Chapter 15: Alterations of Neurologic Function – Part 2
Headache, Infections, Degenerative Diseases, and Tumors

I. Headache

A. Migraine

- Familial, episodic disorder whose marker is headache and is defined as repeated, episodic headache lasting 4 to 72 hours.
- Usually women 25 to 55 years old.
- Caused by combination of multiple genetic and environmental factors.
- Diagnosis:
  - Unilateral, throbbing, worsened by movement, moderate or severe; and any one of the following: nausea, vomiting, accompanied by photophobia or phonophobia.
- Phases:
  - Premonitory - tiredness, irritability or other symptoms that occurs hours to days before onset.
  - Aura - begins around time of onset, may involve visual, auditory, or olfactory perceptions.
  - Headache - usually 4 to 72 hours, including symptoms given above.
- Triggers:
  - Altered sleep patterns, skipping meals, overexertion, weather change, stress or relaxation from stress, hormonal changes (menstrual periods), excess afferent stimulation (bright lights, strong smells), chemicals (alcohol or nitrates).

B. Cluster

- Occur in clusters for a period of days followed by a long period of spontaneous remission.
- Usually men between 20 to 50 years old.
- Trigeminal activation and autonomic dysfunction.
- Unilateral trigeminal distribution of severe pain with ipsilateral autonomic manifestations (tearing on affected side, ptosis of the ipsilateral eye, and stuffy nose).
- Chronic cluster headaches - in 20% of cases headaches occur more frequently and without substantial periods of remission.

C. Tension-type

- Most common.
- Average onset during 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.
- Chronic tension-type headaches - occurs at least 15 days per month for at least 3 months.
II. Infection and Inflammation of the CNS

A. CNS Infection Terminology
- Meningitis – infection limited to the subarachnoid space.
- Meningoencephalitis – infection of the meninges and adjacent brain tissue.
- Encephalitis – infection focused in the brain tissue.
- Abscess – focal infection that may occur at any point in the CNS (or elsewhere in the body).

B. Meningitis
- Can be caused by bacteria, viruses, fungi, protozoa, and rickettsiae.

1. Bacterial meningitis
- Most serious form of meningitis.
- Caused most commonly by *Streptococcus pneumoniae*, but also by *Haemophilus influenza* and *Neisseria meningitides*.
- Bacteria often arise from otitis media, sinusitis, upper respiratory infection, pneumonia, or from a surgical procedure.
- Pathophysiology:
  - Infectious organisms enter CSF through the choroid plexus (specialized capillaries in the ventricles that make CSF) or by crossing the blood brain barrier.
  - Bacteria cause inflammation in the meninges (pia and arachnoid), the CSF, and the ventricles.
  - Meningeal vessels experience increased blood flow and permeability.
  - This allows neutrophils to migrate into the subarachnoid space.
  - Neutrophils produce a purulent exudate that thickens the CSF and interferes with normal flow.
  - Exudate can obstruct the arachnoid villi and produce hydrocephalus (accumulation of CSF).
  - Inflammation causes edema of the meninges and brain, which increases intracranial pressure and decreases cerebral blood flow.
  - Microthrombi may form in subarachnoid vessels, further decreasing blood flow.
  - Infection may spread to brain tissue.
  - Death can result without prompt treatment.
- Symptoms:
  - Nearly always – severe headache, fever, stiff neck (nuchal rigidity).
  - Often – photophobia (sensitivity to light), rash (may be petechial), vomiting, cranial nerve palsies, papilledema (optic disc swelling caused by elevated intracranial pressure), focal neurologic deficits, irritability, and decreased consciousness.
- Diagnosis is confirmed through examination of the CSF obtained from a lumbar puncture.
  - The CSF in bacterial meningitis characteristically reveals increased protein and lactate, normal or decreased glucose, and significant numbers of neutrophils.
2. **Aseptic meningitis** (viral, nonpurulent, lymphocytic meningitis)
   - Usually caused by viruses, but other infectious agents can also be involved.
   - Infection is generally limited to the meninges.
   - Symptoms are less severe than for bacterial meningitis, and include:
     - Mild, generalized throbbing headache, mild photophobia, mild neck pain, stiffness, fever, and malaise.

C. **Encephalitis**
   - Acute febrile illness, usually of viral origin with nervous system involvement
   - Most often caused by a viral infection with West Nile or Eastern equine virus that is carried by mosquitoes; it also can be caused by herpes simplex.
   - Many other viral diseases have been associated with encephalitis, as well as vaccines with live attenuated viruses such as measles, mumps, and rubella.
   - Clinical Manifestations:
     - Symptoms range from mild to life-threatening.
     - They include fever, delirium, or confusion that progresses to unconsciousness, seizure activity, cranial nerve palsies, paresis and paralysis, involuntary movement, and abnormal reflexes.
   - Pathophysiology:
     - Meningeal involvement is present in all types of encephalitis.
     - Various types may cause widespread nerve cell degeneration.
     - Edema, necrosis with or without hemorrhage, and increased intracranial pressure develop.
     - Infectious encephalitis may result from a postinfectious autoimmune response to the virus or from direct invasion of the CNS.

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<tr>
<th>ACTIVITY 1: Match the disorders with their characteristics.</th>
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<tr>
<td>a. Bacterial meningitis  b. Aseptic meningitis  c. Encephalitis</td>
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<tr>
<td>1. Usually caused by a virus.</td>
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<td>2. Purulent exudate enters CSF.</td>
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<td>3. Usually has the least severe symptoms or outcome.</td>
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<td>4. Most likely to be life-threatening if not treated.</td>
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<td>5. Often spread by insect vectors.</td>
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D. Neurologic Complications of AIDS

- 40% to 60% of all persons with AIDS have neurologic complications.
- Result from (1) direct infection by HIV; (2) opportunistic infections, neoplasms, and systemic illness; and (3) complications of therapy.
- The most common neurologic disorder is HIV-associated cognitive dysfunction (*HIV encephalopathy*).
- Others are peripheral neuropathies, vacuolar (spongy softening) myelopathy, opportunistic infections of the CNS, and neoplasms.

III. Degenerative Diseases

A. Multiple sclerosis (MS)

- An inflammatory disease in which the myelin sheaths of axons in the CNS are damaged, leading to demyelination and scarring.
- Pathophysiology:
  - MS involves an autoimmune process that develops when a previous viral insult to the nervous system has occurred in a genetically susceptible individual.
  - T-cells mount an autoimmune attack on CNS myelin.
  - This causes inflammation, and the formation of demyelinated plaques and axonal degeneration.
- Clinical Manifestations:
  - Early stage MS usually begins with a remitting-relapsing pattern, with attacks occurring during increases in body temperature and serum calcium levels.
  - The specific neurologic deficits depend on the parts of the CNS that are most affected.
  - Chronic disease with gliosis (scarring) results in gradual neurologic deterioration.
- MS occurs in 1 of 3 types:
  - Mixed or General MS—Complications are usually visual, but can include brain stem and cognitive dysfunction.
  - Spinal MS—Causes weakness and/or numbness, and bladder and bowel problems.
  - Cerebellar MS—Causes disorders in gait and motor movements.

B. Amyotrophic lateral sclerosis (ALS)

- Classic ALS is also known as “Lou Gehrig disease”
- ALS is a degenerative disorder diffusely involving lower and upper motor neurons of the cerebral cortex, brain stem, and spinal cord (corticospinal tracts and anterior roots).
- Disease leads to progressive weakness leading to respiratory failure and death.
- Patient has normal intellectual and sensory function until death.
• Pathophysiology:
  o Cause of motor neuron death in ALS is unknown, although there may be a genetic factor.
  o Some people with ALS have a genetic mutation in an enzyme that helps destroy free radicals (copper-zinc superoxidase dismutase (SODI)).
  o ALS is also associated with a defect in a gene on chromosome 21, which leads to defective glutamate metabolism. Glutamate is an excitotoxin that causes degeneration of both upper and lower motor neurons without inflammation.
  o Axonal degeneration is followed by gliosis (scarring) and denervation of motor units.

• Clinical Manifestations of ALS:
  o Individuals with ALS experience progressive muscle weakness and atrophy with both flaccid and spastic paralysis.
  o Weakness progresses to involve the muscles of respiration, eventually causing respiratory failure, which requires mechanical ventilation.
  o No associated mental, sensory, or autonomic symptoms are present.
  o On average an individual with ALS lives 2 to 3 years after development of symptoms.

IV. **Neuromuscular Junction Disorders**

A. **Myasthenia gravis**

• A chronic autoimmune disease that affects the neuromuscular junction and is characterized by muscle weakness and fatigability.

• Frequently associated with tumors or pathologic changes in the thymus.

• Associated with an increased incidence of other autoimmune diseases like lupus (SLE).

• Pathophysiology:
  o Due to an autoimmune production of IgG against the postsynaptic acetylcholine receptors on the muscle cell's plasma membrane.
  o IgG attaches to the receptor sites, blocking the binding of acetylcholine, and eventually destroying the receptor sites.
  o This causes diminished transmission of the nerve impulse across the neuromuscular junction and lack of muscle depolarization.

• Clinical Manifestations:
  o Fatigue after exercise.
  o Weakness of muscles, especially those of the eyes, facial expression, neck and limb girdles.
  o Weakness increases with use and improves with rest.

• Myasthenic crisis – occurs when severe muscle weakness causes extreme quadriparesis or quadriplegia, respiratory insufficiency with shortness of breath, and extreme difficulty in swallowing, with danger of respiratory arrest.
ACTIVITY 2: Match the disorders with their characteristics.

a. Multiple sclerosis  
   b. Amyotrophic lateral sclerosis  
   c. Myasthenia gravis

_____ 1. Affects neurons in the peripheral nervous system (not the CNS).
_____ 2. Is NOT caused by an autoimmune response.
_____ 3. May be triggered by a viral infection.
_____ 4. Results in death of motor neurons.
_____ 5. Involves damage to myelin sheath of neurons.
_____ 6. Often associated with problems of the thymus.

V. Central Nervous System Tumors

A. Cranial tumors

1. Primary intracerebral tumors (gliomas)
   - Arise from the supporting cells (neuroglia or glial cells) of the central nervous system.
   - Brain tumors cause symptoms by invading or compressing surrounding tissues and by increasing intracranial pressure.
   - Effects include seizures, visual disturbances, unstable gait, and cranial nerve dysfunction.
   a. Astrocytoma
      - Most common primary brain tumor
      - Develop from astrocytes and expand into and infiltrate normal brain tissue
      - Slow-growing
      - Most commonly located in cerebrum, hypothalamus, or pons
      - Common manifestations: headache, seizure, and neurologic changes that worsen with tumor growth
   b. Oligodendroglioma
      - Develop from oligodendrocytes
      - Slow-growing
      - Usually contain cysts and calcifications
      - Most commonly located in the frontal and temporal lobes
   c. Ependymoma
      - Arise from ependymal cells of ventricular walls
      - Most commonly located in the fourth ventricle
      - Common manifestations: difficulty in motor systems, seizure, visual changes, and contralateral weakness
2. **Primary extracerebral tumors**
   a. **Meningioma**
      - Encapsulated tumors that originate from the dura mater or arachnoid membranes
      - Slow-growing
      - Clinical manifestations: occur after tumor becomes large and usually include seizures, visual disturbances, loss of smell
   b. **Neurilemmoma**
      - Nerve sheath tumor from Schwann cells or due to the inherited disorder neurofibromatosis
      - Benign (nonmetastatic)
      - Tumor causes brain stem displacement that obstructs CSF
      - Common manifestations: headache, hearing and motor disturbances, and facial pain and sensations

3. **Metastatic carcinoma**
   - The majority of tumors in the brain are not primary tumors, but instead are due to metastasis from another site.
   - 50% of metastatic brain tumors arise from the lung, 13% from melanomas, 6% from the breast, and 4% from the kidneys, but tumors from other sites also metastasize to the brain.
   - Carcinomas are disseminated to the brain through the circulation.
   - Usually multiple metastases are found scattered throughout the cerebrum and cerebellum.

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<td>a. Astrocytoma</td>
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<td>b. Oligodendroglioma</td>
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<tr>
<td>____ 1. A tumor that arises in the wall of the ventricles.</td>
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<tr>
<td>____ 2. A tumor that arises from the dura mater or arachnoid.</td>
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<td>____ 3. Most common type of glioma (tumor arising from a neuroglia cell).</td>
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<td>____ 4. A brain tumor due to cells from another site in the body.</td>
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<tr>
<td>____ 5. Type of tumor that often contains cysts and calcifications.</td>
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<td>____ 6. Benign tumor of the cells that form the nerve sheath.</td>
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<td>____ 7. Most tumors that occur in the brain are this type.</td>
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