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Neuropathology Review

Third Edition

Springer

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Preface

The scope of neuropathology continues to expand, as evidenced by increasing numbers of multivolume and specialty texts, which have been published in recent years. For those in the neuroscience disciplines, the ever-increasing amount of information one needs to assimilate and master can be challenging and even at times daunting.

As with the prior two editions, the third edition of *Neuropathology Review* attempts to summarize, in outline form, the essentials of neuropathology. The objectives are twofold: (1) to provide an overview of neuropathology for those initially encountering the discipline and (2) to provide a framework for review for those preparing for in-service and board examinations in the disciplines of neurology, neurosurgery, and pathology, which require some knowledge of neuropathology. Neuropathology is a dynamic field. There is a constant emergence of new information and ideas that continue to shape our understanding. This necessitates the periodic updating of a text such as this to keep abreast of the changes.

The first part of the text (Chaps. 1–11) presents, in outline form, basic updated information on the spectrum of neurologic-related disease. A set of self-assessment questions, some of which include key images for review, are included at the end of each chapter. The second part (Chaps. 12 and 13) presents a series of additional self-assessment questions randomly arranged on material covered in the first 11 chapters. New questions have been added to the bank of questions previously published in the first and second editions.

Cleveland, OH, USA — Richard A. Prayson
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Contents

Normal Histology

1

I. Central Nervous System
  A. Neurons
    - More than 100 billion neurons in the central nervous system (CNS)
    - 5–100 μm in size; Betz cells are the largest neurons of the cerebral cortex
    - Variety of shapes: stellate, oval, round, pyramidal, bipolar, and unipolar
    - Nucleus
      – Vesicular or loose chromatin pattern with prominent nucleolus
      – Scalloped contour—Purkinje cells and pyramidal cells in cortical layer V
    - Cytoplasm
      – Mitochondria prominent
      – Nissl substance—granular basophilic material representing rough endoplasmic reticulum
      – Neurofilaments (60–100 Å, transport function)
      – May have pigments such as lipofuscin and/or melanin
    - Cell processes
      – Axon with terminal synapse—conducts away from cell body, arises from axon hillock which contains no Nissl substance; axoplasm with mitochondria, neurotubules, and neurofilaments
      – Dendrite—conducts toward cell body, contains Nissl substance
    - Neurons in certain highly specialized nuclei produce specific bioaminergic neurotransmitters
      – Substantia nigra—dopamine
      – Locus coeruleus—norepinephrine
      – Raphe nuclei—serotonin
      – Nucleus basalis of Meynert—acetylcholine
    - Pigmented (neuromelanin) neurons—coarse, dark brown granules
      – Substantia nigra (midbrain)
      – Locus coeruleus (pons)
      – Dorsal motor nucleus of the vagus nerve (medulla)
    - Immunostaining
      – Synaptophysin—vesicle protein
      – Neurofilament—neuronal intermediate filaments
      – NeuN—neuronal nuclear stain
    - Lipofuscin (aging pigment, lipochrome)
      – Increases with age
      – Intracytoplasmic
      – Light yellow-brown color on routine hematoxylin and eosin staining
    - Hyaline (colloid inclusion)
      – Cytoplasmic
      – Endoplasmic reticulum dilated cisternae
    - Marinesco bodies
      – Eosinophilic intranuclear inclusions
      – May be multiple within a single nucleus
      – Prominently seen in pigmented neurons
      – Increase with age
    - A variety of other inclusions within neurons may be seen in association with certain disease processes (e.g., Lewy bodies, neurofibrillary tangles, Hirano bodies, Pick bodies, granulovacuolar degeneration, viral inclusions)
    - Ischemic changes—"red and dead"—shrunken cell body with dark nucleus, indistinguishable nucleolus, and hypereosinophilic cytoplasm
    - Central chromatolysis—related to axonal or retrograde degeneration, cytoplasmic swelling with loss of Nissl substance, and peripheralization/flattening of the nucleus; may be reversible to a point
    - Ferrugination of neurons (fossilized neurons)—encrusted with calcium and/or iron, may be seen in old infarcts
    - Neuronophagia—phagocytosis of cell body
    - Axonal spheroids—focal dilation of axon with neurofilaments and organelles, reaction to axon injury, Purkinje cell axonal spheroids called "torpedoes"

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B. Astrocytes
- Largest of glial cells
- Oblong nucleus, vesicular chromatin without nucleolus
- Cytoplasm highlighted with glial fibrillary acidic protein (GFAP) antibody—stains intermediate glial filaments, nucleus stains with Olig 2
- Processes often invest vessels, contribute to blood–brain barrier (BBB)
- Processes also extend to pial surface (glial limitans of brain–cerebrospinal fluid barrier)
- Variety of shapes
  - Star-shaped fibrillary (white matter) and protoplasmic (gray matter) cells
  - Pilocytic astrocytes of periventricular region and cerebellum
  - Bergmann astrocytes of cerebellum
- Corpora amylacea
  - Laminated, basophilic polyglucosan bodies
  - Associated with astrocytic foot processes
  - Increase with age
  - Frequently seen in subpial, subventricular, and perivascular regions
- Reactive astrocytes
  - Cell hypertrophy—increased cell cytoplasm
  - Gliosis may be associated with increased cell number
  - Cells in chronic reactive gliosis have more fibrillar appearance (piloid gliosis)
  - A marker for pathology (normal brain does not demonstrate reactive astrocytosis)
- Rosenthal fibers
  - Cytoplasmic inclusions
  - Brightly eosinophilic, elongated deposits
  - Observed in a number of entities including chronic gliosis, Alexander's disease, pilocytic astrocytoma
- Creutzfeldt astrocyte
  - Reactive astrocytes with increased cytoplasm and fragmented nuclear material (giving the impression of multiple micronuclei) or disarranged mitotic figure
  - Often seen in demyelinative processes
- Alzheimer type I astrocyte
  - Large, bizarre-appearing cell often with multiple nuclei or irregularly lobulated nuclei
  - Seen in progressive multifocal leukoencephalopathy
- Alzheimer type II astrocyte
  - Nuclear swelling and chromatin clearing
  - Prominent nucleation
  - Cell cytoplasm not readily apparent
  - Prominently seen in basal ganglia in hepatic diseases that produce elevated ammonia levels
- Viral inclusions in astrocytes
  - Cowdry A—intranuclear, eosinophilic viral inclusion; displaces the nucleolus (e.g., subacute sclerosing panencephalitis (measles), herpes, cytomegalovirus)
  - Cowdry B—intranuclear, eosinophilic viral inclusion; often multiple and smaller than Cowdry A inclusions, generally do not displace the nucleolus (e.g., polio)

C. Oligodendrocytes
- Most numerous cells in the CNS
- Small cells with no cytoplasmic staining on H&E stain, round dark nucleus without prominent nucleolus
- Thinner and fewer cell processes than astrocytes
- Tend to arrange themselves around neurons (neuronal satellitosis)
- "Fried egg" appearance is a delayed post-formalin-fixation artifact (not apparent at frozen section)
- Cells often arranged in small rows in the white matter between myelinated fibers
- Involved in the formation and maintenance of CNS myelin
- Only weak immunostaining with GFAP, positive staining with S-100 protein and Olig2 antibodies
- Glassy, plum-colored intranuclear inclusions in progressive multifocal leukoencephalopathy (JC virus)

D. Ependymal cells
- Epithelioid cells that line ventricular walls and central canal of the spinal cord
- Columnar/cuboidal cells with cilia, oval hyperchromatic nuclei
- Cilia attached to cell body by blepharoplast
- Tanycytes—specialized ependymal cells of the third ventricle with basal processes extending between astrocytic processes to form an end-foot on blood vessels
- Ependyma-lined central canal is patent in childhood but generally becomes obliterated by puberty
- Ependymal loss with injury accompanied by a proliferation of subependymal glia (granular ependymitis)

E. Microglia
- Small, dark, elongated nuclei with scant cytoplasm

- Derived from a monocytic/macrophage lineage (HAM56, CD68, CD163 positive)
- May proliferate in a diffuse pattern (microgliosis) or nodular pattern (microglial nodule—commonly seen with viral encephalitis)
- With destruction of parenchymal tissue will see a macrophage response (gitter cells)
- Macrophages seen in a variety of pathologies (e.g., infarct, demyelinating disease, radiation, infection)

F. Choroid plexus
- Produces cerebrospinal fluid (400–500 mL daily), usually intraventricular in location
- May see choroid plexus in subarachnoid space in cerebellopontine angle region
- Fibrovascular cores lined by epithelial cells, cobblestoned contour
- May see small nests of arachnoid (meningothelial) cells intermixed
- May be focally calcified

G. Arachnoid cap cells or meningothelial cells
- Seen principally in the arachnoid membrane
- Epithelioid to slightly spindled cells in small clusters, oval nuclei with dispersed chromatin and eosinophilic cytoplasm
- Associated with psammoma body formation (laminated calcifications)
- Dorsal leptomeninges of cord may contain white firm plaques (arachnoiditis ossificans)—laminated dense hyalinized fibrous tissue
- May see melanocytes in the meninges, more prominent in darker skinned individuals overlying the ventral surface of the superior portion of the spinal cord, brainstem, and base of brain
- Dura overlying the leptomeninges comprised primarily of dense fibrous connective tissue

H. Architecture
- Cerebral cortex
  - Six layers, oriented parallel to pial surface
  - Neurons within the layers have their processes oriented perpendicular to the pial surface
  - Layers
    - Layer I. Molecular—few small neurons, glia, outermost layer
    - Layer II. External granular—small neurons with short axons
    - Layer III. Outer pyramidal—medium-size and large neurons
    - Layer IV. Internal granular—small stellate neurons
    - Layer V. Inner pyramidal—medium-size neurons, Betz cells
    - Layer VI. Polymorphic layer—innermost layer
- Cerebellum
  - Three layers
    - Molecular layer—outermost layer
    - Purkinje cell layer—single layer of neurons
    - Granular cell layer—hypercellular, small cells
  - Deep cerebellar nuclei (from lateral to medial)—dentate, emboliform, globose, and fastigial
  - External granular cell layer in infant overlying molecular layer, disappears by age 1 year
- White matter
  - Fibers run at right angles to cortical surface
  - Includes centrum semiovale
  - Bundles in gray matter parallel to surface:
    - Inner line of Baillarger layer V, outer line of Baillarger layer IV
    - Stria (line) of Gennari between layers IV in occipital lobe—widened band of Baillarger, marks the primary visual cortex
- Basal ganglia
  - Includes caudate, putamen, and nucleus accumbens
  - Gray matter tissue
  - Most neurons are GABAergic spiny neurons
  - Caudate and putamen contain thin fascicles of myelinated fibers (pencil fibers of Wilson)
- Thalamus
  - Main integration center and sensory relay to the cortex
  - Most neurons (about 75%) are large projection neurons—smaller population of inhibitory GABAergic interneurons
- Hippocampus
  - Consists of dentate gyrus, Ammon's horn, and subiculum
  - Ammon's horn (CA = cornu ammonis) divided into four regions (CA1–4)
    - CA4 endplate region within the hilus of the dentate gyrus
    - CA3 connects endplate to resistance sector (CA2)
    - CA1 Sommer's sector (most sensitive area of brain to anoxic damage)
- Spinal cord
  - Enlargement of anterior (ventral) horns in cervical and lumbosacral region; neurons = lower motor neurons
  - Intermediolateral cell column between T1 and L3 levels

  - Central canal in middle; generally closes off with age
  - Clarke's nucleus is medial extension of the intermediate gray matter T1–L2 levels
  - Terminates with filum terminale
- Pineal gland
  - Vaguely nodular architectural arrangement of cells (pinealocytes) with glial background
  - Pinealocytes—neuronal cells with rounded nuclei, stippled chromatin, and a moderate amount of pale eosinophilic cytoplasm with short processes
  - Corpora arenacea—calcifications, present after puberty ("brain sand")
  - Pineal cysts—gliotic cysts often with Rosenthal fibers
- Pituitary gland
  - Adenohypophysis (anterior)—nests of epithelioid cells separated by delicate fibrovascular septae, cell types in a given nest are mixed type (50% chromophobes, 40% acidophils, and 10% basophils), geographic predominance of certain cell types; hormonal types include: prolactin (PRL), growth hormone (GH), adrenocorticotropic hormone (ACTH), thyroid stimulating hormone (TSH), follicle stimulating hormone (FSH), and luteinizing hormone (LH)
  - Pars intermedia—at interface between adenohypophysis and neurohypophysis, glandular formations may be seen
  - Neurohypophysis (posterior)—spindled cells (pituicytes) loosely arranged; contains Herring bodies (eosinophilic axonal dilations containing vasopressin and oxytocin)
- Brainstem
  - Base—ventral location, consists mostly of long fiber tracts
  - Tegmentum—dorsal to base and ventral to fourth ventricle, reticular formation (controls basal body activity)
  - Tectum—dorsal to ventricular components
  - Three levels—midbrain, pons, and medulla

II. Artifacts
- Bone dust from craniotomy or skull removal
- Delayed fixation—neuronal shrinkage, perinuclear halos in oligodendrocytes
- Swiss cheese brain—prolonged postmortem period resulting from gas producing bacterial overgrowth
- Cerebellar granular cell conglutination—prolonged postmortem period
- Tangential sectioning—may give impression of hypercellular cortex

III. Skeletal Muscle

A. Muscle fibers arranged in bundles (fascicles) surrounded by perimysium connective tissue; endomysium is connective tissue between muscle fibers

B. Nuclei multiple, peripherally arranged
- Central nuclei abnormal if seen in >3–5% of myofibers
- Increased centralized nuclei in myotonic dystrophy, myotubular myopathy, Charcot-Marie-Tooth disease

C. At muscle–tendon junction, fibers get smaller and often contain internalized nuclei

D. In cross section, fibers are generally the same size
- Atrophy
  - Scattered vs grouped (neurogenic), tend to have angulated contours
  - Rounded fiber atrophy—more likely myopathic except in denervation atrophy in infants (e.g., Werdnig-Hoffmann disease)
  - Perifascicular atrophy—ischemia-related and a characteristic feature of dermatomyositis
  - Fascicular atrophy—spinal muscular atrophy, hereditary motor and sensory neuropathies, vasculitis
  - Type I atrophy—myotonic dystrophy, congenital myopathies, spinocerebellar degeneration
  - Type II atrophy—disuse, steroids (type IIB atrophy), collagen vascular disease, myasthenia gravis, cachexia, paraneoplastic neuromyopathy
- Hypertrophy
  - Normal in athletes (type II fibers)
  - Often associated with central nuclei and split fibers
  - Scattered hypertrophic fibers adjacent to atrophy—compensatory

E. Muscle fiber types (type I, type IIA, type IIB) generally distributed in a mosaic/checkerboard pattern
- Type I fibers—high oxidative, low glycolytic activity
- Type II fibers—low oxidative, high glycolytic activity
- Different muscles contain different proportions of the three fiber types
- Loss of the mosaic distribution of fiber types—fiber type grouping, indicative of chronic denervation and re-innervation

F. Muscle cells of variable length—run from origin to insertion

G. Muscle cells made up of myofilaments
- Two main types: thick myosin filaments and thin actin filaments
- Sarcomere segment is the functional contractile unit of muscle formed by the orderly arrangement of interdigitating myofilaments, runs from Z band to Z band
- Sarcomeric banding patterns
  - Dark central A (anisotropic) band consisting of mostly thick myosin filaments
  - A band is crossed at midpoint by a dark narrow transverse M line consisting of cross-bridges, which link adjacent myosin filaments together
  - M band is surrounded by paler H band, which varies in width as the sarcomeric length changes
  - Pale I (isotropic) band situated on either side of the A band, consisting mostly of thin actin filaments in combination with troponin and tropomyosin proteins
  - Z band divides I band at midpoint and marks the longitudinal boundary of each sarcomere, made of α-actinin material
- During contraction of the myofiber, I filaments slide toward the center of the A band with shortening of the I and H bands
- Desmin intermediate filaments link Z discs together and join them to the plasmalemma

H. Sarcoplasm
- Represents the cytoplasm of the myofiber
- Consists of a variety of structures/organelles
  - Mitochondria—type I > type II
  - T system (transverse tubular system)—network of tubules continuous with the muscle cell plasma membrane, allows for the rapid passage of depolarization into the interior of the myofiber
  - Sarcoplasmic reticulum—a series of flattened sacs between and around myofibrils
  - Lipid—droplets lie between myofibrils and adjacent to mitochondria, type I > type II
  - Glycogen—more prominent in region of I bands than A bands, type II > type I
  - Ribosomes, Golgi membranes, intermediate filaments, microtubules, and lipofuscin also seen

I. Muscle spindle
- Collections of small intrafusal fibers (3–14) enclosed in a connective tissue capsule
- Center of spindle is swollen, ends are tapered
- Located between muscle fascicles in perimysial connective tissue
- Consists of two types of intrafusal fibers: nuclear bag fibers and nuclear chain fibers
- More numerous in muscles involved in delicate movements
- Associated with sensory nerve endings

J. Golgi tendon organ
- Encapsulated sensory nerve terminal
- Located at junction of muscle with tendon or aponeurosis
- Functions to detect changes in muscle tension and inhibit strong muscle contractions

K. Motor unit—consists of anterior horn cell, nerve fiber arising from it, and the muscle fibers supplied by it

L. Neuromuscular junction—interface between the nerve and muscle; acetylcholine is released by the nerve to activate the muscle; the electrical impulse reaches the sarcoplasmic reticulum via the T system

M. Muscle proteins associated with myofibrillar apparatus, membrane cytoskeleton, and extracellular matrix
- Myosin—hexomeric protein; thick filaments of A band
- Actin—thin filaments
- Troponin—calcium-binding complex, releases inhibitory effect of tropomyosin
- Tropomyosin—sterically inhibits actin–myosin interaction
- α-Actinin—anchors thin filaments, Z-band material
- Desmin and vimentin—intermediate filaments, links Z bands of adjacent myofibrils together
- Titin (connectin)—maintains position of thick filaments between Z bands
- Creatinine kinase—resynthesis of ATP
- Nebulin—regulates length of thin filaments
- Dystroglycan—transmembrane protein which links intracellular cytoskeleton with extracellular matrix
- Dystrophin—cytoskeletal protein which links actin with dystroglycans

I. Peripheral Nerve

A. Connective tissue layers
- Epineurium—binds fascicles together, continuous with dura mater at junction of spinal nerves and spinal nerve roots
- Perineurium—concentric layers of flattened cells which are epithelial membrane antigen (EMA) positive, separated by collagen that surrounds individual fascicles, forms part of the blood–nerve barrier, continuous with the pia arachnoid

- Endoneurium—collagen compartment that surrounds individual axons, Schwann cells, and fibroblasts

B. Mast cells also present in endoneurium, increase in number with axonal degeneration and neurofibroma
C. Renaut bodies—cylindrical hyaline bodies attached to inner aspect of the perineurium; composed of collagen fibers, fibroblasts, and epineurial cells; function not known; increase in number in compressive neuropathies
D. Blood supply comes from vasa nervorum
E. Nerve fibers
- Either myelinated or unmyelinated
- Class A fibers
  - Myelinated
  - 1–20 μm diameter; conduction velocity 12–100 m/sec
- Class B fibers
  - Myelinated preganglionic autonomic fibers
  - Up to 3 μm in diameter; conduction velocity 3–15 m/sec
- Class C fibers
  - Unmyelinated
  - Small fibers (0.2–1.5 μm diameter); conduction velocity 0.3–1.6 m/sec

F. Myelin (peripheral nervous system)
- Can be highlighted with certain stains (Luxol fast blue, Loyez, osmium, periodic acid–Schiff, Masson trichrome)
- Formed by fusion of Schwann cell membranes
- 75% lipid and 25% protein
- Major lipids comprising myelin: cholesterol, sphingomyelin, galactolipid
- Myelin-associated glycoprotein (MAG)—associated with Schwann cells and myelination process
- One Schwann cell per myelinated axon (in CNS, one oligodendrocyte supplies myelin to multiple axons)
- Schwann cells S-100 and SOX10 positive by immunohistochemistry
- Pi granules of Reich—lamellated structures, cytoplasm accumulates along with lipofuscin with increasing age
- Corpuscles of Elzholz—spherical bodies in Schwann cell cytoplasm

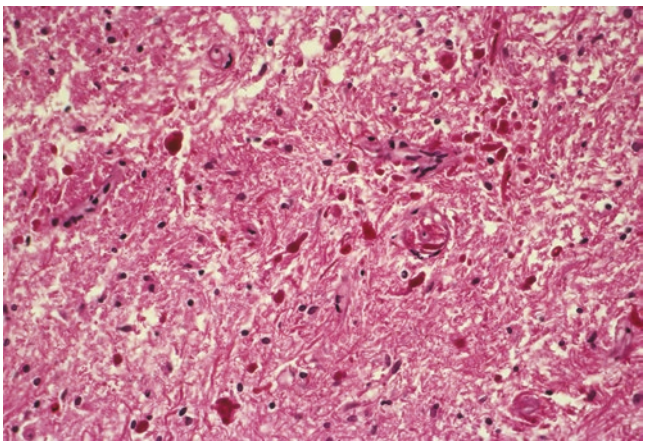
G. Schmidt-Lanterman clefts
- Cleft splits the cytoplasmic membranes and serves as a route of passage for substances from the outer cytoplasmic layer through the myelin sheath to the inner cytoplasm
- The number of clefts correlates with the diameter of the axon

H. Node of Ranvier
- Gaps in the myelin sheath
- Distance between nodes is proportional to myelin thickness
- Conduction of impulses along myelinated fibers proceeds in a discontinuous manner from node to node (saltatory conduction)

I. Myelinated axons
- Axon is delimited by axolemma membrane
- Axolemma separated from adjacent Schwann cell by periaxonal space
- Axonal cytoplasm contains mitochondria, smooth endoplasmic reticulum, glycogen, ribosomes, peroxisomes, neurotransmitter vesicles, filaments/tubules
- Filaments include actin, neurofilaments, and microtubules

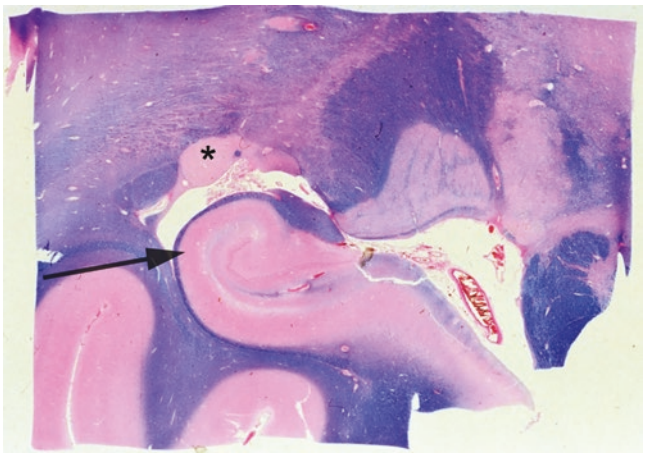
J. Unmyelinated axons
- Best evaluated and studied by electron microscopy
- More numerous than myelinated axons: 3–4:1 unmyelinated:myelinated axons
- Frequently associated with Schwann cells; may be more than one axon per Schwann cell

Self-Assessment



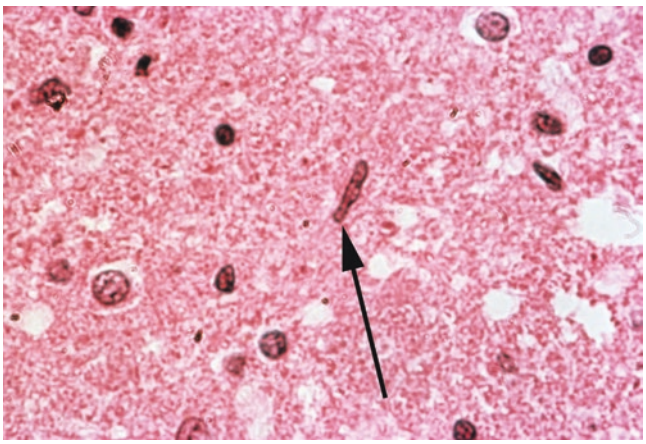
Question 1

1. These brightly eosinophilic staining, irregularly shaped structures in a pilocytic astrocytoma are referred to as
   A. Rosenthal fibers
   B. Granular bodies
   C. Marinesco bodies
   D. Tangles
   E. None of the above



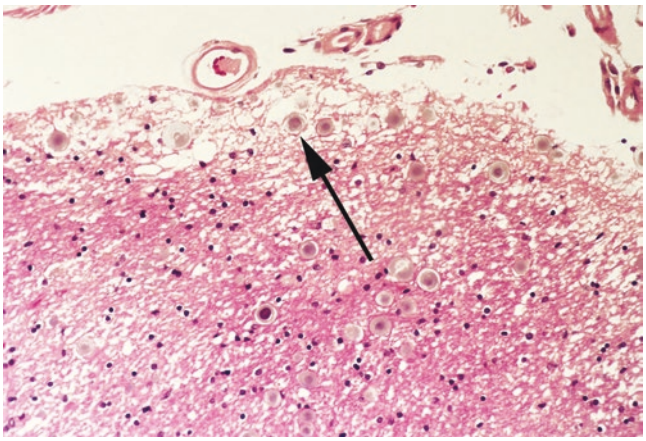
Questions 2–3

2. The region denoted by the arrow represents
   A. Dentate
   B. CA4
   C. CA3
   D. Sommer's sector
   E. Subiculum
3. The structure marked by the asterisk represents
   A. Choroid plexus
   B. Hippocampus
   C. Amygdala
   D. Caudate nucleus
   E. Thalamus



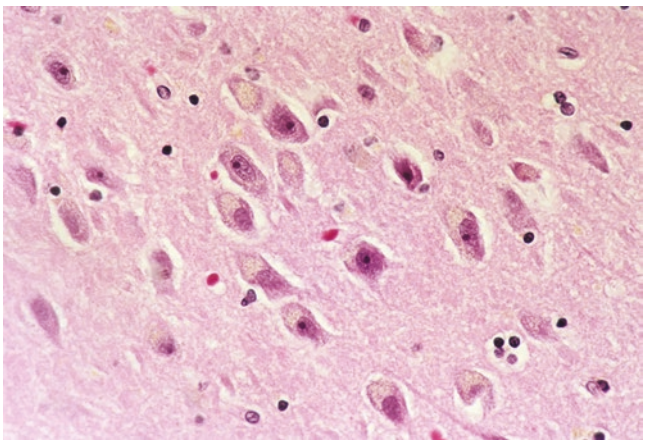
Questions 4–5

4. The cell denoted by the arrow represents a(n)
   A. Neuron
   B. Oligodendrocyte
   C. Ependymal cell
   D. Endothelial cell
   E. Microglial cell
5. The antibody that would best stain this cell would be
   A. Neurofilament
   B. GFAP
   C. Cytokeratin
   D. CD34
   E. CD68



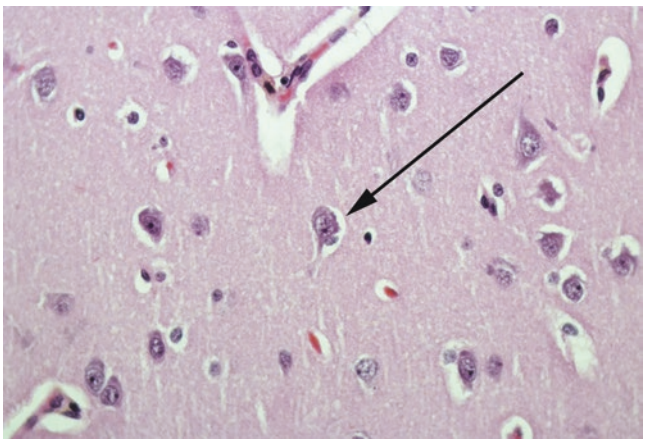
Question 6

6. The structure denoted by the arrow represents a(n)
   A. Marinesco body
   B. Hyaline body
   C. Rosenthal fiber
   D. Corpora amylacea
   E. Alzheimer type I astrocyte



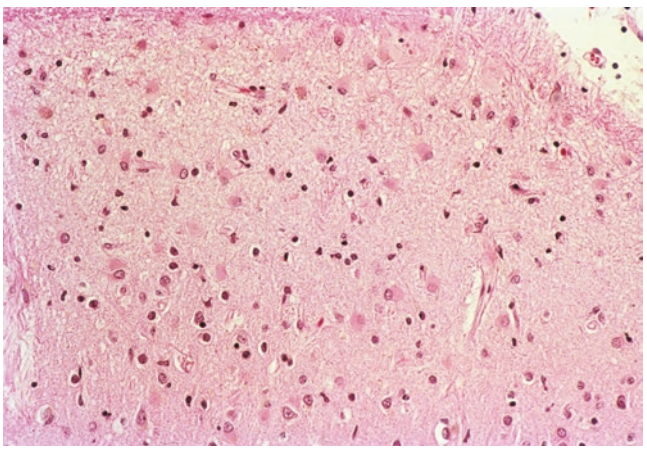
Question 7

7. The cytoplasm of these neurons in this normal brain section are filled with
   A. Neuromelanin
   B. Lipofuscin
   C. Hyaline bodies
   D. Marinesco bodies
   E. Hemosiderin



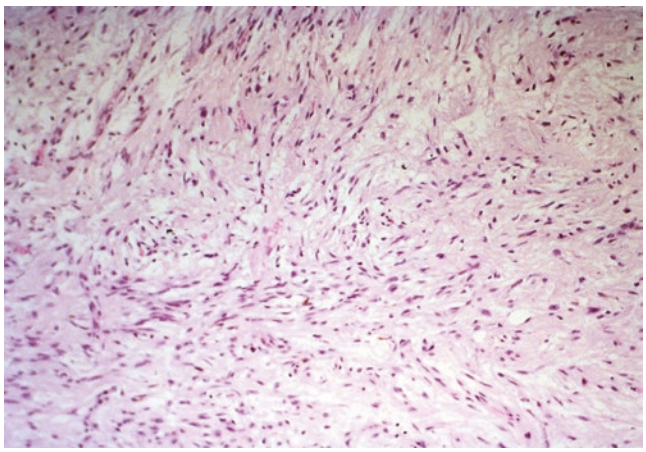
Questions 8–9

8. The cell denoted by the arrow represents a(n)
   A. Astrocyte
   B. Oligodendrocyte
   C. Neuron
   D. Microglial cell
   E. Arachnoidal cap cell
9. This cell is most likely to stain positively with which antibody?
   A. GFAP
   B. Synaptophysin
   C. Epithelial membrane antigen
   D. Common leukocyte antigen
   E. HAM 56



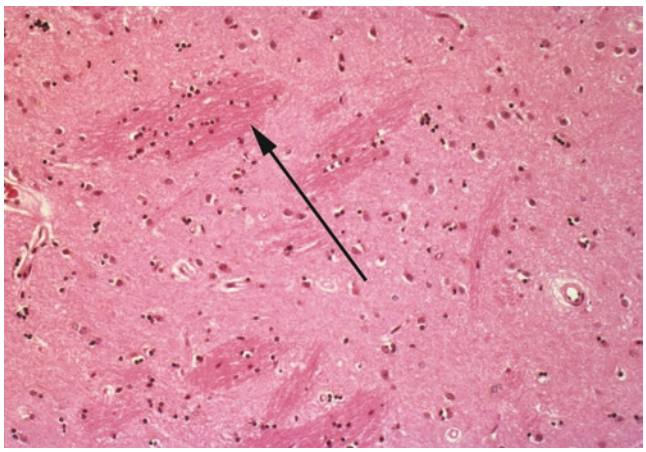
Question 10

10. The histology illustrated here represents
    A. Normal brain
    B. Astrocytoma
    C. Ependymoma
    D. Reactive astrocytosis
    E. Lymphoma



Questions 11–12

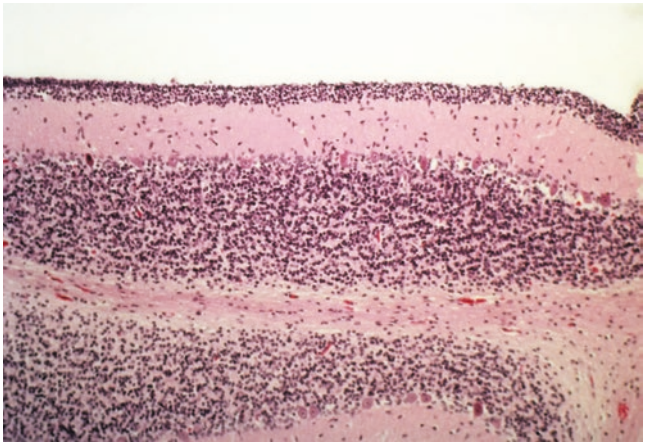
11. The photomicrograph here represents what normal structure?
    A. Pineal gland
    B. Leptomeninges
    C. Pituitary adenohypophysis
    D. Pituitary neurohypophysis
    E. Pituitary pars intermedia
12. Eosinophilic axonal dilations which contain vasopressin that may be found in this location are known as
    A. Pars intermedia
    B. Crooke's hyaline
    C. Fibrous bodies
    D. Herring bodies
    E. Corpora amylacea



Questions 13–14

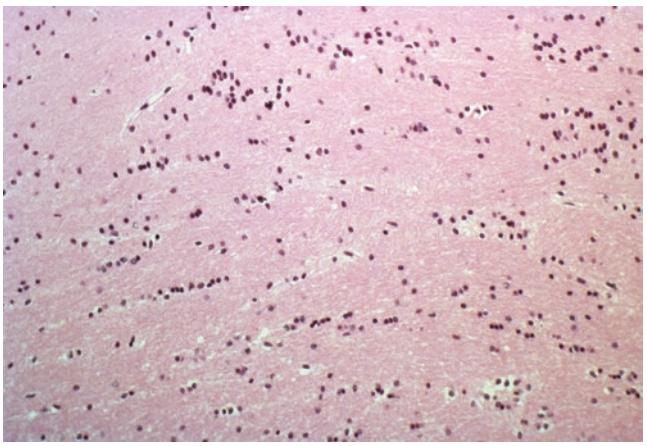
13. The area seen here is consistent with
    A. Caudate nucleus
    B. Hippocampus
    C. Dentate nucleus
    D. Olivary nucleus
    E. None of the above

14. The fascicles of myelinated fibers seen here (arrow) are referred to as
    A. Lines of Baillarger
    B. Stria of Gennari
    C. Fibers of Wilson
    D. Polymorphous bundles
    E. None of the above



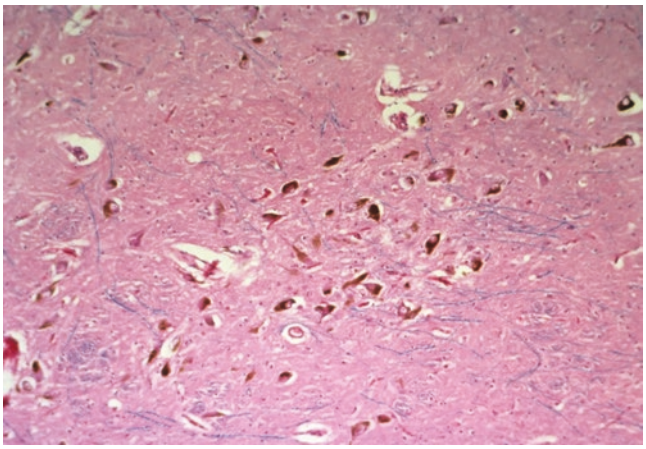
Question 15

15. The age of the patient here most likely is
    A. 3 months
    B. 3 years
    C. 13 years
    D. 30 years
    E. 60 years



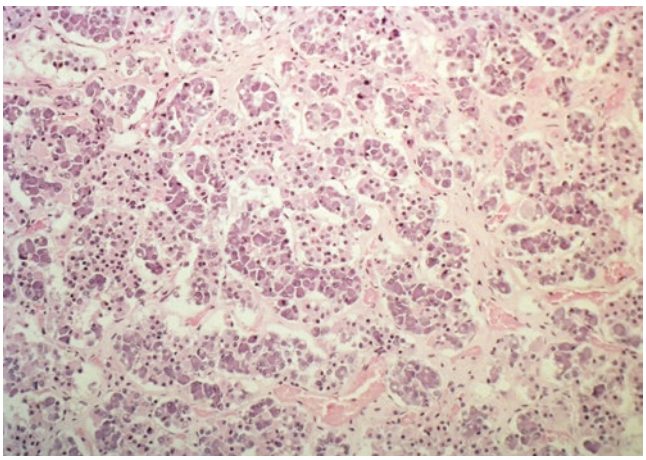
Question 16

16. The photomicrograph here was most likely taken from which location?
    A. Frontal lobe cortex
    B. Frontal lobe white matter
    C. Putamen
    D. Hippocampus
    E. Pineal gland



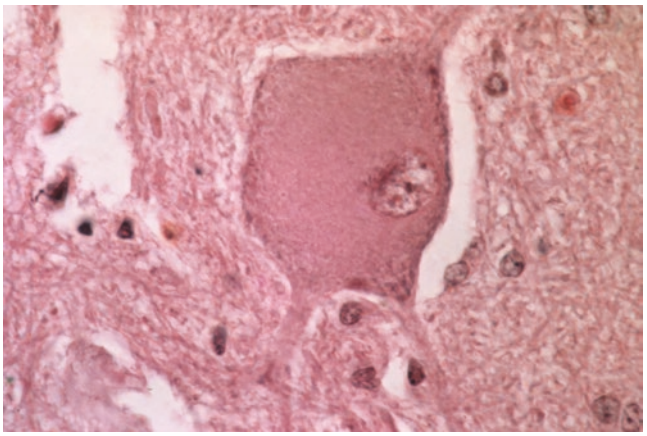
Question 17

17. The melanin-pigmented neurons seen here belong to which neuronal group?
    A. Dentate nucleus
    B. Substantia nigra
    C. Hypoglossal nucleus
    D. Red nucleus
    E. Olivary nucleus



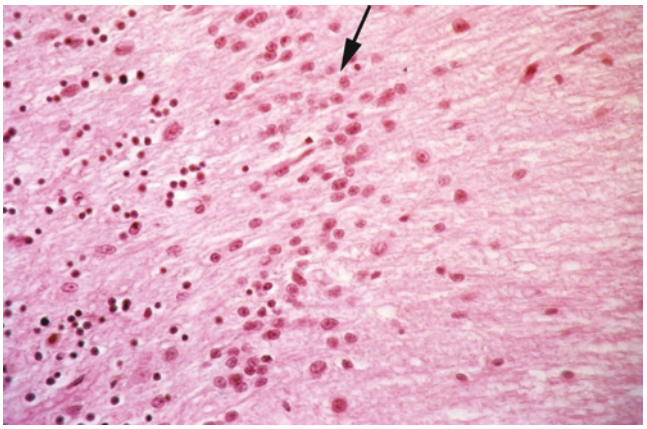
Question 18

18. What normal structure is represented here?
    A. Pineal gland
    B. Arachnoid cap cells
    C. Choroid plexus
    D. Skeletal muscle
    E. None of the above



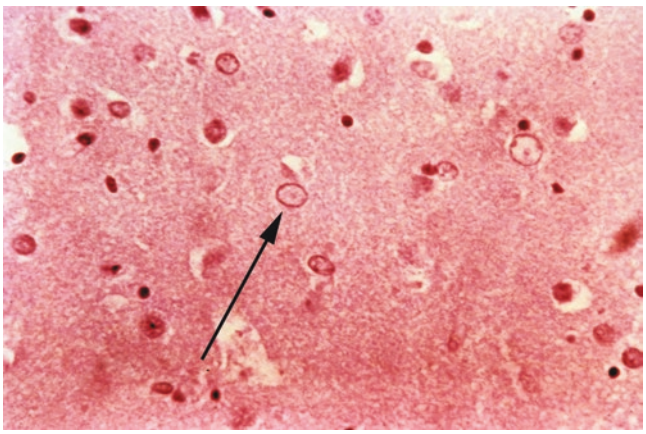
Questions 19–20

19. The cell shown here represents a(n)
    A. Neuron
    B. Astrocyte
    C. Microglial cell
    D. Oligodendroglial cell
    E. Endothelial cell
20. The process shown in this cell represents
    A. Ischemic changes
    B. Central chromatolysis
    C. Ferrugination
    D. Neuronophagia
    E. Creutzfeldt astrocyte



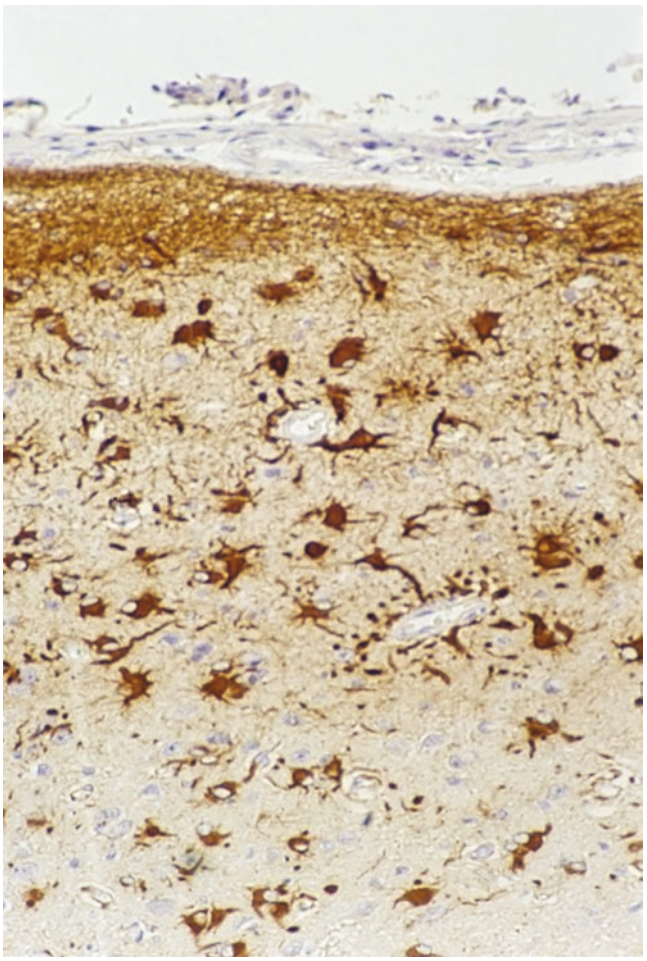
Questions 21–22

21. The paler staining cells denoted by the arrow represent
    A. Purkinje cells
    B. Granular cells
    C. Lymphocytes
    D. Bergmann astrocytes
    E. Corpora amylacea
22. All of the following conditions are likely to result in the pathology seen here except
    A. Chronic ischemic change
    B. Chronic epilepsy
    C. Alcoholism
    D. Infiltrating astrocytoma
    E. Phenytoin toxicity



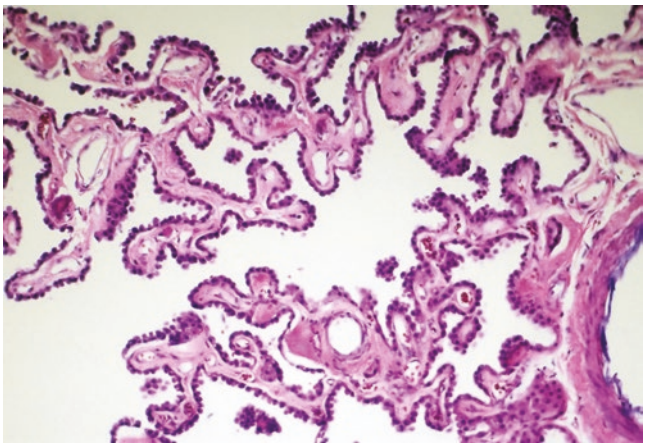
Questions 23–24

23. The cell denoted by the arrow represents a(n)
    A. Reactive astrocyte
    B. Gemistocyte
    C. Creutzfeldt astrocyte
    D. Alzheimer type I astrocyte
    E. Alzheimer type II astrocyte
24. This cell is most likely to be encountered in the setting of
    A. Tumor
    B. Demyelinating disease
    C. Diabetic encephalopathy
    D. Hepatic encephalopathy
    E. Progressive multifocal leukoencephalopathy



Question 25

25. The GFAP immunostain seen here is highlighting what cells?
    A. Ependymal cells
    B. Astrocytes
    C. Microglial cells
    D. Oligodendroglial cells
    E. Neurons



Question 26

26. The structure illustrated represents
    A. Choroid plexus
    B. Choroid plexus papilloma
    C. Choroid plexus carcinoma
    D. Papillary meningioma
    E. Papillary ependymoma
27. Nissl substance is composed of
    A. Smooth endoplasmic reticulum
    B. Rough endoplasmic reticulum
    C. Golgi structures
    D. Neuromelanin
    E. Lipofuscin
28. Marinesco bodies are most likely going to be found in which cell type?
    A. Neuron
    B. Astrocyte
    C. Oligodendrocyte
    D. Ependymal cell
    E. Arachnoid cap cell
29. Bergmann astrocytes are found in the
    A. Basal ganglia
    B. Cerebral cortex
    C. Subcortical white matter
    D. Cerebellum
    E. Hippocampus
30. Rosenthal fibers may be encountered in all of the following conditions except
    A. Alexander's disease
    B. Reactive astrocytosis
    C. Infiltrating astrocytoma
    D. Pilocytic astrocytoma
    E. Pineal gland cyst
31. Alzheimer's II astrocytes are most commonly associated with what condition?
    A. Hepatic encephalopathy
    B. Progressive multifocal leukoencephalopathy
    C. Gliosis
    D. Pilocytic astrocytoma
    E. Alexander's disease

32. The "fried egg" appearance of oligodendrocytes represents
    A. Cell cytoplasm
    B. Perinuclear edema
    C. Artifact of delayed fixation
    D. Increased cytoplasmic lipid
    E. None of the above
33. Ciliary body attachments in ependymal cells are known as
    A. Kinetoplasts
    B. Chloroplasts
    C. Microtubuloblasts
    D. Blepharoplasts
    E. None of the above
34. Which of the following immunostains is a useful marker for microglial cells?
    A. GFAP
    B. Synaptophysin
    C. HAM56
    D. S-100 protein
    E. CLA
35. Layer III of the cerebral cortex is known as
    A. External granular layer
    B. Internal granular layer
    C. Polymorphic layer
    D. Outer pyramidal layer
    E. Inner pyramidal layer
36. The pencil fibers of Wilson are a feature of which structure?
    A. Substantia nigra
    B. Dentate
    C. Putamen
    D. Locus coeruleus
    E. Hippocampus
37. The endplate of the hippocampus (Ammon's horn) is referred to as
    A. Dentate
    B. CA1
    C. CA2
    D. CA3
    E. CA4
38. Perifascicular atrophy is a feature of
    A. Dermatomyositis
    B. Polymyositis
    C. Neurogenic atrophy
    D. Myotonic dystrophy
    E. Steroid use
39. The longitudinal boundaries defining the sarcomere are the
    A. A bands
    B. I bands
    C. M lines
    D. Z bands
    E. H bands
40. Increased myofiber central nuclei may be seen in all of the following except
    A. Exercise-induced hypertrophy
    B. Neurogenic atrophy
    C. Myotubular myopathy
    D. Myotonic dystrophy
    E. Charcot-Marie-Tooth disease
41. Intermediate filaments that link Z discs together in muscle are known as
    A. Actin
    B. Desmin
    C. Myosin
    D. Dystrophin
    E. Vimentin
42. Which of the following cells is a normal constituent of the endoneurial compartment?
    A. Lymphocytes
    B. Eosinophils
    C. Mast cells
    D. Basophils
    E. Neutrophils
43. Lamellated cytoplasmic structures located within the Schwann cell cytoplasm that increase with age are referred to as
    A. Corpuscles of Elzholz
    B. Lipofuscin
    C. Schmidt-Lanterman clefts
    D. Pi granules of Reich
    E. Space of Klebs
44. The ratio of myelinated to unmyelinated axons in a sural nerve biopsy would be best approximated by which of the following?
    A. 1:2
    B. 1:4
    C. 1:6
    D. 1:8
    E. 1:10
45. The saltatory conduction pattern in the peripheral nerve is most closely related to which structure?
    A. Node of Ranvier
    B. Periaxonal space of Klebs
    C. Neurofilaments
    D. Schmidt-Lanterman clefts
    E. Vasa vasorum
46. The glial limitans involves cell processes from which cell type-investing blood vessels?
    A. Neurons
    B. Astrocytes

C. Oligodendrocytes
D. Microglial cells
E. Ependymal cells

47. A structure that is involved in detecting muscle tension and inhibiting strong muscle contractions is
A. Muscle spindle
B. Motor unit
C. Golgi tendon organ
D. Myotendinous insertion
E. H band

48. The most numerous cells in the CNS are
A. Neurons
B. Astrocytes
C. Oligodendrocytes
D. Microglial cells
E. Ependymal cells

49. Which muscle-associated protein is associated with the regulation of thin filament length?
A. Titan
B. Nebulin
C. Dystroglycan
D. Dystrophin
E. Vimentin

50. Deep cerebellar nuclei include all of the following except
A. Dentate
B. Olivary
C. Emboliform
D. Globose
E. Fastigial

51. Corpora arenacea are most likely located where?
A. Meninges
B. Frontal lobe
C. Pineal gland
D. Pituitary gland
E. Pons

52. All of the following are associated with type II myofiber atrophy except
A. Disuse
B. Steroid use
C. Cachexia
D. Collagen vascular disease
E. Myotonic dystrophy

Answers to Self-Assessment

1. A (Chapter 1, I.B. and Chapter 3, I.J.) Rosenthal fibers are a characteristic feature of pilocytic astrocytoma. They can be found in other conditions including gliosis.
2. D (Chapter 1, I.H.) The Sommer's sector (CA1) region is denoted by the arrow.
3. D (Chapter 1, I.H.) The tail of the caudate nucleus is marked by the asterisk.
4. E (Chapter 1, I.E.) The cell characterized by an elongated nucleus and scant cytoplasm represents a microglial cell.
5. E (Chapter 1, I.E.) Microglial cells are immunoreactive to the same antibodies that macrophages are, including CD68, CD163, and HAM56.
6. D (Chapter 1, I.B.) The structure represents corpora amylacea, a laminated basophilic polyglucosan body associated with astrocytic foot processes.
7. B (Chapter 1, I.A.) The intracytoplasmic material in many of the neurons here represents lipofuscin or aging pigment.
8. C (Chapter 1, I.A.) The cell shown represents a neuron.
9. B (Chapter 1, I.A.) Neurons are most likely to stain with an antibody to synaptophysin.
10. D (Chapter 1, I.B.) The mildly increased cellularity and larger cells with abundant eosinophilic cytoplasm are characteristic of reactive astrocytosis.
11. D (Chapter 1, I.H.) The loose arrangement of spindled cells is characteristic of the pituitary neurohypophysis.
12. D (Chapter 1, I.H.) Herring bodies are eosinophilic axonal dilations which contain vasopressin and oxytocin and are located in the neurohypophysis.
13. A (Chapter 1, I.H.) The area seen here may represent either the caudate or putamen.
14. C (Chapter 1, I.H.) The fascicles of myelinated fibers seen in the caudate are known as the fibers of Wilson.
15. A (Chapter 1, I.H.) The presence of the external granular cell layer of the cerebellum is a finding most consistent with an age of less than 1 year (3 months).
16. B (Chapter 1, I.H.) The photomicrograph represents white matter parenchyma.
17. B (Chapter 1, I.A.) Melanin-pigmented neurons are seen in substantia nigra, locus coeruleus and the dorsal motor nucleus of the vagus nerve.
18. E (Chapter 1, I.H.) The nests of epithelioid cells separated by fibrovascular septae is characteristic of the pituitary adenohypophysis.
19. A (Chapter 1, I.A.) The cell shown here represents a neuron.
20. B (Chapter 1, I.A.) Cytoplasmic swelling with loss and peripheralization of Nissl substance and eccentric nucleus are salient features of central chromatolysis.
21. D (Chapter 1, I.B.) The proliferation of cells in the region of the Purkinje cell layer are the Bergmann astrocytes.

22. D (Chapter 1, I.B.) Loss of Purkinje cells with astrocytosis is associated with all of the listed conditions except infiltrating astrocytoma.
23. E (Chapter 1, I.B. and Chapter 7, I.X.) The nuclear swelling and chromatin clearing is characteristic of an Alzheimer type II astrocyte.
24. D (Chapter 1, I.B.) Alzheimer type II astrocytes are most likely encountered in hepatic encephalopathy (elevated ammonia levels).
25. B (Chapter 1, I.B.) The GFAP immunostain is highlighting astrocytic cells in the cortex.
26. A (Chapter 1, I.F.) The structure shown represents normal choroid plexus, marked by fibrovascular cores lined by epithelioid cells.
27. B (Chapter 1, I.A.) Nissl substance is composed of rough endoplasmic reticulum.
28. A (Chapter 1, I.A.) Marinesco bodies are intranuclear neuronal inclusions.
29. D (Chapter 1, I.B.) Bergmann astrocytes are found in the cerebellum near the Purkinje cells.
30. C (Chapter 1, I.B.) Rosenthal fibers are frequently seen in all the listed conditions except infiltrating astrocytoma.
31. A (Chapter 1, I.B.) Alzheimer type II astrocytes may be prominently seen in hepatic diseases marked by elevated ammonia levels.
32. C (Chapter 1, I.C.) The "fried egg" appearance of oligodendrocytes is related to formalin fixation artifact.
33. D (Chapter 1, I.D.) Blepharoplasts are the ciliary body attachments in ependymal cells.
34. C (Chapter 1, I.E.) Microglial cells are HAM56 positive.
35. D (Chapter 1, I.H.) Layer III of the cerebral cortex is known as the outer pyramidal layer.
36. C (Chapter 1, I.H.) The pencil fibers of Wilson are thin fascicles of myelinated fibers seen in the caudate and putamen.
37. E (Chapter 1, I.H.) The endplate of the hippocampus is designated CA4.
38. A (Chapter 1, II.D.) Ischemia-related perifascicular atrophy is a feature of dermatomyositis.
39. D (Chapter 1, II.G.) The sarcomere runs from Z band to Z band.
40. B (Chapter 1, II.B.) Increased central nuclei (normally <3–5% of all fibers) is not typically seen in neurogenic atrophy.
41. B (Chapter 1, II.G.) Desmin filaments link Z discs together and join them to the plasmalemma.
42. C (Chapter 1, III.B.) Mast cells are normally present in the endoneurium in small numbers.
43. D (Chapter 1, III.F.) The pi granules of Reich are lamellated structures that increase in number with increasing age in the Schwann cell cytoplasm.
44. B (Chapter 1, III.J.) The best approximation of a myelinated:unmyelinated axon ratio is 1:4.
45. A (Chapter 1, III.H.) Discontinuous saltatory conduction is most related to the nodes of Ranvier.
46. B (Chapter 1, I.B.) Astrocytes are involved in the formation of the glial limitans.
47. C (Chapter 1, II.J.) The Golgi tendon organ is involved in detecting muscle tension and inhibiting strong muscle contractions.
48. C (Chapter 1, I.C.) Oligodendrocytes are the most numerous cells in the CNS.
49. B (Chapter 1, II.M.) Nebulin is involved with regulating the length of thin filaments in skeletal muscle.
50. B (Chapter 1, I.H.) Olivary nuclei are located in the medulla.
51. C (Chapter 1, I.H.) Corpora arenacea represents calcifications that are located in the pineal gland, usually after puberty.
52. E (Chapter 1, II.D.) Myotonic dystrophy is typically associated with type I muscle fiber atrophy.