



Integrated Neural Science Core Curriculum (Full content outline) December 2008

Goals of the Basic Neuroscience Curriculum

It is our goal to provide guidelines for the development, content and evaluation of neuroscience courses taught primarily in the first and/or second years of medical school. The guidelines were designed to prepare students for future neuroscience clerkship and practice experiences as well as to provide the background to participate in basic, clinical, and translational research in the neurosciences. It is hoped that the construction of such a content outline would help to facilitate integration of basic and clinical neuroscience and promote the inclusion of topics such as genetics, epidemiology, and medical informatics (including critical thinking and analysis skills) early in the curriculum.

Learning Objectives for Students

- Describe the normal structure and function of key components of the human nervous system and molecular, biochemical, and cellular mechanisms required for health and homeostasis.
- Identify common disorders of the nervous system and describe the alterations in structure and functioning underlying diseases.
- Describe the complex interplay of the biological, psychological, and social factors in the genesis and maintenance of psychological health and disease and the nosology and phenomenology of psychiatric disorders.
- Demonstrate the ability to apply basic knowledge and principles in neuroscience (including neuroanatomy, neurophysiology, neuropharmacology, neuropathology, and behavioral science) to permit knowledgeable participation in the diagnosis and care of patients with neurologic and psychiatric disorders.
- Demonstrate skills of medical problem solving, communication, team work, and life-long learning.

Contents

- I. Neural Cell Biology: Morphologic and Physiologic Properties of Cells in the Nervous System
- II. Neural Development
- III. Functional Neuroanatomy
- IV. Clinical Assessment of Neurologic System
- V. Neuropharmacology and Other Therapeutic Modalities
- VI. Neuropathophysiology
- VII. Psychopathologic Disorders
- IX. Interdisciplinary Areas/Psychosocial Issues

I. Neural Cell Biology: Morphological and Physiological Properties of Cell in the Nervous System

- A. Cellular elements of the nervous system
 1. Neurons
 2. Glia
 3. Endothelial cells
- B. Divisions of the nervous system
 1. Central nervous system (CNS)
 2. Peripheral nervous system (PNS)
 3. Autonomic nervous system (ANS)
 4. Enteric nervous system (ENS)
- C. Neuronal morphology and cell biology
 1. Regions of functional morphology
 - a. Cell body
 - b. Dendrites
 - c. Axon
 2. Major morphologic types of neurons
 3. Transport functions
 - a. Slow axoplasmic flow
 - b. Fast anterograde axonal transport

- c. Retrograde axonal transport
- D. Functional classification of neurons
- 1. Sensory
 - 2. Motor
 - 3. Interneurons
- E. Glial cells—greatly outnumber neurons in the CNS
- 1. Schwann cells (PNS)
 - 2. Astrocytes
 - 3. Oligodendroglia
 - 4. Microglia
 - 5. Ependymal cells
- F. Peripheral nerves
- 1. Origins
 - a. Cell bodies of peripheral sensory neurons lie in dorsal root ganglia or brainstem sensory ganglia
 - b. Motor neuron cell bodies lie in the ventral horn of the spinal cord or in certain brainstem nuclei
 - c. Autonomic axons arise from the spinal cord (T1-L2) and sympathetic chain ganglia or from brainstem or sacral cord nuclei (parasympathetic)
 - 2. Connective tissue sheaths envelope peripheral nerves
 - a. Epineurium
 - b. Perineurium
 - c. Endoneurium
 - 3. Axons of peripheral nerves are surrounded by Schwann cells
 - a. Myelinated axons
 - b. Unmyelinated axons
 - 4. Peripheral nerve injury
 - a. Causes (trauma, diseases of myelin or neurons, toxins, and metabolic disorders)
 - b. Wallerian degeneration
 - c. Chromatolysis
 - d. Peripheral neuropathies generally affect small and distal processes first
- G. Neuronal electrical and excitable properties for signaling
- 1. Membranes have selective ion permeability
 - a. Nernst equation describes equilibrium potentials for each major ionic species
 - b. Membrane potential always moves toward the equilibrium potential of the ion(s) to which the cell is most permeable
 - 2. Resting membrane potential due to selective permeability to potassium ions (K⁺)
 - 3. Action potentials
 - a. Caused by a brief increase in sodium ion (Na⁺) conductance followed by an increase in K⁺ conductance
 - b. Channels for Na⁺ and K⁺ permeation involved in the action potential are voltage-gated
 - c. Voltage-gated Na⁺ channels have an activated and inactivated (refractory) state are initiated in the axon-hillock area of neurons
 - d. Propagate undiminished down the axon to cause release of synaptic transmitter from axon terminals
 - e. Large-diameter axons conduct faster than small-diameter axons
 - f. Myelin allows the action potential to conduct very rapidly (saltatory conduction)
 - 4. Neural membranes have passive properties that allow them to integrate incoming signals temporally and spatially
 - 5. The “sodium pump” (Na⁺- K⁺ ATPase) is critical for maintaining ion gradients in neuronal membranes
- H. Synaptic transmission
- 1. Pre-synaptic and post-synaptic specializations, synaptic cleft
 - 2. Release of synaptic vesicles depends on influx of Ca⁺⁺ ions
 - 3. Transmitter chemicals
 - a. Small-molecule transmitters
 - b. Peptide transmitters
 - c. Some neurons use both small-molecule and peptide transmitters
 - d. Each neuron is specified to use only one small-molecule transmitter

4. Production and transport of peptide transmitters
 5. Synthesis and recycling of small-molecule transmitters
 6. Transmitter clearance by degradation, diffusion, or reuptake
 7. Two general families of neurotransmitter receptors
 - a. Ionotropic receptors
 - b. Metabotropic receptors
- I. Trophic and growth factors (Nerve growth factor, brain-derived neurotrophic factor, glial-derived neurotrophic factor, cytokinelike peptides and chemokines)
1. Produced by neurons or target tissue
 2. Critical during development, growth, or repair
 3. Promote axon guidance, neuronal differentiation, survival and synapse formation
 4. Many neurotrophic factors engage tyrosine kinase receptors
 5. In the absence of appropriate neurotrophic signaling, neurons may undergo programmed cell death (apoptosis)
- J. Neurogenetics
1. Inheritance patterns
 2. Mitochondrial DNA
 3. DNA triplet repeat expansion
- K. Homeostasis in the CNS
1. CNS metabolism
 - a. Maintenance of ion gradients (e.g., ATP-requiring sodium pump [Na⁺-K⁺ ATPase])
 - b. Active transport of nutrients and amino acids
 - c. Extensive membranes and membrane proteins
 - d. Synthesis, transport, and release of synaptic transmitters
 - e. High metabolic rate (receives approximately 20% of cardiac output)
 - f. Autoregulation of cerebral blood flow
 2. Blood-brain barrier
 - a. Severely limits the passive movement of most solutes between blood and brain
 - b. Tight junctions found in CNS endothelial and ependymal cells
 - c. End-feet of astrocytes
 - d. Active transport required for exchange of most solutes between brain and blood
 3. Choroid plexus
 - a. Mesodermally derived tissue lying in ventricles
 - b. Composed of “conventional” (leaky) capillaries, connective tissue, and pia mater covered by ependyma
 - c. Ependymal cells secrete CSF
 4. CSF
 - a. Production
 - b. Composition
 - c. Circulation
 - d. Functions

II. Neural Development

- A. Induction
1. Ectoderm, mesoderm, Spemann organizer
 2. Molecular aspects
 3. Primary versus secondary
 4. Neural plate, neural groove, neural tube, neural crest
 5. Timing of anterior, posterior tube closure
- B. Patterning
1. Anterior/posterior, dorsal/ventral
 2. Hox genes
 3. Shh, patched, smoothed
- C. Neurogenesis

1. Ventricular zone
 2. Radial migration, reelin
 3. Progenitors, daughter cells, cleavage plane
 4. Neuronal birthdays
- D. Migration
1. Heterotopia
 2. Attraction/repulsion
 3. Long range/short range
- E. Differentiation
1. Cell fate
 2. Notch, neurogenin
- F. Synaptogenesis
1. Neuromuscular junction clustering and synthesis of nAChRs
- G. Cell survival
1. Neurotrophins (NGF, BDNF)
 2. Trk receptors
 3. Caspases, apoptosis
- H. CNS embryology
1. Neural tube (brain and spinal cord)
 2. Lamina terminalis
 3. Three-vesicle stage
 - a. Prosencephalon
 - b. Mesencephalon
 - c. Rhombencephalon
 - d. Cephalic and cervical flexures
 4. Five vesicle stage
 - a. Telencephalon (cerebral hemispheres, olfactory bulbs, lateral ventricles)
 - b. Diencephalon (thalamus, hypothalamus, infundibulum, third ventricle)
 - c. Mesencephalon (midbrain, cerebral aqueduct)
 - d. Metencephalon (pons, cerebellum, rostral fourth ventricle)
 - e. Myelencephalon (medulla, caudal fourth ventricle)
- I. PNS embryology
1. Neural crest (peripheral ganglia, Schwann cell, afferents)
 2. Neural tube (preganglionic autonomics, muscle efferents)
 3. Mesoderm (dura mater, connective tissue of peripheral nerve)
 4. Placodes (olfactory and otic apparatus, cranial nerve (CN) I and CN VIII)
- J. Histology
1. Layers of the neural tube wall
 - a. Ventricular (ependymal cells)
 - b. Mantle (neuroblasts, glioblasts, alar and basal plates)
 - c. Marginal (white matter of spinal cord)
- K. Cell types
1. Neuroblasts (all neurons)
 2. Glioblasts
 3. Macroglia (astrocytes, oligodendrocytes, radial glia)
 4. Ependymal cells (ependymocytes, choroid plexus)
 5. Microglia (derived from monocytes)
- L. Dorsal-ventral development
1. Alar plate (sensory)
 2. Sulcus limitans
 3. Basal plate (motor)

M. Myelination (from gestational age 4 months)

III. Functional Neuroanatomy

A. Basics

1. Anatomic terminology
 - a. Anatomic position
 - b. Anterior, posterior, dorsal, ventral, rostral, caudal, medial, lateral, superior, inferior
 - c. Proximal, distal, ipsilateral, contralateral
 - d. Anterior, posterior from developmental biology/embryology perspective
2. Section planes
 - a. Coronal, frontal, transverse, longitudinal horizontal, sagittal, parasagittal, midsagittal, oblique
3. Movements
 - a. Flexion, extension, hyperextension, dorsiflexion, plantar flexion, abduction, adduction, inversion, eversion, pronation, supination, circumduction, rotation
4. Anatomic terminology specific to the nervous system
 - a. Gray versus white matter
 - b. Neuron, axon, dendrite, synapse, neuromuscular junction
 - c. Glial cell, supporting cell
 - d. Dorsal root ganglion cell
 - e. Nerve fiber, nerve, tract
 - f. Afferent, efferent, interneuron
 - g. Effector
 - h. Somatic, autonomic
 - i. Dorsal root, ventral root, spinal nerve, ganglion
 - j. Nerve fiber types (Ia, Ib, II, A β , B, C, α , γ)
 - k. Reflex arc
 - l. Spinal segments
 - m. Preganglionic neuron, postganglionic neuron, paravertebral ganglion, prevertebral ganglion
 - n. Enteric nervous system (ENS)

B. Spinal cord

1. Regions (dorsal horn, ventral horn, intermediate zone, central canal, funiculi)
2. Structures (dorsal columns, Lissauer's tract, Clarke's column, substantia gelatinosa, nucleus proprius, intermediolateral cell column)
3. Vascular supply (anterior spinal artery, posterior spinal arteries, radicular arteries)

C. Brainstem

1. Cranial nerves
 - a. Sensory and motor roots, peripheral territory, nuclei, medial longitudinal fasciculus
2. Major Divisions
 - a. Tectum
 - b. Tegmentum
3. Reticular formation
 - a. Raphe
 - b. Locus ceruleus
 - c. Pedunculopontine nucleus
 - d. Horizontal and vertical gaze centers
4. Ventricular system (fourth ventricle, foramina of Luschka and Magendie, cerebral aqueduct)
5. Vascular supply (vertebral arteries, basilar artery, posterior inferior cerebellar artery, anterior internal cerebellar artery, superior cerebellar artery, posterior cerebral artery)
6. Medulla
 - a. Pyramids, olive, cuneate and gracile tubercles
 - b. Cranial nerves (glossopharyngeal, vagus, spinal accessory, and hypoglossal nerves)
7. Pons
 - a. Longitudinal fibers of the pons, transverse fibers of the pons, pontine nuclei, pontine protuberance (basilar or ventral pons), cerebellar peduncles
 - b. Cerebellum
 - i. Deep cerebellar nuclei (fastigial, globose, emboliform, dentate)
 - ii. Cerebellar cortex
 - iii. Medial to lateral organization, vermis, paravermis, hemispheres, tonsils

- iv. Basic circuit diagram
 - c. Cranial nerves (trigeminal, abducens, facial and vestibulocochlear nerves)
 - 8. Midbrain
 - a. Cerebral peduncles, interpeduncular fossa
 - b. Superior and inferior colliculi, posterior commissure
 - c. Cranial nerves (oculomotor and trochlear nerves)
 - d. Red nucleus, decussation of the superior cerebellar peduncle, substantia nigra, periaqueductal gray
- D. Diencephalon
- 1. Thalamus
 - a. Medial and lateral geniculates
 - b. Thalamic tubercle (anterior nucleus)
 - c. Pulvinar
 - d. Brachium of the inferior colliculus
 - e. Massa intermedia
 - f. Other nuclei
 - 2. Hypothalamus
 - a. Optic nerve, chiasm, and tract
 - b. Mammillary bodies, anterior commissure, lamina terminalis
 - c. Infundibulum, pituitary gland
 - d. Hypothalamic-pituitary-adrenal axis
 - e. Control of autonomic function
 - f. Homeostasis
 - g. Interface with the limbic system
 - 3. Subthalamic nucleus
 - 4. Pineal, habenula
 - 5. Circle of Willis
 - 6. Ventricular system: third ventricle, foramen of Monroe
- E. Cerebrum
- 1. Vascular supply
 - a. Anterior circulation (internal carotids, middle cerebral artery, lenticulostriate arteries, anterior choroidal artery, ophthalmic artery, anterior communicating artery (ACA), and posterior communicating artery (PCA))
 - b. Posterior circulation (posterior cerebral artery)
 - c. Watershed areas
 - 2. Lateral ventricles
 - a. Anterior, posterior, inferior horns, trigone, foramen of Monroe
 - 3. Cortex
 - a. Frontal, parietal, occipital, and temporal lobes, insula, paracentral lobule, orbitofrontal cortex
 - b. Major gyri (with functional correlates) and sulci
 - i. Central (rolandic) sulcus, lateral (sylvian) fissure, precentral and postcentral sulci, superior and middle temporal sulci, calcarine fissure
 - ii. Superior, middle, and inferior frontal gyri
 - iii. Precentral and postcentral gyri
 - iv. Superior, middle, and inferior temporal gyri
 - v. Cingulate gyrus
 - vi. Broca's and Wernicke's areas
 - vii. Supramarginal and angular gyri, parahippocampal gyrus
 - c. Primary and secondary cortical regions (motor and premotor, frontal eye fields, somatosensory, visual, auditory, olfactory)
 - d. Association cortex
 - 4. Hippocampus, amygdala, uncus, basal forebrain nuclei, nucleus accumbens, fornix, stria terminalis, stria medullares thalamicus, median forebrain bundle
 - 5. Internal capsule, corpus callosum, anterior commissure, thalamic radiations (especially optic), cingulum
 - 6. Papez circuit
 - 7. Basal ganglia
 - a. Caudate, putamen, globus pallidus
 - b. Substantia nigra, subthalamic nucleus

F. Sensory Systems

1. Receptor and circuit properties
 - a. Generator potential, adaptation, sensory transduction
 - b. Receptive field, lateral or surround inhibition
 - c. Convergence, divergence
2. Somatosensory
 - a. Proprioception
 - i. Muscle spindle, Golgi tendon organ, joint receptors
 - ii. Fiber types (Ia, Ib, II, A β , γ)
 - b. Fine touch, vibration sense
 - i. Merkel cell, Meissner's corpuscle, Pacinian corpuscle, hair follicle afferent
 - ii. Fiber types (A β)
 - c. Dorsal column—medial lemniscal pathway
 - i. Dorsal columns (gracile and cuneate fasciculi)
 - ii. Dorsal column nuclei
 - iii. Internal arcuate fibers cross to form medial lemniscus
 - iv. Ventral posterior lateral nucleus of the thalamus
 - v. Primary somatosensory cortex (postcentral gyrus, Brodmann 3, 1, 2)
 - vi. Descending modulation (corticospinal tract from postcentral gyrus and area 5, 7, dorsal column nuclei, dorsal horn)
 - d. Trigeminal system for fine touch, vibration sense, and proprioception from face and head
 - i. Trigeminal nerve and main sensory nucleus
 - ii. Cross to join ascending medial lemniscus
 - e. Pain and temperature
 - i. Nociceptors, free nerve endings, wide dynamic range neurons
 - ii. A β and C fibers
 - f. Trigeminal system for pain and temperature from face and head
 - i. Trigeminal nerve and spinal nucleus and tract
 - ii. Cross to join ascending anterolateral pathway
 - g. Anterolateral system
 - i. Marginal nucleus, substantia gelatinosa, lamina V cells
 - ii. Ventral white commissure crossing to contralateral anterolateral funiculus
 - iii. Spinothalamic and spinoreticular thalamic projections
 - iv. Ventral posterior lateral nucleus of the thalamus
 - v. Primary somatosensory cortex (postcentral gyrus, Brodmann 3, 1, 2)
 - vi. Descending modulation
 - a) Periaqueductal gray, raphe nuclei, substantia gelatinosa
 - b) Serotonin, enkephalin
3. Vision
 - a. Optics, properties of light
 - b. Eye anatomy, including extraocular muscles
 - c. Pupillary light reflex
 - d. Accommodation
 - e. Refraction (air/tear interface, cornea, lens)
 - f. Retinal anatomy and physiology
 - i. Rods, cones, retinal ganglion cells, pigmented epithelium
 - ii. Rhodopsin, retinal, opsin, transducin
 - iii. Sensory transduction
 - iv. Optic disc, macula, fovea
 - g. Visual pathway
 - i. Visual field map on retina
 - ii. Optic nerve, chiasm, tract
 - iii. Lateral geniculate nucleus of the thalamus
 - iv. Optic radiations
 - v. Primary visual (striate) cortex (area 17)
 - a) Ocular dominance columns
 - b) Stereopsis
 - c) Cortical receptive fields
 - d) Line orientation and movement detection
 - v. Secondary visual cortex (area 18, 19)
 - vi. Parvocellular (“what”) and magnocellular (“where”) visual processing pathways
4. Hearing

- a. Properties of sound
 - ii. Frequency
 - iii. Pitch
 - iv. Amplitude
 - v. Decibel scale
 - b. Ear anatomy
 - i. Pinna, external auditory meatus, tympanic membrane
 - ii. Middle ear malleus, incus, and stapes
 - iii. Inner ear, organ of Corti
 - iv. Cochlea, basilar membrane, scala tympani, vestibule, and media
 - c. Sensory transduction
 - i. Basilar membrane properties
 - ii. Hair cells, endolymph with high K⁺, stria vascularis
 - iii. Efferent control
 - iv. Tonotopy
 - d. Auditory pathways
 - i. Eighth nerve and ganglion to cochlear nuclei at pontomedullary junction
 - ii. Cochlear nuclei bilaterally to superior olive (sound localization)
 - iii. Superior olives to inferior colliculus via lateral lemnisci (visual/auditory map congruence)
 - iv. Inferior colliculus via brachium to medial geniculate nucleus of the thalamus
 - v. Medial geniculate to primary auditory cortex in superior temporal gyrus (Heschl's gyrus)
5. Balance
- a. Labyrinth within inner ear
 - i. Hair cells in semicircular canals sense angular acceleration
 - ii. Hair cells in otolith organs (utricle and saccule) monitor pull of gravity and linear acceleration
 - b. Vestibular pathways
 - i. Eighth nerve and ganglion to vestibular nuclei at pontomedullary junction
 - ii. Direct projections also to flocculonodular lobe of the cerebellum
 - iii. Vestibular nuclei contribute to several pathways
 - a) Ascending median longitudinal fasciculus for control of eye movements via nuclei of CN III, IV, and VI
 - b) Descending median longitudinal fasciculus for control of head and neck muscles
 - c) Lateral vestibulospinal tract for postural control
6. Taste
- a. Sensory transduction is direct or second messenger-mediated ion channel opening in taste buds
 - b. Taste buds innervated by CN VII, IX, and X
 - c. Projects to the nucleus tractus solitarius (NTS) in the medulla
 - i. Via the parabrachial nucleus of the pons to the amygdala and the hypothalamus
 - ii. To the ventral posteromedial nucleus of the thalamus, which then projects to parietal operculum of the postcentral gyrus
7. Olfaction
- a. Olfactory receptor neurons generated throughout life from basal cells in the olfactory epithelium
 - b. Odorants dissolve in mucus of nasal epithelium and stimulate olfactory receptors
 - c. Sensory transduction at olfactory neuron dendrites in olfactory epithelium
 - d. Olfactory nerve projects through cribriform plate to olfactory bulb
 - e. Mitral cells in bulb project via olfactory tract from bulb directly to primary olfactory cortex, entorhinal cortex, and amygdala
 - f. Mitral cell projections to dorsal medial nucleus of the thalamus and from there to frontal cortex for perception of smell

G. Motor systems

- 1. Peripheral receptors and nerves
 - a. Golgi tendon organ
 - b. Muscle spindle
 - c. Fibers
 - i. Ia, Ib, II sensory
 - ii. α and γ motor neurons
- 2. Muscle
 - a. Muscle fiber types

- b. Motor unit recruitment
 - c. Neuromuscular junction, cholinergic synaptic properties
3. Brain, brainstem, and spinal cord
- a. Anatomy
 - b. Decerebrate versus decorticate posture
 - c. Upper and lower motor neuron syndromes
 - d. Motor cortex
 - i. Primary
 - ii. Premotor
 - iii. Supplemental
 - e. Corticospinal tract (lateral [LCST] and anterior [ACST])
 - i. Internal capsule, cerebral peduncles, longitudinal fibers of the pons, pyramids, pyramidal decussation (LCST) in pyramid
 - f. Red nucleus, rubrospinal tract crossed in midbrain
 - g. Reticulospinal, tectospinal, and vestibulospinal tracts
 - h. Postural (medial) versus volitional (lateral) systems
 - i. Motor nucleus of the trigeminal and innervation of muscles of mastication
 - j. Facial nerve and nucleus and innervation of muscles of facial expression
 - k. Control of eye movements
 - i. Oculomotor, trochlear, and abducens nuclei innervating extraocular muscles
 - ii. Ascending median longitudinal fasciculus
 - iii. Vestibular function and nystagmus
 - iv. Vestibuloocular reflexes
 - v. Horizontal and vertical gaze centers
 - vi. Frontal and parietal eye fields
 - l. Spinal motor neurons to body
 - i. Medial to axial musculature
 - ii. Lateral to appendicular musculature
4. Basal ganglia
- a. Anatomy
 - b. Striatum (caudate and putamen)
 - c. Globus pallidus
 - d. Subthalamic nucleus and substantia nigra
 - e. Cortex-basal ganglia- thalamus-cortex loops
 - f. Direct and indirect pathways and dopamine
 - g. Control of selection of movement
 - h. Hyperkinesias, bradykinesias, hemiballism, chorea, tremor
5. Cerebellum
- a. Anatomy
 - b. Cortico-ponto-cerebellar-thalamo-cortical loop
 - c. Cortico-rubro-ponto-cerebellar-rubro-spinal pathway
 - d. Postural (vermal) versus appendicular (paravermal) versus planning (lateral) functions
 - e. Vermal, flocculonodular vestibular function
 - f. Deep cerebellar nuclei and vestibular nuclei
 - g. Superior, middle, and inferior cerebellar peduncles
 - h. Spinocerebellar pathways
 - i. Ataxia, intention tremor
- H. Autonomic nervous system (ANS)
- 1. Parasympathetic, craniosacral, end organ ganglia
 - a. Hypothalamo-brainstem control
 - b. Nucleus tractus solitarius and CN VII, IX, X
 - c. Nucleus ambiguus and dorsal motor nucleus of the vagus, CN IX, X, and XI
 - d. Edinger-Westphal nucleus and CN III
 - 2. Sympathetic, thoracolumbar, paravertebral, prevertebral ganglia, and adrenal
 - a. Hypothalamo-brainstem-spinal control
 - b. Rostral ventrolateral medulla

- I. Limbic system and emotional behavior
 - 1. Papez circuit
 - 2. Amygdala
 - 3. Prefrontal cortex
 - a. Orbitofrontal (emotional behavior)
 - b. Dorsolateral (executive decision making)
 - c. Anterior cingulate (attention)
 - d. Basal ganglia loops

- J. Cognition
 - 1. Hippocampus
 - 2. Neocortex
 - 3. Basal forebrain nuclei

- K. Language
 - 1. Broca's and Wernicke's areas and functions
 - 2. Grammar and syntax versus prosodic lateralization
 - 3. Dyslexia
 - 4. Sign language representation

- L. Memory
 - 1. Hippocampus, temporal lobes, prefrontal cortex
 - 2. Short-term, working, long-term
 - 3. Short-term and long-term potentiation

- M. Sleep
 - 1. Electroencephalography (EEG)
 - 2. Consciousness
 - 3. Circadian rhythms
 - 4. Rapid eye movement (REM) sleep
 - 5. Slow wave sleep

IV. Clinical assessment of neurologic system

- A. Neurologic examination
 - 1. Mental status
 - 2. Cranial nerves
 - 3. Motor function
 - 4. Reflexes
 - 5. Sensation
- B. Diagnostic tests
 - 1. Neuroimaging
 - 2. Lumbar puncture
 - 3. Serologic tests for diagnosis of infectious, autoimmune, and neoplastic conditions
 - 4. Electroencephalography
 - 5. Evoked potentials
 - 6. Nerve conduction studies/electromyography
 - 7. Brain/meningeal biopsy
 - 8. Peripheral nerve/muscle biopsy
 - 9. Genetic testing

V. Neuropharmacology and Other Therapeutic Modalities

Pharmacologic therapies to include mechanism of action, use and adverse effects, pharmacogenetics of drugs for treatment of disorders of the nervous system

- A. Peripheral nervous system (PNS)
 - 1. Autonomic drugs (adrenergic signaling)
 - a. Adrenergic agonists
 - i. Alpha (norepinephrine, epinephrine, phenylephrine, clonidine)
 - ii. Beta (norepinephrine, epinephrine, isoproterenol, dopamine, dobutamine, terbutaline)

- b. Adrenergic antagonists
 - i. Alpha (phenoxybenzamine, labetalol, prazosin)
 - ii. Beta (propranolol, timolol, labetalol, atenolol)
 - c. Indirect-acting adrenergic drugs
 - i. Synthesis (α -methyl dopa (+), α -methyl tyrosine (-))
 - ii. Storage (guanethidine (-), reserpine (-))
 - iii. Release (amphetamine (+), ephedrine (+), tyramine (+))
 - d. Reuptake (cocaine (-))
2. Autonomic and neuromuscular drugs (cholinergic signaling)
 - a. Cholinergic agonists
 - i. Nicotinic agonists (nicotine, carbachol)
 - ii. Muscarinic agonists (methacholine, bethanechol, muscarine, pilocarpine)
 - b. Cholinergic antagonists
 - i. Depolarizing nicotinic antagonists (nicotine, succinylcholine)
 - ii. Non-depolarizing nicotinic antagonists (trimethaphan, mecamlamine, d-tubocurarine, mivacurium, rocuronium)
 - iii. Muscarinic antagonists (atropine, scopolamine, ipratropium)
 - c. Acetylcholinesterase (AChE) inhibitors
 - i. Reversible (edrophonium, tacrine, carbamates—neostigmine, physostigmine)
 - ii. Irreversible (organophosphates—sarin, parathion, malathion, echothiophosphate)
 - iii. AChE reactivators (pralidoxime)
 - iv. Acetylcholine (ACh) release inhibitors (botulinum toxin)
 3. Autocoids and smooth muscle drugs
 - a. Phosphodiesterase inhibitors (sildenafil, vardenafil)
 - b. Histamine
 - i. H1 receptor antagonists (epinephrine, diphenhydramine, promethazine, loratadine, fexofenadine)
 - ii. H2 receptor antagonists (cimetidine, ranitidine)
 - iii. Release inhibitors (β -2 receptor agonists, cromolyn sodium, nedocromil)
 - c. Serotonin
 - i. Agonist (sumatriptan)
 - ii. Antagonist (ondansetron)
 - iii. Ergot alkaloid (ergotamine)
 4. Gastrointestinal drugs
 - a. Antiemetics (promethazine, metochlopramide, prochlorperazine, scopolamine, meclizine, odansetron)
 - b. Irritable bowel syndrome (tegaserod, alosetron)
 - c. Colonic pseudo-obstruction (neostigmine)
 - d. Antidiarrheal (diphenoxylate, loperamide)
 5. Nonsteroidal anti-inflammatory drugs (NSAIDs)
 - a. Salicylates (acetylsalicylic acid, salsalate)
 - b. COX II inhibitors (nabumetone, celecoxib, valdecoxib)
 - c. Propionic acids (ibuprofen, naproxen)
 - d. Indole derivatives (indomethacin)
 - e. Other NSAIDs (meclofenamate, piroxicam, acetaminophen)
 - f. Synthetic PGE1 (misoprostol)
 - g. Suppressive therapy of rheumatoid arthritis (autothioglucose, hydroxychloroquine, d-penicillamine, methotrexate)
 - h. Gout treatment (indomethacin [acute], colchicine, allopurinol)
 6. Local anesthetics (procaine, tetracaine, lidocaine, cocaine)

B. Central nervous system (CNS)

1. General anesthetics
 - a. Inhalation (nitrous oxide, halothane, isoflurane)
 - b. Intravenous (thiopental, propofol, midazolam, morphine, fentanyl, ketamine)

2. Sedatives/hypnotics/anxiolytics
 - a. Barbiturates (phenobarbital, pentobarbital)
 - b. Benzodiazepines (diazepam, triazolam, midazolam)
 - c. Benzodiazepine antidote (flumazenil)
 - d. Other (ethanol, buspirone, zolpidem, propranolol)
 3. Anticonvulsants (carbamazepine, phenobarbital, phenytoin, valproic acid, ethosuximide, gabapentin)
 4. Neuroleptics
 - a. Antipsychotics
 - i. Classic (haloperidol, chlorpromazine)
 - ii. Atypical (clozapine, risperidone, olanzapine, quetiapine, aripiprazole)
 - b. Antiemetics (promethazine, metoclopramide, prochlorperazine)
 5. Psychostimulants (methylphenidate, dextroamphetamine, modafinil)
 - a. Atomoxetine (nonstimulant attention deficit hyperactivity disorder treatment)
 6. Antidepressants
 - a. Tricyclics (imipramine, amitriptyline, nortriptyline, desipramine, doxepin)
 - b. Heterocyclic (bupropion)
 - c. Monoamine oxidase (MAO) inhibitor (phenelzine)
 - d. Selective serotonin reuptake inhibitors (fluoxetine, paroxetine)
 - e. Other (venlafaxine)
 7. Mood stabilizers (lithium, valproic acid, olanzapine)
 8. Opioid analgesics
 - a. Opioid agonists (morphine, meperidine, codeine, heroin, oxycodone)
 - b. Treatment for opioid addiction (methadone)
 - c. Central cough suppressant (dextromethorphan)
 - d. Opioid antagonist (naloxone)
 9. Drugs of abuse (heroin, oxycodone, ethanol, nicotine, caffeine, marijuana, cocaine, methamphetamine, methylenedioxymethamphetamine [MDMA; ecstasy], ephedra, lysergic acid diethylamide [LSD], phencyclidine [PCP], inhalants [nitrous oxide, chloroform, industrial solvents])
 10. Treatment of drug addiction (disulfiram, methadone, bupropion, naltrexone, buprenorphine)
 11. Spasmolytics (diazepam, baclofen, tizanidine, dantrolene, botulinum toxin, cyclobenzaprine)
 12. Drugs for the treatment of stroke (tissue plasminogen activator, clopidogrel, dipyridamole, aspirin)
 13. Antiparkinson's agents
 - a. Dopamine enhancers (levodopa, carbidopa, bromocriptine, pergolide, pramipexole, ropinirole, amantadine)
 - b. Anticholinergics (benztropine, trihexyphenidyl)
 - c. Catechol O-methyltransferase (COMT) inhibitor (entacapone)
 - d. MAO inhibitor (selegiline)
 14. Treatment of multiple sclerosis (interferon β , glatiramer acetate, methylprednisone, mitoxantrone, natalizumab)
 15. Treatment of Alzheimer's disease (donepezil, memantine, rivastigmine)
 16. Treatment of increased intracranial pressure (diuretics, mannitol, steroids, carbonic anhydrase inhibitors)
- C. Nonpharmacologic therapeutic modalities
1. Radiation
 2. Surgery
 - a. CSF shunting for hydrocephalus, increased intracranial pressure
 - b. Drainage of intracranial hemorrhages, abscesses
 - c. Clipping or insertion of intravascular coils for aneurysms
 - d. Resection/debulking for tumors
 - e. Resection of seizure focus for epilepsy
 - f. Thalamic stimulator implantation and ablation for Parkinson's disease, tremors
 - g. Spinal surgery (resection of herniated discs, decompression of spinal stenosis)
 - h. Vascular surgery for stenosis
 - i. Pain (nerve blocks, ablations)
 3. Behavioral therapies, hypnosis
 4. Respiratory

- a. Continuous positive airway pressure
- b. Hyperventilation
- c. Supplemental oxygen
- d. Respiratory therapy
- e. Decompression
- 5. Rehabilitation therapies
 - a. Physical
 - b. Occupational
 - c. Speech and language
- 6. Electrophysiologic techniques
 - a. Deep brain stimulation
 - b. Electroconvulsive therapy
 - c. Transcutaneous nerve stimulation
 - d. Vagal nerve stimulation
- 7. Emerging Therapeutics
 - a. Neuroprotectin
 - b. Neurotransplantation
 - c. Neuroregeneration

VI. Neuropathophysiology (Abnormal Processes)

- A. Congenital disorders (developmental, metabolic)
 - 1. Neural tube defects
 - a. Spina bifida (posterior neural tube closure defect)
 - b. Anencephaly (anterior neural tube closure defect)
 - 2. Arnold-Chiari malformation
 - 3. Dandy-Walker syndrome
 - 4. Fetal alcohol syndrome
 - 5. Hydrocephalus
 - 6. Holoprosencephaly
 - 7. Hydranencephaly
 - 8. Lissencephaly
 - 9. Cerebral palsy
 - 10. Mental retardation, Down syndrome
 - 11. Sphingolipidoses (Tay-Sachs disease, Gaucher disease, Niemann-Pick disease, metachromatic leukodystrophy)
 - 12. Phenylketonuria
 - 13. Lesch-Nyhan syndrome
 - 14. Adrenal leukodystrophy
- B. Infectious, inflammatory, and immunologic disorders
 - 1. Meningitis
 - a. Bacterial (meningococcal, prophylaxis of contacts), pathogens in different situations/ages
 - b. Fungal (cryptococcal)
 - c. Viral
 - d. Parasitic
 - 2. HIV infection, toxoplasmosis
 - 3. Prion diseases (Creutzfeldt-Jacob disease)
 - 4. Encephalitis (viral, herpes simplex encephalitis, arbovirus, West Nile virus)
 - 5. Brain abscess
 - 6. Rabies
 - 7. Poliomyelitis
 - 8. Progressive multifocal leukoencephalopathy
 - 9. Peripheral nerve infections
 - a. Herpes zoster (radicular vesicular eruption, ophthalmic, Ramsay-Hunt syndrome)
 - b. Facial palsy (Bell's palsy, Lyme disease, sarcoidosis)
 - c. Leprosy
 - 10. Biologic neurotoxins (botulism, tetanus)
 - 11. Spirochetal, Rickettsia, and parasitic CNS infections
 - a. Neurosyphilis (*Treponema pallidum*)
 - b. CNS Lyme disease (*Borrelia burgdorferi*)

- c. Rocky Mountain spotted fever (*Rickettsia rickettsii*)
 - d. Neurocysticercosis (*Taenia solium*)
 - 12. Multiple sclerosis (relapse, retrobulbar optic neuritis, Marcus Gunn pupil, internuclear ophthalmoplegia, other symptoms/signs, Lhermitte sign, demyelination, MRI/CSF abnormalities)
 - 13. Other demyelination syndromes (optic neuritis, acute disseminated encephalomyelitis [ADEM])
 - 14. Myasthenia gravis (clinical features, pathology, diagnostic tests, association with thymoma, differentiation from Lambert-Eaton syndrome)
 - 15. Guillain-Barré syndrome
 - 16. Transverse myelitis
 - 17. Vasculitic neuropathy
 - 18. Inflammatory myopathies (polymyositis, dermatomyositis)
 - 19. Congenital CNS infections (rubella, Cytomegalovirus, herpes simplex virus, neurosyphilis, toxoplasmosis, HIV)
- C. Traumatic and mechanical disorders
- 1. Concussion/cerebral contusion
 - 2. Subdural hematoma (bridging veins, slow bleed, MRI appearance)
 - 3. Epidural hematomas (middle meningeal artery, temporal/parietal fracture)
 - 4. Spine fractures (odontoid, hangman's)
 - 5. Cord compression (fracture, epidural abscess, hematoma, tumor)
 - 6. Brown-Séquard syndrome
 - 7. Syringomyelia
 - 8. Peripheral nerve injury (carpal tunnel syndrome, upper and lower brachial plexus injuries, ulnar neuropathy, radial, axial)
 - 9. Increased intracranial pressure due to mass effect
 - a. Herniation syndromes
 - b. Treatment measures
 - 10. CSF flow disorders:
 - a. Hydrocephalus, obstructive
 - b. Normal pressure hydrocephalus (clinical triad, causes)
 - c. Pseudotumor cerebri (symptoms, causes, treatment)
- D. Neoplastic disorders, including primary and metastatic
- 1. Adult (supratentorial location)
 - 2. Glioblastoma multiforme/astrocytoma
 - 3. Meningioma (psammoma bodies)
 - 4. Ependymoma
 - 5. Acoustic neuroma or vestibular schwannoma (neurofibromatosis type 2)
 - 6. Pediatric (infratentorial location)
 - 7. Medulloblastoma, ataxia
 - 8. Cerebellar hemangioblastoma (retinal angiomas)
 - 9. Metastatic (lung, breast, kidney, gastrointestinal)
 - a. Hemorrhagic tumors (breast, melanoma)
 - b. Dissemination (leptomeningeal metastasis)
- E. Acquired metabolic and regulatory disorders
- 1. Delirium (due to electrolyte/metabolic derangement, intoxications, infections, hepatic encephalopathy, renal, hypothyroidism)
 - 2. Vitamin B₁₂ deficiency (subacute combined degeneration, megaloblastic madness)
 - 3. Niacin deficiency—pellagra (skin, gastrointestinal, neuropathy/myelopathy/optic atrophy)
 - 4. Pyridoxine deficiency (precipitated by isoniazid [INH]): sensory neuropathy
 - 5. Reye's syndrome
 - 6. Central pontine myelinolysis
 - 7. Idiopathic orthostatic hypotension, Shy-Drager syndrome, multiple system atrophy
 - 8. Alcohol—neurologic complications
 - a. Intoxication
 - b. Hallucinoses
 - c. Delirium tremens
 - d. Wernicke's encephalopathy (thiamine deficiency)/Korsakoff's syndrome
 - e. Cerebellar degeneration
 - f. Peripheral neuropathy

F. Vascular disorders

1. Transient ischemic attacks
 - a. Risk factors
 - b. Differentiate anterior from posterior circulation
 - c. Carotid stenosis
2. Cerebrovascular occlusive disease
 - a. Specific vessel syndromes
 - b. Lacunar infarcts
3. Venous sinus thrombosis
4. Risk factors for embolic cerebrovascular accident
 - a. Atrial fibrillation
 - b. Cardiomyopathy
 - c. Anticoagulation
5. Subarachnoid hemorrhage/aneurysms
 - a. Presentations
 - b. Association with polycystic kidney disease, aortic coarctation
 - c. Location of berry aneurysms
 - d. Management
6. Intracerebral hemorrhage
7. Vascular dementia
8. Aphasia

G. Systemic disorders affecting the nervous system

1. Uremic neuropathy
2. Diabetic neuropathy
3. Systemic lupus erythematosus

H. Phakomatoses

1. Tuberous sclerosis
2. Neurofibromatosis (type 1 and 2)
3. Sturge-Weber syndrome

I. Degenerative disorders

1. Peripheral neuropathy
 - a. Charcot-Marie-Tooth (hereditary sensorimotor neuropathy)
2. Alzheimer's dementia
 - a. Clinical features
 - b. Plaques and tangles
 - c. Anticholinesterase treatment
3. Parkinson's disease
 - a. Symptoms
 - b. Dopamine
 - c. Substantia nigra
 - d. Lewy bodies
 - e. Levodopa and carbidopa treatment
4. Essential tremor
5. Huntington's disease
6. Motor neuron disease
 - a. Amyotrophic lateral sclerosis
 - b. Spinal muscular atrophy
7. Muscular dystrophy
 - a. Dystrophinopathies (Duchenne's, X-linked)
 - b. Myotonic dystrophy
 - c. Fascioscapulohumeral
8. Friedreich's ataxia
9. Wilson's disease

J. Paroxysmal disorders

1. Epilepsy
 - a. Focal vs. generalized (primary and secondary), simple vs. complex

- b. Types
 - ii. Absence
 - iii. Focal motor
 - iv. Complex partial—temporal lobe most common focus, path: mesial temporal sclerosis
 - v. Generalized, infantile spasms
 - vi. Febrile seizures
 - vii. Nonpileptogenic seizures
 - viii. Post-traumatic
 - ix. Status epilepticus
 - x. Nonconvulsive status epilepticus
 - 2. Headache
 - a. Migraine
 - b. Cluster
 - c. Tension
 - d. Rebound/analgesic headache
 - 3. Transient global amnesia
- K. Pain syndromes
 - 1. Trigeminal neuralgia
 - 2. Peripheral neuropathy—diabetic
 - 3. Sympathetically mediated pain syndromes
 - 4. Low back pain, neck pain
- L. Sleep disorders
 - 1. Narcolepsy
 - 2. Obstructive sleep apnea
 - 3. Parasomnias:
 - a. Sleep terrors
 - b. REM sleep behavior disorder
 - c. Sleepwalking
 - 4. Restless legs syndrome: iron deficiency anemia
- M. Abnormal movements
 - 1. Chorea
 - 2. Myoclonus
 - 3. Asterixis
 - 4. Acute dystonia
 - 5. Tics and Tourette's syndrome
 - 6. Neuroleptic malignant syndrome
 - 7. Tardive dyskinesia
- N. Dizziness and vertigo
 - 1. Ménière's syndrome
 - 2. Benign positional vertigo
 - 3. Vestibular neuronitis
 - 4. Cerebellopontine angle tumor (Schwannoma)
- O. Disorders of special senses
 - 1. Blindness and visual disorders
 - a. Amaurosis fugax
 - b. Anterior ischemic optic neuropathy
 - c. Temporal arteritis
 - d. Optic neuritis
 - e. Retinal artery occlusion
 - 2. Deafness
 - a. Congenital
 - b. Conductive
 - c. Sensorineural
 - d. Acoustic neuroma
 - e. Cortical

VII. Psychopathologic Disorders

- A. Early-onset disorders
 - 1. Mental retardation
 - 2. Learning disorders
 - 3. Attention deficit hyperactivity disorder (ADHD)
 - 4. Pervasive developmental disorders
 - 5. Tic disorders
 - 6. Elimination Disorders

- B. Substance-related Disorders
 - 1. Definitions
 - 2. Neurobiological mechanisms
 - 3. Specific substances

- C. Psychotic disorders
 - 1. Schizophrenia
 - 2. Other psychotic disorders

- D. Mood disorders
 - 1. Basic definitions
 - 2. Neurobiology of mood disorders
 - 3. Assessing suicide risk
 - 4. Major depressive disorder – *DSM-IV* criteria
 - 5. Bipolar I disorder
 - 6. Bipolar II disorder
 - 7. Substance induced mood disorders
 - 8. Mood disorders secondary to medical conditions

- E. Anxiety disorders
 - 1. Basic definitions
 - 2. Theories of pathology
 - 3. Diagnoses
 - a. Panic disorder with or without agoraphobia
 - b. Social phobia
 - c. Obsessive-compulsive disorder
 - d. Generalized anxiety disorder
 - e. Acute stress disorder
 - f. Posttraumatic stress disorder
 - g. Substance induced anxiety disorder
 - h. Anxiety disorder due to medical conditions

- F. Somatoform disorders
 - 1. Psychological mechanisms
 - a. Somatization
 - b. Conversion
 - 2. Types of somatoform disorders
 - a. Somatization disorder
 - b. Conversion disorder
 - c. Pseudoseizures
 - d. Hypochondriasis
 - e. Body dysmorphic disorder
 - f. Pain disorder

- G. Personality disorders
 - 1. Etiologic factors
 - 2. Types

- H. Abuse
 - 1. Epidemiology
 - 2. Identification and recognition of patterns of abuse
 - 3. Behavioral manifestations of victims

4. Reporting abuse

I. Other disorders

1. Dissociative disorders
2. Sexual disorders
3. Gender identity disorders
4. Eating disorders
5. Sleep disorders
6. Impulse control disorders
7. Adjustment disorders
8. Factitious disorders
9. Malingering

VIII. Interdisciplinary Areas/Psychosocial Issues

- A. Ethical issues
- B. Rehabilitation medicine
- C. Complementary medicine
 1. Stress reduction
 2. Acupuncture
 3. Chiropractics
 4. Natural supplements
- D. Coma and persistent vegetative state
- E. End-of-life care
- F. Brain death