Cerebral Palsy

Definition:

- A heterogeneous group of disorders of movement and posture, affecting primarily the motor function, secondary to permanent, non-progressive pathology that formed in utero or early infancy (before 2-3 years of age).
- CP is often accompanied by disturbances of sensation, perception, cognition, communication, behavior, epilepsy, and secondary musculoskeletal problems.

Reference: Dev Med Child Neurol Suppl. 2007 Feb; 109:8-14.

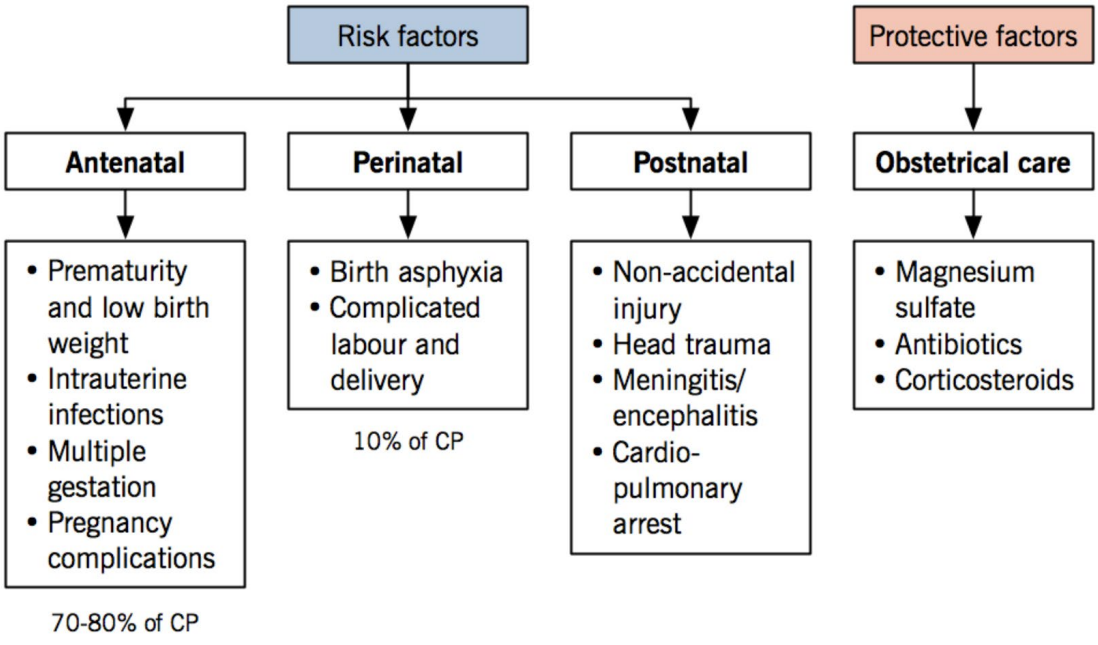
Epidemiology:

- CP affects approximately 2-2.5/1000 live births in the Western world, and more children in the developing world.
- The ratio of affected males to females is 1.4:1.

Risk & protective factors:

Risk factors for development of cerebral palsy

Risk factors can be divided by time period into antenatal, perinatal, and postnatal factors. The majority of the risk occurs in the antenatal period. Prematurity is a significant risk factor, predisposing to development of periventricular leukomalacia (PVL). Prudent obstetrical care, with management of preeclampsia (magnesium), infections (antibiotics), and preterm labour (corticosteroids), can help reduce the risk of CP.



Antenatal (~70-80% of causes)

Prematurity and low birth weight

- Greater risk of CP with preterm deliveries (but since most deliveries happen close to term, most infants with CP (75%) are born after 36 weeks).
- There is a U-shaped association between CP and gestational age, where incidence of CP is increased in both preterm and postterm babies. The mechanism may be related to the physiological changes that trigger labour. Parturition is hypothesized to be partially related to fetal brain maturity, as fetuses with cerebral abnormalities tend to be delivered either preterm or postterm.
- Periventricular leukomalacia (PVL) is a condition of underdeveloped white matter in the brain surrounding the ventricles. It is the leading cause of CP in preterm infants. PVL is discussed in the Pathophysiology section below.
- Intraventricular hemorrhage (IVH) is predominantly associated with prematurity and is due to fragility of developing blood vessels in the infant's brain. IVH may cause PVL or ischemia in other parts of the brain. See Pathophysiology for details.

Infections

- Fetoplacental and uterine infection or inflammation can cause initiation of preterm labour, which can lead to CNS injury and CP. Underdeveloped fetal brains are more susceptible to inflammation and inflammatory cytokines. These cytokines are hypothesized to be responsible for the development of PVL.
    - Chorioamnionitis is the most frequently associated maternal infection in CP.
    - TORCHS infections are associated with ~5% of all CP cases.

Multiple gestation

- Increases the risk of antenatal complications, such as preterm labour, growth restriction, low birth weight, and death of a co-twin.
- Death of a co-twin in utero has been shown to induce neuropathologic changes that can lead to CP in the surviving twin. Prevalence of CP in the surviving twin was found to be 15x higher than average.
- Twinning is the single strongest risk factor for the development of CP.

Pregnancy complications in the mother

- Thrombophilias can lead to placental vascular injury and clotting of the fetal vessels.
- Hemorrhage and preeclampsia (placental abruption, placenta previa, and other causes of third trimester bleeding) seem to lead to premature delivery, conferring the same risks for CP as a premature infant according to some evidence.

Perinatal

- Birth asphyxia (~10%) is commonly associated with CP.
- CP is associated with complicated labour and delivery, but there is not a clear association between CP and the quality of perinatal care.
- Despite the advancement of prenatal and obstetrical care in the past 30 years, the incidence of CP has remained constant. This may be due to increased survival rates of premature and low birth weight babies.

Postnatal

- Non-accidental injury.
- Head trauma.
- Meningitis/encephalitis (including cerebral malaria in the developing world).
- Cardiopulmonary arrest.

Obstetrical care (protective factors)

- Magnesium sulfate may reduce the risk of CP according to some studies, but further research is needed before it is used specifically as a neuroprotective agent for preterm births.
- Antibiotics used to treat bacterial vaginosis may reduce the rate of preterm delivery. In women with premature rupture of membranes, antibiotics reduce the risk of chorioamnionitis.
- Corticosteroids reduce the risk of CP, as steroids inhibit cytokine production, thus preventing PVL.

References:

- *Clin Obstet Gynecol. 2008 Dec;51(4):775-86.*
- *Pediatr Neurol. 2009 Mar;40(3):168-74.*
- *Essentials of Obstetrics and Gynecology, 5E (Hacker).*
- *Nelson Textbook of Pediatrics, 18E.*

Pathogenesis:

Preterm infants

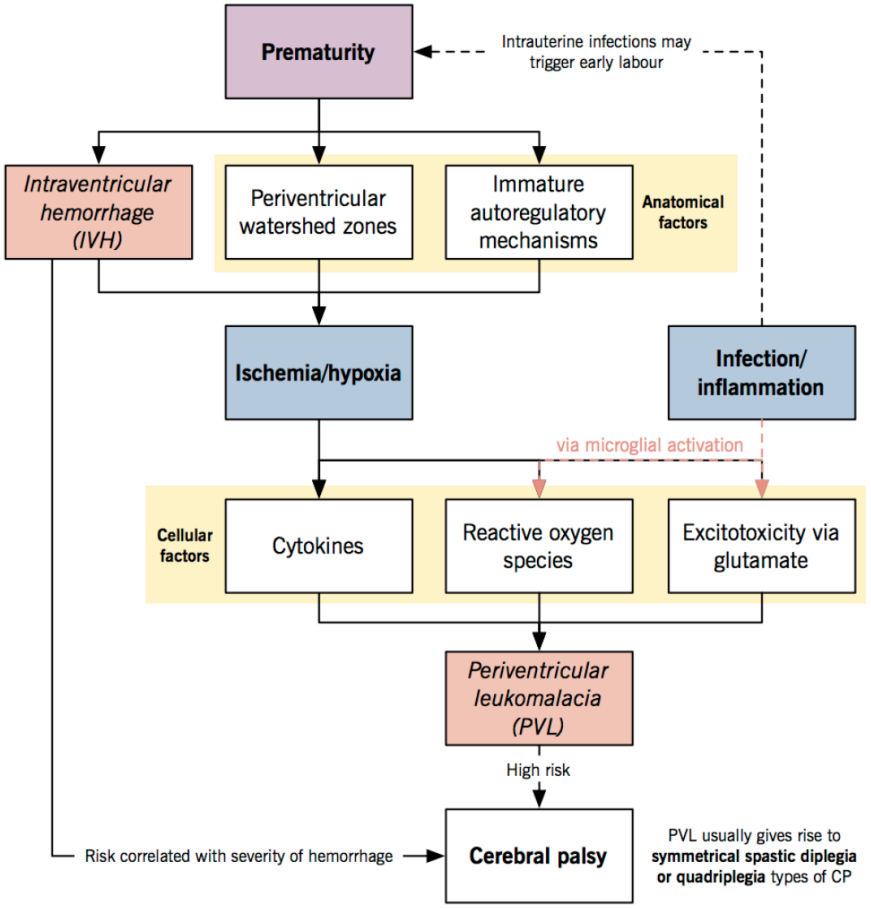
The premature neonatal brain is susceptible to two main pathologies: Intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). Although both pathologies increase the risk of CP, PVL is more closely related to CP and is the leading cause in preterm infants. The term PVL describes white matter in the periventricular region that is underdeveloped or damaged ("leukomalacia"). Both IVH and PVL cause CP because the corticospinal tracts, composed of descending motor axons, course through the periventricular region.

- **Intraventricular hemorrhage (IVH):** IVH describes bleeding from the subependymal matrix (the origin of fetal brain cells) into the ventricles of the brain. The blood vessels around the ventricles develop late in the third trimester, thus preterm infants have underdeveloped periventricular blood vessels, predisposing them to increased risk of IVH. The risk of CP increases with the severity of IVH.
- **Periventricular leukomalacia (PVL):** IVH is a risk factor for PVL, but PVL is a separate pathological process. The pathogenesis of PVL arises from two important factors: (1) ischemia/hypoxia and (2) infection/inflammation.

Pathogenesis of periventricular leukomalacia (PVL)

Source: Arch Dis Child Fetal Neonatal Ed. 2008 Mar;93(2):F153-61. Eric Wong

Prematurity is the main risk factor for CP. Preterm infants are at risk of both intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). **Anatomical factors**, including distal arterial perfusion of watershed zones and immature vessel autoregulation, predispose the premature brain (periventricular area) to ischemia. **Cellular factors** such as cytokines, reactive oxygen species, and excitotoxicity, target the premyelinating oligodendrocytes, interfering with myelination of white matter. Together, these factors give rise to underdevelopment of the white matter in the periventricular area, known as periventricular leukomalacia.



Term infants

- Circulation and autoregulation of cerebral blood flow are similar to that of an adult in a full-term infant. Ischemic and hemorrhagic injuries tend to follow similar patterns of those in adults:
  - Watershed areas where the three major cerebral arteries end in the cortex. This is the most common area of injury.
  - Basal ganglia damage can cause extrapyramidal or dyskinetic CP.

References:

- *Arch Dis Child Fetal Neonatal Ed. 2008 Mar;93(2): F153-61.*
- *Pediatric Ophthalmology: Current Thought and a Practical Guide, 1E (Wilson).*

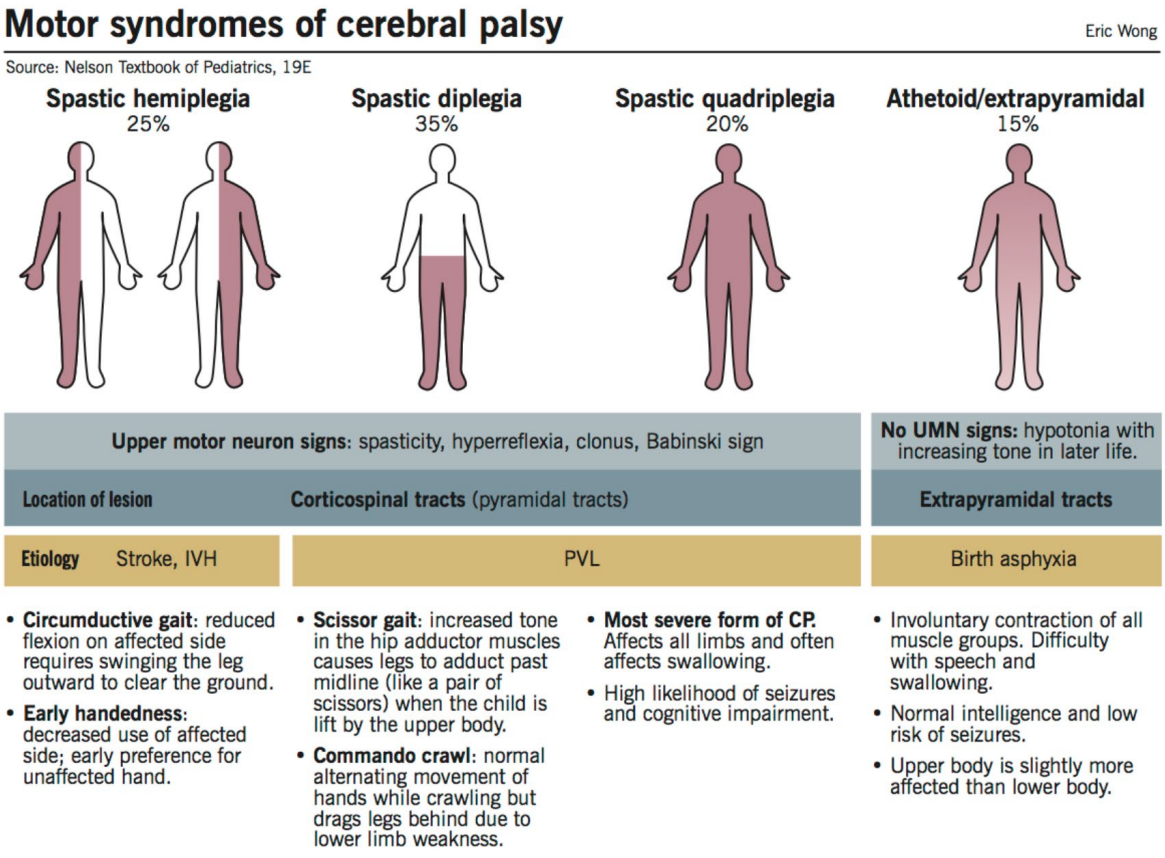
Clinical features:

The clinical features of neurological disorders depend on the location of damage to the nervous system. The location of damage can be divided into upper motor neuron or lower motor neuron. The pathology in CP is in the upper motor neurons.

Comparison of UMN and LMN lesion clinical presentations

Upper motor neuron lesion	Lower motor neuron lesion
Spasticity	Flaccid paralysis
Increased tone	Decreased or absent deep tendon reflexes
Hyperactive deep reflexes	Fasciculations and fibrillations
Clonus	Severe muscle atrophy (from disuse)
Babinski sign	
Little to no muscle atrophy	

Common clinical presentations:



Spastic hemiplegia

- Affects one side of the body more than the other (though both sides may be affected).
- Upper limb affected more than lower.
- Hand preference obvious at an early age (< 12 months old).
- Delayed walking (18-24 months) with a circumductive gait.
    - Circumductive gait: One leg is stiff and upon stepping, it is rotated away from the body, and then towards it (i.e., a semicircle shape). The stiffness in the affected leg limits flexion and the patient has to raise the pelvis to swing the leg out to lift the leg enough to clear the ground.
- On exam:
    - Circumductive gait.
    - On affected side:
        - Growth differences of hand and thumbnail.
        - Tiptoe walking on one side, due to increased tone in the gastrocnemius muscles. Spasticity has a greater effect on the postural (antigravity) muscles, e.g., gastrocnemius and sartorius.
        - Unilateral ankle clonus (usually).
        - Babinski sign.
        - Brisk deep tendon reflexes.
        - Weakness of hand and foot dorsiflexors.
    - Seizure disorder presenting before 2 years of age in 1/3 of children.
    - Cognitive abnormalities in 25% of cases.

Spastic diplegia

- Bilateral spasticity of the limbs with legs more affected than arms.
- First clinical signs appear around the time when the child starts to crawl.
    - Commando crawl: The child uses arms in a normal reciprocal manner but drags legs behind rather than using legs as well.
- On exam:
    - Spasticity of the legs.
    - Brisk reflexes.
    - Ankle clonus.
    - Bilateral Babinski sign.
    - Scissoring posture of legs when held in the air supported by the axillae due to spasticity in the hip adductor muscles.
    - Tiptoe walking.
    - Atrophy and impaired growth of legs in severe cases.
- Strongly associated with white matter damage in utero between 20-34 weeks of gestation.
- Most common neuropathologic feature is PVL.
- Minimal risk of seizure disorder.
- Normal intellectual development is common, but many children still have learning disabilities.
- Other deficits in sensory areas, like vision, may be present.

Spastic quadriplegia

- Most severe form of CP.
- Motor impairment to all extremities.
- High association with cognitive deficiencies and seizure disorders.
- Increased difficulty swallowing due to supranuclear bulbar palsies, which can cause the child to have aspiration pneumonias.
- Most common neuropathologic lesion is PVL but may also include basal ganglia damage.
- On exam:
    - Increased tone and spasticity in all limbs.
    - Decreased spontaneous movements.
    - Brisk reflexes and plantar extension responses.
    - Flexion contractures of knees and elbows commonly present in late childhood.
- Delay in speech and the presence of visual abnormalities are common.

Athetoid (extrapyramidal, dyskinetic)

- Less common than spastic CPs.
- 15-20% of patients with CP.
- On exam:
    - Infants are usually hypotonic with poor head control and head lag.
    - Variably increased tone with rigidity and dystonia with age.
    - Upper extremities more affected than lower extremities.
- Feeding and speech difficulties due to affected oropharyngeal muscles.
- Seizure disorders are uncommon.
- Normal intellectual development in many patients.
- Most commonly associated with birth asphyxia.
- Other causes: Kernicterus, metabolic genetic disorders.
- Neuropathologic lesions of the basal ganglia and thalamus (signals are relayed by the extrapyramidal tracts) are most common.

References:

- *Nelson Textbook of Pediatrics, 18E.*
- *Eur J Neurol. 2002 May;9 Suppl 1:3-9; discussion 53-61.*
- *Neuroscience, 3E (Purves).*
- *Clinical Neuroanatomy, 26E (Waxman).*
- *Rosenbaum P, Rosenbloom L (2012). Cerebral Palsy. From Diagnosis to Adult Life. London: Mac Keith Press.*

Diagnosis

CP is essentially a clinical diagnosis – there are no pathognomonic signs or diagnostic tests.

Clinical assessments:

- **General:**
  - Suspicions of CP are commonly based on a positive history of adverse perinatal or antenatal events.
  - If no positive history, suspicions are often raised by family observations of developmental delays.

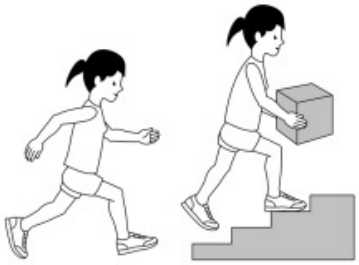
Early signs of CP:

- Head lag/feels stiff or floppy before 6 months.
- Hand preference before 12 months.
- Stiffness or tightness in the legs before 12 months.
- Inability to sit by 9 months.
- Persistent fisting of hands beyond 4 months.
- Asymmetric tonic neck reflex beyond 6 months.
- Mobilizes/crawls not using all limbs (e.g., commando crawl) beyond 10 months.
- Delays or asymmetry in movement or posture.

  - CP is non-progressive but can change its clinical manifestations throughout childhood. Therefore, such changes are important to discuss with parents.
  - In a CP patient, always look for the **associations** (e.g., hearing/vision impairment, cognitive/learning disability, communication problems, behavioral problems, seizures, GERD, constipation, swallowing problems/aspiration, sialorrhea, MSK problems, sleeping problems, feeding problems/poor nutrition/poor growth, pain/irritability).
  - Examine and rule out the possibility of degenerative diseases, metabolic disorders, spinal cord lesions/tumors, muscular dystrophy, and anomalies of the cervical spinal cord and skull.

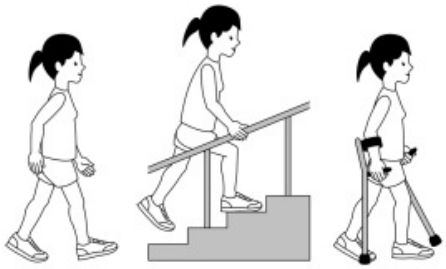
- **Functional:**
  - Gross Motor Function Classification System (GMFCS) is a 5-level classification scheme used to evaluate gross motor function in children with CP.
  - Specific attention to head posture, head control, ability to sit independently, and presence of independent mobility is important.
  - When independent mobility is present, gait, asymmetry, and abnormalities of posture should be assessed.
  - Assessing chewing abilities or oromotor functioning is also important in determining any safety concerns with regards to feeding.
  - Assessing speech production and clarity are important.

Gross Motor Function Classification System (GMFCS)



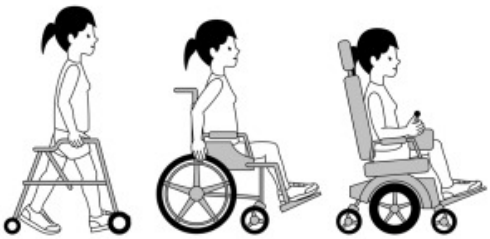
GMFCS Level I

Youth walk at home, school, outdoors and in the community. Youth are able to climb curbs and stairs without physical assistance or a railing. They perform gross motor skills such as running and jumping but speed, balance and coordination are limited.



GMFCS Level II

Youth walk in most settings but environmental factors and personal choice influence mobility choices. At school or work they may require a hand held mobility device for safety and climb stairs holding onto a railing. Outdoors and in the community youth may use wheeled mobility when traveling long distances.

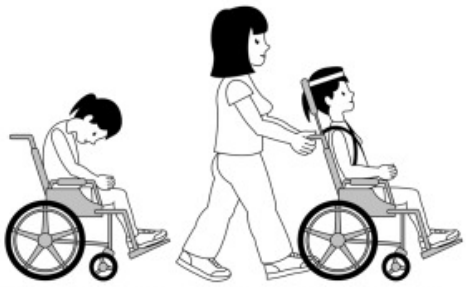


GMFCS Level III

Youth are capable of walking using a hand-held mobility device. Youth may climb stairs holding onto a railing with supervision or assistance. At school they may self-propel a manual wheelchair or use powered mobility. Outdoors and in the community youth are transported in a wheelchair or use powered mobility.

GMFCS Level IV

Youth use wheeled mobility in most settings. Physical assistance of 1-2 people is required for transfers. Indoors, youth may walk short distances with physical assistance, use wheeled mobility or a body support walker when positioned. They may operate a powered chair, otherwise are transported in a manual wheelchair.



GMFCS Level V

Youth are transported in a manual wheelchair in all settings. Youth are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements. Self-mobility is severely limited, even with the use of assistive technology.

Investigations:

- Brain imaging is one of the most useful diagnostic tools.
    - Confirmation of brain/spinal cord lesion via MRI.
        - Location and extent of lesion.
        - Can at times be 'normal' in the face of clear clinical findings.

- Additional tests:
    - Hearing and vision testing.
    - Genetic/metabolic screening in those with congenital malformations or if evidence of a genetic disorder.
    - Tests for thrombophilia in those where a stroke is the suspected cause.

References:

- *Pediatr Neurol. 2010 Mar;42(3):177-80.*
- *Nelson Textbook of Pediatrics, 18E.*
- *Rosenbaum P, Rosenbloom L (2012). Cerebral Palsy. From Diagnosis to Adult Life. London: Mac Keith Press.*

Management:

- Children with CP often have multiple developmental issues that are best managed by a multidisciplinary team of health care professionals.
- Health care professionals usually involved in the care of children with CP include:
    - Developmental pediatricians:
        - Monitor and promote the child's development.
        - Connect with other health care professionals as needed.
    - Occupational therapists:
        - Implement the use of assistive devices (e.g., wheelchairs, ankle-foot orthosis (AFOs), walkers, appropriate toys, and adaptations) that can be made to the home to accommodate the child.
        - Assist with feeding, as these children often have difficulties with chewing and swallowing.
    - Speech therapists:
        - Assist with the development of speech language and the provision of non-verbal communication systems, as necessary.
    - Physiotherapists:
        - Assist with the development of muscle control, overcoming weakness, minimizing spasticity, and preventing contractures.
    - Nutritionists:
        - Malnutrition may be seen in children with feeding difficulties.
        - Food to be given in a form that the child is able to chew and swallow.
        - Energy-rich supplements may be needed.
        - Enteral feeding may also be necessary if oral intake is insufficient.
    - Orthopedic surgeons:
        - Chronic muscle weakness or spasticity can cause orthopedic deformities that need surgical correction, e.g., dislocation of the hips due to spasticity of the thigh adductors, deformity of the ankle from calf muscle spasticity.

References:

- *Nelson Textbook of Pediatrics, 18E.*
- *Rosenbaum P, Rosenbloom L (2012). Cerebral Palsy. From Diagnosis to Adult Life. London: Mac Keith Press.*

Prognosis:

- The use of the GMFCS (in the Ontario Motor Growth Study) has been shown to be an effective tool in assessing outcomes for individuals with CP.
    - Motor assessments have been used alongside growth charts to characterize gross motor development over time.
    - These trends can be divided into 5 distinct motor development curves which children can be categorized into to assist with providing further prognostic information for parents.
    - Prognosis for motor function depends on the type and severity of motor impairment.
    - Individuals with CP on average have a life expectancy that is 44% of normal (this can be applied to countries with varying life expectancy rates).
    - Mortality risk increases with increasing number of impairments (e.g., intellectual, hearing, vision).
    - Research has shown that the strongest predictors of early mortality are immobility and impaired feeding ability (i.e., the need for tube feeding).
        - Shortest life expectancy is associated with individuals who are unable to lift their head in prone position.

References:

- *Clin Obstet Gynecol. 2008 Dec;51(4):816-28.*
- *JAMA. 2002 Sep 18;288(11):1357-63.*
- *Pediatrics. 2011 Aug;128(2):e299-307.*
- *Dev Med Child Neurol. 2008 Jul;50(7):487-93.*