

# WHAT IS HBOT? ITS EFFECTS IN ACUTE AND LONG TERM NEUROLOGY.

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Oxygen was discovered by John Priestly 1774, Lavoissier und Seguin 1789 distributed the idea of toxicity of oxygen in higher concentration. The first noticed pressure chamber was constructed by Dr. Henshaw 1664 using normal air. Pressurized air as a therapeutic method had most active time beginning of the last century. The peak was the construction of a giant chamber by Orwell Cunningham Kansas, 1928, with six floors, with 12 beds in every storage, but it never worked. The German Draeger-Cooperation constructed 1917 a vessel for Hyperbaric Oxygenation to be used in the treatment of diving accidents.

Oxygen in the air is distributed between 19 % till 21 %. In Hyperbaric Oxygenation Therapy (HBOT) a 100 percentage oxygen is used, with a pressure greater than atmospheric pressure. Pressurized oxygen adheres all gas laws. After the law of Henry and Dalton there is a direct relationship between pressure and the amount of gas dissolved in solutes. Oxygen is a pluripotent drug unmatched by any pharmaceutical. Edward Teller stated, that under pressure free clinical molecular oxygen is delivered directly to the cell for immediate metabolic use, without energy exchange and even with compromised circulation. I. Boerema and his group used this knowledge in his open heart surgery under pressurised oxygen (1960). Ingvar and Lassen used HBOT in 4 patients with ischemic stroke (1965).

The biophysical immediate effect of HBO is the reduction of cerebral oedema, limitation of ischemic cascade and reduction of CNS lactate in hypoxia. The plasma oxygen is increased by 2 000 %, oxygen dissolved in CSF, lymph, bone and urine. Metabolically available oxygen is delivered without chemical energy, life is sustained without blood. Some other effects are the perfusion to all tissue spaces, reduction of adhesiveness of white blood cells, neutralisation of toxic amines, deaggregation of platelets, increase of phagozytic activities and as main long term effect the restoration of the integrity of blood brain barrier and cell membrane. An antibiotic effect is known. HBOT may enhance the effectiveness of certain drugs and their longevity .

Pressurised oxygen can be compared to a drug of specific dose for each diagnoses, dose equals are depths of pressure, length of exposure, frequency and total number of treatment. For the administration of HBOT there available multiplace chamber, monoplace chamber and low pressure portable chambers.

HBOT method suffers by lack of knowledge and missing of teaching program in pre- and postgraduate education. There is lack of facilities and last not least nothing is to be patented. Basically research on human and extension of basic research with animal models are necessary.

As current applications in Neurology now 3 groups are to differentiate, the acute group like acute state in stroke and in traumatic brain injury, the group of chronic neurological conditions like CP in children, neurological defects states including apallic syndrome and as a third group of patients brain diseases with progredient cause including apallic syndrome, heredoataxia, etc.

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# ABSTRACTS

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- **I. Velcheva** - Cardiovascular autonomic disorders
- 18.15 – 19.15 • **V. Bossnev, M. Daskalov, Zl Stoyneva, H.Kaji** - Autonomic microvascular disorders  
GLAXO SMITH KLINE Satellite Symposium: - REQUIP IN PARKINSON'S DISEASE.  
PROGRESSIVE THERAPY FOR A PROGRESSIVE DISEASE
- **I.Milanov** - The role of dopamine agonists in the treatment of Parkinson's disease
- **D. Georgiev** - Clinical profile and therapeutic effects of ReQuip (ropinirole)
- 20.00 **Cocktail Party**

**Thursday, September 16, 2004**  
**National Palace of Culture, Hall 3.1**

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**HBO Therapy in Neurology**  
Chair: **Dr. Richard A. Neubauer (USA)**  
**Dr. Franz Gerstenbrand (Austria)**

- 8.00 – 8.20 • **Dr. Franz Gerstenbrand (Austria)**  
What is HBO?  
Its effects in acute and long term Neurologic Problems.
- 8.20 – 8.40 • **Dr. Richard A. Neubauer (USA)**  
How is it Administered  
The use of hyperbaric oxygen in acute and long Term Neurologic deficits
- 8.40 – 9.00 • **Dr. Ivan Chavdarov (Bulgaria)**  
The use of hyperbaric oxygenation in the long-term rehabilitation of the cerebral palsy.
- 9.00 – 9.20 • **Dr. Natalja Kazantseva (Moscow)**  
Cyclosporine A & HBO in Neuro-Degenerative Diseases
- 9.20 – 9.40 • **Dr. Cuauhtemoc Sanchez (Mexico)**  
Early Intervention in neonatals
- 9.40 – 10.00 • **Dr. Arun Mukherjee (India)**  
UDANN and HBO therapy
- 10.00 – 10.20 Coffee
- 10.20 – 10.40 • **Dr. Paul Harch (USA)**  
TBI and Autism
- 10.40 – 11.00 • **Dr. Ignacio Folgel (Argentina)**  
Physiological Bases, Indications and Protocols  
Of the Low, Mild and Ultra Low Hyperbaric  
Treatment Modalities

**P52. PULSE CORTICOSTEROID THERAPY IN RELAPSES OF MULTIPLE SCLEROSIS**

D. Janculjak, D. Vukashinovic, S. Soldo-Butkovic, L. Knazevic, B. Kovac  
Osijek, University Hospital, Department of Neurology, Croatia

**P53. MULTIPLE SCLEROSIS AND AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION –  
OUR TWO PATIENTS EXPERIENCE.**

E. Klímová, Š. Raffaè, J. Rosocha, E. Tóthová.  
Košice, Slovak Republic

**P54. INCREASING OF SERUM URIC ACID LEVELS MAY HAVE THERAPEUTIC VALUE IN MULTIPLE  
SCLEROSIS**

G. Toncev, G. Zlatic, Z. Knezevic, B. Milicic.  
Kragujevac, Belgrade, Serbia&Montenegro

**P55.COMPLEXE KINESITHERAPEUTIC PROGRAM  
FOR PATIENTS WITH CEREBRO-SPINAL FORM OF MULTIPLE SCLEROSIS**

I.Koleva, N.Lishev  
Sofia, Bulgaria

**P56.FUNCTIONAL REHABILITATION AMELIORATING THE QUALITY OF LIFE  
OF MULTIPLE SCLEROSIS PATIENTS**

I.Koleva, I.Milanov, N.Topalov, R. Yoshinov  
Sofia, Bulgaria

**14.00 – 15.00 LIBRA Satellite Symposium:  
Chairperson: I. Milanov**

- I.Milanov - PK Merz in the treatment of chronic fatigue syndrome in patients with multiple sclerosis
- P. Shotekov - Treatment of cerebrovascular disorders with Cefavora

**15.00 – 15.40 Main topic: HEADACHE  
Chairpersons: G. Sandrini, I. Milanov, P. Kolev**

- G. Sandrini - Sensitization phenomena in migraine: clinical and electrophysiological evidence
- P. Kolev - Application of neurophysiological methods in migraine diagnosis.

**15.40 – 16.25 PFIZER Satellite Symposium: RECENT ADVANCES IN THE PREVENTION OF  
CEREBROVASCULAR DISEASE  
Chairperson: P. Stamenova**

- I. Petrov Recent advances in prevention of cerebrovascular disease

**16.25 – 16.40 Coffee Break**

**16.40 – 18.15 Main topic: AUTONOMIC NERVOUS SYSTEM  
Chairpersons: A. Korczyn, M. Hilz, M. Daskalov**

- A. Korczyn - Multiple system atrophy
- M. Hilz - Clinical examples of bedside and research testing of the Autonomic nervous system
- L. Kazakov, M. Vlaskovska - Purinergic neurotransmission in visceral pain: implication to therapy.



**36<sup>th</sup>**

**INTERNATIONAL DANUBE SYMPOSIUM**

**FOR NEUROLOGICAL SCIENCES**

**AND CONTINUING EDUCATION**

**15 - 18 September 2004, Sofia, Bulgaria**

*COLLABORATING SOCIETY*

*OF THE EUROPEAN FEDERATION OF NEUROLOGICAL SOCIETIES*

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## ***Final Programme & Abstracts***



## HBO Therapy in Neurology

**What is HBO?  
Its effect in acute and long term  
neurologic problems**

F. Gerstenbrand<sup>1</sup>, R. Neubauer<sup>2</sup>, W. Struhal<sup>1</sup>  
<sup>1</sup>Wien, <sup>2</sup>Fort Lauderdale

36<sup>th</sup> International Danube Symposium for Neurological  
Sciences and Continuing Education  
September 16<sup>th</sup>, 2004, Sofia

## The Pressurized Environment is Not New

The 1<sup>st</sup> Recorded Use in History  
was a Diving Bell Alexander the  
Great Used in the Siege of Tyre  
in 332 B.C.

Oxygen was discovered by Priestly  
in 1774

He cautioned increased pressure  
may be toxic

this held the field back  
many years

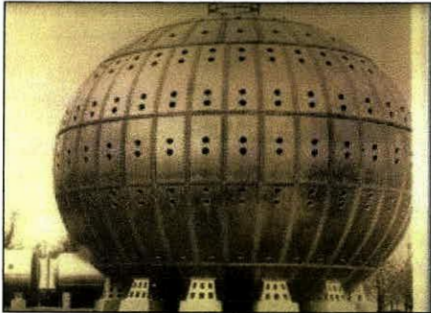
In the Early 19<sup>th</sup> Century  
Pressurized Air Spas Were  
Rampant Throughout Europe

healing properties were  
demonstrated

1920s – 30s Remarkable Clinical  
Results Were Obtained by  
Orville Cunningham, Professor of  
Anesthesia,  
Univ. of Kansas

1928 - The 6 Story Stainless Steel  
Domicilium Was Erected For  
Cunningham by Timken Ball Bearing  
Company in Cleveland

## Cunningham's Domicilium



Hyperbaric Oxygen Therapy is the use of 100% Oxygen at greater than atmospheric pressure

Pressurized  $O_2$  adheres to all gas laws of physics

Henry's Law states there is a direct relationship between pressure and the amount of gas dissolved in solutes

Under HBOT  $O_2$  is increased in the:

- Bone
- Urine
- Plasma
- Lymph
- And most importantly the cerebrospinal fluid

How is  $O_2$  handled in the body ?

Under pressure free molecular oxygen is delivered directly to the cell for immediate metabolic use without energy exchange.

Edward Teller, Ph.D.

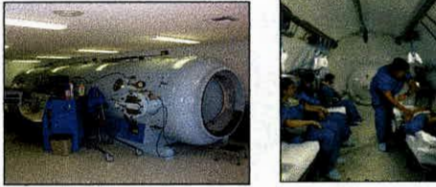
## Dose equals

- Depth of pressure
- Time (length) of exposure
- Frequency
- Total number of treatments

## How is pressure vessel administered

- Multiplace Chamber
- Monoplace Chamber
- Low Pressure Portable Chamber

## Multiplace Chamber



## Monoplace Chamber



## Proper protocols

- For insurance reimbursement 20 – 60 treatments may be recommended
- Some patients may require hundreds of treatments

## Effects of pressurized oxygen in acute brain insult

1/3

- Reduces cerebral edema & ICP
- Limits the ischemic cascade
- Reduces CNS lactate peak in hypoxia
- Neutralizes toxic amines
- Disaggregation of platelets
- Increases phagocytic activity of PMN cells (white blood cells)



### Effects of pressurized oxygen in acute brain insult 2/3

- Reduces adhesiveness of WBCs to endothelium
- Perfuses all tissue spaces
- Life sustaining O<sub>2</sub> available via retrograde perfusion in absence of a trickle phenomena
- Delivers metabolically available O<sub>2</sub> without chemical energy transfer – *enough to sustain life without blood*

### Effects of pressurized oxygen in acute brain insult 3/3

- Under pressure O<sub>2</sub> adheres to all the gas laws of physics
- Displaces all other gases in the body:
  - N<sub>2</sub>, CO
- Follows the law of mass action
- Completely saturates hemoglobin
- Increases plasma O<sub>2</sub> by 2000%
- Dissolves in cerebrospinal fluid, lymph, bone and urine

### Effects of Pressurized Oxygen in Chronic Brain Insult 1/3

- Reactivates idling neurons
- Enhances plasticity
- Efficiently elevates diffusional driving force for O<sub>2</sub> thereby increasing tissue oxygen availability
- Promotes phagocytosis (internal debridement)
- Ameliorates multiple biochemical changes

### Effects of Pressurized Oxygen in Chronic Brain Insult 2/3

- Restores the integrity of the blood brain barrier and cell membranes
- Improves cell respiration, reduces cell byproducts – cytokines
- Promotes neovascularization
- Promotes epithelization

### Effects of Pressurized Oxygen in Chronic Brain Insult 3/3

- Acts as scavenger of free radicals
- Bacteriostatic effects, synergizes with certain antibiotics
- Neutralizes certain toxins: Clostridium, anaerobes
- Stimulates the adaptive immune system, especially in elderly (mice)

### HBOT Treatment in Cerebral Palsy and Brain Injured Child

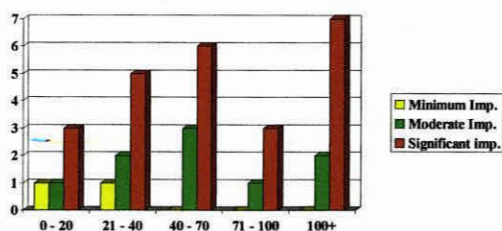
## MATERIALS , METHODS AND CLINIC

- Seizure disorder actively treated
- SPECT scanning was done with a single head scint gamma camera with high resolution
- Technesium 99 Tracer:
  - CeretechTM
  - NeuroliteTM
- nts

## RESULTS

- Showed positive changes in cerebral blood flow and metabolism in 87% of the patients
- The Clinical Correlation Associated With These Changes is 92%

Correlation between number of treatment & degree of improvement



According to the Golden - Neubauer Study there is an 85% correlation between positive changes in the SPECT scan and clinical improvement

Golden Z, Neubauer R, Golden C, et al  
International Journal of Neuroscience,  
112: 119-131, 2002

From extensive data  
the earlier the  
intervention the  
better the results

### ***Delivery Room to Chamber***

HYPERBARIC OXYGEN IN THE  
RESUSCITATION OF THE  
NEWBORN

Hutchison JH, Kerr MM, Williams KG,  
Hopkinson WI  
The Lancet, 1963, Vol. 2, pp 1020-1022

One hour exposure to HBO at  
time of delivery may alter the  
entire life

Dr. E. C. Sanchez, Mexico  
2<sup>nd</sup> International Symposium on  
Hyperbaric Oxygen in Cerebral Palsy  
& the Brain Injured Child  
Boca Raton, FL,  
July 25-28, 2001

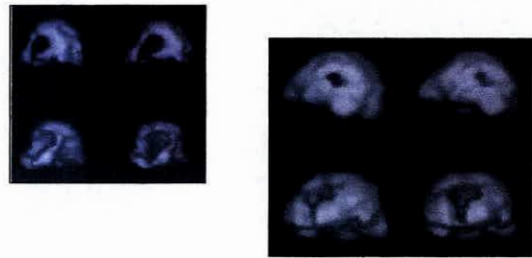
DA

- Age at TX: 5 ½ Yrs
- DX: CP – Anoxia at Birth
- Time to TX: 5 ½ Yrs

DA # of TX 147

- Results:
  - Gross Motor ↑
    - Beginning to walk
  - Spasticity ↓
  - Balance ↑
  - Interaction ↑
  - Nutrition and Growth ↑

DA – Pre & Post



ANOXIC ISCHEMIC  
ENCEPHALOPATHY

AIE

The effect of hyperbaric oxygen  
in prolonged coma. Possible  
identification of marginally  
functioning brain zones

Neubauer, RA  
Minerva Med Subaacqua ed Iperbarica  
5: 75 1985

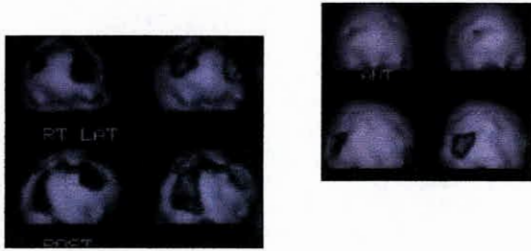
### MC

- Age at TX: 23 y
- Diagnosis: AIE - Near Hanging Apallic, Glasgow scale 3
- Time to TX: 9 y

### MC # of TX 150

- Results:
  - Alertness ↑
  - Glasgow Coma Scale 7
  - Motor ↑
  - Nutrition ↑
  - Some Response

### MC Pre & Post



### MJ

- Age at TX: 32 y
- Diagnosis: CO Poisoning, Semi-Coma
- Time to TX: 13 y

### MJ # of TX 500+

- Results:
  - Dramatic - Returned to Society

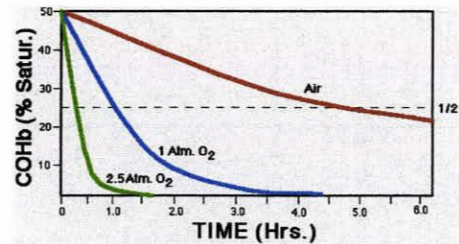
### MJ Post



## Physiology of CO

- Hemoglobin has a greater affinity for CO
- Thus O<sub>2</sub> is displaced producing varying degrees of hypoxia
- Brain and heart are the main target organs

## Left Shifting of the oxyhemoglobin dissociation curve with CO



## Indication for HBOT in CO

- Carboxyhemoglobin above 25%
- COHb below 25% if symptoms
- Abnormal EKG
- Abnormal Neuropsych Testing
- MRI only if positive (basal ganglia)
- SPECT Scan is diagnostic

## Smoke Inhalation Injury

Neubauer RA  
Postgraduate Medicine  
January 1988

## Frequently misdiagnosed especially in:

- Smokers
- Tunnel Workers
- Firefighters
- Passengers in Autos with leaking exhaust
- Often referred to psychiatrist

## The Biggest Unrecognized Group are the Firefighters

- Severe Exposure
- 100% O<sub>2</sub> in the Ambulance
- in ER if Carboxyhemoglobin & MRI are normal, then sent home

### Treatment of Multiple Sclerosis with Monoplace Chamber

Neubauer RA  
J FL Med Soc  
65: 101 1978

Most of these studies have been  
flawed with improper protocol or  
misinterpretation of data

### Hyperbaric Oxygen and Multiple Sclerosis: Final Results of a Placebo Controlled, Double-Blind Study

Barnes MP, Bates D, et al  
J Neurol Neurosurg Psychiatry  
50: 1402-1406 1987

### HBO in MULTIPLE SCLEROSIS

- Not a Cure
- Dose Sensitive
- Requires Follow-up Treatments
- Alters Favorably the natural course of the disease
- Non-Invasive

### MULTIPLE SCLEROSIS

10,000 Patient Series currently ongoing in  
the United Kingdom which began in 1983

D. Perrins, M.D. and P. James, M.D.

These results show a positive trend, but are  
not comparable with the Interferon treatment.

### Animal Studies

CVA and Cerebral Ischemia

### Hyperbaric Oxygen Increases Survival Following Carotid Ligation in Gerbils

Reitan J et al  
STROKE, 1990; 21: 119-123

This investigation demonstrates that graded doses of hyperbaric oxygen given after the insult increase survival in a gerbil model of stroke

### Results of Hyperbaric Oxygen Therapy During Temporary Middle Cerebral Artery Occlusion in Unanesthetized Cats

Weinstein, P, et al  
NEUROSURGERY, 1987; 20(4): 518-524

HBO therapy administered early after middle cerebral artery occlusion had a significant protective effect during temporary regional ischemia in cats

### Clinical Data on HBOT in Stroke

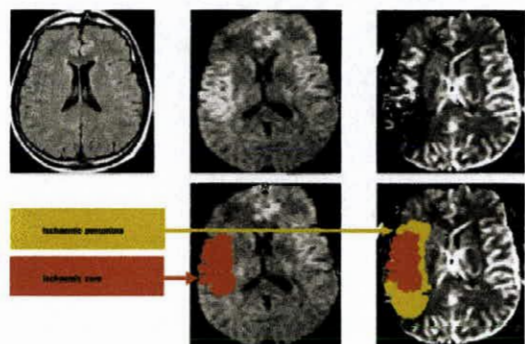
Over 1000 cases of stroke treated with hyperbaric oxygen have been reported in the literature with about 40% favorable response

### Hyperbaric Oxygenation as an adjunct in stroke due to thrombosis: A Review of 122 Patients

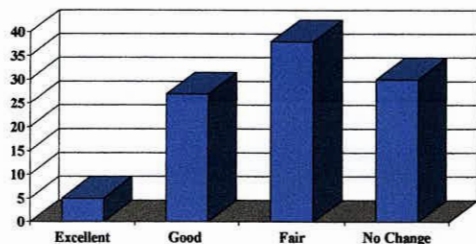
Neubauer R, End E. STROKE 11(3): 297-300, 1980

- 25 % of the group treated within 4 hours of ictus did not require hospital admission longer than 24 hours.
- 1st definitive protocol for the treatment of stroke

### The Ischemic Penumbra

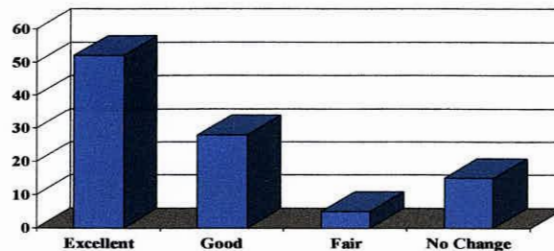


### HBO/Stroke 4 Hours to 1 Week



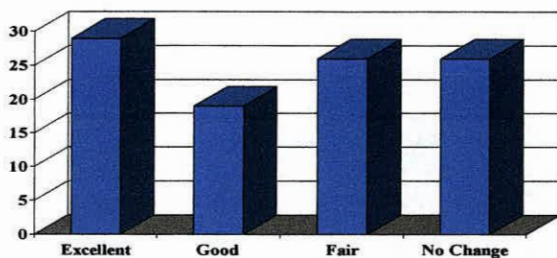
Number of Patients: 7

### HBO/Stroke 1 Week to 2 Months



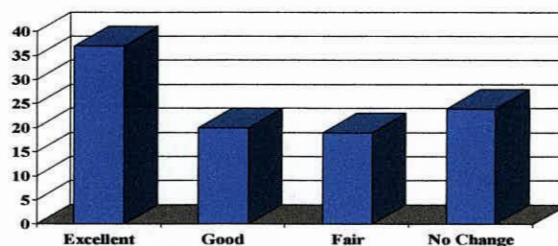
Number of Patients: 10

### HBO/Stroke 2 Months to 1 Year



Number of Patients: 19

### HBO/Stroke 1 Year to 10 Years



Number of Patients: 71

### Recovery of Axonal Transport in "Dead Neurons"

Dai J, Swaab D, Buijs R. THE LANCET Vol  
351 February 14, 1998

"We now present evidence for survival of human brain neurons up to 8 h after death such that they still have the potential to recover their functions of energy metabolism and axonal transport."

### Effects of Tissue Plasminogen Activator for Acute Ischemic Stroke at One Year

Kwiatkowski G, et al. NEJM 1999; 340: 1781 -  
1787

At 1 year follow up patients treated within 3 hours were more likely to have minimal or no disability than patients given placebo.



Conclusion: In the acute brain insult, HBOT is extremely efficient at reducing cerebral edema, ICP, lactate, toxic amine levels as well as limiting the ischemic cascade

The Emerging Role of Hyperbaric Oxygen Therapy in Traumatic Brain Injury  
*Acute and Long Term Neurorehab*

Jim Thorpe Neuroscience and Neurorehabilitation Conference  
September 18 – 20, 2003  
Oklahoma City, Oklahoma

The decrease in mortality and improved outcome for patients with severe traumatic brain injury over the past 25 years can be attributed to the approach of *"squeezing oxygenated blood through a swollen brain"*

Ghajar, "Traumatic Brain Injury"  
Lancet 2000:356:923-29

Presumably, the critical parameter for tissue function is oxygen availability rather than blood flow

Astrup, Siesjo and Simon  
"Thresholds in Cerebral Ischemia – The Ischemic Penumbra"  
STROKE 12:723-725, 1981

Animal Data

Acute TBI

Human Data

Acute TBI

### Improved Reversibility of Traumatic Mid-Brain Syndrome Following the Use of Hyperbaric Oxygen

Mid Brain Syndrome 111 Patients  
= 15.5%  
Total Head Injury 714 Patients  
Selected for Study 99/111 = 89.2

Data Taken From: Holbach, Wassman & Kolberg  
Acta Neurochir 30: 247-256, 1974

### Results of a Prospective Randomized Trial for Treatment of Severely Brain Injured Patients with Hyperbaric Oxygen

Rockswold GL, Ford SE, et al  
J of Neurosurgery 76:929-934, June 1992  
Double Blind Controlled Study (168 pts)  
40% Reduction in Mortality

### Effects of Pressurized Oxygen in Chronic Brain Insult <sup>1/3</sup>

- Reactivates idling neurons
- Enhances plasticity
- Efficiently elevates diffusional driving force for O<sub>2</sub> thereby increasing tissue oxygen availability
- Promotes phagocytosis (internal debridement)
- Ameliorates multiple biochemical changes

### Cognitive and Cerebral Blood Flow Improvements in Chronic Stable Traumatic Brain Injury Induced by 1.5 ATA Hyperbaric Oxygen

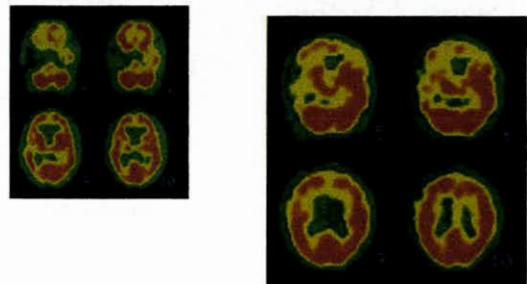
- Controlled Study 5 Patients > 3Yrs Post Injury
- 120 txs @ 1.5 ATA
- Very Good Results - Paralleled by SPECT

Barrett K, Harch P, et al  
1998 Undersea and Hyperbaric Med 25:9  
(abstract)

### TD - MVA

- 26 Yr M: 5 Yrs Post Injury
- Unable to Re-enter Society because of Personality, Cognitive and Memory
- 73 HBO treatments
- Now in College and working as a Model

### TD - Pre & Post



**Life planning estimate  
age 15 to 65 total care**

- Peg Tube
- Tracheotomy
- 24 Hour Attendants
- Multiple Hospitalizations
- Prescription Drugs
- Physical Therapy
- Occupational Therapy
- Speech Therapy
- Handicapped Vans
- Home Modifications

**Life Time Cost - \$82 Million Dollars**

**Cost Effectiveness**

- Reduction in life care expenditures of up to 85%
- Progress in Glasgow Coma Scale from 3 to 14

**The Future**

- Education of the Medical Student & the Practicing Physician
- Continued Education of the Family
- Eventual Insurance Reimbursement

**In the future hopefully  
HBOT will become  
standard treatment rather  
than investigational for TBI**

*“Here is Better than the  
Open Air :  
Take it Thankfully”*

**William Shakespeare  
King Lear III.6.1  
1564 - 1616**