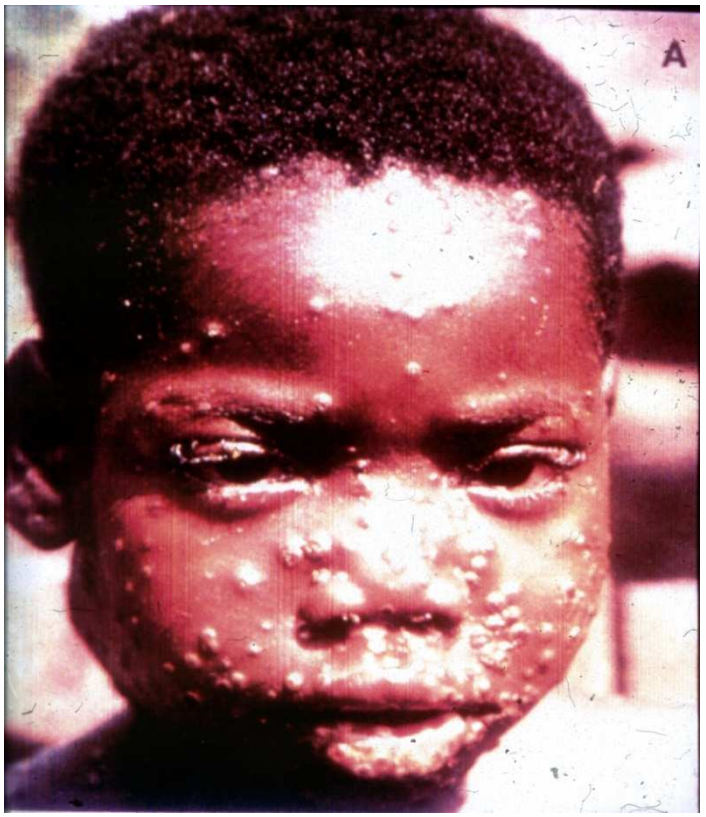
Dr. Gábor Lotz

Infectious Diseases



250 years of EXCELLENCE
in medical education,
research & innovation
and healthcare

Semmelweis University
http://semmelweis.hu
2nd Department of Pathology

INFECTIOUS DISEASES

are disorders in which tissue damage or dysfunction is produced by a microorganism.

Changing pattern of infectious diseases

Vaccines have controled or eliminated:

smallpox, measles, pertussis, poliomyelitis, mumps

Insecticides have helped to control:

malaria, schistosomiasis, thyphus

Purification of drinking water lessened the threat of water-born epidemics:

Amoebiasis and hepatitis A

however,

Occurence of therapy resistent agents

Opportunistic infections have appeared (AIDS, organ transpl.)

Increased speed of disease spreading (globalisation)

Changing geographical distribution (climate changes)

CLASSES OF ORGANISMS THAT CAUSE INFECTIOUS DISEASES

VIRUSES	*Obligate intracellular*
CHLAMYDIAE	*Obligate intracellular*
RICKETTSIAE	*Obligate intracellular*
MYCOPLASMS	*Extracellular*
BACTERIA	*Extracellular*
(Spirochetes, Mycobacteria)	*Facultative intracellular*
FUNGI	*Superficial*
	Deep/Systemic
PROTOZOA	*Extracellular*
	Intracellular
	obligate *facultative*
HELMINTHS	

HOST DEFENCES AGAINST INFECTION

- *» Skin*
- *» Tears*
- *» Normal bacterial flora*
- *» Gastric acid*
- *» Bile*
- *» Salivary and pancreatic secretions*
- *» Filtration system of nasopharynx*
- *» Mucociliary blanket*
- *» Bronchial, cervical, urethral, and prostatic secretions*
- *» Neutrophils*
- *» Monocytes*
- *» Complement*
- *» Stationary, mononuclear phagocyte system*
- *» Immunglobulins*
- *» Cell-mediated immunity*

VIRAL *INFECTION*

Viral replication in host cells

VIRAL *DISEASE*

Viral replication + tissue injury

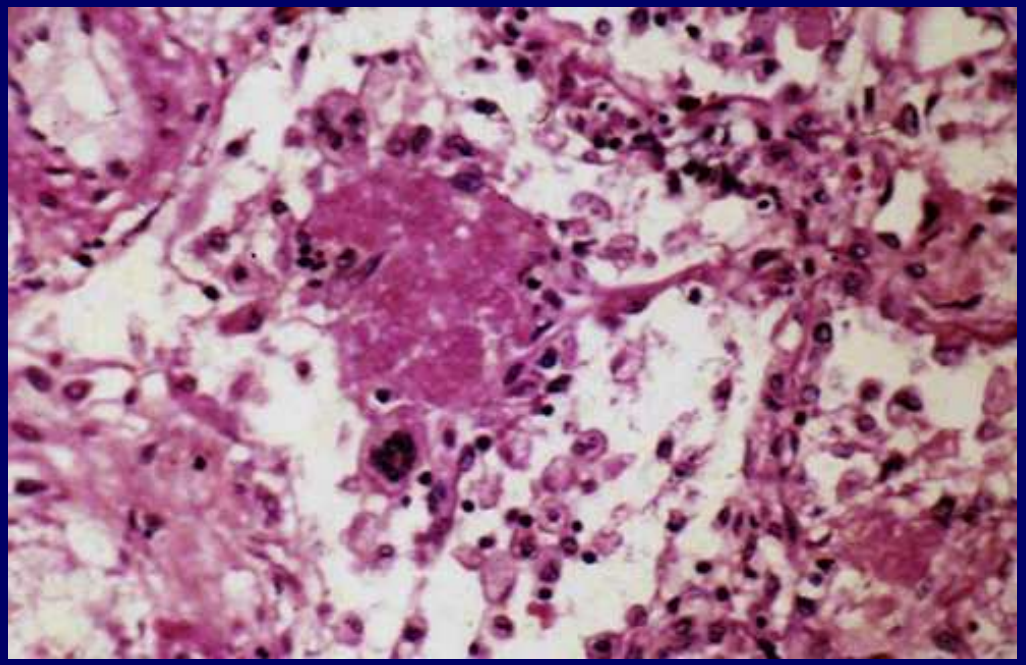
Mechanisms of cell injury in viral infections

Direct

- ***Cell fusion*** */giant cells/*
  HIV, measles
- ***Formation of inclusions***
  HSV, CMV, rabies, smallpox
- ***Cytolysis*** *influenza, yellow fever, poliomyelitis*

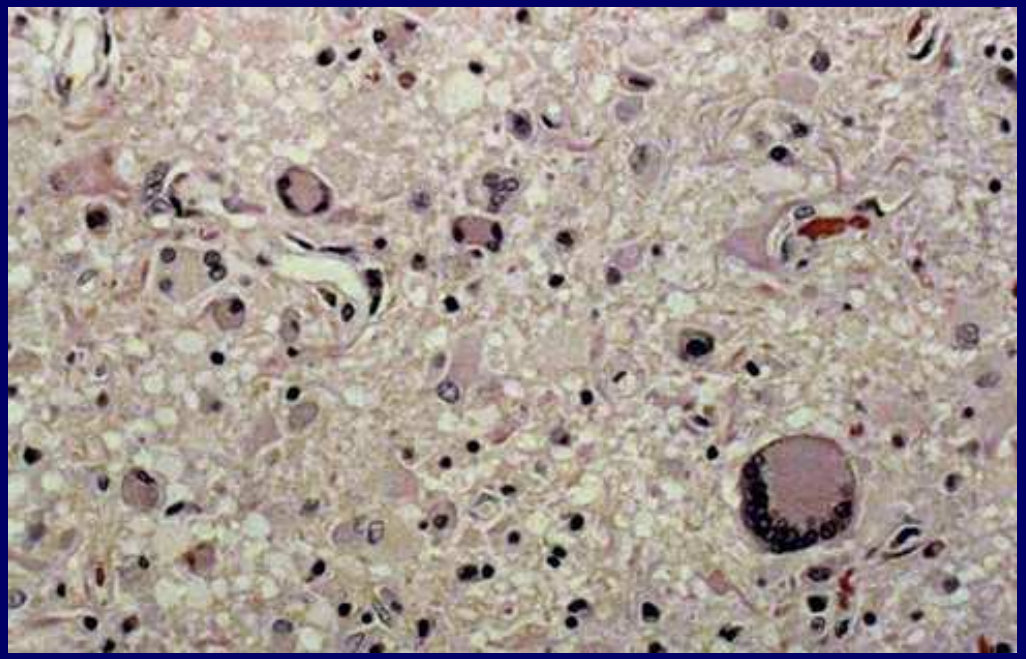
Indirect

- ***Immunmediated cell injury***
  hepatitis B
- ***Secondary infections***

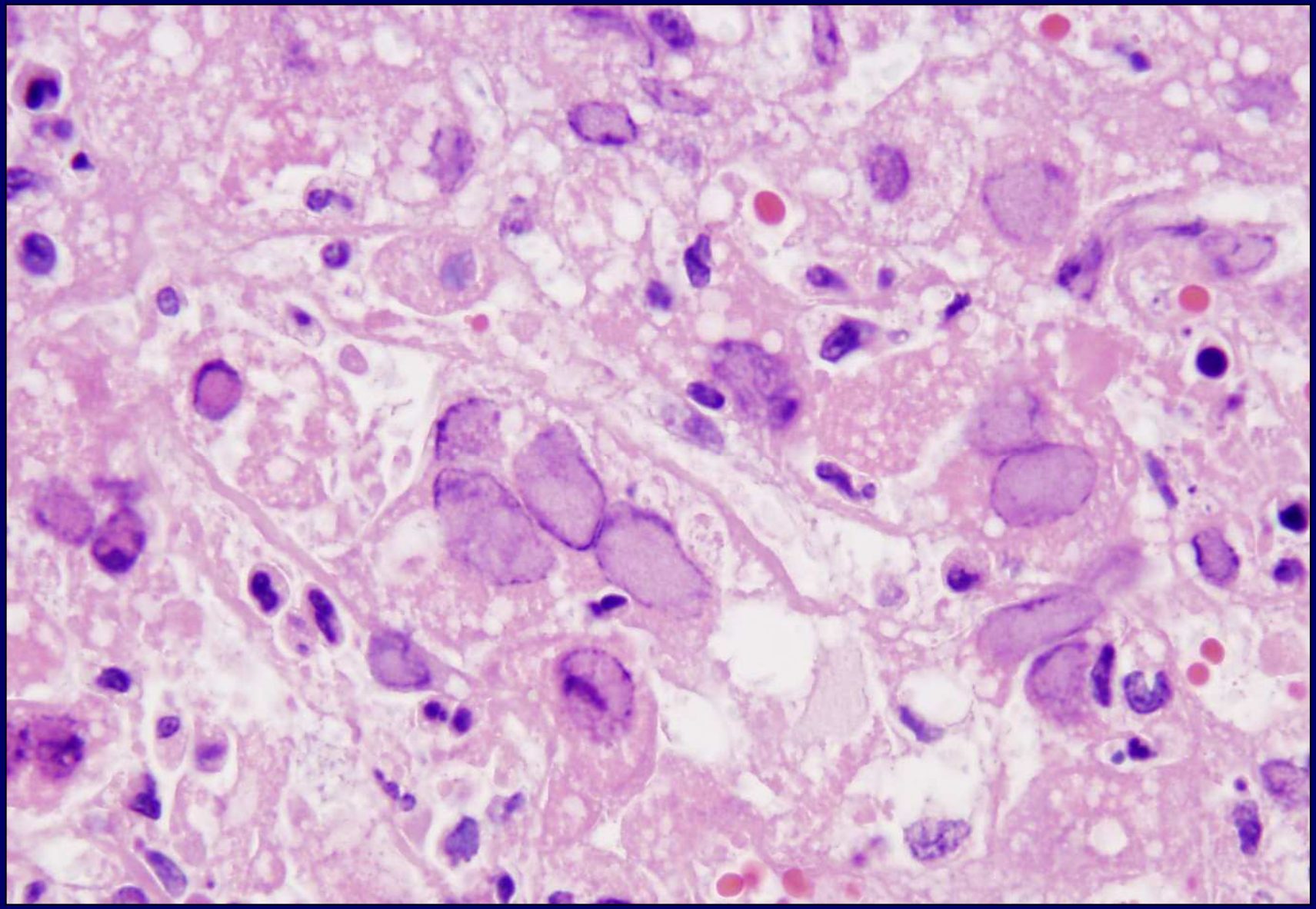


Measles pneumonia

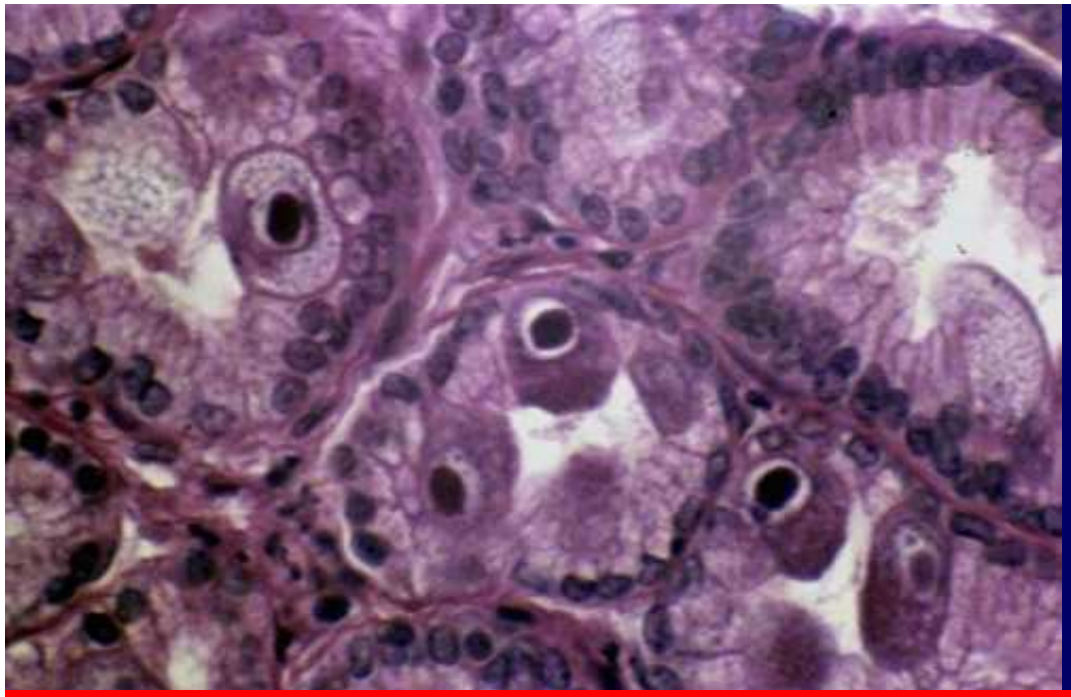
Viral giant cells



AIDS encephalitis



HSV inclusions (in HSV hepatitis)

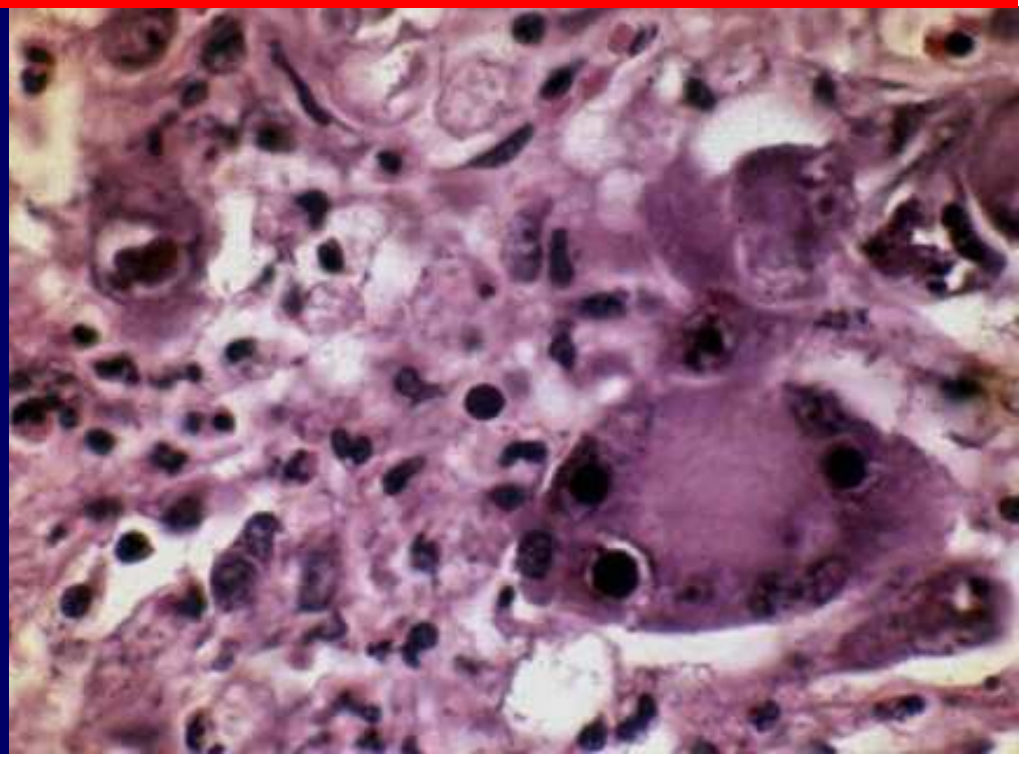


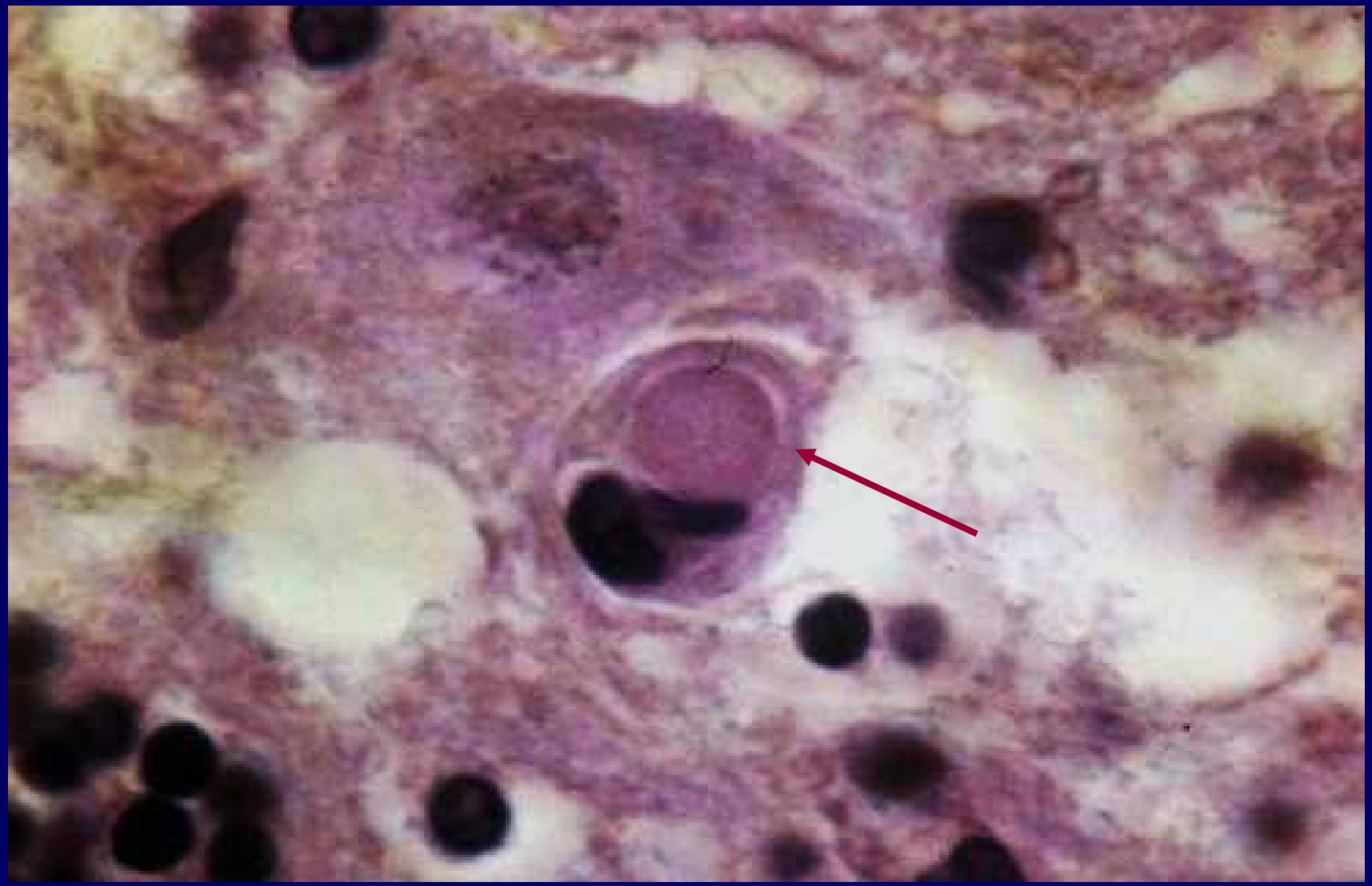
CMV - Inclusions

(owl's eye)

Gastric mucosa

Adrenal in an AIDS patient

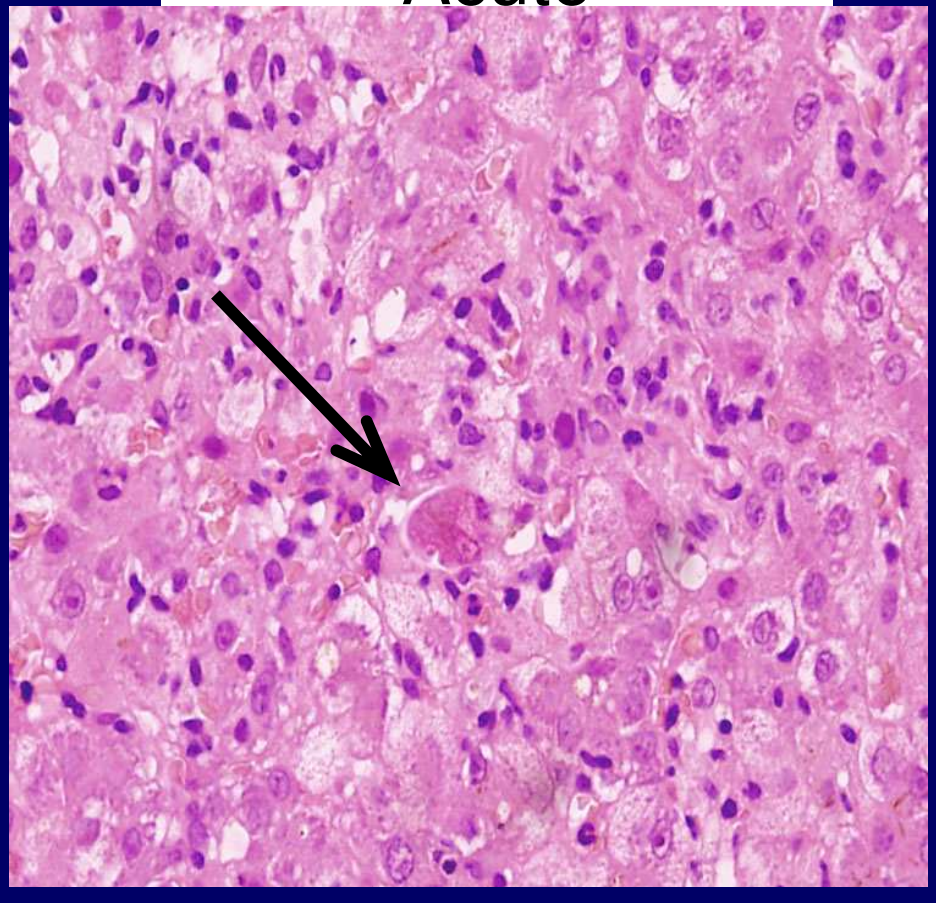




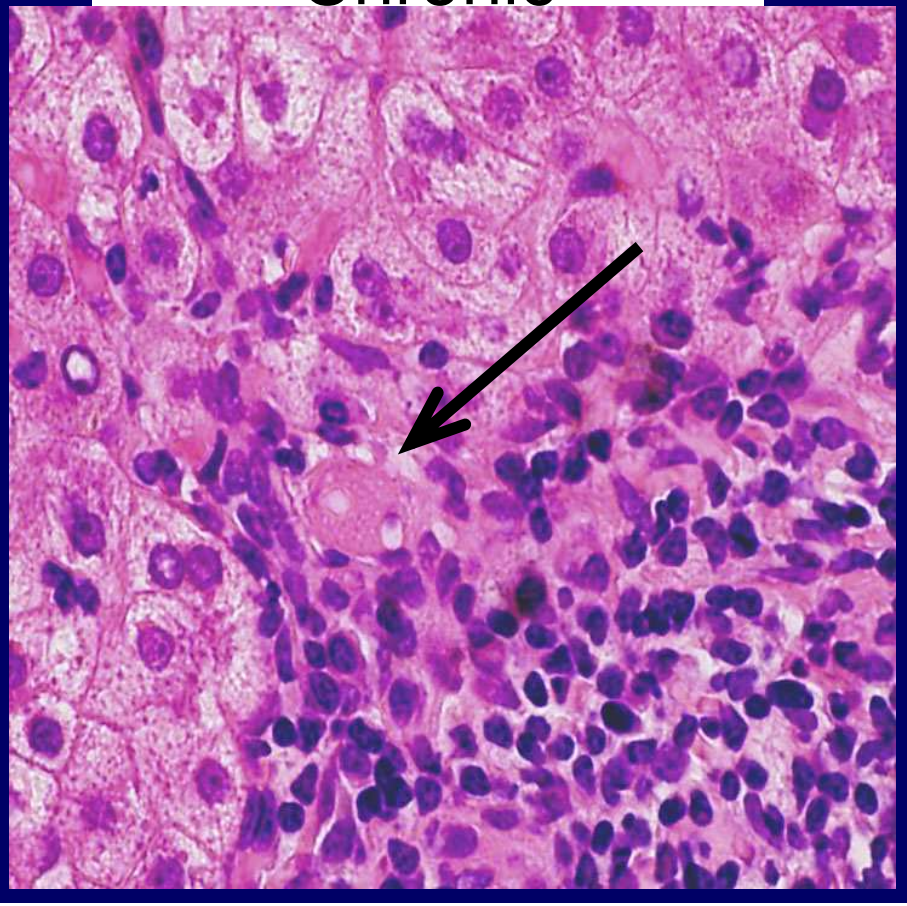
NEGRI BODY in brain / Rabies/

Apoptosis in acute and chronic hepatitis

Acute



Chronic

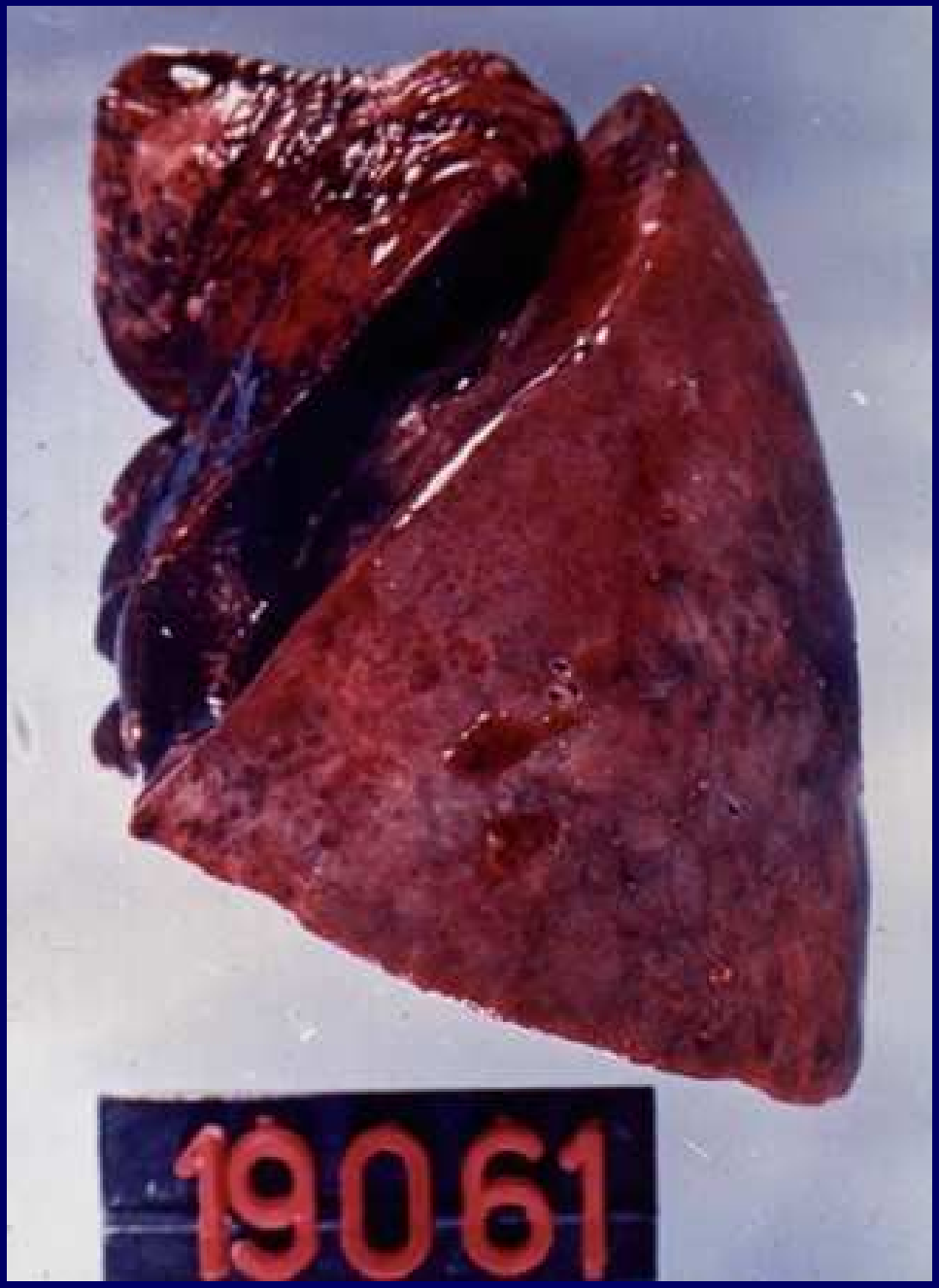


RESPIRATORY VIRUSES

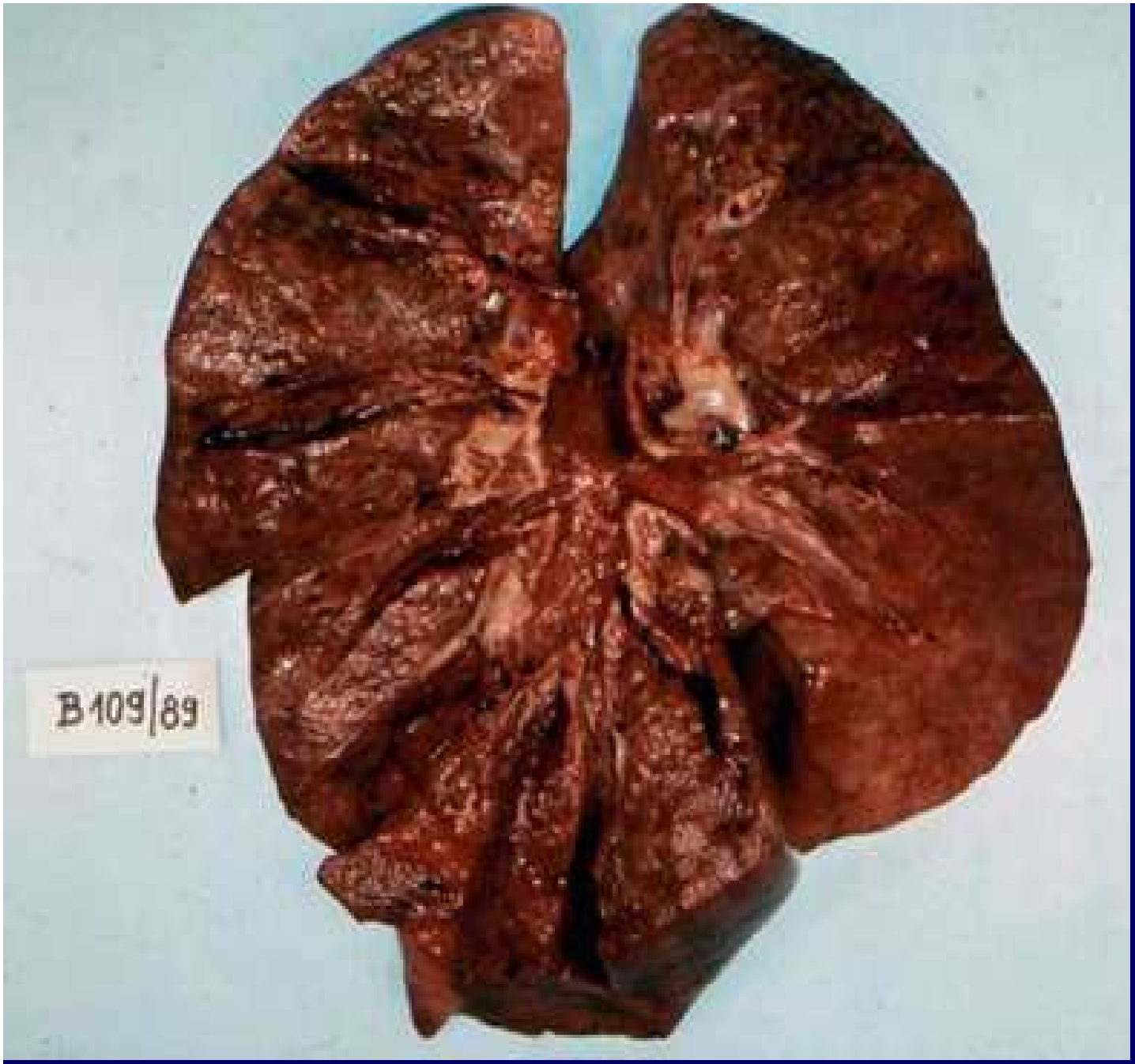
- ***Influenza A,B,C,***
  Changing antigenic identities
- ***Parainfluenza viruses (croup)***
- ***RSV (Paramyxovirus) 1-6 month of age***
- ***Adenoviruses (in children)***
- ***Measles (rubeola)***

VIRAL PNEUMONIAS

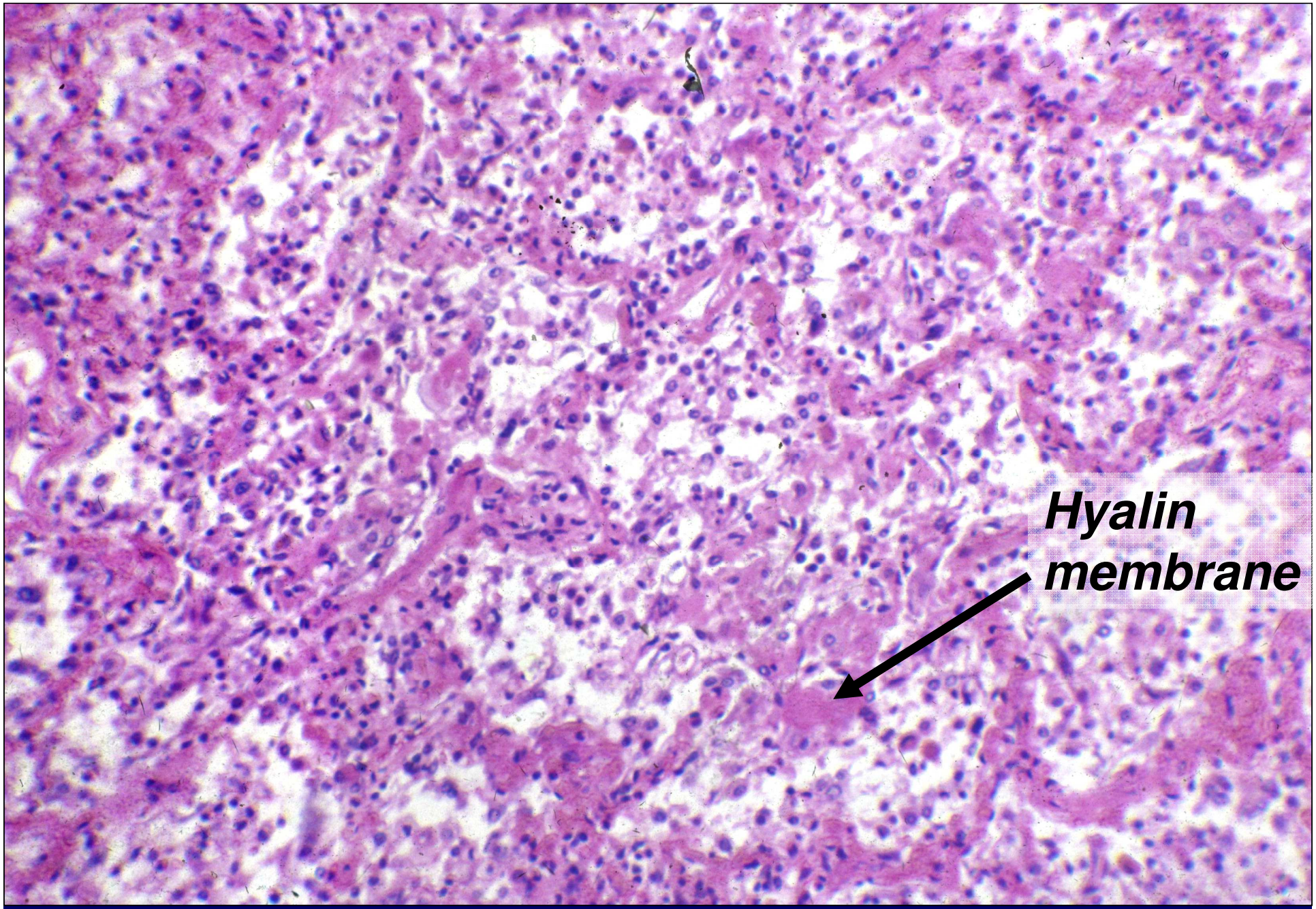
- *MORPHOLOGY*
  Interstitial pneumonia
- *INFLAMMATORY INFILTRATION IN*
  alveolar septa
  peribronchial tissue
- *Diffuse alveolar damage (DAD)*
  → Hyalin membranes (ARDS)
- *Necrotizing bronchiolitis (RSV)*
- *Hemorrhagic feature (Influenza)*
- *Squamous metaplasia of bronchial epithelium*



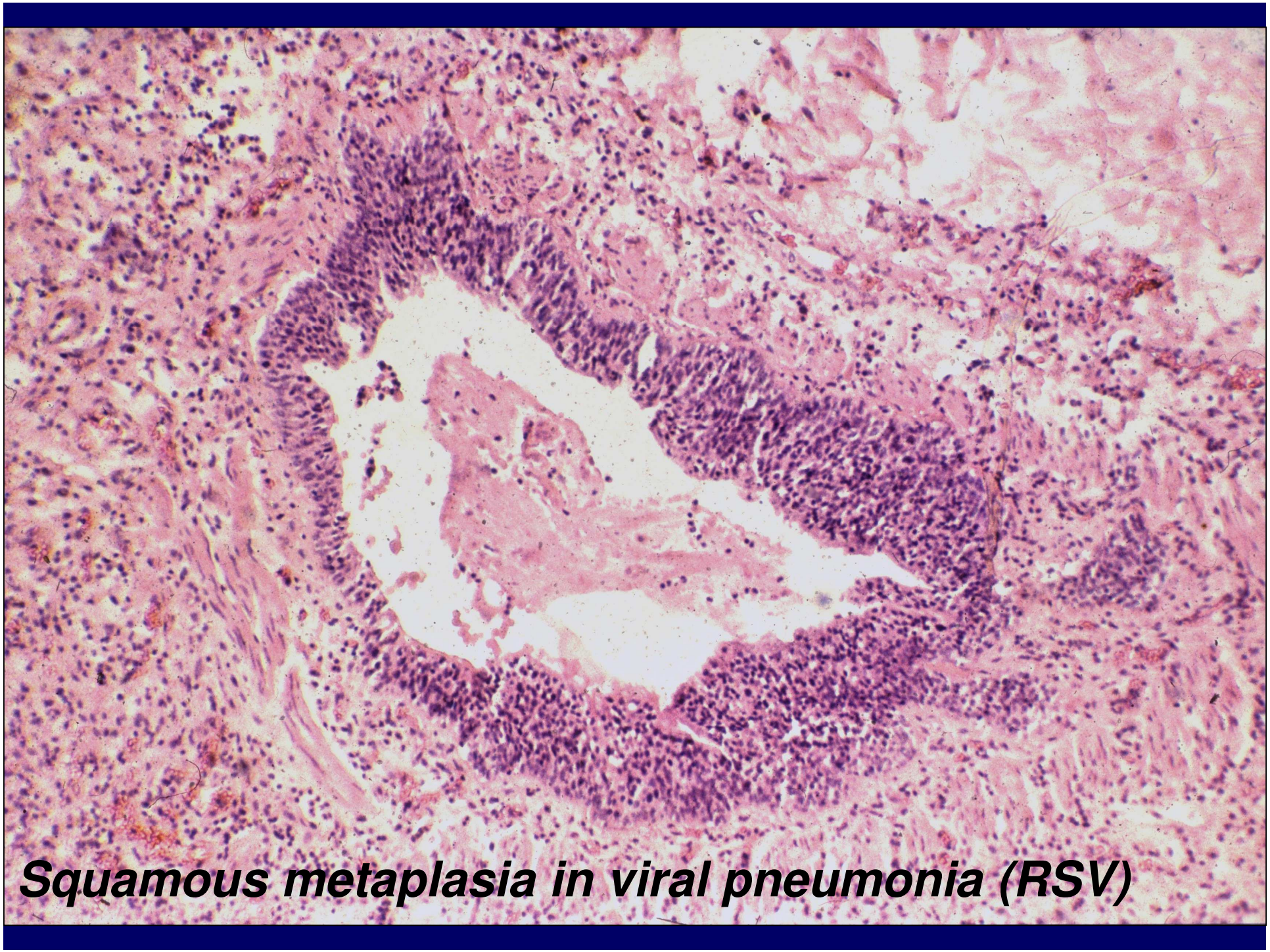
Viral hemorrhagic pneumonia caused by influenza virus



VIRAL PNEUMONIA / Measles/



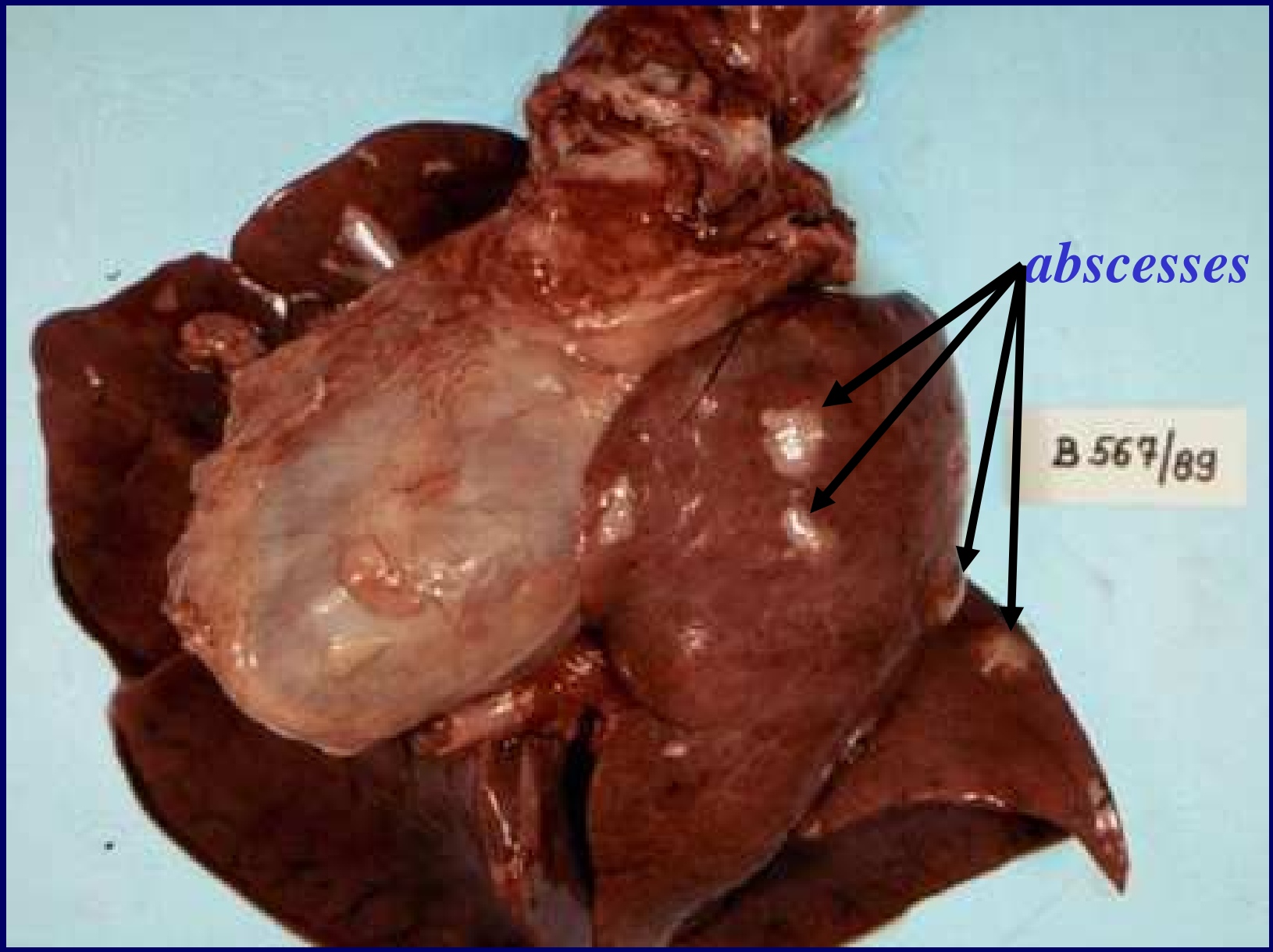
VIRAL PNEUMONIA (measles)



Squamous metaplasia in viral pneumonia (RSV)

Acute viral infection of the respiratory tract

Acute viral infection of the respiratory tract



Viral pneumonia complicated by bacterial infection

COVID-19 (SARS-CoV-2 virus)

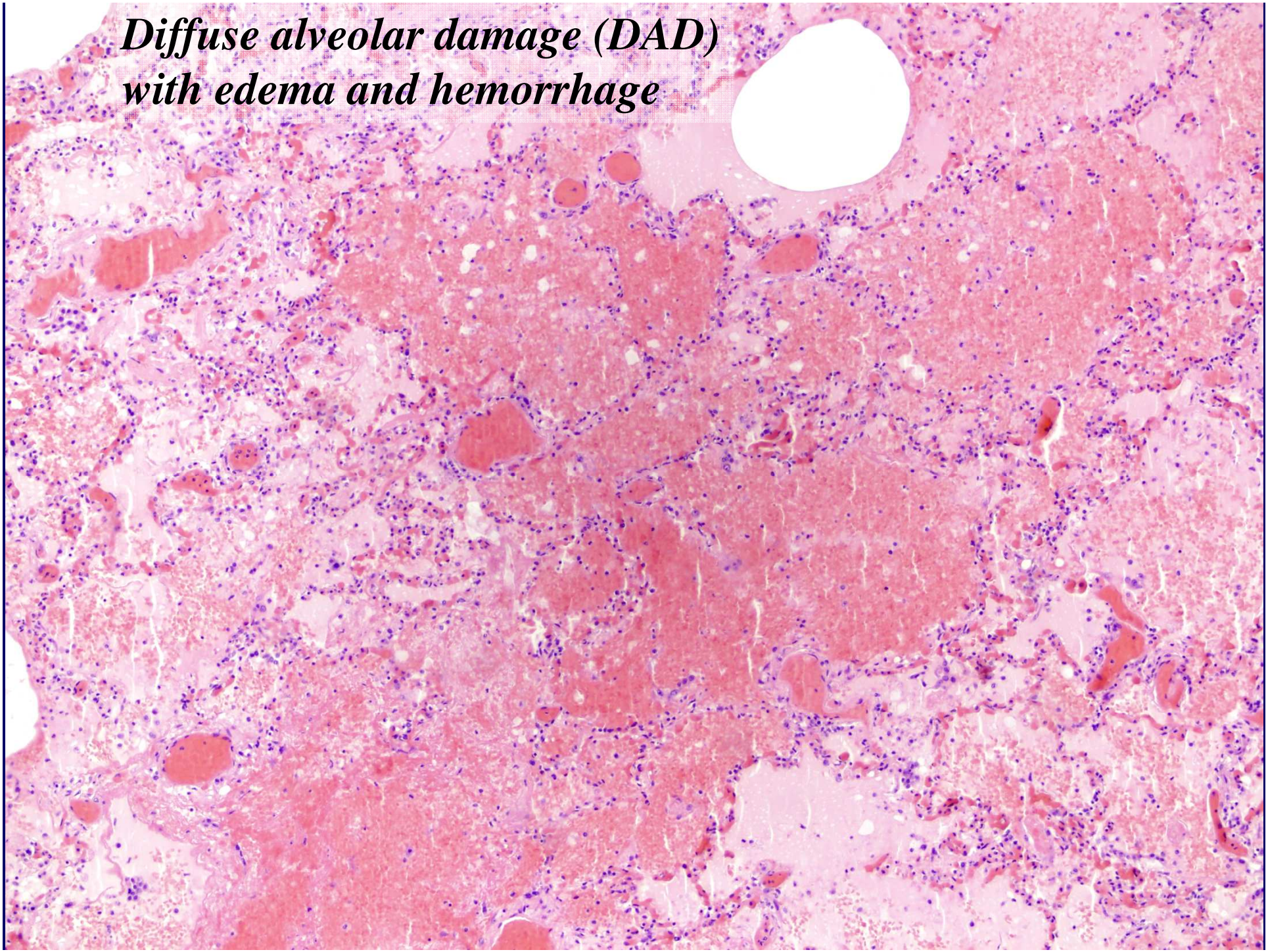
- *Viral replication in the bronchial epithelium and pneumocytes*

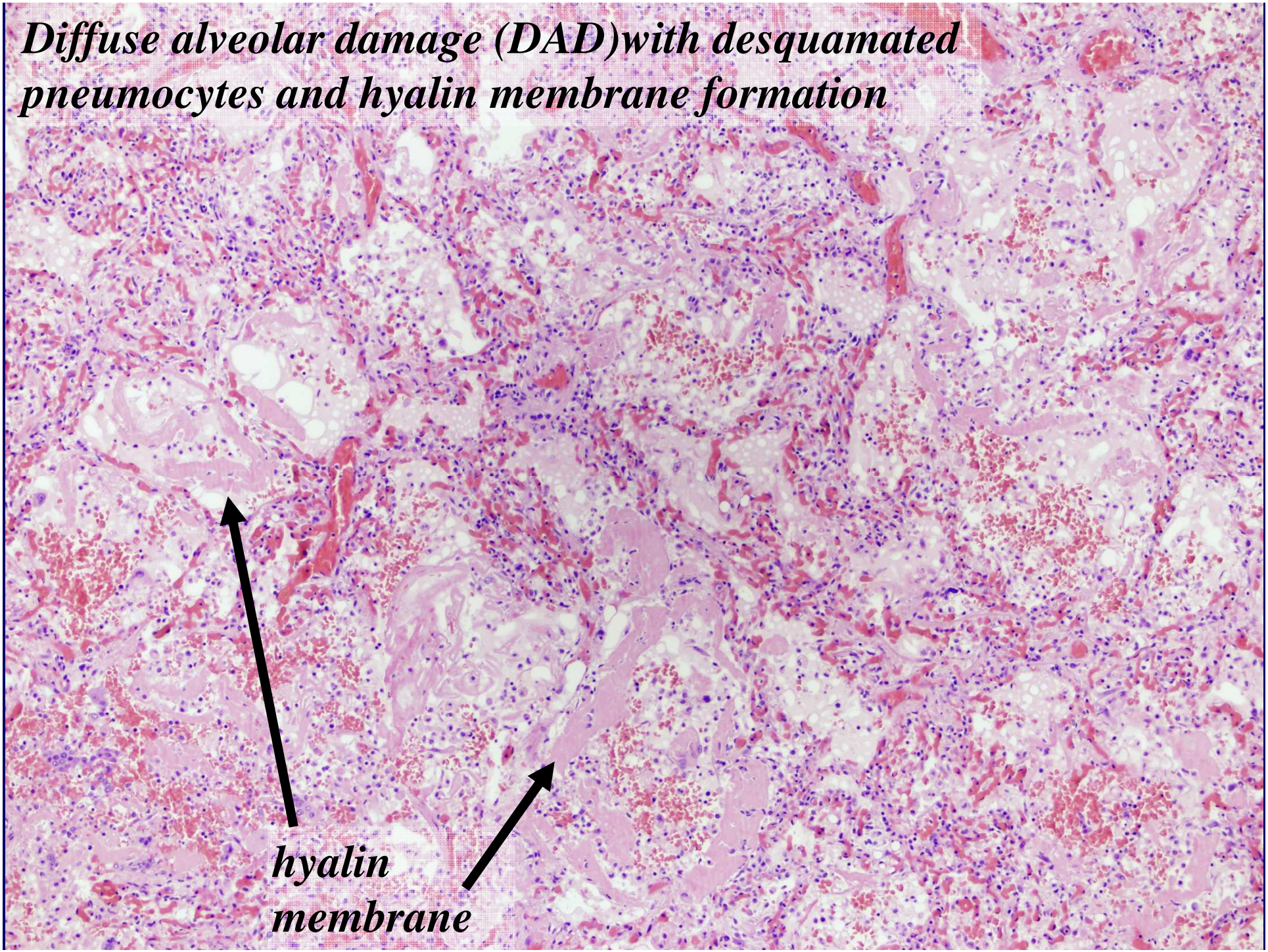
  viral pneumonia, extensive lung damage, cytokine storm in severe cases

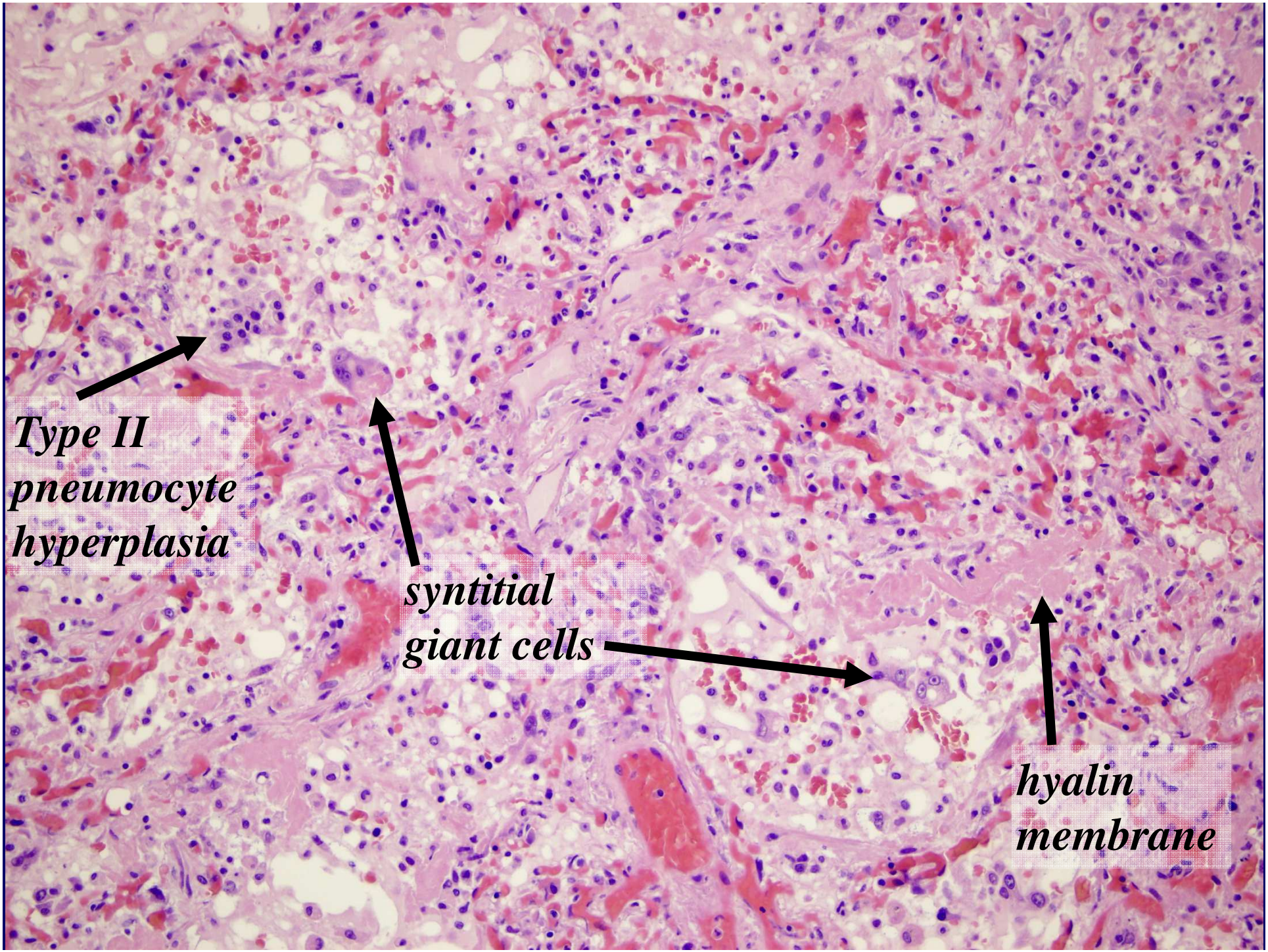
COVID-19 lung features:

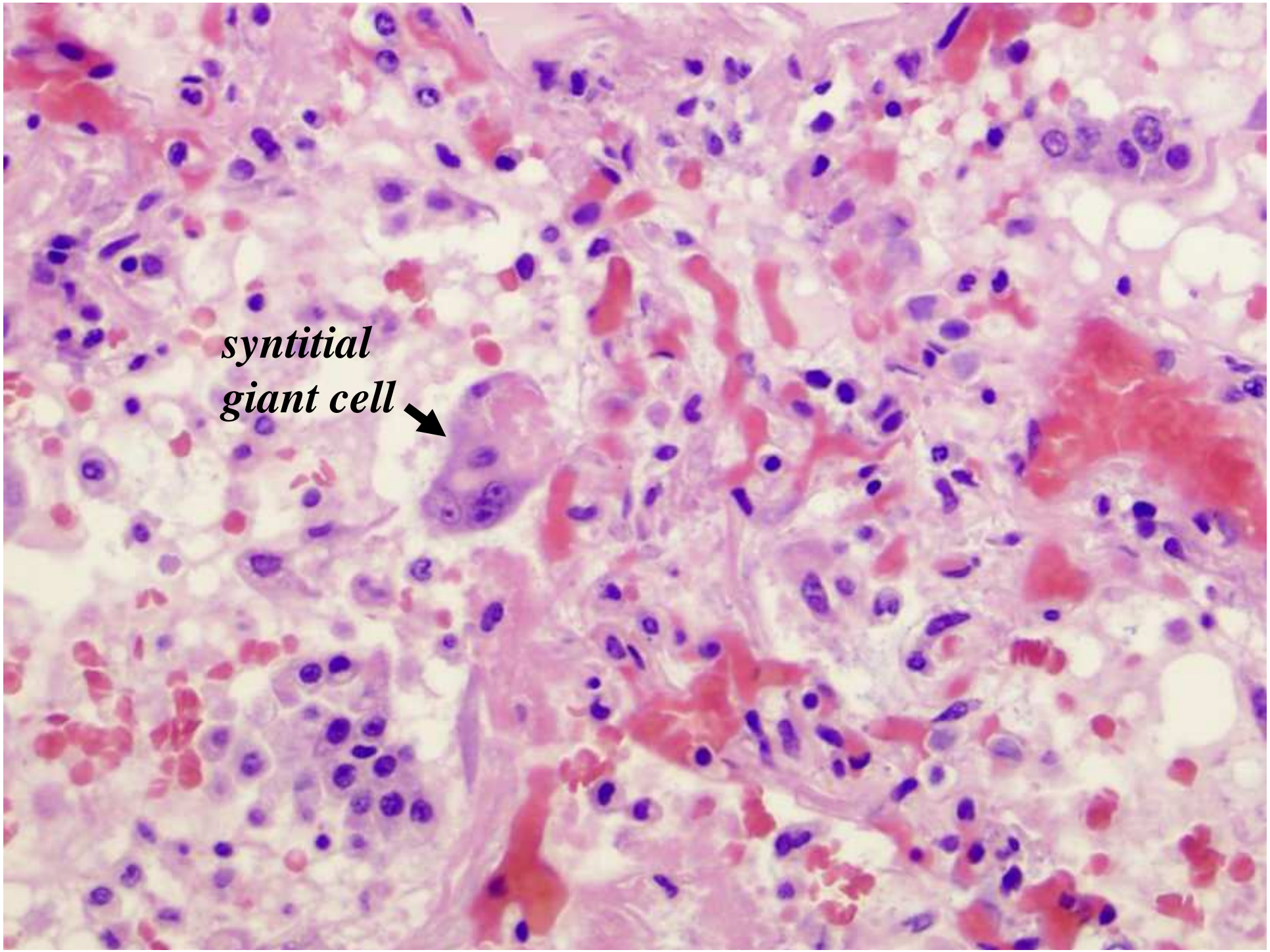
- *Extensive thrombotic / thromboembolic lesions*
- *Hyalin membranes (DAD - ARDS)*
- *Syntitial giant cells (spike protein - ACE2 rec)*
- *Hyperplasia of the type II pneumocytes*
- *Squamous metaplasia in the alveoli*

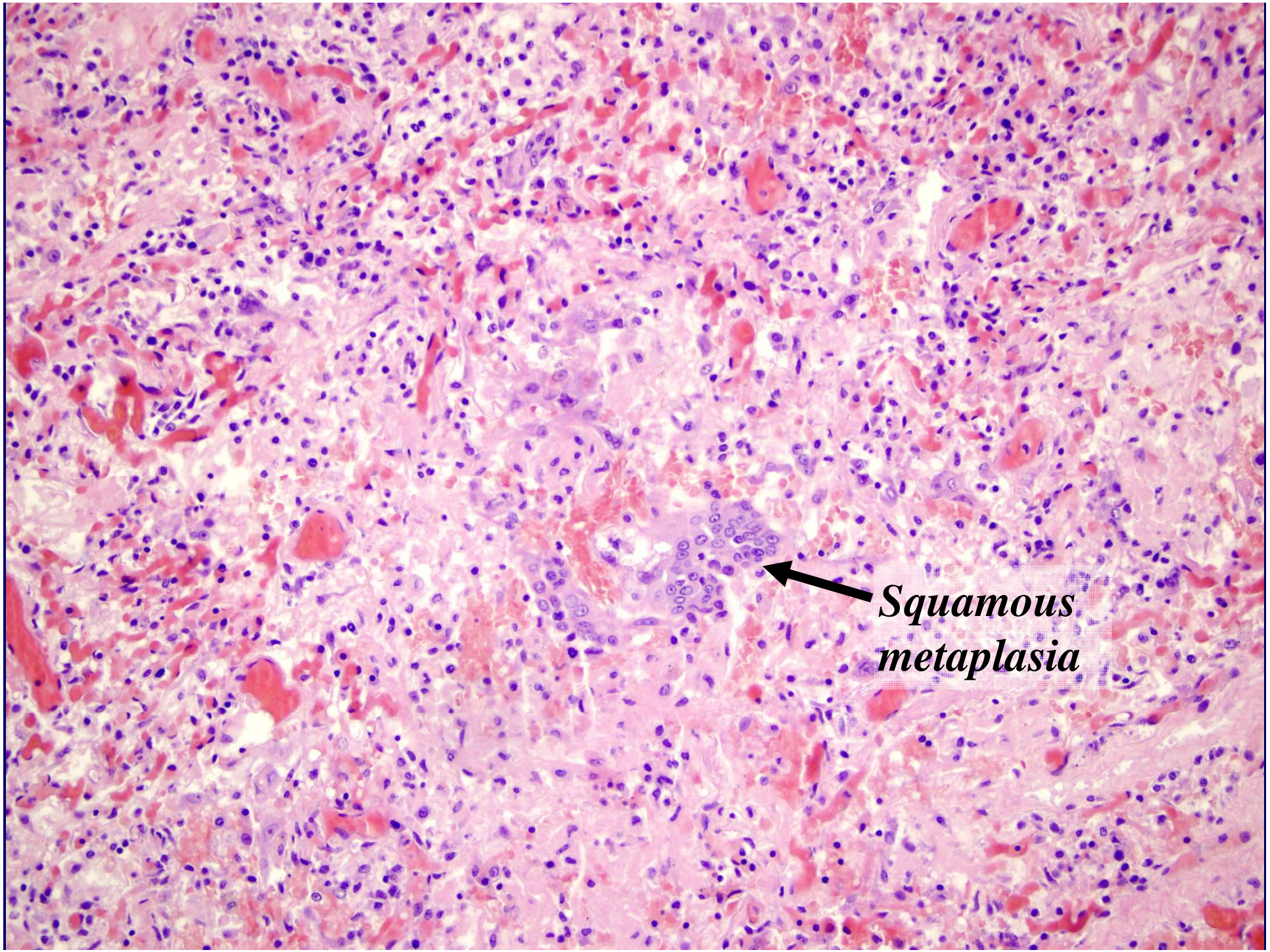

COVID-19 pneumonia
congestion
alveolar overdistension (due to respiratory therapy)
atelectasis

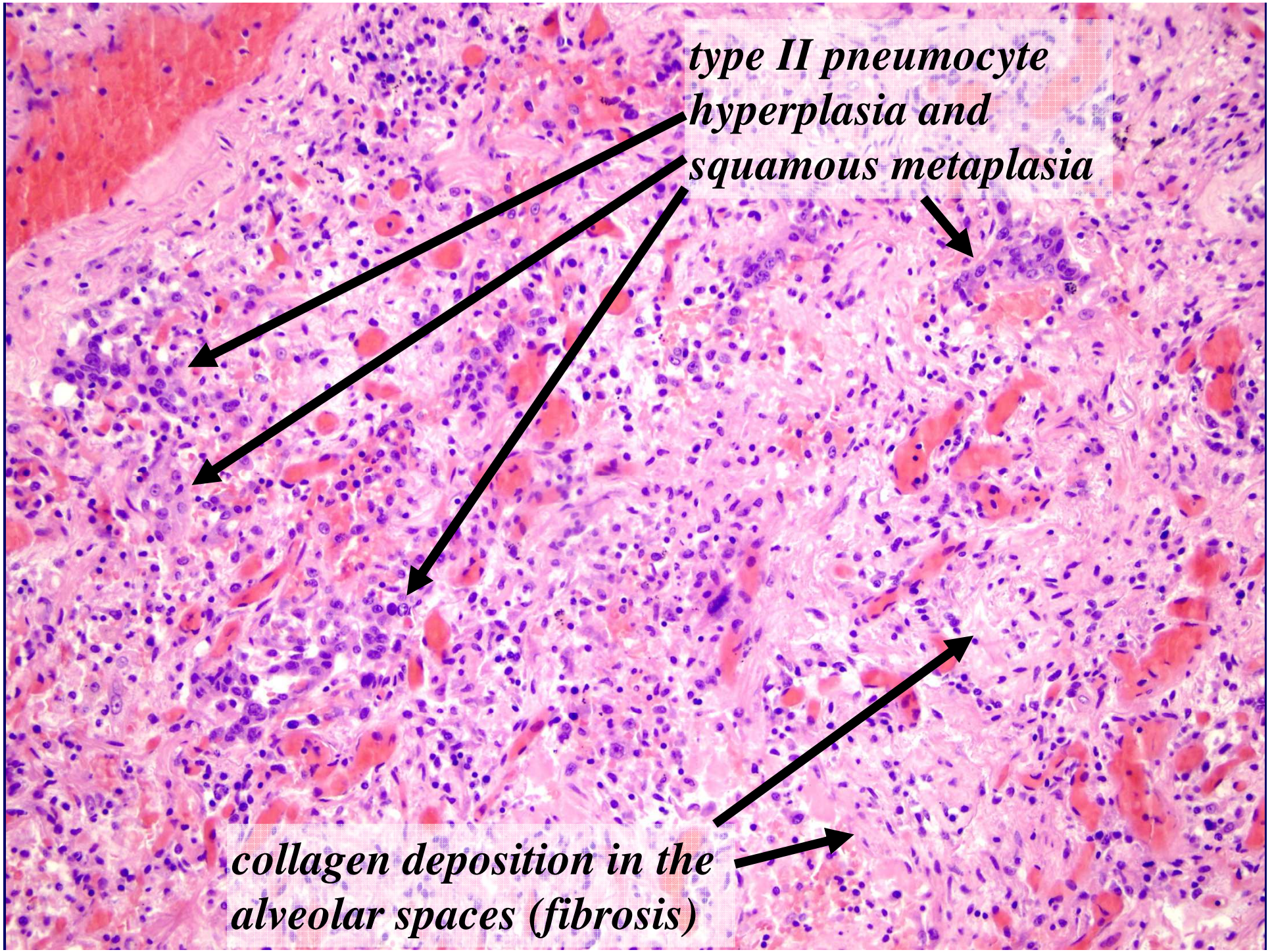

Diffuse alveolar damage (DAD)
with edema and hemorrhage


Diffuse alveolar damage (DAD)with desquamated pneumocytes and hyalin membrane formation
hyalin membrane


Type II pneumocyte hyperplasia
syntitial giant cells
hyalin membrane


syntitial
giant cell


Squamous metaplasia


type II pneumocyte hyperplasia and squamous metaplasia
collagen deposition in the alveolar spaces (fibrosis)

HERPESVIRUS INFECTIONS (DNA viruses)

HERPES SIMPLEX
TYPE 1, TYPE 2
VARICELLA - ZOSTER

} **HSV**, **VZV** — **neurotropic**

HUMAN HERPES VIRUS
TYPE 6, 7
HUMAN HERPES VIRUS Type 8

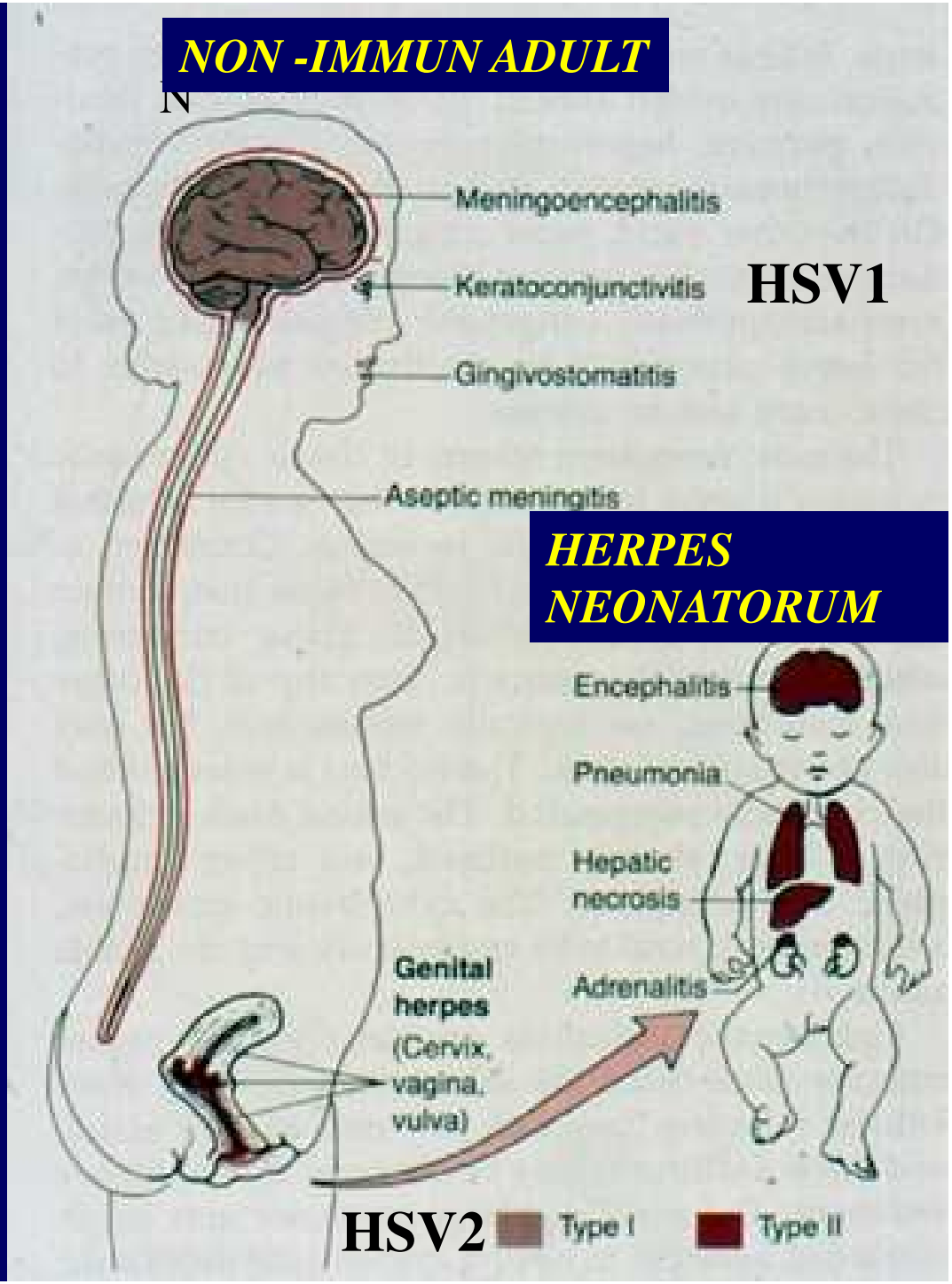
CYTOMEGALOVIRUS

EPSTEIN - BARR VIRUS
(Mononucleosis infectiosa
BURKITT'S lymphoma
Nasopharyngeal carcinoma)

INFECTION WITH

HSV type 1

HSV type2



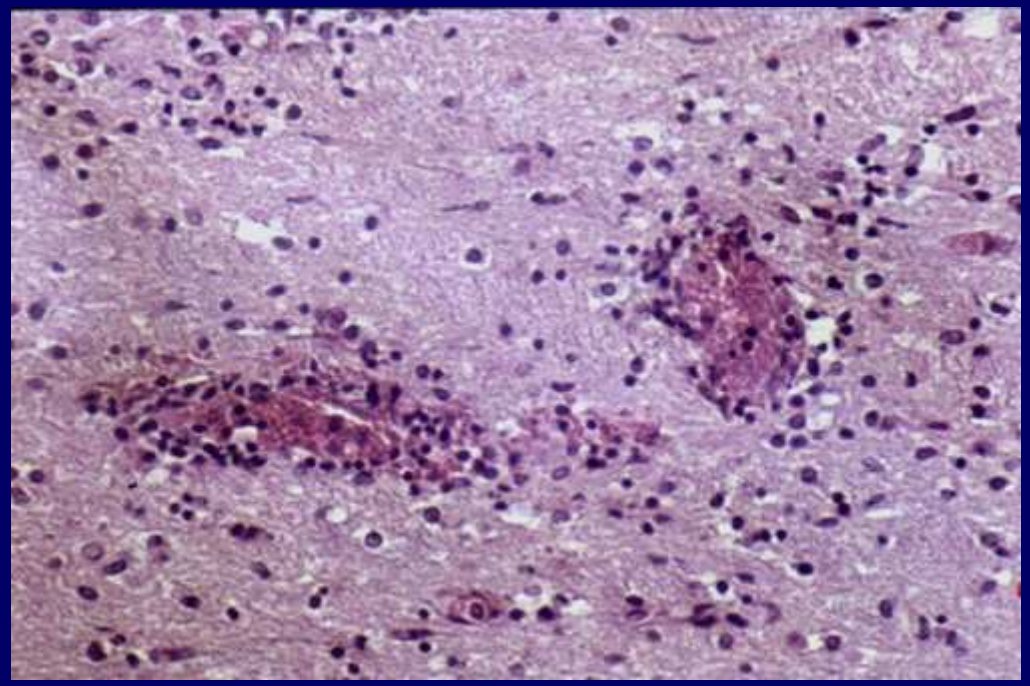
HSV-1 infection

Cold sore

Immunodeficiency

HSV-1 infection in leukaemic patient

HSV-1 encephalitis



HSV type 2

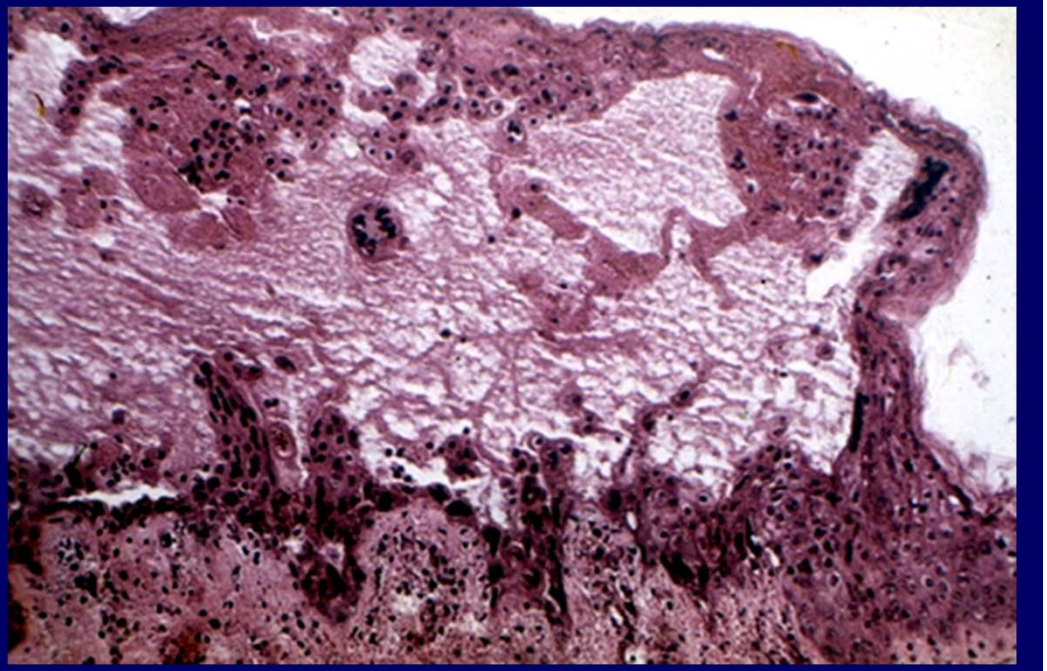
Herpes of the newborne

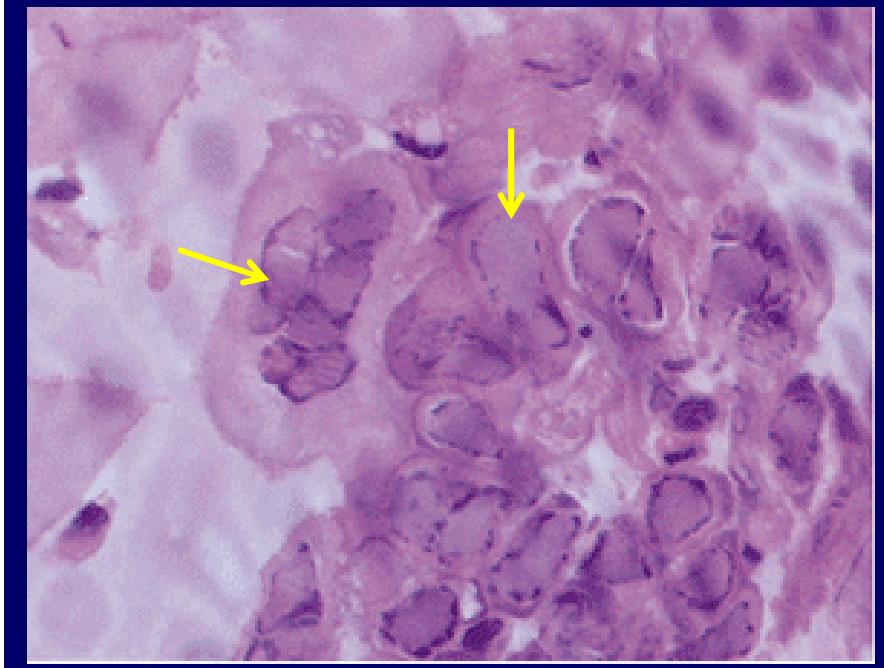
Infection during delivery:

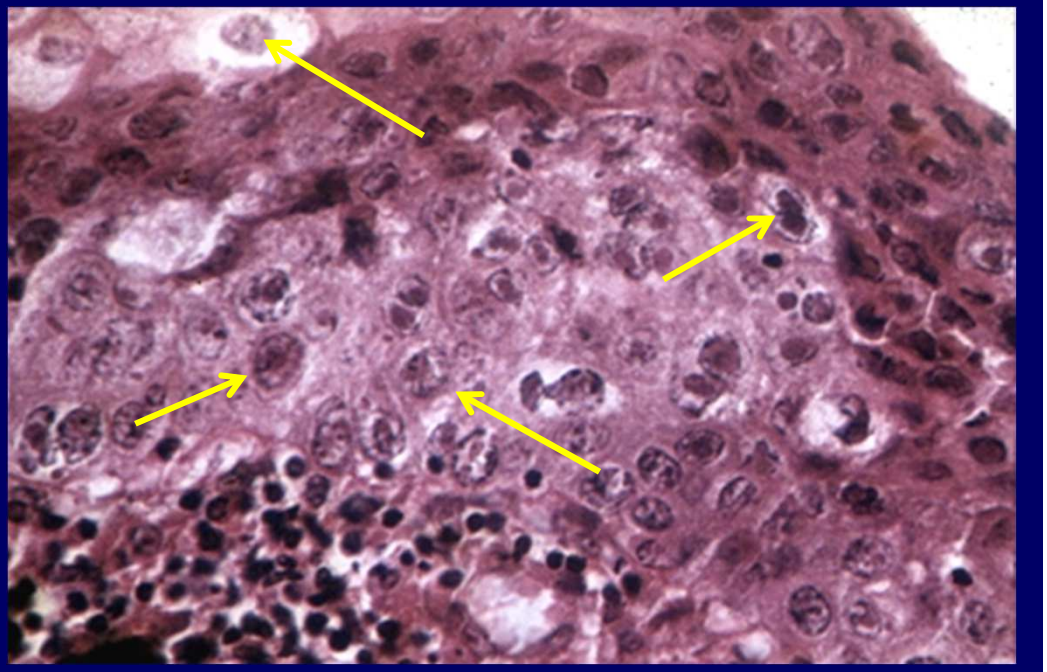
generalised skin and visceral lesions

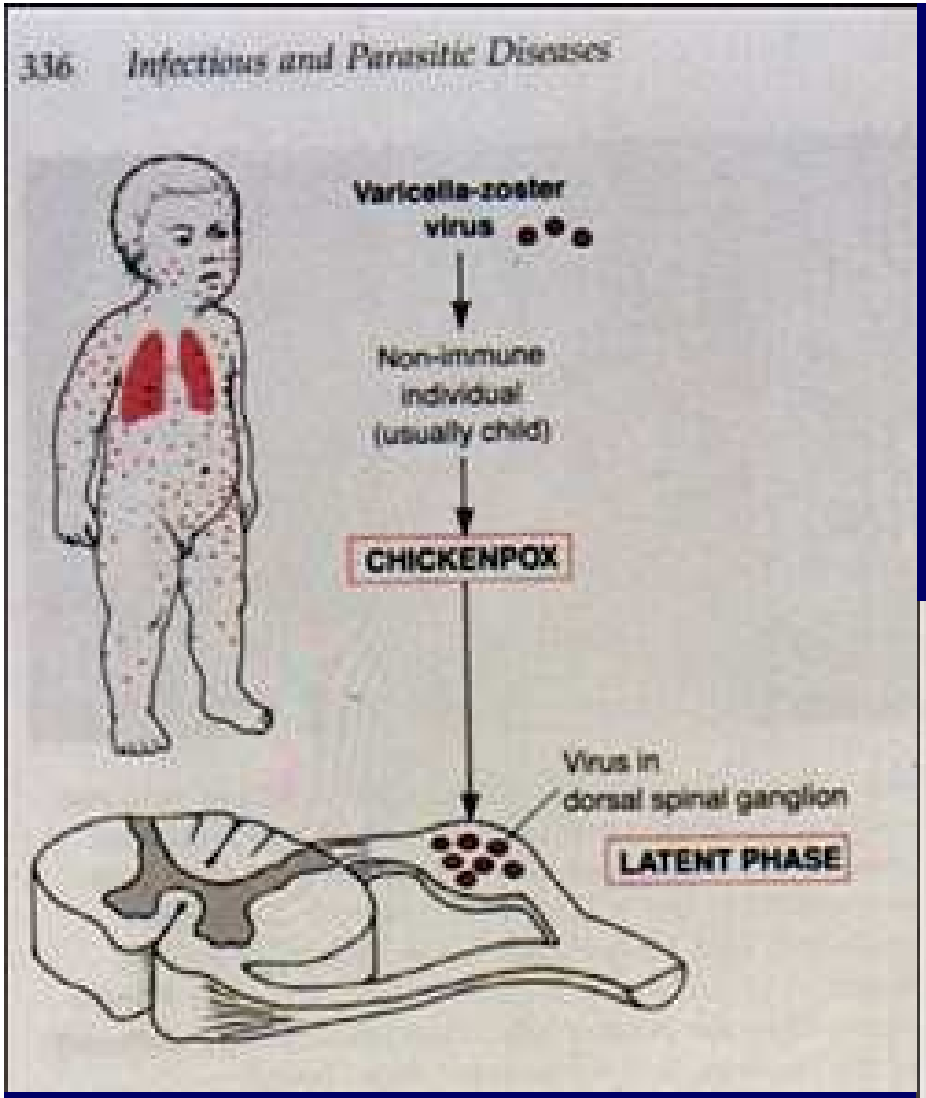
Intraepidermal vesicle

HSV inclusions in epithelial cells





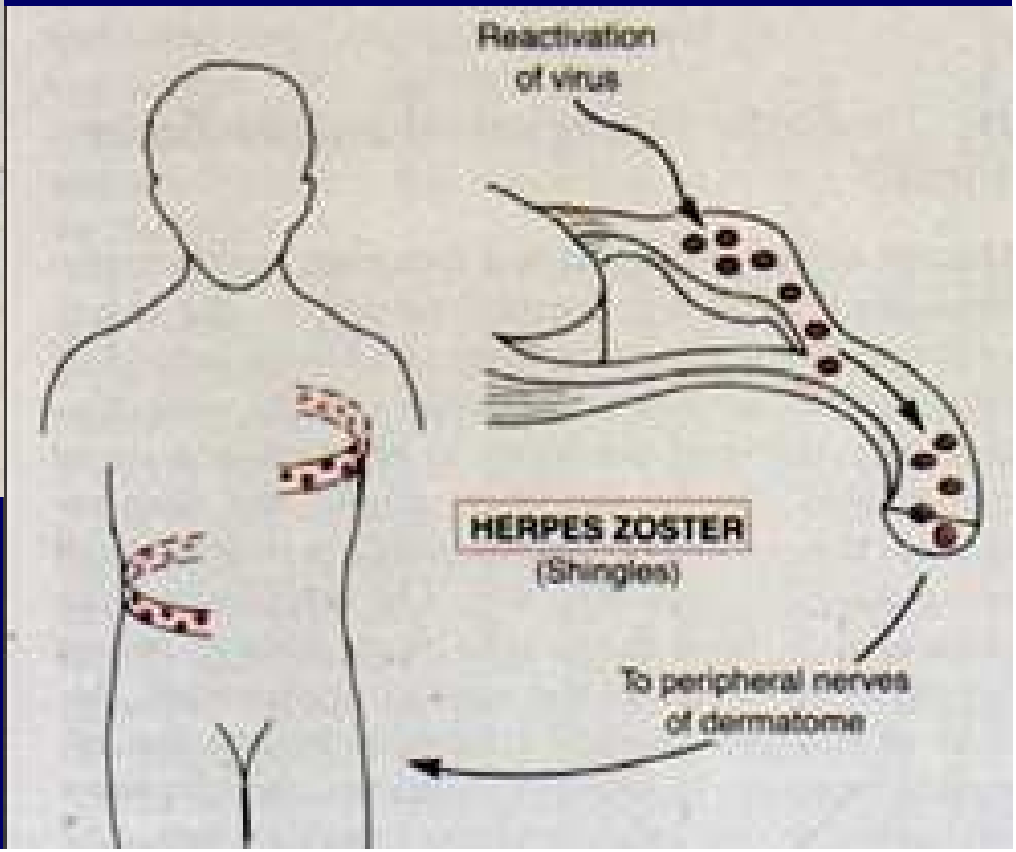




VZV

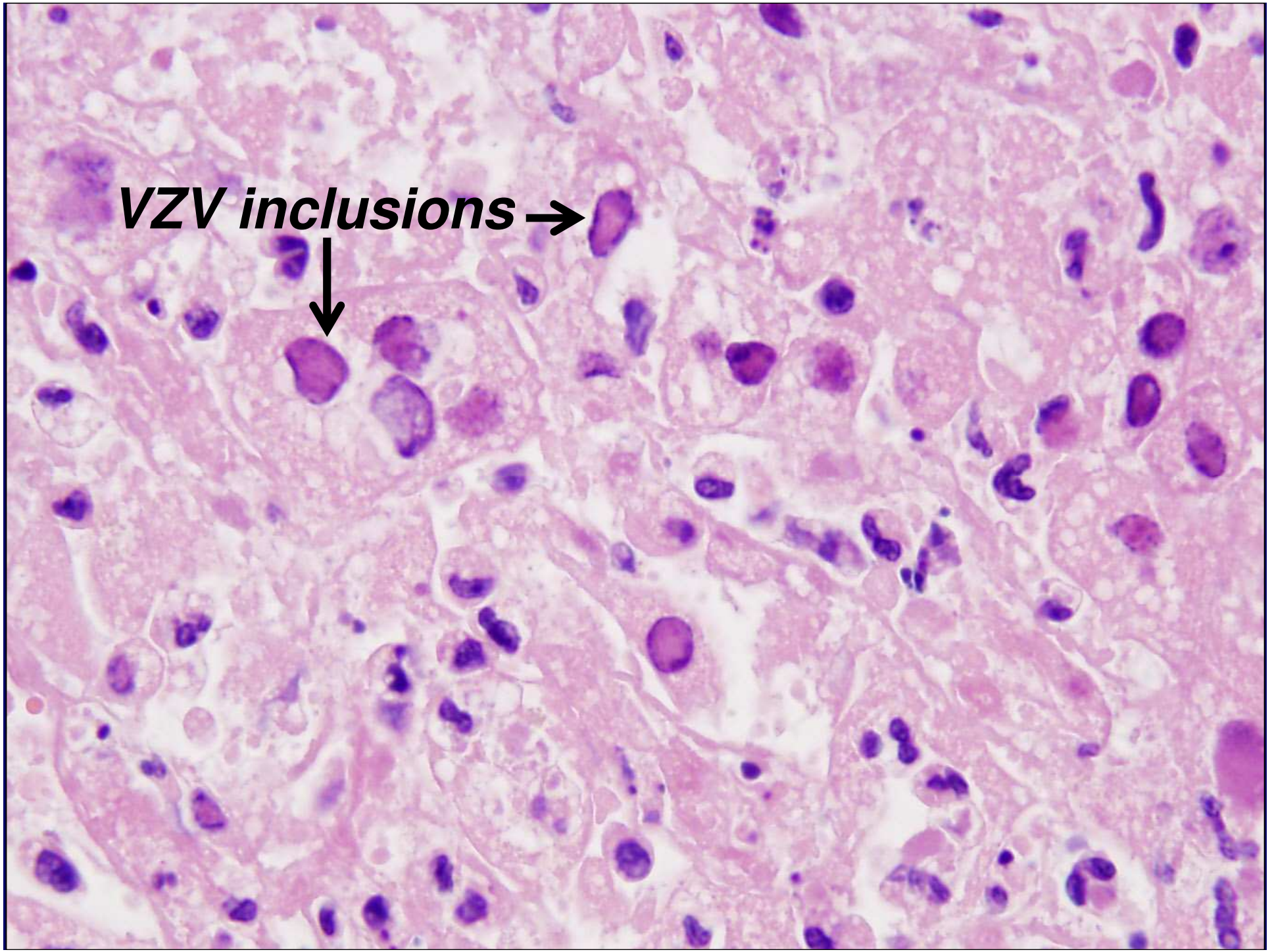
(Varicella Zoster Virus)

Chickenpox



Herpes zoster

Chickenpox in a child with normal immunity

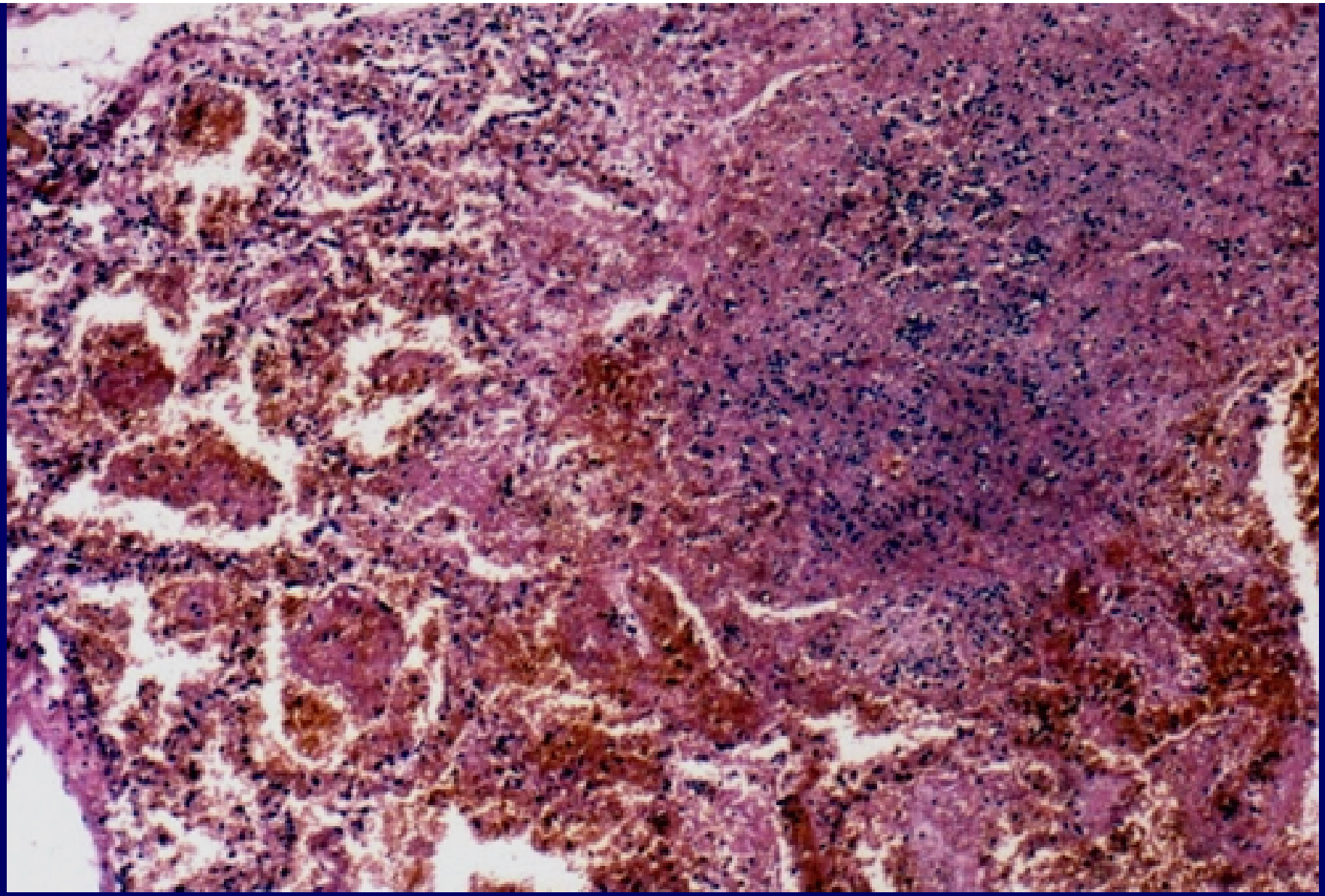

VZV inclusions

Herpes zoster (VZV)

Herpes zoster ophtalmicus

VZV-infection in an immunodeficient patient

Chickenpox and ALL



Necrotizing varicella pneumonia in immunocompromised host

Cytomegalovirus infection

Connatal ***Perinatal*** ***Postnatal***

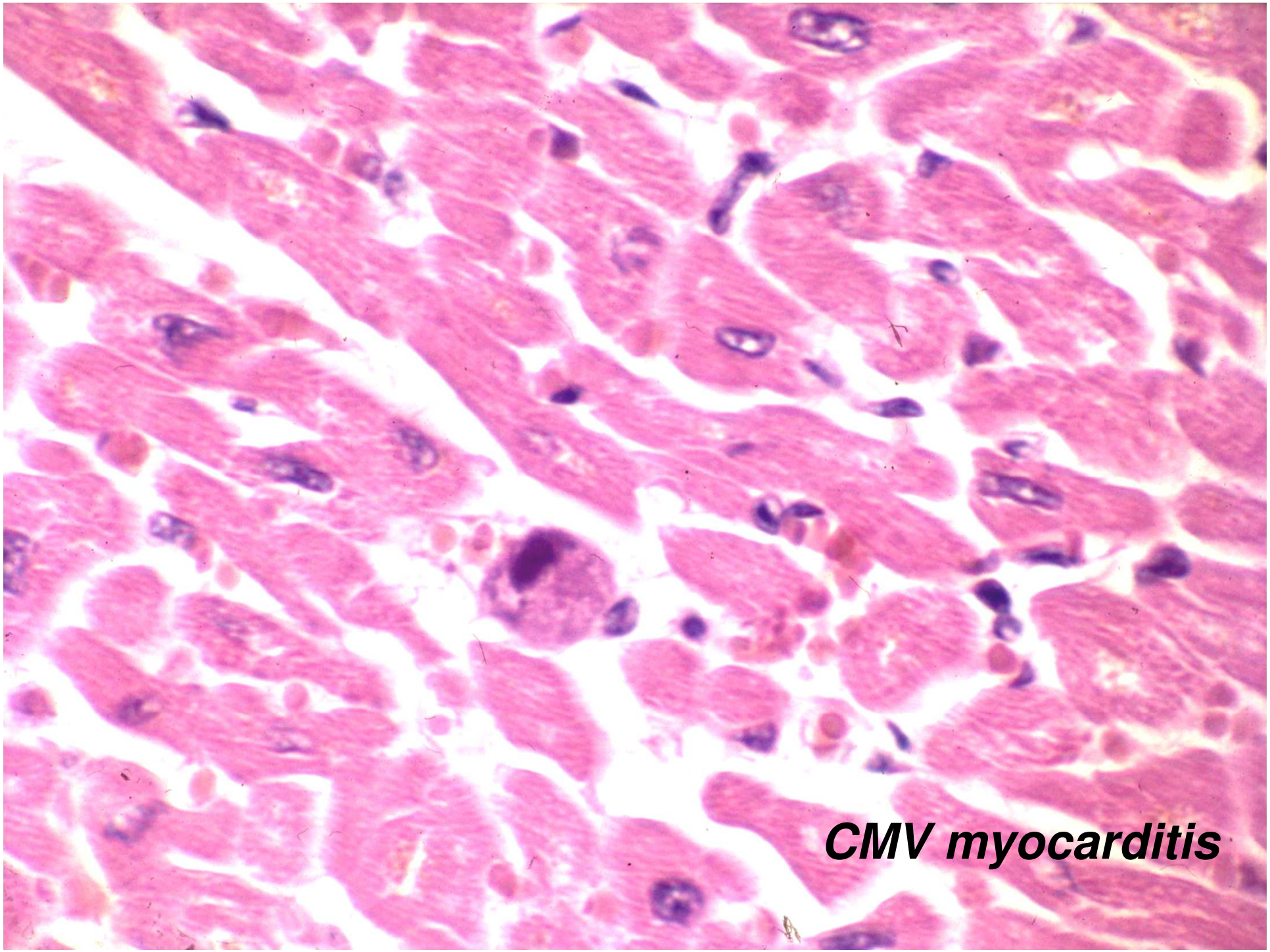
Transmission: intrauterin, perinatal, suckling, body fluids, respiratory, sexual, transfusion, transplantation

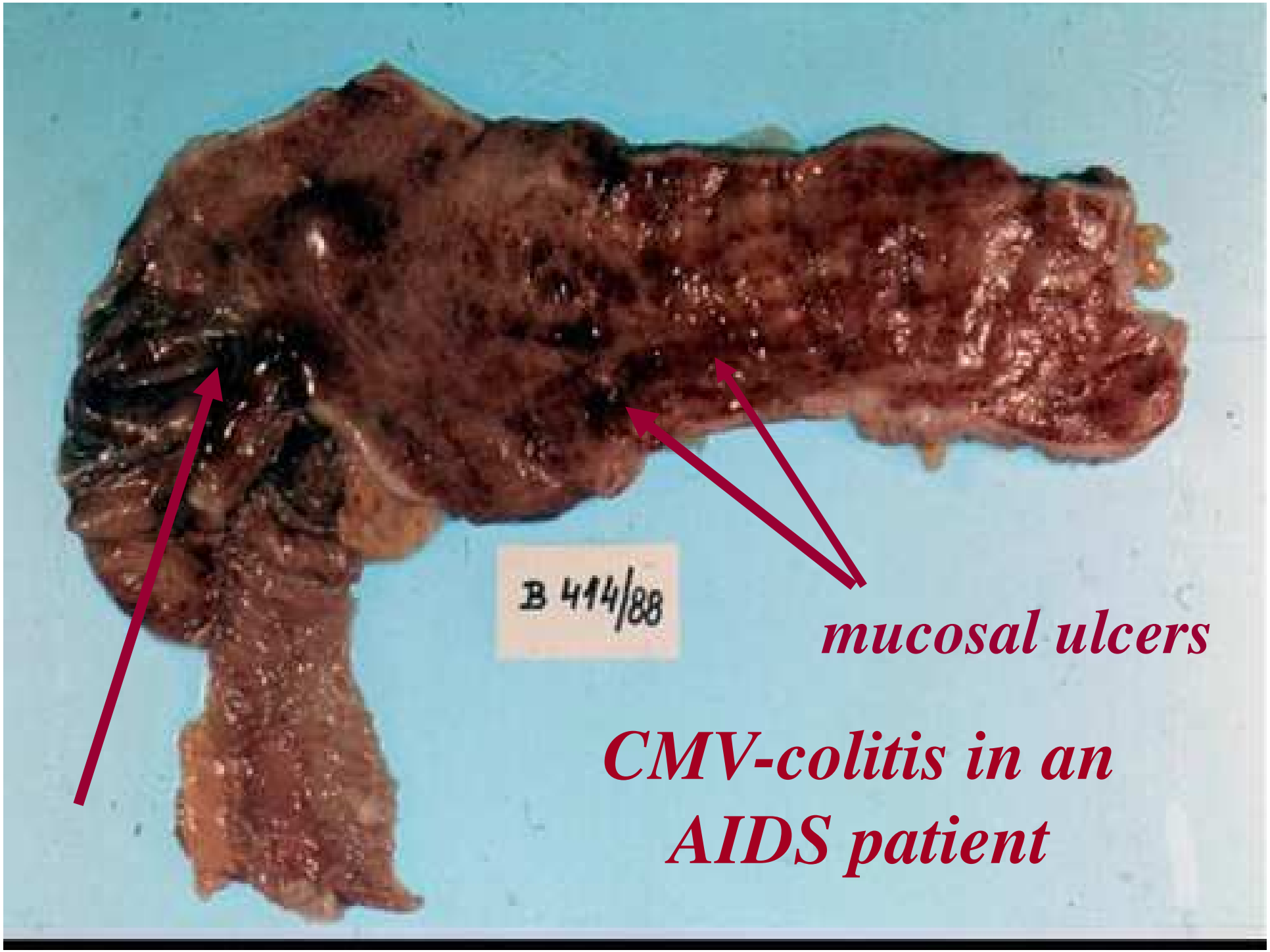
Cytomegalovirus disease

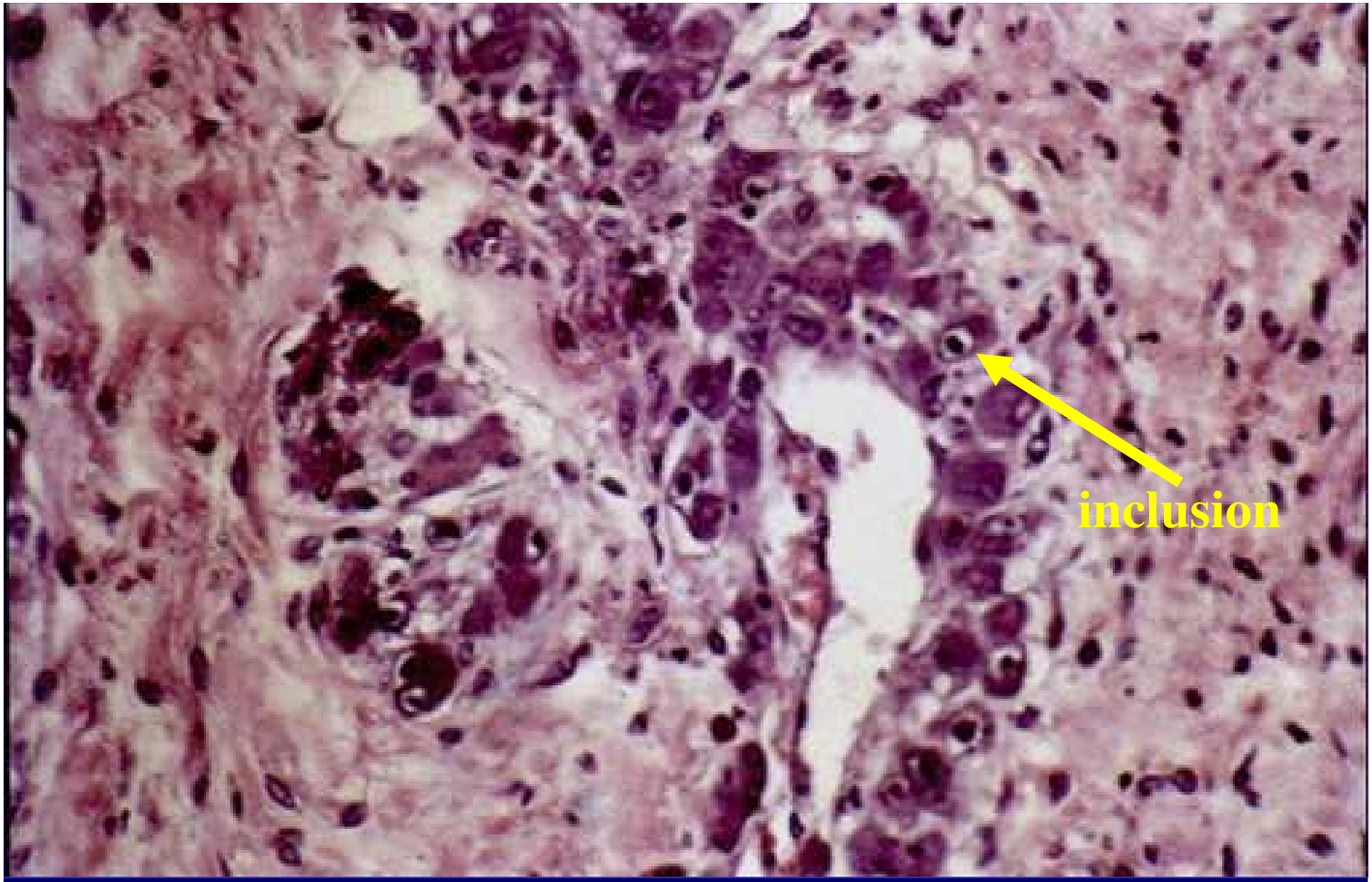
- ***Connatal form: brain lesions***
  (microcephaly, cysts, periventricular calcification, hydrocephaly)

One of the most common opportunistic infections in immunodeficiency

- ***Myocarditis after transplantation***
- ***Generalised viral disease after transplantation***
- ***Generalised infection in AIDS patients***

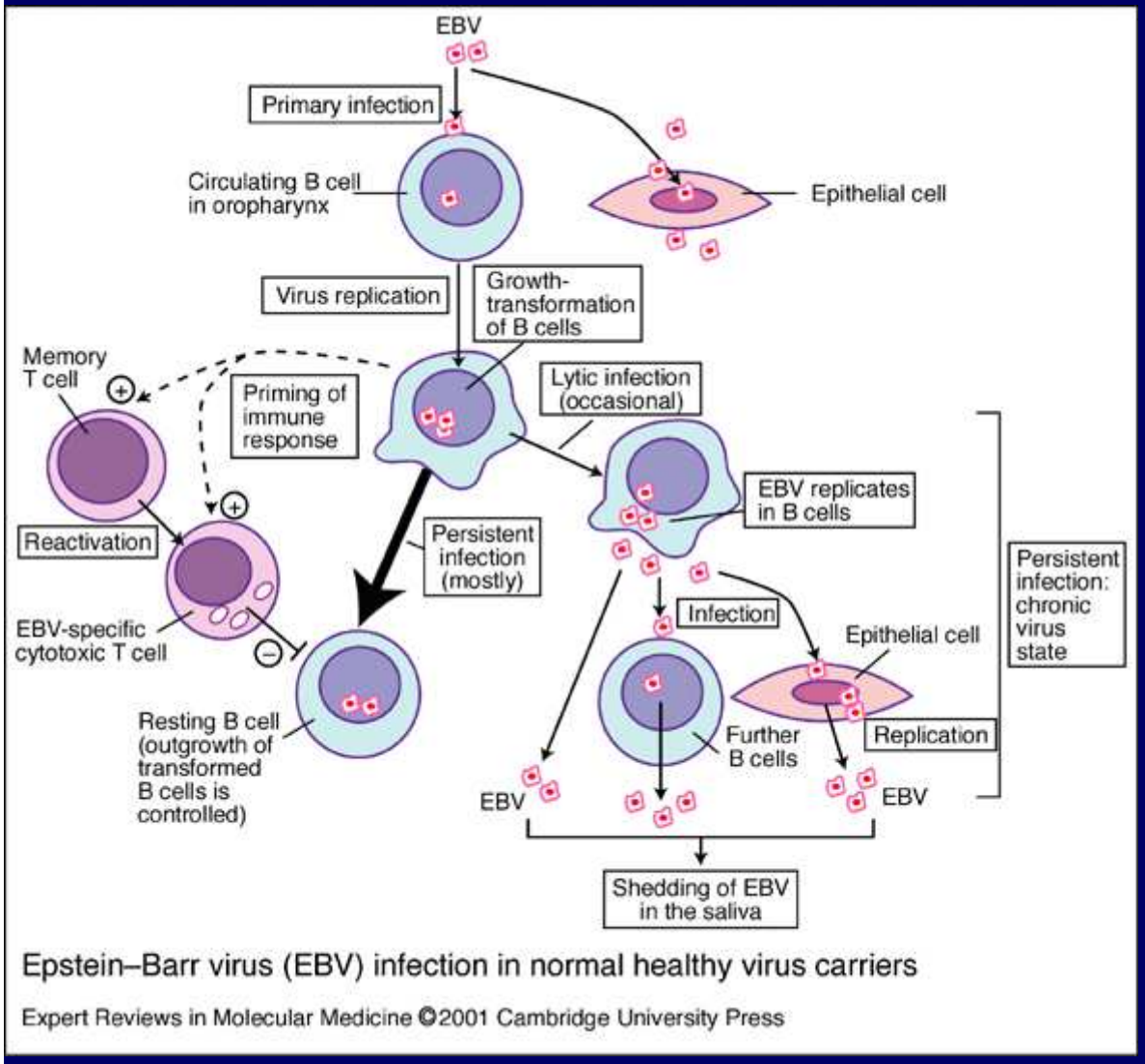

CMV myocarditis


B 414/88
mucosal ulcers
CMV-colitis in an
AIDS patient



CMV vasculitis in an AIDS patient leading to exulceration of the mucosa

EBV-Infection



Epstein–Barr virus (EBV) infection in normal healthy virus carriers

1. Mononucleosis infectiosa

2. Burkitt's lymphoma

3. Nasopharyngeal carcinoma

4. PTLD
(Post-transplant lymphoproliferative disorder)

5. Oral hairy leucoplakia (OHL)

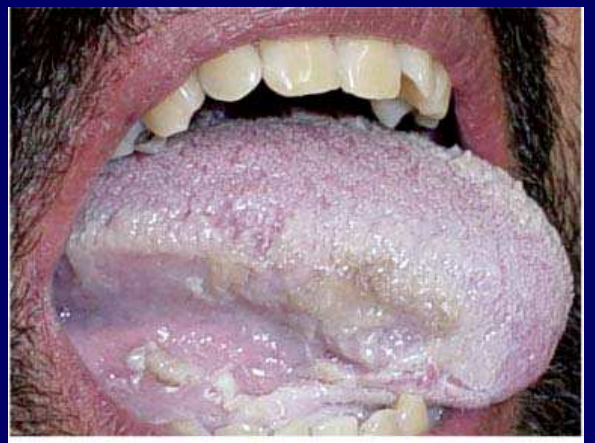
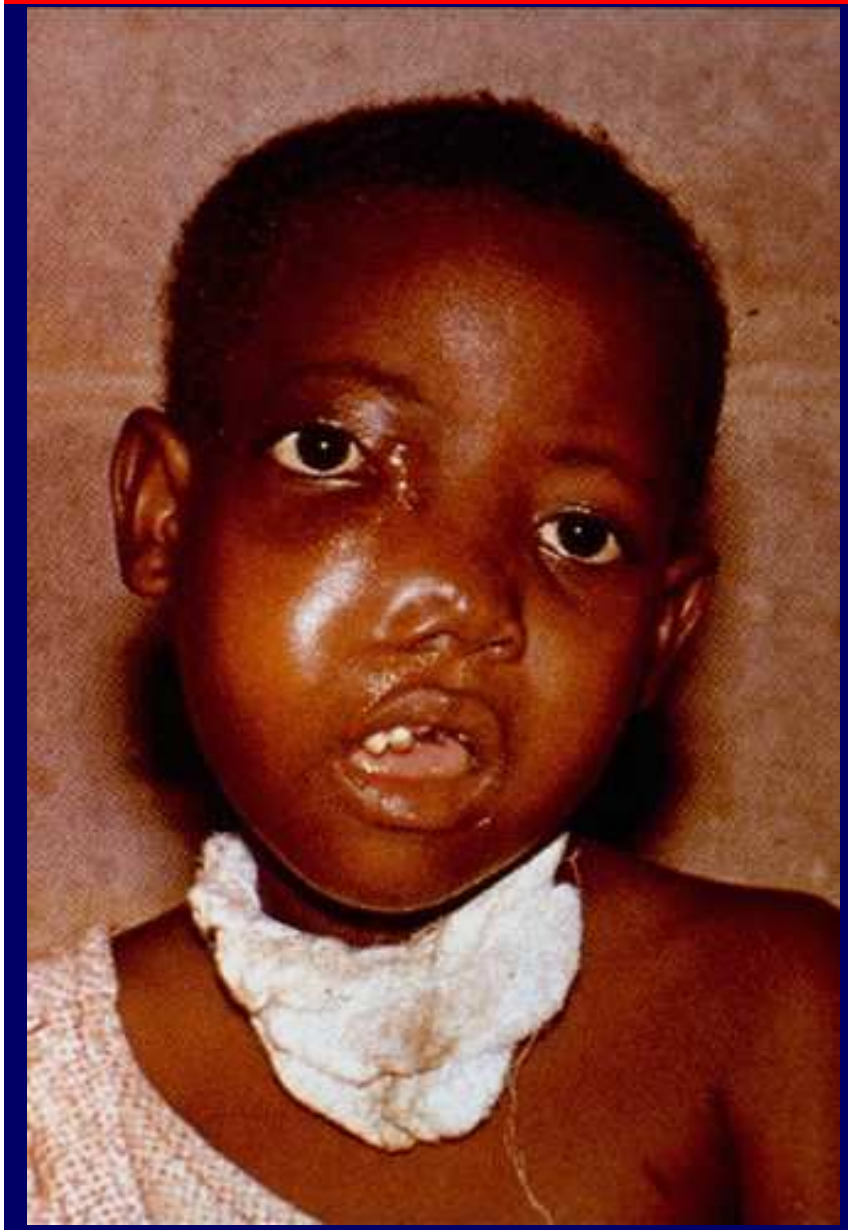


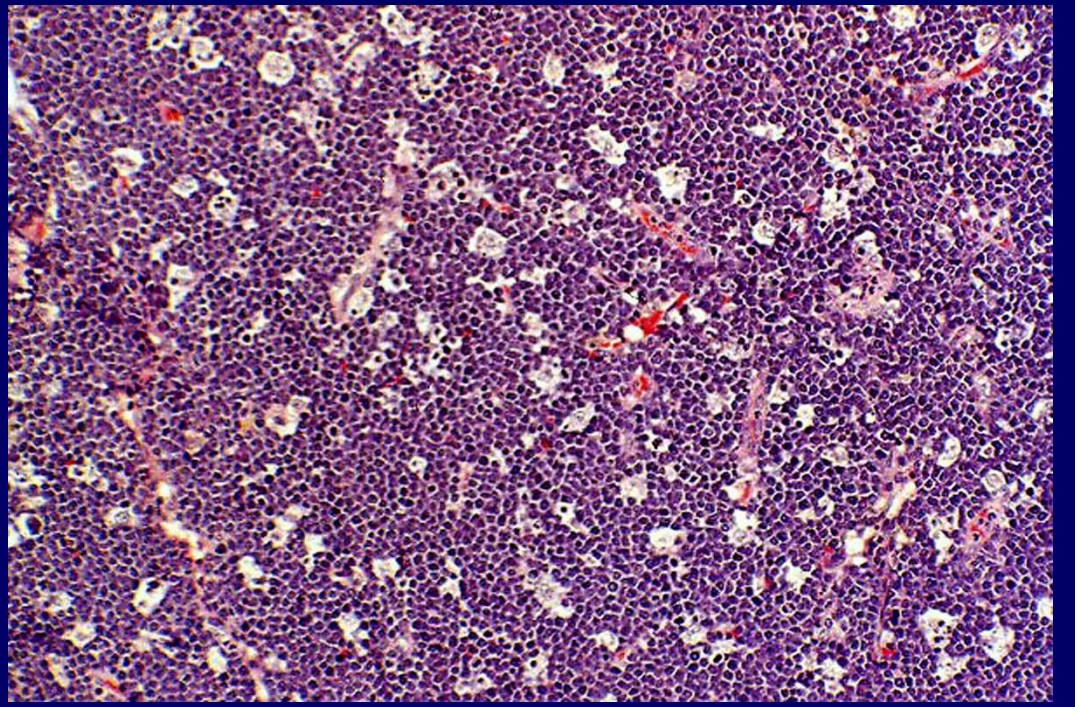
Figure 3 - Adherent white patch on right side of lateral border of tongue.

EBV-Infection



BURKITT'S LYMPHOMA

„Stary sky „



Bacterial infections

RESPIRATORY TRACT INFECTIONS

Lobar (pneumococcal) pneumonia:

Streptococcus pneumoniae

Phases:

I. Congestion (1-2nd days)

(hyperemic capillaries, serous alveolar exsudate)

II. Red hepatization (3rd day)

(red blood cell rich serofibrinous alveolar exsudate)

III. Grey hepatization (4-5th days)

(degradation of RBCs, grey color due to the fibrin-filled alveoli containing macrophages and neutrophils)

IV. Yellow hepatization (7th day)

(massive neutrophil infiltration in the fibrin-filled alveoli)

V. Resolution (8-9th days)

(fibrinolytic dissolution of the exudate by neutrophils & mac.)

BACTERIAL TOXINS

EXOTOXINS

NEUROTOXINS

Clostridium tetani	*TETANUS*
Clostridium botulinum	*BOTULISM*

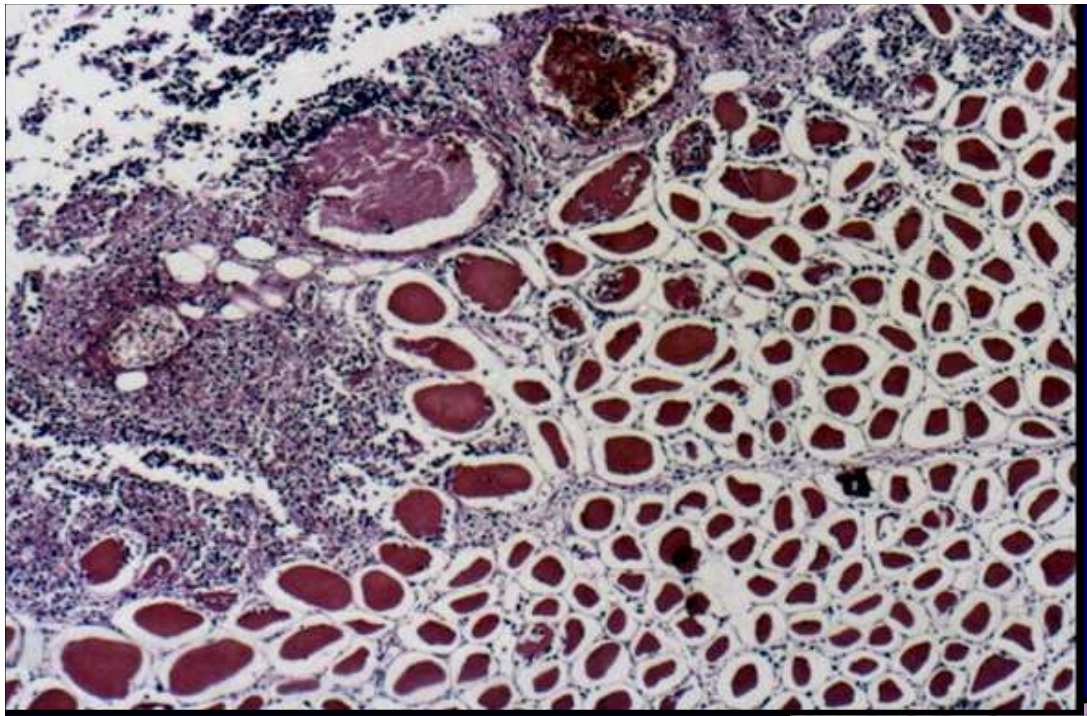
ENTEROTOXINS

Vibrio cholerae	*CHOLERA*
Clostridium difficile	*COLITIS*
S. aureus	*FOOD POISONING*

CYTOTOXINS

Clostridium perfringens	*GAS GANGRENE*
Corynebact. diphteriae	*DIPHTERIA*

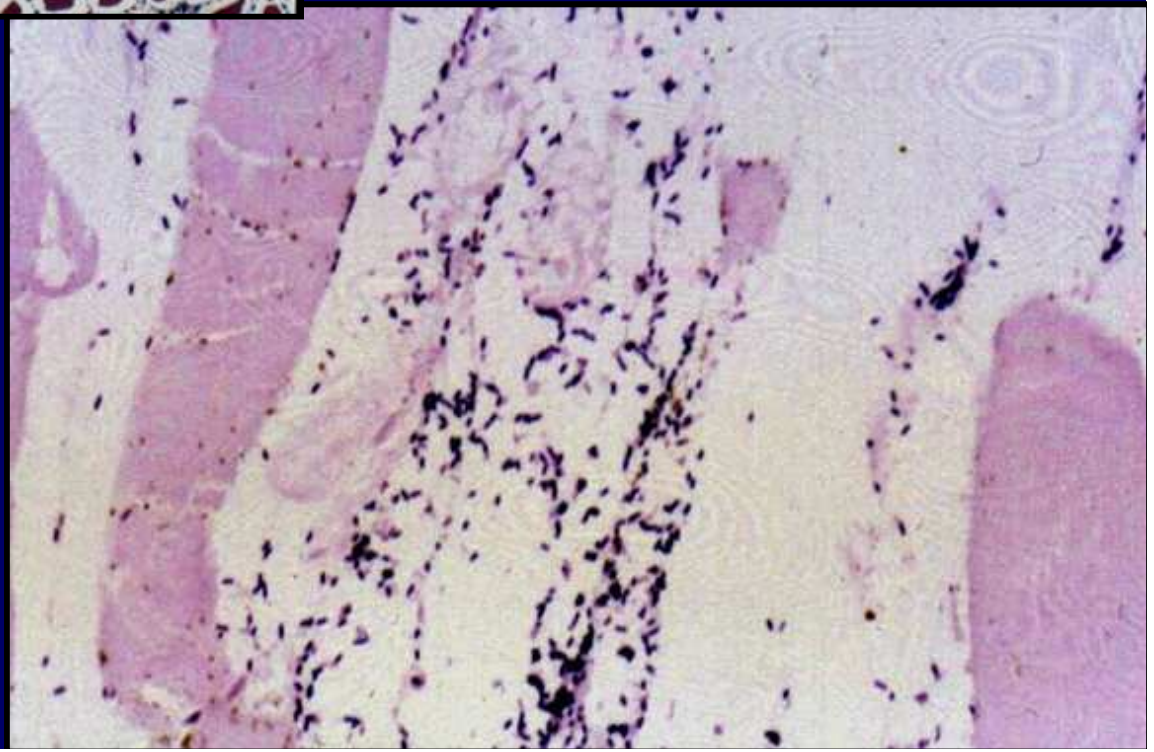
ENDOTOXINS - Gram-negativ bacteria



GAS GANGRENE

Clostridium perfringens

Effect of myotoxin: lysis of muscle cells



Common bacterial infections of the gastrointestinal tract

E. coli diarrhea

Enterotoxigenic E. coli	*travellers*
Enteropathogenic E. coli	*babies*
Enterohemorrhagic E. coli	*colon*
Enteroinvasive E. coli	*colon, distal ileum*

Salmonella enterocolitis

Fecal-oral transmission
superficial ulceration

Typhoid fever

Salmonella typhi ; Fecal –oral transmission; carrier status
Mucosal invasion and swelling, fibrinous necrosis, ulcerations of Peyer patches, S.typhi passes into the circulation leading to systemic infection

Cholera

Exotoxin effect /functional disturbances only/

Shigellosis (shigella dysentery)

Pseudomembranous colitis

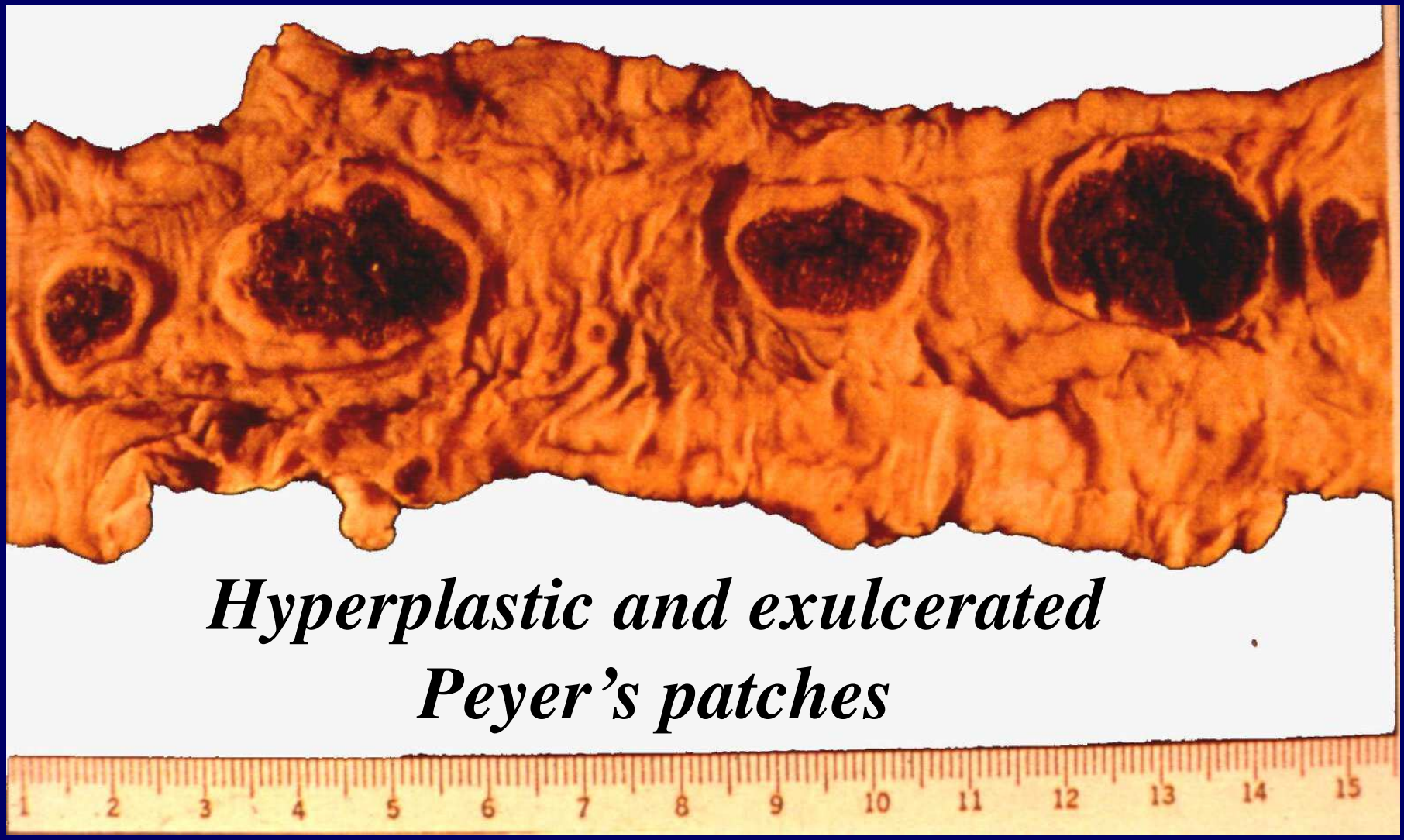
Antibiotics associated colitis

Pseudomembranous colitis caused by Clostridium difficile

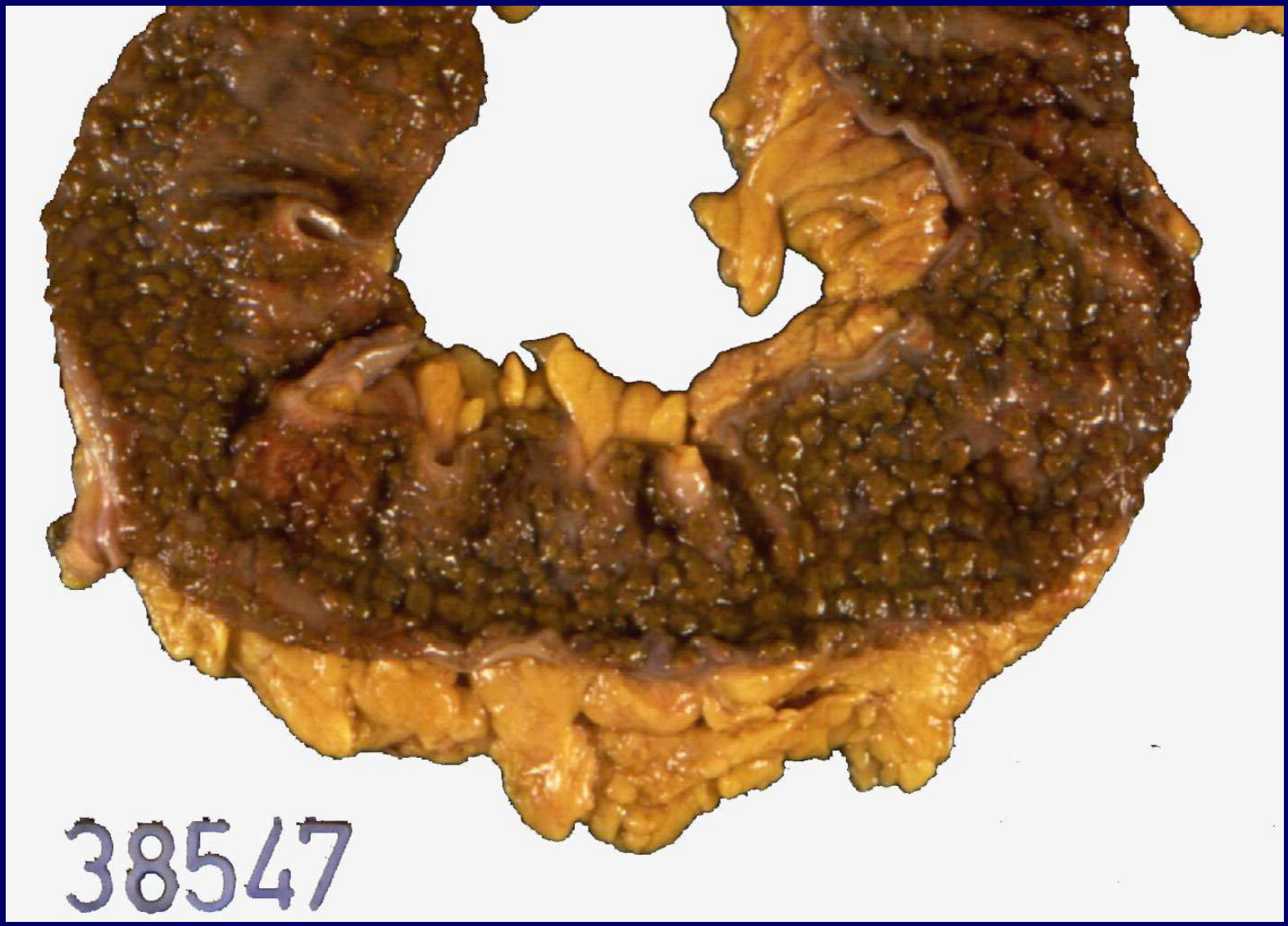
Aucte enterocolitis

(superficial ulceration)

Ulcers of the terminal ileum in fatal typhoid fever (deep ulceration)

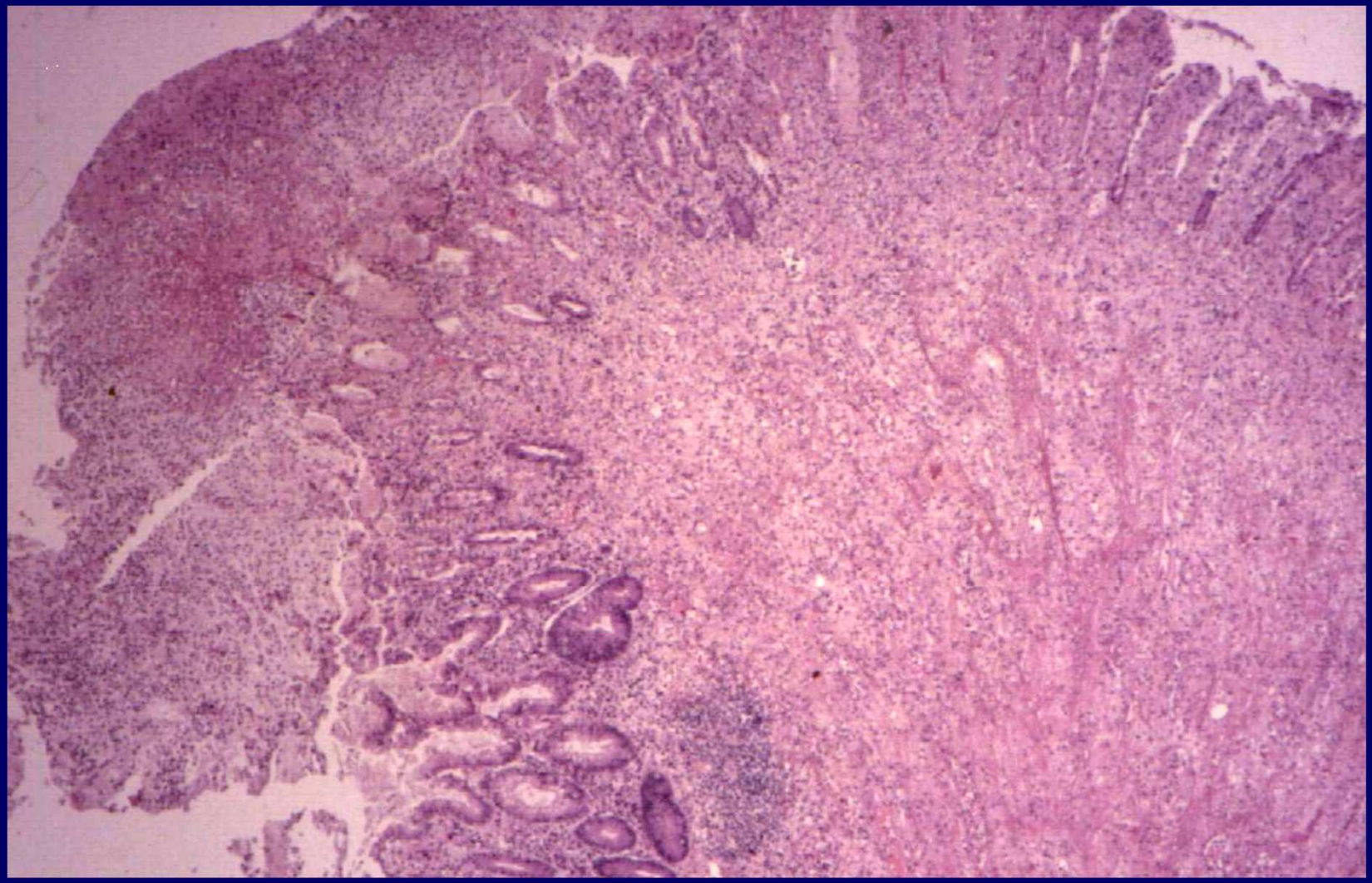


Hyperplastic and exulcerated Peyer's patches



Pseudomembranous colitis *(deep ulceration)*

Pseudopolyps (remaining islands of mucosa in the ulcerated area)



Clostridium difficile colitis

MENINGOCOCCAL INFECTIONS

***GRAM* - DIPLOCOCCUS**

Two fatal lesions:

I. Meningococcal meningitis

FEVER, HEDACHE, STIFF NECK, CONFUSION, VOMITING

Tachycardia, Myocardial damage,

Purulent meningitis

II. Fulminant meningococcemia Waterhouse-Fridericksen syndrome

Purulent meningitis due to Meningococcus

(Neisseria meningitidis)

II.WATERHAUSE -FRIDERICHSEN SY.

(Fulminant meningococcemia)

(IN CHILDREN UNDER 5 YEARS)

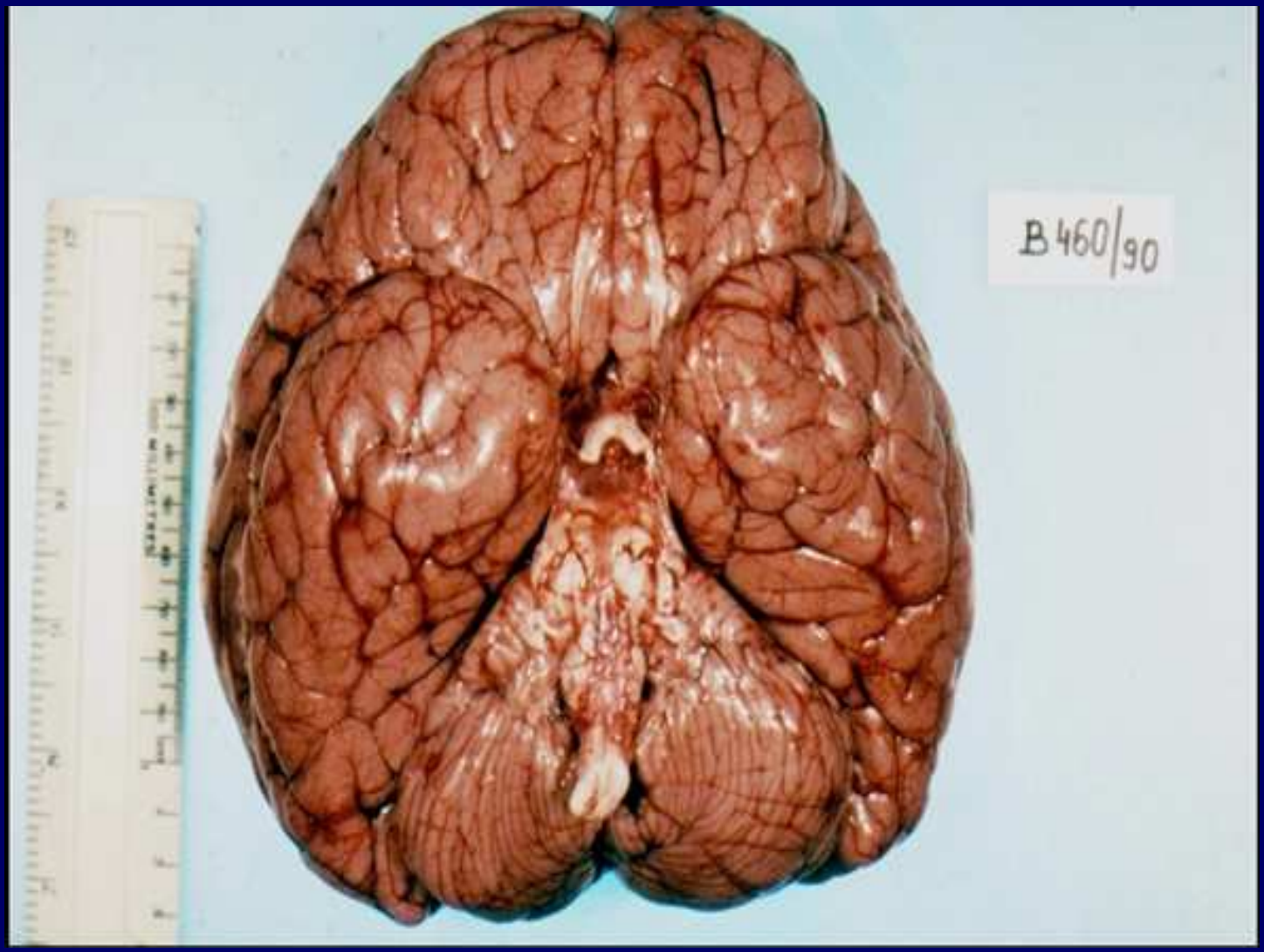
- *Rapid onset, fever, fulminant development of symptoms*
- *Cutan hemorrhages, (purpura)*
- *DIC*
- *Endotoxin shock*
- *Hemorrhagic necrosis of adrenals*

PURULENT MENINGITIS MAY OR MAY NOT BE PRESENT

WATERHOUSE-FRIDERICKSEN SYNDROME

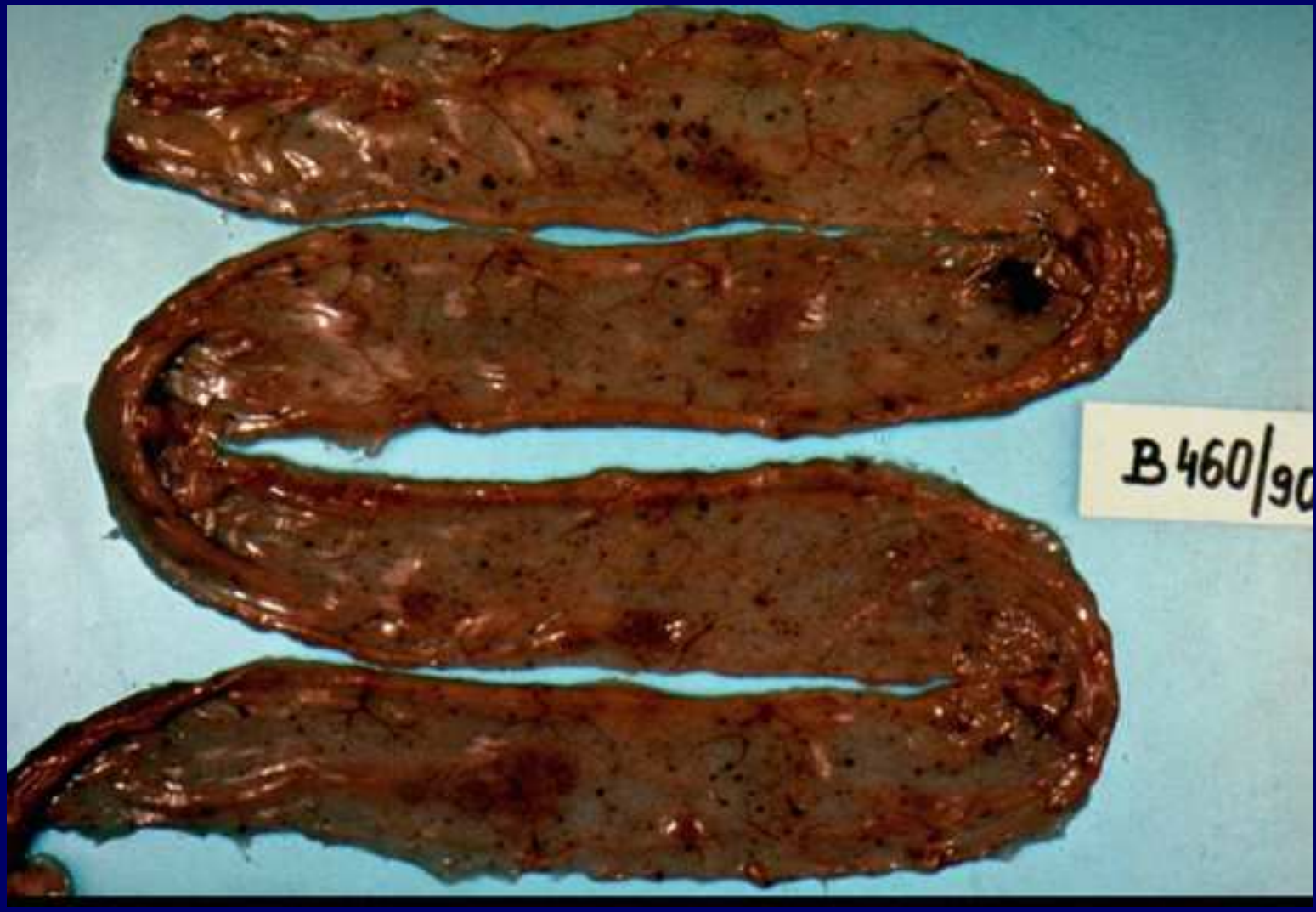
Petechiae and purpura on the skin

Purpura in meningococcaemia



Oedema of the brain and hyperaemia of meninges in Waterhouse-Fridericksen sy.

Haemorrhagic necrosis of adrenals



Petechiae on the bowel mucosa

*ZOONOTIC DISEASES**

** Infection is aquired from ANIMAL RESERVOIR*

BRUCELLOSIS

Granulomatous lesions

TULARAEMIA

Abscedating - granulomatous lesions

ANTHRAX

Haemorrhagic inflammation

LISTEROSIS

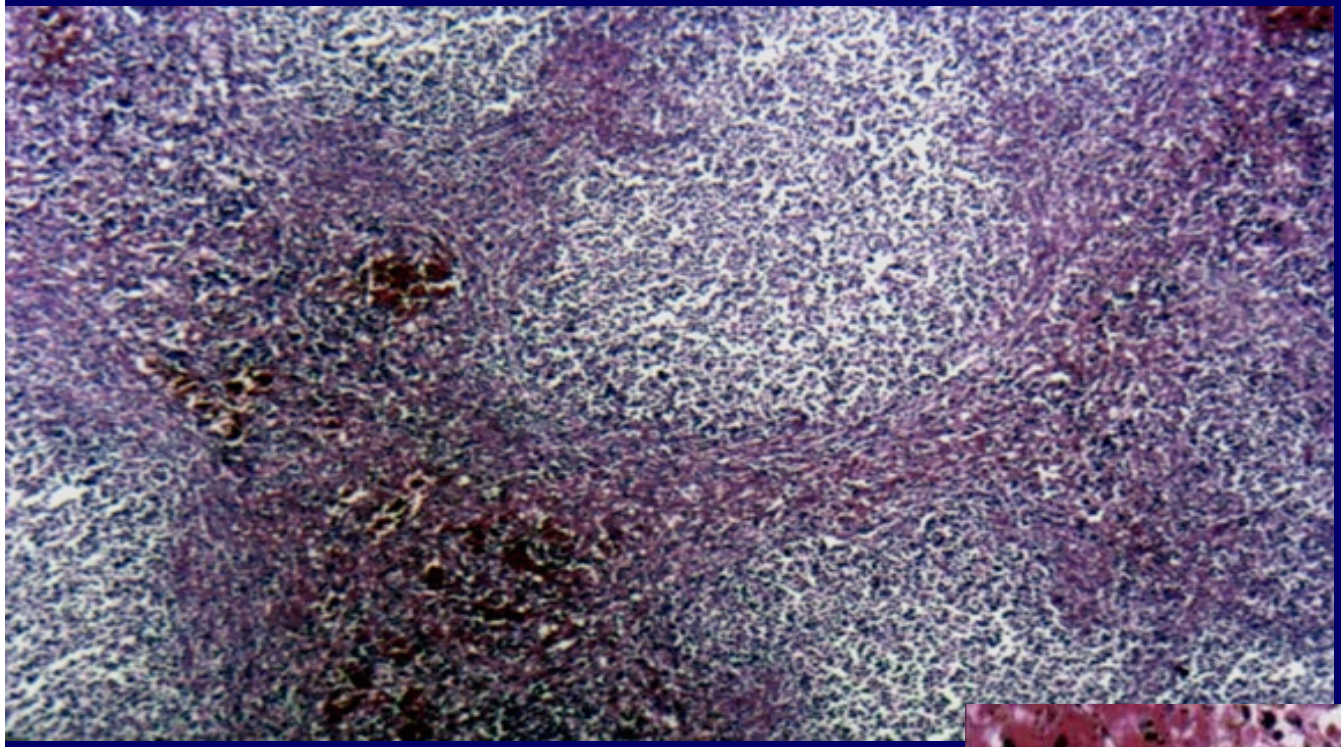
Septicaemia, meningitis

Granulomatosis infantiseptica

CAT-SCRATCH FEVER

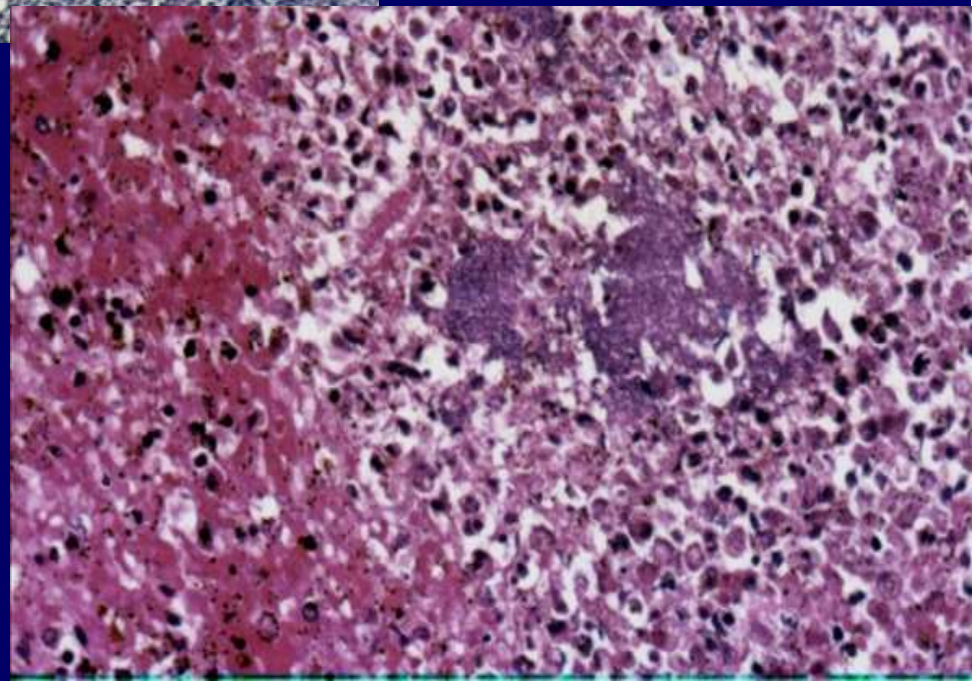
Suppurative - granulomatous lesions

Injury of the skin from the bites of a rabbit infected with Francisella tularensis

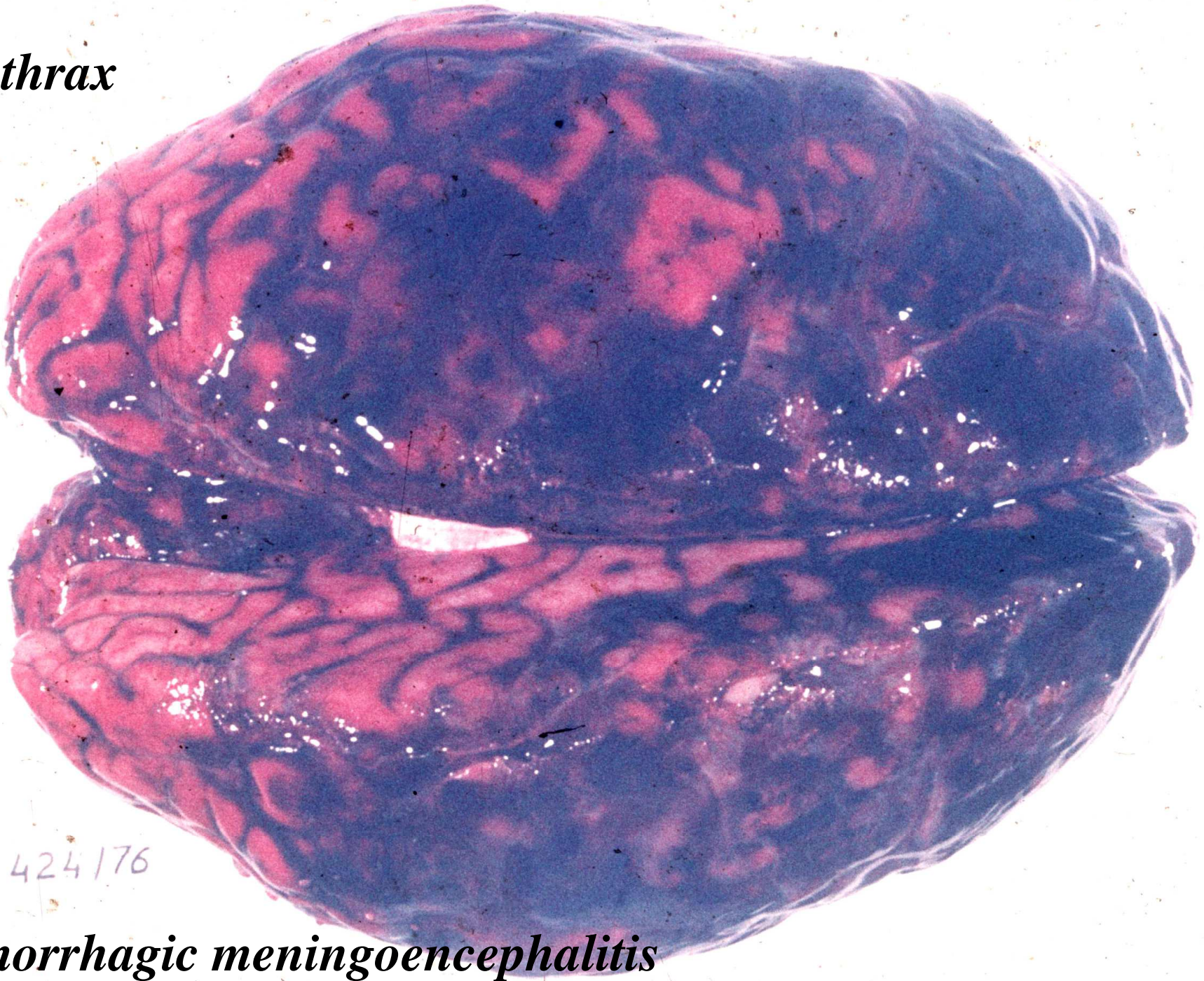


Tularemia

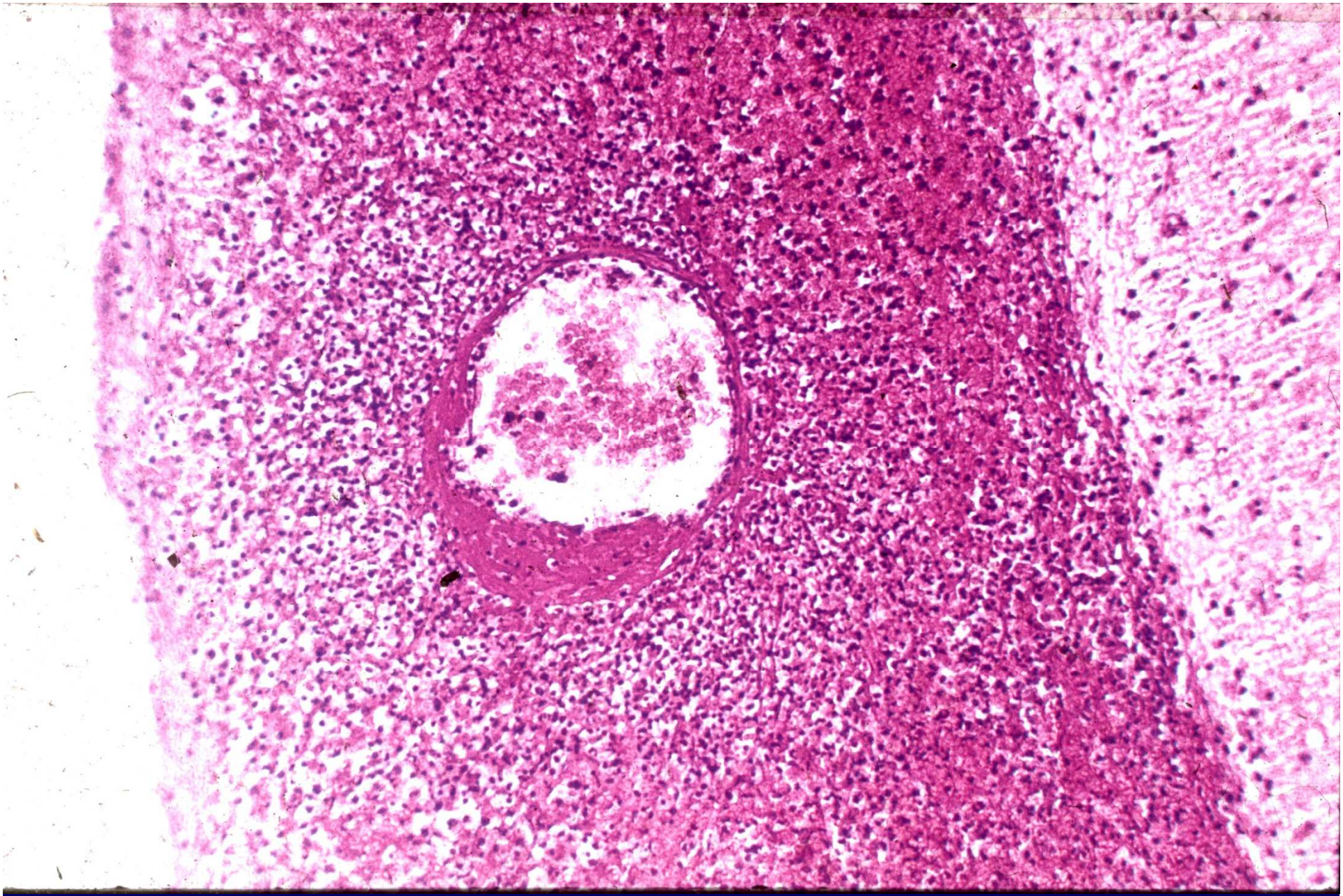
Abscedating lymphadenitis



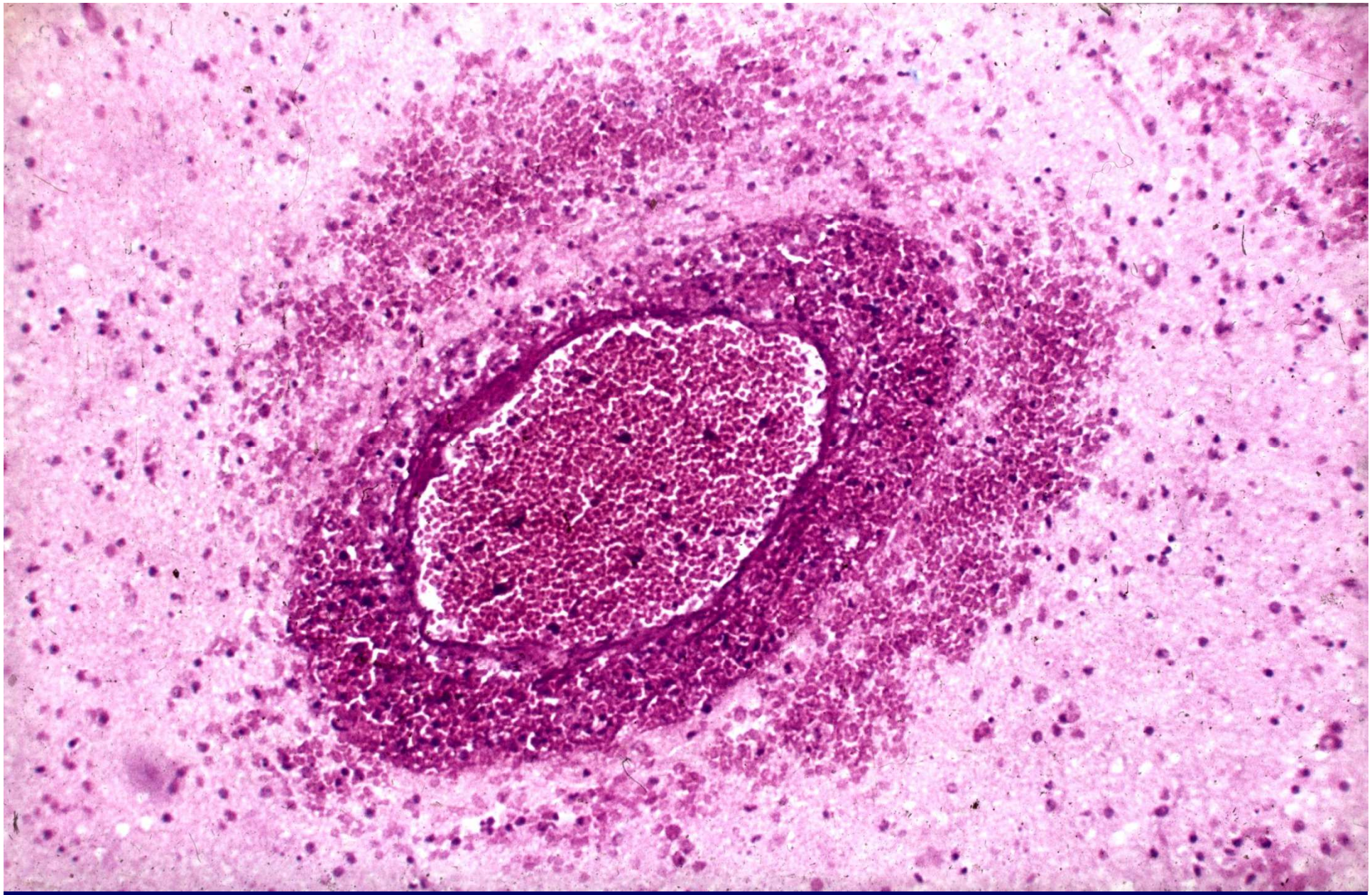
Anthrax



Hemorrhagic meningoencephalitis



Hemorrhagic leptomeningitis. (Anthrax)



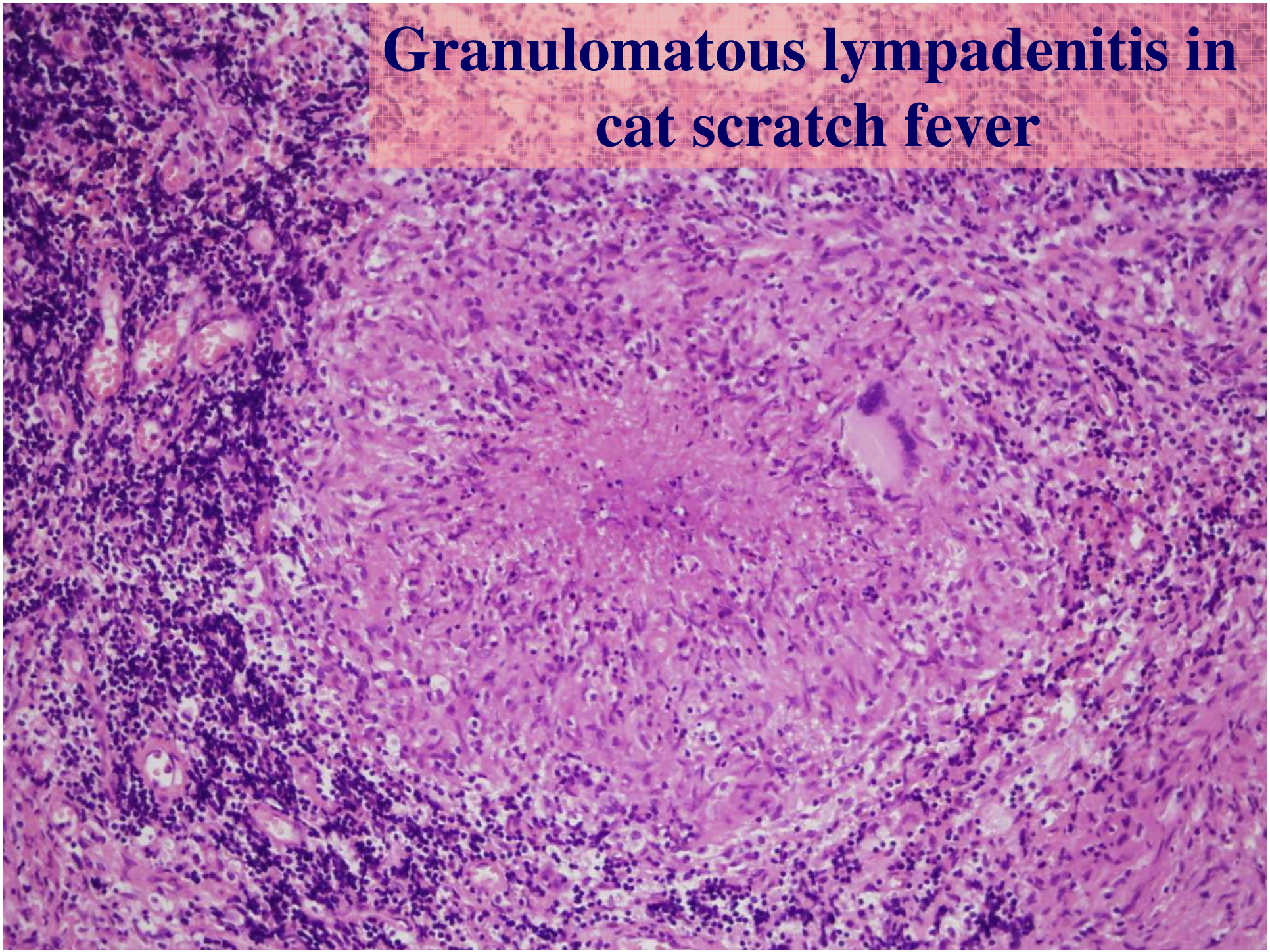
Perivascular hemorrhagic infiltration in the brain. Meningoencephalitis.(Anthrax)

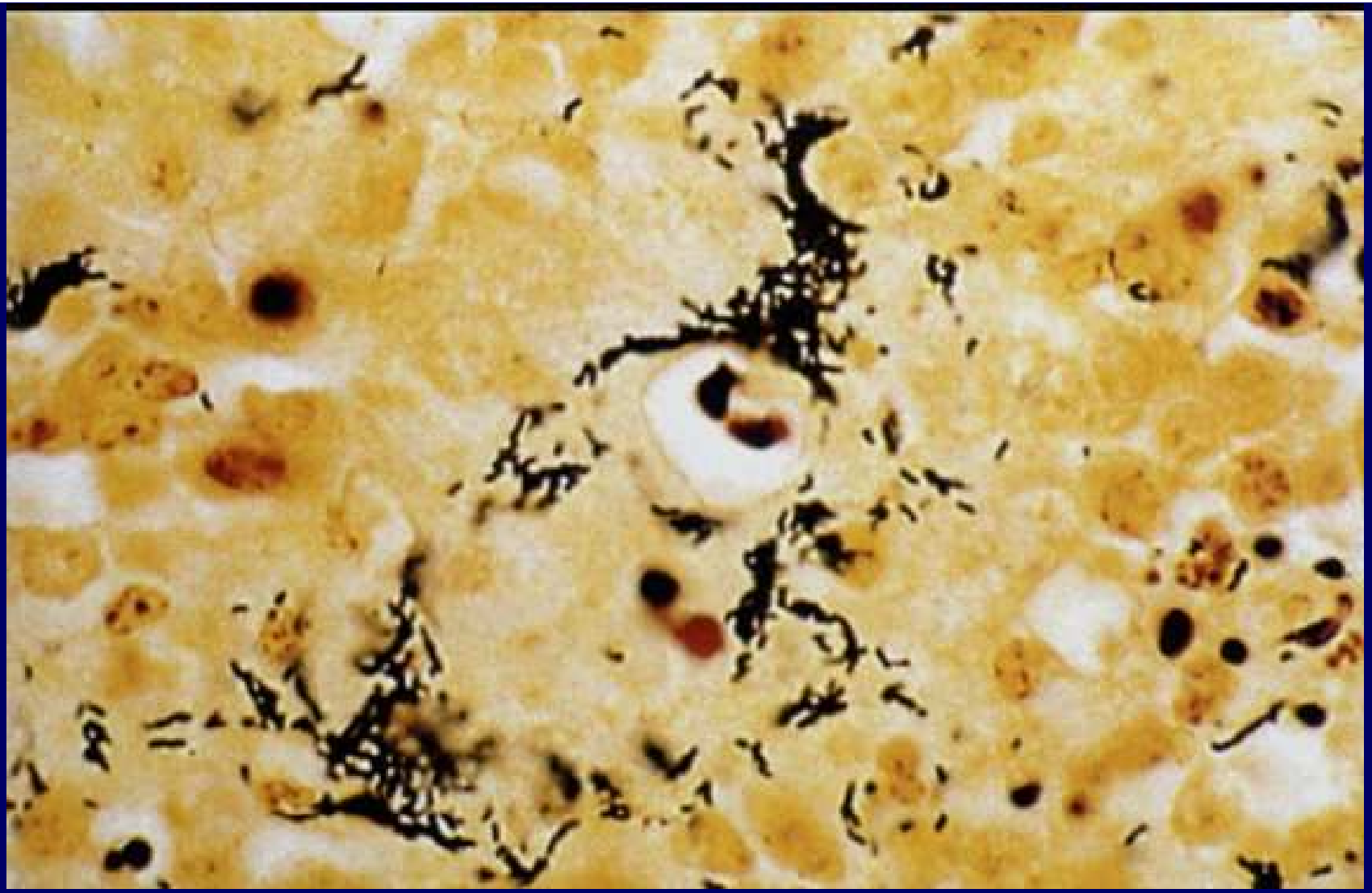
CAT SCRATCH DISEASE

- ***Self limited infection caused by***
  Bartonella henselae
- ***Site of entry: skin, conjunctiva***
  (oculoglandular syndrome)
- ***Lymphadenitis:***
  suppurative and
  granulomatous

Cat scratch fever

Granulomatous lympadenitis in cat scratch fever





Warthin-Starry silver impregnation of Bartonella henselae bacilli in lymph node. Cat scratch disease

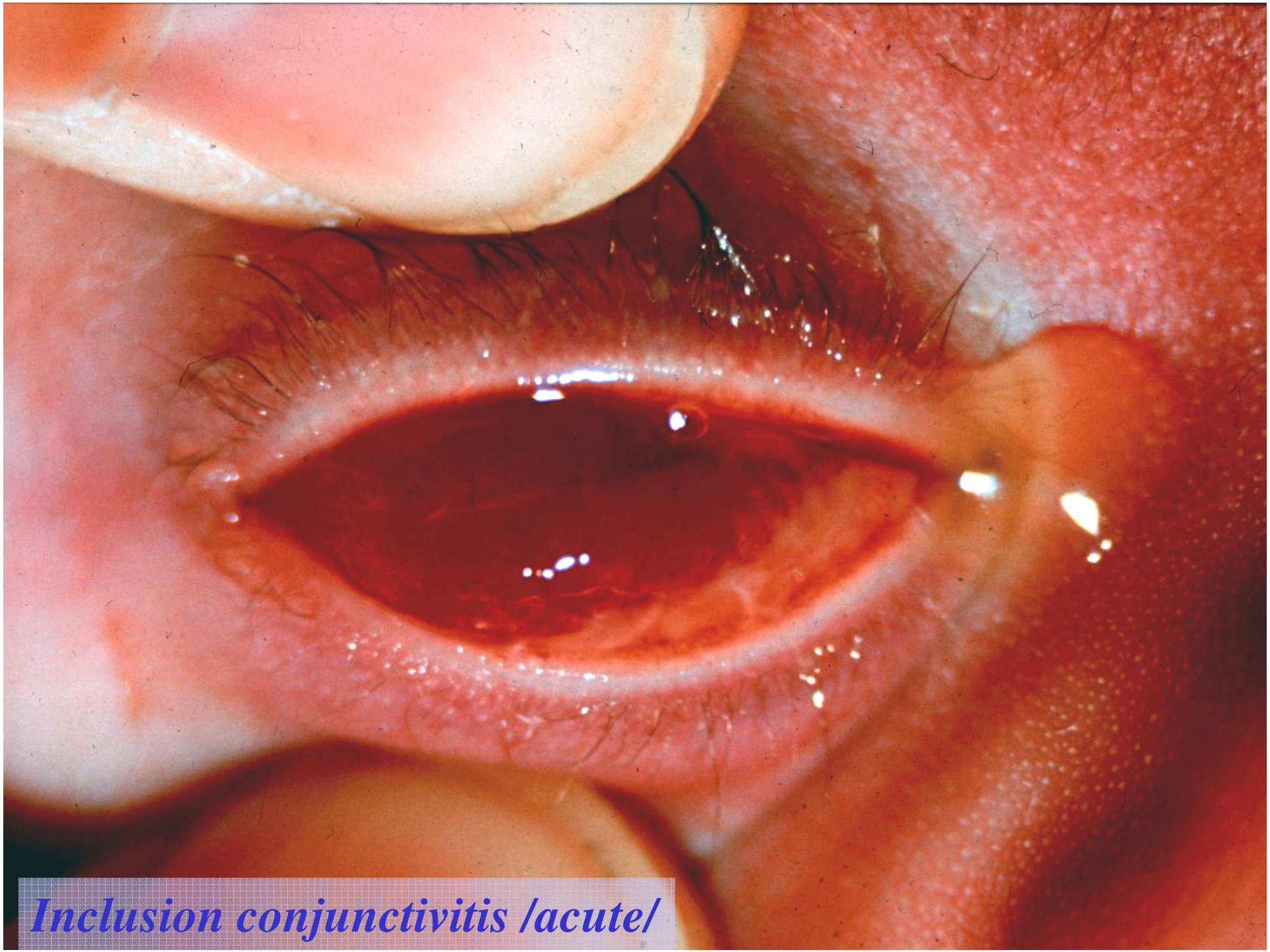
Sexually transmitted bacterial diseases

- *Syphilis (lues)-Treponema pallidum*
- *Gonorrhoea- Gonococcus*
- *Ulcus molle (chancroid)*
  (Hemophilus ducreyi)
- *Granuloma inguinale*
  (Calymmatobacter granulomatis)
- *Lymphogranuloma venereum*
  (Chlamydia trachomatis L1.L3))

CHLAMYDIAL DISEASES

- ***Psittacosis** /parrot fever, ornitosis/; Chl. psittaci*
- ***Trachoma** /leading cause of blindness/; Chl. trachomatis A-C*
- ***Inclusion conjunctivitis** /paratrachoma/; Chl. trach. D-K*
- ***Lymphogranuloma venereum; Chl. trachomatis L1, L3***
- ***Infections of the genital tract; Chl. trachomatis D-K***
- ***Neonatal pneumonitis;***
  Chl. pneumoniae

SEXUALLY TRANSMITTED, Non-gonococcal urethritis (NGU),
SALPINGITIS ⟶ STERILITY

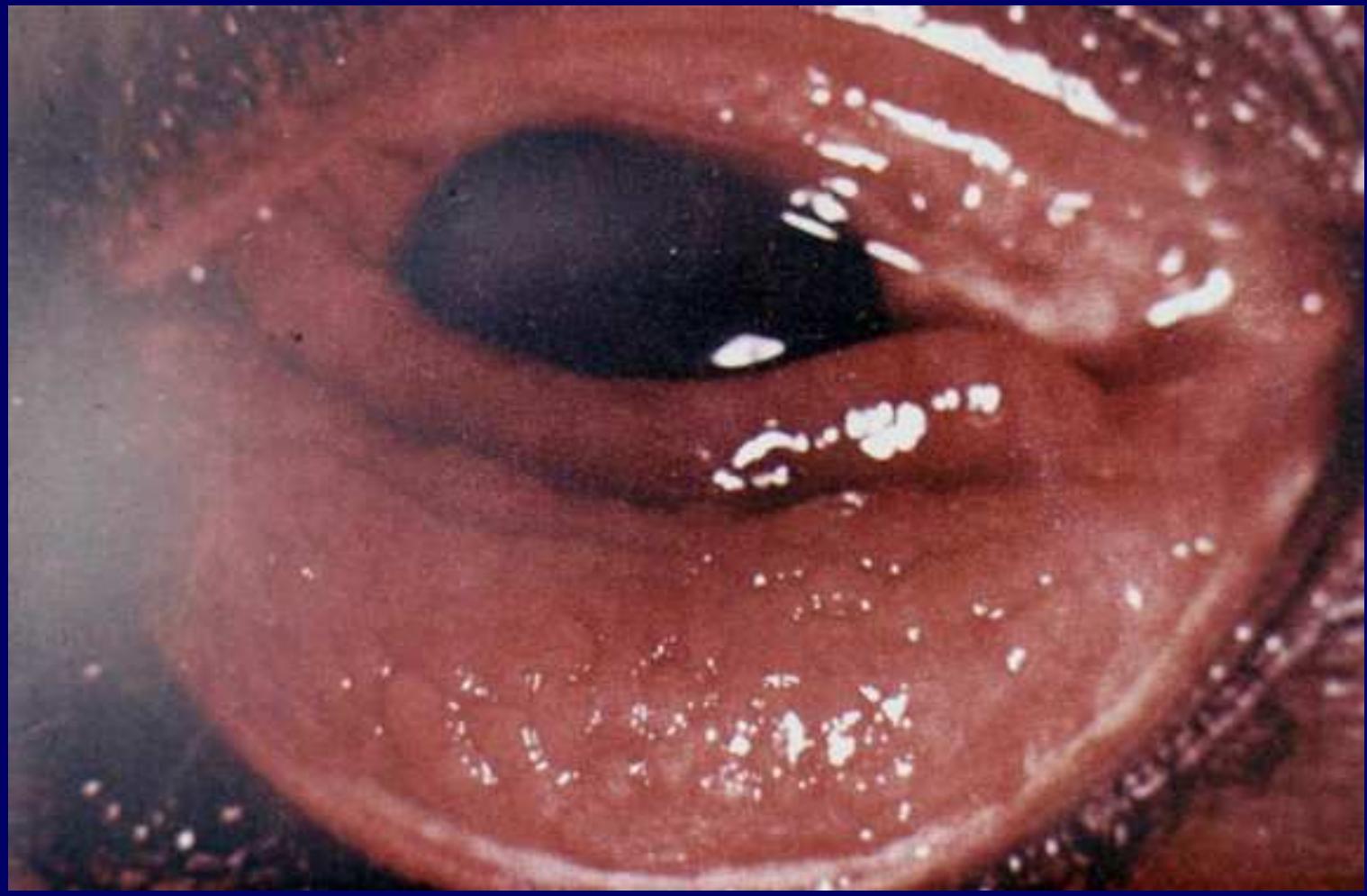


Inclusion conjunctivitis /acute/

Inclusion conjunctivitis / subacute/


Inclusion conjunctivitis

Trachoma



Repeated inflammatory episodes lead to pannus formation (granulation tissue-like fibrovascular hyperplasia of the conjunctival and corneal stroma), scarring → ulcerative keratitis and blindness