Chapter 16

Neurologic & Neuromuscular Disorders

CONTENTS

1. SEIZURES AND EPILEPSY

Convulsions are common in childhood. Nearly 5% of all children suffer one or more convulsions before 5 years of age, more than 50% of these are febrile convulsions.

Definitions:

A seizure: is a sudden,paroxysmal disruption of the brain's normal electrical activity accompanied by altered consciousness and/or other neurological and behavioral manifestations.

Seizures are not a disease in themselves. Instead, they are a symptom of many different disorders that can affect the brain.

Convulsion: This means a motor seizure and consists of abnormal involuntary muscular contractions which may be:

- Sustained (tonic).
- Interrupted (clonic).
- Brief, jerk-like (myoclonic).

Epilepsy: means recurrent seizures.

Causes of convulsions:

1- Acute convulsions:

1- Febrile convulsions.

2- Intracranial infections: meningitis, encephalitis, brain abscess.

3- Head injuries: birth trauma or later in life.

4- Intracranial hemorrhage due to birth or later trauma, hemorrhagic diseases, or vascular malformations.

5- Brain anoxia:

a) Prenatal or perinatal asphyxia.

b) Severe bronchopulmonary disease.

c) Hypercyanotic attacks of congenital cyanotic heart disease.

6- Metabolic: hypocalcemia, hypomagnesemia, hypoglycemia, hypernatremia, alkalosis, post-acidosis.

7- Toxic agents as:

- Bacterial toxins of shigella, salmonalla, tetanus.
- Poisons: insecticides, lead.
- Drugs: theophylline, corticosteroids, strychnine.

8- Intracranial neoplasm (brain tumor).

9- Cerebrovascular:

- Embolism (subacute bacterial endocarditis).
- Thrombosis (cyanotic heart disease, dehydration).
- Hypertensive encephalopathy.

2- Chronic (recurrent) convulsions i.e. epilepsy:

a- Primary (idiopathic).

b- Secondary.

FEBRILE CONVULSIONS

Definition: Febrile convulsions are tonic-clonic convulsions due to rapid rise of body temperature caused by extracranial infections.

Epidemiology:

- They are the most common seizure disorder during childhood. The incidence approaches 3-4 % of young children.
- They are age dependent and are rare before 6 mo and after 5 yr of age. The peak age of onset is approximately 14-18 mo of age.
- There is a strong family history of febrile convulsions in siblings and parents, suggesting a genetic predisposition. An autosomal dominant inheritance pattern is demonstrated in some families.

Types of febrile convulsions:

1- **Typical** (primary, simple or benign).

2- **Atypical** (secondary, complex or complicated).

The typical seizure is characterized by the following:

- Age from 6 mo – 6 yr.
- Generalized tonic-clonic.
- Single during the same febrile illness.
- A few seconds to 10 minutes in duration.
- No neurological abnormalities in the child.
- EEG is normal in between the attacks.

The atypical seizure is diagnosed if one of the following is present:

1. A seizure persisting more than 15 min.
2. Repeated convulsions occur within the same day.
3. A focal seizure.

The risk factors for the development of epilepsy as a complication of febrile seizures include:

1. Atypical febrile seizure.
2. A positive family history of epilepsy.
3. Initial febrile seizure prior to 6 mo or after 6 yr of age.
4. Delayed developmental milestones.
5. An abnormal neurological examination.
6. Abnormal EEG inbetween the attacks.

The incidence of epilepsy is approximately 9 % when several risk factors are present compared with an incidence of 1 % in children who have febrile convulsions and no risk factors.

Management of febrile convulsions:

1. Aborting the attack of convulsion with diazepam 0.3 mg/kg slowly intravenously or rectally. This dose can be repeated after 10 minutes if needed.
2. Lowering the body temperature with tepid sponges (no ice or alcohol) and antipyretics.
3. Treating the cause of fever e.g antibiotics for otitis media.
4. Excluding intracranial infections by doing lumbar puncture and CSF examination if any doubt exists.

Prophylactic therapy:

Diazepam has been shown to be effective in preventing recurrences if given together with a potent antipyretic immediately at the onset of fever and continued until the patient has been a febrile for 24 hours. Diazepam dosage is 0.3 mg / kg orally every 8 hours (1 mg / kg / 24 hr).

Prolonged antiepileptic drug (AED) prophylaxis:

i- May be given for patients with secondary febrile convulsions with risk factors for epilepsy and with abnormal EEG.

ii- No need for long-term AED in primary febrile convulsions because these are ineffective and have many side effects.

EPILEPSY

Definition: Recurrent seizures unrelated to fever or to an acute cerebral insult

(two or more unprovoked seizures occur at an interval greater than 24 hr apart are needed for the diagnosis).

Epidemiology:

Epilepsy has a prevalence of 5-10/1000 population, 60% of cases occur in the pediatric age.

Etiology: Epilepsy is divided into two groups:

A- Idiopathic (primary):

- This is the main group and most of the patients (2/3 of cases) belong to it.
- It is called idiopathic because the etiology is unknown. The only important factor is heredity. In more than 90 % of cases a positive family history of epilepsy is present.

B- Symptomatic (secondary):

- The minority of patients belongs to this group (1/3 of cases).
- It occurs secondary to a brain lesion.
- **The common causes are:**

1- Congenital conditions: e.g. congenital hydrocephalus, microcephaly, cerebral agenesis, and vascular anomalies.

2- Post-infectious: following encephalitis, meningitis and brain abscess.

3- Post traumatic. 4-Post hypoxic. 5-Post–hypoglycemic.

6-Post–toxic (e.g after kernicterus).

7-Degenerative brain diseases.

4- Parasitic e.g. toxoplasmosis.

5- General causes: e.gTetany, Uremia

Classification of epileptic seizures:

A classification useful in delineating childhood epilepsy is shown in **table 1.**

TABLE 1- International classification of seizures

I- Partial (Focal) Seizures

1. Simple partial (consciousness is retained)

- Motor -Sensory -Autonomic -Psychic

2. Complex partial (consciousness is impaired):

3. Partial seizures with secondary generalization

II- Generalized Seizures

a. Absence:

-Typical - Atypical

b. Generalized tonic-clonic:

- Tonic
- Clonic
- Tonic-clonic

c. Myoclonic

d. Atonic (Akinetic)

III-Unclassified seizures

The best example is subtle neonatal seizures

1- Partial (focal) seizures

- Arise from a focal area in brain (cortical or subcortical).
- Give focal manifestations related to the area of origin.
- No loss of consciousness.
- May be associated with a preceding aura which indicates a focal onset of the seizure (usually absent in infants and young children).
- EEG: focal abnormalities.
- Partial seizures may be:

1. Simple (with no loss of consciousness).
2. Complex (consciousness is impaired).

2 - Generalized seizures

- Arise from subcortical structures (thalamus and brain stem)
- Give generalized manifestations (both cerebral hemispheres are involved)
- Consciousness is lost
- EEG: generalized abnormalities
- Generalized seizures may be:

1. Tonic-clonic (grand mal)
2. Absence (petit mal)
3. Myoclonic
4. Atonic (akinetic)

3- Partial with secondary generalization

- Arise from focal area
- Starts with localized manifestations followed by secondary spread to the other side and loss of consciousness
- EEG: focal abnormalities with secondary generalization.

Pathogenesis:

- The normal, spontaneous electrical activity of the brain can be recorded by the electroencephalogram (EEG).
- In epilepsy there is paroxysmal increase in the electrical activity of the brain. For this reason epilepsy has been described as “paroxysmal cerebral dysrhythmia”.
- The zone of origin of the abnormal electrical activity is called the epileptogenic focus which may be:

a) Centrencephalic (subcortical)

b) Cortical.

GENERALIZED TONIC-CLONIC SEIZURES

(Grand mal epilepsy)

May occur at any age. Three clinical stages may be detected to occur successively:

1- **Preconvulsive stage (occurs in few cases)**: As pallor, irritability or behavioral changes. Parents may be familiar with these changes.

2- **Convulsive stage**:

The attack usually occurs without warning. The consciousness is suddenly lost and the child falls to the ground.

a) Tonic phase: during this phase there is sustained contraction of the muscles, apnea, cyanosis and tongue biting.

b) Clonic phase: during this phase there is repetitive contraction of muscles, frothing at the mouth, and at the end of the attack relaxation of sphincters occur leading to bedwetting and sometimes defecation..

The convulsive stage lasts from one to several minutes.

3- Post-ictal stage:

After the attack, the patient falls asleep or suffers from headache, depression and confusion and on rising he is completely normal.

Precipitating factors of generalized tonic-clonic seizures in children:

1. Excessive fatigue.
2. Lack of sleep.
3. Infectious illnesses and fever.
4. Emotional stress.
5. Drugs as theophylline, psychotropic drugs, methylphenidate.
6. Sensory stimuli such as flashing lights, visual patterns, sounds including music and startling by noise or touch.
7. Sudden withdrawal of AED.

Recurrence rate:

- Very low after a single fit.
- About 50% if the child had more than one fit.

ABSENCE (petit mal)

- Usually in children more than five years old, more in females.
- There is sudden loss of voluntary motor activity.
- The child loses consciousness but doesn't lose postural tone (does not fall).
- There is a blank star and rapid eye blinking.
- This lasts around 30 seconds and then the child resumes his / her preseizure activity
- No postictal confusion.
- The attack can be induced by hyperventilation
- Has a charachteristic EEG pattern (3 per second spike and wave pattern).
- May be associated with poor school performance.
- Etiology: idiopathic (genetic).
- Good response to ethosuxcimide and sodium valproate with good prognosis.
- 60% of children experience remissions by late adolescence.

MYOCLONIC SEIZURES

- The attack is characterized by short involuntary muscle contractions usually of a localized group of muscles
- Upper limbs are more commonly affected
- More frequent in the morning after awakening
- Loss of consciousness may not be noticed due to very short duration.

INFANTILE SPASMS

- Also called infantile myoclonic seizures
- Occur in infants below 2 yr of age (usually begin between the ages of 4 and 8 mo).
- There are 3 types of infantile spasms: flexor, extensor, and mixed.
- **Flexor** spasms are more common. Usually occur in clusters or volleys, and consist of sudden dropping of the head, flexion of the arms, flexion of the legs to the abdomen and crying (like colic).
- **Extensor** spasms produce extension of the trunk and extremities.
- **Mixed** spasms consist of flexion in some volleys and extension in others.
- Disappear before the 4^{th} yr of life to be followed by an other type of seizure.
- 10-20 % are idiopathic, and the remainder are **symptomatic**.
- Symptomatic infantile spasms are related to severe prenatal, perinatal, and postnatal factors.
- Have a characteristic EEG pattern (hypsarrythmia).
- May or may not be associated with mental retardation
- Good response to ACTH or prednisone

ATONIC (Akinetic) SEIZURES
(Drop attack)

- Is characterized by sudden loss of muscle tone and fall to the ground.
- In infants it takes the form of sudden drop of the head forward.
- It may be associated with momentary loss of consciousness.
- No tonic or clonic movements

SIMPLE PARTIAL (FOCAL) SEIZURES

- They may be motor (muscle contractions), sensory (numbness, auditory hallucinations, flashes of light) or autonomic (sweating, tachycardia or abdominal pain,…).
- The motor seizure may start locally in a part of the body and then spreads to adjacent parts (with jacksonian march) or may involve the whole limb from the start (without jacksonian march).
- Weakness of the affected limp may follow temporarily (Todd's paralysis).
- The patient remains conscious.
- No postictal phenomenon follows the event.

COMPLEX PARTIAL SEIZURES
(Psychomotor seizures)

Complex partial seizure (CPS) is also called temporal lobe epilepsy.

- Complex = motor + sensory + autonomic
- The early part is often remembered as a dreamy state
- Motor manifestations (**automatism)**:
    - In infants : automatic behavior consists of masticatory movements as lip smacking, chewing, swallowing, and excessive salivation.
    - In older children: automatic behavior consists of semi-purposeful,incoordinated movements including Picking and pulling at clothing or bed sheets, rubbing or caressing objects, and walking or running in a nondirective fashion.
- Sensory manifestations: hallucinations, disturbance of perception
- Autonomic manifestations: fear, anxiety, anger, aggression.
- CPS may be precipitated by sleep deprivation.

- The EEG usually shows a focal discharge in the anterior temporal lobe. In some children the abnormal discharge arises from the frontal, parietal, or occipital lobes.
- Temporal lobe epilepsy may be associated with visual field defects due to involvement of optic radiations in the temporal lobe.
- Spreading of the epileptiform discharge during CPS can result in secondary generalization with a tonic-clonic convulsion.

Diagnosis of epilepsy:

1. This is essentially on clinical basis, through history from the parents and observation by the pediatrician.
2. Investigation of the suspected cause e.g. metabolic studies, CSF examination, MRI.
3. EEG: if positive is confirmatory. It may be normal in more than 30 % of epileptic children. A normal EEG does not exclude epilepsy.

Sometimes prolonged video monitoring of the EEG may be needed to prove the occurrence of seizures.

Differential diagnosis:

Epilepsy should be differentiated from “recurrent events” that mimic epilepsy in childhood. The most common are:

1. Breath holding attack.
2. Syncope.
3. Pseudoseizures (Psychogenic).

Prognosis:

70 % outgrow their seizure tendency with remission.

30 % may have recurrences especially during the first year after withdrawal of treatment.

Recurrence risk factors:

- Age of onset less than 2yr
- Neurological dysfunction
- Mental retardation
- Seizure type: infantile spasms
- Difficult control with polytherapy
- Abnormal EEG at stoppage of treatment

TREATMENT OF EPILEPSY

1- General treatment:

- An epileptic child should, as far as possible, lives a normal life
- The child should attend school
- The patient should avoid situations of obvious dangers e.g. swimming and working at a height
- The parents should avoid the precipitating factors
- Moderate exercise is desirable but violent ones may precipitate fits

2- During the attack of convulsion:

A- First aid:

- Put the patient in semi prone position with the head turned to one side
- Suctioning and cleaning of the airways
- Do not thrust a tongue depressor or spoon handle into clenched teeth.
- Do not try to restrain the patient.

B- Give oxygen if the patient is cyanosed.

C- Correct the cause if it is evident (e.g. glucose in hypoglycemia and calcium in cases of tetany).

D- If the cause is not evident or not readily correctable, give diazepam, 0.3 mg/kg slowly intravenously. This dose can be repeated after 10 minutes.

3- Long term therapy with AEDs:

A- Indications:

AED therapy is indicated only if the patient had more than one fit.

For a patient with isolated fit (i.e a single afebrile fit), AED therapy is indicated only if:

- The patient is neurologically abnormal
- The presence of a focal brain lesion
- Positive family history of epilepsy
- Abnormal EEG

B- Rules:

- Only one drug, known to be effective for the seizure type, should be used in a small dose that is increased gradually at intervals of two weeks till the fit is controlled or the maximum dose is reached.
- If the drug is ineffective, start a 2nd one in a similar way, and once seizures are controlled, start gradual withdrawal of the first one.
- The dose must increase with the increase in age and weight.
- Avoid double or triple drug therapy as far as possible.
- Treatment is continued for at least 2-seizure free years and discontinued gradually over 3-6-month period.

C- Follow up:

I- Because most serious adverse effects of anticonvulsant drugs develop during the initial 2-3 mo of therapy, screening of **complete blood count and liver function studies** should be done every month for the first 3 months. Subsequently, routine blood tests are ordered only when clinically indicated.

II- Routine Serum monitoring of anticonvulsant levels is not recommended.

D- Common AEDs are:

1- Conventional AEDs (Table 2):

Table 2: Conventional antiepileptic drugs

Drug	Seizure type	Oral dose (mg/kg/day)	Most common side effects
Phenobarbital	GTC. Partial Status epilepticus	2 - 6	Drowsiness. Hyperactivity. Impaired cognition.
Phenytoin	GTC Partial Status epilepticus	5 - 8	Hirsutism. Gum hypertrophy. Ataxia. Skin rash. Impaired cognition. Rickets.
Carbamazepine	Partial GTC	10 - 30	Drowsiness. Liver dysfunction. Hematological abnormalities
Sodium valproate	GTC Partial Absence Myoclonic	10 - 60	Weight gain. Alopecia. Tremor. Liver dysfunction. Hematol. abnormalities.
Ethosuximide	Absence	20 - 40	GIT disturbances. Skin rash. Liver dysfunction. Leucopenia.
Clonazepam	Absence Myoclonic Infantile spasm Partial seizures Akinetic Lennox-Gastaut syndrome	0.05 – 0.2	Drowsiness. Irritability. Behavioral abnormalities. Depression. Excessive salivation.

GTC= Generalized tonic clonic

- Valproate: is a broad spectrum AED.
- Carbamazepine: is more preferable in partial seizures.
- Phenobarbital and phenytoin are less frequently used now due to their effects on cognition.

2- Second line AEDs: e.g oxycarbazepine, topiramate, vigabatrin, lamotrigine, leviteracetam

STATUS EPILEPTICUS (SE)

Definition:

Status epilepticus is defined as a continuous convulsion lasting greater than 30 min, or

The recurrence of serial convulsions between which there is no return of consciousness.

Etiology:

1. A prolonged febrile convulsion in a child < 3 yr old, is the most common cause
2. Rapid withdrawal of AED at any age
3. Idiopathic SE: a seizure develops in the absence of an underlying CNS lesion or insult
4. Symptomatic SE: a seizure occurs in association with a longstanding neurological disorder or a metabolic abnormality

Treatment:

A- Airway patency: by suctioning, semi prone position ± put airway tube

B- Breathing: should be adequate

C-Circulation: should be insured

D- Drugs: all drugs should be given IV. AEDs are tried in the following order:

1. Diazepam (0.3mg/kg) is used initially.
2. Phenytoin infusion: IV loading dose 20 mg/kg slowly over 30 min, followed 12 hours later by maintenance dose of 5-8 mg/kg /day in two divided doses.
3. Phenobarbital: IV loading dose 20 mg/kg slowly over 30 min, followed 12 hours later by maintenance dose of 3-5 mg/kg /day in two divided doses.
4. Diazepam IV infusion 2 mg / hour.
5. General anesthesia and assisted ventilation is given if the above-mentioned measures fail.

2. CEREBRAL PALSY (CP)

CP is a non-progressive permanent motor disorder (affecting muscle power, tone, movements, coordination or posture) due to brain insult, which occurs during early brain growth (from conception to 3 yr of age).

It may or may not be associated with epilepsy, mental retardation, visual / hearing impairment, and / or language delay.

Incidence: 2 / 1,000 population.

Etiology:

CP results from damage affecting motor areas of brain (motor cortex, basal ganglia, cerebellum) due to:

1- Prenatal factors (10-20 % of cases):

- Intrauterine infection: TORCH, other viruses
- Prenatal anoxia
- Fetal irradiation
- Congenital CNS malformations
- Primary microcephaly
- Placental insufficiency

2- Natal factors (40-60 % of cases):

- Birth trauma
- Neonatal anoxia

3- Postnatal factors (20-30 %):

- Kernicterus
- Intracranial infections e.g. meningitis, encephalitis
- Brain trauma
- Dehydration
- Cerebral anoxia
- Vascular lesions e.g. cerebral hemorrhage and thrombosis

Early detection of CP in high risk neonate:

- Poor suckling ability
- Increased or decreased muscle tone
- Abnormal reflexes
- Irritability

Detection of CP later in life:

1- Delayed motor development (e.g. lack of head control at 3 months)

2- Abnormal motor development:

- Baby is stiff on handling
- Early handedness (before one year) may be early sign of hemiplegic CP
- Very early neck support or persistent toe walking **(may be early sign of spastic CP)**
- Persistent hand clenching (after 3 months)
- Persistence of primitive reflexes (tonic neck reflex, Moro reflex, grasp reflex) beyond their age limit
- Absence of normal protective cortical reflexes as parachute reaction
- Floppiness, hypotonia, and involuntary movements

Clinical types of CP:

1- **Spastic CP**: lesion in pyramidal area.

2- **Extrapyramidal CP**: Lesion in basal ganglia.

3- **Ataxic CP**: lesion in cerebellum.

4- **Atonic CP**: an evolutional stage in the development of spastic CP.

5- **Mixed CP**.

Spastic Cerebral palsy

It is the commonest type of CP. It accounts for 70 % of cases.

It is caused by affection of motor cerebral cortex and its connections (pyramidal area).

There is increased tone (clasp knife), increased tendon reflexes, extensor planter responses, clonus, scissoring of legs.

Spastic quadriplegia, double hemiplegia and diplegia are commonly associated with:

1. Mental retardation
2. Seizures
3. Swallowing difficulties due to supranuclear bulbar palsies
4. Persistence of primitive reflexes.

Topographically it includes:

TYPE	AFFECTED LIMB	COMMENTS
Monoplegia	One limb	
Paraplegia	Both lower limbs	
Triplegia	Both lower limbs and one upper limb	
Hemiplegia	One side of the body	Upper limb is more affected than lower limb
Quadriplegia	Affection of 4 limbs + trunk	
Tetraplegia	4 limbs	All limbs are equally affected
Double hemiplegia	4 limbs	Upper limbs are more affected than lower limbs
Diplegia	4 limbs	Lower limbs are more affected than upper limbs

Extrapyramidal (Athetoid) Cerebral Palsy

- Accounts for 10 % of cases of CP.
- It is caused by a lesion of the basal ganglia, usually as a sequel of kernicterus.
- Early in life: Infants are characteristically hypotonic and have poor head control and marked head lag.
- At about one year of age, involuntary movements in the form of choreo-athetosis and dystonia appear and the muscle tone is increased (rigidity).
- Speech is typically affected owing to involvement of the oropharyngeal muscles.
- Seizures are uncommon, and intellect is preserved in most patients.

Ataxic Cerebral Palsy

- Accounts for 10 % of cases of CP.
- It is caused by affection of the cerebellum.
- Early in life: association of hypotonia, floppiness and weakness.

Later on it is characterized by:

1) Ataxia (disturbed gait)
2) Incoordination of movements
3) Ataxic speech
4) Intention tremors
5) Nystagmus may be present
6) Hypotonia and diminished deep tendon reflexes
7) Mental retardation is slight

Atonic Cerebral Palsy

It is characterized by:

- It will be changed into a spastic type after a period of time.
- Generalized hypotonia.
- Exaggerated deep tendon reflexes.
- Mental retardation.

Mixed Cerebral Palsy

- Accounts for 10 % of cases of CP.
- Usually one type is more manifest.
- The common mixed CP is spastic and athetoid type.

Differential diagnosis:

1. Degenerative CNS diseases
2. Spinal cord tumor
3. Muscular dystrophy

Investigations:

1. Brain CT scan or magnetic resonance imaging (MRI)
2. EEG
3. Tests for auditory and visual acuity

Associated disabilities with CP:

1- Epilepsy:

Occur in 30 % of cases.

It is of the symptomatic rather than the idiopathic type.

Treatment may need more than one drug and usually given for life.

2- Mental retardation, and learning problems:

60 % of children with CP have some degree of mental retardation.

However, many children with severe CP, especially the dystonic type may have normal intelligence.

3- Perceptual defects:

Visual impairment due to refractive errors, optic atrophy or visual cortical damage occurs in 20 % 0f cases.

Squint in 30 % 0f cases. Early treatment is needed.

Hearing loss of sensory neural type is common in 20 % of cases.

4- Speech disorders: common and may be due to

- Hearing loss
- Mental retardation
- Muscular incoordination

Management of CP:

Management of CP is a teamwork aiming at offering the child the best quality of life he can have and to reduce parent's stress.

This needs the cooperation of pediatrician, physiotherapist, orthopedist, speech therapist and nutrionist.

Treatment consists of:

1. **Education:** depends on the degree of brain affection
2. **Drugs:** Muscle relaxants: (oral diazepam, baclofen, IM botulinum toxin type A, intrathecal baclofen). Anticonvulsant drugs if epilepsy is present.
3. **Physiotherapy:** to avoid contractures.
4. **Use of some aids:**

   Sitting: special chairs.

   Walking: special calipers.

   Toilet: special seats.
5. **Speech therapist**
6. **Orthopedic correction of deformities and contractures.**

3. Intellectual disability (ID)

Definition: It is a deficit in intellectual and adaptive functioning presenting before 18 years of age.

The term improves upon and replaces the older term, mental retardation.

The term global developmental delay (GDD) is used to describe children younger than age three who fail to meet expected developmental milestones in multiple areas of intellectual functioning, and whose severity level of impairment cannot be reliably assessed; not all children with GDD will meet criteria for ID as they grow older.

Etiology:

Genetic and Environmental causes

I- Genetic causes:

A- Chromosomal abnormalities: Chromosomal aberrations are the most common known cause of ID.

e.g Down syndrome and other trisomies, Turner syndrome

B- Single-gene disorders:

- Inborn errors of metabolism: phenylketonuria, galactosemia.
- Neurocutaneous syndromes e.g. tuberous sclerosis.
- Cerebral malformation e.g. lissencephaly.

II- Environmental causes

A- Prenatal causes

- Congenital infections
- Environmental toxins or teratogens (eg, alcohol, lead, mercury, phenytoin, valproate).
- Radiation exposure
- Fetal anoxia or trauma.
- Placental insufficiency.

B- Perinatal brain insult:

- Extreme prematurity.
- Neonatal asphyxia.
- Intracranial hemorrhage.
- Birth injuries.
- Neonatal meningoencephalitis.
- Hypoglycemia.
- Hyperbilirubinemia.

C- Postnatal brain insult:

- Congenital hypothyroidism.
- CNS infections: meningitis, encephalitis, brain abscess.
- Brain trauma
- Hypoxia (eg, near-drowning)
- Environmental toxins: Poisoning e.g. CO, lead.

- Post-immunization e.g. after rabies or pertussis Vaccination.
- Psychosocial deprivation
- Malnutrition

CLINICAL FEATURES

Presenting symptoms —Language delay, behavior difficulties, immature self-help skills, or difficulty in learning.

Diagnostic criteria:

1. Subaverage intellectual functioning with an Intelligence quotient (IQ) of 70 or less when intelligence is tested .
2. Defect in adaptive behavior (ability to adapt to environment) taking in consideration his/her age and environment.
3. Onset of impairment before age of 18 years.

Assessment of Intellectual Function:

Many intelligence (psychometric) tests are available to judge the mental age of the child.

These tests assess verbal and performance functions.

The normal IQ is in the range of 90-110.

$$IQ = \frac{\text{Mental age}}{\text{Chronological age}} \times 100$$

In infant and children less than 3 years and in those with developmental, behavioral, or emotional problems, the developmental tests are used to judge the developmental age of the child.

These tests assess gross motor, fine motor, social-adaptive, and language functions.

This is used to calculate the developmental quotient (DQ).

Normally DQ is above 70.

$$DQ = \frac{\text{Developmental age}}{\text{Chronological age}} \times 100$$

Grades of Intellectual disability

IQ	Type	Comment
90 – 71	Borderline	Not handicapped but have some learning problems. Can function independently.
70 – 51	Mild (educable)	May not be apparent till school age. In special schools, they can attain 4^{th} – 6^{th} grade reading level, able to function independently as adult.
50 – 36	Moderate (trainable)	Cannot be learned to read or write, but can talk Have maximal self-care skills if trained. Can be trained to do simple tasks. Able to function semi independently.
35 - 21	Severe	Non-educable, non-trainable. Minimal self-care, no language development.
20 - 0	Profound	Non educable, non trainable. No self-care, no language development.

Evaluation of the child with Intellectual disability /GDD:

History: prenatal, perinatal , and postnatal history; developmental history; and family history.

Physical examination and neurologic examination

Investigation:

1. Standardized intelligence tests: Intellectual function is measured by the administration of intelligence tests in children >3 yr of age .
2. Brain imaging: Plain x-ray, brain CT scan, MRI.
3. Chromosomal studies.
4. Thyroid function tests: Serum T3, T4, and TSH.
5. Serum for TORCH.
6. Blood lead level.
7. Metabolic screening: Urine for urine organic acids, serum amino acids, serum ammonia, and lactate.

Treatment:

1. Treat the cause if possible.
2. Interventions that should be applied early to improve short-term and long-term outcomes, including

   ●Speech and language therapy

   ●Occupational therapy

   ●Physical therapy and rehabilitation, including mobility and postural support

   ●Family counseling and support

   ●Behavioral intervention

   ●Educational assistance: Special schools for education and training.
3. Treat associated diseases e.g epilepsy, visual, or auditory impairment, malnutrition.
4. Specific drug therapy**:**

   - No drugs has been found to improve intellectual function, except for specific defects as thyroxine for hypothyroidism
   - Treating associated disorders: ADHD (stimulant medication), self-injurious behavior and aggression (neuroleptics).
   - Piracetam may cause some improvement.

Prevention of Intellectual disability

Primary prevention

1. Routine childhood immunizations
2. Biochemical neonatal screening for hypothyroidism, galactosemia, and phenylketonuria .
3. Genetic counseling & antenatal diagnosis (amniocentesis) for genetic causes of ID.
4. Rubella vaccination before marriage.
5. Good antenatal & intrapartum care.
6. Adequate management of neonatal problems as hyperbilirubinemia.
7. Adequate management of intrauterine and postnatal infections.
8. Prevention and treatment of PEM.
9. Prevention of accidents.

4.FLOPPY INFANT SYNDROME

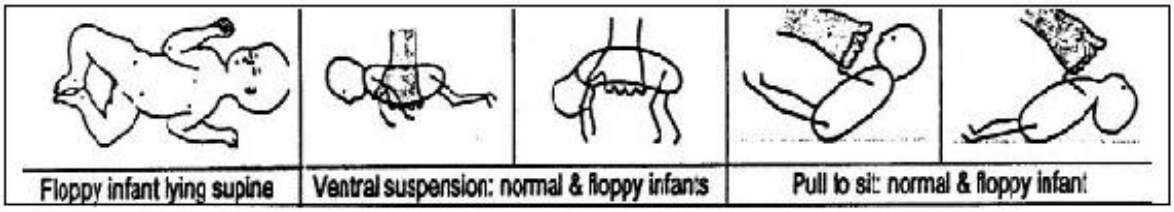
Definition: The term describes the infant who has marked generalized hypotonia

Criteria for diagnosis:

1- Lying supine: No spontaneous movements, and Frog-leg position.

2- Ventral suspension: head is down and the arms hang helplessly giving inverted U posture

3- Vertical suspension: may slip from your hands



4- Pull to sit maneuver: marked head lag

Causes:

Central causes:

1- Cerebral plasy.

- Generalised hypotonia
- Exaggerated deep tendon reflexes
- Mental retardation

2- Chromosomal as Down syndrome.

3- Congenital anomalies of the cerebellum.

Spinal cord diseases

Spinal cord diseases cause hypotonia only if the lesion is acute as a result of shock stage e.g. hypoxic ischemic myelopathy and injuries.

The lesion is characterized by:

- Sphincter disturbances are very prominent from the start
- Anethesia of lower limbs with sensory level on the trunk
- Planter response becomes extensor within few days.

Neuro-muscular causes.

Werdnig – Hoffman disease:

- The commonest cause of floppy infant
- Autosomal recessive
- Characterized by degeneration of anterior horn cells.
- Absent tendon reflexes.
- Bulbar palsy: Weak cough and cry.
- Visible tongue fasciculations.
- Normal mentality.
- Two thirds of infants die by 2 years of age.
- EMG: is diagnostic

Polyneuropathies: e.g Guillain Barre Syndrome

- Post-infectious(demyelination of spinal roots)
- Bilateral and symmetrical weakness
- Absent deep tendon reflexes
- Glove and stocking hypothesia
- CSF: protein cell dissociation
- Slow nerve conduction velocity
- EMG: normal

III-Disorders of neuromuscular transmission: e.g. infantile botulism caused by toxin of Clostridium Botulinum in contaminated food, and congenital myasthenia gravis.

The lesion is characterized by:

- *Acute flaccid paralysis of the limbs and extraocular muscles*
- *Diminished or absent deep tendon reflexes*
- No sensory changes
- EMG is diagnostic

Primary muscle diseases:

E.g. Non progressive congenital myopathy and congenital muscular dystrophy which is a progressive degenerative disease of muscles. Primary muscle diseases are characterized by:

- Bilateral and symmetrical weakness
- Hypotonia and diminished reflexes
- No sensory changes
- No excretory changes
- CPK is elevated in muscular dystrophy
- Muscle biopsy is diagnostic.

Benign congenital hypotonia:

- Non-progressive hypotonia of unknown etiology.
- Normal tendon reflexes
- Mentality is normal.
- Delayed motor development.
- Gradual improvement, sometimes complete.
- CPK, EMG,and nerve conduction velocity are normal.
- Normal muscle biopsy & C.T. Scan of brain