MODULE 3

CNS DISORDERS

DISEASE OF THE NERVOUS SYSTEM

- **Learning objectives:** at the end of this lesson the student will be able to:
- *1. Understand the epidemiologic significance of Headaches.*
- *2. Understand the classification of common headaches.*
- *3. Identify the clinical manifestation of common headaches.*
- *4. Manage patients with acute common headache and prevention of recurrent attacks.*

DISEASE OF THE NERVOUS SYSTEM

- ***1. Headache***
- Headache is one of the commonest complaints in medical practice.
- As many as 90% of individuals have at least one episode of headache per year.
- Severe disabling headache is reported to occur at least annually by 40% of individuals worldwide.
- It results from distention, stretching, inflammation or destruction of pain sensitive cranial structures.
- These pain sensitive structures are the scalp, dura, sinuses, falx cerebri, middle meningeal arteries, proximal segments of large pial arteries and cranial nerves 5, 9 and 10.
- Brain parenchyma is not pain sensitive.
- A pain (sensory stimuli) from these structures is conveyed to the brain either via trigeminal nerve or first three cervical nerves.

Classification of headaches

- Headache can be clarified pathophysiologically as:
- ***1. Vascular headache***
  - Migraine headache
  - Cluster headache
  - Miscellaneous (orgasmic, Hangover)
- ***2. Cranial Neuralgias***
- ***3. Tension headache***

Classification of headaches

- ***4. Traction –inflammation headache***
  - Cranial arteritis
  - Meningitis
  - Brain tumor
  - Increased /Decreased ICP
- ***5. Extra cranial lesions***
  - Paranasal sinusitis
  - Dental problems
  - Ear problems
  - Ocular problems
  - Cervical problem

Evaluation of patients presenting with Headache

- ***Appropriate History*** is critical in evaluating a patient with headache.
- ***Characterize the headache:*** the quality, location, duration, time course, the conditions that produce, exacerbate or relieve it should be reviewed.
- ***Look also for associated symptoms, medication history and psychiatric history.***
- ***Physical Examination:***
- *I*s important to search for underlying serious illnesses. It should include
- *Vital signs* (Blood pressure, temperature)
- *Head and neck examination*: scalp tenderness, sinus tenderness, examination of the oral cavity and tempromandibular joint.

Evaluation of patients presenting with Headache

- ***Ophthalmologic evaluation including*** : fundoscopic examination pupillary size, corneal clouding
- ***Systematic evaluation of other systems*** (Glands, chest, CVS, abdomen, GUS, MSS, and Integumentary system)
- ***Neurological examination*** including change in mental status, focal neurological deficit, neck stiffness and other meningeal signs
- ***Investigation***
- Diagnosis of common primary headache syndromes is clinical. No specific test is available.
- Occasionally investigations including Neuro-imaging studies are important if the headache is atypical or it is associated with abnormalities on physical examination.
- After appropriate evaluation of the headache the following clinical features should be considered as indicators of serious underlying disease.

Evaluation…

- 1. First severe headache ever described as the worst type of headache in the patient's life may suggest subarachnoid hemorrhage
- 2. Subacute worsening over days or weeks (tumor)
- 3. Disturbs sleep or present immediately upon awakening (tumor)
- 4. Abnormal neurological exam (space occupying lesions)
- 5. Fever or other unexplained systemic signs (meningitis)
- 6. Vomiting precedes headache
- 7. Headache induced by bending, lifting or cough
- 8. Known systemic illnesses
- 9. Onset of headache in patients older than 55 yrs.

1. Vascular headache

- Vascular headaches refers to a group of headache syndromes, of unknown cause, in which pain results from dilation of one or more of branches of carotid arteries.
- Migraine headache and cluster headache account for the majority of the cases.
- ***A) Migraine Headache***
- ***Definition:*** migraine headache is a benign and episodic disease, characterized by headache, nausea, vomiting and/ or other symptoms of neurological dysfunction.
- It is the most common cause of vascular headache. It approximately affects 15% of women and 6% men.
- It usually begins in childhood or young adult life.

Vascular headache…

- ***Etiology***: the cause of migraine is often unknown, but several common precipitants have been observed.
- ***1) Family history*** of migraine present in nearly 2/3 of patients.
- ***2) Environmental, dietary and psychological factors.***
- Emotional stress , depression
- Altered sleep pattern or sleep deprivation
- Menses , Oral contraceptives
- Alcohol intake especially red wine
- Caffeine withdrawal
- Various food staffs (e.g. . chocolates, nuts, aged , cheese , meals containing nitrates
- Perfumes

Vascular headache…

- ***3) It may develop after seemingly minor head injury.***
- ***Pathogenesis:*** different hypothesis are proposed including:
- *1)* ***Vascular theory:*** in this theory it is said that migraine and neurological symptoms are results of extracranial vasodilatation and intracranial vasoconstriction.
- *2)* ***Neuronal theory***: a slowly spreading neuronal depolarization is considered as a cause.
- *3)* ***Trigeminovascular system abnormality***: this theory says dysfunction of trigeminal nucleus caudalis leads to release of vasoactive neuropeptides resulting in migraine.

Vascular headaches…

- ***Clinical feature***
- Migraine may be precipitated by some of the factors mentioned above. It is relieved by sleep and exhilaration, Sumatriptan and pregnancy.
- ***The syndrome of Classical migraine has five phases:***
- ***Prodromal phase***: characterized by lassitude, irritability difficulty in concentrating
- **Aura phase:** patients with aura often report visual complaints, vertigo, aphasia or other neurological deficit before the onset of the headache
- ***Headache phase*** – characteristic migraine headache
- ***Headache termination*** – usually occurs within 24 hours
- ***Post headache phase*** – feeling of fatigue. Sleepiness and irritability

Vascular headaches…

- ***Characteristic Migraine head ache is:***
- Moderate to severe head pain , pulsating quality often unilateral (affecting half part of the head)
- It is exacerbation by physical activity and relived by sleeping
- It is often associated with Nausea and/or vomiting, photophobia, phonophobia/sonophobia (dislike ad avoidance of laud sounds or noises).
- Multiple attacks may occur, each lasting 4 – 72 hrs.
- ***There are different variants of Migraine***
- ***Common migraine***
- This is the commonest variation of migraine headache
- No focal neurological disturbance precedes the recurrent headache

Vascular headaches…

- ***Classic migraine***
- It is associated with characteristic premonitory sensory, motor or visual symptoms.
- Most common symptoms reported are visual which include scotomas and/or hallucinations.
- **Complicated migraine**
- Migraine associated with dramatic transient neurological deficit, or a migraine attack that leaves a persisting residual neurological deficit.

Vascular headaches…

- ***Treatment***
- Therapy should first involve removal of inciting agents when possible.
- ***1. Acute/abortive treatment of migraine***
- These are lists of drugs effective for acute management of migraine attack
- **a) NSAIDS (Nonsteroidal antinflamatory agents):** such as ASA, paracetamol, Ibuprofen, Diclofenac may reduce the severity and duration of migraine attack.
- These drugs are effective for mild to moderate attacks and are most effective when taken early.
- ***Side effects:*** Dyspepsia and GI irritation are common side effects..

Vascular headaches…

- **b) 5-Hydroxytryptophan-1 Agonists:** is a serotonin agonist that decreases substance P release at the trigeminovascular junction.
- **i. Nonselective (Ergot preparations: Ergotamine and dihydro-ergotamine)**
  - Widely used for relief of acute attacks
  - Has oral, sublingual, rectal, nasal and parentral preparation. Parenteral forms are used for rapid relief of the attack.
  - Usually prepared combined with caffeine which potentiates the effect by improving absorption..

Vascular headaches…

- ***Dose: Initial*** dose: 1 – 2 mg oral /SL/ rectal and repeat every hour if there is no relief of headache to a maximum of 6 – 8 mg over 24 hrs
- ***Side effects:*** are nausea, vomiting, myalgias, chest discomfort, peripheral ischemia and even angina. Excess use may lead to rebound headache and dependency
- ***Contraindication:*** patients with vascular diseases like coronary heart disease
- **ii. Selective - Triptans including** (Naratriptan, Ritatriptan, Sumatriptan, and Zolmitriptan): are new drugs in management of migraine.
- ***Sumatriptan* –** single 6 mg SC dose is effective in 70 – 80% of patients
- **c) Dopamine agonists:** are used as adjunctive therapy.
- ***2. Prophylactic Treatment:*** includes drug regimens and changes in patients behavior

Vascular headaches…

- ***Medical therapy:***
- These are drugs that have capacity to stabilize migraine. Prophylactic treatment is indicated if the patient has three or more attacks per month.
- Drugs used for this purpose include β-blockers (propranolol), Tricyclic antidepressants (amitriptyline), and Calcium channel blockers (Verapamil), Valproic acid.
- Start with low dose and gradually increase if there is no adequate response.
- **Biofeedback therapy**
- It is simple and cost effective. It lessens migraine attacks by helping patients deal more effectively with stress

Vascular headaches…

- ***B) Cluster Headache***
- Cluster head ache is a vascular headache syndrome, characterized by severe, acute headache that occurs in clusters lasting several weeks followed by pain free intervals that averages a year.
- Common in men than women. Male: Female ratio is 8:1
- Usually begins 3rd to 6th decades
- Cluster headache is periorbital less commonly temporal. It has rapid onset without warning. It is also severe and explosive in quality lasting 30 min to 2hrs, subsiding abruptly.

Vascular headaches…

- Clusters characteristically occur in the spring and fall several times a day particularly at night and stay for 3 – 8 weeks
- During attack patients often have associated nasal stiffness, lacrimation and redness of the eye ipsilateral to the headache.
- Alcohol provokes attacks in about 70% of patients
- ***Treatment***
- **Acute attack /abortive therapy (Treatment)**
- Inhalation of 100% oxygen and
- ***Sumatriptan*** 6 mg S.C. stat said to be helpful and ergotamine or other analgesics may also be used.
- **Preventions/prophylactic therapy:** clusters attacks can be prevented effectively by:
- Prednisolone , Lithium, Methysergide, Ergotamine, Sodium valproate and verapamil

C) Tension headache (Tension type headache)

- Most common cause of headache in adults
- Common in women than men
- Can occur at any age, but onset during adolescence or young adulthood is common.
- ***Etiology:*** various precipitating factors may cause tension headache in susceptible individual including.
- Stress – usually occurs in the afternoon after long stressful work hours
- Sleep deprivation
- Uncomfortable stressful position and/or bad posture
- Hunger (Irregular meal time)
- Eye strain resulting from continuous TV watching, working on computer screen for a long time.

Tension headache…

- ***Clinical feature***
- Tension headache is characterized by mild or moderate, bilateral pain.
- Headache is a constant, tight, pressing or band like sensation in the frontal, temporal, occipital or parietal area.
- Usually lasts less than 24 hrs but can persist for days or weeks.
- Prodromal symptoms are absent some patients have neck, jaw or temporomandibular joint discomfort.
- On examination some patients may have tender spots in the pericranial or cervical muscles.

Tension headache…

- ***Treatment:*** management of tension headache consists:-
- ***1. Pharmacotherapy***
- **Abortive therapy/acute treatment**
  - Stop or reduce severity of individual attacks
  - This can be done with simple analgesics like paracetamol, ASA, Ibuprofen, and Diclofenac.
- If treatment is unsatisfactory addition of caffeine or other analgesic is beneficial.
- **Long term preventive therapy**
  - Main form of therapy for chronic form of tension headache
  - This kind of treatment is indicated if the headache is :

Tension headache…

- Long term treatment is indicated for headaches that are:
- Frequent (> 2 attacks / week),
- Of long duration (> 3hrs)
- Severe (cause significant disability)
- Associated with overuse of abortive medication
- Commonly used drug for long term treatment is Amitryptilline.

Tension headache…

- **2. *Physical Therapy:*** different techniques can be used including
- Hot or cold application
- Positioning
- Stretching exercises
- Traction
- Massage

Tension headaches…

- **3. Psychological Therapy**
- Includes reassurance, Counseling, relaxation, stress management programs and biofeedback techniques reduce both the frequency and severity of chronic headache.
- ***D) Headache Associated with Brain Tumor***
- About 30% of patients with brain tumor present with headache.
- Brain tumor can affect all ages and both sexes.
- Headache of brain tumor is usually intermittent dull aching, moderate intensity which worsens with time.
- It disturbs sleep in about 10% of patients, exacerbated by exertion and postural changes.
- With time patients can develop nausea and vomiting.
- Upon examination focal neurological deficit may be detected.

E) Temporal Arteritis

- It is also called giant cell arteritis. It is an inflammatory disorder of the carotid artery and its branches.
- It is common in elderly, and women account for 65% of cases.
- ***Clinical feature***
- Typical presenting symptom includes headache, polymyalgia rheumatica, jaw claudication, fever and weight loss.
- Headache is located to temporal or occipital area, described as dull and boring. It is usually worse at night and is often aggravated by exposure to cold.
- Scalp tenderness is often found over temporal artery.
- 50% of patients with untreated temporal arteritis develop blindness due to involvement of ophthalmic artery and its branches.

Temporal arteritis…

- ***Diagnosis***
- ESR is often elevated.
- Biopsy of temporal artery confirms the diagnosis.
- ***Treatment***
- Prednisolone 80 mg /day for 4 – 6 weeks

F) Lumbar Puncture headache

- Occurs in 10 – 30% of patients having LP
- Usually begins within 1 – 2 days and persists for 3 – 4 days.
- Headache of lumbar puncture is usually bifrontal or occipital, dull aching aggravated by sitting or standing, head shaking, jugular vein compression and disappears in prone or supine position.
- ***Treatment:*** simple analgesics and lie the patient supine.

References:

- 3) Kasper L., Braunwald E., Harrison's principles of Internal medicine, 16th Edition, Headache, pages 85-93.
- 4) Myers R. Allen, National Medical Series for independent Study (NMS) 3rd edition Medicine, Headache, pages 61—613.

UNIT 2

DISEASES OF THE SPINAL CORD

2. Diseases of the Spinal cord

- **Learning objectives:** at the end of this lesson the student will be able to:
- *1. Identify the characteristic features of diseases of the spinal cord.*
- *2. Describe the Etiologies of diseases of the spinal cord.*
- *3. Identify the clinical manifestation of common diseases of the spinal cord.*
- *4. Understand the diagnostic wok up for common diseases of the spinal cord.*
- *5. Understand the management of common diseases of the spinal cord.*

Introduction…

- Spinal Cord is part of the central nervous system contained in the spinal canal.
- The adult spinal cord is 18 cm long, oval or round in shape in cross section.
- It has two parts, white matter and gray matter, with central canal at the center.
- The white matter contains ascending sensory and descending motor fibers and gray matter contains nerve cell bodies.
- Spinal cord is organized into 31 somatotropic segments, i.e. 8 cervical, 12 thoracic, 5 Lumbar, 5 sacral and 1 coccygeal segments.
- Diseases of the spinal cord are frequently devastating, because the spinal cord contains, in a small cross-sectional area, almost the entire motor output and sensory input of the trunk and the limbs.

Characteristics of spinal cord diseases

- **Generally diseases of spinal cord are characterized by:**
- ***The presence of a level below which motor/sensory and/or autonomic function is disturbed.***
- ***1. Motor disturbance*** causes weakness (paraplegia, quadriplegia), spasticity, hypereflexia and extensor plantar response, which is due to disruption of descending corticospinal fibers.
- ***2. Impaired sensation*** results from disordered function of ascending spinothalamic and dorsal column pathways.
- ***3. Autonomic disturbance*** leads to disturbed sweating, bladder, bowel and sexual dysfunction.

Aetiology

- ***Some causes of spinal cord diseases***
- **1) *Compressive*** : lesions may be epidural, intradural or intramedullary
  - i) TB spodylitis
  - ii) Neoplasms
  - iii) Epidural abscess
  - iv) Epidural hemorrhage
  - v) Cervical spondylosis
  - vi) Herniated disc /disc prolapse
  - vii) Fractured / displaced vertebral body

Aetiology…

- ***2) Vascular***
  - i) AV – malformation
  - ii) Spinal artery thrombosis or embolization
- ***3) Inflammatory***
  - i) Transverse myelitis, Borrelia, Syphilis
  - ii) MS (multiple sclerosis)
  - iii) Vasculitis

Aetiology…

- ***4) Infections***
  - i) Viral : Varicella zoster virus , HSV-1 and HSV-2 , CMV , HIV
  - ii) Bacterial : Myocobaterial
  - iii) Parasitic : Schistosomaisis, Toxoplasmosis
- ***5) Developmental :*** syringomyelia , meningomyelocel
- ***6) Metabolic***
- i) V-B 12 deficiency
- ii) Neurolathrism: that is a spastic paraparesis resulting from consumption of "Guaya", which grows in the northern part of Ethiopia. This cereal has neurotoxin which causes paraparesis when consumed in large amount for relatively long period of time.

Common Spinal Cord Diseases

- ***A. Neoplastic spinal cord compression***
- ***May be classified as:***
- **1)** ***Extramedullary:*** tumor outside the spinal cord.
- i) ***Epidural:*** outside the dural layer
- Commonest cause of neoplastic compression of spinal cord in adults. Usually results from metastasis to adjacent vertebral bone or direct compression of the spinal cord.
- Commonest neoplasm include: breast, lung, prostate, kidneys, lymphoma and multiple myeloma
- Most frequently involved site is thoracic cord

Common Spinal Cord Diseases…

- ii) ***Intradural:*** inside the dural layer
- These are slowly growing benign tumors like meningioma, neuroblastoma, lipoma
- **2) *Intra medullary:*** tumors within the spinal cord.
- These are uncommon tumors , including ependymoma, hemangioblastoma low grade astrocytoma

Clinical features

- Initial symptom is backache, which is localized, and which worsens with movement, coughing or sneezing.
- The pain may radiate to the legs, trunk or following dermatomal distribution.
- The pain may be sever and awaken the patient at night.
- As compression progresses patient develops progressive weakness, sensory abnormalities and autonomic disturbances change in bladder function and constipation.

Clinical features…

- **Physical findings include:**
- Weakness, spasticity, hyperreflexia
- Loss of or decreased sensations to pinprick in the lower extremities
- Extensor plantar response , and loss of abdominal reflexes and anal sphincter tone
- Urinary retention

Clinical features…

- ***Investigations***
- Check for primary tumor sites
- Plain X-ray of the spine
- Myelography
- Radionuclide bone scan
- CT/MRI
- Biopsy usually unnecessary in patients with known pre-existing cancer.

Therapy

- ***Therapy:*** depends on site and type of tumor.
- Treatment modalities include
- ***Steroids:*** help to reduce the interstitial edema
- Should be started immediately with in the first 12 hrs of occurrence of symptoms
- Prednisolone 40 mg PO BID , or Dexamethason 12 mg IV followed by 4 mg IV QID may be used

Therapy…

- ***Radiotherapy.***
- Is effective even for classically radio-resistant tumors
- Prevents new weakness and may give recovery of function
- ***Surgery:*** decompression or vertebral body resection
- Useful especially for intradural and intramedullary tumors
- ***Note:*** Treatment should be started as soon as possible (with in 12 hrs). Fixed motor deficits (paraplegia or quadriplegia), once established for > 12 hrs, do not usually improve, and beyond 48 hrs the prognosis for substantial motor recovery is poor.

B. Tuberculosis of the spine (Pott's disease)

- One of commonest causes of myelopathy in developing countries where Tuberculosis is endemic.
- Often Involves two or more adjacent vertebral bodies
- Commonest site is lower thoracic and upper lumbar vertebrae
- ***Clinical features***
- Patients present with insidious on set of back pain, which progressively get worse.
- Gibus deformity (kyphotic swelling over the back)
- Numbness and loss of sensation with a sensory level
- Weakness of the lower limbs, often spastic in nature, with exaggerated deep tendon reflexes and up going plantar (Babinisky's sign)
- Bladder and /bowel dysfunction (Urinary retention with overflow incontinence, constipation or fecal incontinence)
- In about 65% of cases evidences of extra spinal tuberculosis is present

Tuberculosis of the spine (Pott's disease)…

- ***Diagnostic workup:***
- **1. Imaging studies**
- Plain radiograph show characteristically destructive process of the vertebrae, involvement of disc space with deformity.
- CT/MRI may show the lesion more clearly
- ***Treatment***
- ***Medical Therapy***
  - ***DOTS: short course anti tuberculosis chemotherapy*** is mainstay of therapy.
  - ***Steroids*** can be added it there is neurological deficit
- ***Surgery:*** is indicated if there is spinal instability or deformity and unresponsiveness to medical treatment.

C. Prolapse of intervertebral disc

- It occurs due to trauma, sudden severe strain or degenerative changes.
- Commonest site of for disc prolapsed is the lumbar region.
- **Clinical feature**
- Localized back pain aggravated by straining with or without
  - Radiculopathy
  - Segmental sensory loss
  - Changes in deep tendon reflexes (asymmetrical)
- ***Straight leg raising sign is positive:*** the patient will have back pain, when stretched leg is raised / flexed at the hip joint.

Prolapse of intervertebral disc…

- ***Diagnostic workup***
- Myelography: may help to localize the site of prolapse
- CT/MRI: can easily demonstrate the prolapsed disk
- ***Therapy:***
- ***Medical therapy***: is often supportive ad include Bed rest, adequate analgesics and physical therapy
- Supporting belts or corsets
- ***Surgery***: is the definitive treatment for disk prolapse.

D. Transverse Myelitis

- It is an acute or sub acute inflammatory disorder of the spinal cord.
- It occurs associated with;
  - Antecedent infection (*either viral or Mycoplasmal.*)
  - Recent vaccination
  - Multiple sclerosis
  - Collagen vascular disease (SLE)

Transverse Myelitis…

- ***Clinical feature***
- Initial symptom is localized back or neck pain or radicular pain followed by various combinations of paresthesia, sensory loss, motor weakness and sphincter disturbances, which can evolve within hours to several days.
- ***Investigation***
- CSF: may be normal or show pleocytosis and increased protein.
- ***Treatment***
- Steroids can be used in moderate to severe cases.

E. Metabolic and toxic myelopathies

- ***i) Subacute combined degeneration of spinal cord***
- Neurologic disease mainly affecting the spinal cord, resulting from severe Vit-B12 deficiency.
- Vit-B12 deficiency results abnormalities on myelin basic protein leading to swelling of myelin sheath followed by demyeliniation and gliosis.
- These changes mainly affect the posterior and lateral columns of spinal cord.
- ***Clinical Feature:*** patients present with;-
- Paresthesia in the hands and feet.
- Early loss of position and vibration senses (loss of propioreceptor sensations).
- Progressive spastic and ataxic weakness
- Some patients may develop optic atrophy and encephalopathy

Metabolic and toxic myelopathies…

- ***Treatment***
- ***Vitamin B12:*** 1000µg IM/d for 5 – 10 days, followed by 1000 µg IM/week for 1 month, and then 1000 µg IM month lifelong.
- ***iii) Neurolathrism***
- Neurolathrism is syndrome that affects the nervous system of man due to consumption of peas of the lathyrus species ("Guaya" seeds) that contains neurotoxic amino acid.
- Excessive consumption of these (Guaya) seeds occurs during times of food shortage
- It affects predominantly young men.

Metabolic and toxic myelopathies…

- ***Clinical feature***
- Onset can be acute /subacute usually precipitated by manual labour, febrile illness or diarrhea then the patients will develop weakness, spasticity and rigidity progressively preventing them from walking.
- Usually no sensory abnormality is seen.
- Some of severely affected cases may develop incontinence and impotence.
- ***Investigation***
- No specific laboratory test required.
- Diagnosis of neurolathrism is by exclusion of other causes and taking proper dietary history and understanding the geographic distribution of the diseases.

Metabolic and toxic myelopathies…

- ***Treatment***
- No cure once established
- ***Prevention***
- Banning cultivation and consumption of the seed (" Guaya").
- Breeding of nontoxic variant if possible.
- Use of certain preparation methods (Cooking or soaking in excess water) makes the seed less toxic.

References:

- 1) Kasper L., Braunwald E., Harrison's principles of Internal medicine, 16th Edition, Diseases
- of the Spinal cord, pages 2438-2446.
- 2) Myers R. Allen, National Medical Series for independent Study (NMS) 3rd edition Medicine,
- Myelopathy and other spinal cord disorders, pages 635-637.

3. Cerebrovascular diseases

- **Learning objectives:** at the end of this lesson the student will be able to:
- *1. Define cerebrovascular diseases/stroke.*
- *2. Understand the epidemiologic significance of stroke.*
- *3. Understand the classification of stroke and the etiologies.*
- *4. Identify the clinical manifestation of different types of stroke.*
- *5. Understand the diagnostic approach of patients with stroke.*
- *6. Understand the principles of management of patients with stroke.*
- *7. Understand the preventive strategies for stroke.*

Cerebrovascular diseases…

- ***Definition***: Syndrome of an abrupt onset of nonconvulsive, focal neurologic deficit resulting from sudden interruption of the blood supply to parts of the brain, lasting 24 hours or longer.
- **Classification of stroke**
- ***I. Etiologic classification***
- 1) **Ischemic** -stroke accounts for 80 – 90% of all stroke in developed countries
- a) Embolic
- b) Thrombotic
  - i) Large vessel disease: resulting from narrowing of cerebral arteries doe to atherosclerosis.
  - ii) Small vessel disease (Lacunar infarct)
  - iii) Miscellaneous: E.g. Vasculitis resulting thrombus formation

Cerebrovascular diseases…

- *2) **Hemorrhagic Stroke:***
- ***A**ccounts for 10-20 % of cerebrovascualr accidents in developed nations.*
- *It is a much more commoner cause of stoke in developing countries , mainly associated with unrecognized or poorly controlled hypertension*
- *a) Primary Intracerebral Hemorrhage (PICH)*
- *b) Subarachnoid Hemorrhage (SAH)*

Cerebrovascular diseases…

- ***II. Classification based on the duration of stroke***
- 1) ***Transient Ischemic attack:*** TIAs are focal neuralgic deficit lasting < 24 hrs confined to an area of brain perfused by specific artery , and neurologic deficit resolves in less than
- 2) ***Reversible Ischemic neurologic deficit:*** sudden onset focal neurologic deficit which lasts for more than 24 hours, but the neurologic deficit recovers / resolves /.
- 3) ***Stroke in evolution:*** a focal neurologic deficit, the degree of which is progressing over a couple of hours or days.
- 4) ***Complete stroke:*** sudden onset of focal neurologic deficit, in which the deficit neither improves nor gets worse over time. It is often associated with infarction of part of the brain.

Cerebrovascular diseases…

- ***Epidemiology and risk factor***
- Stroke is prevalent all over the worldwide. It is third commonest cause of death in developed world following Coronary heart diseases and cancer. It is a leading cause of disability.
- The prevalence and incidence of stroke is also on the rise in developing countries.
- ***Major risk factors associated with stroke include***
  - *Incidence is higher in men and old age*
  - *Hypertension*
  - *Smoking*
  - *Diabetic mellitus*
  - *Hyperlipidemia*
  - *Atrial fibrillation*
  - *Myocardial infarction*
  - *Congestive heart failure*
  - *Acute alcohol abuse.*

Cerebrovascular diseases…

- **Approach to a patient with stroke:**
- ***Goals /Steps***
- **1.** Assessment and maintenance of vital functions
- **2.** Determination of presumptive diagnosis of stroke subtype
- **3.** Confirmation of stroke subtype
- **4.** Management of a patients with stroke

Cerebrovascular diseases…

- ***1. Initial Assessment and maintenance of vital functions/stabilizing the patient***
- Stroke should be considered as medical emergency, as it affects vital functions of an individual.
- For this reason the initial step in management of patients with acute stroke should be rapid assessment and maintenance of vital functions. This includes:
- ***a) Maintenance of air way and ventilation***
- ***b) Control of blood pressure***
- Acute stroke alters autoregulation of cerebral blood flow, compromising the blood supply to an already damaged brain. Close monitoring of blood pressure and correction of both hypotension and hypertension reduces this risk.
- If the patient is hypertensive treatment is recommend only when the DBP ≥120 and SBP ≥ 200 mmHg. Short acting antihypertensive drugs are preferred.
- If the patient is hypotensive, it should be corrected by fluid administration and treatment of the underlying cause for the hypotension.

Cerebrovascular diseases…

- ***c) Control of body temperature.***
- Fever occurs in 44% of patients with acute stroke. The fever may be due to stoke or infections. Because fever worsens the prognosis of stroke body temperature should be controlled appropriately.
- **d) Fluid management**
- Maintenance of euvolumic state and establishment of IV access using normal saline (rather than glucose solutions) is also important. Glucose is said to be neurotoxic and it is better avoided in patients with stroke.
- ***N.B Exclude causes of brain dysfunction, which mimic stroke like states like syncope, migraine, hysteria and trauma.***

Cerebrovascular diseases…

- ***2. Determine Presumptive Diagnosis of Stroke Subtype***
- Numbers of clinical features are useful in determining the type of stroke. A good history taking, and proper physical examination may suggest the possible cause of the stroke.
- **Important historical information includes:**
- ***Mode of onset and pattern of progression***
  - Embolisms usually occur suddenly when the patient is awake, most often early in the morning, giving maximum deficit at onset.
  - Hemorrhagic stokes also occur suddenly while the patient is awake, any may be physically active or straining, and progresses within minutes to hours.
  - Thrombosis often occurs during sleep hour or present upon arising from bed progressing in a stepwise fashion.

Cerebrovascular diseases…

- ***Associated symptoms***
  - Headache, vomiting, reduced alertness suggest hemorrhagic stroke than ischemic stroke. Very severe headache with altered consciousness without major neurologic deficit may suggest subarachnoid hemorrhage.
  - If patient is having fever raises suspicion of infective endocarditis.
  - Seizure is common in embolic stroke.
- ***Look for risk factors for stroke***
- ***Looking for other medical conditions*** associated with stroke such as hypertension, diabetes, smoking and use of drugs like OCP* may suggest the diagnosis.

Cerebrovascular diseases…

- **Physical Examination**
- Physical Findings may give clue to the type of stroke the patient is suffering from.
- Absent/reduced peripheral pulses suggest atherosclerosis or embolism
- Presence of neck bruit suggests extra cranial occlusion of carotid arteries
- Cardiac abnormalities: such as atrial fibrillation, murmurs or cardiac enlargement may suggest embolic stroke, the embolus originating from the heart.
- Fever raises concern for infectious etiologies
- Ophthalmoscopic examination: papilledma or retinal hemorrhage may suggest subarachnoid hemorrhage or increased intracranial pressure.

Table VIII-3-1. Characteristic features of different

	Embolic stroke	**Intracerebral hemorrhage**	**Large vessel thrombosis**	**Lacunar infarctions**	**Subarachnoid hemorrhage**
Onset	Sudden onset with maximum deficit at onset	Sudden (deficit Progresses over minutes to hours)	Sudden, Gradual, stepwise, or Stuttering	Sudden, Gradual, Stepwise or Stuttering	Sudden, Usually few or not focal signs
Time of occurrence	When the patient is Awake	When the patient is Awake and active	When the patient is Asleep or inactive	When the patient is Asleep or inactive	When the patient is Awake and active

Table VIII-3-1. Characteristic features of different

	Embolic stroke	**Intracerebral hemorrhage**	**Large vessel thrombosis**	**Lacunar infarctions**	**Subarachnoid hemorrhage**
Warning signs (TIA)	None	None	Usually	Variable, TIA's may occur	None
Associated symptoms (Headache Vomiting)	Sometimes	Usually	Sometimes	No	Always (stiff neck)
CT scan	Decreased density	Increased density	Decreased density	Usually normal	Usually abnormal
LP	Usually clear	Usually bloody	Clear	Clear	Invariably blood

Cerebrovascular diseases…

- These characterizations are generally accepted principles regarding stroke; however, it is good to remember that stroke can present atypically.
- **3. *Confirmation of Diagnosis:*** different investigations are needed to confirm the diagnosis.
- ***Imaging studies (CT or MRI):*** are the most important initial diagnostic tests in patients with stroke (if available and affordable by the patient). CT can identify or excludes hemorrhagic stroke and other conditions which simulate stroke (like Neoplasm and abscesses). Complete Infarction is usually seen after 24 hours. MRI is more sensitive than CT for early diagnosis of brain infarction.

Cerebrovascular diseases…

- **Other Tests are:**
- ***Lumbar puncture*** – may be needed to make a diagnosis of small SAH which can be missed by CT or MRI.
  - Carotid Doppler studies : to look for carotid artery narrowing
  - Angiography : to identify the exact location and the specific artery blocked
  - Echocardiography : to look for cardiac sources of embolization
  - ECG: to look for arrhythmias such as atrial fibrillation
  - CBC, ESR, VDRL
  - Tests for HIV infection : stroke associated with vasculitis is common in HIV positive patients
  - FBS, Lipid profile : to look for diabetes and hyperlipidemia 9 risk factors for stroke
  - Coagulation profile: to look bleeding tendencies.

Cerebrovascular diseases…

- ***4. Management of specific stroke***
- **Goal of Treatment**
- Interruption of further brain damage
- Prevention and management of complication

Cerebrovascular diseases…

- ***A. General Measures***
- Admit the patients where close follow up can be given
- Continue follow up and maintenance of vital functions.
  - Airway and ventilation
  - Controlling of blood pressure
  - Controlling body temperature
  - Fluid administration /Hydration
- If the patient is comatose or has impaired mental status
  - Changing the patients position every 2 hrs and avoid the occurrence of bed sores
  - Bladder and bowel care: if the patient has incontinence – catheterize
- Infections such as aspiration pneumonia should be treated with antibiotics

Cerebrovascular diseases…

- ***B. Management of Specific Etiologies***
- ***1) Atherosclerotic stroke (Thrombotic stroke)***
- ***i)*** Thrombolytic therapy: in developed countries thrombolytic therapy with medications such as rt-PA (plaminogen activator), to patients who present within 3 hrs of onset of stroke, helps to lyse the thrombus and restore perfusion to the affected brain.
- ***Contraindications:***
  - Extensive infarct on CT,
  - Recent surgery, Head trauma
  - GI or urinary hemorrhage, bleeding disorders, Anticoagulation with prolonged PT/PT
  - Seizure at stroke onset
  - Severe uncontrolled hypertension.

Cerebrovascular diseases…

- ***ii) Anticoagulants:*** use of Heparin and Warfarin is controversial. Low dose heparin can be given for prevention of thromboembolism.
- ***iii) Anti-platelet aggregation agents:***
- Aspirin reduces the incidence of stroke and vascular mortality. General recommendation is to give 325 mg of ASA once daily. It may not help to resolve the already formed thrombus, but ASA prevents recurrence of stroke.
- ***2) Embolic stroke: (Cardiogenic embolus)***
- Anticoagulation is indicated to prevent recurrent embolic stroke. Anticoagulation with heparin should be initiated when the acute phase of stroke is over. Care should be taken to avoid hemorrhagic transformation of infarct. Warfarin is used for chronic anticoagulation.

Cerebrovascular diseases…

- ***3) Intracerebral hemorrhage***
- Continue supportive measures
- Control very high blood pressure
- Surgical consultation is indicated for removing cerebellar hematoma, as it may compress vital centers in the brainstem.
- ***4) Subarachnoid Hemorrhage***
- ***Medical therapy:***
- (a) Supportive measures include bed rest, sedatives, analgesic, laxative,
- (b) Control of hypertension and
- **(c)** Nimodipin (calcium channel blocker) is given to prevent neurologic deterioration due to vasospasm.
- ***Surgical therapy***: Saccular aneurysms are treated surgically

Cerebrovascular diseases…

- ***C. Prevention of further stroke:***
- Control of hypertension
- Control blood sugar in diabetics
- Ceasation of smoking
- Physical activity and weight reduction
- Anticoagulation for atrial fibrillation
- ASA 75 mg Po daily in individuals older than 50 and have history of TIA
- Surgery (Endarterioactomy): if a narrowed artery is detected

Cerebrovascular diseases…

- **D. *Rehabilitation:*** is a very important part of management, and it shall be started early and include:-
- Physiotherapy
- Occupational and speech therapy.
- ***References:***

- 1) Kasper L., Braunwald E., Harrison's principles of Internal medicine, 16th Edition, Cerebrovascular diseases, pages 2372-2392.
- 2) Myers R. Allen, National Medical Series for independent Study (NMS) 3rd edtion Medicine, Stroke, pages 619-625.

4. Impairment of consciousness and Coma

- **Learning objectives:** at the end of this lesson the student will be able to:
- *1. Define different levels of Impairment of consciousness and Coma.*
- *2. List the etiologies of Impairment of consciousness and Coma.*
- *3. Understand the diagnostic approach of Impairment of consciousness and Coma.*
- *4. List differential diagnosis to Impairment of consciousness and Coma.*
- *5. Understand the principles of management of patients with coma.*

Impairment of consciousness and Coma…

- ***Introduction***
- Maintenance of conscious state requires proper functioning of the cerebral hemispheres, reticular activating system found in brain stem and corticothalmic connections. If there is structural, metabolic or toxic insult of diffuse nature to these structures results in alteration of conscious level of different degree.
- ***Coma*** is severe degree of reduced consciousness (alertness and responsiveness) from which the patient cannot be aroused.
- ***Stupor*** is a sleep like unarousability, from which the patient can be awakened by vigorous stimuli.

Impairment of consciousness and Coma…

- ***Drowsiness:*** is a state of reduced consciousness characterized by easy arousal that can be maintained only for brief period of time.
- ***Vegetative state:*** is characterized by the patient's unawareness of self or external stimuli. Autonomic functions are relatively well maintained, and a sleep-wake cycle exists. The patient cannot interact with others in a meaning full fashion. The patient can survive with medical and nursing support.
- ***Brain death:*** This is a state in which there has been cessation of cerebral blood flow; as a result there is global loss of brain function while respiration is maintained by artificial means and the heart continues to pump.

Impairment of consciousness and Coma…

- ***Etiologies***
- ***1. Diseases that cause no focal neurologic deficit or lateralizing neurologic signs***. The loss of consciousness in such patients is diffuse bilateral hemispheric impairment, and such patients have normal brainstem function. Some of the causes include :-
- ***Metabolic disturbances such as :*** hepatic encephalopathy ,uremic encephalopathy ,hypoglycemia, diabetic ketoacidosis. Electrolyte imbalance (hyponatremia, hypernatremia, Hyperkalemia, Hypocalcaemia), Hypoxia, Hypercapnia etc

Impairment of consciousness and Coma…

- ***Etiologies***
- ***Intoxications:*** alcohol, sedative drugs, opiates
- ***Sever systemic or CNS infections*** : meningitis, encephalitis, cerebral malaria, cerebral abscess
- ***Post seizure state*** : status epilepticus
- ***Hypertensive encephalopathy , eclampsia***
- ***Severe hyperthermia or hypothermia***
- ***Head trauma:*** brain concussion

Impairment of consciousness and Coma…

- ***Etiologies***
- ***2. Diseases that cause focal neurologic deficit:*** these disorders cause coma by affecting the reticular activating system. They are classified in to two depending on the location of the lesion.
- ***a) Supratentorial (hemispheric) lesions***
  - Epidural or subdural hematoma
  - Intraparenchymal hemorrhage (hemispherical hemorrhage)
  - Large ischemic infarction
  - Tumor , Abscess , Trauma
- ***b) Infratentorial lesions***
  - Pontine or cerebellar hematoma
  - Basilar artery thrombosis
  - Ischemic cerebellar infarction
  - Tumor , abscess

Impairment of consciousness and Coma…

- ***Approach to a patient in Coma***
- **Complete and rapid assessment of the patient is critical for optimal care.**
- ***A. Assessment and maintenance of vital function is the initial step***
- Maintain the air ways and ensure adequate breathing (ABC of life)
- Maintain circulation
- ***B. Establishment of cause of coma***: is done by taking a careful history, doing rapid but through physical examination and investigations.

Impairment of consciousness and Coma…

- ***Patient History:***
- **Past medical history:** looking for disease like diabetes, hypertension, cirrhosis, chronic renal disease, malignancies and other diseases.
- History of medications: legal or illicit drugs (sedatives, hypnotics, narcotics) and history of drug abuse
- Circumstances and rapidity with which change in mental status developed (sudden onset indicating vascular causes, gradual onset indicating metabolic and infectious causes fluctuations suggest subdural hematoma)
- Recent patient complaints preceding loss of consciousness: medical and neurologic symptoms (fever suggesting infections, polyuria and polydypsia indicating DKA)
- Details regarding the site where the patient was found (e.g. the presence of empty drug vials or evidence of fall or trauma

4. Impairment of consciousness and Coma

- ***Physical examination should be through.***
- ***Vital signs*:** Extremes of BP, pulse or temperature and abnormal pattern of breathing.
  - Fever suggests systemic or CNS infections or Neurogenic fever
  - Tachypnea – in pulmonary infections or acidosis
  - Hypertension – hypertensive encephalopathy
- ***Head and neck*:** evidence of trauma and the presence of meningismus
- ***Skin:*** look for signs of trauma or injection.

4. Impairment of consciousness and Coma

- ***Physical examination should be through.***
- **General systemic examination:** looking for evidences of systemic illnesses like cirrhosis, chronic renal, failure, meningococcemia etc.
- ***Neurologic examination:*** is the cornerstone of assessment of comatose patient. It should be descriptive and systematic.
- ***1. Level of consciousness:*** can be assessed semi quantitatively using the Glasgow coma Scale.

Table VIII-4-1 Glasgow coma Scale:

Points are given for best response in each category and are added giving a score between 3 (deep coma) and 15(normal)

Eye opening	Score
Spontaneous To verbal stimulus To painful stimulus None	4 3 2 1
Best verbal response	Score
Oriented Confused Inappropriate words Unintelligible words None	5 4 3 2 1
Best motor response	Score
Best motor response Obeys commands Localizes pain Withdrawal from pain Extensor response Flexor response None	6 5 4 3 2 1

2. Brain stem reflexes

- Assessment of brainstem functions helps to localize the cause of coma. This can be done using brain stem reflexes including, pupillary light response, ocular movements, corneal reflex and the respiratory pattern. If the brainstem functions are normal, coma must be ascribed to bilateral hemispherical disease.
- ***a) Pupillary light response***
- Pupillary reactions are examined with a bright, diffuse light. During examination size, shape, symmetry and reaction to light should be noted on both eyes.
- Normally reactive and round pupils of midsize (2.5 to 5 mm) essentially exclude midbrain damage.
- Enlarged (>6mm) and unreactive pupil on one side signifies a compression or stretching of the third nerve from the effects of a mass above.

Brain stem reflexes…

- ***a) Pupillary light response***
- Bilaterally dilated and unreactive pupils, indicates severe midbrain damage, usually from compression by a mass.
- Bilaterally small (1 to 2.5 mm) and reactive pupils (not pinpoint) are seen in metabolic encephalopathies or in deep bilateral hemispheral lesions such as hydrocephalus or thalamic hemorrhage.
- Very small but reactive pupils (< 1 mm)/pinpoint pupils, characterize narcotic or barbiturate overdoses but also occur with extensive pontine hemorrhage the thalamus.

Brain stem reflexes…

- ***b) Ocular Movements***
- Before maneuvers the eyes are observed by elevating the lids and noting the resting position and spontaneous movements of the eyeballs.
- Lid tone is tested by lifting the eyelids and noting their resistance to opening and the speed of closure. Resistance to opening the eye lids may suggest hysteric conversion. Easy eyelid opening with slow closure indicates sever coma.
- Midline deviation suggests frontal/pontine damage.
- Dysconjugate gaze (abduction or adduction) suggests cranial nerve abnormalities.
- Spontaneous eye movements roving, dipping, bobbing suggest damages being at different sites.
- The eyes look towards a hemispheric lesion and away from a brainstem lesion.

Brain stem reflexes…

- ***i. Occulocephalic reflex***
- Oculocephalic reflex is elicited by moving the head from side to side or vertically with eyes held open. In comatose patient with intact brainstem
- If the eyeballs move to the opposite direction of the head movement-intact brainstem function ("doll's eyes" movement is positive.)
- If the eyeballs move to the same direction of the head movement- Brainstem dysfunction.
- ***ii. Caloric (occulovestibular) reflex***
- This test is performed by irrigating the ear with ice (cold) to stimulate the vestibular apparatus. In patients with intact brain stem the eyes move to the irrigated ear.

2. Brain stem reflexes

- **c) Corneal reflex**
- This test assesses the integrity of dorsal midbrain and pontine. It is lost if the reflex connections between the fifth (afferent) and the seventh (efferent) cranial nerves within the pons are damaged.
- ***d) Respiration:***
- Abnormalities of respiratory pattern can help in coma diagnosis but are of less localizing value in comparison to other brainstem signs.
- ***Shallow, slow, but regular breathing*** suggests metabolic or drug depression.

Brain stem reflexes…

- ***d) Respiration:***
- ***Cheyne-Stokes respiration*** signifies bihemispherical damage or metabolic suppression, and commonly accompanies light coma.
- ***Rapid, deep (Kussmaul) breathing*** usually implies metabolic acidosis but may also occur with pontomesenephalic lesions and severe pneumonia.
- ***Agonal gasps*** reflect bilateral lower brainstem damage and are indicators of severe brain damage and a near death situation.

3. Motor function /response

- ***Posture of the patient*:**
- ***Quadriparesis and flaccidity*:** suggest pontine or medullary damage
- ***Decorticate posturing:*** flexion of the elbows and the wrists with supination of the arms, and extension of the legs, suggests severe bilateral or unilateral hemispheric or diencephalic lesion (damage above the midbrain.)
- ***Decerebrate posturing*** (extension of elbows and the wrist with pronation of the forearm and extension of the legs) indicates damage to the brainstem(midbrain or pontine compromise)

Motor function /response…

- ***Posture of the patient*:**
- ***Spontaneous activities*** – if the patient is yawning, swallowing, coughing or moaning the coma is not deep.
- ***Abnormal body movements*** – seizure, myoclonus may suggest the cause of the coma is status epelepticus, uremia etc.
- Assess tone, response to painful stimuli and presence of asterixes. Asymmetric motor responses have localizing value.

Motor function /response…

- ***Differential Diagnosis:***
- ***Psychogenic Coma (hysteric coma):*** patient often has history of psychiatric illness, and non physiologic response on physical examination.
- Resistance to having the eyelids opened (the patient resists eyelid opening when the examiner tries to open it)
- Failure of the patient's arm, when held by the examiner over the patent's face, to fall up on the face when released by the examiner.
- Nystagmus when the ear is irrigated with cold water
- Adversive head and eye movements

Laboratory investigations

- ***Blood film, CBC, urine analysis***
- ***Measurements of serum glucose level, renal and liver function test.***
- ***Lumbar puncture and CSF examination*** should be done as soon as possible unless increased intracranial pressure is suspected to exclude infections and subarachnoid hemorrhage.
- Measurements of serum electrolytes, cultures, toxicological analysis, arterial blood gas analysis, EEG and imaging studies are also helpful in diagnosis of coma if available.

Management

- ***Management***
- Ideally the, care of comatose patient is started together with the initial assessment to identify the etiology.
- ***a) Initial therapy*** : Maintaining an adequate airway, optimal ventilation and maintaining adequate perfusion (blood pressure)
- If there is possibility of cervical fracture, immobilization of the neck is essential
- Endothracheal intubation is often indicated to protect the airways
- Blood samples for CBC, electrolyte glucose, RFT, LFT etc should be obtained.

Management

- ***a) Initial therapy*** **:**
- Intravenous thiamine: 100 mg IV with 50 % glucose solution is given. This treatment is given if hypoglycemia is even remote possibility, and thiamine is given with glucose in order to avoid eliciting Wernicke disease in malnourished
- Naloxone(0.4mg) is administered in case of opiate intoxication
- Flumazenil can be given if benzodiazepine or hepatic coma is suspected
- Correct any associated problem like hypertension, hypoglycemia hyperthermia and hypoxia

Management

- ***b) Give care of comatose patient:***
- Monitor vital signs
- Provide adequate ventilation and oxygenation.
- Maintain appropriate position and change position frequently
- Catheterize and insert nasogastric tube
- ***c)*** Manage the primary cause of coma.

Unit 5

Seizure and Epilepsy

5. Seizure and Epilepsy

- **Learning objectives:** at the end of this lesson the student will be able to:
- *1. Define Seizure and epilepsy.*
- *2. Describe the international classification of Seizure.*
- *3. Understand the epidemiology of Seizure and epilepsy.*
- *4. List the etiologies or risk factors for Seizure disorder.*
- *5. Identify the clinical manifestation of different types of Seizure disorders.*
- *6. Understand the Evaluation and diagnostic approach to Seizure.*
- *7. Identify complications of Seizure.*
- *8. List differential diagnosis for Seizure.*
- *9. Manage patients with Seizure or epilepsy.*
- *10. Understand status epileptics and its management.*

Seizure and Epilepsy…

- **Definition:** *Seizure* is a paroxysmal event due to abnormal excessive discharge of cerebral neurons.
- The paroxysmal event may be subtle or dramatic.
- Depending on the distribution of the discharge, the manifestations may be:
  - Motor
  - Sensory
  - Autonomic or
  - Psychiatric manifestation.

Seizure and Epilepsy…

- ***Epilepsy* –** is a syndrome characterized by recurrent (two or more) unprovoked seizure attacks, due to a chronic, underlying process in the brain.
- This definition implies that a person with a single seizure, or recurrent seizures due to correctable or avoidable circumstances, does not necessarily have epilepsy.

International classification of seizures:

- Epileptic seizures can be classified in many different ways. Commonly used classification is the one developed by International League against Epilepsy.
- ***1) Partial seizures: beginning locally***
  - a) Simple partial seizure: (with motor, somatosensory, autonomic or psychiatric symptoms
  - b) Complex partial seizure
  - c) Partial seizures with secondarily generalization

International classification of seizures…

- ***2) Generalized seizures***
  - a) Absence seizures (petit mal)
  - b) Tonic – clinical seizures (grand mal)
  - c) Myoclonic seizures
  - d) Clonic seizures
  - e) Tonic Seizures
  - f) Atonic seizures

International classification of seizures…

- ***3) Unclassified***
  - a) Neonatal seizures
  - b) Infantile spasm
- The basis for this classification is manifestations during seizure attack and EEG feature between attacks.
- This classification is useful in understanding underlying etiology, selecting appropriate treatment and understanding the prognosis of seizure type.

Epidemiology

- Epilepsy is estimated to affect 0.5-4% of the population around the world.
- The prevalence is said to be higher in developing countries.
- Grand mal seizure account for 40 to 80 %of all types of epileptic seizures.
- It is estimated that 5-10 % of the population will have at least one seizure attack in their life time, with the highest incidence occurring in early childhood and late adulthood.

Etiology of seizure or risk factors:

- The causes of epilepsy/seizure are vary greatly in different age groups and across different regions of the world
  - ***Idiopathic or cryptogenic*:** in which the cause is unknown, accounts for the majority.
  - ***Genetic factor*** (Family History)
  - ***Perinatal causes*:** perinatal asphyxia, birth trauma, perinatal infection
  - ***CNS infections*:** encephalitis, toxoplasmosis, cerebral malaria,
  - ***Head trauma*:** penetrating head injury, depressed skull fracture, intracranial hemorrhage and prolonged post traumatic coma are associated with increased risk of having seizure disorder.

Etiology of seizure or risk factors…

- ***Neoplasms***: metastatic or primary brain tumors
- ***Vascular causes***: Infarction or stroke, vascular malformations
- ***Metabolic abnormalities***: hyponatremia, hypo or hyperglycemia, Uremia
- ***Inflammatory causes***: Systemic lupus erythromatus
- ***Degenerative diseases:*** Alzheimer's disease
- ***Drugs:*** Theophylline, Cocaine, Lidocaine

Clinical features

- ***I. Partial Seizures:*** these are seizures, which arise from localized region of the brain.
- ***a) Simple partial/focal seizures***
  - These are seizure activities in which consciousness is not impaired.
  - Manifestation can be motor, sensory, autonomic or psychiatric.
  - Motor manifestation is usually focal clonic or tonic movement of angle of mouth, finger or thumbs. This seizure activity may spread over one side of the body (Jacksonian march) to involve larger body part. (E.g. the convulsive activity can start in the face, move to ipsilateral arm, and then to the leg)
  - The rest of manifestations include transient sensory abnormalities, flushing and sweating or odd feelings.

Clinical features

- ***b) Complex partial seizure***
- These are focal seizures activities accompanied by impairment of the patient's ability to maintain normal contact with the environment. The patient is unable to respond appropriately to visual or verbal commands during the seizure, and has impaired recollection or awareness of ictal phase.
- The seizure frequently begins with an aura , which may manifest with hallucination (e.g. Olfactory . visual , auditory or gustatory) and complex illusions (e.g. having experienced a new event)

Clinical features…

- ***b) Complex partial seizure…***
- The start of the ictal phase is often a sudden behavioral arrest or motionless stare, which is often accompanied by automatism, which is involuntary automatic behavior (repeated complex activities like chewing, lip smoking, "picking movement" of the hands , and display of emotions).
- They have also post-ictal confusion and transition to full recovery may take minutes to hours.
- ***c) Partial seizure with secondary generalization***
- These are focal seizures, which evolve into a generalized seizure. These are usually tonic-clonic type and difficult to differentiate from primary generalized tonic-clonic seizure.

Clinical features…

- ***II. Generalized seizures***
- There are seizure disorders which arise from both cerebral hemispheres simultaneously, with without any detectable focal onset.
- **a) *Absence seizure* :**
- It is characterized by sudden and brief lapses of consciousness without loss of postural control.
- The seizure typically lasts for only few seconds, consciousness returns as sudden as it was lost.
- It usually manifests with blank staring and they may have also subtle motor manifestations like blinking of the eyes, chewing movements.
- There is no post-ictal confusion.
- The seizure may occur as many as hundreds of times per day
- It is usually detected by unexplained daydreaming and decline in school performance.
- It usually begins in childhood (4- 8 yrs) , and it often has a good prognosis, with 60-70% of such patients will have spontaneous remission during adolescence.

Clinical features…

- ***b)* Generalized tonic clonic seizure (Grand mal)**
- Is the most common seizure type.
- The seizure usually begins abruptly without warning (no aura or focal manifestations.)
- ***The ictal phase*** is begins with tonic contraction of muscles throughout the body , which is responsible for loud moan or cry (due tonic contraction of the muscles of respiration and the larynx), tonic posturing, respiration is impaired and the patient falls to the ground, and there may be tongue biting due to tonic contraction of the jaw muscles.
- After 10 – 20 seconds the tonic phase evolves to clonic phase characterized by bilateral jerking clonic movement involving the whole body. This lasts for another 1 minute.

Clinical features…

- ***b)* Generalized tonic clonic seizure (Grand mal)**
- ***The post-ictal phase*** is characterized by unresponsiveness, muscle flaccidity, excessive salivation and frothing of saliva which may cause stridorous breathing and partial airway obstruction. Bladder or bowel incontinence may occur at this point.
- Patients gradually regain consciousness over minutes to hours, and during this transition there is typically a period of postictal confusion, headache, muscle ache and fatigue that can last for many hours.

Clinical features…

- ***c) Atonic Seizures*:**
- Are characterized by sudden loss of postural muscle tone, lasting 1 to 2 seconds.
- Consciousness is briefly impaired.
- It usually manifest as a head drop or nodding movement, while a longer seizure may cause the patient to collapse
- ***d) Myoclonic seizure* :**
- Is characterized by a sudden and brief muscle contraction that may involve one part of the body or the entire body.
- A normal common physiologic form of myoclonus is sudden jerking movement observed while falling asleep.
- Pathologic myoclonus is most commonly seen with metabolic disorders, degenerative diseases of the CNS or anoxic brain injury .

Complications

- Status epilepticus
- Accidents
- Hypoxic brain damage
- Mental retardation and impairment of intellectual function
- Sudden death
- Psychosocial (Social stigma).

Diagnostic approach/Evaluation

- Patient's history and physical examination can aid in the determination of whether or not a seizure or some other transient event was responsible for the patient's symptoms
- ***History should include: -***
- ***History of the event***
- Presence of any prodromal symptoms
- Description of seizure by reliable observer
- Post ictal symptoms
- Urinary incontinence, myalgia and tongue bite or oral lacerations are clues to the proper diagnosis.

Diagnostic approach/Evaluation

- ***History of suggesting cause and risk factors***
- Febrile convulsion (history of high grade fever)
- CNS infections (current /Previous)
- Head injury
- Stroke
- Developmental abnormality
- Family history
- Social history (like alcohol abuse)

Diagnostic approach/Evaluation…

- ***Physical examination:*** features that should be looked for include
- Skin for evidence of Neurofibromatosis
- Organomegaly: Metabolic storage diseases
- CVS/ carotid artery - stroke
- Complete neurological exam.
- **Investigations**
- ***EEG (Electroencephalography)*** is most useful test in diagnosis of seizure disorder.
- It should be performed while the patient is asleep and awake. Abnormal EEG supports the diagnosis of seizure and may give information about the type of seizure.
- However abnormal EEG is not adequate for diagnosis of seizure and normal EEG can be found in epileptics.

Diagnostic approach/Evaluation…

- **Investigations**
- ***Neuroimaging preferably MRI*** : may help to see any space occupying lesion in the brain
- ***Other routine laboratory assessment*** may be required in management of patients with epilepsy (CBC. Urinalysis, serum glucose, liver function test, renal function test electrolytes, toxicological screening).
- ***Differential Diagnosis for Seizure***
- Syncope
- Psychogenic seizure (hysteric conversion)
- Transient Ischemic attack
- Migraine

Management:

- **Goal of therapy:**
- Complete control of seizure
- Prevent development of complications and socioeconomic consequences.
- ***Treatment of seizure includes:-***
- ***1. Treatment of underlying condition***
- Metabolic disorders such as hypoglycemia, hyponatremia or drug intoxication should be corrected
- Structural CNS lesion lie tumors may be removed surgically.
- ***2. Avoidance of precipitating factor***
- Maintain normal sleep schedule
- Avoid taking excess alcohol
- Reduce stresses using , physical Exercise , meditation or counseling

Management:

- ***3. Suppression or control of recurrent seizure***
- ***Antiepileptic drug therapy (AEDT)***
- The Goal of antiepileptic therapy is to achieve complete control of seizure with no or minimal side effects, preferably using single agent and easy dosing schedule
- **When do we start anti epileptic drugs?**
- ***Recurrent seizure of unknown cause or a known cause that cannot be reversed***
- ***Single seizure due to :***
  - Identified CNS lesion (tumor, infection, trauma)
  - With abnormal neurologic exam
  - Presenting as status epilepticus
  - With post-ictal Todd's paralysis
  - With strong family history of seizure disorder
  - With abnormal EEG

Management…

- ***Note:*** anticonvulsant therapy is not often initiated in patients with a single, unprovoked convulsion, a normal neurologic examination, and a normal neuroimaging study and EEG unless they experience a second seizure.
- ***General principles*:**
- An attempt is usually made to prevent subsequent seizure using a single agent , in order to limit side effects.
- The drugs should be administered in progressive dose until seizure control has been achieved or until drug toxicity occurs.
- Only if monotherpay fails should a second drug be added to the patient's regimen. If control is achieved, then the first agent might be carefully withdrawn.
- A number of drugs are available for treatment of epilepsy and the choice of medication is based on the seizure type

Table VIII-5-1 Selection of antiepileptic drugs

	Primary GTCS	**Partial**	**Absence**	**Atypical absence , myoclonic, Atonic**
First line	Valproic acid Lamotrigine	Carbamazepine Phenytoin Valproic acid	Valproic acid Ethusuximide	Valproic acid
Second line	Phenytoin Carbamazepine Phenobarbitone	Topiramate Phenobarbitone	Lamotrigin Clonazepam	Clonazepam Lamotrigin Clonazepam Topiramate

Management…

- ***i. Phenobarbitone***
- In developing countries, Phenobarbitone is the drug of choice for the control of partial and GTC seizures, due to the wide availability and cheaper cost of the drug.
- Its efficacy is quite acceptable in comparison to most of the AEDS, but it has some side effects that might interfere with compliance. These side effects have to be explained to the patient and his family early on.
- This drug is available in the following dosage forms: 15, 30, 60 and 100 mg tablets.
- ***Dosage:***
- The usual starting dose for adults is 60 PO daily. If seizure is not controlled the dosage may be increased gradually at intervals of no less than 2-3 weeks to a maximum dose of 200 mg PO BID.

Management…

- **Common side effects of Phenobarbitone**
- Fatigue , Listlessness , depression
- Insomnia (especially in children)
- Distractibility and short attention span (especially in children) and Hyperkinesia, Irritability
- Poor memory
- Decreased libido

Management…

- **Common side effects of Phenobarbitone**
- In cases of treatment failure or poor control with maximum tolerable doses of drug, a second AEDS is often added to the regimen. The addition of a second drug is associated with worsening of adverse effects; hence care should be taken, before one decides to add a second drug to the original regimen.

Management…

- ***ii. Phenytoin:*** is the usual prescribed as a second line drug in resource limited settings like ours mainly because of its availability and cost.
- ***Dosage***:
- 100 mg PO BID or TID , which may be gradually increased to a maximum of 200 mg PO TID (i.e. 600 mg daily)
- ***Side effects:***
- CNS : nystagmus , ataxia
- Gingival hyperplasia
- Coarsening of facial feature
- Toxic hepatitis and liver damage

Management…

- ***iii. Carbamazepine***: is also available in Ethiopia. It is often given for the treatment of partial seizure
- ***Dosage:*** a low initial dosage with gradual increase is advised.
- 200 mg Po BID and gradually increase the dosage by 200 mg every week until the best response is achieved or maximum dose of 1600 mg daily.
- ***Side effects***
- Aplastic anemia
- Dizziness drowsiness
- Skin rash
- Transient diplopia

Management…

- ***When to stop antiepileptic drugs?***
- It is common practice to continue treatment until the patient has been seizure free for at least 3 years.
- Thereafter, consideration of drug withdrawal is based on a number of factors like:-
  - The ease with which control was achieved starting from the time of AED drug initiation.
  - The type of seizure
  - The presence of other neurological co-morbidity e.g. mental retardation, focal neurological deficit.
- The probability of relapse after stopping treatment is somewhere around 10-40%
- It is not known whether remissions for 3 or more years consist of "cure" or " control" and so drug withdrawals have to be gradual, over a period of months to minimize the risks of relapse.
- Most relapses occur within a year of discontinuing of medications. The more severe and long lasting a patient's active epilepsy before remission, the greater the risk of relapse.

Management…

- ***When to refer patients to a neurologist or tertiary level hospital***
- Failure to respond to treatment
- Recurrence of previously controlled seizure
- Change in clinical pattern of seizure
- Appearance of previously absent symptoms/sign
- Development of side effects of a drug

Management…

- ***4. Managing psychosocial issues***
- ***Social stigma*** : avoid misconceptions in the public through health education
- ***Psychiatric problems*** : depression , psychosis ,anxiety should be treated
- ***Social problems*** (education, employment, marriage): encourage patients to go school /work to get married and establish family.
- ***Educate Patients and families:*** about the diseases and what precautions patient should take.
  - Seizure /epilepsy can be controlled by drugs
  - Drug discontinuation creates problem and follow up is important

Management…

- ***4. Managing psychosocial issues***
- ***Advice Patients to avoid***
  - Alcohol/ other drugs or substances like “Chat”
  - Heights
  - Cooking with open fire
  - Machineries that may cause injury
  - Swimming
  - Driving

Management…

- ***4. Managing psychosocial issues***
- ***What should families or attendants do during active seizure***
  - No traditional treatment is beneficial
  - To be calm
  - Loosen patient's clothing
  - Keep from injury
  - Turn head to side
  - Do not insert anything into the month

Management…

- ***Surgical Therapy:*** Patient's refractory to medical control of seizure may benefit from surgery to control the epilepsy. Surgical interventions include
- Temporal lobe resection
- Corpus callosum sectioning
- ***Status epilepticus***
- A condition characterized by continuous or repetitive discrete seizure with
- impairment of consciousness during interictal period, which lasts for more than 30 minutes. It is a medical emergency

Management…

- ***It can be caused or precipitated by***
- Non compliance with AED
- CNS infections
- Metabolic derangement
- Tumors
- Trauma
- Stroke
- Refractory epilepsy

Management…

- ***Clinical features:***
- Generalized status epilepticus is obvious when the patient is having over convulsion, however after 30-35 min of uninterrupted seizure, the signs may become increasingly subtle. Patients may have mild clonic movement of only the fingers, or fine, rapid movement of the eyes.
- ***Complications of Status epilepticus:***
- Aspiration
- Hypoxia
- Metabolic acidosis
- Hypotension
- Hyperthermia
- Rhabdomyolysis and associated myoglobinuria
- Multiple physical injures including vertebral bone fracture
- Irreversible neuronal injury

Management…

- ***Management***
- ***1. Emergency supportive measures***
  - Keep Airway patent and maintain breathing
  - Secure IV line and take blood for laboratory investigation
  - Give glucose IV with Thiamine
- ***2. Control the seizure*** with anticonvulsant
  - 1st step: Lorazepam 0.1 mg/kg IC at a rate of 2mg/min or Give diazepam IV 5- 10 mg IV
  - 2nd step: Phenytoin 20 mg/kg IV at a rate of 50 mg /min if seizure continues
  - 3rd step: Phenobarbital 20 mg/kg IV at a rate of 50 -75 mg/min, if seizure still continues
  - 4th Step: General anesthesia with Medazolam, Propofol or pentobarbitol, if seizure becomes refractory In resource limited setting Diazepam 5-10 mg IV is given 2-3 times, and if the seizure is not controlled Phenytion 1000 mg PO is given through NG tube. Phenobarbitone can also be used.

Management…

- ***Management***
- ***3. Treat the precipitating cause (metabolic abnormalities or infections)***
- ***4. Give maintenance antiepileptic drug:*** after the acute condition is controlled.
- ***References:***

- 1) Kasper L., Braunwald E., Harrison's principles of Internal medicine, 16th Edition, Seizure and Epilepsy, pages 2357-2371.
- 2) Myers R. Allen, National Medical Series for independent Study (NMS) 3rd edition Medicine, Seizure, pages 626-628.

UNIT 5

PARKINSONS DISEASE

6. Parkinson's Diseases and other movement disorders

- **Learning objectives:** at the end of this lesson the student will be able to:
- *1. Define Parkinsonism and Parkinson's disease.*
- *2. List the etiologies or Parkinsonism.*
- *3. Understand the epidemiology and risk factors for Parkinsonism.*
- *4. Describe the clinical manifestation of Parkinson's diseases.*
- *5. Understand the principles of management of Parkinson's diseases.*
- *6. Understand the basic clinical features of other movement disorders.*

Parkinsonism:

- ***Definition*:** Parkinsonism is a clinical syndrome characterized by:-
- ***Bradykineisa*:** slowness and paucity of movement
- ***Tremor*:** This occurs at rest
- ***Rigidity***
- ***Snuffling gate*** and
- ***Flexed posture*.**

Parkinsonism…

- **Etiologies:**
- ***1*. Parkinson's Diseases:** It is sporadic and idiopathic with unknown etiology.
- Is the commonest cause of Parkinsonism accounting for 75 % of all cases?
- It is characterized by degeneration of cells in the ***substantia nigra,*** which causes deficiency of dopamine (a neurotransmitter) in the CNS, leading to a series of changes in motor control pathways.
- These degenerative changes are believed to be due to accumulation of the presynaptic protein α-synuclien.

Parkinsonism…

- **Etiologies:**
- ***2. Other known causes :*** *account for 25 % of all cases*
- ***a) Familial (primary Parkinson's diseases)***
- ***b) Other neurodegenerative diseases***
  - Shy-Drager syndrome
  - Motor neuron disease with PD features
  - Dementia with Lewy bodies
  - Progressive supranuclear palsy
  - Wilson's disease
  - Huntington's diseases.

Parkinsonism…

- ***c) Miscellaneous acquired conditions***
- Vascular parkinsonism (stroke affecting the extrapyramidal structures)
- Normal pressure hydrocephalus
- Cerebral palsy
- Repeated trauma:“ dementia puglistica” with parkisonian features (e.g. seen in professional boxers like Mohamed Ali)
- Infectious : post encephalitis PD , Neurosyphilis
- Hypothyroidism or pseydohypoparathyriodism
- Drugs:
- Neroleptics (antipsychotics e.g. Haloperidol ,Chlorpromazine
  - Antiemetics : metoclopromide ,
  - Methyldopa
  - Valproic acid
- Toxins : Cyanide , Methanol , Carbon monoxide, manganese

Parkinsonism…

- **Epidemiology:**
- PD affect > 1 million people in US (1 % of those > 55 years)
- The peak age of onset is the 60s (range is 35-85 years)
- Familial PD tend to have an earlier age of onset (typically before the age of 50 year)
- **Risk factors for Parkinsonism include**
- *Positive family history*
- *Male gender,*
- *Head injury*
- *Exposure to pesticides*
- *Consumption of well water*
- *Rural living*

Parkinsonism…

- ***Clinical Features***
- A diagnosis of PD can be made with some confidence in patients with some confidence in patients who present with at least 2 of the three cardinal signs:
  - Rest tremor
  - Rigidity and
  - Bradykinesia

Parkinsonism…

- ***Motor Features***
- ***Resting tremor:***
- It is present in 85 % of patients with true PD, and a diagnosis of PD is difficult when tremor is absent.
- It starts unilaterally and has a gradual onset, affecting first distally involving the digits and wrist where it may present with “pill –rolling” character.
- Tremor usually spreads proximally, ipsilaterally and occasionally to the leg, before crossing to other side after a year or two.
- It may appear later in the lips, tongue, and jaw but spears the head.

Parkinsonism…

- ***Motor Features***
- ***Bradykinesia/akinesia:***
- It is the most disabling feature which interferes with all aspects of daily living. Patients have trouble in walking, rising from seated position, turning over in bed, dressing etc.
- Fine motor movement is also impaired as evidenced by decreased manual dexterity and hand writing (micrographia)
- Soft speech (hypophonia) is the other of bradykinesia.
- Masked face , decreased eye blinking

Parkinsonism…

- ***Motor Features***
- ***Rigidity:***
- Is felt as a uniform resistance to a passive movement about a joint throughout the full range of motion.
- Brief regular interruption of resistance during passive movement may give rise to“cogwheels rigidity.

Parkinsonism…

- ***Gait disturbance:***
- Patients have shuffling short steps, and a tendency to turn en bolc ,
- ***Festinating gait,*** a typical feature of Parkinsonism, result from a combination of flexed posture and loss of postural reflux, which causes the patient to accelerate in an effort to catch up with the body's centre of gravity.
- ***Freezing of gait***: is a feature of more advanced PD, occurs commonly at the onset of locomotion (start hesitation), when attempting to change direction to turn around and upon entering narrow space such as a doorway.
- Abnormalities of balance and posturing: tends to increase as the disease progress
- ***Stooped posture***: flexion of the head, stooping and tilting of the upper trunk, and tendency to hold the arm in flexed posture while waking is common.
- In advanced diseases postural instability may lead to frequent falls and injuries.

Parkinsonism…

- ***Non motor features:***
- ***Loss of sense of smell*** (anosmia)
- ***Sensory abnormalities*** often manifest as distressing sensation of inner restlessness and aching pain in the muscles of the extremities which often develops as anti-Parkinson's medications are wearing off.
- ***Sleep disorders*** are common in PD, which may manifest as day time drowsiness frequent napping. This may result from disrupted sleep from night time worsening of symptoms and difficulty of turning over in bed
- **Autonomic dysfunction:** may manifest with orthostatic hypotension, constipation urinary urgency and frequency , excessive sweating

Parkinsonism…

- **Neuropsychiatric System**
- ***Depression*** affects approximately half of patents
- ***Anxiety* disorders**
- ***Cognitive abnormalities***: affect many patients and it may manifest with difficulty of doing complex tasks, long term planning, and memorizing or retrieving new information.
- Dementia is 6X more common in PD patients than their age matched controls.
- ***Psychotic symptoms***: affect 6 – 40 % of patients with PD, visual hallucination are common symptoms, and depression and dementia are risk factors for developing psychiatric symptoms.

Parkinsonism…

- ***Treatment***
- The goal of therapy in PD is to maintain function and quality of life and to avoid drug induced complications
- Parkinson's disease is a progressive disease, therefore management protocols vary depending on the patient symptoms and the extent of functional impairment.
- ***1. Pharmacotherapy of motor symptoms:***
- Therapy to control motor symptoms should be initiated as soon as the patient's symptoms begin to interfere with the quality of life.

Parkinsonism…

- ***Early Parkinson's disease:***
- ***a) Selegilline*** is selective and irreversible mono aminoxide (MAO) inhibitor.
- It may slow the clinical progression of Parkinson's diseases and delay the need for other medication.
- This drug has minimal effect on symptoms when used as monotherapy or as an adjuvant to Carbidopa/levodopa.
- Selegilline is used as an initial therapy or added to alleviate tremor of Carbidopa/levodopa associated wearing effect
- ***Dose:*** 5 mg PO with breakfast and lunch

Parkinsonism…

- ***b) Dopamine agonists***: have direct post synaptic effect on do dopamine receptors.
- Dopamine agonist monotherpay is well tolerated and significantly reduced the risk of later treatment –related complications such as motor fluctuation and dyskinesia associated with Carbidopa/levodopa treatment.
- ***Non Ergot alkaloids:***
  - ***Rupinirole:*** Initial dose 0.25 mg Po TID to maximum target dose as monotherapy is 12-24 mg/day
  - ***Parmipexole*** ; Initial dose 0.125 mg PO TID maximum target dose as monotherapy is 1.5-4.5 mg /day

Parkinsonism…

- ***Ergot alkaloids***
- ***Pergolide;*** Initial dose 0.05 mg PO TID to maximum dose 1.5-6 mg /day
- ***Bromocriptine***: Initial dose 1.25 mg Po BID or TID, to maximum target dose as monotherapy 7.5-15 mg/day
- When dopamine agonists are used as monotherapy, higher doses are required to control symptom. However the dose should be titrated gradually.
- Most patients require the addition of levodopa or another agent, within 1-3 yrs of initiating dopamine agonists
- Older patients and those with akinetic rigidity have a low risk of motor complications and dyskinesia, and may be satisfactorily treated with levodopa as an initial therapy.

Parkinsonism…

- ***Advanced Therapy***
- ***c) Levodopa/Carbidopa Formulation (Sinemet®, Atamet®)***
- ***Levodopa***: is converted to dopamine by presynaptic neuron and therefore increase the amount of neurotransmitter available to the post synaptic dopamine receptor.
- ***Carbidopa:*** blocks systemic/peripheral conversion of levodopa to dopamine, thereby decreasing the undesirable systemic effects of levodopa such as nausea and orthostatic hypotension.
- ***Dose:***
- ***Carbidopa/levodopa*** IR 25/100 mg Initial dose: t/2 tab PO TID, to maximum target dose of 3-6 25/100 mg tabs /day (i.e. 1 -2 tabs PO TID)
- ***Carbidopa/levodopa*** CR 50/200 mg tabs : dose 1tab BID or TID

Parkinsonism…

- ***Advanced Therapy***
- The dosage of these drugs should be escalated gradually
- ***Wearing- off effects:*** management of Parkinson's disease becomes increasingly difficult as the disease progresses. Late treatment related complications include.
- ***Dsykineisa:*** refers to choreiform and dytonic movements that occur as a peak dose effect or at the beginning or end of the dose.
- ***Motor fluctuation:*** (on and off phenomenon) these are wide random swings in the patient's mobility or exaggerated ebb and flow of Parkinsonian signs, experienced by many patients between doses of anti-Parkinson medication.
- *More than 50 % of patients with PD treated over five years with levodopa will develop these complications*

Management…

- ***d) Levodopa Augmentation :***
- ***i) Catechol O-methytransferase (COMT) inhibitors***
- Estacapone and tolcapone offer augmentation of the effect of levodopa by blocking enzymatic degradation of levodopa and dopamine.
- These drugs are used in conjunction with Carbidopa/levodopa , they alleviate the wearing off symptoms
- ***ii) Anti-cholinergics*** :are given as adjuncts to dopaminomimetic therapy
- They are useful in controlling resting tremor and dystonia
- Bezhexol is a drug which is available and commonly used

Management…

- ***iii) Amantadine*** : has anti-cholinergic and dopaminomimetic properties
- It helps to reduce drug induced dyskinesia
- Can be effective early in the course of the diseases, or as an adjunct therapy later in the diseases course to help " smooth out " motor function
- ***2. Neuroprotective therapy***
- Reducing the progression of PD through neuroprotective or restorative therapy is a major focus of research.
- Some of the neuroprotecitve treatment trails arte

Management…

- ***Non steroidal anti-inflammatory agents***
- ***Estrogens replacement therapy*** in post menopausal women
- ***Selegilline therap***y delays the need for levodopa therapy by 9 -12 months in newly diagnosed patients. Studies demonstrated that patients who remain on Selegilline for 7 yrs experienced slower motor decline.

Management…

- ***3. Therapy of non motor symptoms***
- ***Insomnia due to nocturnal akinesia*** **:** treated with night time supplemental dose of Carbidopa /levodopa
- ***Depression :*** Responds to anti depressants like Amitriptyline
- **Psychotic patients:** first remove anticholinergics and amantadine if the patient is taking.
- Reduce the dose of dopaminomimetic if the patient is not responding. If still the patient has psychotic symptoms and signs, start antipsychotics with minimal extrapyramidal side effects.

Management…

- ***3. Therapy of non motor symptoms***
- ***Dietary manipulation*** : limiting protein intake during the day may improve levodopa's efficacy
- ***Physical therapy*** and an exercise program help to optimize mobility.
- ***Surgical therapy***
- ***Pallidotomy , and thelamothomy*** ; may be a therapeutic option for refractory Parkinson's diseases
- ***Neurotransplantation***: Transplantation of fetal substantia nigra tissue or cells.

Hyperkinetic disorders

- These are disorders associated with increased movement.
- ***1. Tremor***
- a) Benign essential tremor is characterized by posture related 5-9 Hz oscillation of hands and forearms that impairs performance of fine motor tasks.
- This type of tremor is familial and may be accompanied by titubation (head tremor/bobbing)
- Consumption of alcohol may temporarily suppress the tremor: stress , caffeine or sleep deprivation may exacerbation the condition
- β-adrenergic blocking agents are effective in controlling tremor.
- a) An Action (kinetic) tremor is evident when the patient moves his or her arms; there may be a relatively mild accompanying postural and intention component.
- Clonazepam treatment can be useful.

2. Myoclonus

- **Definition:** a brief, lightning-like contraction of a muscle or group of muscles.
- **Etiology:**
  - Metabolic derangements (e.g. uremia)
  - Degenerative diseases (e.g. Alzheimer's)
  - Slow virus infections (Creuzfeldt-Jakob disease, subactue sclerosing panencephalitis)
  - Severe closed head trauma
  - Hypoxic-ischemic brain injury

Myoclonus…

- **Signs and symptoms:**
  - Myoclonus may occur normally as a person falls asleep (nocturnal myoclonus).
  - Common hiccup (singultus) is a form of myoclonus affecting the diaphragmatic muscles.
  - Action myoclonus: is a myoclonus that increases with intended movements, It occurs typically after brain injury;
  - Palatal myoclonus is a continuous, rhythmic contraction of posterior pharyngeal muscles.
- **Treatment:**
  - Correct underlying metabolic abnormalities.
  - Clonazepam 0.5-2 mg PO. TID or valproate may be effective.

3. *Tics*

- Brief, rapid, simple or complex involuntary movements, which are stereotypical and repetitive, but not rhythmic.
- ***Simple motor tics*** (e.g. blinking) often begin as nervous mannerisms in childhood or later, and disappear spontaneously.
- ***Complex motor tics*** often resemble fragments of normal behaviour such as touching, smelling and jumping.
- ***Simple phonic tics*** include throat clearing, sniffing and grunting and complex phonic tics include the repetition of words and coprolalia.
- ***Tourette's syndrome***: a complex type of tics disorder characterized by multiple motor and one or more phonic tics that may occur many times a day, nearly every day for more than 1 year.
- ***Treatment***
- Education of patients and their family
- Drugs: Clonidine, Haloperidol

3. Chorea and Athetosis

- **Definition:**
- ***Chorea:*** is brief, purposeless involuntary movements of the distal extremities and face, which may merge imperceptibly into purposeful or semi purposeful acts that mask the involuntary motion.
- ***Athetosis:*** is writhing movements, often with alternating postures of the proximal limbs that blend continuously into a flowing stream of movement. Both often occur together (choreoathetosis).
- ***Etiology:***
- Huntington's disease (see below)
- Thyrotoxicosis
- SLE
- Drugs (antipsychotics)

4. Chorea gravidarum

- It is choreiform movement occurring during pregnancy, often in patients with a history of rheumatic fever.
- Chorea usually begins during the first trimester and resolves spontaneously by or after delivery.
- Rarely, a similar disorder occurs in women taking oral contraceptives.
- Treatment consists of sedation with barbiturates, because other drugs may harm the fetus.

5. Hemiballismus

- It is violent, continuous proximal limb flinging movements confined to one side of the body, usually affecting the arm more than the leg.
- It is caused by a lesion, usually an infarct, in the region of the contralateral sub-thalamic nucleus of Luys.
- Differential diagnosis includes acute hemichorea, usually due to tumor or infarct of the caudate nucleus, and focal seizures. Although disabling, hemiballismus is usually selflimited, lasting 6 to 8 wk.
- Treatment with antipsychotics is often effective.

6. Huntington's Disease

- **Definition:** also called Huntington's chorea, chronic progressive chorea or hereditary chorea.
- It is an *autosomal dominant disorder characterized by choreiform movements and progressive intellectual deterioration, usually beginning in middle age.*
- ***Etiology:*** *Genetically determined.*
- ***Signs and symptoms:*** *Develop insidiously.*
- *Dementia or psychiatric disturbances may precede the disease or develop during the course (anhedonia, asocial behaviour).*

Huntington's Disease…

- *Motor manifestations:* flicking movements of the extremities, a lilting gait, motor impersistence (inability to sustain a motor act, such as tongue protrusion), facial grimacing, ataxia, and dystonia.
- Disorder is always progressive; patients ultimately lose physical and mental abilities to care for themselves.
- ***Treatment:***
- No treatment for the underlying cause.
- Antipsychotics may control behaviour problems (e.g. chlorpromazine 100-900 mg/d PO or haloperidol 10-90 mg/d PO).

7. Dystonia

- **Definition:** Sustained abnormal posture and disruptions of ongoing movement, resulting from alterations in muscle tone; it is classified as generalized, focal or segmental:
- **Generalized dystonia (dystonia musculorum deformans)**
- It is a rare progressive syndrome characterized by movements that result in sustained, often bizarre postures.
- Symptoms usually begin in childhood with inversion and plantar fixation of the foot while walking.
- Generalized dystonia is often hereditary.
- In its most severe form, the disorder can be relentlessly progressive. Severely affected patients may become twisted into grotesque fixed postures.
- Mental function is usually preserved.

Dystonia…

- **Focal dystonia** affects a single body region. Rarely, dystonic movements spread to an adjacent region **(segmental dystonia)**, and even more rarely, the process generalizes.
- **Treatment:**
- Treatment is often unsatisfactory.
- For **generalized dystonia,** high-dose anticholinergics and/or the dopamine-depleting drug reserpine 0.1-0.6 mg/d PO are most often used. Levodopa and carbamazepine benefit a few patients.
- For **focal or segmental dystonias** or for generalized dystonia that severely affects specific body regions, local injection of purified botulinum a toxin is the treatment of choice.

7. Peripheral neuropathy

- ***Definition:*** A general term indicating peripheral nerve disorder of any cause.
- ***Classification of neuropathies***
- Neuropathies may be classified based on:
- ***1. The type of symptoms and signs*** *: Sensory , Motor , Autonomic , Or any combination*
- ***2. Distribution***
- ***Mononeuropathy:*** single nerve affected
- ***Multiple mononeuropathy(mononeuritis multiplex):*** two or more nerves in separate areas affected
- ***Polyneuropathy:*** many nerves simultaneously affected
- ***3. Course*** *:* (acute , subacute or chronic)
- ***4. Nerve conduction test (NCT):*** Axonal or Myelin sheath

Table VIII-7-1 Etiologies of neuropathies based the predominant symptoms or signs

	Causes	
Neuropathy	Acute	Subacute of Chronic
Sensory neuropathy		Sensory neuropathy Diabetes mellitus Leprosy Uremia Alcohol abuse Vitamin deficiency: Vit B1, B6, B12 HIV Hereditary neuropathies Drugs : Cisplatin , Phenytoin Paraneoplatic syndrome
Motor neuropathy	Guillain-Barre syndrome Porphyria Critical illness Poliomyelitis	Chronic inflammatory demyelinating polyneuropathy (CIDP) Lead intoxication
Sensorimotor neuropathy		Diabetes mellitus Uremia Vasculitis Hypothyroidism Paraprotinemias CIDP Drugs Toxins
neuropathy	Guillain-Barre syndrome Porphyria	Diabetes mellitus Amyloidosis Familial dysautonomia

Peripheral neuropathy…

- **Etilogoies based on distribution**
- **1. Mononeuropathy:**
- ***Trauma***: most common cause of localized injury to single nerve
- ***Focal neuropathy***: violent muscular activity, forcible overextension of joint, repeated small traumas
- ***Pressure or entrapment paralysis:*** affects superficial nerves at bony prominences or at narrow canals; also from tumors, bony hyperostosis, casts, crutches, prolonged cramped postures.
- ***Haemorrhage*** into a nerve, exposure to cold or radiation
- ***Tumor invasion***

Peripheral neuropathy…

- **Etilogies based on distribution…**
- **Multiple mononeuropathy (*mononeuritis multiplex)*:**
- ***Collagen vascular disorders*** (polyarteritis nodosa, SLE, Sjörgen's, RA)
- ***Sarcoidosis***
- ***Metabolic diseases*** (diabetes, amyloidosis)
- ***Infectious diseases*** (e.g. HIV, leprosy)

Peripheral neuropathy…

- **Polyneuropathy:**
- Acute febrile diseases: from toxin (e.g. diphtheria), autoimmune reaction (Guillain-Barré syndrome)
- Immunization
- Toxic agents: barbital, phenytoin, heavy metals, carbon monoxide etc.
- Nutritional deficiencies, metabolic disorders: B vitamin deficiency, hypothyroidism, porphyria, sarcoidosis, amyloidosis, uremia, diabetes mellitus.
- Malignancy

Peripheral neuropathy…

- ***Signs and symptoms:***
- **Specific mononeuropathies:**
- Are characterized by pain, weakness and paresthesias in distribution of affected nerve; multiple mononeuropathy is asymmetric; nerves may be involved all at once or progressively.
- **Ulnar nerve palsy:**
- Often caused by trauma to nerve in the ulnar groove of the elbow, or due to compression at cubital tunnel;
- Paresthesia and sensory deficit in 5th and medial half of the 4th fingers is a common finding.
- Thumb adductor, 5th finger abductor and interossei muscles are weak and atrophied.
- Claw hand deformity may occur.

Peripheral neuropathy…

- **Carpal tunnel syndrome:**
- Is compression of median nerve in volar aspect of wrist, may be unilateral or bilateral.
- Paresthesia in radial-palmar aspect of hand and pain over the wrist and palm; pain may be more severe at night.
- Sensory deficit in palmar aspect of first three fingers may follow; thumb abduction and opposition may become weak and muscles atrophied.
- For all, conservative treatment should be tried first, with surgical exploration taking place if no success or worsening of symptoms occurs.

Neuropathies…

- **Radial nerve palsy:**
- Is due to compression of nerve against humerus;
- Weakness of wrist and finger extensors (wrist drop),
- Sensory loss over dorsal aspect of 1st finger.
- **Peroneal nerve palsy:**
- It is usually caused by compression of nerve against fibular neck.
- Weakness of foot dorsiflexion and eversion (foot drop) occurs;
- Sensory deficit over anterolateral aspect of lower leg and dorsum of foot or web space between 1st and 2nd metatarsals can occur.

Neuropathies…

- **Specific polyneuropathies:**
- Are relatively symmetric, often affecting sensory, motor, and vasomotor fibers simultaneously.
- They may affect the axon cylinder or the myelin sheath and, in either form, may be acute (e.g. Guillain-Barré syndrome) or chronic (e.g., renal failure).
- ***Diabetic neuropathy-See section on diabetes***

Diabetes neuropathies…

- ***Sensory polyneuropathy***
- Develops slowly over months or years.
- Sensory abnormalities are common, usually starting in the lower extremities, more severe distally than proximally.
- Peripheral tingling, numbness, burning pain, or deficiencies in joint proprioception and vibratory sensation are often prominent.
- Pain is often worse at night and may be aggravated by touching the affected area or by temperature changes.
- In severe cases, there are objective signs of sensory loss, typically with stocking-and glove distribution.
- Achilles and other deep tendon reflexes are diminished or absent.
- Painless ulcers on the digits or Charcot's joints may develop when sensory loss is profound. Sensory or proprioceptive deficits may lead to gait abnormalities.

Neuropathies…

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Neuropathies…

- ***Motor neuropathy***: results in distal muscle weakness and atrophy.
- ***Autonomic neuropathy***: Autonomic nervous system may be additionally or selectively involved, leading to:
- Nocturnal diarrhoea
- Urinary and faecal incontinence and impotence (erectile dysfunction)
- Postural hypotension.
- Vasomotor symptoms vary. The skin may be paler and drier than normal, sometimes with dusky discoloration; sweating may be excessive.
- Trophic changes (smooth and shiny skin, pitted or ridged nails, and osteoporosis) are common in severe, prolonged cases.

Neuropathies…

- **Polyneuropathy due to nutritional deficiencies:**
- Is commonly seen among alcoholics and the malnourished patients.
- Wasting and symmetric weakness of the distal extremities is usually insidious but can progress rapidly, sometimes accompanied by sensory loss, paresthesia, and pain.
- Aching, cramping, coldness, burning, and numbness in the calves and feet may be worsened by touch.
- Multiple vitamins may be given when etiology is obscure, but they have no proven benefit.

Neuropathies…

- ***Diagnostic approach to neuropathies***
- **History and physical examination**
- **CBC:** e.g. megaloblasts in pernicious anaemia may suggest Vit-B12 deficiency or stippled RBCs indicate lead poisoning.
- **LFT, AP,**
- **Renal function test:** creatinine to assess for renal function test
- **glucose**
- **Urine analysis**
- **Serum protein and electrophoresis** (e.g. multiple myeloma)
- **TFT** if suspicion of thyroid dysfunction
- **Electromyography, nerve conduction velocity tests**
- **Muscle biopsy, sural nerve biopsy** as needed

Neuropathies…

- ***Treatment:***
- Treatment of the underlying cause or systemic disorder; recovery is usually slow
- Traumatic lesions with complete transection of nerve require surgery.
- Entrapment neuropathies may require corticosteroid injections or surgical decompression. Physical therapy and splints reduce the likelihood or severity of contractures.
- If impaired sensation renders the patient prone to injury, protective measures should be taken.
- Autonomic insufficiency is difficult to manage ; orthostatic hypotension can be treated with agents that expand blood volume (e.g. fludrocortisone) and increase vascular tone (epinephrine and yohimbine)
- Tricyclic antidepressants, carbamazepine, phenytoin and capsaicin can help patients suffering room pain.

Guillain-Barré syndrome

- **Definition:** also called Landry's ascending paralysis
- It is an acute inflammatory demyelinating polyradiculoneuropathy.
- It is predominantly motor neuropathy characterized by muscular weakness and arflexia (loss of deep tendon reflexes)
- It has an acute onset and it is usually rapidly progressive in nature.
- There may be also mild distal sensory loss.
- ***Etiology and pathogenesis:***
- The etiology is not known but it is believed to be due to autoimmune damage to the myelin sheath of peripheral nerves.
- In about 2/3 of cases, the disease begins 5 days to 3 wk following an antecedent event such as:
  - *Non specific viral syndrome*
  - *May be associated with HIV infection*
  - *Campylobacter jejuni infection*

Guillain-Barré syndrome…

- Etiology
- *Hepatitis , infectious mononucleosis*
- *Mycoplasma pneumonae infection*
- *Vaccination*
- *Surgery*
- *Lymphoma or*
- *SLE*
- It is the most common acquired demyelinating neuropathy.

Guillain-Barré syndrome…

- ***Signs and symptoms:***
- Relatively symmetric weakness with paresthesia usually begins in the legs and progresses to the arms.
- Weakness typically evolves over hours to a few days, and for 90% of patients, weakness is maximal at 3 wk after which the patent reaches a plateau, and further progression is unlikely.
- Weakness is always more prominent than sensory abnormalities and legs are usually more affected than the arms.

Guillain-Barré syndrome…

- ***Signs and symptoms:***
- Deep tendon reflexes are lost.
- Sphincters (both bladder and bowel) are usually spared.
- More than 50% of patients with severe disease have weakness of facial muscles (diaparesis).
- The lower cranial nerves are also frequently involved, causing bulbar weakness and difficulty of swallowing difficulty of handling secretions and maintaining the airways.

Guillain-Barré syndrome…

- ***Signs and symptoms:***
- Most patients need hospitalization, and almost 30 % require ventilator assistance at some time during their illness due to possible respiratory failure.
- Autonomic dysfunction: wide fluctuation in BP, postural hypotension, and inappropriate ADH secretion, cardiac arrhythmias and pupillary changes occur in severe cases. These complications need close monitoring as they may be fatal.
- Pain is another common feature of GBS. The usual type of pain is deep aching pain in the weakened muscles. Back pain involving the entire spine may also be felt.
- Respiratory paralysis and autonomic dysfunction may be life-threatening.
- About 5% of patients die.

Guillain-Barré syndrome…

- **Diagnosis:**
- ***Presumptive diagnosis is made based on history and physical examination.***
- ***CSF analysis:*** elevated protein but few (<50 mononuclear cells) or no cells not cells (albumino-cytologic dissociation).
- ***Nerve conduction test (NCT):*** slow nerve conduction velocity, evidence of conduction block, and prolonged distal latencies, which suggest demyelination is the usual finding.
- **Differential diagnosis:**
  - Toxins (organic phosphate, botulism),
  - Acute poliomyelitis.
- ***Treatment:***
- *Guillain-Barré syndrome is a medical emergency,* requiring constant monitoring and support of vital functions.

Guillain-Barré syndrome…

- ***General supportive measures:***
- The airway must be kept clear, and vital capacity should be measured frequently, so that respiration can be assisted if necessary.
- Fluid intake should be sufficient to maintain a urine volume of at least 1 to 1.5 L/d.
- Extremities should be protected from trauma and from the pressure of bed rest.
- Heat helps relieve pain, making early physical therapy possible.
- Immobilization, which may cause ankylosis, should be avoided. Passive full-range joint movement should be started immediately and active exercises begun when acute symptoms subside.
- Heparin 5000 U SC BID may help to avoid thromboembolism in bedridden patients.

Guillain-Barré syndrome…

- ***Immunotherapy:***
- ***Plasmapheresis:*** can shorten the length of time that the patient is dependent on respirator and unable to ambulate. Criteria to initiate plamapheresis include the inability of the patient to walk or rapid progression of the diseases.
- ***Immunoglobulin treatment:*** it is also effective and decreases morbidity and hastens recovery.
- Plasmapheresis and immunoglobulin treatment may be given in combination
- ***Steroids are not effective in GBS,*** but in chronic relapsing Polyneuropathy, corticosteroids improve weakness and may be needed for a long time.
- Immunosuppressive drugs (azathioprine) and plasmapheresis benefit some patients.

8. CNS infections

- ***I. Pyogenic (bacterial) meningitis***
- ***Learning Objective***: At the end of this unit the student will be able to
- ***1.*** *Define Bacterial meningitis.*
- ***2.*** *List the etiologies of Bacterial meningitis.*
- ***3.*** *Describe the mode of transmission Bacterial meningitis.*
- ***4.*** *Describe the epidemiology of Bacterial meningitis.*
- ***5.*** *Identify the clinical features of Bacterial meningitis.*
- ***6.*** *List the common complications of Bacterial meningitis.*
- ***7.*** *Describe the most commonly used tests for the diagnosis of Bacterial meningitis.*
- ***8.*** *Make an accurate diagnosis of Bacterial meningitis.*
- ***9.*** *Understand the management of Bacterial meningitis.*
- ***10.*** *Understand methods of prevention Bacterial meningitis.*

CNS infections…

- **Definition:** is an inflammation of the arachnoid layer of the meninges and the fluid that circulates, in the ventricles and sub-arachnoid space (CSF), caused by bacterial infection
- **Etiologic agents:** the causes of bacterial meningitis vary with age:
- ***Infants (< 1 year)***: *E. coli, group-B streptococcus, Listeria monocytogenous* are the commonest causative agents.
- ***Young children/toddlers (age 1- 6 years)*** : *Haemophilus influenza, Meningococcus* account for > 50 % of cases
- ***Adolescents and Adults:*** *Meningococcus, Pneumococcus* are the commonest etiologies
- ***In immunocompromised hosts and cancer patients***: *Listeria, Staphylococcus, Pseudomonas aeruginosa* etc.

CNS infections…

- **Route of infection:**
- ***Droplet infection through the upper airways:*** E.g. In *Meningococcus meningitis,* with possibly epidemic spread
- ***Haematogenous spread:*** e.g. in Pneumococcus pneumonia
- ***Contagious spread from adjacent sites :*** e.g. in otitis media , sinusitis
- ***Direct:*** e.g. in open head injury

CNS infections…

- ***Epidemiology:***
- Bacterial meningitis is the most common form of suppurative CNS infection.
- In the West due to the availability of vaccines for *N. meningitidis* and *H. influenza, S.pneumonae* has become the leading cause of bacterial meningitis.
- However, in African and most developing countries, *N. meningitidis* is still the leading cause of bacterial meningitis in adolescents and adults.
- An outbreak of meningitis epidemic has been documented to occur every 7-10 years in the meningitis belt in African, which includes Kenya.

CNS infections…

- ***Clinical presentation;***
- **Incubation period:** the incubation period for Meningococcal meningitis may range from 1-10 days, but mostly the clinical manifestations occur within in 2-4 days
- Meningitis may manifest as an acute fulminant illness that progress rapidly in few hours or as a subacute infection that progressively worsens over several days.
- The classic clinical triad of meningitis is ***fever, headache and nuchal rigidity (neck stiffness)*** , which are seen in > 90 % of patients .
- Alteration in metal status can occur in > 75 % of patients and can vary from lethargy to comma.
- Nausea and vomiting are common symptoms.

CNS infections…

- ***Clinical presentation;***
- Avoiding light (photophobia) is seen in some patients.
- Seizure occurs as part of the initial presentation of bacterial meningitis, or during the course of the illness in 20-40 % of patients
- In Meningococcal meningitis of sudden onset with severe course, patients develop diffuse erythromatus maculopapular rash which rapidly becomes petechial, purpural or bullos lesions.
- The petichiae are found on the trunk, lower extremities, in the mucous membrane and the conjunctiva, and occasionally on the palms and soles.
- In older and debilitated patients the symptoms of meningitis may be subtle.

CNS infections…

- ***Meningeal signs*** are clinical signs often sound in patients with meningitis
- ***Neck stiffness*** when head is flexed passively
- ***Kerning's sign***: when one leg which is flexed at the hip and knee joints, is passively extended at the knee joint, the other leg flexes at the knee.
- ***Brudzinski's sign:*** Upon passively flexing the head, one notices flexion of both legs at the knees
- ***Note:*** These classic meningeal signs may not be seen in infants, old persons and patients in coma.

CNS infections…

- **Complications:**
- Brain edema,
- Hydrocephalus
- Brain abscess,
- Septic vein thrombosis
- Hearing impairment
- Fulminant meningococcal sepsis: Waterhouse-Friedrichsen syndrome is a clinical condition resulting from hemorrhagic necrosis of the adrenal gland, with multi-organ failure. Patients are hypotensive or in shock. Disseminated intravascular coagulation (DIC) with skin and mucosal purpura and bleedings are commonly seen associated features.

CNS infections…

- **Diagnostic approach**
- History, physical examination,
- Search for possible source of infection(pneumonia , otitis media , sinusitis , head injury)
- CSF analysis
- Identify the organism from CSF and blood (culture, PCR etc.)
- Serologic antibody test : latex agglutination test

CNS infections…

- ***Laboratory findings:***
- ***General signs of inflammation:*** leukocytosis, CRP and ESR ↑
- ***CSF analysis:***
- Gross appearance and opening pressure : CSF looks turbid and the opening pressure is increased (due to raised intra cranial pressure)
- Cell count and differential : polymorphonuclear leukocytosis
- Biochemical tests : glucose is decreases and protein in the CSF is elevated
- Gram stain Culture and sensitivity
  - Meningococcus are seen as gram negative intracellular diplococcic

Table VIII-8-1, CSF analysis findings in different types of meningitis .

	Bacterial meningitis	Viral meningitis	Tuberculous meningitis
Appearance	Turbid	Clear	Cob-web appearance
Cell count/µl	Several thousand	Several hundreds	Several hundreds
Cell type	Granulocytes(PMNLs)	Lymphocytes	Lympho-, monocytes
Glucose	↓ (< 30 mg/dl)	Normal	↓ (< 30 mg/dl)
Protein	↑ (> 120 mg/dl)	Normal ↑	↑ (> 120 mg/dl)
Lactate dehydrogenase (LDH)	> 3.5 mmol/L	< 3.5 mmol/l > 3.5 mmol/l	***Lactate dehydrogenase (LDH)*** > 3.5 mmol/L < 3.5 mmol/l > 3.5 mmol/l

CNS infections…

- **Differential diagnosis:**
- Virally caused meningoencephalitis (Coxsackie-, Echo-, Mumps-virus, HIV, measles, CMV, VZV, HSV)
- Chronic meningitis : Tuberculous meningitis , Cryptococcal meningitis
- Subarachnoid hemorrhage
- **Treatment:**
- ***A. Antibiotic Therapy***
- **1. Empirical antibiotic therapy:**
- Bacterial meningitis is a medical emergency and antibiotics should be initiated immediately before the results of the CSF gram stain and culture are known.
- Antibiotics should be given intravenously, at higher doses
- In adults without underlying disease: Ceftriaxone 2 gm IV BID plus Ampicilline 2 gm IV QID for 2 weeks.

CNS infections…

- Crystalline Penicillin 3-4 million IU, IV every 4 hours plus Choramphnicole 1gm IV QID are alternative antibiotics for a resource limited setting .
- Patients with ENT infection or head injury: Ceftriaxone 2 gm IV BID and Vancomycin 1gm IV BID + treatment of the underlying cause.
- If suspected hospital-acquired infection: Ceftriaxone 2 gm IV BID plus Vancomycin 1 gm IV BID plus Gentamycin (80 mg TID)
- In immunodeficient patients: Ceftriaxone 2 gm IV BID plus Vancomycin 1 gm IV BID plus Ampicillin (2g IV QID)

CNS infections…

- **2. *Specific antibiotic therapy*:** is given when the specific etiologic agent is identified through gram stain or culture
- ***N. meningitidis*** : Even though Ceftriaxone or Cefotaxim provide adequate empirical coverage , Penicillin G remains the drug of choice for *N. Meningitides*
- Crystalline Penicillin 3-4 million IU, IV every 4 hours for 7 -10 days may be adequate.
- ***Pneumococcal meningitis*:** Antibiotic therapy in initiated with Cephalosporins plus Vancomycine
- Ceftriaxone 2 gm IV BID and Vancomycin 1 gm IV BID for 2 weeks
- ***H. influenza*** : Ceftriaxone 2 gm IV BID for 1- 14 days may be enough Choramphnicole 1gm IV QID may be an alternative antibiotic, for patients who may not afford Ceftriaxone.

CNS infections…

- ***B. Symptomatic and adjunctive Therapy***
- ***Steroids:***
  - ***Dexamethasone*** when initiated before antibiotic therapy reduces the number of unfavourable outcomes, including death and neurologic complications. It is mainly advantageous in children, predominantly with meningitis due to *H.Influenza and S. Pneumoniae.*
- ***Dose***: Dexamethason10 mg IV 15-20 minutes before the first dose of antibiotics and 4 mg IV QID for 4 days

CNS infections…

- ***B. Symptomatic and adjunctive Therapy***
- ***Treat increased intracranial pressure:***
  - Elevation of the patients head to 30-45°
  - Intubation and hyperventilation (till PaCO2 is lowered to 25-30 mmHg)
  - Mannitol IV infusion
- ***Regulate water and electrolyte balance,***
- ***Thromboembolism prophylaxis***
- ***Patients with meningococcal meningitis should be isolated.***

CNS infections…

- ***Chemoprophylaxis:*** In case of *N. Meningitides,* all close contact to the patient should be given chemoprophylaxis with:-
- Rifampicin 600 mg PO BID for 2 days in adults and 10mg/kg PO BID for children > 1 yr.
- Ciprofloxacin 750 mg PO stat can be given as an alternative for adults.

II. Viral encephalitis

- ***Learning Objective***: At the end of this unit the student will be able to
- *1. Define viral encephalitis.*
- *2. List the etiologies of viral encephalitis.*
- *3. Identify the clinical features of viral encephalitis.*
- *4. Describe the most commonly used tests for the diagnosis of viral encephalitis.*
- *5. Understand the management of viral encephalitis.*

Viral encephalitis…

- **Definition:** Inflammation of the brain parenchyma, with or without involvement of the meninges, caused by virus. The spinal cord and/or nerve roots may also involved rarely.
- **Signs and symptoms:**
- Acute febrile illness with evidence of meningeal involvement (meningeal signs)
- Altered level of consciousness (ranging from lethargy to coma)
- Abnormal mental state (hallucinations, agitation, personality change, behavioural disorder, psychosis)
- Evidence of either focal or diffuse neurologic signs or symptoms.
- Focal or generalized seizures occur in > 50 % of cases.
- Most common focal findings are aphasia, ataxia, hemiparesis (with hyperactive tendon reflexes), involuntary movements and cranial nerve deficits.

Organisms: Viruses causing encephalitis

Common	Less common Rare	Common Less common Rare
Arboviruses, enteroviruses, HSV-1, mumps	CMV, EBV, HIV, measles, VZV	Adenoviruses, CTFV, influenza A, LCMV, parainfluenza, rabies, rubella

Viral encephalitis…

- **Laboratory findings:**
- ***CSF examination:*** check for increased intracranial pressure first. Characteristic profile is undistinguishable from viral meningitis and consists of lympocytic pleocytosis, elevated protein, normal glucose level
- CSF PCR, if available
- CSF culture, usually negative (esp. in HSV-1 infections)
- Serologic studies and antigen detection, if available
- MRI, CT, and EEG: if available, done to exclude alternative diagnoses, and assist in differentiation between focal and diffuse encephalitic process (e.g. 90 % of patients with HSV-1 infection have abnormalities in the temporal lobe on MRI).
- ***Brain biopsy:*** reserved for patients with unclear diagnosis, lack of response to therapy and who have abnormalities on imaging techniques.

Viral encephalitis…

- **Treatment:**
- ***Supportive therapy (usually in ICU):***
- Check vital signs, restrict fluid, and give antipyretics.
- Treat seizures and/or give prophylactic therapy (high risk for seizures!).
- ***Medication:***
- Acyclovir 10 mg/kg TID for at least 14 days (adult dose).
- Gancyclovir (5 mg/kg BID) or Foscarnet (60 mg/kg TID) are especially recommended for CMV infections.