

A Review on Current therapy and surgery of Cerebral palsy

Dharmesh Sisodiya^{1*}, Poornima Pandey², Kamlesh Dashora³ and RK. Agrawal⁴

¹Institute of Pharmacy Vikram University, Ujjain, Madhya Pradesh, India.

²Mahakal Institute of Pharmaceutical Studies, Ujjain, Madhya Pradesh, India.

³Head of Department, Institute of Pharmacy Vikram University, Ujjain, Madhya Pradesh, India

⁴Pharmaceutical Chemistry Department of Pharmaceutical Sciences, Vishwavidyalaya, Sagar, Madhya Pradesh, India.

ABSTRACT

Cerebral palsy is an abnormality of motor function (as opposed to mental function) and postural tone that is acquired at an early age even before birth. Signs and symptoms of cerebral palsy usually show in the first year of life. This abnormality in the motor system is the result of brain lesions that are non-progressive. The motor system of the body provides the ability to move and control movements. A brain lesion is any abnormality of brain structure or function. "Non-progressive" means that the lesion does not produce ongoing degeneration of the brain. It also implies that the brain lesion is the result of a one-time brain injury that will not occur again. Whatever the brain damage that occurred at the time of the injury is the extent of damage for the rest of the child's life.

Cerebral palsy affects approximately one to three out of every thousand children born. However it is much higher in infants born with very low weight and in premature infants. Interestingly new treatment methods that resulted in an increased survival rate of low birth weight and premature infants actually resulted in an overall increase number of children with cerebral palsy. The new technologies however did not change the rate of cerebral palsy in children born full term and with normal weight.

Keywords: per ventricular leukomalacia [PVL], Cerebral dysgenesis, intracranial hemorrhage.

INTRODUCTION

Cerebral palsy (CP) is an umbrella term encompassing a group of non-progressive, non-contagious motor conditions that cause physical disability in human development, chiefly in the various areas of body movement. Cerebral refers to the cerebrum, which is the affected area of the brain (although the disorder most likely involves connections between the cortex and other parts of the brain such as the cerebellum) and palsy refers to disorder of movement. Cerebral palsy's nature as an umbrella term means it is defined mostly via several different subtypes, especially the type featuring spasticity and also mixtures of those subtypes.

Cerebral palsy is caused by damage to the motor control centers of the developing brain and can occur during pregnancy, during childbirth or after birth up to about age three. Resulting limits in movement and posture cause activity limitation and are often accompanied by disturbances of sensation, depth perception and other sight-based perceptual problems, communication ability; impairments can also be found in cognition, and epilepsy is found in about one-third of cases. CP, no matter what the type, is often

accompanied by secondary musculoskeletal problems that arise as a result of the underlying etiology.

CLASSIFICATION

Cerebral palsy (CP) is divided into four major classifications to describe different movement impairments. These classifications also reflect the areas of the brain that are damaged. The four major classifications are: spastic, ataxic, athetoid/dyskinetic and mixed.

Spastic cerebral palsy

Spastic cerebral palsy is by far the most common type of overall cerebral palsy, occurring in 80% of all cases. People with this type of CP are hypertonic and have what is essentially a neuromuscular mobility impairment (rather than hypotonia or paralysis) stemming from an upper motor neuron lesion in the brain as well as the corticospinal tract or the motor cortex. This damage impairs the ability of some nerve receptors in the spine to properly receive gamma amino butyric acid, leading to hypertonia in the muscles signaled by those damaged nerves.

Ataxic cerebral palsy

Ataxia type symptoms can be caused by damage to the cerebellum. The forms of ataxia are less common types of cerebral palsy, occurring in at most 10% of all cases.[citation needed] Some of these individuals have hypotonia and tremors. Motor skills such as writing, typing, or using scissors might be affected, as well as balance, especially while walking. It is common for individuals to have difficulty with visual and/or auditory processing.

Athetoid cerebral palsy

Athetoid cerebral palsy or dyskinetic cerebral palsy is mixed muscle tone – both hypertonia and hypotonia mixed with involuntary motions. People with Dyskinetic CP have trouble holding themselves in an upright, steady position for sitting or walking, and often show involuntary motions. For some people with dyskinetic CP, it takes a lot of work and concentration to get their hand to a certain spot (like scratching their nose or reaching for a cup). Because of their mixed tone and trouble keeping a position, they may not be able to hold onto objects, especially small ones requiring fine motor control (such as a toothbrush or pencil). About 10% of individuals with CP are classified as dyskinetic CP but some have mixed forms with spasticity and dyskinesia. The damage occurs to the extrapyramidal motor system and/or pyramidal tract and to the basal ganglia. In newborn infants, high bilirubin levels in the blood, if left untreated, can lead to brain damage in the basal ganglia which can lead to dyskinetic cerebral palsy.

Children with cerebral palsy exhibit a wide variety of symptoms including:

- Lack of muscle coordination when performing voluntary movements (ataxia).
- Stiff or tight muscles and exaggerated reflexes (spasticity).
- Walking with one foot or leg dragging.
- Walking on the toes a crouched gait or a “scissor” gait.
- Variations in muscle tone either too stiff or too floppy.
- Excessive drooling or difficulties swallowing or speaking.
- Shaking (tremor) or random involuntary movements.
- Difficulty with precise motions such as writing or buttoning a shirt.

CAUSES

The majority of children with cerebral palsy are born with it although it may not be detected

until months or years later. This is called *congenital cerebral palsy*. In the past if doctors couldn't identify another cause they attributed most cases of congenital cerebral palsy to problems or complications during labor that caused *asphyxia* (a lack of oxygen) during birth. However extensive research by NINDS scientists and others has shown that few babies who experience asphyxia during birth grow up to have cerebral palsy or any other neurological disorder. Birth complications including asphyxia are now estimated to account for only 5 to 10 percent of the babies born with congenital cerebral palsy.

A small number of children have *acquired cerebral palsy* which means the disorder begins after birth. In these cases doctors can often pinpoint a specific reason for the problem such as brain damage in the first few months or years of life, brain infections such as bacterial meningitis or viral encephalitis or head injury from a motor vehicle accident, a fall or child abuse.

Research has given us a bigger and more accurate picture of the kinds of events that can happen during early fetal development or just before during or after birth that cause the particular types of brain damage that will result in congenital cerebral palsy. There are multiple reasons why cerebral palsy happens as the result of genetic abnormalities, maternal infections or fevers or fetal injury for example. But in all cases the disorder is the result of four types of brain damage that cause its characteristic symptoms.

Damage to the white matter of the brain (*periventricular leukomalacia* [PVL])

The white matter of the brain is responsible for transmitting signals inside the brain and to the rest of the body. PVL describes a type of damage that looks like tiny holes in the white matter of an infant's brain. These gaps in brain tissue interfere with the normal transmission of signals. There are a number of events that can cause PVL including maternal or fetal infection. Researchers have also identified a period of *selective vulnerability* in the developing fetal brain a period of time between 26 and 34 weeks of *gestation* in which periventricular white matter is particularly sensitive to insults and injury.

Abnormal development of the brain (*cerebral dysgenesis*)

Any interruption of the normal process of brain growth during fetal development can cause brain malformations that interfere with the transmission of brain signals. The fetal brain

is particularly vulnerable during the first 20 weeks of development. Mutations in the genes that control brain development during this early period can keep the brain from developing normally. Infections, fevers, trauma or other conditions that cause unhealthy conditions in the womb also put an unborn baby's nervous system at risk.

Bleeding in the brain (*intracranial hemorrhage*)

Intracranial hemorrhage describes bleeding inside the brain caused by blocked or broken blood vessels. A common cause of this kind of damage is fetal stroke. Some babies suffer a stroke while still in the womb because of blood clots in the *placenta* that block blood flow. Other types of fetal stroke are caused by malformed or weak blood vessels in the brain or by blood-clotting abnormalities. Maternal high blood pressure (hypertension) is a common medical disorder during pregnancy that has been known to cause fetal stroke. Maternal infection especially *pelvic inflammatory disease* has also been shown to increase the risk of fetal stroke.

Brain damage caused by a lack of oxygen in the brain (*hypoxic-ischemic encephalopathy or intrapartum asphyxia*)

Asphyxia a lack of oxygen in the brain caused by an interruption in breathing or poor oxygen supply is common in babies due to the stress of labor and delivery. But even though a newborn's blood is equipped to compensate for short-term low levels of oxygen if the supply of oxygen is cut off or reduced for lengthy periods an infant can develop a type of brain damage called hypoxic-ischemic encephalopathy which destroys tissue in the cerebral motor cortex and other areas of the brain. This kind of damage can also be caused by severe maternal low blood pressure, rupture of the uterus, detachment of the placenta or problems involving the umbilical cord.

THERAPIES

Physical therapy

Physical therapy usually begun in the first few years of life or soon after the diagnosis is made is a cornerstone of cerebral palsy treatment. Physical therapy programs use specific sets of exercises and activities to work toward two important goals preventing weakening or deterioration in the muscles that aren't being used (*disuse atrophy*) and keeping muscles from becoming fixed in a rigid abnormal position (*contracture*).

Resistive exercise programs (also called strength training) and other types of exercise are often used to increase muscle performance especially in children and adolescents with mild cerebral palsy. Daily bouts of exercise keep muscles that aren't normally used moving and active and less prone to wasting away. Exercise also reduces the risk of contracture one of the most common and serious complications of cerebral palsy.

Normally growing children stretch their muscles and tendons as they run, walk, and move through their daily activities. This insures that their muscles grow at the same rate as their bones. But in children with cerebral palsy spasticity prevents muscles from stretching. As a result, their muscles don't grow fast enough to keep up with their lengthening bones. The muscle contracture that results can set back the gains in function they've made. Physical therapy alone or in combination with special braces (called *orthotic devices*) helps prevent contracture by stretching spastic muscles.

Occupational therapy

This kind of therapy focuses on optimizing upper body function, improving posture and making the most of a child's mobility. An occupational therapist helps a child master the basic activities of daily living, such as eating, dressing, and using the bathroom alone. Fostering this kind of independence boosts self-reliance and self-esteem and also helps reduce demands on parents and caregivers.

Recreational therapies

Recreational therapies such as therapeutic horseback riding (also called hippotherapy) are sometimes used with mildly impaired children to improve gross motor skills. Parents of children who participate in recreational therapies usually notice an improvement in their child's speech, self-esteem, and emotional well-being.

Controversial physical therapy

"Patterning" is a physical therapy based on the principle that children with cerebral palsy should be taught motor skills in the same sequence in which they develop in normal children. In this controversial approach the therapist begins by teaching a child elementary movements such as crawling regardless of age before moving on to walking skills. Some experts and organizations including the American Academy of Pediatrics have expressed strong reservations about the

patterning approach because studies have not documented its value. Experts have similar reservations about the Bo bath technique (which is also called "neurodevelopment treatment" named for a husband and wife team who pioneered the approach in England. In this form of physical therapy instructors inhibit abnormal patterns of movement and encourage more normal movements.

The Bo bath technique has had a widespread influence on the core physical therapies of cerebral palsy treatment but there is no evidence that the technique improves motor control. The American Academy of Cerebral Palsy and Developmental Medicine reviewed studies that measured the impact of neurodevelopment treatment and concluded that there was no strong evidence supporting its effectiveness for children with cerebral palsy. Conductive education developed in Hungary in the 1940s is another physical therapy that at one time appeared to hold promise. Conductive education instructors attempt to improve a child's motor abilities by combining rhythmic activities such as singing and clapping with physical maneuvers on special equipment. The therapy however has not been able to produce consistent or significant improvements in study groups.

Speech and language therapy

About 20 percent of children with cerebral palsy are unable to produce intelligible speech. They also experience challenges in other areas of communication such as hand gestures and facial expressions and they have difficulty participating in the basic give and take of a normal conversation. These challenges will last throughout their lives.

Speech and language therapists (also known as speech therapists or speech-language pathologists) observe, diagnose and treat the communication disorders associated with cerebral palsy. They use a program of exercises to teach children how to overcome specific communication difficulties.

For example if a child has difficulty saying words that begin with "b" the therapist may suggest daily practice with a list of "b" words increasing their difficulty as each list is mastered. Other kinds of exercises help children master the social skills involved in communicating by teaching them to keep their head up maintain eye contact and repeat themselves when they are misunderstood.

Speech therapists can also help children with severe disabilities learn how to use special communication devices such as a computer with a voice synthesizer or a special board covered with symbols of everyday objects and

activities to which a child can point to indicate his or her wishes. Speech interventions often use a child's family members and friends to reinforce the lessons learned in a therapeutic setting. This kind of indirect therapy encourages people who are in close daily contact with a child to create opportunities for him or her to use their new skills in conversation.

Treatments for problems with eating and drooling are often necessary when children with cerebral palsy have difficulty eating and drinking because they have little control over the muscles that move their mouth, jaw and tongue. They are also at risk for breathing food or fluid into the lungs. Some children develop *gastro esophageal reflux disease* (GERD commonly called heartburn) in which a weak diaphragm can't keep stomach acids from spilling into the esophagus. The irritation of the acid can cause bleeding and pain.

Individuals with cerebral palsy are also at risk for malnutrition, recurrent lung infections and progressive lung disease. The individuals most at risk for these problems are those with spastic quadriplegia. Initially children should be evaluated for their swallowing ability, which is usually done with a modified barium swallow study. Recommendations regarding diet modifications will be derived from the results of this study.

In severe cases where swallowing problems are causing malnutrition a doctor may recommend tube feeding in which a tube delivers food and nutrients down the throat and into the stomach or *gastrostomy* in which a surgical opening allows a tube to be placed directly into the stomach.

Although numerous treatments for drooling have been tested over the years there is no one treatment that helps reliably. *Anticholinergic drugs* such as glycopyrolate can reduce the flow of saliva but may cause unpleasant side effects such as dry mouth, constipation and urinary retention. Surgery while sometimes effective carries the risk of complications. Some children benefit from biofeedback techniques that help them recognize more quickly when their mouths fall open and they begin to drool. Intraoral devices (devices that fit into the mouth) that encourage better tongue positioning and swallowing are still being evaluated but appear to reduce drooling for some children.

Hyperbaric oxygen therapy

Some children have cerebral palsy as the result of brain damage from oxygen deprivation. Proponents of hyperbaric oxygen therapy propose that the brain tissue

surrounding the damaged area can be "awakened" by forcing high concentrations of oxygen into the body under greater than atmospheric pressure. A recent study compared a group of children who received no hyperbaric treatment to a group that received 40 treatments over 8 weeks. On every measure of function (gross motor, cognitive, communication, and memory) at the end of 2 months of treatment and after a further 3 months of follow up the two groups were identical in outcome. There was no added benefit from hyperbaric oxygen therapy.

Aquatic Therapy

Aquatic Therapy or pool therapy, as it's often called, consists of an exercise program done in the water. The buoyancy of the water supports the weight of the child and allows him/her to move in ways that would be impossible on land. Physical Therapists insist the pool relaxes muscles and reduces the force of stress placed on the joints. This, in turn, makes it easier to work and strengthen muscles. Aquatic Therapy may be used in conjunction with other therapies for children with Cerebral Palsy, Muscular Dystrophy, Down's Syndrome and a number of other childhood diagnosis.

G Therapy

G Therapy is described as "a pioneering treatment for a variety of Neurodevelopment disorders and neurological conditions including cerebral palsy, mental sub normality, autism, Down's Syndrome, global delays, etc as well as a range of other chronic conditions". It's a treatment that consists of "combinations of pharmacopeia-based homeopathic medicines derived from herbal remedies and body salts".

Highlights of G Therapy:

G Therapy has shown positive results in over 70% of cases in conditions considered to be irreversible by modern medicine.

G Therapy consists of combinations of pharmacopeia-based homeopathic medicines derived from herbal remedies and body salts.

The exact treatment can differ from patient to patient and is prescribed after an extensive analysis of the patient's conditions by our staff of experts.

Stem cell treatment

Cerebral palsy refers to a group of non-progressive, non-contagious conditions that cause physical disability and applies to the cerebrum in the brain and the disorder of movement. The brain damage normally doesn't worsen but secondary diseases are

very common. Most notable are various orthopedic difficulties and motor disorders, arthritis and osteoporosis. Cerebral palsy cannot be cured. Standard treatments include drugs, mechanical aids, physical therapy, behavioral therapy, occupational therapy and speech therapy. All these approaches are focused at helping the patient overcome developmental disabilities or learn new ways to accomplish difficult tasks.

The Xcell-Center Cerebral Palsy Stem Cell Treatment

The XCell-Center's cerebral palsy treatment differs from standard methods because it attacks the root cause of CP inside the brain. Stem cell therapy is a drug-free alternative focused on affecting physical changes in the brain that can improve a child's quality of life. Almost 70% of the cerebral palsy patients treated with stem cells at the XCell-Center show improvement. Cerebral palsy patients are treated by lumbar puncture injecting the stem cells into the cerebrospinal fluid which transports them up the spinal canal and into the brain. Lumbar puncture is an outpatient procedure that requires patients to stay in Germany 4 or 5 nights.

DRUG TREATMENT

As a muscle-relaxing therapy the baclofen pump is most appropriate for individuals with chronic severe stiffness or uncontrolled muscle movement throughout the body. Doctors have successfully implanted the Medication Choices pump in children as young as 3 years of age.

Antispasmodics are the most common medicines used for people with CP.

Injectable antispasmodics which are injected directly into stiff or spasmodic muscles are sometimes used to help them relax. These medicines typically remain effective for about 3 to 8 months depending on the type used. Injectable antispasmodics used for treating CP include:

Phenol or alcohol "washes."

Anticonvulsants are used as treatment for people with CP who have seizures. Most commonly used anticonvulsants include: Gabapentin (Neurontin), Lamotrigine (Lamictal), Oxcarbazepine (Trileptal), Topiramate (Topamax), Zonisamide (Zonegran).

Anticholinergics help a minority of people with CP who have uncontrollable body movements (dystonic cerebral palsy) or who drool frequently. These include:

Benzotropine mesylate, Carbidopa-levodopa (Sinemet), Glycopyrrolate

(Robinul), Procyclidine hydrochloride
(Kemadrin), Trihexyphenidyl hydrochloride.

RECENT DRUGS AND DRUG TRIALS

Glycopyrrolate treatment

This is a drug candidate designed to treat drooling in children with cerebral palsy and other neurological disorders. The 24-week trial compared liquid Glycopyrrolate to a placebo.

According to the company, after eight weeks of taking the drug, patients drooled significantly less. The drug is intended to treat chronic moderate to severe drooling in children 3 to 18 with cerebral palsy, mental retardation, or any other neurological conditions.

Botox treatment

Botulinum Toxin A (aka Botox or BTA) has been used in treating various effects of cerebral palsy for years. Some success has been seen in treatments of muscle spasms, "tiptoe" walking, and, more recently, the side effect of drooling. Varying degrees of the medicine are injected into different parts of the body, depending on the severity or instance of the offending symptom.

BTA injections can help with providing relief to certain cerebral palsy children by straightening their spasmodic legs, which can cramp up and either prevent ambulation, or make walking very difficult and awkward. BTA can also be effective when injected into hip muscles, upper body problems, or any localized muscle spasmodic occurrence. BTA treatment can also be used for tiptoe walking, known as "pes equinus," which has been used with varying degrees of success. Tiptoe walking occurs when a child with cerebral palsy has a certain amount of spasticity in the legs and cannot place their feet flatly onto the floor. Using BTA to relax the muscles of the calves, medical practitioners have seen some success in helping children regain a short-term flat footedness, which relieves some of the spasmodic contractions in their legs and calves. This treatment can help with balance improvement and stability as well. Botox injections are also seen as helpful in preventing any problems that may develop on top of existing ones, such as permanent fixed contractures (shortening of muscles), abnormality in bone structure, and joint weakness.

BTA injections have a low rate of side effects. The therapeutic sessions involving the injections require multiple visits, however, and involve needle injections that may produce pain or discomfort in the child. As with all sorts of therapy, BTA treatments should only be

administered after a clear success rate and low incidence of side effects in the afflicted child and only by a board-certified surgeon.

SURGERIES

Orthopedic surgery

Orthopedic surgery is often recommended when spasticity and stiffness are severe enough to make walking and moving about difficult or painful. For many people with cerebral palsy improving the appearance of how they walk their gait is also important. A more upright gait with smoother transitions and foot placements is the primary goal for many children and young adults.

In the operating room surgeons can lengthen muscles and tendons that are proportionately too short. But first they have to determine the specific muscles responsible for the gait abnormalities. Finding these muscles can be difficult. It takes more than 30 major muscles working at the right time using the right amount of force to walk two strides with a normal gait. A problem with any of those muscles can cause an abnormal gait. In addition because the body makes natural adjustments to compensate for muscle imbalances these adjustments could appear to be the problem instead of a compensation. In the past doctors relied on clinical examination, observation of the gait and the measurement of motion and spasticity to determine the muscles involved. Now doctors have a diagnostic technique known as *gait analysis*. Gait analysis uses cameras that record how an individual walks force plates that detect when and where feet touch the ground a special recording technique that detects muscle activity (known as *electromyography*) and a computer program that gathers and analyzes the data to identify the problem muscles. Using gait analysis doctors can precisely locate which muscles would benefit from surgery and how much improvement in gait can be expected.

The timing of orthopedic surgery has also changed in recent years. Previously orthopedic surgeons preferred to perform all of the necessary surgeries a child needed at the same time usually between the ages of 7 and 10. Because of the length of time spent in recovery which was generally several months doing them all at once shortened the amount of time a child spent in bed. Now most of the surgical procedures can be done on an outpatient basis or with a short inpatient stay. Children usually return to their normal lifestyle within a week.

Consequently doctors think it is much better to stagger surgeries and perform them at times

appropriate to a child's age and level of motor development. For example, spasticity in the upper leg muscles (the adductors) which causes a "scissor pattern" walk is a major obstacle to normal gait. The optimal age to correct this spasticity with adduction release surgery is 2 to 4 years of age. On the other hand, the best time to perform surgery to lengthen the hamstrings or Achilles tendon is 7 to 8 years of age. If adduction release surgery is delayed so that it can be performed at the same time as hamstring lengthening the child will have learned to compensate for spasticity in the adductors. By the time the hamstring surgery is performed the child's abnormal gait pattern could be so ingrained that it might not be easily corrected.

With shorter recovery times and new less invasive surgical techniques doctors can schedule surgeries at times that take advantage of a child's age and developmental abilities for the best possible result.

Selective dorsal rhizotomy (SDR)

Selective dorsal rhizotomy (SDR) is a surgical procedure recommended only for cases of severe spasticity when all of the more conservative treatments physical therapy, oral medications and intrathecal baclofen have failed to reduce spasticity or chronic pain. In the procedure a surgeon locates and selectively severs over activated nerves at the base of the spinal column. Because it reduces the amount of stimulation that reaches muscles via the nerves SDR is most commonly used to relax muscles and decrease chronic pain in one or both of the lower or upper limbs. It is also sometimes used to correct an overactive bladder. Potential side effects include sensory loss, numbness or uncomfortable sensations in limb areas once supplied by the severed nerve.

Even though the use of microsurgery techniques has refined the practice of SDR surgery there is still controversy about how selective SDR actually is. Some doctors have concerns since it is invasive and irreversible and may only achieve small improvements in function. Although recent research has shown that combining SDR with physical therapy reduces spasticity in some children particularly those with spastic diplegia whether or not it improves gait or function has still not been proven. Ongoing research continues to look at this surgery's effectiveness.

Spinal cord stimulation was developed in the 1980s to treat spinal cord injury and other neurological conditions involving motor neurons. An implanted electrode selectively stimulates nerves at the base of the spinal

cord to inhibit and decrease nerve activity. The effectiveness of spinal cord stimulation for the treatment of cerebral palsy has yet to be proven in clinical studies. It is considered a treatment alternative only when other conservative or surgical treatments have been unsuccessful at relaxing muscles or relieving pain.

CONCLUSION

Cerebral palsy diseases are an abnormality of motor function and postural tone that is acquired at an early age even before birth. New treatment methods that resulted in an increased survival rate of low birth weight and premature infants actually resulted in an overall increase number of children with cerebral palsy. So it was concluded that the new technologies however did not change the rate of cerebral palsy in children born full term and with normal weight. Ongoing research continues to look at this surgery's and therapies effectiveness.

REFERENCES

1. "Cerebral Palsy – Facts & Figures: History". United Cerebral Palsy Research and Education Foundation (U.S.). Retrieved 2007-07-06.
2. "Cerebral Palsy: Hope Through Research". National Institute of Neurological Disorders and Stroke (U.S.). NIH Publication No. 06-159. July 2006. Retrieved 2010-04-26.
3. Access Economics. The Economic Impact of Cerebral Palsy in Australia in 2007. Access Economics, Canberra, ACT, 2008.
4. "Cerebral Palsy: a Guide for Care". Retrieved 2007-07-29.
5. Brindle, David (2002-05-22). "A very telling tale". The Guardian (London). Retrieved 2007-07-29.
6. Zimmer, Benjamin (2007-02-05). "A brief history of "spaz"". Language Log. University of Pennsylvania. Retrieved 2007-07-29.
7. Erickson and Glenn . "DVD Savant Review: Goodbye CP". DVDtalk, 2007.
8. Borah and Prabalika. "Movie with a twist". The Hindu (Chennai, India), 2011.
9. Alawadhi and Neha. "Charting unexplored territory in Indian cinema". The Hindu (Chennai, India), 2011.
10. Rai and Ashutosh. "spandan" "Review of Marathi Film "SPANDAN"". The Newsleak.in, 2012.

11. "Vegitha, carving a niche for herself". *The Deccan Chronicle*. 2011;7.
12. Champlin, Charles "My Left Foot". *Los Angeles Times*, 1989.
13. Josh Blue wins "Last Comic Standing". Retrieved 2010-12-06.
14. Mulligan S and Neistadt ME. Occupational therapy evaluation for children: a pocket guide. : Lippincott Williams & Wilkins; 2003.
15. Steultjens E, Dekker J, Bouter LM, JCM, Lambregts B and CHM. Occupational therapy for children with cerebral palsy: a systematic review. *Clin.Rehabil*. 2004; 18(1):1-14.
16. Neistadt ME. Occupational therapy evaluation for adults: a pocket guide. : Lippincott Williams & Wilkins; 2000.
17. Guidetti S and Söderback I. Description of self-care training in occupational therapy: case studies of five Kenyan children with cerebral palsy. *Occup Ther Int*. 2001;8(1):34-48.
18. Heinen F, Desloovere K, Schroeder AS, Berweck S, Borggraefe I and van Campenhout. The updated European Consensus 2009 on the use of Botulinum toxin for children with cerebral palsy. *Eur J Paediatr Neurol*. 2010;14(1):45-66. Epub 2009;14. Review. PubMed PMID 19914110.
19. Schejbalová A . "[Derotational subtrochanteric osteotomy of the femur in cerebral palsy patients]" (in Czech). *Acta chirurgiae orthopaedicae et traumatologiae Cechoslovaca*. 2006;73(5):334-9. PMID 17140515.
20. Farmer JP and Sabbagh AJ. Selective dorsal rhizotomies in the treatment of spasticity related to cerebral palsy. *Child s Nervous System*. 2007;23(9):991-1002. DOI:10.1007/s00381-007-0398-2. PMID 17643249.
21. Balaban B, Yasar E, Dal U, Yazicioglu K, Mohur H and Kalyon TA. The effect of hinged ankle-foot orthosis on gait and energy expenditure in spastic hemiplegic cerebral palsy". *Disability and rehabilitation*. 2007;29(2):139-144. DOI:10.1080/17483100600876740. PMID 17373095.
22. White H, Jenkins J, Neace WP, Tylkowski C and Walker J . "Clinically prescribed orthoses demonstrate an increase in velocity of gait in children with cerebral palsy: a retrospective study". *Developmental medicine and child neurology*. 2002;44(4):227-32. DOI:10.1017/S0012162201001992. PMID 11995890.
23. Shankaran S, Laptook AR and Ehrenkranz RA. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med*. 2005;353(15): 1574-1584. DOI:10.1056/NEJMcps050929. PMID 16221780.
24. Ehrenkranz RA, Dusick AM, Vohr BR, Wright LL, Wrage LA and Poole WK . "Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants". *Pediatrics*. 2006;117(4): 1253-1261. DOI:10.1542/peds.2005-1368. PMID 16585322.
25. McDonagh MS, Morgan D, Carson S, Russman BS . "Systematic review of hyperbaric oxygen therapy for cerebral palsy: the state of the evidence". *Dev Med Child Neurol*. 2007;49(12): 942-947. DOI:10.1111/j.1469-8749.2007.00942.x. PMID 18039243.
26. Jenks KM, de Moor J, van Lieshout EC, Maathuis KG, Keus I and Gorter JW . The effect of cerebral palsy on arithmetic accuracy is mediated by working memory, intelligence, early numeracy, and instruction time. *Dev Neuropsychol*. 2007;32(3): 861-79. DOI:10.1080/87565640701539758. PMID 17956186.
27. Medicaid.gov: Self Directed Services. Retrieved 2012-03-03.