“General Neuroanatomy/Staining: an Introduction to Neuropathology for Neuropathologists”

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AMERICAN ASSOCIATION
OF NEUROPATHOLOGISTS

Disclosures

- I have no relevant financial relationships to disclose. (I wish I did.)

Learning objectives

- Name histochemical stains ordered by neuropathologists, both currently and in the past, and their uses
- Explain the vascular territories that correspond to gross neuroanatomic structures
- Identify selected neuroanatomic structures and interesting facts about them

Neuropathology board exam blueprint

ABPath Exam Blueprint

Updated for 2021

Neuropathology Exam Blueprint	Approximate %		
	Written/Practical I	Written/Practical II	Micro/Virtual
General neuroanatomy, pathology, and staining	8	8	11
Developmental neuropathology	8	8	5
Epilepsy	4	4	0
Vascular disorders	9	9	6
Trauma	7	7	5
Infectious/inflammatory disease	8	8	11
Demyelinating diseases	6	6	6
Complications of systemic disorders	5	5	3
Aging and neurodegenerative diseases	12	12	6
Prion diseases	2	2	3
Neoplasms-Nonpitiuitary	13	13	23
Pituitary	5	5	6
Skeletal Muscle	5	5	8
Peripheral Nerve	2	2	5
Ophthalmic pathology	3	3	2
Management & Informatics-General	3	3	0
Total Percentage	**100**	**100**	**100**
Total Number of Questions in Each Section	**95**	**95**	**66 (55/11)**
Total Hours Allotted for Each Section	**1 Hrs 45 Mins**	**1 Hrs 45 Mins**	**3 Hrs 30 Mins**

https://www.abpath.org/images/blueprints/2021_blueprints/Subspecialty/NP_-SS_2021.pdf

Outline (based on objectives)

- Neuropathology-specific histochemical stains (with absolutely no immunohistochemistry photographs)
- Gross neuroanatomy from the perspective of vascular territories
- Selected microscopic neuroanatomic structures with etymologies and tidbits
- Virtual slide

Section #1

NEUROPATHOLOGY-SPECIFIC HISTOCHEMICAL STAINS

Histochemical staining in general

- Reagents
- Differentiating solutions
- Recipes
- Discussing all of these in-depth is beyond the scope of this lecture (and my experience)
- Some stains require special preparation and/or fixation (e.g., frozen sections, free-floating sections, celloidin-embedding, non-Formalin fixation)

Neuropathology-specific stains: central myelin

- **Luxol fast-blue (LFB)**
- **Weil (similar to Loyez; requires thicker sections)**
- Loyez (FFPE; alternative to LFB; myelin dark-brown to black)
- Marchi (FFPE; degenerated myelin; contains osmium tetroxide)
- Osmium tetroxide-alpha naphthylamine (degenerated myelin; frozen tissue; carcinogenic)
- Pal-Weigert (lengthy technique; requires celloidin embedding)
- Woelke modification of Heidenhain stain (requires celloidin)

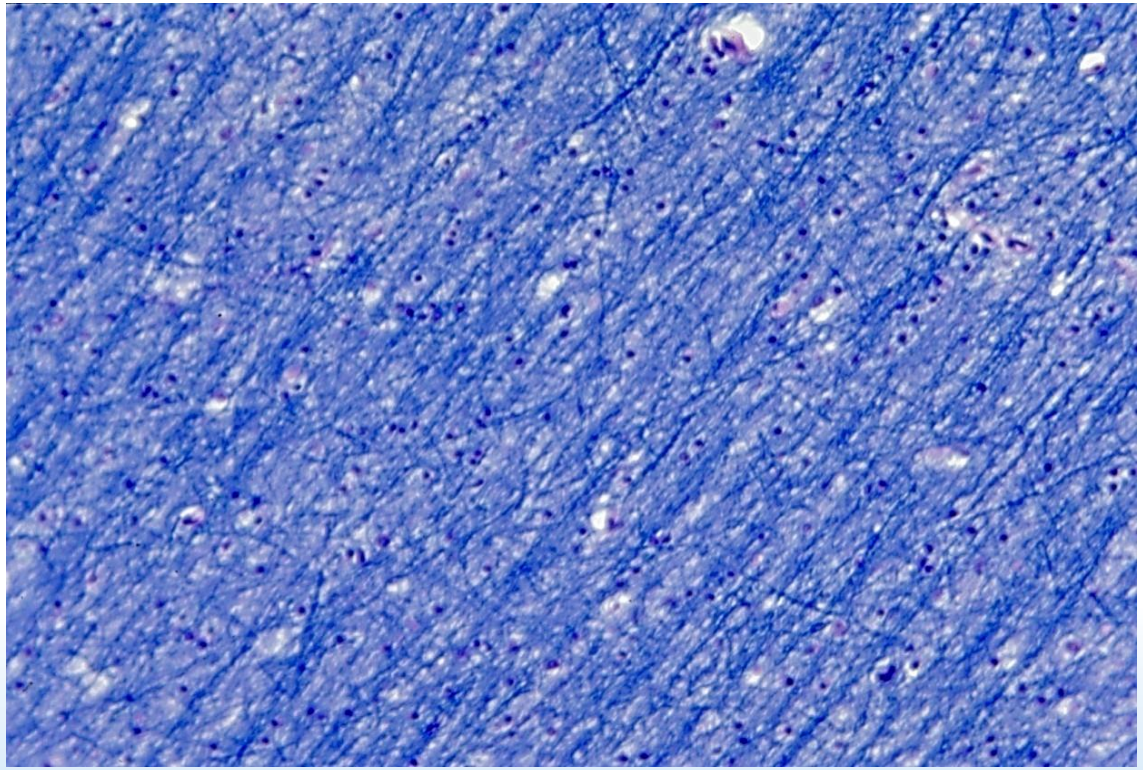
From Dawson TP, Neal JW, Llewellyn L, Thomas C. "Neuropathology Techniques." London: Hodder Arnold, 2003.

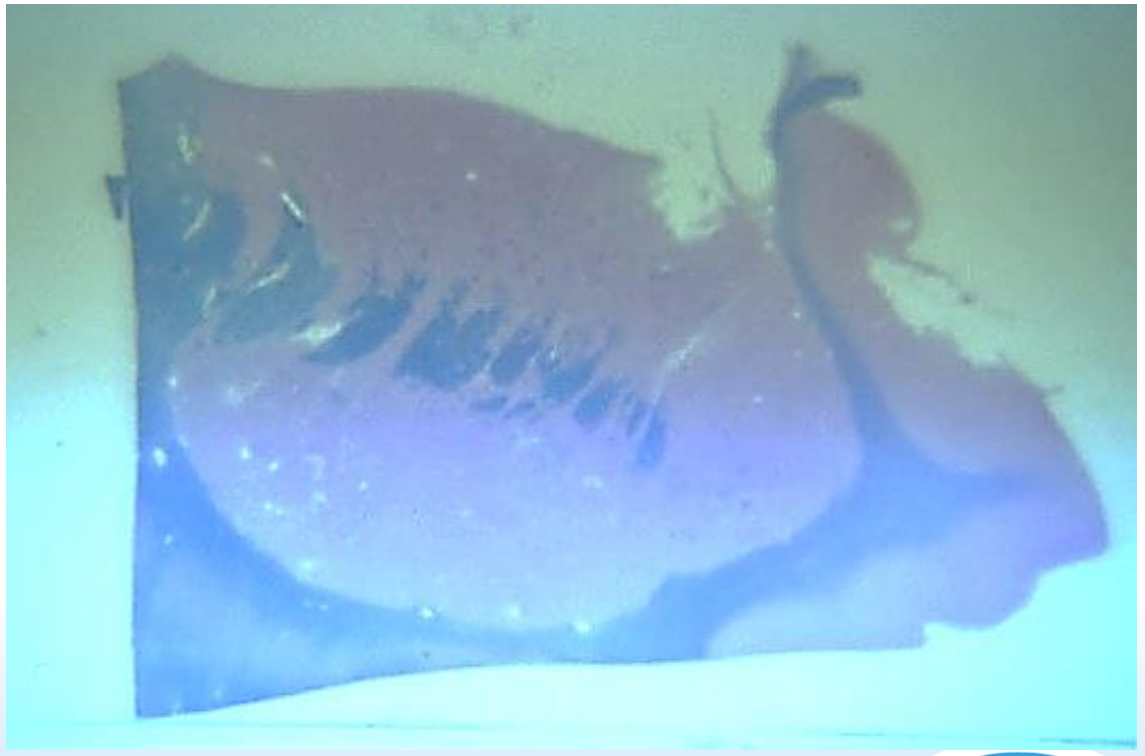
Luxol fast-blue (LFB)

- The best stain currently for assessing myelin in formalin-fixed, paraffin-embedded (FFPE) brain tissue
- Central myelin is blue to dark green; peripheral myelin is light green to green-purple; easy to see difference at the Obersteiner-Redlich zone
- Combine with H&E for routine assessment of brain and spinal cord autopsy sections (though may take an extra day or two to process)
- Immunohistochemical equivalent: myelin-basic protein or myelin-associated glycoprotein

From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

Luxol fast-blue (LFB)—FFPE sections



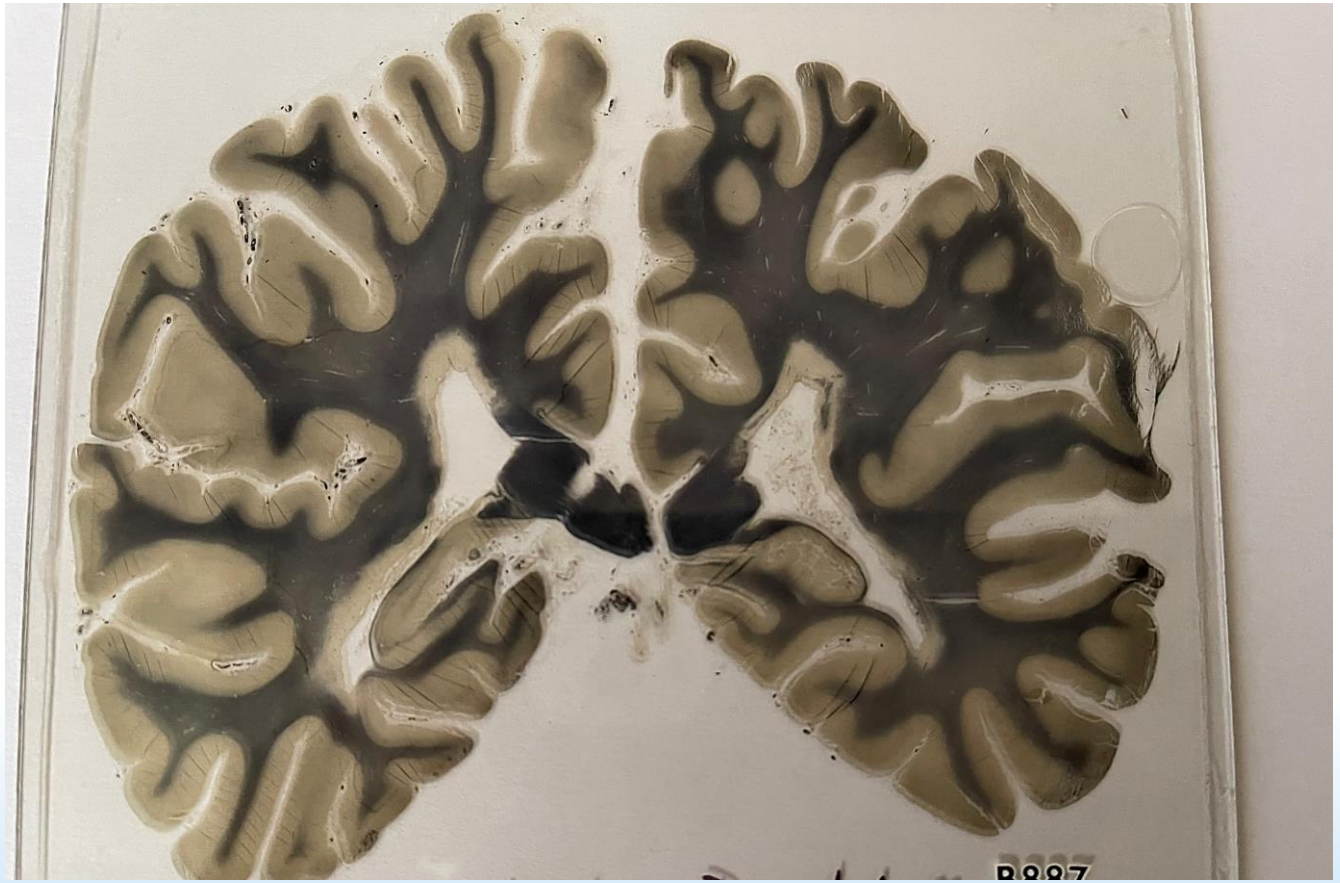


Weil

- Similar to Loyez but requires thicker sections
- Great for celloidin-embedded tissue
- Reagents include aqueous iron alum and Loyez hematoxylin (containing lithium carbonate)
- Myelin is dark-brown to black
- Gray matter is light-beige
- Background is a very pale yellow

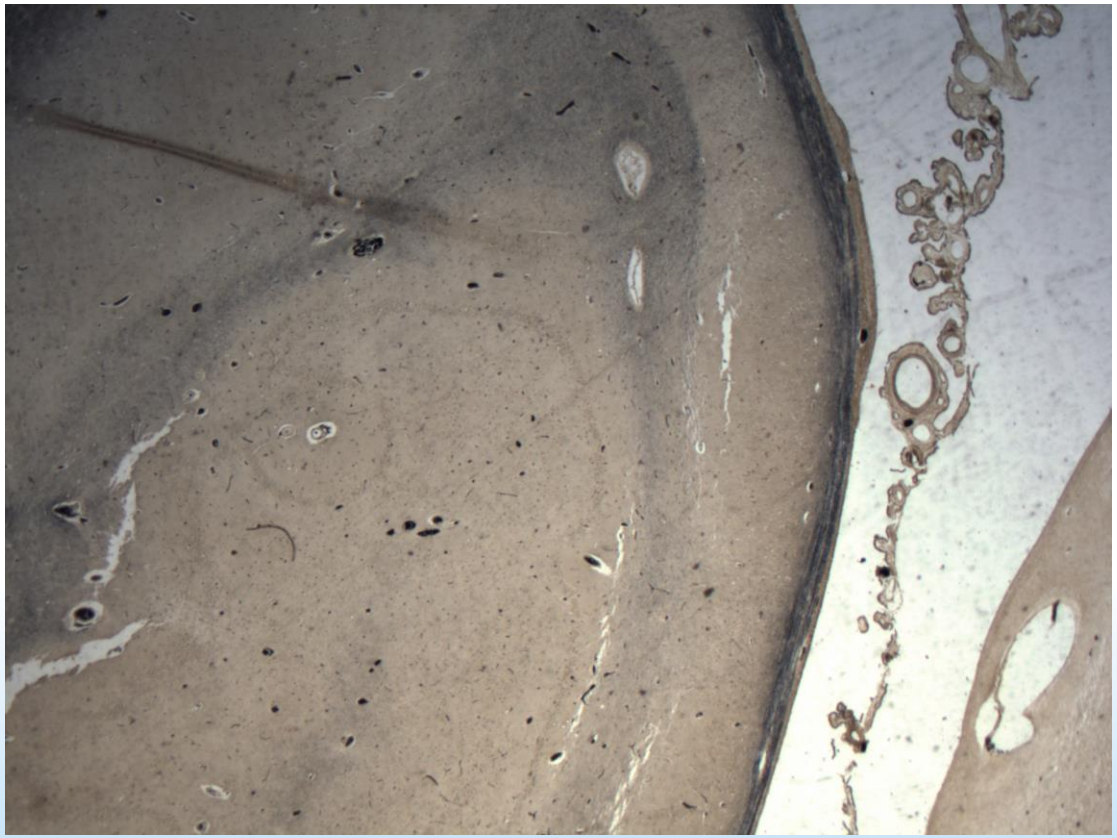
From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

Weil—whole-mount, celloidin-embedded section

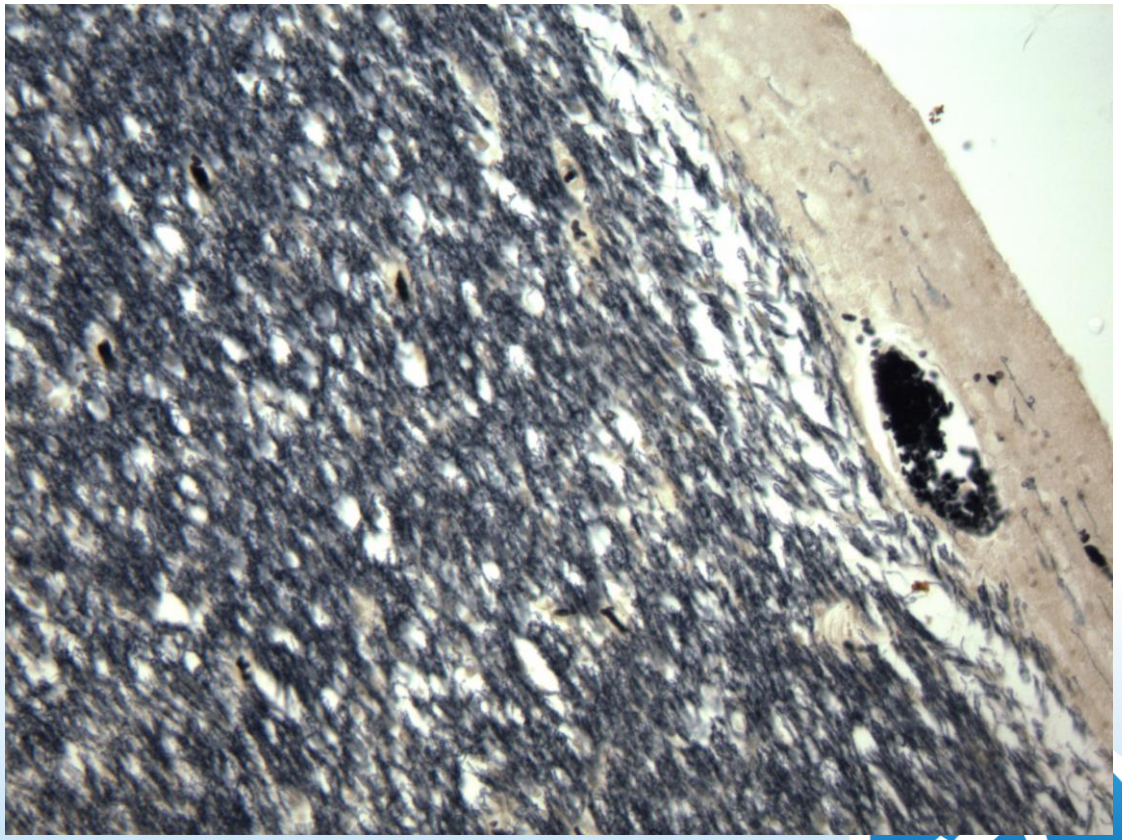


Weil—whole-mount, celloidin-embedded section

Hippocampus



Subependymal region



Neuropathology-specific stains: peripheral myelin

- **Toluidine blue (glutaraldehyde-fixed; resin-embedded with hardener/accelerator; “semi-thin” sections)**
- **Osmium tetroxide (glutaraldehyde-fixed; resin-embedded without hardener/accelerator; teased nerve fibers)**
- Modified Kultschitsky-hematoxylin (Flemming’s fixation—chromic acid, osmium tetroxide, and glacial acetic acid)
- Page’s solochrome cyanin stain (FFPE; less contrast than Kultschitsky; no connective tissue staining)

From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

Toluidine blue

- One of the best stains for highlighting peripheral myelin (in semithin resin section)—mandatory to assess the state of the axons and determine axonal vs. demyelinating neuropathy
- In aqueous form can be used for rapid smears and staining the storage product brown in metachromatic leukodystrophy

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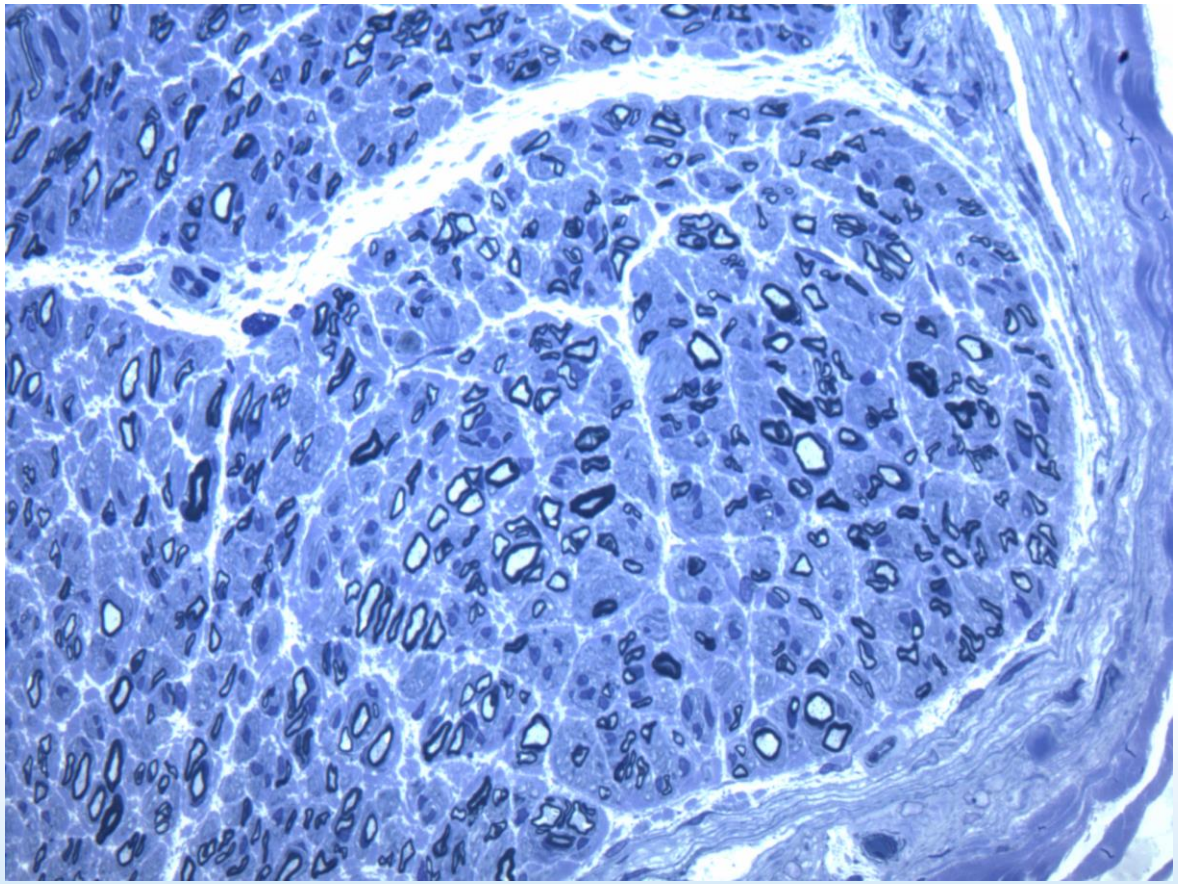
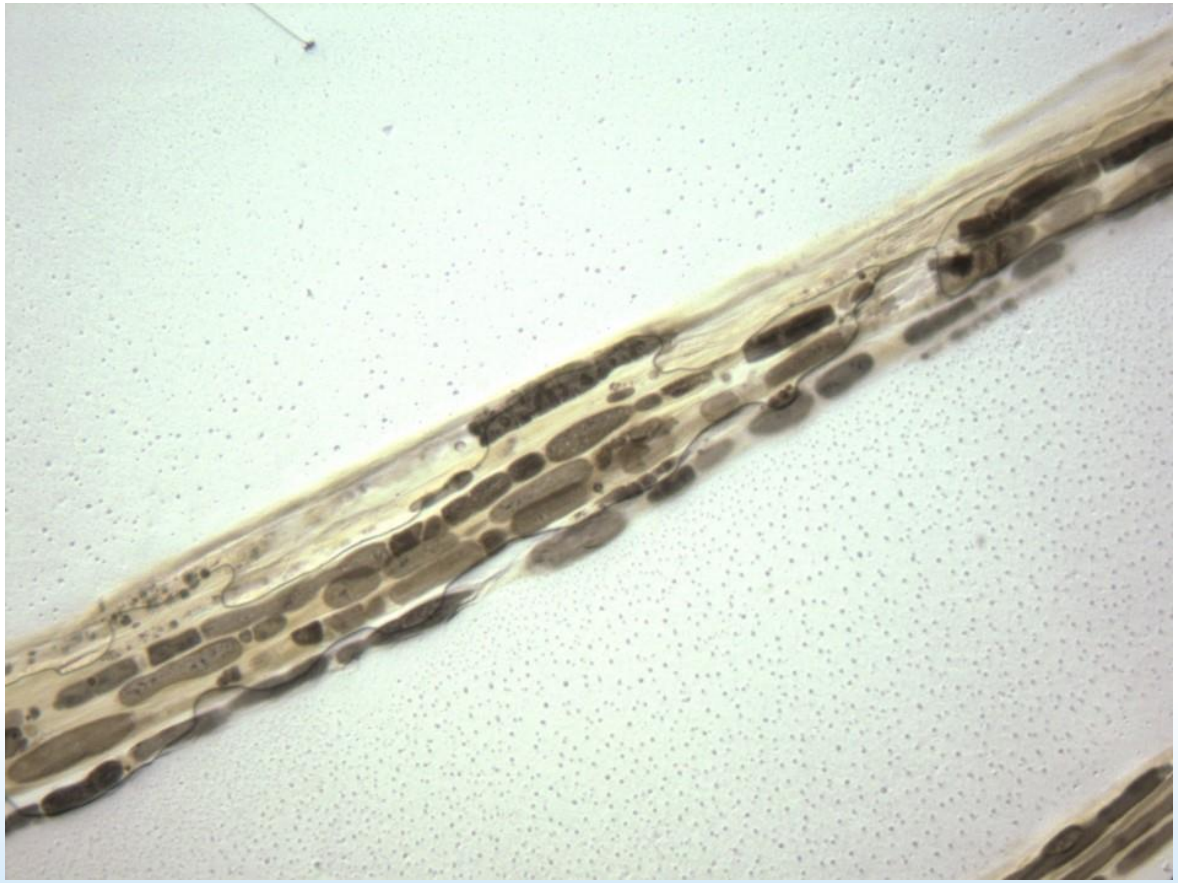
Toluidine blue—semithin section



Osmium tetroxide—teased nerve fiber preparation

- Assessment of internodal distances
- Visualization of myelin ovoids in acute axonal neuropathy
- Optimal view of segmental demyelination

Osmium tetroxide—teased nerve fiber preparation



Neuropathology-specific stains: neurons

- **Cresyl violet ("Nissl" stain)**
- Cajal stains
  - Requires free-floating sections
  - Reagents include pyridine, which can cause sterility
- Golgi Cox block method
  - Tissue hardened with dichromate solution; combine with silver or mercury
  - Only small percentage of neurons stained (black); great 3D structures seen
- Marsland, Glees, and Erikson stain
  - Uses silver nitrate and ammonia; good for FFPE tissue
  - Neurons (and axons) dark-brown to black

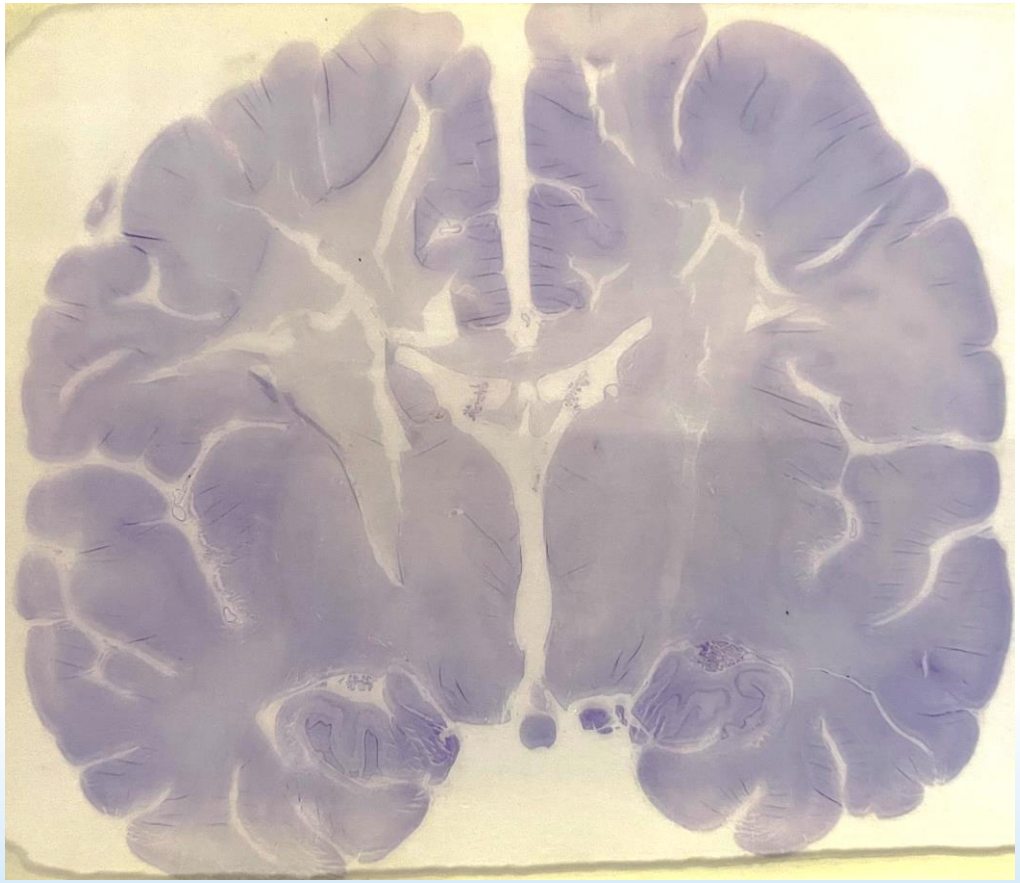
From Dawson TP, Neal JW, Llewellyn L, Thomas C. "Neuropathology Techniques." London: Hodder Arnold, 2003.

Cresyl violet ("Nissl" stain)

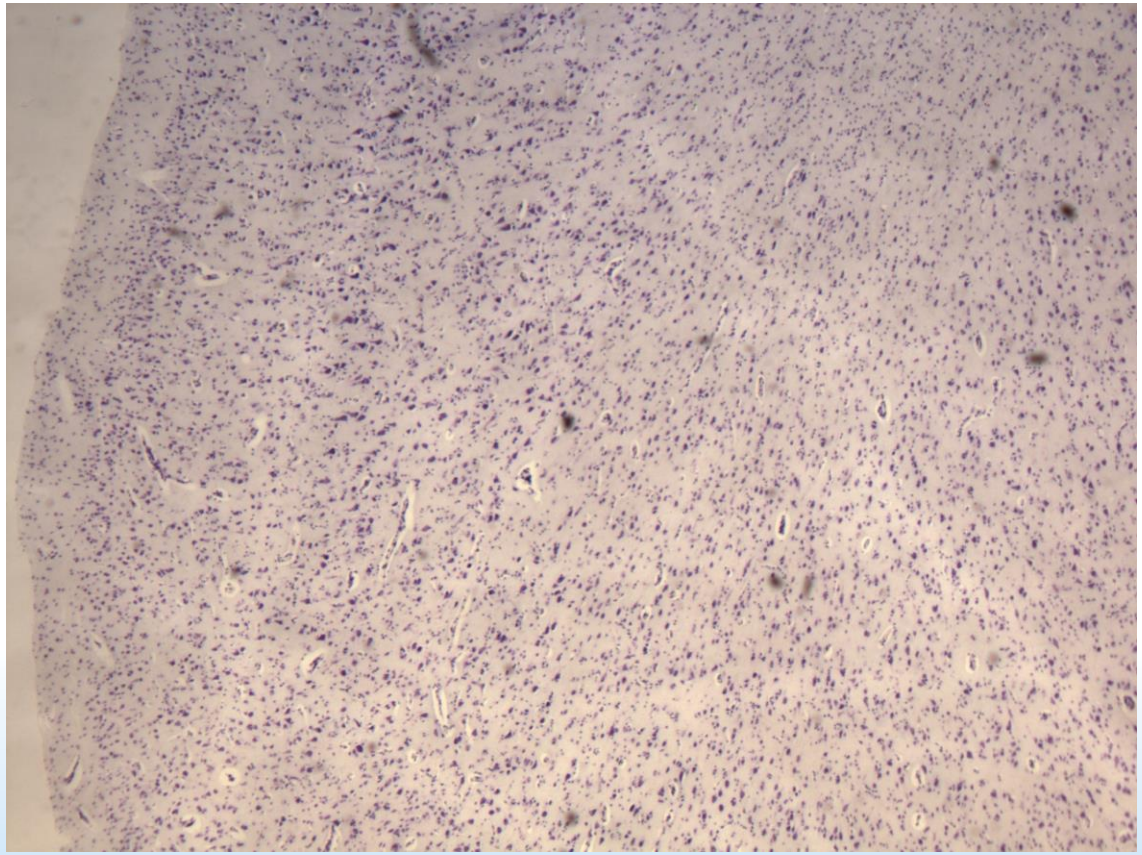
- Supposed to highlight Nissl substance (rough endoplasmic reticulum)
- FFPE or celloidin-embedded tissue
- Good for highlighting neurons without much background, useful for morphometric analysis
- Nissl substance and nuclei are dark-purple to blue
- Immunohistochemical equivalent: Neu-N
- (Cresyl violet or toluidine blue stains the storage product brown in metachromatic leukodystrophy)

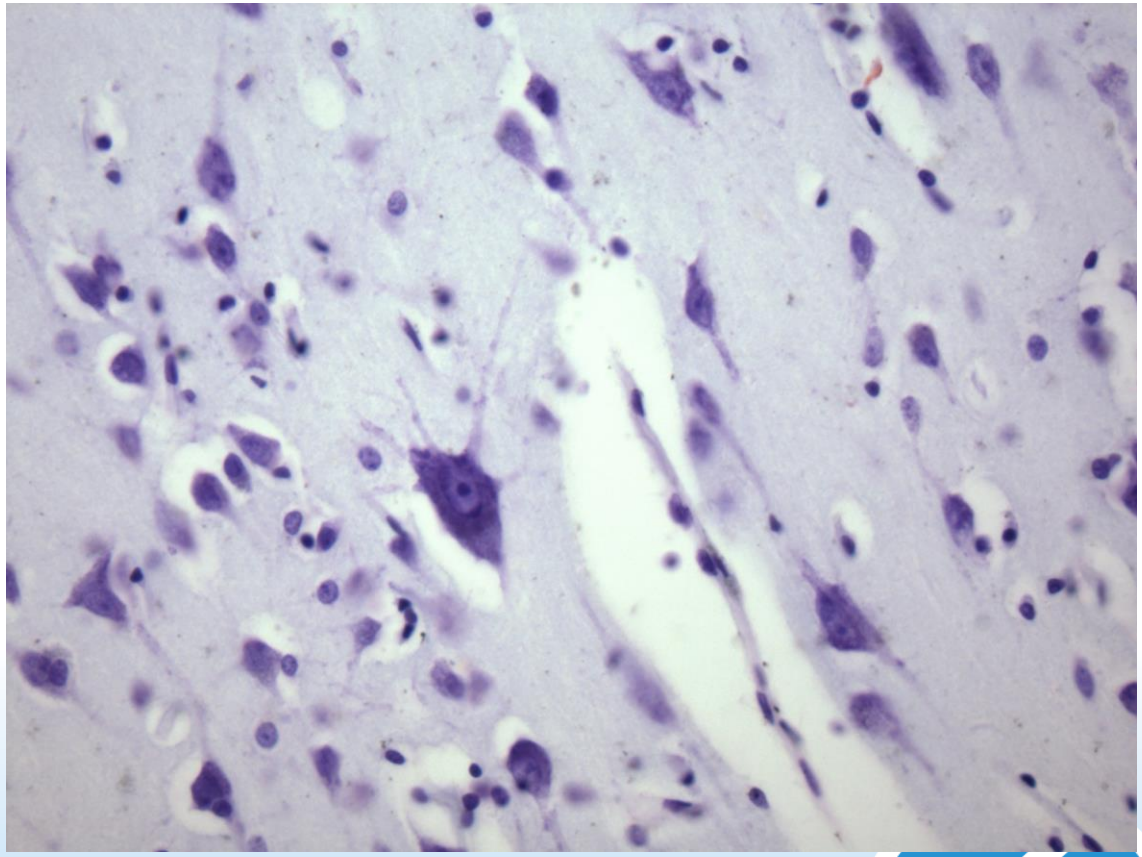
From Dawson TP, Neal JW, Llewellyn L, Thomas C. "Neuropathology Techniques." London: Hodder Arnold, 2003.

Cresyl violet (“Nissl” stain)—whole-mount, celloidin-embedded section



Cresyl violet (“Nissl” stain)—whole-mount, celloidin-embedded section





Neuropathology-specific stains: axons and neurites

- **Bielschowsky**
- **Bodian**
- Eager (frozen sections; degenerating axons)
- Fink-Heimer (free-floating frozen sections)
- Gallyas (FFPE; abnormal neurites around neurofibrillary tangles)
- Guillery, Shirra, and Webster (FFPE; uses pyridine—sterility)
- Holmes (FFPE; uses pyridine—sterility)
- Marsland, Glees, and Erikson (see neuronal section)
- Palmgren (FFPE; central or peripheral axons)

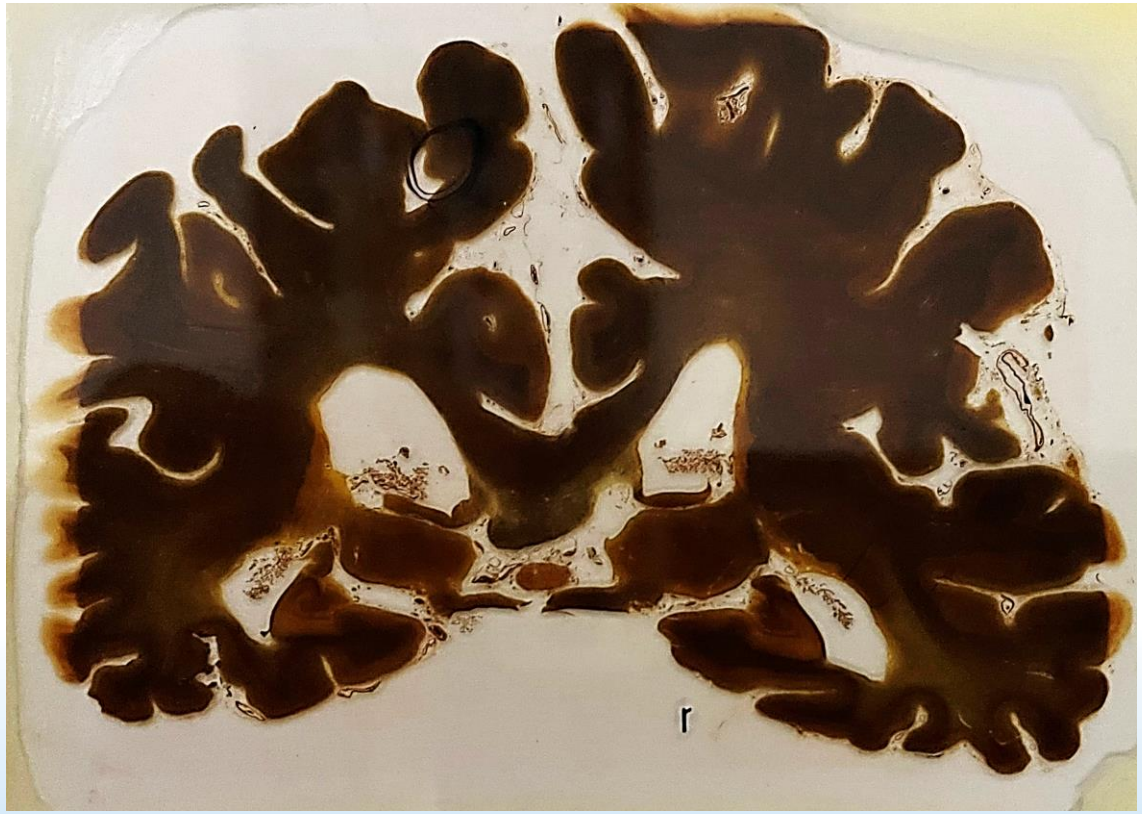
From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

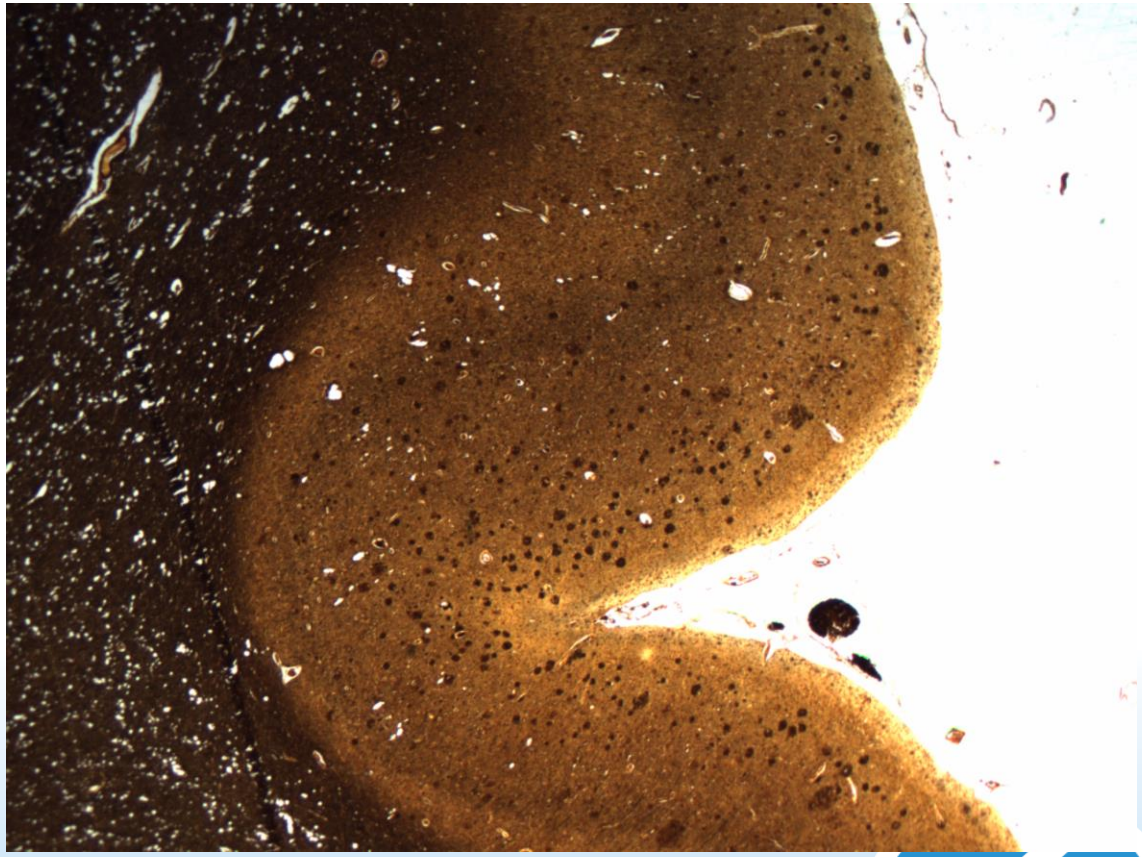
Bielschowsky

- Commonly-used silver stain
- Can be used on frozen, celloidin, or FFPE sections
- Axons and neurites stain black
- Great for neuritic plaques and neurofibrillary tangles
- Background is colorless or counterstained (mine is yellowish-brown)
- Immunohistochemical equivalent: neurofilament (for axons)

From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

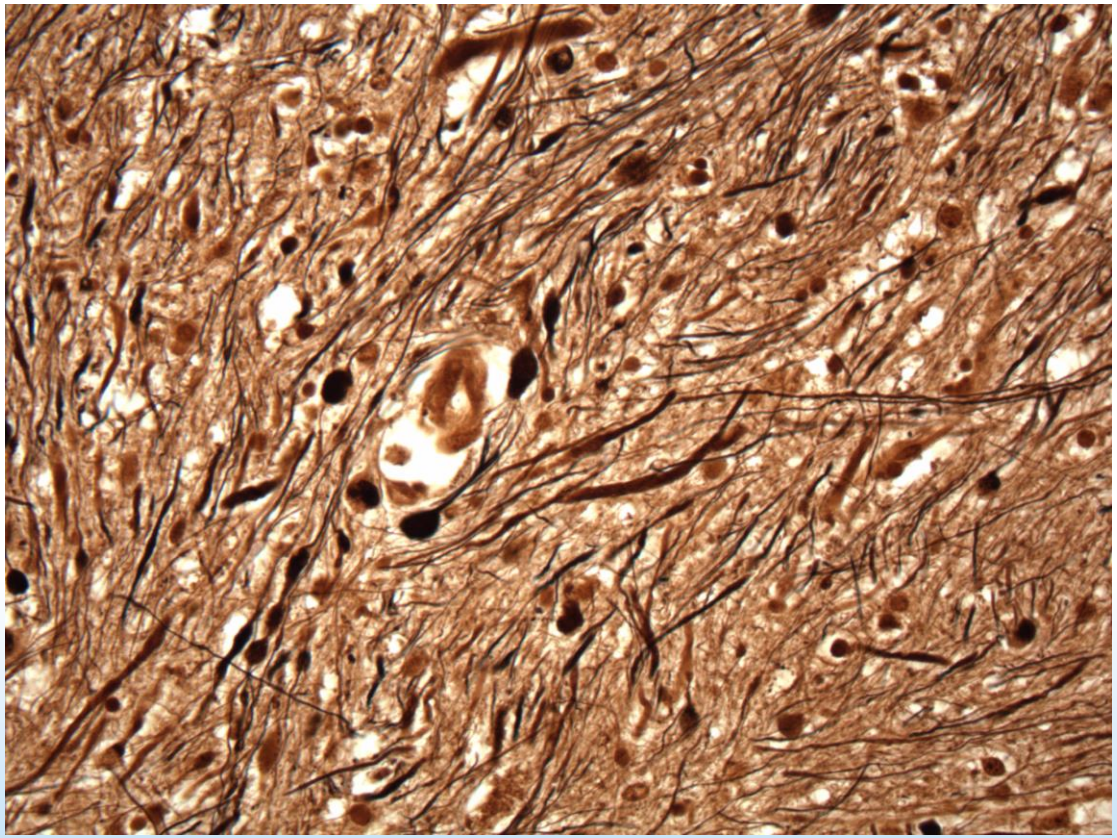
Bielschowsky—whole-mount, celloidin-embedded sections



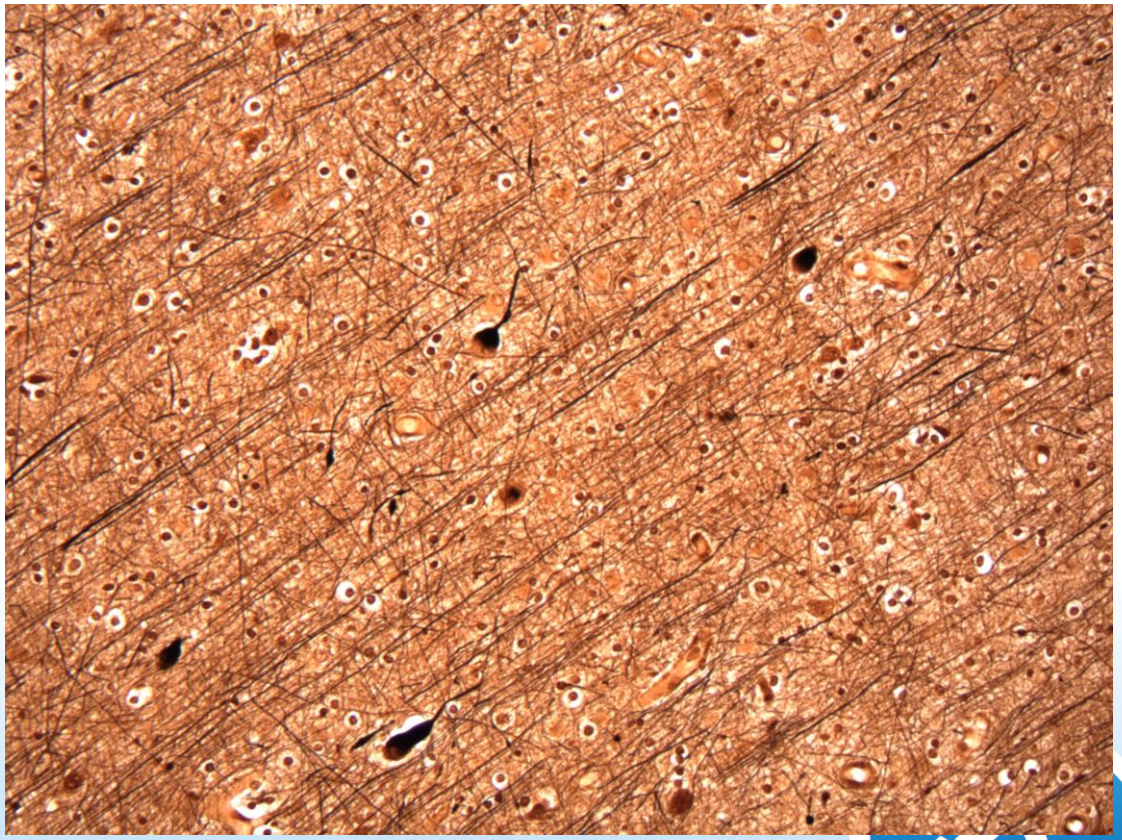


Bielschowsky—FFPE sections

Diffuse axonal injury



Possible infarct?

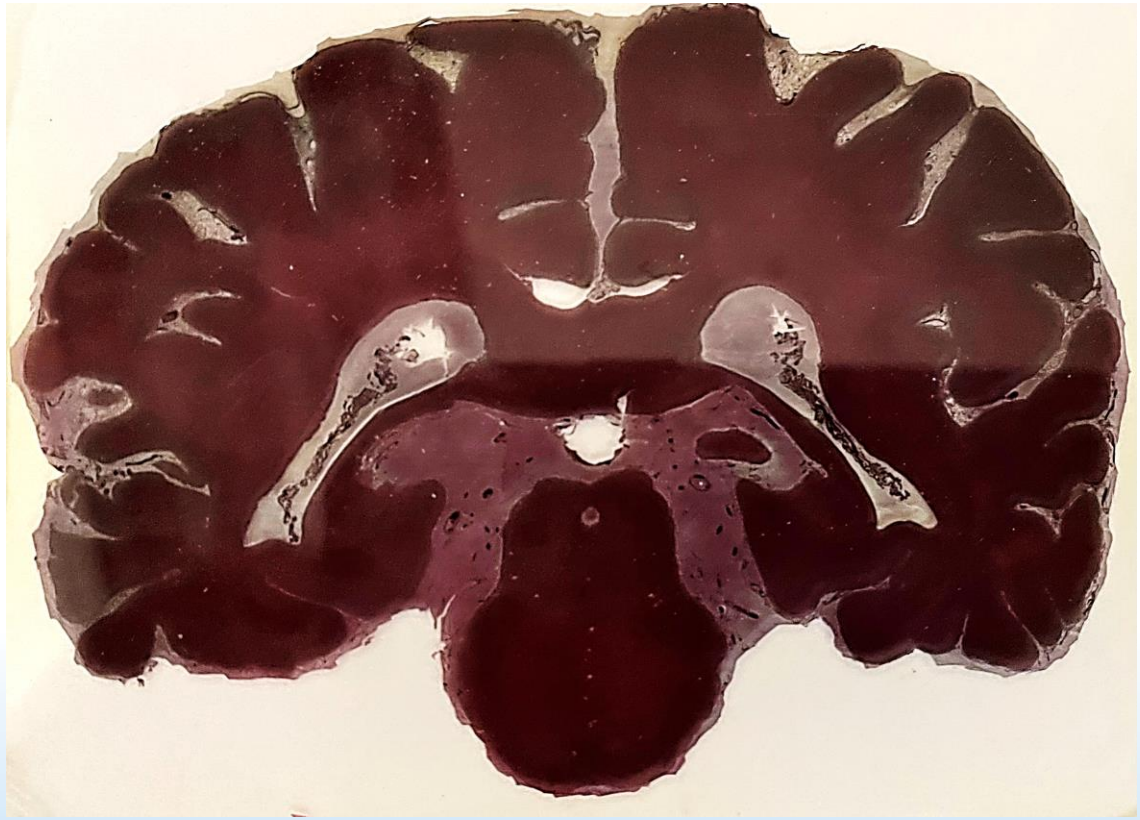


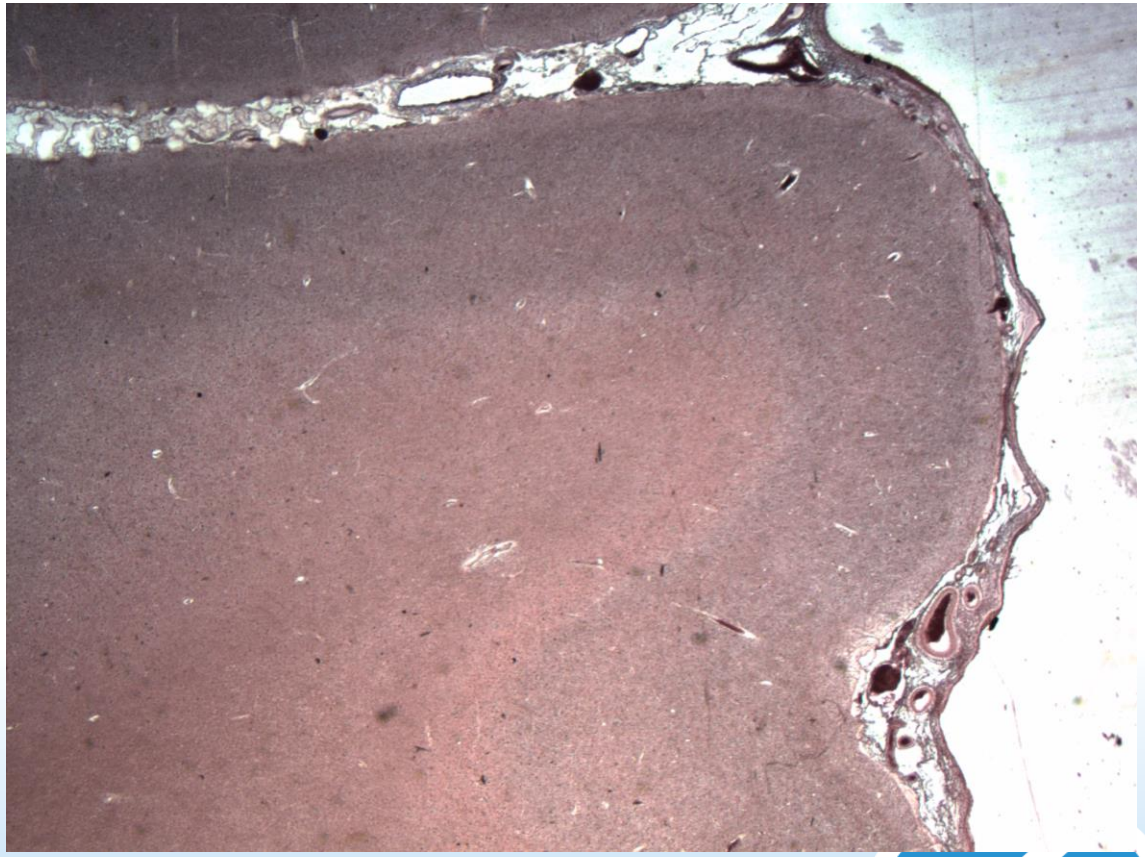
Bodian

- Uses silver proteinate (brand name Protargol) to highlight the axons and neurites; allegedly difficult to obtain
- Good for celloidin-embedded and FFPE tissue, and likely frozen tissue as well
- Method has variable reliability (but then again, so does Bielschowsky)

From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

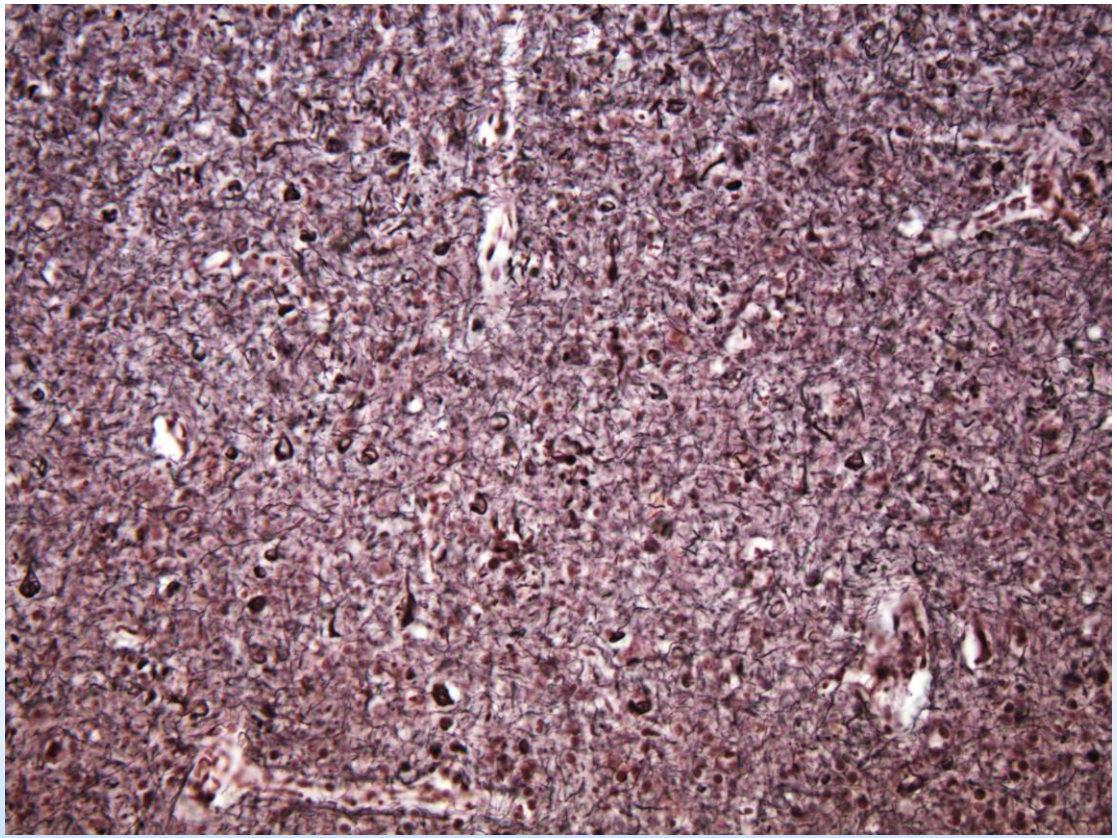
Bodian—whole-mount, celloidin-embedded section





Bodian—whole-mount, celloidin-embedded section

Gray matter



White matter

Neuropathology-specific stains: glia

- **Phosphotungstic acid-hematoxylin (PTAH)**
- **Holzer**
- Cajal gold sublimate (free-floating frozen sections; fixation in formol ammonium bromide; no pyridine fortunately)
- Hortega (free-floating frozen sections; not very specific for astrocytes)
- Penfield modification of Hortega (microglia/oligodendrocytes; free-floating frozen sections; uses hydrobromic acid)
- Nauomenko and Feigin method for microglia (silver nitrate and sodium carbonate; unreliable and nonspecific)
- Weil and Davenport (microglia/oligodendrocytes; frozen sections; silver nitrate; older tissue leaves ugly granular deposits over gray matter)

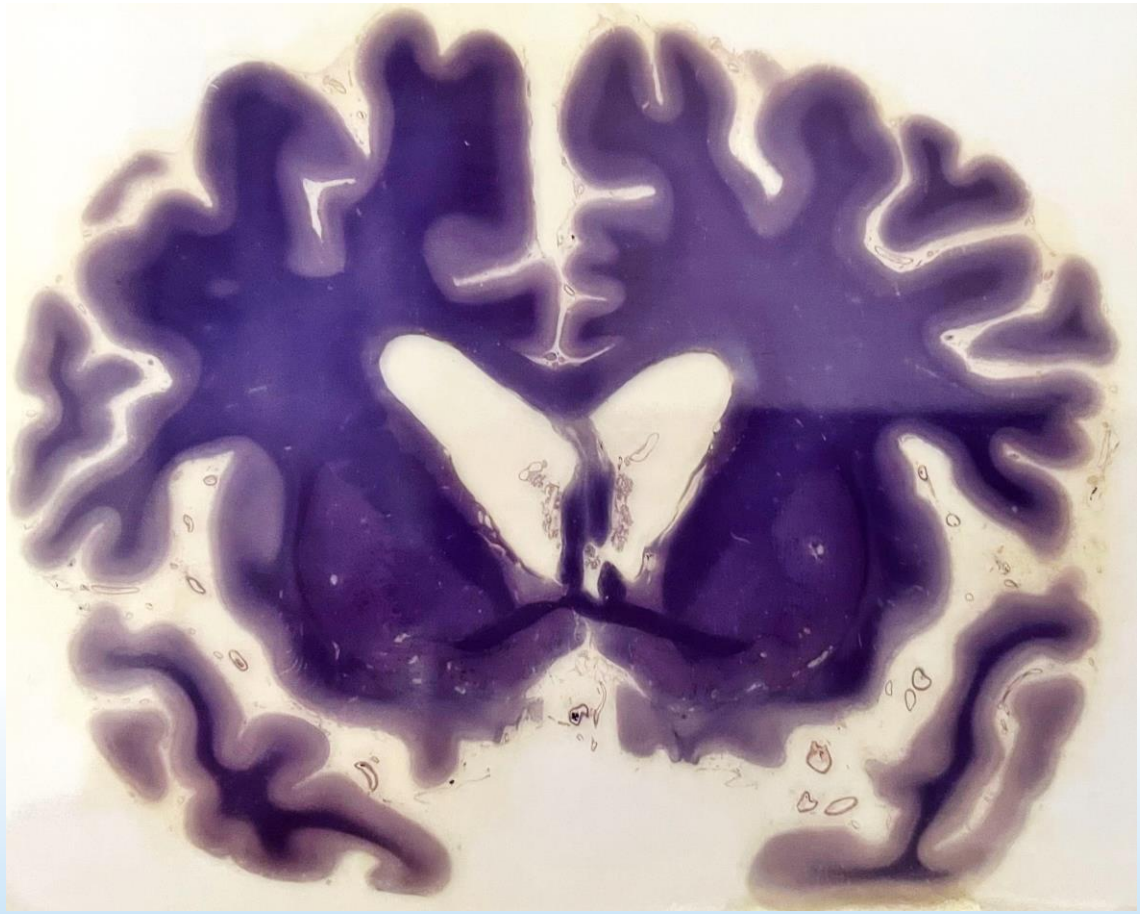
From Dawson TP, Neal JW, Llewellyn L, Thomas C. "Neuropathology Techniques." London: Hodder Arnold, 2003.

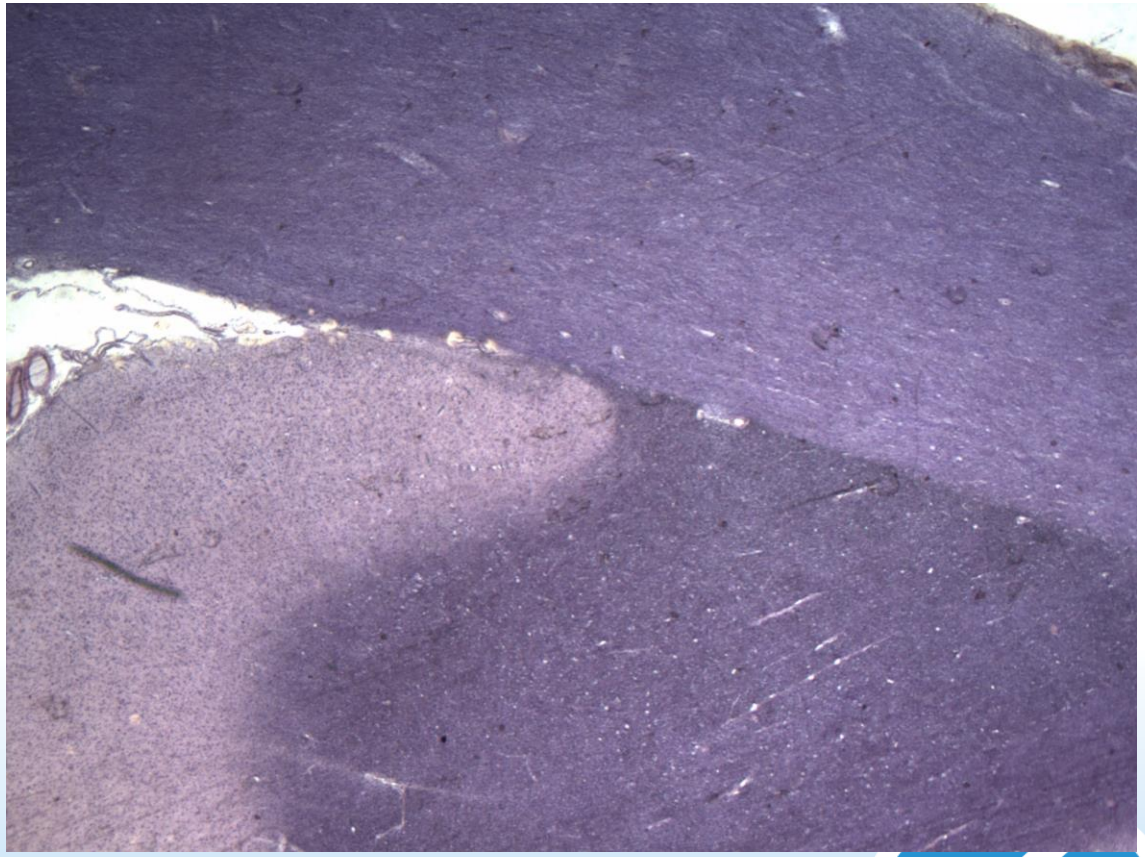
Phosphotungstic acid-hematoxylin (PTAH)

- Typically an astrocytic stain; used with FFPE or celloidin
- Obscured by incidental myelin staining in white matter
- Most useful in gray matter, foci of demyelination, and reactive astrocytes that stain well over the background
- Stains for intracytoplasmic filaments like GFAP
- Also useful for demonstrating banding in longitudinal sections of skeletal and cardiac muscle fibers
- Immunohistochemical equivalent: GFAP (in brain)

From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

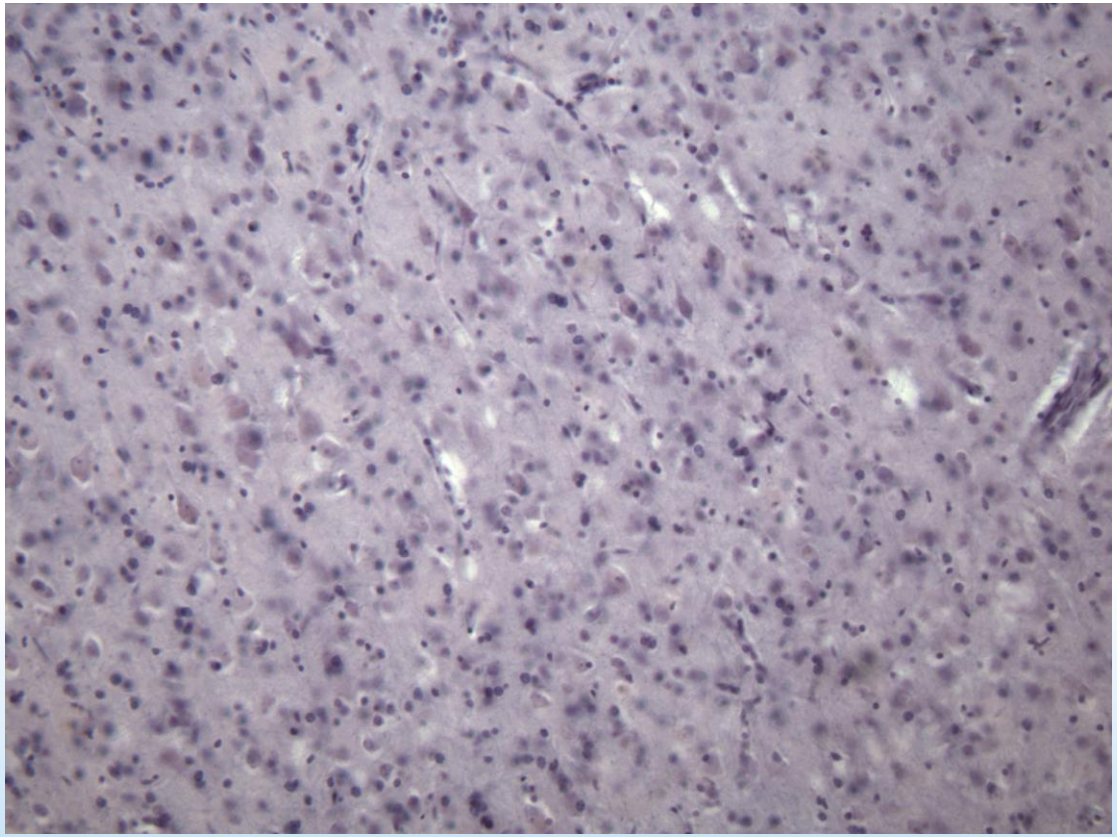
PTAH—whole-mount, celloidin-embedded section



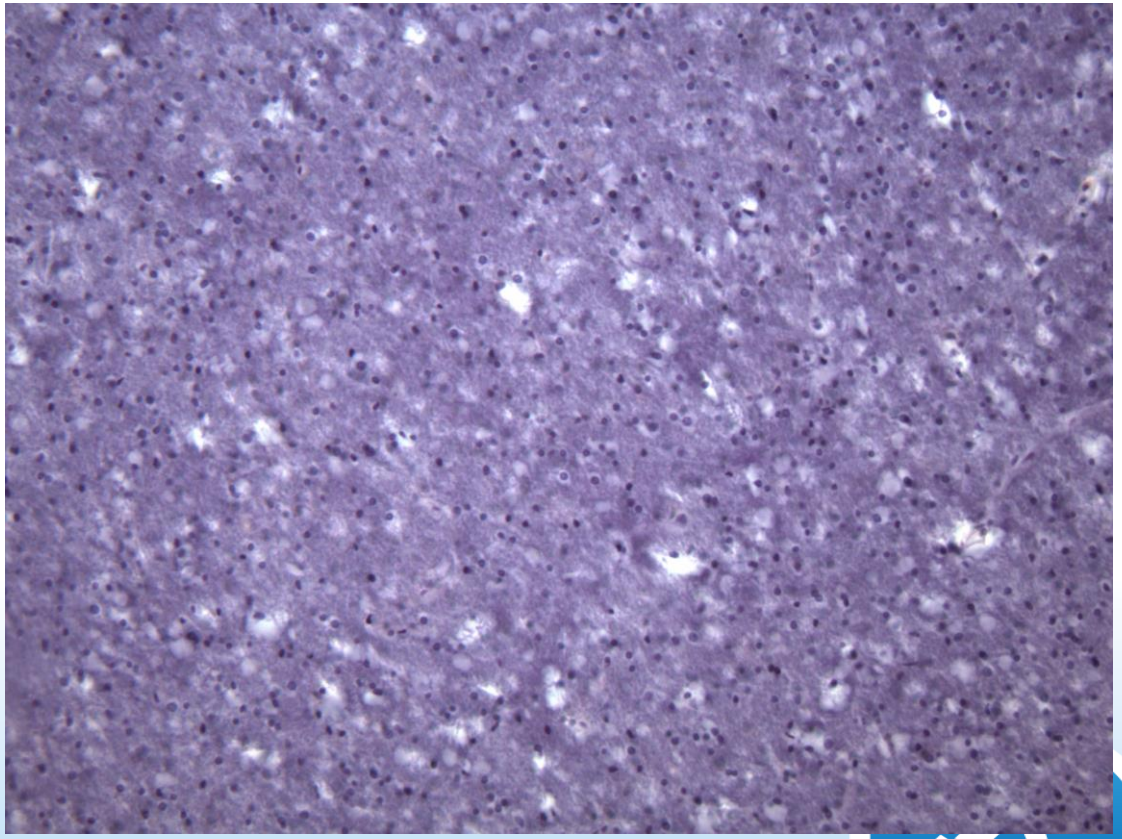


PTAH—whole-mount, celloidin-embedded section

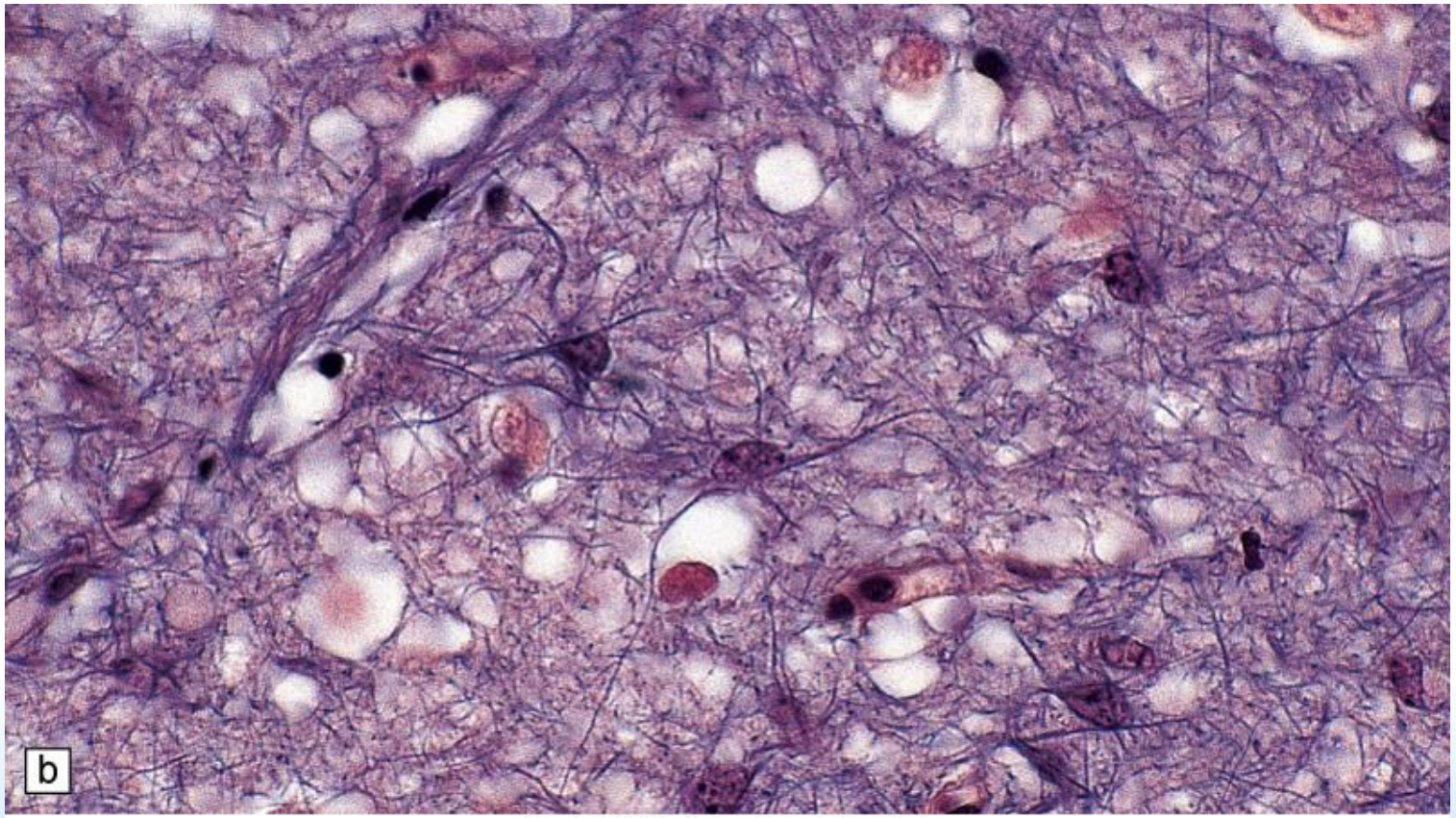
Gray matter



White matter



PTAH—stock photo



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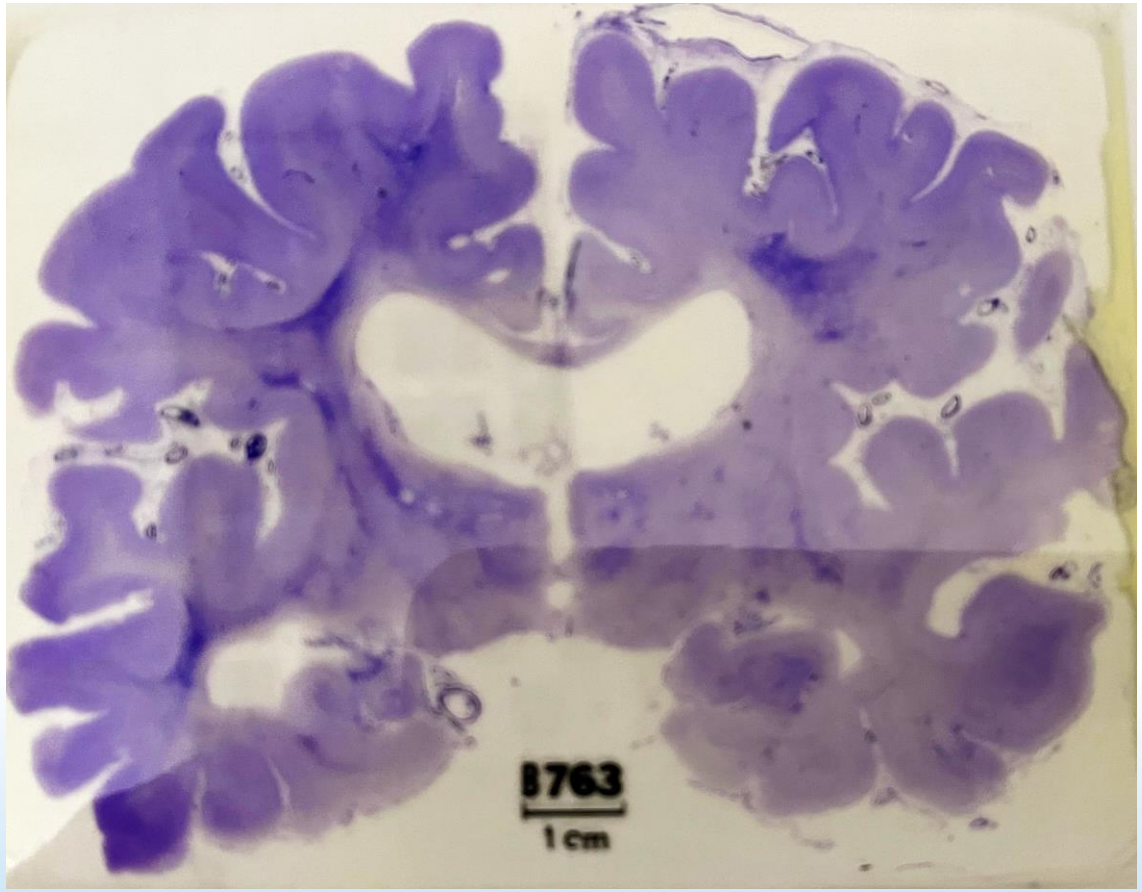
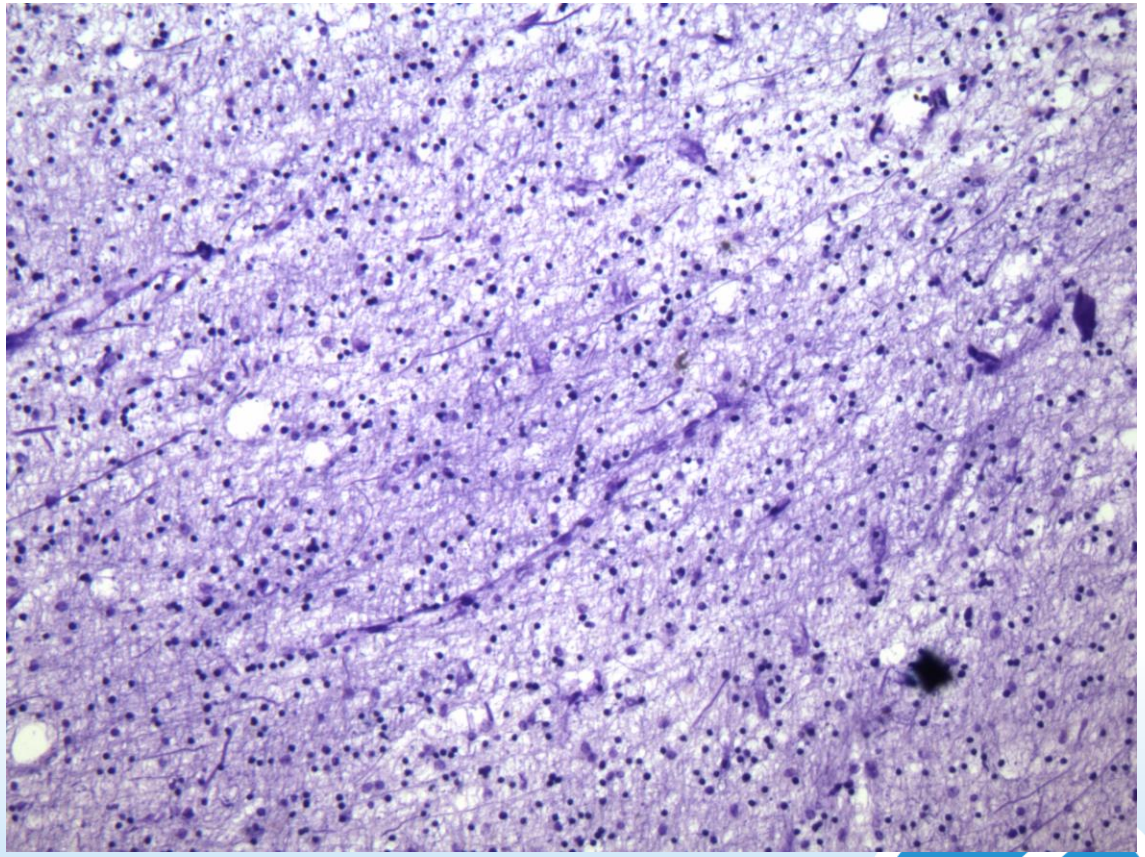
Holzer

- Good stain for demonstrating astrocytes and their processes; used with FFPE or celloidin
- Less incidental staining than with PTAH—astrocytes more easily identified, even in white matter
- Requires aniline oil in the differentiating solution, which is carcinogenic and been withdrawn from use
- Immunohistochemical equivalent: GFAP

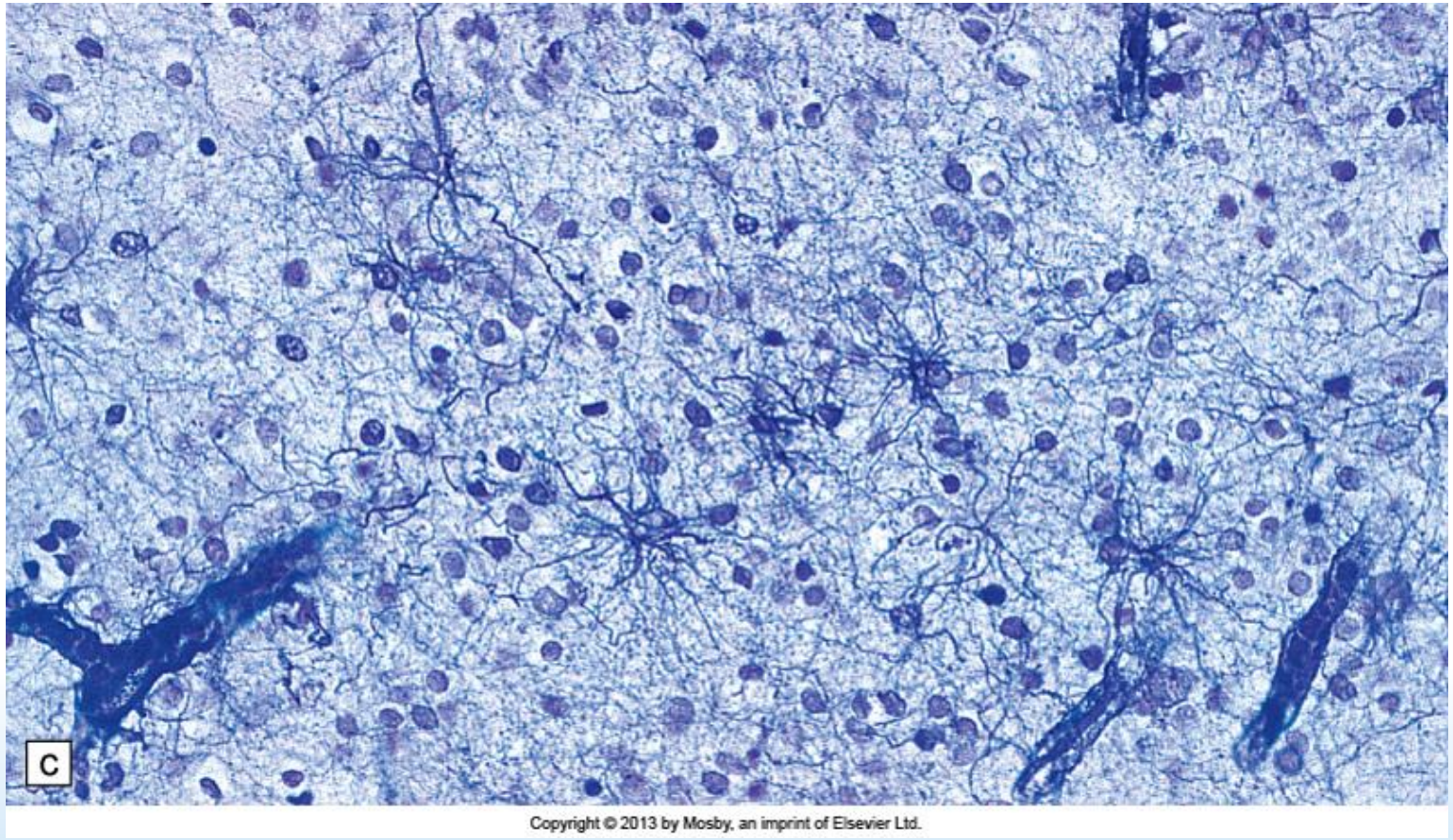
From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

Holzer—whole-mount, celloidin-embedded section





Holzer—stock photo



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Neuropathology-specific stains: neuroendocrine

- **Grimelius**
- Churukian-Schenk (alternative silver stain; FFPE; pink background with red nuclei)
- Periodic acid-Schiff-Orange G (PAS-OG; FFPE; provided basis for categorizing pituitary cells as acidophils, basophils, and chromophobes)

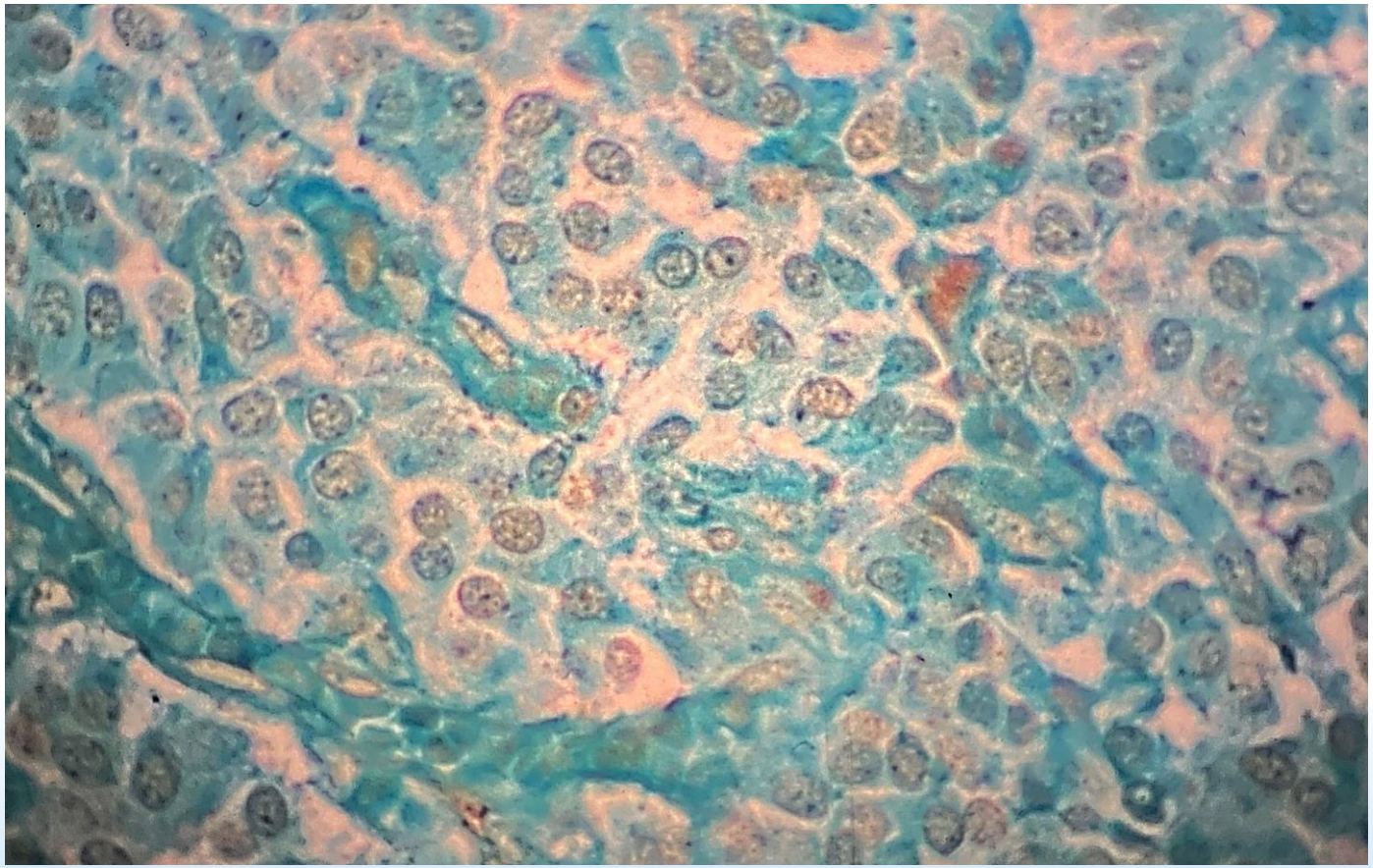
From Dawson TP, Neal JW, Llewellyn L, Thomas C. "Neuropathology Techniques." London: Hodder Arnold, 2003.

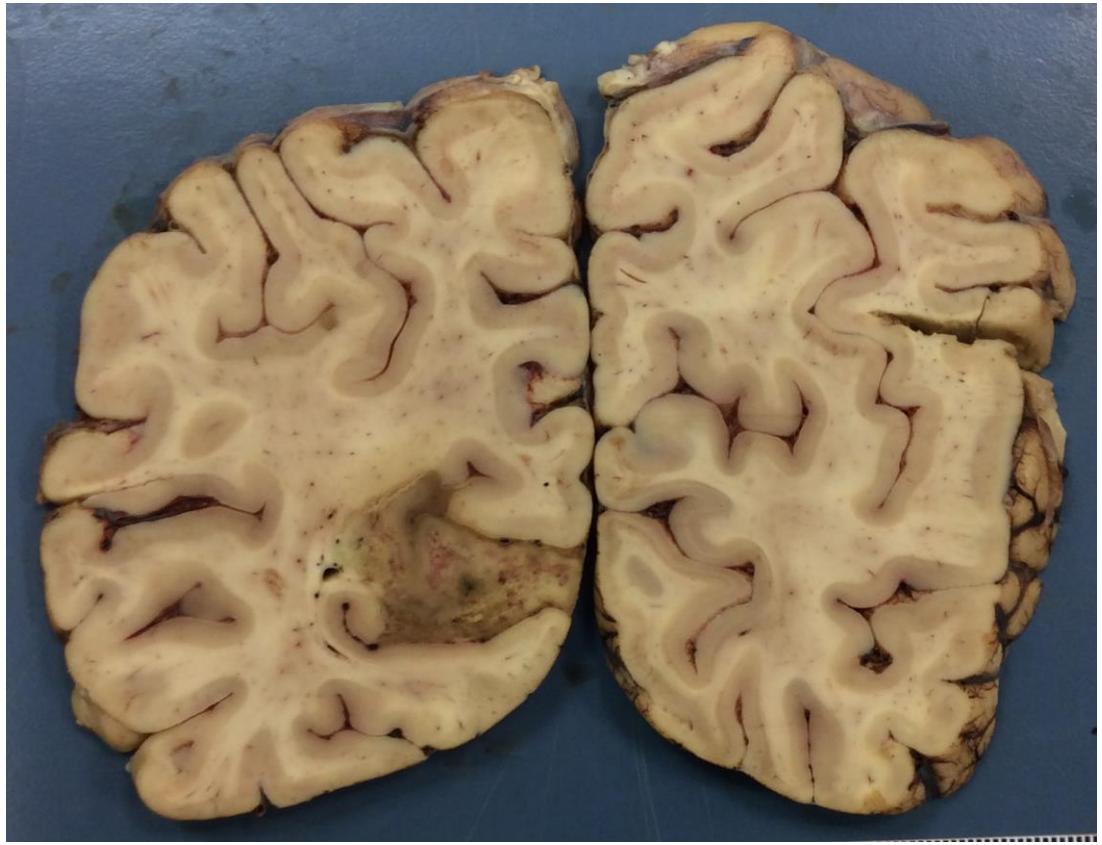
Grimelius

- Argyrophilic silver stain that highlights neuroendocrine granules
- FFPE
- Neuroendocrine cells are black
- Background is pale yellow to green
- Immunohistochemical equivalent: chromogranin, synaptophysin, neuron-specific enolase (NSE)

From Dawson TP, Neal JW, Llewellyn L, Thomas C. “Neuropathology Techniques.” London: Hodder Arnold, 2003.

Grimelius—1997 paraganglioma kodachrome

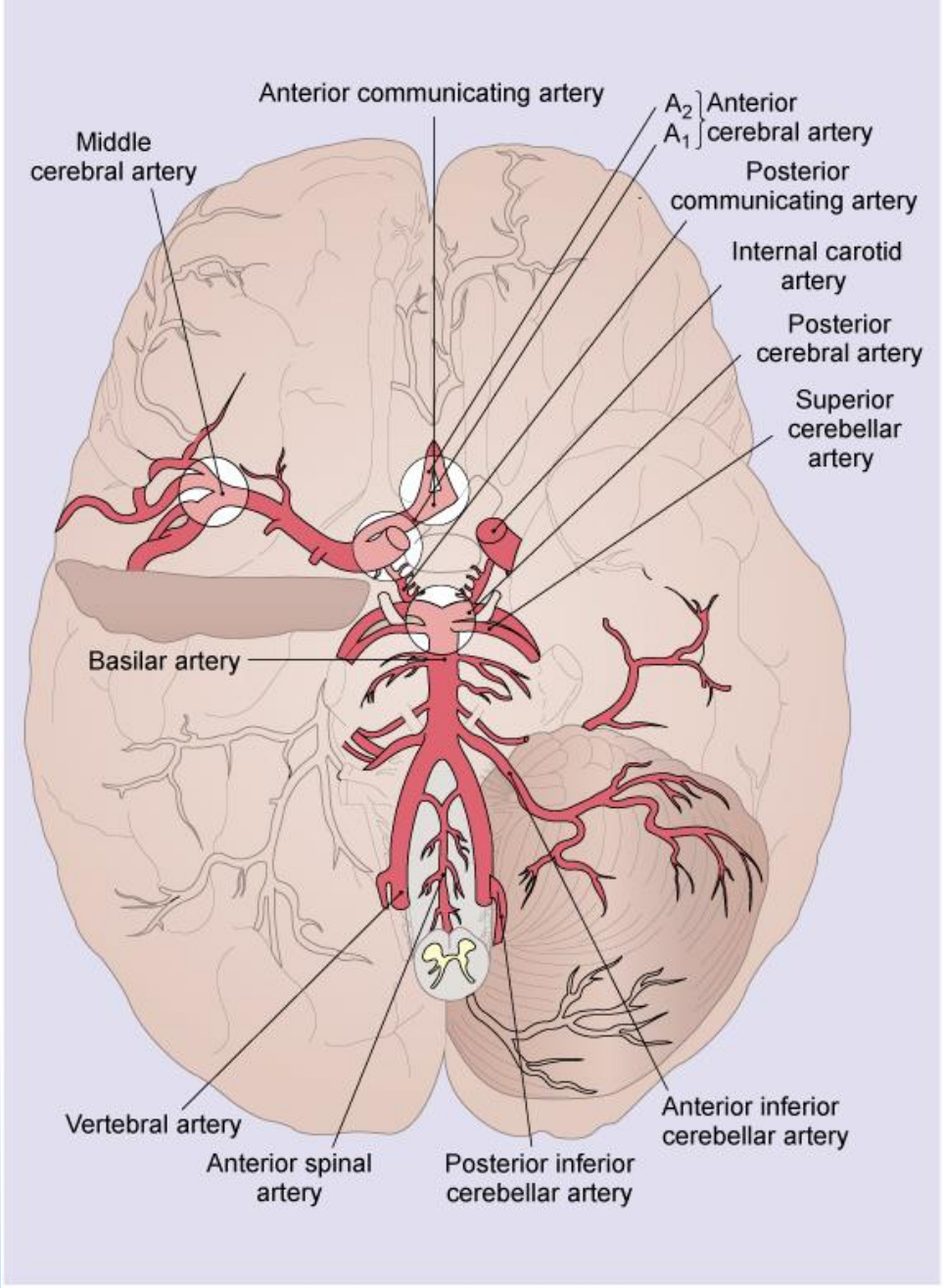




Section #2

GROSS NEUROANATOMY: VASCULAR TERRITORIES

Circle of Willis



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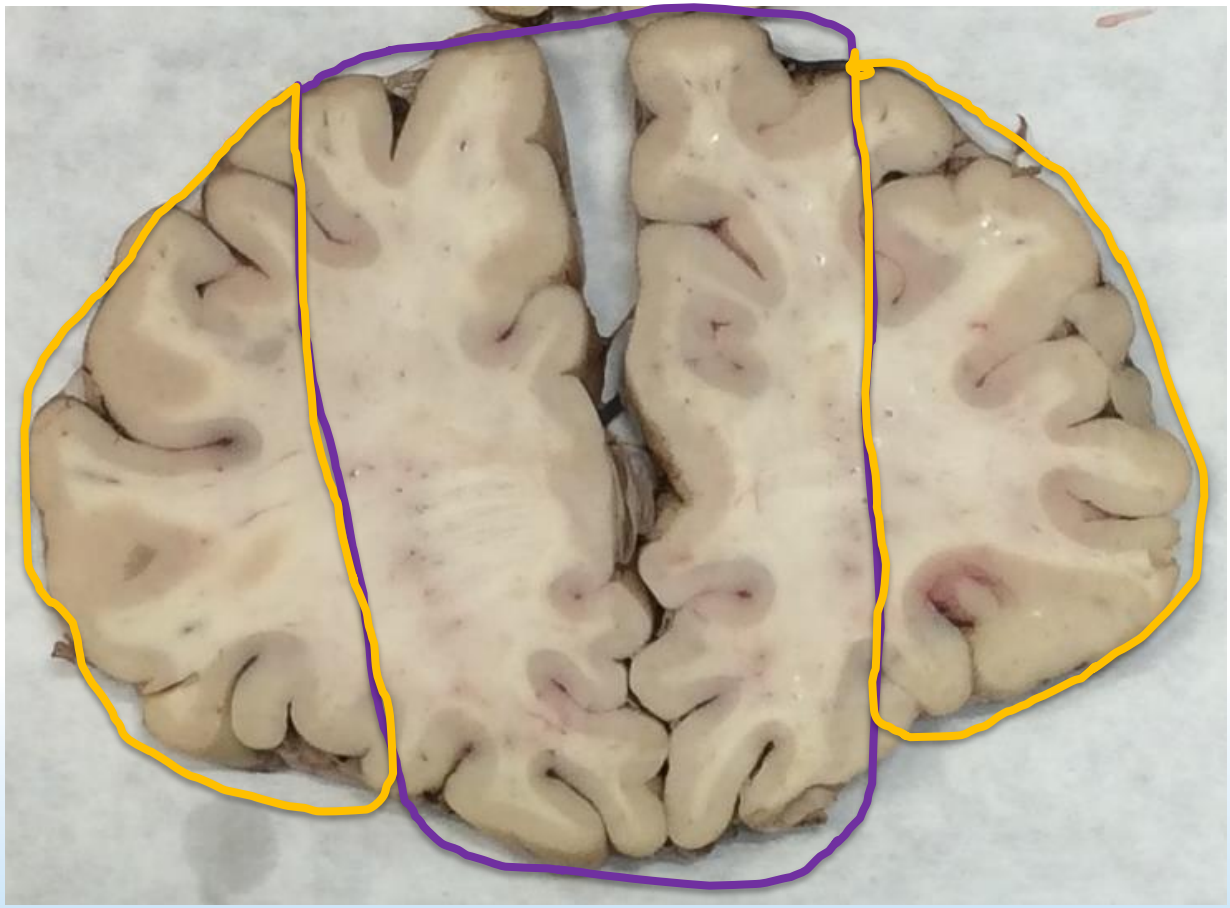
Vascular territories

Anterior cerebral artery

Middle cerebral artery

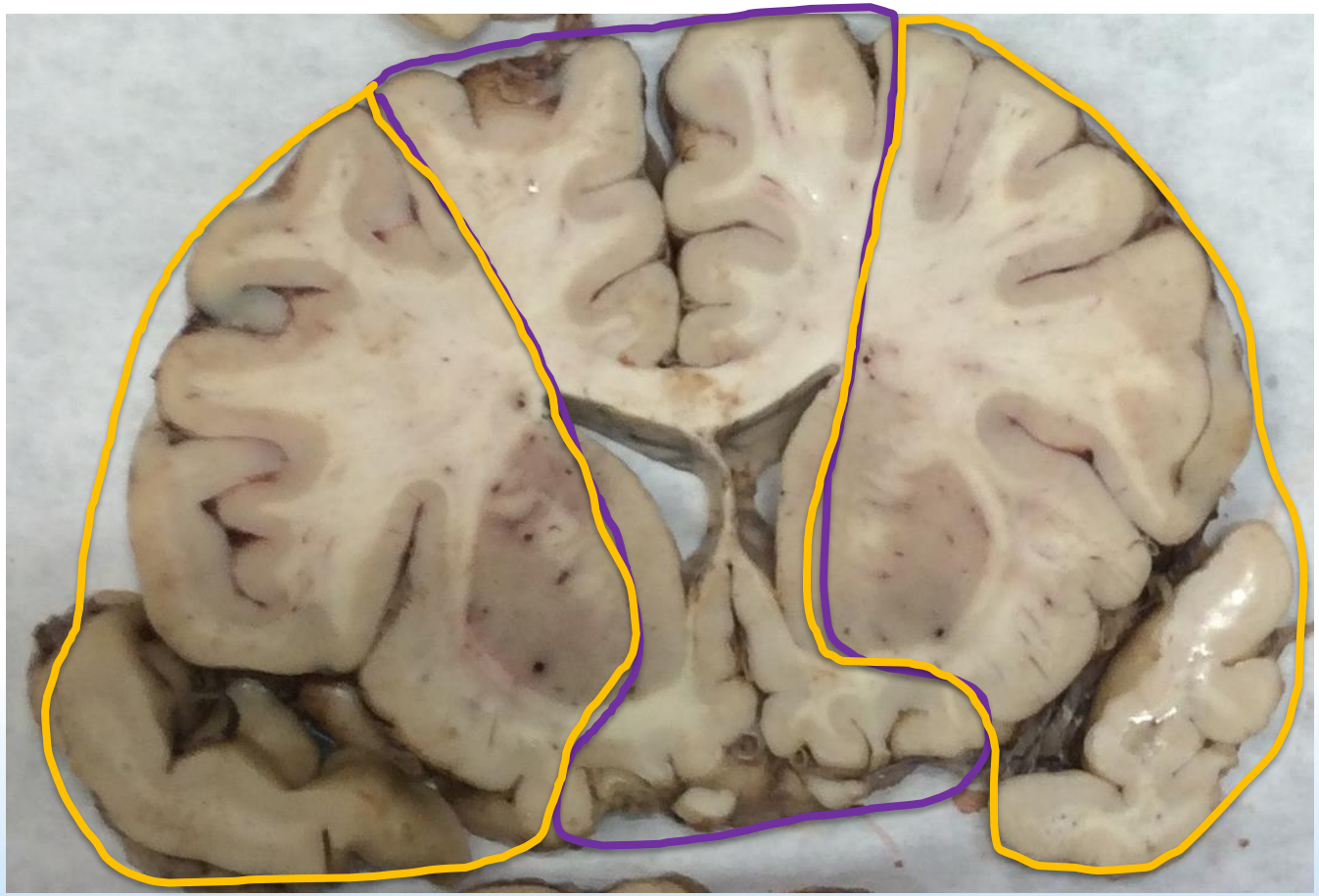


Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

Vascular territories

Anterior cerebral artery

Middle cerebral artery



Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

Vascular territories

Anterior cerebral artery

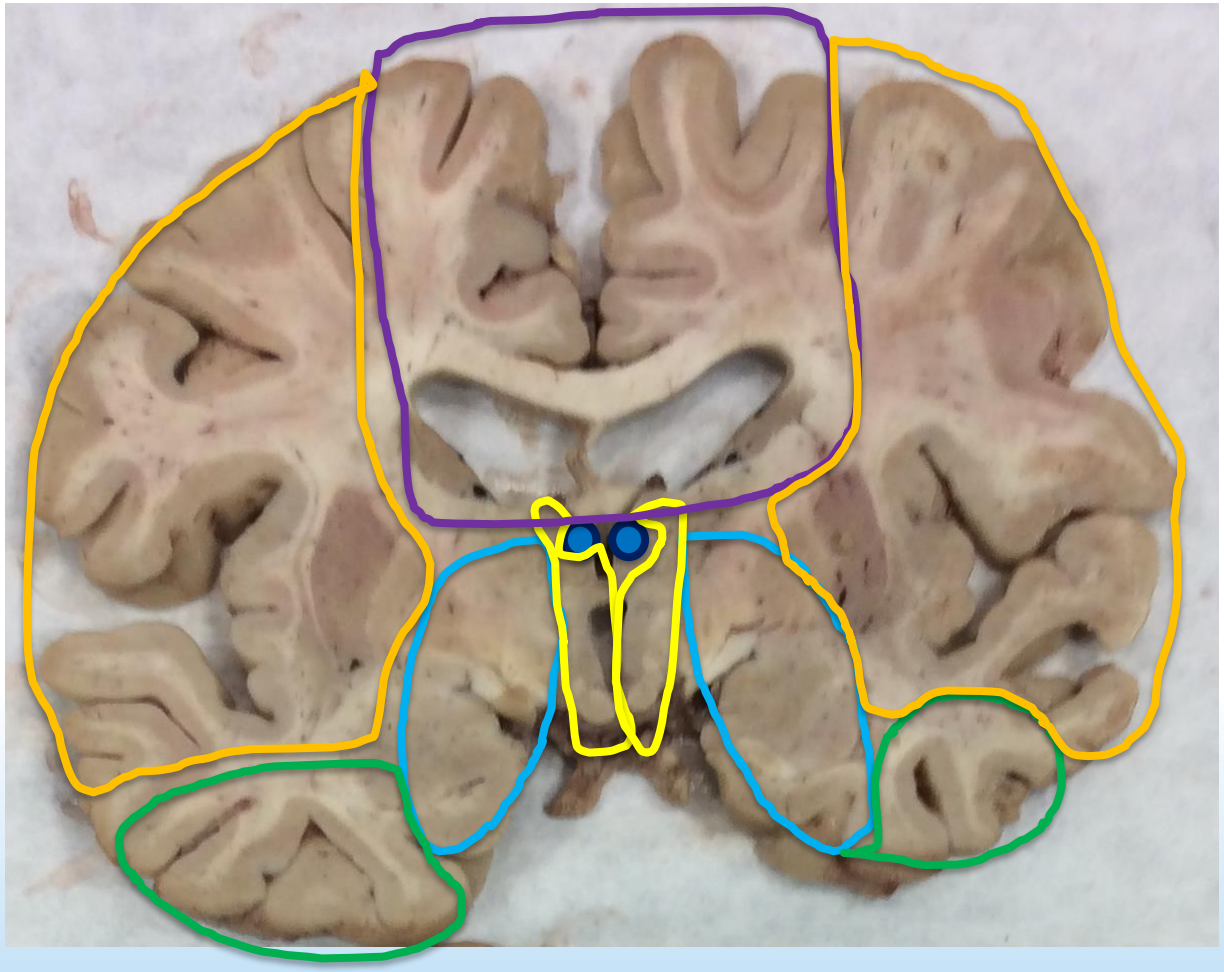
Middle cerebral artery

Posterior cerebral artery

Anterior choroidal artery

Posterior choroidal artery

Posterior communicating artery



Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

Vascular territories

Anterior cerebral artery

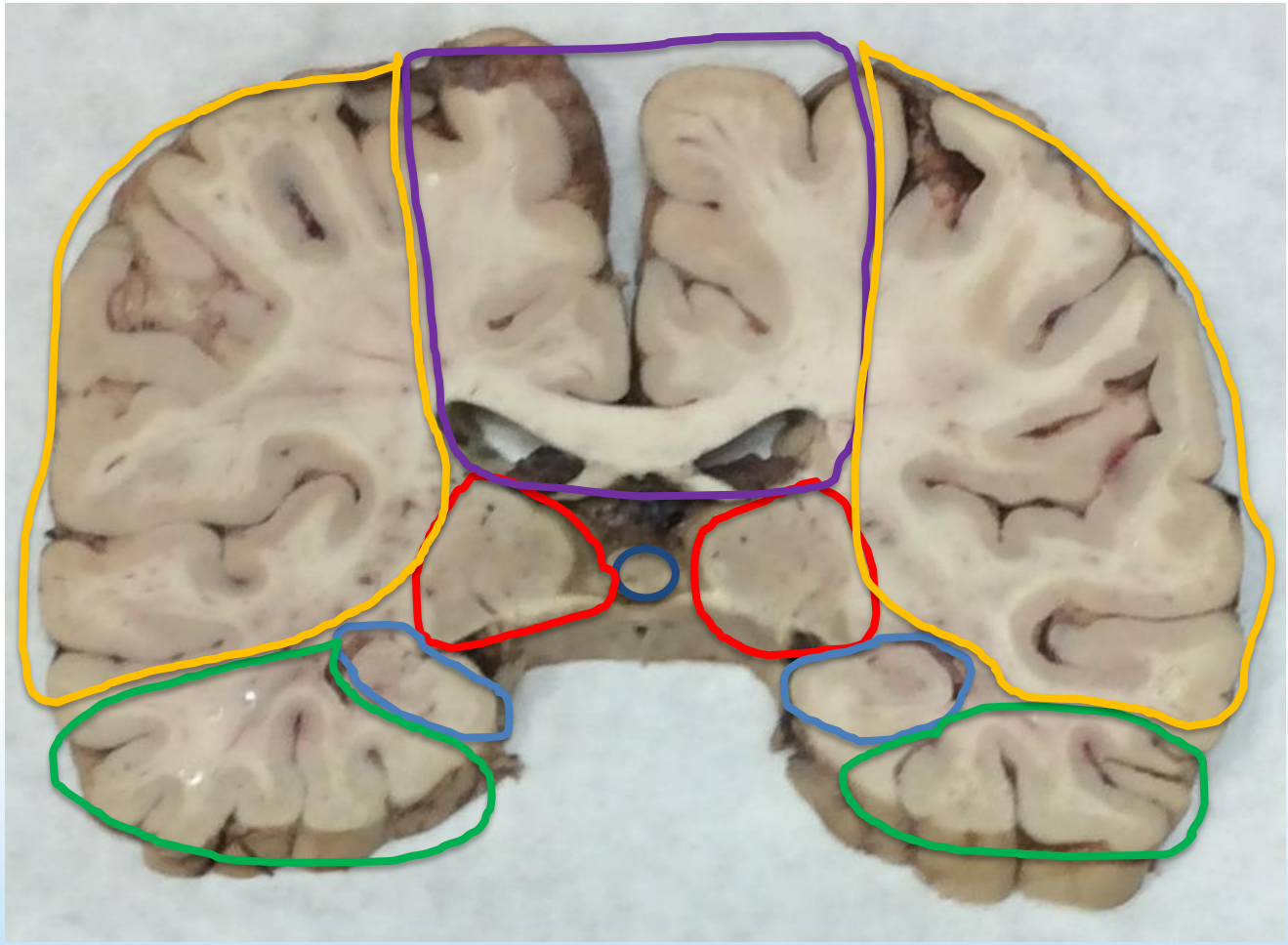
Middle cerebral artery

Posterior cerebral artery

Anterior choroidal artery

Posterior choroidal artery

Thalamic perforating arteries



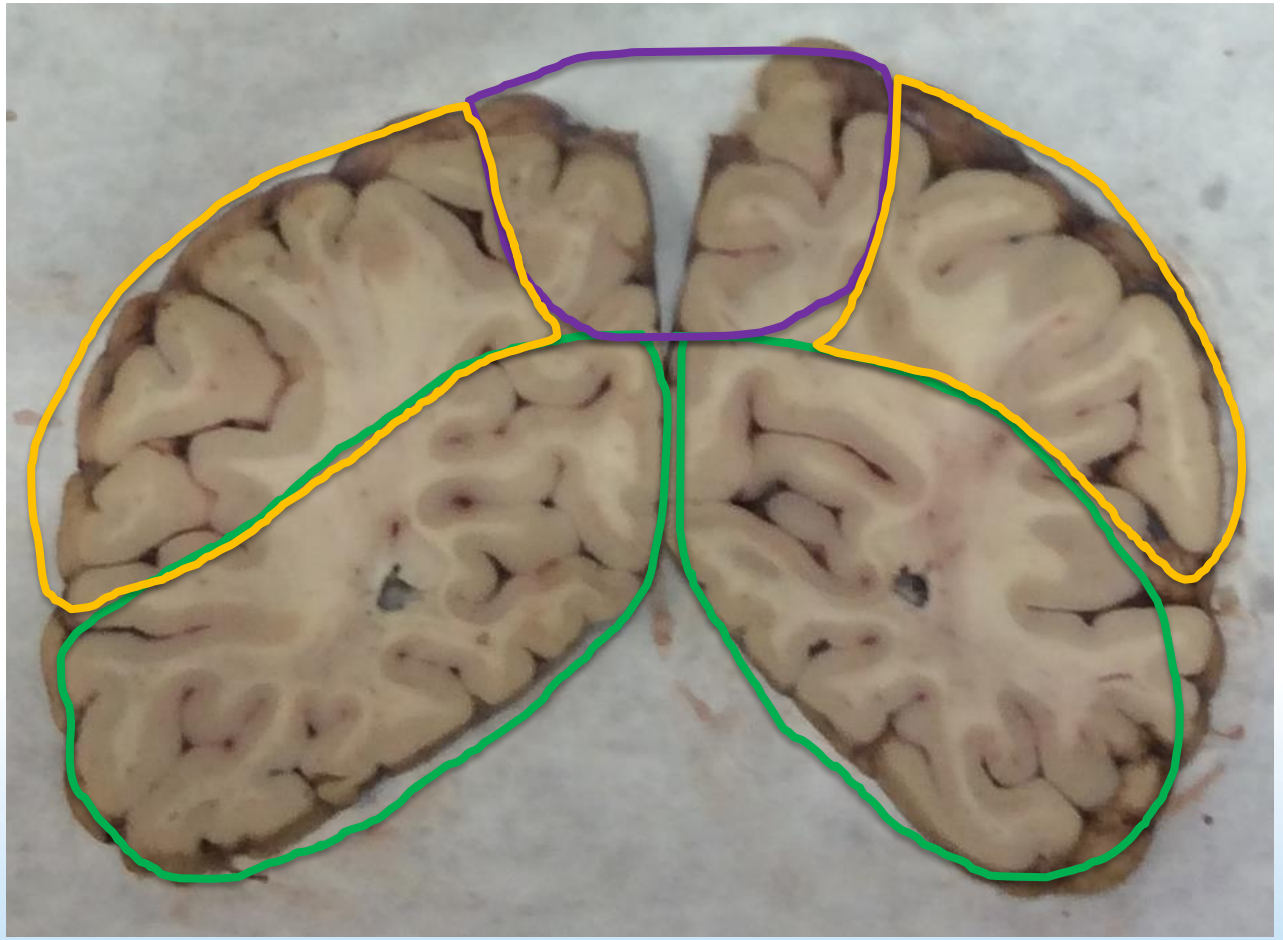
Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

Vascular territories

Anterior cerebral artery

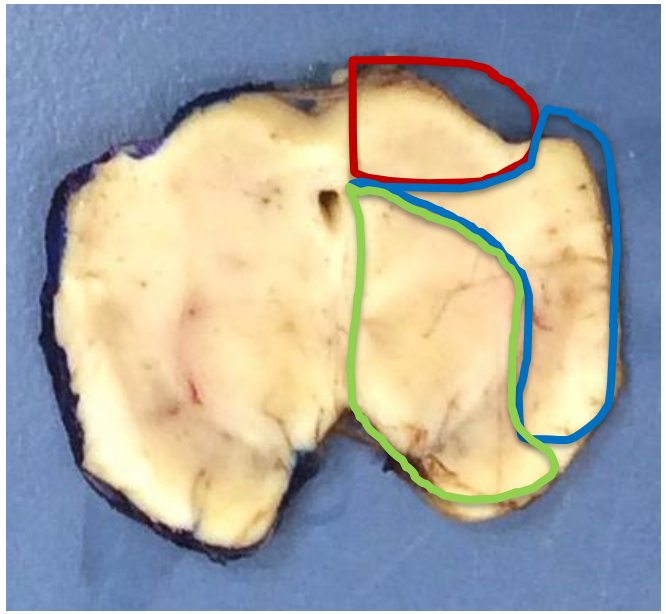
Middle cerebral artery

Posterior cerebral artery



Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

Vascular territories



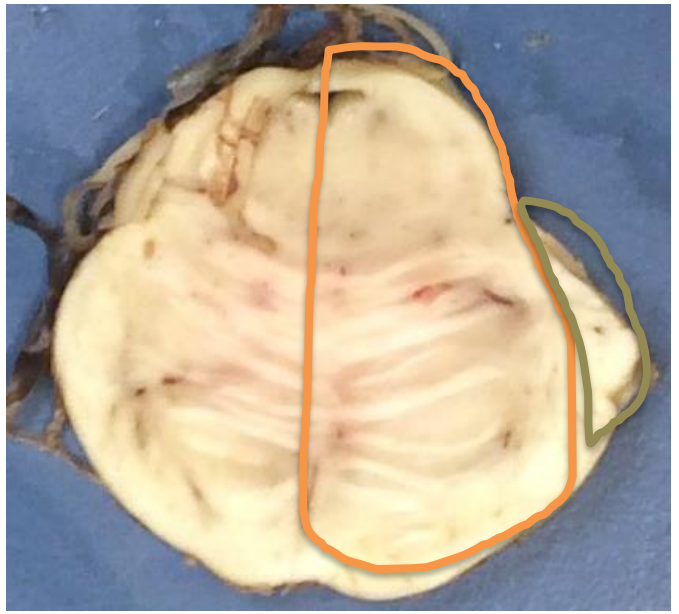
Superior cerebellar artery

Posterior choroidal artery

Posterior cerebral artery perforators

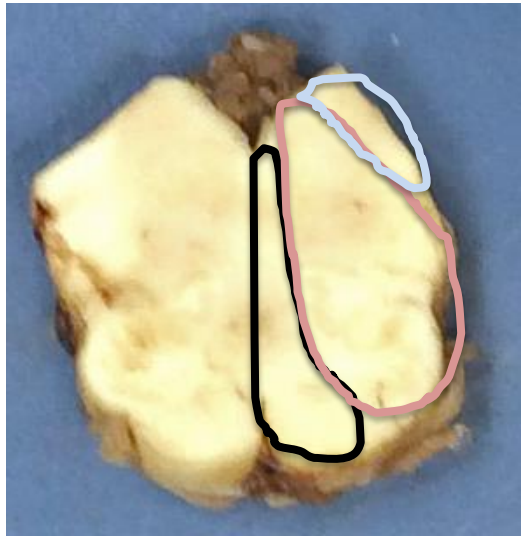
Basilar artery

Anterior inferior cerebellar artery



Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

Vascular territories



Anterior spinal artery

Vertebral artery

Posterior inferior cerebellar artery

Superior cerebellar artery

Anterior inferior cerebellar artery

Adapted from figures in Hanaway J, Woolsey TA, Gado MH, Roberts MP Jr. “The Brain Atlas: A Visual Guide to the Human Central Nervous System.” Fitzgerald Science Press Inc., 1998.

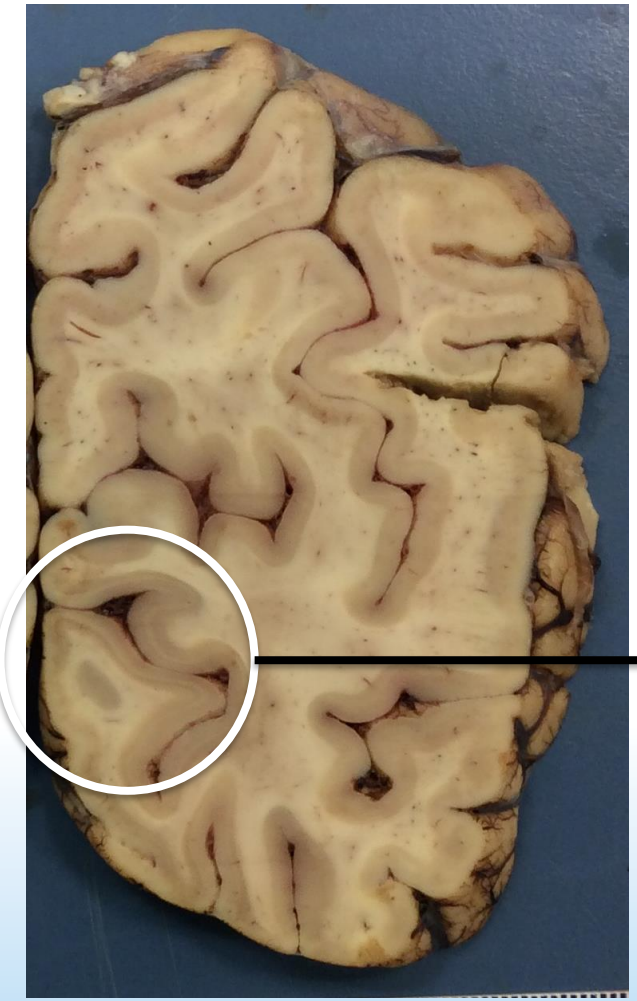
Section #3

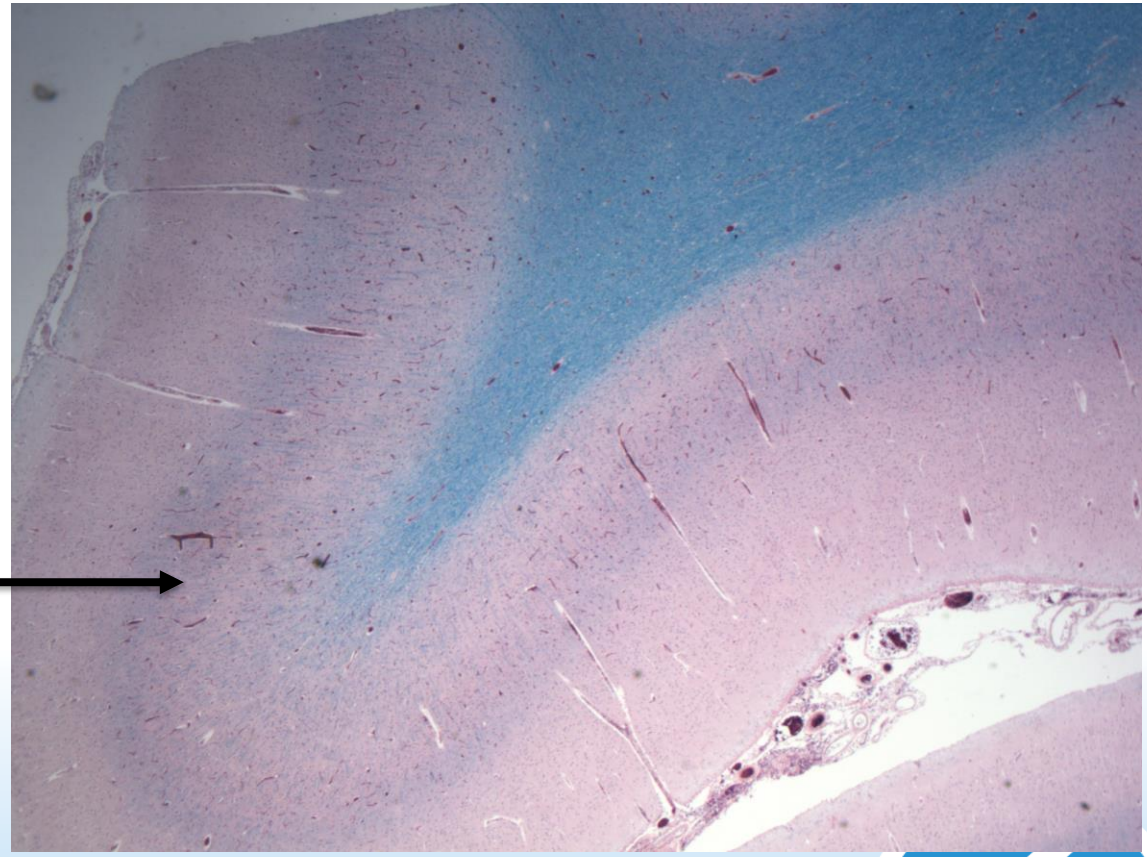
MICROSCOPIC NEUROANATOMY: ETYMOLOGIES AND TIDBITS

Unifying theme of section #3

- You’re sitting around the multiheaded scope with me reviewing brain slides to sign out a case
- I’m rattling off random factoids off the top of my head about some of the brain structures that we are examining to make the signout interesting and educational
- It’s impossible to cover all of neuroanatomy and every tidbit in this limited time

Calcarine cortex: line (stria) of Gennari





Line of Gennari

- Named after Francesco Gennari, 18th-century Italian physician
- Originally described when a medical student but didn't publish until 1782
- Also described by French anatomist Félix Vicq d'Azyr (of "tract of Vicq d'Azyr" fame—the mammillothalamic tract)
- Was knows as the "line of Vicq d'Azyr" for about a century
- Henrich Obersteiner suggested "line of Gennari" in 1888

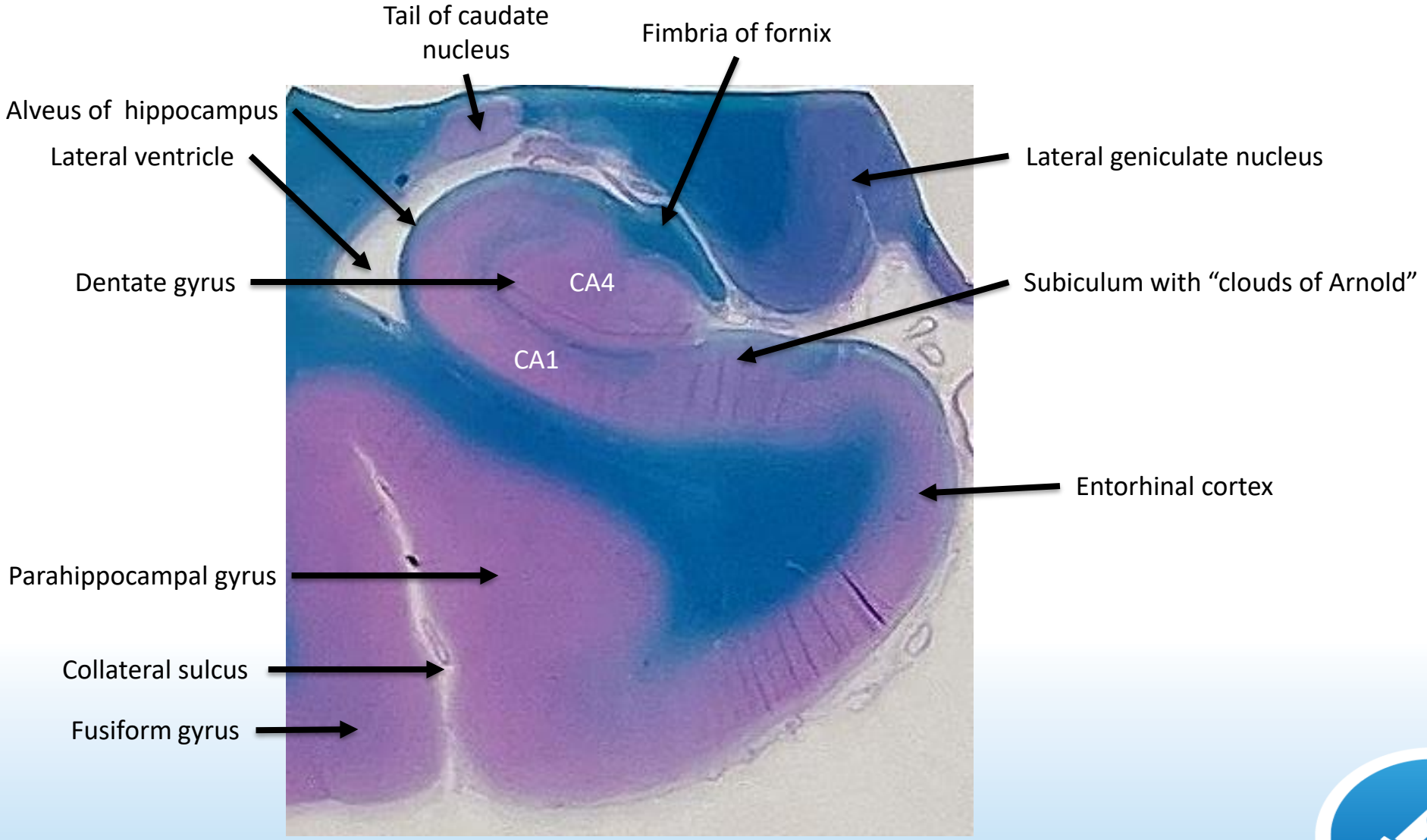
Bakkum BW, "The Line of Gennari—Sometimes History Gets It Right," *J Hist Neurosci* 2015; 24: 95-101.

Bands of Baillarger

- Line of Gennari is the outer band of Baillarger in the primary visual cortex
- Outer (layer IV) and inner (layer V) bands of Baillarger are tangential myelinated fibers in the cerebral cortex running parallel to the surface
- Most prominent in sensory areas due to high concentration of thalamocortical fibers
- Described by French neurologist/psychiatrist Jules Baillarger in 1840

Snell RS. "Clinical Neuroanatomy, Seventh Edition." Lippincott Williams & Wilkins, 2010.
Leblanc R, "The perversion of language: Jules Baillarger on aphasia, the lateralization of speech, and the Baillarger-Jackson principle," *J Hist Neurosci* 2021; 30: 277-299.

Hippocampus/medial temporal cortex

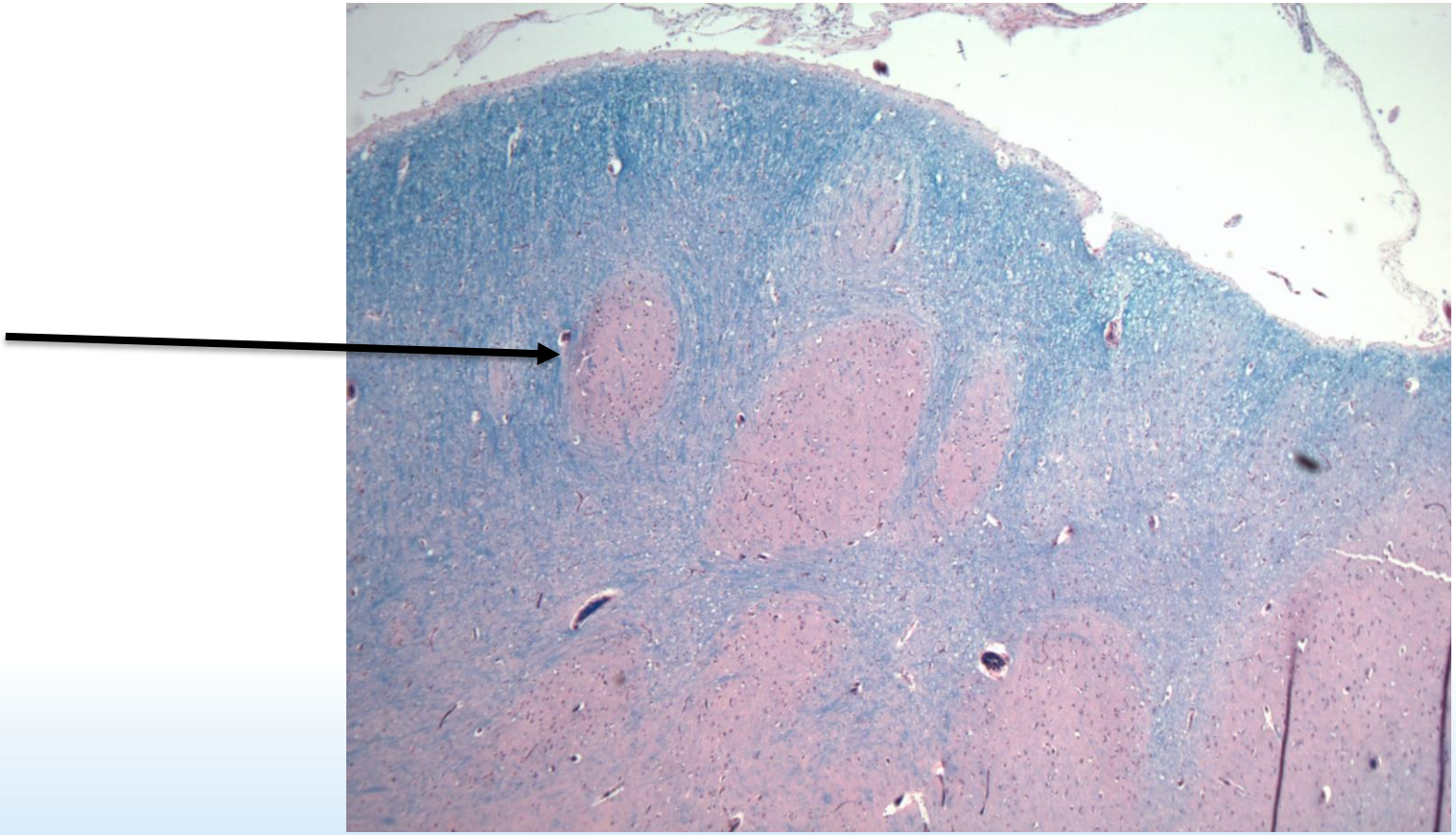


Sampling of limbic system structures

- Limbic system (Latin *limbus*, “border”—limbic system forms a border around the brainstem)
- Cingulate gyrus (Latin *cingulum*, “belt”—above corpus callosum)
- Hippocampus (Greek, “seahorse”)
- CA = *Cornu Ammonis*, “Ammon’s horn”
- Uncus (Latin, “hook”)—anterior end of parahippocampal gyrus
- Alveus (Latin, “trough” or “canal”)
- Fornix (Latin, “arch”)
- Fimbria (Latin, “fringe”)
- Amygdala (Greek, “almond”)
- Thalamus (Greek, “bridal couch” or “wedding chamber“)

Afifi AK, Bergman RA. “Functional Neuroanatomy: Text and Atlas.” McGraw-Hill, 1998.

Clouds of Arnold

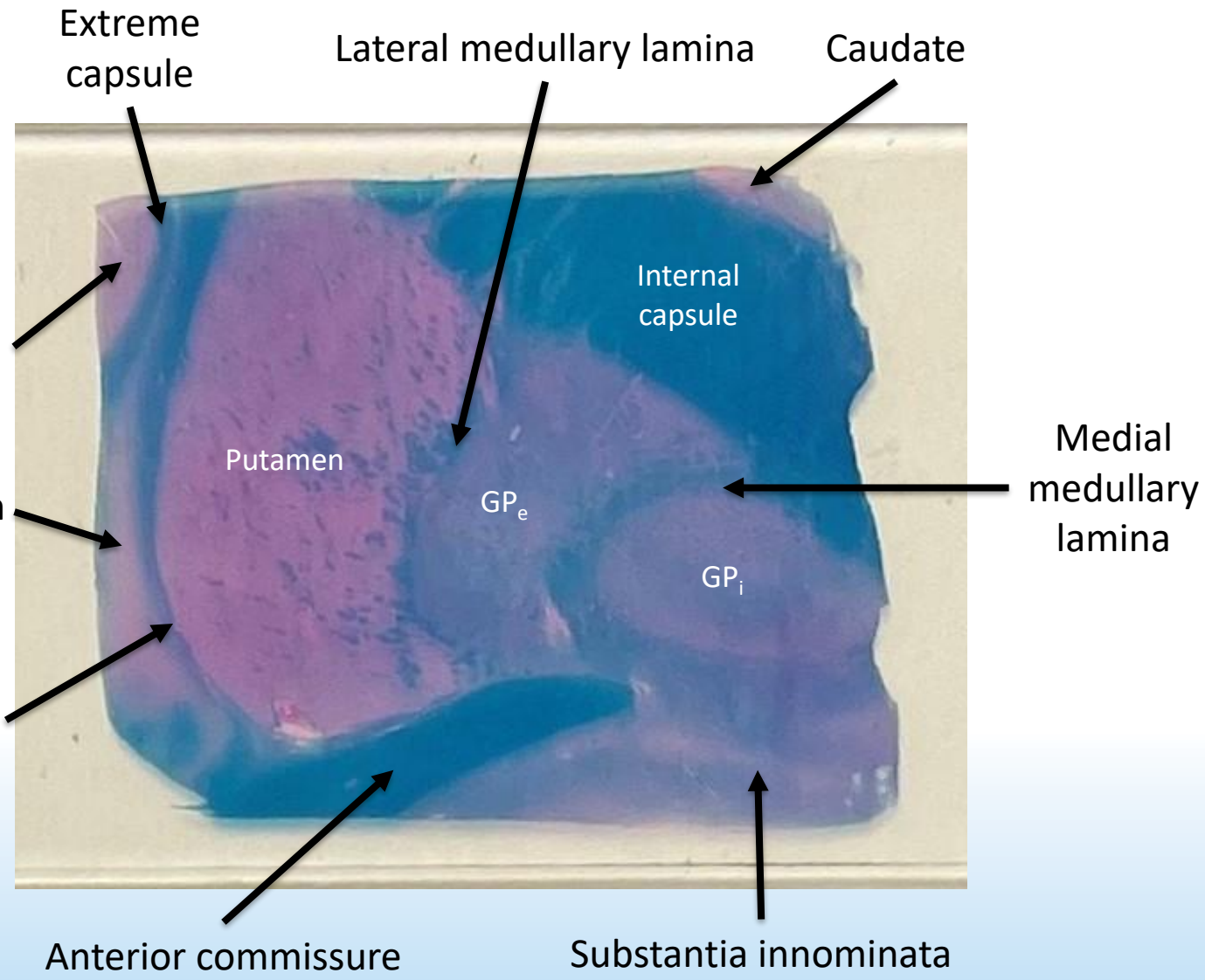


Clouds of Arnold

- Clusters of neurons appearing just below the pial surface as the temporal neocortex transitions into the subiculum (Latin for “support”—it’s the “support” beneath the central hippocampus)
- Named for German neuroanatomist Friedrich Arnold
- *Handbuch der Anatomie des Menschen* (1851)

Louis DN, Frosch MP, Mena H, Rushing EJ, Judkins AR. “Atlas of Nontumor Pathology: Non-Neoplastic Diseases of the Central Nervous System.” AFIP, 2009.
Adanir SS, Bahşi I, Orhan M, “Contributions to our modern understanding of cranial nerves and brain: Friedrich Arnold,” *Childs Nerv Syst* 2019; 35: 577-580.

Basal ganglia



Sampling of basal ganglia and adjacent structures

- Caudate (Latin, “having a tail”)
- Putamen (Latin, “shell”)
- Globus pallidus (Latin, “pale sphere”)
- Striatum (Latin *striatus*, “striped”)
- Lentiform nucleus (Latin *lens*, “lentil” and *forma*, “shape”)
- Substantia nigra (Latin, “black substance”)
- Insula (Latin, “island”)
- “Island of Reil”—Johann Christian Reil, Danish physiologist, anatomist, and psychiatrist (late 18th, early 19th centuries)

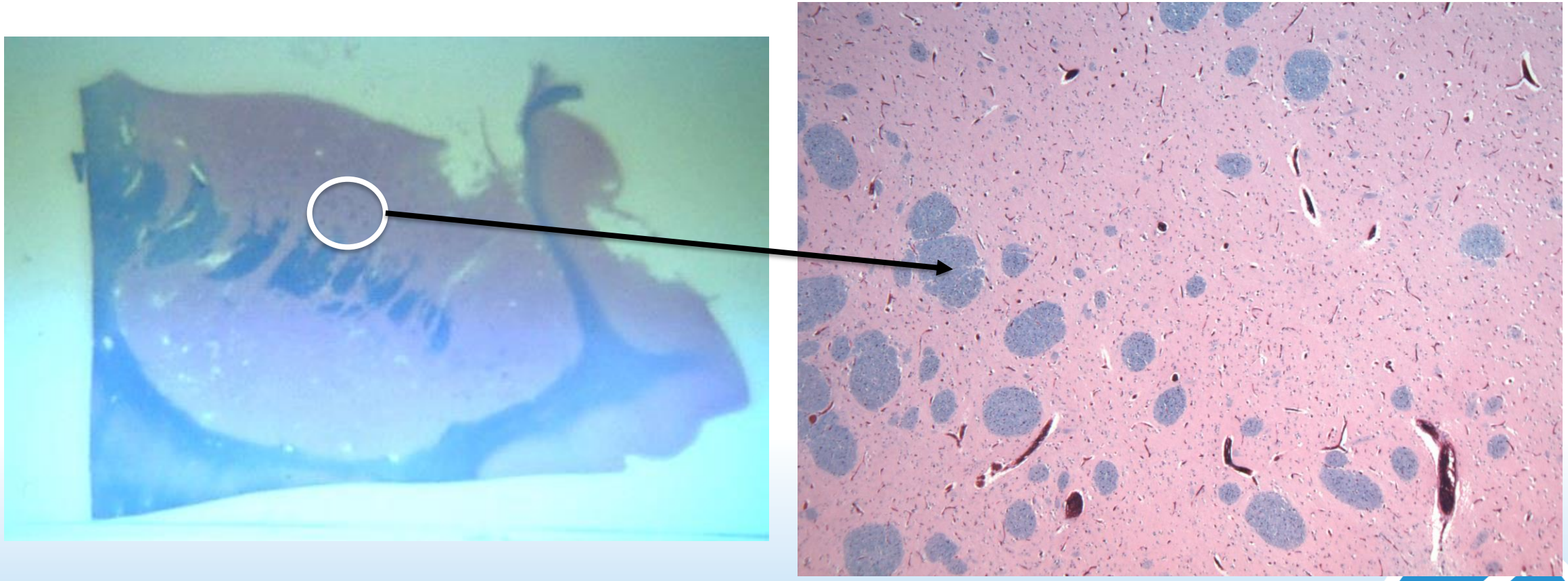
Afifi AK, Bergman RA. “Functional Neuroanatomy: Text and Atlas.” McGraw-Hill, 1998.

Claustrum

- Latin for “wall” or “barrier”
- Poorly-understood structure: complex shape/deep location
- Thought to be crucial to neural homeostasis
- Integrates multiple sensory inputs to promote reward-related behavior
- Changes in structure and volume in neurodegenerative diseases

Nikolenko VN, Rizaeva NA, Beeraka NM, *et al.*, “The mystery of claustral neural circuits and recent updates on its role in neurodegenerative pathology,” *Behav Brain Funct* 2021; 17**:** 8. https://doi.org/10.1186/s12993-021-00181-1.

Pencil fibers of Wilson

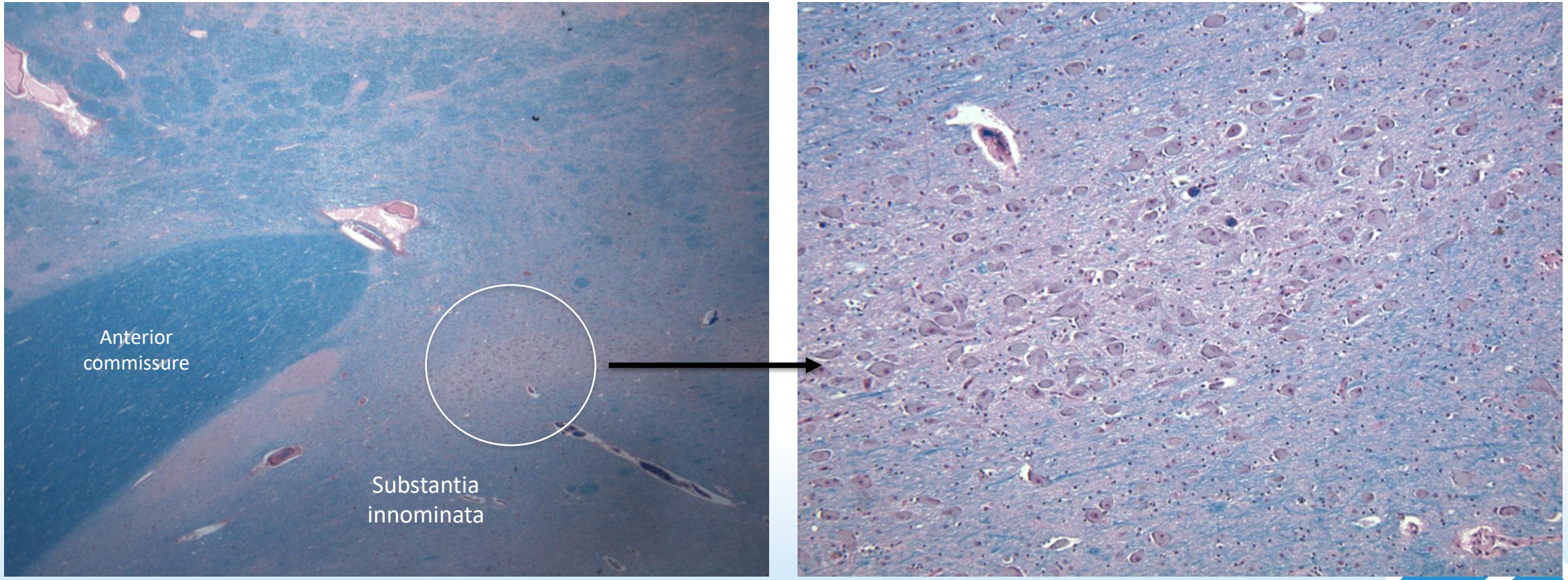


Pencil fibers of Wilson

- Small white matter bundles of the internal capsule that are specific for the caudate and putamen (striatum)
- “Striatopallidal fibers”—connect to globus pallidus
- Described by Samuel Alexander Kinnier Wilson (American-born British neurologist of “Wilson disease” fame) using the Marchi staining method for myelin

Broussolle E, Trocello J-M, Woimant F, Lachaux A, Quinn N, “Samuel Alexander Kinnier Wilson. Wilson’s disease, Queen Square, and Neurology,” *Rev Neurol (Paris)* 2013; 169: 171-184.
Wilson CJ, “Chapter 3—The history of the basal ganglia: cells and circuits,” *Handb Behav Neurosci* 2016; 24: 45-62.

Nucleus basalis of Meynert



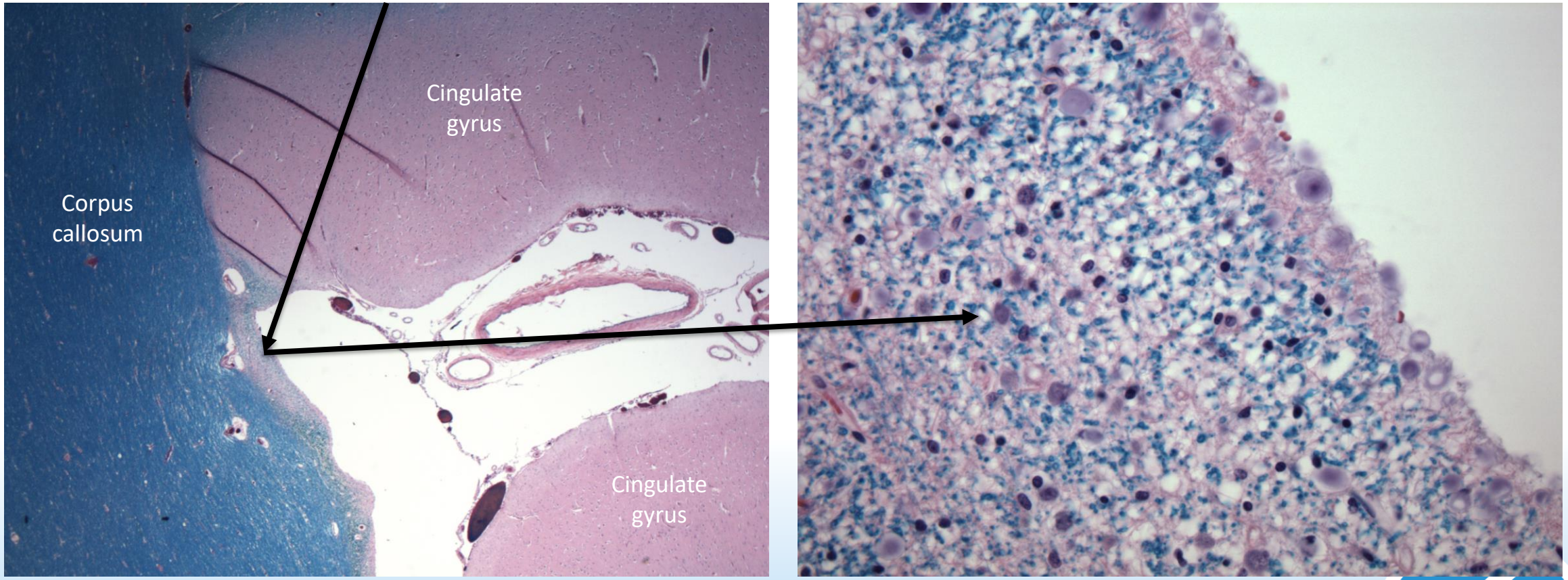
Nucleus basalis of Meynert

- Part of the substantia innominata (Latin for “unnamed substance”) below the anterior thalamus and lentiform nucleus
- The major source of cholinergic input to the cerebral cortex
- Named after Theodor Meynert, a 19th-century German-Austrian psychiatrist, neuropathologist, and anatomist

Seitelberger F, “Theodor Meynert (1833-1892): pioneer and visionary of brain research,” *J Hist Neurosci* 1997; 6: 264-274.

Indusium gresium (IG)

Indusium gresium



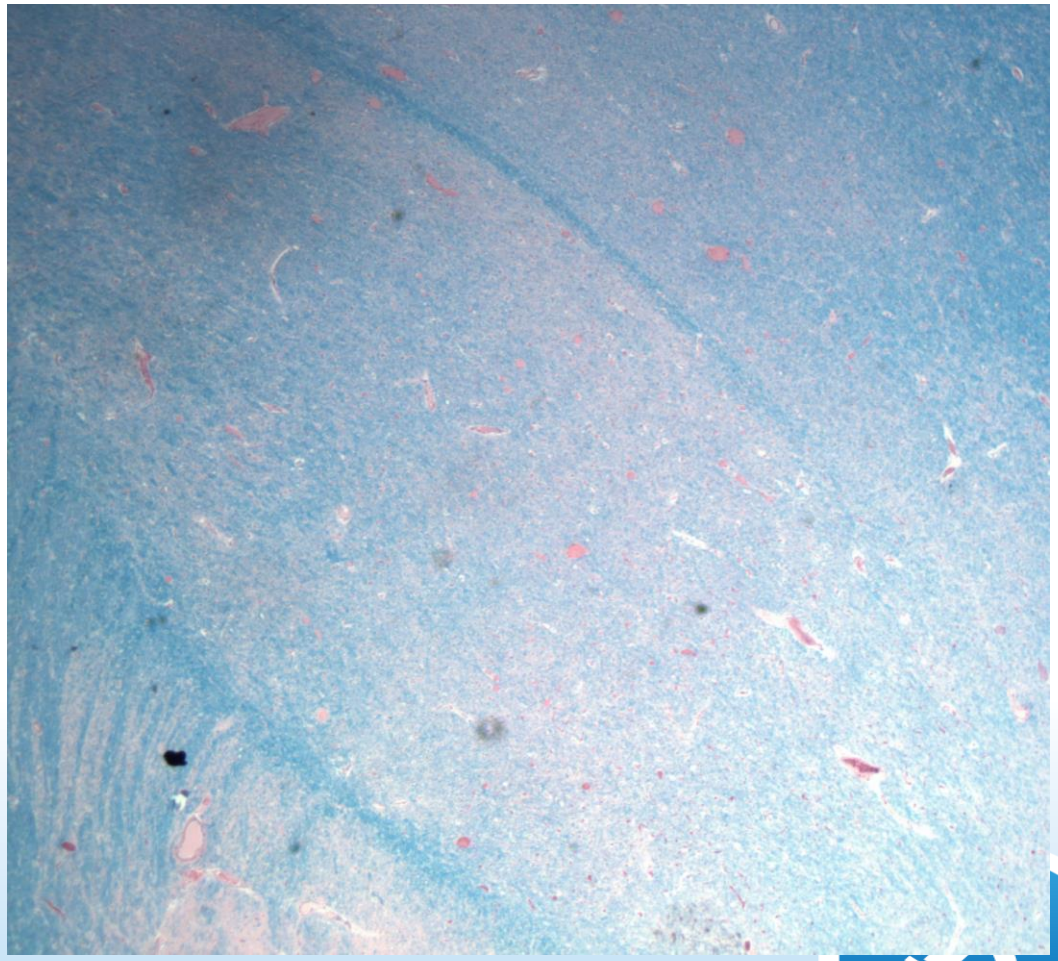
Indusium gresium (IG) and longitudinal stria (LS) of the corpus callosum (CC)

- IG is Latin for “gray underwear”; CC is Latin for “tough body”
- Described by Giovanni Maria Lancisi of Italy in 1712
  - CC was the “seat of the soul” and medial LS (“nerves of Lancisi”) was pathway for consciousness
  - Thought lateral LS were merely folded-up edges of the CC
- Embryologic dorsal remnants of hippocampus and fornix—part of limbic system
- IG innervated by cholinergic, dopaminergic, noradrenergic, serotonergic, and GABA-ergic neurons
- True function unknown

Di Ieva A, Tschabitscher M, Rodriguez y Baena R, “Lancisi's nerves and the seat of the soul,” *Neurosurgery* 2007; 60: 563-568.
Di Ieva A, Fathalla H, Cusimano MD, Tschabitscher M, “The indusium griseum and the longitudinal striae of the corpus callosum,” *Cortex* 2015; 62: 34-40.

Subthalamic nucleus ("body of Luys")

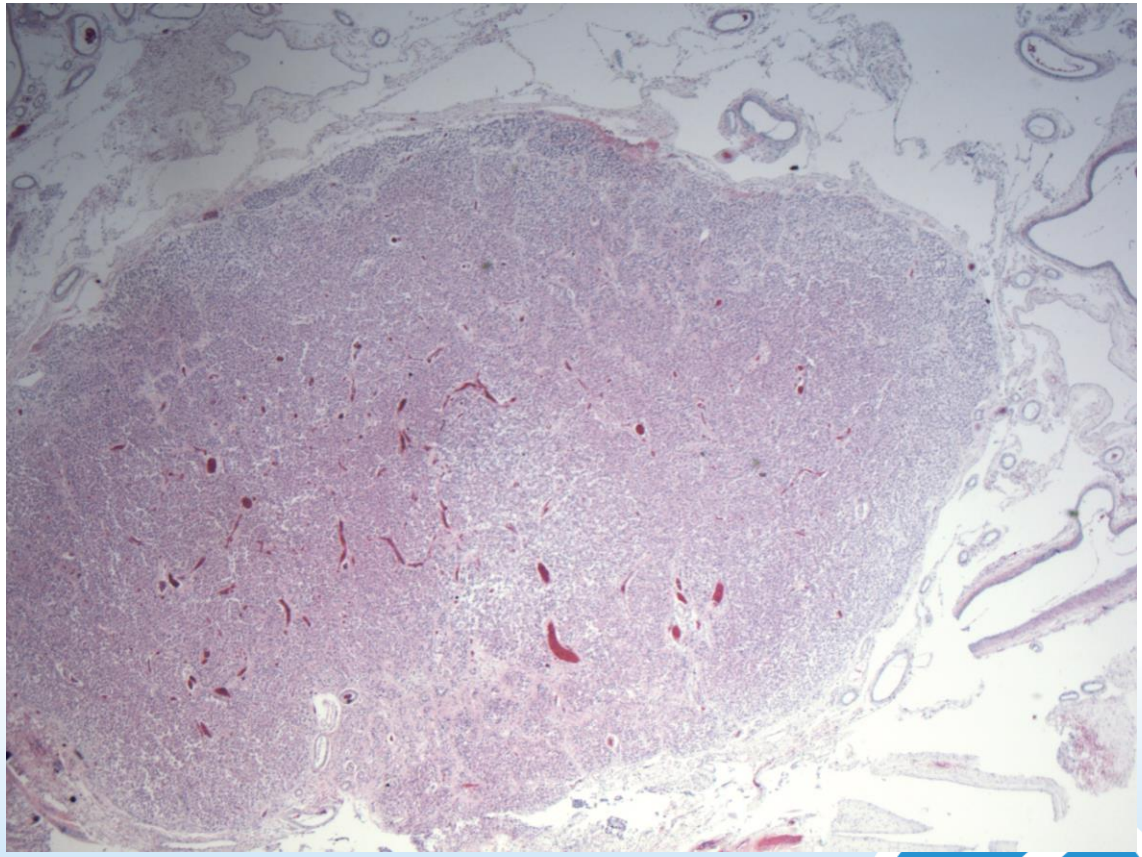
- Named after Jules Bernard Luys, a 19th-century French neurologist who made important contributions to neuroanatomy and neuropsychiatry
- Where "luysian" comes from in dentatorubropallidoluysian atrophy (DRPLA)
- Lesions can cause hemiballismus



Parent A, Parent M, Leroux-Hugon V, "Jules Bernard Luys: a singular figure of 19th century neurology," *Can J Neurol Sci* 2002; 29: 282-288.

Pineal gland

- Derived from Latin *pinea*, “pine cone”
- Considered the “seat of the soul” by Descartes (17th century)
- Secretes melatonin; involved in circadian rhythms
- One of the “circumventricular organs” (parts of the brain that lack a blood-brain barrier)



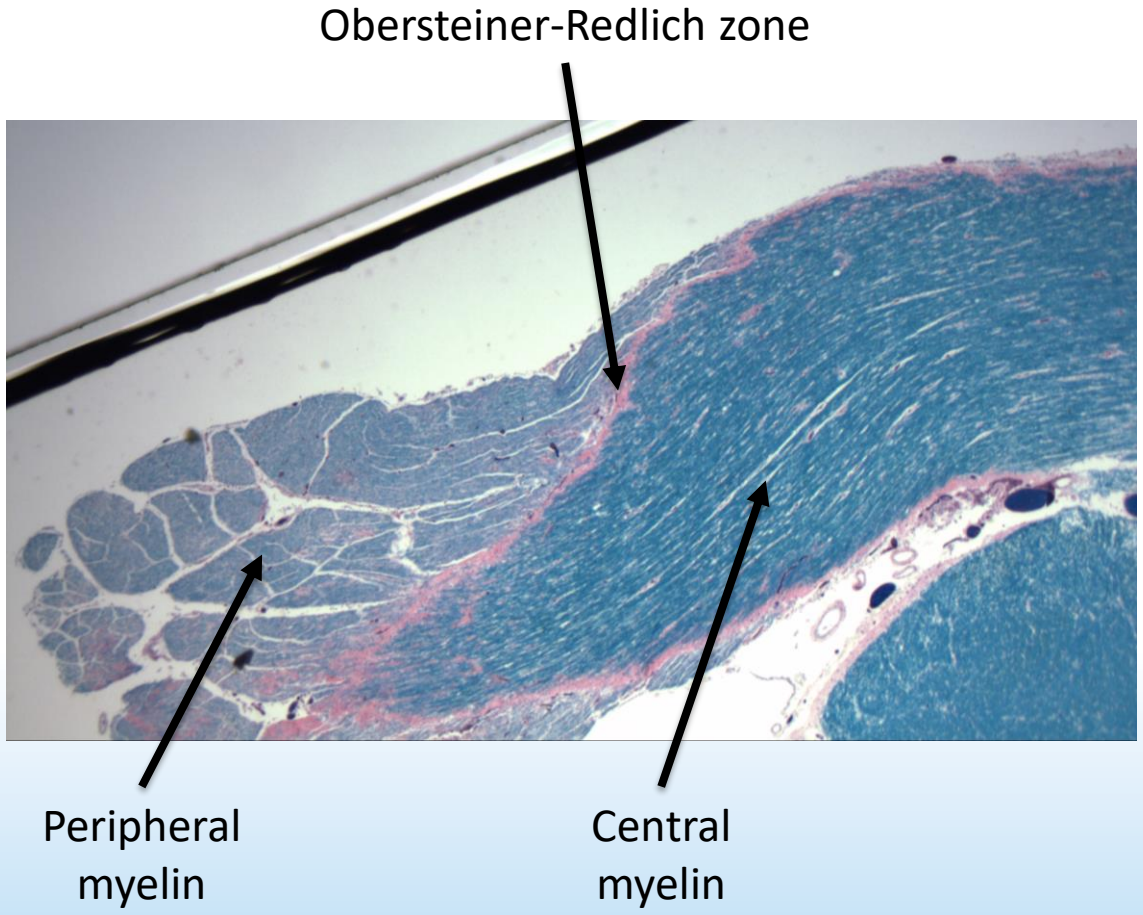
Abhyankar R, “On the seat of the soul: Descartes’ pineal gland,” *Neurology* 2020; 94 (15 Supplement): 914.
Blumenfeld H. “Neuroanatomy through Clinical Cases, Second Edition.” Sinauer Associates Inc., 2010.

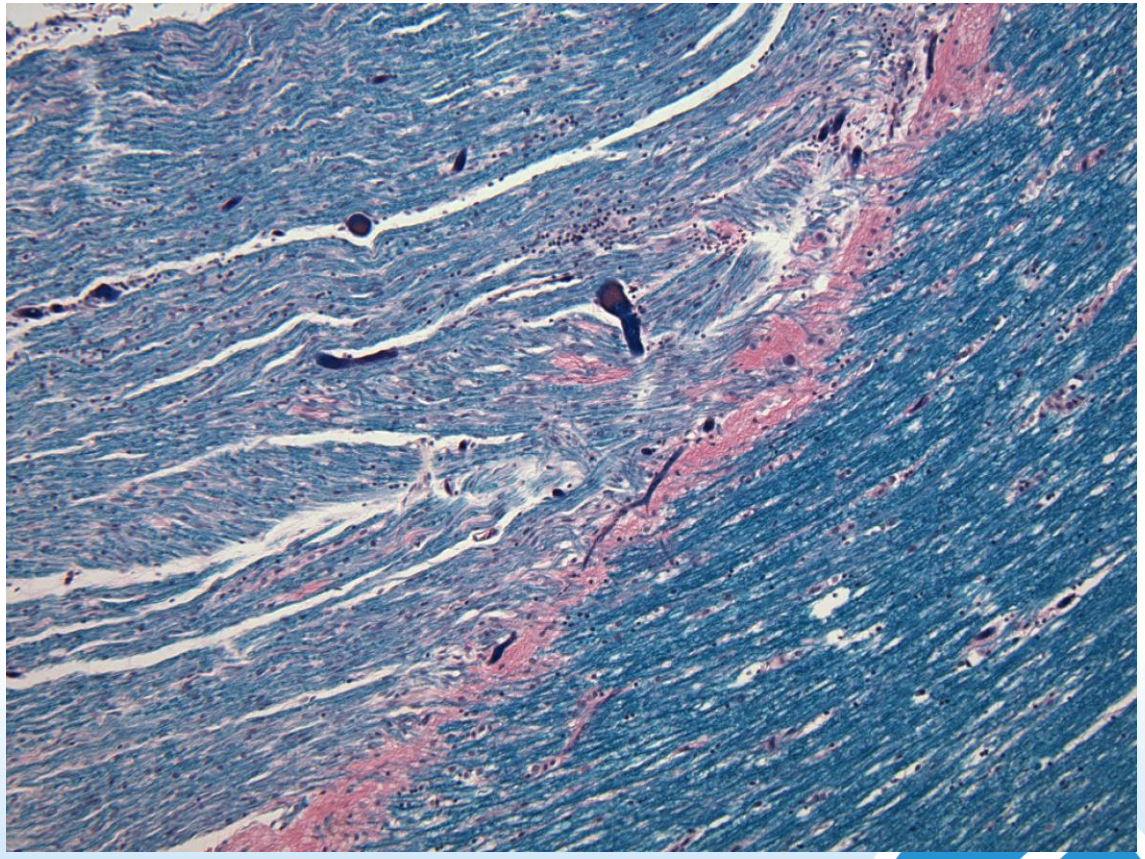
Habenular nuclei

- Derived from Latin *habenula* (diminutive form of *habena*, a "small strap or rein"): the pineal gland runs the brain via the reins of the habenular nuclei
- Comprise epithalamus along with pineal gland
- Projects to interpeduncular nucleus of midbrain via habenulo-interpeduncular tract ("fasciculus retroflexus of Meynert")
- Modulates fear/anxiety, risk/reward, pain, sleep, and reproductive and aggressive behaviors

Roberson S, Halpern ME, "Development and connectivity of the habenular nuclei," *Semin Cell Dev Biol* 2018; 78: 107-115.

Obersteiner-Redlich zone of trigeminal (V) nerve



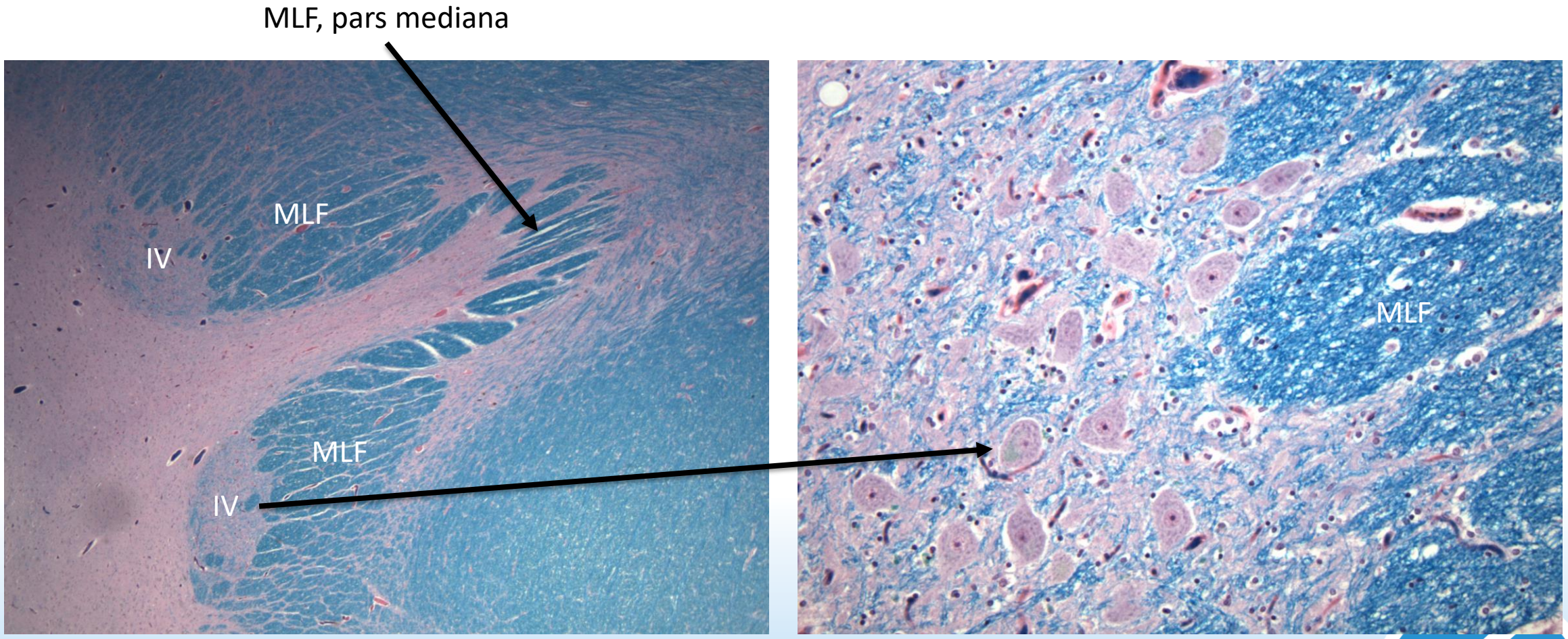


Obersteiner-Redlich zone

- The “root entry zone” where central myelin meets peripheral myelin and oligodendrocytes meet Schwann cells
- Potential site of vascular compression in trigeminal neuralgia
- Most common tumor in the zone thought to be schwannoma; however, some feel it arises lateral to the zone
- Named after Austrian neurologists Henrich Obersteiner and Emil Redlich who first described it in the spines of patients with tabes dorsalis

Alfieri A, Fleischhammer J, Strauss C, Peschke E, “The central myelin-peripheral myelin transition zone of the nervus intermedius and its implications for microsurgery in the cerebellopontine angle,” *Clin Anat* 2012; 25: 882-888.
Xenellis JE, Linthicum FH Jr., “On the myth of the glial/Schwann junction (Obersteiner-Redlich zone): origin of vestibular nerve schwannomas,” *Otol Neurotol* 2003; 24: 1.

Trochlear (IV) nucleus

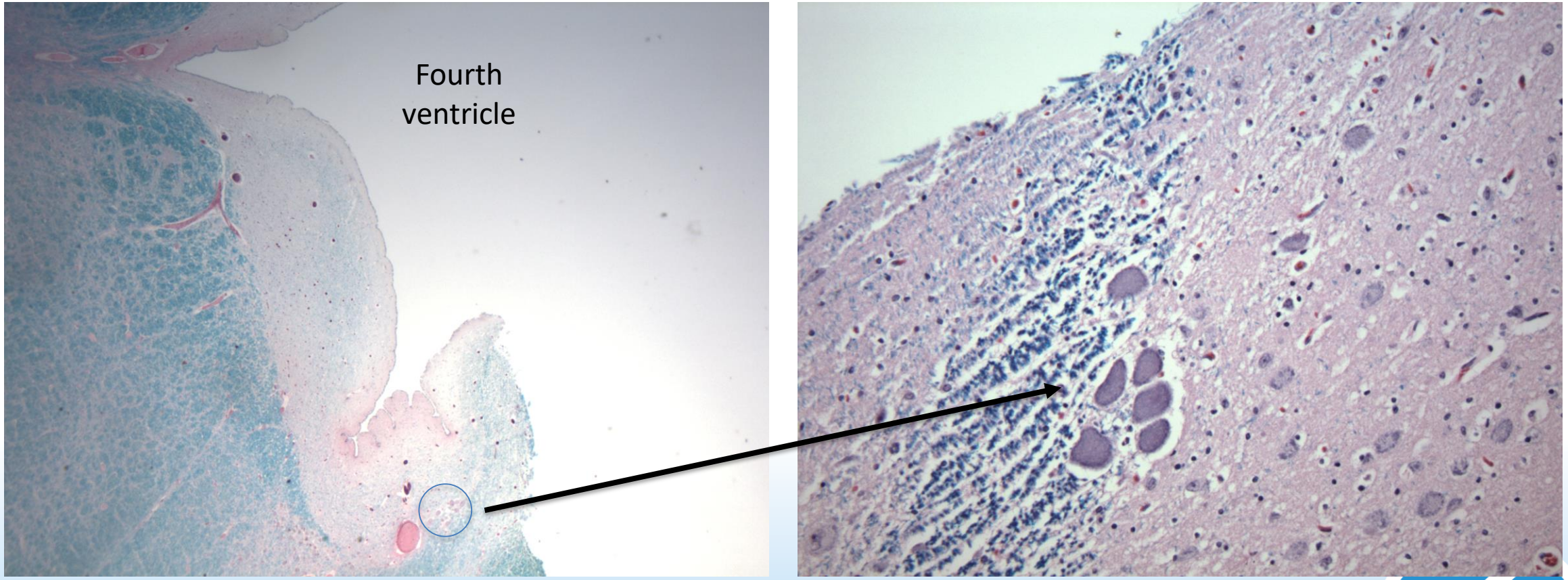


Trochlear (IV) nucleus

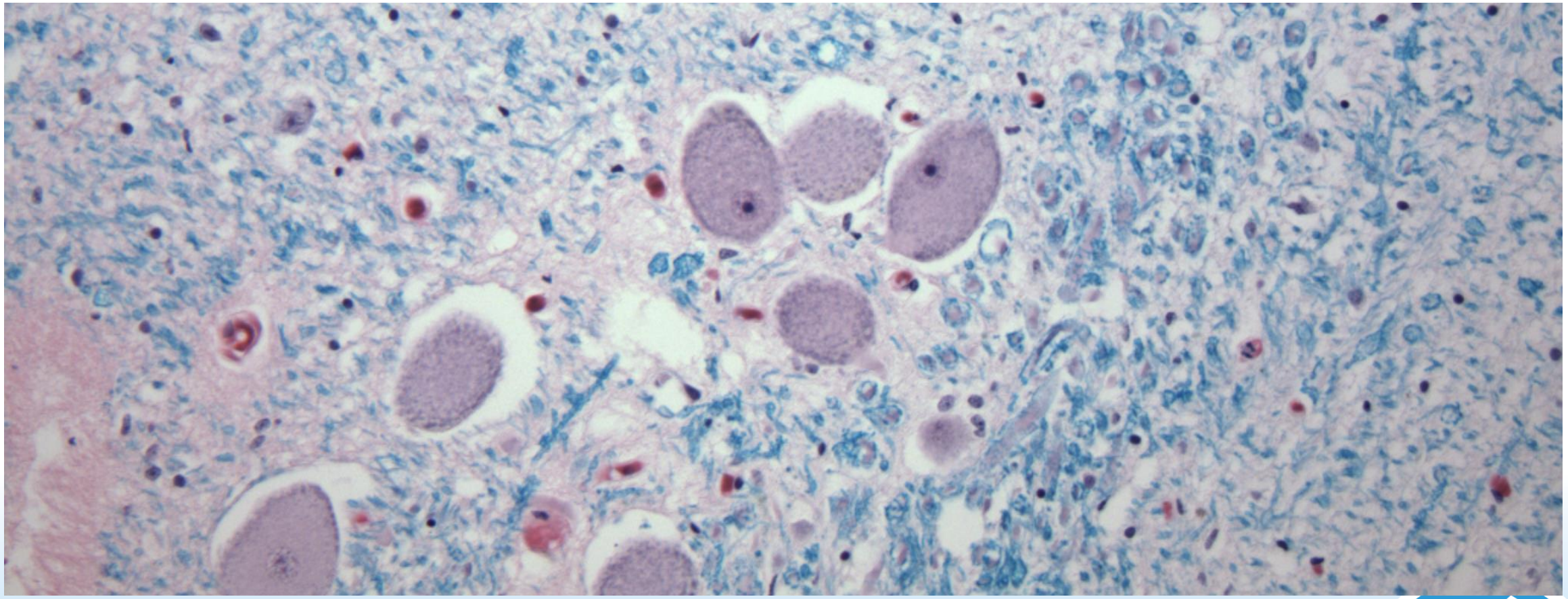
- Located medially in the caudal midbrain at the level of the decussation of the superior cerebellar peduncle and the medial longitudinal fasciculus, pars mediana
- Axons form the trochlear nerve which is responsible for depression and intorsion of the eye
- Lesions cause vertical diplopia

Alsop Riley H, “An Atlas of the Basal Ganglia, Brain Stem and Spinal Cord Based on Myelin-Stained Material.” Hafner Publishing Company, 1960.
Blumenfeld H. “Neuroanatomy through Clinical Cases, Second Edition.” Sinauer Associates Inc., 2010.

Pons (Latin, “bridge”) with mesencephalic trigeminal (V) nucleus



Mesencephalic trigeminal (V) nucleus



Mesencephalic trigeminal (V) nucleus

- The ONLY first-order, primary sensory neurons that are completely within the CNS parenchyma (like having a dorsal root ganglion inside the brain)
- Run along lateral edge of periaqueductal gray (but do focally extend into the superior pons)
- Responsible for proprioceptive input from the face
- Part of the jaw jerk reflex

Blumenfeld H. "Neuroanatomy through Clinical Cases, Second Edition." Sinauer Associates Inc., 2010.

Cranial nerves of the cavernous sinus

O

C A T

O

M

- O = Oculomotor (III) nerve
- T = Trochlear (IV) nerve
- O = Ophthalmic (V_1) nerve
- M = Maxillary (V_2) nerve
- C = Carotid (internal) artery
- A = Abducens (VI) nerve

Cranial nerves of the cavernous sinus

O

C A T

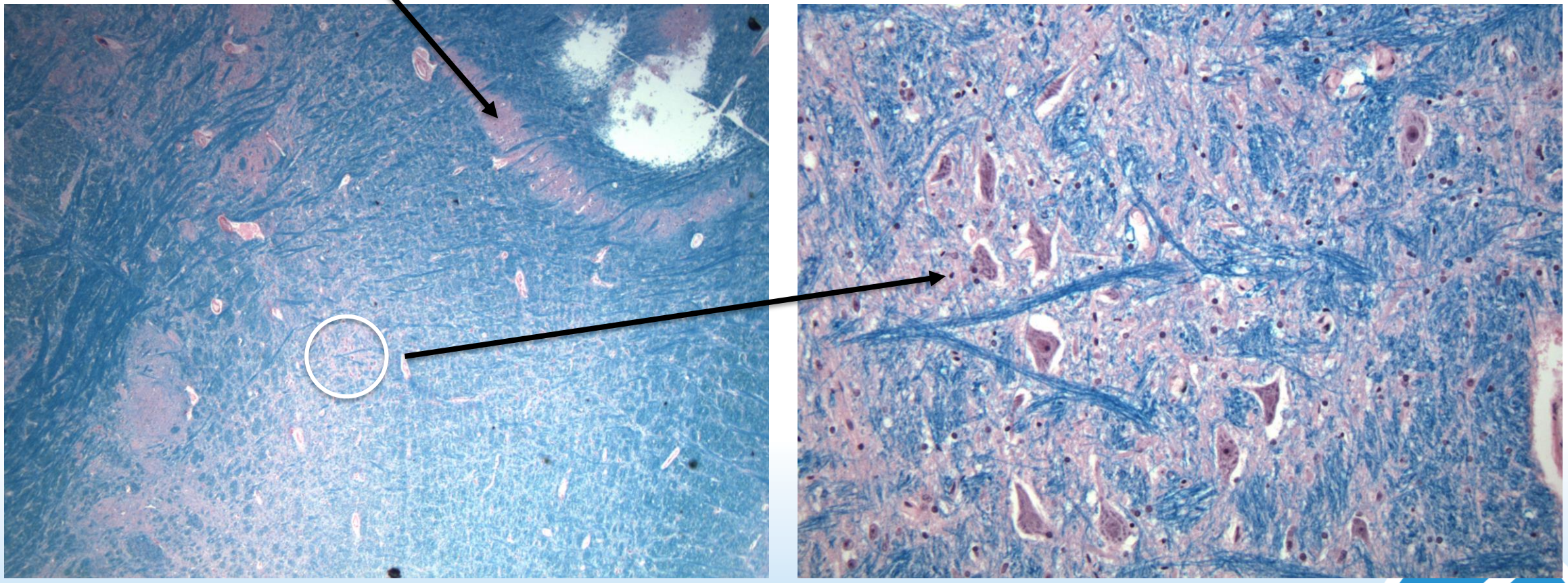
O

M

- Recall that the mandibular (V_3) nerve does NOT pass through the cavernous sinus
- The abducens (VI) nerve is closest to the carotid artery within the cavernous sinus

Nucleus ambiguus

Dorsal accessory nucleus (part of ION)

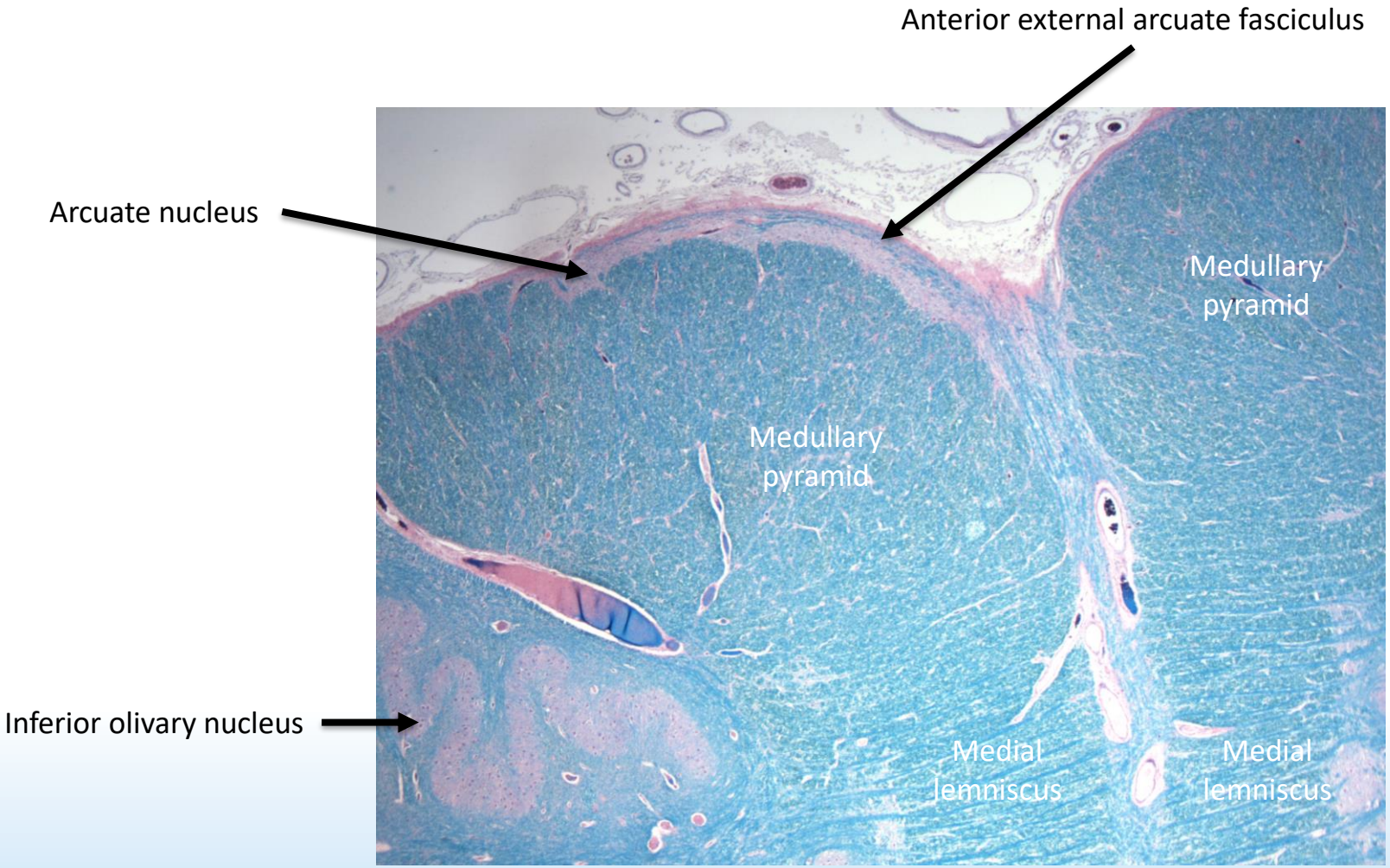


Nucleus ambiguus

- Ambiguous location in medulla at the level of the dorsal accessory nucleus (part of inferior olivary nucleus)
- Supplies branchial motor fibers via the vagus (X; Latin for “wandering”) nerve to palatal, pharyngeal, upper esophageal, and laryngeal muscles and glossopharyngeal (IX) nerve to the stylopharyngeus muscle
- Affected in “lateral medullary syndrome”

Blumenfeld H. “Neuroanatomy through Clinical Cases, Second Edition.” Sinauer Associates Inc., 2010.

Arcuate nucleus

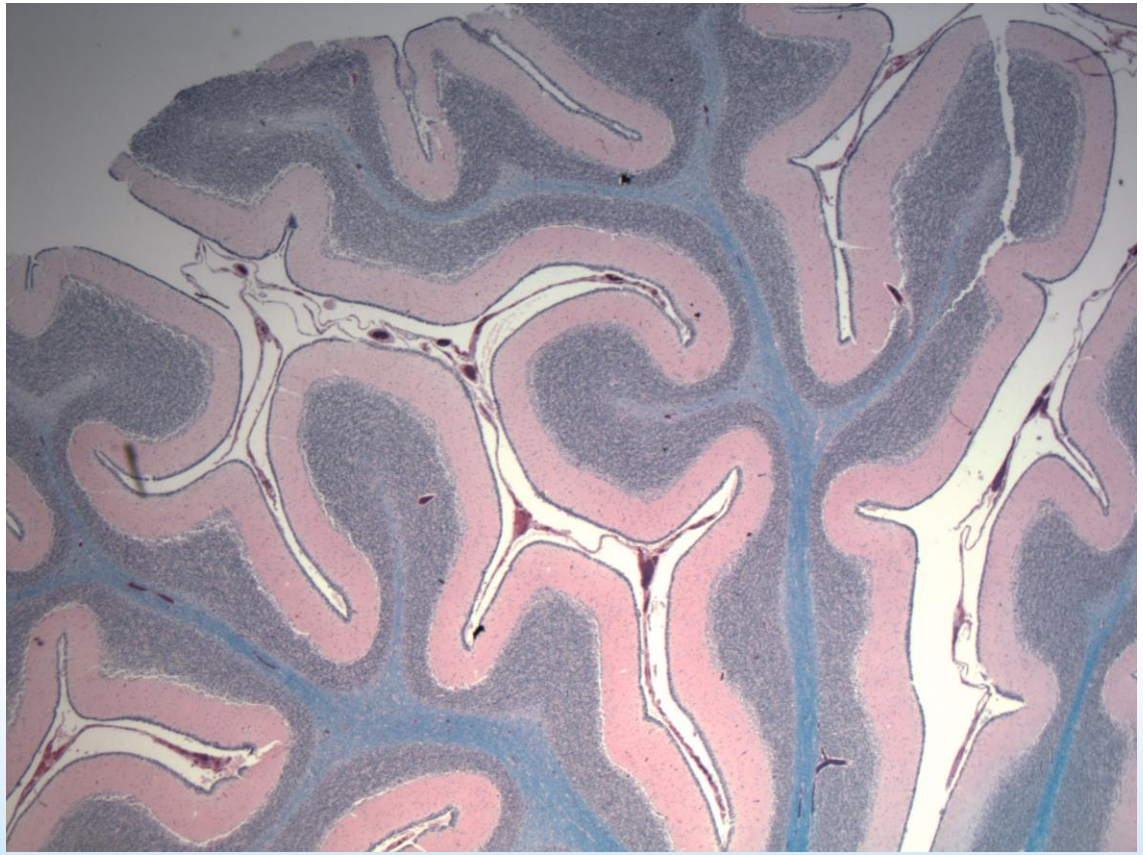


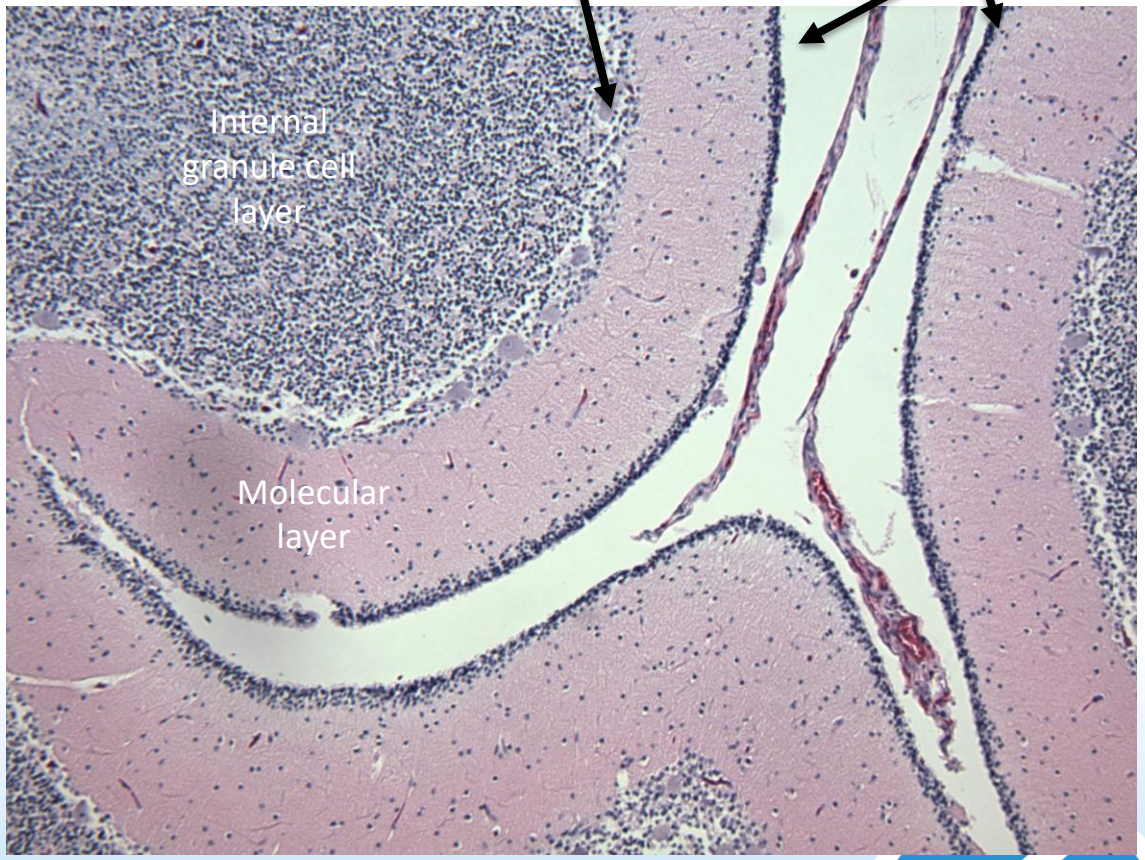
Arcuate nucleus

- On ventral surface of medulla overlying the pyramid
- Pre-cerebellar nucleus
- Proposed to play a role in regulating respiration ($\uparrow CO_2$)
- Some axons project to the anterior exterior arcuate fasciculus and then to the cerebellum via the inferior cerebellar peduncle
- Other axons project posteriorly to the medullary reticular formation

Stonebridge R, Taliano RA, Velilla TD, Anthony DC, "Hypertrophy of the anterior exterior arcuate fasciculus: a rare variant with implications for the development of the arcuate nucleus," *Front Neuroanat* 2020; 14: 595500. Published online 2020 Nov 27. doi: 10.3389/fnana.2020.595500.

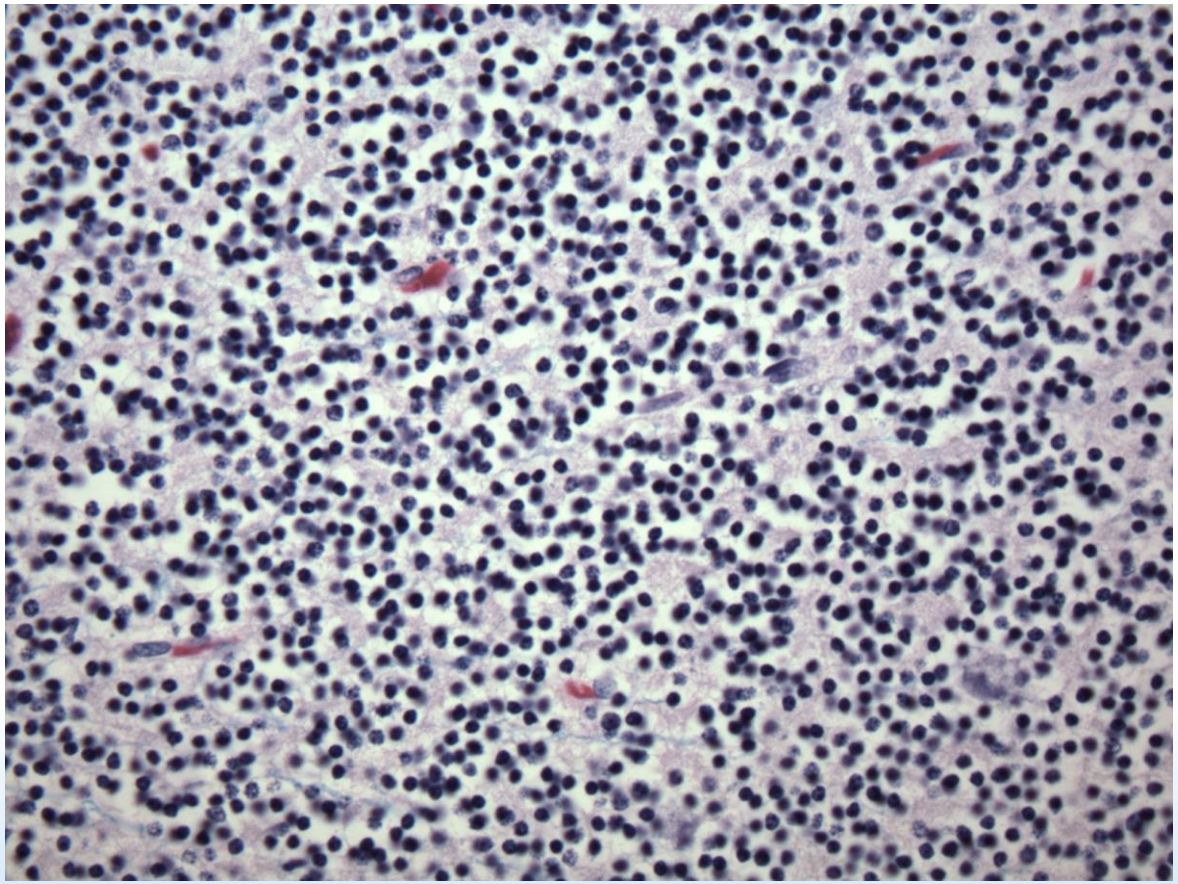
Cerebellar cortex—4-month-old





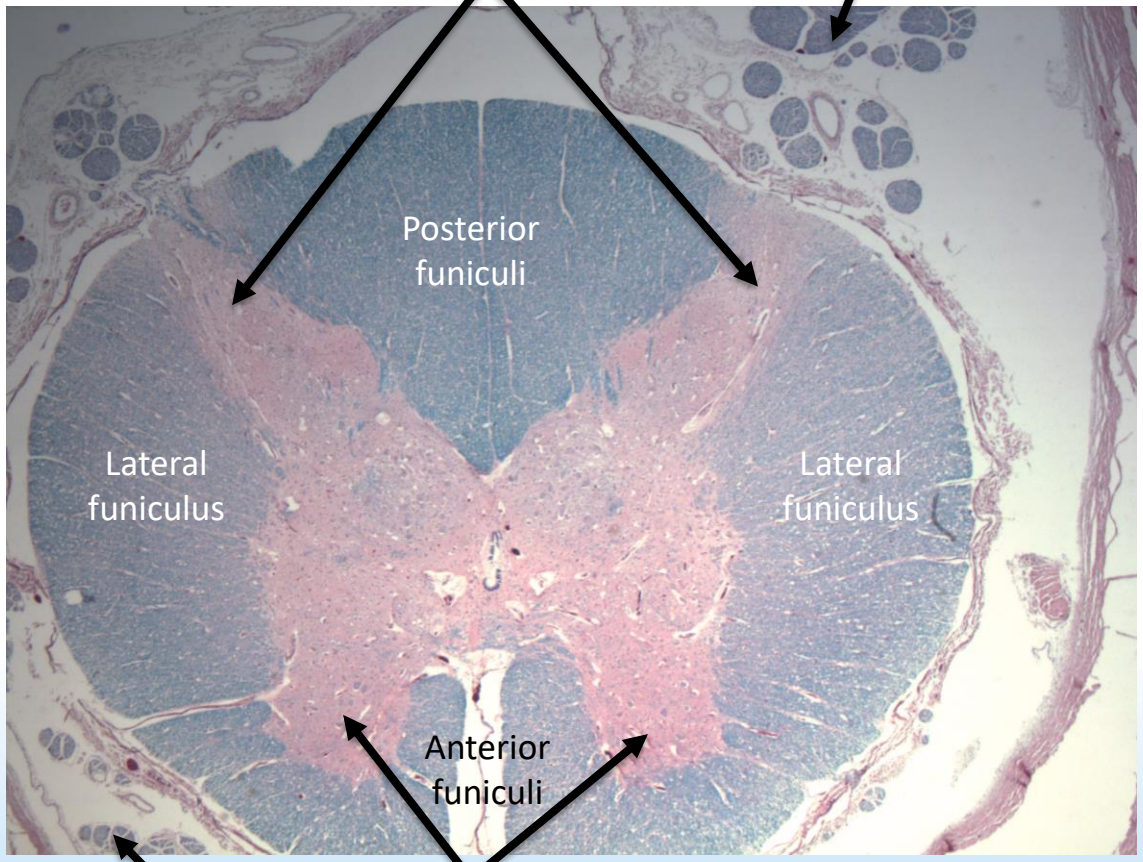
Cerebellar granule cell layer, high-power

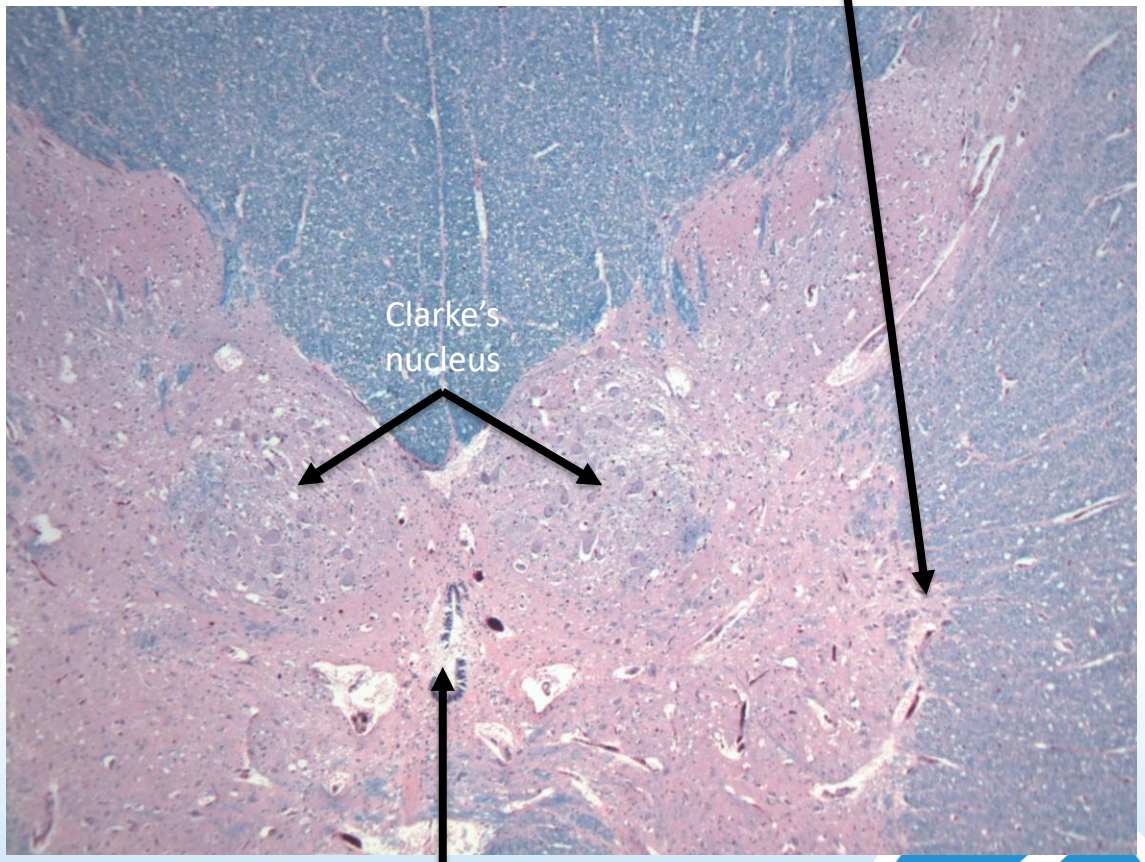
Resembles benign neuroendocrine tumor!!!



Thoracic spinal cord

Funiculus: Latin for “cord” or “rope”





Clarke's nucleus

- The posterior thoracic nucleus ("Clarke's column"; "nucleus dorsalis of Clarke"); in the intermediate zone of the spinal cord
- Major relay center for unconscious proprioception
- Axons form the dorsal spinocerebellar tract and ascend through the inferior cerebellar peduncle to the ipsilateral cerebellum
- Named after Jacob Lockhart Clarke, a 19th-century British anatomist and neurologist

Ramachandran M, Aronson JK, "Jacob Lockhart Clarke's and John Hughlings Jackson's first description of syringomyelia," *J R Soc Med* 2012; 105; 60-65.

51-year-old man with seizure disorder and sudden death; medical examiner case

https://pathpresenter.net/public/display?token=7eba43ec

VIRTUAL SLIDE

Q&A