Cerebral Palsy-An Update

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Introduction
Cerebral palsy is the leading cause of childhood disability affecting function and development and was first described in 1862 by an orthopedic surgeon named William James Little. Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, 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, perception, cognition, communication, and behavior; by epilepsy, and by secondary musculoskeletal problem. So, screening for these conditions should be part of the initial assessment¹.

Modern brain imaging techniques have shed new light on the nature of the underlying brain injury and studies on the neurobiology of and pathology associated with brain development have further explored etiologic mechanisms.

For classification of CP, use of the four major dimensions of classification listed in table I is recommended.

Table: I. Components of CP classification²

1. MOTOR ABNORMALITIES
   A. Nature and typology of the motor disorder:
   The observed tonal abnormalities assessed on examination (e.g. hypertonia, hypotonia) as well as the diagnosed movement disorders present, such as spasticity, ataxia, dystonia, athetosis.

   B. Functional motor abilities:
   The extent to which the individual is limited in his or her motor function, including oromotor and speech function.

2. ACCOMPANYING IMPAIRMENTS
   The presence or absence of later-developing musculoskeletal problems and/or accompanying non-motor neurodevelopmental or sensory problems, such as seizures, hearing or vision impairments, or attentional, behavioral, communicative and/or cognitive deficits, and the extent to which impairments interact in individuals with cerebral palsy.

3. ANATOMICAL AND NEURO-IMAGING FINDINGS
   A. Anatomic distribution:
   The parts of the body (limbs, trunk, bulbar region, etc.) affected by motor impairments or limitations.

   B. Neuro-imaging findings:
   The neuroanatomic findings on CT or MRI imaging, such as ventricular enlargement, white matter loss or brain anomaly.

4. CAUSATION AND TIMING
   Whether there is a clearly identified cause, as is usually the case with post-natal CP (e.g. meningitis, head injury) or when brain malformations are present, and the presumed time frame during which the injury occurred, if known.

Prevalence and incidence
The overall prevalence of CP has remained constant in recent years despite increased survival of at-risk preterm infants³. In developed countries, the overall estimated prevalence of CP is 2-2.5 cases per 1000 live births. The prevalence of CP among preterm and very preterm infants is substantially higher⁴. In the developing world, the prevalence of CP is not well established but estimates are 1.5-5.6 cases per 1000 live births⁵.

Etiology and risk factors
Upto 50% of CP cases have no identifiable underlying etiology⁶. The etiologies can be classified according to the timing of the insult as prenatal (commonest), natal, or postnatal⁷. Risk factors for CP are multifactorial and can 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 deficiency⁸. There also seems to be an association between autoimmune and coagulation disorders and CP. Preterm infants are at the highest risk for developing CP. The vulnerable brain is harmed during a critical period of development primarily by known CNS complications of prematurity such as intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL)⁹. PVL is the strongest and most independent risk factor for the development of CP. A recent study found that cerebral malformations were much more frequent among children with CP than among all live births in the population¹⁰. Children with cerebral malformations tends to be of greater gestational age and birth weight, or the product of a twin gestation¹¹. Study suggests that genetic abnormalities may cause cerebral palsy. For years it was thought that a difficult birth and other perinatal factors were the leading causes of CP. Now, researchers find that the majority of CP cases may in fact be caused by genetic abnormalities. There is a growing body of evidence that suggests mutations in multiple genes are responsible for CP¹². In about 10-20% of patients CP is acquired postnatally mainly because of brain damage from bacterial meningitis, viral encephalitis, hyperbilirubinemia, motor vehicle collisions, falls or child abuse¹³.

Pathogenesis
Cerebral palsy is restricted to lesions of the brain only. The brain lesions of CP occur from the fetal or neonatal period up to early childhood¹⁴. Insults resulting in neuronal loss can be 1) cortical...
Cerebral Palsy displays a combination of features, such as spasticity and leading cause of extrapyramidal CP. Congenital ataxia cannot be diagnosed until about six months, because one cannot be sure until ataxoid movement develops which may not be one or two years after birth. The ataxoid form cannot usually be diagnosed early, because one cannot be sure until athetoid movement occurs when the child displays a combination of features, such as spasticity and choreoathetosis. Congenital 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 focal or multifocal cerebral injury. The brain lesions seen in preterm infants include germinal matrix/intraventricular hemorrhage and white matter damage.

An algorithm for the evaluation of the child with CP according to the American Academy of Neurology (AAN) practice parameter on CP (2004)

1. Confirm that the history does not suggest a progressive or degenerative central nervous system disorder
2. Assure that features suggestive of progressive or degenerative disease are not present on examination
3. Classify the type of CP (quadriplegia, hemiplegia, diplegia, ataxic, etc)
4. Screen for associated conditions including:
   - Development delay/mental retardation
   - Ophthalmologic/hearing impairments
   - Speech and language delay/difficulties
   - Feeding/swallowing dysfunction
   - If history of suspected seizures, obtain an EEG

Did the child have previous neuroimaging or other laboratory studies? (e.g., in neonatal period) that determined the etiology of CP?

- Yes: No need for further diagnostic testing
- No: Obtain Neuroimaging study (MRI preferred to CT)

Abnormal MRI

1. Determine if neuroimaging abnormalities in combination with history and examination establishes a specific etiology of CP
2. If developmental malformation is present, consider genetic evaluation
3. If previous stroke, consider evaluation for coagulopathy or other etiology

Normal MRI

1. Consider metabolic/genetic testing if on follow-up the child has:
   - Evidence of deterioration or episodes of metabolic decompensation
   - No etiology determined by medical evaluation
   - Family history of childhood neurologic disorder associated with CP

Figure 1: (A) Eight-year-old girl with cerebral palsy: spastic diplegia grade II, right > left. Focal epilepsy. An axial-plane, fluid-attenuated inversion recovery sequence revealed bilateral hyperintense lesions of the basal ganglia and thalamus. (B) Twenty-year-old boy with cerebral palsy: tetraplegia grade IV, right > left. Intractable epilepsy. An axial-plane, fluid-attenuated inversion recovery sequence revealed bilateral lenticulostriate hyperintensities and atrophy. (C) Ten-year-old boy with cerebral palsy: spastic diplegia grade III, left > right. Enlargement of the cerebellar vermis, cerebellar atrophy, and increased signal intensity of the cerebellar white matter. (D) Same patient as in C. (E) One-year-old boy with cerebral palsy: spastic diplegia grade II, left > right. Axial-plane, fluid-attenuated inversion recovery sequence revealed symmetrical atrophy of the body vertebrae.
Complications
Complications of CP include spasticity and contractures; feeding difficulties, choking, gagging, drooling, aspiration pneumonia, GERD, communication difficulties; osteopenia, osteoporosis, fractures, pain, bladder dysfunction, sleep disturbances and functional GI abnormalities contributing to bowel obstruction, vomiting, and constipation.

Management
The management of patients with cerebral palsy must be individualized based on the child's clinical presentation and requires a multidisciplinary approach that provides a combination of interventions. Specific treatment options include physical, occupational, and speech therapy, drug treatment for spasticity (local, intrathecal, systemic) and orthopedic and neurosurgical interventions. The primary care physician should provide anticipatory guidance, immunizations, and developmental surveillance.

Children with CP are at high risk of incomplete and delayed immunization and their increased vulnerability to the complications of vaccine-preventable diseases. All routine immunization should be provided, including pertussis vaccine, even if the child has epilepsy. Progressive uncontrolled epilepsy indicates DT rather than DPT vaccine. Annual influenza vaccine and pneumococcal immunization is recommended for those with recurrent or chronic respiratory illnesses.

Spasticity and other forms of muscle overactivity caused by cerebral palsy may impair function or ease of care or may cause discomfort or poor body image. The treatment program for a child with spasticity may include allied health therapy, exercise, casting, constraint-induced therapy, oral medications, chemodenervation, intrathecal baclofen, selective dorsal rhizotomy, and orthopedic surgery. Techniques may be combined for greater efficacy and better tailoring to the needs of the child. Systemic treatments for spasticity include Baclofen, Diazepam, Dantrolene, and Tizanidine alone or in combination. Baclofen is the most commonly used oral medication in children with generalized spasticity.

Children with spasticity that are refractory or intolerant to oral medications may be candidates for intrathecal baclofen therapy. In general, oral medications and intrathecal baclofen are used for treating generalized spasticity, while chemodenervation agents (botulinum toxin, phenol or alcohol) are used to treat localized spasticity.

Chemical denervation
Injection Botulinum toxin type A can be an effective treatment for pain in children with hip spasms and cerebral palsy. With ongoing active physiotherapy, longer benefits from the injections can occur. A new guideline from the AAN and the child neurology society finds Injection Botulinum toxin type A to be an effective and generally safe treatment for spasticity in children and adolescents with CP but there is some risk of isolated cases of generalized weakness following its use. Chemical denervation using phenol injections are some times used in larger muscles where botulinum toxin would be ineffective. How ever there is insufficient data to support or refute the use of phenol or alcohol.

Non-pharmacological therapy
Selective dorsal rhizotomy (SDR): Selective dorsal rhizotomy is a well accepted neurosurgical procedure for the relief of lower limb spasticity in children with spastic diplegic CP. SDR plus physical therapy decreases spasticity, improves joint range of motion and have a positive effect on gross motor function, and gait.

Neuromuscular electrical stimulation (NMES): There is evidence to support the use and effectiveness of NMES in children with CP. Electrical stimulation to the hip adductor and abductor muscles simultaneously at the sensory and motor levels respectively improves the gait of spastic diplegic CP children. How ever the use of dynamic splinting with NMES has been shown to be more effective than either treatment alone, or its own in improving function and posture. A neurostimulation device (the L 300 Foot Drop System), for the treatment of footdrop in children with cerebral palsy, was the first device of its kind approved by the US Food and Drug Administration (FDA) in January 2013 for use in children.

Orthotic management in cerebral palsy: Children with CP may have many musculoskeletal deformities depending on the type of CP. Rehabilitation, orthopedic surgical intervention and additional orthotic management can prevent and correct these deformities. Orthoses are frequently used to improve the gait efficiency of ambulant children with CP and the most common orthoses used is the ankle-foot orthoses (AFO).

Rehabilitation: Traditional Physiotherapy and Occupational therapy are widely used interventions and have been shown to be of benefit in the treatment of cerebral palsy. Children with CP who require intensive physical, occupational, and speech therapy may need to be admitted for rehabilitation. These patients receive therapy in at least 2 disciplines for 3 hours daily.

Physiotherapy: Physiotherapy is the most common intervention in cerebral palsy and is usually a component of mandated program of management. Physiotherapy program consists of Neuro-developmental Treatment (NDT) and Therapeutic Exercises (TE).

Occupational therapy (OT): Occupational therapy focuses on the development of skills necessary for the performance of activities of daily living. These activities include play, self-care activities such as dressing, grooming and feeding, and fine motor tasks such as writing and drawing. OT also addresses cognitive and perceptual disabilities, especially in the visual-motor area.

Constraint-Induced Movement Therapy: Researchers report that children with CP who underwent C1 movement therapy saw a significant increase in grey matter volume in areas of the brain associated with movement.

Training for sensory and perceptual integration: This is provided by giving various types of sensory stimulation. Most of this training is given in the form of play. Children not only accept this, they often enjoy learning these skills.

Table 2: Oral Agents Used in the Treatment of Spasticity Due to Cerebral Palsy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tr>
<td>Baclofen</td>
<td>2-7 years: 10-15 mg/day divided every 8 h; titrate dose every 3 days in increments of 5-15 mg/day to a max of 40 mg/day</td>
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<tr>
<td>Diazepam</td>
<td>0.12-0.8 mg/kg/day divided every 6-8 h</td>
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<tr>
<td>Dantrolene sodium</td>
<td>0.5 mg/kg/day twice daily; increase frequency to 3-4 times a day at 4-7 day intervals</td>
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<tr>
<td>Clonidine</td>
<td>5-10 mcg/kg/day, in 2-3 divided doses</td>
</tr>
<tr>
<td>Tizanidine</td>
<td>pediatric dosing is unavailable</td>
</tr>
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* Oral baclofen is FDA approved for use in children 12 years of age and older.

Figure 2: Global therapeutic approach to the child with spasticity.
Cerebral Palsy

Speech/Language Therapy: focuses on talking, using sign language, or using a communication aid.

Vagal nerve stimulation (VNS): Jaseja has shown the efficacy of VNS in CP patients on account of its dual therapeutic effectiveness, i.e. anti-epileptic and IED-suppression. These two effects are likely to control seizures that are quite often drug-resistant and also improve neurorecovery in CP patients, thus hoping for a better overall prognostic outcome and an improved quality of life.

Cognitive stimulation: Cognitive stimulation may be performed with an occupational therapy, physiotherapy, speech/language therapy.

Developmental Therapy (DT): The "developmental therapy" is best done in a holistic interdisciplinary approach that draws on the expertise of many specialists in different disciplines comprising of a physiotherapist, occupational therapist, speech and language therapist preferably under one roof.

Nutritional support: Some 35% of children with CP are malnourished. They may have difficulty in coordinating their muscles in their tongue and mouth to chew and swallow correctly. Extra nutritional supplements may be necessary in order to prevent malnutrition. Speech therapy provides some aid in the form of muscle exercises that can develop the muscles around the mouth. Those who require NG tube feeding during the first year of life have a 5-times greater mortality rate than children with oral feeding. Due to limitations of long term use of NG tube feeds, the American Academy for Cerebral Palsy and Developmental Medicine (AACDPM) addressed gastrostomy as an option for long –term treatment and supports gastrostomy as beneficial to most, but not all patients with CP.

Oral health: Drooling occurs in up to 30% of children with CP. Intrasalivary gland injection of botulinum toxin type A is known to treat sialorrhoea effectively in children with CP.

Bone Strength in Children with Cerebral Palsy: There are sufficient data to support that there may be significantly decreased bone mass in children with cerebral palsy. If there is evidence of vitamin D deficiency or poor dietary calcium intake, replacement would be appropriate. Several studies have shown that vitamin D and a third generation bisphosphonate (risedronate) have a larger increase in bone mineral density compared with children treated with vitamin D alone.

Vitamin K: In a child with hemiplegia treated with vitamin K alone, the cortical bone geometric strength of the hemiplegic tibia increased compared with the non-hemiplegic tibia.

New advances: In a study, allometric umbilical cord blood (UCB) infusion potentiated with recombinant human erythropoietin (rEPO) ameliorated motor and cognitive impairment in children with CP, suggesting that this therapy could be developed as a novel therapeutic approach. A comprehensive evaluation of the adverse effects of this therapy is, however, necessary before its clinical application. Rabbits with CP treated with D-NAC, a dendraimer conjugated with a drug known as NAC (N-acetyl-L-cysteine) showed a dramatic improvement and within 5 days were able to walk and hop. While still in pre-clinical testing in animals, the dendraimer-drug conjugate shows promise for postnatal treatment of babies suspected of having CP.

Prognosis: In general, some children who sit between three and four years of age eventually walk, but most require aids or braces or have restricted functional ambulation. A child who does not walk by nine years of age is unlikely to ever walk, even with support. Overall, the probability of reaching the age of 20 years in child with severe CP is 50%. Respiratory infections, aspiration, epilepsy, and cerebral malformation are leading causes of death.

Conclusion: Various Medical efforts failed to prevent the occurrence of CP. CP is a very diverse diagnosis with substantial variation in impairments and severity. Care and research in childhood CP is evolving. Management is not curative; however, if provided optimally it can improve the quality of life of these children and their families.

References: