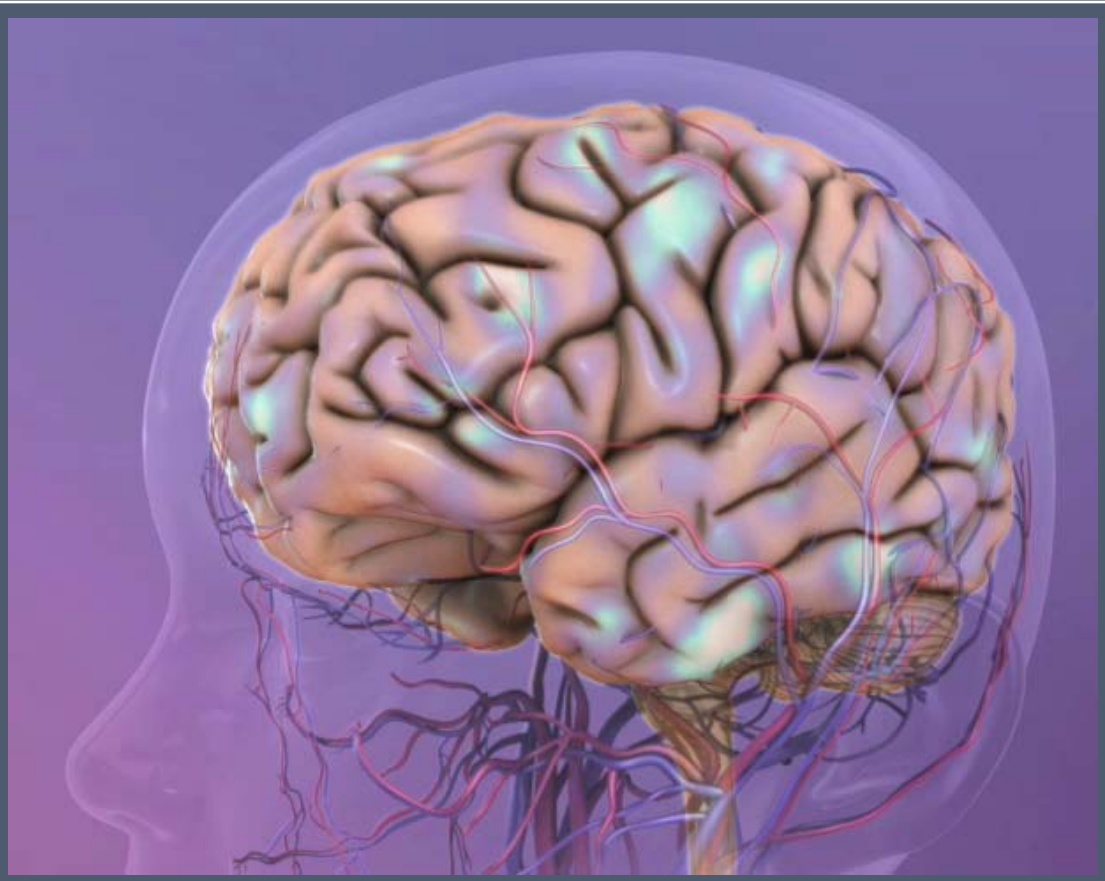
BRAIN INJURY & UMBILICAL CORD BLOOD TRANSPLANT

March is National Brain Injury Awareness Month



What is Brain Injury

- **As defined by the National Head Injury Foundation**
  "a traumatic insult to the brain capable of producing physical, intellectual, emotional, social and vocational changes."
- The brain controls everything we say, do, think, and feel. It controls the very functions that keep us alive: breathing, circulation, digestion, hormones, and the immune system. It is through the brain that we experience emotion and express ourselves.
- Brain injury refers to an injury in which an insult to the brain causes damage to the brain.
- Because of the fact that each injury does damage to a different part of the brain, every brain injury is unique.

A CT of the head years after a traumatic brain injury showing an empty space marked by the arrow were the damage occurred

Classification of Brain Injury

- Generally Brain injuries are classified as;
  - **Direct**

    Primary injury caused by forces of trauma
  - **Indirect**

    Secondary injury caused by factors resulting from the primary injury
- Also, Brain injuries can be classified along several dimensions;
  - Classification of brain injury w.r.t. injury processes:
    - **Primary Brain Injury**
    - **Secondary Brain Injury**
  - Classification is also done on the basis of extent & location of brain injury:
    - **Focal Brain Injury**
    - **Diffuse Brain Injury**

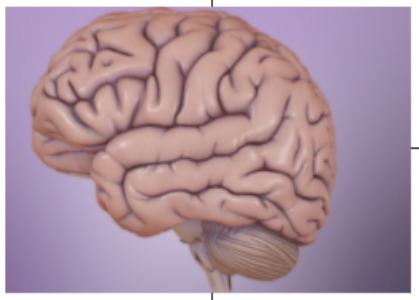
Types of Brain Injury

The type of injury the brain receives may affect just one functional area of the brain, various areas, or all areas of the brain. There are three main types of brain injuries;

1. **Traumatic Brain Injury** - "An insult to the brain, not of degenerative or congenital nature caused by an external physical force that may produce a diminished or altered state of consciousness, which results in an impairment of cognitive abilities or physical functioning. It can also result in the disturbance of behavioral or emotional functioning."
2. **Acquired Brain Injury** - Acquired Brain Injury (ABI), results from damage to the brain caused by strokes, tumors, anoxia, hypoxia, toxins, degenerative diseases, near drowning and/or other conditions not necessarily caused by an external force.
3. **Levels of Brain Injury** - Mild Traumatic Brain Injury, Moderate Traumatic Brain Injury & Severe Brain Injury.

Types of Brain Injury

Unmet Treatment Needs



TRAUMAS & CONCUSSIONS

Traumatic brain injury ("TBI") is a devastating event for an estimated 1.4 million Americans annually,[6] resulting in about 50,000 deaths and 90,000 life-long injuries with substantial loss of function.[7] Current TBI treatment is insufficient, with the end result being significant motor, cognitive and social impairment.

CEREBRAL PALSY

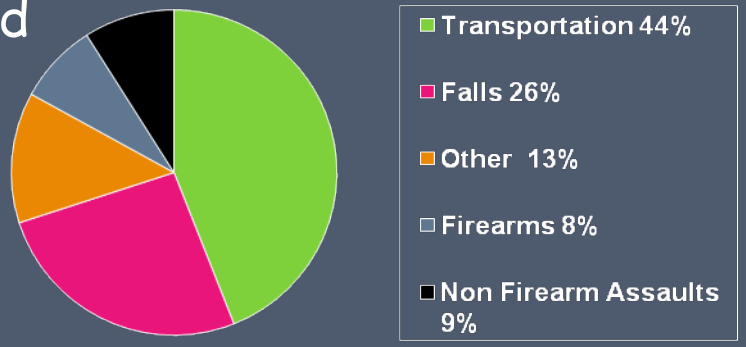
Cerebral palsy is a broad term referring to neurological disorders affecting body movement and muscle coordination. The cause varies from case to case and can include oxygen-depriving (hypoxic) injury to the brain, traumatic injury, infection and stroke. Affects two million children and adults in the United States, with an additional 10,000 babies and infants diagnosed with the condition annually.[8] There is currently no cure for cerebral palsy and no standard therapy.

STROKE

Stroke. Over four million individuals in the U.S. are living with a neurological impairment due to stroke.[9] Since the brain is extremely sensitive to oxygen deprivation, some degree of tissue death from stroke is likely.[1]

What causes brain injury?

- The damage may be caused by an
  - external physical force,
  - insufficient blood supply,
  - toxic substance,
  - malignancy,
  - disease-producing organisms,
  - congenital disorders,
  - birth trauma or degenerative processes
- An outside force impacts the head causing the brain to move
- A direct blow to the head
- A rapid acceleration and deceleration of the head



Epidemiology of brain injury

- According to Centers for Disease Control and Prevention (CDC), every year, at least **1.7 million** TBIs occur either as an isolated injury or along with other injuries.[1]
- TBI is a contributing factor to a third (30.5%) of all injury-related deaths in the United States.[1]
- As perNIMHANS (National Institute of Mental Health & Neuro Science), it is estimated that nearly **1 million persons are injured**, **200,000 people die** and nearly **1 million require rehabilitation** services every year in India.[2]

1. http://www.cdc.gov/traumaticbraininjury/statistics.html
2. http://www.nimhans.kar.nic.in/epidemiology/doc/ep_ft25.pdf

What are the symptoms?

There are numerous symptoms of brain damage, whether traumatic or acquired. They fall into four major categories:

Cognitive symptoms of brain damage include:

- Difficulty processing information
- Difficulty in expressing thoughts
- Difficulty understanding others
- Shortened attention span
- Inability to understand abstract concepts
- Impaired decision-making ability
- Memory loss

Physical symptoms of brain damage include:

- Persistent headaches
- Extreme mental fatigue
- Extreme physical fatigue
- Paralysis
- Tremors
- Seizures
- Sensitivity to light
- Sleep disorders
- Slurred speech
- Loss of consciousness

Perceptual symptoms of brain damage include:

- Change in vision, hearing, or sense of touch
- Spatial disorientation
- Inability to sense time
- Disorders of smell and taste
- Balance issues
- Heightened sensitivity to pain

Behavioral/emotional symptoms of brain damage include:

- Irritability and impatience
- Reduced tolerance for stress
- Sluggishness
- Flattened or heightened emotions or reactions
- Denial of disability
- Increased aggressiveness

What are the consequences?

Cognition: concentration, memory, judgment, communication, sleep.

Movement abilities: strength, coordination, balance, fatigue.

Sensation: tactile sensation, vision, hearing, headaches.

Emotion: instability, impulsivity, mood.

Community integration: impacts family, work, economic/ social wellbeing

How is Brain Injury diagnosed?

- History of TBI
- Length of unconsciousness, post traumatic amnesia
- Physical examination
- Imaging: CT, MRI
- Neuropsychology

Glasgow Coma Scale:

- Eye Opening (1-4)
- Best Motor Response (1-6)
- Verbal Response (1-5)

Scoring:

- Mild 13-15
- Moderate 9-12
- Severe <12

How is Brain Injury diagnosed?

- **X-Ray:** Radiation view bone structure
- **CT Scan (CAT scan):** Different type of X-ray shows brain and soft tissue (15-30 min)
- **MRI (magnetic resonance imaging):** Large magnet and radio waves used, 60 min
- **Angiogram:** views damaged or spasming blood vessels by injecting dye into an artery through a catheter, 1-3 hours
- **ICP Monitor:** measures intracranial pressure by inserting small tube into/on top of brain through small hole in skull
- **EEG (electroencephalograph):** measures electrical activity in brain by placing electrodes on head, painless and time varies.

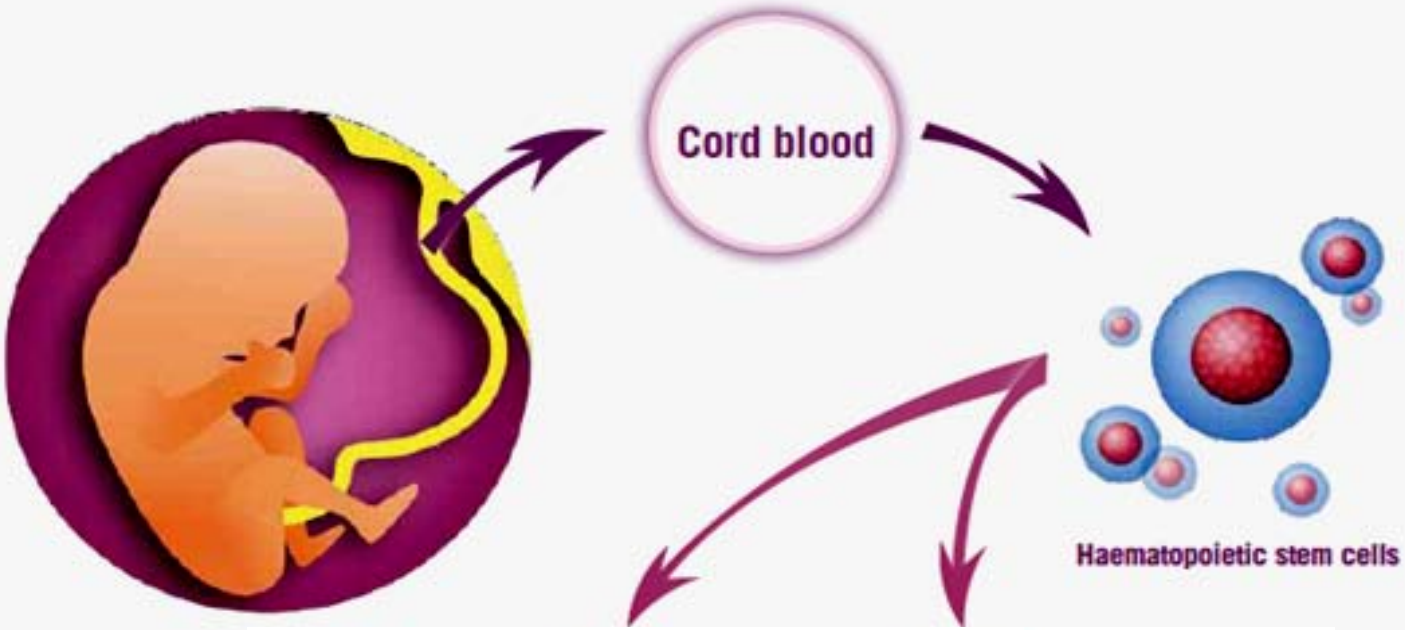
How is it treated?

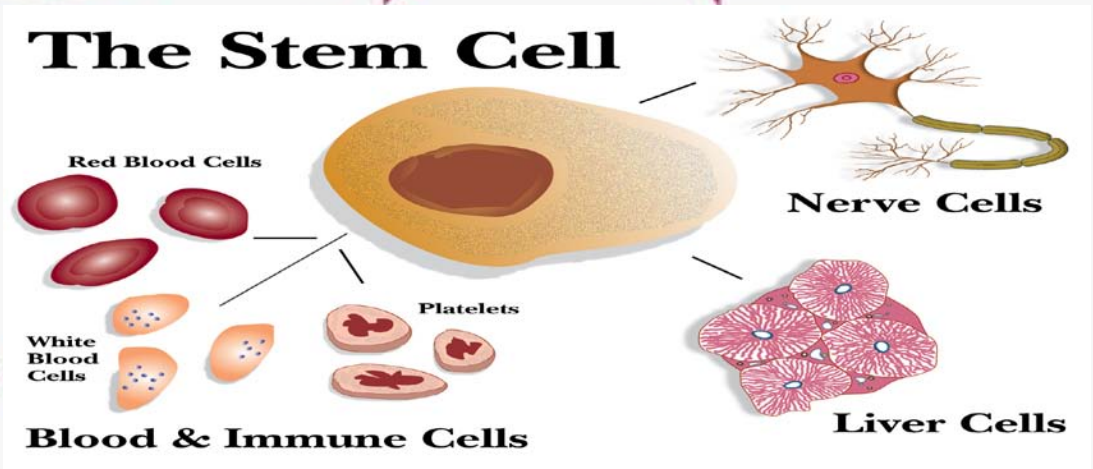
- **Initial Treatment: Evaluation**
  - Emergency Response
    - level of consciousness, ABC's (airway, breathing, circulation) and vital signs assessed & treated
    - Neurological Assessment
    - Imaging
- **Patient's condition determines next level of treatment:**
  - May be released from ER with Dr's orders
  - ICU treatment for more severe injuries that may include LOC, contusion, lesions, edema, hematoma, ↑ ICP, fracture, etc.

- Other treatments for brain injury include medication, psychotherapy, neuropsychological rehabilitation, snoezelen, surgery, or physical implants such as deep brain stimulation.

- Umbilical Cord Blood stem cell transplant is one of the most effective treatment to treat Brain Injuries.

Cord Blood Stem cell transplant in Brain Injuries





Cord Blood Stem cell transplant in Brain Injuries

- Umbilical cord blood is playing an important and growing role in the treatment of Brain Injuries i.e. Traumatic or Acquired Brain Injury and other life-threatening blood diseases.

- The use of cord blood transplants has increased for both children and adults. Cord blood is used more often in children because a cord blood unit has a limited amount of blood-forming cells. Smaller patients need fewer cells and larger patients need more cells.

Published Articles

Umbilical Cord Blood-Derived Stem Cells and Brain Repair

PAUL R. SANBERG[1,*], ALISON E. WILLING[1], SVITLANA GARBUZOVA-DAVIS[1], SAMUEL SAPORTA[2], GUOQING LIU[1], CYNDY DAVIS SANBERG[3], PAULA C. BICKFORD[1], STEPHEN K. KLASKO[1], NAGWA S. EL-BADRI[1] Article first published online: 9 JAN 2006, DOI: 10.1196/annals.1334.008

- HUCB cells are enriched for stem cells that have the potential to initiate and maintain tissue repair.
- The therapeutic potential of HUCB cells may be attributed to inherent ability of stem cell populations to replace damaged tissues. Alternatively, various cell types within the graft may promote neural repair by delivering neural protection and secretion of neurotrophic factors.
- In this review, we evaluate the preclinical studies in which HUCB was applied for treatment of neurodegenerative diseases and for traumatic and ischemic brain damage.
- Furthermore, HUCB cells are easily available and less immunogenic compared to other sources for stem cell therapy such as bone marrow

http://onlinelibrary.wiley.com/doi/10.1196/annals.1334.008/abstract;jsessionid=D74E980CD310E9E440322B1C26B393CF.f04t01?deniedAccessCustomisedMessage=&userIsAuthenticated=false

Case Reports

Restorative Neurology and Neuroscience 31 (2013) 397–410
DOI 10.3233/RNN-120289
IOS Press

Allogenic umbilical cord blood therapy combined with erythropoietin for patients with severe traumatic brain injury: Three case reports

- Three Patients with TBI over 6 months post injury.
- Intravascular administration of allogenic UCB and injection of rhEPO, and rehabilitation therapy.
- Patient 1 demonstrated improvements in motor and cognitive function.
- Patient 2 displayed improvements in activities of daily living.
- In Patient 3, neurogenic fever vanished and Brain PET revealed increased glucose metabolism at basal ganglia, thalami, and cerebellum.
- The allogenic UCB therapy combined with rhEPO in the present study was safe and suggested potential therapeutic efficacy for patients with TBI.

Brain injury (Cerebral Palsy) cured using cord blood stem cells

Bochum's medics have succeeded in treating cerebral palsy with autologous cord blood. http://www.sciencedaily.com/releases/2013/05/130523101822.htm

2.5 year old boy had been in a persistent vegetative state with minimal chances of survival. Just two months after treatment with the cord blood containing stem cells, the symptoms improved significantly; over the following months, the child learned to speak simple sentences and to move.

Reasons to choose cord blood for stem cell Transplant

A doctor might choose cord blood because of some of the ways it differs from marrow or peripheral blood.

- **More tolerant matching**

  A close match between the patient and the donor or cord blood unit can improve a patient's outcome after transplant. If you have an uncommon tissue type, you may not find a closely matched adult donor for you. However, a cord blood unit may be the best option.

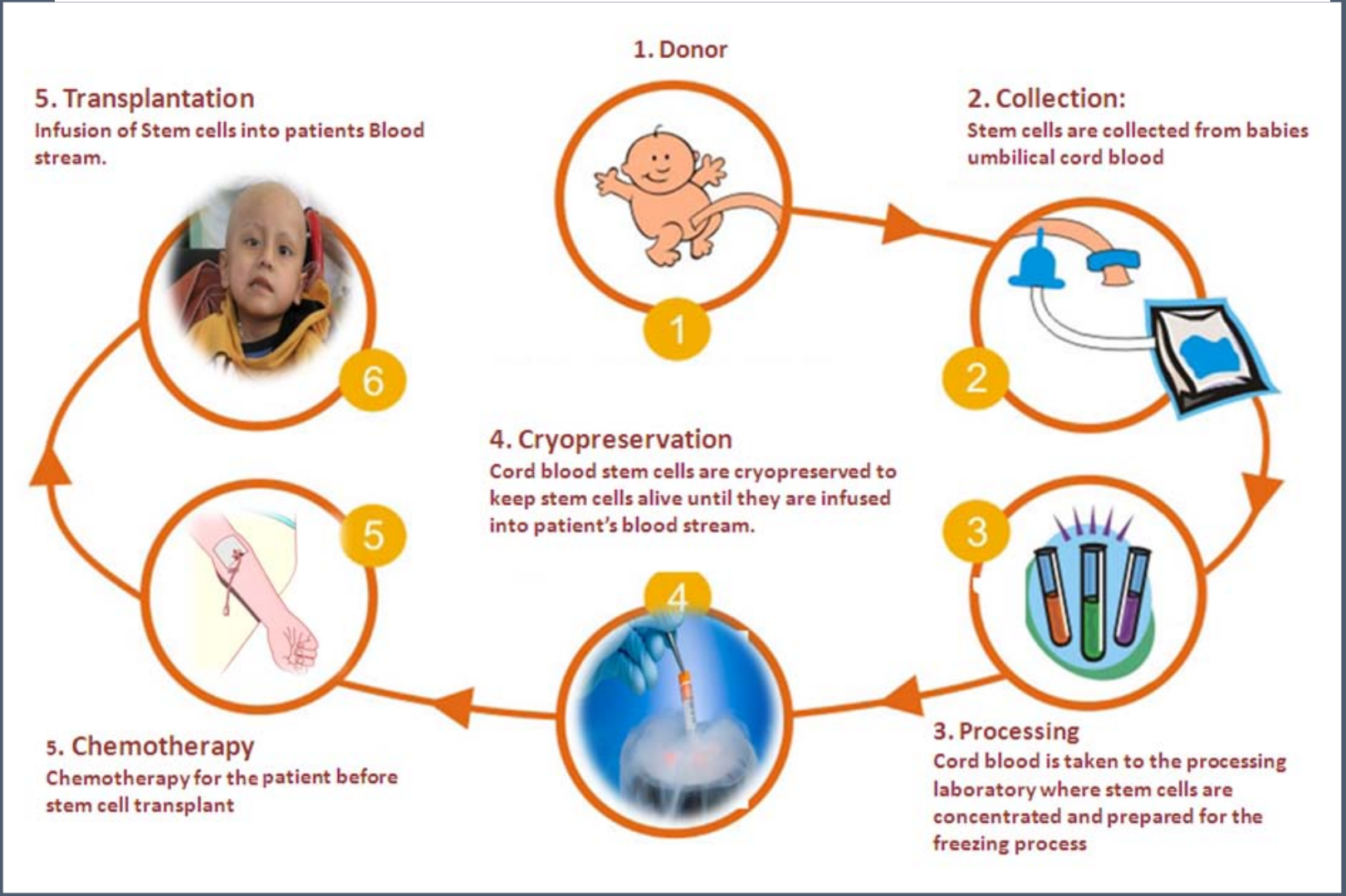
- **More quickly available**

  Cord blood units are stored and ready to use. A cord blood unit can be selected and delivered to the transplant center in less than two weeks whereas it can take two months or more to find an unrelated marrow or peripheral blood donor.

- **Less graft-versus-host disease**

  Graft-versus-host disease (GVHD) is a common complication after an allogeneic transplant (which uses cells unrelated donor). GVHD can range from mild to life-threatening. There is less chance of GVHD when the cord blood transplant is done using cells from a family member.

Cord Blood Transplant for Brain Injury



UCB transplantation Flowchart

Step 1
- Collection, Storage and Cryopreservation of Umbilical Cord Blood

Step 2
- Day -30 to -11: HLA typing and donor/recipient matching

Step 3
- Day -10: Patient Admission and Isolation in ICU Room

Step 4
- Day -8: Pre Transplantation conditioning Regimen for 8-10 day before transplantation

Step 5
- Day 0: Umbilical Cord Blood transplantation in Patient

Step 6
- Day 1 to Day 25: Post Transplantation follow up and Monitoring

Step 1 - Collection of UCB

- Umbilical cord Blood is collected by trained paramedic as per standard procedure and transported for storage.

- Collected cord blood sample is stored at GMP laboratory for future use.

Step 2- HLA typing

- Before implantation, HLA typing (Cross matching) is need to do for checking donor- recipient compatibility.
- Also attention requires in the case of Blood Groups of both donor- recipient for ABO incompatibility.
- Assessment of medical history and reports.

Step 3- Hospitalization

- Patient is admitted to the hospital before 8-10 days of transplantation date.
- Patient is completely isolated from the outside and keep in ICU unit to avoid contamination.
- Access is restricted to limited personnel only

Step 4- Pre-operative Regimen

- Preparative regimen is given to the patient to prepare for implantation.
- This includes medication, antibiotics and chemotherapy to ablate the patient's immune system and avoid GVHD after transplantation.

Step 5- UCB transplantation

- Stored umbilical cord blood sample is procured from the lab before transplantation.
- Physician transplant the required quantity of umbilical cord blood cells intravenously into the patients body.
- The intravenous part of the transplant takes approximately 15 minutes.

Step 6- Post transplantation Follow up

- After transplantation, patient will be under strict monitoring for 4-5 weeks for any side effects or complications.

- It can takes months to recover full immune power for patient after transplantation.

Centers where UCB can be done

- AIIMS, New Delhi
- Apollo Specialty Hospitals, Chennai
- Global Hospitals, Hyderabad
- Tata Memorial Hospital, Mumbai
- KDA hospital Mumbai
- Jaslok Hospital Mumbai
- Christian Medical College Hospital
- Sahyadri Speciality Hospital,Pune

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