Universitas Kristen Indonesia
Fakultas Kedokteran

SURAT KEPUTUSAN
No. : 143/UKI.F5.D/HKP.3.5.6/2021
tentang

PENUGASAN TENAGA AKADEMIK DALAM MEMBERIKAN KULIAH PAKAR PIMPINAN FAKULTAS KEDOKTERAN UNIVERSITAS KRISTEN INDONESIA

MENIMBANG : Bahwa untuk kelancaran proses belajar mengajar dan meningkatkan mutu pendidi di FKUKI diperlukan penugasan tenaga akademik FKUKI untuk memberi Kuliah Pakar

MENGINGAT :
1. Peraturan Pemerintah No. 60 tahun 1999 tentang Pendidikan Tinggi
2. Surat Keputusan Dekan FKUKI No. 53/SK/FKUKI/11.2006 tanggal November 2006 tentang Pemberlakuan Kurikulum Berbasis Kompetensi (K di FKUKI
3. Surat Keputusan Rektor UKI No. 90/UKI.R/SK/SDM.8/2018 tent pengangkatan Dekan Fakultas Kedokteran UKI
4. Surat keputusan pengangkatan sebagai tenaga akademik

MEMUTUSKAN

MENETAPKAN : 1. Penugasan dalam memberikan Kuliah Pakar :

Nama	dr. Fajar L. Gultom, Sp.PA
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Judul Materi	Histopatologi saraf
Semester	genap 2020/2021
Kelas	A : 0,21 SKS
	B : 0,21 SKS
SKS	0,42 SKS

2. Apabila dikemudian hari ternyata terdapat kekeliruan dalam Surat Kepu ini akan diperbaiki sebagaimana mestinya

Asli Surat Keputusan ini disampaikan kepada yang bersangkutan untuk diketahui

Ditetapkan di : Jakarta
Pada tanggal : 09 Maret 2021
Dekan,

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NIP. UKI. 031 545

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Neuropathology

Fajar L. Gultom
Departemen Patologi Anatomik
FK UKI
Maret 2021

1

SISTEM SARAF

No		Daftar Penyakit	Tingkat Kemampuan
Geneti	**Tumor Sistem Saraf Pusat**		
1	19	Tumor primer	2
2	20	Tumor sekunder	2
Gangg	**Penurunan Kesadaran**		
3	21	Ensefalopati	3B
4	22	Koma	3B
Infeksi	23	Mati batang otak	2
5	**Nyeri Kepala**		
6	24	*Tension headache*	**4A**
7	25	Migren	**4A**
8	26	Arteritis kranial	**1**
9	27	Neuralgia trigeminal	**3A**
10	28	*Cluster headache*	**3A**
11	**Penyakit Neurovaskular**		
12	29	TIA	**3B**
13	30	Infark serebral	**3B**
14	31	Hematom intraserebral	**3B**
15	32	Perdarahan subarakhnoid	**3B**
16	33	Ensefalopati hipertensi	**3B**
17			
18			

	Penyakit pada Tulang Belakang dan Sumsum Tulang Belakang		
	47	*Amyotrophic lateral sclerosis (ALS)*	1
	48	*Complete spinal transaction*	3B
	49	Sindrom kauda equine	2
	50	*Neurogenic bladder*	3A
	51	Siringomielia	2
	52	Mielopati	2
Lesi Kra	53	*Dorsal root syndrome*	2
34	54	*Acute medulla compression*	3B
35	55	*Radicular syndrome*	3A
Ganggua	56	*Hernia nucleus pulposus (HNP)*	3A
36	**Trauma**		
37	57	Hematom epidural	2
38	58	Hematom subdural	2
	59	Trauma Medula Spinalis	2
Defisit M	**Nyeri**		
39	60	*Reffered pain*	3A
40	61	Nyeri neuropatik	3A
Ganggua	**Penyakit Neuromuskular dan Neuropati**		
41	62	Sindrom Horner	2
42	63	*Carpal tunnel syndrome*	3A
Epilepsi d	64	*Tarsal tunnel syndrome*	3A
43	65	Neuropati	3A
44	66	*Peroneal palsy*	3A
45	67	*Guillain Barre syndrome*	3B
	68	Miastenia gravis	3B
Penyakit	69	Polimiositis	1
46	70	Neurofibromatosis (*Von Recklaing Hausen disease*)	2
	Gangguan Neurobehaviour		
	71	Amnesia pascatrauma	3A
	72	Afasia	2
	73	*Mild Cognitive Impairment (MCI)*	2

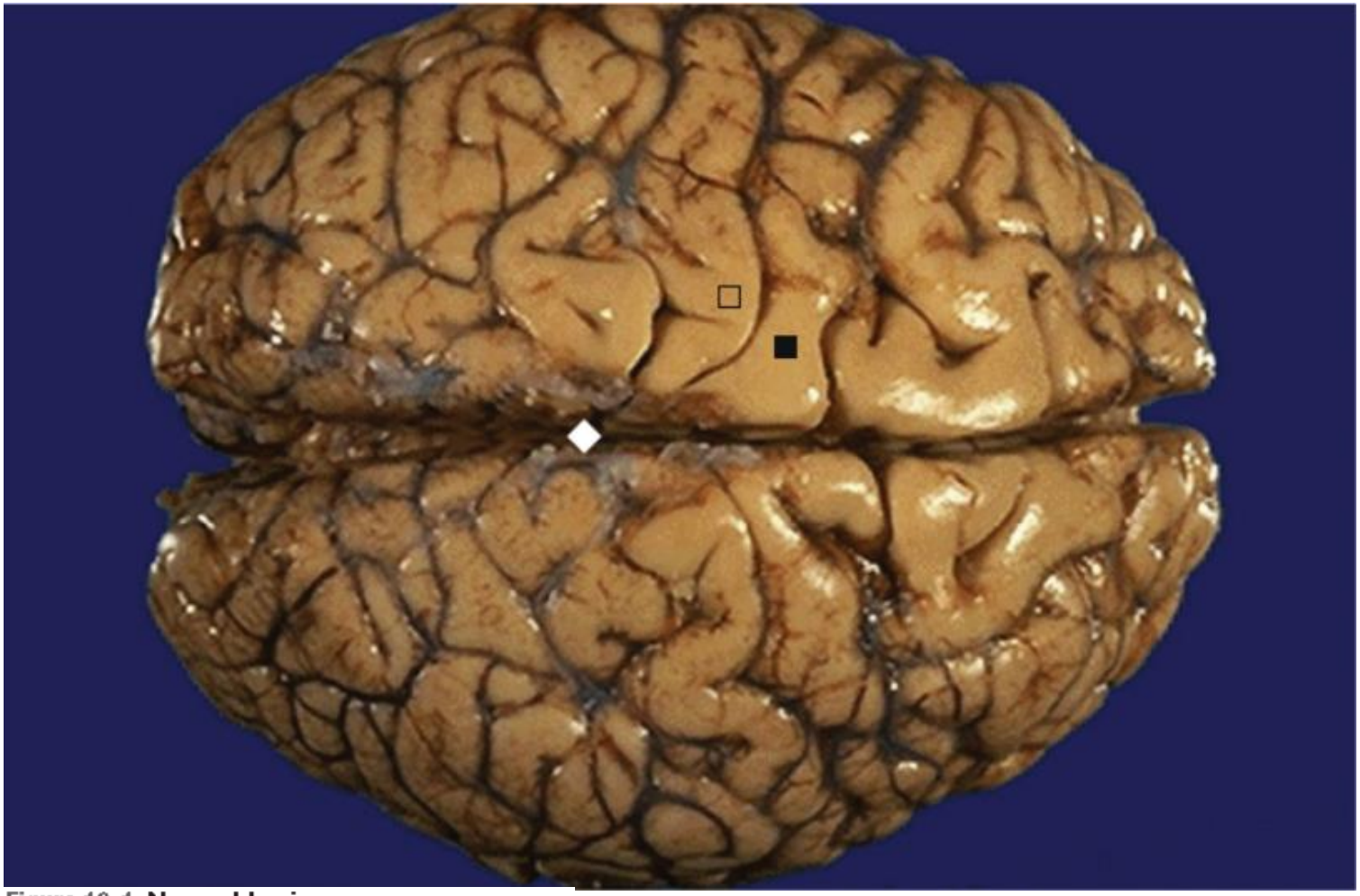


Figure 19-1 Normal brain, gross
The superior aspect at the vertex of an adult brain is shown here with the central sulcus (◆) between the right and left hemispheres. Note the pattern of gyri and sulci beneath the thin, filmy meninges (pia and arachnoid layers; the overlying dura has been removed). The rolandic fissure with the precentral gyrus (■) (motor cortex) and the postcentral gyrus (□) (somesthetic cortex) are shown here. The normal adult brain weighs 1100 to 1700 g.

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

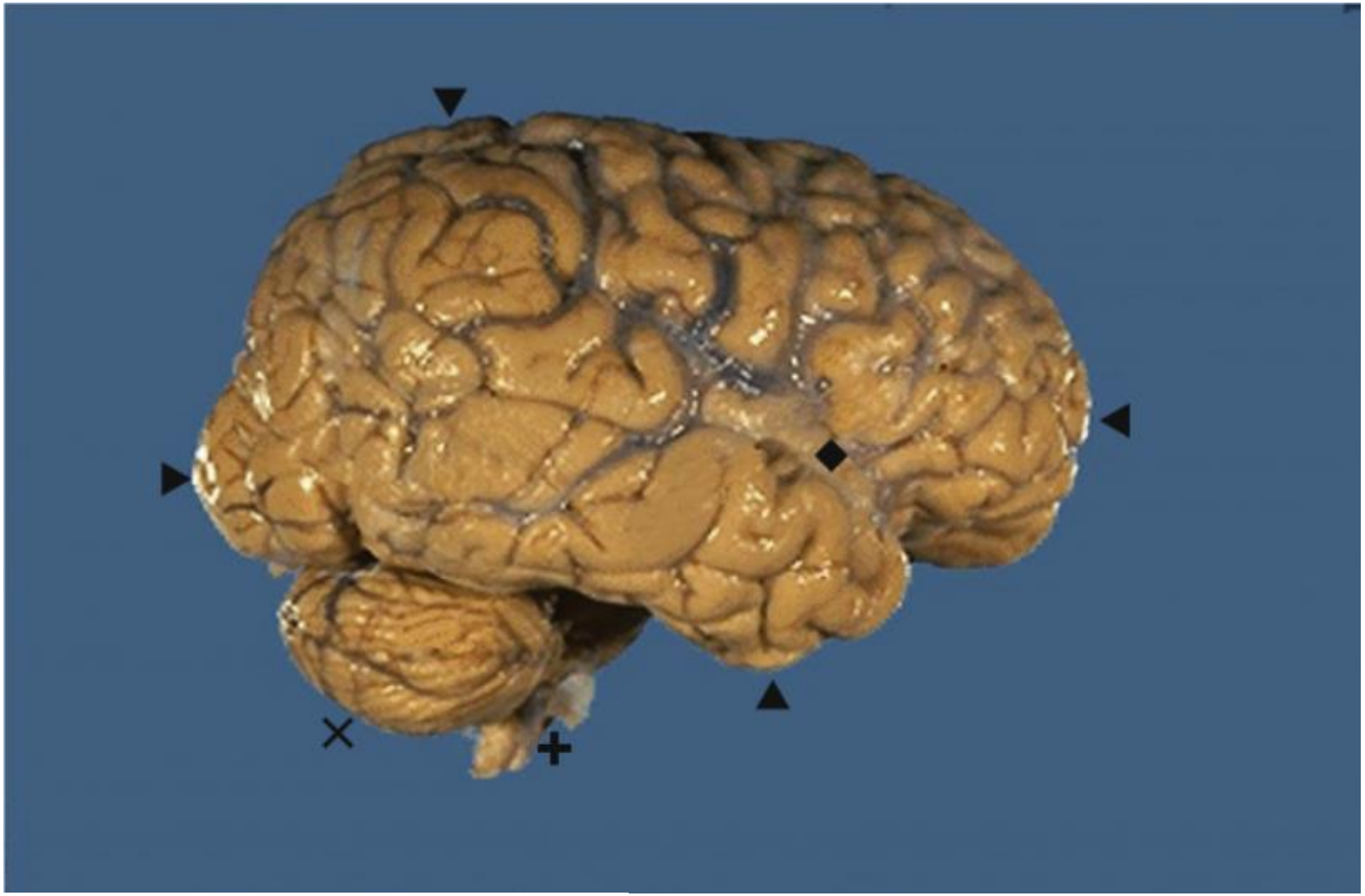


Figure 19-2 Normal brain, gross
The lateral view of the brain reveals the frontal lobe (◀), parietal lobe (▼),temporal lobe (▲), occipital lobe (▶), cerebellum (✕), and brain stem (✚). Note the sylvian fissure (◆) separating the frontal lobe from the temporal lobe.

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

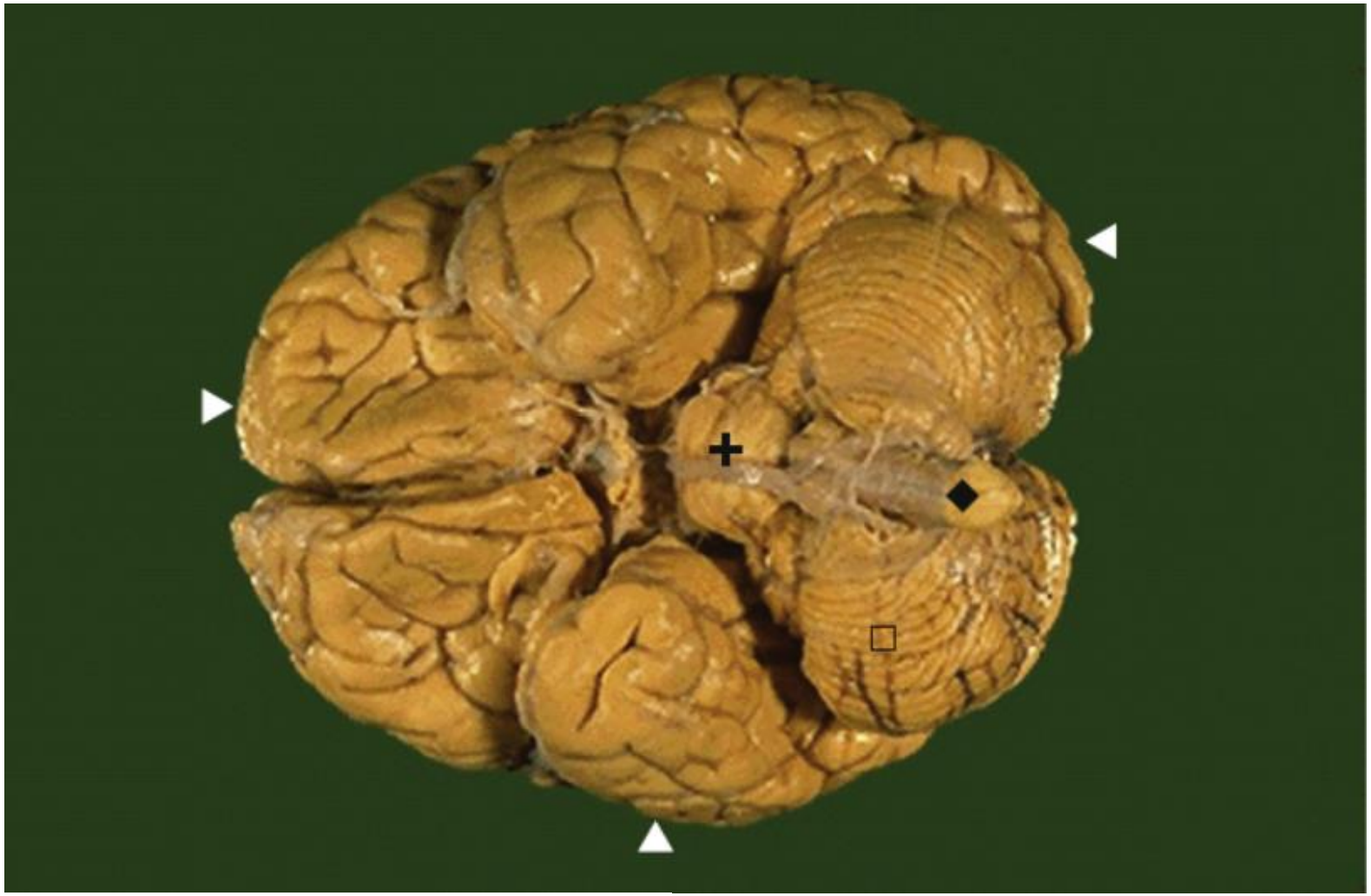


Figure 19-3 Normal brain, gross
At the base of the brain can be seen the inferior frontal lobes (▶), temporal lobes (▲), pons (✚), medulla oblongata (◆), cerebellar hemispheres (□), and occipital lobes (◀).

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

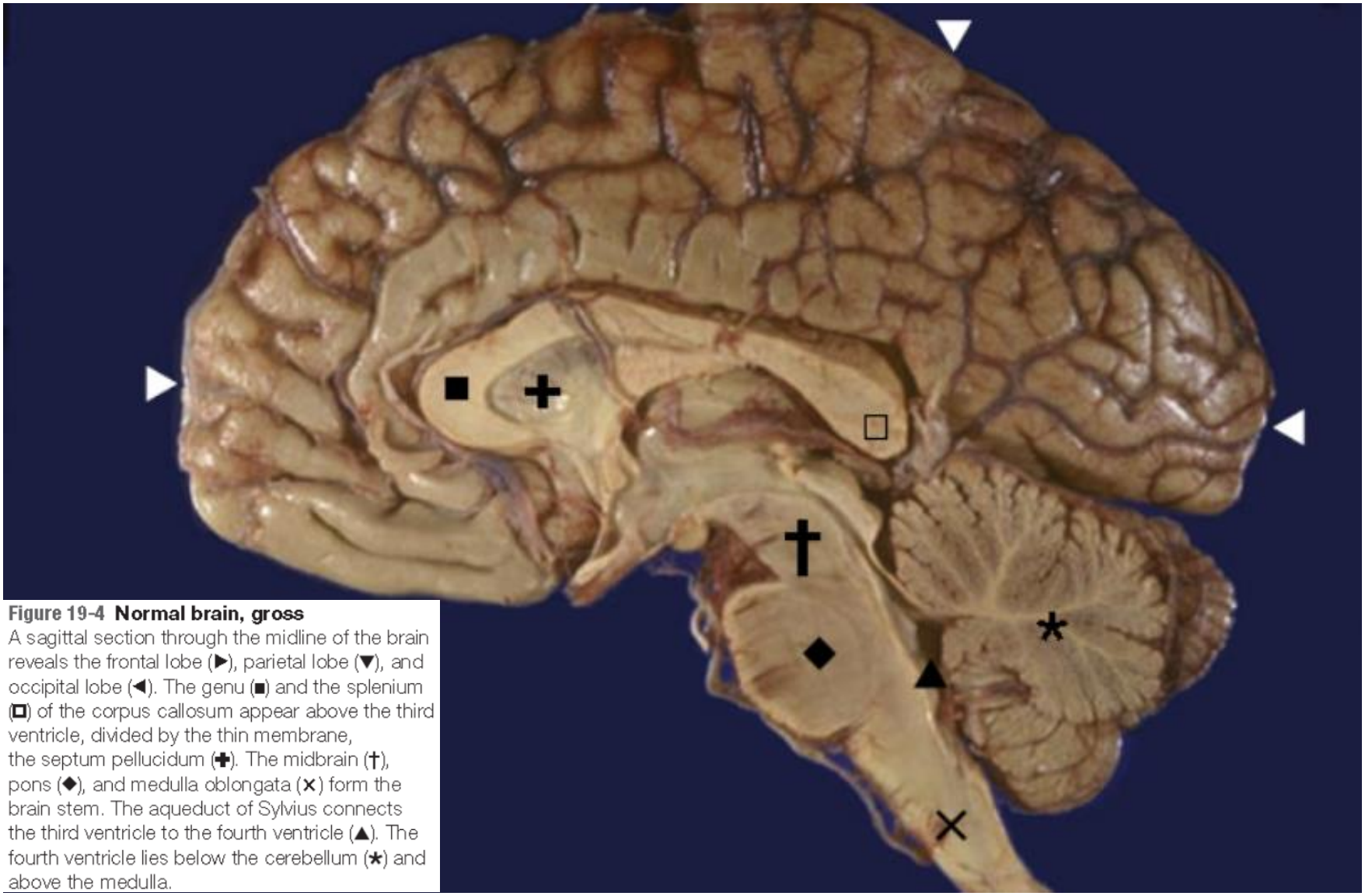


Figure 19-4 Normal brain, gross
A sagittal section through the midline of the brain reveals the frontal lobe (▶), parietal lobe (▼), and occipital lobe (◀). The genu (■) and the splenium (□) of the corpus callosum appear above the third ventricle, divided by the thin membrane, the septum pellucidum (✚). The midbrain (†), pons (◆), and medulla oblongata (✕) form the brain stem. The aqueduct of Sylvius connects the third ventricle to the fourth ventricle (▲). The fourth ventricle lies below the cerebellum (★) and above the medulla.

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

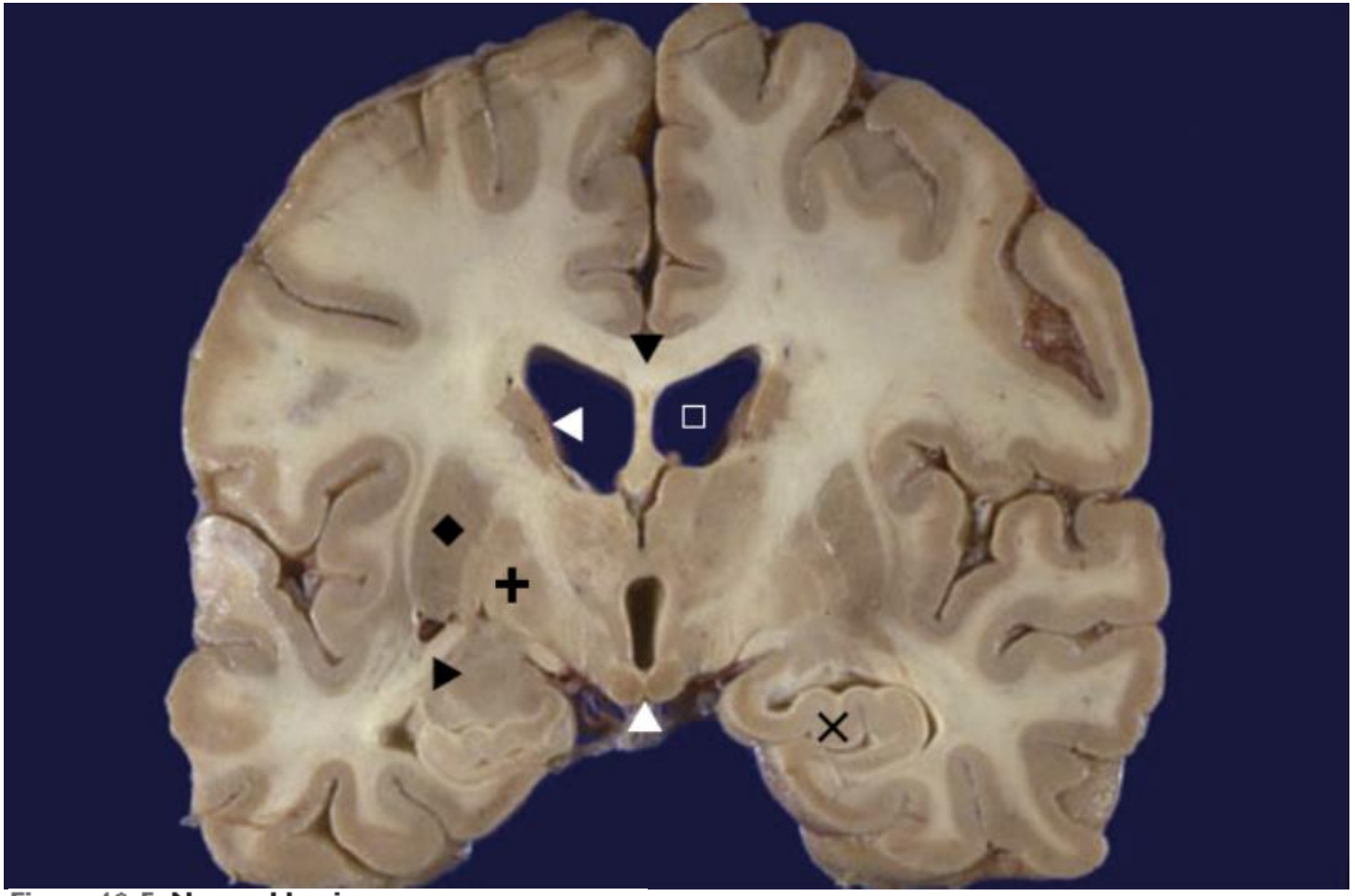


Figure 19-5 Normal brain, gross
This coronal section through the center of the brain reveals the mammillary bodies (▲), globus pallidus (✚), putamen (◆), caudate nucleus (◀), lateral ventricles (◘), corpus callosum (▼), and hippocampus (✕). This section is not completely symmetrical (as is the case with many CT scans and MRI images), so the amygdala (▶) appears on just one side.

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

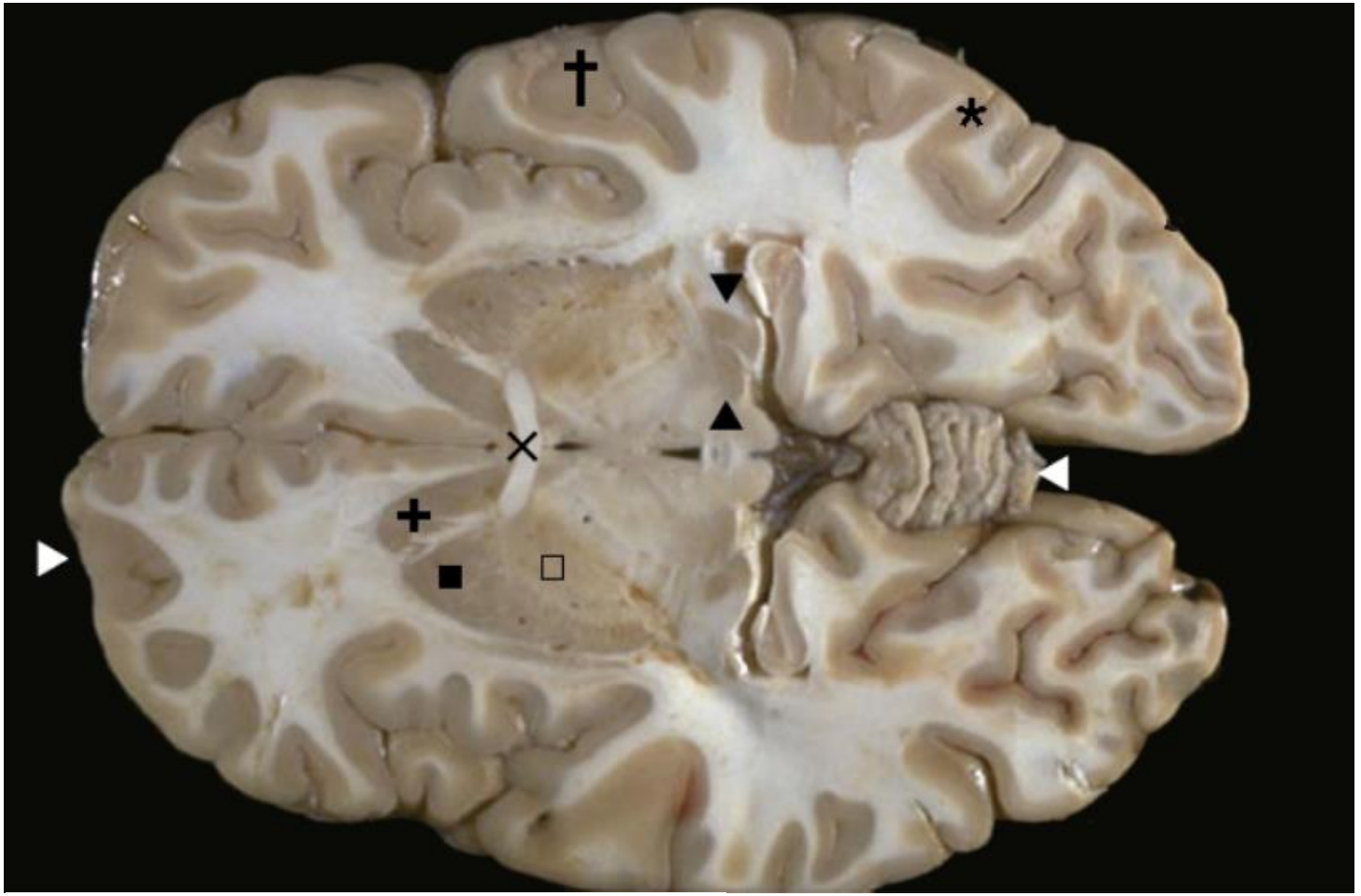


Figure 19-6 Normal brain, gross
This axial (transverse) section through the brain reveals the frontal lobe (▶), caudate nucleus (✚), anterior commissure (✕), putamen (■), globus pallidus (□), medial (▲) and lateral (▼) geniculate nuclei, temporal lobe (†), parietal lobe (✱), and anterior vermis (◀) of the cerebellum.

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

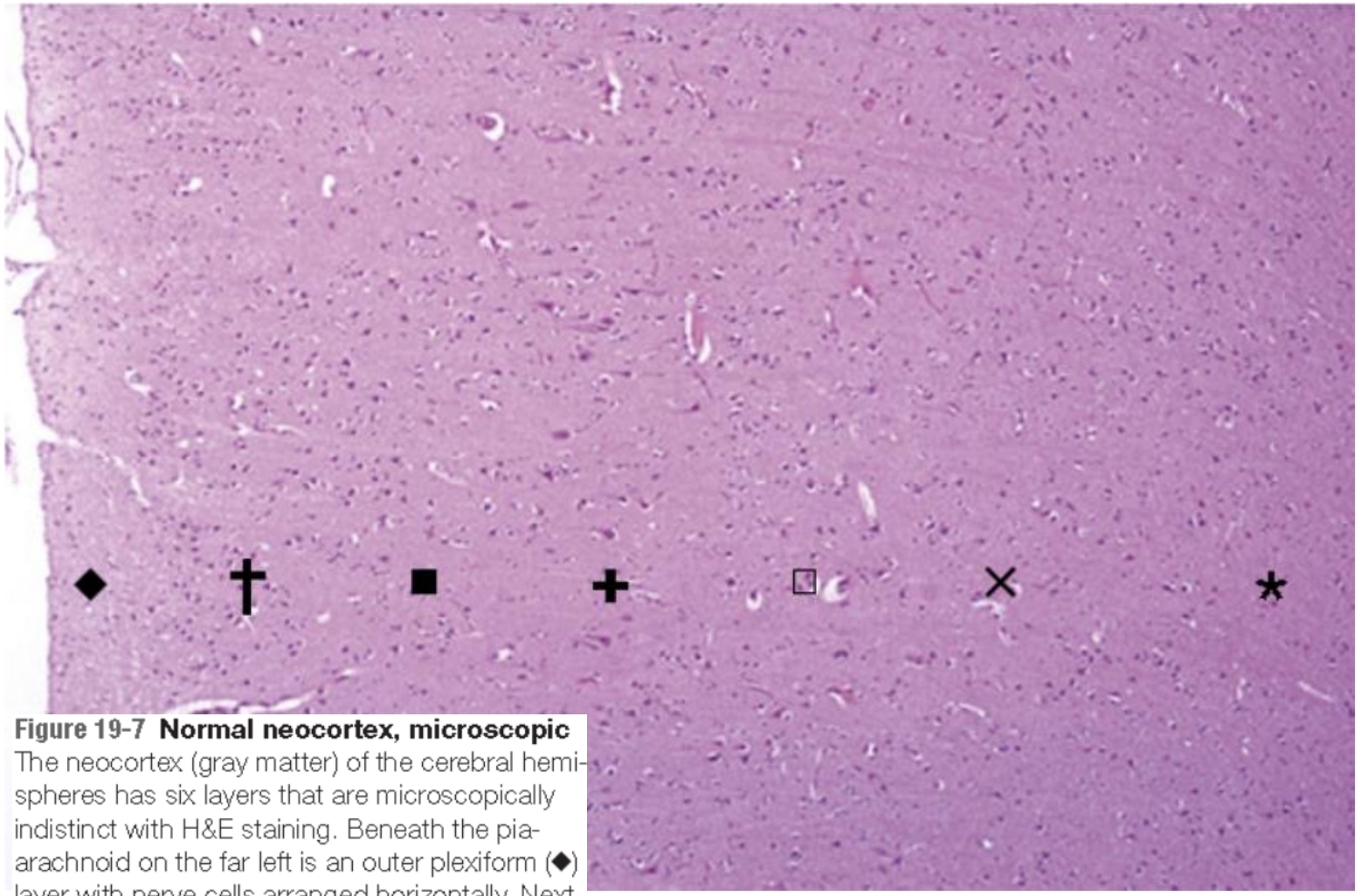


Figure 19-7 Normal neocortex, microscopic
The neocortex (gray matter) of the cerebral hemispheres has six layers that are microscopically indistinct with H&E staining. Beneath the pia-arachnoid on the far left is an outer plexiform (◆) layer with nerve cells arranged horizontally. Next is the outer granular layer (†) containing small pyramidal neurons. Next is the outer pyramidal cell layer (■) with medium-sized pyramidal neurons. Below this is the inner granular layer (✚) of larger pyramidal neurons. Beneath this is the inner pyramidal layer (□) of larger pyramidal neurons. The innermost cortical layer is the polymorphous layer (×), which lacks pyramidal cells. Beneath the cortex is the white matter (★).

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

Cellular in CNS

- Neurons
- Glial: astrocyte, oligodendrocyte, ependyma
- Microglia → macrophages CNS

Neurons

- Principal functional unit of the CNS.
- Receive and transmit information.
- Components:
  - Soma/ body
  - Dendrites
  - Axon
- **Incapable** of cell division → destruction → **neurologic deficit.**

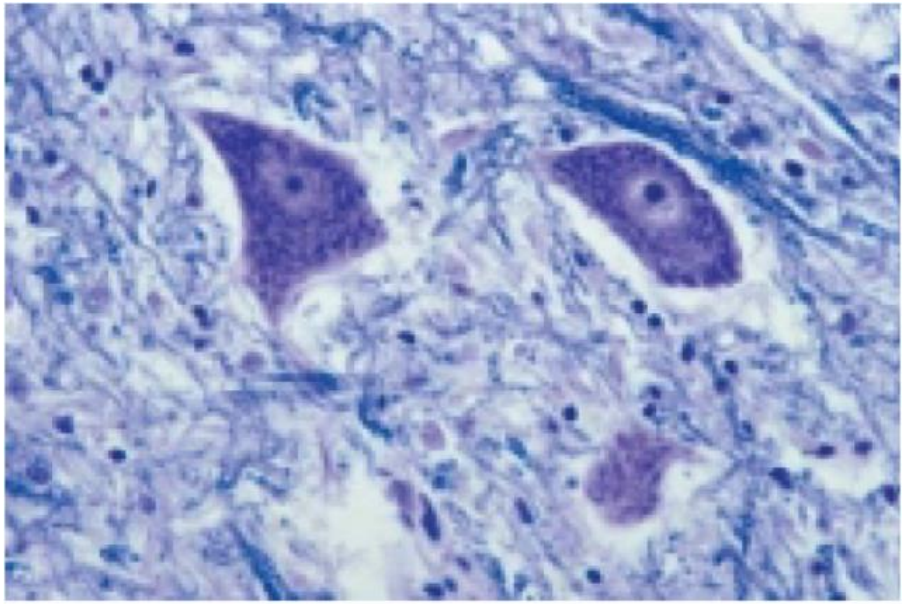


Figure 3.1 Normal neuron. Ventral horn cells from human lumbar spinal cord. The nucleus is round and centrally placed, and contains a prominent nucleolus: the cytoplasm contains large numbers of Nissl bodies that extend into dendrites. Luxol fast blue/cresyl violet.

Adam and Graham's introduction to neuropathology, 2006

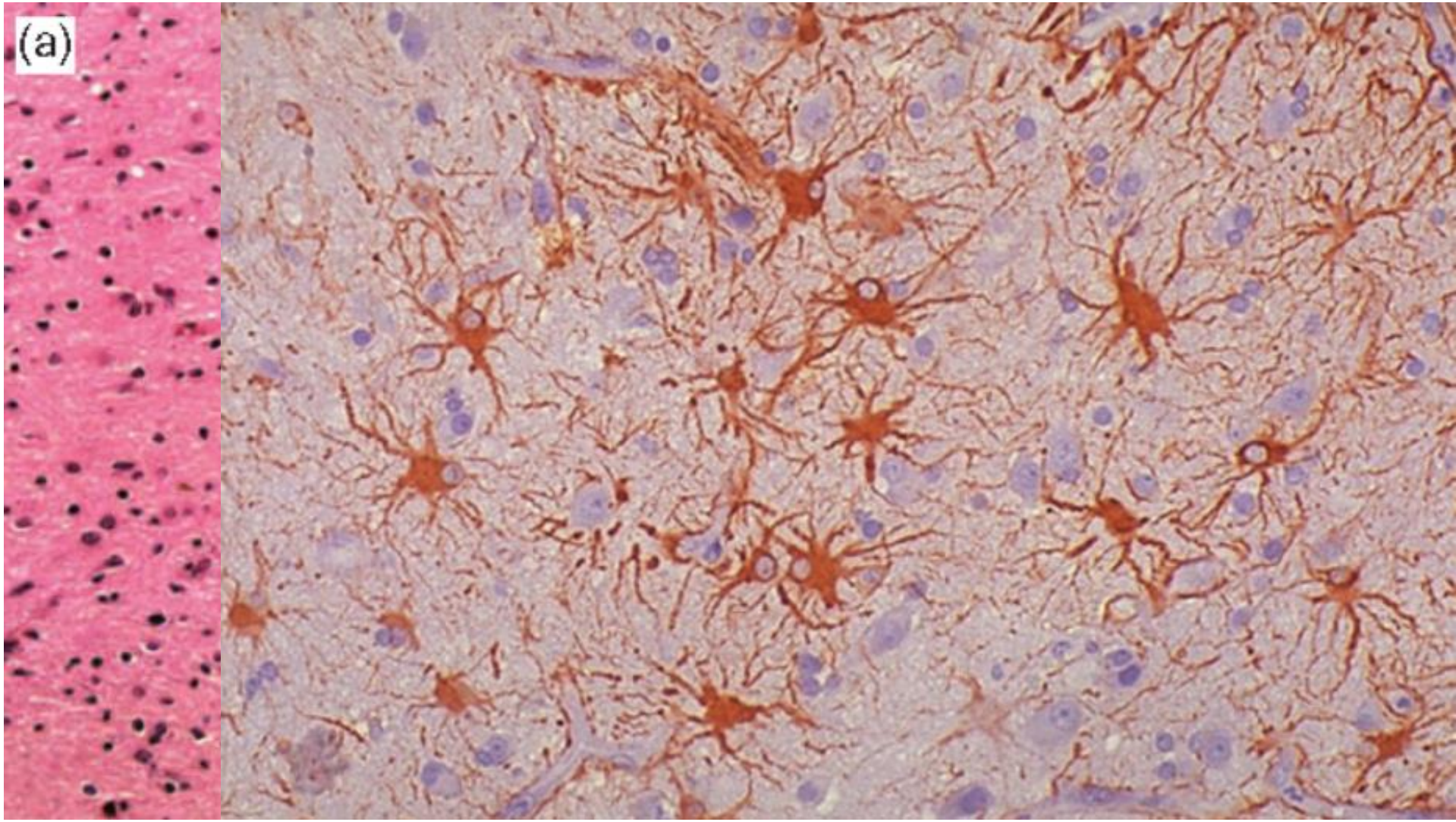
Glial

- More numerous than neuron (± 90% CNS cells).
- Retain capacity to **proliferate**.
- "Glue" → providing structural and functional support for neuron.
- CNS injury → glial cells mobilize, clean up debris, seal off local area → glial scar (gliosis).
- Most brain tumors (benign/ malignant)→ glial origin!!

Astrocyte

- Star shaped appearance.
- Two categories: fibrous and protoplasmic.
- Presence of large number glial filament → GFAP (Glial Fibrillary Acidic Protein).
- Metabolic buffers, detoxifiers, CNS development & regeneration, barrier function (foot process surround capilers).

Astrocyte

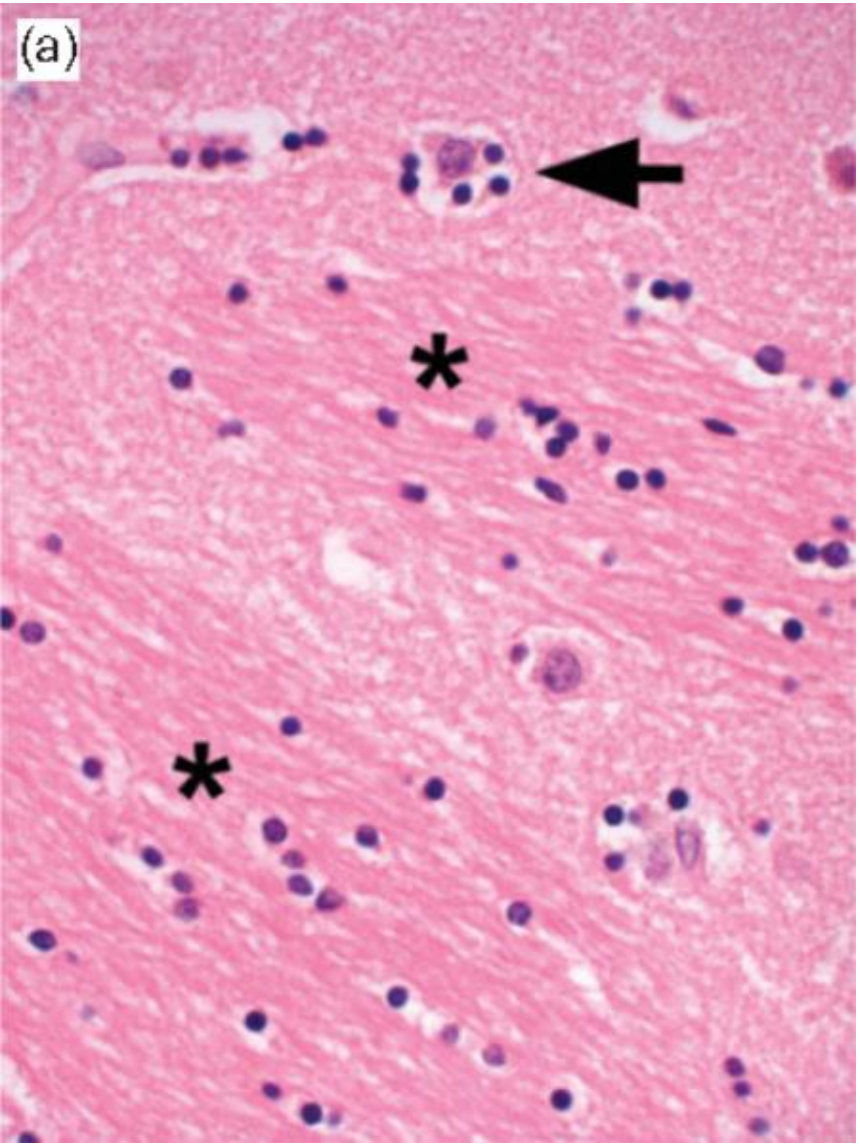


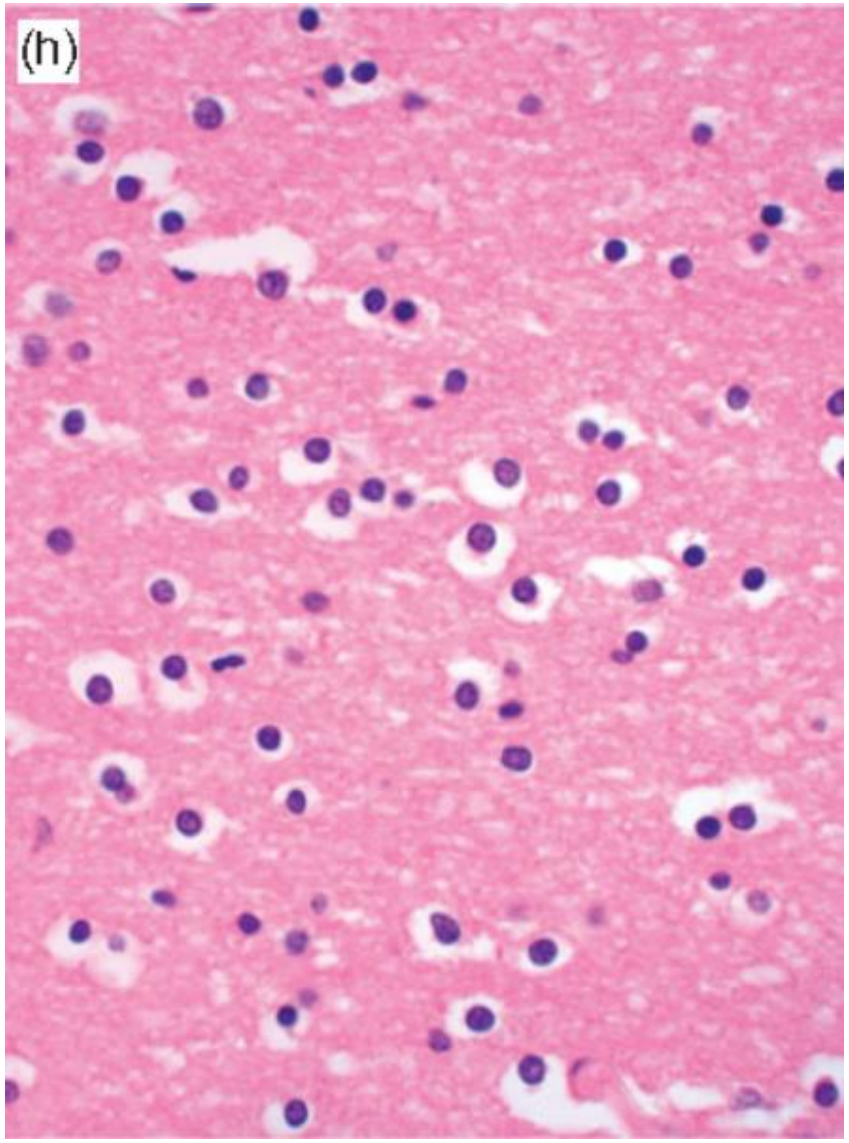
Histology and cell biology an introduction to pathology. 4ed. 2016.

Oligodendrocyte

- Small cell bodies, few short processes and no cytoplasmic filaments.
- Cluster around neuron cell.
- Function: myelin formation, axonal support and maintenance.
- H&E stain: round nucleus, evenly dispersed chromatin, no nucleolus, no visible cytoplasm (perinuclear halo/ fried egg appearance)

Oligodendrocyte





Greenfield's neuropathology, 8th ed. 2008

Reactions of Neurons to Injury

- Neurons → continuos supply glucose and oxygen.
- Acute process: depletion of glucose/ oxygen, trauma.
- Slower process, subacute/ chronic: accumulation of abnormal protein aggregates → degenerative disorder of brain (amyotrophic lateral sclerosis, Alzheimer disease)

Acute Neuronal Injury
Red Neurons

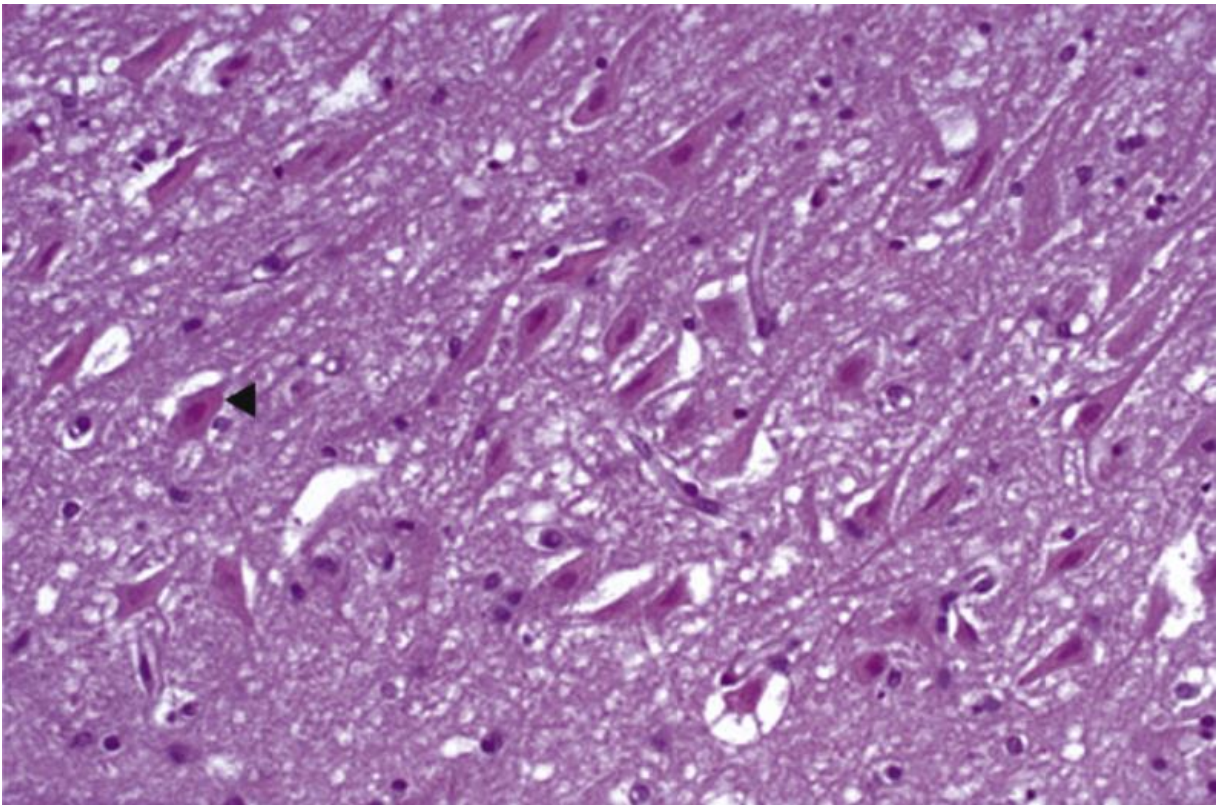


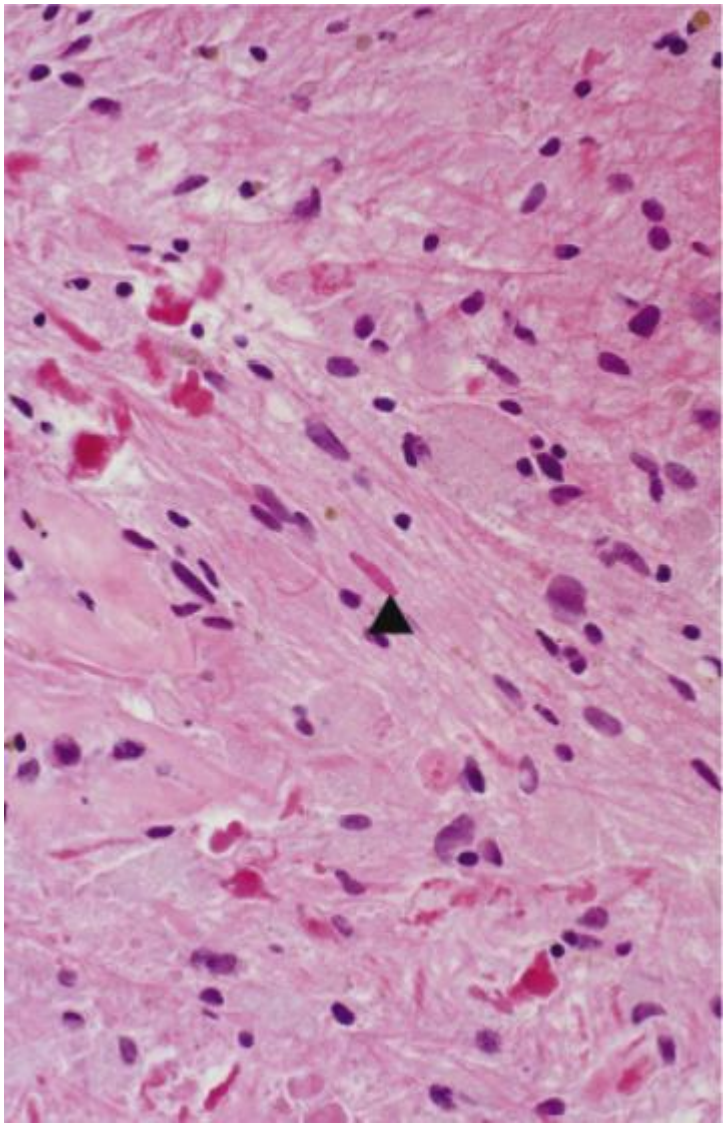
Figure 19-63 Hypoxic encephalopathy, microscopic
Neurons are highly differentiated cells that depend on glucose and oxygen for continued function, and they are very sensitive to hypoxic injury. Shown here are red neurons (◀) in cortex, which are dying 12 to 24 hours after onset of hypoxia. One of the most sensitive areas in the brain to hypoxic injury is the hippocampus. Cerebellar Purkinje cells and neocortical pyramidal neurons are also very sensitive to ischemic events. A global hypoxic encephalopathy occurs with reduction of all cerebral perfusion with reduced cardiac output and with hypotension. Intracranial vascular diseases may reduce blood flow focally to the brain, and the extent of injury depends on collateral circulation

Shrinkage, pyknosis nuclei, loss nucleoli, loss nissl substance, intense eosinophilia cytoplasm

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

Reactions of Astrocytes to Injury

- Gliosis → CNS injury → hypertrophy and hyperplasia of astrocytes.
- Nuclei enlarged, vesicular, prominent nucleoli
- Rosenthal fiber: longstanding gliosis



Robbins and Cotrans Atlas of pathology 3rd ed. 2015

Infection

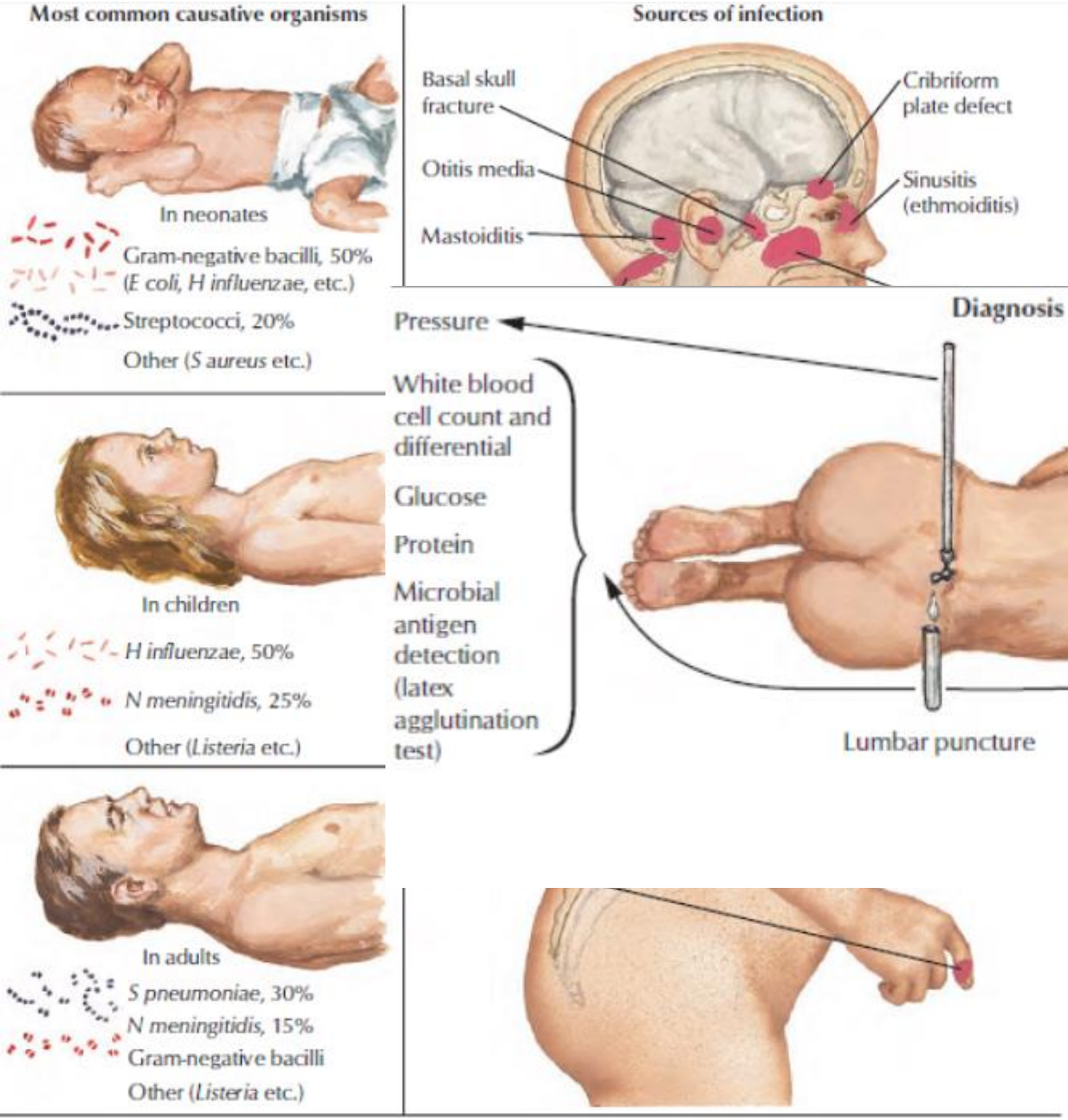
- Pathogens (virus, parasite, bacteria) → infect brain
- Routes (4):
  - Hematogenous **(most common)** → arterial circulation
  - Direct implantation → trauma/ congenital malformation
  - Local extention → infected adjacent structure (air sinuses, teeth, skull)
  - Retrograde transport along nerves → herpes zoster, rabies

Infection

- Meningitis → inflammatory process leptomeninges and CSF within subarachnoid space usually caused by infection.
- MeningoEncephalitis: meninges + brain parenchyme.
- Acute pyogenic (bacterial), aseptic (viral), chronic (tuberculous).

Infection

- Meningeal irritation and neurologic impairment: headache, photophobia, irritability, neck stiffness, consciousness <<
- Lumbal puncture:
  - WBC count → ?
  - Protein → ?
  - Glucose → ?
  - Bacteria → smear (gram) or cultured?



Bacterial meningitis: inflammation of leptomeninges and CSF, caused by spread of microorganism through blood stream from another sites.

Meningitis

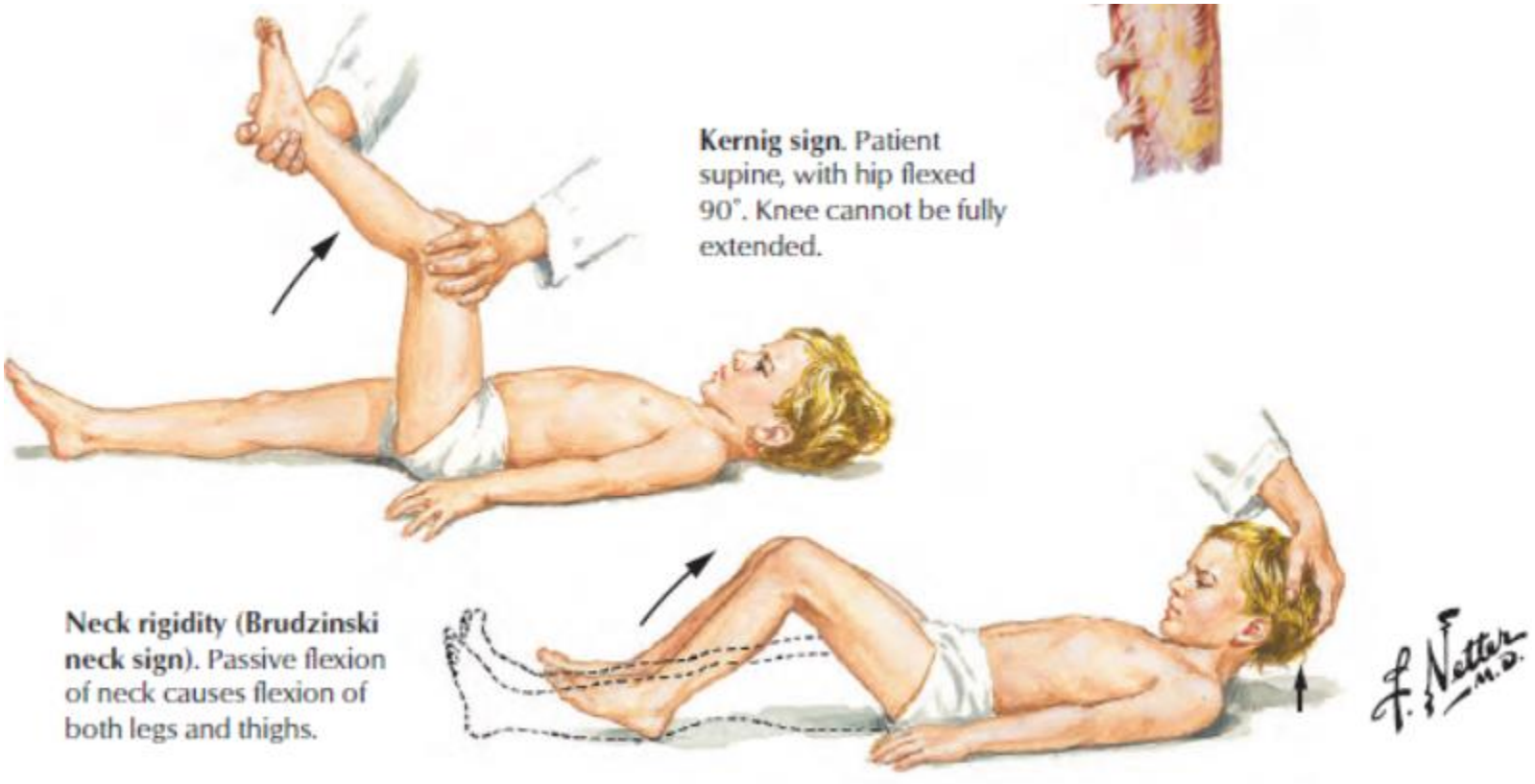

Kernig sign. Patient supine, with hip flexed 90°. Knee cannot be fully extended.
Neck rigidity (Brudzinski neck sign). Passive flexion of neck causes flexion of both legs and thighs.
F. Netter M.D.

Table 28-2 Com

Type of Infection			
Bacterial Infecti			
Meningitis	Meningitis	Acute aseptic meningitis	Enteroviruses Measles (subacute sclerosing
	Encephalitis		Venezuelan equine encephalitis virus Japanese encephalitis virus Tick-borne encephalitis virus
Localized infections	Brainstem and spinal cord syndromes	Rhombencephalitis Spinal poliomyelitis	Rabies Polio West Nile virus
	Rickettsia, Spirochetes, and Fungi		
	Meningitic syndromes	Rocky Mountain spotted fever	*Rickettsia rickettsii*
		Neurosyphilis	*Treponema pallidum*
		Lyme disease (neuroborreliosis)	*Borrelia. burgdorferi*
		Fungal meningitis	*Cryptococcus neoformans* *Candida albicans*
	Protozoa and Metazoa		
	Meningitic syndromes	Cerebral malaria	*Plasmodium falciparum*
		Amebic encephalitis	*Naegleria* species
	Localized infections	Toxoplasmosis	*Toxoplasma gondii*
		Cysticercosis	*Taenia solium*

Robbins Pathologic Basis of Disease 9th ed, 2015

Acute Meningitis

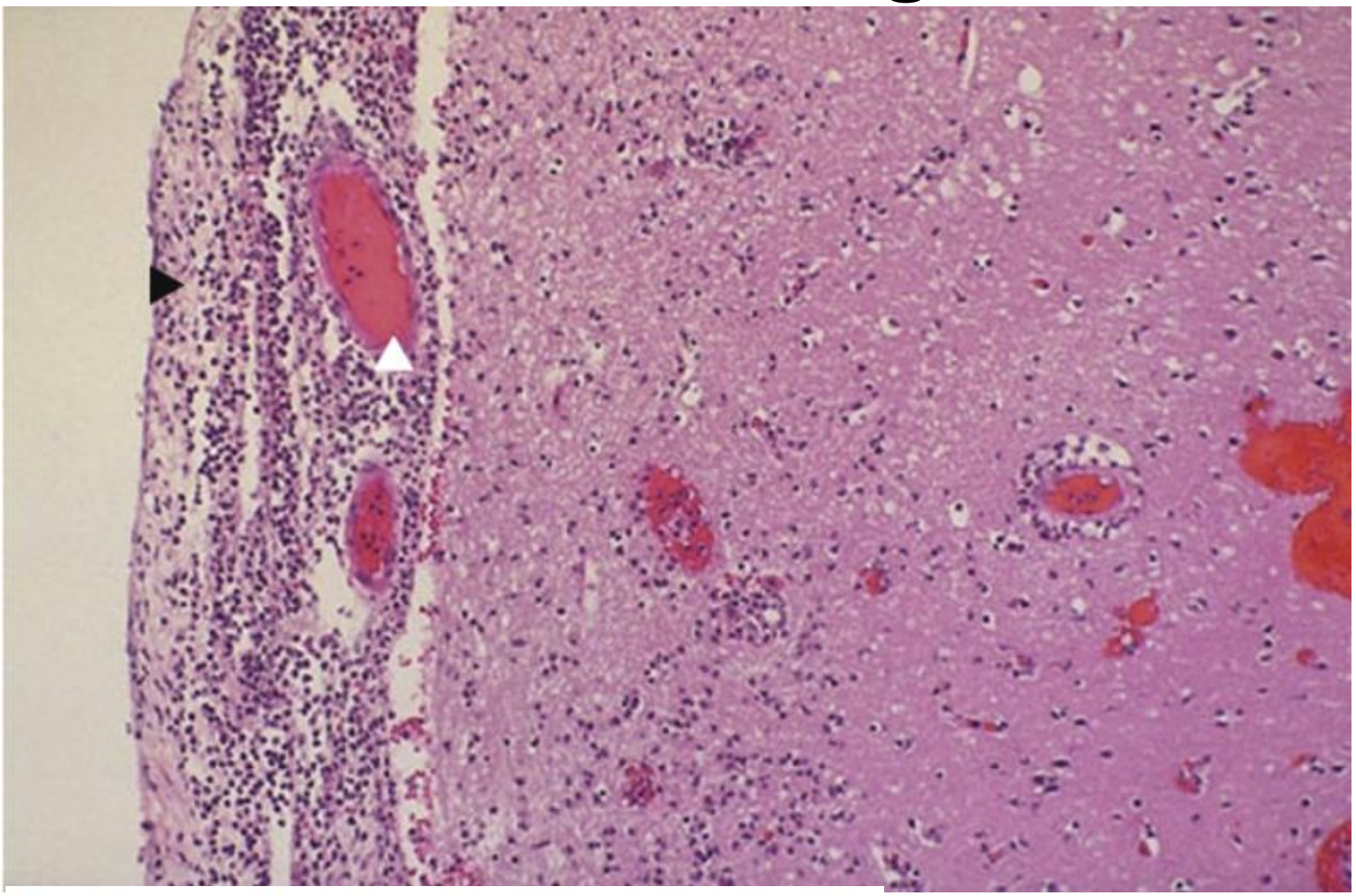


Figure 19-84 Acute meningitis, microscopic
A neutrophilic exudate (▶) involves the meninges on the left, with prominent dilated vessels (▲).

Robbins and Cotrans Atlas of pathology 3rd ed. 2015

Cerebral Abscess

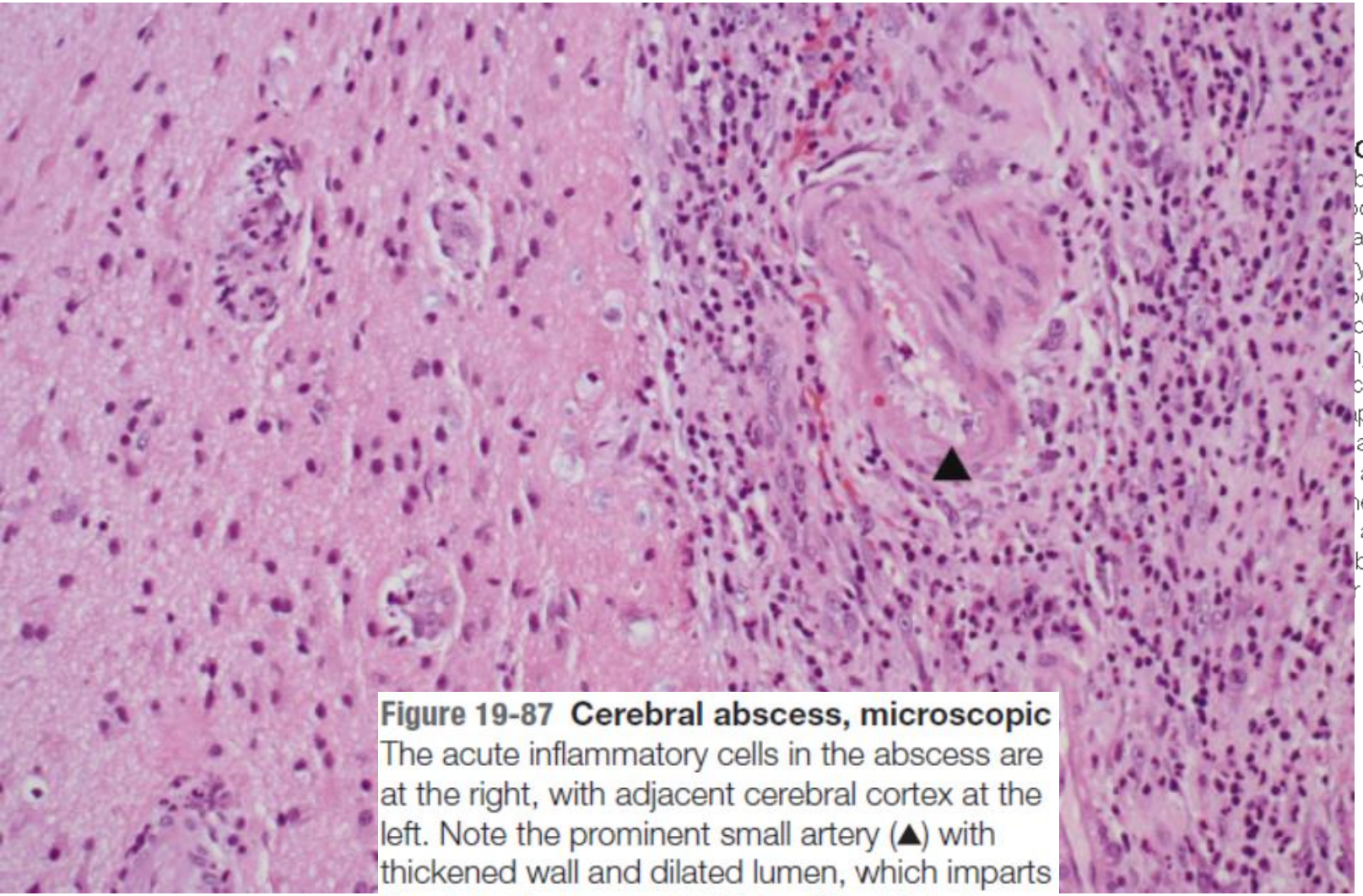
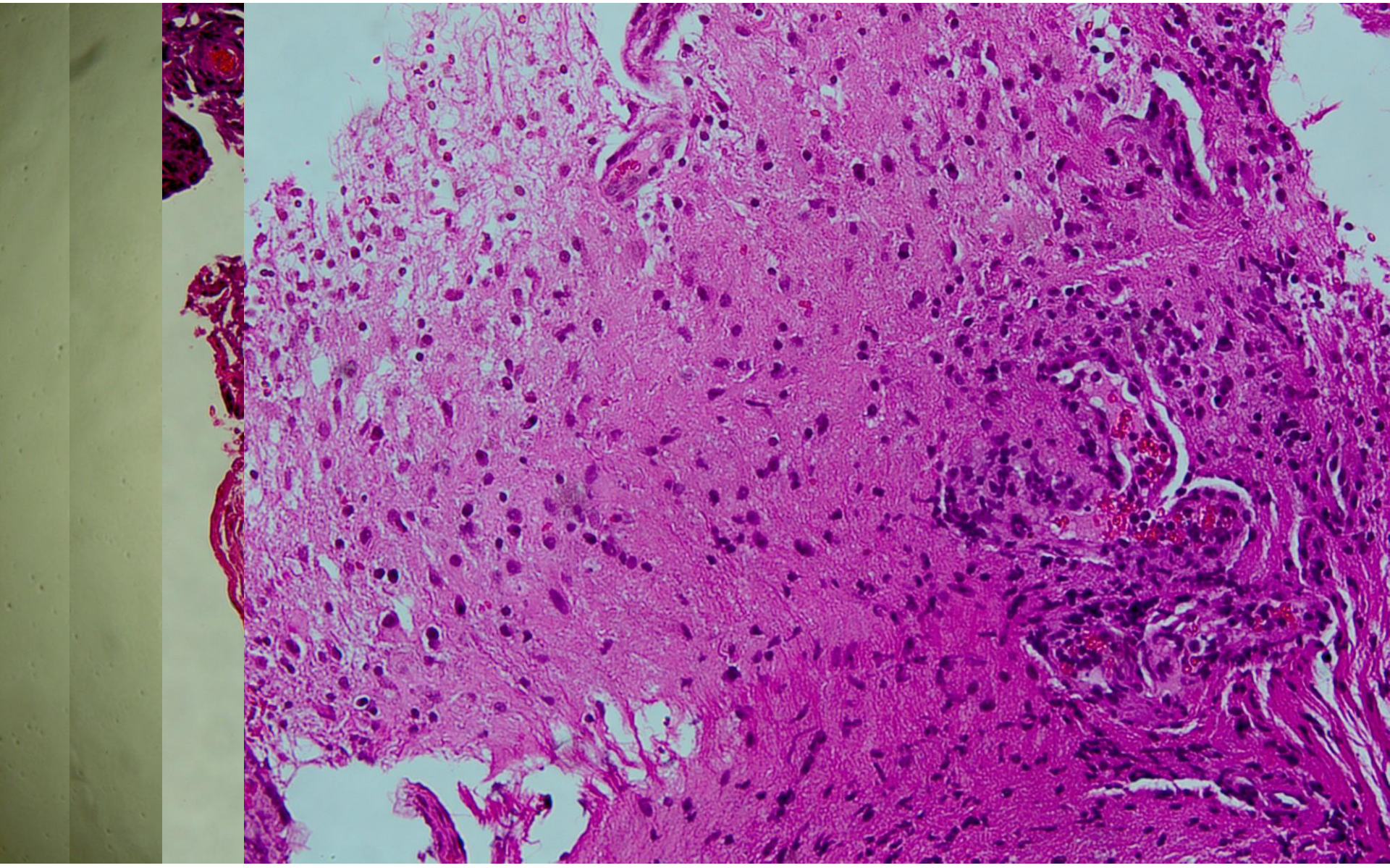


Figure 19-87 Cerebral abscess, microscopic The acute inflammatory cells in the abscess are at the right, with adjacent cerebral cortex at the left. Note the prominent small artery (▲) with thickened wall and dilated lumen, which imparts the ring enhancement visible with radiologic scans.

CT image
be displays prominent
order (▼) caused by the
ation tissue that contains
y of the abscess. Most
ococcal or streptococc-
destructive of brain
n, often with surrounding
cause herniation. The
pilledema observed on
a lumbar puncture, an
and examination of the
eutrophilia, along with
a decrease in glucose.
by rupture and spread
cerebral venous sinus

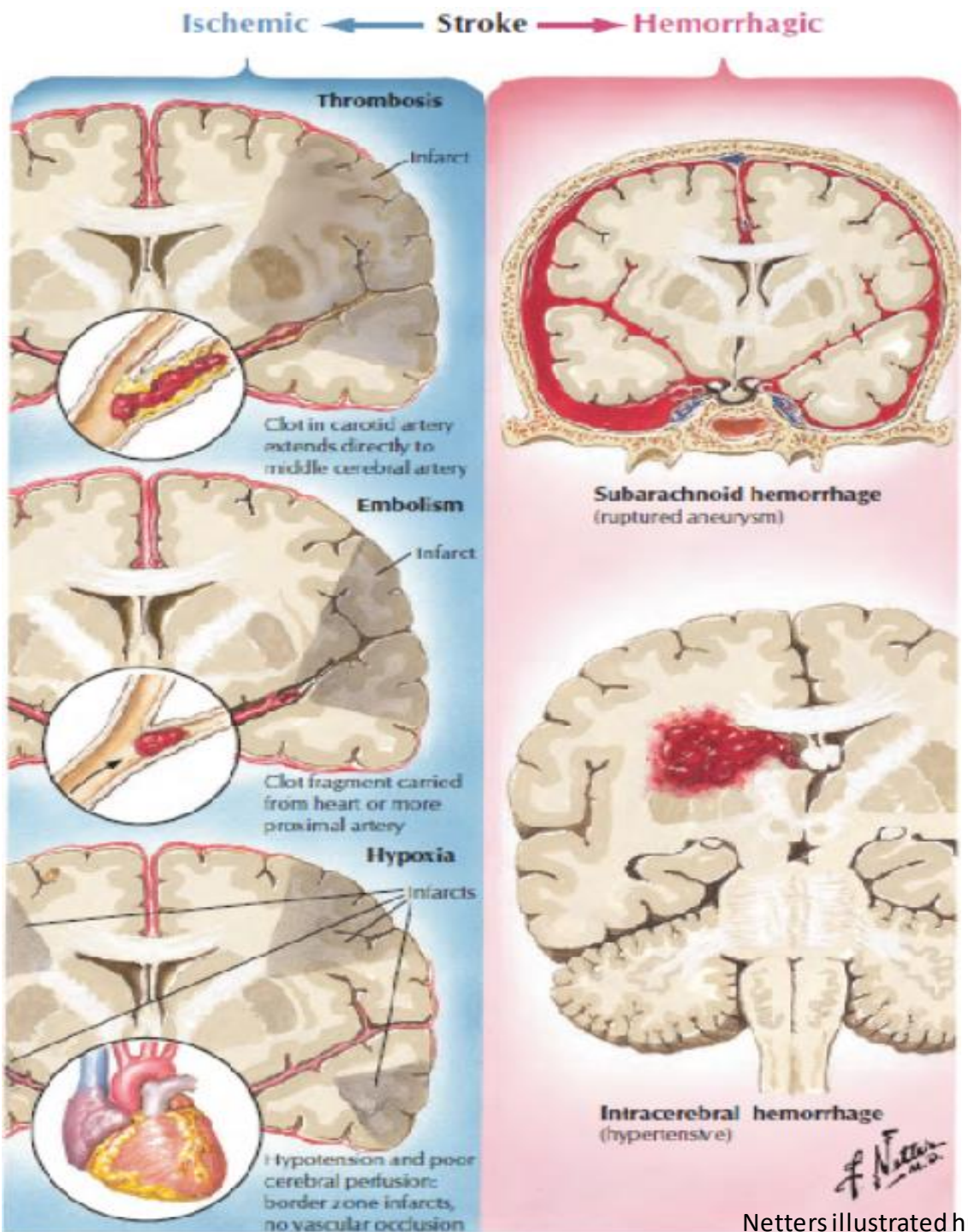
Robbins and Cotrans Atlas of pathology 3rd ed. 2015

Chronic Meningitis ec M. Tb

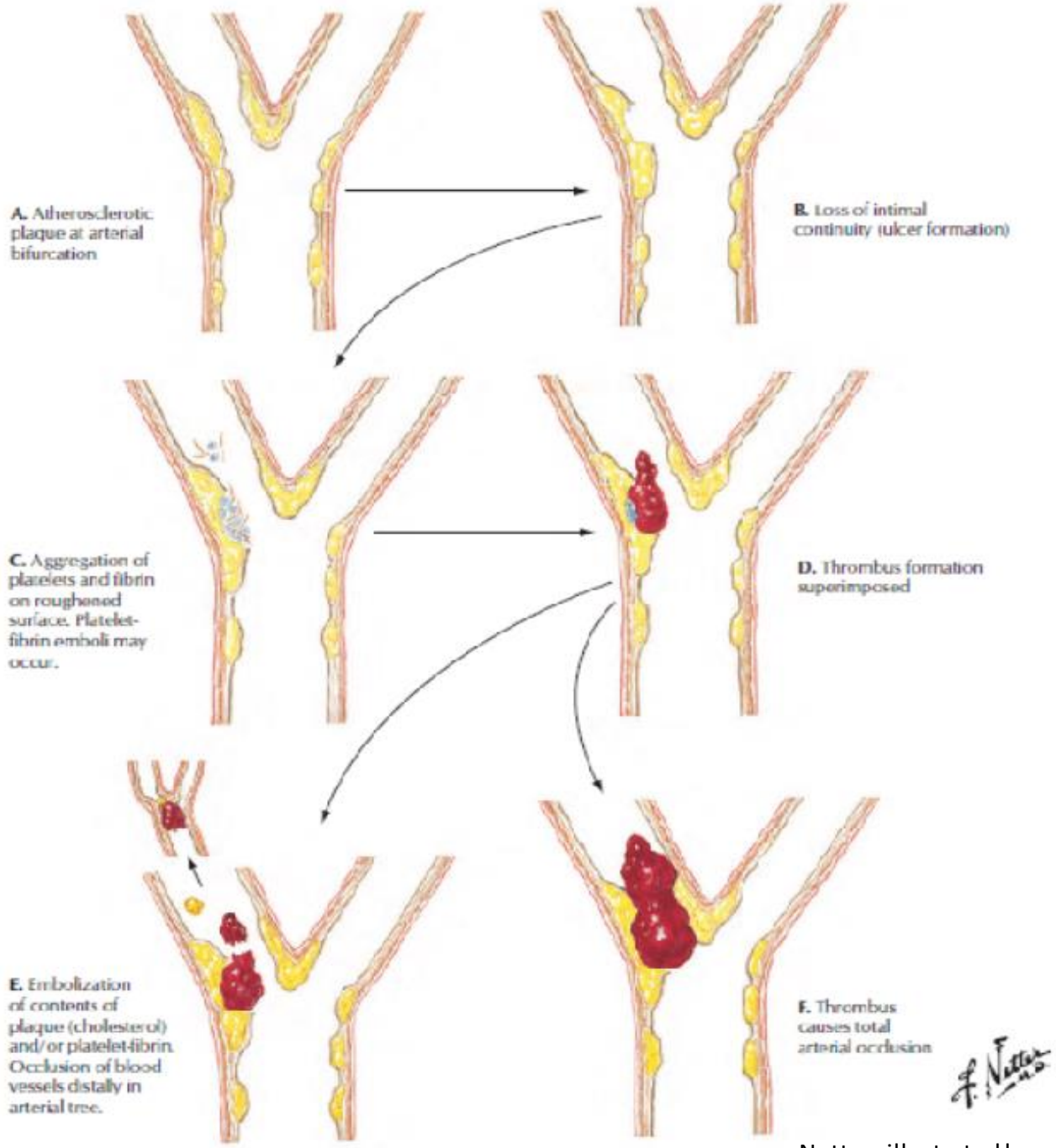


Cerebrovascular Disease

- Injury to brain → altered blood flow
- Etiologies: ischemic – hemorrhagic
- Stroke → Clinical term **acute onset neurologic deficit** resulting from hemorrhagic/ obstructive **vascular lesion**
- 3rd COD in US after heart disease and cancer
- Two process → ischemic – hemorrhagic



Netters illustrated human pathology, 2nd ed. 2014

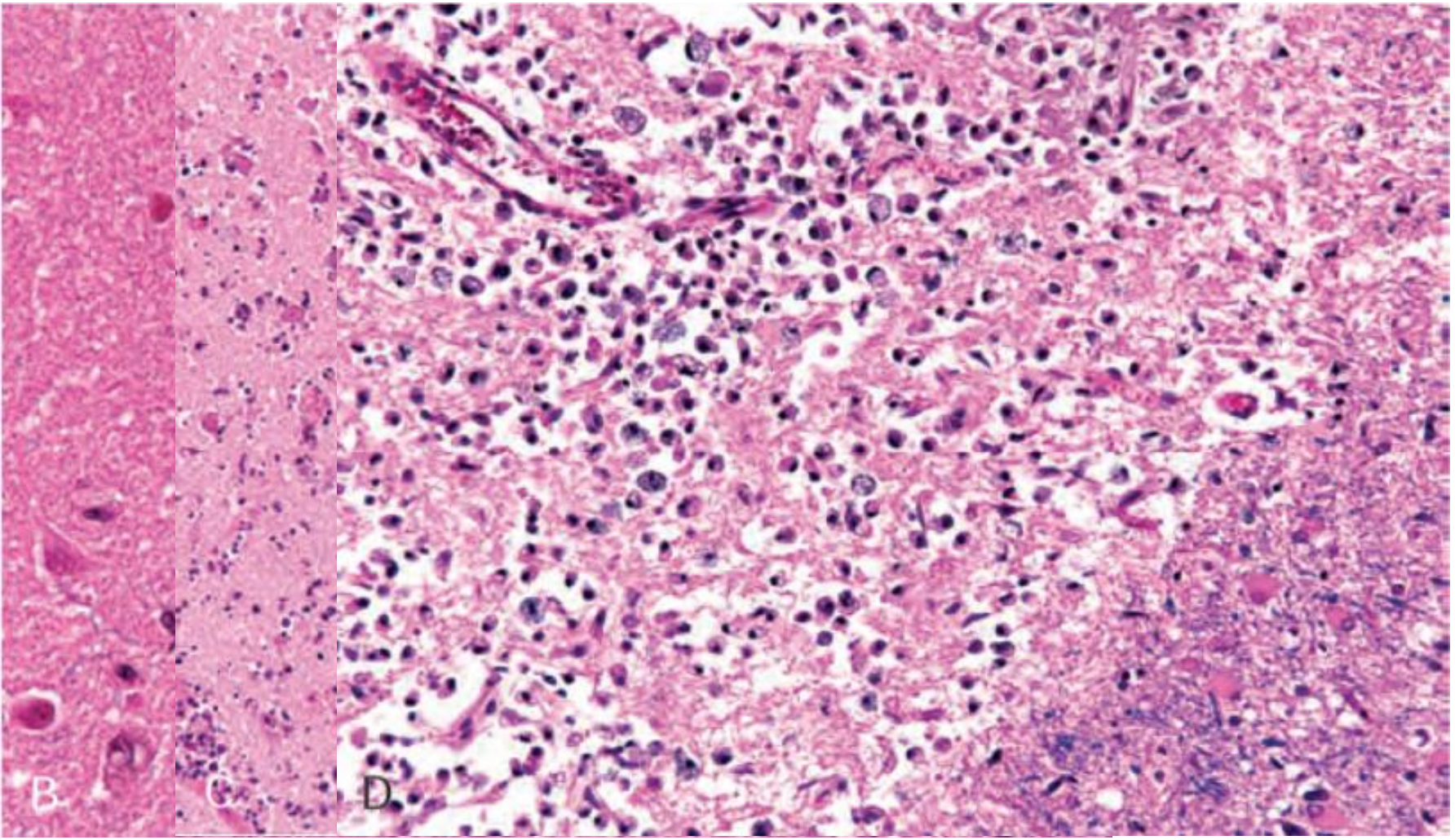


Netters illustrated human pathology, 2nd ed. 2014

Hypoxia, Ischemic and Infarction

- Brain → constant supply glucose and oxygen
- Deprivation O2:
  - Hypoxia
  - Ischemia
- Tissue survival: collateral circulation, duration ischemia, magnitude n rapidity flow reduction
- Global cerebral ischemia (diffuse): cardiac arrest, shock, severe hypotension.
- Focal cerebral ischemia

Cerebral Infarction



Acute ischemic injury. B. diffuse neuronal injury (shrink). C. infiltration of neutrophils. D. After 10 days, macrophages and reactive gliosis.

Robbins Pathologic Basis of Disease 9th ed, 2015

Hypertensive Cerebrovascular Disease

Effect of Hypertension on brain:

- Lacunar infarcts
- Slit hemorrhages
- Hypertensive encephalopathy
- Massive hypertensive intracerebral haemorrhage

Hypertensive Cerebrovascular Disease

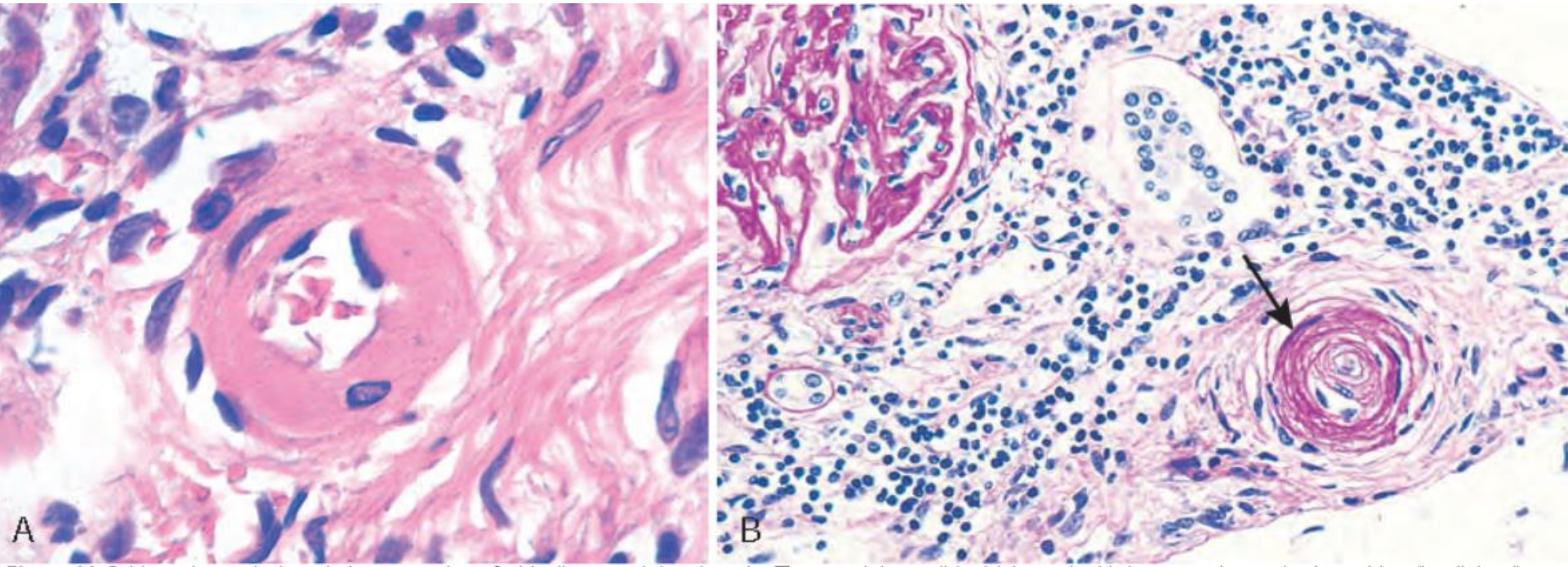


Figure 11-6 Vascular pathology in hypertension. **A,** Hyaline arteriolosclerosis. The arteriolar wall is thickened with increased protein deposition (hyalinized), and the lumen is markedly narrowed. **B,** Hyperplastic arteriolosclerosis (onion-skinning) causing luminal obliteration (periodic acid–Schiff [PAS] stain). (Courtesy Helmut Rennke, MD, Brigham and Women's Hospital, Boston, Mass.)

Robbins Pathologic Basis of Disease 9th ed, 2015

Hypertensive Cerebrovascular Disease

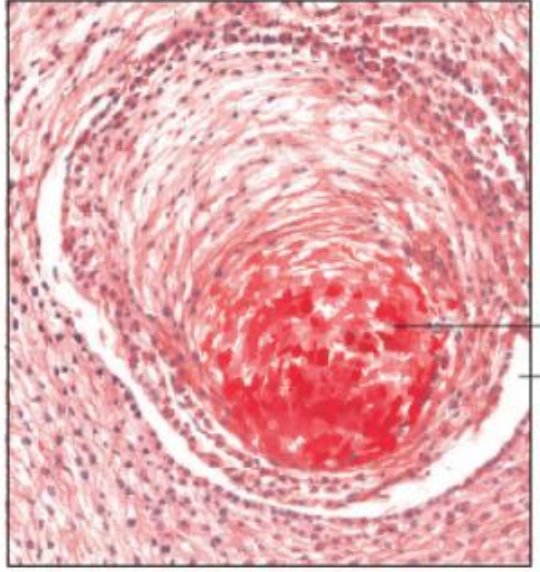
Lacunar infarcts (Ø <15 mm)

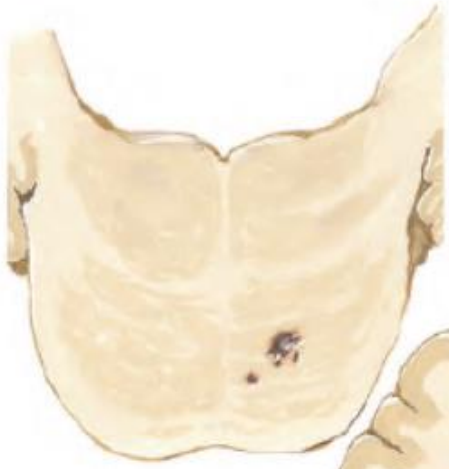
- Cerebral vessel → arteriolar sclerosis → occluded
- Single, multiple cavitary infarcts → lacuna

Figure 28-17 Lacunar infarcts in the caudate and putamen *(arrows)*.

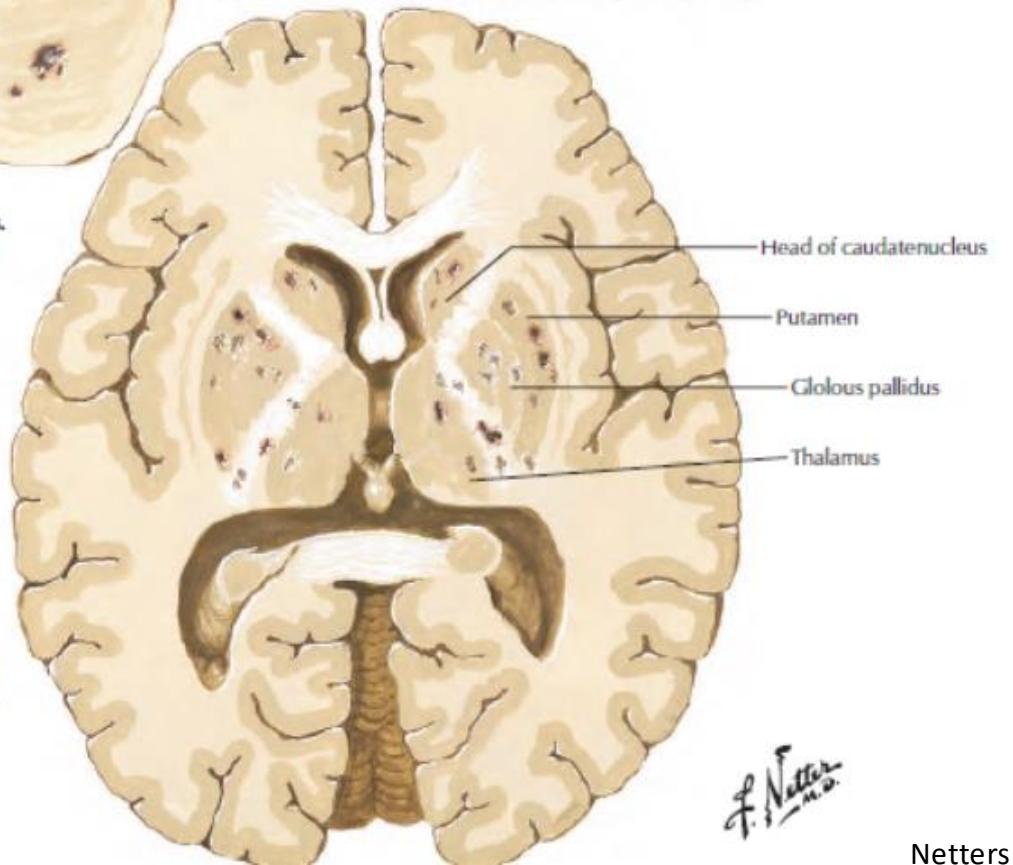
Robbins Pathologic Basis of Disease 9th ed, 2015

Small (100 μm) artery within brain parenchyma. Showing typical pathologic changes secondary to hypertension. Vessel lumen almost completely obstructed by thickened media. Pink-staining fibrinoid material within walls.





Lacunar infarcts in base of pons. Interrupting some corticospinal (pyramidal) fibers. Such lesions cause mild hemiparesis.



Multiple bilateral lacunae and scars of healed lacunar infarcts. In thalamus, putamen, globus pallidus, caudate nucleus, and internal capsule. Such infarcts produce diverse symptoms.

F. Netter M.D.

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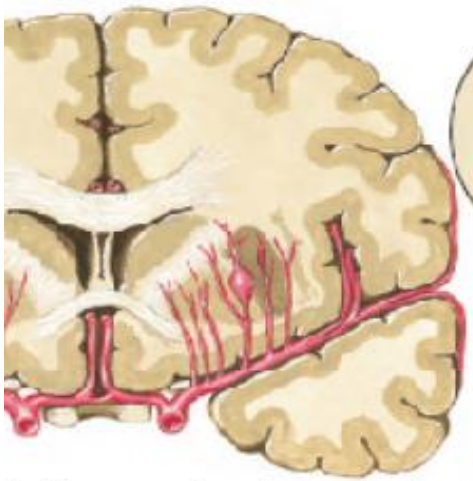
Pathogenesis

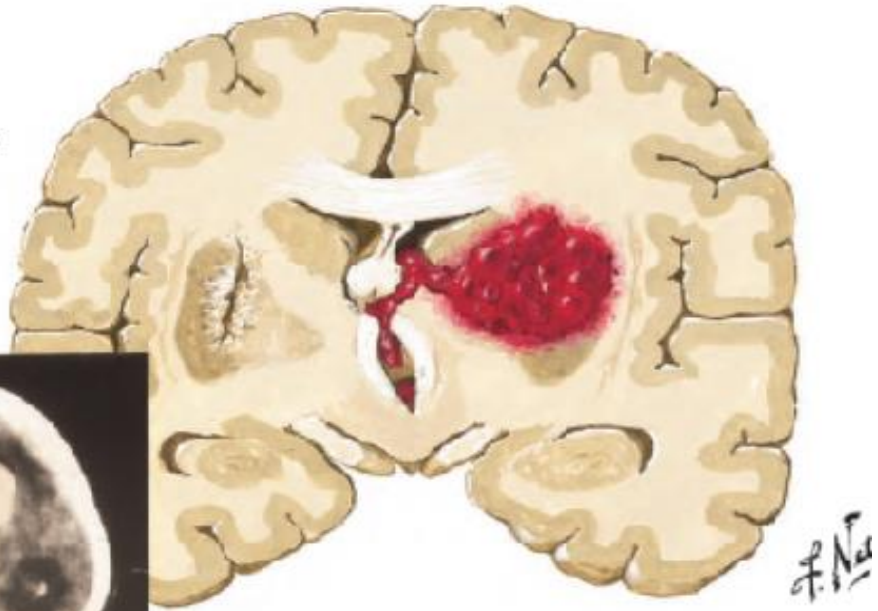


A. Microaneurysm formed in parenchymal artery of brain as result of hypertension. Lenticulostriate vessels (shown) most commonly involved, but similar process may occur in other parts of brain, especially lobar white matter, thalamus, pons, and cerebellum.

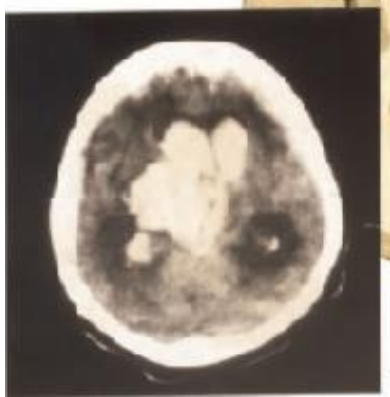
B. Microaneurysm ruptures, causing pressure on adjacent (satellite) vessels.

C. Satellite vessels rupture.

D. Amount of blood extravasated into brain tissue depends on tissue turgor opposed to intravascular blood pressure.



Moderate-sized intracerebral hemorrhage involving left putamen, with rupture into lateral ventricle. Brain distorted to opposite side. Scar of healed hemorrhage on right side.



CT scan. Showing large putaminal hemorrhage with blood in ventricles.

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Tumors

- Cells of the covering (meningiomas), brains (gliomas), other CNS cell populations (primary CNS lymphoma) or metastatic (lung, breast).
- Clinical course: pattern of growth and location.
- Histologic grade WHO grade I – IV.
- Tumors recur → progression to higher grade.
- Tumor initiating (stem-like) cells → key target of new therapy.
- Mutations of PTEN tumor suppressor gene, deletions chromosome 10, amplification EGFR oncogene, mutation TP53.

WHO Grading

- Predict biologic behaviour of a neoplasm
- Grading influence choice of therapy
- WHO grading ←→ malignancy scale
- Useful addition to the diagnosis

WHO grading: grade I-IV

- Grade I: tumors with low proliferative potential, possibility of cure following resection alone.
- Grade II: generally infiltrative, low level proliferative, often recur.
- Grade III: histological evidence of malignancy.
- Grade IV: cytologically malignant, mitotically active, necrosis prone neoplasm, fatal outcome.

Gliomas

- Most common group primary brain tumors.
- Glial cells: astrocytes, oligodendrocytes, ependymal.
- Progenitor cells → differentiate to one of cellular lineage.
- Astrocytoma, oligodendroglioma, ependymoma.

Astrocytoma

- WHO grade I – IV
- **Pilocytic astrocytoma (WHO gr I)**
- **Diffuse infiltrating astrocytoma (WHO gr II)**
- Anaplastic astrocytoma (WHO gr III)
- Glioblastoma (Primary or secondary) (WHO gr IV)
- Signs n symptoms: seizures, headache, focal neurologic deficit.

Glioblastoma

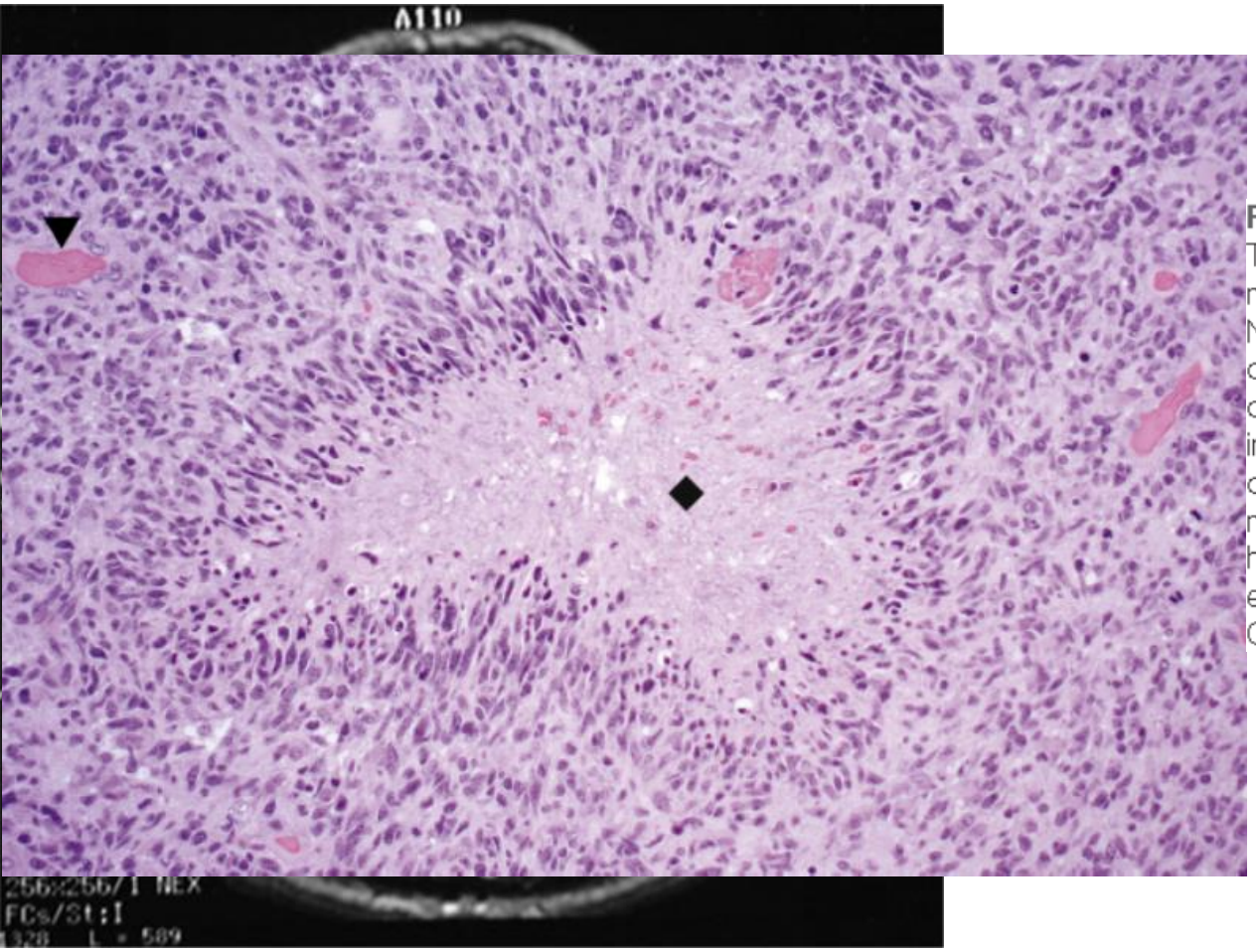

Figure 19-128 Glioblastoma, microscopic This malignant glioma is highly cellular with marked hyperchromatism and pleomorphism. Note the prominent vascularity (▼) and the area of pale necrosis (◆) in the center, with neoplastic cells concentrated around it. This pseudopalisading necrosis is characteristic of glioblastoma. The cells can infiltrate widely, particularly along white matter tracts, and even through the CSF. Such highly anaplastic cells may be difficult to differentiate from metastases, but gliomas should be GFAP positive with immunohistochemistry.

Highly cellular, pleomorphism, prominent vascularity and necrosis

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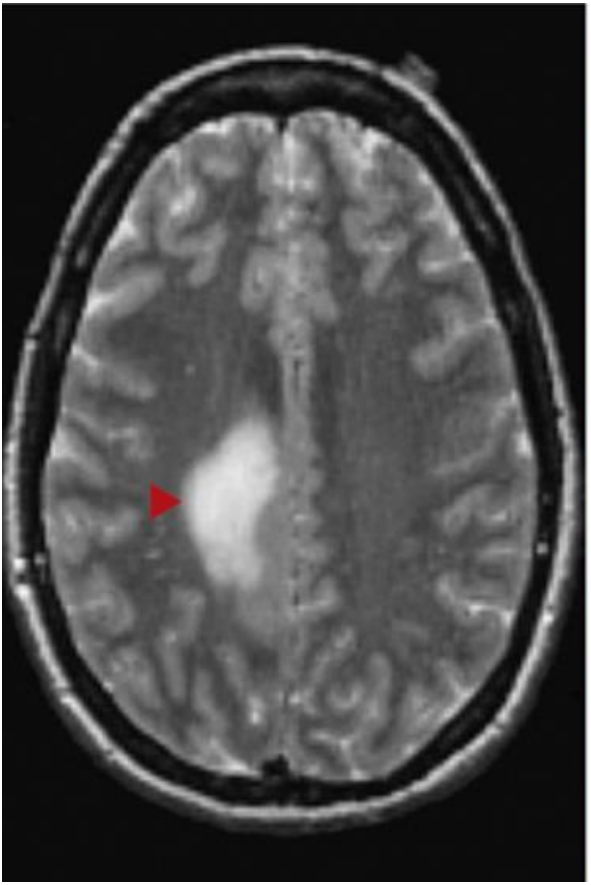
Astrocytoma



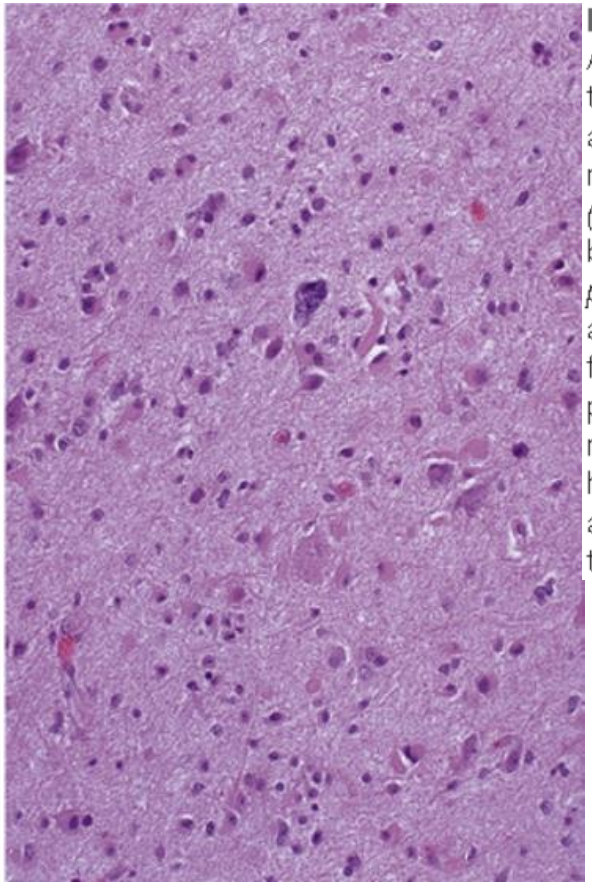


Figure 19-129 Astrocytoma, MRI and microscopic A diffuse fibrillary astrocytoma (▶) is a form of glioma that is lower grade and not as extensively invasive as a glioblastoma, but it is still not a highly discrete mass, as visible in the T2-weighted axial MRI image *(left panel)*. These gliomas tend to enhance brightly because of their abnormal vascularity. In the *right panel* this astrocytoma shows increased cellularity and pleomorphism compared with normal brain, but far less than a high-grade glioma. Note the one very pleomorphic cell at the top center. The clinical course may be slowly progressive for years, but astrocytomas have a tendency to become more anaplastic with time as genetic alterations accumulate within the neoplastic cells, and then more rapid deterioration ensues.

Diffuse astrocytoma

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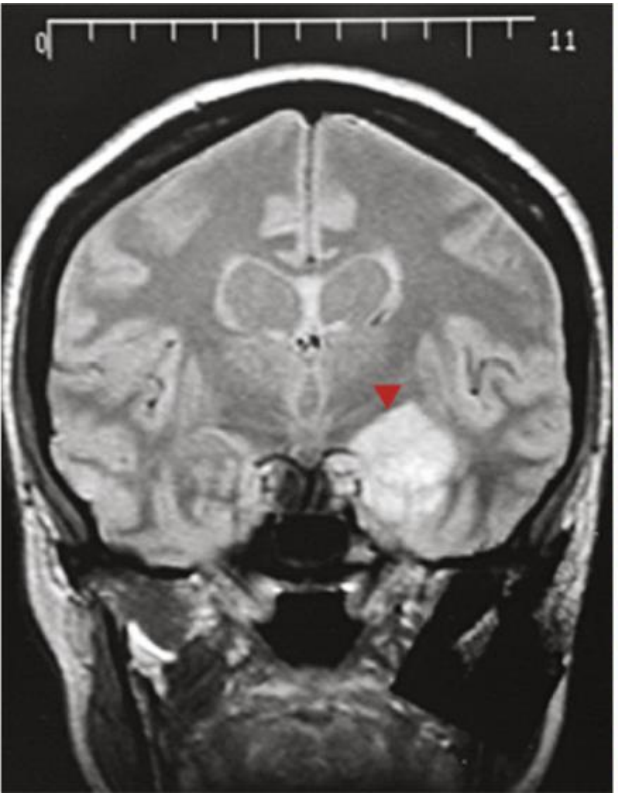
Oligodendroglioma



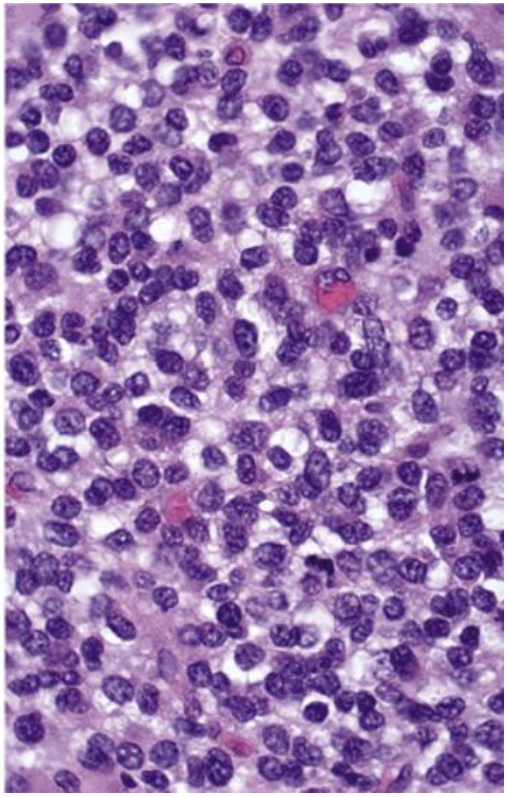


Figure 19-130 Oligodendroglioma, MRI and microscopic

The enhanced MRI image in coronal view *(left panel)* shows a mass (▼) within the left temporal lobe. This type of glioma tends to be well circumscribed, with cystic areas and focal calcification. It enhances as a result of the rich vascular network of anastomosing capillaries within the tumor. Oligodendrogliomas constitute about 5% to 15% of all gliomas; they typically occur within the cerebral hemispheres, usually in white matter, of adults in their 30s and 40s. Typical oligodendrogliomas have round blue nuclei with clear cytoplasm *(right panel)*. Most have cytogenetic abnormalities involving chromosomes 1p and 19q. They tend to be slowly progressive over years and can have a better prognosis than other adult gliomas.

Well circumscribed, cystic and calcification

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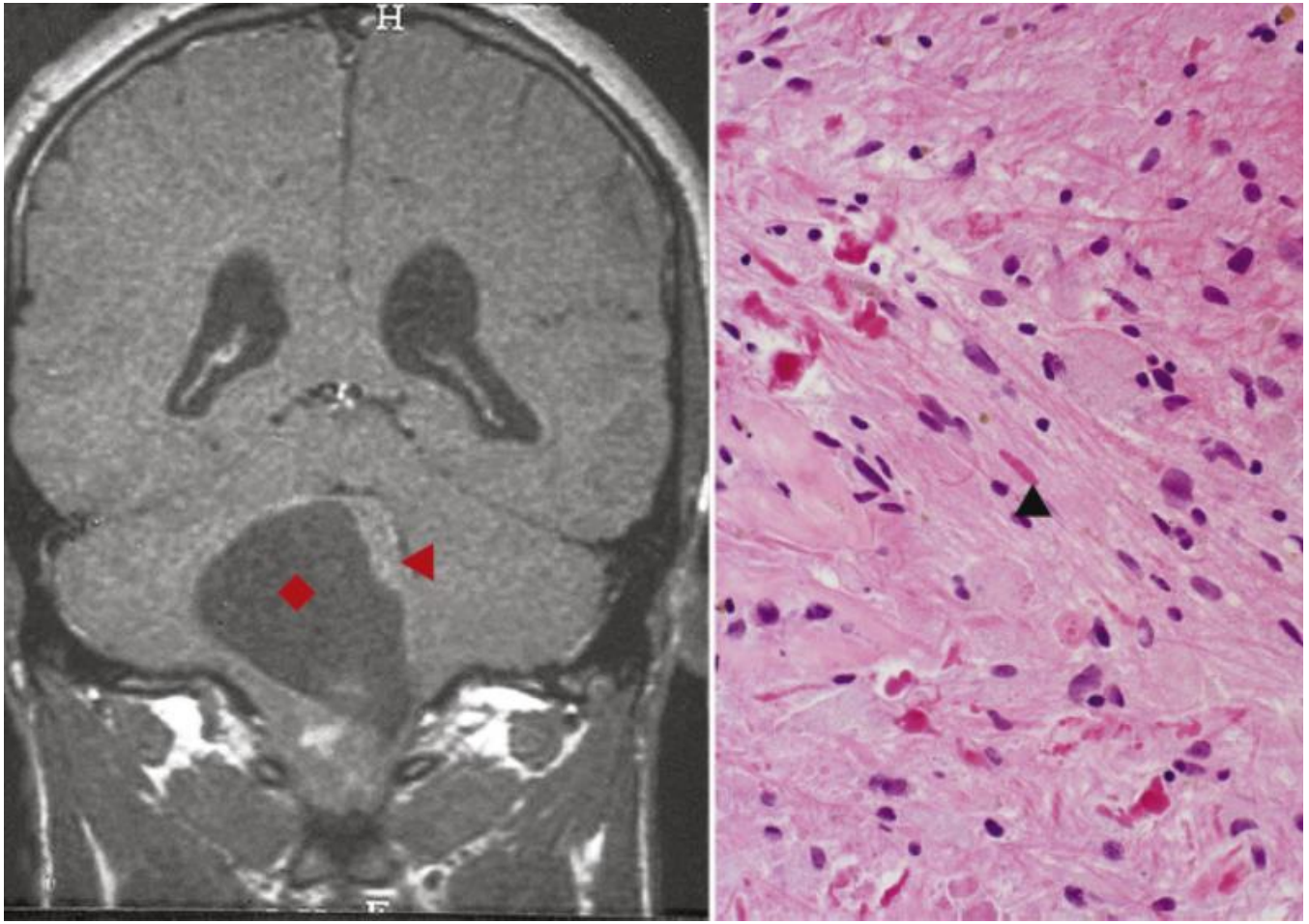
Pilocytic Astrocytoma



Children, slow growing, low grade astrocytic tumor, very god prognosis

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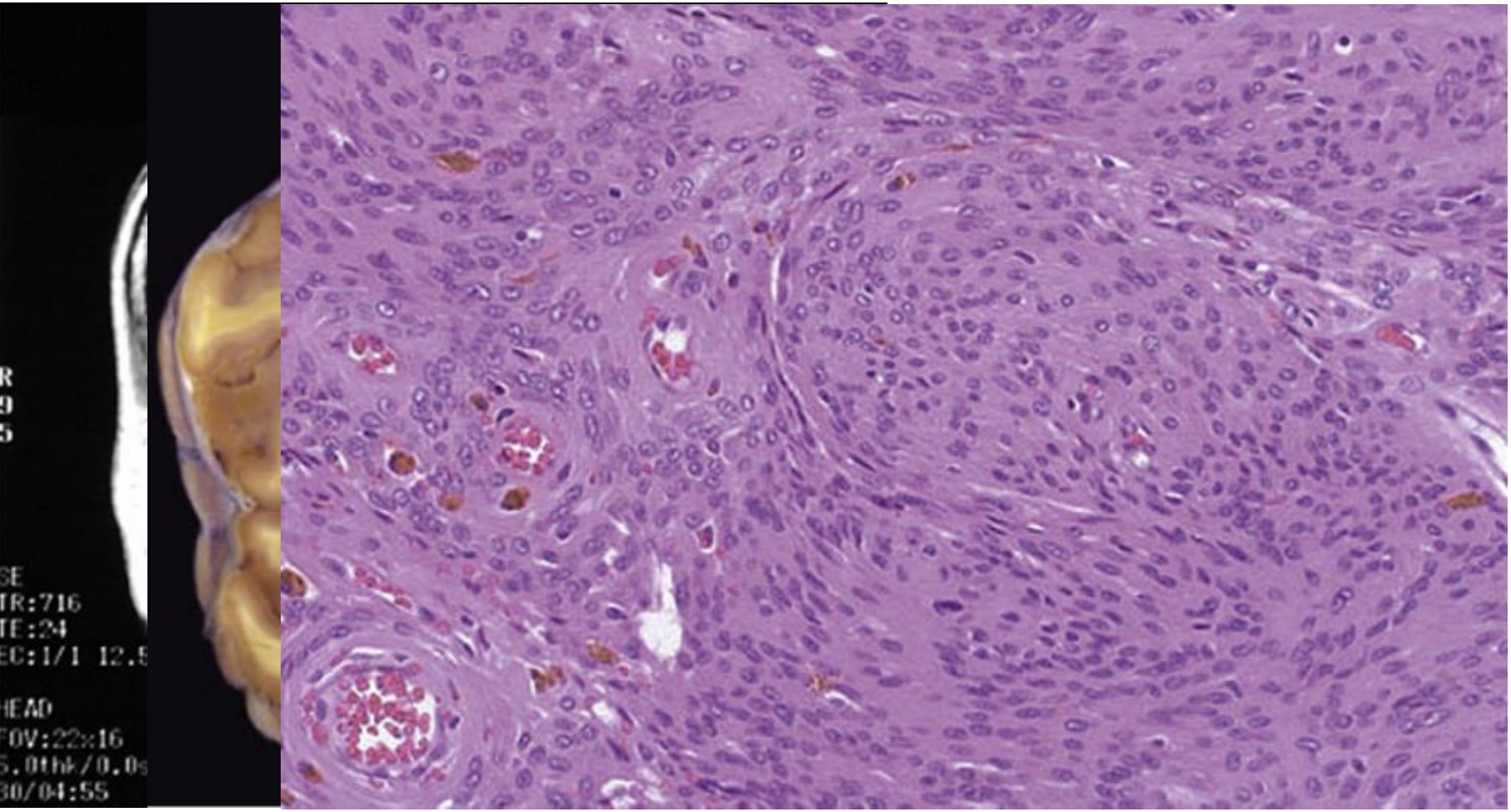
Meningioma

- Benign tumor, usually attached to dura, arise form meningothelial cells of the arachnoid
- Slow growing, solitary or multiple

Meningioma



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Thank You