7: Alterations of the Nervous System

Learning Objectives

- Describe the anatomy of the nervous system: Somatic and Autonomic divisions (review).
- Describe the sensory and motor functions of the peripheral nervous system (review).
- Explain the pathophysiology of traumatic brain injury
- Explain the pathophysiology of various spinal cord injuries and degenerative diseases of the spine (spinal shock, autonomic hyperreflexia, degenerative disk disease; spondylolysis, spondylolisthesis, and spinal stenosis)
- Explain the pathophysiology and types of CVA and aneurysms. Compare and contrast the types of CVA: *thrombotic stroke, transient ischemic attack (TIA), stroke-in-evolution, completed stroke, embolic stroke, and hemorrhagic stroke.*
- Explain the pathophysiology and types of headache
- Explain the pathophysiology of common CNS infections
- Explain the pathophysiology and clinical manifestations of multiple sclerosis
- Explain the pathophysiology and clinical manifestations Guillain-Barré Syndrome and Myasthenia gravis
- Explain the physiology of consciousness, arousal and pathophysiological impairment, describe the patterns of clinical manifestations (level of consciousness, pattern of breathing, vomiting, pupillary changes, oculomotor responses, and motor responses) that are used to evaluate the level of arousal and the differences between brain death and cerebral death
- Explain briefly the pathophysiology and types of data processing deficits, define and describe the following terms used to characterize specific data processing disorders: *agnosia*, *dysphasia*, aphasia, acute confusional states, and dementias.
- Explain pathophysiological basis and types of seizures, differentiate among the different types of seizures and seizure syndromes
- Explain the pathophysiology of Dementia and Alzheimer ‘s disease
- Characterize cerebral hemodynamics and stages of increased intracranial pressure and describe the four types of cerebral edema: vasogenic, cytotoxic, ischemic, and interstitial. Describe hydrocephalus
- Review nervous system infections and distinguish bacterial meningitis, viral meningitis, fungal meningitis and tubercular meningitis and central nervous system abscesses. Compare and contrast *meningitis* and *encephalitis*
- Describe extrapyramidal motor disorders: basal ganglia and cerebellar impairments.
- Explain the pathophysiology and clinical manifestations of Huntington's disease

- Explain the pathophysiology of Parkinson's disease and differentiate between the types of hypokinetic disorders: akinesia, bradykinesia, and loss of associated movement.
- Describe the alterations in movement & related terminology and compare upper and lower motor neuron lesions
- Explain briefly the pathophysiology of pain, temperature and sleep disorders
- Describe *nociception* (perception of pain), *nociceptors*, *pathways of nociception,* and *neuromodulation of pain, d*ifferentiate among *acute pain, chronic pain, somatic pain, visceral pain, referred pain, neuropathic pain, peripheral pain* and *central pain and* define *pain threshold* and *pain tolerance*
- Describe the process of normal thermoregulation and discuss briefly impairments of thermal regulation

Definitions: Alterations of the Nervous System

Term	Definition
Pain transmission via δ (delta) and C fibers	Pain transmitted along A-delta nerve fibres is sharp and well localized Pain transmitted along C nerve fibers is dull, aching, and poorly localized
ACUTE PAIN	
Acute somatic	Pain due to organic cause or pathology related to external structure
Acute visceral	Pain due to organic cause or pathology related to internal structure
DEGENERATIVE DISEASES OF THE SPINE	
Spondylolisthesis	Spinal vertebra slipping out of place
Spondylolysis	Structural defect in lamina or neural arch of vertebra (in pars interarticularis)
Herniated intervertebral disc	Displacement of nucleus pulposus or annulus fibrosus of vertebral disc
DISORDERS OF EXPRESSION	
Hypermimesis	Pathologic laughter or crying
Hypomimesis	Loss of emotion in language (arhapsody)
Dyspraxias/ Apraxias	Difficulty planning and executing coordinated motor movements
DISORDERS OF GAIT	

Basal ganglia/Senile gait	Stooped, hyperflexed posture with narrow base and short-stepped gait with decreased arm swing
Cerebellar gait	Wide base with feet often turned inward or outward for stability
Scissors gait	Legs adducted so they touch and then swing around each other
Spastic gait	Shuffling gait with one leg extended and the other held stiff, which can often lead to it being dragged
DISORDERS OF POSTURE/STANCE	
Dystonia	Maintenance of abnormal postures through muscular contractions
Decerebrate posturing	Extension outwards from body
Decorticate posturing	Flexion inwards towards ‘core’ of body
DYSSOMNIAS	
Insomnia	Poor or lack of ability to sleep
Obstructive sleep apnea (OSA)	Most common sleep disorder with complex pathology including hypoxia and oxidative stress
FRACTURES	
Simple	Single break in a vertebra that usually affects transverse or spinous process
Comminuted	Vertebral body shattered into several fragment
Compression	Vertebral body compressed anteriorly
Dislocation	Vertebral body slides on another
Nociception	Perception of pain
Nociceptors	Receptors for pain
PARASOMNIAS	
Somnambulism	Sleep walking
PROCESSES OF NOCICEPTION	
Transduction	Activation of nociceptors
Transmission	Conduction to dorsal horn and up via spinal cord

Perception	Awareness of pain
Modulation	Facilitation or inhibition of transmission before during, or after perception
Pain dominance	Pain at one location may cause an increase in the threshold in another location
Pain threshold	Point at which a stimulus is perceived as pain
Pain tolerance	The intensity or duration of pain that a person will endure before initiation of pain responses
Referred pain	Pain in an area distant from its point of origin

Review: Nervous System Anatomy and Physiology

Quick and critical facts:

- Sensation does NOT mean awareness
  - For a person to be aware of a sensation it must reach the cortex
- There is typically no awareness of visceral (those from organs) sensations
- There is awareness of somatic sensations
  - I.e. those coming from environment. General (pain, temp, touch). Special (vision, smell, sound, equilibrium)
- The somatic nervous system is voluntary and consists of nerves and skeletal muscles
- The *autonomic nervous system* (ANS) is involuntary and consists of autonomic nerves and:
  - Smooth muscle (walls of viscera and glands)
  - Cardiac muscle
- The ANS is further divided into sympathetic and parasympathetic branches
  - The sympathetic branch stimulates the body in preparation for action
    - Also known as the "*fight or flight*" response
  - The parasympathetic branch relaxes muscles to promote repair and restoration
    - Also known as "*rest and digest*"

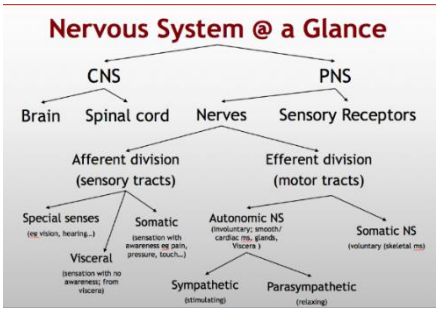

Figure 1: Divisions and structure of the nervous system

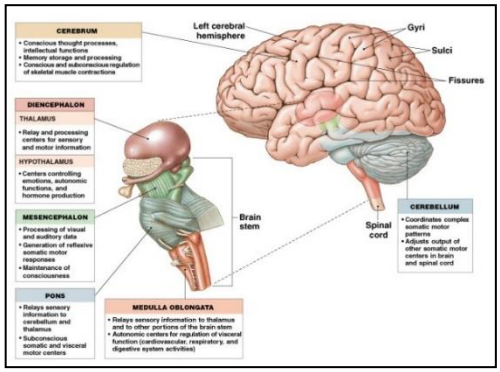

Figure 2: Anatomy of the brain and brainstem

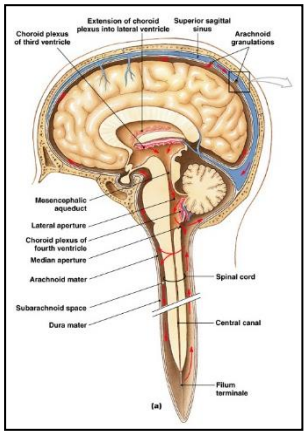

Figure 3: Anatomy of brain and brainstem

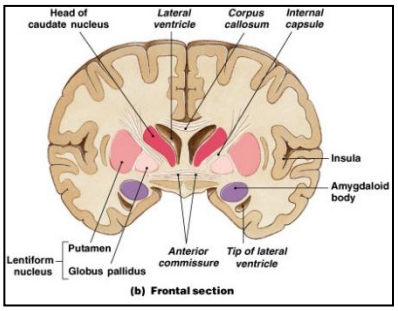

Figure 4: Frontal cross of brain

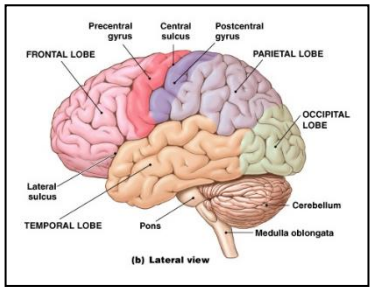

Figure 5: Surface anatomy of the brain

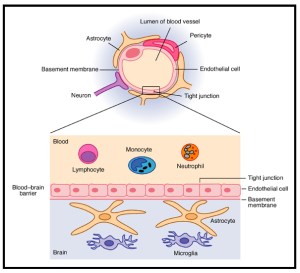

Figure 6: Cells of the nervous system and blood brain barrier

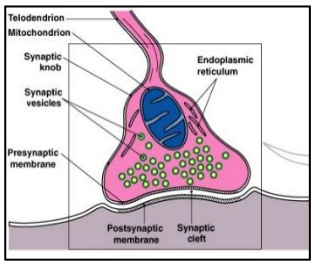

Figure 7: Neuronal synapse

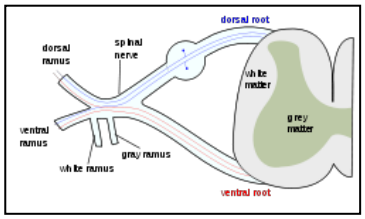

Figure 8: Peripheral nerves

- The nervous system is composed of gray and white matter in different configurations depending on the location within the nervous system
    - Within the brain, grey matter is on the outside and white matter on the inside, while in the spinal cord this is the reverse (see Figures 4, 11)

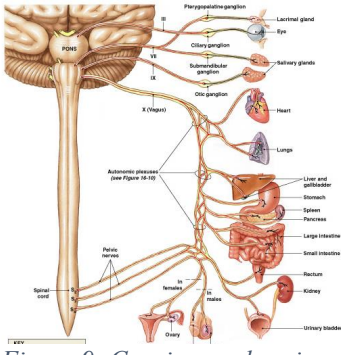

Figure 9: Craniosacral regions of the autonomic nervous system

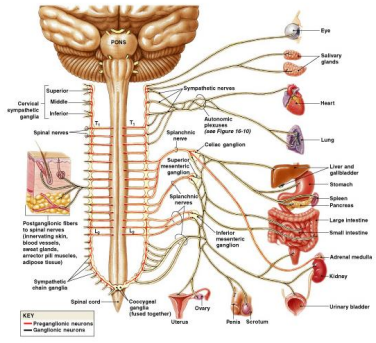

Figure 10: Thoracolumbar region of the autonomic nervous system

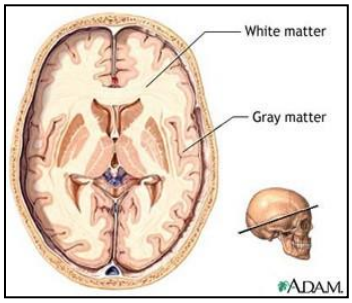

Figure 11: Brain cross section showing white and grey matter

Table: Configurations of Grey and White Matter of the Nervous System by Location		
Region of Nervous System	**White Matter (myelinated)**	**Grey Matter (unmyelinated)**
Brain	*Inside*	*Outside*
Spinal Cord	*Outside*	*Inside*

- SAME DAVE is the mneumonic that can be used for remembering the relationships and locations between nerves and the spinal cord
    - **SAME**: Sensory-Afferent; Motor-Efferent
    - **DAVE**: Dorsal-Afferent; Ventral-Efferent
- Ependymal cells line the ventricles and the choroid plexus
    - Responsible for cerebrospinal fluid (CSF), approximately 150mL, in circulation

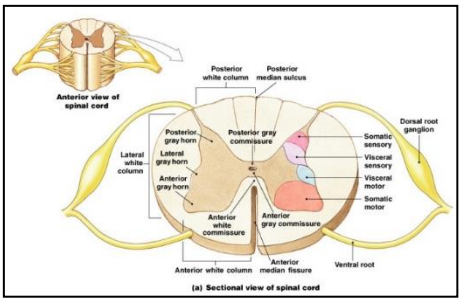

Figure 12: Relationship between central and peripheral nervous system in the spinal cord

Disorders of the Central and Peripheral Nervous Systems and the Neuromuscular Junction

Traumatic Brain Injury (TBI)

- Brain injury is **leading cause of death** and disability for Canadians under the age of 40
- ~1.5 M Canadians live with the effects of an acquired brain injury
- The annual incidence of ABI is > that od MS, SCI, HIV/AIDS and Breast Cancer combined!

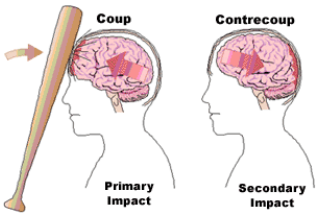

Figure 13: Coup versus contrecoup impact in TBI

Etiology

Caused by any accident in which head trauma occurs

- Damage can be at the site of impact (coup) or opposite (contrecoup) from recoil, and often both occur as the brain impacts the interior of the cranium
- Common examples include: Transportation (vehicle and pedestrian collisions), falls (particularly in older adults), sports-related, violence

Types of trauma:

- Closed (blunt, non-missile) trauma

- Open (penetrating, missile) trauma

Pathophysiology:

- Brain hematoma develops following trauma
- May be located in one of 3 spaces between meningeal layers
    - Epidural
    - Subdural
    - Intracerebral
- Focal or diffuse neuronal injury occurs
    - As blood accumulates, there is increased pressure within the cranium which damages neurons to produce clinical symptoms
    - Clinical symptoms are dependent on the location of injury
- *Focal injury* is localized to specific brain regions area
- *Diffuse neuronal (axonal) injury (DAI)* occurs when there is a twisting of the brain within the cranium producing shearing forces that effectively shred the axons themselves
    - DAI generally produces more severe symptoms and prognosis

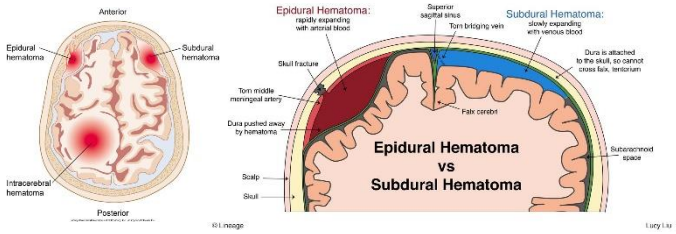

Figure 14: Types of hematoma by location (epidural, subdural, intracerebral)

Concussion

- Mild TBI causing alteration in brain functions +/- loss of consciousness
- Common causes include (blunt head trauma, car crash, physical assault, falls)

Clinical manifestations:

- **Mild concussion:**
    - Immediate but transient clinical manifestations; 1 to several minutes, possibly with amnesia
- **Classic cerebral concussion**
    - Loss of consciousness < 6 hours
    - Amnesia with confusional state lasting hours to days
- **General manifestations of concussion**
    - Headache
    - Sleep disturbance
    - Nausea and/or vomiting
    - Blurred vision
    - Attention impairment

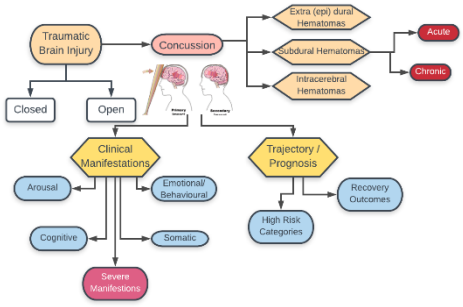

Figure 15: Classifying TBI and manifestations

- Reduced processing speed
- Drowsiness
- Emotion/behavior changes
- Posttraumatic seizure
    - If the patient is going to have a seizure it will usually occur within the first 24h following the traumatic event

Prognosis

- Symptoms are usually transient, with peak of symptoms occurring in the first 18-36 hours
- May experience full recovery or a range of residual impairments from mild (i.e. increased sensitivity to sound or light) to severe (i.e. permanent cognitive or physical impairment)

Fractures of the Spine

Types:

- *Simple fracture*
    - Single break usually affects transverse or spinous process
- *Compression fracture*
    - Vertebral body compressed anteriorly
- *Comminuted (burst) fracture*
    - Vertebral body shattered into several fragment
- *Dislocation*
    - Vertebral body slides on another

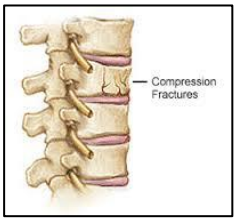

Figure 16: Compression fracture of the spine

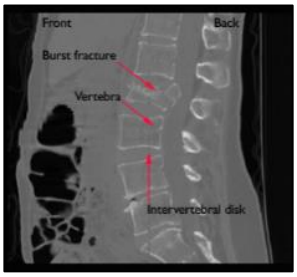

Figure 17: Comminuted (burst) fracture on x-ray

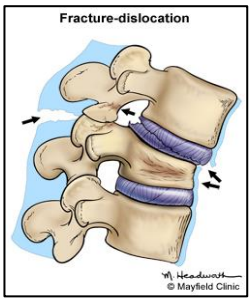

Figure 18: Dislocation fracture of the spine

Location:

- Most common fracture locations are:
    - Cervical (1, 2, 4-7)
    - T1-L2

Pathology and complications:

- Spinal cord injuries due to compression of spinal cord parenchyma, central canal and vascular structures

Spinal Cord Injuries (SCI)

Causes:

- Hyperextension injury
- Flexion injury
- Axial compression injury

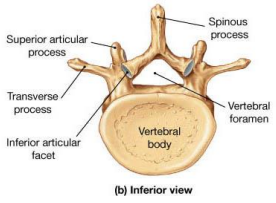

Figure 19: Anatomy of a vertebra

- Flexion-rotation injury

Pathophysiology:

- Hemorrhage in grey matter and pia-arachnoid region of the meninges
  - Increases in size until entire grey matter is hemorrhagic and necrotic
- Edema in white matter
  - Microcirculation block that reduces vascular perfusion to the region leading to ischemia and necrosis
  - Maximum pathology from hemorrhages and edema occur at the level of injury + 2 segments above and below
- It takes 24 h regain circulation in white matter and longer to gray matter
- Inflammation and healing start 36-48 h
- Collagen replacement/repair in 3-4 weeks

Spinal shock:

- Stopping of spinal cord activities at and below the level of injury
- Complete loss of reflex function (skeletal, bladder, bowel, thermal control, and autonomic control) below level of lesion
  - May last from a few days to 3 months with an average of 7-20 days
  - Ends with reappearance of reflex activity, hyperreflexia, spasticity, and reflex emptying of the bladder

Complications of spinal cord injuries

Paraplegia:

- Lesion in thoracic, lumbar, or sacral regions
- Impairment in motor, sensory functions of the lower limbs

Quadriplegia:

- Lesion at high level C1–C7
- Impairment in motor or sensory function of all limbs and torso

Degenerative Disorders of the Spine

Degenerative Disc Disease (DDD)

- Progressive disease common in individuals over the age of 30 related to structural defects from loss of cartilage in the spine leading to vertebral compression
- Both part of the normal aging process as well as having genetic component involving genes that code for cartilage in the spine
  - **Potential environmental causes include:**

- Decrease/ loss of blood supply
- Biochemical factors (e.g. inflammatory mediators)
- Biomechanical factors of the intervertebral disc tissue (e.g. mechanical loading and compression of vertebra)

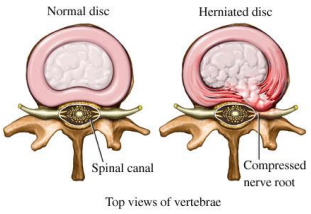

Figure 20: Comparison of normal and herniated intervertebral disc

- Pathological findings include spondylolysis, spondylolisthesis, disc protrusion (herniation), and spinal stenosis

Spondylolysis:

- Structural defect in lamina or neural arch
- Defect in pars interarticularis (small segment of bone connecting facet joints in the spine)
- Sports related, common in L5
- Cause pain, reduced mobility
- Can progress to *spondylolisthesis* **(**vertebra slipping out of place)

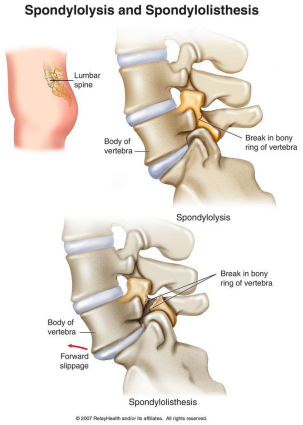

Figure 21: Spondylolysis and spondylolisthesis of the lower spine

Herniated intervertebral disc:

- Displacement of nucleus pulposus or annulus fibrosus
- **Clinical manifestations**:
  - Pain, paresthesia

Spinal stenosis:

- **Causes**:
  - Herniated disk, trauma, tumor
- **Pathophysiology**:
  - Abnormal narrowing of spinal canal
  - Mostly cervical and lumbar
- **Clinical manifestations:**
  - Could be asymptomatic
  - Symptoms are typically bilateral
  - Discomfort/pain of the neck/ lower back
  - Numbness, tingling
  - Weakness of (upper/ lower limb)

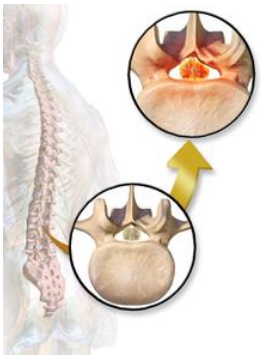

Figure 22: Spinal stenosis

Cerebrovascular Accident (CVA)

- Also known as stroke
- Leading cause of death and disability worldwide
- Loss of brain function due to impaired blood supply
- Brain vasculature = Circle of Willis (review)

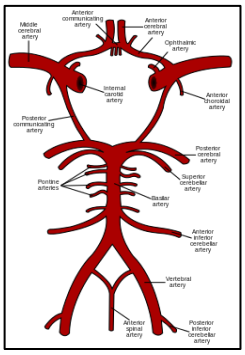

Figure 23: Cerebral vasculature

Causes

- Majority caused by cerebral ischemia
  - *Thrombotic stroke*
    - Block by *thrombus* in a cerebral vessel directly leading to the brain
    - *Middle cerebral artery* is a major site
  - *Embolic stroke*
    - Block by *embolus* (e.g. thrombus fragments, air, fat) from other locations in the body's vasculature that migrates to the brain and block a cerebral vessel
- Another, less common, cause is cerebral hemorrhage (*hemorrhagic stroke*):
  - Due to trauma or ruptured aneurysm
  - A medical emergency

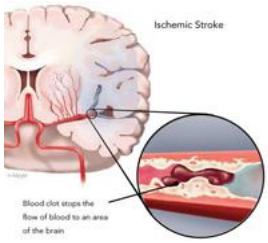

Figure 24: Ischemic stroke

Risk factors:

- Hypertension, DM, high cholesterol, smoking, atrial fibrillation, previous stroke (or transient ischemic attack)
- Consistent with risk factors for myocardial infarction

Pathophysiology:

- *Review Atherosclerosis - lecture 6*

Clinical manifestations:

- Depends on site and extent of occlusion. potential symptoms include:
- Transient ischemic attacks (TIAs)
- Altered level of consciousness, confusion
- Unilateral motor, sensory impairment
- Aphasia (failure to understand or formulate speech)
- Vision impairment of one side of the visual field
- Kernig sign
- Brudzinski sign

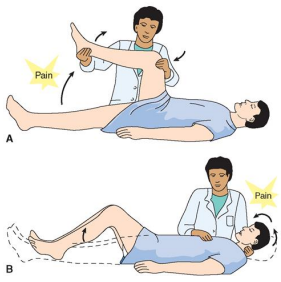

Figure 25: Kernig (A) and Brudinski (B) Signs

Intracranial Aneurysm

- Localized, blood-filled bulge in the blood vessel wall

Cause:

- Weakened vessel wall
  - May be congenital or acquired
  - Any blood vessel can be affected

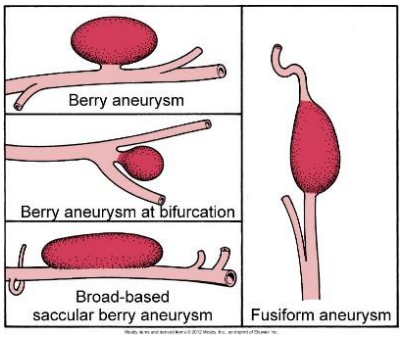

Figure 26: Types of aneurysms

Examples:

- Common sites for intracranial aneurysms within the Circle of Willis:
  - Anterior communicating artery (35%)
  - Internal carotid artery (30%-including the carotid artery itself, the posterior communicating artery, and the ophthalmic artery)
  - Middle cerebral artery (22%)
  - Posterior circulation sites, most commonly the basilar artery tip.

- Outside the brain, Aorta is a common site

Complications:

- Bulge may increase in size leading to rupture
  - Characterized by a "thunder clap" headache
- Continuous bleeding into subarachnoid space leading to hemorrhage
  - Person may get sentinel 'warning' headaches related to increase in the size of the bulge and/or leakage of blood into subarachnoid space
  - May experience subsequent hypovolemic shock, death

Headache

- Pain anywhere in the region of the head or neck
- Non-specific symptom with many causes (mild benign & serious)

Pathophysiology:

- Many theories! Traction/irritation of meninges and spasm/ dilation of blood vessels, stimulating nociceptors
- Brain tissue lacks pain receptors, is insensitive to pain

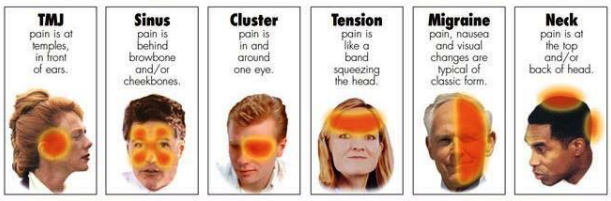

Figure 27: Types of Headache

- Pain originates from nearby pain-sensitive structures: periosteum, muscles, subcutaneous tissues, etc.

Headache - Migraine

- Familial, episodic disorder with headache as a marker
- **Characteristic features:**
  - Repeated, episodic headache lasting 4 to 72 hours
  - Usually women 25 - 55 y (More than men)
- **Causes**:
  - Genetic/environmental, neuronal dysfunction
- **Diagnosis**
  - Unilateral, throbbing pain, moderate or severe, worsened by movement
  - Associated with any one of the following:
  - Nausea, vomiting
  - Photophobia or phonophobia
- **Triggers**:
  - Altered sleep patterns
  - Overexertion
  - Weather change
  - Stress or relaxation from stress
  - Hormonal changes (menstrual periods)
  - Excess afferent stimulation (bright lights, strong smells)
  - Skipping meals
  - Chemicals (alcohol or nitrates)

Figure 28: Unilateral location of migraine headache

Headache - Cluster

- Chronic, in clusters (minutes to hours) for a period of days, followed by a long period of spontaneous remission
- Usually men 20 - 50 y
- **Cause**
  - Trigeminal activation and autonomic dysfunction
- **Associated clinical features**:
  - Tearing on affected side, ptosis of the ipsilateral eye, stuffy nose

Headache - Tension

- Most common
- **Cause**:

- Stress and fatigue (most common causes)
- Muscular tension

- **Features**:
  - Average onset 2nd decade
  - Mild to moderate bilateral headache with a sensation of a tight band or pressure around the head with gradual onset of pain
  - Occurs in episodes and may last for several hours or several days

*Infection/Inflammation of the CNS

Meningitis

- Inflammation of meninges
  - Bacterial meningitis
  - Non- bacterial, or aseptic (viral, non-purulent) meningitis

Encephalitis

- Inflammation of brain tissues
- Commonly caused by arthropod-borne viruses and herpes simplex virus

Meningo-encephalitis

- Inflammation of both the meninges and brain tissues

Infection/Inflammation of the CNS - *Abscess*

- Localized collection of pus within the parenchyma
  - Divided into three classifications:
    1. **Extradural**: Associated with osteomyelitis of the cranial bone
    2. **Intracerebral**: Arising from a vascular source
    3. **Spinal**: Located within the spinal cord
  - Pus may collect anywhere within the nervous system and lead to manifestations as it compresses nearby nerves
- **Causes**:
  - Open trauma
  - Post neurosurgery
  - Spread from nearby septic foci
    - Primarily the middle ear, mastoid air cells, nasal cavity, nasal sinuses
  - Hematogenous spread from distant foci

Clinical Manifestations – Brain abscess

- Early:
  - Low-grade fever

- Headache (most common symptom)
- Neck pain/ stiffness (more often in extradural abscesses)
- Confusion
- Drowsiness
- Sensory/communication deficits

- Late:
  - Distractibility
  - Memory deficits
  - Visual impairment
  - Ataxia
  - Dementia

Spinal cord abscess

- Severe pain, spasms of the back muscles and limited movement
- Progressive compression symptoms
- Paralysis

DEMYELINATING DEGENERATING DISORDERS

Multiple Sclerosis (MS)

- Demyelinating disorder of the **CNS**
- Acquired, progressive, autoimmune-inflammatory disorder
- Cause not totally understood, antibodies that destroy myelin sheath

Pathophysiology:

- Inflammation/autoimmune response targeting myelin sheaths of neurons
  - A previous viral illness in a susceptible individual, leads to inflammation
  - Early inflammation and demyelination lead to irreversible damage and scarring (sclerosis)
- *MS Lesions*: Scar-like plaques that develop throughout the CNS
  - They can appear in wherever there is localized demyelination (plaques)
  - Can be focal or diffuse
  - Can occur anywhere within in the brain, spinal cord, white, and/or grey matter
- There is thinning, then complete loss of myelin and breakdown of axons
  - Leads to impaired conduction of electrical signals
- Re-myelination takes place but becomes successively less effective with time, aggravating symptoms

Clinical Manifestations

- Onset usually between 20-40 years
- More common in women, however, males often have a more aggressive course
- Phenotypes (based on the clinical course):
  - Relapsing-remitting (90% initial representation)
    - Without treatment these persons will progress to the progressive types
  - Primary progressive (PPMS)
  - Secondary progressive (SPMS)
  - Progressive relapsing
- Symptoms include:
  - Paresthesia
  - Weakness
  - Impaired gait
  - Visual disturbances
  - Urinary incontinence

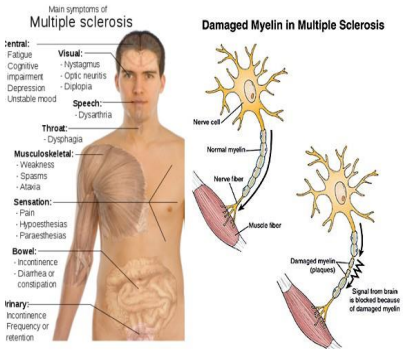

Figure 29: Pathophysiology and manifestations of multiple sclerosis

Guillain-Barré Syndrome

- Demyelinating disorder of the peripheral nervous system (LMN)

Pathophysiology:

- Days or weeks after flu-like illness
  - Most often respiratory or gastrointestinal viral illness
  - E.g. *Campylobacter jujini*
- Acute, autoimmune inflammatory polyneuropathy
  - Axonal demyelination as antibodies form to attack the myelin covering peripheral nerves
  - Acute onset of motor, sensory, or autonomic symptoms

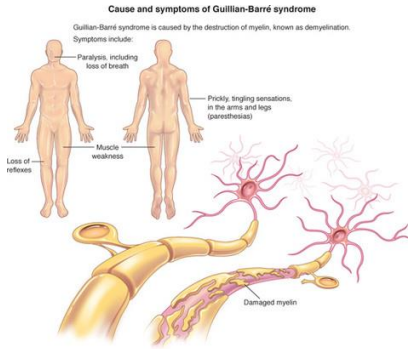

Figure 30: Causes, pathophysiology, and manifestations in Guillain-Barre syndrome

Clinical manifestations:

- Symptoms are related to antibody subtypes
- Most common form is ascending motor paralysis:
  - Rapid-onset of muscle weakness starts at lower limbs
  - Demyelination works upwards and can affect the lungs leading to cessation of breathing
  - It can affect respiratory muscles causing respiratory failure (~25% of cases)

- Loss of deep tendon reflex
- Blood pressure fluctuations and irregularities in the heartbeat

Myasthenia Gravis

- A disorder of the neuromuscular junction (NMJ) whereby autoantibodies damage/destroy acetylcholine (Ach) receptors affecting transmission of nerve impulses to the muscle
- Acquired chronic autoimmune disease

Pathophysiology:

- Circulating IgG against Ach receptors
    - Inhibit the excitatory effects of Ach on nicotinic receptors (post synaptic) at NMJ.
    - No nerve impulse transmission and subsequently excitation of the muscle
- Targets the head and neck
- Usually unilateral

Clinical Manifestations:

- Progressive weakness and fatigue
- Affects muscles of eyes & throat causing diplopia and difficulty chewing, talking, swallowing
- Manifestations of other associated autoimmune diseases