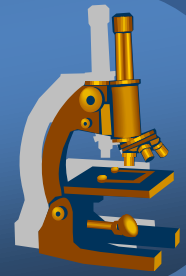


Systemic pathology



Nervous system



Brain swelling, ischemia

Brain swelling



- × generalised increase in the volume of brain (blood, water, ions) → clinical signs related to raised intracranial pressure / intracranial shift / herniation
- × **diffuse** (vasodilatation, oedema – vasogenic, cytotoxic, interstitial)
- × **focal** (space-occupying lesions – inflammation, tumor, trauma, vascular lesion)
- × **herniations:**
 - ⇒ *supracallosal – interhemispheric under falx cerebri*
 - ⇒ *transtentorial – temporal (3rd nerve, secondary brainstem haemorrhage)*
 - ⇒ *tonsillar – foramen magnum, vital centres compressed*

Brain swelling



xgross:

⇒ *flattened gyri, narrow sulci, slit-like ventricles*

xmicro:

⇒ *neuropil vacuolation*

⇒ *swelling of the cytoplasm and processes of astrocytes*

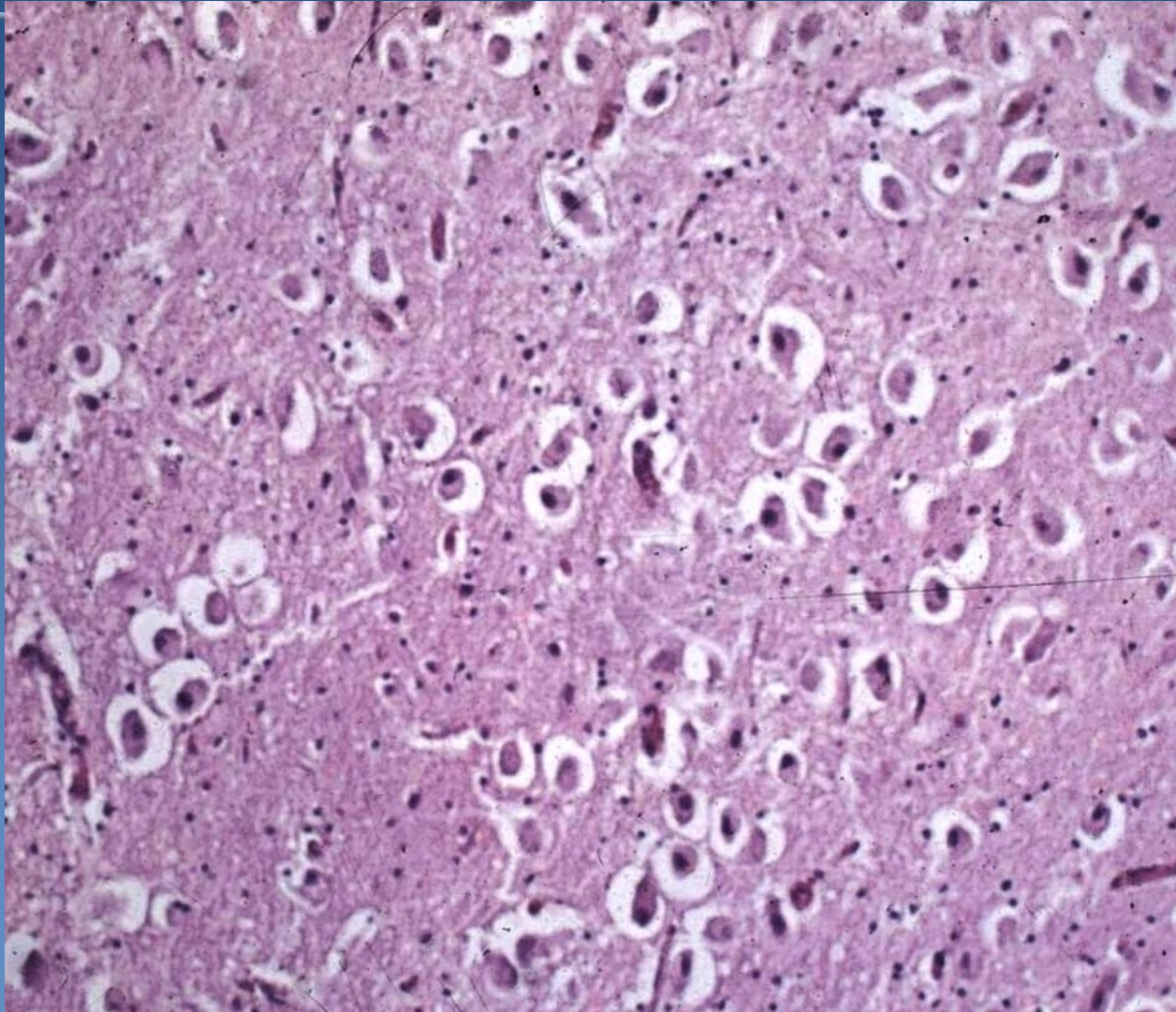
⇒ *perivascular optically empty spaces*

⇒ *myelin less vividly colored*

Diffuse brain swelling



Diffuse brain swelling



Brain swelling - pathogenesis



× main types:

⇒ *vasogenic*

- due to increased cerebral vascular permeability (esp. by neoangiogenesis)
- adjacent to tumors, abscesses, haemorrhage, ischemia

⇒ *cytotoxic*

- due to hypoxia / ischemia , toxic damage – cell membrane injury, ↑intracellular fluid

⇒ *interstitial*

- due to damage of ventricular lining (hydrocephalus, CSF diffusion into the white matter)

Hydrocephalus



- ✗ increased amount of CSF, ↑ intracranial pressure
- ✗ infants x older children, adults
- ✗ caused by:
 - ⇒ *increased CSF production*
 - ⇒ *decreased CSF resorption*
 - meningitis, subarachnoid haematoma
 - ⇒ *obstruction to CSF flow*
 - congenital x acquired – trauma, tumors, infection, blood coaguli, cyst
 - ⇒ *hydrocephalus e vacuo (secondary/compensatory)*

Hydrocephalus



Encephalomalatia ***(cerebral infarction)***



- × **colliquative necrosis**
- × **„white“ ischemic x haemorrhagic – blood reflux, venous**

- × **clinically: stroke or transient ischaemic attack – TIA**

- × **pathogenesis:**
 - ⇒ *arterial thrombosis (AS, arteritis, arteriopathy)*
 - ⇒ *thrombembolia*
 - ⇒ *venous thrombosis*
 - ⇒ *diffuse small vessel problems – spasm, vasculitis*
 - ⇒ *external pressure (haematoma)*
 - ⇒ *systemic hypoxia*

- × **the size and distribution depends on:**
 - ⇒ *diameter and localisation of affected artery*
 - ⇒ *closure promptness*
 - ⇒ *possibilities of collateral circulation*

Encephalomalatia



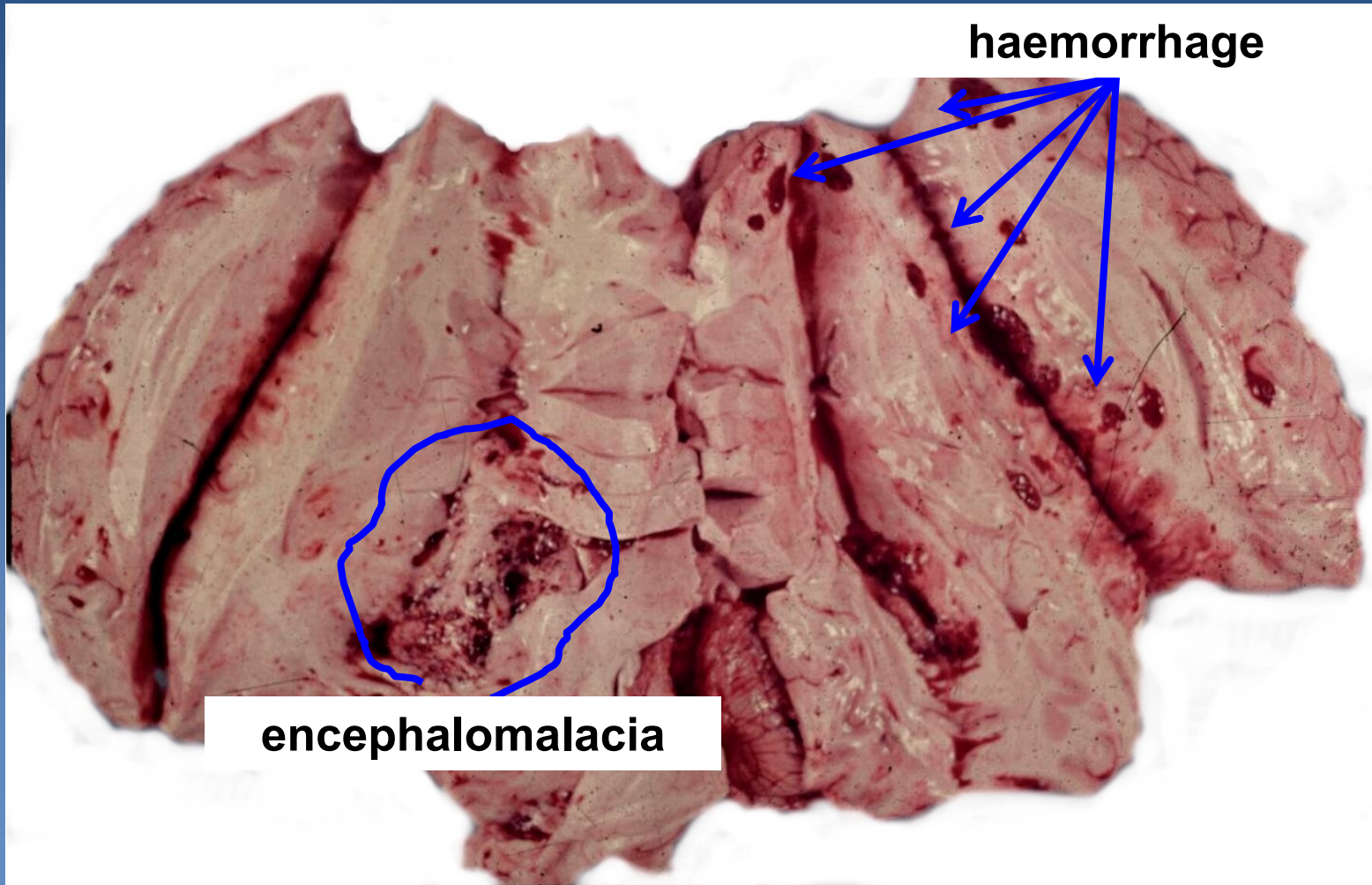
× gross:

- ⇒ approx. 24hours – affected tissue softened and swollen, loss of border between grey and white matter
- ⇒ oedema
- ⇒ infarcted tissue undergoes colliquative necrosis

× micro:

- ⇒ **neuronal ischemia** (loss of cytoplasmic basophilia, nuclei), endothelial + glial oedema
- ⇒ **neutrophils, after 2 days infiltration with macrophages** (cytoplasm filled with the lipid products of myelin breakdown)
- ⇒ **reactive astrocytes and proliferating capillaries at the edge of the infarct**
- ⇒ **Necrotic tissue phagocytosed → fluid-filled pseudocystic cavity lined by glial tissue**

Encephalomalacia (cerebral infarction)

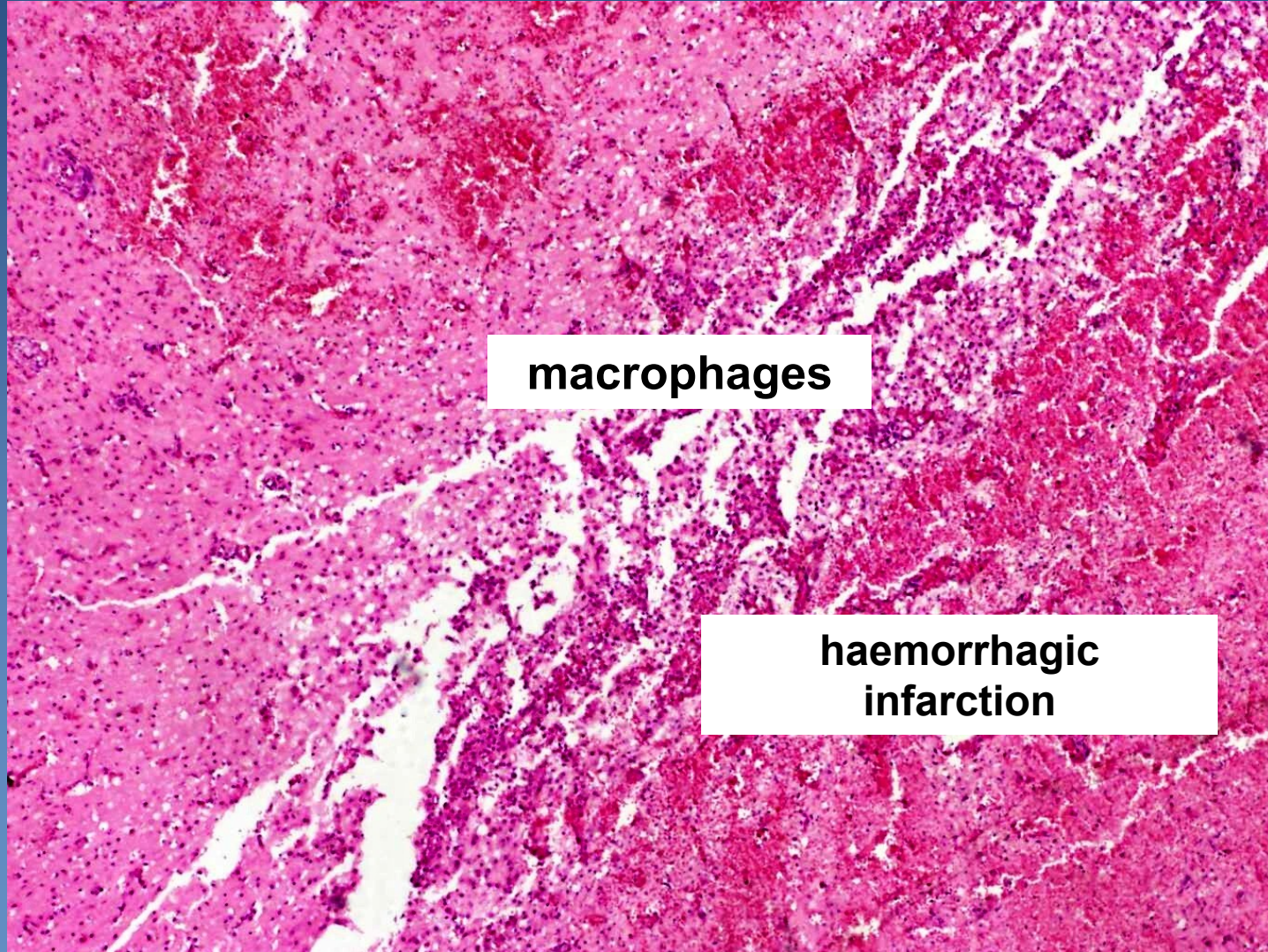


haemorrhage

encephalomalacia

Encephalomalacia

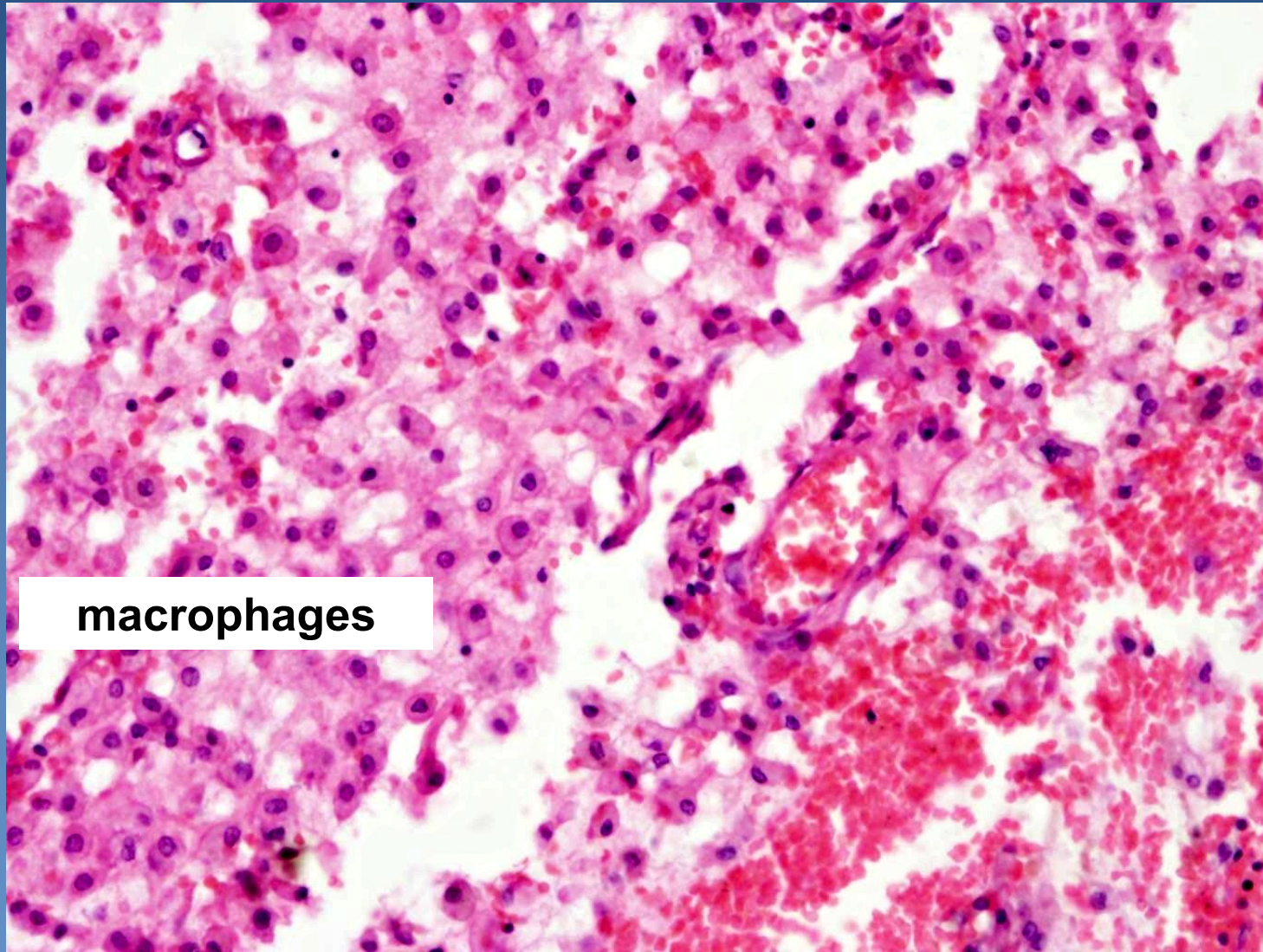
(+ reactive macrophages)



macrophages

**haemorrhagic
infarction**

Encephalomalatia



macrophages

Intracranial haemorrhage



- × **Extradural – epidural** (haemorrhage between skull and dura mater)
 - ⇒ mostly due to skull fracture (rupture of *a. meningea media*)
 - ⇒ arterial, traumatic, acute,
 - ⇒ clinically: variable lucid interval later onset of signs - increased intracranial pressure
- × **Subdural** (haemorrhage between dura and arachnoid matter)
 - ⇒ rupture of venous sinuses or small bridging veins
 - ⇒ acute x chronic (particularly in elderly - headache, memory loss and confusion, personality change)
- × **Subarachnoid** (haemorrhage between arachnoid matter and pia mater)
 - ⇒ inborn defect: aneurysm (saccular „berry“ aneurysm on the circle of Willis)
 - ⇒ AS, hypertension, tumor, coagulative disorders

Intracranial haemorrhage



× Intracerebral

⇒ nontraumatic arterial

- hypertension + regressive vessel wall changes → rupture of blood vessel
- AS
- vasculitis, amyloid angiopathy, tumors

⇒ traumatic

⇒ *premature newborn*

- extension into ventricular system, subarachnoid space - possible hydrocephalus

× Intraventricular (haemocephalus)

⇒ secondary after haemorrhage extension into ventricular system

CNS infections



xetiology

- ⇒ *bacterial incl. tb, rickettsia*
- ⇒ *viral*
- ⇒ *fungus, parasitic (protozoan, etc.)...*

- ⇒ *haematogenous spread*
- ⇒ *local extension – direct spread (adjacent inflammations)*
- ⇒ *trauma – direct implantation*
- ⇒ *along the peripheral nerves*
- ⇒ *iatrogenic infection*

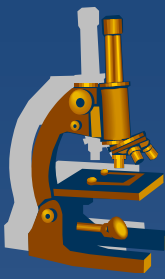
Leptomeningitis



- ⇒ *chemical (irritation)*
- ⇒ *acute pyogenic (bacterial)*
- ⇒ *acute aseptic – lymphocytic (viral)*
- ⇒ *chronic (granulomatous tuberculous; fungal)*

direct spread x blood-borne

Bacterial leptomeningitis



× symptoms:

- ⇒ *headache, joint + muscle pain*
 - ⇒ *sleepiness, fever, vomiting, loss of consciousness, convulsion*
 - ⇒ *petechial rash*
 - ⇒ *photophobia*
 - ⇒ *signs of meningeal irritation*
 - ⇒ *sepsis*
-
- ⇒ *!! acute onset, rapid diagnosis + ATB therapy necessary*

Bacterial leptomeningitis



×etiology:

- ⇒ *In neonates: E. coli, Str. agalactiae, Listeria*
- ⇒ *2-5 years.: Str. pneumoniae (Haemophilus now rare)*
- ⇒ *5-30 years: Neisseria meningitidis (type B)*
- ⇒ *over 30 years: Str. pneumoniae, staph., etc.*

×Gross:

- ⇒ *pia mater hyperemic, pus deposits*
- ⇒ *opaque CSF*
- ⇒ *brain swelling, sometimes cortical necrosis*

Bacterial leptomeningitis



Bacterial leptomeningitis



× micro:

⇒ *hyperemia, neutrophilic + macrophagic infiltrate, secondary phlebitis + thrombosis*

× complications:

⇒ *cerebral abscess*

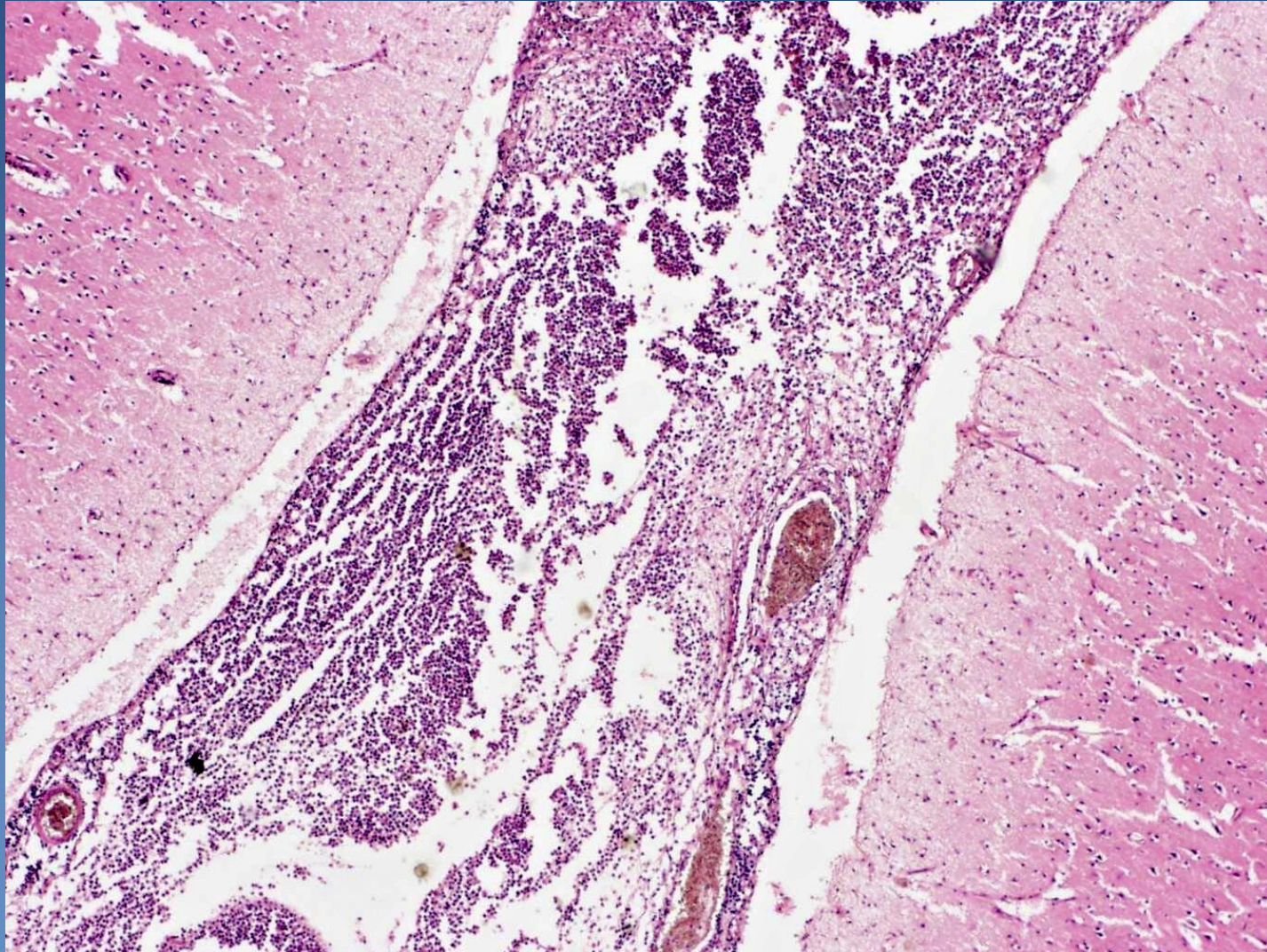
⇒ *subdural empyema*

⇒ *cerebral infarction*

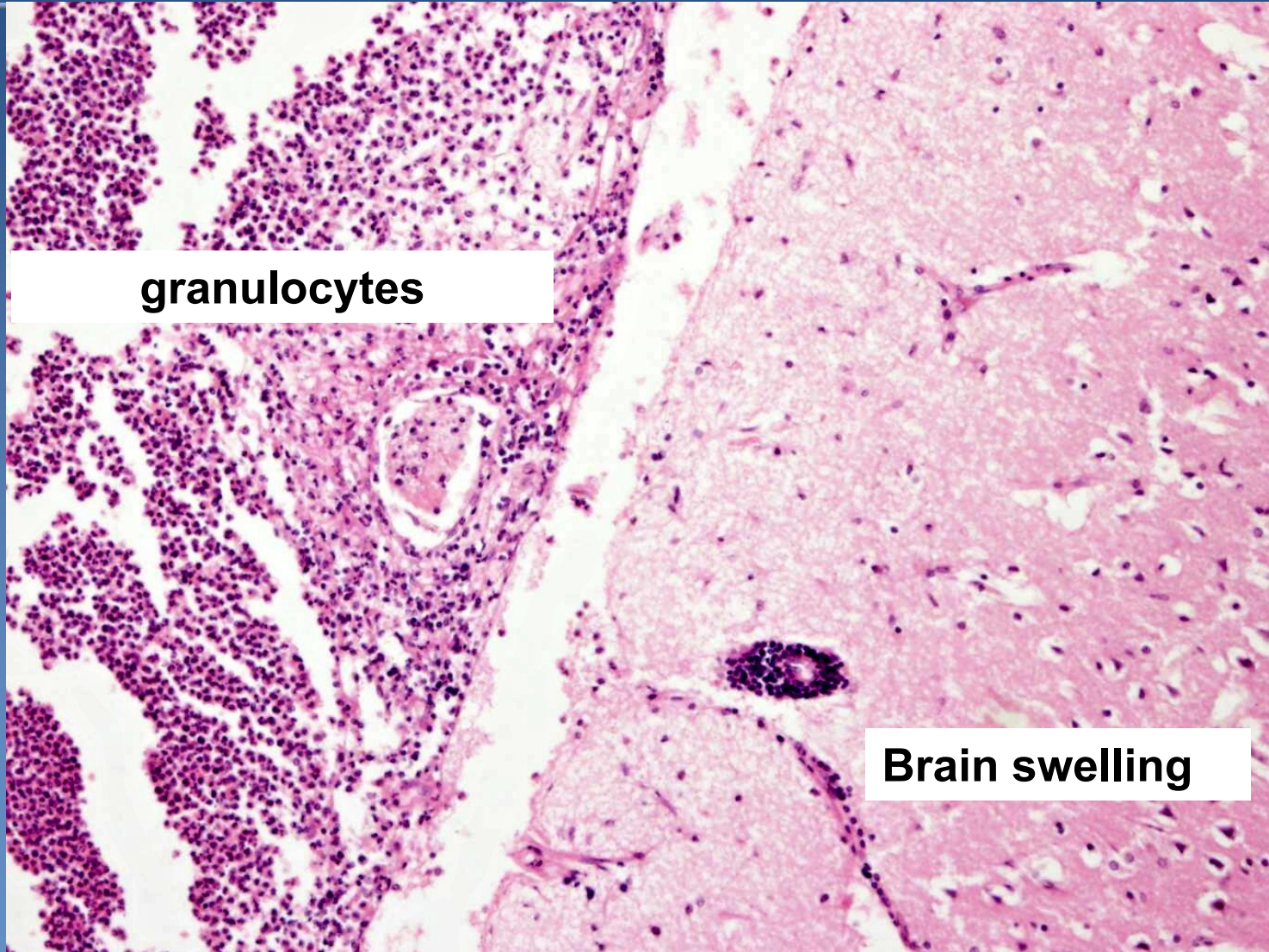
⇒ *epilepsy*

⇒ *leptomeningeal fibrosis, subarachnoid cysts, obstructive hydrocephalus*

Bacterial leptomeningitis



Bacterial leptomeningitis



granulocytes

Brain swelling

Acute aseptic meningitis



x infectious

⇒ *viral (mumps, coxackie, echoviruses, EBV, HSV)*

⇒ *usually self-limited*

⇒ *gross: hyperemic pia mater, slight edema*

⇒ *micro: lymphocytic infiltration*

x chemical or other irritant

Chronic meningitis



x granulomatous

⇒ *Mycobacterium tbc.*, granulomas, obliterative endarteritis

⇒ meningovascular neurosyphilis

⇒ fungi: *Cryptococcus neoformans*, *Aspergillus*, etc.

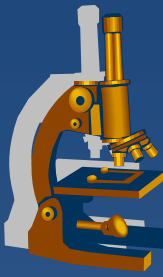
x chronic

⇒ Lyme disease – aseptic meningitis

x immune deficiency

⇒ AIDS, immunosuppression, cachexia

Tuberculous meningitis

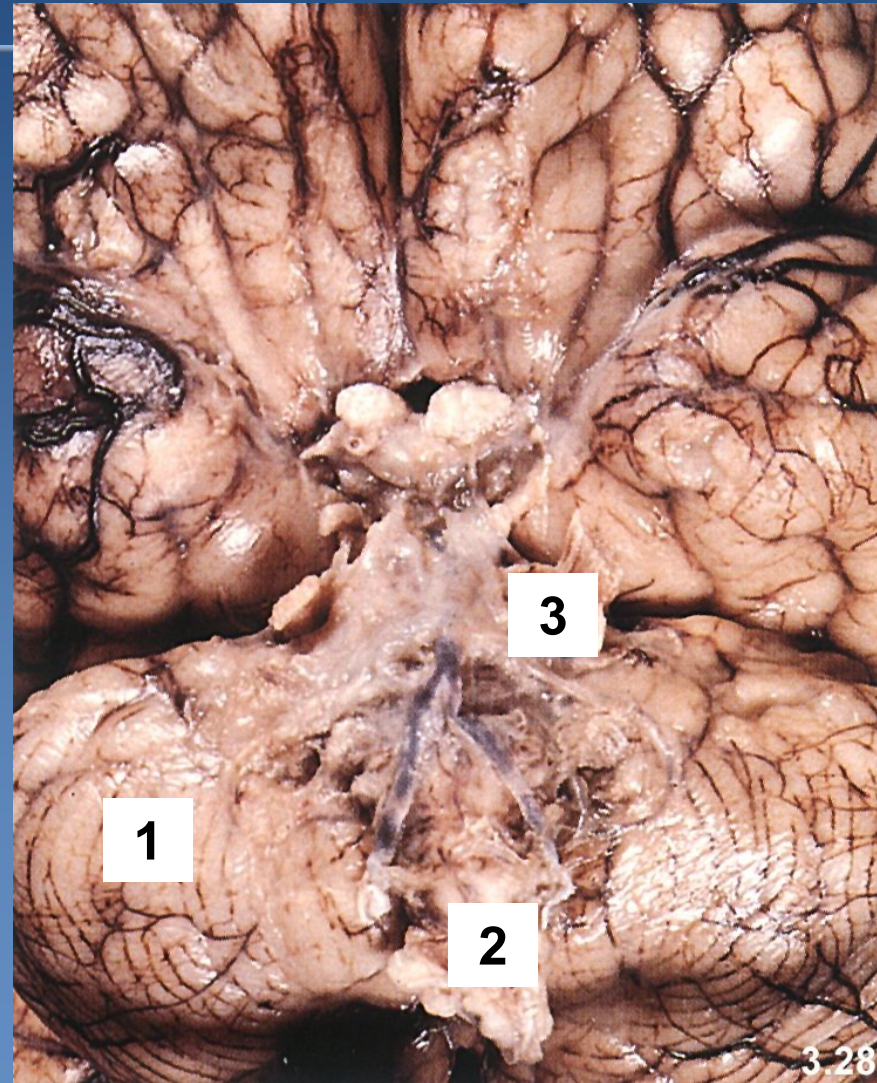


- × **etiology:** *mycobacterium tuberculosis*
- × **spread:** *usually hematogenous in primary pulmonary tuberculosis*
- × AIDS (M. avium-intracellulare complex)
- × **gross: exudative** - *thick gelatinous exudate, most marked at the base of the brain;*
 - proliferative: small white granulomas*

tuberculous meningitis



1 cerebellum
2 oblongata
**3 gelatinous
inflammatory infiltrate**



Encephalitis



× primary

⇒ *neurotropic viruses*

⇒ *anthropozoonoses - from animals transmitted to humans*

× secondary

⇒ *other underlying disease*

- *viruses (HSV, enterovirus), rickettsiae, parasites (toxoplasmosis...), spirochetes (lues),...*

× micro (viral encephalitis):

⇒ *neuronal damage, reactive glial changes*

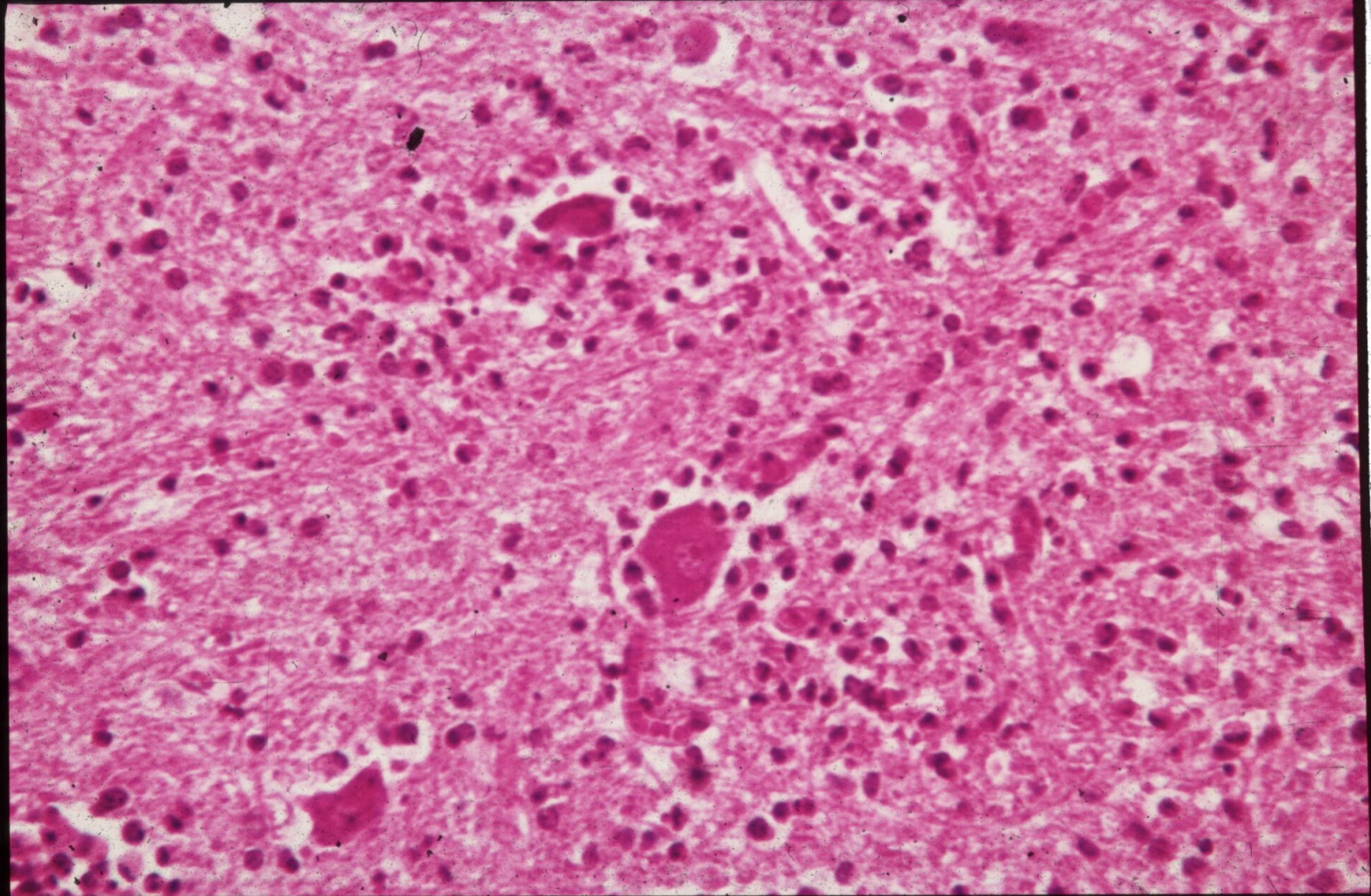
⇒ *perivascular „cuff“ infiltrate of lymphocytes, plasma cell*

Viral encephalitis - myelitis

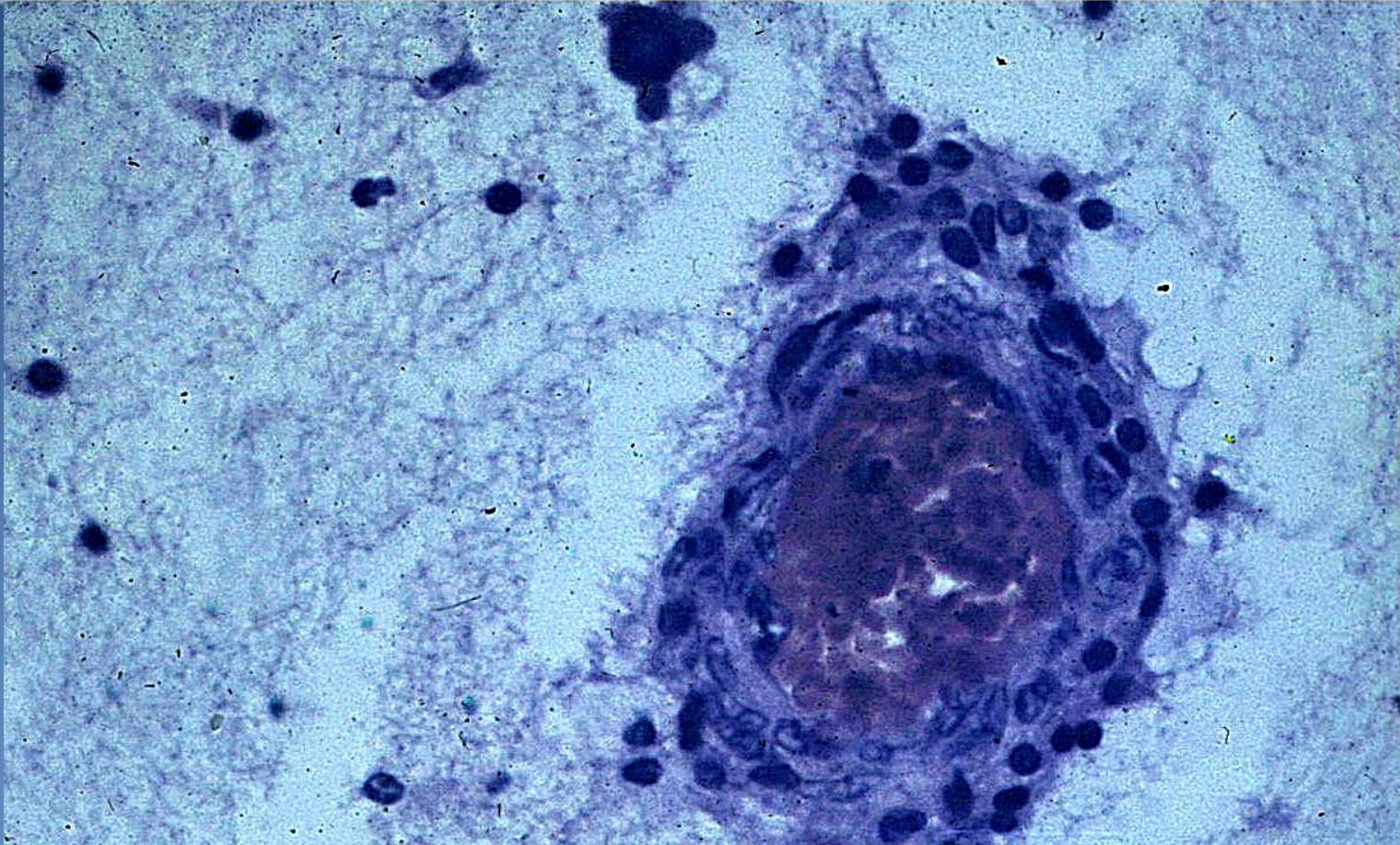


- × **usually + meningitis**
- × **spread:** *haematogenous x neural (retrograde)*
- × **tropism** - specific cell type or area involved
- × **etiology:**
 - ⇒ *arthropod-borne (tick-borne), mumps, enteroviruses (poliomyelitis), HSV, CMV, EBV, HIV, rabies*
- × **gross:**
 - ⇒ *hyperemic meninges, brain edema*
- × **micro:**
 - ⇒ *perivascular, parenchymal mononuclear cell infiltrate, glial cell reaction, oedema, neuronophagia, viral inclusions*
- × *possibility of latency, immune-mediated disease, late sequelae*

Viral encephalitis - myelitis



Viral encephalitis



perivascular infiltrate of lymphocytes + plasma cell

Viral encephalitis



x with the formation of inclusion bodies

⇒ *Rabies*

⇒ *HSV1, HSV2*

⇒ *Poliomyelitis*

x Without inclusion bodies

⇒ *tick-borne viral encephalitis*

⇒ *HIV-associated encephalitis*

Encephalitis



x Others

- ⇒ *Acute disseminated encephalomyelitis – immune-associated demyelination*
- ⇒ *Subacute sclerosing panencephalitis (measles virus)*
- ⇒ *Typhus fever - rickettsiae*
- ⇒ *Neurosyphilis*

Viral encefalitis with inclusion bodies



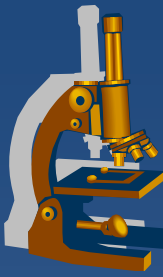
x rabies, lyssa

- ⇒ *incubation 3-8 weeks → with axonal retrograde flow to the brainstem, spinal cord, dorsal root ganglia, cerebral cortex, cerebellum, hippocampus*
- ⇒ *micro **Negri bodies** (eosinophilic inclusions of the size of red blood cells in the cytoplasm of neurons)*

x herpetic encephalitis (HSV1, HSV2)

- ⇒ *Frontal cortex, other parts of the gray matter*
- ⇒ *hemorrhagic necrosis, intranuclear inclusions*
- ⇒ *severe (sometimes fatal) course*

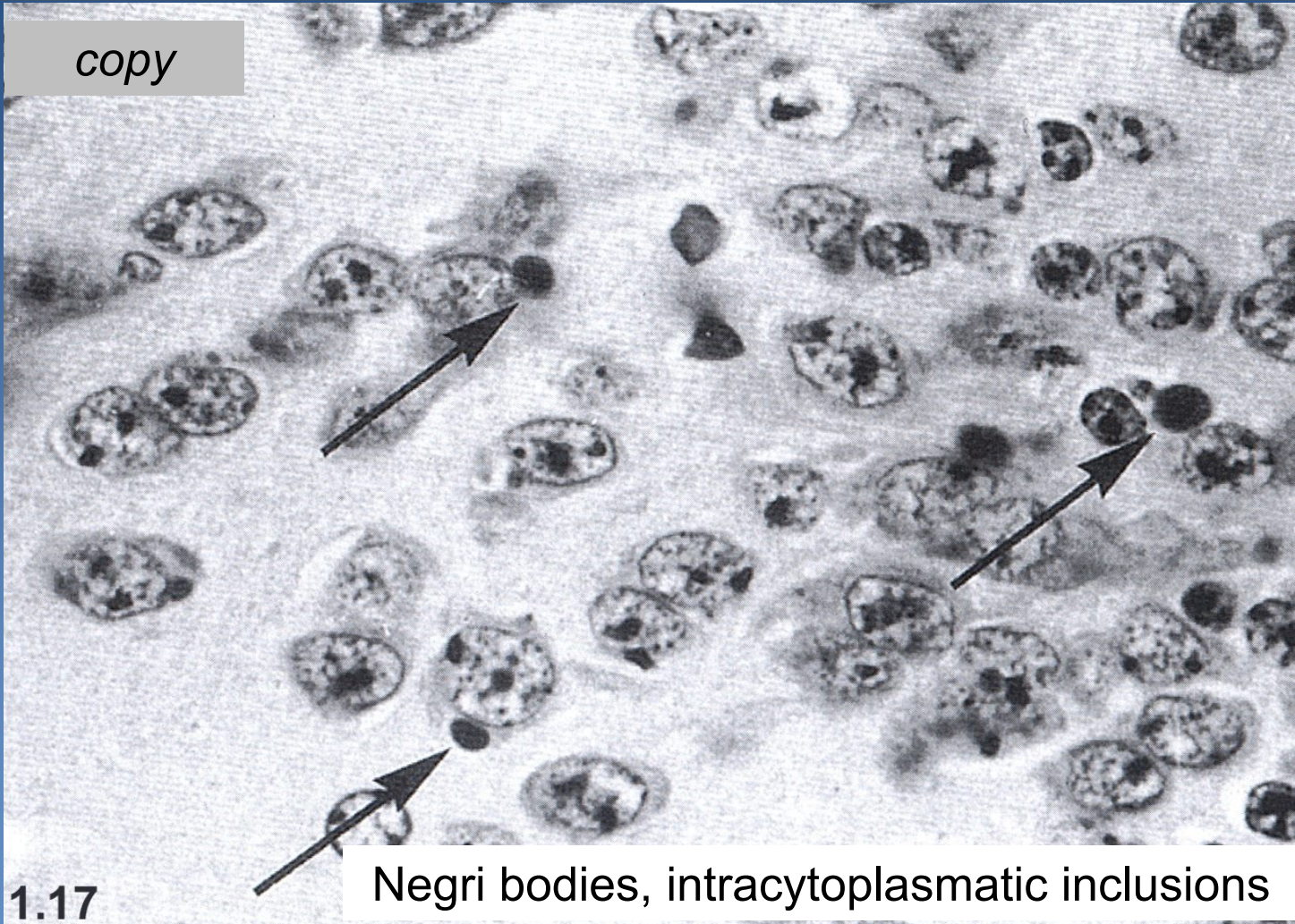
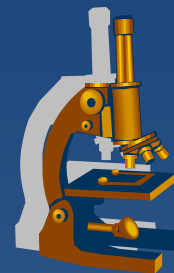
Viral encefalitis with inclusion bodies



x Poliomyelitis

- ⇒ *enteroviruses, coxsackie, ECHO*
- ⇒ *pharyngitis, enteritis, myocarditis, myositis...*
- ⇒ *approx. in 10% affinity to the motoric neurons → anterior horns of the spinal cord, (gyrus precentralis) → symptoms of paralysis*
- ⇒ *anterior horns of the spinal cord markedly swollen, hyperemic*
- ⇒ *small intranuclear inclusions → neuronal necrosis → inflammatory reaction + neuronophagia → gliosis*

Rabies

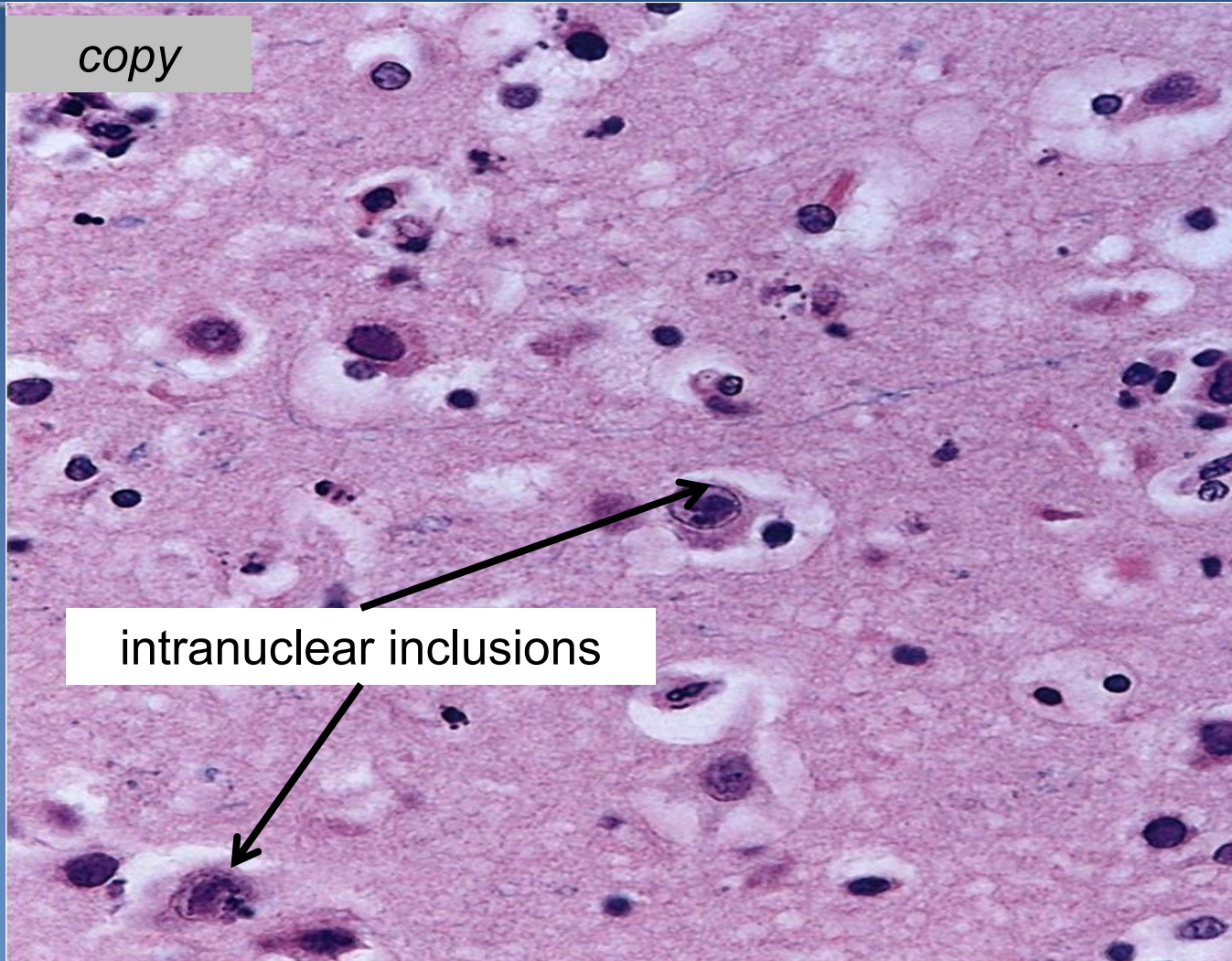


copy

1.17

Negri bodies, intracytoplasmic inclusions

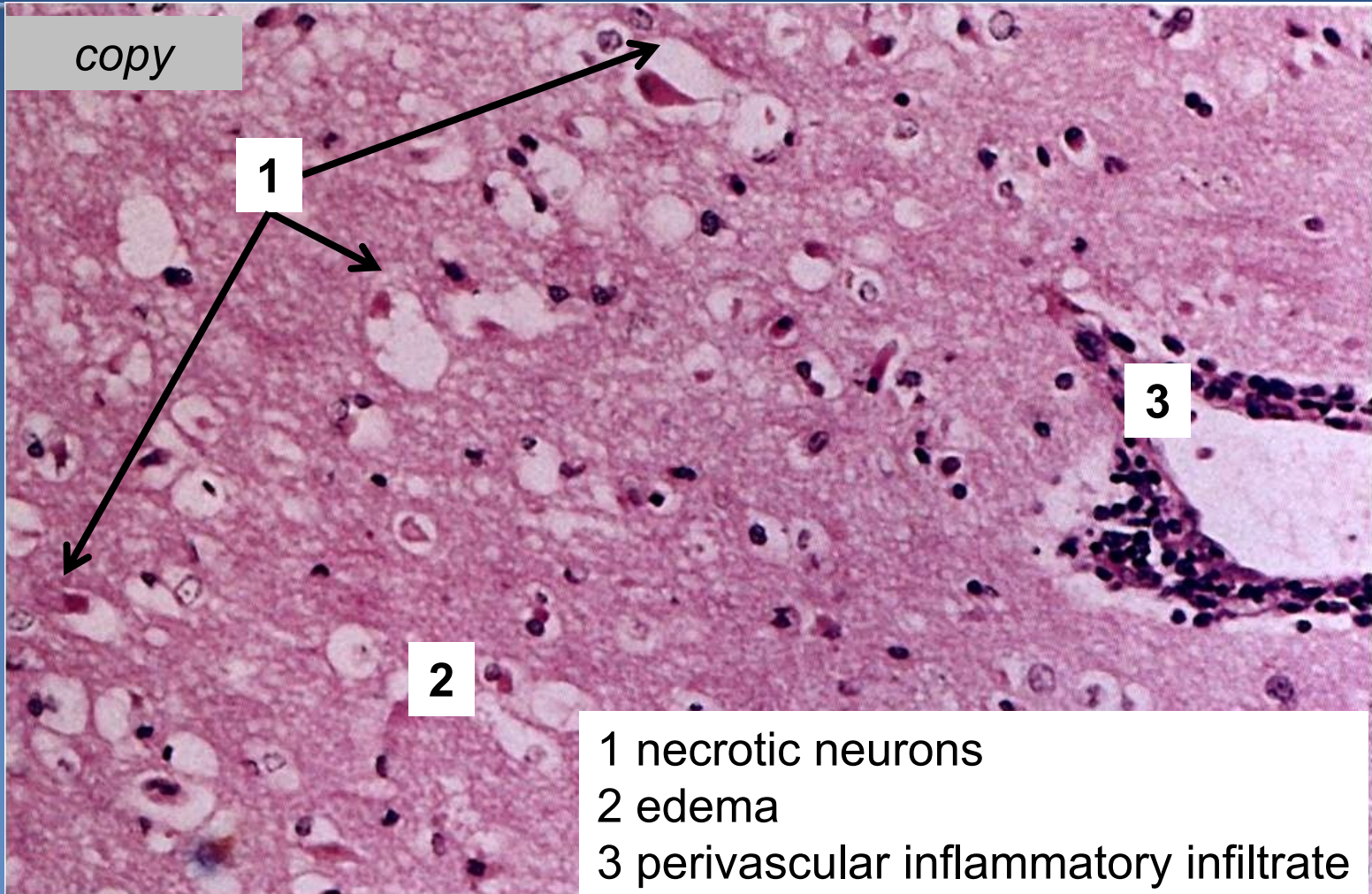
Herpetic encephalitis



copy

intranuclear inclusions

Herpetic encephalitis



copy

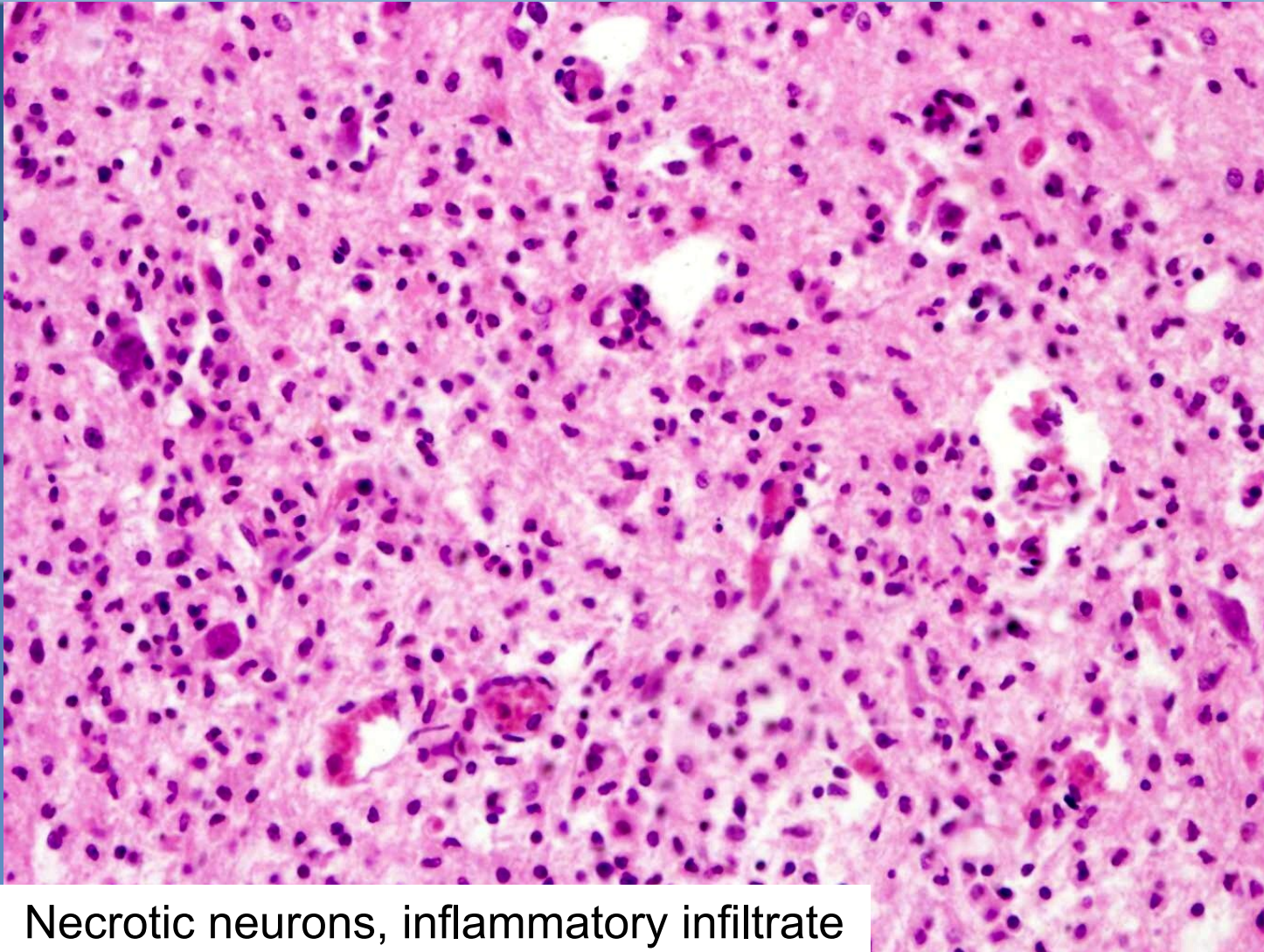
1

3

2

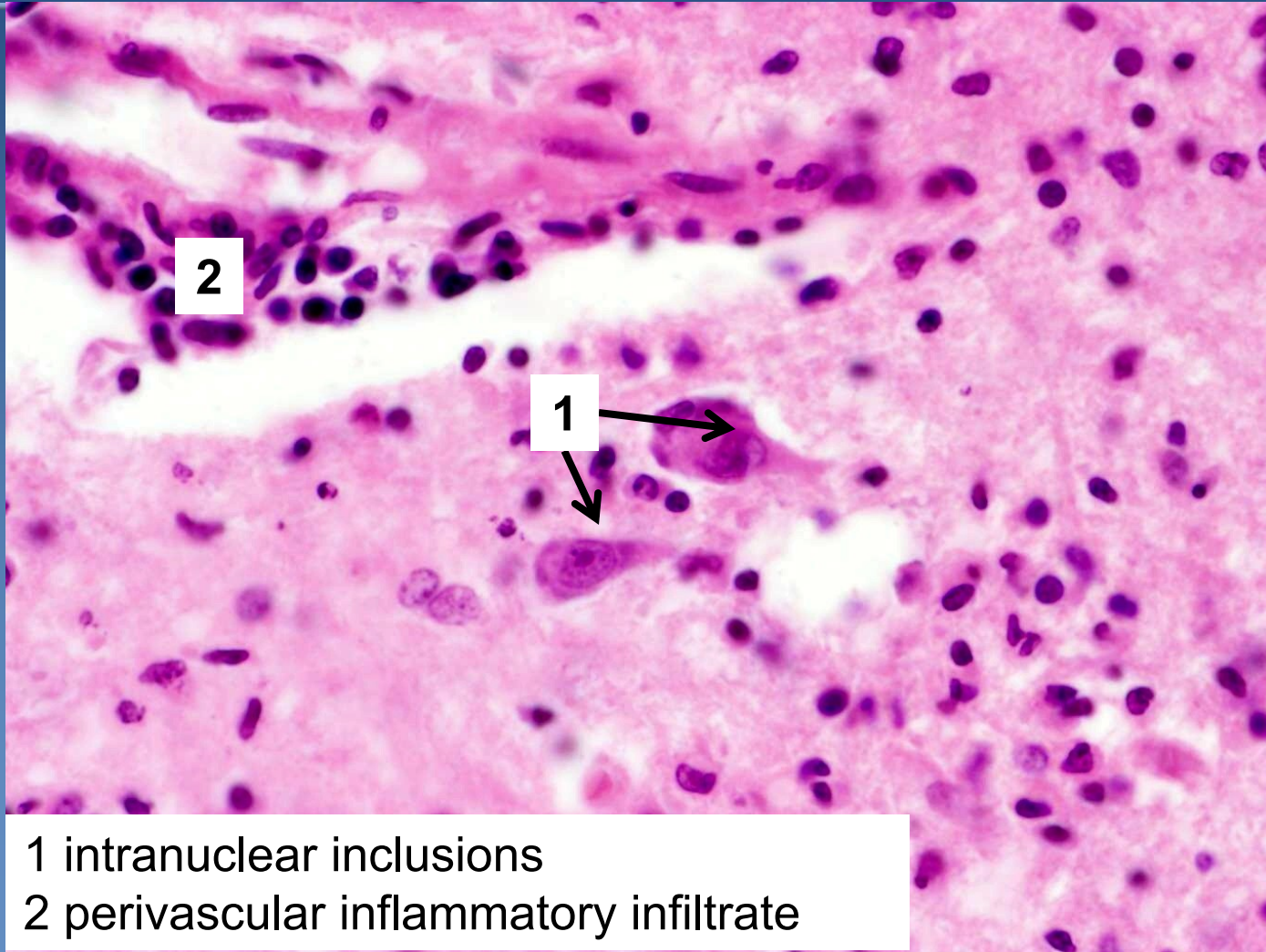
- 1 necrotic neurons
- 2 edema
- 3 perivascular inflammatory infiltrate

Poliomyelitis



Necrotic neurons, inflammatory infiltrate

Poliomyelitis



1 intranuclear inclusions
2 perivascular inflammatory infiltrate

Viral encephalitis without inclusion bodies



x Tick-borne encephalitis (Middle Europe)

⇒ ***mostly asymptomatic***

⇒ ***symptoms rarely***

- convulsions, confusion, delirium, coma, often with focal neurological deficits such as reflex asymmetry

⇒ ***meningeal form, meningoencephalitic or
encephalomyelitic form***

- both gray and white matter affected (panencephalitis)

Viral encephalitis without inclusion bodies



- x HIV encephalitis**

- x HIV-associated dementia**

- ⇒ *acute aseptic meningitis in 10% of HIV + patients*
- ⇒ *subacute/chronic HIV encephalitis*
- ⇒ *vacuolar myelopathy*
- ⇒ *opportunistic encephalitis (herpetic, CMV, toxoplasmosis)*

Neurosyphilis



⇒ *different CNS changes in the 2nd, 3rd stage*

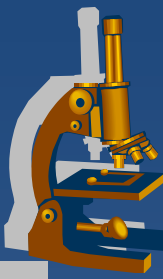
⇒ *meningovascular form*

- chronic meningitis
- obliterative (Heubner) endarteritis

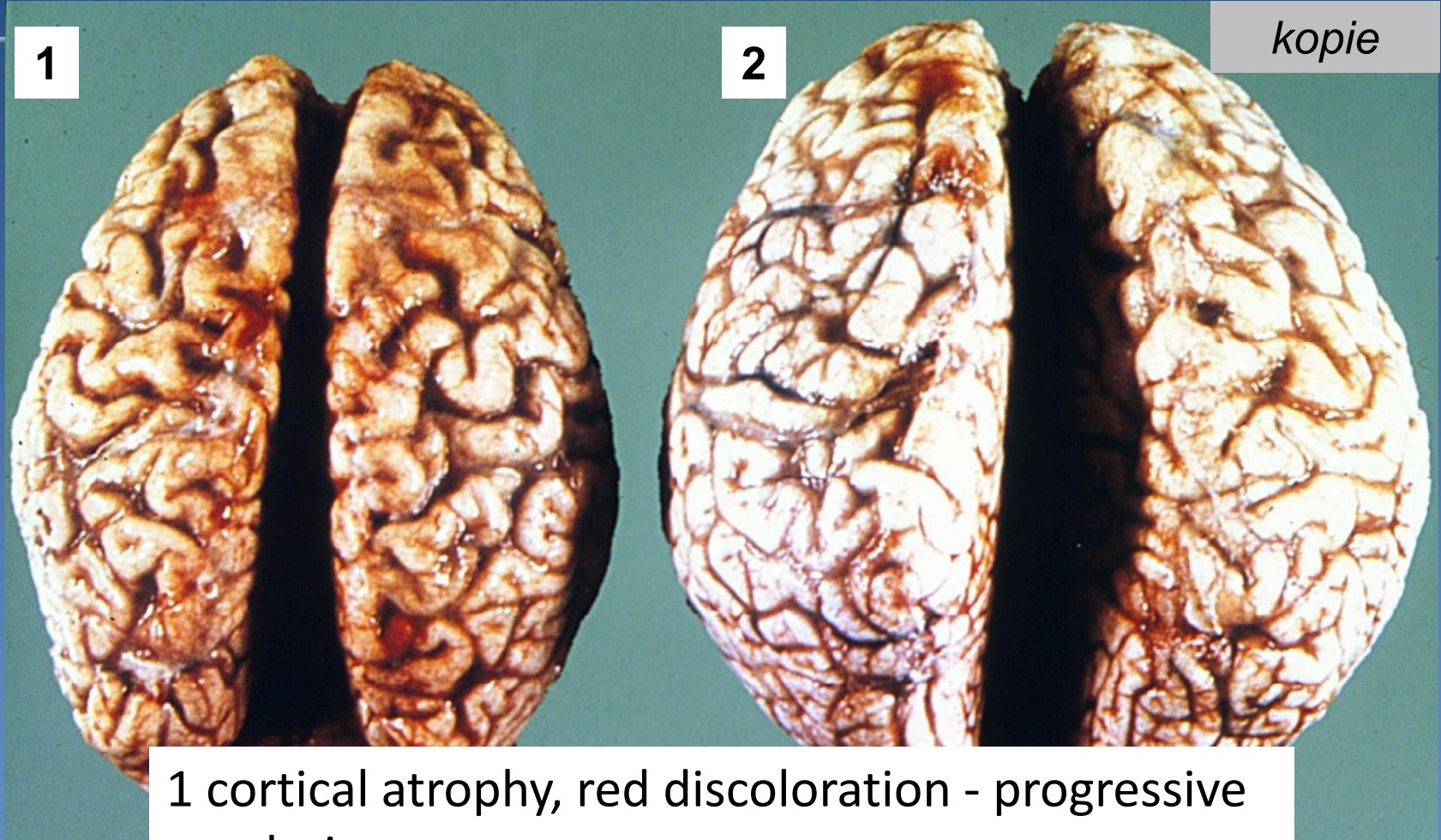
⇒ *parenchymatous form*

- atrophic cortex + hemosiderin; gummata
- progressive mental deficit → dementia
- tabes dorsalis – sensory nerves of the dorsal roots

Neurosyphilis



kopie



1

2

1 cortical atrophy, red discoloration - progressive paralysis
2 initial stage

prion encephalopathy



xPrions (*proteinaceous infectious particles*)

⇒ *protein particles capable of inducing conformational change of tissue PrPc to pathogenic PrPSc*

⇒ *micro:*

- *spongiform encephalopathy – microscopic vacuolisation*
- *numerical atrophy of neurons*
- *reactive gliosis*
- *missing inflammatory response!!*

⇒ *long incubation period, rapid progression (dementia) → ☹️*

prion encephalopathy



✘ Creutzfeldt-Jacob disease

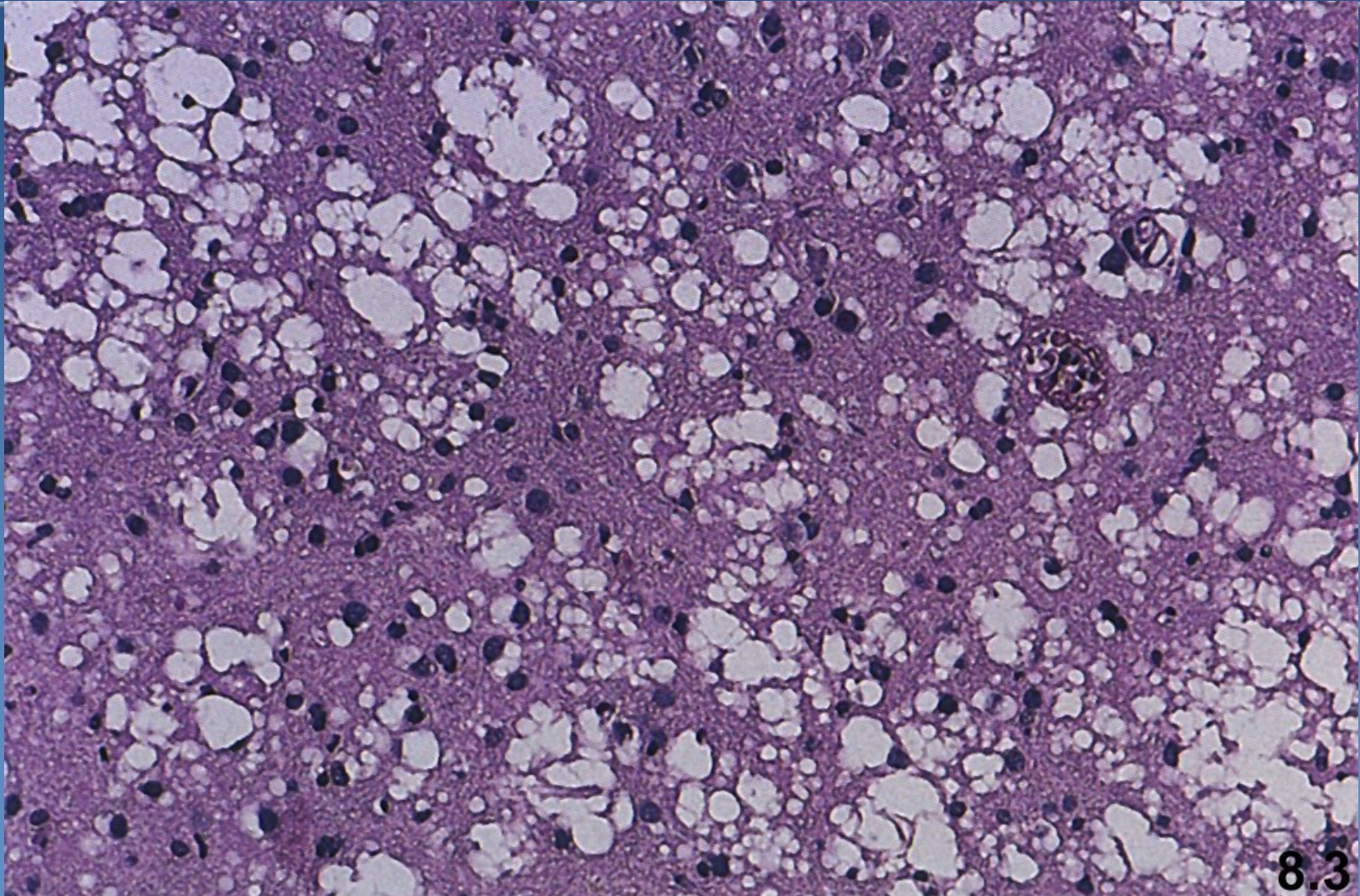
⇒ *sporadic*

⇒ *familial*

⇒ *iatrogenic*

⇒ *variant (BSE?)*

Creutzfeldt-Jacob disease





Neurodegenerative diseases

Neurodegenerative diseases



x loss of specific groups of neurons → typical clinical signs

⇒ *apoptosis + oxygen radicals – neuronal damage*

⇒ *pathological protein aggregates*

- disease-specific – classification

⇒ *genetic risk*

Degenerative diseases



- ✗ cortex – Alzheimer disease – dementia
- ✗ subcortical – Parkinson d. – tremor, dyskinesia, rigidity
- ✗ amyotrophic lateral sclerosis – motor neurone loss

- ✗ **Pick's disease**
- ✗ **Huntington's disease**
- ✗ **Parkinson's disease, parkinsonism**

Alzheimer's disease



✗ the most common neurodegenerative condition

✗ pre-senile dementia

⇒ possible start at the age of 50 (or sooner) → slow progression (-> 8-10+ years) → death due to inanition, bronchopneumonia

⇒ M:F 1:2

⇒ sporadic x familial (about 5%)

Alzheimer's disease



x gross:

- ⇒ *marked cortical atrophy (frontal, temporal)*
- ⇒ *loss of cortical grey and white matter, secondary hydrocephalus*
- ⇒ *limbic system affected - hippocampus*

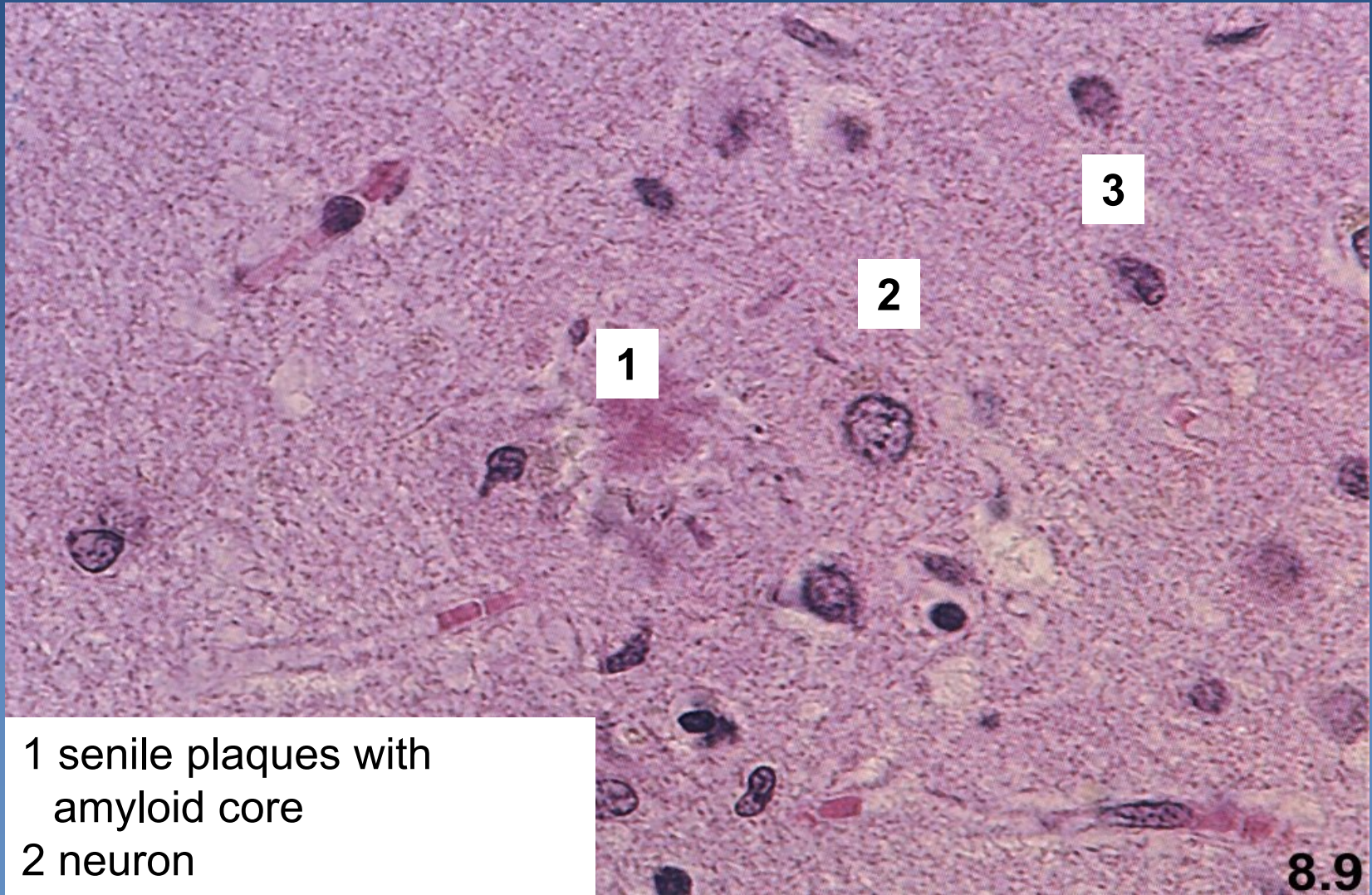
x micro:

- ⇒ *neuronal loss*
- ⇒ *A-beta amyloid plaques and neurofibrillary tangles*
- ⇒ *amyloid angiopathy - deposits in the wall of capillaries and arterioles*
- ⇒ *non-specific changes, only more pronounced*

Alzheimer's disease



Alzheimer's disease

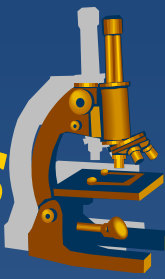


1 senile plaques with amyloid core

2 neuron

3 neurofibrilla

Frontotemporal dementias



- ✗ similar clinical picture – language deterioration, personality changes
- ✗ may have specific protein aggregates - deposits (tau)
- ✗ sporadic or rare familial
- ✗ approx. 10% of dementias

Pick's disease

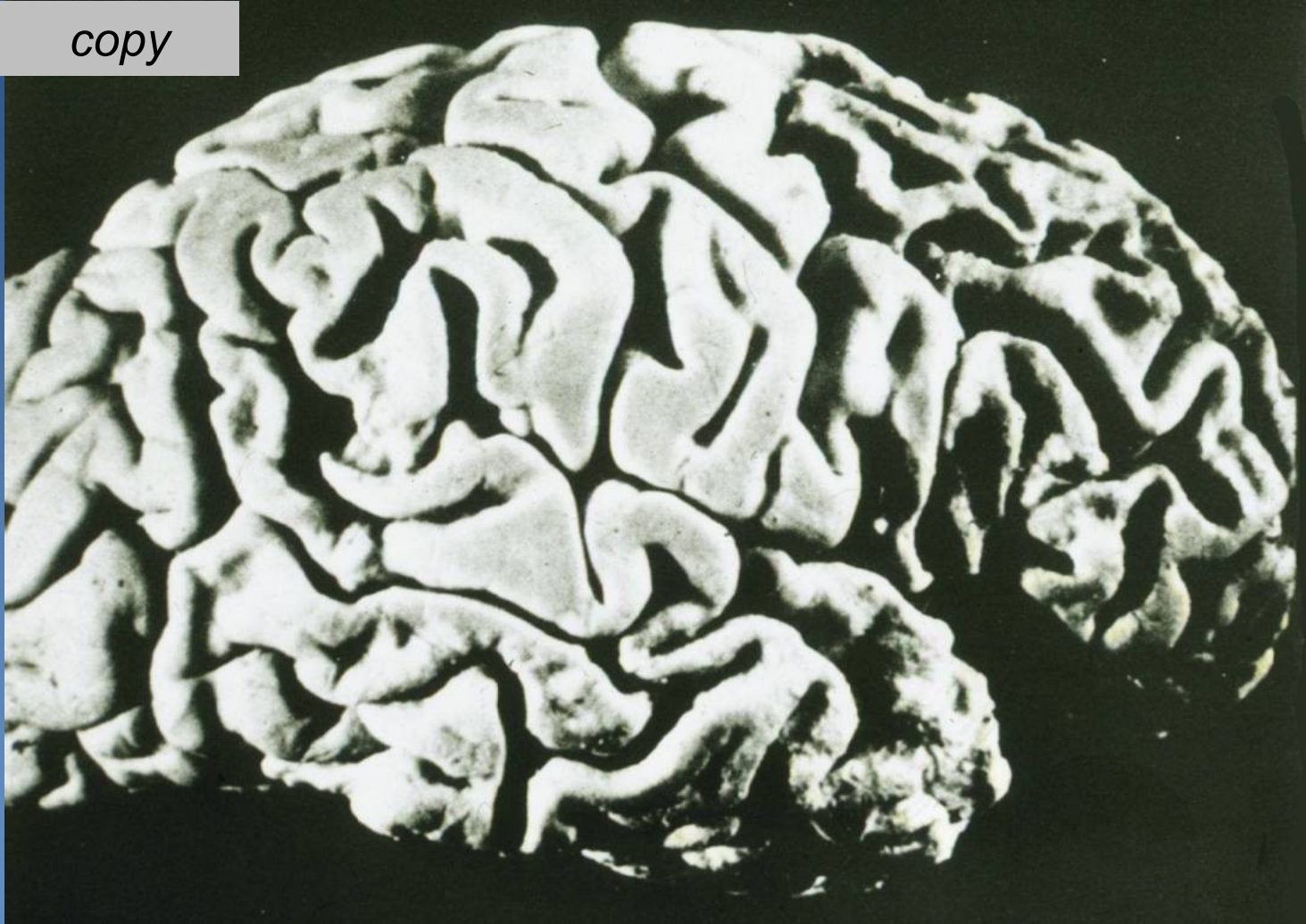


- × 5% of dementias, M>F
- × **gross**
 - ⇒ max. atrophy in **the frontal and temporal lobe** (foliate threads) - lobar atrophy
- × **micro**
 - ⇒ loss of neurons in the I.-III. cortical layers
 - ⇒ demyelination in the white matter
 - ⇒ neuron's cytoplasm with Pick bodies (filamentous inclusions), Hirani bodies, granulovacuolar degeneration

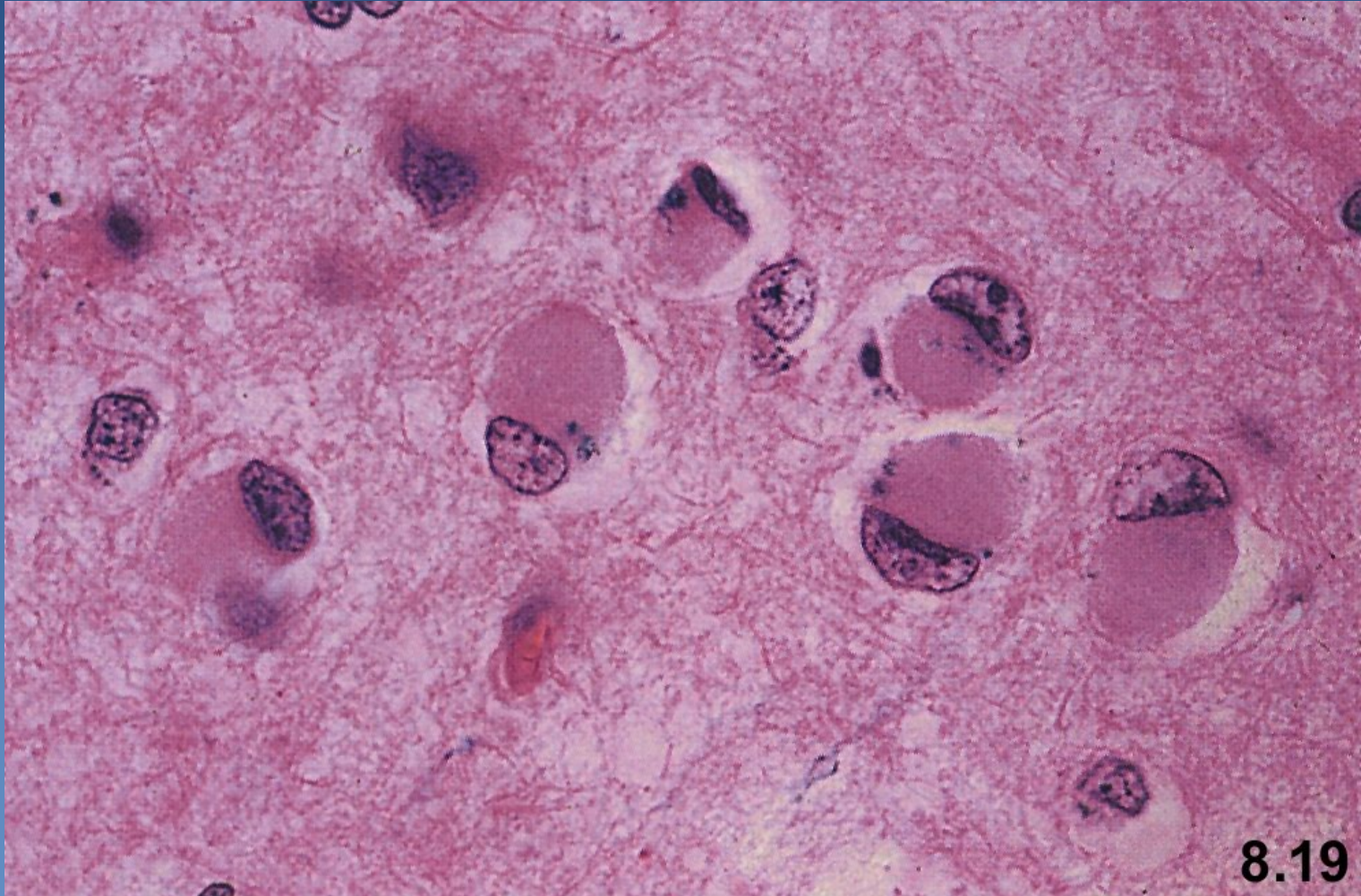
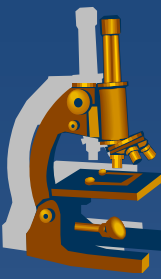
Pick's disease



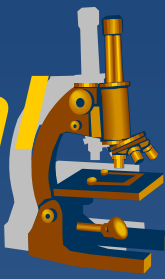
copy



Pick's disease



Degenerative diseases of basal ganglia and brainstem



x movement disorders

⇒ *rigidity*

⇒ *abnormal posturing*

⇒ *chorea*

x reduction of voluntary movements

x increase of involuntary movements

Huntington's disease



x AD

⇒ *gene on chromosome 4p – huntingtin protein*

- CAG triplet repeat, if > 35 → disease
- ↑ number of repeats → earlier onset, more rapid course

x begins after age of 30 (4th, 5th decade)

x progressive course (15-20 years)

x uncoordinated, jerky body movements, gradually dementia

Huntington's disease



x gross:

- ⇒ Atrophy of *n. caudatus* a *putamen*
- ⇒ **dilated** lateral + 3rd ventricle
- ⇒ *cortical atrophy*
- ⇒ *brain weight reduction of up to 30%*

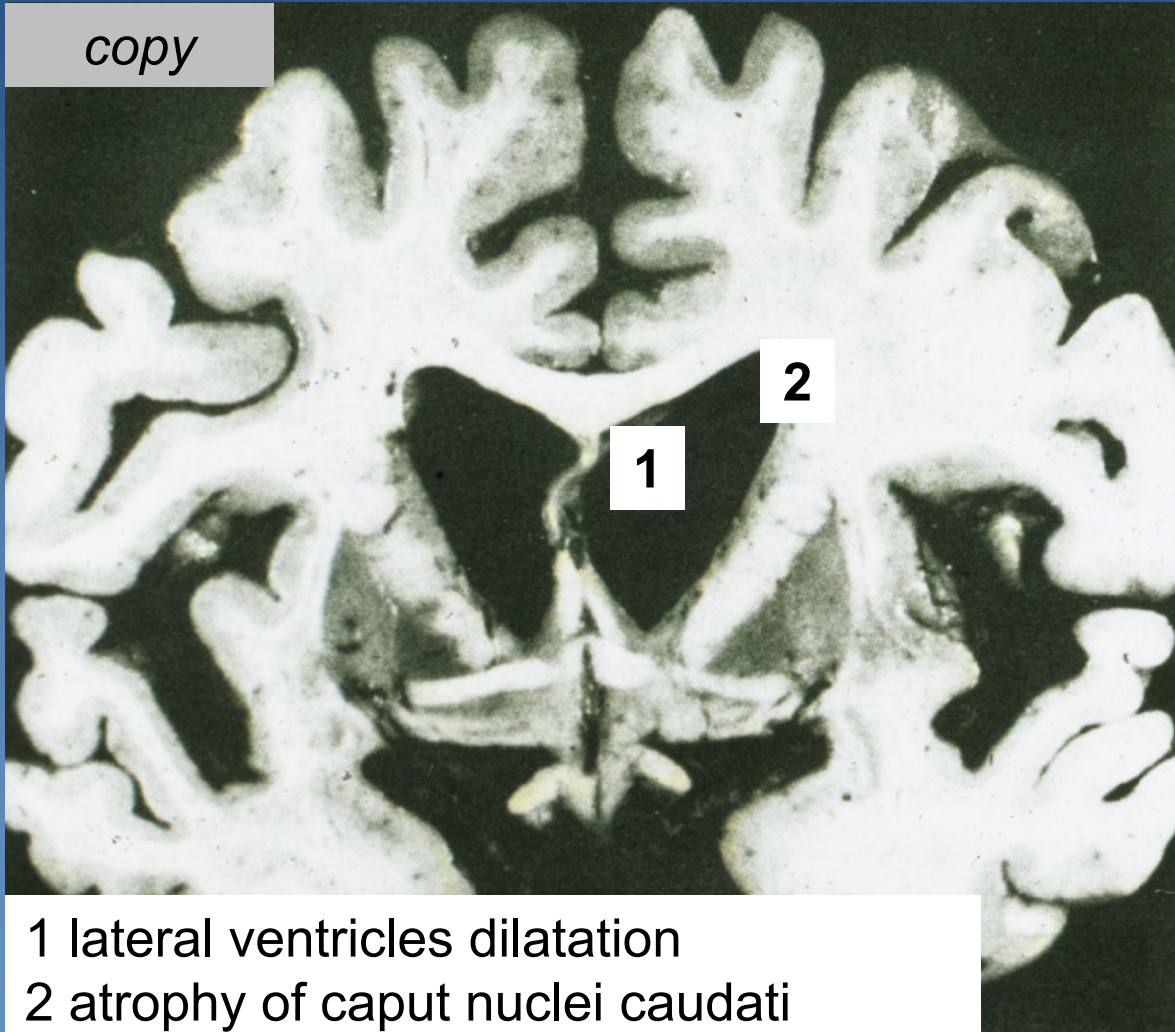
x micro:

- ⇒ *loss of neurons*
- ⇒ *fibrillary gliosis*

Huntington's disease



copy



- 1 lateral ventricles dilatation
- 2 atrophy of caput nuclei caudati

Parkinsonism



- × **clinical condition due to the damaged nigro – striatal dopaminergic system**
- × ↓ inhibitory neurotransmitter
- × stiff facial expression, muscle rigidity, slowness of voluntary movements (bradykinesia), tremor
- × **forms:**
 - ⇒ *Primary PS:*
 - **Parkinson's disease**
 - multiple system atrophy, i. e. striatonigral degeneration
 - ⇒ *Secondary PS:*
 - after encephalitis, in arteriosclerosis, after CO poisoning, other toxins, tumors, etc.

Parkinson's disease



x idiopathic

- ⇒ *mostly sporadic (exogenous, mitochondrial dysfunction?), minority familial*
- ⇒ *progressive course (10 years), may be + dementia*

x gross:

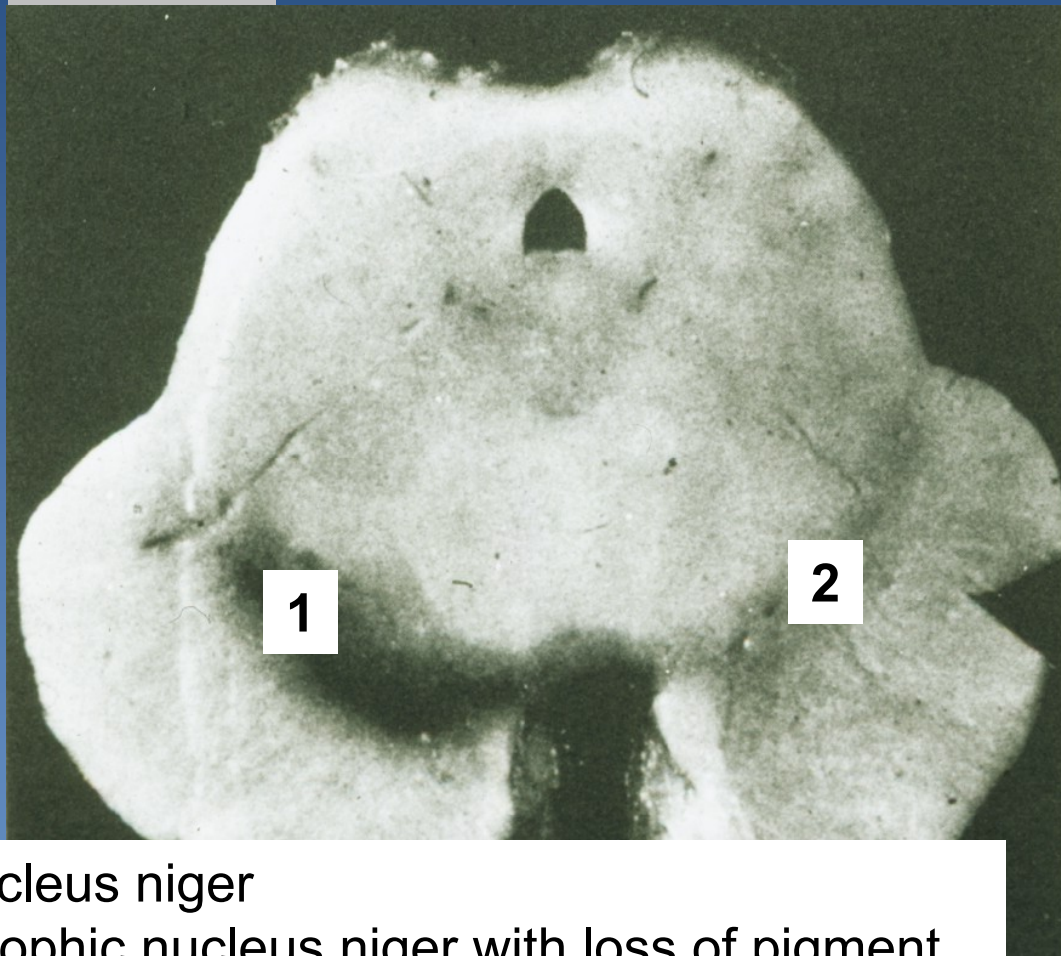
- ⇒ *minor general changes, decolorization of substantia nigra*

x micro:

- ⇒ *loss of neurons → astrogliosis*
- ⇒ *numerous Lewy bodies (α -synuclein) in the cytoplasm of damaged neurons*

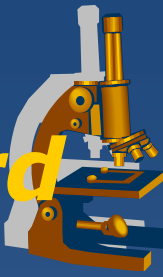


Parkinson's disease - brainstem



1 nucleus nigra
2 atrophic nucleus nigra with loss of pigment

Degenerative diseases of spinal cord



- x Amyotrophic lateral sclerosis**
 - ⇒ *loss of motor neurons*
- x Spinocerebellar hereditary ataxia**
- x Spinal muscular atrophy**

Demyelinating diseases



- ✗ **disintegration of myelin sheaths**
 - ⇒ *axonal regression*
- ✗ primary x secondary (after axonal damage)

- ✗ **multiple sclerosis**
- ✗ progressive multifocal leukoencephalopathy (JC virus)
- ✗ acute disseminated encephalomyelitis
(after viral infection, rarely vaccination)

Multiple sclerosis



✗ more frequent in **women** between 20 and 40

✗ **unclear etiology**

⇒ *autoimmune disorder triggered by exogenous factor (virus?) in susceptible host (genetics)*

✗ **progressive course, episodic acute relapses** with neurologic deficit

⇒ *variable presentation*

⇒ *sensoric, sensitive, motor dysfunction*

⇒ *ends in severe psychomotoric disturbance + cachexia*

⇒ *trophic ulcers, pressure sores, sepsis*

Multiple sclerosis



× gross:

- ⇒ *white (less commonly gray) matter with multiple, well-demarcated, gray-tan solid lesions – plaques*
 - variable size mm-cm
- ⇒ **Mostly periventricular**, but also in optic fasciculus....

× micro:

- ⇒ **Active plaques, early (pink, softer)**
 - myelin reduction, perivascular monocyctic infiltrate + activation of macrophages → axonal destruction
- ⇒ **Inactive plaques:**
 - disappearance of oligodendrocytes and myelin, reactive gliosis, persistence of numerous nerve fibers without inflammation

Multiple sclerosis



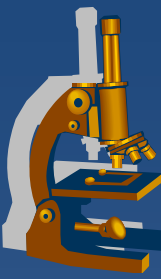
× Acute form

- ⇒ *fatal within a few weeks / months*
- ⇒ *may be in children*
- ⇒ *pink lesions (plaques) in white matter of the brainstem, spinal cord*

× Neuromyelitis optica

- ⇒ *fasciculus opticus → bilateral blindness*
- ⇒ *necrotic centre of plaques*

Multiple sclerosis



active (pink) plaques

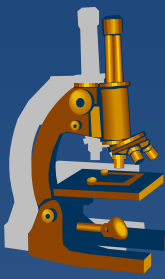


Tumors of the nervous system

neuroectodermal tumors



- x tumors of the central nervous system**
- x peripheral neuroectodermal tumors**
- x tumors of the autonomic nervous system**
- x melanocytic tumors**



INTRACRANIAL TUMORS

Intracranial tumors



- ✗ primary extracerebral (meningioma, schwannoma, neurofibroma)
- ✗ primary intracerebral (gliomas – astrocytoma, oligodendroglioma, ependymoma, neuronal tumors, primitive neuroectodermal tumors PNET – medulloblastoma, endocrine t., vascular t., lymphomas)
- ✗ secondary tumors – metastases, leukemic infiltration

Intracranial tumors



- ✘ focal signs according to the localisation (excitation, later loss of function)
- ✘ general raised intracranial pressure (seizures, headache, visual defects, nausea etc.)
- ✘ histologically benign brain tumors can kill the patient – growing in a position where they cannot be completely resected !

Metastatic tumors of the CNS



- ✗ CNS metastases in 25% of cancer deaths
- ✗ most common origin in adults
 - ⇒ lung ca (*small cell, adenocarcinoma*)
 - ⇒ breast ca
 - ⇒ melanoma
 - ⇒ renal
 - ⇒ colorectal
- ✗ most common origin in children
 - ⇒ leukaemia, lymphoma
 - ⇒ osteosarcoma, rhabdomyosarcoma

Biologic potential



- ✗ possible infiltrating growth of histologically benign tumors
- ✗ localisation highly important (grave consequences even in benign tumors)
- ✗ rare metastases outside the CNS

Age factor



- ✗ in children - mostly primary intracerebral
incl. PNET; infratentorially (posterior fossa)
- ✗ in adults – number of secondary t. rises
with age; mostly supratentorially

classification of intracranial tumors



- × Astrocytic tumors
- × Oligodendroglial tumors
- × Ependymal tumors
- × Choroid plexus tumors
- × Neuronal/glioneuronal tumors
- × Pineal tumors
- × Embryonal tumors

Astrocytic tumors



- × **Diffuse (fibrillary) astrocytoma (Grade II)**
- × **Anaplastic astrocytoma (Grade III)**
- × **Glioblastoma (Grade IV)**

- × **Pilocytic astrocytoma (Grade I)**
- × **Pleomorphic xanthoastrocytoma (Grade II)**
- × **subependymal giant cell astrocytoma (Grade I)**

Astrocytic tumors

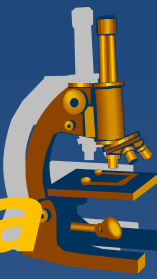
Diffuse (fibrillary) astrocytoma



- × low grade - grade II/IV (WHO)
- × slow growth, high degree of differentiation
- × !! intrinsic tendency for malignant progression to anaplastic astrocytoma → glioblastoma
- × in all age groups
 - ⇒ mostly young adults, $M > F$
- × **Anywhere in the brain** - poorly demarcated or infiltrative tumor

Astrocytic tumors

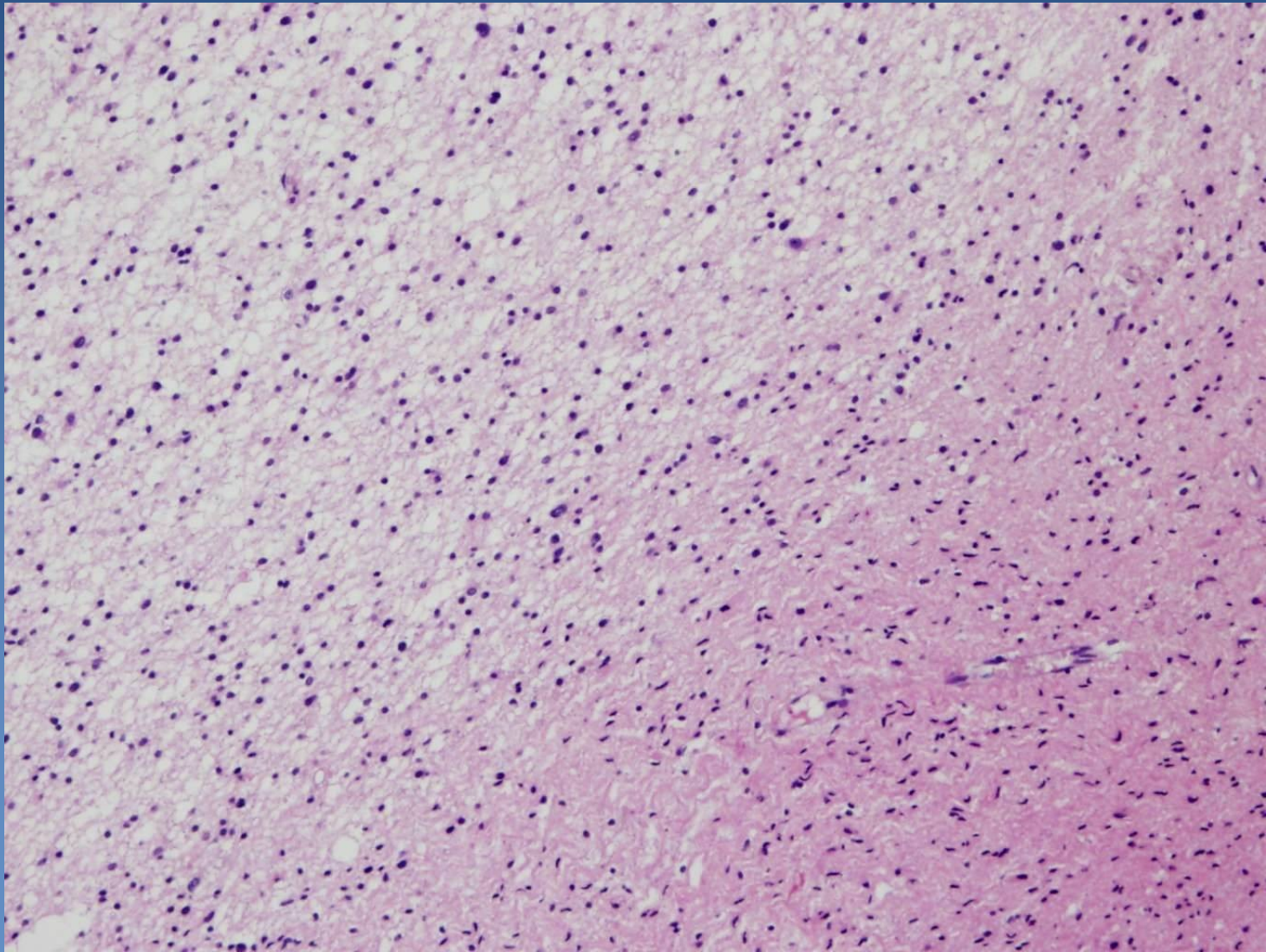
Diffuse (fibrillary) astrocytoma



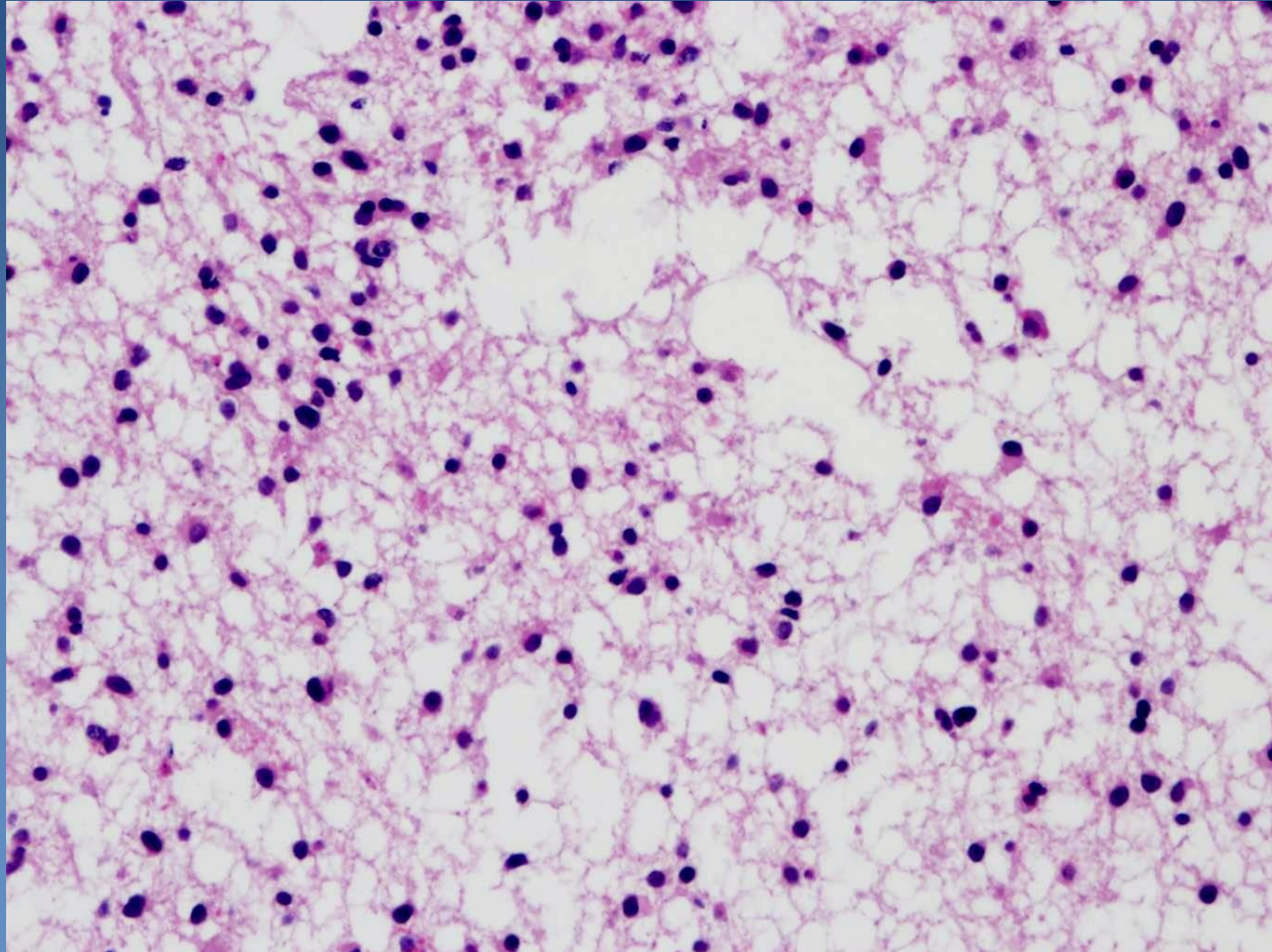
xmicro:

- ⇒ *well-differentiated fibrillary, gemistocytic (mass of eosinophilic cytoplasm), rare protoplasmic astrocytes*
- ⇒ *slightly increased cellularity in comparison with normal tissue tumor*
- ⇒ *stroma often microcystic*
- ⇒ *usually no mitotic activity*
- ⇒ *without necrosis or microvascular proliferation*

Diffuse (fibrillary) astrocytoma



Diffuse (fibrillary) astrocytoma



Astrocytic tumors

Glioblastoma



- x grade IV/IV (WHO) – anaplastic glioma**
- x most common and most malignant primary brain tumor**
- x typically in adults, usually 45-75 years of age**
- x mostly de novo – primary glioblastoma**
 - ⇒ *short history, >60 years of age*
- x possible transformation from preexisting astrocytoma gr. II or III – secondary glioblastoma,**
 - ⇒ *history 1-10 yrs, around 45 years of age*
- x rapidly growing, infiltrative (very poor prognosis)**
- x gross:**
 - ⇒ *variable appearance – white and firm regions, yellow and soft parts, foci of necrosis, cysts, hemorrhages*

Astrocytic tumors

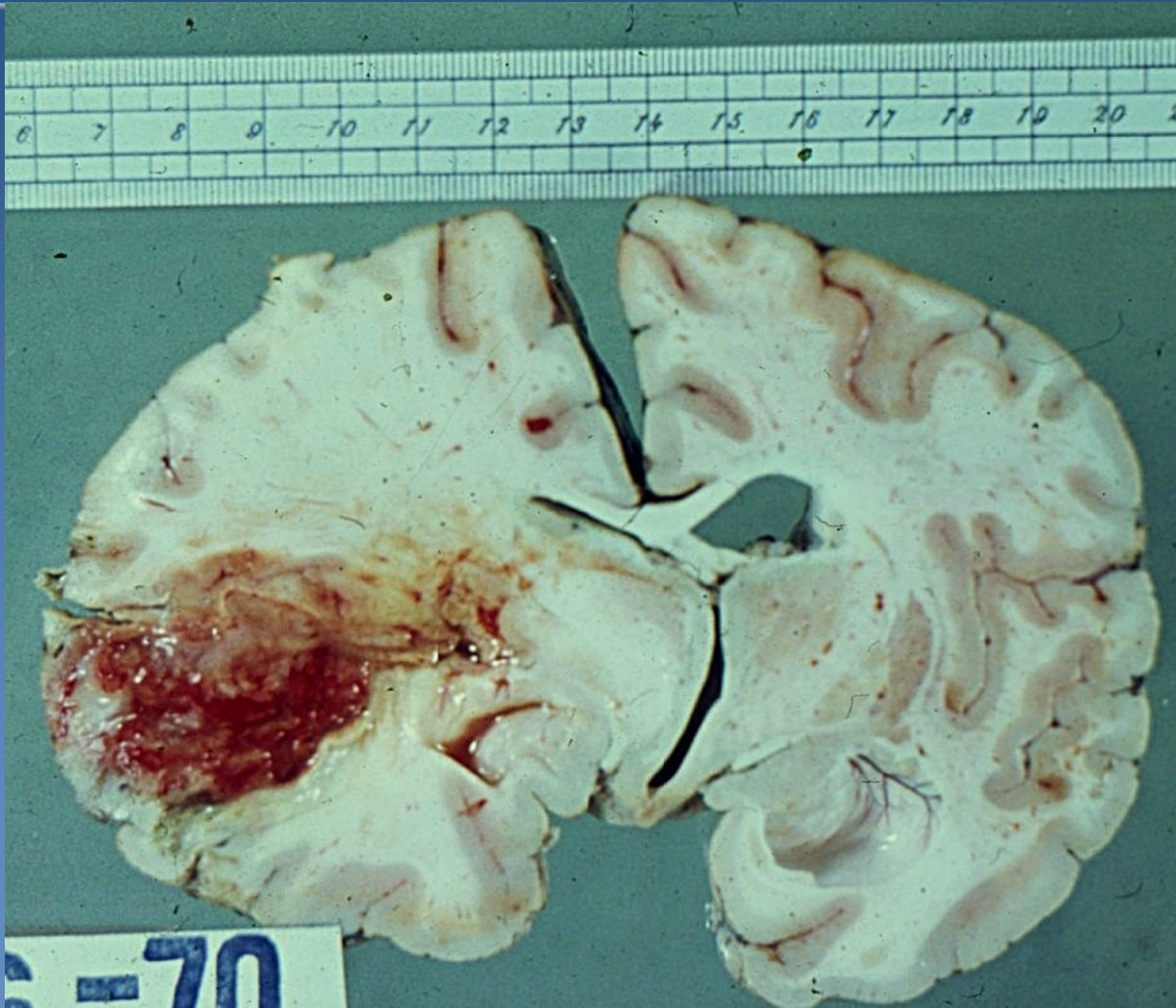
Glioblastoma



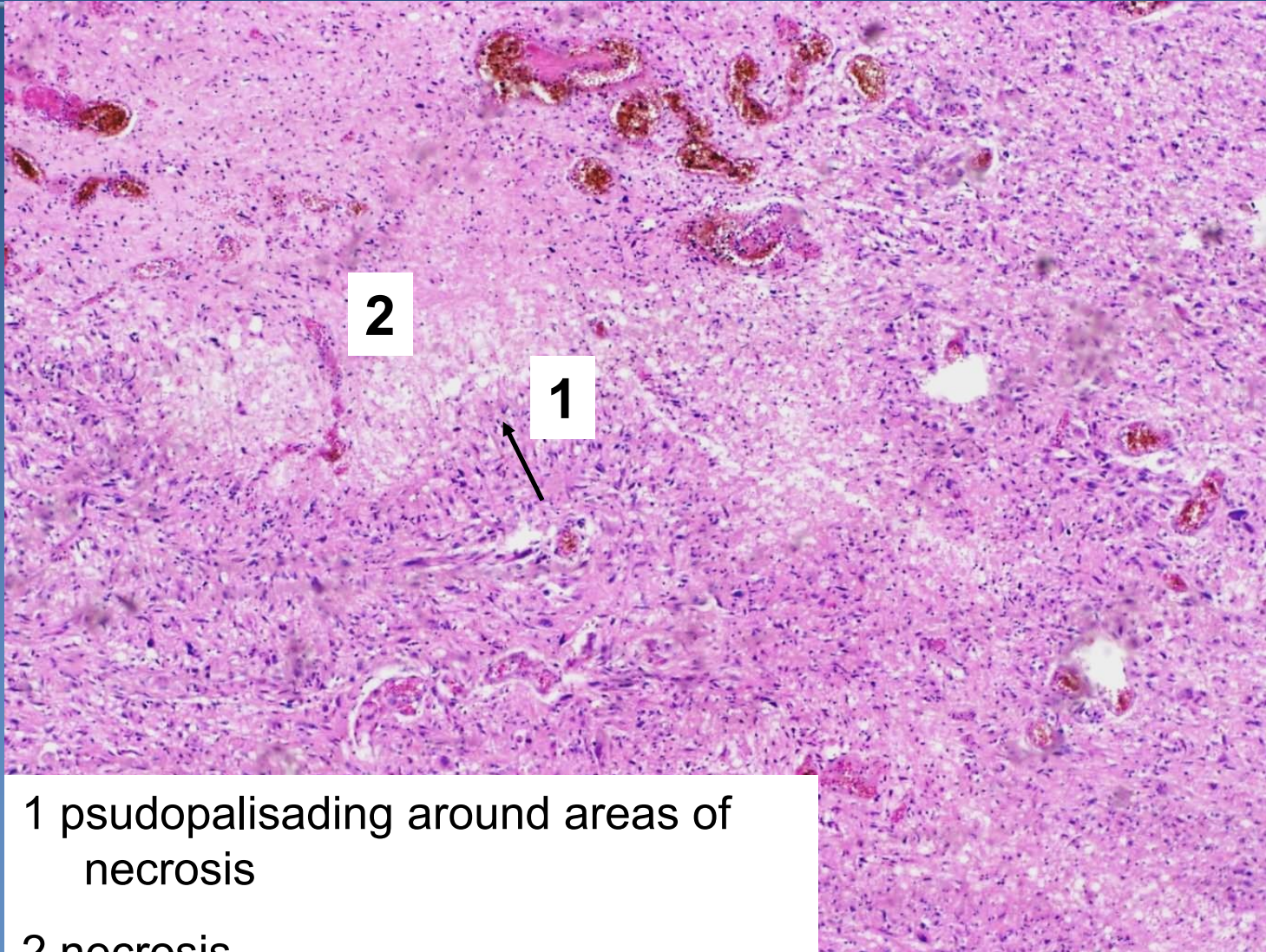
xmicro:

- ⇒ *pleomorphic tumor cells - severe cellular and nuclear atypia*
- ⇒ *tumor is regionally heterogeneous*
 - alternation of pleiomorphic and more regularly arranged areas
- ⇒ *high mitotic rate*
- ⇒ *conspicuous microvascular proliferation and / or necrosis*
- ⇒ *pseudopalisading of tumor cells around necrotic areas*

Glioblastoma



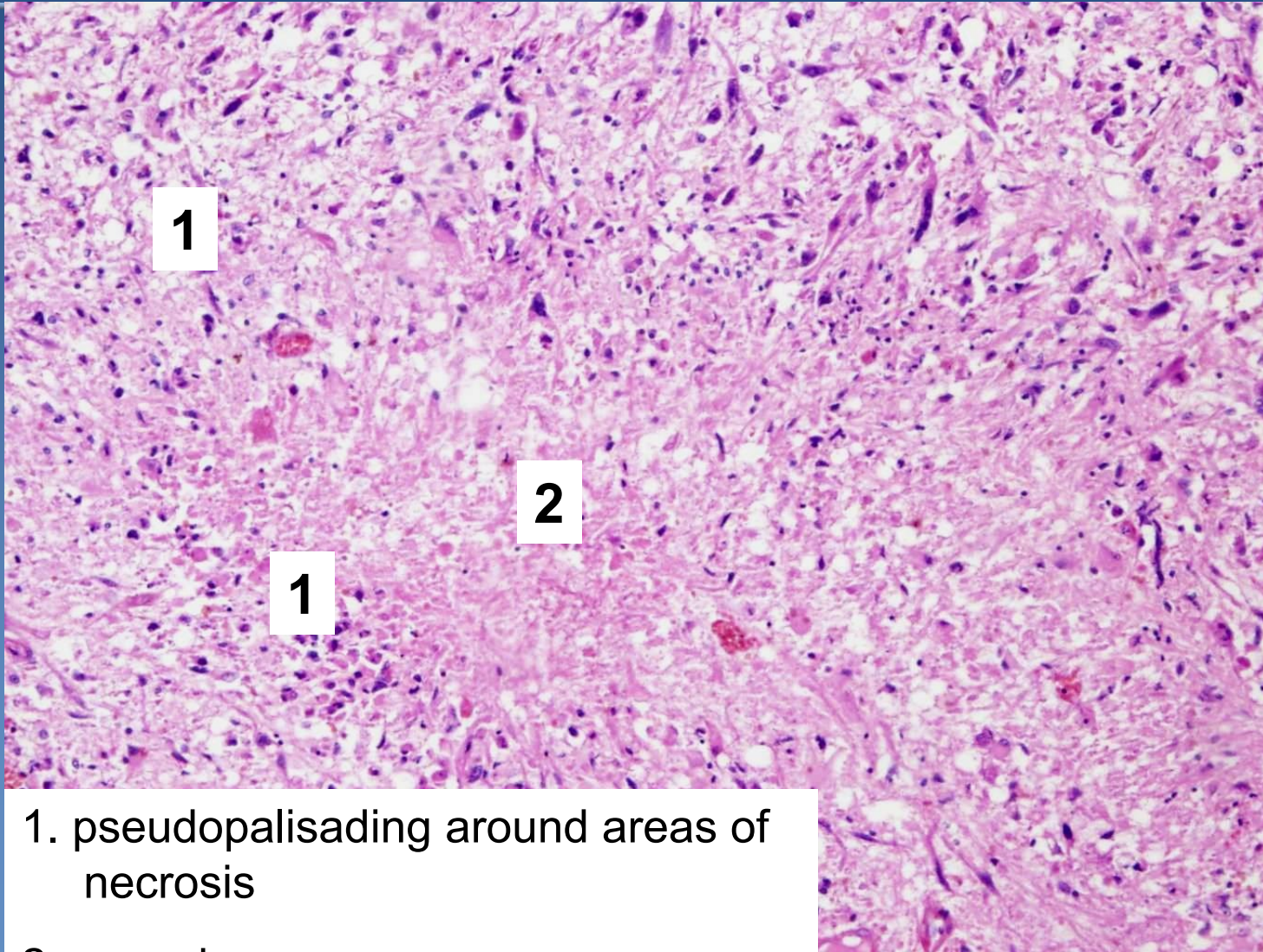
Glioblastoma



1 pseudopalisading around areas of
necrosis

2 necrosis

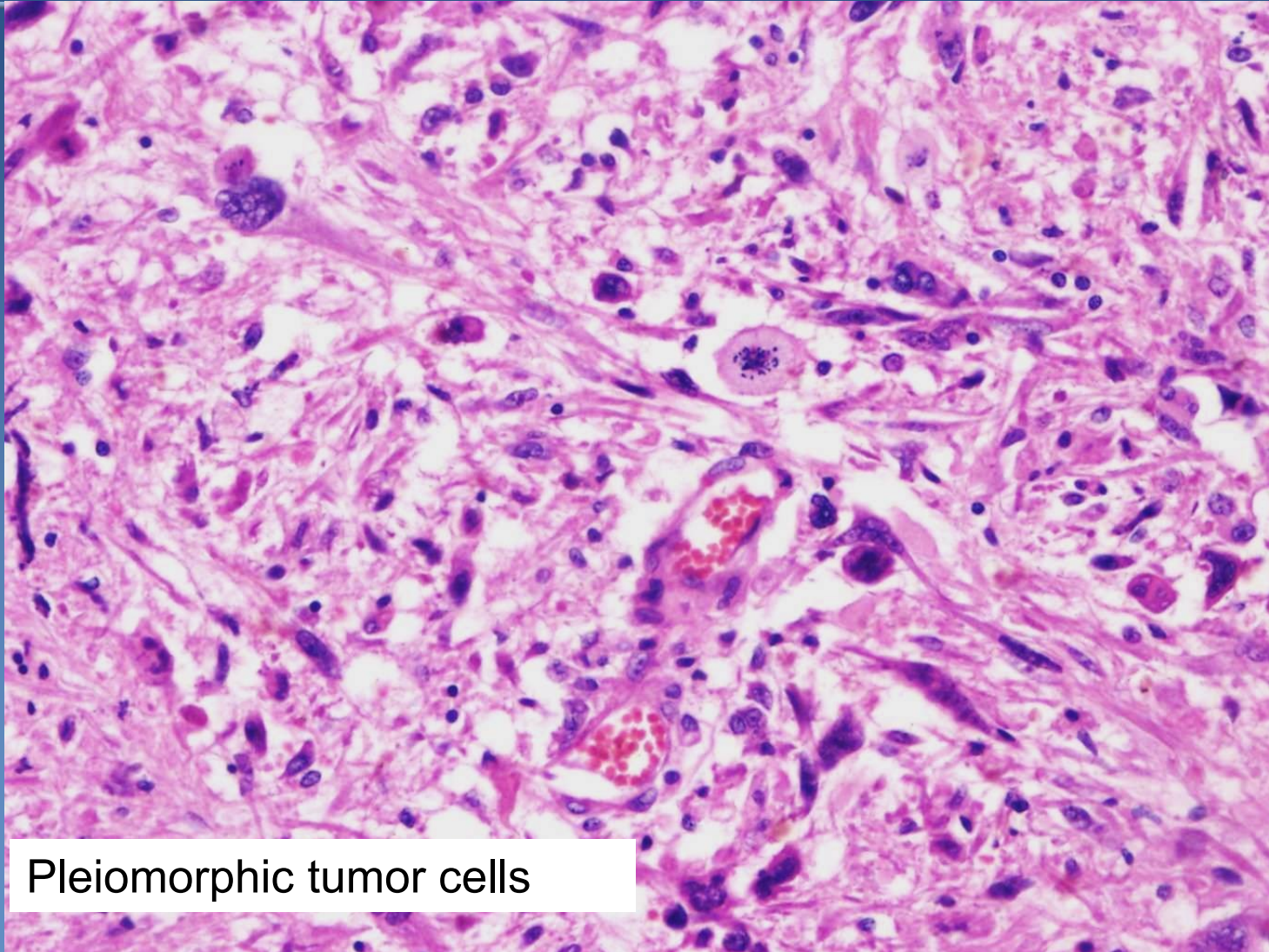
Glioblastoma



1. pseudopalisading around areas of necrosis

2 necrosis

Glioblastoma



Pleiomorphic tumor cells

Astrocytic tumors

Pilocytic astrocytoma



× **grade I (WHO)**

× **grows very slowly**

× growth begins in childhood - clinical signs manifest around age of 20 (and later); in cerebellum or near III. and IV. ventricle, resection possible

× **micro:**

⇒ ***biphasic structure solid / cystic***

- compact region with bipolar tumor astrocytes with eosinophilic Rosenthal fibers
- microcystic, sparsely cellular areas with multipolar tumor cells with granular eosinophilic bodies and eosinophilic globules

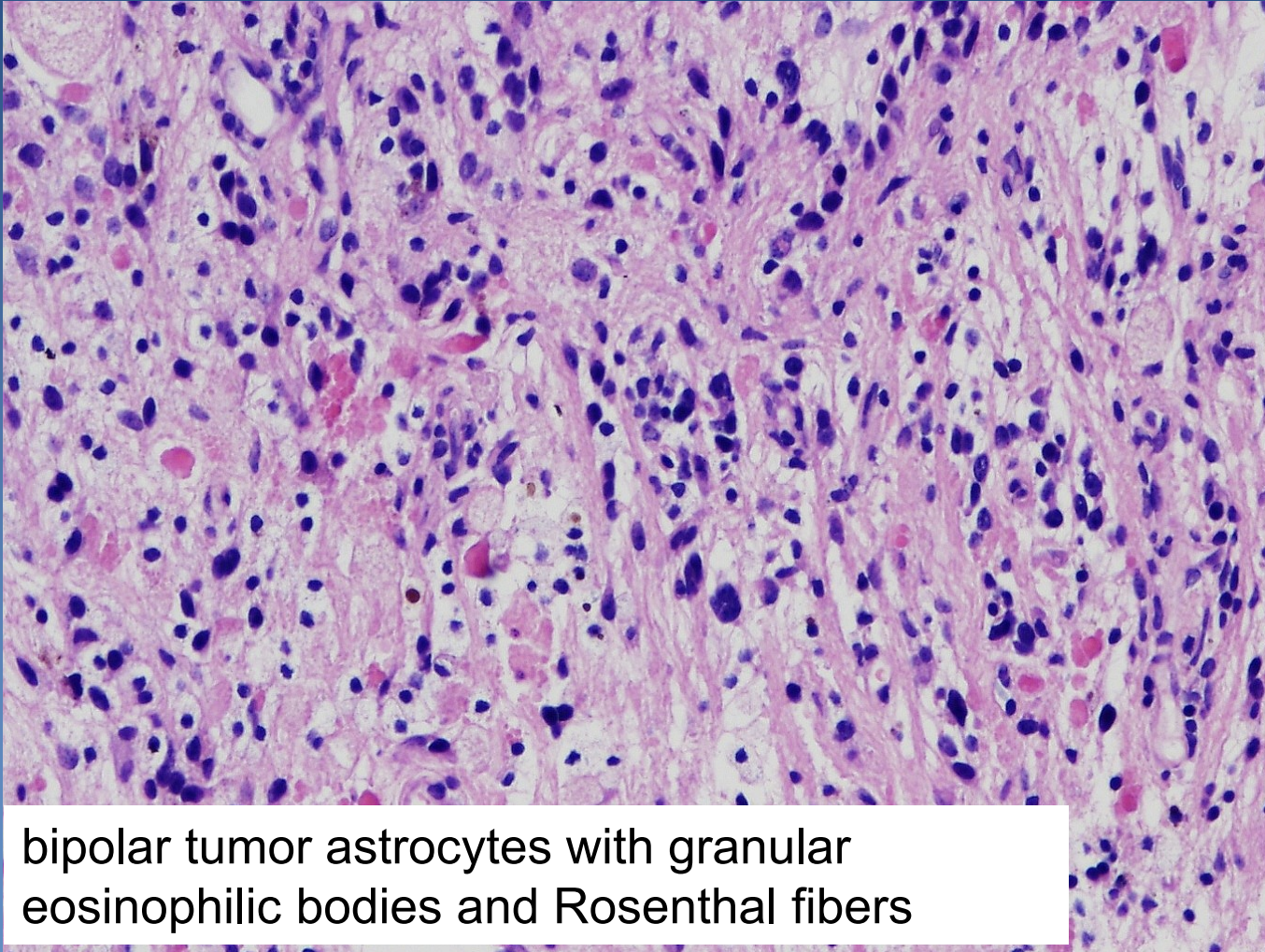
⇒ *degenerative atypia and calcification*

⇒ *infrequent mitosis, sm. nuclear pleiomorphism and hyperchromasia*

⇒ *glomeruloid vascular endothelial proliferation often*

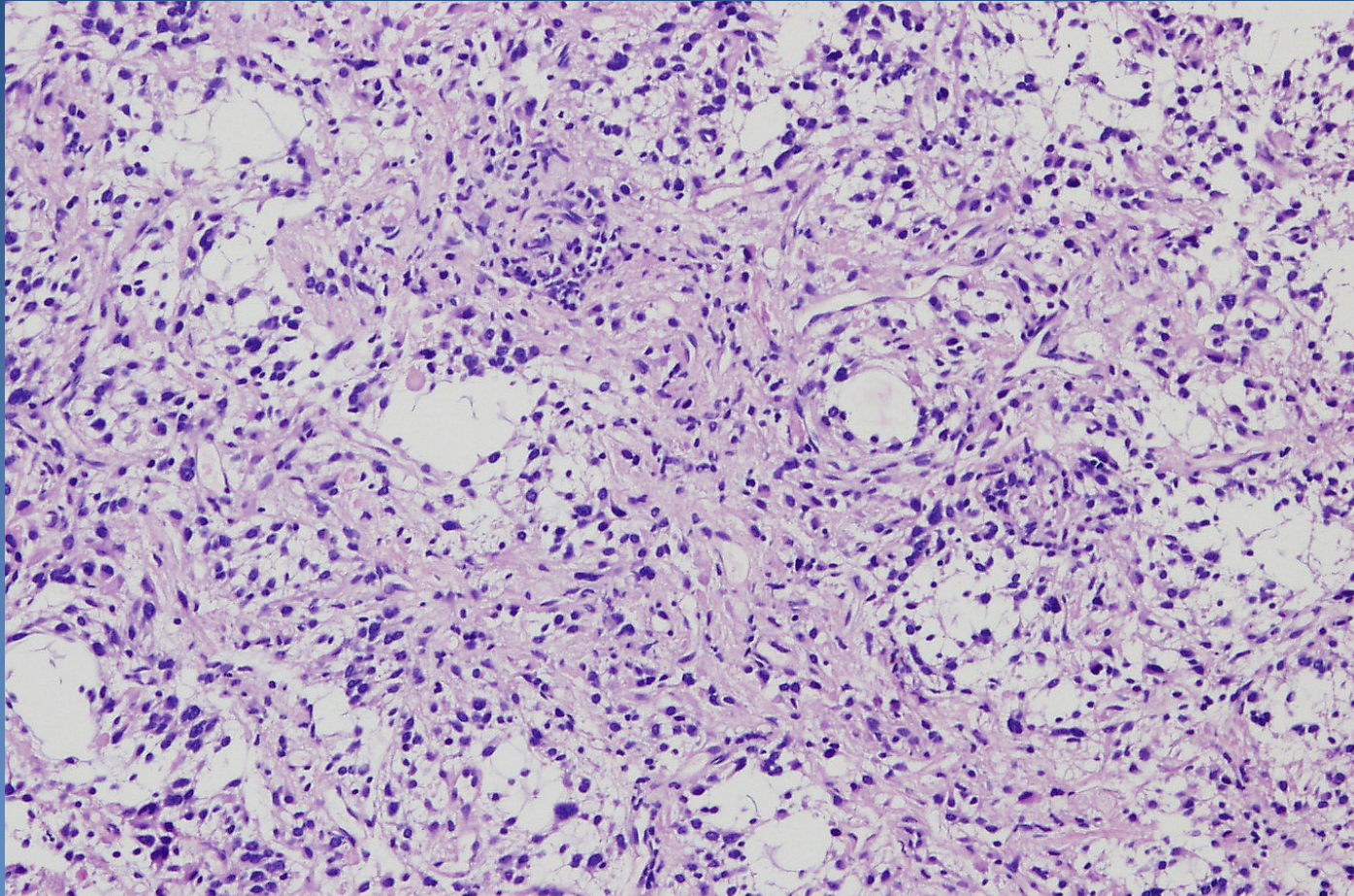
⇒ *small necrosis possible*

Pilocytic astrocytoma



bipolar tumor astrocytes with granular eosinophilic bodies and Rosenthal fibers

Pilocytic astrocytoma



Microcystic areas with multipolar tumor cells

Oligodendroglial tumors



- × **Oligodendroglioma (Grade II/IV)**
- × Anaplastic oligodendroglioma (Grade III)
- × Mixed oligoastrocytomas (Grade II, III)

Oligodendroglial tumors

Oligodendroglioma



× grade II (WHO)

× in adults; slow growth

× **Micro:**

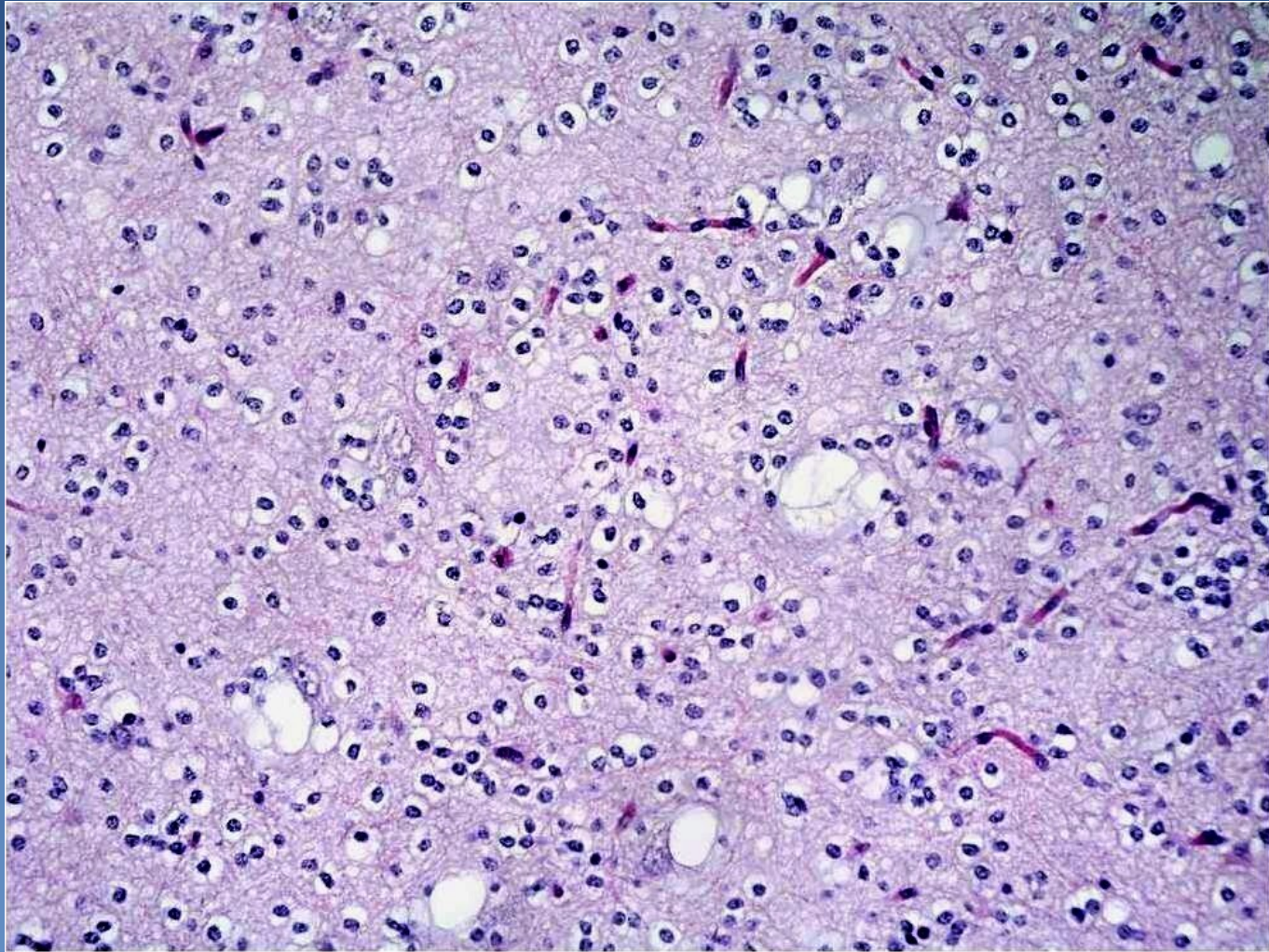
⇒ *uniform tumor cells with round nuclei and perinuclear halos*

⇒ *microcalcifications (X-ray)*

⇒ *areas of mucoid degeneration*

⇒ *abundant branching capillaries*

Oligodendroglioma



Ependymal tumors



- × Ependymoma (grade II)
- × Anaplastic ependymoma (grade III)
- × Myxopapillary ependymoma (grade I)
- × Subependymoma (grade I)

Ependymal tumors

Ependymoma



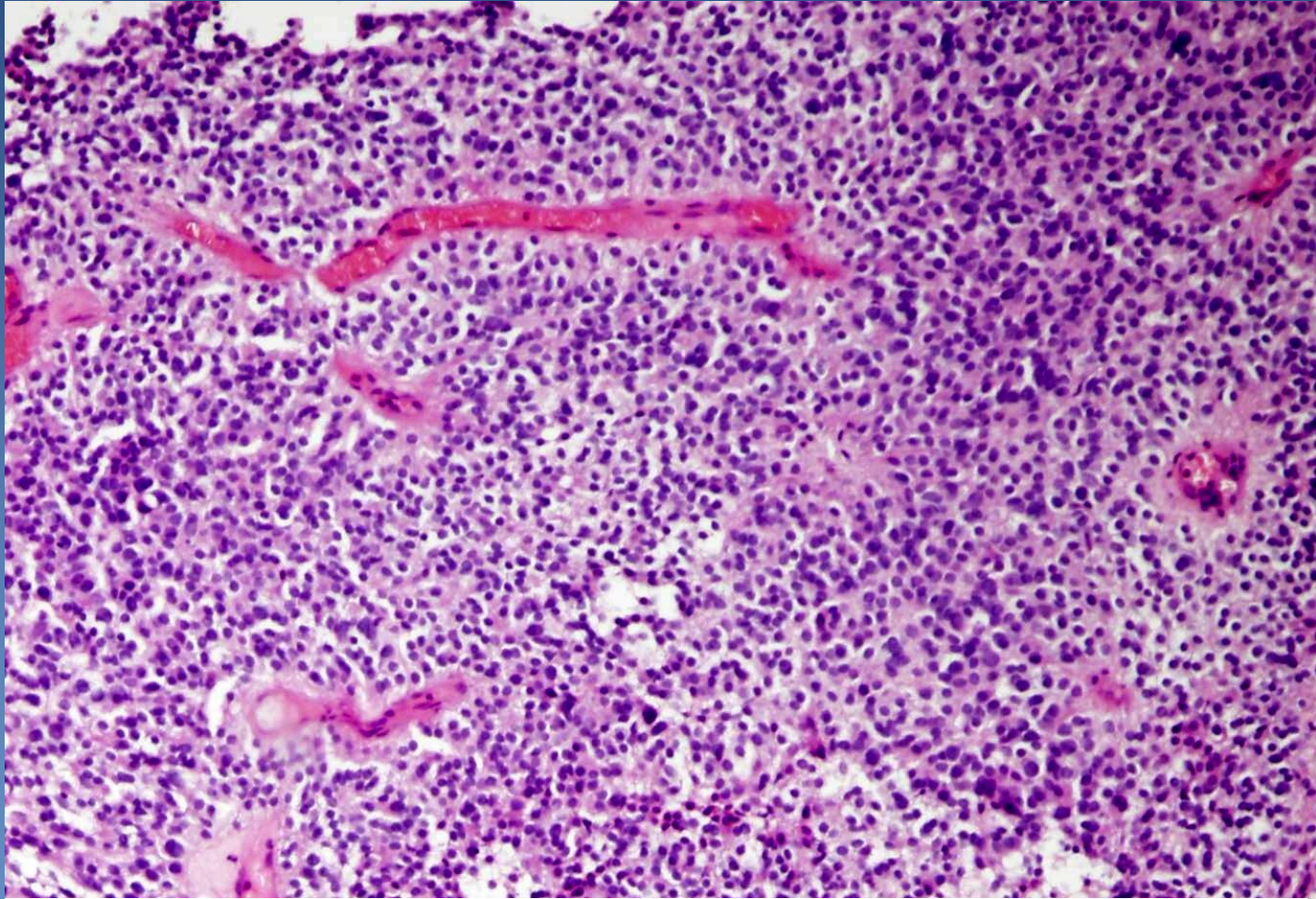
x grade II (WHO)

x in children - usually around IV. ventricle, in adults - spinal cord, with neurofibromatosis type 2

x micro:

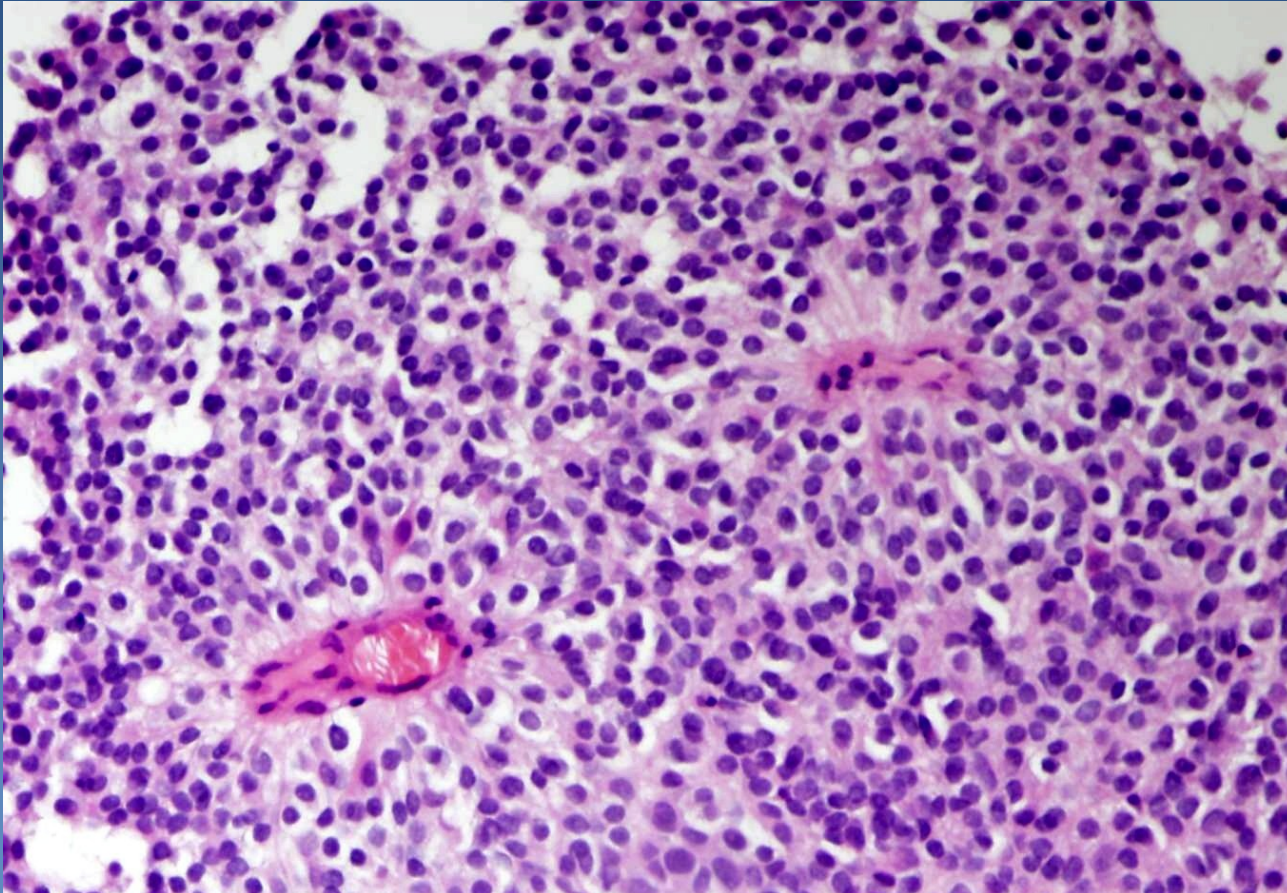
- ⇒ *fusiform cells with long processes, uniform round to oval nuclei*
- ⇒ *fine fibrillary background*
- ⇒ *canalicular formations, perivascular pseudorosettes*
- ⇒ *sporadic or no mitotic figures*

Ependymoma



Perivascular pseudorosettes, uniform population of tumor cells

Ependymoma



Perivascular pseudorosettes, uniform population of tumor cells

Tumors of the choroid plexus



- × Choroid plexus papilloma (grade I)
- × Atypical choroid plexus papilloma (grade II)
- × Choroid plexus carcinoma (grade III)

Embryonal tumors



- ✗ Primitive aggressive malignant tumors of childhood

- ✗ Tumors "of small blue cells" grade IV
 - ⇒ *Medulloblastoma*
 - ⇒ *Supratentorial primitive neuroectodermal tumor*
 - ⇒ *Ependymoblastoma*
 - ⇒ *Retinoblastoma*
 - ⇒ ...

Embryonal tumors

Medulloblastoma



x grade IV (WHO)

x tumor of first two decades of life

x highly malignant but radiosensitive

x in cerebellum, midline in children

⇒ *local infiltration, meningeal and CSF spread → hydrocephalus*

⇒ *gross – focal pink/grey tumor*

x micro:

⇒ *highly cellular*

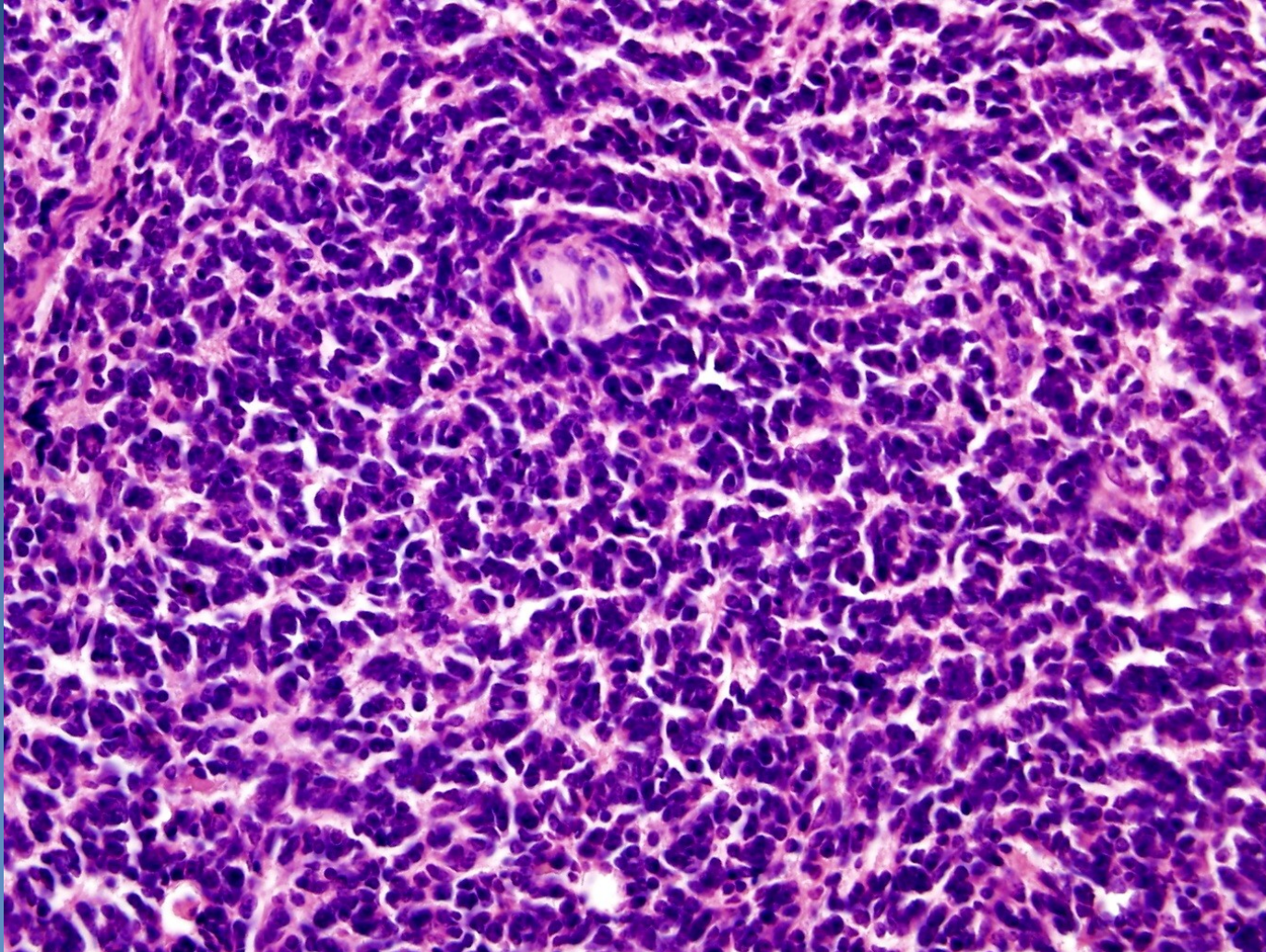
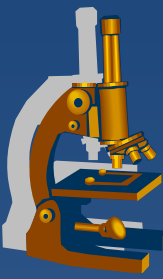
⇒ *small hyperchromatic nuclei, carrot-shaped*

⇒ *neuroblastic Homer-Wright's rosettes*

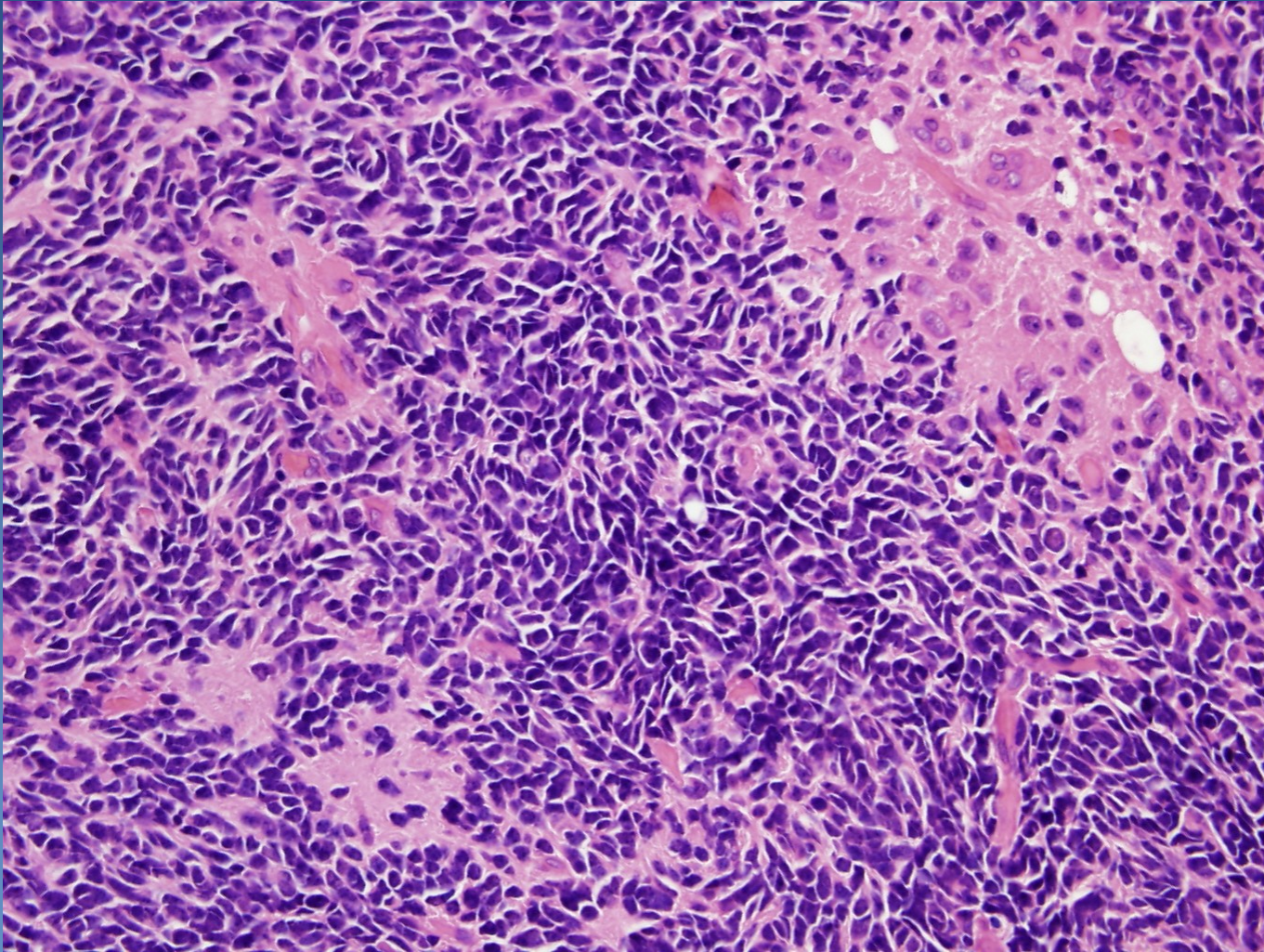
⇒ *high mitotic activity*

⇒ *differentiation to neuronal / other cells possible*

Medulloblastoma



Medulloblastoma



Tumors of the meninges



× Meningioma (Grade I)

- ⇒ *(Syncytial (+)*
- ⇒ *Fibroblastic (+)*
- ⇒ *Transitional (+)*
- ⇒ *Psammomatous*
- ⇒ *Angioblastic*
- ⇒ *Microcystic)*

× (Atypical meningioma, chordoid and clear cell (Grade II)

× Rhabdoid, papillary, anaplastic (Grade III)

× + solitary fibrous tumor of meninges,
(hemangiopericytoma), sarcomas,....)

Tumors of the meninges

Meningioma

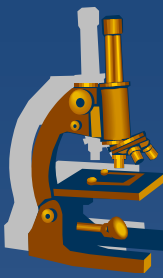


- x grade I (WHO classification)**
- x usually benign, common (20% of all intracranial tumors), adults**
- x predominantly on the hemispherical convexity**
- x origin from arachnoidal cap cells**

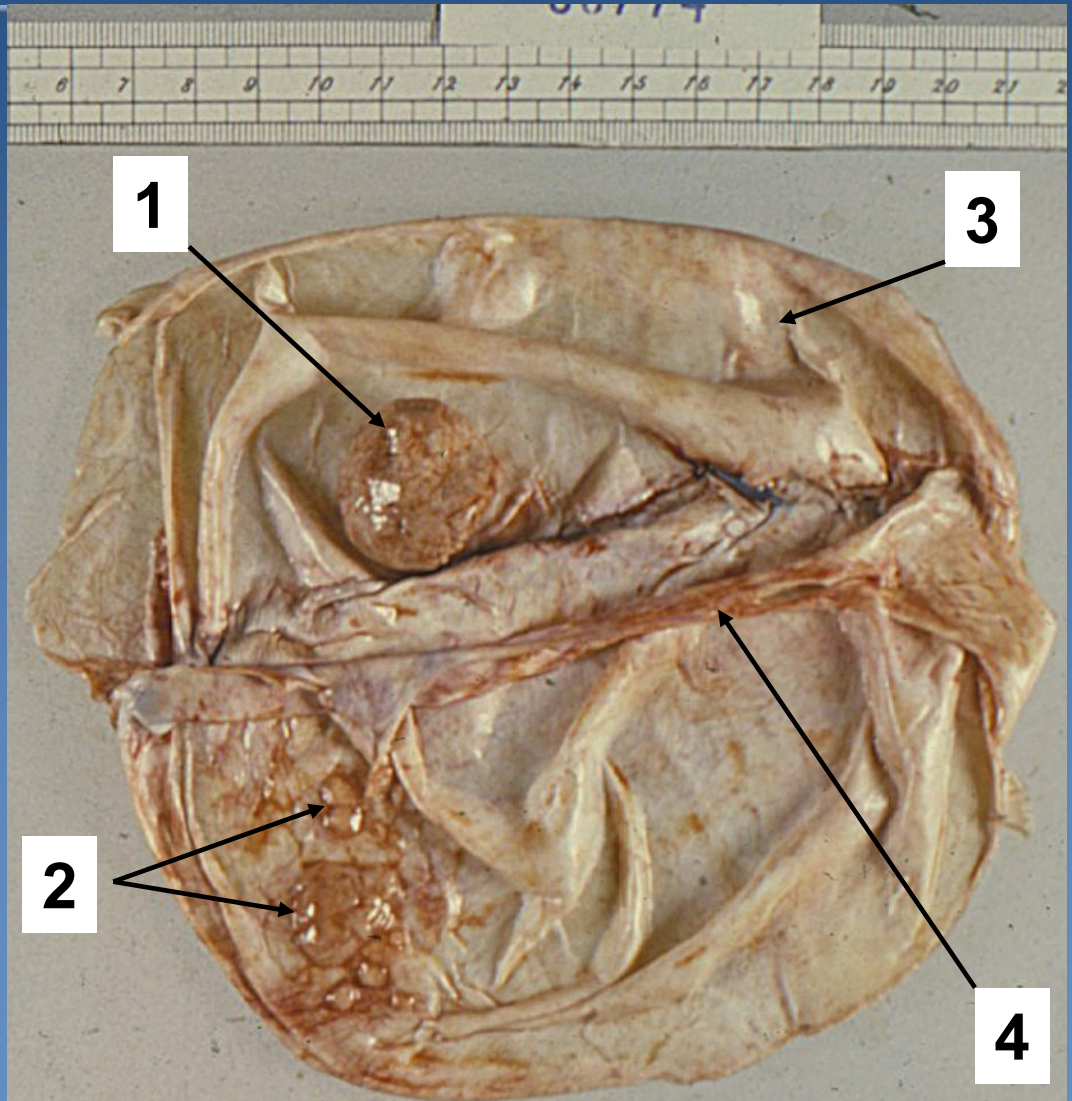
- x gross:**
 - ⇒ *usually solitary , well demarcated, firm, whorl-like pattern on cut surfaces*
 - ⇒ *attached to the dura, cortical compression, rare skull invasion*

- x micro:**
 - ⇒ *highly variable*
 - ⇒ *whorls, bundles*
 - ⇒ *common laminated calcific concretions – psammoma bodies (X-ray)*

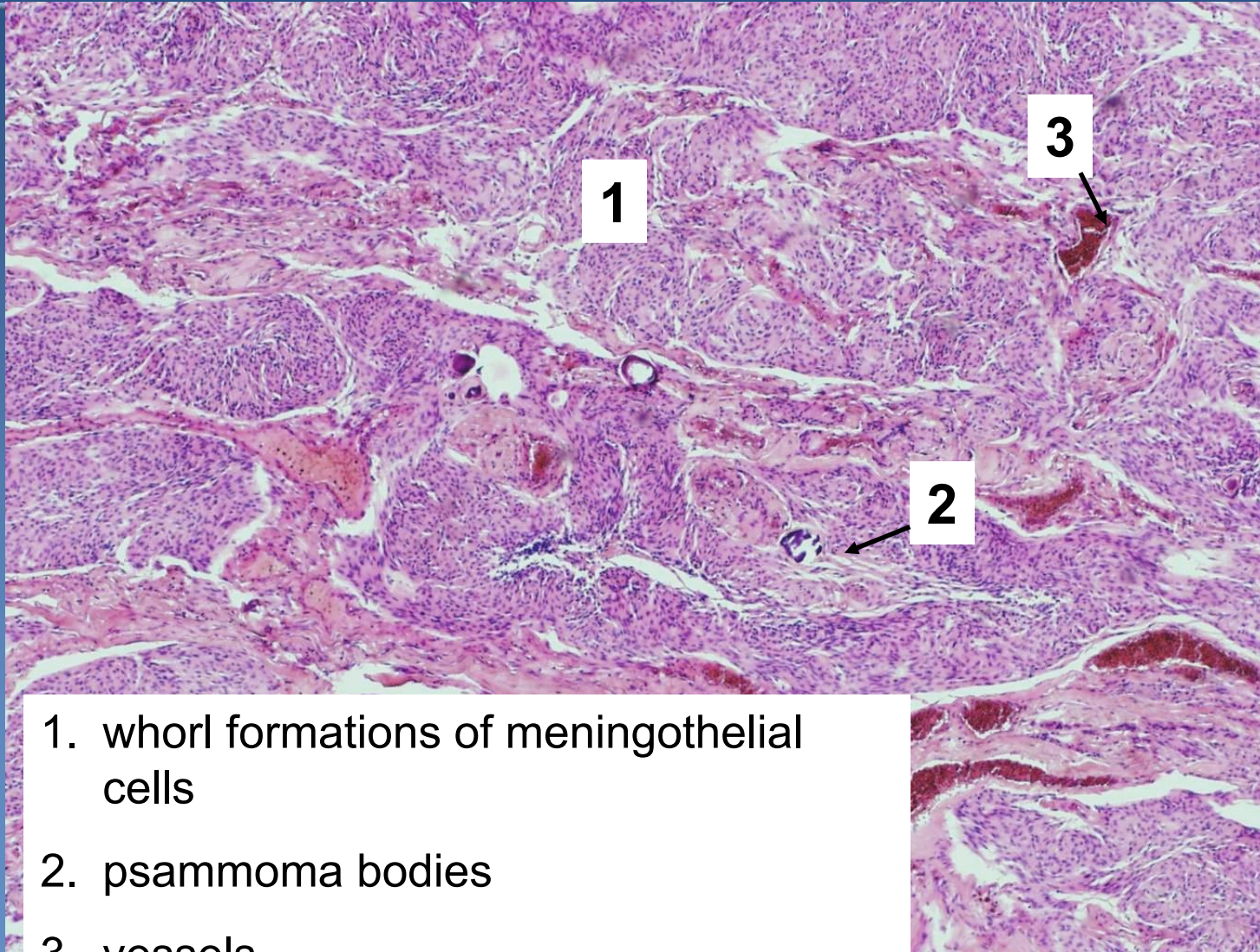
Meningioma



1. Lobular meningioma
2. Flat meningiomas
3. Dura mater
4. Falx cerebri

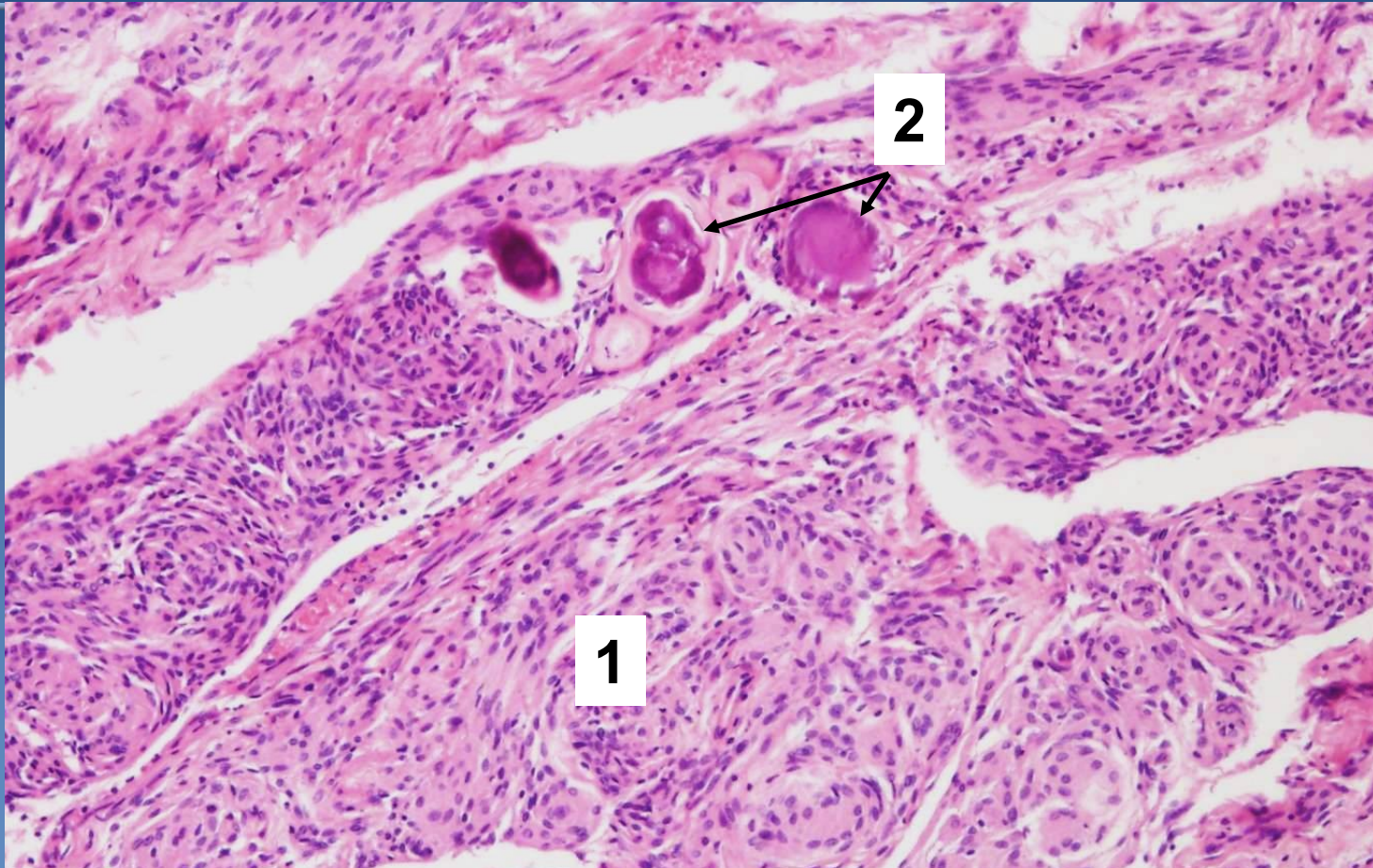


Meningioma



1. whorl formations of meningothelial cells
2. psammoma bodies
3. vessels

Meningioma



- 1. whorl formations of meningothelial cells
- 2. psammoma bodies



Peripheral nerve sheath tumors

Benign tumors



- × Schwannoma
- × neurofibroma (solitary; multiple - neurofibromatosis type 1)
- × perineurioma
- × neurothecoma
- × granulosa cell tumor

Schwannoma



- peripheral myelinisation

- ✗ in connection with **peripheral nerve**
- ✗ **intracranial - cerebellopontine angle – VIII. nerve „acoustic neuromas**
- ✗ **compression (excitation, later loss of function)**

✗ **gross:**

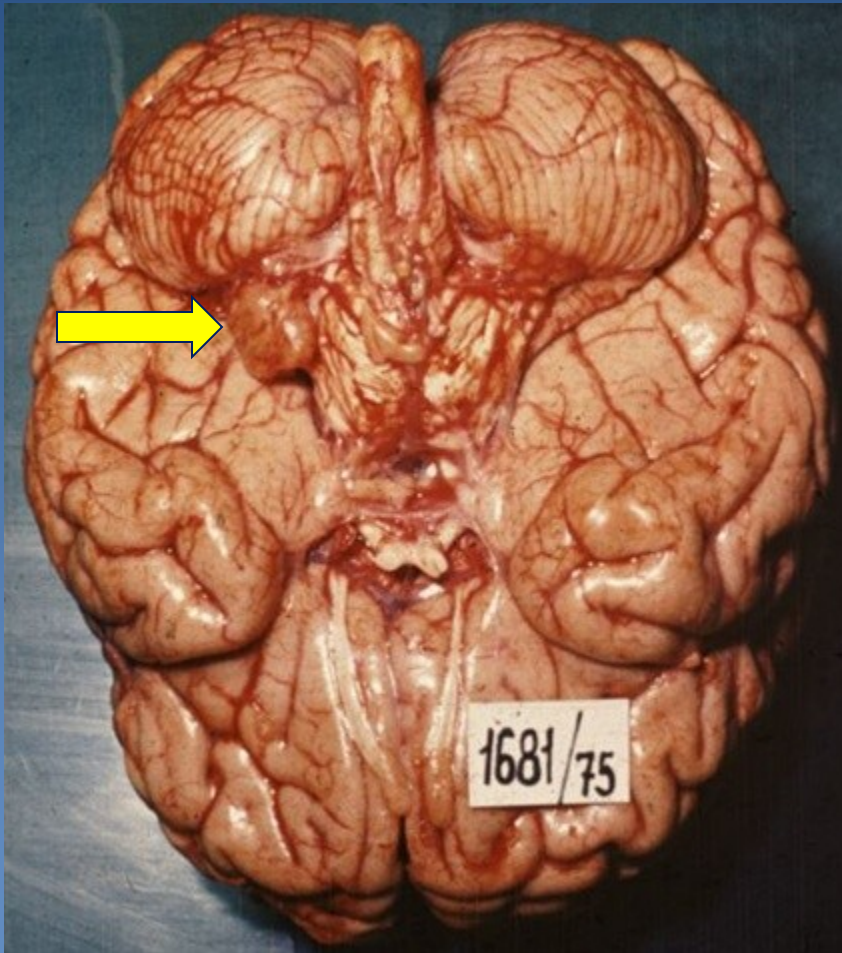
⇒ *well-circumscribed encapsulated lesion, may be attached to the nerve*

✗ **micro:**

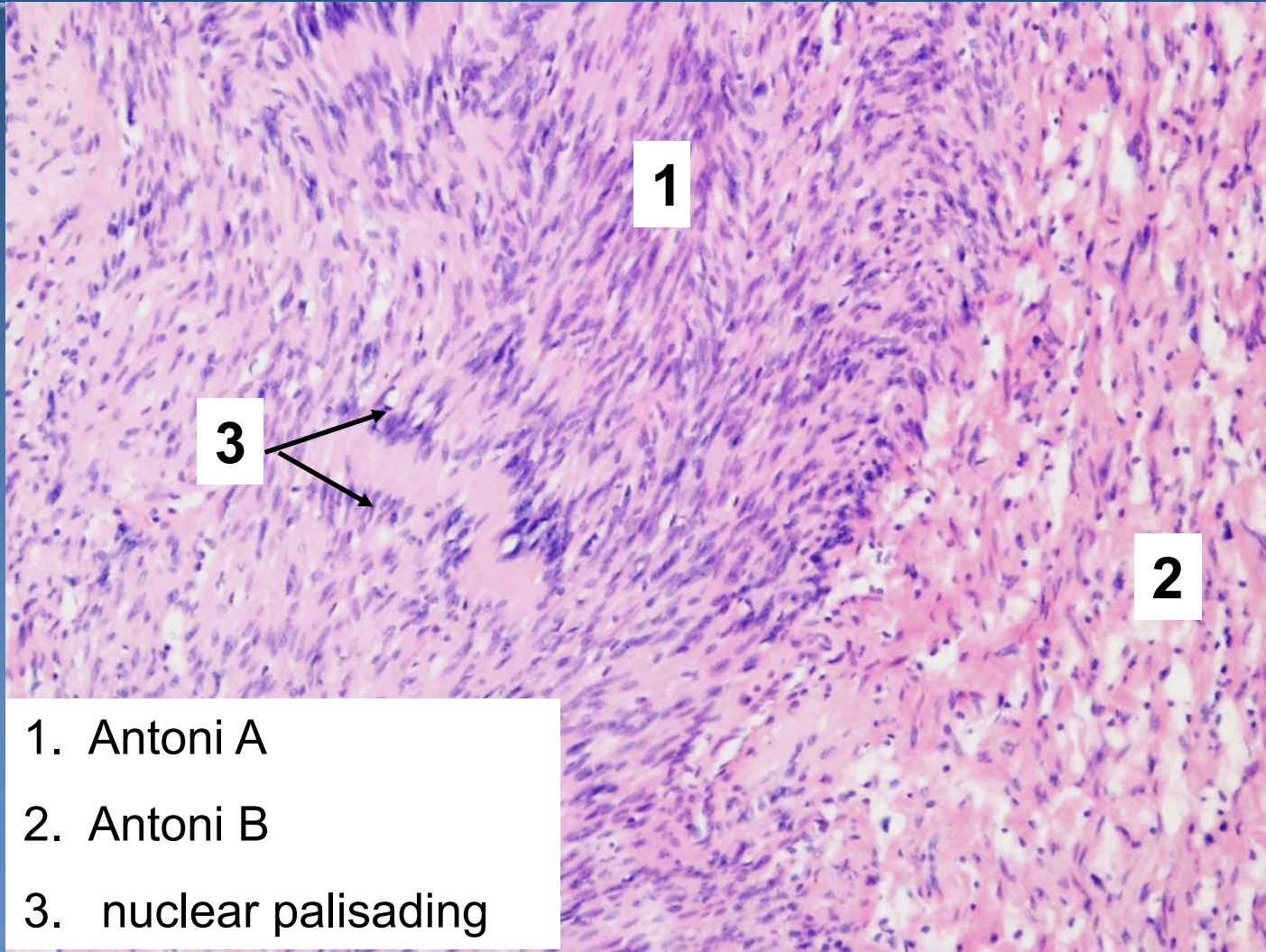
⇒ *cellular areas of densely packed spindle cells (**Antoni A pattern**, Verocay bodies – nuclear palisading)*

⇒ *intermixed with looser, myxoid regions (**Antoni B pattern**)*

Schwannoma

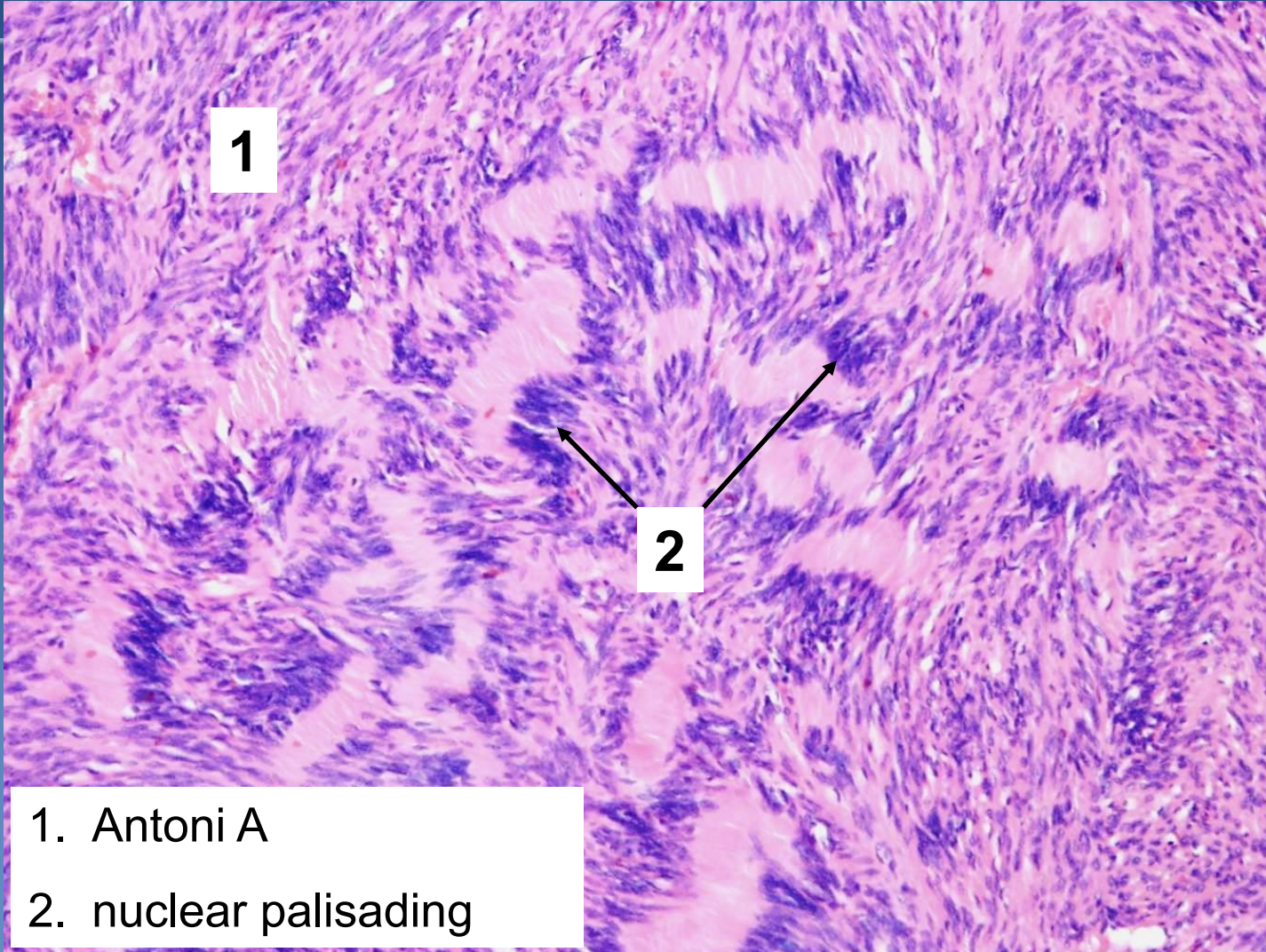


Schwannoma



1. Antoni A
2. Antoni B
3. nuclear palisading

Schwannoma



1. Antoni A
2. nuclear palisading

Neurofibroma



- × peripheral nerve sheath tumor
- × solitary x multiple (neurofibromatosis I. , II. type)
- × **cutaneous x plexiform** (*along nerves, possible malignant transformation*)

× gross:

⇒ *unencapsulated soft roundish nodules*

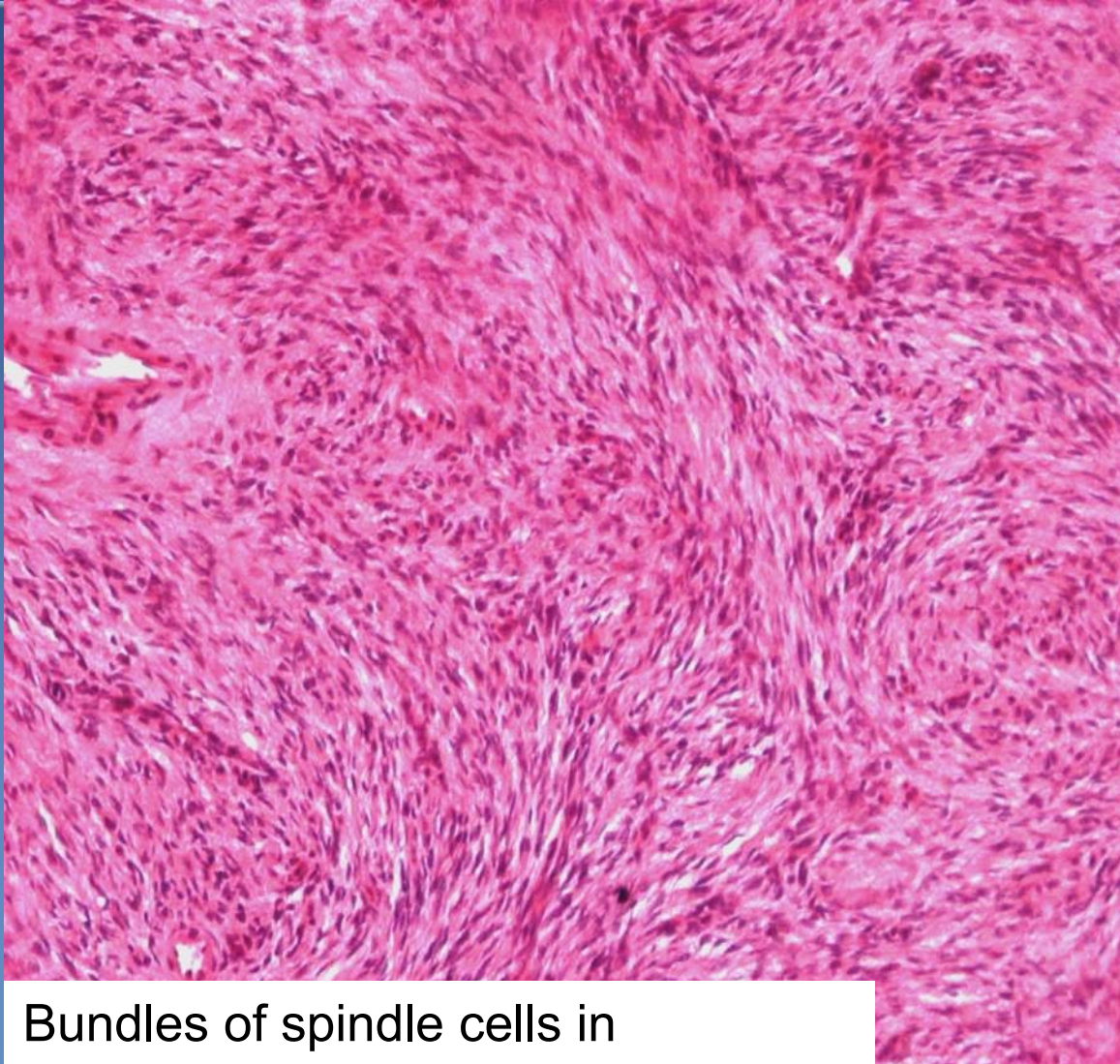
× micro:

⇒ *spindle cells, „S“ and „C“ shaped*

⇒ *extracellular loose myxoid or collagenous matrix*

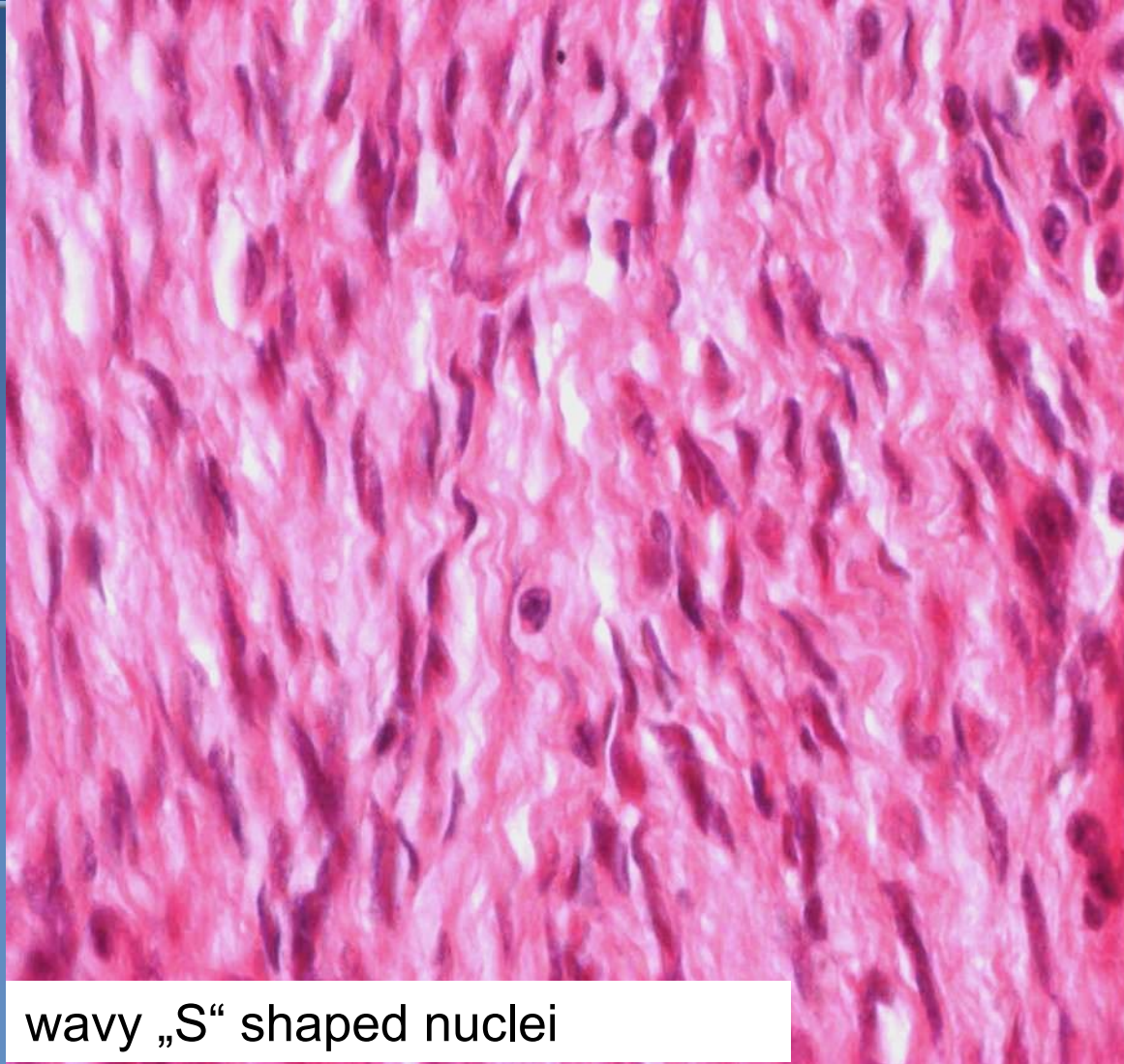
⇒ *sporadic small vascular lumina*

neurofibroma



Bundles of spindle cells in collagenous stroma

neurofibroma



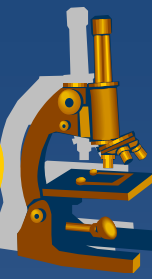
wavy „S“ shaped nuclei

Neurofibromatosis (type I)



- ✗ von Recklinghausen's disease
 - ⇒ AD, frequency 1:3000, chromosome 17, defect of tumor suppressor gene
- ✗ **multiple neurofibromas, mostly on skin**, in any localisation - retroperitoneum, orbit, tongue, GIT, melanin-containing variants
- ✗ **hyperpigmented skin lesions** (café-au-lait spots), **pigmented iris hamartomas** (Lisch nodules)
- ✗ in approx. 3% of patients malignant transformation
- ✗ ↑ **risk of development of other tumors** (*optic gliomas, meningiomas, pheochromocytomas*)

Neurofibromatosis (type I)



Malignant tumors



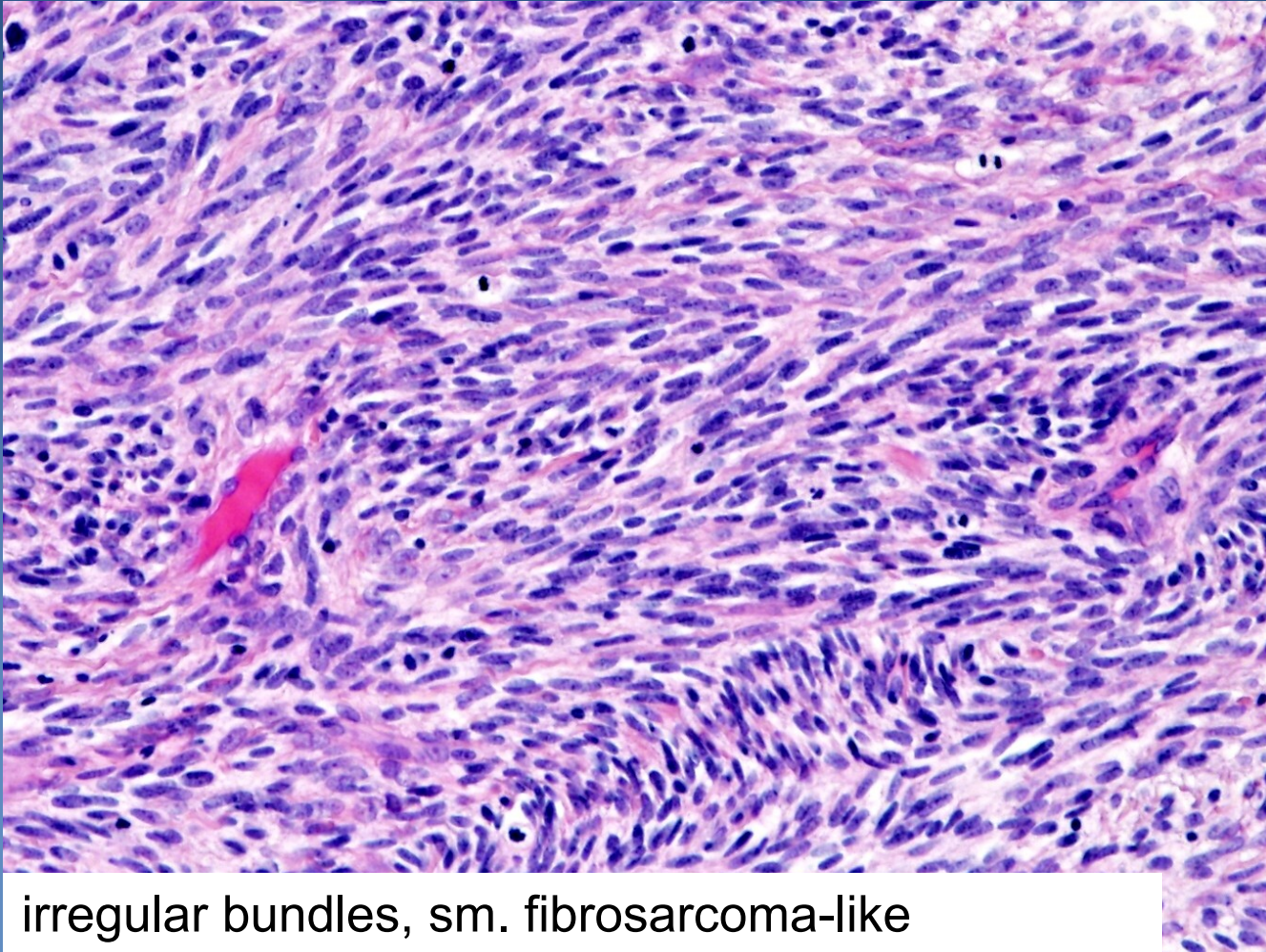
x malignant peripheral nerve sheath tumor (MPNST)

- ⇒ „neurogenic sarcomas“ arising from the peripheral nerve sheath
- ⇒ 50% occur in patients with neurofibromatosis type 1, adults
- ⇒ aggressive, recurrent, metastases (lung, bones)
- ⇒ gross: foci of necrosis, hemorrhage
- ⇒ micro: fibroblast-like cells with elongated nuclei, frequent mitotic figures, areas of necrosis

x primitive neuroectodermal tumors (PNET)

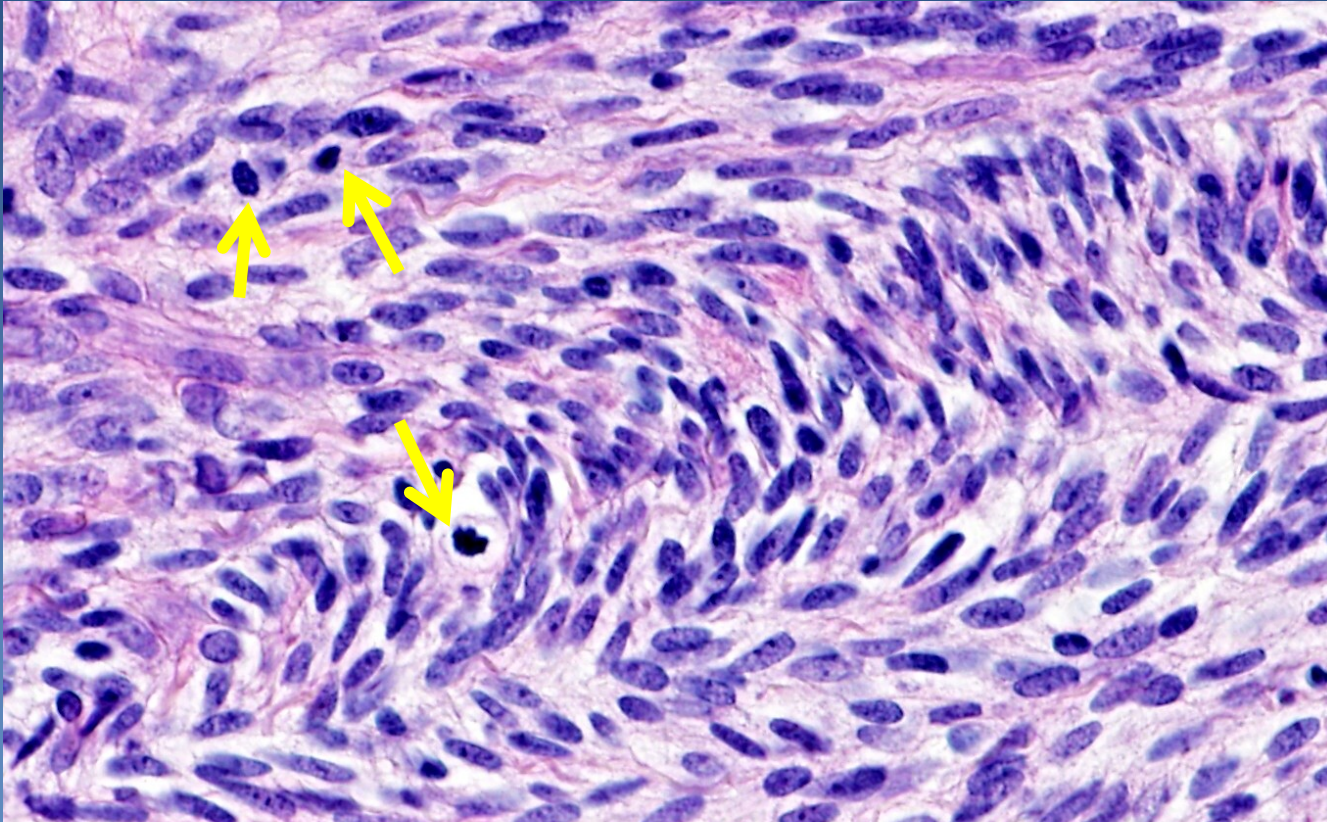
- ⇒ bone tumor

MPNST



irregular bundles, sm. fibrosarcoma-like

MPNST



Hyperchromatic nuclei of spindle cells

Mitoses (arrows)



TUMORS OF THE AUTONOMIC NERVOUS SYSTEM

Tumors of the parasympathetic system



× paraganglioma, chemodectoma

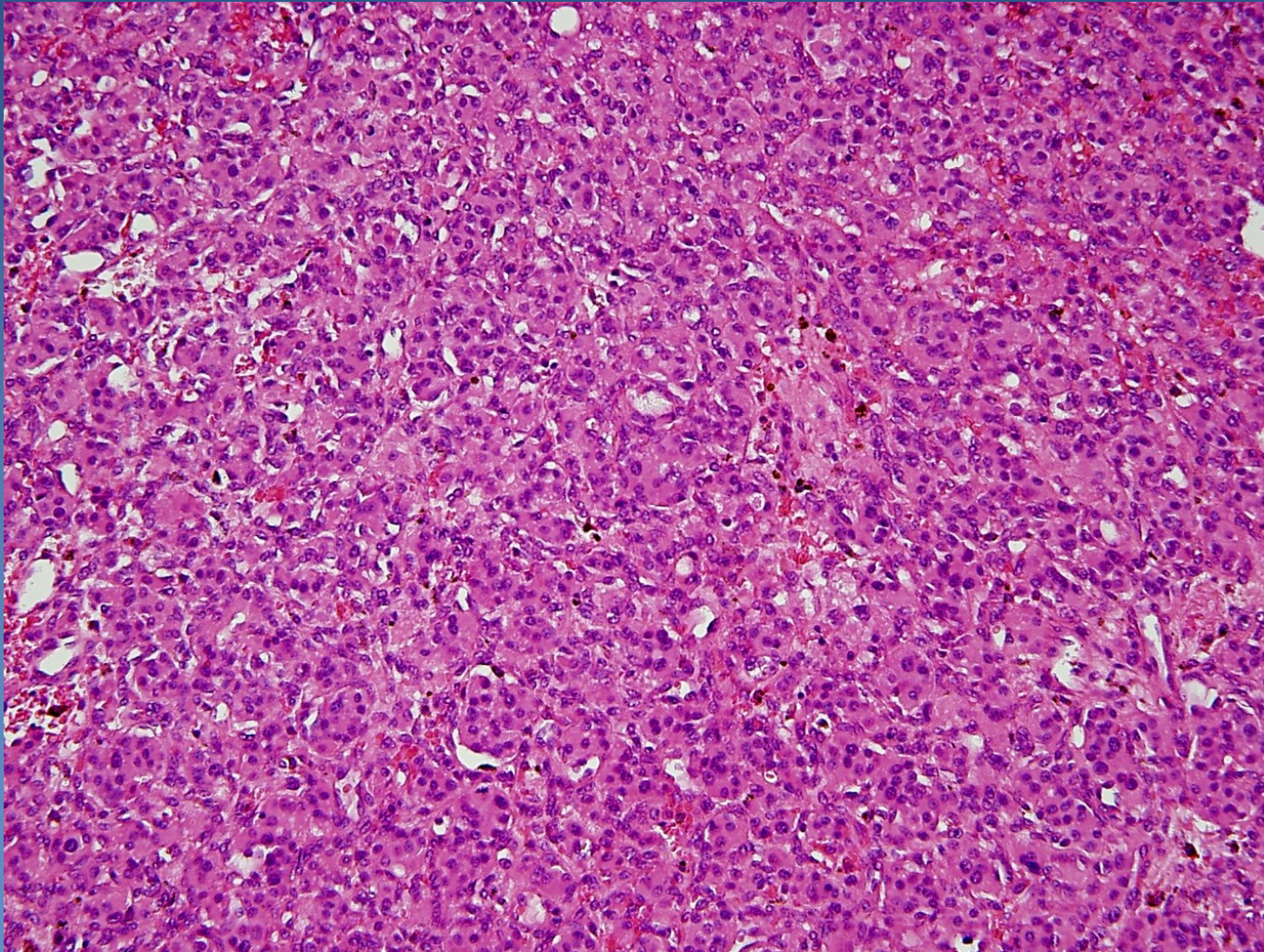
⇒ *originate from extraadrenal paraganglia*

- glomus tympanicum and jugulare, vagal bodies, carotid bodies, laryngeal, aorticopulmonary
 - pressure changes: $\downarrow P_a O_2$, $\uparrow P_a CO_2$ a $\uparrow pH$ → reflex stimulation of respiratory and cardiovascular system

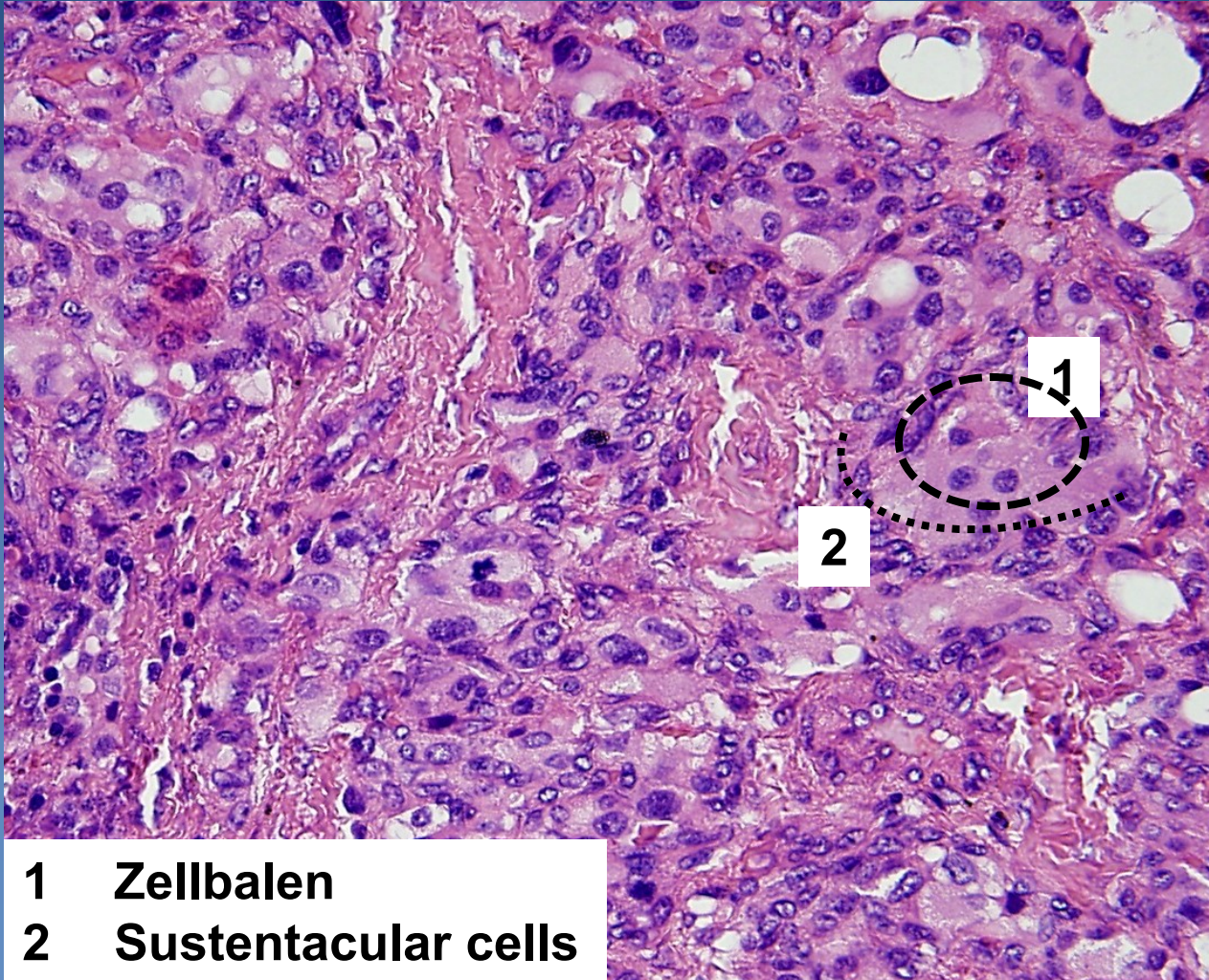
⇒ *micro:*

- organoid (solid alveolar) formation of cells:
 - chief cells - polygonal to oval; in distinctive cell nests, „Zellballen“)
 - **supporting** (sustentacular) **spindle cells**
- separated by thin fibrovascular stroma

Paraganglioma

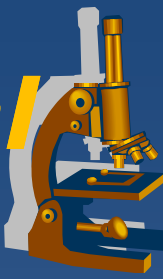


Paraganglioma



- 1 Zellbalen
- 2 Sustentacular cells

Tumors of the sympathoadrenal system



× Paragangliomas

× Pheochromocytoma

⇒ Adrenal medullary paraganglioma

⇒ **Gross:**, circumscribed lesions, usually confined to the adrenal, yellow-tan (hemorrhage, necrosis)

⇒ 10% associated with familial syndromes (MEN 2A, 2B, ..), 10% extra-adrenal, in adrenal location 10% bilateral, 10% biologically malignant)

× Neuroblastoma → ganglioneuroblastoma → ganglioneuroma

⇒ spontaneous or chemotherapy-induced maturation

⇒ even regression possible

⇒ variable prognosis, according to age and stage

Neuroblastoma



- ✗ most common extracranial solid tumor in childhood
- ✗ usually sporadic, 1% germline mutation of ALK (anaplastic lymphoma kinase)-gene
- ✗ mostly in adrenal medulla, paravertebral sympathetic ganglia
- ✗ large tumors haemorrhagic, necrotic

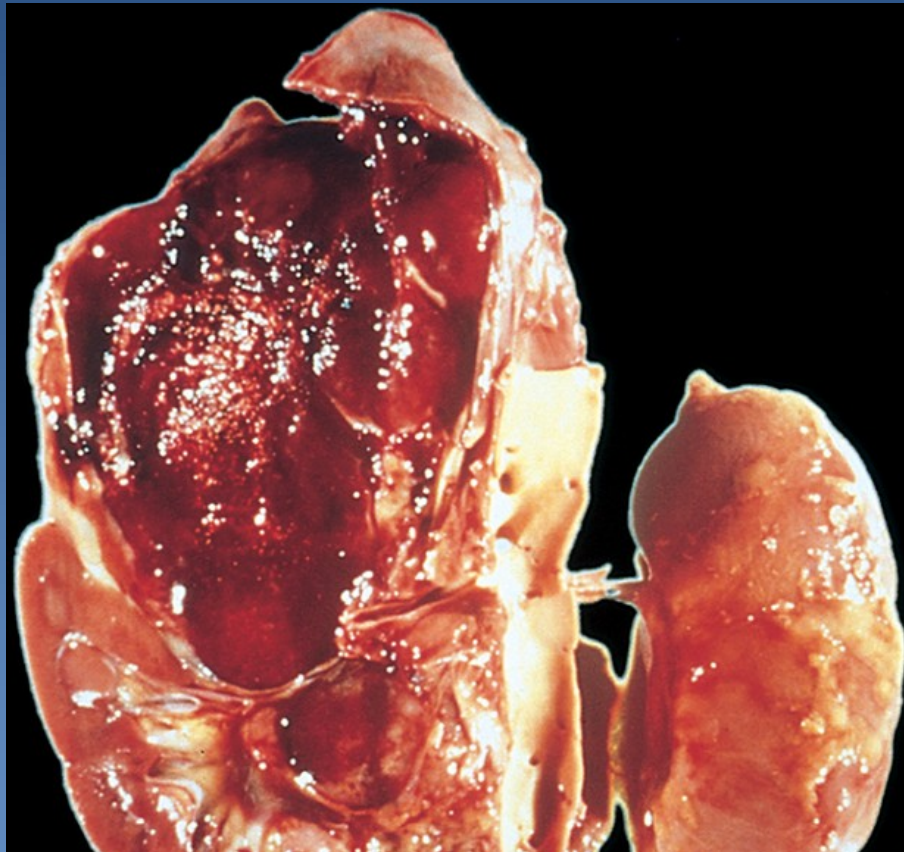
Neuroblastoma



xMicro:

- ⇒ *small round cells, hyperchromatic nuclei („small blue cells“)*
- ⇒ *extracellular eosinophilic fibrillary stroma*
- ⇒ *Homer-Wright rosettes*
- ⇒ *commonly high mitotic activity, caryorrhexis*

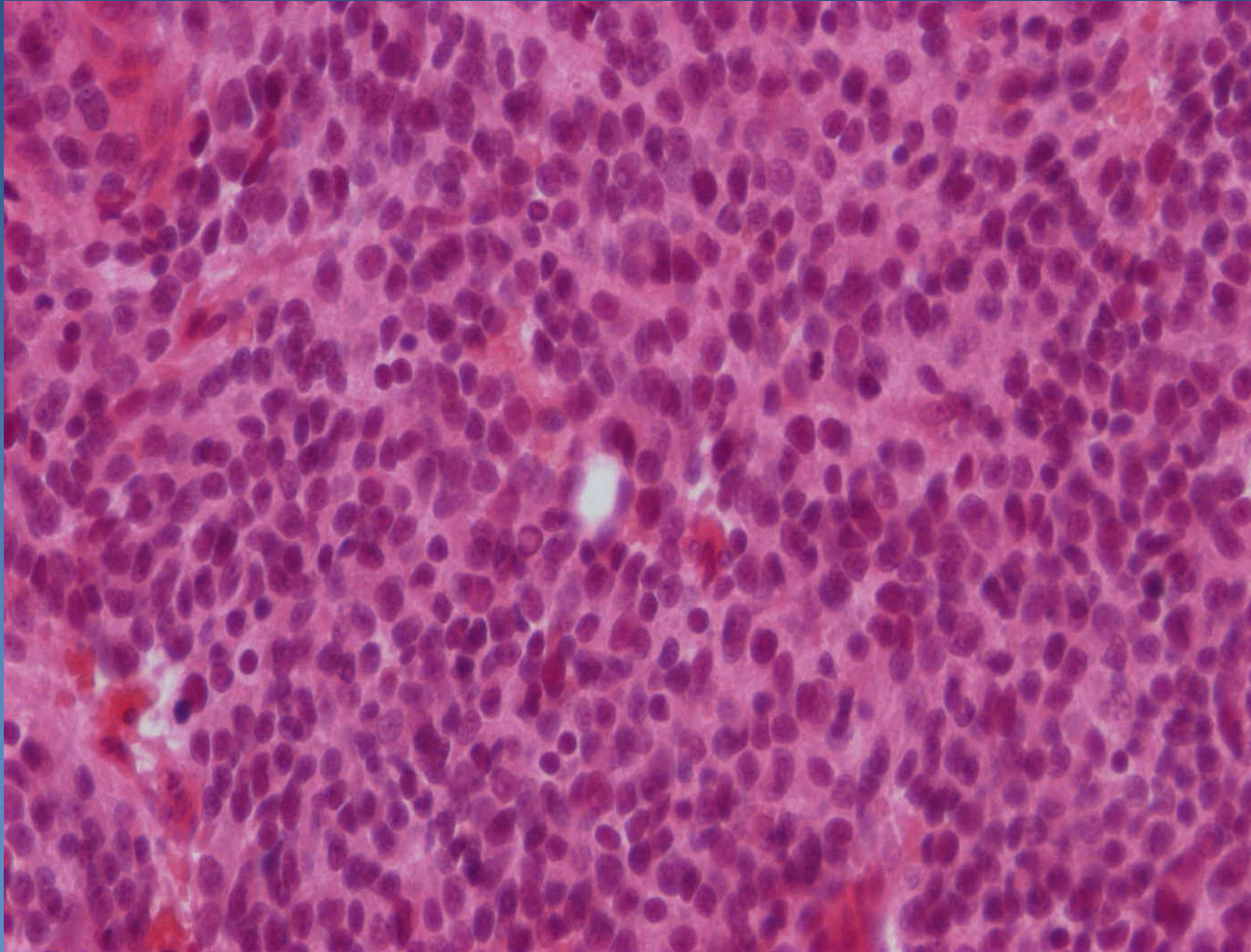
Neuroblastoma



Necrotic haemorrhagic adrenal tumor

Kumar et al: Robbins & Cotran Pathologic Basis of Disease, 9th Edition.
Copyright © 2009 by Saunders, an imprint of Elsevier, Inc. All rights reserved.

Neuroblastoma



Neuroblastoma



Homer-Wright rosettes