

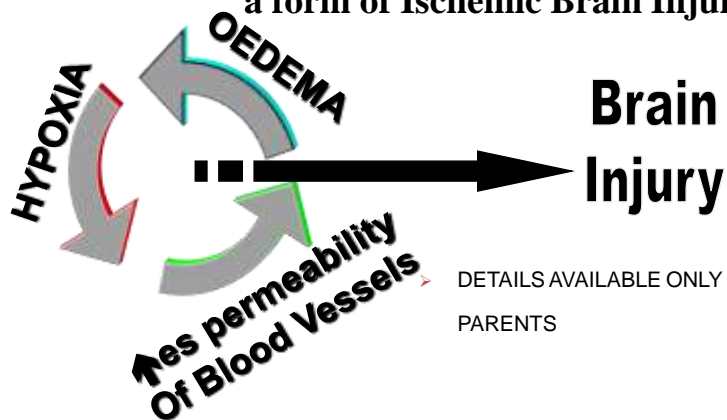
Stem Cell: A hope in intractable Neuro problems, provided done scientifically

Dr. Arun Mukherjee, MD
 Director & Team Leader: **UDAAN for the Disabled**
 A project for therapy for children with moderate to severe CP, Autism, MR and allied Neurodevelopmental Delays
 Under Min. of Social Justice & Empowerment, Govt. of India
 C-27 Dayanand Colony, Lajpatnagar – 4; New Delhi 110019;
Website: www.udaan.org



CP PATHOLOGY

The end result of various etiologies in C.P. is a form of Ischemic Brain Injury, where



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Autism pathology

- Abnormal heavy metals
- Somehow, propensity to AND specific parts of that control involuntary functions and emotions

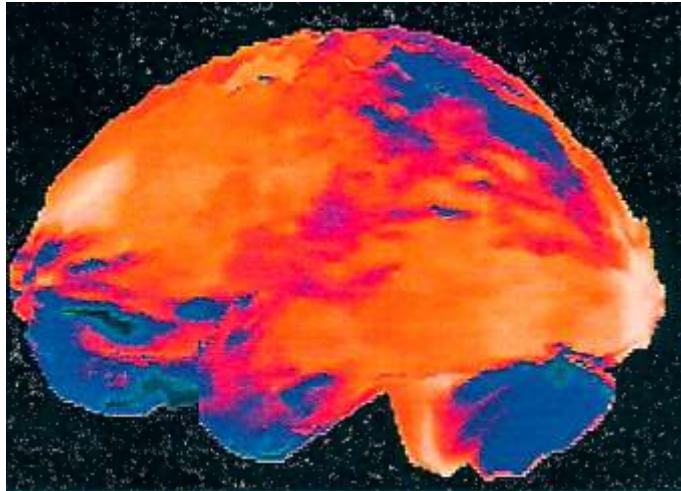


End of the day, what do we have?

- **Various means to damage brain:**
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- ALL OF THEM CAUSE ➔
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- **This generic pathology needs a generic therapy:**
Stem cells with or without mHBOT / HBOT



SPECT Scan of brain in **CEREBRAL PALSY** helps us to identify areas where we may not achieve anything much (blue areas) and areas where variable degree of recovery is possible (deep red areas), and areas that are functioning normally (white to pink areas)



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Correlating SPECT in **CEREBRAL PALSY** with clinical findings, we suggest to parents where HBOT or Stem cells or both **MAY** help in about 80 to 90% children, with no guarantee it definitely will. Then leave it to parents to decide whether they want to try HBOT/Stem cell Therapy or not.

Overlay of scan with functional correlation
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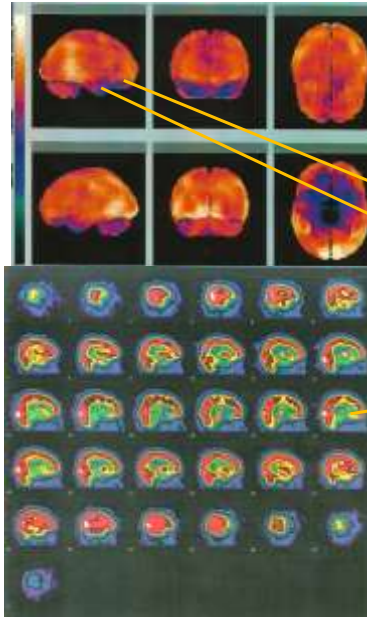
SPECT Scan in ASD before Stem cell Therapy

Case No. 1

J. S. is an 8 yrs old male child with the diagnosis of ASD (Autism Spectrum Disorder).

His main problem areas were:

- Poor Eye Contact
- Very hyperactive
- Decreased sitting behavior
- Aggressive
- Not following age appropriate commands
- Decreased social skills
- Not playing meaningfully
- Lots of self-stimulatory behaviors like playing with fingers, rocking and mouthing non-edible things
- Decreased Attention Span



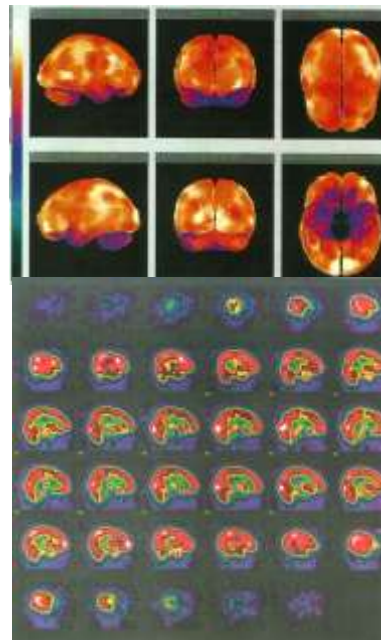
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SPECT Scan 2 month after SCT

2 Month Post SC therapy:

- Better Eye contact (on command)
- Decreased hyperactivity
- Can sit at one place for a structured activity
- Command following is better.





Management in CP

- As per established guidelines,
- All established Rehab centers generally agree & somewhat accept there is some role for:
 -



Where does that leave us?

- are the **foundation** of any rehab therapy.
- Children initially show good progress in motor (Body Control & Speech) and educational/ psychosocial abilities.
- After a few years, there is a stagnation in neurodevelopmental growth rate in spite of best efforts, with **NO rise in cognitive abilities / intellectual functions**



Regenerative Medicine

- Regenerative Medicine has a role to play to restore lost ground in the brain.
- HBOT since the last 2 decades and Stem Cells for a decade, has been the subject of intense research, and has shown promising results
- **Stem Cells in particular have shown a rapid revival of damaged neurons.**

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Hyperbaric Oxygen Therapy (HBOT)

➤ Definition: DETAILS AVAILABLE ONLY FOR
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- The Lancet Study and our own 9 years experience suggests 1.3 (Air) to 1.5 ATA (100% O₂) HBOT best for children
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Physiological Basis

- How does HBOT act ?
- Oxygen exists in the Blood in two forms
 - Combined with Hb (19.5ml/100ml)
 - Dissolved in Plasma (0.3ml/100ml)
- More oxygen is transported by Hb
- But O₂ is delivered to the tissues in dissolved form by the liquid portion of blood



Theory of HBOT: Highway Truck

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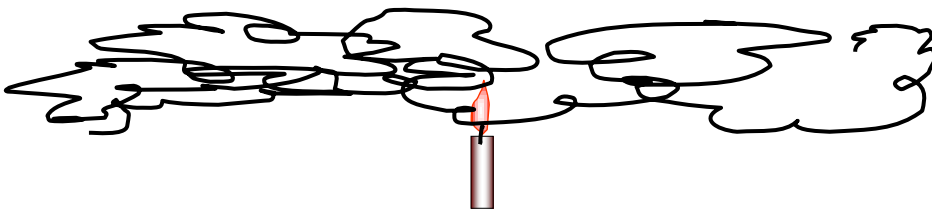


Oxygenated Fluid

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Recall what is simple Diffusion

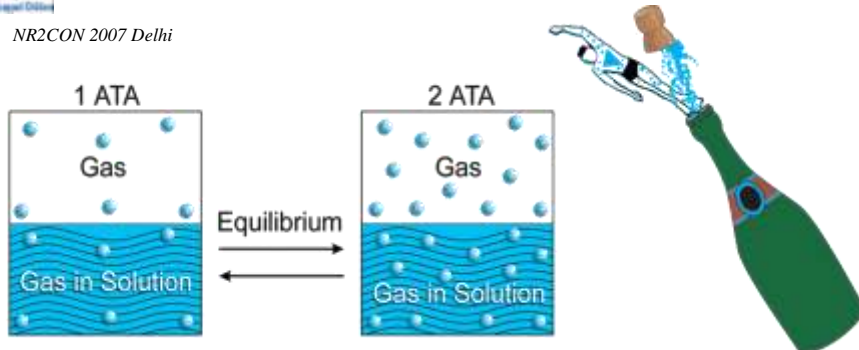


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NR2CON 2007 Delhi

Soda Water Bottle



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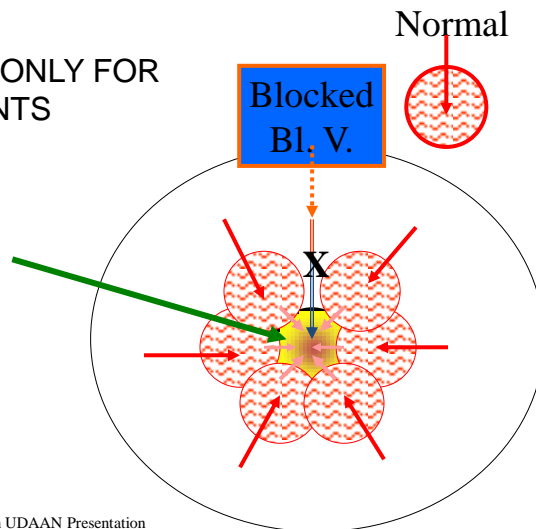


Paul Harch



How Damaged areas remain Non-dead

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An UDAAN Presentation



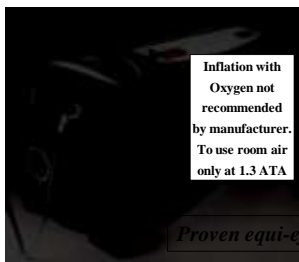
4 Centuries ago



Accepted HBOT

"Negative" HBOT

History of Hyperbaric THERAPY
(HBOT / HBA):
Medicinal use after mid-1800s



Proven equi-effective in CP



Accepted HBOT

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Dose of HBO Treatment in Severe Brain Lesion - n= 30

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1.3 1.75

— EPE alpha
— Lact.
— CBF L
— ICP

Adapted from paper presented by Wassman et al
at the 5th Int.Symp. on HBO & the Recoverable Brain
Fort Lauderdale, Florida, July 2006



Detailed Effects of HBOT

- Increased Fibroblast Proliferation
 - 1997; 5: 147-50
- Increased Bone Mineral Density & Healing
 - 1998; 44(4): 676-81
- Angiogenesis
 - 11/90; 160: 519-24
 - 1980; 31: 564-66
- Epithelialization
 - 1994; 93: 835-41
 -; 31: 564-66
- Ischemic Tissue Oxygen Capacitance
 - 1997; 99: 148-55
- Mobilization of Bone Marrow Stem Cells
 - 2006; 290: 1378-86.
- Enhanced Neuro-Plasticity to allow unused areas of brain to take over function of fully damaged areas, and also normalization of Metabolic Apoptosis & DNA signaling
 -; Sept. 2007

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IN CONCLUSION

HYPERBARIC O₂ / Air THERAPY

AS PRACTICED **TODAY IS QUITE SAFE IF
ALL PRECAUTIONS FOLLOWED**



Introducing Stem cells

- Called Master Cells of the body.
 - Undifferentiated cells that have the ability to divide & differentiate into other 200 cell types.
- Stem cells are distinguished from other cell types by two important characters
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Stem Cells

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Totipotent Stem Cells →

→ *Safer Multipotent Stem Cells* →

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↓ *Pleuriotent Stem Cells*

← ← ←

Potency of Stem Cell ?

Differentiation potential

Ethical considerations

- **Toti-potent**
 - Can be any type of cell in the body
 - If split in early stage, develops identical monozygotic twins
- **Pluri-potent**
 - Can become almost any kind of cell in the body (an example would be fetal cells)
- **Multi-potent**
 - Can differentiate into only a limited range of cell types (examples include umbilical cord and adult stem cells)
 - May be from self (autologous) or donor (allogenic)
 - For our Study, we have applied for the more tried, tested and proven safe autologous variety. There is virtually no risk of infection, transplant rejection, allergy, etc. The child either improves or does not improve. No deterioration in any case.

X

?



Composition of Adult Stem cells

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- Brain damage to neurons, nerves, supporting fibers, blood vessels, with inflammation, defective blood flow, etc. need various types of Stem cells, hence this cocktail

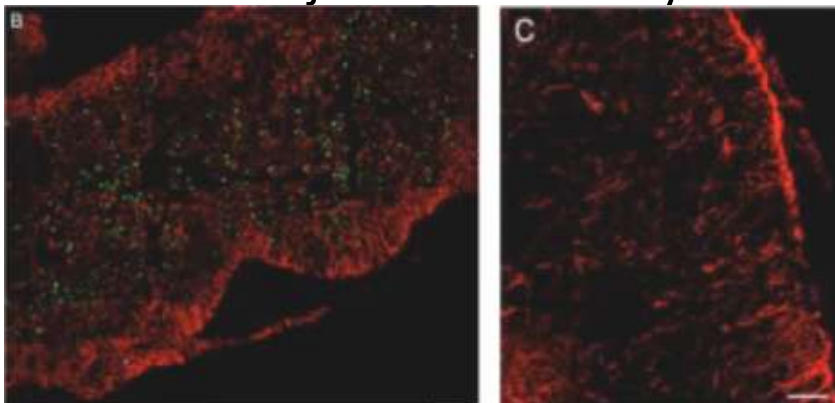


Mechanism of Action

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Stem cells cross BBB & home
on to injured tissues only



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Mechanism of Action Cont..

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New Brain tissue formation

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CD34+ stem cells can:

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Safety

Autologous Stem Cell Transplantation by lumbar puncture:

A safety Follow-up in 870 Patients

February 4th, 2009

Johannes P.J.M. de Maat, Director Research and Development

XCell-Center Cologne and Düsseldorf Germany

Report file:

Official Safety Report XCell-Center GmbH Germany 2009: XC20091107B5

Title:

Autologous Stem Cell Transplantation by lumbar puncture

A safety Follow-up in 870 Patients

Author:

J.P.J.M. de Maat, Director Research and Development XCell-Center GmbH

Release date:

February 4th, 2009

Conclusions

Within XCell-Center, the incidence of Post Dural Puncture Headache is estimated as low as 11.9% (103 cases out of 870 patients). There were no reported side effects concerning fever, skin rashes, shock or tachycardia. Therefore, the transplantation of autologous stem cells seems to be safe and the lumbar puncture is a safe and non-invasive procedure to inject the stem cells into the intrathecal space. The Post Treatment Survey is a useful tool to monitor the safety of the procedures.



Some hiccups we face today

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That is where we are headed

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What about Stored Cord Blood

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- **IS BEING USED at some places as donor cells for some other patient = Allogenic SCT**
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Our Inclusion Criteria in CP

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Our Inclusion Criteria in ASD

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Unmodified Autologous Bone Marrow derived Stem Cell Therapy

- DETAILS AVAILABLE ONLY FOR REGISTERED PARENTS .
- **Intensive Standard Therapies mandatory THROUGHOUT.**
- ***Follow up:***
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Criteria for Evaluation: CP

- **Physical Progress**
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- **Cognitive Progress**
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- **Speech, Language and Communication Progress**
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- **Any other relevant Internationally accepted scale as applicable to a particular child to help his therapy**



Criteria for Evaluation: ASD

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- The **Criteria of Evaluation** shall be on two hallmarks:
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PRE-THERAPY PROTOCOL

- Informed voluntary written consent
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- Proper balanced diet and micronutrient support and general health improvement.



Investigations

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Side Effects

- DETAILS AVAILABLE ONLY FOR REGISTERED PARENTS
- No specific side effects as child's own blood used



Take Home Message

- Standard therapy is sheet anchor of therapy.
- A time comes when in spite of best efforts by parents and therapists, mental faculties and body control improvement rate stagnates at a constant rate.
- That is when Experimental Therapies like Stem cell and HBOT have a place, by reviving some damaged brain areas, gives the therapist some extra RAM Chip to train and thus improve the quality of life.



Thank You