In 1662, the British Clergyman Henshaw built his a chamber driven by organ bellows with valves to control the flow of air, this sealed chamber was used to create both hyper- and hypobaric conditions.

- Chamber was sealed and unventilated.

"In times of good health this domicilium is proposed as a good expedient to help digestion, to promote insensible respiration, to facilitate breathing and expectoration and consequently, of excellent use for prevention of most affections of the lungs."

History - “Domicilium”
France in the 1830’s

• Hyperbaric chamber exposures of between 2 and 4 atmospheres absolute were stated to increase the circulation to the internal organs, improve the cerebral blood flow, and produce a feeling of well being.

• Junod 1834 commissioned a hyperbaric chamber based upon a design by James Watt (steam engine fame). Capable to compression to 4 ATA. He described a sense of well-being in his patients.
France in the 1830’s

- 1837- Pravaz built a large hyperbaric chamber using it to treat a variety of ailments.
  - used specifically for pulmonary diseases, including tuberculosis, laryngitis, tracheitis and pertussis
  - as well as apparently unrelated diseases such as deafness, cholera, rickets, menorrhagia and conjunctivitis.
• Late 1800s -> pneumatic institutes
M. Paul Bert, French physiologist - the father of high pressure physiology – 
– *La Pression barometrique* (1878),

- Studied the effects of various gas mixtures
- Recognized the toxic effects of oxygen at high pressures on the CNS
  -> Paul Bert effect.
- Rec’d slow ascent to allow for nitrogen off-gassing.
- Beginning of scientific scrutiny of HBO.
• Fontaine (1879) invented mobile HBO chamber
• A well-known French surgeon, M Pean, used it to perform 27 different operations over a 3 month period. All were considered successful and pt’s were noted to recover from anesthesia much quicker.
• Plan for a 300 person surgical amphitheatre.
• Fontaine was first reported hyperbaric practitioner fatality following a decompression accident.
"The use of atmospheric air under different degrees of atmospheric pressure, in the treatment of disease, is one of the most important advances in modern medicine and when we consider the simplicity of the agent, the exact methods by which it may be applied, and the precision with which it can be regulated to the requirements of each individual, we are astonished that in England this method of treatment has been so little used".
Industrial Revolution

- Triger 1841, a French paleontologist and mining engineer, first to utilize a submersible caisson. Submerged at the bottom of a river to recover otherwise inaccessible coal deposits (industrial revolution).

- Miners would return to the surface after many hours in the caisson and describe joint pain and CNS disturbances.
• Civil engineers were quick to adopt caisson technology which allowed for construction of bridges across large bodies of water and underground tunnels.

• Workers were exposed to compressed air for long hours and upon reexposure to surface pressures nitrogen would be supersaturated and bubble
• First steel arch bridge span in St. Louis 1869 required exposures up to 4.45 ATA.
  – 352 workers, 5% died, 10% suffered serious decompression sickness.
• Brooklyn Bridge (1869-83)
  – Several hundred workers had decompression sickness, 27 mortalities
• 2 tunnels under the East River (1906-8), pressures up to 3.9 ATA with frequent twice daily exposures

- Several thousand cases of decompression illness were recorded and there were 20 fatalities from the 500,000 exposures.
• New York’s Hudson tunnel
  – 1882, 25% mortality recorded
  – 1890, a decompression lock (chamber) was installed
  – Protracted decompression was instituted and the 18 following months saw a marked reduction in morbidity and mortality (only 3 more fatalities).
In 1921 Dr. Orville J. Cunningham constructed a 10’ x 88’ chamber in Kansas City.

- Spanish influenza (500-675,000 deaths in US alone).
- Began treating these pts and then expanded tx to include HTN, DM, syphillis, and cancer.
- Believed that anerobes played a role in these diseases.
- $3 for a am or pm session, $6 for an entire night
- One night pressure suddenly was lost and al the occupants died.
• H.H. Timken, The head of Timken Ball Bearing Company, gave Cunningham $1 million to build additional chambers.
  – Cunningham Ball in Cleveland, 1928
  – 5 stories high, 64 ft in diameter, 12 bedrooms per floor, and was elaborately furnished.
Oxygen Treatment Tanks
Cunningham Sanitarium
Cleveland, O.
A Bedroom in Main Tank
Cunningham Sanitarium
Cleveland, O.
No published results, AMA concerned, Cunningham did not address concerns, AMA condemned HB tx and forced his retirement.

Bells were dismantled and the steel was used to build tanks during WWII.
Renewed Interest

• Alvaro Ozorio de Almeida, Prof of physiology at the U of Rio de Janeiro, published basic and clinical research in 3 languages in 1934 of HB oxygen tx.
  – Cancer
  – Leprosy
  – Gas gangrene
• 1st use of HBO
US Navy used HBO in the late 1930’s to enhance inert gas elimination during decompression of divers. Breathing O2 during staged decompression significantly reduced the time necessary to reach surface pressure.
Churchill-Davidson, London radiotherapist, reported his clinical experience with HBO as a tumor radiosensitizer in 1955.

- First clinical application of monoplace chambers
- Wide variety of tumors were irradiated during HBO during 1960’s.
- Long term outcomes didn’t support use and interest waned in 1970’s.

Recent interest renewed – Japanese researches irradiate pts 15-30 min after HBO tx – malignant gliomas.

• Dr. Ite Boerema was first to report use of hypothermia as an aid to cardiac surgery.

• 1956 demonstrated that dogs could tolerate much longer periods of arrest while cooled and breathing 3.0 ATA oxygen

• Life without Blood (1960)

• Began performing cardiac surgery on infants and adults within a specially built HBO OR with impressive results.

• International interest, orders for HBO ORs
• Bernhard and colleagues at Harvard were first to perform experimental HBO surgery in the US in 1963.
  – Pressures between 3.0-3.6 ATA
  – Greater the cyanosis, greater the pressure
  – Compression began once the chest was opened and decompression started when repair of the defect was completed.
• Extracorporeal circ technology became perfected shortly after and was approved for routine use.
• HBO ORs were either converted for use for other treatments or scrapped.
• the lay press and non-medical hyperbaric gurus had begun treating people with little to no scientific basis. Hyperbaric oxygen treatments became a bit of a circus show.
CO poisoning

• Smith and Sharp (1962) reported great benefit of HBO for CO poisoning
  – Resurgence in interest and growth of HBO units
• Undersea Medical Society, founded in 1967 by six Navy diving and submarine medical officers.
• By the mid 1970s, UMS began working with practitioners to rebuild the credibility of the field. A multi-authored textbook, Hyperbaric Oxygen Therapy (edited by Jefferson Davis and Thomas Hunt) was published in 1977.
• That same year, the UMS formulated a set of medical diagnoses which were appropriate for HBO therapy, and this report was accepted by the major insurance carriers as a basis for payment.
• With the guidance of the leaders in the field, UMS developed certification programs.
NORMAN KNIGHT HYPERBARIC MEDICINE CENTER

GIFT OF NORMAN KNIGHT

IN HONOR OF

THE HEROIC FIREFIGHTERS OF MASSACHUSETTS

JUNE 28, 1999
Multiplace chambers
Physical aspects of hyperbaric medicine

• Dalton’s law: in a gas mixture, each gas exerts its pressure according to its proportion of the total volume.
  – Partial pressure of a gas = % gas x ATA
  – Air = 78% nitrogen, 21% O2, 0.04% trace gases

• Boyle’s law: at constant T, the volume of a gas will vary inversely with the absolute pressure.
Figure 4. Muscle tissue oxygen and carbon dioxide, means and standard deviations, eight male volunteers. (Modified from C. H. Wells, J. E. Goodpasture, D. J. Horrigan & G. B. Hart [14].)
Mechanisms of action

• Hyperoxygenation
• Bubble size reduction
• Vasoconstriction
• Fibroblast proliferation/collagen synthesis
• Neovascularization
• Leukocyte oxidative killing
• Toxin production inhibition/inactivation
• Antibiotic synergism
HBO Indications (2014)

Approved by UHMS

• 1. Air or Gas Embolism
• 2. Carbon Monoxide Poisoning
• 3. Clostridial Myositis and Myonecrosis (Gas Gangrene)
• 4. Crush Injury, Compartment Syndrome and Other Acute Traumatic Ischemias
• 5. Decompression Sickness
• 6. Arterial Insufficiencies: Central Retinal Artery Occlusion
• 7. Severe Anemia
• 8. Intracranial Abscess
• 9. Necrotizing Soft Tissue Infections
• 10. Osteomyelitis (Refractory)
• 11. Delayed Radiation Injury (Soft Tissue and Bony Necrosis)
• 12. Compromised Grafts and Flaps
• 13. Acute Thermal Burn Injury
• 14. Idiopathic Sudden Sensorineural Hearing Loss (New! approved on October 8, 2011 by the UHMS Board of Directors)
Late Radiation Tissue Injury

• Chronic effects of xrt:
  – Epithelial destruction (hair follicles, sub-Q glands)
  – Endarteritis obliterans
  – Progressive fibrosis and decreased vascularity
  – Decreased blood flow, low tissue pO2
  – Fibrosis, necrosis, ulceration, fistula formation
  – Three H’s
Incidence of ORN per Radiation Dose
- retrospective review of 104 cases

<table>
<thead>
<tr>
<th>Total Radiation Dose</th>
<th>No. Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>(range 3-7,400 cGy)</td>
<td></td>
</tr>
<tr>
<td>&lt; 5,000 cGy</td>
<td>5</td>
</tr>
<tr>
<td>5 - 6,000 cGy</td>
<td>24</td>
</tr>
<tr>
<td>6 - 7,000 cGy</td>
<td>33</td>
</tr>
<tr>
<td>&gt; 7,000 cGy</td>
<td>42</td>
</tr>
</tbody>
</table>

~ 89.4% trauma-induced
~ 10.6% spontaneous

J. Oral Maxillo Surg: 55
1.0 ATA Air

HBO at 2.4 ATA

$\Delta = 10-20$ mmHg

$\Delta = 230$ mmHg
Blood Flow in Non-irradiated Bone

mg/ml x 100g tissue

Temporal  Frontal  Zygoma  Maxilla  Mandible

Granstrom G. et al. 1993
XIXth Annual Meeting EUBS
Blood Flow in Irradiated Bone after HBO and Bone Grafting

Temporal | Frontal | Zygoma | Maxilla | Mandible | Mand. grafted

XIXth Annual Meeting EUBS
The Marx Protocol

-all treatments at 2.5ATA x 90 mins.

Stage I: Small area of exposed bone

30 treatments

Stage I responder:

- decreased amount of exposed bone
- resorption or spontaneous sequestration
- softening of exposed bone

10 additional treatments to achieve full mucosal cover, if necessary.
Stage II: Stage I non-responder

Following initial 30 treatments, local surgical debridement

10 additional treatments if wound is progressing without complications

If wound dehisces, leaving exposed bone, pt. is advanced to Stage III.
Stage III:

Stage II non-responder, or pts. with fistulae, pathological fx. or x-ray evidence of bone resorption.

Following initial 30 treatments:

- transoral partial jaw resection, with fixation
- primary closure of fistulae

10 additional treatments
Stage III R:

Following an 8-10 week period from resection, pt. undergoes bony reconstruction.

- ten additional treatments
- jaw fixation maintained for 8 weeks
<table>
<thead>
<tr>
<th>Stage</th>
<th>Resolved Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>38 (14%)</td>
</tr>
<tr>
<td>Stage II</td>
<td>48 (18%)</td>
</tr>
<tr>
<td>Stage III</td>
<td>182 (68%)</td>
</tr>
<tr>
<td></td>
<td>268 (100%)</td>
</tr>
</tbody>
</table>
## Cost Analysis Of ORN - 2001 US Dollars

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. Pts.</th>
<th>Avg. 1 yr. Cost</th>
<th>Total Cost</th>
<th>Resol. Rate(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-HBO</td>
<td>116</td>
<td>44,000</td>
<td>152,000</td>
<td>10</td>
</tr>
<tr>
<td>HBO- no surg.</td>
<td>81</td>
<td>38,000</td>
<td>79,000</td>
<td>18</td>
</tr>
<tr>
<td>Marx Protocol</td>
<td>492</td>
<td>48,000</td>
<td>48,000</td>
<td>100</td>
</tr>
<tr>
<td>Marx Protocol</td>
<td>112</td>
<td>41,000</td>
<td>41,000</td>
<td>100</td>
</tr>
</tbody>
</table>
"Osteoradioneucrosis is best managed with HBO therapy oxygen alone, or in conjunction with surgery"

...in high-risk patients, pre-extraction hyperbaric oxygen therapy should be considered

National Cancer Institute
Monographs 1990: No. 9
<table>
<thead>
<tr>
<th>GRADE</th>
<th>INDICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>~ strong evidence</td>
</tr>
<tr>
<td>Level 2</td>
<td>Mandibular ORN</td>
</tr>
<tr>
<td></td>
<td>Radiation cystitis</td>
</tr>
<tr>
<td></td>
<td>Dental extraction</td>
</tr>
<tr>
<td>Level 3</td>
<td>Radionecrosis of other bones</td>
</tr>
<tr>
<td></td>
<td>Radiation proctitis: Radiation enteritis</td>
</tr>
<tr>
<td>Level 4</td>
<td>Laryngeal radionecrosis</td>
</tr>
<tr>
<td></td>
<td>CNS radionecrosis</td>
</tr>
</tbody>
</table>

~ indicates strength of evidence:
- strong evidence
- convincing evidence
- evidence of beneficial action, weakly supported
- anecdotal evidence
Level I evidence, but interpretation issues...

A double-blind, placebo-controlled mandibular ORN RCT

Primary Outcome Measure

Recovery at one year. HBO 6/31 (19%); Placebo 12/35 (32%)

✓ ruled out Stages II and III
✓ failed to apply standard care

They appeared to ask the question... 'Does HBO in the absence of multi-disciplinary care obviate the need for complete surgical care?'

EBM includes knowledgeable interpretation of published material
• Does HBO promote cancer recurrence, proliferation and metastasis?!!!!!
• No enhancing effect of growth on primary or mets

• No initiator or promotor effect on cancer de novo

• Targeted Oncology, 2012
  – “The consensus today is that research performed hitherto has failed to demonstrate that HBO has a cancer-promoting effect or that it enhances recurrence. Nevertheless, both recent and older research studies have shown that HBO can be inhibitory and reduce cancer growth in some cancer types.”
This study suggests HBO therapy does accelerate the growth of microscopic foci of squamous cell carcinomas (but does not increase met rate).
Compromised skin grafts/flaps

• HBO:
  – Stimulates fibroblast proliferation and collagen synthesis
  – Enhances leukocyte killing and bacterial clearance
  – Promotes angiogenesis via steep O2 gradient
  – Promotes epithelialization
Flaps

• When surgical correction not possible or appropriate
  – HBO antagonizes the effect of ischemia/reperfusion injury
  – Increases microvascular blood flow
  – Reduces neutrophil endothelial adherence
  – Blocks progressive arteriolar vasoconstriction

- Composite grafts – Level IV
- Skin grafts – Level IB (from 1967)
- Random flaps – Level IV
- Distant flaps – Level V
- Free flaps – Level VI

- Level 4. Historic, nonrandomized cohort or case-control studies
- Level 5. Human case series
- Level 6. Animal or mechanical model studies
Nolen et al., Head Neck. Comparison of complications in free flap reconstruction for osteoradionecrosis in patients with or without hyperbaric oxygen therapy.

- Multi-institutional, retrospective analysis of ORN patients undergoing free flap recon.
- 39/89 patients (43.8%) had HBO while 50/89 (56.2%) did not.
- There was no statistical difference in overall complication in patients between groups (p=0.5478).
- Marginal significance of increased infections in the patients with a history of HBO (p=0.0545).
HBO combined with XRT

• Studies have shown beneficial results on local tumor control, mortality, and local tumor recurrence
  – But the protocols of the reviewed literature made them conclude that they could not justify the routine use of HBO in combination with radiation [55].
  – No consensus
<table>
<thead>
<tr>
<th>Condition</th>
<th>Year</th>
<th># RCTs</th>
<th># patients</th>
<th>Quality of Evidence</th>
<th>Effect</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant Otitis Externa</td>
<td>2013</td>
<td>0</td>
<td></td>
<td>none</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Irradiated pts needing dental implants</td>
<td>2013</td>
<td>1</td>
<td>26</td>
<td>low</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>Late radiation tissue injury</td>
<td>2012</td>
<td>11</td>
<td>669</td>
<td>moderate</td>
<td>positive</td>
<td>mucosal coverage with osteoradionecrosis 1.3(ORN) 8.7surgical flaps 1.4hemimandibulectomy</td>
</tr>
<tr>
<td>Acute surgical and traumatic wounds</td>
<td>2013</td>
<td>4</td>
<td>229</td>
<td>low</td>
<td>positive</td>
<td>irradiated tooth sockets following dental 1.4extraction</td>
</tr>
<tr>
<td>Acute idiopathic SSNHL</td>
<td>2012</td>
<td>7</td>
<td>392</td>
<td>moderate</td>
<td>positive</td>
<td>no effect on tinnitus or chronic SSNHL</td>
</tr>
</tbody>
</table>