Cerebral Palsy: A Multisystem Review

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ABSTRACT: Most cases of cerebral palsy (CP) are the result of congenital, genetic, inflammatory, anoxic, traumatic, toxic, and metabolic disorders. A minority of cases result from asphyxia at birth. Nearly three-quarters of children with CP aged 7 years had a normal neurological evaluation at birth. Abnormal motor development usually provides the first diagnostic clue. Neuroimaging is recommended if the cause of CP has not been established with perinatal imaging. MRI is preferred to CT. Management of the multisystemic manifestations begins with a comprehensive medical evaluation by a multidisciplinary team that includes family members. Therapy is aimed at maximizing the patient's level of function. Key areas include ambulation, cognitive skills, activities of daily living, hygiene, and rehabilitation into society.

Cerebral palsy (CP) refers to a group of nonprogressive neurological conditions defined by specific motor deficits or movement disorders. It is often associated with other systemic sequelae. Because 65% to 90% of children with CP survive into adulthood, it is important for clinicians to understand the multisystemic nature of CP. Here we present an overview.

PREVALENCE/RISK FACTORS
The incidence of CP is relatively low. Prevalence in surviving neonates is about 0.2%. CP accounts for 2% to 8% of office visits to the pediatric neurologist. The spastic types are the most common, followed by the ataxic and athetoid types. Visits to the doctor are often precipitated by comorbidities involving organ systems other than the nervous system. Historically, CP was thought to be associated with birth trauma. Although the percentage of CP cases attributable to birth asphyxia is debatable, Nelson and Ellenberg estimated that 6% to 7% of cases resulted from asphyxia at birth—and that 80% of cases were associated with prenatal complications. Congenital, genetic, inflammatory, anoxic, traumatic, toxic, and metabolic conditions all have been implicated as causes of CP. Prenatal risk factors include intrauterine infections; choioamnionitis; fetal thrombophilia; exposure to teratogens; placental complications; multiple births; and maternal conditions, such as mental retardation, history of seizures, and hyperthyroidism. New models that look at the inflammatory-mediated model of CP and its developmental sequelae are being developed.

Perinatal events such as preterm birth, low birth weight, intracranial hemorrhage, infection, seizure, hypoglycemia, and hyperbilirubinemia are well-known risks for neurological sequelae. Careful developmental and neurological screening is warranted in pediatric patients who have been affected by these conditions in the perinatal period. Furthermore, accurate determination of the cause of CP has specific implications for prevention in future pregnancies, treatment, prognosis, and medicolegal issues.

DIAGNOSIS
History and physical examination. The parents' and pediatrician's concerns about abnormal motor development provide the first clue to a possible diagnosis of CP and may initiate referral to a pediatric neurologist. The history may reveal risk factors; findings from the physical examination may identify the type of CP. For guidance on diagnostic assessment, see "Practice parameter: diagnostic assessment of the child with cerebral palsy: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society." The traditional diagnostic approach consists of early assessment of impairments in muscle tone, strength, and control; assessment of involuntary movements; asymmetry; persistence of primitive reflexes; and late development of postural responses. Only about one quarter of children with CP aged 7 years had an abnormal neurological examination at birth.
In reviewing the differential diagnosis, conditions such as metabolic disorders should not be overlooked. Also be aware that genetic syndromes such as Lesch-Nyhan syndrome can mimic CP and should be considered in the differential diagnosis if the pregnancy and birth history are unremarkable.8 CP also can be detected based on functional limitations. Estimating functional limitations using the motor quotient (motor age divided by chronological age times 100) is one diagnostic tool. A motor quotient below 50 predicts gross motor delay.9

**Neuroimaging.** Neuroimaging is recommended in the evaluation of a child with CP if the cause has not been previously established by perinatal imaging. MRI is preferred to CT because it is more likely to identify a cause.6,10 Cranial ultrasonography is recommended for infants between 7 and 14 days old and near term-corrected age to identify intraventricular hemorrhage, periventricular leukomalacia, and low-pressure ventriculomegaly.

**Other investigations.** When an asphyxial episode during gestation is suspected, cord and serum laboratory studies (ie, hemoglobin/hematocrit, platelet count, pH, liver, and renal function tests) help determine the timing and severity of the insult. Metabolic and genetic studies should not be routinely ordered but should be considered when clinical history or findings and neuroimaging do not identify a specific structural abnormality.6 Coagulation studies should be obtained in hemiplegic CP.6 A genetics consultation may be useful to further evaluate specific conditions and dysmorphologies in which CP is one characteristic. An electroencephalogram should be obtained only when a child with CP has a history that suggests epilepsy.6

**MULTISYSTEM MANIFESTATIONS**

**Neurological.** CP is associated with motor and mental disabilities of variable severity in a growing child. The motor abnormalities include spasticity (spastic quadriplegia, hemiplegia, and diplegia) and movement disorders that may coexist in the same patient. Because bone growth exceeds muscle growth in the presence of spasticity in a growing child, contractures and bone deformities often develop.11

Dystonia, athetosis, or both are present in 10% to 20% of patients, and children with dystonia may have eye movement and oromotor abnormalities.12 The ataxic form of CP is uncommon and presents with gait abnormalities and fine motor dysfunction. Although not a defining feature of CP, cognitive impairment occurs in many patients and ranges from learning disabilities to attention deficit disorders to severe mental retardation. Motor development is not a reliable predictor of cognitive development.13 For example, children with athetotic CP may be of normal intelligence.14

Hearing loss of the sensorineural or conductive type and visual impairment (refractory errors, visual field defects, cortical visual impairment, faulty accommodation, strabismus, nystagmus, and optic atrophy) are common.14 Other sensory defects may include impairment of touch and pain perception, proprioception, and stereognosis in spastic forms of CP.15 Seizures—typically grand mal, which often are difficult to treat—occur in many children with CP. They usually manifest in the first year of life, more so in children with spastic hemiplegia or quadriplegia.

**Musculoskeletal.** Dislocations and bony deformities are not uncommon in the CP population. Spinal deformities such as kyphoscoliosis and lordosis develop in children with CP, particularly those who cannot ambulate. The incidence is as high as 60%.16 Spinal deformities progress despite skeletal maturity and may interfere with good seating posture and cause pain, pelvic misalignment, and pressure sores. Cervical and lumbar spondylosis and myelopathy may occur in athetoid CP secondary to stresses incurred by repetitive complex trunk movements.17 Nonambulators also are at high risk for osteopenia and fractures. Reduced bone mineral density is attributed mainly to immobility, poor nutrition, and anticonvulsant medication.18 Fractures usually occur at the metaphysis of the distal femur and proximal tibia and may be caused by contractures, falls, seizures, and overzealous physical therapy.19 Contractures at the hip and knee in particular are a source of pain and disruption to daily activities such as sitting, standing, and perineal hygiene.19 Equinus deformity occurs in almost all patients with spastic CP secondary to gastrocnemius and soleus muscle spasticity, which results in toe walking. Upper limb deformities are seen in patients with spastic hemiplegia and quadriplegia. The shoulders are internally rotated and flexion contractures occur at the elbow and wrist. Forearm pronations, fisted hand with thumb in palm, and swan finger deformities also are common.

**Oromotor.** Oromotor muscle incoordination and spasticity may interfere with speech, the ability to suck, and swallow mechanisms and may cause temporomandibular joint contractures.15 Speech delay and dysarthria are potential sequelae. Also, dental hygiene can be difficult to maintain.
Malocclusion, enamel dysplasia, and dental caries occur frequently. Gastroesophageal reflux disease (GERD) has been associated with dental erosion in CP, and degree of GERD severity has been correlated with degree of tooth erosion. Dripping is one of the most troublesome oromotor problems for patients with CP. Poor head control and posture, impaired lip closure, abnormal tongue movements, and oral sensory impairment may contribute.

Swallowing difficulties, GERD, and constipation also contribute to feeding problems, which may occur very early in life. In a population survey of children with CP aged 12 to 72 months, more than 90% had clinically significant oromotor dysfunction. Severe feeding problems preceded the CP diagnosis in 60% of these children. The undernourishment that results from feeding problems leads to growth failure. In those children who do not have major feeding disturbances, however, excessive weight gain can occur because of their inability to participate in physical activities.

**Cardiopulmonary.** Congenital heart disease may be a component of genetically mediated CP. Pneumonia may occur frequently in the severely affected patient secondary to immobility, weak cough, contorted posture (scoliosis or chest wall deformities), GERD, and risk of aspiration.

**GI.** Over 90% of children with CP have associated GI symptoms, including constipation, swallowing problems, regurgitation and/or vomiting, and abdominal pain. GERD, which is often difficult to control, has been found in up to 75% of patients and increases the risk of hematemesis, rumination, and dental erosion. Constipation has been associated with transit time delay in at least 1 segment of the colon and with ambulatory function.

**Genitourinary.** Bladder difficulties often occur concurrently with bowel difficulties in children with CP. Dysfunctional voiding symptoms, such as incontinence and urinary urgency, have been noted in more than half of all CP patients. Reproductive issues are often overlooked in the adolescent patient with CP. According to a recent cross-sectional survey, puberty tends to begin earlier in children with CP than in the general population. However, menarche occurs later: the median age is 14 years, as compared with 12.8 years in the general population.

Children with developmental disabilities are vulnerable to sexual abuse. Findings based on data from the National Center on Child Abuse and Neglect suggest that children with disabilities are twice as likely to be sexually abused than children in the general population. Furthermore, the US Department of Justice reports that up to 83% of women with developmental disabilities are sexually abused at some point in their lives.

**Behavioral.** Behavioral disorders, including attention deficit hyperactivity disorder, are more prevalent in children with CP. Frustration, aggression, and mood disturbances may be part of the picture. A change in behavior may signal that the child is in pain, especially in a child with communication difficulties. The degree of pain is difficult to assess and may also manifest as sleep disturbance, decreased appetite, or intolerance to movement. Several potential sources of pain include dental caries, GERD and esophagitis, constipation, infections, and musculoskeletal abnormalities.

**MANAGEMENT**

**General.** Management of the child with CP begins with a comprehensive medical evaluation by a multidisciplinary team that includes a pediatrician; a pediatric neurologist; physical, occupational, and speech therapists; an audiologist; an ophthalmologist; a social worker; and possibly, a neurosurgeon and an orthopedic surgeon. Family members are the most important part of the treatment team. Hearing tests and early referrals to audiologists and speech therapists are necessary to prevent delays in language and learning skills. Use of electronic communication devices may help alleviate frustration caused by communication difficulties. Screening for visual defects and ophthalmological referrals should take place within the first year of life. Cognitive delays warrant careful assessment, initiation into early intervention programs, and the development of an individualized education plan in the face of severe motor and communication difficulties. The goals of overall therapy should be aimed at maximizing the patient's level of function. Important areas of focus include ambulation, cognitive skills, activities of daily living, personal hygiene, and rehabilitation into society. The primary care physician will probably play the central role in coordinating care, but the pediatric neurologist will be called on for expert guidance.

**Neurological.** Pharmacotherapeutic resources are available to manage symptoms such as spasticity and sleep disturbances and to manage seizures and movement disorders in general. Oral antispasticity medications include benzodiazepines, baclofen, a2-adrenergic agonists, and dantrolene sodium (Dantrium). Injectable medications include botulinum toxin A (Botox). Invasive procedures include placement of an intrathecal infusion pump for continuous delivery of...
baclofen to the CNS for the treatment of severe spasticity. Several studies have shown that intrathecal baclofen therapy is safe and effective in children with CP.\textsuperscript{34-36}

Another neurosurgical procedure for spasticity is highly selective dorsal root rhizotomy. This procedure attempts to cut fewer than 50% of the sensory fascicles from each cauda equine nerve root, guided by intraoperative neuromuscular testing to identify the most abnormal nerve fascicles that should undergo ablation.\textsuperscript{37-39}

Few studies have directly compared the safety, efficacy, and long-term outcomes or relative costs of dorsal root rhizotomy and the baclofen pump. Therefore, the use of either of these interventions must be decided on a case-by-case basis.\textsuperscript{40} Seizure control with antiepileptic drugs or use of a ketogenic diet or surgery also should be considered on a case-by-case basis, depending on patient presentation and seizure type.

Therapies for dystonia include anticholinergics and dopamine agonists. Sleep problems, which can be attributed to pain and motor dysfunction, can be managed with melatonin and other sleep aids and by simply establishing an appropriate bedtime routine.

**Musculoskeletal.** Management of the musculoskeletal sequelae of CP should include the participation of the pediatric orthopedic surgeon and physical therapist. Treatment needs to be tailor-made for the specific orthopedic abnormality present. Consultation with the specialists will determine optimum timing and type of treatment.

**Oromotor.** Of various strategies studied to reduce plaque and gingivitis in patients with CP, an electric toothbrush was found most effective in optimizing oral hygiene.\textsuperscript{41} The use of cryotherapy to enhance mouth opening by providing a temporary reduction in masseter spasticity has been shown to improve oral access and thus facilitate preventive dental care and other dental procedures.\textsuperscript{42}

Occupational and behavioral therapy using oral stimulation techniques, such as stroking, tapping, and blowing exercises, has been shown to diminish drooling.\textsuperscript{43} The centrally acting antispastic agent modafinil (Provigil)\textsuperscript{44} and anticholinergic medications, such as scopolamine, glycopyrrolate (Robinul), and benztropine reduce drooling but are associated with significant systemic adverse effects.\textsuperscript{45}

Ultrasound-guided intraglandular injection of botulinum toxin A can successfully reduce drooling without major adverse effects.\textsuperscript{45} Surgical options include submandibular gland excision, parotid duct ligation, duct rerouting, and transystympanic neurectomy.\textsuperscript{46}

Placement of gastrostomy tubes (G-tubes) for non-oral feeding should be considered in patients at high risk for chronic undernourishment because of severe impairment of oromotor function. Oral feeding interventions for such patients have not been effective in promoting feeding efficiency or weight gain.\textsuperscript{47} Although concerns have been raised, no correlation between respiratory problems and G-tube placement has been found.\textsuperscript{48}

The placement of a G-tube improves the caregiver’s quality of life as measured by a significant reduction in feeding times, increased ease of drug administration, and reduced parental concern regarding the child’s nutritional status.\textsuperscript{49} Consultation with a nutritionist may benefit the child with CP who experiences either poor weight gain or obesity.

**Cardiopulmonary.** Any evidence of heart or lung disease should be aggressively evaluated.

Pediatric cardiology consultation should be sought for definitive diagnosis and treatment of the cardiac abnormality. Effective pulmonary toileting and administration of antibiotics, including anaerobic coverage, are essential for the treatment of pneumonia in the patient with CP.

**GI.** In patients with GERD who do not respond to medical management with proton pump inhibitors, Nissen fundoplication may be undertaken. A study of gastrojejunal tube placement suggested that this surgical procedure may be equally helpful in improving GERD.\textsuperscript{50} Oral administration of baclofen via a nasogastric tube to reduce symptoms of GERD also has been shown to reduce the frequency of emesis and the total number of events of acid reflux.\textsuperscript{51}

Treatment of chronic constipation demands a multifaceted approach that includes a regular toileting schedule, proper toilet positioning, dietary modifications, and medication. In patients with impacted stool, it is important to begin with a "clean-out" regimen using either oral osmotic agents or serial enemas. After the impacted stool is removed, a maintenance program using titrated agents such as polyethylene glycol to achieve daily soft stool should be continued on a long-term basis. Oral mineral oil should not be used because of risk of aspiration.

**Genitourinary.** Highly selective dorsal root rhizotomy may improve spasticity and bladder storage capacity in appropriate patients. Neurogenic detrusor overactivity—the most common finding in patients with lower urinary tract symptoms—can most often be controlled with a clean intermittent catheterization protocol and concomitant anticholinergic medication.\textsuperscript{28}

For precocious puberty, a pediatric endocrinologist may be consulted. Gonadotropin-releasing hormone agonists remain the mainstay treatment.\textsuperscript{52}
Behavioral. An integrative team approach, including monthly meetings between the rehabilitation therapist, child psychiatrist, developmental pediatrician, psychologist, and preventive medicine specialist, has been shown to improve standardized measures of family stress associated with the parents' attitude toward the child with a disability. This approach has yielded significant improvements in the subscales of the Vineland adaptive skills assessment of the child. Mood and behavioral disturbances are treated on a case-by-case basis, with behavior modifications and medication that depend on the individual patient's circumstances. If pain is the possible trigger for the behavior change, for example, management should focus on uncovering and treating the underlying cause.


