Year 2, CENTRAL NERVOUS SYSTEM BLOCK - PATHOLOGY

Pathology of brain tumors – Two lectures

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

Upon completion of this lecture, students should be able to:

- Appreciate how the anatomy of the skull and the spinal column influences the prognosis of both benign and malignant primary CNS tumors.

- List the principal clinicopathological features of some of the main types of tumors that can arise within the central and the peripheral nervous systems.

**Background:**

CNS tumors exhibit unique characteristics that make them different from tumors of the other body sites. Also childhood CNS tumors differ from those in adults, both in histologic subtypes and locations. Although histological classification and grading play a major rule in predicting the outcome a CNS tumor, the anatomic site of the neoplasm can have lethal consequences irrespective of histologic classification.

**Key principles to be discussed:**

- CNS tumors incidence and classification, with special consideration of the general differences between the pediatric and the adult population

- The unique characteristics that set CNS tumors apart from neoplastic processes elsewhere in the body

- The incidence, common clinical presentation, location, macroscopic appearances, microscopic features, pattern of spread and prognosis of the following neoplasms will be explained and discussed (within the context of the recommended textbook):

- Astrocytic neoplasms: Pilocytic astrocytoma, diffuse astrocytoma, anaplastic astrocytoma and gliobastoma

- Oligodendroglioma

- Ependymoma

- Medulloblastoma

- Meningioma

- Metastatic tumours

- Peripheral nerve sheath tumours: schwannoma and neurofibroma

**Key principles to be covered by self-directed learning:**

- The inheritance pattern and the main features of:

* + - Type 1 Neurofibromatosis
    - Type 2 Neurofibromatosis

**Take home messages:**

- Histologic distinction between benign and malignant lesions may be more subtle in comparison to other body systems.

- Even low-grade or benign tumors can have a poor clinical outcome depending on their location.

- The most aggressive and poorly differentiated glial tumor is glioblastoma; it contains anaplastic astrocytes and shows striking vascular abnormalities.

- Metastatic spread of brain tumors to other regions of the body is rare, but the brain is not comparably protected against spread of tumors from elsewhere.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell , Robbins Basic Pathology, 8th Edition

**Key words:**

CNS tumors, astrocytoma, glioblastoma, oligodendroglioma, ependymoma, medulloblastoma, meningioma, metastatic tumours, peripheral nerve sheath tumours, schwannoma, neurofibroma and neurofibromatosis.

Year 2, CENTRAL NERVOUS SYSTEM BLOCK - PATHOLOGY

Pathology and pathogenesis of multiple sclerosis

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

The student should:

- Appreciate the critical role of myelin in maintaining the integrity of the CNS system.

- Understand the pathogenesis and the clinic-pathological features of multiple sclerosis as the classical and the commonest example of CNS demyelinating diseases.

**Background**:

In general, diseases involving myelin are separated into two broad groups. Demyelinating diseases of the CNS are acquired conditions that are classically represented by multiple sclerosis. Other processes that can cause this type of disease include viral infection, drugs and other toxic agents.

When myelin is not formed properly or has abnormal turnover kinetics, the resulting diseases are referred to as”dysmyelinating”. These are associated with mutations affecting the proteins required for the formation of normal myelin or in mutations that affect the synthesis or degradation of myelin lipids.

**Key principles to be discussed:**

- Myelin function

- The differences between CNS and PNS Myelin

- Primary Demyelinating disease classification

- Multiple sclerosis: definition, epidemiology, pathogenesis and clinicopathological features; with special emphasis on CSF analysis findings, morphology and distribution of MS plaques.

**Take home messages:**

- In view of the critical role of myelin in nerve conduction; diseases of myelin can lead to widespread and severe neurologic deficits.

- Diseases of myelin can be grouped into demyelinating diseases (in which normal myelin is broken down for inappropriate reasons-often by inflammatory processes), and dysmyelinating diseases (which are metabolic disorders that include the leukodystrophies in which the underlying structure of the myelin is abnormal or its turnover is abnormal).

- Multiple sclerosis, an autoimmune demyelinating disease, is the most common disorder of myelin, affecting young adults often with a relapsing-remitting course and eventual progressive accumulation of neurologic deficits.

- Other less common forms of immune-mediated demyelination often follow infections and are more acute illnesses.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell , Robbins Basic Pathology, 8th Edition.

**Key words:**

Multipsle sclerosis, demyelination, dysmyelination, leukodystrophy, plaques, T cell-mediated delayed type hypersensitivity, oligoclonal bands and optic neuritis.

Year 2, CENTRAL NERVOUS SYSTEM BLOCK – PATHOLOGY

Pathogenesis and risk factors of cerebrovascular accidents - Two lectures

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

The student should:

- Explain the concepts of brain “Hypoxia”, “Ischemia” and “Infarction”.

- Understand the pathogenesis of thrombotic and embolic stroke and be able to identify clinical risk factors.

- Identify the causes and consequences of subarachnoid and intracerebral hemorrhage.

- Build a list of the different causes that can lead to cerebrovascular accident.

**Background:**

Cerebrovascular disease is one of the leading causes of death and morbidity in Saudi Arabia. It is the most prevalent neurologic disorder in terms of both morbidity and mortality. The term cerebrovascular disease denotes any abnormality of the brain caused by a pathologic process involving blood vessels. The three basic processes are (1) thrombotic occlusion of vessels, (2) embolic occlusion of vessels, and (3) vascular rupture.

**Key principles to be discussed:**

- The concept of “stroke”.

- Thrombotic and embolic stroke: incidence, significance of classification, causes and major clinicopathological features.

- Global Cerebral Ischemia, Border zone ("watershed") infarcts and focal Cerebral Ischemia: definition, causes and main gross and histopathological features.

- Intracerebral and subarachnoid hemorrhage: causes and major clinicopathological features.

- Vascular malformations: definition

- The main possible CNS cerebrovascular complications of hypertension including intracerebral hemorrhage, lacunar infarct, slit hemorrhages and hypertensive encephalopathy: definitions

- Vasculitis: possible causes.

**Key principles to be covered by self-directed learning:**

- Hypoxia, Ischemia, and Infarction: revision of definitions.

- Risk factors of cerebrovascular accidents.

- Transient ischemic attacks: definition.

**Take home messages:**

- Stroke is the clinical term for a disease with acute onset of a neurologic deficit as the result of vascular lesions, either hemorrhage or loss of blood supply.

- Cerebral infarction follows loss of blood supply and can be widespread, focal or affect regions with the least robust vascular supply ("watershed" infarcts).

- Focal cerebral infarcts are most commonly embolic; if there is subsequent fragmentation of an embolism, a non-hemorrhagic infarct can become hemorrhagic.

- Primary intraparenchymal hemorrhages are typically due to either hypertension (most commonly in white matter, deep gray matter, or posterior fossa contents) or cerebral amyloid angiopathy.

- Spontaneous subarachnoid hemorrhage is usually caused by a structural vascular abnormality, such as an aneurysm or arteriovenous malformation.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell , Robbins Basic Pathology, 8th Edition

**Key words:**

Stroke, infarction, watershed infarct, embolism, hemorrhage, hypertension, amyloid, aneurysm, arteriovenous malformation, vasculitis, lacunar infarct, slit hemorrhage, encephalopathy, hypoxia and ischemia.

Year 2, CENTRAL NERVOUS SYSTEM BLOCK – PATHOLOGY

Introduction to degenerative brain disease

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

The student should:

- Explain the basic pathological concepts of neurodegenerative disease, using Alzheimer’s and Parkinson disease as a classical example.

- Know the definition of “dementia” syndrome.

- List the possible causes of dementia.

- Explain the basic pathological concepts of a neurodegenerative disease, using Alzheimer’s disease as a classical example.

- Understand the major clinic-pathological features of Alzheimer’s disease.

- Hypothesize the possible etiologies of Alzheimer’s disease.

- List the causes of Parkinsonism.

- Understand the major clinical and pathological feature of Parkinson disease.

- Hypothesize the possible etiologies of Parkinson disease.

**Background:**

Degenerative brain disease is an umbrella term for the progressive loss of structure or function of neurons, including death of neurons. Classical examples on this group of diseases are Alzheimer’s disease and Parkinson’s disease.

Dementia is a serious loss of cognitive ability in a previously unimpaired person, beyond what might be expected from normal aging. It has many causes. Alzheimer’s disease is the most common cause of dementia in people at the age of 65 years and older.

Parkinsonism is a clinical syndrome characterized by diminished facial expression, stooped posture, slowness of voluntary movement, festinating gait, rigidity, and a "pill-rolling" tremor. This syndrome can be seen in a number of conditions that damage to dopaminergic neurons of the substantia nigra or to their projection to the striatum. Idiopathic Parkinson disease is the most common neurodegenerative disease associated with Parkinsonism; the diagnosis is made in patients with progressive Parkinsonism in the absence of a toxic or other known underlying etiology and if they show clinical response to L-DOPA.

**Key principles to be discussed:**

- Neurodegenerative diseases definition.

- The definition and etiology of dementia.

- Alzheimer disease:

- Definition.

- Clinical findings including age of onset and progression pattern.

- Morphologic abnormalities including the gross brain changes, neurofibrillary tangles, and neuritic plaques deposition.

- Parkinsonism: definition and etiology.

- Parkinson disease: definition, epidemiology, pathogenesis and clinicopathological features.

**Take home messages:**

- Neurodegenerative diseases cause symptoms that depend on the pattern of involvement of the brain.

- Diseases that affect cerebral cortex primarily (e.g., Alzheimer disease) are more likely to cause cognitive change, alterations in personality and memory disturbance.

- Accumulation of the Aβ peptide, derived from amyloid precursor protein, is central to the pathogenesis of Alzheimer disease.

- Dementia is a non-specific illness syndrome that has many causes.

- Diseases that affect basal ganglia (e.g. Parkinson disease) have motor symptoms as prominent clinical features.

- Parkinson disease is caused by loss of dopaminergic neurons.

- Parkinsonism is not Parkinson’s disease.

- Parkinson’s disease is associated with abnormal aggregation of proteins, which may lead to loss of function or may trigger apoptosis. Familial forms are associated with mutations in the genes encoding these proteins.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell , Robbins Basic Pathology, 8th edition

**Key words:**

Dementia, Alzheimer disease, neurofibrillary tangles, neuritic plaques, amyloid beta and phosphorylated tau. Lewy bodies, cholinergic cells, αlpha-synuclein, parkin, UCHL-1, Parkinson disease, Parkinsonism and substantia nigra.

Year 2, CENTRAL NERVOUS SYSTEM BLOCK - PATHOLOGY

Pathology of meningitis and its complication

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

The student should:

- Revise the spectrum of organisms that can cause meningitis.

- Explain the terms used in the description of CNS infections patterns.

- Understand the pathology of acute bacterial and tuberculous meningitis and the information that can be obtained from investigation of cerebrospinal fluid in suspected meningitis.

**Background:**

The brain and its coverings, as with all other parts of the body, can be affected by infections.

Damage to nervous tissue may be the consequence of direct injury of neurons or glia by the infectious agent or it may occur indirectly through the elaboration of microbial toxins, the destructive effects of the inflammatory response or the influence of immune-mediated mechanisms.

**Key principles to be discussed:**

- Meningitis and meningoencephalitis: definition and a list of the possible infectious etiologies.

- Ports of entry of infection into the CNS.

- Pyogenic meningitis: etiology, clinic-pathological features and CSF findings.

- Viral (aseptic) meningitis: clinic-pathological features and CSF findings.

- Tuberculous Meningitis: clinic-pathological features and CSF findings.

- The definition and pathogenesis of epidural abscess, subdural empyema and brain abscess.

**Take home messages:**

- Different pathogens may use distinct routes to reach the brain, and will cause different patterns of disease.

- Bacterial infections may cause meningitis, cerebral abscesses or a chronic meningoencephalitis. Viral infections can cause meningitis or meningoencephalitis.

- Lumbar puncture plays an important role in the diagnostic process of some CNS infections.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell , Robbins Basic Pathology, 8th Edition

**Key words:**

CNS infection, virus, bacteria, meningitis, cerebral abscesses, chronic meningoencephalitis, viral meningitis, epidural abscess, subdural empyema and tuberculosis.

Year 2, CENTRAL NERVOUS SYSTEM BLOCK – PATHOLOGY

Congenital malformations and hydrocephalus

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

The student should:

- Know the common types of congenital malformations of the CNS and have a basic knowledge of their pathological features.

- Correlate CNS normal development with the classification of congenital CNS malformations.

- Appreciate the role of folate deficiency as an etiological factor in neural tube defects and understand the role of Alpha feto-protein measurement and ultrasound in antenatal diagnosis of neural tube defects.

- Understand the various mechanisms that lead to the development of hydrocephalus.

- List and classify the main causes of hydrocephalus.

**Background:**

The incidence of CNS malformations, giving rise to mental retardation, cerebral palsy, or neural tube defects, is estimated at 1% to 2%. Malformations of the brain are more common in the setting of multiple birth defects. Prenatal or perinatal insults may either cause failure of normal CNS development or result in tissue destruction.

Hydrocephalus is abnormal buildup of cerebrospinal fluid (CSF) in the ventricles of the brain. It can result from congenital and acquired etiologies. The fluid is often under increased pressure (but not always) and can compress and damage the brain.

**Key principles to be discussed:**

1] CNS congenital malformation incidence and introduction to the basic concepts behind the pathogenesis. These include genetic and environmental factors and the role of the stage of gestation development.

- Definition and pathological changes in forebrain anomalies:

- Megalencephaly, microencephaly and lissencephaly.

- Microencphaly causes.

- Definition and pathological changes in neural tube defects:

- Meningomyelocele, spina bifida, anencephaly and encephalocele.

- Pathogenesis with special emphasis on the role of folate and alpha fetoproteins and their clinical significance.

- Definition and pathological changes in posterior fossa anomalies:

- Arnold Chiari malformation.

2] Hydrocephalus:

- Definitions of normal pressure hydrocephalus, noncommunicating hydrocephalus and communicating hydrocephalus - Pathophysiology and etiology.

**Key principles to be covered by self-directed learning:**

- Define: meningocele.

- Define: polymicrogyria.

- What is the difference between microcephaly and microencephaly?

- Define: hydrocephalus ex vacuo.

**Take home messages:**

- Malformations of the brain can occur because of genetic factors or external insults.

- The timing of the injury will determine the pattern of the injury, based on the type of developmental processes occurring at the point of injury.

- Patterns of malformation include alterations in the closure of the neural tube, proper formation of the separate portions of the neural tissue, and migration of neurons to the appropriate locations.

- Hydrocephalus is an increase in CSF volume within all or part of the ventricular system.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell , Robbins Basic Pathology, 8th edition

<http://www.medterms.com>, for additional explanation of terms definitions.

**Key words:**

CNS malformations, hydrocephalus, noncommunicating hydrocephalus, communicating hydrocephalus, hydrocephalus ex vacuo, Arnold Chiari malformation , folate, alpha fetoproteins, meningomyelocele, meningocele, spina bifida, anencephaly, encephalocele, megalencephaly, microencephaly, lissencephaly and polymicrogyria.

Year 2, CENTRAL NERVOUS SYSTEM BLOCK – PATHOLOGY

Cellular aspects of injury and pathological aspects of trauma

Dr Hisham Alkhalidi

Assistant professor of Pathology

Phone: 4670862

Email: [**halkhalidi@ksu.edu.sa**](mailto:halkhalidi@ksu.edu.sa)

**Objectives:**

The student should:

- Understand the role of the different constituents of CNS cells in the disease status.

- Compare the “trauma” and “injury” concepts.

- Explain the basic pathological descriptive terms used in CNS cellular injury and trauma.

- Correlate the different patterns of cellular injury with some important clinical examples.

-Analyze the clinical entities that result from CNS trauma.

**Background:**

The central nervous system cells are unique in many pathological aspects. A good example is the CNS cellular reaction to injury.

CNS trauma is very serious and crucial subject; considering the high rate of road traffic accidents in Saudi Arabia. Trauma to the brain and the spinal cord is a significant cause of death and disability (6000 deaths in 2009/ KSA traffic police statistics). Understanding classification of the CNS trauma patterns is of particular importance for any clinician regardless of his/ her specialty.

**Key principles to be discussed:**

Cellular aspects of injury:

-The definition of and an example for each of the following terms:

- Markers of Neuronal Injury: Acute neuronal injury, red neurons, spheroids, central chromatolysis, intracellular inclusions and dystrophic neuritis

- Marker of Astrocytes reaction to injury: gemistocytic astrocytes, fibrillary astrocytes and Rosenthal fibers

- Microglia (microglial nodules and neuronphagia)

CNS trauma:

- The rule of the severity and site of injury in deciding the outcome

- Traumatic parenchymal Injuries: The definition of and an example for each of the following terms:

- Contusion, laceration, diffuse axonal injury and concussion.

- The classification of traumatic Vascular Injury entities, including the mechanisms and the clinical presentation of epidural Hematoma (with special emphasis on the lucid interval) and subdural Hematoma (with special emphasis on the pathological features).

**Key principles to be covered by self-directed learning:**

- The definition of Corpora amylacea and its relation to CNS cellular injury.

- The definition and an example for: Coup injury, countercoup injury.

**Take home messages:**

- The cellular constituents of the nervous system respond in different ways to various forms of injury.

- Physical injury to the brain can occur when the inside of the skull comes into forceful contact with the brain. If the head is able to move there may be contact between the skull and brain, both at the original point of contact (coup injury) and the opposite side where the brain eventually hits the skull as it moves within it (countercoup injury).

- Rapid displacement of the head and brain can lead to tearing of axons (diffuse axonal injury), which often causes immediate onset of severe and minimally reversible neurologic deficits.

- Tearing of blood vessels associated with trauma can lead to accumulation of blood in any of three spaces: epidural hematoma, subdural hematoma, or subarachnoid hemorrhage.

**Further reading (Prescribed book):**

Vinay Kumar, Abul K. Abbas, Nelson Fausto, & Richard Mitchell, Robbins Basic Pathology, 8th Edition

**Key words:**

Cellular injury, neurons, glial cells, hemorrhage, epidural hematoma, subdural hematoma, subarachnoid hemorrhage, diffuse axonal injury, coup injury, countercoup injury, oligodendrocytes, ependymal cells, microglia, neuronophagia, acute neuronal injury, red neurons, spheroids, central chromatolysis, dystrophic neuritis, gemistocytic astrocyte, fibrillary astrocyte, Rosenthal fibers and Corpora amylacea.