NSC 4V90 Medical Neuropathology
Fall 2016 Syllabus

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Office Hours: **M, W 12-12:45 PM** and by arrangement

Graduate TAs: none

Textbook
Required: *None.* We will use this web site:
http://neuropathology-web.org/chapter1/chapter1aNeurons.html and perhaps a few others.

Recommended: *Clinical Neuropathology*, Catherine Hagerland. Ebook at the UTD library.

Course Content
Neuropathology is the study of disease of nervous system tissue, usually in the form of either small surgical biopsies or whole autopsy brains. Neuropathology is a subspecialty of anatomic pathology, neurology, and neurosurgery. This course will cover what goes wrong with the human brain, at all these levels. As you expect, our study will be of human clinical cases. You will have the chance to diagnose unknown neuropath cases, given the brain appearance and a brief clinical history. It should be fun.

Learning objectives
NEUROCYTOLOGY

Know all the types of glial cells, their normal functions, and their reactions to injury.

Understand the significance of the RER (Nissl substance) and how it reacts to axotomy.

Know the basic components of the neuronal cytoskeleton and how alterations of some of these components are associated with neurodegenerative diseases.

Understand the uses of silver stains in the histological study of the CNS.

Know that GFAP is a key protein of astrocytes.

Understand how myelin is formed and what cells make myelin in the CNS and PNS.

Understand the role of microglia in CNS inflammation and repair.

Locate the hippocampus in coronal brain sections and understand its significance in memory and learning.

CEREBRAL ISCHEMIA AND STROKE

Understand the role of energy deficiency, free radicals, and glutamate toxicity in the pathogenesis of hypoxic- ischemic encephalopathy.

Understand the clinical distinction and pathological substrate of brain death vs. the persistent vegetative state.

What is the significance of the hippocampus in the pathology and the clinical sequelae of HIE?

Distinguish ischemic stroke (cerebral infarct) from hemorrhagic stroke (intracerebral hemorrhage) in terms of etiology and pathology.

What is the difference between a bland and hemorrhagic infarct?

What is the difference between hemorrhagic infarct and a cerebral hemorrhage?

Should anyone with a stroke be treated with thrombolytic agents?
What is the difference between a hemispheric and a lacunar infarct, and implications for survival and neurological function?
What is "small vessel disease", name 2 conditions that cause it, and what are its effects in the brain?
When and why do patients with hemispheric infarcts die?
Name five causes of ischemic infarct besides atherosclerosis and embolism.
Name an angiopathy that can cause infarcts, white matter degeneration, and dementia.
Name four causes of intracerebral hemorrhage, and know which of the four is preventable.
Describe the pathology, clinical implications, and pathogenesis of hippocampal sclerosis.
Discuss the role of glutamate and other factors in the pathogenesis of brain damage associated with seizures.
Name 3 brain lesions that can cause focal seizures.

PERINATAL DISORDERS

What does the term "neonatal asphyxia" mean?
Name three situations that can cause perinatal asphyxia.
What does multicystic encephalopathy mean and what are its causes?
Name parts of the brain that are especially vulnerable in perinatal HIE.
Describe the pathology and pathogenesis of porencephaly, schizencephaly, and hydranencephaly.
Name an ischemic white matter lesion in premature babies and discuss its pathogenesis.
Know the frequency, clinical setting, and complications of germinal matrix hemorrhage.
Describe the clinical setting, pathology, and sequelae of bilirubin encephalopathy.

CRANIOCEREBRAL TRAUMA AND INCREASED INTRACRANIAL PRESSURE

Understand the difference in pathogenesis between epidural and subdural hematoma and clinical implications of it.
Name three types of traumatic hemorrhage that do not involve brain parenchyma and know which of the three is most common.
Understand the pathogenesis of diffuse axonal injury and the shaking baby syndrome.
Name five components of the shaking baby syndrome.
Understand the importance of fundoscopic examination in the shaking-impact syndrome.
Name three conditions besides traumatic brain injury in which increased intracranial pressure may cause death.
Understand what herniation means and name three types of herniation.
Understand the pathogenesis and significance of the fixed, dilated pupil.
Name vascular complications of temporal lobe (uncal) herniation.
Understand the importance of fundoscopic examination in detecting increased intracranial pressure.
Name six causes of increased intracranial pressure.
Understand the pathogenesis of complications from doing a lumbar puncture in a patient with increased intracranial pressure.

CNS INFECTIONS

Understand the difference in anatomical location between epidural abscess, subdural empyema, and bacterial meningitis.
Understand why epidural abscess, subdural empyema, and brain abscess are life-threatening processes.
Know the most common organisms that cause bacterial meningitis in newborn infants and in adults.
Know the CSF findings in meningitis.
Understand the pathogenesis of altered mental status and cerebral edema in acute meningitis.
Why patients develop cranial nerve deficits, ischemic infarction, and hydrocephalus following meningitis?
How does tuberculous meningitis differ histologically from meningococcus meningitis?

Know the CSF findings in tuberculous meningitis and the differential diagnosis of such findings.
Know the main fungi that affect the central nervous system and the clinical settings of such infections.
Name two angioinvasive fungi.
Recognize the gross findings of cryptococcus meningitis.
What are the CSF findings in viral diseases of the nervous system?
Name three key pathological changes in viral meningoencephalitis.
Name three viruses that cause intranuclear inclusions.
What parts of the brain are most severely affected in adult HSV encephalitis and what are the clinical sequelae of this localization?
How does adult HSV infection differs from neonatal HSV infection?
Distinguish HIV encephalitis from secondary (opportunistic) infections in AIDS.
Describe the key pathological feature of HIV encephalitis.
What does prion mean?
What are prions?
Name five human prion diseases.
Name four naturally occurring animal prion diseases.
Describe the key pathological finding in CJD.
Know that CJD can occur in sporadic and familial settings.
Understand the molecular basis of familial CJD.
Describe how CJD can be transmitted to humans.

DEMYELINATING DISEASES

Name the most common CNS and PNS demyelinative diseases.
Name two variants of MS.
Does MS cause axonal loss and what are the implications of this?
Name the two key pathological findings in MS.
Describe common anatomical locations of MS plaques, and parts of the CNS that are particularly prone to developing lesions.
Discuss the pathogenesis of MS.
Understand why MS patients have neurologic deficits and why sometimes they recover.
Name an experimental model of MS.
Name a demyelinating disease that occurs following infections and discuss its pathogenesis.
Know what CSF studies are ordered in a patient suspected of MS.
Name an infectious demyelinative disease that occurs in patients with immunodeficiency, and understand its pathogenesis.
Understand the clinical setting and pathogenesis of central pontine myelinolysis.

BRAIN TUMORS

Name three glial tumors and one embryonal tumor of the CNS.
Understand the difference between intra-axial and extra-axial tumors.
Name the two most common extra-axial CNS tumors.
Name the two most common brain tumors in adults and in children.
Name four genetic conditions associated with brain tumors, and know their inheritance pattern and the most common tumors associated with each.
Describe the key gross and microscopic differences between astrocytoma and glioblastoma.
Know the grading of astrocytoma.

Describe the pathological diagnostic criteria for glioblastoma.
What is the difference between pilocytic and other astrocytomas?
Name the two most common locations of pilocytic astrocytoma.
Name two key histological features of oligodendroglioma.
Name a key chromosomal abnormality of oligodendroglioma.
What is the most common location of the ependymoma?
Know the histological appearance of medulloblastoma.
Know about the propensity of medulloblastoma to seed the subarachnoid space, and CSF findings associated with such spread.
Describe the most common clinical presentation of posterior fossa tumors in children.
Know the overall prevalence, age, and sex distribution of meningiomas.
Understand why meningiomas are extra-axial, and the clinical implications of such localization.
Recognize classic meningioma histologically.
Describe the gross and microscopic findings of cerebral lymphoma.
Name three conditions that predispose patients to developing cerebral lymphoma.
Distinguish parenchymal from meningeal metastases, and describe the clinical presentation in CSF findings in the latter.

NUTRITIONAL DISORDERS

Name 3 conditions that can cause the Wernicke-Korsakoff syndrome (WKS).
Know the key clinical findings of the WKS and how they correlate with the topography of the lesions.
Know the hallmark lesion of the WKS.
Name two lesions that can cause Korsakoff amnesia.
Name clinical settings (other than alcoholism) in which the WKS occurs.
Recognize the pathology of midline cerebellar degeneration.
Name a spinal cord lesion caused by vitamin B12 deficiency and describe its pathology.

DEGENERATIVE DISEASES

Name six conditions (other than neurodegenerative diseases) that can cause dementia.
Recognize the two key histological lesions of Alzheimer's disease.
Understand the role of amyloid in Alzheimer's disease.
Know the chemical composition of paired helical filaments.
Name three mutations that can cause autosomal dominant Alzheimer's disease.
Understand the significance of Apolipoprotein E (ApoE) in Alzheimer's disease.
Discuss the role of environmental factors in the pathogenesis of Alzheimer's disease.
Name the best known frontotemporal dementia and how it differs grossly and microscopically from Alzheimer's disease.
Name three tauopathies.
Describe the genetics and pathology of Huntington's disease.
Recognize the key gross and microscopic pathology of Parkinson's disease.
Discuss how the pathology correlates with the neurotransmitter abnormality in Parkinson's disease.
Name a neurotoxin that causes Parkinson's disease and its mechanism of action.
Recognize the upper and lower motor neuron pathology in amyotrophic lateral sclerosis and the clinical manifestations that correspond to this pathology.
Name a motor neuron disease that affects infants and children, and describe its pathology and the gene mutation that is associated with it.

Understand the concept of spinal and cerebellar ataxia.

Is Friedreich's ataxia spinal or cerebellar?

Describe the key pathology of Friedreich's ataxia.

Describe two conditions that may occur together with olivopontocerebellar atrophy.

METABOLIC DISORDERS

Understand the basic biochemical principles and pathogenesis of lysosomal, peroxisomal, and mitochondrial disorders.

Know how the inheritance of mitochondrial disorders differs from that of lysosomal and peroxisomal disorders.

Recognize neuronal storage and leukodystrophy on a representative image.

Name 3 gangliosidoses causing neuronal storage.

Name one LSD and one peroxisomal disorder that cause leukodystrophy.

Recognize key skeletal and visceral changes in the mucopolysaccharidoses.

Name a common LSD that involves the bone marrow, spleen, and lymph nodes.

Have an approach for diagnosis of LSDs.

Name the 2 peroxisomal disorders.

Describe a key biochemical change in the peroxisomal disorders.

Know that peroxisomal disorders are associated with neuronal migration defects.

Name 2 mitochondrial disorders.

Recognize ragged red fibers on a light microscopic image and understand their significance.

Name 2 amino acid disorders that cause neonatal encephalopathy and one that causes vascular disease.

CONGENITAL MALFORMATIONS

Name 2 neural tube defects (NTDs) involving the cranial region and one involving the spinal cord.

Describe 3 grades of spina bifida.

Name a key micronutrient that is important in prevention of NTDs.

Describe the key pathology of holoprosencephaly (HPE).

What is the difference between alobar and lobar HPE?

Name one crucial gene and one chromosomal abnormality associated with HPE.

Name a brain malformation causing disconnection between the cerebral hamispheres.

When is neuronal migration to the cortex completed?

Name 3 neuronal migration defects (NTDs)

What does "lissencephaly" mean?

What are the clinical consequences of severe NMDs?

Describe polymicrogyria and name one condition in which it occurs.

Name three mechanisms by which hydrocephalus may occur.

Which of the three is most common?

Name five cause of obstructive hydrocephalus.

Distinguish obstructive hydrocephalus from hydrocephalus ex vacuo.

Describe the three components of the Chiari type II malformation.

What is the Chiari I malformation?

Describe disruptive and genetic lesions of the aqueduct that cause hydrocephalus.

What is the key cerebellar pathology of the Dandy-Walker syndrome?

What is the first pathological change that occurs in hydrocephalus?

Describe the white matter and cortical pathology in hydrocephalus.
Understand the pathology of syringomyelia and its clinical sequelae.

MYOPATHOLOGY

Describe the structure of the sarcolemma and key intracellular, transmembrane, and extracellular proteins associated with it, and how they are involved in the pathogenesis of muscular dystrophies.
Describe how type I and type II fibers are distributed in normal muscle and in the denervation atrophy.
Name two types of conditions that cause denervation atrophy.
Describe the microscopic and histochemical findings in denervation atrophy.
Describe the pathogenesis of Duchenne and Becker muscular dystrophies.
Discuss the pathogenesis of limb-girdle and other dystrophies.
What is the most useful laboratory study in distinguishing denervation atrophy from muscular dystrophy and inflammatory myopathy?
What are the key pathological findings in Duchenne muscular dystrophy?
Discuss the genetics and key pathological changes of myotonic dystrophy.
Name three congenital myopathies.
Discuss the differential diagnosis of neonatal hypotonia.
What are ragged red fibers and what is their significance?
Name the three most common types of inflammatory myopathy.
Discuss the differences in pathology and pathogenesis between polymyositis and dermatomyositis.
Discuss the pathology and chemistry of inclusion body myositis.

CEREBROSPINAL FLUID

Discuss normal cerebrospinal fluid in terms of its formation, circulation, and laboratory parameters (protein, glucose and cellular elements).
Describe CSF findings in: Subarachnoid hemorrhage, Viral meningitis, Guillain-Barré syndrome, Multiple sclerosis, Primary and metastatic malignant tumors

Elearning

Lecture slides are posted on elearning. Discussion boards and Chat are available for your use. I will not monitor them unless I receive complaints about inappropriate posting. Grades will be posted as soon as they are available. Announcements will be made from time to time.

Attendance

Your performance in this course will be greatly enhanced by your attendance. Duh. Recall the wisdom of Woody Allen: “Ninety percent of life is just showing up”. Your grade may be penalized for poor attendance.

Assessment

Exams (75%): There will be three exams during the course. Each exam will be worth 25% of your final grade and will cover the material from the third of the course preceding the exam. Material covered on the exams will be taken from the assigned readings and class lectures, as well as any additional material that I may provide. Exams will consist of multiple choice questions and short answers, and a slide identification part. Missed exams may be made up by taking a comprehensive final.

Biweekly unknowns: Biweekly case studies will be worth a total of 25%. These are done online at your convenience, but the deadline is absolute. I will include in this grade the best 5 of your efforts.

Clickers will be used; the points gained count as bonus. Clicker grading: You receive 2 points for every correct clicker question answer, and 1 point for every incorrect answer. For the final clicker grade computation, I will average the top three students' total clicker points and set that as 100%. So, if the top three students earned 130, 129 and 128 points, 100% is the average of these: 129. If you scored 112 total points, then your grade for the clickers is 112/129: 87%, and you receive 5 x .87 = 4.5 points added to your final course grade.

Grading scheme

Final Grades: A final grade will be submitted: A+: 97-100%, A: 93-96.9%, A-: 90-92.9%, B+:87-89.9%, B: 83-86.9%, B-: 80-82.9%, C+: 77-79.9%, C: 73-76%, C-: 70-72.9%, D: 50-69.9%, F < 50

Medical Neuropathology 2016 topics

Date	Lecture Topic	Lecture	Reading
Week 1 (8/23)	Introduction / Neuroimaging	1, 2	Basics of CT and MRI (in Useful Files and Links folder)
Week 2 (8/30)	Neurocytology / Hypoxia	3, 4	http://neuropathology-web.org/chapter1/chapter1aNeurons.html Neurons | Astrocytes | Oligodendroglia | Ependymal Cells | Microglia-Macrophages |Tissue Patterns
Week 3 (9/6)	Hypoxia / Stroke	5, 6	http://neuropathology-web.org/chapter2/chapter2aHIE.html HIE General Principles | HIE Pathology | HIE-Clinical Findings | The White Matter in HIE | Cerebral infarcts-Clinical Findings | Pathology | Hemorrhagic Infarct |Lacunar Infarct |Causes of Ischemic Infarction | Small Vessel Disease | Venous Infarct |Vascular Dementia | Cerebral Hemorrhage |Hypertensive Hemorrhage |Hypertensive Encephalopathy| Cerebral Amyloid Angiopathy |
Week 4 (9/13)	Trauma	7, 8	http://neuropathology-web.org/chapter4/chapter4aSubduralepidural.html General Principles | Skull Fractures | Epidural Hematoma | Subdural Hematoma | Subarachnoid Hemorrhage |Cerebral Contusion | Diffuse Axonal Injury | Chronic Traumatic Encephalopathy | Concussion | Shaken Baby Syndrome |Intracerebral Hematoma | Hypoxic-Ischemic Lesions | Increased Intracranial Pressure | Herniations |Cerebral Edema
Week 5 (9/20)	CNS Infections	9, 10	http://neuropathology-web.org/chapter5/chapter5aSuppurative.html Suppurative Infections | Subdural Empyema | Bacterial Meningitis | Brain Abscess | Mycobacterial Infections | Treponemal Infections | Fungal Infections | Cryptococcosis| Viral Diseases | Herpes Simplex Encephalitis | CMV Encephalitis | HIV infections | Prion Diseases | Pathogenesis of Prion diseases | Pathology of Prion Diseases | Creutzfeldt-Jakob Disease
Week 6	**Review; Catchup /**		

(9/27)	**Exam 1 (9/29)**		
Week 7 (10/4)	Demyelinating Diseases	11, 12	http://neuropathology-web.org/chapter6/chapter6aMs.html MS and its Variants |Neuromyelitis Optica | CSF Findings in MS | Pathogenesis of MS | Pathophysiology of MS| Acute Disseminated Encephalomyelitis | Progressive Multifocal Leukoencephalopathy | Central Pontine Myelinolysis
Week 8 (10/11)	Degenerative Diseases	13, 14	http://neuropathology-web.org/chapter9/chapter9aDementia.html Dementia |Alzheimer's Disease | AD Pathogenesis | AD Pathology | AD Genetics | AD Risk Factors |Old Age and AD |Vascular Disease in AD | AD Neurotransmitters | AD Diagnosis | FrontotemporalDementia|Tauopathies |Parkinson's Disease |Diffuse Lewy Body Disease |MPTP Parkinsonism |Huntington's Disease |Motor Neuron Diseases |Amyotrophic Lateral Sclerosis |
Week 9 (10/18)	Perinatal Disorders	15, 16	http://neuropathology-web.org/chapter3/chapter3bAsphyxia.html Periventricular Leukomalacia |Germinal Matrix Hemorrhage | Bilirubin Encephalopathy|Porencephaly | Schizencephaly | Hydranencephaly |
Week 10 (10/25)	Brain Tumors	17, 18	http://neuropathology-web.org/chapter7/chapter7aTumorsgeneral.html Histogenesis-Classification; Molecular-Genetic Aspects; Etiology-Pathogenesis; Genetic Tumor Syndromes; Diagnosis; Gliomas; Low-Grade Astrocytoma; Astrocytoma; Glioblastoma; Pilocytic Astrocytoma; Pleomorphic Xanthoastrocytoma; Oligodendroglioma; Ependymoma; Choroid Plexus Tumors; Medulloblastoma; Meningioma; Craniopharyngioma; Metastatic Tumors; The Effects of Brain Tumors
Week 11 (11/1)	**Review; Catchup / Exam 2 (11/3)**		
Week 12 (11/8)	CNS Malformations	19, 20	http://neuropathology-web.org/chapter11/chapter11aGeneral.html General Principles | Neural Tube Defects | Anencephaly |Spina Bifida |Encephalocele | Holoprosencephaly |Agenesis of the Corpus Callosum | Neuronal Migration Defects | Periventricular Heterotopia |Lissencephaly-Pachygyria |Polymicrogyria |Hydrocephalus |Pathogenesis of Brain Damage in Hydrocephalus | Chiari Malformations |Aqueductal Atresia and Stenosis |Dandy-Walker Malformation |Syringomyelia |
Week 13 (11/15)	Metabolic Disorders: Hereditary/Acquired	21, 22	http://neuropathology-web.org/chapter8/chapter8Nutritional.html The Wernicke-Korsakoff Syndrome | Midline Cerebellar Degeneration | Vitamin E Deficiency | Vitamin B12 Deficiency | Subacute Combined Degeneration
Week 14 (11/29)	Metabolic Disorders: Hereditary/Acquired	23, 24	http://neuropathology-web.org/chapter10/chapter10aLSDgeneral.html Lysosomal Disorders |LSD Phenotypes |Classification of LSDs |Diagnosis of LSDs |Metachromatic Leukodystrophy |Globoid Cell Leukodystrophy | Peroxisomal Disorders | Zellweger Syndrome |Neonatal Adrenoleukodystrophy |Mitochondrial Disorders |Genetics of Mitochondrial Disorders | Clinical Aspects | Pathology |Diagnosis | Most Common Mitochondrial Disorders | Disorders of Amino Acid Metabolism | Alexander Disease | Canavan Disease |
Week 15	**Exam 3 12/6 or TBA**		

(12/6)			
TBA	**Final Exam**		

Syllabus may be changed at any time during the course, as needed.

UT Dallas Syllabus Policies and Procedures

The information contained in the following link constitutes the University's policies and procedures segment of the course syllabus. Please go to http://go.utdallas.edu/syllabus-policies for these policies.