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Review

Cerebral Palsy: An Overview of Etiology, Types and Comorbidities

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Abstract

Cerebral Palsy (CP) is the most frequent cause of childhood disability. CP occurs in 1 out of every 345 children in the United States. CP is primarily a motor disease that is the result of an insult to the brain that occurs during the prenatal or early postnatal period when the brain is still developing. CP is not a single disease but a physical description of motor impairments that originate from multiple etiologies. This article briefly discusses the etiologies, classification and management of the neurologic medical comorbidities that are associated with CP. Proactive management can assist in minimizing morbidity and maximizing outcomes and improving quality of life.

Keywords

Cerebral palsy; comorbidity; etiology; types; diagnosis

1. Introduction

French pathologists in the 1820's first started correlating brain injuries to clinical manifestations [1]. In 1843, orthopedic surgeon William Little is credited with first describing *cerebral paralysis* in

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a series of lectures entitled “Deformities of the Human Frame [1].” Although his lecture was focused on the muscle contractures and boney deformities as a result of paralysis and spasticity, he was credited with being the first to identify preterm and birth asphyxia as the cause of the brain damage that led to spasticity and paralysis in children [1] However, many notable names in medicine also contributed to the recognition and definition of cerebral palsy (CP). Sir William Osler, the father of modern medicine, first coined the term “cerebral palsy” and explored other etiologies aside from birth asphyxia. It was Osler who began classifying CP based upon “distribution of paralysis [1].” Sigmund Freud, although known for psychiatry, was a trained neurologist and neuropathologist who first suggested that, in addition to the intranatal and postnatal period, CP may also result from maternal and idiopathic congenital factors [1]. Freud also advocated for classifying CP based upon clinical presentation as opposed to pathologic findings. These initial observations that began nearly 180 years ago still remain an integral part of how CP is viewed and classified today.

1.1 Incidence and Etiology

Since Freud’s initial observations, CP has been recognized as a spectrum of disorders that are linked to an injury to the developing infant brain that occurs in the prenatal, perinatal or postnatal period. CP remains the most common childhood motor disability. It occurs in one out of every 345 children in the United States and occurs throughout the world in one to four children per 1,000 [2]. It was initially believed that CP was due to hypoxia during labor or the perinatal period. The etiology is likely multifactorial. In the majority of cases, the initial event causing damage to the infant’s brain may be indeterminable. Estimates suggest that approximately 75% of cases may have originated from a prenatal cause, whereas the perinatal and neonatal period risk factors account for 10-18% of cases [3] There have been multiple risk factors attributed to the development of CP (see Table 1). Although these identified risk factors place children at higher risk for developing CP, the vast majority of children with risk factors do not develop CP [4]. Furthermore, nearly 50% of children diagnosed with CP are term births without any identified neonatal risk factors [5].

Table 1 Risk Factors for Cerebral Palsy.

Prenatal	Perinatal	Postnatal
Systemic Diseases During Pregnancy	Prematurity	Head Trauma Accidental/ Non-Accidental
Brain Abnormalities	CNS Infections, i.e. viral encephalitis Bacterial meningitis	CNS infections
Multiple Gestation Pregnancy	Stroke	Infections
Assisted Reproduction Technology	Hypoxic-Ischemic Insults	Stroke
Placenta Abnormalities, i.e. abruption	Prolonged Labor	Anoxic Insults

Premature Rupture of Membranes	Neonatal Seizures
Oligohydramnios/ Polyhydramnios	Hyperbilirubinemia
Intrauterine Hypoxia	
Intrauterine Infections	
Potential pathogenic genetic variants	

Premature birth has been identified as one of the largest risk factors for development of CP. Children born prematurely account for nearly 35% of cases of CP [6]. Risk factors most commonly associated with CP in premature infants include: lower gestational age, small for gestational age, infection, chorioamnionitis, multiple births, male gender, postnatal corticosteroids, and early surgery [7]. Among identifiable risk factors, preterm birth has the highest correlation with CP [7]. An infant born prior to 28 weeks of gestation is 50 times more likely to have CP than a term child [8]. Children born at term have different risk factors for CP than children born preterm. McIntyre et al 2012 completed a systemic review to determine the most statistically significant risk factors for CP in term infants CP [4]. These included placental abnormalities, major and minor birth defects, low birthweight, meconium aspiration, instrumental/emergency caesarean delivery, birth asphyxia, neonatal seizures, respiratory distress syndrome, hypoglycemia, and neonatal infections [4]. Sadowska et al looked at risk factors for developing a specific motor type of CP [9]. They found that respiratory failure, infections, intraventricular bleeding and prematurity were common risk factors among all CP motor types. Many different pathways may lead to CP; however, direct causal relationships are not always clear.

Infection is also a significant risk factor for both preterm and term infants. Premature infants who have evidence of post-natal systemic inflammation, such as from an infection, will have an increased risk of developing CP [10, 11] Placental infection may lead to hypoxia-ischemia which increase inflammatory cytokine levels in the fetus. High levels of cytokines have been associated with intraventricular hemorrhage and periventricular leukomalacia in preterm infants [12]. This “two-hit model” suggests that infants already at risk by being premature may increase the risk of developing CP once the additional insult of systemic inflammation is added [11]. Chorioamnionitis by itself is associated with a 4-fold increased risk for CP in term infants [13].

Although birth asphyxia is commonly linked to CP, this may not necessarily be a primary contributing factor as once thought. The term “birth asphyxia” was initially associated with the need for oxygen after birth [14]. However, this term historically played a key role in the definition of CP from both a medical and legal aspect. Ellenberg and Nelson argue that birth asphyxia cannot necessarily be attributed as the direct causative factor of clinical signs such as APGAR scores, respiratory depression, neonatal seizures, or aberrant fetal heart rate patterns [15]. Previous definition of CP overly attributed asphyxia to CP and the meta-analysis of these studies to determine an estimate case exposure rate of birth asphyxia is indeterminate given the heterogeneity of study designs [15]. Perinatal factors previously associated with birth asphyxia such as respiratory difficulties after birth, neonatal seizures, caesarean delivery and meconium delivery may be associated with other factors that occurred earlier in development and not directly related to

delivery [4]. A more accurate estimation of children who develop CP as a result of birth asphyxia is most likely less than 10% [15]. The term hypoxic ischemic encephalopathy (HIE) is more specific to an intrauterine hypoxic event but may require supporting evidence such as: metabolic acidosis on cord blood gas or arterial blood within an hour of birth, low APGAR scores, seizures, evidence of multiorgan failure and/or MRI findings [13]. However, this is suggestive of an event that occurred but not causation of the event. A study in Western Australia followed term newborn children with CP for 6 years. Only 13% of the infants with moderate to severe HIE developed CP [16]. Of the children with CP, 24% had a history of HIE whereas the other 76% did not have a history of HIE during first week of life [16]. However, those with HIE did have a poorer prognosis.

Brain imaging in children with CP may demonstrate combinations of injury, not just the effects of hypoxia. The stage of brain maturation at the time the injury occurs can be determined by the type of lesion, site of lesion, and brain response to injury [17]. In the preterm infant, the structural and functional immaturity of the blood vessels make them extremely vulnerable to both ischemic and hemorrhagic injury [18]. Beginning at mid-gestation, the arterial branches start to penetrate the cerebral wall and grow towards the ventricles. However, they are thin walled and have poor intrinsic regulation of blood flow, making them vulnerable to hypoxic ischemic insults [18]. The oligodendrocyte, which makes myelin, is located in the deep periventricular white matter [18]. Thus, this makes the immature oligodendrocyte vulnerable to those vascular changes as well and ultimately affects periventricular white matter [18]. Thus, necrosis of the white matter around the lateral ventricles, periventricular leukomalacia and multicystic cortical encephalomalacia is a characteristic pattern seen in preterm CP [19]. Diffuse injury during the second trimester may cause liquefaction necrosis, porencephalic cysts [20]. The brain of the term infant is affected by global hypoxia-hypoperfusion events to the entire brain or focal infarctions [18]. As this results in abruption of major arterial supplies or disruption of intravascular boundaries (watershed areas), the cerebral cortex and its underlying subcortical and periventricular white matter are affected.

Genetics are now becoming more recognized as a contributing factor to CP. Previously it was thought to contribute to 1-2% of cases that had familial links [6]. Recent studies utilizing exome sequencing show that 14% of cases have single gene mutations and 31% have clinically relevant copy number variations [6]. The utilization of next generation sequencing in individuals with CP have demonstrated quite variable results, from 14-80% [6, 21, 22]. Although, it is difficult to understand the significance of these findings given the large variability, it is clear that the interaction of genetics may play a larger role in the manifestation of CP than previously thought. As many as 1/3 of patients diagnosed with CP do not have traditional risk factors, and it is likely that there may be a genetic component to their diagnosis [23]. In a recent study 45% of children who were diagnosed with cerebral palsy without risk factors were found to have detrimental genetic variants [24]. In addition, children with more significant motor and intellectual disabilities were more likely to contain these variants [24]. In a recent study by Chopra et al, the researchers found that 29% of children with CP who had no risk factors for CP contained genetic variants discovered in whole exome sequencing [25]. Surprisingly, 15% of children with CP who had identifiable risk factors for CP also contained genetic variants [25]. Multiple methods in human genome sequencing have discovered multiple genetic mutations that are linked to CP, but not a specifically associated variant [13]. It is speculated that genetic variations may be similar to other disabilities such as autism in which causative variants may not be directly determined [24]. Multiple variations have been identified including single-gene mutations, copy number variants, single nucleotide polymorphisms, and candidate CP genes The

OMIM Mendelian genetic database contains more than 800 genetic conditions that includes CP as part of their phenotype [21]. Although clinicians tend to focus on genetic conditions that mimic CP, there is growing data to suggest that there are susceptibility genes that may be contributing factors to developing CP as well [21]. Chopra et al found that 26% of subjects with CP who had whole exome sequencing were found to have a pathogenic or likely pathogenic variant in 13 unique genes [25]. Our understanding of genetic factors that lead to CP is still developing [23]. In some cases, identifying potentially detrimental genes may lead to identification of unrecognized comorbidities or changing of care plans. In addition to phenotyping patients, future researchers will need to characterize genotype relationships in order to determine if specific molecular subtypes of CP may be more or less amenable to specific therapies or treatments [23, 26]. It may be possible that identifying genes that cause specific motor types may help develop personalized treatments [26].

2. Diagnosis

The most widely accepted definition is from the 2007 consensus which defines CP as "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 [27]. In addition to motor disturbances, there may be associated disorders of "sensation, perception, cognition, communication and behavior [27]."

When making a clinical diagnosis of CP, the following criteria must be met [27]:

1) motor involvement
2) Timing of insult to brain must occur in the perinatal/infant period when the brain is developing
3) Nonprogressive course from neurological standpoint

Recently Aravamuthan et al completed a study demonstrating that even among experts there is variability in diagnosis, especially in the setting of known genetic etiology and hypotonia [28]. Forty percent of the respondents felt that a known genetic etiology was a reason not to diagnose CP [28]. However, this would be contested by both the 2007 consensus definition recognizing that CP is a phenotypic and not an etiologic diagnosis and the 2019 international consensus statement stating that "genetic or other causation should not change the clinical diagnosis of cerebral palsy [27, 29]."

There is a large variability in when children are diagnosed with CP. Typically children with CP are diagnosed between the ages of 12-24 months when clinical motor signs of impaired movement, balance or posture became more apparent [30-32]. Hubermann et al found that primary care providers referred children to neurologists for diagnosis of CP at an average of 28.8 months +/- 27.1 months in comparison to other pediatric medical specialties at 12.6 +/- 15.7 months [32]. Children who had a neonatal intensive care stay tended to be referred significantly earlier for diagnosis and interventions at a mean age of 9m [32]. Prior studies cited that physicians would adopt a "wait and see" approach to see if the child would "catch up [5]." There was a belief that there was a "silent" or latent period that often prevented early diagnosis [33]. However, research has demonstrated that parents experienced more grief when diagnosis was delayed [34]. Equally important, an earlier diagnosis leads to earlier initiation of therapeutic interventions during critical periods of brain growth and neuroplasticity as well as initiating treatment plans for medical comorbidities [32, 33].

Diagnosis of CP is dependent on a combination of several factors, a history consistent with clinical risk factors, physical exam, neurodevelopmental assessments, and/or neuroimaging. However, CP or "high risk CP" can be accurately predicted prior to 6m of age using neurodevelopmental screening and MRI [33]. In 2017, an international group of experts recommended best practices for early detection of CP using MRI and neurodevelopmental screening [33]. Despite MRI having a sensitivity of 86-89%, neurodevelopmental screening is a more sensitive test [35]**.** Prior to 5 months of age, the Prechtl Quantitative Assessment of General Movements (GM) has a sensitivity of 98% and the Hammersmith Infant Neurologic Exam (HINE) has a sensitivity of 90% [35, 36]. Conversely, normal MRI and GM completed as early as three months can assure that a high risk term infant is at low risk for moderate to severe CP [37]. After 5 months, the HINE and the Development Assessment of Young Children are preferred screening exams [36]. Where costs or feasibility of an MRI is not possible, the HINE can provide early diagnosis as well as objective evidence regarding the severity of CP [33]. In a recent study by Straathoif et al, they found that high risk infants who had hypertonia in the upper extremity after 7 months had a higher association with CP at 21months, whereas the association of ankle hypertonia was not associated with CP at 21months unless it persisted after 18 months of age [38].

MRI findings that are suggestive for high risk for CP include white matter injury (i.e.: cystic periventricular leukomalacia, and periventricular hemorrhagic infarction), injury to deep grey matter structure (i.e. basal ganglia lesion or watershed injuries), brain malformations (i.e. cortical dysplasia) or stroke [38]. In term infants, an MRI should always be performed as part of the initial evaluation if there is no other neonatal imaging that supports the diagnosis [30]. MRI's can be helpful in establishing a diagnosis as well as helping determine the cause of CP [33]. In addition to establishing causation, it can help differentiate between structural abnormalities, vascular abnormalities, or help in identifying metabolic or genetic syndromes [35]. In 10-15% of children diagnosed with CP, those children have normal MRI's [39, 40].

Although CP is a phenotypical diagnosis, it is important to have a correct diagnosis. There are many metabolic and genetic disorders that can present with motor dysfunction that are very similar to CP but are not CP. These disorders are frequently referred to as "CP mimics" [41]. This is an important distinction in that they may have potential treatments which can lessen or reverse neurologic course if identified in time [41]. Disorders such as aromatic L-amino acid decarboxylase (AADC) and dopa-responsive dystonia are frequently mistaken for CP, as they have early onset motor disorder [41]. A thorough medical history and clinical examination is essential in detecting suspected cases (History and physical exam findings suggestive of CP mimic can be found in Table 2). An accurate diagnosis may assist the family with treatment options, disease modifying therapies and prognosis. Furthermore, it may provide the family options for genetic counseling which may help educate in regards to cause of the disorder, risk of recurrence in future children, and prognosis.

Table 2 Clinical Features of Cerebral Palsy Mimics [21, 41].

Absent history of any perinatal risk factor for brain injury
Family history of sibling with similar neurological symptoms
Family Hx of Consanguinity
Motor symptom onset after an initial period of normal development
Developmental regression Progressive neurological symptoms

Paroxysmal motor symptoms or marked fluctuation of motor symptoms
Clinical exacerbation in the setting of a catabolic state (e.g., febrile illness) Isolated generalized hypotonia
Prominent ataxia
Isolated hypotonia
Rigidity
Signs of peripheral neuromuscular disease (reduced or absent reflexes, sensory loss)
Eye movement abnormalities (e.g., oculogyria, oculomotor apraxia, or paroxysmal saccadic eye-head movements)
Normal MRI
MRI with abnormalities isolated to Globus Palidus

There are many different management strategies for sending genetic testing for children with CP. Children with brain malformations, dysmorphic features, or family history of CP or consanguity, or multiple miscarriages in mother should have a genetic work-up [21, 30, 41]. Typically these patients would start with a chromosome microarray [21]. If the patient has a history of developmental regression, then metabolic screening is recommended [21]. If a patient has a nonspecific CP phenotype, such as hypotonia, then send whole-exome sequencing after muscular dystrophies have been ruled out [21]. There are also gene panels for specific phenotypes such as ataxia and central nervous system migrational disorders which are searchable on the Genetic Testing Registry (www.ncbi.nlm.nih.gov/gtr).

3. Classification of CP

CP is typically described based on movement disorder, anatomic distribution and severity of the impairment [27]. There are 4 motor types that present and may change during the first two years [33]. These include: spastic (85-91%), dyskinetic (4-7%), ataxic (4-6%) and hypotonic (2%) [33]. Dyskinetic CP includes dystonia and choreoathetosis. CP is also classified by anatomic distribution of the motor disorder. Diplegia CP affects primarily the lower extremities, but there may be some fine motor impairments in the upper extremities [33, 42]. Hemiplegic CP affects one side of the body, although there may be greater impairments in the upper extremity [33, 42]. Quadriplegia affects all 4 limbs and may include the trunk as well [33, 42]. As a total population, approximately 23% of children with CP have quadriplegia, 39% have hemiplegia and 38% have diplegia [43]. However, the majority of patients with severe CP will have quadriplegia [43]. Approximately three-quarters of children with quadriplegia will have severe CP in contrast to diplegia and hemiplegia where severe CP compose approximately 2% and 1%, respectively [43]. However, the Surveillance of Cerebral Palsy in Europe uses a slightly different topographic description in which they subclassify CP into unilateral and bilateral [44]. Using these subclassifications has allowed some authors to further subdivide the unilateral classification into hemiplegic and monoplegic [45]. The bilateral designation allows for further descriptive terms to be further subcategorized into diplegic, triplegic or quadriplegic. Quadriplegic may also be used interchangeably with tetraplegic or “whole-body involvement [45].” These designations are felt to be more descriptive.

Despite the physical description, this nomenclature tells the physician very little regarding what the child is doing functionally. Twenty-five years ago Palisano et al developed a five-level ordinal

grading system to classify gross motor function in children with CP [46]. The Gross Motor Function Classification System (GMFCS) has become the most common way for clinicians to describe mobility in their patients with CP. It was initially created to be used with children aged 2-12 years old, but was later expanded and validated to include children from 2-18 years old [47]. However, the function of a child is more than their ability to ambulate. Other classification systems were also developed using a similar five point ordinal grading systems in order to describe other aspects of function that were important to track. The Manual Ability Classification System (MACS) was developed in 2006 by Eliasson et al to grossly classify upper extremity and hand use in children with CP ages 4-18 years old [48]. A general description is provided in Table 3. As CP is a motor disorder, it can affect all the motor systems in the body, not just "arms and legs." Oral motor control can also significantly be affected in children with CP. It is estimated that anywhere from 21-88% of individuals with CP have communication difficulties [17, 49, 50]. Following the previous mentioned scales, Hideckler et al created a five-point ordinal scale to classify communication for children with CP [51]. The Communication Functional Classification Scale (CFCS) was designed to assess the ability of the individual to both send and receive information. The CFCS also allows for nonverbal communication, such as sign and adaptive communication methods to be included in the assessment. However, oral motor dysfunction is not limited to communication. Children with CP may also have impairments in eating and drinking. The Eating and Drinking Ability Classification System (EDACS) was developed to assess these skills in children 3 years old and older [52]. In addition to using a five- point ordinal scale to classify safety and efficiency, there is also an additional three -point scale to assess the amount of assistance an individual may need (independent, requires assistance, dependent) [52]. A brief summary of all the classification systems described above can be found in Table 3. When used in conjunction with each other, these classification systems can provide complementary information to determine the individual's functional profile [53, 54].

Table 3 Overview of Cerebral Palsy Classification Systems.

	GMFCS	MACS	CFCS	EDACS
I	Walks without Limitations	Handles Objects easily	Effective senders and receiver	Eats and drinks safely and efficiently
II	Walks with Limitations	Handles most objects with reduced speed/Quality	Effective but slow paced sender and receiver	Eats and drinks safely but some limitations in efficiency
III	Walks with Hand-Held Mobility Device	Handles Objects with difficulty, needs help to prepare or modify activity	Effective sender and receiver with familiar partners	Eats and drinks with some limitations to safety; some limitations in efficiency
IV	Self-Mobility with limitations	Handles a limited number of objects in adaptive setting	Inconsistent sender and receiver with	Eats and drinks with a significant limitations to safety; some

			familiar partners	gastrostomy/jejunostomy tube supplementation
V	Transported in Manual Wheelchair	Does not handle objects	Seldom effective sender and receiver with familiar partners	Unable to eat or drink safely; primarily gastrostomy/jejunostomy tube supplementation

GMFCS: Gross Motor Functional Classification System. MACS: Manual Ability Classification System. CFCS: Communication Functional Classification System. EDACS: Eating and Drinking Ability Classification System.

4. Prognosis

Many families become focused on their child's ability to walk. The prognosis for walking in children with CP is poor if they are unable to achieve head control by 20 months, have not extinguished primitive reflexes by 24 months, have not achieved postural reactions by 24 months, or do not sit independently by 48 months [55]. Many children who are able to sit between three and four years may be able to walk with orthosis, gait aids for limited distances. A child who does not walk by 9 years old is unlikely to walk, even with maximum assistance [55]. Many children with CP will have reached 90% of their gross motor capacity by the age of 5 years old [56]. Recent meta-analysis by Keeratisiroj et al found additional predictors of walking also include: type of CP, visual impairment, intellectual disability, epilepsy and ability to self-feed as potential indictors of independent ambulation [57]. However, their meta-analysis distinguished independent sitting by 2 years old, absence of visual impairment, absence of intellectual impairment and absence of seizures as the most important prognostic predictors for ambulation [57].

The vast majority of children with CP will survive into adulthood. Between 1980-1994, the 20 year survival rate in the United Kingdom ranged from 87-94% [58]. The majority of children with CP have mild impairment. As a result, approximately 80% of individuals with CP have similar survival rates to the general population [59, 60]. However, this figure is calculated across all GMFCS levels and does not necessarily correlate to children with severe CP. There is a correlation between reduced life expectancy in relationship to the medical complexity of the child. For example, the probability a 3 year old child with GMFCS V will survive to age 20 is approximately 50-60% [61, 62]. In higher income countries, mortality rates for children with severe CP are comparable [63, 64] However, in lower income countries, such as South Africa, mortality rate is 20% higher for children with CP GMFCS V [64]. Various studies have looked at multiple factors which may impact mortality in individuals with CP. These have included: degree of motor impairment [58-60, 65, 66], self-feeding ability [59, 60, 66, 67], cognition [58, 60, 65, 68], epilepsy [60, 65, 68], scoliosis [65], visual deficits [58, 60, 68] and hearing deficits [60, 68].

Over recent years, medical care for children with CP has improved. Blair et al noted that since 1990 mortality of children with CP has shifted from childhood to early adulthood [60]. Aggressive management of medical issues such as seizures, hypertonia, nutrition, respiratory issues, scoliosis and orthopedics are likely responsible for improvement in childhood mortality in children with CP [69]. However, these factors likely impact childhood survival and likely do not significantly alter adult

life expectancy. Direct determination of causes of premature death in children and young adults with CP can somewhat be obscured by poor documentation. In studies looking at the cause of death in individuals with CP 30-60% of the time "CP" is listed as the cause of death. However, when recoded, respiratory and disease of the circulatory system are the leading causes of death in adults with CP [60, 65, 70, 71]. There are multiple potential causes of respiratory insufficiency in individuals with CP. For example, malnutrition, hypertonia, scoliosis, and poor trunk control can all lead to weak respiratory muscles and/or ineffective cough which can lead to respiratory insufficiency. Oropharyngeal dysphagia and chronic gastroesophageal reflux can also lead to chronic aspiration, recurrent pneumonias, and respiratory insufficiency in children with CP. Hence, multiple medical issues may be contributing factors leading to respiratory disease. Blair et al suggest that a barrier to improving survival may be that adult care services tend to be more highly specialized and may not be prepared to address the CP patient who has multiple medical problems and may require a more holistic approach to their complex healthcare needs [60].

5. Management of CP

Medical treatment for CP should be focused on treating disability and managing associated comorbidities. Management of the medical conditions associated with CP contribute not only to the patient's overall health but quality of life as well. Children with CP may also have significant associated medical comorbidities (see Table 4). Frequency of medical comorbidities are strongly associated with severity of motor impairments [72]. Many children with CP see multiple subspecialists and require a general health framework, planning, and guidance.

Table 4 Comorbidities Associated with Cerebral Palsy.

Gastroenterology	Poor nutrition and growth
	Oral motor dysfunction leading to poor feeding
	Sialorrhea
	Dysphagia
	Gastroesophageal Reflux
	Constipation
Vision	Cortical Visual Impairment
	myopia
	Strabismus
	Nystagmus
	Optic Atrophy
Hearing	Sensoneural Hearing Loss
	Hearing Impairment
Dental	
	Malocclusion
	Bruxism
	Poor Hygiene/ Dental Caries
Neurologic	Seizures
	Hypertonia: Spasticity/Dystonia

	Ataxia
	Athetosis
	Learning/ Attention Problems
	Cognitive Deficits
	Speech and Language Impairments
Respiratory	Restrictive Lung Disease
	Chronic Lung Disease
	Recurrent Aspiration
	Obstructive Sleep Apnea
Sleep	Insomnia/ Frequent Wakening
Endocrine	Osteopenia/Osteoporosis
	Precocious puberty
PAIN	Chronic pain
Orthopedics	Scoliosis
	Hip Subluxation/ Dislocation
	Bony deformities
	Muscle and Joint Contractures
	Foot deformities

In addition to the patient's primary care physician, a specialist who is familiar with CP plays a crucial role in the coordination, identification, and maintenance of care. This role may be filled by a pediatric physiatrist, pediatric neurologist, or a developmental pediatrician who is familiar with many of the comorbidities associated with CP. In addition to the medical knowledge and training the specialist brings to the team, it is important for the specialist to recognize the impact the family has on the child's care as well. Family -centered care helps the physician understand how the child interacts at home, school, and the community and how the medical decisions impact the child's participation in those different environments. Parental involvement allows the clinician to understand barriers to treatment plans and to formulate a collaborative plan that will optimize adherence and outcomes. Treating disability by focusing on interventions that work towards improving health and participation is provided by the International Classification of Functioning, Disability and Health (ICF) [73].

5.1 Neurologic and Neuromuscular Comorbidities Associated with CP

5.1.1 Hypertonia

Over 90% of children with CP have hypertonia [42]. Hypertonia can be identified as spasticity, dystonia, or rigidity. These abnormal tone patterns do not always occur in isolation, and often children will demonstrate a combination of patterns. Spasticity is typically defined as "a motor disorder characterized by a velocity- dependent increase in [muscle tone] with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex [74]." Dystonia by contrast, is abnormal involuntary contractions in agonist and antagonist muscle groups causing abnormal posturing of the neck, torso, and extremities [75]. Sometimes clinicians can have difficulty differentiating between them. The Hypertonia Assessment Tool can be performed easily in the office setting to help distinguish spasticity from dystonia [76]. Although spasticity and dystonia have different origins and

management strategies, they can have similar effects on the child with CP. Hypertonia may cause secondary changes to occur in muscle, tendon, and collagen tissue properties such as stiffness, fibrosis, and atrophy [77]. Uncontrolled hypertonia may interfere with mobility, exercise, range of motion, and ADLs and cause chronic pain and contribute to contractures and/or pressure sores [78]. However, there are some positive effects associated with hypertonia. It may help maintain muscle tone in patients who are unable to ambulate, help support circulatory function, may prevent formation of deep venous thrombosis, and may assist in ambulation or transfers [79]. When managing hypertonia, the physician must balance both the positive and negative effects of increases in muscle tone.

Spasticity and dystonia alone do not explain the deficits in motor function. Furthermore, correcting hypertonia does not correct motor control [80]. Children with CP also have deficits in their selective muscle control. This causes impairments such as weakness, hyperreflexia, decreased speed of movement and lack of reciprocal inhibition [81]. They may retain obligatory co-activation synergy patterns instead of being able to activate typical recruitment patterns [82]. This leads to difficulties in balance, loading responses and limb stabilization [82]. Furthermore, this can lead to gait instability, decreased endurance, and abnormal forces through joints. Children with CP are at significant risk for developing growth related musculoskeletal deformities such as lever arm deformities and joint contractures that can significantly affect function, care and comfort [83].

Treatment for hypertonia requires a multidisciplinary team and management. As CP is a motor disability, physical therapy and occupational therapy remain the backbone of a rehabilitation program. Oral medications may also play a role in managing hypertonia. The most common medications used to treat spasticity include baclofen, gabapentin, diazepam, clonazepam, dantrolene, and tizanidine [84, 85]. Common side effects of many antispasticity medications include sedation, confusion, confusion, ataxia and liver toxicity [86]. Dystonia can also be treated with gabapentin, baclofen, clonazepam and diazepam [87]. However, levodopa, amantadine, trihexyphenidyl, or tetrabenazine may also play a role [87]. Medications used for dystonia may have a risk of additional side effects such as confusion, nausea, constipation, dyskinesias or hallucinations [86]. The role of levodopa in management of CP remains controversial. There is poor evidence that levodopa is helpful in children with dystonic CP who have secondary dystonias [88-90]. However, due to the heterogenicity of CP, it continues to remain in the clinician's arsenal. However, response to levodopa may prompt the physician to consider a workup for dopamine responsive dystonia [91].

Chemodenervation is also frequently used in the management of hypertonia in patients with CP. Botulinum Toxin A has been used in the treatment of CP since 1993 [92]. Several formulations of Botulinum Toxin (BoNT)are commercially available. They all have a similar mechanism of action: chain protein that binds to synaptobrevin at the neuromuscular junction and inhibits vesicles from anchoring to the cell membrane, thus preventing acetylcholine release. It is the binding of acetylcholine to the post-synaptic receptors at the neuromuscular junction that is required to initiate a muscle contraction [93]. BoNT injections are well tolerated with a low risk of adverse events if dosing guidelines are followed [94]. Risks for BoNT include fever, muscle weakness, respiratory difficulties, seizures, swallowing difficulties, bleeding, infections, allergic reaction, generalized muscle weakness, and death. On review of the literature, systemic reaction to BoNT-A injections in children occur at a rate of approximately 1-3.6% [94]. Pre-existing medical comorbidities such as orofacial weakness and respiratory weakness may increase a patient's risk of having an adverse event related to BoNT [95, 96]. Children with CP who are GMFCS IV and V are

more likely to have these risk factors and may place them at greater risk after BoNT injections [95, 96].

Phenol or alcohol can be used for a similar purpose. As opposed to BoNT which works directly on the muscle, alcohol and phenol reduce hypertonia by targeting nerves. The mechanism of action for alcohol and phenol to reduce spasticity is the reduction of neural transmission by chemically denaturing nerve fibers [78]. In comparison to BoNT, phenol and alcohol injections are considerably more painful and require more time which frequently will require sedation in the pediatric patient. In addition, phenol and alcohol have less versatility than BoNT in that it is limited to nerves that can be localized to focal areas. Commonly injected areas for phenol and alcohol include obturator nerve to adductors, motor branch of tibial nerve to hamstrings, tibial nerve to gastrocnemius, musculocutaneous nerve to brachialis/biceps muscles, radial nerve to brachial radialis, pectoralis nerve to pectoralis muscle, and thoracodorsal nerve to latissimus dorsi. It is common for oral pharmacology to be used in conjunction with injectable medications. Many children have multiple areas of spasticity that cannot be safely managed with toxicity limits of injectable medications. In addition, there are concerns regarding the effects chemodenervation may have on muscle health in the long term, prompting many clinicians to re-evaluate the frequency of using these medications [97, 98].

In addition to pharmacologic options, surgical options also exist for treating spasticity in children with CP. An intrathecal baclofen pump (ITB) can be implanted in the patient directly infusing baclofen into the intrathecal space around the spinal cord. This allows high concentrations of baclofen to be infused to the spinal cord without the risks of systemic side effects. The position of the catheter in the spinal cord can be strategically lower to affect primarily the lower extremities or placed higher to affect both upper and lower extremities. Risks associated with an intrathecal baclofen pump include cerebrospinal fluid lead, catheter migration, disconnection or blockage [99]. Children with spastic diplegic CP GMFCS 3 have demonstrated improvement in tone and knee flexion at initial contact with ITB [100]. ITB contributes to a better quality of life in children with GMFCS IV and V [101]. In addition to patients with spasticity, ITB has been shown to be effective in improving symptoms of dyskinetic CP as well [102]. Children with dyskinetic CP did not demonstrate improvement in gross motor function with ITB, but did demonstrate improvements in pain, sitting balance, activities of daily living, sleep, and fine motor function [102].

Selective dorsal rhizotomy (SDR) is a surgical intervention in which a neurosurgeon will selectively separate the L2-S1 motor and sensory nerve roots [103]. The surgeon will then stimulate the nerve roots and ablate the roots that demonstrate abnormal sensory feedback [103]. Approximately 50% of the roots are ablated. Potential risks include loss of bladder function, hyperesthesia, and loss of previous ability to walk. Traditionally, the best candidates were felt to be between the ages of three to seven, without visual impairment, dystonia, athetosis or ataxia and who were cognitively capable of participating in an intense post-operative therapy regimen [104]. Children who are GMFCS I and II will show more improvement in their gait than GMFCS III [105]. Customarily, children who were ambulatory were considered for SDR, and children who were non-ambulatory were considered candidates for ITB. However, research has shown this not necessarily to be the case. An SDR can be considered for spastic children with CP who are GMFCS IV and V in order to focus on reduction of spasticity for care, comfort and hygiene [106]. However, a recent study has demonstrated an increased risk for unmasking dystonia in non-ambulatory children after SDR [107]. The authors suggested careful screening with an MRI prior to SDR in order to exclude children with dystonia as

well as screening for underlying congenital disorders that may place the child at risk for dystonia [107]. A systematic review published in 2020 by Novak et al evaluated 64 interventions for CP [108]. The interventions shown to be the most effective in reducing muscle spasticity were botulinum toxin, diazepam, and selective dorsal rhizotomy [108]. Dantrolene, tizanidine, and alcohol/phenol injections were considered "probably effective [108]."

5.1.2 Epilepsy

The incidence of epilepsy among individuals with CP is 15-55% [109]. However, this number rises to 71% when associated with intellectual disability [110]. Epilepsy is most commonly associated with quadriplegia CP (50–94%) but is also prevalent in hemiplegia (33–50%) [111]. Just as motor dysfunction in CP varies based upon the area of the brain that is affected, so does seizure type. Partial seizures are the most common type and are more common in children with hemiplegic CP, with a prevalence of 70% [112]. Children who have spastic diplegia or quadriplegia are more likely to have generalized tonic clonic seizures [113].

Epilepsy is a significant issue among children with CP, as it can significantly affect both clinical prognosis and mortality [57, 114]. Increase seizure frequency may result in progressive motor disability, intellectual disability, sensory dysfunction, and behavioral problems in children with CP [115]. Risk factors associated with epilepsy development in children with CP include family history of epilepsy, neonatal seizure in the first 72 hours of life and in the neonatal period, quadriplegic type of CP, severe gross motor and fine motor impairment, and moderate to severe intellectual disability [116]. Maternal hypertension, neonatal seizures, and delivery by cesarean section were also shown to increase the risk of epilepsy and drug resistant epilepsy in children with CP [117].

Pharmacologic management of the medical comorbidities of children with CP may also be complicated by their epilepsy. Baclofen, a medication used for the management of hypertonia, has a risk of lowering seizure threshold [77]. Furthermore, there is a risk of antiepileptic medication side effects exacerbating pre-existing comorbidities such as topiramate impacting cognitive difficulties or feeding problems [118, 119]. In general, antiepileptic medications affect normal brain function and make learning more difficult by causing side effects such as drowsiness, inattention and restlessness [120]. A common overlooked comorbidity is the effect of seizure medications on bone health. Medications that induce the enzymes of the cytochrome P450 system such as carbamazepine, phenobarbital, and phenytoin are well known to decrease bone density [121, 122]. Vitamin D catabolism is accelerated by cytochrome P450 system [122]. Valproic Acid is also associated with a decrease in bone mineral density as well, causing increased bone turnover by changing osteoblast and osteoclast activity [122]. Children with CP may have additional risk factors that contribute to poor bone health such as poor growth and nutritional status, limited sunlight exposure, low vitamin D / calcium intake, lack of weight bearing, feeding difficulties, and poor mobility [122]. A recent system review demonstrated that use of antiepileptic medications are the most significant risk factor for loss of bone mineral density [123]. However, only approximately 25% of pediatric neurologists surveyed screen their patients for bone health [124].

Seizures also play a role in prognosis in children with CP. The presence of seizures is known to have an association with lower full-scale intelligent quotient scores (IQ) and memory performance in children with hemiplegic CP when compared to children with hemiplegic CP without seizures [125]. Although most children with CP have a normal life expectancy, children with CP who have

epilepsy in combination with intellectual and motor disability have the greatest risk of premature death [42].

5.1.3 Learning and Cognition

Approximately half of children with CP will have an associated cognitive impairment [72]. However, children with CP who have cognitive skills in the normal range are still at significant risk for significant deficits in learning and/or attention [126]. The degree of cognitive impairment does not correlate with degree of motor impairment. The risk for cognitive impairments is highest in patients with quadriplegia and lowest in patients with hemiplegic CP. However, there is a strong association between intellectual impairment and the presence of epilepsy, abnormal EEG, or abnormal imaging [109].

Approximately 25% of patient with CP are unable to talk and up to 85% exhibit speech and language impairments [17, 50]. Research suggests that children with CP should receive a speech and language evaluation by 2 years of age in order to implement early treatment [50]. Difficulties with communication can lead to frustration and behavioral problems. Clinicians should be aware of this and alternative communication such as sign language or augmentative communication should be sought. Children with CP also are subject to nonverbal learning impairments as well that lead to difficulty in visual-spatial skills [127]. In addition to limitations in academic achievement, there is also a poorer prognosis for independent ambulation and achieving continence [72]. As demonstrated in the Table 4, children with CP haver impaired oral-motor skills that can contribute to feeding problems. However, the same impaired oral motor skills and gross motor skills can also cause significant delays or deficits in language skills as well. These delays may lead to a significant underestimation of intelligence in children with CP [128]. Hearing problems, which occur in 30-40%, of children with CP, may also contribute to language delays [129]. It is the clinician's responsibility to be aware of these potential limiting factors and advocate for hearing screenings and augmentative communication so that children can communicate and have access to teaching at their appropriate cognitive level. Standard measures for grading intelligence may not be fair assessments for some children with CP as they rely on motor, speech, visual and auditory function that may be impaired [130]. Appropriate school placement can be challenging. Children with spastic diplegia who were placed in a mainstream classroom demonstrated an increase in verbal IQ but not performance IQ in comparison to similar peers who were placed in special education classrooms [130]. However, children in special education classes demonstrated increases in performance IQ [130]. It is crucial that children with CP have access to appropriate resources so that they can achieve optimal education services to achieve their appropriate potential.

5.1.4 Pain

Pain is unfortunately a common problem in children with CP. Unlike other medical comorbidities which are frequently related to severity of motor dysfunction, pain is likely to be at all motor level functions [72]. Between half to two-thirds of children with CP report pain [131-133]. Children with CP are 4.5 times more likely to have chronic pain than their typically developing peers [134]. Jacobson et al reported a pain prevalence of 49 present across all GMFCS level [135]. Unfortunately, pain in children with CP can be difficult to address if the child has limited verbal or cognitive skills and is unable to express their concerns. Often pain behaviors in non-verbal children can be observed

in a child's crying, moaning, increase in ton, or agitation [136]. However, parents and caregivers may also may have to be aware of idiosyncratic behaviors such as drooling, grunting, self-abusive behaviors and laughing [136]. The most common sources of pain are associated with muscle spasms (from hypertonia) or associated musculoskeletal disorders such as hip subluxation, charcot joints or scoliosis [137]. Other causes of pain include constipation, gastroesophageal reflux, dental abscess, corneal abrasions, headaches, pressure sores, and urolithiasis [138]. Pain has been shown to negatively influence function and sleep in individuals with CP [132, 135, 139]. This ultimately can have negative consequences for eating, learning and general well-being [135, 140, 141]. Pain behaviors in non-verbal children can be quite frustrating for parents who are desperate to find the cause of their child's discomfort and will visit multiple medical specialists who do medical work ups that are limited to their area of specialization [138]. Often a detailed history and physical, with attention to progression of symptoms and associated behaviors, can suggest potential causes and solutions [138]. It may take time to explore possibilities and interventions in order to find a solution. However, assuming ownership of a potential problem as opposed to "turfing" them to another provider is often appreciated by the family.

5.1.5 Sleep

Children with CP are at high risk of having sleep disorders. In addition to pain described above, frequent repositioning, medications, and/or overnight feeds can be disruptive to the child as well as to the entire family [142, 143]. In addition, children with CP may have direct disruption to the sleep architecture including high incidence of sleep awakenings, abnormalities in sleep spindles and absence of rapid-eye movement (REM) [144]. Medical comorbidities also may interfere with sleep in children with CP. Medical influences such as gastro-esophageal reflux, nocturnal seizures, antiepileptic medications, upper airway obstruction, restrictive lung disease, spasticity, vision abnormalities and cognitive impairments have all been associated with sleep disorders in children with CP [145]. Parents of children with neurodevelopmental disabilities have poorer quality of sleep than parents of typical children [146]. It is important for the clinician to take a sleep history to address sleep behavior and sleep hygiene. Parents of children with CP feel that clinicians often neglect the impact of the child's sleep on parental sleep and the family [142] Understanding the patient's medication, nap frequency, snoring, breathing difficulties, sleep length, bedtime routine, activities in bed, and behavioral reinforcements can help the provider make appropriate behavioral, positional, or pharmacologic recommendations to improve sleep for the patient and for the family [144].

5.1.6 Musculoskeletal

Although many clinicians are familiar with the CNS injury, they often forget that there are changes in the skeletal muscle of children with CP.

Children with CP have neural impairments that contribute to the motor dysfunction associated with CP: hypertonia, poor selective muscle control, and poor balance [83]. The primary cause of muscle weakness in CP is alterations to the descending pathway in the CNS. These alterations limit the way an individual can maximally contract a muscle as well as cause co-contractures of antagonist muscles. This can lead to musculoskeletal impairments such as muscular contractures, bony

deformities, as well changes to intrinsic muscle structure. Sometimes it can be difficult to assess functional strength in children with CP based on the child's age, cognition, and motivation.

When compared to typically developing children, the muscles of children with CP have structural and mechanical changes that reduce the force potential of their muscles [147, 148]. Muscles of children with CP have shown to have reduced contractile tissue, overstretched sarcomeres, and reduced muscle size [148]. The muscles of children with CP have demonstrated increase in fibrosis and the replacement of connective tissue, primarily fat. Replacement of contractile tissue has been present in both ambulatory children and nonambulatory children [149, 150]. These changes increase the passive properties of the muscle and muscle stiffness [148]. However, these changes do not entirely explain the degree of passive muscle stiffness associated with CP [148]. The sarcomere the functional unit of the muscle in individuals with CP is structurally different in comparison to typical individuals. The sarcomeres in children with CP are almost twice the length of typical children but less in number [147]. The optimal sarcomere length in order to generate maximum force is between 2.64 μm and 2.81 μm [147]. Functionally long sarcomeres would generate low active tension. Lieber et al measured the length of sarcomere length in the wrists of children with CP and found the length to be within the range of 3.5-4.0 μm. This would functionally reduce the force to approximately 20% of maximal tetanic tension [151]. Similarly, Leonard et al found similar results in hip adductors of children with CP and estimated a loss of 55% of active power [152]. Children with CP have also been shown to have a decrease in the number of satellite cells [148]. Normal muscle growth and regeneration requires satellite cells [147]. Reduced number of satellite cells may be related to decreased longitudinal growth of muscles but further studies are needed to determine an actual relationship [148]. Recent studies by Dayanidhi et al demonstrated skeletal muscle mitochondrial electron chain enzymatic activity is reduced by 45-65% children with CP compared to typically developing peers, which may also account for increased energy expenditure of movement and fatigue experienced in ambulatory children with CP [153].

When comparing muscle volumes to typically developing children, children with CP have significantly smaller muscle volumes [154-157] Davids et al completed a case series of 255 children with spastic diplegia GMFCS I-III and used linear regression to predict the rate of change in lower extremity muscle strength in relation to body weight and strength normalized for age [158]. Although strength and weight increased over time for the entire cohort, strength normalized to weight decreased as the children aged. They also found that children were 90% likely to maintain independent ambulation when strength was 49% that of typically developing children [158]. In a systemic review of evidence in treating CP, Novak et al recognized that strength training in combination with functional mobility training will likely improve functional mobility [108]. Furthermore, strength training in combination with exercise, activity training and behavioral change strategies may demonstrate improvement in ambulation, mobility, participation and quality of life, but not gross motor skills [108].

However, in that same study, Novak et al note that there is good evidence to support the use of botulinum toxin (BoNT) to improve motor function, treat tone, and to use in conjunction with casting to improve contracture and alignment [108]. However, as noted in the hypertonia section, there is controversy in the literature regarding the use of BoNT injections in children with CP. There is a concern that because BoNT can potentially decrease muscle volume it may potentiate muscle weakness and further contribute to sarcopenia [97, 159]. Although some studies demonstrate sustained atrophy for periods longer than 6 months [160-162], other studies demonstrated recovery

and improvement in muscle volume [154, 163-165]. The question is whether function is a direct correlation to muscle volume. Williams et al demonstrated that children with CP who received injections to their gastrocnemius may have had a decrease in muscle volume in their gastrocnemius by 4.47% but had increases in soleus by 4%, quadriceps by 4.23%, and biceps femoris by 4.67% [161]. Alexander et al also demonstrated a sustained gastrocnemius reduction in volume of 6.8% at 25 weeks but an increase in soleus volume of 10.8%, resulting in total gastrocnemius-soleus complex increase of 5.1% [162]. In addition, the subjects also demonstrated functional improvements in the 6 -minute walk test and the timed up -and- go test [162]. Using ultrasound, Schless et al compared the gastrocnemius muscles of typically developing children, BoNT naïve children with CP, and children with CP who received 3 or more recurrent BoNT injections [166]. The results of this study demonstrated that compared to the typically developing children, both groups of children with CP had significantly different volume and echo intensity on ultrasound [166]. However, both GMFCS and BoNT intervention was associated with smaller volumes and higher echo intensity. On clinical evaluation of the two CP groups, there were no functional differences aside from slightly weaker dorsiflexion in the CP group that received BoNT. The authors hypothesized that increase in ankle joint resistance may be due to reduced muscle growth and changes in the tissue properties as opposed to spasticity that requires BoNT [166].

5.1.7 Orthopedic Surgeries

Orthopedic surgeries are reserved to correct contractures, bony deformities and muscle imbalances. Orthopedic surgeons will perform tendon lengthening to correct contractures, rotational osteotomies for bony torsional deformities, tendon transfers to rebalance muscle forces, and scoliosis corrections.

Due to the abnormalities in the sarcomere, the muscle tendon units in children with CP fail to lengthen in proportion to bony growth [147]. Muscles that cross two joints are at bigger risk for contracture: i.e. hamstrings and gastrocnemius muscles. Surgical correction can either be a muscle-tendon lengthening, muscle release, fascial and aponeurotical transection, or aponeurectomy [148]. The goal of surgical correction is to allow the muscle to shorten but allow the supporting connective tissue to lengthen. Children with CP are prone to hip subluxation that can progress to dislocation. As opposed to other orthopedic issues that are indirectly related to hypertonia, hip subluxation is a result of “persistent fetal alignment” [167]. In utero, the angle of the femoral neck is approximately 55 º. When a child begins to walk, bony remodeling occurs, and it assumes the typical adult shape of 15-20 º [167] A combination of delayed walking, excessive hip flexion and spastic hip internal rotators (adductors and medial hamstrings) create abnormal forces that do not allow for typical remodeling [168]. If the hip becomes dislocated, it can significantly impact quality of life and function by interfering with sitting, walking, completing activities of daily living and causing pain [150]. The risk of hip displacement increases linearly with GMFCS score [169]. Overall hip displacement affects 1/3 of patients with CP and up to 90% of GMFCS V [170]. Screening for hip subluxation starts at approximately 2 years of age and is followed closely by examination and serial x-rays. Surgical treatment involves femoral derotational osteotomy. Using spasticity related hip surveillance program has shown to reduce hip pain, hip dislocations and salvage surgery [170]

Scoliosis monitoring is crucial in children with CP. It is estimated that between 21-64% of children with CP will develop scoliosis [171]. Children with GMFCS IV-V have a 50% chance of developing a

severe scoliosis [172]. Spasticity, weakness, and poor muscle control have been contributing factors to developing spinal curvature. Children who had a Cobb angle >40º by 12 years of age were more likely to progress [173]. Furthermore, scoliosis in children with CP can progress beyond skeletal maturity [174]. Rate of progression in a non-ambulatory adult with CP can progress 3-4.4 per year [171]. Use of thoracolumbosacral orthosis has not been shown to be effective or well tolerated in children with CP [171]. Surgical intervention is typically considered in patients with curvatures > 45-50º in children older than 10 years, curves that are causing functional problems, or at risk for increasing medical comorbidities [171, 172].

Approximately 1/3 of children with CP will develop upper limb contractures [175, 176]. Hypertonia and muscle imbalances play a large role in the formation of contracture and joint deformity. Decreases in passive range of motion can be seen as early as the first year of life and become more significant for wrist extension by 4 years old and elbow extension by 7 years of age [176]. Risk of contractures increased with GMFCS level, MACS level, and dyskinetic CP [176]. The most common impairment is decreased passive range of motion in the wrist and fingers [175]. Shortened wrist and finger flexors create an overflexed wrist and decreased finger dexterity which makes it difficult to perform ADL's. Eliason et al demonstrated that children who underwent tendon transfer and muscle releases, regardless of degree of impairment, had benefits ranging from functional improvement to cosmetic appearance [177].

5.1.8 Multi-Specialty Team

A crucial component to a multidisciplinary care team is a dedicated therapy team that assists the family in developing a tailored approach to their child's needs. Members of the therapy team can include physical therapists, occupational therapists and speech-language pathologists. Physical therapist's interventions range from designing exercise programs to utilizing modalities such as electrical stimulation and selecting durable medical equipment. The goals are to help promote posture, seating, mobility, transfers and ambulation. Occupational therapists focus on improving upper extremities tone, range of motion, and dexterity to maximize the child's ability to participate in activities of daily living, school, recreational activities and work. Speech language therapists play a crucial role in optimizing a child's feeding and communication skills. Other crucial members to consider are neuropsychologists and educational specialists who develop strategies to address cognitive deficits and learning disabilities and optimize learning. Recreational therapists can help coordinate and create recreation -based treatment programs. Assistive technology specialists are able to fit and provide appropriate durable medical equipment to help the child adapt and overcome physical limitations.

It is difficult for both physicians, therapists and parents to maintain realistic therapeutic goals. Therapeutic management of CP can be classified as "child-passive" and "child-active" [42]. Child-passive therapies are therapies where activities are "done to the child", where the child plays a passive role in the activity [42]. Child-active therapies are therapies where the child plays a role in practicing real-life tasks. This approach is more in line with inducing neuroplasticity by engaging in goal-based, specific practices. It is important for the entire team to determine what are realistic goals within the child's motor potential and their developmental trajectory. For example it is not reasonable to expect a child who is GMFCS IV to achieve community walking, and it may be more reasonable to pursue a compensatory and environmental adaption approach to the treatment plan

[42]. Therapeutic walking and active stretching may be an important part in health maintenance but appropriate attention needs to be given to considering equipment needs and environmental adaptions that improve inclusion, function, independence and quality of life.

6. Conclusion

CP is a common and complex motor disease that affects children world-wide. It is not a single disease but a phenotypic description of children who acquired a non-progressive brain injury in the perinatal/infant period when the brain was still developing. The etiologies remain complex and multifactorial. In addition to established risk factors for CP, there is growing evidence to strongly suggest that there may be a genetic variants that contribute to the development of CP warranting genomic sequencing in all CP cases. Clinical management focuses on awareness and treatment of the numerous potential medical comorbidities. Proactive management and focused goals can assist in maximizing function and quality of life. Multidisciplinary management and communication are essential in achieving best outcomes for children with CP.

Author Contributions

The author did all the research work of this study.

Competing Interests

Dr. Vova has served on advisor boards for Ipsen Pharmaceuticals.

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