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Cerebral Palsy

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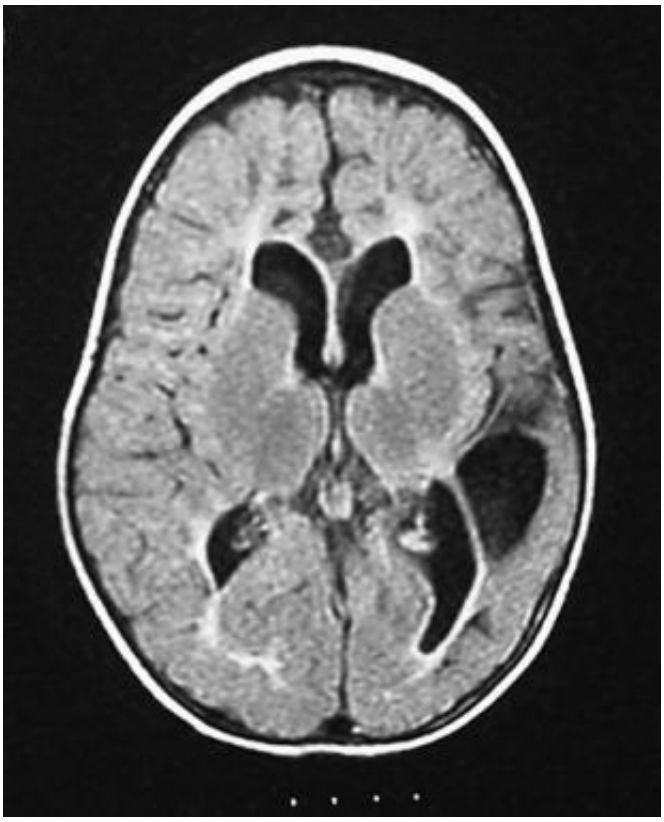
Overview

Practice Essentials

Cerebral palsy is the leading cause of childhood disability affecting function and development. The incidence of the condition has not changed in more than 4 decades, despite significant advances in the medical care of neonates.

The magnetic resonance image (MRI) below illustrates the findings in a 16-month-old boy with cerebral palsy.



Magnetic resonance image (MRI) of a 16-month-old boy who was born at term but had an anoxic event at delivery. Examination findings were consistent with a spastic quadriplegic cerebral palsy with asymmetry (more prominent right-sided deficits). Cystic encephalomalacia in the left temporal and parietal regions, delayed myelination, decreased white matter volume, and enlarged ventricles can be seen in this image. These findings are most likely the sequelae of a neonatal insult (eg, periventricular leukomalacia with a superimposed left-sided cerebral infarct).

Signs and symptoms

Signs of cerebral palsy include the following:

- History of gross motor developmental delay in the first year of life
- Abnormal muscle tone: The most frequently observed symptom; the child may present as either hypotonic or, more commonly, hypertonic, with either decreased or increased resistance to passive movements, respectively. Children with cerebral palsy may have an early period of hypotonia followed by hypertonia. A combination of axial hypotonia and peripheral hypertonia is indicative of a central process.
- Definite hand preference before age 1 year: A "red flag" for possible hemiplegia
- Asymmetrical crawling or failure to crawl
- Growth disturbance, especially failure to thrive
- Increased reflexes: Indicating the presence of an upper motor neuron lesion; this condition may also present as the persistence of primitive reflexes
- Underdevelopment or absence of postural or protective reflexes

The patient’s overall gait pattern should be observed, and each joint in the lower and upper extremity should be assessed for signs of cerebral palsy, including the following:

- Hip: Excessive flexion, adduction, and femoral anteversion make up the predominant motor pattern; scissoring of the legs is common in spastic cerebral palsy
- Knee: Flexion and extension with valgus or varus stress occur
- Foot: Equinus, or toe walking, and varus or valgus of the hindfoot is common in cerebral palsy

See Clinical Presentation for more detail.

Diagnosis

Laboratory studies

The diagnosis of cerebral palsy is generally made based on the clinical picture. There are no definitive laboratory studies for diagnosing the condition, only studies, including the following, to rule out other symptom causes:

- Thyroid function studies: Abnormal thyroid function may cause abnormalities in muscle tone or deep tendon reflexes or movement disorders
- Lactate and pyruvate levels: Abnormalities may indicate an abnormality of energy metabolism (ie, mitochondrial cytopathy)
- Ammonia levels: Elevated ammonia levels may indicate liver dysfunction or urea cycle defect
- Organic and amino acids: Serum quantitative amino acid and urine quantitative organic acid values may reveal inherited metabolic disorders
- Chromosomal analysis: Chromosomal analysis, including karyotype analysis and specific DNA testing, may be indicated to rule out a genetic syndrome, if dysmorphic features or abnormalities of various organ systems are present
- Cerebrospinal protein: Levels may support asphyxia in the neonatal period; protein levels can be elevated, as can the lactate-to-pyruvate ratio

Imaging studies

Cranial imaging studies to help evaluate brain damage and identify persons who are at risk for cerebral palsy include the following:

- Cranial ultrasonography: Can be performed in the early neonatal period to delineate clear-cut structural abnormalities and show evidence of hemorrhage or hypoxic-ischemic injury
- Computed tomography scanning of the brain: Is particularly helpful for imaging of blood, calcification, and bone, and may be performed quickly in a sleeping infant, but emits radiation. Helps to identify congenital malformations, intracranial hemorrhage, and periventricular leukomalacia or early craniosynostosis.
- Magnetic resonance imaging of the brain: The diagnostic neuroimaging study of choice because this modality defines cortical and white matter structures and abnormalities more clearly than does any other method; MRI also allows for the determination of whether appropriate myelination is present for a given age. However, sedation in a young child is required to prevent movement artifact.

Other

Additional studies in cerebral palsy can include the following:

- Electroencephalography: Important in the diagnosis of seizure disorders
- Electromyography and nerve conduction studies: Helpful when a muscle or nerve disorder is suspected

See Workup for more detail.

Management

Management of abnormal movements

Numerous medications, including the following, may relieve the movement difficulties associated with cerebral palsy:

- Botulinum toxin with or without casting: Botulinum toxin (Botox) type A may reduce spasticity for 3-6 months and should be considered for children with cerebral palsy with spasticity.[1, 2, 3, 4, 5]
- Phenol intramuscular neurolysis: This agent can be used for some large muscles or when several muscles are treated. Phenol therapy is more painful, but lasts longer than botulinum toxin injections.
- Antiparkinsonian, anticonvulsant, antidopaminergic, and antidepressant agents: Although antiparkinsonian drugs (eg, anticholinergic and dopaminergic drugs) and antispasticity agents (eg, baclofen) have primarily been used in the management of dystonia, anticonvulsants, antidopaminergic drugs, and antidepressants have also been tried.

Surgery

Surgical treatments used in patients with cerebral palsy include the following:

- Intrathecal baclofen pump insertion: To treat spasticity and/or dystonia[6]
- Selective dorsal rhizotomy: To treat velocity-dependent spasticity in the lower extremities[7, 8]
- Stereotactic basal ganglia surgery: May improve rigidity, choreoathetosis, and tremor
- Orthopedic surgical intervention: To treat scoliosis, joint contractures or dislocation

See Treatment and Medication for more detail.

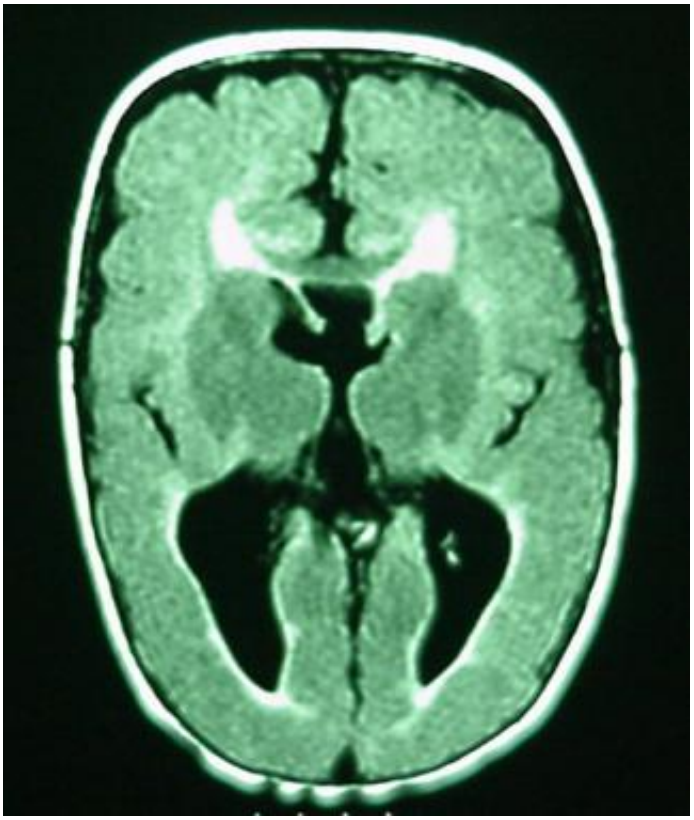
Background

The term cerebral palsy (CP) was originally coined more than a century ago and loosely translates as "brain paralysis." However, cerebral palsy is not a single diagnosis but an "umbrella" term describing motor or postural abnormalities that are noted during early development, and are due to nonprogressive brain lesions.[9] Cerebral palsy has been described as follows:[10]

"A group of disorders of the development of movement and posture causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior and/or a seizure disorder."

Cerebral palsy is the leading cause of childhood disability affecting function and development. The brain lesions that cause cerebral palsy occur from the fetal or neonatal period to up to age 3 years. Although insults to the brain that occur after age 3 years through adulthood may manifest clinically similar to cerebral palsy, by definition, these clinical scenarios are not described as cerebral palsy. In addition, despite the fact that the lesion to the developing brain occurs before age 3 years, the diagnosis of cerebral palsy may not be made until after that time. Some authorities advocate not making a definitive diagnosis in selected cases until age 5 years or later. This approach allows the clinical picture to be clear and potentially allows exclusion of progressive diseases.[11, 12] In addition, some children have been diagnosed with cerebral palsy at an early age, only to have the symptoms resolve later.[13]

The magnetic resonance image (MRI) below illustrates the findings in a 1-year-old former preterm boy with cerebral palsy.



Magnetic resonance image (MRI) of a 1-year-old boy who was born at gestational week 27. The clinical examination was consistent with spastic diplegic cerebral palsy. Pseudocolpocephaly and decreased volume of the white matter posteriorly were consistent with periventricular leukomalacia. Evidence of diffuse polymicrogyria and thinning of the corpus callosum is noted in this image.

Approximately 30–50% of patients with cerebral palsy have mental retardation, depending on the type.[14, 15] However, because of oromotor, fine motor, and gross motor difficulties, communication in these patients may be impaired and

expression of intellectual capacity may be limited. However, if cerebral palsy is approached in a multidisciplinary manner, with physical, occupational, and nutritional therapy to maximize rehabilitative efforts, patients can be more fully integrated academically and socially.

Approximately 15–60% of children with cerebral palsy have epilepsy, and epilepsy is more frequent in patients with spastic quadriplegia or mental retardation.

See also the following:

- Rehabilitation and Cerebral Palsy
- Epilepsy and Seizures
- Antiepileptic Drugs
- Cerebral Venous Thrombosis
- Periventricular Hemorrhage-Intraventricular Hemorrhage
- Pediatric Periventricular Leukomalacia

Classification

Cerebral palsy is classified according to resting tone and what limbs are involved (called topographic predominance). Spastic cerebral palsy, due to cortex/pyramidal tract lesions, is the most common type and accounts for approximately 80% of cases[12] ; this type of cerebral palsy is characterized by spasticity (velocity-dependent increase in tone), hyperreflexia, clonus, and an upgoing Babinski reflex.

Extrapyramidal or dyskinetic cerebral palsy comprises 10-15% of this disorder and is characterized more by abnormal involuntary movements. Ataxic cerebral palsy comprises less than 5% of cerebral palsy.

Many patients have characteristics of both spastic and extrapyramidal cerebral palsy. The typical types of cerebral palsy are as follows:

- Spastic hemiplegia (20-30%) – Cerebral palsy predominantly affecting 1 side of the body, including an arm and a leg, with involvement of upper extremity spasticity more than lower extremity spasticity (eg, right side involved with right arm more than right leg). If both arms are more involved than the legs, the condition can be classified as a double hemiplegia.
- Spastic diplegia (30-40%) – Cerebral palsy affecting bilateral lower extremities more than upper extremities; in some cases, the lower extremities are solely involved
- Spastic quadriplegia (10-15%) – Cerebral palsy affecting all 4 extremities and the trunk (full body)
- Dyskinetic cerebral palsy (athetoid, choreoathetoid, and dystonic) – Cerebral palsy with extrapyramidal signs characterized by abnormal movements; hypertonicity is often associated
- Mixed cerebral palsy – Cerebral palsy with no single specific tonal quality predominating; typically characterized by a mixture of spastic and dyskinetic components
- Hypotonic cerebral palsy – Cerebral palsy with truncal and extremity hypotonia with hyperreflexia and persistent primitive reflexes; thought to be rare
- Monoplegia - Rare; involvement is noted in 1 limb, either an arm or a leg. If a patient has monoplegia, an effort should be made to rule out causes other than cerebral palsy.

Functional classification systems generally divide patients into mild, moderate, and severe types (depending on functional limitations). Alternatively, patients may be categorized more comprehensively by their abilities and limitations, as was proposed by the World Health Organization in 2001. See International Classification of Functioning, Disability and Health

(ICF).

Cerebral palsy is generally considered a static encephalopathy (ie, nonprogressive in nature). However, the clinical presentation of this condition changes as children and their developing nervous systems mature.

Advances in neonatal neurology

Advances in neonatal neurology continue to focus on potentially modifiable factors during the neonatal period that contribute to the development of cerebral palsy. In recent years, several studies have shown that antenatal magnesium sulfate given to mothers at risk for preterm delivery is associated with a significant reduction in the risk of cerebral palsy.[16, 17, 18] Many other studies focus on the role of excitable amino acids and their role in neurologic injury. The hope is that more can be done in the neonatal period to prevent the permanent neurologic deficit resulting in cerebral palsy.

In summary, no set rules exist as to where or when the brain injury can occur, and injury may occur at more than one stage of fetal brain development. Additionally, causes are multiple and potentially multifactorial, including vascular insufficiency, infection, maternal factors, or underlying genetic abnormalities. Regardless of the etiology, however, the underlying brain anomaly in cerebral palsy is static, although the motor impairment and functional consequences may vary over time. By definition, cases associated with underlying disorders of a progressive or degenerative nature are excluded when diagnosing cerebral palsy.

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Anatomy

Cerebral palsy is restricted to lesions of the brain only; diseases specific to the peripheral nerves of the spinal cord (eg, spinal muscular atrophy, myelomeningocele) or to the muscles (eg, muscular dystrophies), although causing early motor abnormalities, are not considered cerebral palsy.

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Pathophysiology

Major events in human brain development and their peak times of occurrence include the following[19] :

- Primary neurulation – Weeks 3–4 of gestation
- Prosencephalic development – Months 2–3 of gestation
- Neuronal proliferation – Months 3–4 of gestation
- Neuronal migration – Months 3–5 of gestation
- Organization – Month 5 of gestation to years postnatal
- Myelination – Birth to years postnatal

Cohort studies have shown an increased risk in children born slightly preterm (37–38 weeks) or postterm (42 weeks) compared with children born at 40 weeks.[20]

Brain injury or abnormal brain development

Given the complexity of prenatal and neonatal brain development, injury or abnormal development may occur at any time, resulting in the varied clinical presentations of cerebral palsy (whether due to a genetic abnormality, toxic or infectious

etiology, or vascular insufficiency). For example, cerebral injury before the 20th week of gestation can result in a neuronal migration deficit; injury between the 26th and 34th weeks can result in periventricular leukomalacia (foci of coagulative necrosis in the white matter adjacent to the lateral ventricles); injury between the 34th and 40th weeks can result in focal or multifocal cerebral injury.

Brain injury due to vascular insufficiency depends on various factors at the time of injury, including the vascular distribution to the brain, the efficiency of cerebral blood flow and regulation of blood flow, and the biochemical response of brain tissue to decreased oxygenation.

Prematurity and cerebral vasculature

The physical stress on premature infants and the immaturity of the brain and cerebral vasculature likely explain why prematurity is a significant risk factor for cerebral palsy. Before term, the distribution of fetal circulation to the brain results in the tendency for hypoperfusion to the periventricular white matter. Hypoperfusion can result in germinal matrix hemorrhages or periventricular leukomalacia. Between weeks 26 and 34 of gestation, the periventricular white matter areas near the lateral ventricles are most susceptible to injury. Because these areas carry fibers responsible for the motor control and muscle tone of the legs, injury can result in spastic diplegia (ie, predominant spasticity and weakness of the legs, with or without arm involvement of a lesser degree).

Periventricular leukomalacia

When larger lesions extend past the area of descending fibers from the motor cortex to involve the centrum semiovale and corona radiata, both the lower and upper extremities may be involved. Periventricular leukomalacia is generally symmetric and thought to be due to ischemic white matter injury in premature infants. Asymmetric injury to the periventricular white matter can result in one side of the body being more affected than the other. The result mimics a spastic hemiplegia but is best characterized as an asymmetric spastic diplegia. The germinal matrix capillaries in the periventricular region are particularly vulnerable to hypoxic-ischemic injury because of their location at a vascular border zone between the end zones of the striate and thalamic arteries. In addition, because they are brain capillaries, they have a high requirement for oxidative metabolism.

Periventricular hemorrhage-intraventricular hemorrhage

Many authorities grade the severity of periventricular hemorrhage-intraventricular hemorrhage using a classification system originally described by Papile et al in 1978 (see Periventricular Hemorrhage-Intraventricular Hemorrhage), as follows:[21]

- Grade I – Subependymal and/or germinal matrix hemorrhage
- Grade II – Subependymal hemorrhage with extension into the lateral ventricles without ventricular enlargement
- Grade III – Subependymal hemorrhage with extension into the lateral ventricles with ventricular enlargement
- Grade IV – A germinal matrix hemorrhage that dissects and extends into the adjacent brain parenchyma, irrespective of the presence or absence of intraventricular hemorrhage, is also referred to as an intraparenchymal hemorrhage when found elsewhere in the parenchyma. Hemorrhage extending into the periventricular white matter in association with an ipsilateral germinal matrix hemorrhage/intraventricular hemorrhage is termed a periventricular hemorrhagic venous infarction.

Term cerebral vascular and hypoperfusion injuries

At term, when circulation to the brain most resembles adult cerebral circulation, vascular injuries at this time tend to occur most often in the distribution of the middle cerebral artery, resulting in a spastic hemiplegic cerebral palsy. However, the term brain is also susceptible to hypoperfusion, which mostly targets watershed areas of the cortex (eg, end zones of the major cerebral arteries), resulting in spastic quadriplegic cerebral palsy. The basal ganglia also can be affected, resulting in extrapyramidal or dyskinetic cerebral palsy.

Etiology

The clinical presentation of cerebral palsy may result from an underlying structural abnormality of the brain; early prenatal, perinatal, or postnatal injury due to vascular insufficiency; toxins or infections; or the pathophysiologic risks of prematurity. Risk factors may include preterm birth, multiple gestation, intrauterine growth restriction, male sex, low Apgar scores, intrauterine infections, maternal thyroid abnormalities, prenatal strokes, birth asphyxia, maternal methyl mercury exposure, and maternal iodine deficiency.[12, 13, 22, 23]

Evidence suggests that prenatal factors result in 70-80% of cases of cerebral palsy. In most cases, the exact cause is unknown but is most likely multifactorial.[13]

Interpretation of the literature is limited by the lack of strict definitions in studies attempting to define a pathogenesis of cerebral palsy and the relatively small size of certain studies. An increasing amount of literature suggests a link between various prenatal, perinatal, and postnatal factors and this disorder. Epidemiologic studies suggest that prenatal factors play a predominant role in the etiology of cerebral palsy.

A Norwegian study involving children with cerebral palsy diagnosed before 5 years of age suggested that a low Apgar score at 5 minutes is associated with cerebral palsy in all birth weights.[23] The prevalence of cerebral palsy was highest in children with a low birth weight; however, the odds ratio of this disorder being associated with a low Apgar score (< 4) was highest in normal weight children. Nonetheless, most children with cerebral palsy had Apgar scores higher than 4 at 5 minutes.[23]

Although preterm delivery is a well-established risk factor for cerebral palsy, a recent study suggests that postterm pregnancy at 42 weeks or later has been associated with an increased risk of this condition.[20]

Maternal, prenatal, gestational risk factors

The following maternal and prenatal risk factors statistically correlate with cerebral palsy:

- Long menstrual cycle
- Previous pregnancy loss
- Previous loss of newborn
- Maternal mental retardation
- Maternal thyroid disorder, especially iodine deficiency
- Maternal seizure disorder
- History of delivering a child weighing less than 2000 g
- History of delivering a child with a motor deficit, mental retardation, or a sensory deficit

The following factors during pregnancy also correlate statistically with cerebral palsy:

- Polyhydramnios
- Treatment of the mother with thyroid hormone, estrogen or progesterone
- Maternal seizure disorder
- Maternal severe proteinuria or high blood pressure
- Maternal methyl mercury exposure

- Congenital malformations in the fetus
- Male sex of fetus
- Bleeding in third trimester
- Intrauterine growth retardation
- Multiple gestation

The apparent overrepresentation of cerebral palsy in multiple gestation pregnancies may relate more to the presence of prematurity or intrauterine growth retardation. Multiple gestations may not be an added risk for this disorder. The exception is when one twin dies; the surviving twin has a higher chance than a singleton of developing cerebral palsy.

Perinatal risk factors

The following perinatal factors are associated with an increased risk of cerebral palsy:

- Prematurity
- Chorioamnionitis
- Nonvertex and face presentation of the fetus
- Birth asphyxia

In 10% or less of cerebral palsy cases, birth asphyxia can be determined as the definitive cause. Even when birth asphyxia is thought to be associated clearly with cerebral palsy, abnormal prenatal factors (eg, intrauterine growth retardation, congenital brain malformations) may have contributed to perinatal fetal distress. Cases of cerebral palsy attributed to birth asphyxia must document clear evidence of acidosis, moderate to severe neonatal encephalopathy, restriction to spastic quadriplegia, dyskinetic or mixed types of cerebral palsy, and exclusion of other etiologies. Additionally, an intrapartum event must be suggested by a sentinel event, fetal heart rate changes, Apgar score less than 4 at 5 minutes, organ system damage related to tissue hypoxia, and early imaging abnormalities.[24]

Although Apgar scores provide a method for documenting cardiopulmonary and neuromotor status in the minutes following birth, low scores alone cannot be used as an indicator of birth asphyxia. Such scores may reflect circumstances unrelated to birth asphyxia, such as infections and other preexisting prenatal conditions.

Postnatal risk factors

The following postnatal factors may contribute to cerebral palsy:

- Infections (eg, meningitis, encephalitis)
- Intracranial hemorrhage (eg, due to prematurity, vascular malformations, or trauma)
- Periventricular leukomalacia (in premature infants)
- Hypoxia-ischemia (eg, from meconium aspiration)
- Persistent fetal circulation or persistent pulmonary hypertension of the newborn
- Kernicterus

Possible causes of cerebral palsy by type are discussed below.

Spastic hemiplegic

Of all cases of cerebral palsy, 70-90% are congenital and 10-30% are acquired (eg, vascular, inflammatory, traumatic). In

unilateral lesions of the brain, the vascular territory most commonly affected is the middle cerebral artery; the left side is involved twice as commonly as the right. Other structural brain abnormalities include hemi-brain atrophy and posthemorrhagic porencephaly. In premature infants, this may result from asymmetric periventricular leukomalacia.

Spastic diplegic

In premature infants, spastic diplegia may result from parenchymal-intraventricular hemorrhage or periventricular leukomalacia. In term infants, no risk factors may be identifiable, or the etiology might be multifactorial.

Spastic quadriplegic

Approximately 50% of spastic quadriplegic cerebral palsy cases are prenatal, 30% are perinatal, and 20% are postnatal in origin. This type is associated with cavities that communicate with the lateral ventricles, multiple cystic lesions in the white matter, diffuse cortical atrophy, and hydrocephalus.

The patient often has a history of a difficult delivery with evidence of perinatal asphyxia. Preterm infants may have periventricular leukomalacia. Full-term infants may have structural brain abnormalities or cerebral hypoperfusion in a watershed (ie, major cerebral artery end zone) distribution.

Dyskinetic (extrapyramidal)

Dyskinetic (extrapyramidal) cerebral is associated with several unique etiologies. Historically, kernicterus, or acute neonatal bilirubin encephalopathy, was a major cause. With improvement in early management of hyperbilirubinemia, the vast majority cases of dyskinetic cerebral palsy are currently associated with presumed hypoxic ischemic injury rather than with hyperbilirubinemia.[25] In the absence of hypoxia, hyperbilirubinemia, or prematurity, the possibility of a metabolic or neurodegenerative disorder as a basis for this presentation must be considered.

Thus, dyskinetic cerebral palsy may be associated with hyperbilirubinemia in term infants or with prematurity without prominent hyperbilirubinemia. Hypoxia affecting the basal ganglia and thalamus may affect term infants more than preterm infants.

Epidemiology

The incidence of cerebral palsy has not changed in more than 4 decades, despite significant advances in the medical care of neonates.

In developed countries, the overall estimated prevalence of cerebral palsy is 2–2.5 cases per 1000 live births.[26] The prevalence of this disorder among preterm and very preterm infants is substantially higher.[27, 28] In the developing world, the prevalence of cerebral palsy is not well established but estimates are 1.5–5.6 cases per 1000 live births. These figures may represent an underestimation because of a paucity of data, the lack of healthcare access, an overrepresentation of severe cases, and inconsistent diagnostic criteria.[12]

All races are affected by this disorder. Lower socioeconomic status[29] and male sex[12] may be increased risk factors for cerebral palsy.

With relation to age, the insult that gives rise to cerebral palsy occurs during immature brain development. According to most references, this initiating event can take place anytime between prenatal development and age 3 years. However, children are usually not diagnosed until after age 1 year, with the condition becoming identifiable as children fail to meet developmental milestones. Often, children who are older and are diagnosed as having cerebral palsy—as a result of having presenting symptoms or problems that are similar to those of cerebral palsy—should instead be labeled with the etiology of their brain injury (ie, traumatic brain injury secondary to a motor vehicle accident, stroke, metabolic condition, etc.).

Prognosis

With appropriate therapeutic services, patients may be able to fully integrate academically and socially.

The morbidity and mortality of cerebral palsy relate to the severity of this condition and concomitant medical complications, such as respiratory and gastrointestinal difficulties. In patients with quadriplegia, the likelihood of epilepsy, extrapyramidal abnormalities, and severe cognitive impairment is greater than in those with diplegia or hemiplegia.

Cognitive impairment occurs more frequently in persons with cerebral palsy than in the general population. The overall rate of mental retardation in affected persons is thought to be 30–50%. Some form of learning disability (including mental retardation) has been estimated to occur in perhaps 75% of patients. However, standardized cognitive testing primarily evaluates verbal skills and may result in the underestimation of cognitive abilities in some individuals.

In some studies, 25% of patients with cerebral palsy are unable to walk. However, many patients with this disorder (particularly those with spastic diplegia and spastic hemiplegia types) can ambulate independently or with assistive equipment. Thus, approximately 25% of children with cerebral palsy have mild involvement with minimal or no functional limitation in ambulation, self-care, and other activities. Approximately half are moderately impaired to the extent that complete independence is unlikely but function is satisfactory. Only 25% are so severely disabled that they require extensive care and are nonambulatory.

A prospective study of children has suggested that being able to sit by age 2 years is a good predictive sign of eventual ambulation. The suppression of obligatory primitive reflex activity by age 18–24 months was a sensitive indicator for distinguishing children who ultimately walked from those who were not expected to walk. Children who did not sit by age 4 years did not ambulate.

In patients with spastic quadriplegia, a less favorable prognosis correlated with a longer delay in the resolution of extensor tone. At times, hypertonicity and spasticity may improve or resolve over time in patients with cerebral palsy. Spasticity in patients with spastic quadriplegia can be more resistant even with services and orthopedic and rehabilitative intervention.

Patients with severe forms of cerebral palsy may have a significantly reduced life span, although this continues to improve with improved health care and gastrostomy tubes.[30] Patients with milder forms of this disorder have a life expectancy close to the general population, although it is still somewhat reduced.[31, 32, 33]

Complications

Cerebral palsy complications may affect multiple systems. For example, skin complications include decubitus ulcers and sores; orthopedic complications may include contractures, hip dislocation, and/or scoliosis.

Maintaining weight close to idea body weight is important for wheelchair-bound patients or those with ambulatory dysfunction. Nutrition consultation should be done early and periodically to ensure proper growth. Parents and medical professionals must keep on top of the potential nutritional difficulties in children with cerebral palsy. These patients are especially at risk of developing osteoporosis because of decreased weight bearing, so following their calcium intake and vitamin D levels is important.[34]

Gastrointestinal and nutritional complications include the following:

- Failure to thrive due to feeding and swallowing difficulties secondary to poor oromotor control; patients may require a gastrostomy tube (G-tube) or a jejunostomy tube (J-tube) to augment nutrition.
- Obesity, less frequently than failure to thrive
- Gastroesophageal reflux and associated aspiration pneumonia
- Constipation

- Dental caries

Dental problems also include enamel dysgenesis, malocclusion, and gingival hyperplasia. Malocclusion is twice as prevalent as in the normal population. The increased incidence of dental problems is often secondary to the use of medications, especially drugs administered to premature infants and antiepileptic agents.

Respiratory complications include the following:

- Increased risk of aspiration pneumonia because of oromotor dysfunction
- Chronic lung disease/bronchopulmonary dysplasia
- Bronchiolitis/asthma

Neurologic complications include the following:

- Epilepsy
- Hearing loss (particularly in patients who had acute bilirubin encephalopathy [kernicterus]; also seen in patients who were born prematurely or who were exposed to ototoxic drugs)
- Vision
- Visual-field abnormalities due to cortical injury
- Strabismus

Epilepsy occurs in 15-60% of children with cerebral palsy and is more common in patients with spastic quadriplegia or mental retardation. When compared with controls, children with cerebral palsy have a higher incidence of epilepsy with onset within the first year of life and are more likely to have a history of neonatal seizures, status epilepticus, polytherapy, and treatment with second-line anticonvulsants. Factors associated with a seizure-free period of at least 1 year include normal intelligence, single seizure type, monotherapy, and spastic diplegia.

Visual acuity decreases in premature infants because of retinopathy of prematurity with hypervascularization and possible retinal detachment.

Cognitive/psychologic/behavioral complications include the following:

- Mental retardation (30-50%), most commonly associated with spastic quadriplegia
- Attention-deficit/hyperactivity disorder
- Learning disabilities
- Impact on academic performance and self-esteem
- Increased prevalence of depression
- Sensory integration difficulties
- Increased prevalence of pervasive developmental disorder or autism associated with concurrent diagnosis of cerebral palsy

Patient Education

Patients with cerebral palsy and their caregivers should be aware that oromotor dysfunction may require limitations in the texture of food and liquid, feeding only by gastrostomy or jejunostomy tube, supplemental feedings via gastrostomy or jejunostomy tube to increase energy intake, and aspiration precautions.

In addition, regular physical therapy and occupational therapy are crucial in these individuals. The goal should be to maximize the functional use of limbs and ambulation and to reduce the risk of contractures.

For patient education information, see Brain and Nervous System Center as well as Cerebral Palsy.

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Presentation

History

The child with cerebral palsy can present after failing to meet expected developmental milestones or failing to suppress obligatory primitive reflexes. The 2003 American Academy of Neurology (AAN) practice parameter suggests screening for the following potential cerebral palsy–associated deficits at the initial assessment:[24]

- Mental retardation
- Ophthalmologic and hearing impairments
- Speech and language disorders
- Oromotor dysfunction

The diagnosis begins with a history of gross motor developmental delay in the first year of life. Cerebral palsy frequently manifests as early hypotonia for the first 6 months to 1 year of life, followed by spasticity.

Abnormal muscle tone is the most frequently observed symptom. The child may present as either hypotonic or, more commonly, hypertonic with either decreased or increased resistance to passive movements, respectively. Children with cerebral palsy may have an early period of hypotonia followed by hypertonia. The longer the period of hypotonia before hypertonia, the greater the likelihood that the hypertonia will be more severe.

Definite hand preference before age 1 year is a "red flag" for possible hemiplegia. Asymmetric crawling or failure to crawl may also suggest cerebral palsy. Growth disturbance is often noted in children with cerebral palsy, especially failure to thrive.

The general medical history should include a review of systems to evaluate for the multiple complications that can occur with cerebral palsy (see Complications under Prognosis).

Prenatal history

The prenatal history should include information on the mother's pregnancy, such as prenatal exposure to illicit drugs, toxins, or infections; maternal diabetes; acute maternal illness; trauma; radiation exposure; prenatal care; and fetal movements.

A history of early frequent spontaneous abortions, parental consanguinity, and a family history of neurologic disease (eg, hereditary neurodegenerative disease) is also important.

Perinatal history

The perinatal history should include the child's gestational age (ie, degree of prematurity) at birth, presentation of the child and delivery type, birth weight, Apgar score, and complications in the neonatal period (eg, intubation time, presence of

intracranial hemorrhage on neonatal ultrasonogram, feeding difficulties, apnea, bradycardia, infection, and hyperbilirubinemia).

Developmental history

The child's developmental history should review his/her gross motor, fine motor, language, and social milestones from birth until the time of evaluation.

The age at which gross motor milestones are achieved in typically developing children include head control at age 2 months, rolling at age 4 months, sitting at age 6 months, and walking at age 1 year. Infants with cerebral palsy may have significantly delayed gross motor milestones or show an early hand preference when younger than 1.5 years, suggesting the relative weakness of one side (eg, reaching unilaterally).

The presence of an unexplained regression would be more suggestive of a hereditary neurodegenerative disease than cerebral palsy.

Current social skills, academic performance, and participation in an early intervention program (if < 3 y) or school support (if > 3 y) should be reviewed, including resource room assistance; physical, occupational, and speech and language therapy; and adaptive physical education.

Standardized cognitive and educational testing and a current individualized education plan can be used to determine whether speech therapy, occupational therapy, and physical therapy referrals are needed, if not already in place.

Review the patient's equipment or need for equipment such as adaptive and communication devices (eg, computer-assisted speech programs), orthotics (eg, ankle-foot orthoses, walkers, wheelchair), and/or seating (may require straps to keep in place). See Rehabilitation and Cerebral Palsy.

Physical Examination

Physical indicators of cerebral palsy include joint contractures secondary to spastic muscles, hypotonic to spastic tone, growth delay, and persistent primitive reflexes.

The initial presentation of cerebral palsy includes early hypotonia, followed by spasticity. Generally, spasticity does not manifest until at least 6 months to 1 year of life. The neurologic evaluation includes close observation and a formal neurologic examination.

Before the formal physical examination, observation may reveal abnormal neck or truncal tone (decreased or increased, depending on age and type of cerebral palsy); asymmetric posture, strength, or gait; or abnormal coordination.

Patients with cerebral palsy may show increased reflexes, indicating the presence of an upper motor neuron lesion. This condition may also present as the persistence of primitive reflexes, such as the Moro (startle reflex) and asymmetric tonic neck reflexes (ie, fencing posture with neck turned in same direction when one arm is extended and the other is flexed). Symmetric tonic neck, palmar grasp, tonic labyrinthine, and foot placement reflexes are also noted. The Moro and tonic labyrinthine reflexes should extinguish by the time the infant is aged 4–6 months; the palmar grasp reflex, by 5–6 months; the asymmetric and symmetric tonic neck reflexes, by 6–7 months; and the foot placement reflex, before 12 months. Cerebral palsy may also include the underdevelopment or absence of postural or protective reflexes (extending arm when sitting up). For a good discussion of this topic, see Capute AJ, Accardo PJ, eds. Developmental Disabilities in Infancy andChildhood. 2nd ed.2001;95-100.[25]

The overall gait pattern should be observed and each joint in the lower extremity and upper extremity should be assessed, as follows:

- Hip – Excessive flexion, adduction, and femoral anteversion make up the predominant motor pattern. Scissoring of the legs is common in spastic cerebral palsy.

- Knee – Flexion and extension with valgus or varus stress occur.
- Foot – Equinus, or toe walking, and varus or valgus of the hindfoot is common in cerebral palsy.

Gait abnormalities may include the crouch position with tight hip flexors and hamstrings, weak quadriceps, and/or excessive dorsiflexion.

Spastic (pyramidal) cerebral palsy

Patients with spastic (pyramidal) cerebral palsy evidence spasticity (ie, a velocity-dependent increase in tone) and constitute 75% of patients with cerebral palsy. Patients have signs of upper motor neuron involvement, including hyperreflexia, clonus, extensor Babinski response, persistent primitive reflexes, and overflow reflexes (crossed adductor). This may be observed by the child's tendency to keep the elbow in a flexed position or the hips flexed and adducted with the knees flexed and in valgus, and the ankles in equinus, resulting in toe walking.

Dyskinetic (extrapyramidal) cerebral palsy

Dyskinetic (extrapyramidal) cerebral palsy is characterized by extrapyramidal movement patterns, abnormal regulation of tone, abnormal postural control, and coordination deficits. Abnormal movement patterns may increase with stress, excitement, or purposeful activity. Muscle tone is usually normal or can be decreased during sleep. Intelligence is normal in 78% of patients with athetoid cerebral palsy. A high incidence of sensorineural hearing loss is reported. Patients often have pseudobulbar involvement, with dysarthria, swallowing difficulties, drooling, oromotor difficulties, and abnormal speech patterns. Thus, the classic physical presentations of dyskinetic cerebral palsy include the following:

- Early hypotonia with movement disorder emerging at age 1-3 years
- Arms more affected than legs
- Deep tendon reflexes usually normal to slightly increased
- Some spasticity
- Oromotor dysfunction
- Gait difficulties
- Truncal instability
- Risk of deafness in those affected by kernicterus

These patients with dyskinetic cerebral palsy may have decreased head and truncal tone and defects in postural control and motor dysfunction such as athetosis (ie, slow, writhing, involuntary movements, particularly in the distal extremities), chorea (ie, abrupt, irregular, jerky movements) or choreoathetosis (ie, combination of athetosis and choreiform movements), and dystonia (ie, slow, sometimes rhythmic movements with increased muscle tone and abnormal postures, eg, in the jaw and upper extremities)

Spastic hemiplegic cerebral palsy

Hemiplegia is characterized by weak hip flexion and ankle dorsiflexion, an overactive posterior tibialis muscle, hip hiking/circumduction, supinated foot in stance, upper extremity posturing (that is, often held with the shoulder adducted, elbow flexed, forearm pronated, wrist flexed, hand clenched in a fist with the thumb in the palm), impaired sensation, impaired 2-point discrimination, and/or impaired position sense. Some cognitive impairment is found in about 28% of these patients. Thus, spastic hemiplegic cerebral palsy includes the following classic physical presentations:

- One-sided upper motor neuron deficit
- Arm generally affected more than leg; possible early hand preference or relative weakness on one side; gait possibly characterized by circumduction of lower extremity on the affected side

- Specific learning disabilities
- Oromotor dysfunction
- Possible unilateral sensory deficits
- Visual-field deficits (eg, homonymous hemianopsia) and strabismus
- Seizures

Spastic diplegic cerebral palsy

Patients with spastic diplegia often have a period of hypotonia followed by extensor spasticity in the lower extremities, with little or no functional limitation of the upper extremities. Patients have a delay in developing gross motor skills. Spastic muscle imbalance often causes persistence of infantile coxa valga and femoral anteversion. Cognitive impairment is present in approximately 30% of spastic diplegic patients. Spastic diplegic cerebral palsy includes the following classic physical presentations:

- Upper motor neuron findings in the legs more than the arms
- Scissoring gait pattern with hips flexed and adducted, knees flexed with valgus, and ankles in equinus, resulting in toe walking
- Learning disabilities and seizures less commonly than in spastic hemiplegia

Spastic quadriplegic cerebral palsy

Most patients with spastic quadriplegic cerebral palsy have some cognitive impairment and demonstrate the following classic physical presentations:

- All limbs affected, either full-body hypertonia or truncal hypotonia with extremity hypertonia
- Oromotor dysfunction
- Increased risk of cognitive difficulties
- Multiple medical complications (see Complications under Prognosis)
- Seizures
- Legs generally affected equally or more than arms
- Categorized as double hemiplegic if arms more involved than legs

DDx

Diagnostic Considerations

The diagnosis of cerebral palsy is generally made based on the clinical picture; however, some authors propose that the diagnosis should be deferred until the child is age 2 years or older. As the brain continues to develop postnatally, abnormalities of motor tone or movement in the first several weeks or months after birth may gradually improve over the first year of life (or even later). The Collaborative Perinatal Project found that almost 50% of individuals diagnosed with cerebral palsy and 66% of children diagnosed with spastic diplegia outgrew findings that were suggestive of cerebral palsy by age 7 years. Others did not manifest full motor signs suggestive of this disorder until aged 1-2 years.

Other conditions that should be considered when evaluating a patient with suspected cerebral palsy include metabolic and genetic diseases, hereditary spastic paraplegias, Rett syndrome, and tethered spinal cord.

Differential Diagnoses

- Inherited Metabolic Disorders
- Intellectual Disability
- Metabolic Myopathies
- Metabolic Neuropathy
- Traumatic Peripheral Nerve Lesions
- Tumors of the Conus and Cauda Equina
- Vascular Malformations of the Spinal Cord

Workup

Approach Considerations

The 2003 American Academy of Neurology (AAN) practice parameter on cerebral palsy suggests laboratory studies if:[24] (1) the clinical history or findings from neuroimaging do not indicate a specific structural abnormality, (2) additional and atypical features are present in the history or clinical examination, or (3) a brain malformation is detected in a child with cerebral palsy. In addition, diagnostic testing for coagulation disorders is recommended if a cerebral infarction is seen; however, available data were insufficient for guiding what precise studies should be ordered.

If a diagnosis of a hereditary or neurodegenerative disorder is suspected, screening for an underlying metabolic or genetic disorder should be performed. However, specific studies were not recommended by the AAN practice parameter as such studies should be guided by the clinical picture, such as clinical features suggestive of a particular syndrome.[24] However, since the 2003 practice parameter, there have been studies demonstrating clinically significant copy number variants on chromosomal microarray in patients with clinical diagnoses of cerebral palsy. These were found in patients with more severe motor impairment, dysmorphisms, or non-motor comorbidities as well as patients with cerebral palsy of unknown cause.[35, 36]

The AAN practice parameter did not recommend an electroencephalogram (EEG) unless suspicion for epilepsy or an epileptic syndrome is present, but it did recommend neuroimaging "to establish that a brain abnormality exists in children with cerebral palsy, that may, in turn, suggest an etiology and prognosis."[24] Note that a normal brain imaging study does not mean that the child does not have cerebral palsy, because the diagnosis is always based only on physical examination findings.

Potentially Helpful Laboratory Tests

There are no definitive laboratory studies for diagnosing cerebral palsy, only studies to rule out other symptom causes,

such as metabolic or genetic abnormalities, as deemed necessary based on clinical examination. Such studies may include the following:

- Thyroid function studies - Abnormal thyroid function may be related to abnormalities in muscle tone or deep tendon reflexes or to movement disorders.
- Lactate and pyruvate levels - Abnormalities may indicate an abnormality of energy metabolism (ie, mitochondrial cytopathy).
- Ammonia levels - Elevated ammonia levels may indicate liver dysfunction or urea cycle defect.
- Organic and amino acids - Serum quantitative amino acid and urine quantitative organic acid values may reveal inherited metabolic disorders.
- Chromosomal analysis - Chromosomal analysis, including karyotype analysis, chromosomal microarray, or specific DNA testing, may be indicated to rule out a genetic syndrome, particularly if dysmorphic features or abnormalities of various organ systems are present, or etiology of the cerebral palsy is undetermined.
- Cerebrospinal protein - Levels may assist in determining asphyxia in the neonatal period. Protein levels can be elevated, as can the lactate-to-pyruvate ratio.

Cranial Imaging Studies

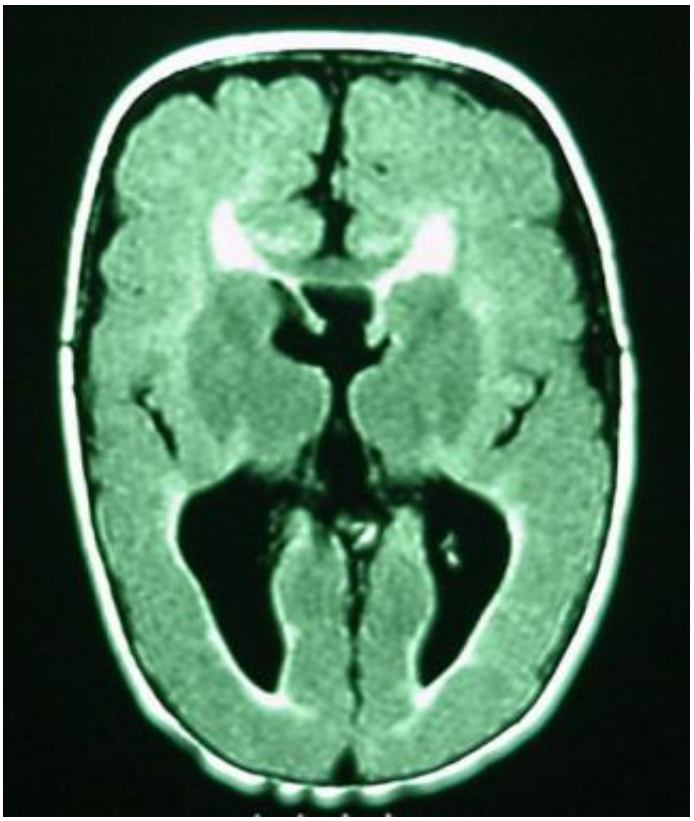
Neuroimaging studies can help to evaluate brain damage and to identify persons who are at risk for cerebral palsy. Data to support a definitive diagnosis of cerebral palsy are lacking.

Cranial ultrasonography performed in the early neonatal period can be helpful in medically unstable infants until they are able to tolerate transport for more detailed neuroimaging. Ultrasonography can delineate clear-cut structural abnormalities and show evidence of hemorrhage or hypoxic-ischemic injury. For example, neonatal cranial ultrasonography provides information about the ventricular system, basal ganglia, and corpus callosum, as well as diagnostic information on intraventricular hemorrhage and hypoxic-ischemic injury to the periventricular white matter. Periventricular leukomalacia initially appears as an echodense area that converts to an echolucent area when the patient is approximately age 2 weeks. Periventricular leukomalacia is strongly associated with cerebral palsy.

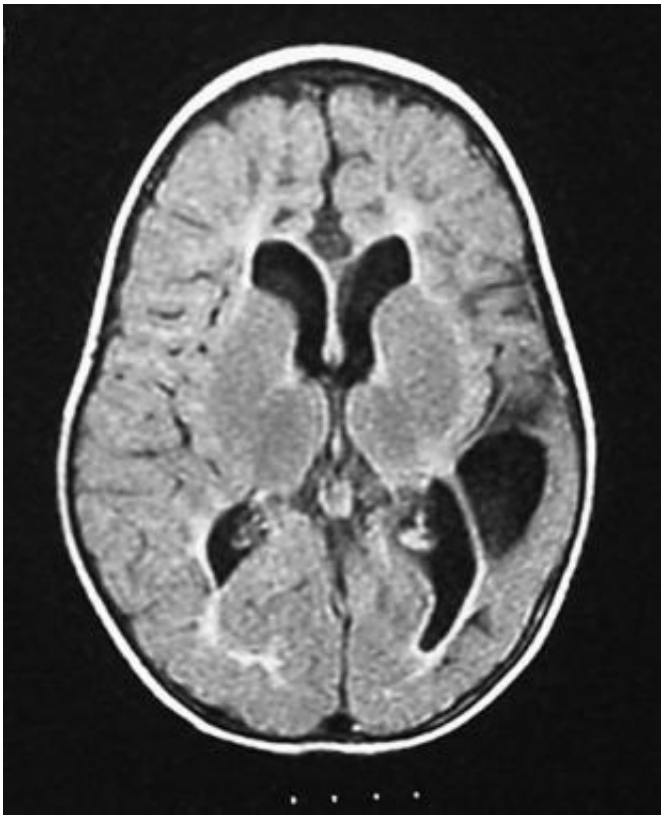
In infants, computed tomography (CT) scanning of the brain helps to identify congenital malformations, intracranial hemorrhage, and periventricular leukomalacia more clearly than ultrasonography.

Magnetic resonance imaging (MRI) of the brain is most useful after 2-3 weeks of life and is the diagnostic neuroimaging study of choice for older children, because this modality defines cortical and white matter structures and abnormalities more clearly than any other method. MRI also allows for the determination of appropriate myelination for a given age. In children with spasticity of the legs and worsening of bowel and bladder function, a spine MRI may help identify a tethered spinal cord.

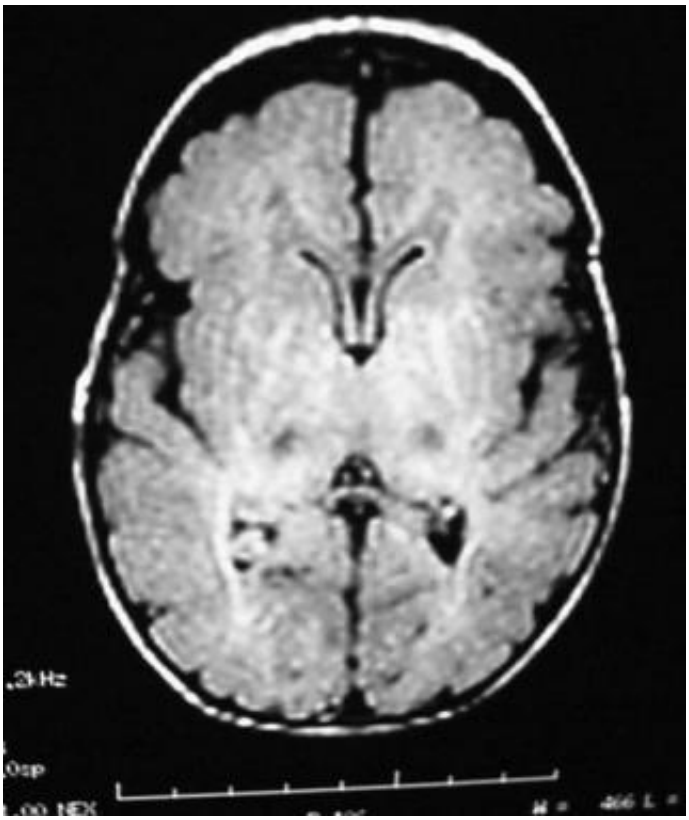
Although the precise role for MRI in the diagnosis and workup of children with cerebral palsy or suspected cerebral palsy has not been fully elucidated, the literature suggests that MRI should be strongly considered in all cases; in one study, 89% children with cerebral palsy were found to have abnormal MRIs.[37] Additionally, MRI may have a role in predicting neurodevelopmental outcomes in preterm infants.[38] See the following images.



Magnetic resonance image (MRI) of a 1-year-old boy who was born at gestational week 27. The clinical examination was consistent with spastic diplegic cerebral palsy. Pseudocolpocephaly and decreased volume of the white matter posteriorly were consistent with periventricular leukomalacia. Evidence of diffuse polymicrogyria and thinning of the corpus callosum is noted in this image.



Magnetic resonance image (MRI) of a 16-month-old boy who was born at term but had an anoxic event at delivery. Examination findings were consistent with a spastic quadriplegic cerebral palsy with asymmetry (more prominent right-sided deficits). Cystic encephalomalacia in the left temporal and parietal regions, delayed myelination, decreased white matter volume, and enlarged ventricles can be seen in this image. These findings are most likely the sequelae of a neonatal insult (eg, periventricular leukomalacia with a superimposed left-sided cerebral infarct).



Magnetic resonance image (MRI) of a 9-day-old girl who was born at full term and had a perinatal hypoxic-ischemic event. Examination of the patient at 1 year revealed findings consistent with a mixed quadriparetic cerebral palsy notable for dystonia and spasticity. Severe hypoxic-ischemic injury to the medial aspect of the cerebellar hemispheres, medial temporal lobes, bilateral thalami, and bilateral corona radiata is observed in this image.

Head ultrasonography, CT scanning, and MRI may be helpful for diagnosing and monitoring findings of hydrocephalus.

Patients who present clinically with cerebral palsy may have normal results from brain imaging studies. Normal results from neuroimaging studies do not exclude a clinical diagnosis of this disorder. However, in these cases, other underlying metabolic and genetic etiologies should be considered and excluded before diagnosing a child with cerebral palsy.

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Electroencephalography

Electroencephalography (EEG) is useful in evaluating severe hypoxic-ischemic injury. Findings initially show marked suppression of amplitude and slowing, followed by a discontinuous pattern of voltage suppression, with bursts of high-voltage sharp and slow waves at 24–48 hours. EEG can also be used to confirm a clinical diagnosis of epilepsy. However, EEG is not indicated if seizures are not suspected along with cerebral palsy.

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EMG and Nerve Conduction Studies

Electromyography (EMG) and nerve conduction studies are helpful when a muscle or nerve disorder is suspected (eg, a hereditary motor or sensory neuropathy as a basis for equinus foot deformities and toe walking).

Evoked potentials are used to evaluate the anatomic pathways of the auditory and visual systems.

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Treatment

Approach Considerations

The management of patients with cerebral palsy must be individualized based on the child's clinical presentation and requires a multidisciplinary approach (see Consultations). Rehabilitation is a "comprehensive intervention strategy designed to facilitate adaptation to and participation in an increasing number and variety of settings in a particular society and culture."

Neurologists and rehabilitation medicine specialists (physiatrists) play significant roles in the management of antispasticity medications. The physician's responsibility is to closely supervise and manage the multiple medical complications associated with cerebral palsy (see Complications under Prognosis).

Parents frequently inquire about and seek complementary and alternative therapies; however, more research is needed. A randomized, controlled trial to determine whether cranial osteopathy affects the general health and wellbeing of children with cerebral palsy found no evidence that cranial osteopathy leads to sustained improvement in motor function, pain, sleep, or quality of life in children aged 5–12 years.[39]

In addition, seizure disorders are common in persons with cerebral palsy. Thus, the clinician should be comfortable with the management of anticonvulsant medications (see Antiepileptic Drugs).

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Management of Abnormal Movements

Numerous medications, although often used off label for age and indication, may relieve the movement difficulties associated with cerebral palsy. These drugs target spasticity, dystonia, myoclonus, chorea, and athetosis. For example, baclofen, administered either orally or intrathecally, is often used for treating spasticity in these patients.

Botulinum toxin with or without casting

AbobotulinumtoxinA (Dysport) is the first botulinum toxin to gain FDA approval for the treatment of lower limb spasticity in children aged 2–17 years. Approval was based on a randomized, multicenter, double-blind, placebo-controlled, international Phase III study in 235 pediatric patients (158 received abobotulinumtoxinA and 77 received placebo) aged 2 to 17 years with lower limb spasticity due to cerebral palsy causing dynamic equinus foot deformity. Patients treated with abobotulinumtoxinA showed statistically significant improvement in efficacy assessments (ie, mean change from baseline in Modified Ashworth scale [MAS] in ankle plantar flexor muscle tone and mean Physician’s Global Assessment [PGA]) response to treatment score at Week 4 and Week 12.[40]

OnabotulinuimtoxinA (Botox) may reduce spasticity for 3-6 months and may be considered for off-label use in children with

cerebral palsy with spasticity in the lower extremities (gastrocnemius, in particular).[1, 2, 3, 4, 5, 41] This therapy can allow for improved range of motion, reduced deformity, improved response to occupational and physical therapy, and delay in the need for surgical management of spasticity. Casting, with or without botulinum toxin type A, may be an additional option for children with an equinus deformity, although the evidence is still somewhat conflicting.[42]

The established total body dose of onabotulinumtoxinA is limited to 12 U/kg, to a maximum of 400 U per visit. (Many practices, however, have been safely using 20 U/kg, to a maximum of 600 U). Each small muscle receives 1–2 U/kg, and large muscles, 4–6 U/kg. The interval between doses should be at least 4 months in order to help prevent antibody formation, which could make subsequent botulinum toxin procedures less effective. Note that large muscles may not respond to this limiting dose, or quite often, patients need several muscles done at each visit.

Phenol intramuscular neurolysis

Historically, phenol intramuscular neurolysis has been considered another medication option. This agent can be used for some large muscles or when several muscles are treated, but phenol therapy is more difficult to administer than other agents. Because phenol is administered using a nerve stimulator, this treatment is more painful, and anesthesia is often used when the therapy is performed. In addition, phenol can, in certain nerves, cause unpleasant sensory dysesthesias, therefore, its use is often limited to nerves with only motor innervation, such as the musculocutaneous (for decreasing arm flexion) and the obturator (for decreasing hip adduction). Phenol treatment is also used for hamstring motor point blocks (for knee flexion).

Antiparkinsonian, anticonvulsant, antidopaminergic, and antidepressant agents

Although antiparkinsonian drugs (eg, anticholinergic and dopaminergic drugs) and antispasticity agents (eg, baclofen) have primarily been used in the management of dystonia, anticonvulsants, antidopaminergic drugs, and antidepressants have also been tried.

Anticonvulsants (including benzodiazepines such as diazepam, valproic acid, and barbiturates) have been useful in the management of myoclonus. Chorea and athetosis are often difficult to manage, although benzodiazepines, neuroleptics, and antiparkinsonian drugs (eg, levodopa) have been tried. Benzodiazepines and baclofen are commonly used to manage spasticity.

Management by spasticity type

A multidisciplinary panel conducted a systematic evaluation of published evidence of efficacy and safety of pharmacologic treatments for childhood spasticity due to cerebral palsy.[43] The panel members consisted of the Quality Standards Subcommittee of the American Academy of Neurology (AAN), and the Practice Committee of the Child Neurology Society.[43]

Localized or segmental spasticity

For localized or segmental spasticity, results of the panel found botulinum toxin type A is effective treatment in the upper and lower extremities; however, conflicting evidence exists regarding functional improvement.[43] Botulinum toxin type A was found to be generally safe in children with cerebral palsy; however, the US Food and Drug Administration (FDA) investigated isolated cases of generalized weakness resulting in poor outcomes and issued a black box warning, as follows:

"Effects of all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These symptoms may include asthenia, generalized muscle weakness, diplopia, blurred vision, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening, and death have been reported. The risk of symptoms is probably greatest in children treated for spasticity, but symptoms can also occur in adults treated for spasticity and other conditions, particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and adults, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses."

Generalized spasticity

For generalized spasticity, the panel listed diazepam as probably effective and tizanidine as possibly effective, although insufficient data exist regarding motor function and side-effect profile.[43] The panel recommends diazepam for short-term use, and tizanidine may also be considered as a treatment option. Data were insufficient for use of dantrolene, oral baclofen, and intrathecal baclofen, and toxicity was frequently reported.[43]

Neurosurgery and Orthopedic Surgery

This section will briefly discuss the following:

- Intrathecal baclofen pump insertion
- Selective dorsal rhizotomy
- Stereotactic basal ganglia
- Orthopedic surgical intervention

Intrathecal baclofen pump insertion

Intrathecal insertion of a baclofen pump to treat spasticity and/or dystonia is useful in the patient with diffuse spasticity or dystonia[6] ; the baclofen pump is most useful in helping to decrease spasticity in the lower extremities and trunk, but it can also reduce spasticity in the upper extremities and improve speech. The pump is placed in the anterior abdominal wall and connects to a catheter inserted in the subarachnoid space overlying the conus of the spinal cord. Intrathecal baclofen can allow more local presynaptic inhibition of I-a sensory afferents and has fewer adverse effects than oral baclofen.

The degree of improvement in the upper extremities is increased with higher placement of the pump catheter. The dose can be adjusted by the physician with an external handheld programmer, with different doses administered during the day and evening, depending on the patient's needs. The patient will need monthly appointments to refill the pump with intrathecal baclofen. The monthly refills are performed in the physician's office, with a single percutaneous needlestick used to access the pump's refill port.

Selective dorsal rhizotomy

Another neurosurgical treatment is that of selective dorsal rhizotomy, which may be beneficial in both the short term[7] and long term[8] to treat velocity-dependent spasticity. This procedure includes a laminectomy and then surgical ablation of 70-90% of the dorsal or sensory nerve roots. By cutting I-a sensory fibers, selective dorsal rhizotomy decreases spasticity by decreasing reflexive motoneuron activation, which is thought to result from the lack of descending fiber input.

Gait analysis has revealed improved range of motion at the knee and hip, with improved stride length following selective dorsal rhizotomy. Patients must be selected carefully for this procedure, because the weakness produced may decrease the level of functional independence. Underlying weakness is uncovered with the decrease in spasticity. Some patients also depend on some of their spasticity to stand or walk.

This surgery has come to be performed less frequently since the advent of the baclofen pump. Because of the laminectomies, some of the earlier surgeries had complications of more severe lumbar lordosis several years after surgery. Most surgeons are currently doing smaller laminectomies of only 1-2 levels.

Stereotactic basal ganglia

Although data are limited in this population, stereotactic basal ganglia surgery may improve rigidity, choreoathetosis, and tremor. A meta-analysis published in 2017 found variable results, depending upon severity of dystonia and presence of

either no or minimal spasticity or ataxia, and thus concluded that there needs to be better markers to define appropriate candidates.[44]

Orthopedic surgical intervention

Scoliosis and hip dislocation are the most common conditions requiring surgery. Tendon lengthening or transfer can decrease spastic muscle imbalance and deforming forces, and osteotomy can realign limbs, including the femoral neck, tibia, and calcaneus.

Additionally, reconstructive surgery to the upper extremities can restore muscle balance, release contractures, and stabilize joints to improve placement of the hand in space, as well as voluntary grasp, release, and pinch functions.

Combined use of a continuous-infusion device and oral analgesics has been shown to be more effective than oral medications alone in reducing pain intensity in children with cerebral palsy undergoing lower extremity orthopedic procedures.[45]

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Special Considerations

Given that prenatal factors greatly outnumber perinatal and postnatal factors in the origin of cerebral palsy and that prenatal factors are difficult to isolate from perinatal and postnatal factors as a cause for this disorder, determining causality due to intrapartum asphyxia or medical neglect is difficult.

Medicolegal issues were outlined extensively in a 1997 review article by Perlman.[46] Obstetricians are at risk of malpractice claims because of the association of cerebral palsy with birth asphyxia, even though most cerebral palsy cases are thought to be caused by prenatal insult.

To determine the presence of medical negligence related to birth asphyxia, the following must be documented:[46]

- An adverse outcome occurred (eg, cerebral palsy as a consequence of intrapartum asphyxia).
- The standard of care was breached during labor or delivery, directly causing the asphyxia.
- An alternative medical strategy more likely than not would have altered the outcome in a positive fashion.

To ascribe the cause of cerebral palsy to intrapartum asphyxia, the following must not be present: (1) clinical evidence indicating any potential antenatal injury, (2) neuroimaging evidence of antenatal cerebral injury, (3) clinical evidence of severe perinatal asphyxia, and (4) evidence of other causes of neonatal encephalopathy.

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Consultations

As previously mentioned, a multidisciplinary team approach is needed in the management of patients with cerebral palsy. Among the specialists who should be consulted are physiatrists; orthopedic surgeons; neurologists and neurosurgeons; geneticists; gastroenterologist, nutritionist, and a feeding and swallowing team; pulmonologists; learning disability team; and other specialists.

Physiatrist

A rehabilitation medicine specialist (physiatrist) should be consulted for the evaluation and management of the rehabilitation program. This specialist can help with many aspects of care, including, but not limited to, those relating to

spasticity management, therapies, modalities, bracing, sialorrhea, and insomnia. Physiatrists may also administer intramuscular botulinum toxin type A.

Orthopedic surgeons

An orthopedic surgeon may be needed to help correct any structural deformities and should be consulted for the surgical management of hip dislocation, scoliosis, and spasticity (eg, tenotomy, a tendon-lengthening procedure). Orthopedic surgeons may also administer intramuscular botulinum toxin type A.

Neurologists and neurosurgeons

A neurologist may help with differential diagnosis and with ruling out other neurologic disorders. Consultation with a neurologist may also be helpful in the treatment of patients with seizures.

A neurosurgeon should be consulted for identifying and treating hydrocephalus, a tethered spinal cord, or spasticity. Neurosurgeons perform the dorsal rhizotomy procedure.

Geneticists

A specialist in genetics may help with the differential diagnosis and with ruling out other disorders. For example, a geneticist should be consulted to evaluate for an underlying genetic syndrome, particularly in the setting of dysmorphic features, multiple organ abnormalities, or a family history of a similar neurologic syndrome.

Gastroenterologist, nutritionist, and feeding/swallowing team

The gastroenterologist, nutritionist, and a feeding and swallowing team provide management of feeding and swallowing difficulties and gastroesophageal reflux and assess nutritional status.

A gastroenterologist may help with reflux and constipation and may aid in coordinating feedings to regulate weight gain or loss, if needed. A G-tube or J-tube also may be needed to help augment nutrition.

A periodic nutrition consultation is important to make sure that the child does not suffer from growth failure or nutritional deficiencies.

Pulmonologists

A pulmonologist should be consulted for the management of chronic pulmonary disease due to bronchopulmonary dysplasia and frequent or recurrent aspiration.

Learning disability team

A multidisciplinary learning disability team specializing in children with special needs should be consulted to identify specific learning disabilities, monitor cognitive progression, and guide services through early intervention and school. The child should be evaluated by a communication enhancement center to guide speech and language treatment and the use of communicative devices.

Other specialists

Consultation with an ophthalmologist may be indicated for follow-up of any patient experiencing visual deficits, and an audiologist may help to screen for hearing deficits. In addition, regular dental visits are important.[47] An endocrinologist is occasionally needed for precocious puberty or treatment of osteoporosis.

Long-Term Monitoring

Multidisciplinary cerebral palsy clinics can allow for the frequent, comprehensive follow-up of children with this disorder while decreasing the need for patient travel. Close neurologic follow-up is required for patients with cerebral palsy.

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Medication

Medication Summary

The goal of pharmacotherapy in patients with cerebral palsy is to reduce symptoms (eg, spasticity) and prevent complications (eg, contractures). Most of the medications used for this disorder in children are off label for age and indication and should be used only by physicians experienced in their use and familiar with their adverse effects.

Note that the indications and doses listed in this section are from a general formulary. A wide range of dosing can be encountered in clinical practice, because information in the literature regarding medication for cerebral palsy in children is scant.

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Neuromuscular Blockers, Botulinum Toxins

Class Summary

Botulinum toxins cause presynaptic paralysis of myoneural junctions and reduces abnormal contractions by preventing acetylcholine release from the presynaptic membrane. The therapeutic effects may last 3-6 months.

AbobotulinumtoxinA (Dysport)

First botulinum toxin to gain FDA approval for the treatment of lower limb spasticity in children aged 2-17 years. The dose is selected based on affected muscle, spasticity severity, and treatment history with botulinum toxins. Total dose per treatment session should not exceed 10-15 units/kg for unilateral lower limb injections or 20-30 units/kg for bilateral lower limb injections or 1000 units, whichever is less. Divide the total dose between the affected spastic muscles of the lower limb(s).

OnabotulinumtoxinA (BOTOX)

OnabotulinumtoxinA treats excessive, abnormal contractions associated with blepharospasm, hemifacial spasm, and cervical dystonia. This drug binds to receptor sites on motor nerve terminals and inhibits release of acetylcholine, which, in turn, inhibits transmission of impulses in neuromuscular tissue. This indication is off-label use in children.

Reexamine patients 7-14 days after the initial dose to assess for a treatment response. Increase the doses 2-fold over the previous doses for patients experiencing incomplete paralysis of the target muscle. The procedure needs to be repeated every 3-6 months depending on the response.

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Muscle relaxants

Class Summary

The muscle-relaxing effects of muscle-relaxant agents may come from inhibition of the transmission of monosynaptic and polysynaptic reflexes at the spinal cord level. These are thought to work centrally by suppressing conduction in the vestibular cerebellar pathways. They may have an inhibitory effect on the parasympathetic nervous system.

Baclofen (Lioresal, Gablofen)

Baclofen is a gamma-aminobutyric acid (GABA) analogue that inhibits calcium influx into presynaptic terminals and suppresses the release of excitatory neurotransmitters.

Baclofen may induce hyperpolarization of afferent terminals and inhibit both monosynaptic and polysynaptic reflexes at the spinal level. This agent undergoes rapid gastrointestinal absorption, which peaks in 1-2 hours. It is primarily excreted renally and is partially metabolized by the liver. Baclofen works better in the treatment of spinal spasticity than it does against cerebral spasticity, but the drug should be tried in both conditions.

This drug's use is often limited by central nervous system (CNS) adverse effects, and thus, an effective dose is usually not obtainable with oral dosing. Intrathecal baclofen is available for use with a surgically implanted pump, which may improve the effectiveness of dosing.

Dantrolene (Dantrium, Revonto)

Dantrolene inhibits the release of calcium into the sarcoplasmic reticulum. This agent may weaken even nonspastic muscles and is generally used only in patients with severe hypertonicity.

Benzodiazepines

Class Summary

Benzodiazepines are used in the acute management of seizures that may accompany cerebral palsy. By binding to specific receptor sites, these agents appear to potentiate the effects of gamma-aminobutyric acid (GABA) and facilitate neurotransmission of GABA and other inhibitory transmitters. Benzodiazepines may act in the spinal cord to induce muscle relaxation.

Diazepam (Valium, Diastat)

Diazepam is effective in treating seizures by depressing all levels of the central nervous system (CNS) (eg, limbic and reticular formation), possibly by increasing the activity of GABA at the spinal and supraspinal sites. Individualize the dosage, and increase cautiously to avoid adverse effects. Diazepam undergoes rapid gastrointestinal absorption; renal excretion and hepatic metabolism occur.

Sedation is common. Diazepam may worsen swallowing problems. This drug is generally used only in patients in whom severe hypertonicity is compromising care.

Anticholinergic Agents

Class Summary

Anticholinergic agents provide benefit for tremor in approximately 50% of Parkinson's disease patients, but they do not improve bradykinesia or rigidity. If 1 anticholinergic does not work, try another. Adverse effects include dry mouth and dry eyes, memory difficulty, confusion, and rare urinary retention.

Trihexyphenidyl

Trihexyphenidyl is a synthetic tertiary amine anticholinergic agent that reduces the incidence and severity (by 20%) of akinesia, rigidity, tremor, and secondary symptoms such as drooling. Besides suppressing central cholinergic activity, these agents may inhibit reuptake and storage of dopamine at central dopamine receptors, thereby prolonging the action of dopamine.

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Dopamine Prodrugs

Class Summary

Dopamine does not the cross blood-brain barrier, but levodopa (L-dopa) (the metabolic precursor of dopamine) does. L-dopa is decarboxylated to dopamine in the brain and in the periphery. The formation of dopamine in the blood causes many of the adverse effects associated with L-dopa. When administered alone, levodopa induces a high incidence of nausea and vomiting.

A peripheral decarboxylase inhibitor such as carbidopa is combined with levodopa to reduce the incidence of nausea and vomiting by inhibiting the peripheral conversion of levodopa to dopamine. Levodopa/peripheral decarboxylase inhibitor is the criterion standard of symptomatic treatment for Parkinson disease; it provides the greatest antiparkinsonian efficacy in moderate to advanced disease with the fewest acute adverse effects.

Because dopaminergic drugs block cholinergic nerve impulses that affect the muscles in the arms, legs, and other parts of the body, these agents may help patients with cerebral palsy. These medications help regulate muscle movement and motor function.

Levodopa/carbidopa (Sinemet, Sinemet CR, Parcopa)

Levodopa/carbidopa is a large, neutral amino acid absorbed in the proximal small intestine by a saturable carrier-mediated transport system. Absorption of this drug is decreased by meals that include other large, neutral amino acids. Only patients with meaningful motor fluctuations need to consider a low-protein or protein-redistributed diet.

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Anticonvulsant Agents

Class Summary

Anticonvulsant drugs are used to terminate clinical and electrical seizure activity as rapidly as possible and to prevent seizure recurrence.

Levetiracetam (Keppra)

Levetiracetam is used as adjunct therapy for partial seizures and myoclonic seizures. This agent is also indicated for primary generalized tonic-clonic seizures. The mechanism of action of levetiracetam is unknown.

Oxcarbazepine (Trileptal)

The pharmacologic activity of oxcarbazepine is primarily by the 10-monohydroxy metabolite (MHD) of oxcarbazepine. This agent may block voltage-sensitive sodium channels, inhibit repetitive neuronal firing, and impair synaptic impulse propagation. The anticonvulsant effect of oxcarbazepine may also occur by affecting potassium conductance and high-voltage activated calcium channels.

The drug pharmacokinetics of oxcarbazepine are similar in older children (>8 y) and adults. Young children (< 8 y) have a 30-40% increased clearance compared with older children and adults. Children younger than 2 years have not been studied in controlled clinical trials.

Valproic acid (Depakote, Depakene, Depacon)

Valproic acid is chemically unrelated to other drugs used to treat seizure disorders. Although its mechanism of action is not established, the activity of valproic acid may be related to increased brain levels of gamma-aminobutyric acid (GABA) or enhanced GABA action; it may also potentiate postsynaptic GABA responses, affect potassium channels, or have a direct membrane-stabilizing effect.

Phenobarbital

Phenobarbital exhibits anticonvulsant activity in anesthetic doses and can be administered orally; in status epilepticus, it is important to achieve therapeutic levels as quickly as possible. The intravenous (IV) dose may require approximately 15 minutes to attain peak levels in the brain. If injected continuously until convulsions stop, brain concentrations may continue to rise and can exceed that which is required to control seizures. It is important to use the minimal amount required and to wait for an anticonvulsant effect to develop before giving a second dose.

Restrict IV use to conditions in which other routes are not possible, either because the patient is unconscious or because prompt action is required.

If an intramuscular (IM) route is chosen, administer phenobarbital into areas with little risk of encountering a nerve trunk or major artery, such as a large muscle (eg, gluteus maximus, vastus lateralis). A permanent neurologic deficit may result from injecting into or near peripheral nerves.

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Alpha2 Adrenergic Agonist Agents

Class Summary

These agents are used for their antispasticity effects.

Tizanidine (Zanaflex)

Tizanidine is an imidazoline derivative and a central alpha2 noradrenergic agonist. The antispasticity effects are the probable result H-reflex inhibition. The drug may facilitate the inhibitory actions of glycine, reduce the release of excitatory amino acids and substance P, and produce analgesic effects. Tizanidine is a centrally acting muscle relaxant that is metabolized in the liver and excreted in the urine and feces.

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Questions & Answers

Overview

Presentation

DDX

Which specialist consultations are beneficial to patients with cerebral palsy?

What is included in long-term monitoring of patients with cerebral palsy?

Medications

What is the goal of drug treatment for cerebral palsy?

Which medications in the drug class Alpha2 Adrenergic Agonist Agents are used in the treatment of Cerebral Palsy?

Which medications in the drug class Anticonvulsant Agents are used in the treatment of Cerebral Palsy?

Which medications in the drug class Dopamine Prodrugs are used in the treatment of Cerebral Palsy?

Which medications in the drug class Anticholinergic Agents are used in the treatment of Cerebral Palsy?

Which medications in the drug class Benzodiazepines are used in the treatment of Cerebral Palsy?

Which medications in the drug class Muscle relaxants are used in the treatment of Cerebral Palsy?

Which medications in the drug class Neuromuscular Blockers, Botulinum Toxins are used in the treatment of Cerebral Palsy?

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