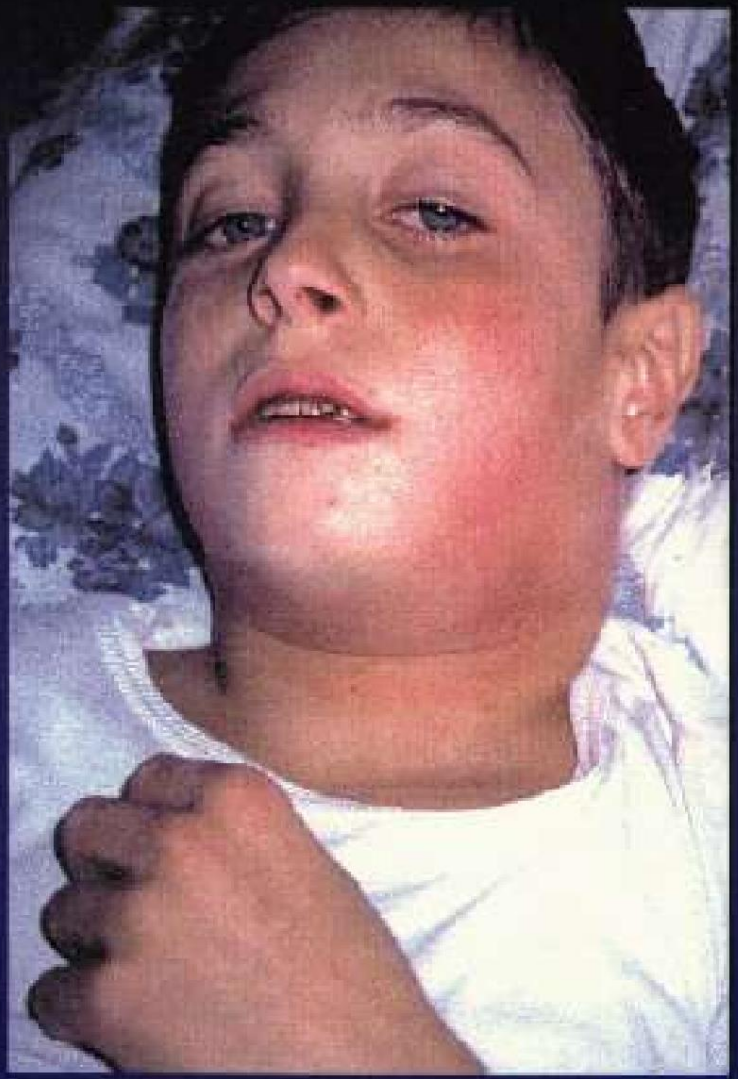
Cutaneous diphtheria

- Common in tropical areas
- Secondary infection of previous infection or skin abrasion
- Presenting lesion-an ulcer surrounded by erythema and covered with membrane.







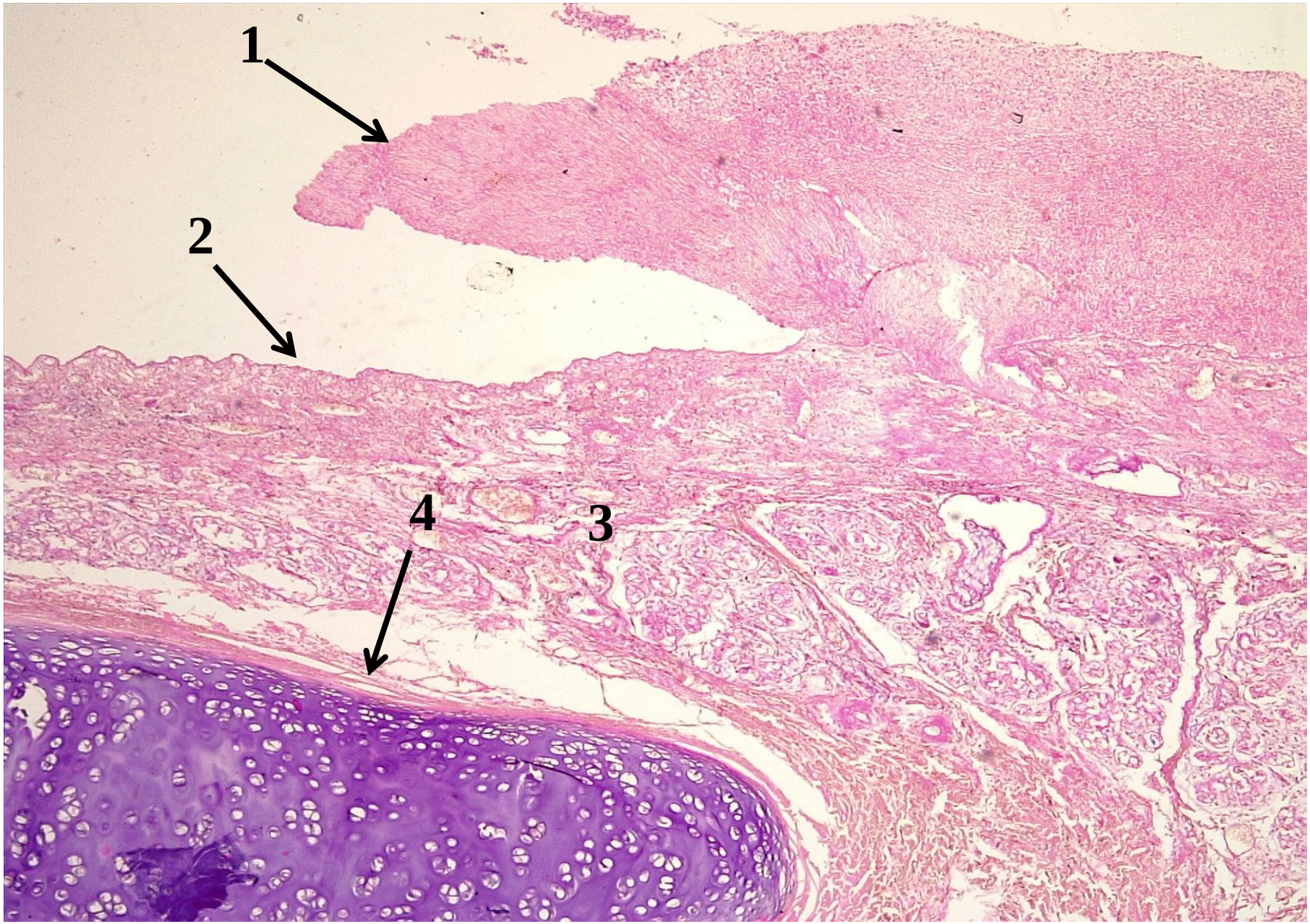


10 y/o boy with severe diphtheria

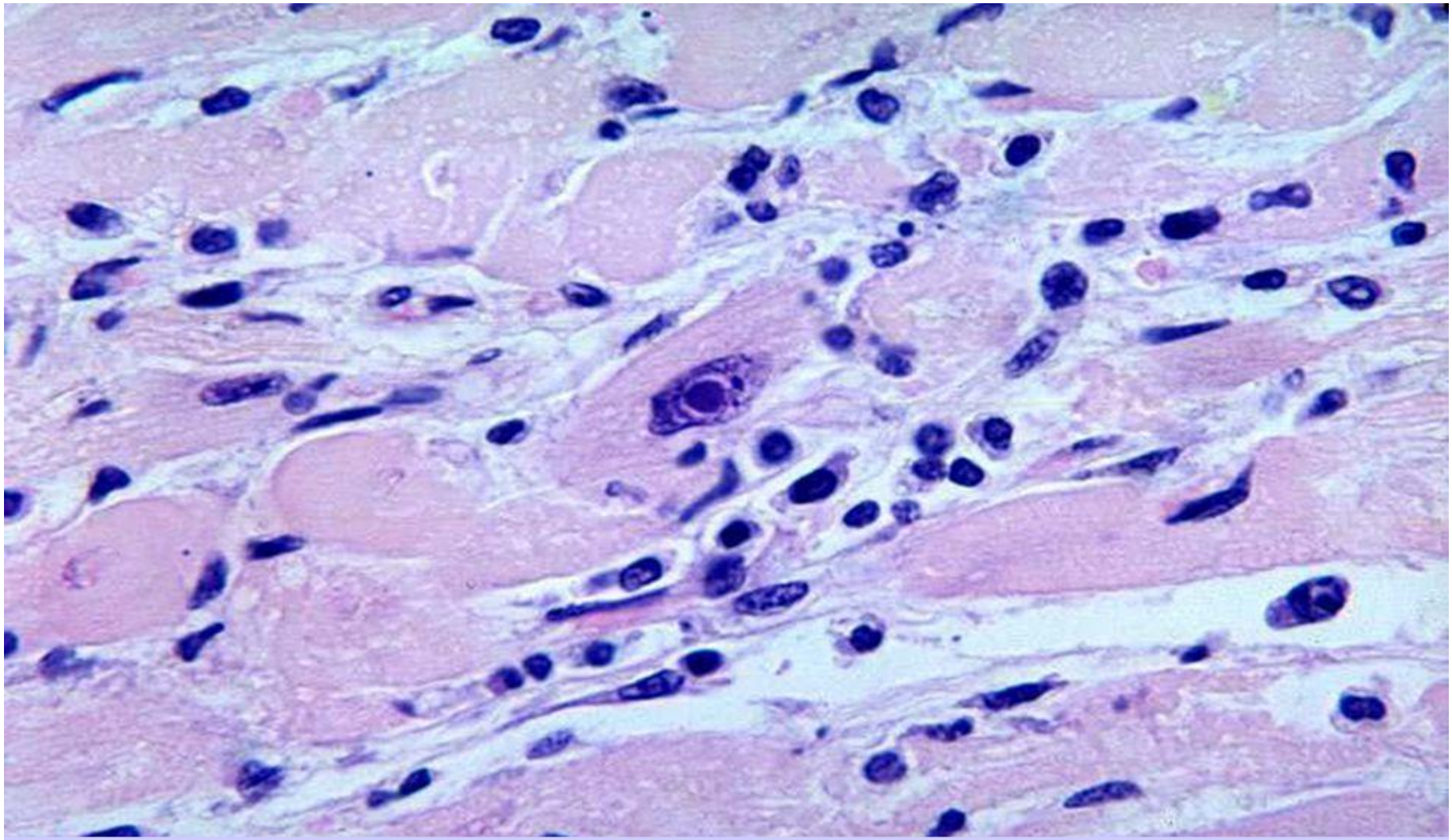
- conjunctivitis
- pharyngeal membrane
- bull neck
- severe myocarditis

CDC

Diphtheria tracheitis



Diphtheria tracheitis *(H-E)*



Diphtheria myocarditis – due to a toxin rather than bacterial invasion. There is some inflammation, myocyte changes (see the big nucleolus). Myocyte necrosis (not shown) also happens.

Scarlet Fever

Is an upper respiratory tract infection associated with a characteristic rash which is caused by an infection with pyrogenic exotoxin (erythrogenic toxin)-producing group A streptococcus in individuals who do not have antitoxin antibodies.

Scarlet Fever (cont.)

The incidence is cyclic, depending on:

1. **The prevalence of toxin-producing strains**
2. **The immune status of the population**

- **The epidemiologic features which include:**
  1. **Modes of transmission**
  2. **Age distribution**

  are otherwise similar to those for group A streptococcal pharyngitis.

The rash of Scarlet Fever

- **The rash appears within 24-48 hr after onset of symptoms, although it may appear with the first signs of illness.**
- **It often begins around the neck and spreads over the trunk and extremities.**
- **It is a diffuse, finely papular, erythematous eruption producing a bright red discoloration of the skin, which blanches on pressure.**
- **It is often more intense on the elbows, axillae, and groin.**

The rash of Scarlet Fever (cont.)

- **The skin has a goose-pimple appearance and feels rough.**
- **The face is usually spared, although the cheeks may be erythematous with pallor around the mouth.**

  After 3-4 days, the rash begins to fade and is followed by desquamation, first on the face progressing downward, and often resembling that seen subsequent to a mild sunburn.
- **Occasionally, sheetlike desquamation may occur around the free margins of the fingernails, the palms, and the soles.**

Scarlet Fever (cont.)

Examination of the pharynx of a patient with scarlet fever reveals essentially the same findings as with group A streptococcal pharyngitis.

- **In addition, the tongue is usually coated and the papillae are swollen.**
- **After desquamation, the reddened papillae are prominent, giving the tongue a strawberry appearance.**