

An Introduction to the Brain Autopsy

Vanessa L. Smith, MD

Molecular Genetic Pathology Fellow

Pathology Department

Duke University

Disclosures

- I have no relevant financial relationships to disclose



Learning Objectives

- Discuss different approaches to brain autopsy in varied neuropathology settings (i.e. Medical Examiner, Alzheimer's Disease Research Center, general academics, etc.).
- Illustrate a basic brain autopsy .
- Identify appropriate sections to take during brain autopsy for histologic examination dependent upon the patient's history and gross findings.

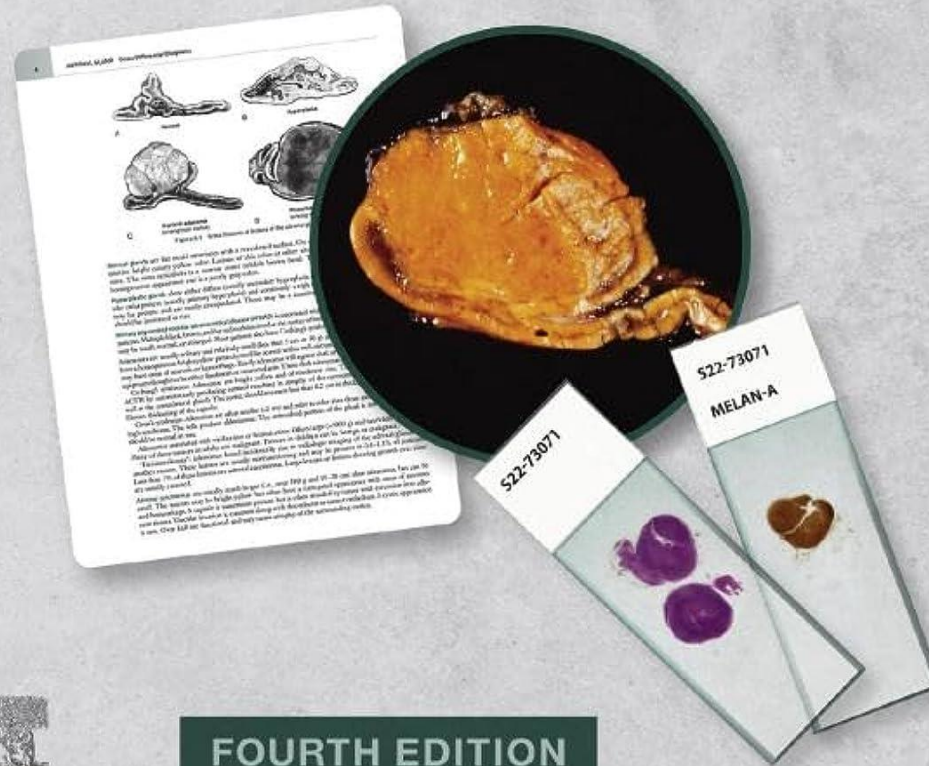


Copyrighted Material

Susan C. Lester

Enhanced
DIGITAL
VERSION
Included

Manual of SURGICAL PATHOLOGY



FOURTH EDITION

Copyrighted Material



Copyrighted Material

ATLAS OF **Gross Neuropathology**

A Practical Approach



Kathreena M. Kurian
Tim H. Moss
Sandra Camelo-Piragua

CAMBRIDGE

Medicine

Copyrighted Material



Brain Autopsy Settings

- Medical Examiner
- Hospital
- Alzheimer's Disease Research Center
- Other research centers
- Private

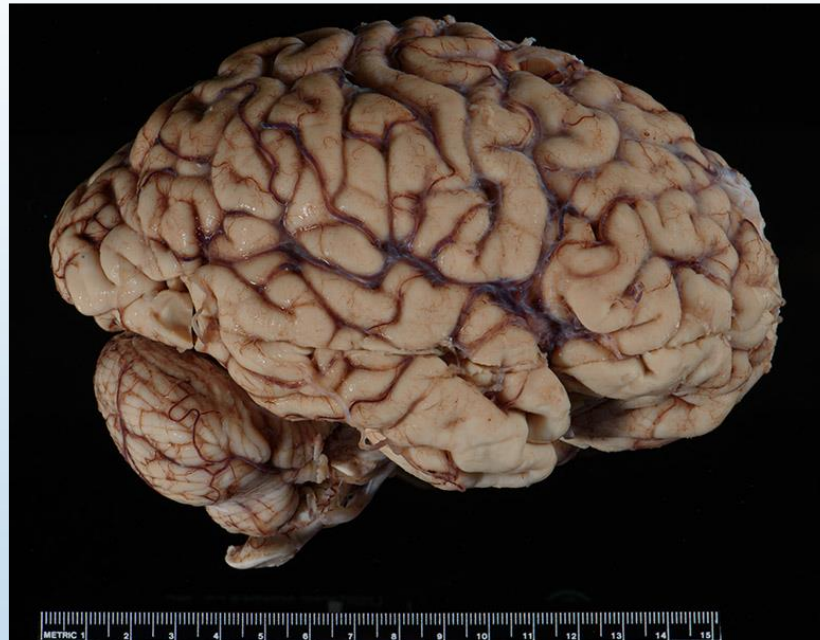


Patient History

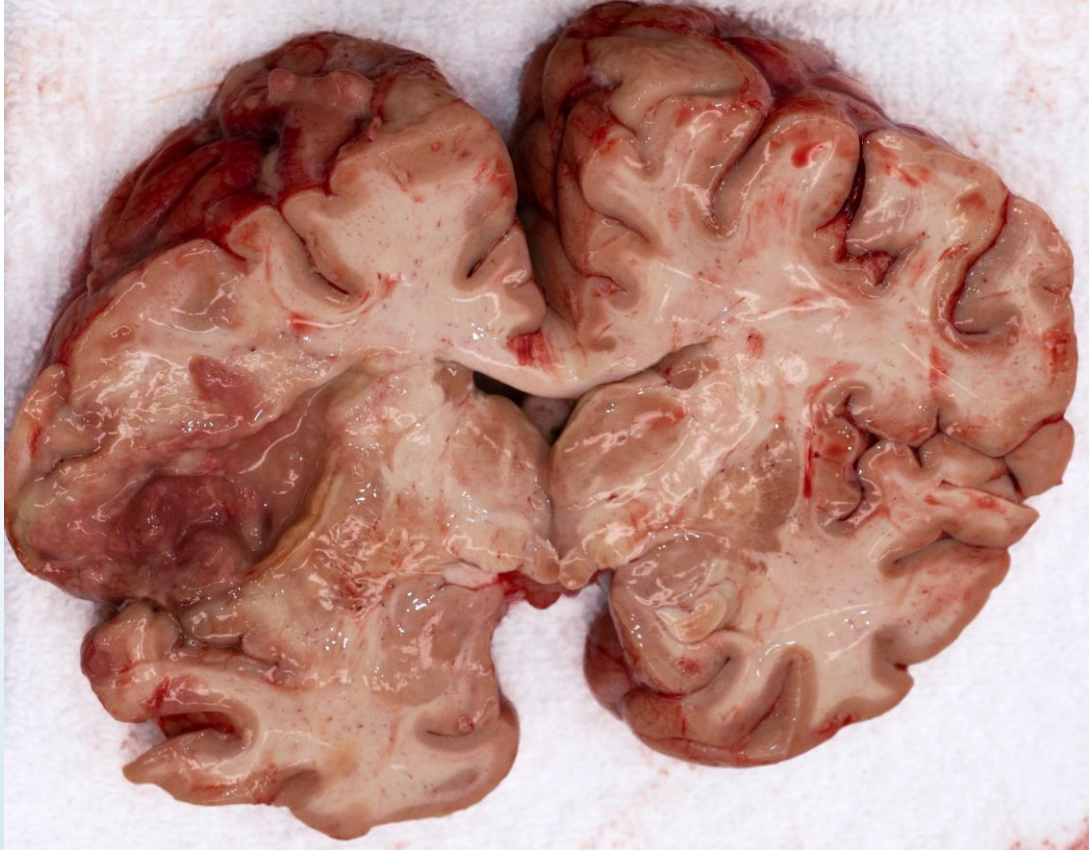
- Age?
- Imaging?
- Known history – documented in medical record, official records, received with autopsy consent/request, etc.



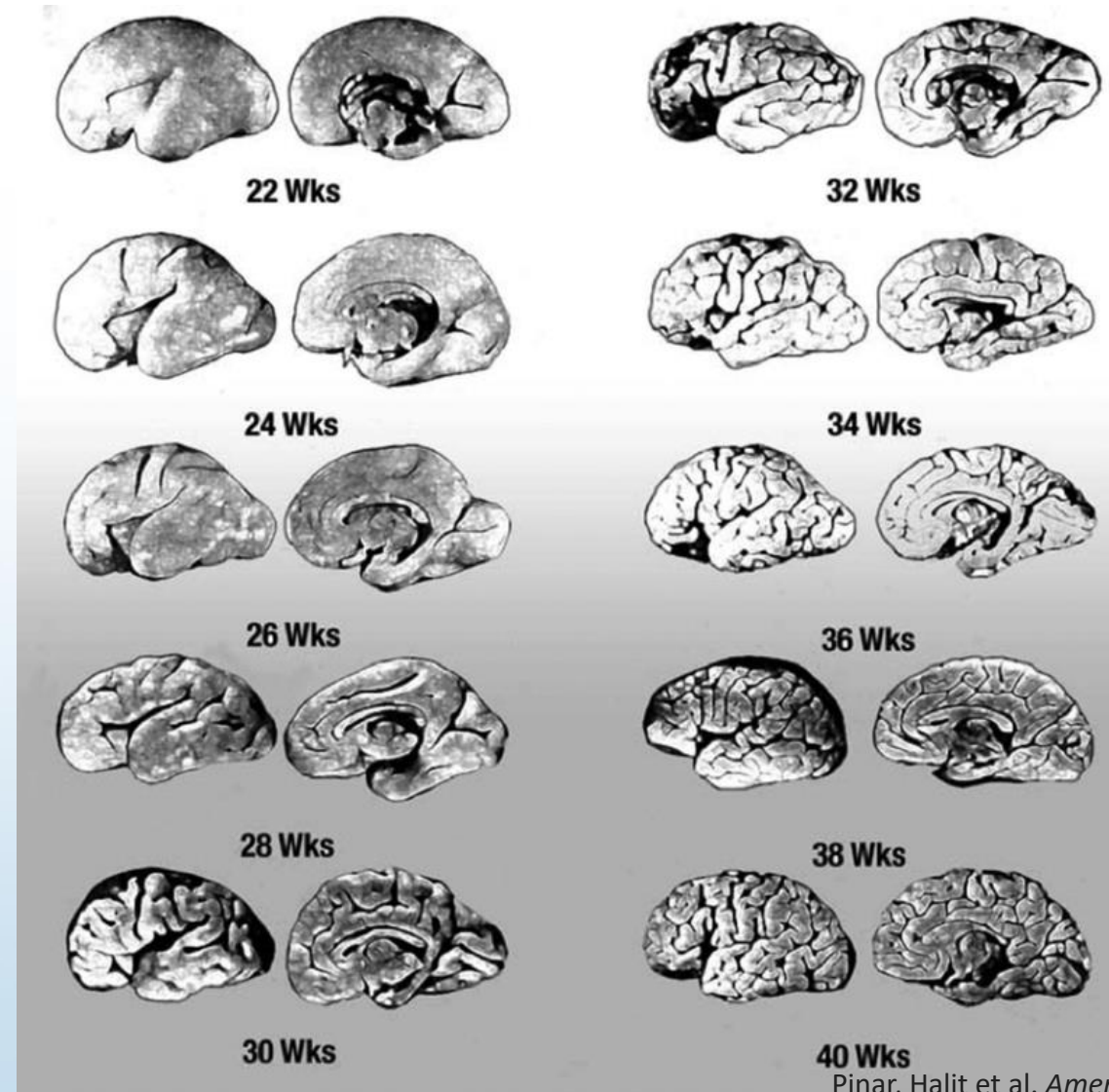
Fresh vs Fixed



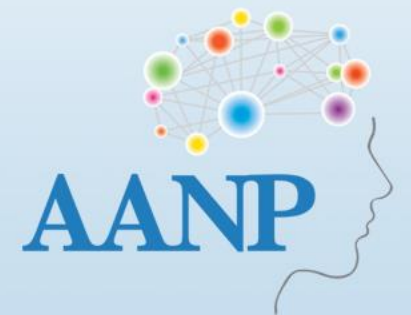
Fresh vs Fixed



A note on intrauterine demise...



Basic Procedure Video



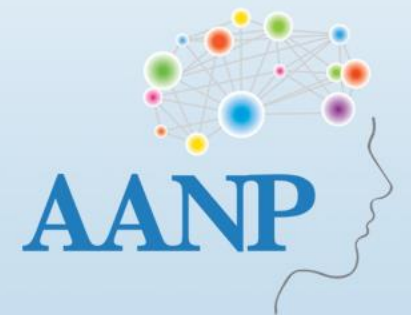


Brain blocking for histological examination

- Dependent on setting of autopsy, history, and findings on gross exam
- May not be necessary or possible depending on setting and gross findings



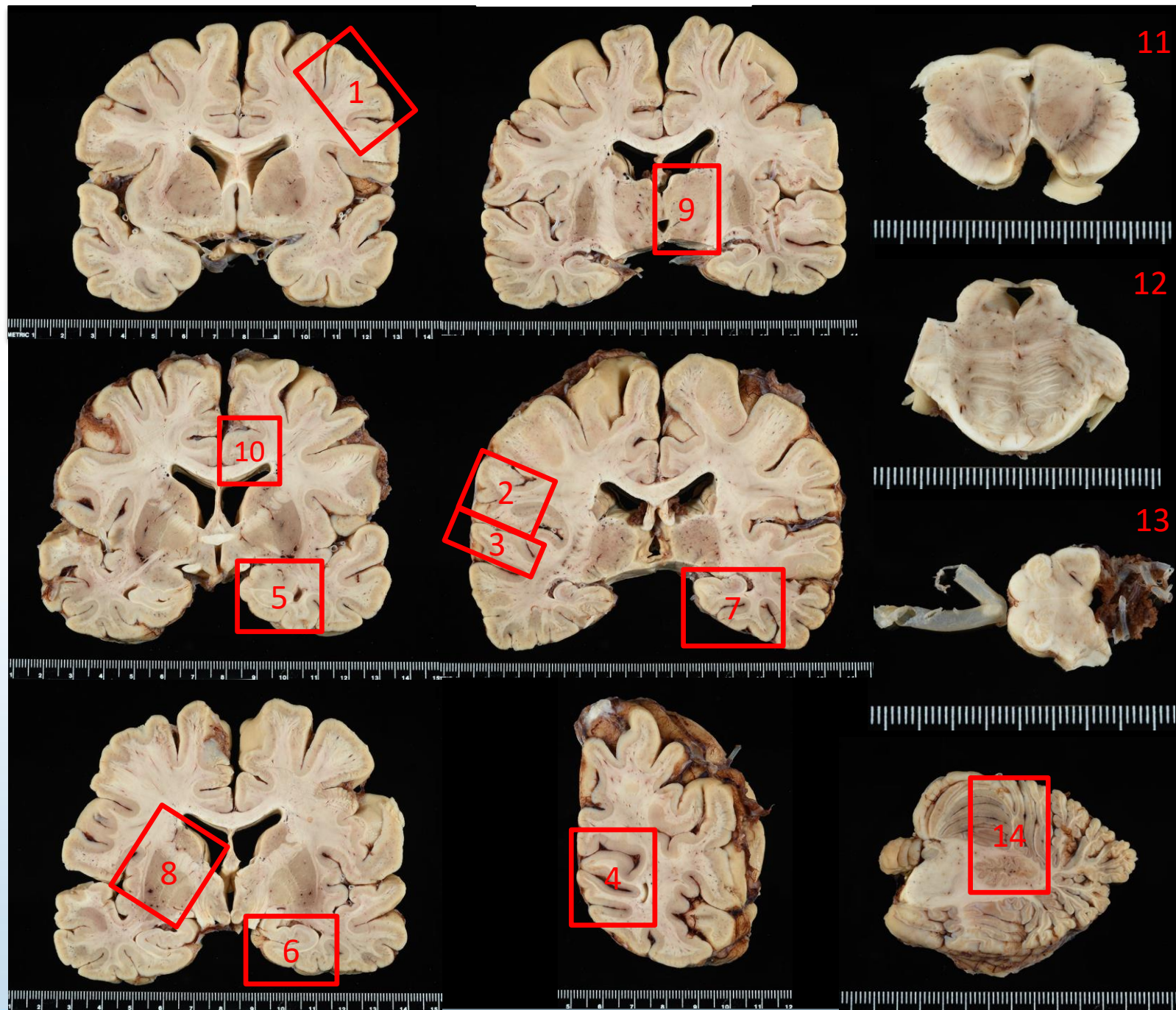
Neurodegenerative



Neurodegenerative workup: MARDC sections

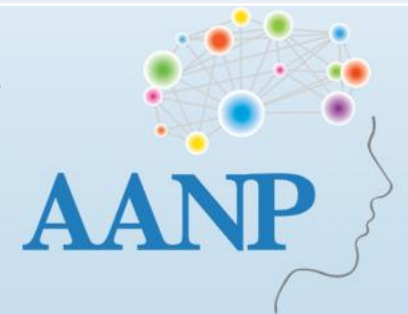
Block	Location
1	Superior frontal cortex (Brodmann Area [BA] 8, 9)
2	Primary motor/sensory strip (BA 3, 4)
3	Superior parietal cortex (BA7)
4	Calcarine cortex (BA17)
5	Hippocampus at lateral geniculate nucleus (LGN)
6	Caudate, putamen, nucleus accumbens
7	Globus pallidus, putamen, substantia innominate
8	Amygdala and entorhinal cortex
9	Thalamus (level of centrum medianum)
10	Midbrain
11	Upper pons (level of locus ceruleus)
12	Lower pons (at inferior border of cranial nerve V)
13	Medulla oblongata
14	Cerebellum (with dentate nucleus)
15	Temporal pole (BA38)
16	Cingulate gyrus (BA24)
17	Thalamus with anterior nucleus, ventral anterior, ventral lateral, and subthalamic nucleus
18	Inferior frontal cortex (BA 10, 11, 12)
19	Inferior parietal cortex (BA 39, 40)



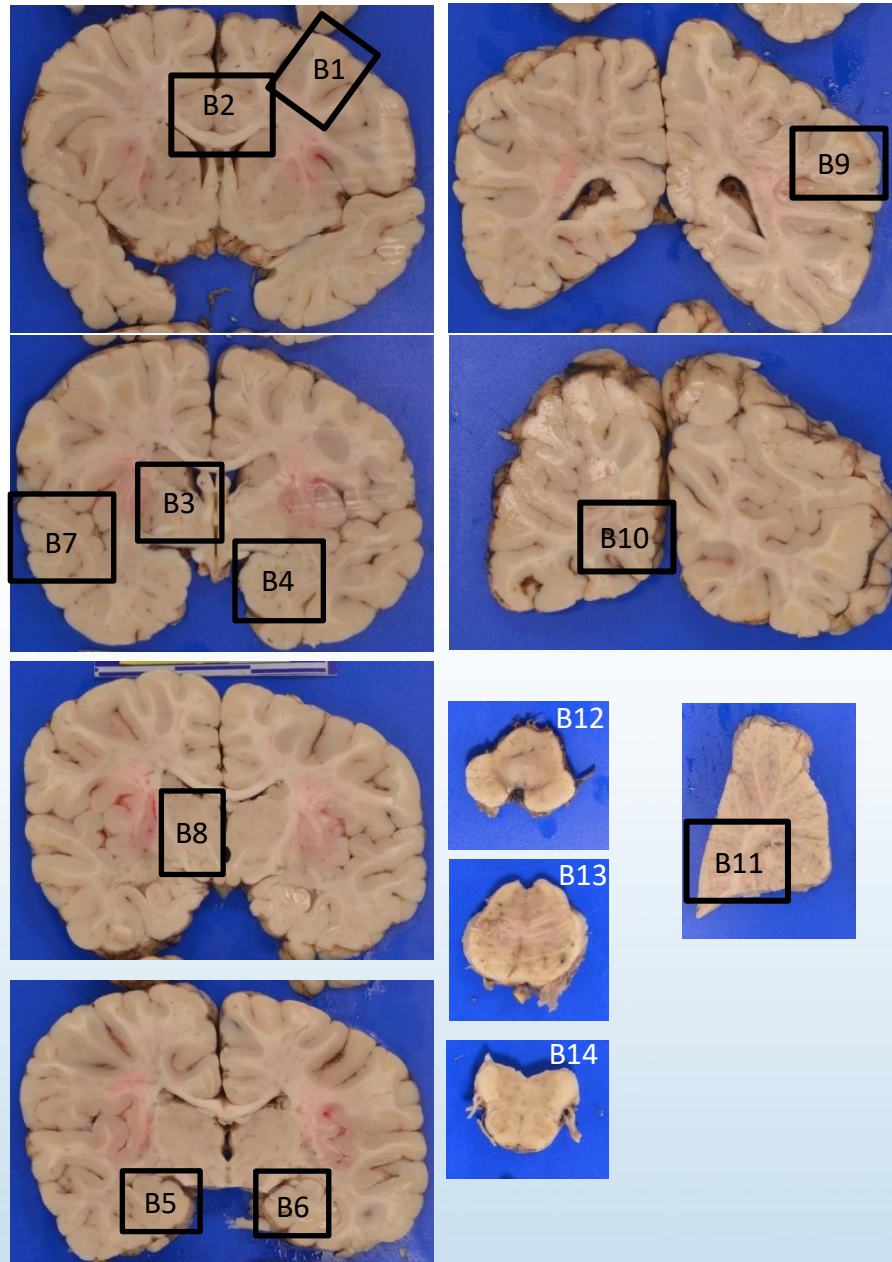


Block	Location
1	Mid-frontal gyrus
2	Inferior parietal lobule
3	Superior temporal gyrus
4	Occipital lobe
5	Amygdala
6	Head of hippocampus
7	Posterior hippocampus
8	Caudate, putamen, globus pallidus
9	Thalamus, subthalamic nucleus
10	Anterior cingulate gyrus
11	Midbrain
12	Pons
13	Medulla
14	Cerebellum

Courtesy of Dr. Jerry Wang and Duke PhotoPathology



Alternative Neurodegenerative Workup Sections



Block and Location	Amyloid*	Tau	TDP43	ASYN
B1. Middle frontal gyrus	+	+	+	+
B2. Cingulate, anterior				+
B3. Basal ganglia at level of AC				
B4. Amygdala			+	+
B5. Left posterior hippocampus	+	+	+	
B6. Right posterior hippocampus	++	++	++	
B7. Superior temporal gyrus	+	+		
B8. Thalamus and subthalamus nucleus				
B9. Inferior parietal lobule				
B10. Occipital (calcarine) cortex		+		
B11. Cerebellar cortex and dentate nucleus	+			
B12. Midbrain	+			+
B13. Pons				
B14. Medulla				
Any lesions				

*Please note this is beta-amyloid, NOT amyloid precursor protein.

+Stains can be done on either hippocampus section, pick the one with the most obvious pathologic findings on H&E



Slide courtesy of Dr. Karra A. Jones

Simplified Brain Blocking Protocol



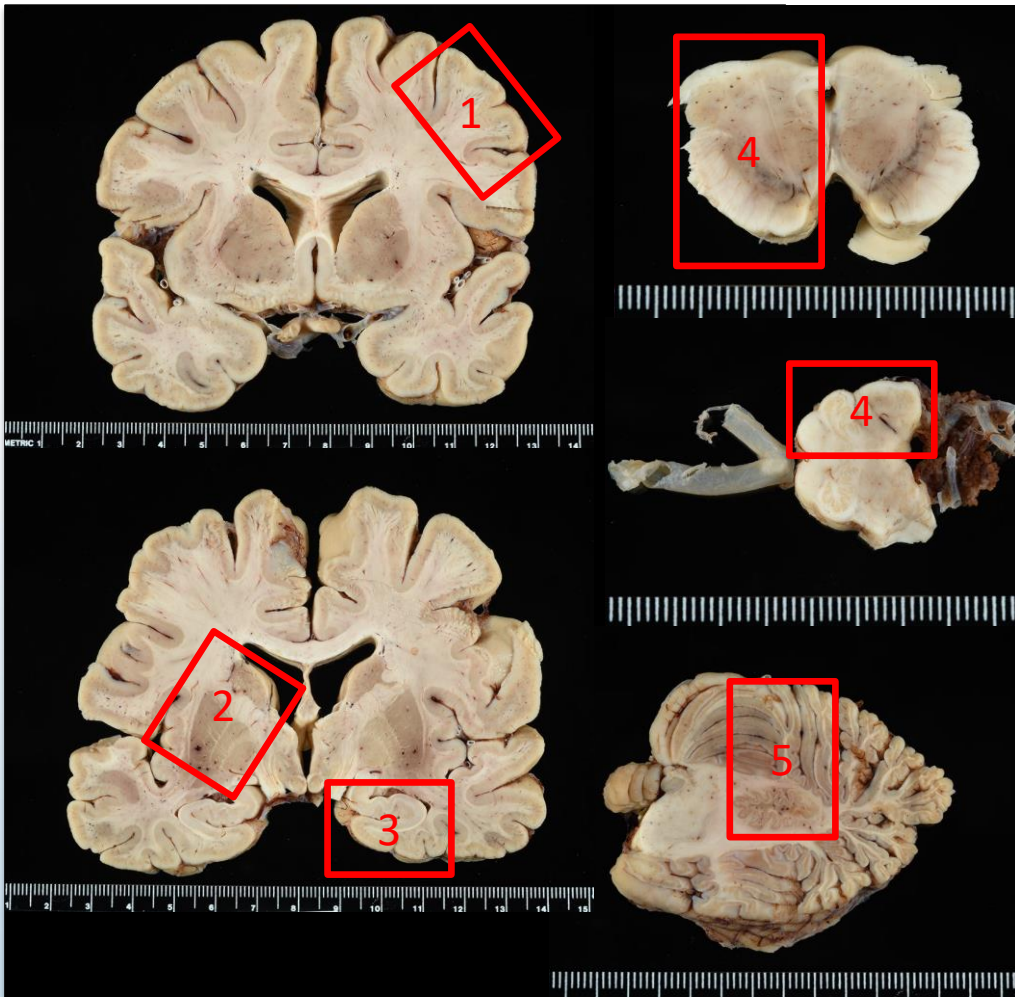
Block	Location
1	Cerebellum; basal ganglia
2	Hippocampus at lateral geniculate nucleus (LGN); Superior frontal cortex (Brodmann Area [BA] 8, 9)
3	Midbrain; Cingulate gyrus (BA24)
4	Medulla oblongata; Pons
5	Calcarine cortex (BA17); Superior frontal cortex (BA7)
6	Thalamus; Temporal pole (BA38)



Other settings and situations



Basic hospital workup – one approach



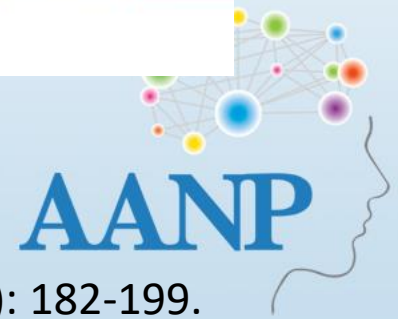
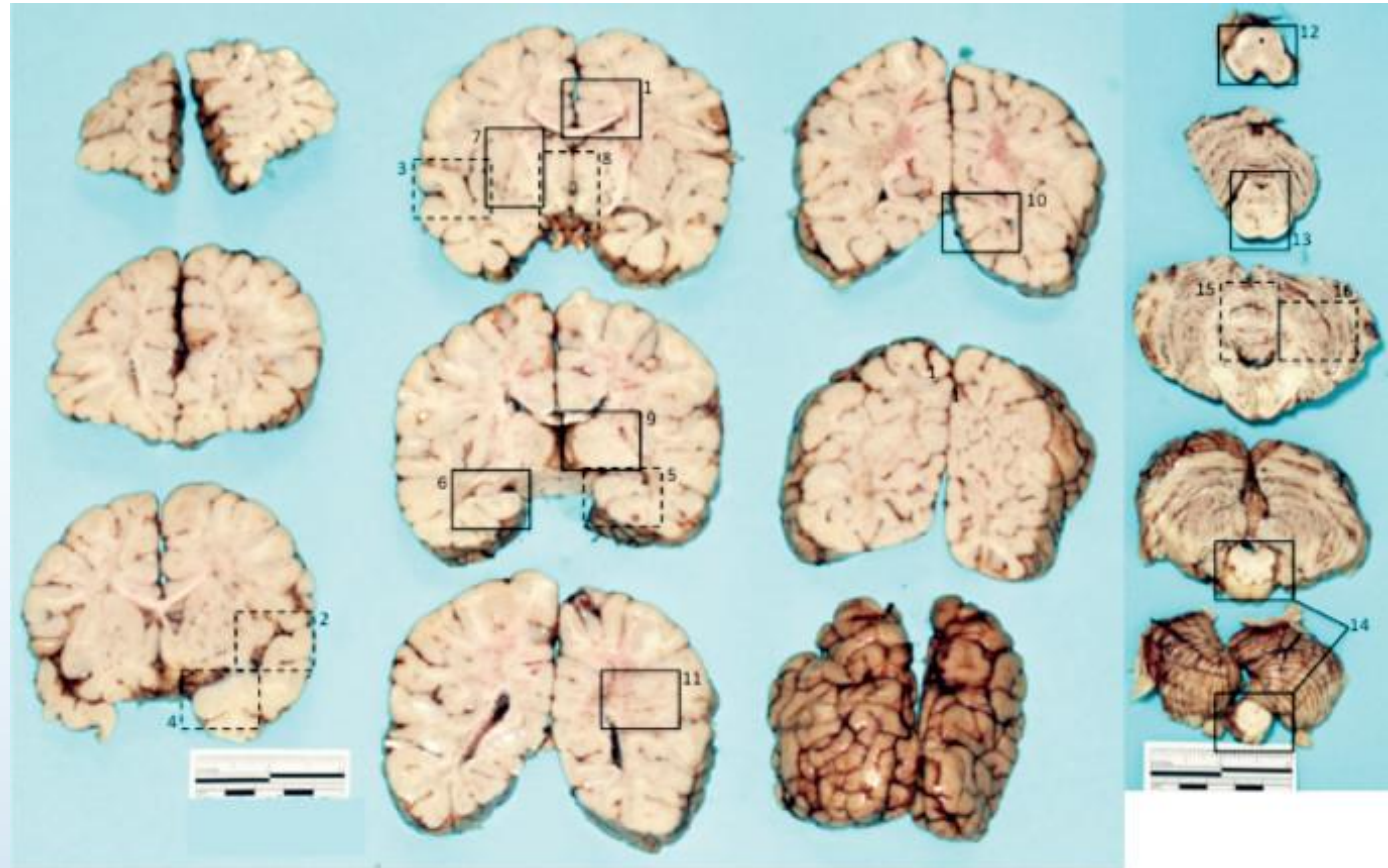
Block	Location
1	Mid-frontal gyrus
2	Caudate, putamen, globus pallidus
3	Hippocampus
4	Midbrain and Medulla
5	Cerebellum

*Courtesy of Dr. Jerry Wang and
Duke Photopathology*



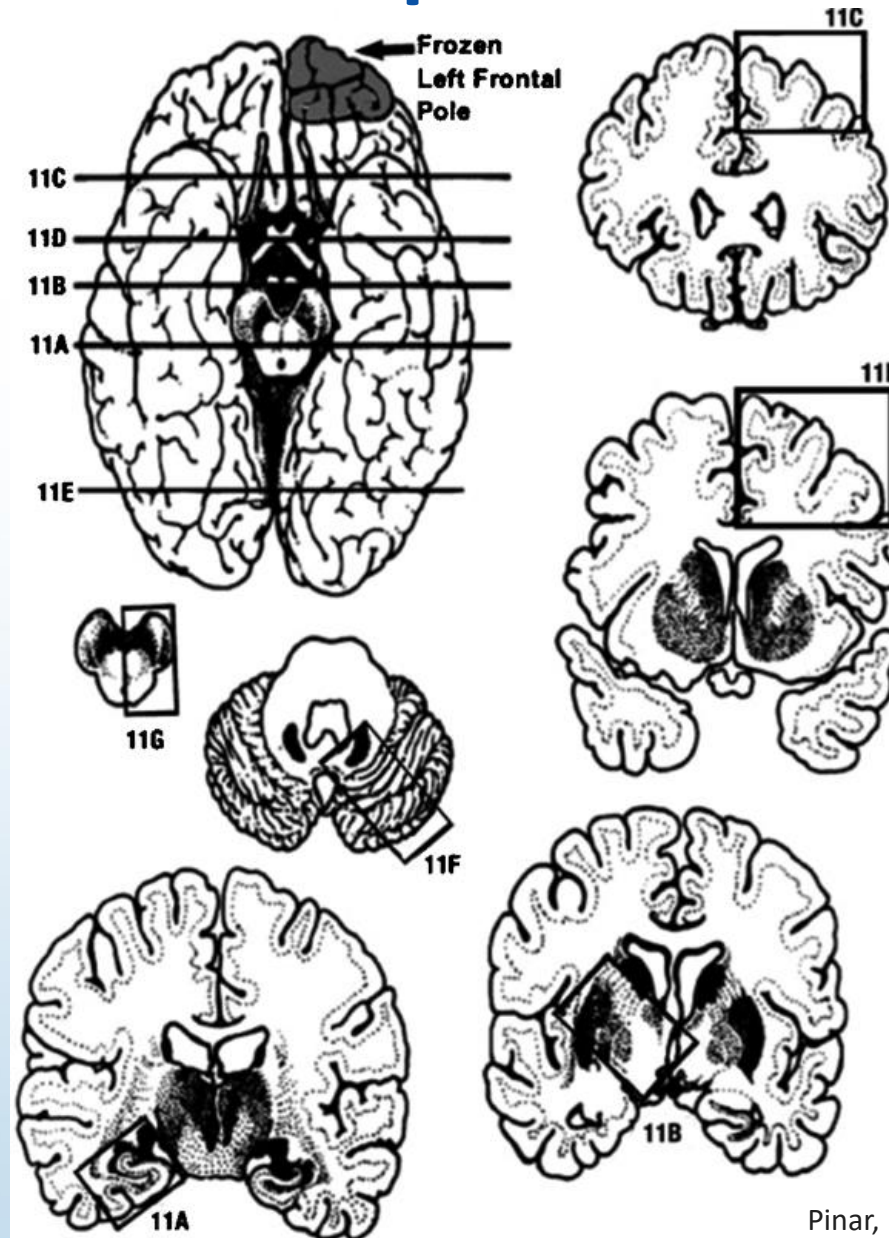
Block	Location
1	Posterior cingulate gyrus, including corpus callosum
2	Right insula and superior temporal gyrus
3	Left insula and superior temporal gyrus
4	Amygdala
5	Right hippocampus at level of lateral geniculate nucleus
6	Left hippocampus at level of lateral geniculate nucleus
7	Basal ganglia (caudate, internal capsule, globus pallidus, putamen)
8	Hypothalamus (mamillary bodies)
9	Thalamus, posterior, including internal capsule
10	Calcarine cortex
11	Parietal cortex and white matter at atrium of lateral ventricle
12	Midbrain
13	Pons
14	Medulla (rostral and caudal)
15	Cerebellar vermis
16	Cerebellar hemisphere including dentate nucleus
17	Spinal cord

Sudden Unexpected Death in Infancy and Childhood

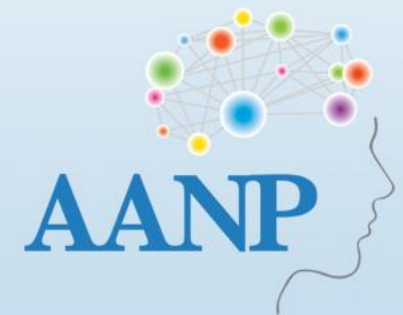
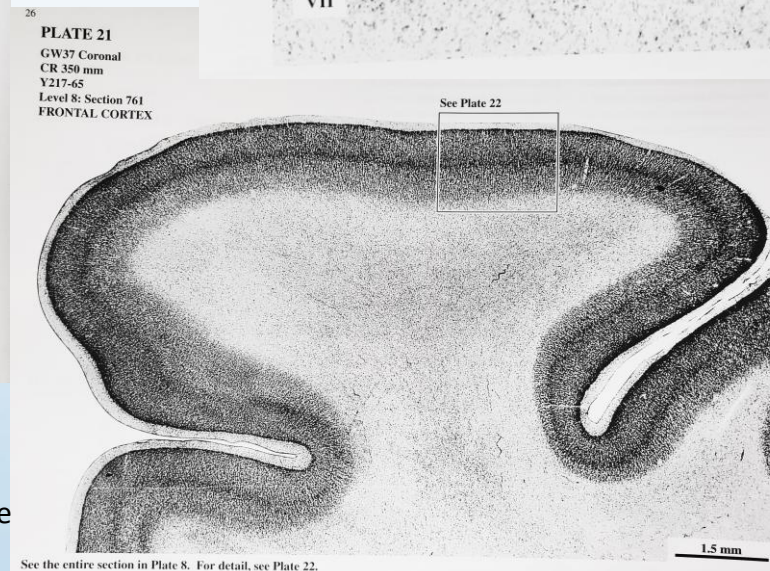
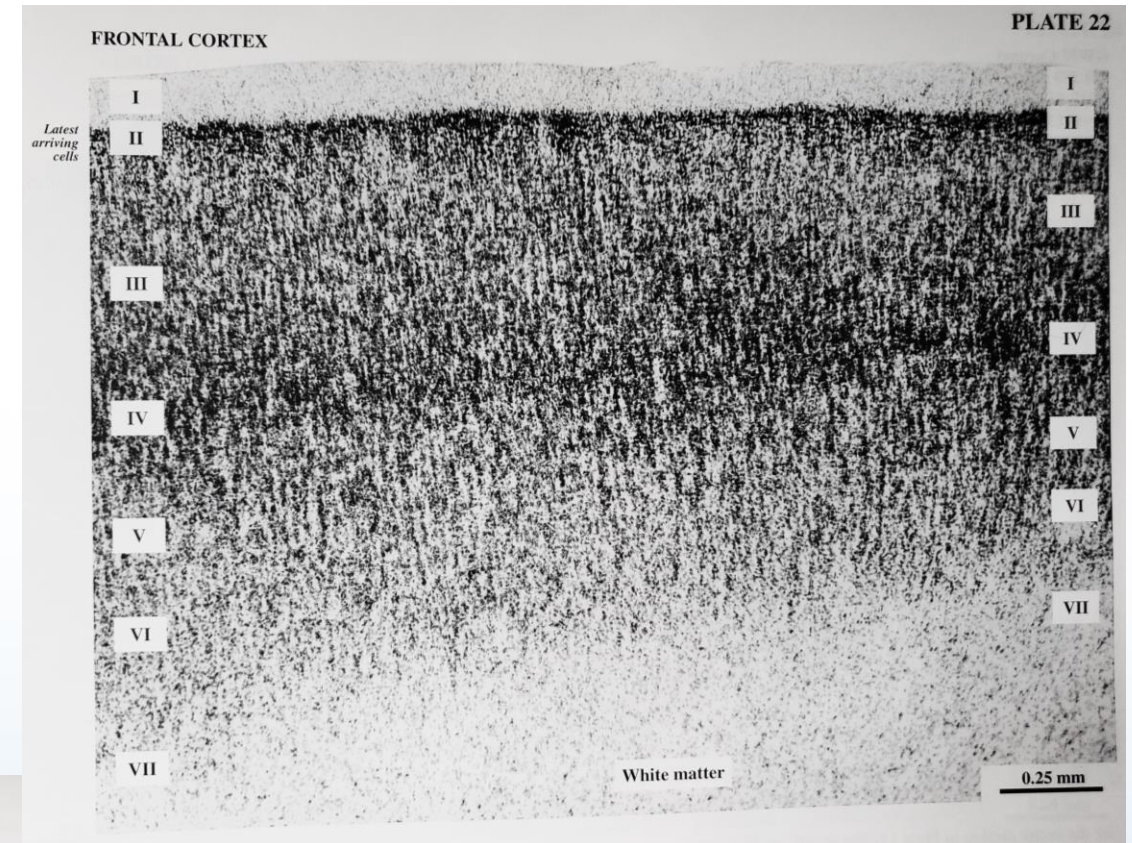
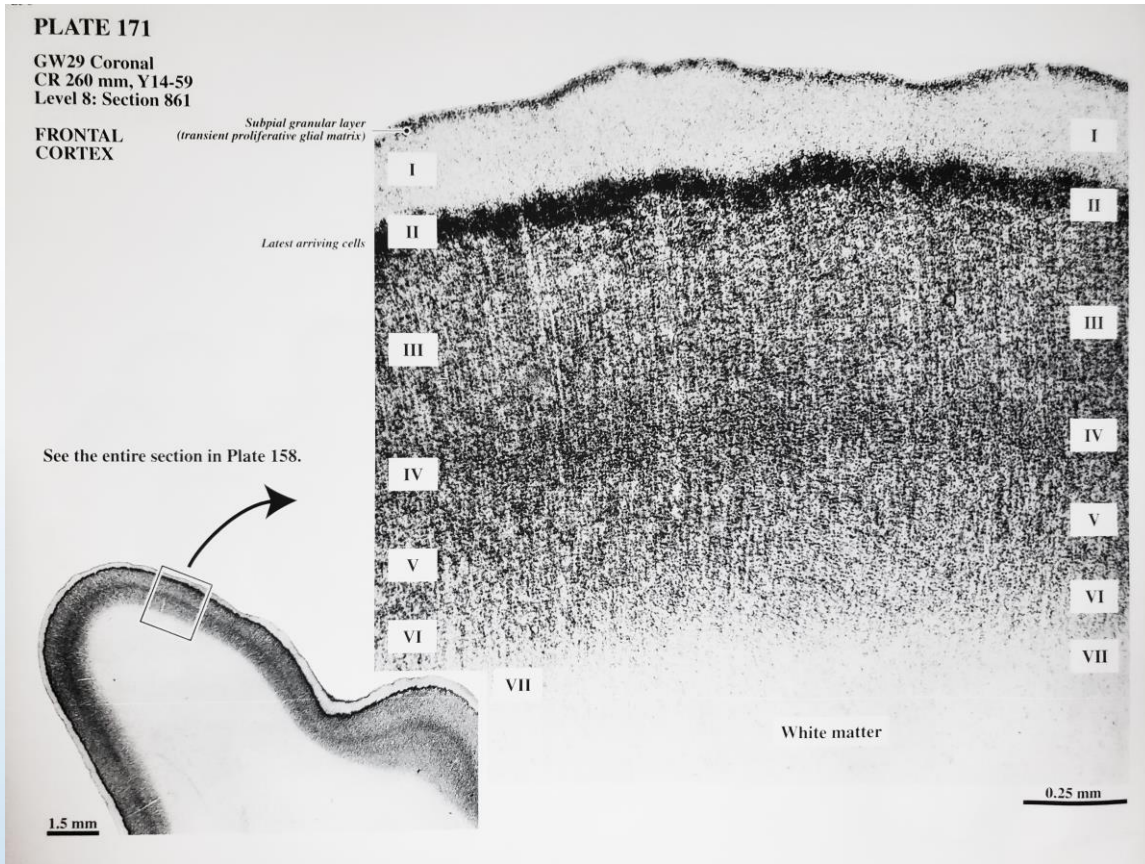


Folkerth, *et al.* Academic forensic pathology vol. 7,2 (2017): 182-199.

Pre- and perinatal workup



Developmental Assessment



Acknowledgements

- Duke Neuropathology
 - Thomas Cummings, MD
 - Anne F. Buckley, MD, PhD
 - Jerry Wang, MD, PhD
 - Karra A Jones, MD, PhD
 - Giselle Y López, MD, PhD
 - Christine Hulette, MD
 - Greg Chamberlin, MD
- Duke Photopathology
 - Steve Conlon
- AANP Website Committee and AANP Education Committee
- Additional NP colleagues
 - Jolee Suddock, DO
 - Rhonda Mittenzwei, MD
 - Michael Williams, MD, MSc
 - Neda Wick, MD
 - Melissa Blessing, DO
 - Maria Gubbiotti, MD
 - Jared Ahrendsen, MD, PhD
 - Yanel De Los Santos, MD
 - Cassie MacRae, MD



References

1. Kurian KM, Moss TH, Camelo-Piragua S. Preface. In: Atlas of Gross Neuropathology: A Practical Approach. Cambridge University Press; 2014:vii-vii.
2. Flanagan ME, Marshall DA, Shofer JB, et al. Performance of a Condensed Protocol That Reduces Effort and Cost of NIA-AA Guidelines for Neuropathologic Assessment of Alzheimer Disease. *J Neuropathol Exp Neurol.* 2017;76(1):39-43.
3. Bayer, SA., and Altman, J. Atlas of Human Central Nervous System Development -5 Volume Set. United States, Taylor & Francis, 2007.
4. Folkerth, Rebecca D et al. "Neuropathologic Examination in Sudden Unexpected Deaths in Infancy and Childhood: Recommendations for Highest Diagnostic Yield and Cost-Effectiveness in Forensic Settings." *Academic forensic pathology vol. 7,2 (2017): 182-199.* doi:10.23907/2017.020
5. Clement NF, DeWitt JC, Frosch MP, Martinez-Lage M, Samore WR, Hedley-Whyte ET. A Simplified Brain Blocking Protocol Optimized for the Diagnosis of Neurodegenerative Disease Saves Time and Money While Preserving Anatomic Relationships. *Arch Pathol Lab Med.* 2021;145(8):960-968. doi:10.5858/arpa.2020-0322-OA
6. Multz RA, Spencer C, Matos A, et al. What every neuropathologist needs to know: condensed protocol work-up for clinical dementia syndromes. *J Neuropathol Exp Neurol.* 2023;82(2):103-109. doi:10.1093/jnen/nlac114
7. Prayson, RA. *Neuropathology: A Volume in the Series: Foundations in Diagnostic Pathology.* Netherlands, Elsevier Health Sciences, 2022.
8. Pinar H, Koch MA, Hawkins H, et al. The Stillbirth Collaborative Research Network neuropathologic examination protocol. *Am J Perinatol.* 2011;28(10):793-802.

