


Are you also suffering symptoms
associated with **Cytokine Storm**?

A lifebuoy with orange and white segments floats on a dark, choppy sea. The sky is a heavy, greyish-blue, suggesting an approaching storm or a difficult situation.

Workshop 14 August 2019

OXYMED

ARE YOU SUFFERING SYMPTOMS ASSOCIATED WITH "CYTOKINE STORM"?

WORKSHOP - WEDNESDAY 14TH AUGUST 6.00PM

CYTOKINES DRIVE AUTOIMMUNE DISORDERS

DEVELOPMENTAL DELAY, AUTISM, CHRONIC FATIGUE, FIBROMYALGIA, CHRONIC PAIN SYNDROMES, MENTAL HEALTH, SLEEP APNEA, IRRITABLE BOWEL & COLITIS, REPRODUCTIVE DISORDERS, COGNITIVE DECLINE, DEMENTIA, STROKE, NEURODEGENERATIVE CONDITIONS, CANCERS AND OTHER DISORDERS

ELITE SPORTS RECOVERY & PERFORMANCE

- Cytokines are key mediators and provide homeostasis and immune control as part of the innate immune system through an intricate interplay with mutually dependent positive and negative feedback mechanisms [4]. In healthy individuals, equilibrium exists between pro- and anti-inflammatory cytokines.

- Data from patients with advanced cancer and other diseases show a cytokine pattern indicating a state of simultaneous immunostimulation and immunosuppression. Pro-inflammatory cytokines predominate driving autoimmune illness.

- * Hyperbaric Oxygen Therapy increases stem cell production modulating cytokine expressions reducing proinflammatory cytokines and upregulating anti inflammatory (reparative) cytokine gene expressions. (Thoms 2005)

- ** Life style, diet and supplements based on cytokine markers will also be discussed.

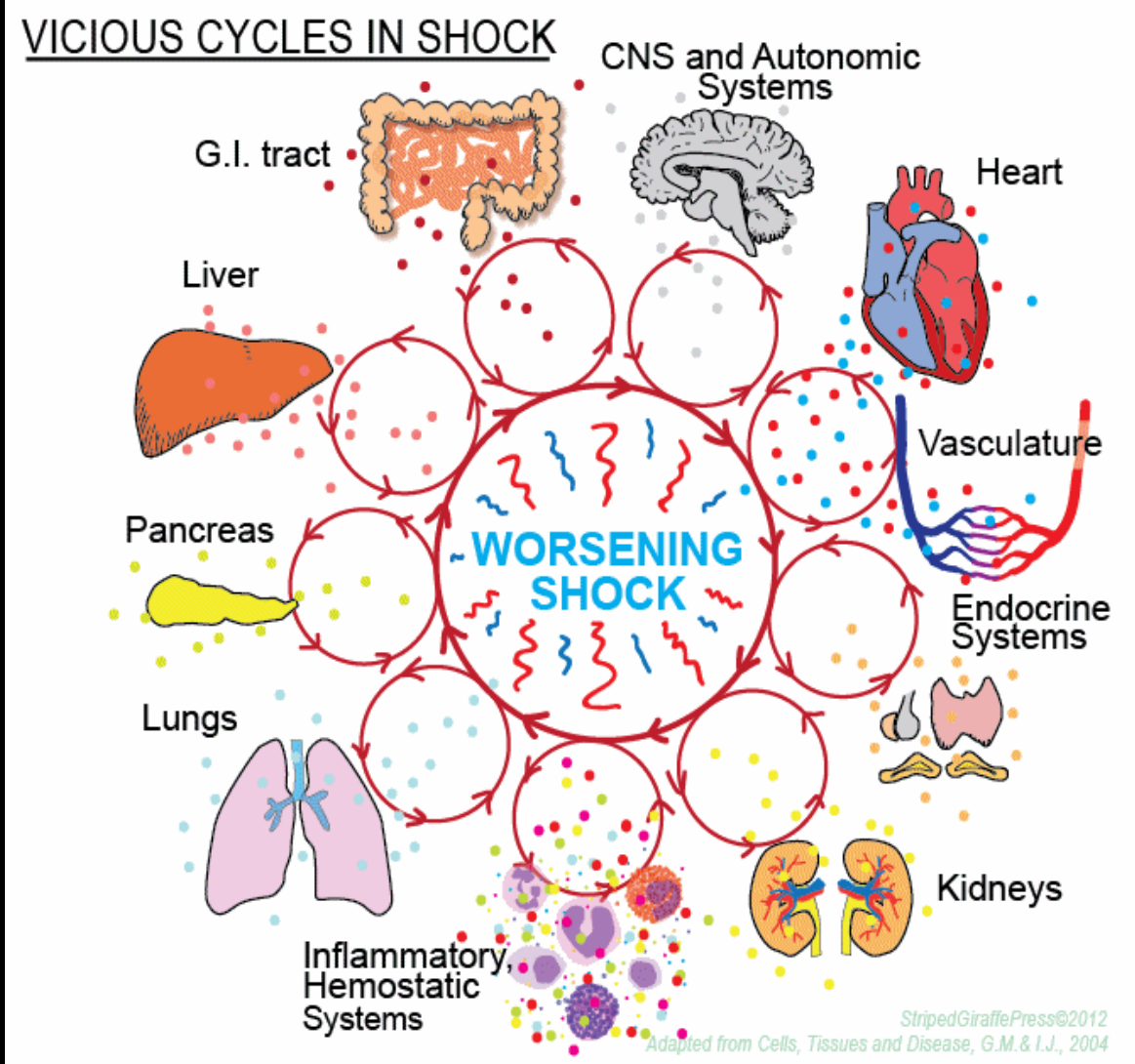


BOOK YOUR SEAT, BRING A FRIEND, THIS IS A NO CHARGE SERVICE (KNOWLEDGE IS POWER)

BOOKINGS info@oxymed.com.au

OXYMED

Cytokines Storms are progressive and culminate in Cytokine Shock



We live technology abundance

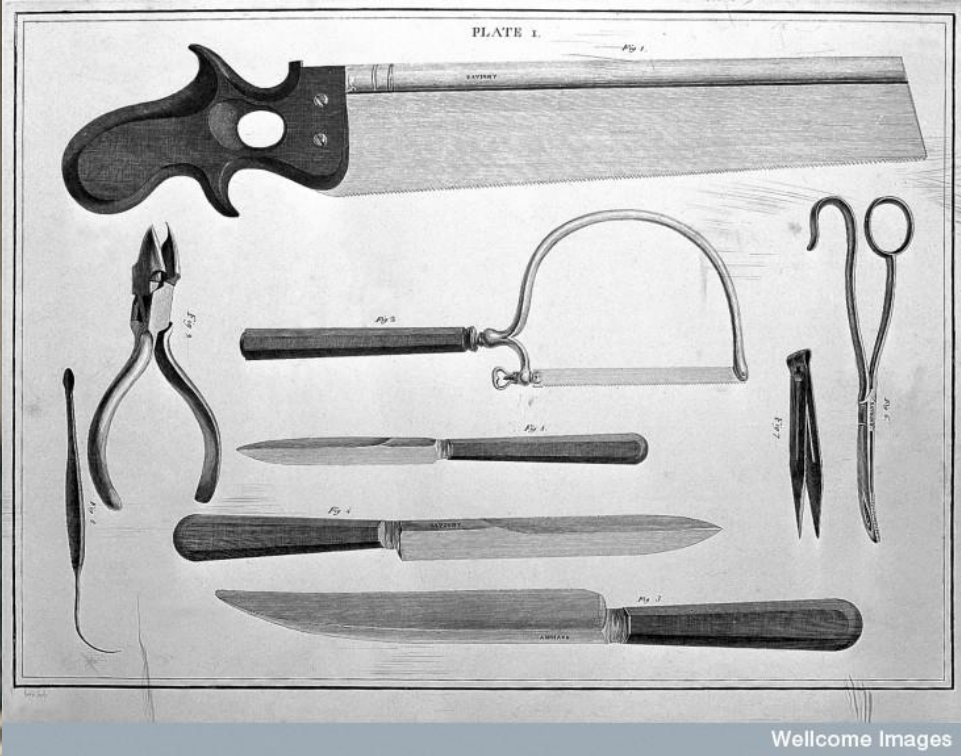
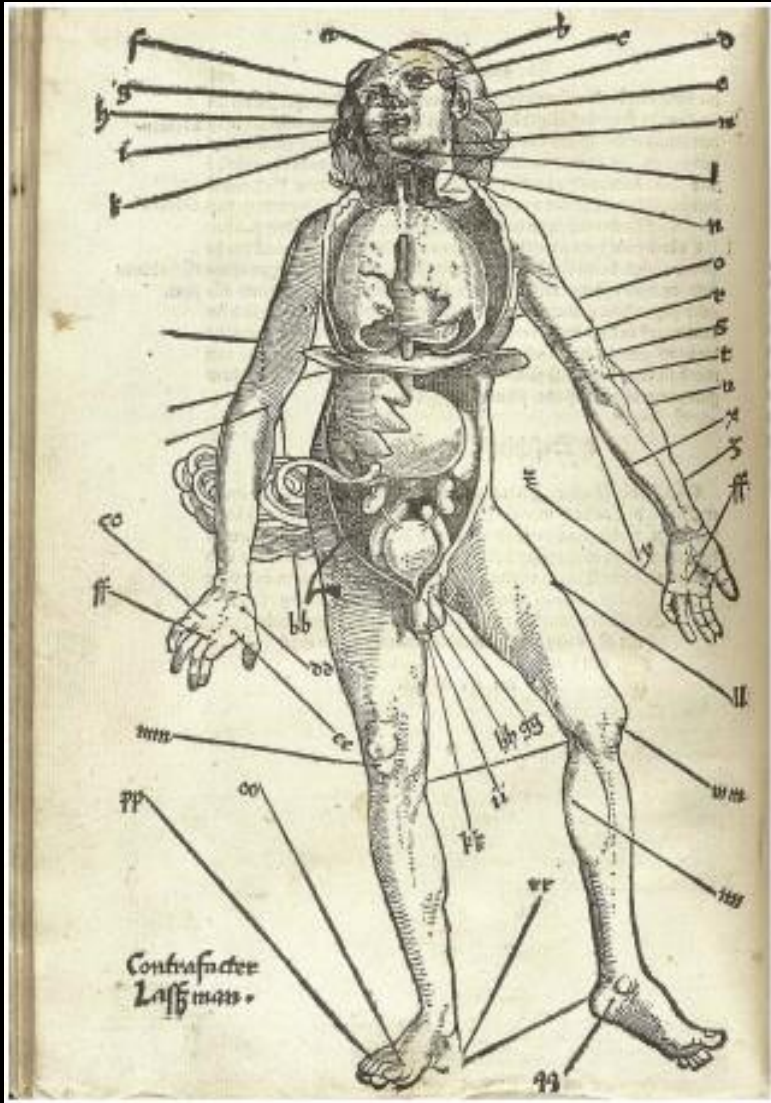


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Artificial Intelligence, 3-D Printing



The past



Wellcome Images

Today – assistive Robotic guided surgery




©2013 Intuitive Surgical, Inc.

The future – who will you trust for your next surgery?



Robots will dominate every part of our life – the race is on


Articles in Medical Robotics



Could You Sue Diagnostic Algorithms or Medical Robots in the Future?

What if a deep learning algorithm misses a diagnosis, the doctor accepts the judgment and the patient dies? What if a surgical robot injures a [...]


Artificial Intelligence in Medicine | Bioethics | Medical Robotics | Policy Makers | Researchers



Top Healthcare Companies in Robotics

Robotics has the power to completely reshape the landscape of healthcare both in its structure and its operation. Here, you find my own list about [...]


Future of Medicine | Medical Robotics



The Technological Future of Surgery

The future of surgery offers an amazing cooperation between humans and technology, which could elevate the level of precision and efficiency of surgeries so high [...]


Future of Medicine | Medical Augmented Reality | Medical Robotics | Virtual Reality in Medicine



Robotics in Healthcare — Get Ready!

In the near future we will inevitably work closely with medical robots. If we take the necessary steps now to gain better understanding of how [...]


Future of Medicine | Future of Pharma | Medical Robotics



9 Exciting Facts About Medical Robots

Medical robots do not only exist in sci-fi movies, they are coming to healthcare. If medical professionals want to utilize them successfully and do not [...]


Medical Robotics



5 Heart-Warming Stories of Digital Health Saving Lives

There are truly heartwarming stories of digital health technology saving lives or helping patients live better.


3D Printing in Medicine | Biotechnology | Future of Medicine | Medical Robotics



The Coolest Medical Robots in Sci-fi Movies

Here are my top 9 movies with medical robots.


Medical Robotics | Medical Science Fiction



10 Exciting Medical Technologies That Will Make You Hopeful About Our Future

Here are the science fiction technologies that make us believe the future of medicine is bright.

Biotechnology | Genomics | Health Sensors & Trackers | Medical Robotics | Medical Science Fiction | Virtual Reality in Medicine

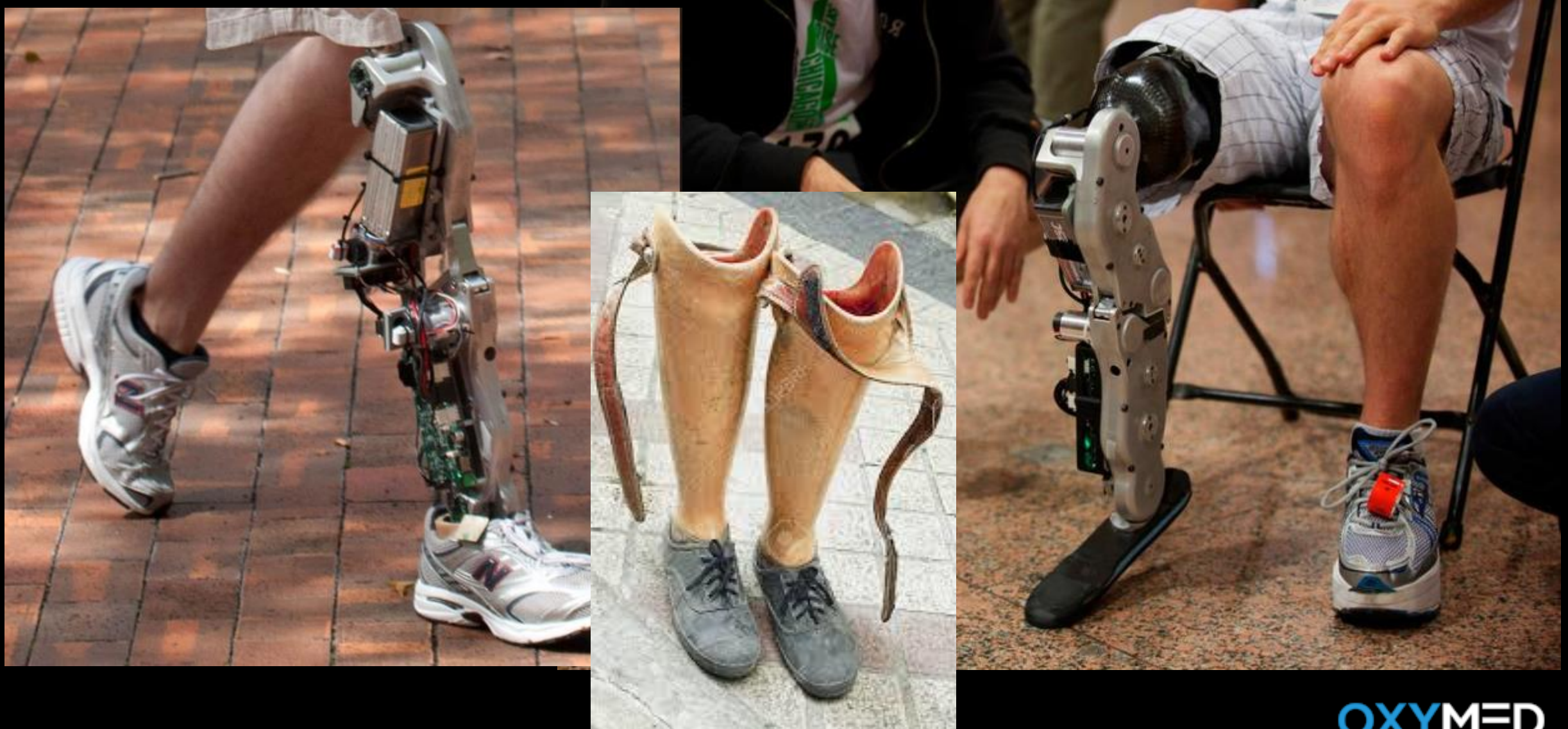


10 Promising Technologies Assisting the Future of Medicine

Ray Kurzweil says technology is improving at an exponential rate. Peter Thiel says technological innovations couldn't live up to the expectations. There are plenty of [...]




'Learning to live with disability' is being challenged by Robotic Assisted Prosthetics



Future Medical Robots

Scientists believe that tiny robots (called “nanorobots”) will be developed which will be used in patients’ bloodstreams to cure illness.



How Blood Swimming Robots Work

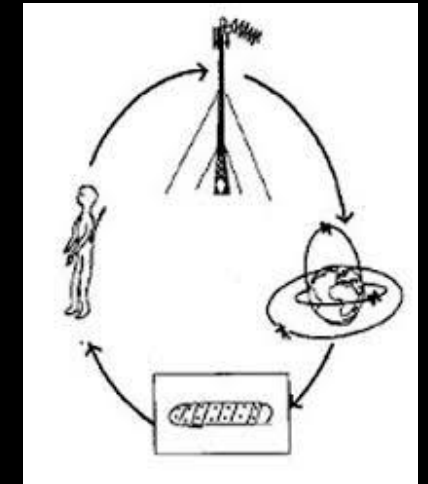
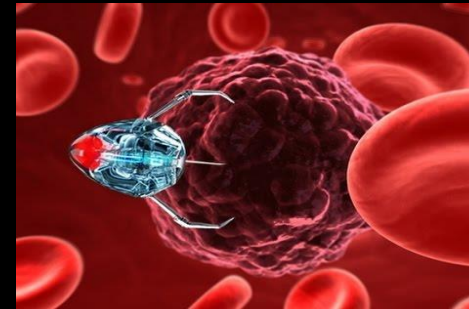
Micro-Camera, Fuel cell, Capacitor, Swimming tail

Bacteria-hunter nanobot

Image courtesy: Medical nanorobots

This nanobot grabs bacteria on its rotating spheres and then digests them inside the body

Saudi files for 'killer' tracking chip patent - The L



<https://www.thelocal.de/20090515/19313> ▼

May 15, 2009 - A **Saudi Arabian** inventor has filed for a **patent** on a potentially lethal science ... the **German Patent and Trademark Office (DPMA)** told The Local on Friday. ... The **patent application** – entitled “Implantation of electronic **chips** in the human ... or 18 months after **submission as required by German law**, she said.

Spinal Cord Injury – nanoscaffolding ‘seeded’ with “growth factors”

Regeneration strategies after the adult mammalian central nervous system injury—biomaterials

Yudan Gao, Zhaoyang Yang , Xiaoguang Li 

Regenerative Biomaterials, Volume 3, Issue 2, 1 June 2016, Pages 115–122,

Mater Sci Eng, C Mater Biol Appl. 2017 Feb 1;71:1122-1134. doi: 10.1016/j.msec.2016.11.100. Epub 2016 Nov 26.

Investigation of cell adhesion in chitosan membranes for peripheral nerve regeneration.

Proc Natl Acad Sci U S A. 2018 Jun 12;115(24):E5595-E5604. doi: 10.1073/pnas.1804735115. Epub 2018 May 29.

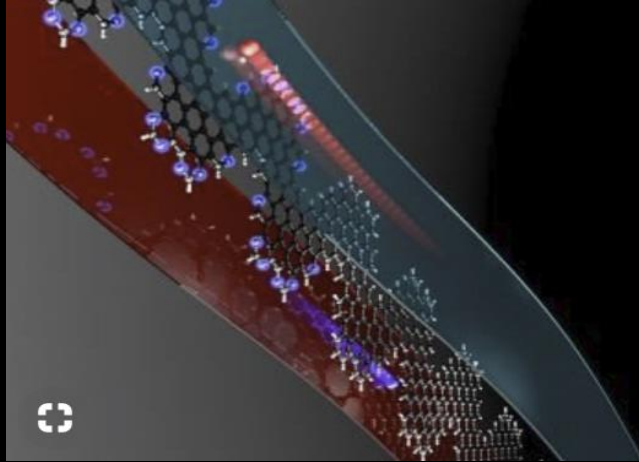
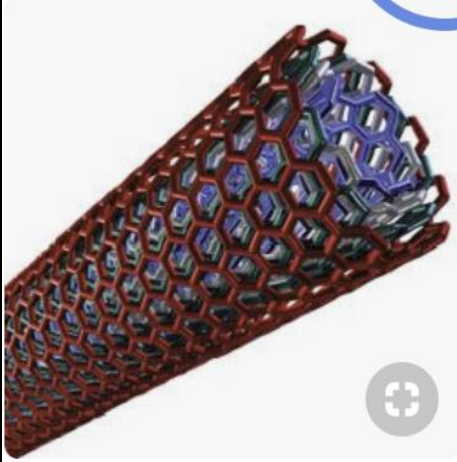
NT3-chitosan enables de novo regeneration and functional recovery in monkeys after spinal cord injury.

Biomaterials. 2017 Sep;138:91-107. doi: 10.1016/j.biomaterials.2017.05.024. Epub 2017 May 19.

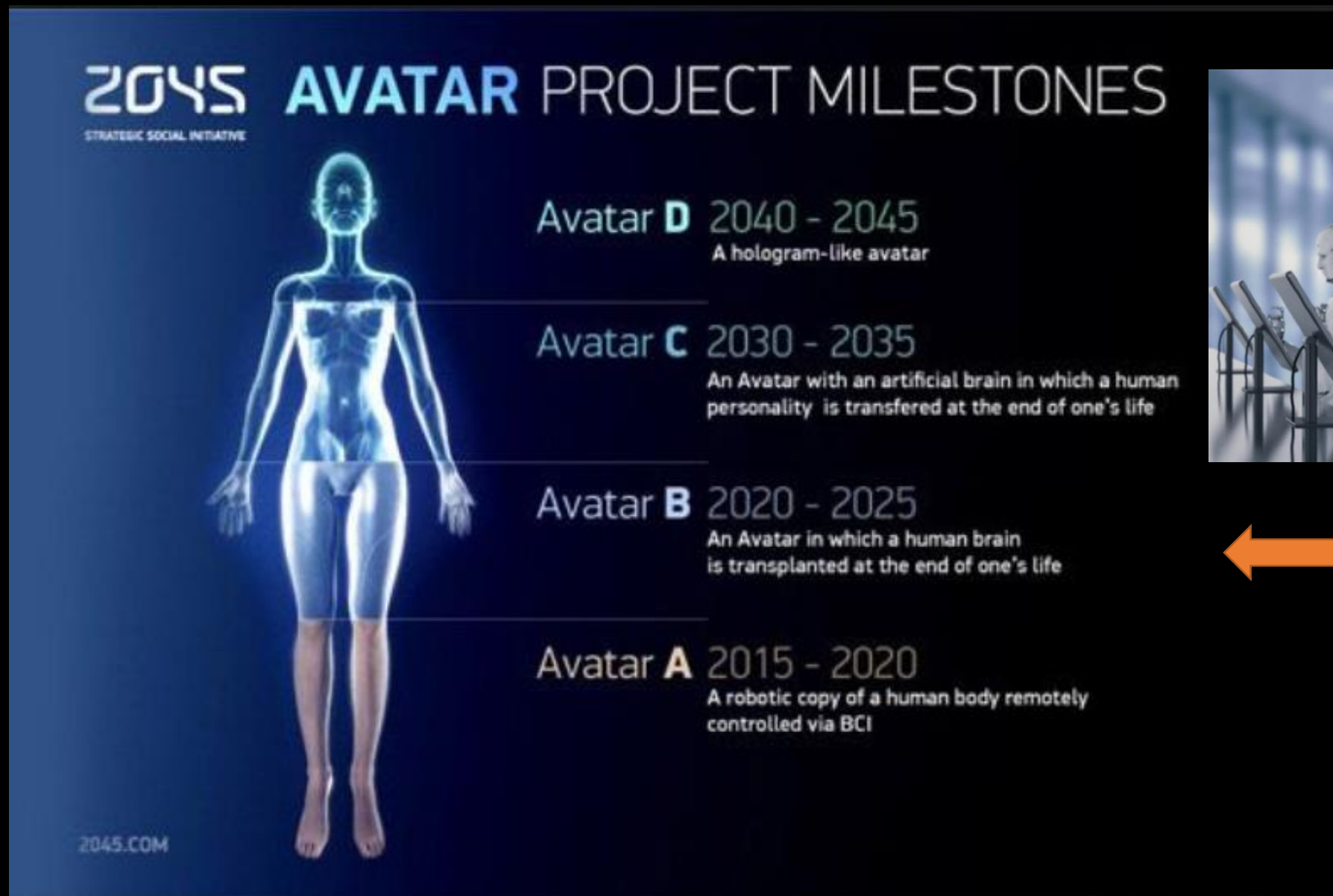
Physical chitosan microhydrogels as scaffolds for spinal cord injury restoration and axon regeneration.

Neural Regen Res. 2018 Jul;13(7):1231-1240. doi: 10.4103/1673-5374.235061.

A partition-type tubular scaffold loaded with PDGF-releasing microspheres for spinal cord repair facilitates the directional migration and growth of cells.



2045.COM AVATAR PROJECTS – ‘human brain interface’ by 2025






Elon Musk – Neuralink brain interface (2017)

SCIENCE / TECH / ARTIFICIAL INTELLIGENCE

Elon Musk launches Neuralink, a venture to merge the human brain with AI

Rockets, cars, and now brain chips

By Nick Statt | @nickstatt | Mar 27, 2017, 4:10pm EDT

   SHARE





Photo by Justin Sullivan / Getty Images

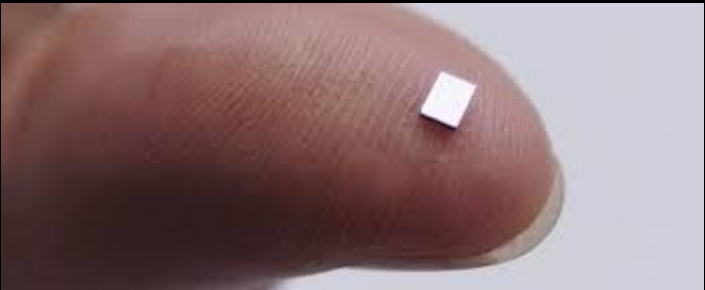
SWINBURNE



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AUGUST INTAKE NOW OPEN

LEARN MORE



Nootropics – ‘Limitless Pill’



Sex robots - how close to reality are we really?



'Reverse sex robots' with REAL BRAINS could be granted human rights

REVERSE engineered sex robots implanted with a human brain “must be granted rights” if they “have a consciousness”, a machine ethics expert has said.

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By **Joshua Nevett** / Published 29th December 2018



Controversy surrounds 'robot sex brothel' set to open

50,903 views



KHOU 11 ✓
Published on Sep 21, 2018

The "sex robot brothel" will be open for business in Houston within the next 10 days, says the business partner for Canadian sex-doll rental company Kinky S Dolls.

The era of “AvaStars”



Drag Queens being 'sent' to spread the message to children



Drag queens read to kids, spreading message of acceptance, and some adults don't like that

USA TODAY NETWORK Amanda McElfresh, Lafayette Daily Advertiser

Published 9:42 a.m. ET Aug. 23, 2018 | Updated 7:05 p.m. ET Aug. 23, 2018

Politics and Hollywood are 'sending' the message

'Panto/drag queen Mama G', booked for the launch, promotes 'her' work as 'Stories about being who you are and loving who you want' and says they are suitable for children aged three and over and their families.

These are not panto dames. Gay men promote 'sexual diversity' to very young children with the blessing of the library authorities and the librarians' professional organisations. Libraries have also promoted 'teen pride events' where children are told 'how to trans' and how to practise 'safe sex'.

With a lack of background checks, unsurprisingly some of these 'drag queen' events have included convicted sex offenders. ←

Children as young as **FOUR** being given transgender lessons which encourage them to explore their 'gender identities'

- Lessons led by campaigners including 'trans man' who was born female
- Up to 20 primary schools per year pay for classes by Gendered Intelligence
- Parents' groups reacted with concern that pupils might be 'frightened'

By [SANCHEZ MANNING FOR THE MAIL ON SUNDAY](#)

PUBLISHED: 13:37 AEST, 1 November 2015 | **UPDATED:** 13:58 AEST, 1 November 2015



Senator Wiener with fellow LGBT Legislative Caucus members Susan Eggman, Todd Gloria, Toni Atkins, Ricardo Lara, Cathleen Galgiani, Evan Low, and Sabrina Cervantes. (Sen. Wiener photo gallery)

HIGHLIGHT **LEGISLATURE**

CA Democrats Author Bill to Protect Sex Offenders Who Lure Minors

No sex offender registry if perpetrator within 10 years of age of the minor ←

By [Katy Grimes](#), February 19, 2019 3:03 pm

Exclusive movies on Netflix, Stan, Prime Video and Foxtel | Finder

<https://www.finder.com.au/exclusive-movies-on-netflix-stan-prime-video-and-foxtel>

Jul 15, 2019 - Alphabet, Phonics, & More Kids Songs! by English Tree TV, 2019 Are All Men

Pedophiles? 2012 Baby Shark - **Nursery Rhymes** & Kids Songs, 2018 **Charged:** The Eduardo Garcia Story, 2017 Confessions Of A Teenage Drama **Queen**, 2004 Fastest Street Car Shootout: **Drag Time**, 2019.

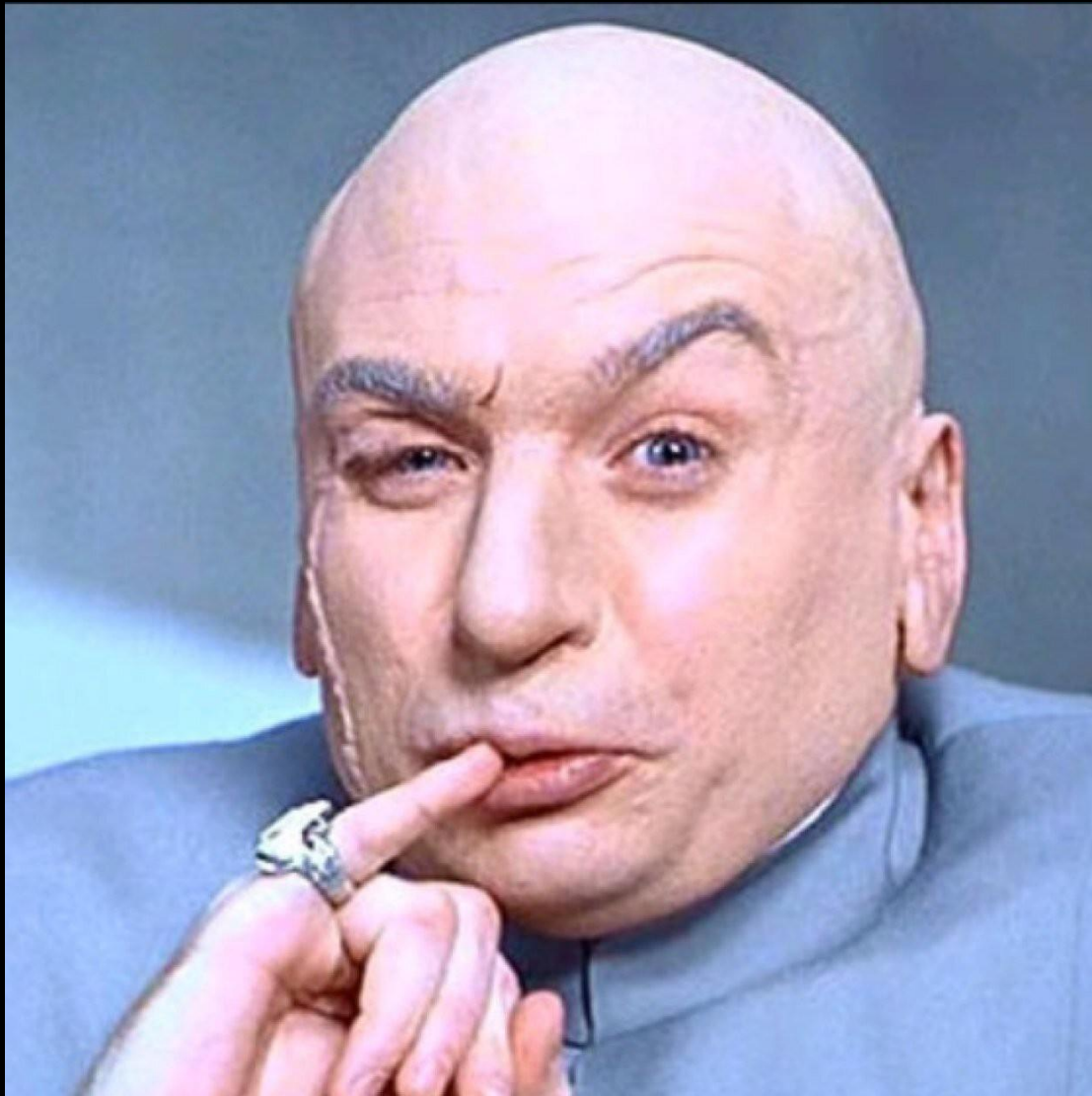
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Opinion | Pedophilia: A Disorder, Not a Crime - The New York Times

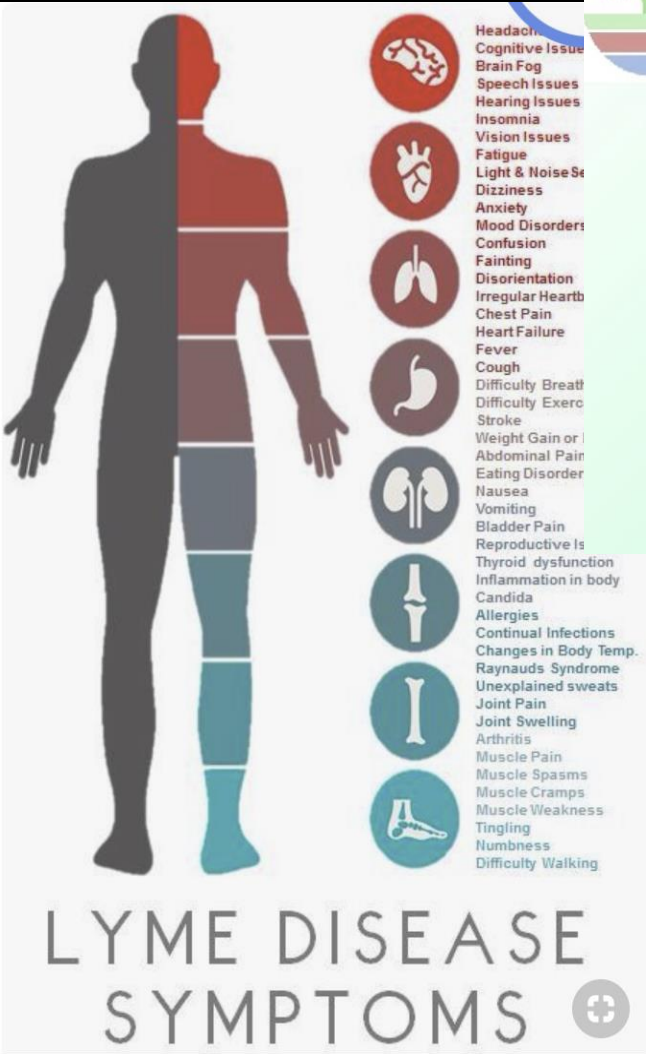
<https://www.nytimes.com/2014/10/06/.../pedophilia-a-disorder-not-a-crime.html> ▾ ←

Oct 5, 2014 - These people are living with **pedophilia**, a sexual attraction to ... more lax than for **ordinary** "civil commitment" for people with mental illness.

Distraction or not? Do we have a choice?



Distraction whilst there are new emerging diseases. Choice?



LYME DISEASE SYMPTOMS

The infographic features a human silhouette with various body parts highlighted in different colors (red, orange, yellow, green, blue). To the right of the silhouette, a list of symptoms is provided, each accompanied by a small circular icon representing the affected body part or system.

- Headache
- Cognitive Issues
- Brain Fog
- Speech Issues
- Hearing Issues
- Insomnia
- Vision Issues
- Fatigue
- Light & Noise Sensitivity
- Dizziness
- Anxiety
- Mood Disorders
- Confusion
- Fainting
- Disorientation
- Irregular Heartbeat
- Chest Pain
- Heart Failure
- Fever
- Cough
- Difficulty Breathing
- Difficulty Exercising
- Stroke
- Weight Gain or Loss
- Abdominal Pain
- Eating Disorder
- Nausea
- Vomiting
- Bladder Pain
- Reproductive Issues
- Thyroid dysfunction
- Inflammation in body
- Candida
- Allergies
- Continual Infections
- Changes in Body Temperature
- Raynaud's Syndrome
- Unexplained sweats
- Joint Pain
- Joint Swelling
- Arthritis
- Muscle Pain
- Muscle Spasms
- Muscle Cramps
- Muscle Weakness
- Tingling
- Numbness
- Difficulty Walking



“MORGELLONS DISEASE”

Individuals report disturbing symptoms of seeing and feeling crawling, stinging and biting organisms on and in their skin. These organisms are described as fiber-like or black specks, and are accompanied by skin lesions. Sufferers also report chronic joint pain, disabling fatigue, cognitive difficulties, mental confusion, memory loss, behavioral effects, and mood disorders.



www.webmd.com

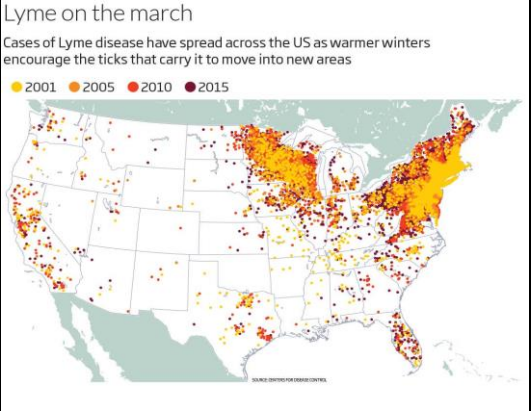
Morgellons Disease: What Is It?



Is Lyme Disease a “bioweapon”?

POLITICS · Published July 17

House orders Pentagon to reveal whether it turned ticks into biological weapons



Lyme disease is one of the fastest-growing vector-borne infections in the United States. The CDC estimates that there are over 329,000 new cases of Lyme disease each year here in the US.

Health · Perspective

No, Lyme disease is not an escaped military bioweapon, despite what conspiracy theorists say

By Sam Telford
August 11

Could Lyme disease in the United States be the result of an accidental release from a secret bioweapons experiment? Could the military have specifically engineered the Lyme disease bacterium to be more insidious and destructive — and then let it somehow escape the lab and spread in nature? Is this why [300,000 Americans are diagnosed annually](#) with this potentially debilitating disease?

It's an old conspiracy theory [enjoying a resurgence](#) with lots of sensational headlines and tweets. Even Congress has ordered that the [Pentagon must reveal whether it weaponized ticks](#).

And it's not true.

[GOP lawmaker thinks rise in Lyme disease is due to a secret tick experiment. A scientist squashes that idea](#)

Ticks can indeed carry infectious agents that could be used as biological weapons. Military research [has long focused on ticks](#). Sites around Long Island Sound, near the military's Plum Island research lab, were some of the first places where the American Lyme disease epidemic was identified.

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Secondary dementia due to Lyme neuroborreliosis

[Wolfgang Kristoferitsch](#),¹ [Fahmy Aboulenein-Djamshidian](#),^{1,2} [Julia Jecel](#),³ [Helmut Rauschka](#),^{1,2} [Michael Rainer](#),^{4,5} [Gerold Stanek](#),⁶ and [Peter Fischer](#)⁴

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REVIEW ARTICLE

Lyme Carditis—Diagnosis, Treatment and Prognosis

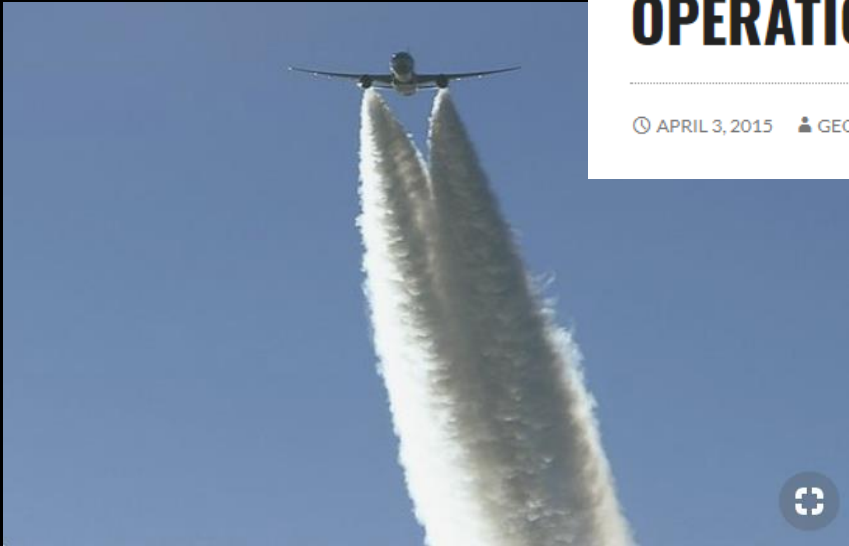
Norbert Scheffold, Bernhard Herkommer, Reinhard Kandolf, Andreas E. May

ChemTrails – debate or not? Distraction? Choice?



**Chemtrail Pilot Blows the Lid Off
OPERATION INDIGO SKYFOLD**

🕒 APRIL 3, 2015 👤 GEOPOLITICS101 💬 152 COMMENTS



“No ChemTrails” – so exactly what are they spraying?



Mornington Peninsula mosquito spray plan: bee keeper fears honey ...

<https://www.heraldsun.com.au/...spraying.../d8f4d3030c182f7ae42829b7a3e16cf7>

3 days ago - A Mornington Peninsula bee keeper says Melbourne Universitys ... Buruli ulcer: Rye bee keeper says mozzie **spraying** killed three colonies.

Missing: [cem](#) | Must include: [cem](#)

Buruli ulcer: Mornington Peninsula 'controls' mozzie spray plan | Leader

<https://www.heraldsun.com.au/...mornington-peninsula.../3e00395622645eae68c05365...>

Aug 5, 2019 - Federal Liberal MP Greg Hunt has slammed Mornington Peninsula Shires claims it had no prior knowledge of a controversial plan to **spray** ...

Missing: [cem](#) | Must include: [cem](#)

Buruli ulcer: Bellarine Peninsula bug's Mornington Peninsula ...

<https://www.geelongadvertiser.com.au/...spray...mornington-peninsula.../a0949ebd7650...>

Jul 17, 2019 - Industrial-strength Morteinwill be **sprayed** from Rosebud to Portsea in the battle against the spread of a flesh-eating ulcer common on the ...

Missing: [cem](#) | Must include: [cem](#)



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Dr Russell Blaylock Neurosurgeon – “Airborne Nanoparticles”

ALUMINIUM nanoparticles

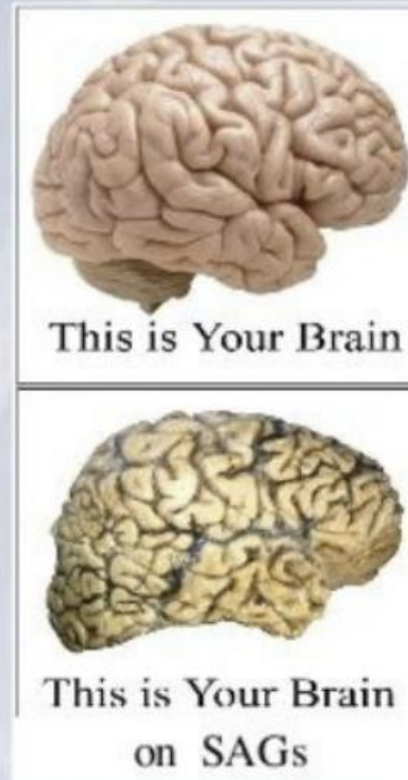


Russell L. Blaylock, MD

neurodegenerative and neurodevelopmental effects

- easily penetrate the brain via the blood and olfactory neural tracts
- infinitely more reactive ⇒ inflammation
- Alzheimer's, A.L.S., Parkinson's
- inflammatory reaction in the lungs
- pulmonary diseases, asthma

nanoparticles are worse than asbestos



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Mind & Brain » Reuters

1 :: Email :: Print

Autism Risk Linked to Particulate Air Pollution

Children whose mothers were exposed to high levels of fine particulate pollution in late pregnancy have up to twice the risk of developing autism as children of mothers breathing cleaner air, scientists reported

REUTERS

December 18, 2014

www.theguardian.com

Toxic air pollution
particles found in
human brains |
Society | The
Guardian

www.newstarget.com

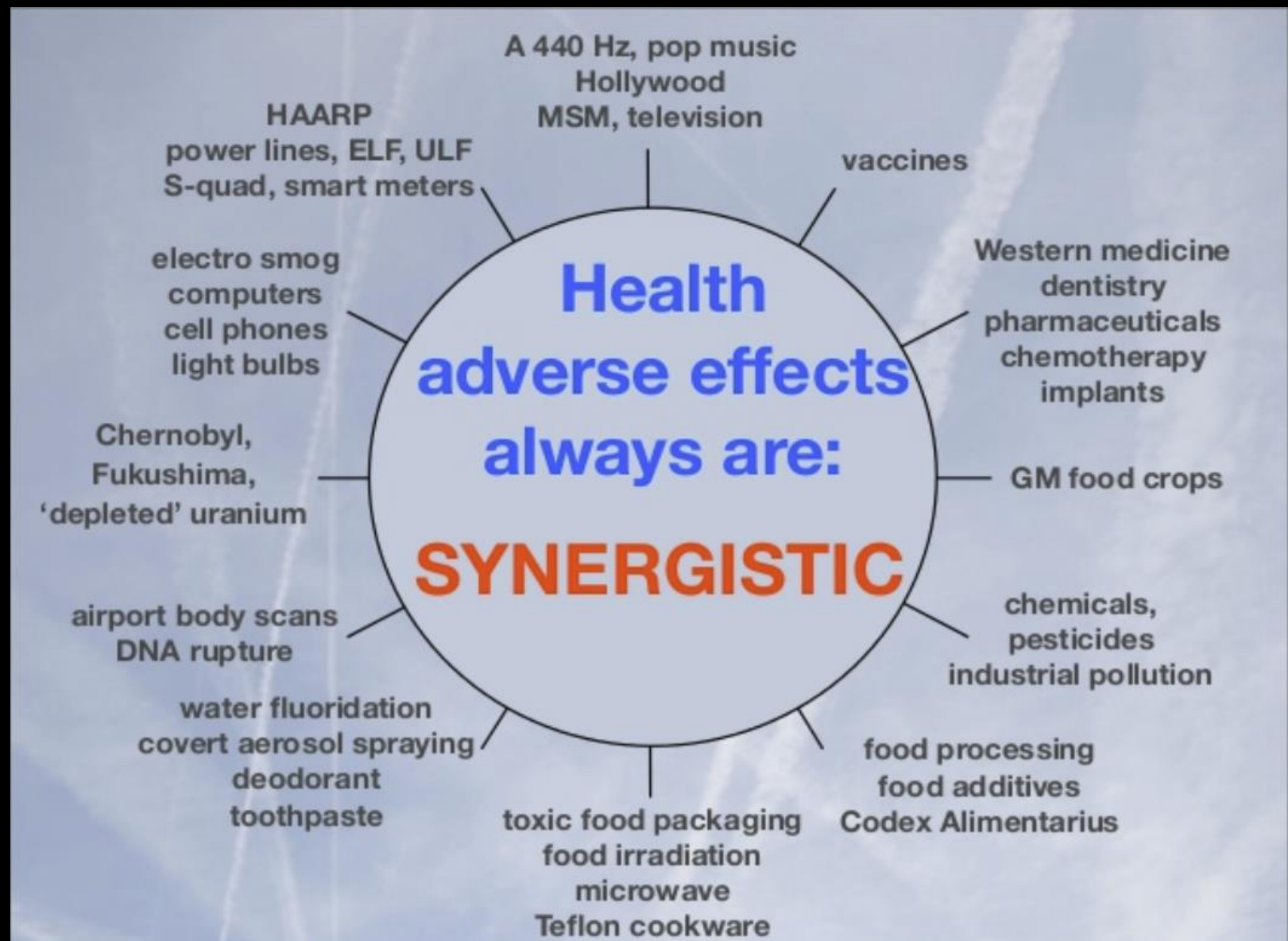
Geoengineering
expert: Chemtrails
used for forced
airborne
vaccinations



OXYMED

<http://www.geoengineeringwatch.org/neurologist-warns-aluminum-in-chemtrails-could-cause-explosive-increase-in-neurodegenerative-diseases/>

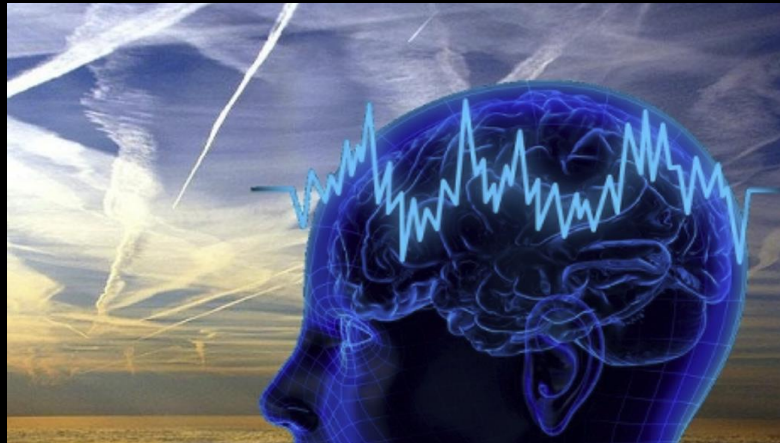
Dr Blaylock – ‘The effects of Cytokine Storm culminate’



LONG TERM EFFECTS OF CHEMTRAIL EXPOSURE

1. Acid Reflux	23. High Cholesterol
2. (ADHD) Attention Deficit Hyperactivity Disorder	24. Hypoglycemia
3. Allergies	25. Hyperglycemia
4. Alzheimer's Disease	26. Irritable Bowel Syndrome (IBS)
5. Aluminum build up in Pineal Gland	27. Insomnia
6. Asthma	28. Learning Disabilities
7. Autism (evidence links autism to mercury)	29. Lung diseases
8. Autoimmune Diseases	30. Lupus Erythematosus
9. Blood in the Urine	31. Multiple Sclerosis
10. Borderline personality disorder	32. Oily Skin (Elevated DHT)
11. Cancer (linked to many types of cancers)	33. Parkinson's Disease
12. Chronic Fatigue	34. Rheumatoid Arthritis
13. Constipation	35. Schizophrenia
14. Depression	36. Short-Term Memory Loss
15. Easy Bruising	37. Sleep Disorders
16. Eye problems	38. Spider Veins
17. pressure)	39. Tinnitus
18. Fibromyalgia	40. White Coating On the Tongue
19. Floaters In the Eyes	41. And many other symptoms
20. Gastritis	
21. Heart Arrhythmia (irregular heartbeat)	
22. Heart Disease	

STOP CHEMTRAILS

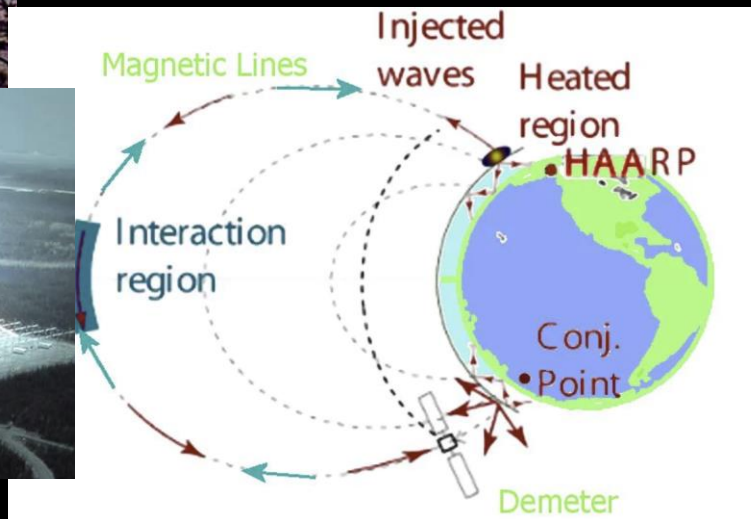


HAARP – High Frequency Active Auroral Research Program

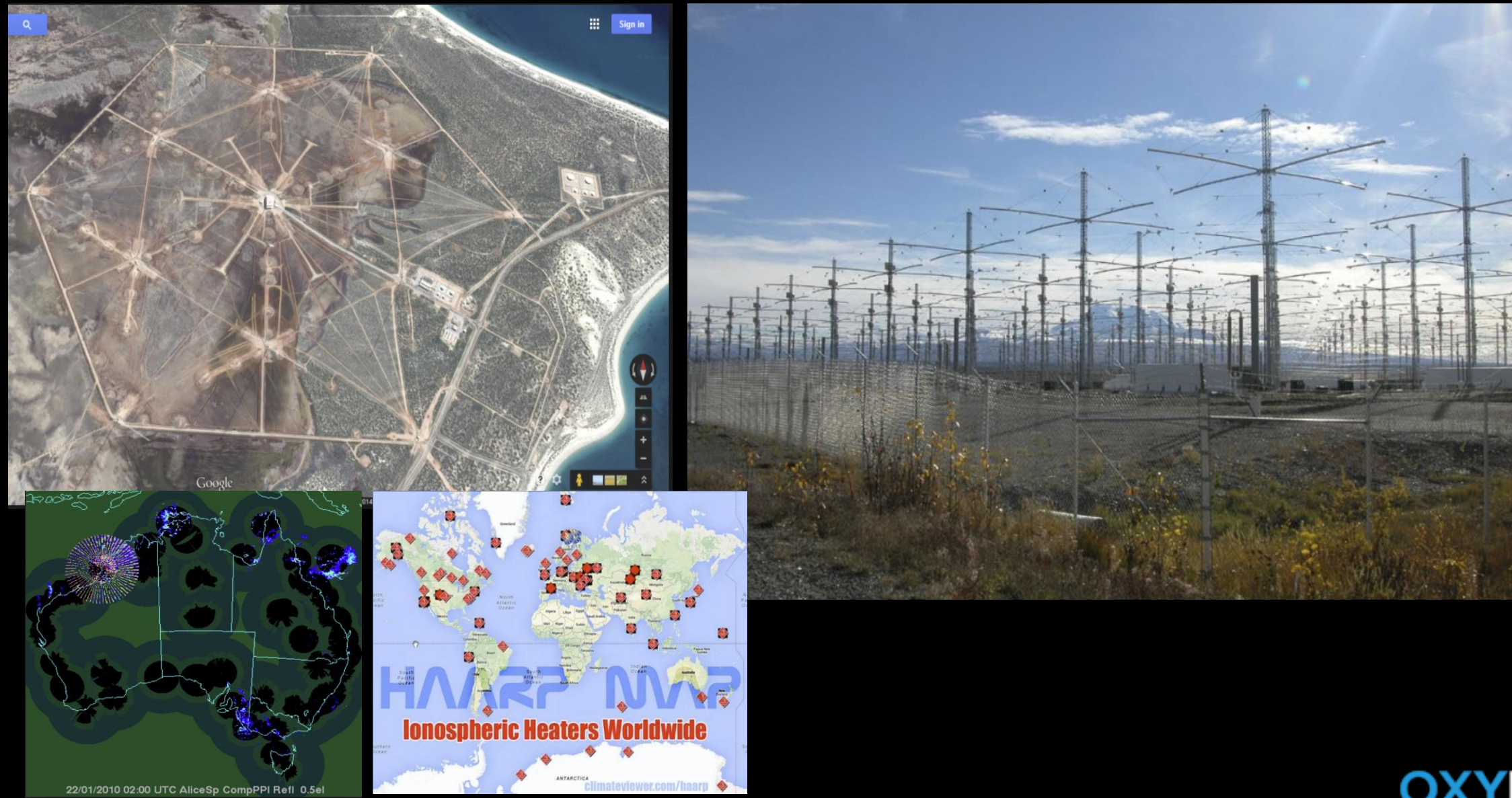
- HAARP, is a scientific endeavor aimed at studying the properties and behavior of the ionosphere. Operation of the research facility was transferred from the United States Air Force to the University of Alaska Fairbanks on Aug. 11, 2015, allowing HAARP to continue with exploration of ionospheric phenomenology via a land-use cooperative research and development agreement.
- HAARP is the world's most capable high-power, high-frequency transmitter for study of the ionosphere. The HAARP program is committed to developing a world-class ionospheric research facility consisting of:
- The Ionospheric Research Instrument, a high power transmitter facility operating in the High Frequency range. The IRI can be used to temporarily excite a *limited area of the ionosphere for scientific study*.
- A sophisticated suite of scientific or diagnostic instruments that can be used to observe the physical processes that occur in the excited region."



HAARP - high-power, high-frequency transmission



Exmouth - Western Australia – who is controlling HAARPs?



The Final Frontier – The Power Within



Tony Robbins 'Unleash the POWER within'

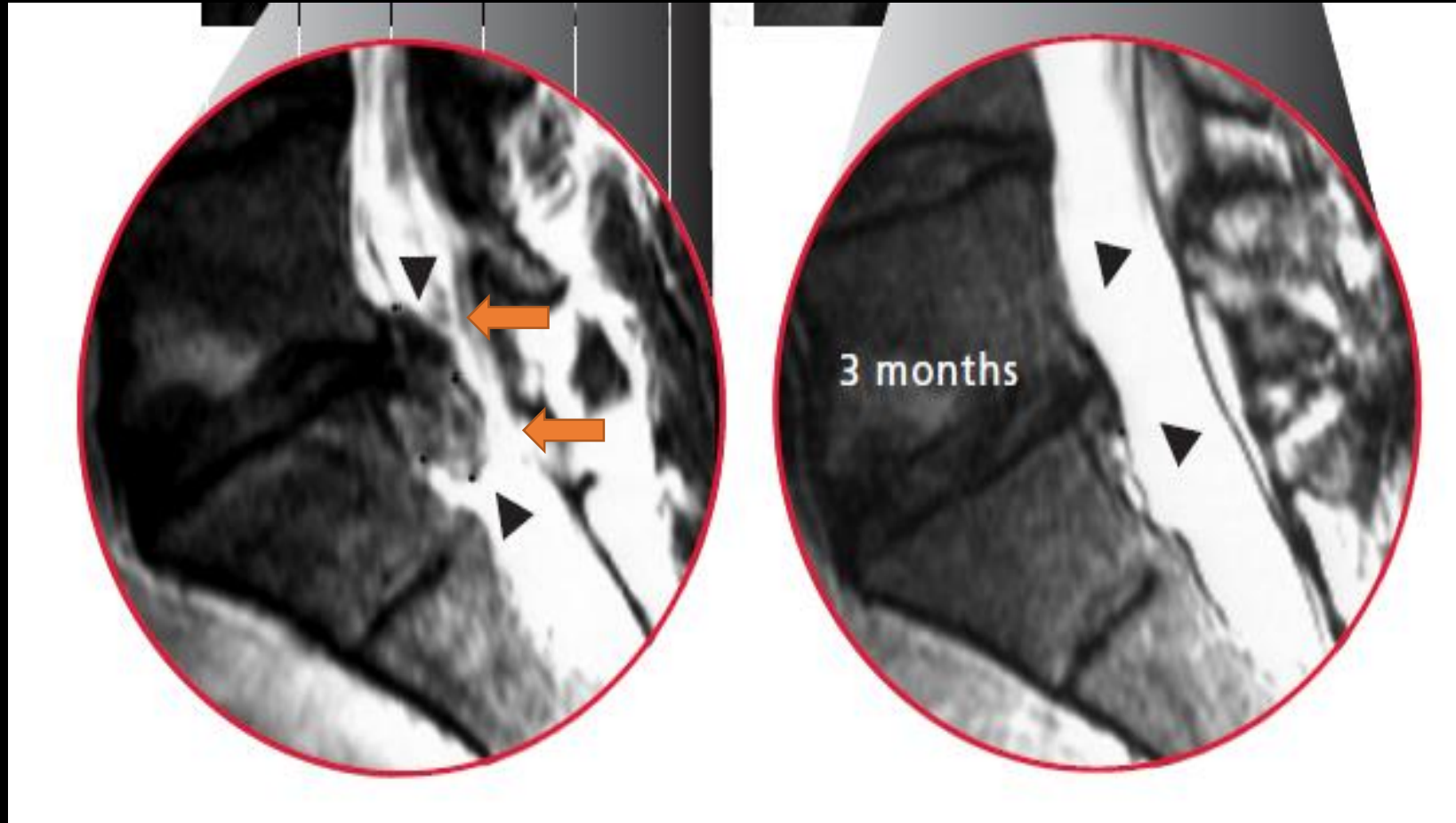
Ephesians 3 vs 20

'God can do exceedingly and abundantly above all that we can think or ask of him – the Power within'

The Story - 1993



HBOT 1995-1999: Chronic Pain, Disc Prolapse, Failed Back Surgery



94 Herald Sun, Monday, February 27, 2006 www.heraldsun.com.au

health&fitness

■ DIET ■ WORKOUTS ■ ADVICE

One doctor believes an oxygen pressure chamber helps spinal patients, writes **Daniel Hoy**

WHEN most people think of hyperbaric chambers, they think of footballers trying to get fit for the finals.

Melbourne doctor Mai Hooper has gone a step further, pioneering the application and role of hyperbaric oxygenation in the treatment of chronic spinal injury — disc prolapse, failed back surgery and spinal-cord injuries.

HyperMed Australia offers the only private hyperbaric treatment unit in Melbourne.

"Infections thrive in low oxygen sites. Spinal conditions, neurovascular disorders, strokes, cancers, slow wound healing are all greatly helped by the introduction of oxygen saturation to the cells," Hooper says.

Hooper does not guarantee any miracle cures, but says any low treatments continue to demonstrate dramatic improvements in immune responses, ranging from simple but difficult-to-treat conditions such as slow wound healing to major disabilities. He says that in some cases, the treatment can make some difference to spinal patients, depending on the injury.

"Many spinal patients improve and gain functional returns, not because they continue to sit in a wheelchair but because the body is finding a way to decrease the inflammation within the damaged section of the spinal cord, reactivating nerve cells that are not dead but simply non-functional," he says.

Visit www.hypermed.com.au or call 1800 3116 or email info@hypermed.com.au

HOW IT WORKS

Hyperbaric Oxygen Therapy (HBOT) is a method of safely delivering high doses of oxygen to the body, by breathing 100 per cent oxygen through a mask or hood while inside a pressurised air chamber.

The pressure inside the chamber causes the oxygen breathed to be dissolved at greater than normal levels in the blood. This provides an additional 15-20 fold (2000 per cent) increase in tissue oxygenation, significantly accelerating the rate of healing, stabilisation and repair.

Hyperbaric oxygenation and its application are global

In the US and many other countries, HBOT is commonly used to treat sports-related injuries. It can also have clinical benefits by:

- **INCREASING** the saturative effects of dissolved oxygen into compromised tissues;
- **DECREASING** swelling, edema and painful inflammation, while providing the growth of new capillary blood vessels (neovascularisation);
- **DEACTIVATING** and clearing toxins (acute and);
- **INCREASING** the body's ability to fight infections; and
- **PROMOTING** neurovascular salvage.

House call
BROKEN COLLARBONE

A common injury among cyclists and footballers, such as St Kilda's Nick Riewoldt (above), the collarbone more often than not takes the brunt of a fall. The symptoms of a broken collarbone include pain, swelling, trouble moving your shoulder and weakness. It is best to visit your doctor after any violent fall, but if the pain does not start to subside, get to the doctor as soon as possible. The good news is that a broken collarbone usually heals without complications.

Number cruncher **1496**

The number of kilojoules in a Mango Magic from Boost Juice.

The BIG EVENT

The SP Ultimate/BW Corporate Trailblaze is on Sunday and you can be assured of one thing: it will attract a huge field. The venue at Ellwood has a carnival atmosphere with more than 80 corporate marquee and thousands of competitors. www.supperite.com.au

See it WIRED TO WIN

Marie de Touffville

The new Inna documentary explores cutting-edge brain science through the dramatic story of the 2003 Tour de France. The film concentrates on the human brain's amazing ability to overcome adversity, and accomplish the near impossible. The film features Melbourne cyclist Benoit Coste (above) as he battles to win the Green Jersey, awarded to the tour's best sprinter.

BACK TRACK

GOOD VIBRATIONS

HyperMed does not offer only hyperbaric chamber treatment. It also uses a technique called Advanced Vibration Training.

The machine allows an athlete recovering from injury to work out while experiencing varying degrees of vibration through their muscles.

It is being used by most major sports in the US, including the NFL and NBA, has been used by Tour de France great Lance Armstrong, and AFL club Collingwood uses a vibration machine as part of pre-match and post-game conditioning.

Dr Mai Hooper says vibration therapy's use is related to rehabilitation include:

HELPING to better use what the patient has left. In a stroke patient, for example, it improves neuromuscular co-ordination, balance, gait (walking) and circulation, and decreases chronic pain and swelling. It is also time and cost effective.

A PATIENT with severe disability can have access to a home unit, meaning several times a day the application of vibration can be directed without having to go through the difficulty of attending a special gym that requires supervision and additional expense.

THE FUTURE

Hooper says that in some cases, stem cells can help spinal victims to walk again.

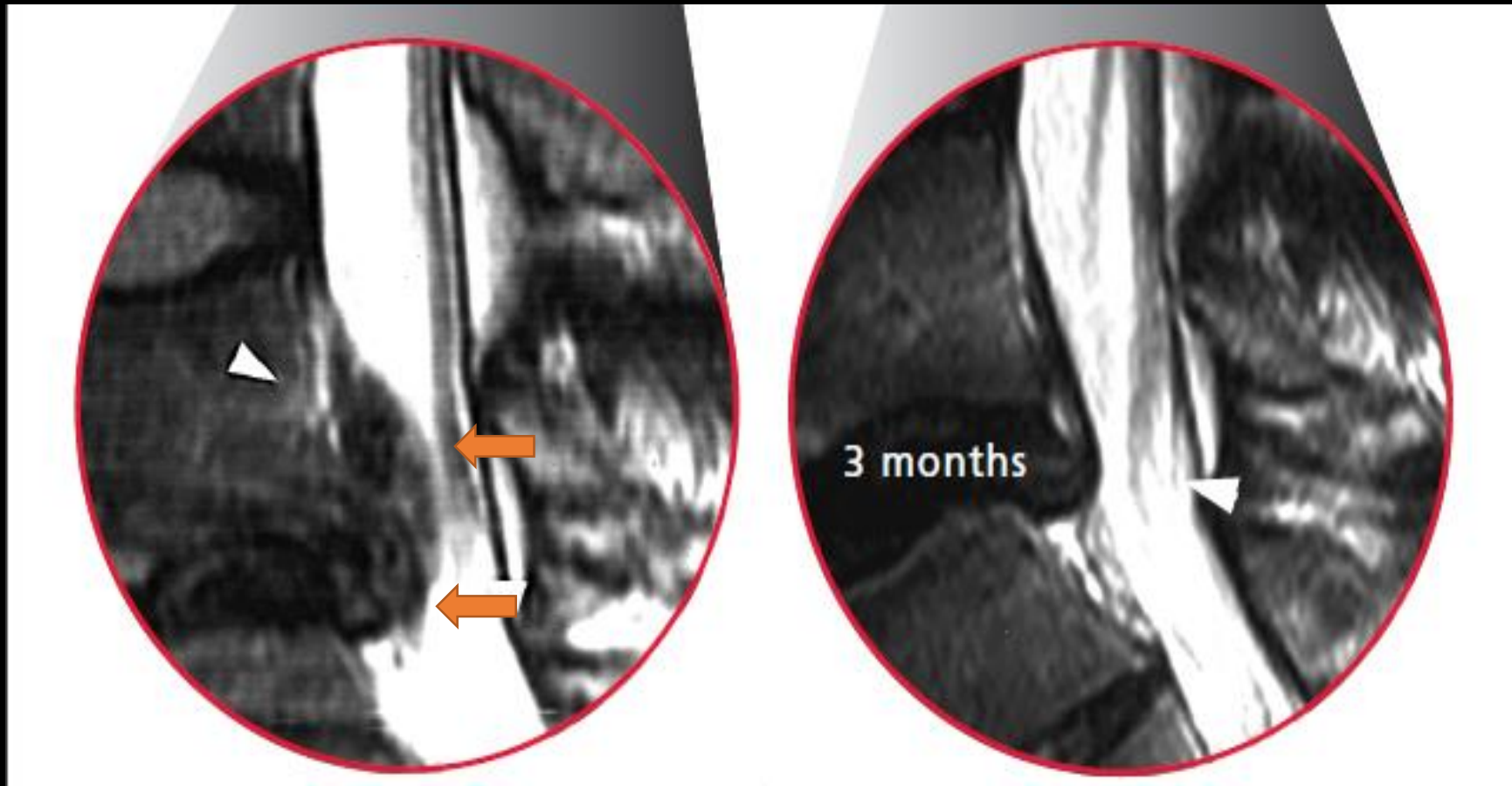
"Stem cells for spinal cord injury are available throughout the world," he says.

Depending on the level of injury and the degree of compromise, if there remains some viable tissue, then stem cells combined with appropriate medical management including Hyperbaric Oxygenation and neuro-robotic rehabilitation, walking is possible.

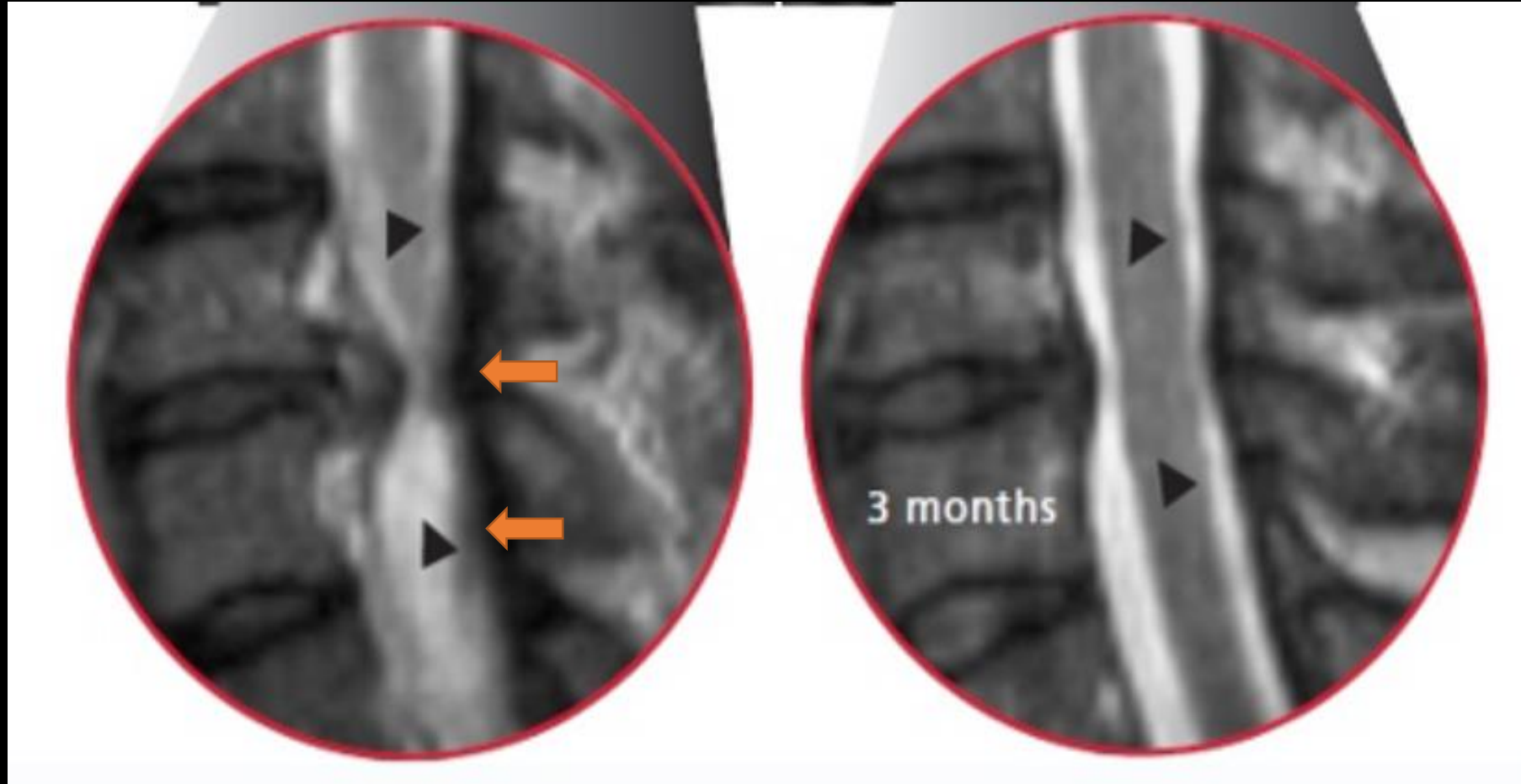
HEALTHFACTS

Editor: Daniel Hoy
Phone: 9292 1831 Fax: 9292 1177
Email: hoy@hypermed.com.au
Advertising:
Hung Nguyen Phone: 9292 2808

Disc sequestration, haematoma



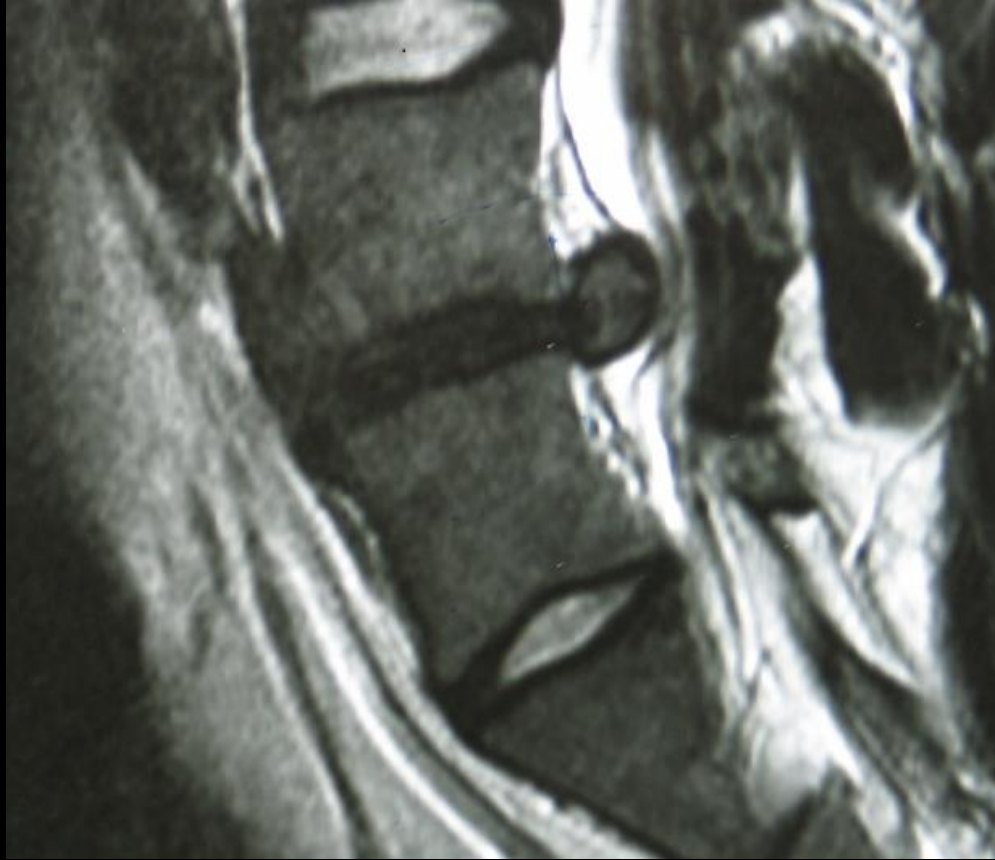
Disc Prolapse, T2 hyperintensity cord signal



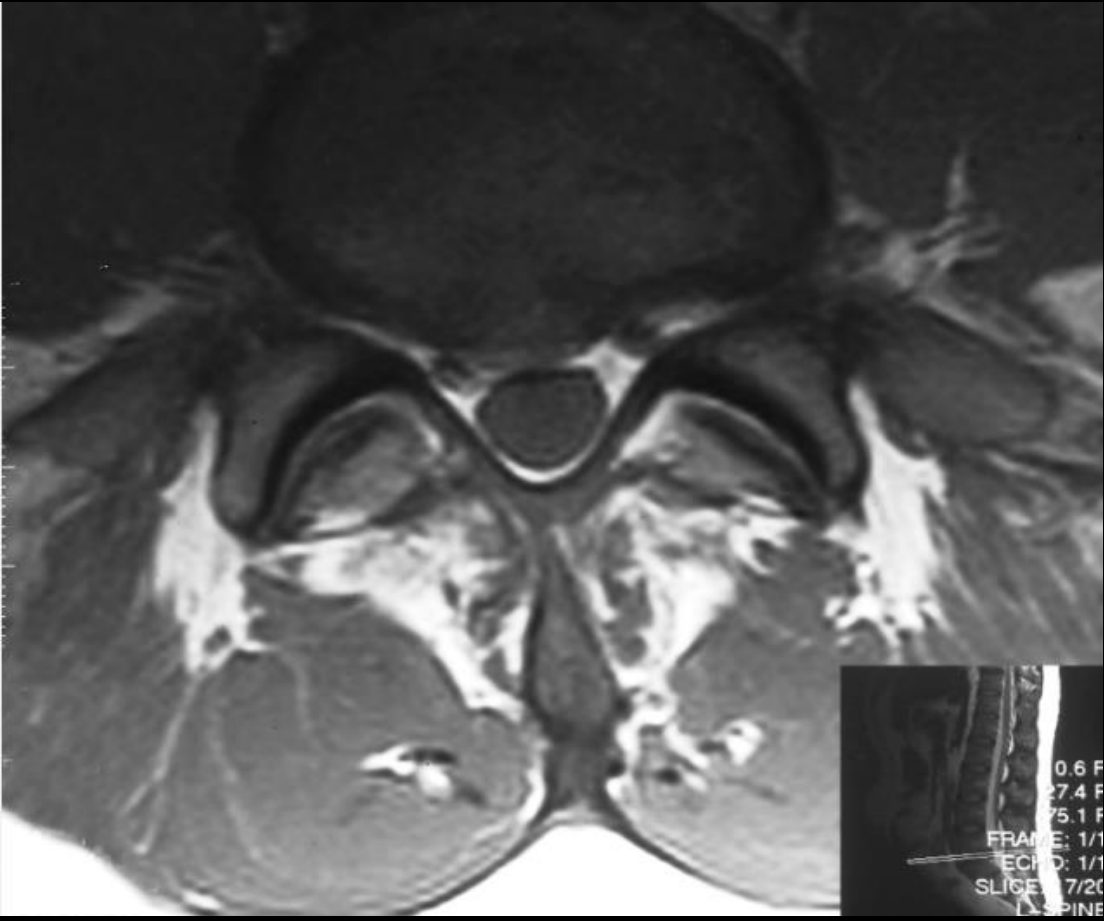
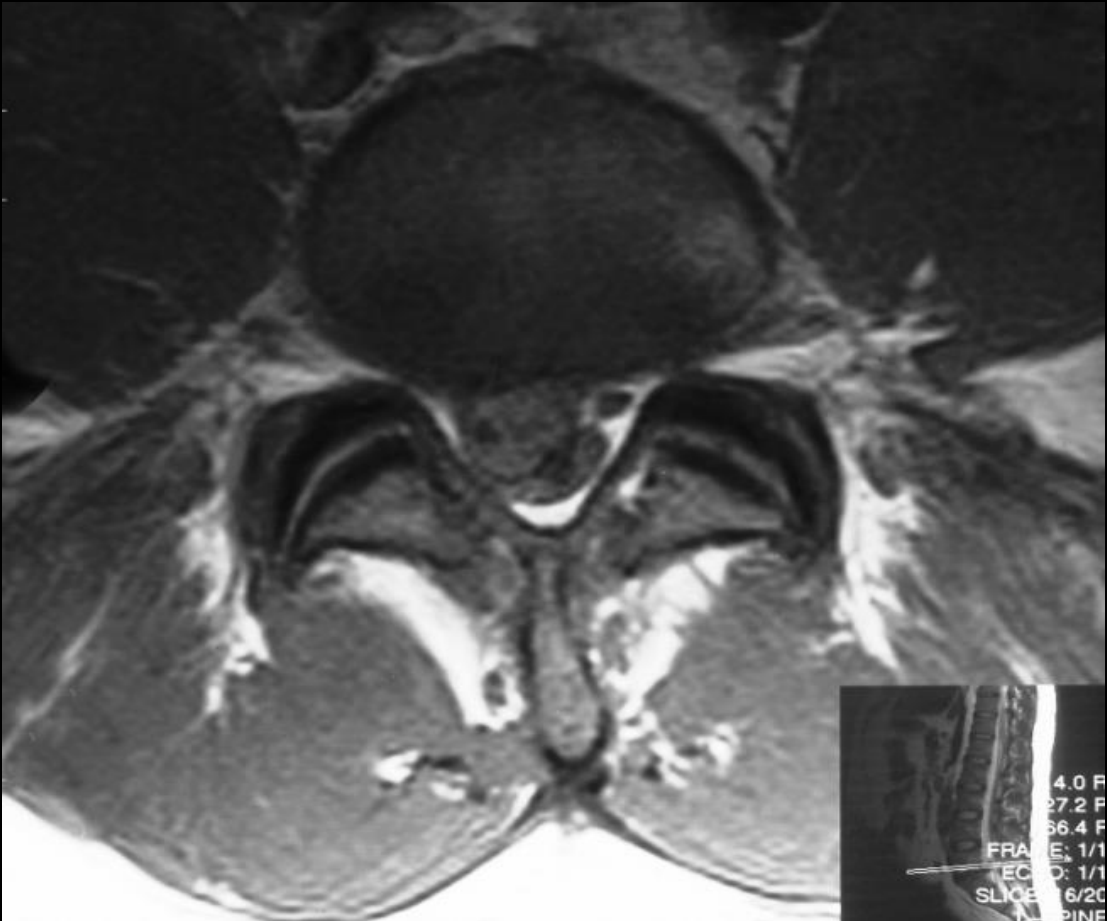
Disc sequestration, disc fragment



Disc Prolapse – 14 days



Large L5/S1 disc sequestration



Failed Back Surgery Syndrome (FBSS) – 2x past discectomy



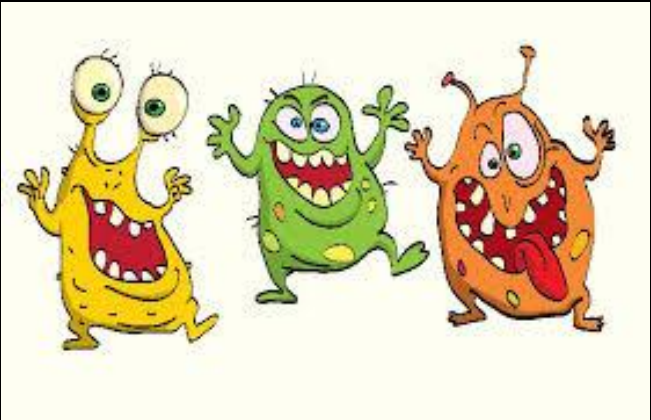
ANTIMICROBICS AND INFECTIOUS DISEASES NEWSLETTER

Editor-in-Chief
Charles W. Stratton, MD
Vanderbilt University
School of Medicine
Nashville, Tennessee

Full editorial board
appears on back cover

Volume 18, Number 7
July 2000

Association of *Chlamydia pneumoniae* with Chronic Human Diseases



OXYMED

Chronic pain syndromes associated with chronic infections

Does antibiotic or anti-viral medication reduce your back pain?

[antibiotics-could-cure-40-cent-chronic-back-pain \(AMA 2013\)](#)

* Blood investigations may include specific testing for Mycoplasma profile, Chlamydia profile, Rickettsia profile, Herpes strains, Cytomegalovirus, Epstein Barr Virus, Borrelia species (Lyme Disease). Chlamydia pneumonia and other chronic anaerobic based infections are associated with arthritis and chronic pain syndromes.

Opportunistic Infections act as a 'triggering agent' driving chronic pain cycles and progressive degeneration. Chlamydia Pneumonia and chronic diseases

** If you are considering the antibiotic approach, then ask your doctor to trial **Minocycline which elevate IL10, IL4, IL15** (pro anti-inflammatory cytokines - 'good guys')

[Minocycline modulates cytokine and gene expression profiles in the brain after whole-body exposure to radiation.](#)

[Mehrotra S1, Pecaut MJ, Gridley DS.](#)

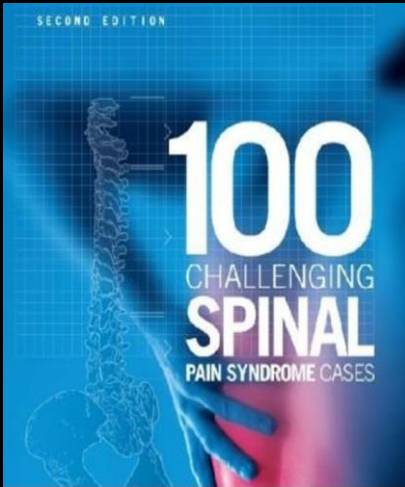
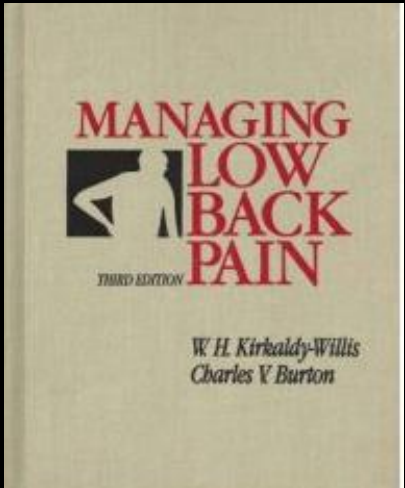
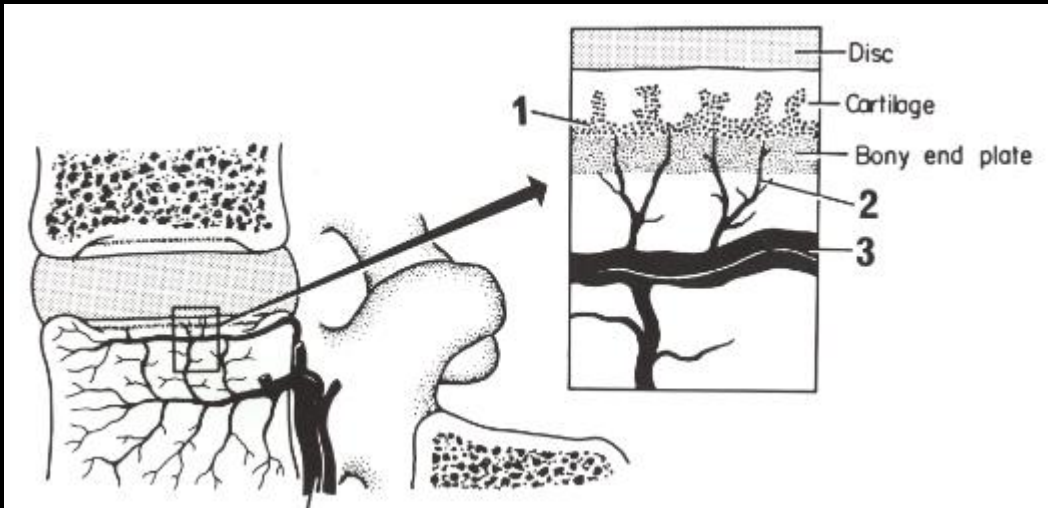
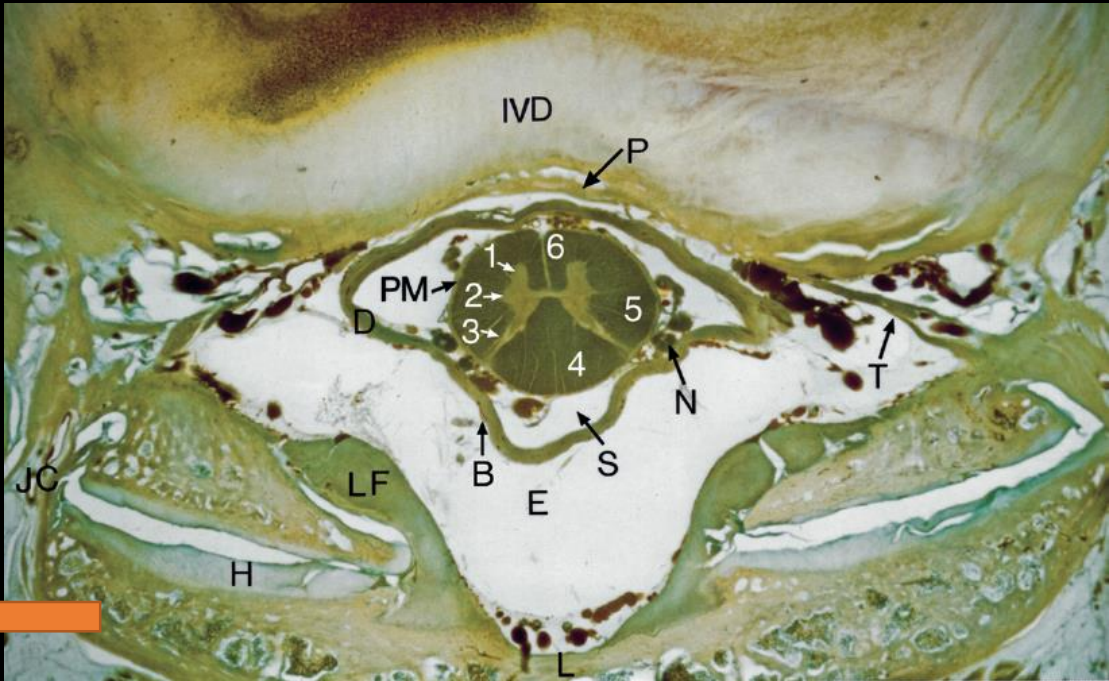
Author information - Chan Shun Pavilion, Room A-1010, 11175 Campus Street, Loma Linda University, Loma Linda, CA 92354, U.S.A. dgridley@llu.edu.

Abstract

An effective countermeasure against radiation damage to normal tissues is urgently needed. The major goal of the present study was to determine if minocycline could modify the immunomodulatory effects of radiation on the brain. C57BL/6 mice were treated with minocycline intraperitoneally for 5 days beginning immediately before total-body exposure to 0, 1, 2 and 3 Gray (Gy) (60)Co γ-rays. Brains were collected on days 4 and 32 post-irradiation for cytokine and gene analyses.

- **Minocycline treatment significantly increased the levels of interleukin (IL)-10, IL-15 and vascular endothelial growth factor (VEGF) in the brain on day 4 in one or more irradiated groups compared to radiation-alone ($p < 0.05$). IL-10 is anti-inflammatory, IL-15 can prevent apoptosis and VEGF is neuroprotective.** On day 32, the drug decreased IL-1 β in the 2- Gy group ($p < 0.05$ vs. 2-Gy alone); this cytokine is implicated in immune-related central nervous system pathologies. Microarray analysis of brains on day 32 showed that while radiation increased expression of inflammatory genes such as Il1f10, Il17, Tnfrsf11b, Tnfrsf12, Il12b and Il1f8, these were no longer up-regulated in the minocycline-treated groups. Similarly, the pro-apoptotic gene Bik and nitric oxide synthase producer (Nostrin) were no longer up-regulated in the drug-treated groups. Pathway analysis based on gene data suggested that catenin- β 1 and tumor suppressor-related transcription regulation were significantly activated by radiation and/or minocycline (activation z-score > 2.0). Overall, the data warrant further testing of minocycline as a potential neuroprotectant against radiation-induced damage.

Ischemic Model of Degeneration (Kirkaldy Willis 1986, L. Giles 2nd Ed)



Stem Cell Mobilization (2005) – ‘Pluripotent’ CD34+ plus Colony Forming Cells (GMCSF)

[Am J Physiol Heart Circ Physiol](#). 2006 Apr;290(4):H1378-86. Epub 2005 Nov 18.

Stem cell mobilization by hyperbaric oxygen.

[Thom SR¹](#), [Bhopale VM](#), [Velazquez OC](#), [Goldstein LJ](#), [Thom LH](#), [Buerk DG](#).

Author information

Abstract

We hypothesized that exposure to hyperbaric oxygen (HBO(2)) would mobilize stem/progenitor cells from the bone marrow by a nitric oxide (*NO) -dependent mechanism. The population of CD34(+) cells in the peripheral circulation of humans doubled in response to a single exposure to 2.0 atmospheres absolute (ATA) O(2) for 2 h. Over a course of 20 treatments, circulating CD34(+) cells increased eightfold, although the overall circulating white cell count was not significantly increased. The number of colony-forming cells (CFCs) increased from 16 +/- 2 to 26 +/- 3 CFCs/100,000 monocytes plated. Elevations in CFCs were entirely due to the CD34(+) subpopulation, but increased cell growth only occurred in samples obtained immediately posttreatment. A high proportion of progeny cells express receptors for vascular endothelial growth factor-2 and for stromal-derived growth factor. In mice, HBO(2) increased circulating stem cell factor by 50%, increased the number of circulating cells expressing stem cell antigen-1 and CD34 by 3.4-fold, and doubled the number of CFCs. Bone marrow *NO concentration increased by 1,008 +/- 255 nM in association with HBO(2). Stem cell mobilization did not occur in knockout mice lacking genes for endothelial *NO synthase. Moreover, pretreatment of wild-type mice with a *NO synthase inhibitor prevented the HBO(2)-induced elevation in stem cell factor and circulating stem cells. We conclude that HBO(2) mobilizes stem/progenitor cells by stimulating *NO synthesis.

1998: Peter R. C7 'complete' – 6 years post injury

Hyperbaric Oxygen is breathing 100 per cent oxygen at pressures greater than normal. HBOT increases dissolved oxygen into the into the damaged regions of the body.

HBO increases blood plasma by 10-15 fold (1000-1500 per cent).

The normal blood plasma carry only 1-2 per cent oxygen with red blood cells carrying approximately 98 per cent oxygen.

“Hyperbaric Oxygen Therapy creates a ‘fertile neurovascular platform’ for emerging stem cell, immunotherapies and nanotechnology techniques. The impact and success of these and future procedures are dependent on the integrity of the underlying supporting neurovascular bed.” (Hooper 2005).

HBO acts as a 'catalyst' promoting immune modulation.

HBO results in increased blood flow by fostering the **formation of existing and new capillary dynamics** (neovascularization) **activating damaged and dormant nerve cells** (penumbral state).

HBO accelerates **neuroplasticity**.



Old Model – Living & coping with disability



2006: 'World first' - HBOT combined with Robotic LOKOMAT

OLD REHABILITATION MODEL - "Living and coping with disability"

BODY WEIGHT SUPPORT TREADMILL TRAINING

- **Two or more physical therapists manually move the patient's legs in a walking pattern.**
However, the labour-intensive, strenuous nature and variability of the manual method can limit the frequency, quality and duration of the therapy.



ROBOTIC EXOSKELETON ASSISTIVE TECHNOLOGIES

- The patient is suspended in a harness over a treadmill and the exoskeleton frame of the robot, attached to the outside of the legs, moves the legs in a natural walking pattern.
- **Neuroplasticity mechanisms work on the basis that by controlling the repetitive walking pattern we can help the brain and spinal cord work together to re-route signals that were interrupted by injury or illness.**
- Robotics assisted walking helps to strengthen muscles and improve circulation.
- **The robotic device does the heavy work** - pattern and pace are consistent and the exercise can be sustained over longer training time.
- Typically patients undertake 3-5 sessions per week for 30-60 minutes durations over 8-12 weeks initially.



Case Study – T4 ‘complete’

Young Isabel has never walked.

At 8-months age Isabel, was operated on for a benign tumour resulting in her becoming a ‘T4 complete paraplegic’.



Syringomyelia, cord atrophy

MRI 13-03-07:

- "Comparison is made with the last examination dated 10-10-05. A demonstrating the enhancing intraspinal lesion posteriorly in the spinal cord at the level of T4-T6.
- It is again seen to measure 2.8cm cranio caudal and 1cm AP. The imaging again shows cord atrophy with hydromyelia from T1 to at least inferior border of the lesion".



2007 Channel 7 News - OXYMED YouTube

<https://youtu.be/f6lCtNzU6gM>



<https://youtu.be/ZfzWSKIKcvM>



OXYMED

Case Study – T12 Spinal Cord Injury – now walking

Kyle was told he would “never walk again”.

Kyle is walking limited distance with the assistance of calipers.

<https://youtu.be/tml5KjZEBp0?t=5>



Case Study – Stroke Victim

Marco - massive arteriovenous malformation (AVM).

<https://youtu.be/OMqty6COs8E?t=39>



OXYMED

Case Study – Drowning Victim

Young Chloe – near drowning victim.

<https://youtu.be/3XCL1mocf1c>



Adult Cerebral Palsy

<https://youtu.be/vOZcfL8KRAk>



Maladaptive Neuroplasticity



Activity Based Neurorehabilitation



Periventricular Leukomalacia (PVL) – low tone, development delay



Hypoxic Ischemic Encephalopathy (HIE) – microcephaly, spastic quadriplegia, PANDAS



Spinal Cord Injury Exoskeleton Neural Priming



Functional 'Activity based' Neuroplasticity



NeuroRecovery Gymnasiums



Whole Body Vibration

[Clin Rehabil](#). 2017 Jan;31(1):23-33. doi: 10.1177/0269215515515621117. Epub 2016 Jul 11.

Effects of whole body vibration on muscle spasticity for people with central nervous system disorders: a systematic review.

[Huang M](#)¹, [Liao LR](#)^{1,2}, [Pang MY](#)¹.

 Author information

Abstract

OBJECTIVES: To examine the effects of whole-body vibration on spasticity among people with central nervous system disorders.

METHODS: Electronic searches were conducted using CINAHL, Cochrane Library, MEDLINE, Physiotherapy Evidence Database, PubMed, PsycINFO, SPORTDiscus and Scopus to identify randomized controlled trials that investigated the effect of whole-body vibration on spasticity among people with central nervous system disorders (last search in August 2015). The methodological quality and level of evidence were rated using the PEDro scale and guidelines set by the Oxford Centre for Evidence-Based Medicine.

RESULTS: Nine trials with totally 266 subjects (three in cerebral palsy, one in multiple sclerosis, one in spinocerebellar ataxia, and four in stroke) fulfilled all selection criteria. One study was level 1b (PEDro \geq 6 and sample size $>$ 50) and eight were level 2b (PEDro $<$ 6 or sample size \leq 50). All three cerebral palsy trials (level 2b) reported some beneficial effects of whole-body vibration on reducing leg muscle spasticity. Otherwise, the results revealed no consistent benefits on spasticity in other neurological conditions studied. There is little evidence that change in spasticity was related to change in functional performance. The optimal protocol could not be identified. Many reviewed studies were limited by weak methodological and reporting quality. Adverse events were minor and rare.

CONCLUSION: Whole-body vibration may be useful in reducing leg muscle spasticity in cerebral palsy but this needs to be verified by future high quality trials. There is insufficient evidence to support or refute the notion that whole-body vibration can reduce spasticity in stroke, spinocerebellar ataxia or multiple sclerosis.




Cerebral Palsy: Joint position, balance, joint sense

[Physiother Can.](#) 2016;68(2):99-105.

Effects of Three Weeks of Whole-Body Vibration Training on Joint-Position Sense, Balance, and Gait in Children with Cerebral Palsy: A Randomized Controlled Study.

[Ko MS](#)¹, [Sim YJ](#)², [Kim DH](#)³, [Jeon HS](#)⁴.

 [Author information](#)

Abstract in [English](#), [French](#)

Purpose : To observe the effects of whole-body vibration (WBV) training in conjunction with conventional physical therapy (PT) on joint-position sense (JPS), balance, and gait in children with cerebral palsy (CP). **Methods**: In this randomized controlled study, 24 children with CP were randomly selected either to continue their conventional PT or to receive WBV in conjunction with their conventional PT programme. Exposure to the intervention was intermittent (3 min WBV, 3 min rest) for 20 minutes, twice weekly for 3 weeks. JPS, balance, and gait were evaluated before and after treatment. **Results**: Ankle JPS was improved after 3 weeks of WBV training ($p=0.014$). Participants in the WBV group showed greater improvements in speed ($F_{1,21}=5.221$, $p=0.035$) and step width ($F_{1,21}=4.487$, $p=0.039$) than participants in the conventional PT group. **Conclusion**: Three weeks of WBV training was effective in improving ankle JPS and gait variables in children with



Bone density, muscle mass

[Sci Rep.](#) 2016 Mar 3;6:22518. doi: 10.1038/srep22518.

Effects of whole-body vibration training on physical function, bone and muscle mass in adolescents and young adults with cerebral palsy.

[Gusso S](#)¹, [Munns CF](#)², [Colle P](#)¹, [Derraik JG](#)¹, [Biggs JB](#)¹, [Cutfield WS](#)¹, [Hofman PL](#)¹.

Author information

Abstract

We performed a clinical trial on the effects of whole-body vibration training (WBVT) on muscle function and bone health of adolescents and young adults with cerebral palsy. Forty participants (11.3-20.8 years) with mild to moderate cerebral palsy (GMFCS II-III) underwent 20-week WBVT on a vibration plate for 9 minutes/day 4 times/week at 20 Hz (without controls). Assessments included 6-minute walk test, whole-body DXA, lower leg pQCT scans, and muscle function (force plate). Twenty weeks of WBVT were associated with increased lean mass in the total body (+770 g; $p = 0.0003$), trunk (+410 g; $p = 0.004$), and lower limbs (+240 g; $p = 0.012$). Bone mineral content increased in total body (+48 g; $p = 0.0001$), lumbar spine (+2.7 g; $p = 0.0003$), and lower limbs (+13 g; $p < 0.0001$). Similarly, bone mineral density increased in total body (+0.008 g/cm²; $p = 0.013$), lumbar spine (+0.014 g/cm²; $p = 0.003$), and lower limbs (+0.023 g/cm²; $p < 0.0001$). Participants reduced the time taken to perform the chair test, and improved the distance walked in the 6-minute walk test by 11% and 35% for those with GMFCS II and III, respectively. WBVT was associated with increases in muscle mass and bone mass and density, and improved mobility of adolescents and young adults with cerebral palsy.



Stroke – sitting, balance, trunk control

[Top Stroke Rehabil.](#) 2017 Mar 23;1-6. doi: 10.1080/10749357.2017.1305655. [Epub ahead of print]

The effect of a whole-body vibration therapy on the sitting balance of subacute stroke patients: a randomized controlled trial.

[Lee JH¹](#), [Kim SB¹](#), [Lee KW¹](#), [Lee SJ¹](#), [Park H²](#), [Kim DW¹](#).

Author information

Abstract

BACKGROUND: The use of a whole-body vibration (WBV) therapy has recently been applied and investigated as a rehabilitation method for subacute stroke patients.

OBJECTIVE: To evaluate the effects of a WBV therapy on recovery of balance in subacute stroke patients who were unable to gain sitting balance.

METHODS: The conventional rehabilitation group (CG) received conventional physical therapy, including sitting balance training by a physical therapist, for 30 min a one session, for twice a day for five days a week for two weeks. The whole-body vibration group (VG) received one session of conventional physical therapy, and received WBV therapy instead of conventional physical therapy for 30 min a day for five days a week for two weeks.

RESULTS: There were 15 patients in the CG and 15 patients in the VG who completed the two-week therapy. After the two-week therapy, both groups showed functional improvement. Patients in the VG improved functional ambulation categories, Berg balance scale, trunk impairment scale scores. But, no statistically significant correlations between the therapeutic methods and outcomes were observed in either group.

CONCLUSION: Our results suggest that WBV therapy led to improvement of the recovery in balance recovery for subacute stroke patients. Because the WBV therapy was as effective as conventional physical therapy, we can consider a WBV therapy as a clinical method to improve the sitting balance of subacute stroke patients.



Cerebral Palsy spasticity - reduction of Satellite Cells

[J Orthop Res.](#) 2015 Jul;33(7):1039-45. doi: 10.1002/jor.22860. Epub 2015 Apr 10.

Reduced satellite cell number in situ in muscular contractures from children with cerebral palsy.

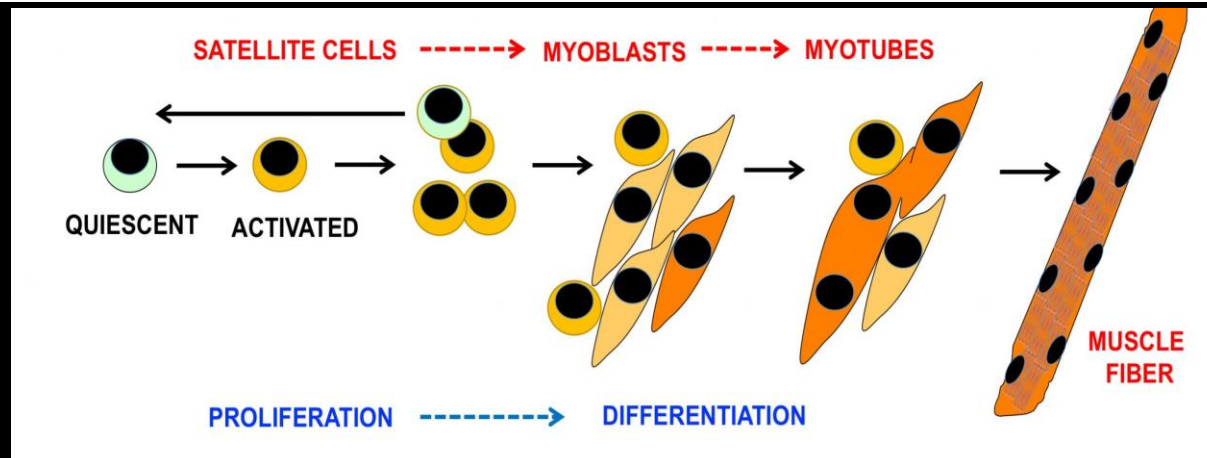
[Dayanidhi S](#)^{1,2}, [Dykstra PB](#)¹, [Lyubasyuk V](#)¹, [McKay BR](#)³, [Chambers HG](#)^{1,4}, [Lieber RL](#)^{1,2,5}.

Children with cerebral palsy suffer impaired muscular growth and contractures.

Satellite cells are muscle stem cells critical for post-natal growth, regeneration and repair of skeletal muscles.

Conclusion:

- Loss of satellite stem cells results in increase in collagen deposition causing muscle stiffness - a result of non-use.
- Children with spastic CP have a reduced number of satellite stem cells.
- Reduced satellite stem cells results in impaired muscle growth and a decreased responsiveness of CP muscle to exercise.



HBOT increases production and satellite cell differentiation

[J Appl Physiol \(1985\)](#). 2014 Jan 15;116(2):149-55. doi: 10.1152/jappphysiol.00235.2013. Epub 2013 Dec 12.

Enhancement of satellite cell differentiation and functional recovery in injured skeletal muscle by hyperbaric oxygen treatment.

Horie M¹, Enomoto M, Shimoda M, Okawa A, Miyakawa S, Yagishita K.

Abstract:

- The use of hyperbaric oxygen (HBO) treatments by elite athletes to accelerate recovery from muscle injuries has become increasingly popular.
- Study: Rats were placed in an animal chamber with 100% oxygen under 2.5 atmospheres absolute for 2 h/day, 5 days/wk. for 2 wk.

Results:

- The cross-sectional areas and maximum force-producing capacity of the regenerating muscle fibers were increased by HBO treatment after injury.
- The mRNA expression of MyoD, myogenin, and IGF-1 increased significantly in the HBO group at 3 and 5 days after injury. The number of Pax7(+)/MyoD(+), Pax7(-)/MyoD(+), and Pax7(+)/BrdU(+) positive nuclei was increased by HBO treatment.

Conclusion:

- HBO treatment accelerated satellite cell proliferation and myofiber maturation in rat muscle.
- HBO treatment accelerates healing and functional recovery after muscle injury.



SPECT Hypoperfusion Cerebral Palsy

Int J Clin Exp Med. 2015 Jan 15;8(1):1101-7. eCollection 2015.

99mTc-ECD brain perfusion SPECT imaging for the assessment of brain perfusion in cerebral palsy (CP) patients with evaluation of the effect of hyperbaric oxygen therapy.

Asl MT¹, Yousefi F², Nemati R², Assadi M³.

11 CP patients were enrolled in this study, of which 4 patients underwent oxygen therapy.

Before oxygen therapy and at the end of **40 sessions of oxygen treatment**, SPECT was performed, and the results were compared.

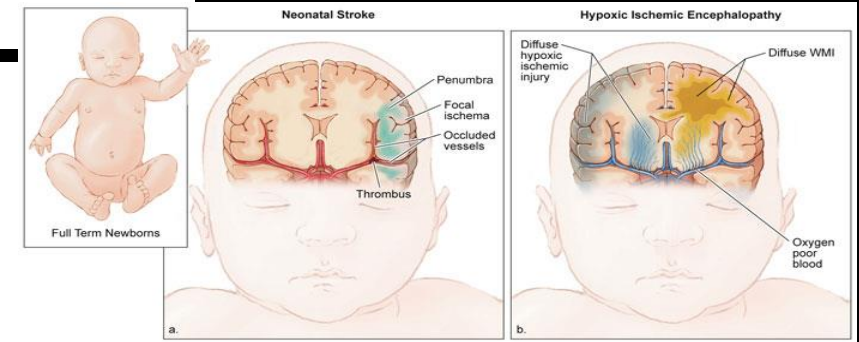
RESULTS:

- 11 CP patients; 7 females and 4 males age range of 5-27 years.
- SPECT studies - all the patients showed perfusion impairments.
- The region most significantly involved was **frontal lobe (54.54%), followed by temporal lobe (27.27%), occipital lobe (18.18%), visual cortex (18.18%), basal ganglia (9.09%), parietal lobe (9.09%), and the cerebellum (9.09%).**
- **Frontal-lobe hypoperfusion was seen in all types of cerebral palsy.**



CONCLUSION:

- Study demonstrated decreased cerebral perfusion in CP patients.
- Two out of 4 patients (2 males and 2 females) who underwent oxygen therapy revealed brain perfusion improvement. **HBOT improved cerebral perfusion.**
- Larger study is required to strengthen a link this approach may have some value.



LOKOMAT - Australian experience

LOKOMAT Australian Experience: Robotically Gait Assisted Body Weight Support Treadmill Training (BWSTT) – Lokomat Gait Training.

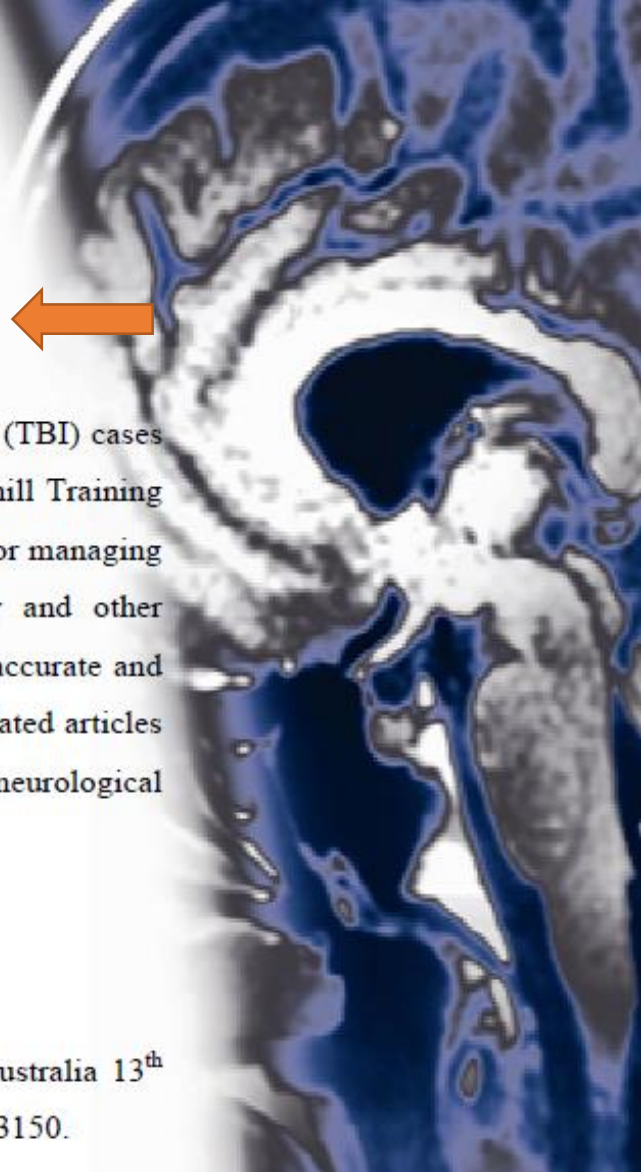
Is it an effective and financially feasible treatment?

HyperMED NeuroRecovery Centre – Melbourne, Australia. M. R. Hooper, T. Chamacham 2008.

Abstract: Growing number of adult and pediatric spinal cord injury (SCI) and traumatic brain injury (TBI) cases each year indicates an increasing need for treatment modalities, like Body Weight-Supported Treadmill Training (BWSTT) to assist functional recovery. In addition to treatment of SCI cases, BWSTT has been used for managing other various neurological diseases such as stroke and multiple sclerosis (MS), cerebral palsy and other neurodegenerative states. Robotically Gait Assisted BWSTT (Lokomat) has been shown to be more accurate and financially feasible, compared to the other BWSTT modalities. In this article, we intend to review related articles and evidence to explain the medical and financial feasibility of using this treatment modality for neurological diseases.

Keywords: locomotion, exoskeleton, locomotor training, bodyweight support, robotics

Corresponding author: Malcolm R. Hooper Director Rehabilitation HyperMED NeuroRecovery Australia 13th floor 15 Collins St Melbourne 3001. Email info@hypermed.com.au T: +61 3 9650 3136 F: +61 3 9650 3150.

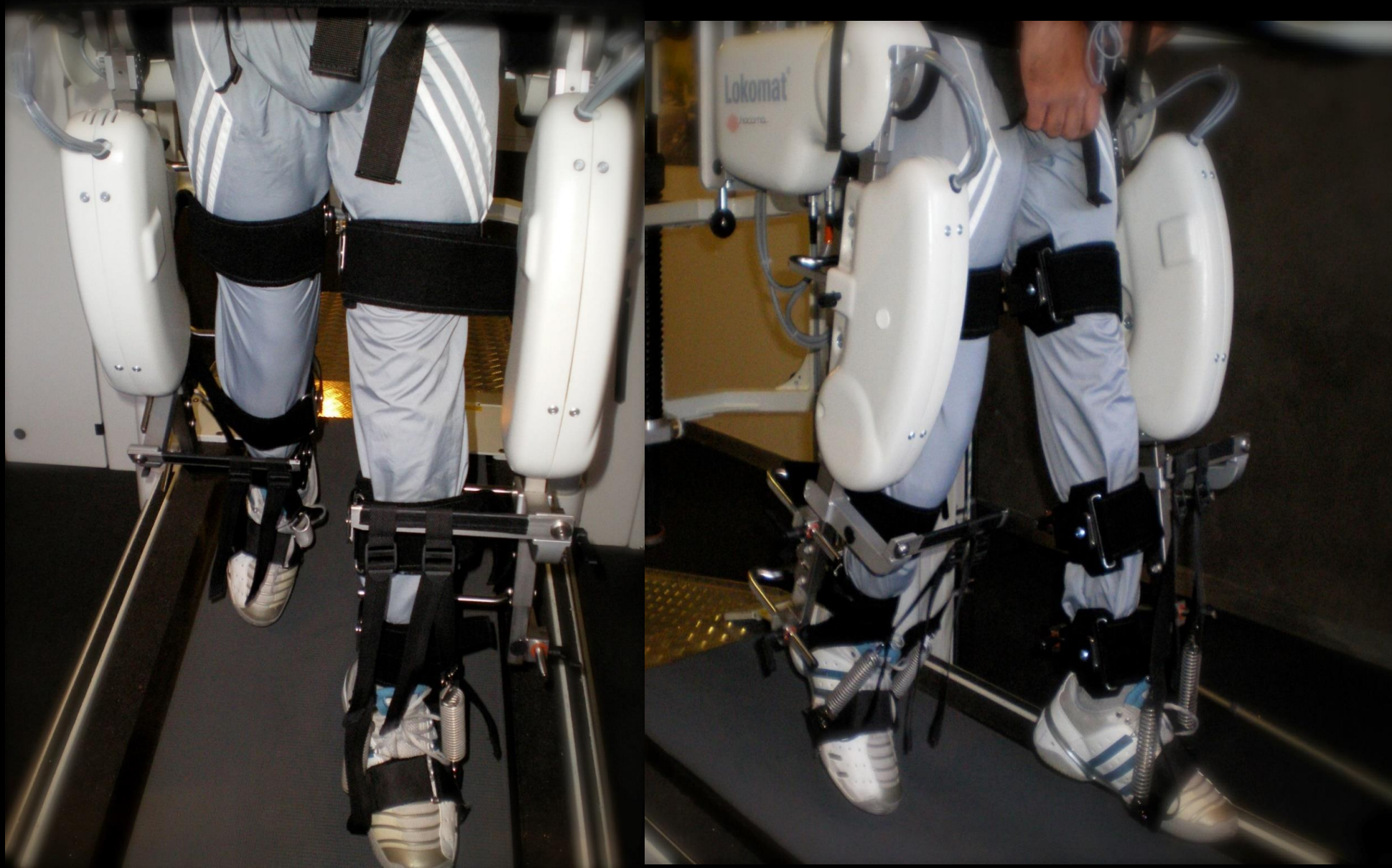


Acquired Gait Dysfunction

Children with cerebral palsy have an acquired dysfunction which their central nervous system function deems normal. This is evident when CP children undertake an intensive Lokomat Gait Training protocol. Many of these children demonstrate a 'normal gait' whilst on the Lokomat which raises question of acquired neural pathways and motor function wrongly developed and reinforced over time. When these same children come off the Lokomat they immediately return back to the acquired gait. Intensity and repetition enables the CP child to generate a new functionality which resembles a 'normal gait'. It is a frequent finding to observe the bewilderment of both parents and CP child when the child sees themselves 'walking normal' on the Lokomat. Visualization whilst on the Lokomat is an important paradigm shift for not only the CP child and parent but also the therapist.




Matching the patient



LOKOMAT Settings

Lokomat®Pro



ADJUST GAIT PATTERN

CHALLENGE PATIENT ▶

DISPLAYED ON PATIENT SCREEN

CURVE PURSUIT

||

□

SYMMETRIC

ASYMMETRIC

SENSITIVITY

▼

2

▲

PELVIS LATERAL MOVEMENT [cm]

▼

2

▲

HIP LEFT ROM [°]

▼

30

▲

HIP LEFT OFFSET [°]

▼

0

▲

KNEE LEFT ROM [°]

▼

62

▲

KNEE LEFT OFFSET [°]

▼

0

▲

HIP RIGHT ROM [°]

▼

30

▲

HIP RIGHT OFFSET [°]

▼

0

▲

KNEE RIGHT ROM [°]

▼

62

▲

KNEE RIGHT OFFSET [°]

▼

0

▲

PATHCONTROL ACTIVATION

ON

OFF

TUNNEL WIDTH

▼

SMALL

▲

ASSIST THROUGH TUNNEL [%]

▼

100

▲

BWS LATERAL MOVEMENT [% OF PELVIS LATERAL MOVEMENT]

▼

2

▲

PELVIS TIME OFFSET [%]

▼

1

▲

STOP

TREADMILL SPEED [km/h]

▼

1.5

▲

ORTHOSIS SPEED

▼

AUTO

▲

GUIDANCE FORCE [%]

▼

R 50

▲

▼

L 50

▲

○

REAL BODY WEIGHT SUPPORT

34 kg

50 %

⏻

📄

🔧

🕒

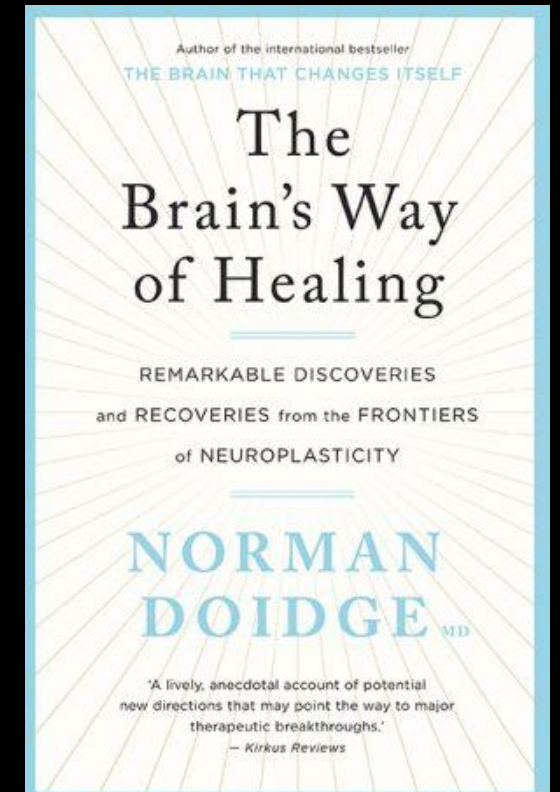
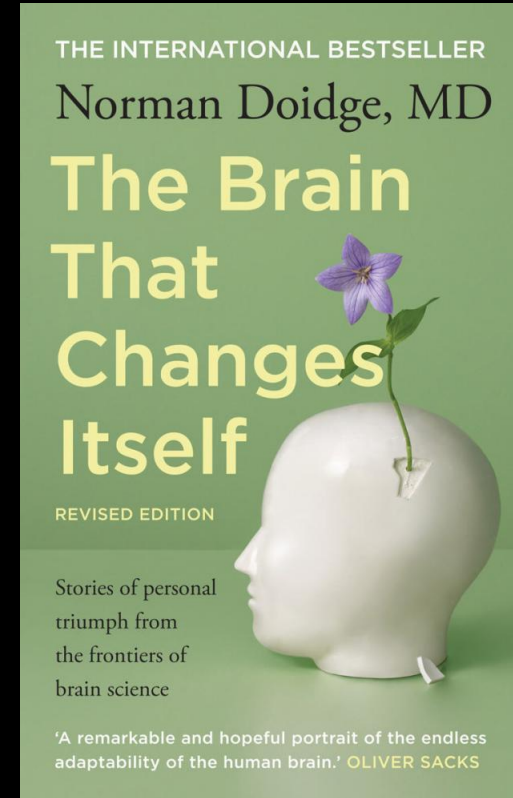
DISTANCE: 125 m

TIME: 5 min

END SESSION ▶

OXYMED

Practise makes perfect



Work with your patient



Neuroplasticity – “finding new connections”



Neuroplasticity recruitment with purpose



Hard work is required by therapist and patient

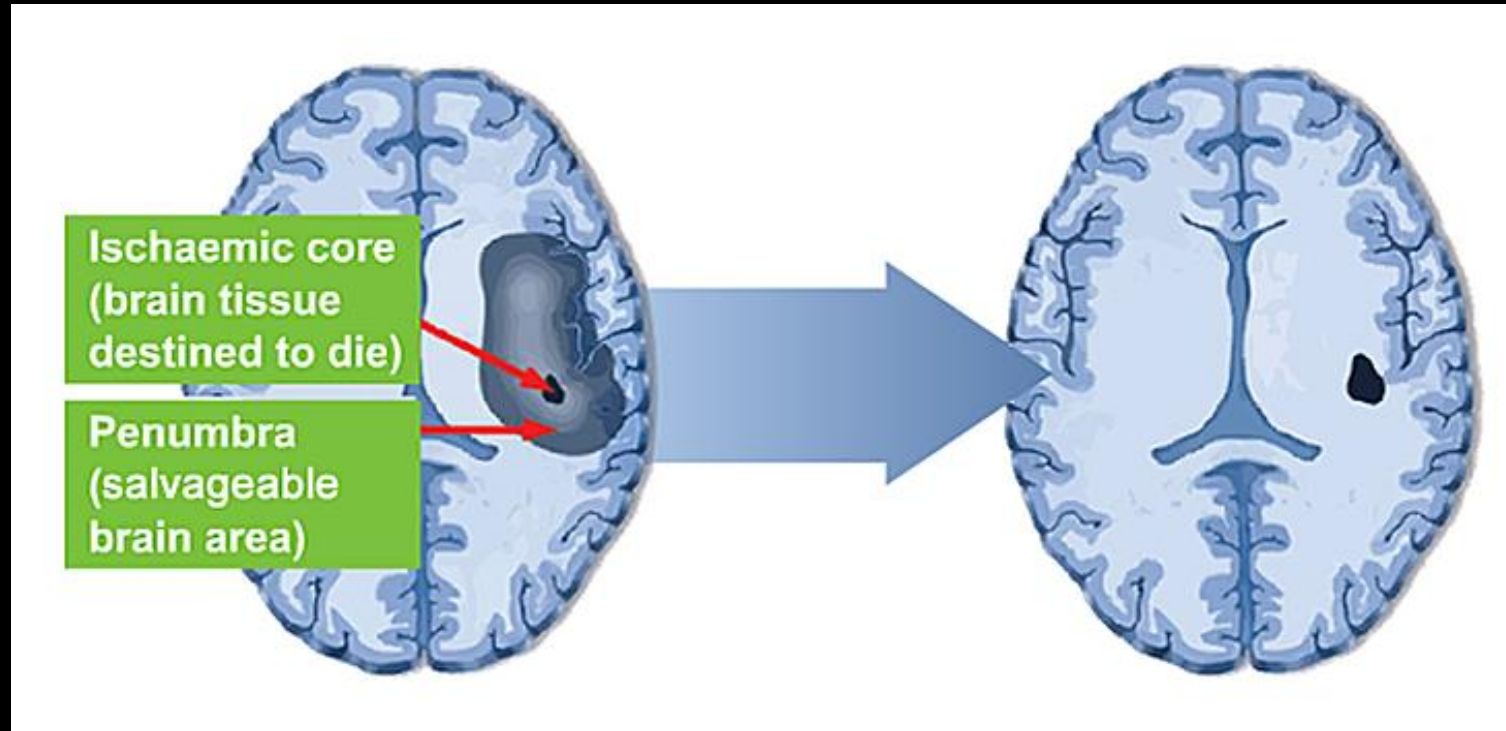


Activity based rehabilitation promotes neurovascular regeneration

THREE KEY PRINCIPLES OF MOTOR LEARNING

- **Practice** - more functional learning will occur with more **accurate practice**.
- **Specificity** - the best way to improve performance of a motor task is to **execute that specific motor task repeated many times**.
- **Effort** - individuals need to **maintain a high degree of focus, participation and involvement** to facilitate motor learning – not watching “days of our lives” and taking another ‘generic’ tablet.

These principles are critical to **promoting activity-dependent plasticity – altering the excitation patterns of neural pathways by activating those pathways**. Plasticity occurs in neural pathways that are both active and inactive



Activity stimulates plasticity, neurogenesis – “if you don’t use it ...”

[Dev Disabil Res Rev. 2009;15\(2\):112-6. doi: 10.1002/ddrr.61.](#)

Activity-based restorative therapies: concepts and applications in spinal cord injury-related neurorehabilitation.

[Sadowsky CL¹](#), [McDonald JW](#).

- The field of neurorehabilitation is changing. After years of evidence the old, deep rooted rehabilitative principles of compensation and adaptation are slowly starting to change.
- The adult injured central nervous system is capable of reorganization allowing for significant improvement following injury.
- Reorganization and plasticity occurs: cortical, subcortical, spinal cord, and in the peripheral nervous system.
- The repair process is referred to as synaptic plasticity and occurs in pre-existing connections (peripheral and central) resulting in sprouting and formation of new connections.
- “Neuroplasticity” refers to the remyelination and new cell birth correcting, restoring, and replacing the damaged nerve cells.
- Neurogenesis reported in adult brain: hippocampus and olfactory system.
- Physical activity stimulates neurogenesis - proliferation of neuronal stem cells.
- Activity reverses decline in neurogenesis associated with aging.
- Exercise activates neighbouring axons and proliferates precursor cells.



'Neural Plasticity occurs through life' (contrary to VCAT Expert Dr Churchyard 2013)

[Cell Mol Life Sci.](#) 2016 Mar;73(5):975-83. doi: 10.1007/s00018-015-2102-0. Epub 2015 Dec 8.

Physical exercise, neuroplasticity, spatial learning and memory.

[Cassilhas RC](#)^{1,2}, [Tufik S](#)³, [de Mello MT](#)⁴.

NEURONAL PLASTICITY OCCURS THROUGHOUT LIFE

- **neurogenesis, synaptic-dependent activity and the reorganization of neuronal networks.**
- The hippocampus dentate gyrus is a 'highly plastic region' able to **generate new neurons**, and can **double or triple in size after physical exercise**.
- Physical exercise induces hippocampal plasticity – **neurogenesis, cell proliferation and dendritic branching**.
- **Brain Derived Neurotrophic Factor (BDNF)** is one of the major modulators of the CNS and brain plasticity. In 1995, Neeper et al. demonstrated that physical exercise enhanced **BDNF gene expression in the hippocampus**.

NEUROTROPHIC FACTORS UP-REGULATED BY PHYSICAL EXERCISE

- **Nerve Growth Factor (NGF), Vascular Endothelial Growth Factor (VEGF), Fibroblast Growth Factor 2 (FGF-2), BDNF and Insulin Growth Factors (IGFs).**
- **Insulin Growth Factor (IgF1)** - promotes **growth, differentiation and cellular survival**. Is **upregulated in the hippocampus**. Has neurotrophic effects in the CNS and involved in **differentiation, proliferation, synaptic plasticity and neurogenesis**. IgF1 is increased in **neurogenesis & cognitive function**.
- **Physical task specific activity** requiring **hippocampus-dependent memory** expressed higher circulating levels of **IgF1 and BDNF in the hippocampus, cerebellum and spinal cord**. HBOT elevates all neurotrophic factors (IgF1, BDNF, VEGF etc).



A patient-specific muscle force estimation model for the potential use of human-inspired swing-assist rehabilitation robots

Ye Ma ✉, Shengquan Xie & Yanxin Zhang

Pages 948-964 | Received 13 Feb 2016, Accepted 27 Mar 2016, Published online: 22 Apr 2016

GAIT REHABILITATION ROBOTS, WHICH ARE PRECISE

- Swing-phase deviations are related to quadriceps spasticity, hip flexion weakness, ankle dorsiflexion weakness or spasticity, hamstring contracture, spasticity and quadriceps weakness, which will lead to inadequate knee joint flexion and extension as well as excessive knee joint flexion and extension.
- Clinical evidence shows that task-oriented repetitive intensive movement swing-phase training improved walking speeds, endurance and performance on functional tasks for individuals with neurologic gait disability.
- Gait rehabilitation robots, which are precise, rehabilitation effectiveness with high accuracy, could yield better training outcomes than traditional physiotherapists.
- Optimal control strategy should comprise task-specificity, repeatability, intensity and optimal physical and mental engagement.
- Robotic swing-assistance task-specific, intensive and non-fatigue training, can improve the locomotion ability of the incomplete SCI patient and other neurologic gait dysfunction.



Robotic Neurologic Assistance

[Dev Neurorehabil](#). 2016 Dec;19(6):410-415. Epub 2015 Apr 2.

Robot-assisted gait training might be beneficial for more severely affected children with cerebral palsy.

[van Hedel HJ](#)^{1,2,3}, [Meyer-Heim A](#)^{1,2,3}, [Rüsch-Bohtz C](#)^{1,2}.

[Eur J Paediatr Neurol](#). 2017 May;21(3):557-564. doi: 10.1016/j.ejpn.2017.01.012. Epub 2017 Feb 2.

Robotic-assisted gait training improves walking abilities in diplegic children with cerebral palsy.

[Wallard L](#)¹, [Dietrich G](#)², [Kerlirzin Y](#)², [Bredin J](#)³.

[Sci Rep](#). 2017 Oct 18;7(1):13512. doi: 10.1038/s41598-017-13554-2.

The Effects of Exoskeleton Assisted Knee Extension on Lower-Extremity Gait Kinematics, Kinetics, and Muscle Activity in Children with Cerebral Palsy.

[Restor Neurol Neurosci](#). 2017;35(5):527-536. doi: 10.3233/RNN-170745.

Robotic-assisted gait training combined with transcranial direct current stimulation in chronic stroke patients: A pilot double-blind, randomized controlled trial.

[Arch Phys Med Rehabil](#). 2018 Jul 25. pii: S0003-9993(18)30448-9. doi: 10.1016/j.apmr.2018.06.020. [Epub ahead of print]

Effects of Electromechanical Exoskeleton-assisted Gait Training on Walking Ability of Stroke Patients: A Randomized Controlled Trial.

[J Clin Neurosci](#). 2018 Feb;48:11-17. doi: 10.1016/j.jocn.2017.10.048. Epub 2017 Dec 6.

What does best evidence tell us about robotic gait rehabilitation in stroke patients: A systematic review and meta-analysis.

[Int J Neurosci](#). 2017 Nov;127(11):996-1004. doi: 10.1080/00207454.2017.1288623. Epub 2017 Feb 13.

Robotic-assisted gait training in Parkinson's disease: a three-month follow-up randomized clinical trial.

Optimal rehabilitation – combination robotics and over ground walking

Journal of Motor Behavior, Vol. 47, No. 1, 2015
Copyright © Taylor & Francis Group, LLC

REVIEW ARTICLE

Science-Based Neurorehabilitation: Recommendations for Neurorehabilitation From Basic Science

Jens Bo Nielsen¹, Maria Willerslev-Olsen¹, Lasse Christiansen¹, Jesper L. Jakob Lorentzen²

¹Department of Neuroscience and Pharmacology and Department of Nutrition, Exercise and Sport, University of Copenhagen, Copenhagen, Denmark. ²Helene Elsass Center, Charlottenlund, Copenhagen, Denmark.

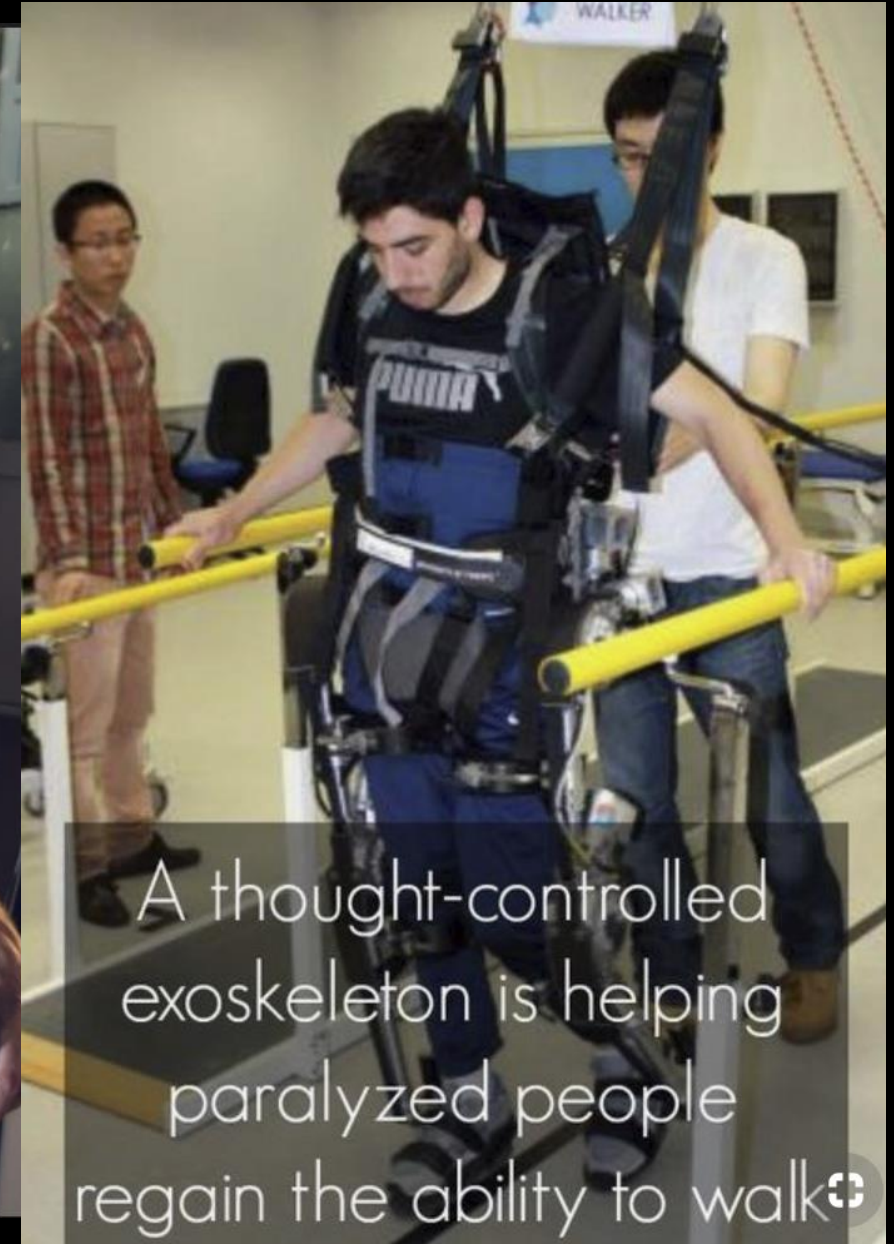
Optimal rehabilitation should involve :

- Robotic assisted devices combined with overground walking
- Active (patient) participation and engagement
- Training involving many repetitions, continues to challenge skill
- Resistance training
- Feedback error learning – changing and challenging environment
- Motivation and reward
- Intensive training and practice over a long time
- Combination training - overground training activities
- “Learn to walk by learning not to fall”



OXYMED

Robotic Virtual Reality Rehabilitation



A thought-controlled exoskeleton is helping paralyzed people regain the ability to walk 🔄

Passive Assistive Exoskeletons - Ambulatory



Passive Assistive Exoskeletons



“Variable Assist” Exoskeletons - Functional

- Today and emerging - new powered gait orthosis featuring programmable “variable assist” movements in the hip and knee joints enabling independent training and neurorehabilitation in a clinical environment and at home.



Parker



OXYMED

Adaptive Exoskeletons



Industrial Exosuits



Wearable Exosuits



Workplace Exoskeltons



A man in a blue work shirt is shown from the waist up. He is wearing a black belt-mounted battery pack and holding a wrench. The battery pack is labeled with 'GM' and 'NASA'.

GM/NASA ROBOGLOVE

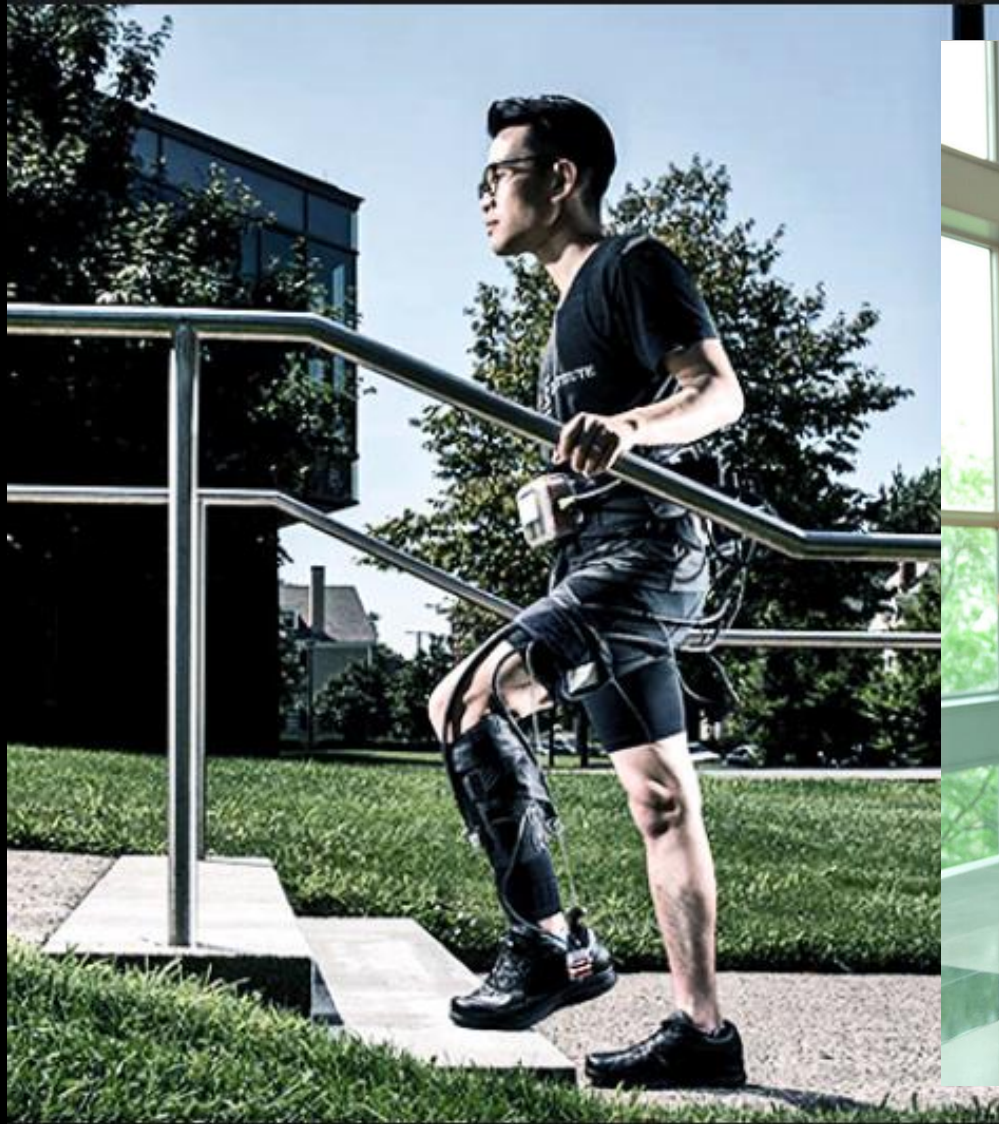
FINGER
SENSORS

PALM
SUPPORT

A close-up of the Roboglove, showing the finger sensors and palm support. The glove is black with blue accents and has a textured palm side.

BELT MOUNTED
BATTERY PACK
(actuators,
micro-controllers,
batteries)

Wearable Exosuits



OXYMED

Military Exoskeletons



Military Lite Exoskeletons



SOFT ROBOTIC EXOSUIT

*Next generation wearable robot
can enhance or restore human
movement*



Exosport suits for optimal motion and speed



Skiing, Snow Boarding



OXYMED

Tesla Exosuits

TESLASUIT TECHNOLOGY



OXYMED

Tesla Interface Exosuits

68

Haptic points

Haptic Animations

Real-time
Simulations

Weight Simulation



User calibration
profiles

Capillary system

Haptic Library

Users can create
custom animations
with Haptic Editor
application

Tesla Rehabilitation

AxonSkeleton

- Force-feedback exoskeleton
- Pairs with AxonSuit

Motion simulator

- Four-axis rotation
- Enables unlimited locomotion



AxonSkin interior lining

- Thermal and tactile feedback

Two-piece suit with gloves and boots

- Full-body coverage

Quick “snap” connectors

- Pair AxonSuit with AxonStation





Telasuit

virtual reality reinvented

The world's first full-body haptic feedback, motion capture, thermo controlled suit. Enjoy incredible real world sensations as never before.

Exo-Panda Statue - Shenyang, China



Time To Connect The Dots



The Global Crisis - Inflammation

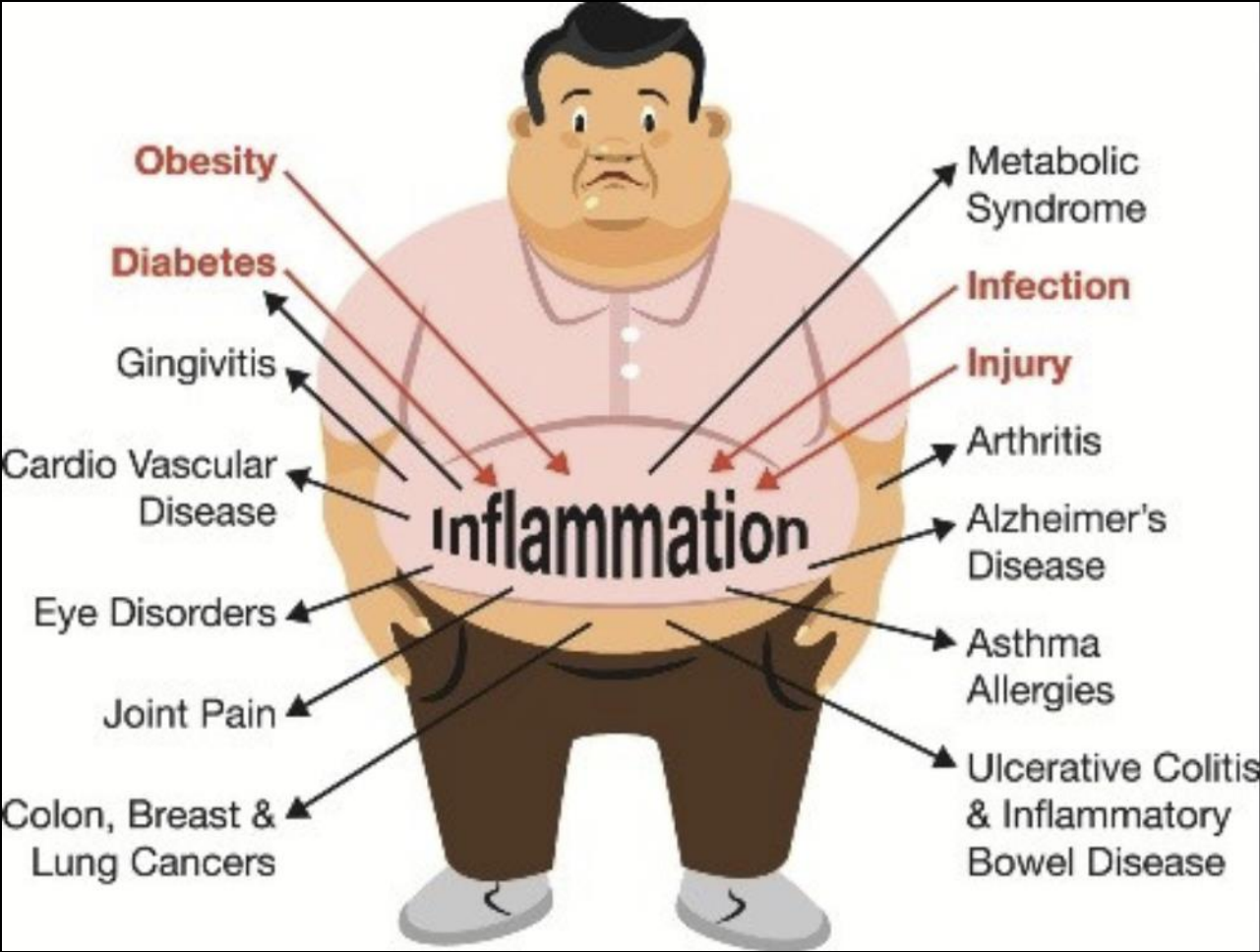
The Economist

Events

GLOBAL CRISIS OF OBESITY

Stepping up the battle against diabetes

November 2nd 2016
Madinat Jumeirah, Mina A'Salam, Dubai



Google your condition and “Cytokines” – the elephant in the room

Google cancer cytokines

All Images News Videos Shopping More Settings Tools

About 19,400,000 results (0.74 seconds)

Google autoimmune disease cytokines

All Images News Videos Shopping More Settings Tools

About 16,900,000 results (0.91 seconds)

Google proinflammatory cytokines aging and age-related diseases

All Images News Videos Shopping More Settings Tools

About 9,280,000 results (0.69 seconds)



Inflammaging and Anti-inflammaging

Arch Immunol Ther Exp (Warsz).

2016 Apr;64(2):111-26. doi: 10.1007/s00005-015-0377-3. Epub 2015 Dec 12.

The Role of Cytokines in Extreme Longevity.

Abstract

- Longevity and aging are two sides of the same coin, as they both derive from the interaction between genetic and environmental factors. Aging is a complex, dynamic biological process characterized by continuous remodeling. One of the most recent theories on aging focuses on immune response, and takes into consideration the **activation of subclinical, chronic low-grade inflammation** which occurs with aging, named "inflammaging".
- Long-lived people, especially centenarians, seem to cope with chronic subclinical inflammation through an anti-inflammatory response, called therefore "anti-inflammaging".
- In the present review, we have focused our attention on the contrast between inflammaging and anti-inflammaging systems, by evaluating the **role of cytokines and their impact on extreme longevity**.
- Cytokines are the expression of a network involving genes, polymorphisms and environment, and are involved both in inflammation and anti-inflammation.
- We have described the role of IL-1, IL-2, IL-6, IL-12, IL-15, IL-18, IL-22, IL-23, TNF- α , IFN- γ as pro-inflammatory cytokines, of IL-1Ra, IL-4, IL-10, TGF- β 1 as anti-inflammatory cytokines, and of lipoxin A4 and heat shock proteins as mediators of cytokines.
- We believe that "inflammaging is a key to understand aging".
- "Anti-inflammaging may be one of the secrets of longevity".

Cytokines 'orchestrate' immune modulation

- Cytokines 'orchestrate' & modulate immune response & gene expression.
- Cytokines modulate cell growth and differentiation, cell death (apoptosis), angiogenesis, normal development and neuromodulations.
- They are known as either **pro-inflammatory** or **anti-inflammatory**.

Biomarkers – 'The Burden of Disease'

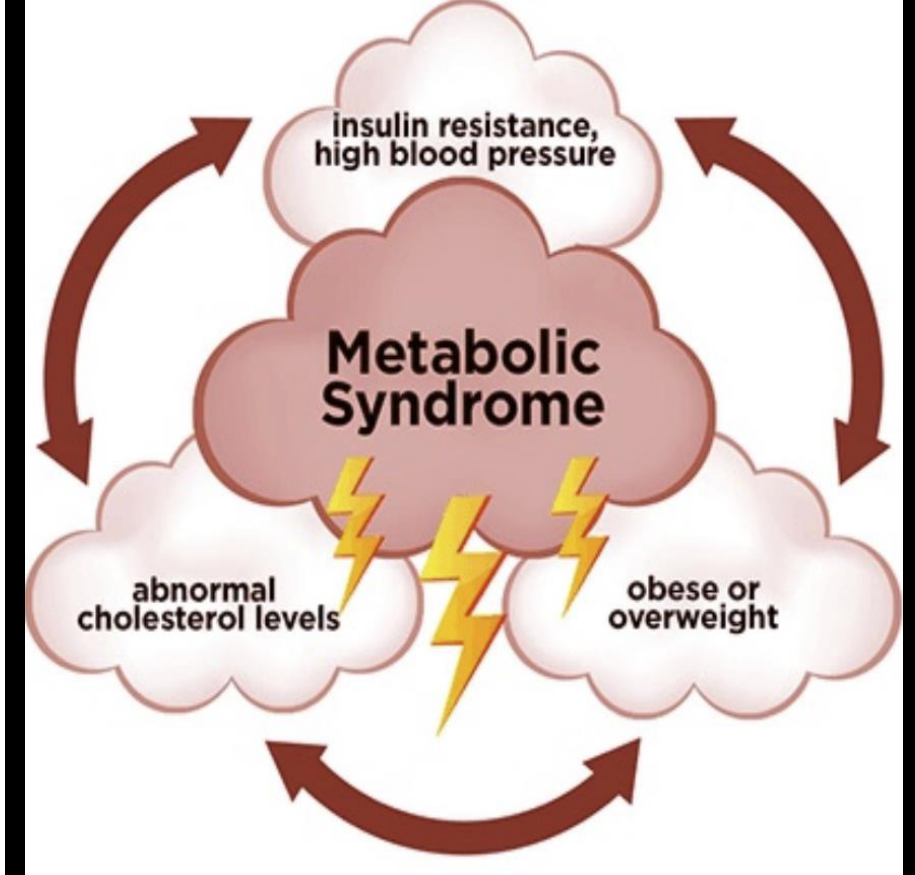
- Cytokines are both "Predictive" and "preventative analysis".

Rotten Apples

- "Autophagy Cross Talk" - Cells 'talk' to other cells – mediated by pro-inflammatory Cytokines and other glycoproteins including HIF other factors including NFkB, TGFb.

Hypoxia drives Cross-Talk accelerating disease

- Hypoxia drives molecular crosstalk of multiple pro-inflammatory loops.
- NFkB is also another key regulator in the crosstalk among the pathways leading to: arthritis, inflammatory bowel disease (IBD), colorectal cancer (CRC) and type 2 diabetes mellitus (T2DM), systemic inflammation.
- 'Hypoxic Cross Talk' plays a major role in linking inflammation to cancer development through its ability to up regulate inflammatory tumor promoting cytokines - IL6, IL1 α and TNF α and genes like BCL2 and BCLXL.
- Chronic 'over-expression' and 'cross-talk' of HIF, TGF β , NFkB, TNF α , IL1, IL6, IL8 could be considered as the matchmaker between inflammation, IBD, cancer and diabetes – referred to as the Metabolic Syndrome



Mitochondria – “The Oxygen Money Meter”

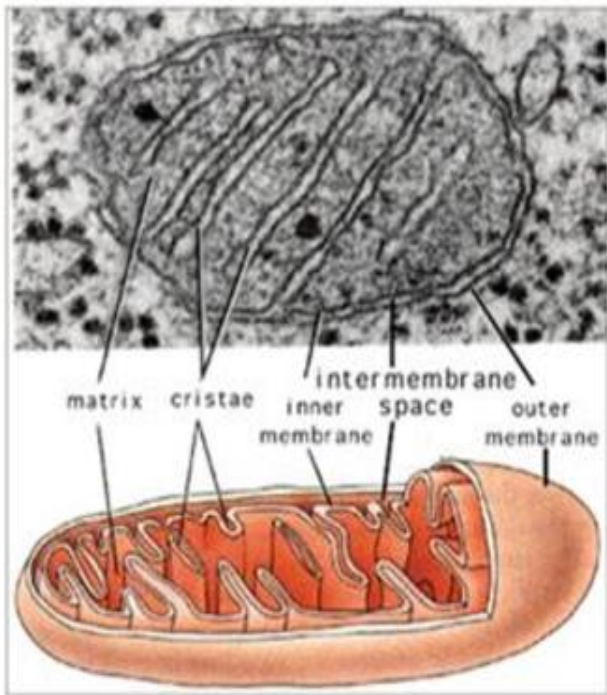
Cancer as a metabolic disease: implications for novel therapeutics

Thomas N. Seyfried, Roberto E. Flores, Angela M. Poff, Dominic P. D’Agostino

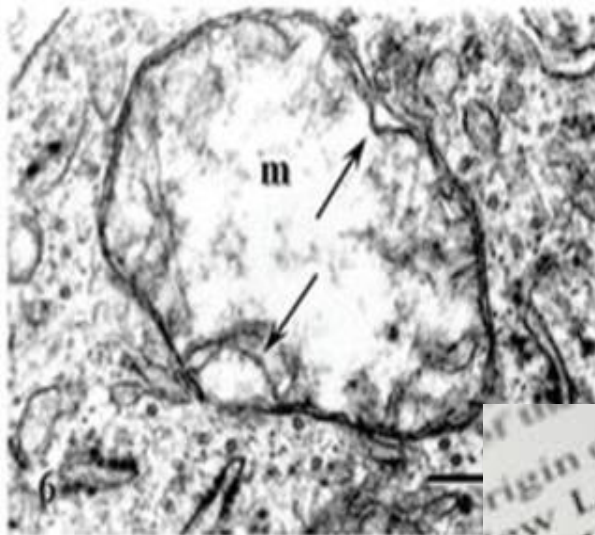
Carcinogenesis, Volume 35, Issue 3, 1 March 2014, Pages 515–527,



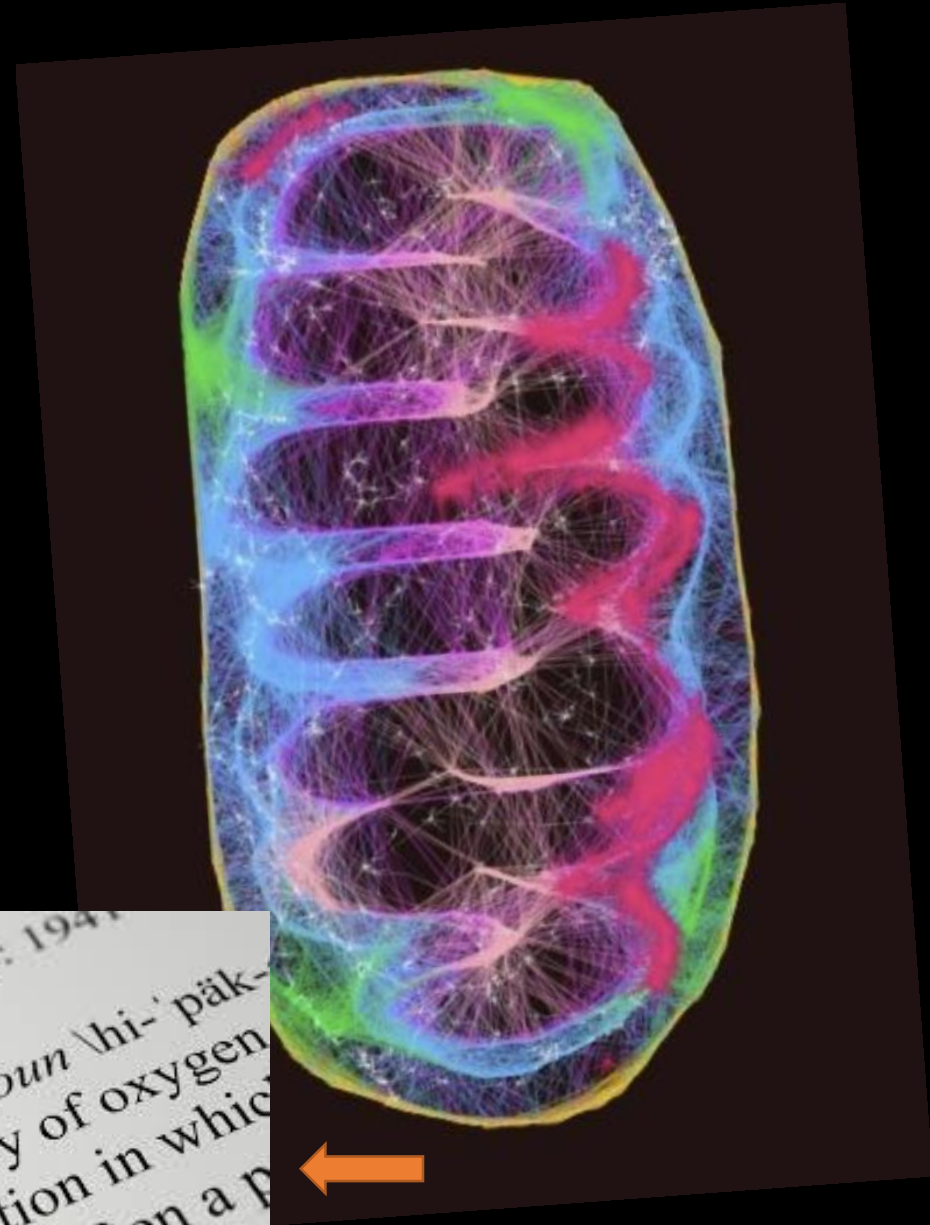
Normal Mitochondria



GBM Mitochondria

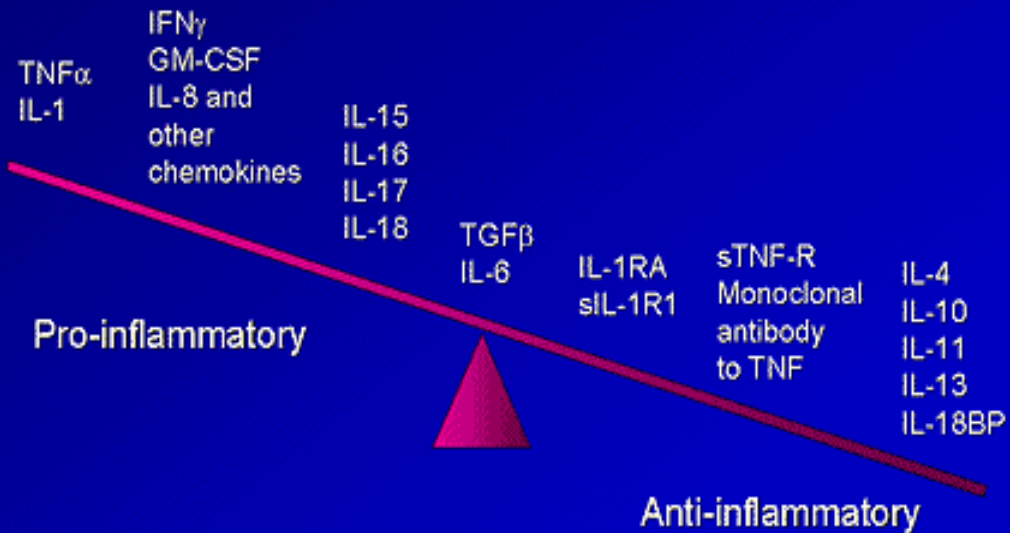


hypoxia noun \hi-'pāk-
: a deficiency of oxygen
: is a condition in which
poxia is often a p
ial oxygen



Cytokine Balance

Role of Cytokines and Cytokine Inhibitors in Chronic Inflammation



Arend. *Arthritis Rheum* 2001.

But Cytokine Storm Masks the Injury Site

Cytokine Storm makes the entire body looks inflamed, injured and infected



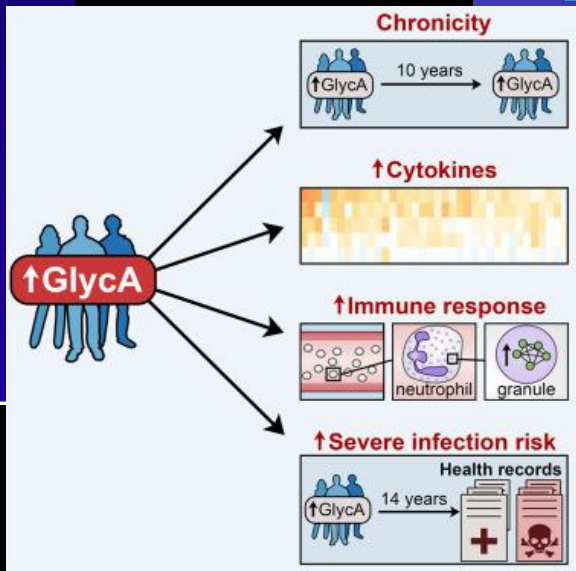
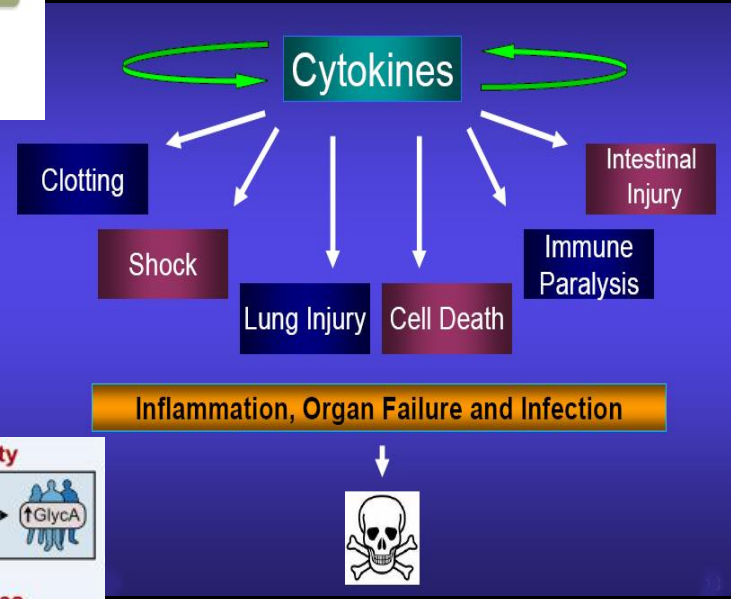
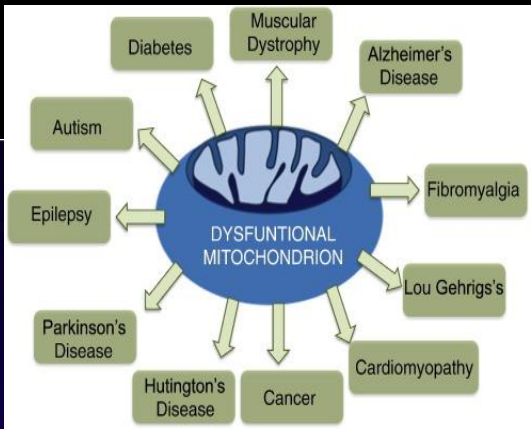
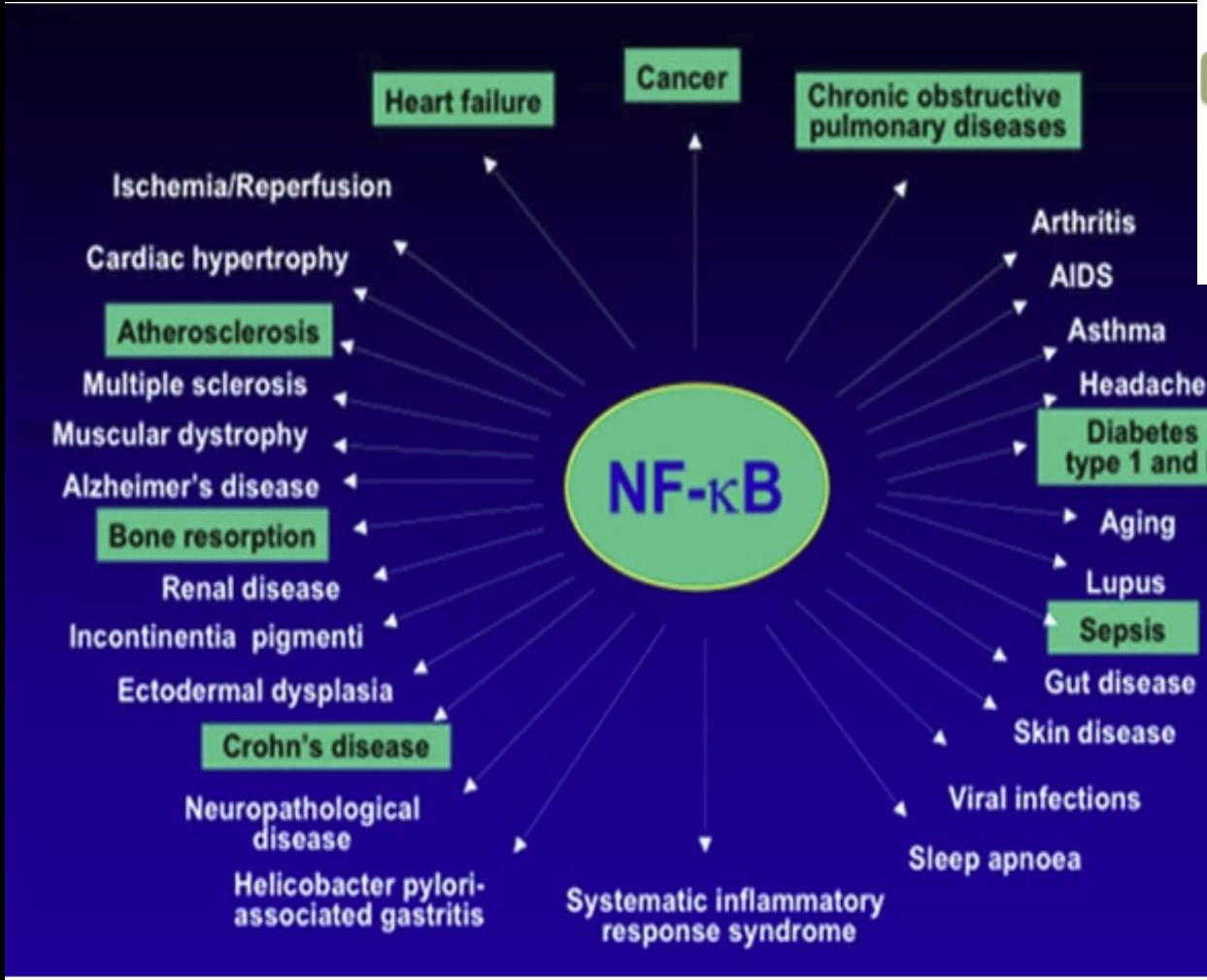
Cytokine Storm
→



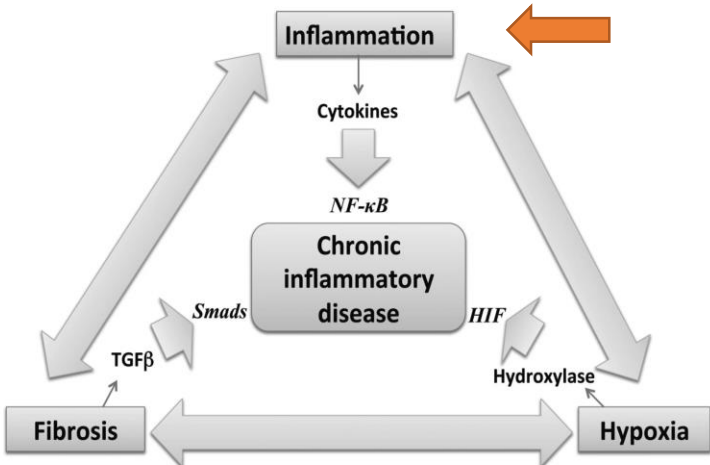
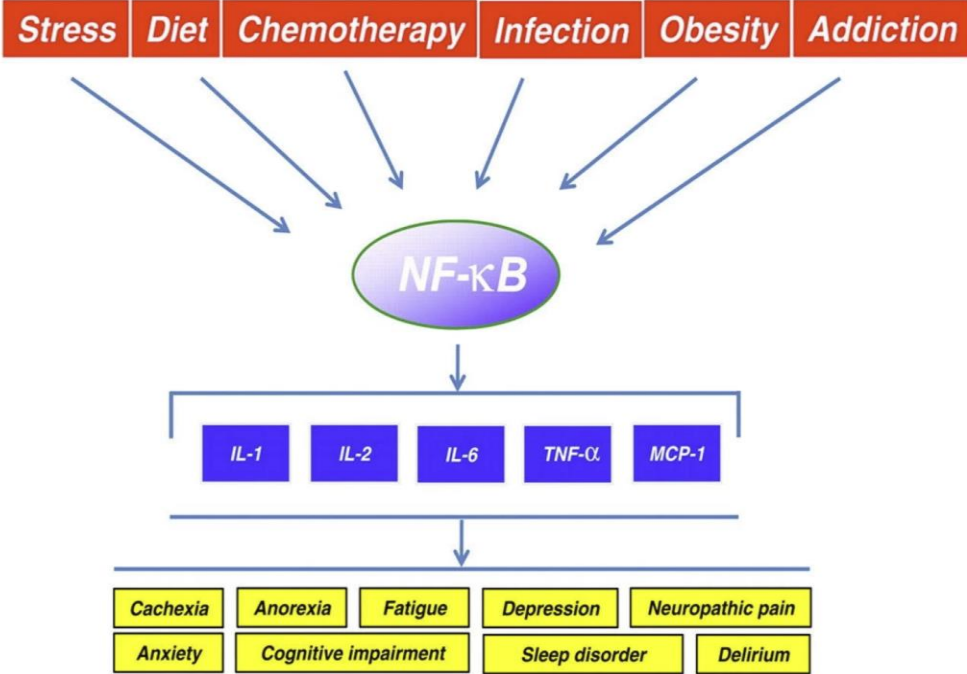
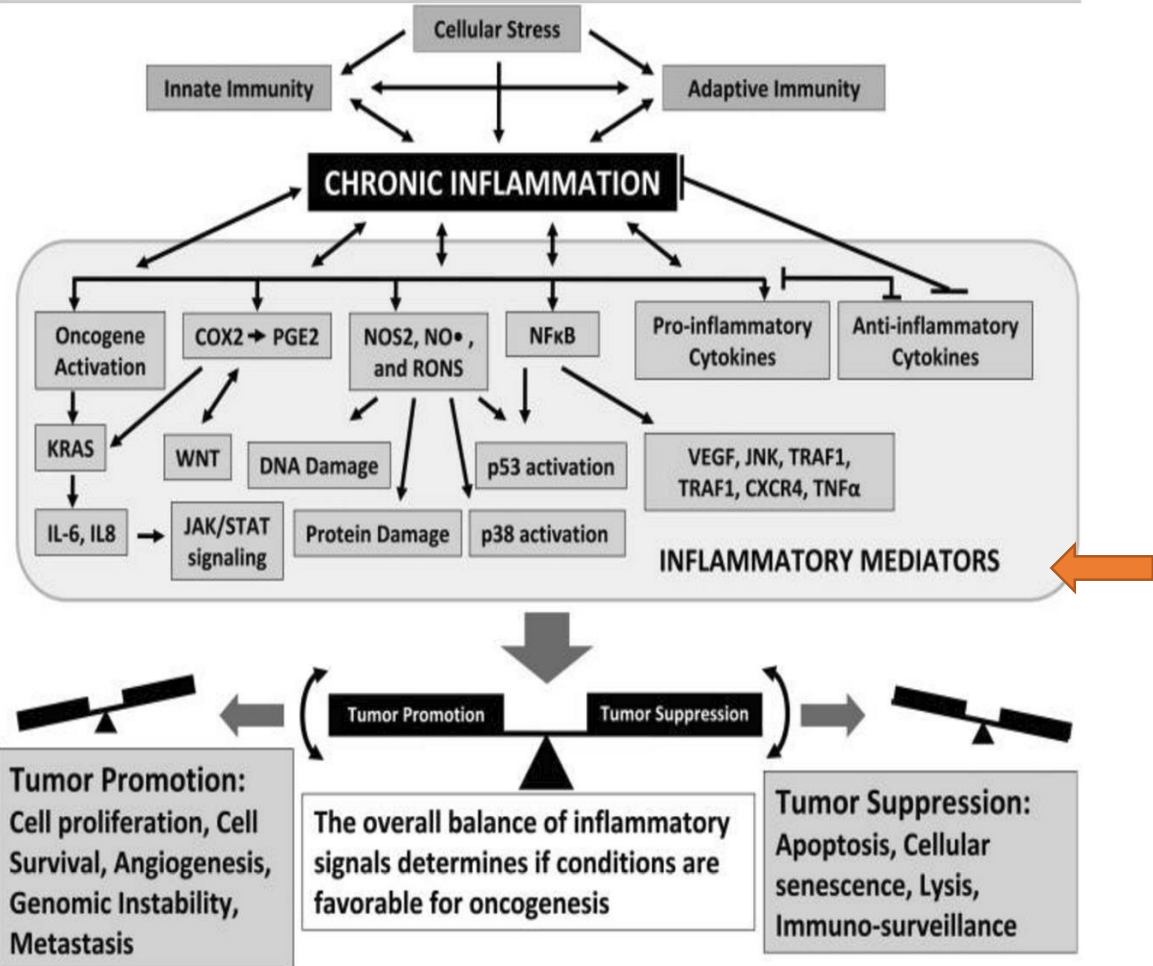
CytoSorbents

24

Pro - Inflammatory Cytokine Cascades



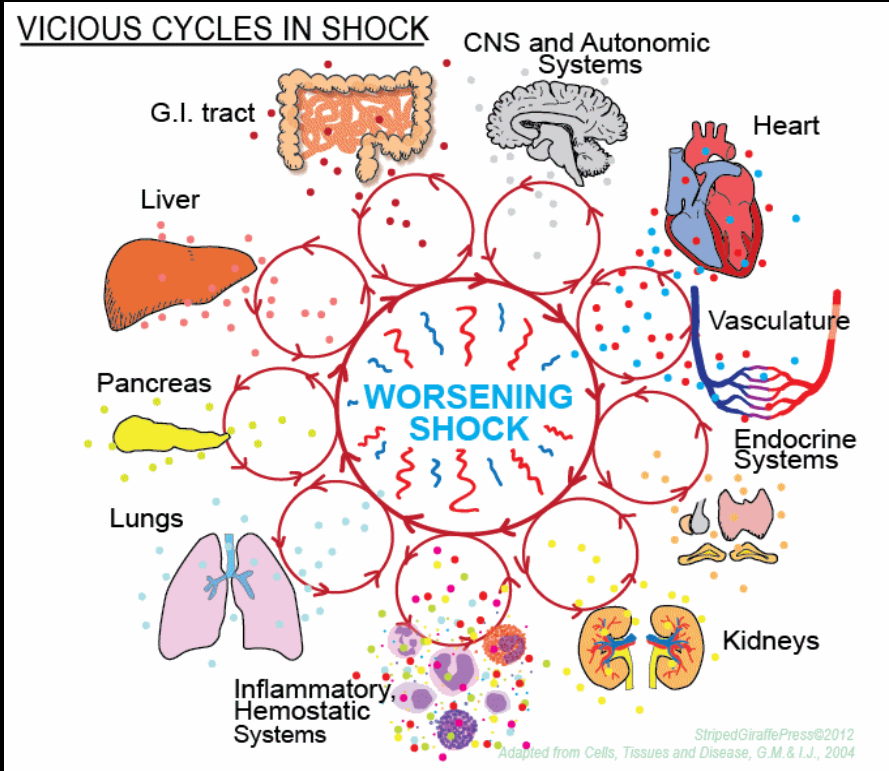
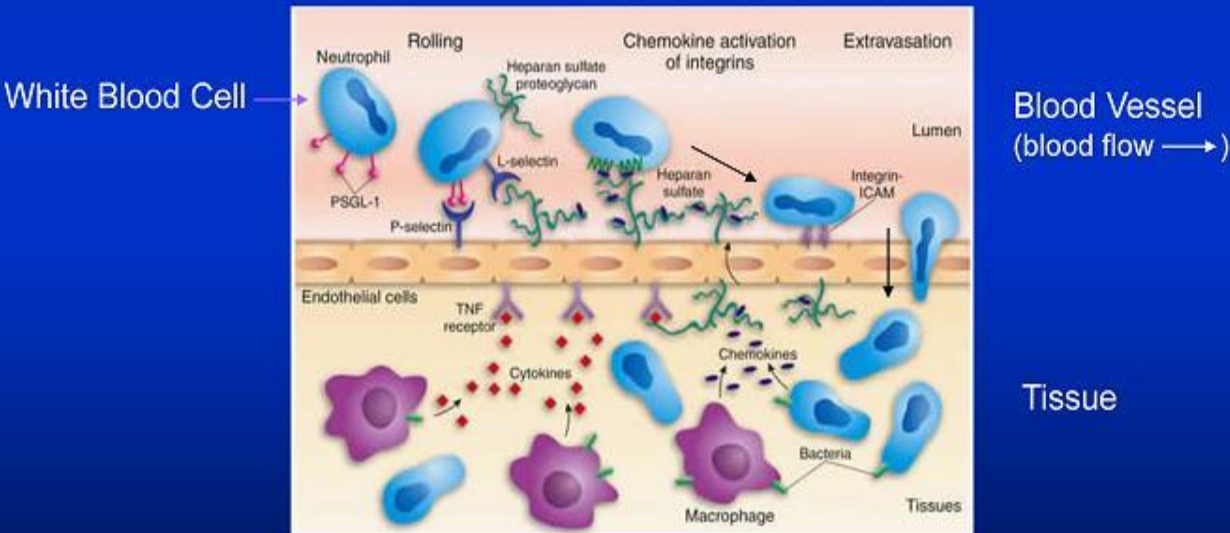
Cytokines Autophagy



Cytokine Shock – Chronic Immune Confusion

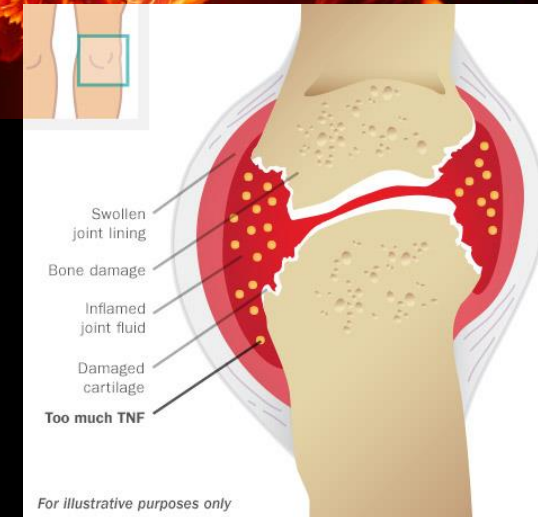
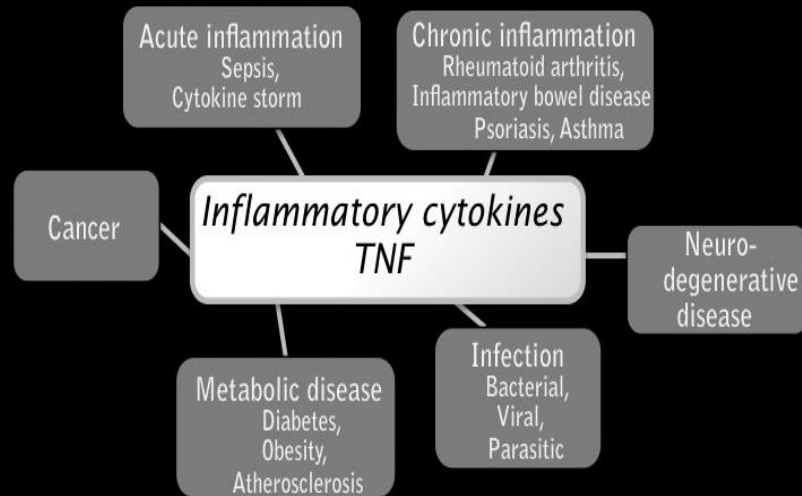
Cytokine Storm Also Causes “Immune Confusion” ←

An injury or infection usually leads to the local production of cytokines. Normally, these cytokines allow white blood cells to home in on the infection and migrate from the blood stream into the affected area.



Tumor Necrosis Factor Alpha – master regulator of inflammation

- TNF α is a cytokine produced by white blood cells, released during the **acute inflammatory response**. It plays a pivotal role in **systemic inflammation** as it induces the **synthesis of C-reactive protein, vasodilatation, and vascular permeability**.
- **Master regulator of the human inflammatory response.**
- Linked with autoimmune disorders including **chronic pain, arthritis, tendinitis**.
- **Elevated TNF α in the brain hippocampus results in atrophy** and associated with **traumatic brain injuries, chronic traumatic encephalopathy (CTE), post traumatic stress disorders, concussion syndrome and conditions depression, psychosis, addiction and dementia**.
- Elevated pro-inflammatory cytokines (IL1, IL6, IL7, IL8, S100B) and TNF α are linked with **chronic and progressive neurodegenerative disease** - often referred to as **Cytokine Storm leading to multisystem inflammatory cascade** (autoimmune erosion). The body due to autoimmune dysfunction - attacks itself!
- Reason for many 'retired' athletes combating depression and other progressive mental health issues.



Tumor Necrosis Factor Alpha – chronic pain syndromes, arthritis

[Pain](#). Author manuscript; available in PMC 2013 Sep 1.

Published in final edited form as:

[Pain](#). 2012 Sep; 153(9): 1871–1882.

Published online 2012 Jul 4. doi: [10.1016/j.pain.2012.05.028](#)

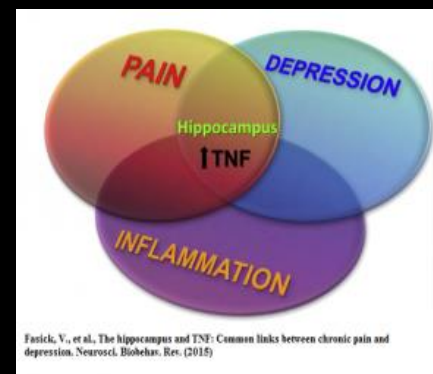
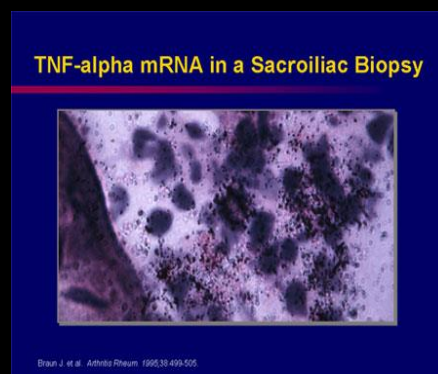
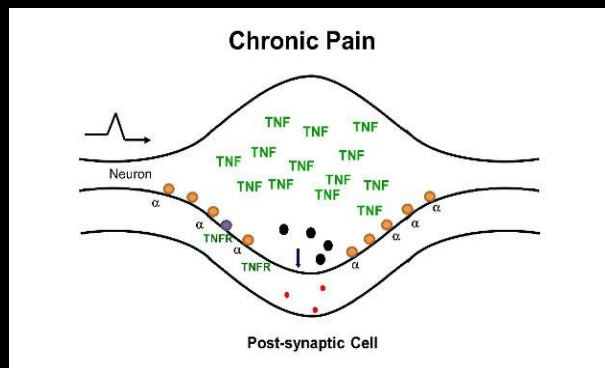
PMCID: PMC3417838

NIHMSID: NIHMS391887

PMID: 22770843

Increasing TNF Levels Solely in the Rat Hippocampus Produces Persistent Pain-like Symptoms

- This review discusses the interaction between **depression and chronic pain**, emphasizing the fundamental role of the **hippocampus** in the development and maintenance of both disorders. **Reduced CBF to the hippocampus results in TNF α overexpression** coupled with other proinflammatory chemokines.
- **Hippocampus expressed TNF α serves as a therapeutic target for management of chronic pain and major depressive disorder.**
- **A novel method of reducing TNF - increasing BDNF levels.**
- In animal subjected to **chronic stress and pain** demonstrated **elevated TNF α associated with decreased BDNF expression in the hippocampus**. Administration BDNF synthesis exerts **antidepressant and analgesic effects on chronic pain** via induction of BDNF in the brain.
- Increasing BDNF may be a novel treatment strategy for **chronic pain associated with depression**.
- HBOT down regulates TNF and upregulates BDNF.



Tumor Necrosis Factor Alpha - Etanercept



International Journal of
Molecular Sciences



Review

A New Venue of TNF Targeting

Sophie Steeland ¹ , Claude Libert ² and Roosmarijn E. Vandenbroucke ^{1,*}

¹ Barriers in Inflammation, VIB Center for Inflammation Research, Ghent, Department of Biomedical Molecular Biology, Ghent University, 9052 Ghent, Belgium; Sophie.Steeland@irc.VIB-ugent.be

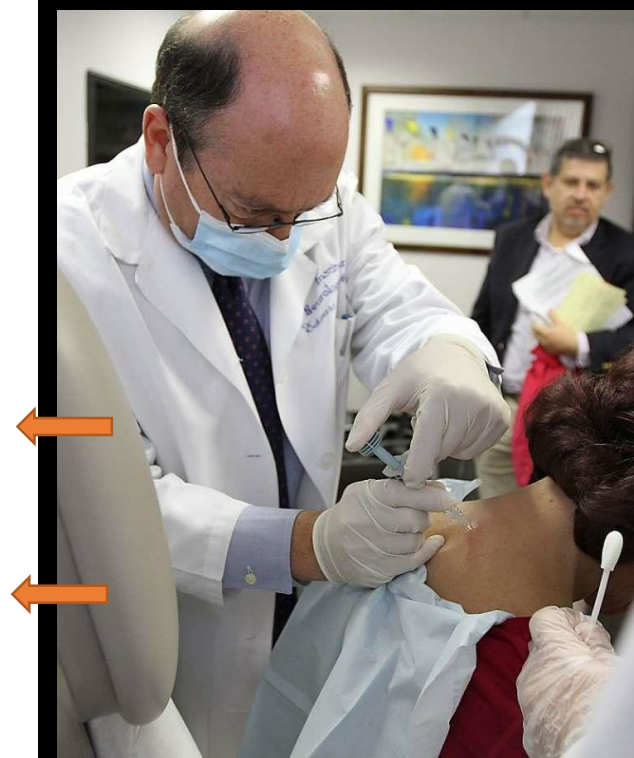
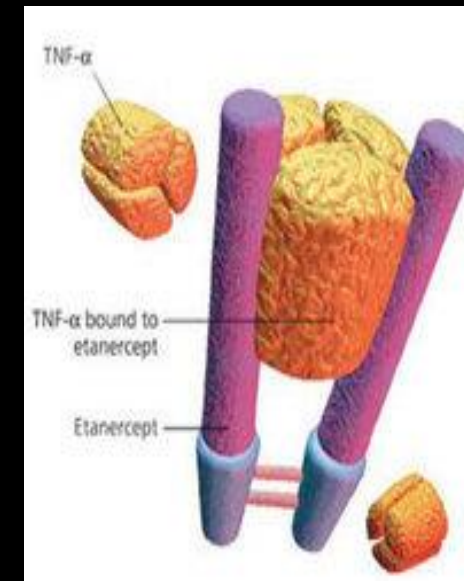
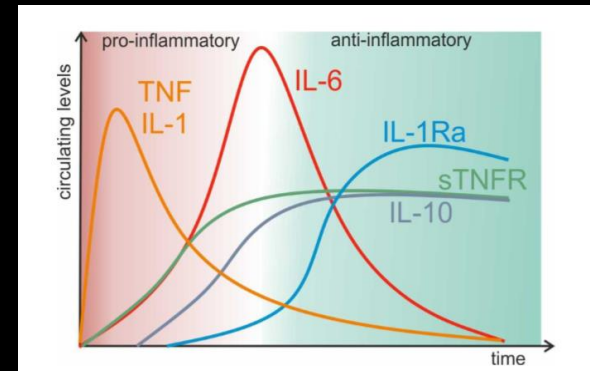
² Mouse Genetics in Inflammation, VIB Center for Inflammation Research, Ghent, Department of Biomedical Molecular Biology, Ghent University, 9052 Ghent, Belgium; Claude.Libert@irc.VIB-ugent.be

* Correspondence: Roosmarijn.Vandenbroucke@irc.VIB-ugent.be; Tel.: +32-9-331-35-87

Received: 31 March 2018; Accepted: 3 May 2018; Published: 11 May 2018



Abstract: The first Food and Drug Administration (FDA)-approved drugs were small, chemically-manufactured and highly active molecules with possible off-target effects, followed by protein-based medicines such as antibodies. Conventional antibodies bind a specific protein and are becoming increasingly important in the therapeutic landscape. A very prominent class of biologicals are the anti-tumor necrosis factor (TNF) drugs that are applied in several inflammatory diseases that are characterized by dysregulated TNF levels. Marketing of TNF inhibitors revolutionized the treatment of diseases such as Crohn's disease. However, these inhibitors also have undesired effects, some of them directly associated with the inherent nature of this drug class, whereas others are linked with their mechanism of action, being pan-TNF inhibition. The effects of TNF can diverge at the level of TNF format or receptor, and we discuss the consequences of this in sepsis, autoimmunity and neurodegeneration. Recently, researchers tried to design drugs with reduced side effects. These include molecules with more specificity targeting one specific TNF format or receptor, or that neutralize TNF in specific cells. Alternatively, TNF-directed biologicals without the typical antibody structure are manufactured. Here, we review the complications related to the use of conventional TNF inhibitors, together with the anti-TNF alternatives and the benefits of selective approaches in different diseases.



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Past head injuries – Single Photon Emission Tomography

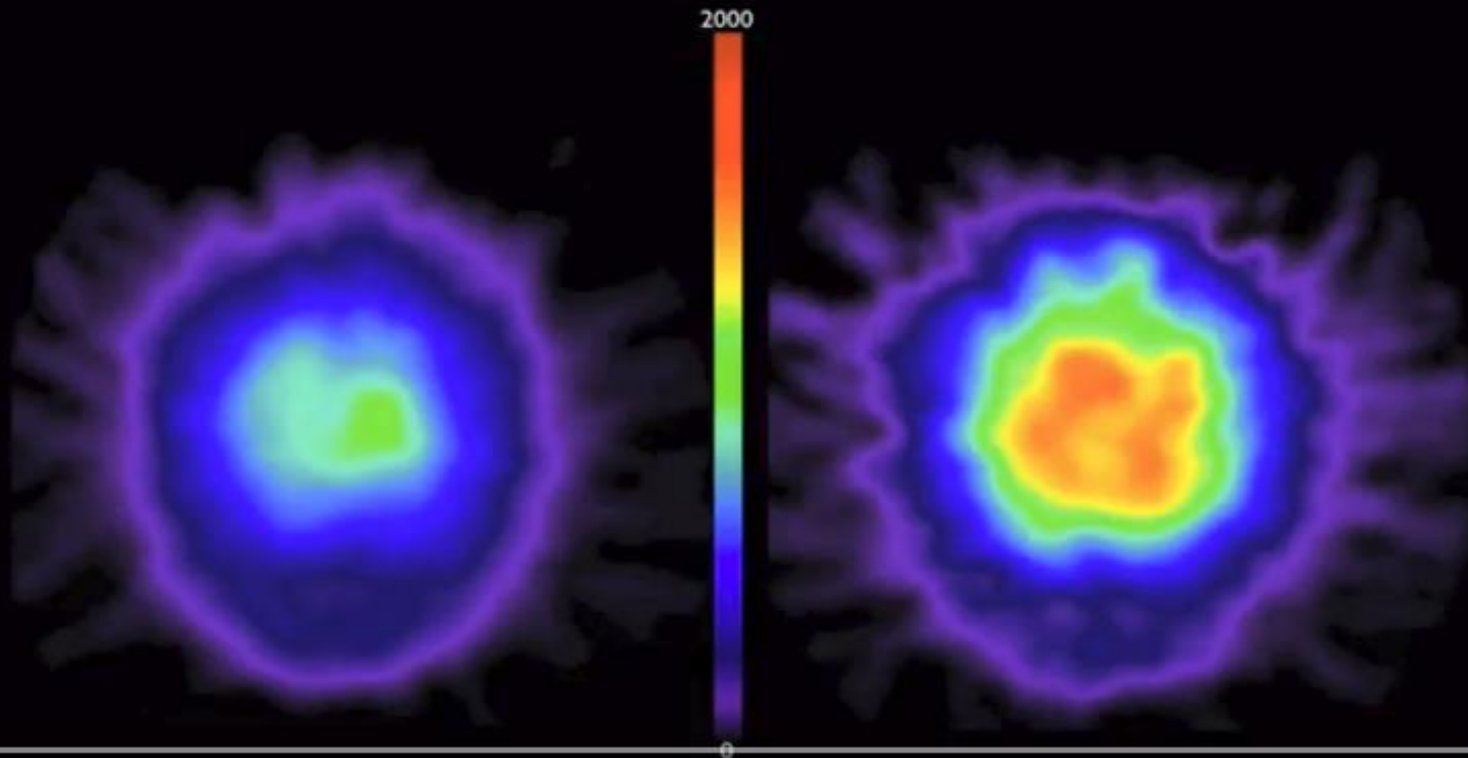
Hyperbaric Brain Scans - Before and After



Case 3

Pre-HBOT

Post HBOT(40 Dives)



▶ 🔊 0:00 / 0:14

⚙️ YouTube 🗉

"A picture is worth a 1000 words. These are side by side pre and post HBOT metabolic SPECT scans showing the improvement over time in the brain function of the individual with 40 hyperbaric therapy treatments" Dr. Ted Fogarty, MD IHMF President & Dr. Paul Harch, MD IHMA Executive Board

OXYMED

S100B – Chronic Traumatic Encephalopathy (CTE)

- S100B is a **neurobiochemical marker of brain damage** and used as a measure of BBB dysfunction.
- Elevated with **mental health** issues including **dementia, Alzheimer's** but also a marker of other systemic issues including **circulatory arrest, stroke and traumatic brain injury**.
- Elevated with **Chronic Traumatic Brain Injury (TBI and CTE), Post Traumatic Stress Disorders (PTSD), shock blast injury, concussions syndromes, blunt head injury and progressive neurodegeneration disorders**.



S100 β as marker of BBB function



S100B and the Blood Brain Barrier

Neurol Sci. 2016 Apr;37(4):533-9. doi: 10.1007/s10072-016-2521-1. Epub 2016 Feb 29.

Re-exposure to the hypobaric hypoxic brain injury of high altitude: plasma S100B levels and the possible effect of acclimatisation on blood-brain barrier dysfunction.

Winter CD^{1,2}, Whyte T³, Cardinal J^{4,5}, Kenny R⁶, Ballard E⁷.

- Hypobaric hypoxic brain injury results in elevated peripheral S100B levels which may relate to blood-brain barrier (BBB) dysfunction.

Curr Med Chem. 2016;23(15):1571-96.

Identifying S100B as a Biomarker and a Therapeutic Target For Brain Injury and Multiple Diseases.

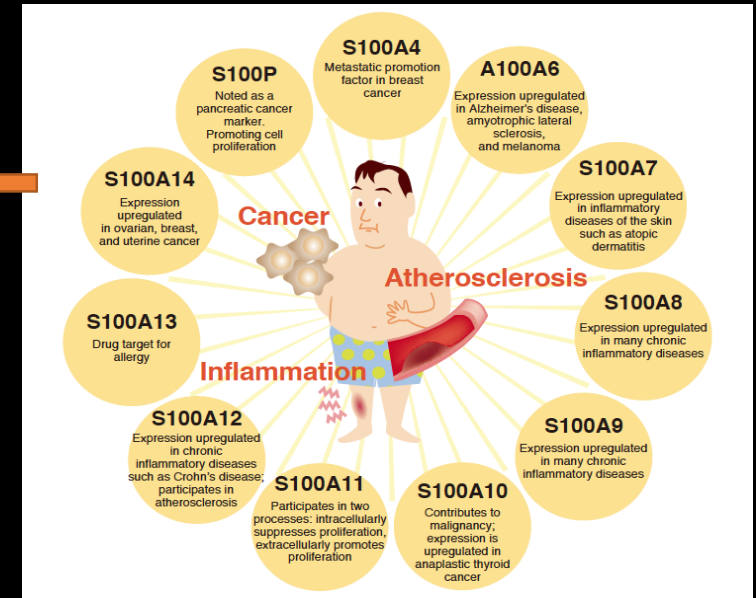
Chong ZZ¹, Changyaleket B, Xu H, Dull RO, Schwartz DE.

- S100B has attracted great attention as a biomarker for a variety of diseases.
- S100B is mainly expressed in glial cells.
- The levels of S100B in the blood may function to predict the progress or the prognosis of many kinds of diseases, such as cerebrovascular diseases, neurodegenerative diseases, motor neuron diseases, traumatic brain injury, schizophrenia, depression, diabetes mellitus, myocardial infarction, cancer, and infectious diseases.
- S100B has been implicated in the pathological process of these diseases, S100B should not be simply regarded as a biomarker, it may also function as therapeutic target for these diseases.
- The role of S100B may formulate innovative therapeutic strategies for multiple diseases.



HEAL THE WARRIORS

Traumatic Brain Injury (TBI) | Post-Concussion Syndrome (PCS)
Post-Traumatic Stress Disorder (PTSD)
Hyperbaric Oxygen Therapy - Fighting to treat the effects of TBI and PTSD



S100B – neuroinflammation regardless of location

[J Neurochem](#). 2018 Aug 24. doi: 10.1111/jnc.14574. [Epub ahead of print]

The S100B story: From biomarker to active factor in neural injury.

[Michetti F](#)^{1,2}, [D'Ambrosi N](#)³, [Toesca A](#)¹, [Puglisi MA](#)¹, [Serrano A](#)¹, [Marchese E](#)¹, [Corvino V](#)¹, [Geloso MC](#)¹.

Author information

Abstract

S100B is a Ca^{2+} -binding protein mainly concentrated in astrocytes. Its levels in biological fluids (cerebrospinal fluid, peripheral and cord blood, urine, saliva, amniotic fluid) are recognized as a reliable biomarker of active neural distress. Although the wide spectrum of diseases in which the protein is involved (acute brain injury, neurodegenerative diseases, congenital/perinatal disorders, psychiatric disorders) reduces its specificity, its levels remain an important aid in monitoring the trend of the disorder. Mounting evidence now points to S100B as a Damage Associated Molecular Pattern molecule which, when released at high concentration, through its Receptor for Advanced Glycation Endproducts, triggers tissue reaction to damage in a series of different neural disorders. This review addresses this novel scenario, presenting data indicating that S100B levels and/or distribution in the nervous tissue of patients and/or experimental models of different neural disorders, for which the protein is used as a biomarker, are directly related to the progress of the disease: acute brain injury (ischemic/haemorrhagic stroke, traumatic injury), neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis), congenital/ perinatal disorders (Down syndrome, spinocerebellar ataxia-1), psychiatric disorders (schizophrenia, mood disorders), inflammatory bowel disease. In many cases, overexpression/administration of the protein induces worsening of the disease, while its deletion/inactivation produces amelioration. This review points out that the pivotal role of the protein resulting from these data, opens the perspective that S100B may be regarded as a therapeutic target for these different diseases, which appear to share some common features reasonably attributable to neuroinflammation, regardless their origin. This article is protected by copyright. All rights reserved.

S100B – marker to burden of disease, treatment resistance

[Biol Trace Elem Res.](#) 2018 Aug 14. doi: 10.1007/s12011-018-1463-2. [Epub ahead of print]

Chronic Oral Arsenic Exposure and Its Correlation with Serum S100B Concentration.



[Hum Mol Genet.](#) 2018 Aug 2. doi: 10.1093/hmg/ddy288. [Epub ahead of print]

Targeting RAGE as a potential therapeutic approach to Duchenne muscular dystrophy.



[Eur Arch Psychiatry Clin Neurosci.](#) 2018 Aug 6. doi: 10.1007/s00406-018-0928-9. [Epub ahead of print]

Cerebrospinal fluid markers analysis in the differential diagnosis of dementia with Lewy bodies and Parkinson's disease dementia.

[Cancer Lett.](#) 2018 Aug 1. pii: S0304-3835(18)30498-1. doi: 10.1016/j.canlet.2018.07.034. [Epub ahead of print]

S100B Suppression Alters Polarization of Infiltrating Myeloid-Derived Cells in Gliomas and Inhibits Tumor Growth.



[Ageing Res Rev.](#) 2018 Jul 30. pii: S1568-1637(18)30093-X. doi: 10.1016/j.arr.2018.07.004. [Epub ahead of print]

Towards frailty biomarkers: Candidates from genes and pathways regulated in aging and age-related diseases.



[Oncol Rep.](#) 2018 Sep;40(3):1574-1582. doi: 10.3892/or.2018.6527. Epub 2018 Jun 27.

S100B promotes chemoresistance in ovarian cancer stem cells by regulating p53.



[Alcohol Clin Exp Res.](#) 2018 Jun 28. doi: 10.1111/acer.13796. [Epub ahead of print]

S100B and Inflammatory Cytokine Levels in Blood as Potential Markers of Blood-Brain Barrier Damage and Psychiatric Impairment in Comorbid Hepatitis C Viral Infection and Alcohol Use Disorder.



TNF α , IL1, S100B elevation suppresses BDNF

[Neural Regen Res.](#) 2018 Oct;13(10):1693-1704. doi: 10.4103/1673-5374.238604.

Depression following a traumatic brain injury: uncovering cytokine dysregulation as a pathogenic mechanism.

[Bodnar CN](#)¹, [Morganti JM](#)², [Bachstetter AD](#)¹.

Author information

Abstract

A substantial number of individuals have long-lasting adverse effects from a traumatic brain injury (TBI). Depression is one of these long-term complications that influences many aspects of life. Depression can limit the ability to return to work, and even worsen cognitive function and contribute to dementia. The mechanistic cause for the increased depression risk associated with a TBI remains to be defined. As TBI results in chronic neuroinflammation, and priming of glia to a secondary challenge, the inflammatory theory of depression provides a promising framework for investigating the cause of depression following a TBI. Increases in cytokines similar to those seen in depression in the general population are also increased following a TBI. Biomarker levels of cytokines peak within hours-to-days after the injury, yet pro-inflammatory cytokines may still be elevated above physiological levels months-to-years following TBI, which is the time frame in which post-TBI depression can persist. As tumor necrosis factor α and interleukin 1 can signal directly at the neuronal synapse, pathophysiological levels of these cytokines can detrimentally alter neuronal synaptic physiology. The purpose of this review is to outline the current evidence for the inflammatory hypothesis of depression specifically as it relates to depression following a TBI. Moreover, we will illustrate the potential synaptic mechanisms by which tumor necrosis factor α and interleukin 1 could contribute to depression. The association of inflammation with the development of depression is compelling; however, in the context of post-TBI depression, the role of inflammation is understudied. This review attempts to highlight the need to understand and treat the psychological complications of a TBI, potentially by neuroimmune modulation, as the neuropsychiatric disabilities can have a great impact on the rehabilitation from the injury, and overall quality of life.



[J Stroke Cerebrovasc Dis.](#) 2018 Aug 24. pii: S1052-3057(18)30356-2. doi: 10.1016/j.jstrokecerebrovasdis.2018.06.032. [Epub ahead of print]

Brain-Derived Neurotrophic Factor Levels are Lower in Chronic Stroke Patients: A Relation with Manganese-dependent Superoxide Dismutase ALA16VAL Single Nucleotide Polymorphism through Tumor Necrosis Factor- α and Caspases Pathways.



IL1- systemic inflammation, stroke, gut & brain link

J Transl Med. 2009; 7: 97.

PMCID: PMC2780998

Published online 2009 Nov 17. doi: [10.1186/1479-5876-7-97](https://doi.org/10.1186/1479-5876-7-97)

Inflammatory mechanisms in ischemic stroke: therapeutic approaches

- IL1 is linked with **systemic inflammation** including the '**gut and brain connection**'.
- Patients with **chronic irritable bowel** and chronic disease are often elevated with IL1 and IL8.
- In stroke patients, IL1 caused a **severe reduction in cerebral blood flow and an increase in infarct volume**. Blockade of endothelin-1 receptors reversed this hypoperfusion, reduced tissue damage, and improved functional outcome.
- Post stroke, IL1 mediates inflammatory effects (in red) – **negative cascade** - including **increased adhesion molecules, neutrophil infiltration, reduced BBB integrity, decreased blood flow**.
- Elevated IL1 on astrocytes reveal increased IL6, TNFα and other chemokines.
- Elevated IL1 inhibits stroke repair – **reduced neurogenesis**.
- Elevations in serum levels and **joint fluids** (synovial fluids) are detected in **rheumatoid arthritis**.

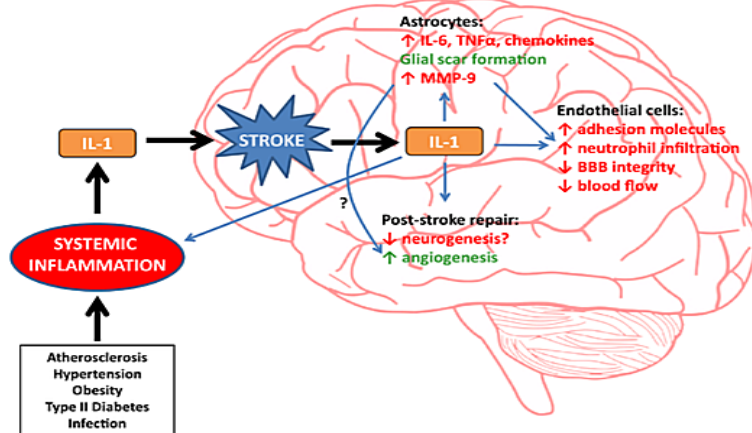


Figure. Mechanisms of interleukin-1 (IL-1) action in stroke. Stroke-related comorbidities and risk factors are associated with a raised systemic inflammatory profile, mediated in part by IL-1. Post-stroke increases in IL-1 in the brain mediate detrimental (indicated in red) inflammatory processes in the acute phase that contribute to worse outcome. In the subacute and chronic phase after stroke, certain actions of IL-1 may be beneficial (indicated in green). Figure provided and used with permission courtesy of Christopher Hoyle, University of Manchester, United Kingdom. MMP indicates matrix metalloproteinases; and TNF, tumor necrosis factor.

IL6 – systemic blood vessel inflammation, neurovascular degeneration

Published online 2014 Oct 13. doi: [10.1016/j.ygeno.2014.10.003](https://doi.org/10.1016/j.ygeno.2014.10.003)

Whole Blood Gene Expression and Interleukin-6 Levels

Shock. 2013 Dec; 40(6): 471–475.
doi: [10.1097/SHK.0000000000000037](https://doi.org/10.1097/SHK.0000000000000037)

INTERLEUKIN 6 MEDIATES NEUROINFLAMMATION AND MOTOR COORDINATION DEFICITS AFTER MILD TRAUMATIC BRAIN INJURY AND BRIEF HYPOXIA IN MICE

Atherosclerosis. 2018 Aug 24. pii: S0021-9150(18)31247-4. doi: [10.1016/j.atherosclerosis.2018.07.037](https://doi.org/10.1016/j.atherosclerosis.2018.07.037). [Epub ahead of print]

Corrigendum to "Interleukin-6 is an independent predictor of progressive atherosclerosis in the carotid artery: The Tromsø study" [*Atherosclerosis* 271 (April 2018) 1-8].

- IL6 is an important biomarker in monitoring inflammatory responses. IL-6 is involved in the **induction of acute phase responses and induction of fever**.
- Elevated serum levels of IL6 are also found in patients with **chronic inflammatory arthritis and traumatic arthritis**. IL6 is a cytokine with a wide variety of biological functions. It is a potent lymphoid cell growth factor that stimulates the growth and survivability of certain B cells and T cells. It plays an essential role in the final differentiation of b-cells into Ig-secreting cells, it induces myeloma and plasmacytoma growth, it induces nerve cells differentiation and in hepatocytes it induces acute phase reactants.
- IL6 can increase up to a **1,000-fold during trauma and infection**. Chronic elevation of serum IL-6 is associated with the **progression of atherosclerosis** in patients with **vascular risk factors**.
- Elevated IL6 but not CRP in midlife, **predicts cognitive decline and dementia**.
- IL6 elevation associated with **chronic lumbar radicular pain**. Persistent increase of the pro-inflammatory substances IL6 and IL8 in serum after **disc herniation**.
- IL6 is a **growth and survival factor in human glioblastoma cells** and plays an important role in **malignant progression**. Its increased levels have been associated with **elevated cancer risk**, and also these levels have been found to be a prognostic factor for several cancer types. In addition, increased levels have been found in **coronary heart disease, insulin resistant patients, advance stage cancer patients, atopy/asthma and in patients with blood circulating micro metastasis (circulating tumour cells)**.

IL7 - promotes tumour development, progression & resistance

Interleukin-7 (IL-7) and IL-7 receptor (IL-7R) signalling complex in human solid tumours

M.A.A. Al-Rawi, R.E. Mansel and W.G. Jiang
Metastasis Research Group, University Department of Surgery, University of Wales College of Medicine, Heath Park, Cardiff, UK

Interleukin-7: from bench to clinic

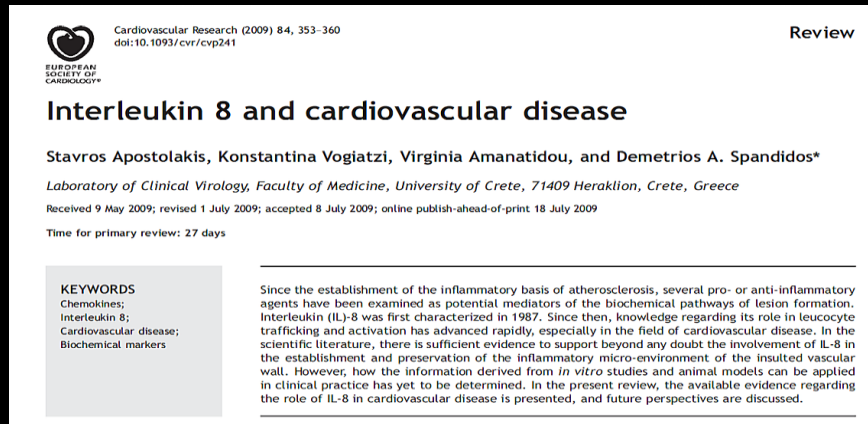
Terry J. Fry and Crystal L. Mackall

Blood 2002 99:3892-3904; doi: <https://doi.org/10.1182/blood.V99.11.3892>

- Hematopoietic growth factor secreted by red marrow and thymus.
- Stimulates the differentiation of multipotent (pluripotent) hematopoietic stem cells.
- Elevated levels detected in the plasma of HIV-infected patients.
- Elevated IL7 promotes tumour development and progression.
- Linked with NFkB in malignancies (acute lymphoblastic leukemia).
- Proliferative and trophic cytokine that induces the development and proliferation of haematopoietic cells and malignancies.
- The production of IL7 linked in the process of tumourgenesis upregulated in several solid tumours including breast, lung, prostate, renal, ovarian, melanomas as well as head and neck tumours.
- An important marker in cancer activity.



IL8 – vascular inflammation, cardio & cerebrovascular disease, thrombosis, DVT



- IL8 was first characterized in 1987.
- Identified with **systemic inflammation of the blood** and involved in **cerebrovascular disorders and cardiovascular disease**.
- IL8 and other chemokines are produced in several tissues upon infection, inflammation, ischemia, trauma etc
 - main cause of local **neutrophil accumulation**.
- **Gross overproduction of IL8 from Endothelial cells in presence of hypoxia.**
- **Chronic systemic inflammation** including: **Progressive vascular disease, atherosclerosis lesions, main source for atherosclerosis plagues, predictive biomarker for ischemia induced oxidative stress.**
- Pathogenesis of **hypertension**, and in the **progression of ischemic induced necrosis**.
- IL8 elevated in **ventricular fibrillation complicating myocardial infarction**.
- IL8 is a **powerful independent predictive factor for cardiovascular disease** and overall mortality in patients with end stage renal disease. **Biomarker of outcome following cardiopulmonary arrest.**
- SPECT Imaging (Single Photon Emission Computed Tomography) demonstrates regions of **cerebral hypoperfusion**. Typically, these are the regions of the brain associated with chronic 'over expression' of pro-inflammatory cytokines including IL1, IL8, TNFa, S100B and lowered BDNF.

IL8 – Neurodegenerative disorders, Dementia, MS, PD, MND



Journal of
Alzheimer's Disease & Parkinsonism

McLennan, J. *Alzheimer's Dis Parkinsonism* 2018, 6:5
DOI: 10.4172/2181-0480.1000273

Mini Review

Open Access

Chemokine Interleukin-8 (IL-8) in Alzheimer's and Other Neurodegenerative Diseases

- IL8 linked with **neuroinflammation** associated with **activated microglia** resulting in neurotoxicity in the inflamed brain.
- IL8 are significantly elevated in **neurodegenerative disease**.
- Activated microglia increased levels of IL8 which contribute to a **positive feedback process amplifying and sustaining inflammatory reactivity in Alzheimer's Disease brain**.
- **Chronic microglial activation** is associated with sustained cellular production of a **milieu of inflammatory mediators** including pro-inflammatory cytokines including IL8, reactive oxygen species and matrix metalloproteinases which cause **abnormalities to blood vessels (weak VEGF) and neurotoxicity**.

Alzheimers Dement. 2018 Aug 8. pii: S1552-5260(18)33035-8. doi: 10.1016/j.jalz.2018.06.2857. [Epub ahead of print]

Blood-brain barrier breakdown, neuroinflammation, and cognitive decline in older adults.

Front Immunol. 2018 Jul 30;9:1767. doi: 10.3389/fimmu.2018.01767. eCollection 2018.

Adipocytes Promote Early Steps of Breast Cancer Cell Dissemination *via* Interleukin-8.

Curr Neurovasc Res. 2018 Jul 17. doi: 10.2174/1567202615666180717161807. [Epub ahead of print]

Pivotal pathogenic and biomarker role of Chlamydia Pneumoniae in neurovascular diseases.



OXYMED

IL8 – cancer proliferation & treatment resistance; autism, development delay – gestational

Hyperbaric Oxygen: Does it promote growth or recurrence of malignancy?

J. FELDMEIER¹, U. CARL², K. HARTMANN³, P. SMINIA⁴.

¹Radiation Oncology Department, Medical College of Ohio, Toledo, OH, USA; ²Department of Radiation Oncology and Nuclear Medicine, Diakonieklinik Rotenberg, Germany; ³Department of Radiation Oncology, Heinrich Heine University, Duesseldorf, Germany; ⁴Department of Radiation Oncology, VU University Medical Center, The Netherlands

iii. Interleukin-8 release is increased by hypoxia⁶⁸ This has been demonstrated in human glioblastoma cells in culture. IL-8 has been shown to have angiogenic properties in this model. The work of Shi and associates⁶⁹ confirms an increase in IL-8 by hypoxia and acidosis and suggest this contributes significantly to the aggressive biology of pancreatic cancer.

- Hypoxia, IL8 and acidity contributes to the aggressive biology of pancreatic cancer growth (UHMS 2003)

Vaccines (Basel). 2016 Jun 24;4(3). pii: E22. doi: 10.3390/vaccines4030022.

The IL-8/IL-8R Axis: A Double Agent in Tumor Immune Resistance.

David JM¹, Dominguez C², Hamilton DH³, Palena C⁴.



- Tumorigenesis analysis proved that patients with higher serum IL-8 levels grew faster than those with lower IL-8 levels.

Arterioscler Thromb Vasc Biol. 2017 Oct;37(10):1819-1827. doi: 10.1161/ATVBAHA.117.309794. Epub 2017 Aug 3.

Clots Are Potent Triggers of Inflammatory Cell Gene Expression: Indications for Timely Fibrinolysis.



J Pediatr. 2017 Jan;180:116-123.e1. doi: 10.1016/j.jpeds.2016.09.054. Epub 2016 Oct 24.

Circulating Inflammatory-Associated Proteins in the First Month of Life and Cognitive Impairment at Age 10 Years in Children Born Extremely Preterm.



IL17 – tendinopathy, rotator cuff injuries, relapsing MS

SCIENTIFIC REPORTS

OPEN IL-17A mediates inflammatory and tissue remodelling events in early human tendinopathy

IL17A interleukin 17A [*Homo sapiens* (human)]

Gene ID: 3605, updated on 13-Aug-2017

J Leukoc Biol. 2016 Sep;100(3):589-98. doi: 10.1189/jlb.4A0715-331R. Epub 2016 Apr 21.

Autophagy suppresses host adaptive immune responses toward *Borrelia burgdorferi*.

Buffen K¹, Oosting M¹, Li Y², Kanneganti TD³, Netea MG¹, Joosten LA⁴.

- High levels of this cytokine IL17 are associated with **several chronic inflammatory diseases** including **rheumatoid arthritis, psoriasis and multiple sclerosis**.
- IL17 is an inflammatory infiltrate in **tendinopathy, rotator cuff injuries and repetitive strain injuries**. Increased levels of IL17 coupled with **TNF- α , IL-6** in torn supraspinatus promoting tissue destruction and degeneration during inflammation.
- IL17 has been linked with **inflammatory arthritis** and more recently associated with **chronic symptoms associated with Lyme like illness**.
- High levels of IL17 have been found in patients with confirmed, severe, **chronic 'borreliosis'** in conjunction with elevated IL1, IL6, TNFa.
- **Oral high dose vitamin D intake** reducing IL17 levels in **MS patients** in a double blind randomized clinical trial. 94 patients with a diagnosis of **relapsing remitting multiple sclerosis (RRMS)**. **50,000 IU vitamin D3** every five days for 12 weeks showed **significant reduction change in RRMS patients**.

Curr Rheumatol Rep. 2016 Jun;18(6):33. doi: 10.1007/s11926-016-0585-9.

The Bench-to-Bedside Story of IL-17 and the Therapeutic Efficacy of its Targeting in Spondyloarthritis.

J Neuroimmunol. 2015 Aug 15;285:125-8. doi: 10.1016/j.jneuroim.2015.05.022. Epub 2015 Jun 12.

Effect of high dose vitamin D intake on interleukin-17 levels in multiple sclerosis: a randomized, double-blind, placebo-controlled clinical trial.

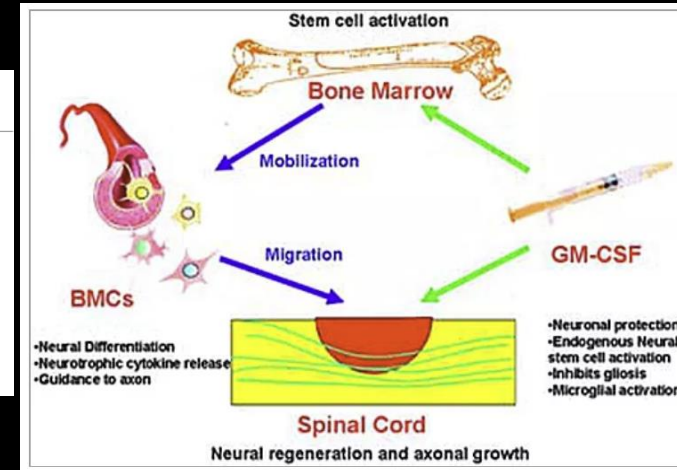


Granulocyte Colony Stimulating Factor (GMCSF)

STEM CELLS®

TRANSLATIONAL AND CLINICAL RESEARCH

Complete Spinal Cord Injury Treatment Using Autologous Bone Marrow Cell Transplantation and Bone Marrow Stimulation with Granulocyte Macrophage-Colony Stimulating Factor: Phase I/II Clinical Trial



- GMCSF are glycoprotein **growth factors**.
- Stimulates blood stem cells to **produce more white blood cells** (neutrophils, eosinophils, basophils, and monocytes) to **reduce the risk of infection** notably after **types of cancer treatment**.
- GMCSF stimulates **bone marrow and make stem cells move from the bone marrow into the blood**.
- GMCSF can have intrinsic spinal cord repair mechanisms including **neuroprotection from apoptosis, endogenous stem cell activation, inhibition of glial scar formation, and microglial cell activation**.
- GMCSF **decreased neuronal apoptosis and improved the functional outcome** in SCI animal models.
- GMCSF stimulates microglial cells to **increase brain-derived neurotrophic factor** (BDNF) synthesis.
- The total number of recruited white blood cells in the peripheral blood was elevated after GMCSF (SGS) administration. The number of white blood cells in patients showing **improved neurologic function was significantly higher**.
- Following GMCSF - Spinal MRI Findings - **42.9% of patients in the GMCSF treated group showed an increase in the diameter of the spinal cord** at the cell transplantation site. **28.6%** showed evidence of spinal cord enhancement.

GMCSF – Sargramostim – stem cell mobilisation – Stroke, ALS, PD, MS

[Eur J Neurosci.](#) 2018 Aug 11. doi: 10.1111/ejn.14106. [Epub ahead of print]

Granulocyte-macrophage colony-stimulating factor improves mouse peripheral nerve regeneration following sciatic nerve crush.

[Cytotherapy.](#) 2010;12(1):50-9. doi: 10.3109/14653240903300682.

Consistent bone marrow-derived cell mobilization following repeated short courses of granulocyte-colony-stimulating factor in patients with amyotrophic lateral sclerosis: results from a multicenter prospective trial.

[J Neuropathol Exp Neurol.](#) 2006 Aug;65(8):816-25.

Intrathecal upregulation of granulocyte colony stimulating factor and its neuroprotective actions on motor neurons in amyotrophic lateral sclerosis.

[J Vis Exp.](#) 2018 Aug 10;(138). doi: 10.3791/57365.

Generation of Large Numbers of Myeloid Progenitors and Dendritic Cell Precursors from Murine Bone Marrow Using a Novel Cell Sorting Strategy.

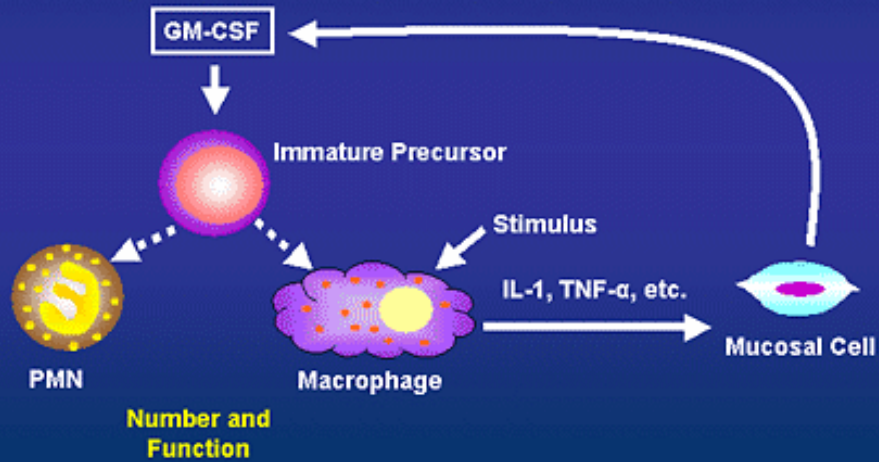
[Int J Inflam.](#) 2018 Aug 1;2018:2027856. doi: 10.1155/2018/2027856. eCollection 2018.

Association of Elevated Serum GM-CSF, IFN- γ , IL-4, and TNF- α Concentration with Tobacco Smoke Induced Chronic Obstructive Pulmonary Disease in a South Indian Population.



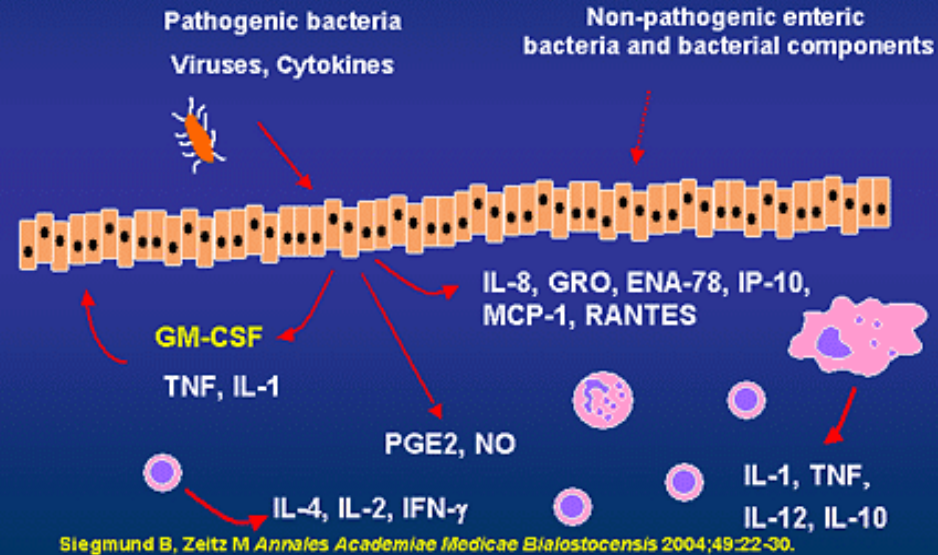
GM-CSF – Innate Immunity

GM-CSF Is a Central Regulator of Innate Immunity



Hamilton J. *Trends in Immunology* 2002;23:403-408.

GM-CSF Is a Central Regulator of Innate Immunity



Siegmund B, Zeltz M *Annales Academiae Medicae Bialostocensis* 2004;49:22-30.

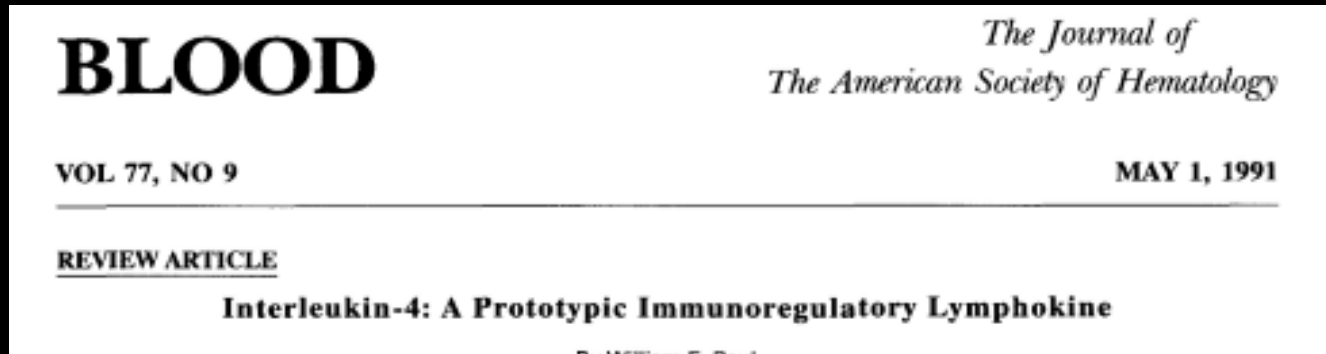


Filgrastim - Drug Information - Chemocare

chemocare.com/chemotherapy/drug-info/filgrastim.aspx ▼

Filgrastim is used to stimulate the production of granulocytes (a type of white blood cell) in patients undergoing therapy that will cause low white blood cell counts. This medication is used to prevent infection and neutropenic (low white blood cells) fevers caused by chemotherapy.

IL4 – Diverse Immune Modulation, Anti Tumour



INTERLEUKIN-4, INTERLEUKIN-10, AND INTERLEUKIN-13

- Can all be regarded as *inhibitory, anti-inflammatory, or counter-regulatory* cytokines.
- All three of these cytokines are produced by TH2 cells
- serve to modulate the production and effects of proinflammatory cytokines such as TNF and IL-1.

- Studies of IL-4 have revealed a wealth of information on the diverse roles of this cytokine in homeostatic regulation and disease pathogenesis.
- IL4 is an Th2 anti-inflammatory cytokine, acting synergistic with IL10 and IL13 responsible for cell growth factor that stimulates the growth and survivability of B cells and T cells.
- IL4 inhibits the production of pro-inflammatory cytokines including TNF, IL1, and IL6.
- IL4 is an immune-stimulating molecule. More recent targets being studied for new asthma treatments.
- IL4 has striking antitumor activities expressing potent biologic agents to enhance immune elimination of certain tumor cells.
- Ameliorates non-resolving neuro-inflammation that causes neuropathic pain after nerve injury (crush injury).

[Neural Regen Res.](#) 2018 Oct;13(10):1743-1752. doi: 10.4103/1673-5374.238615.

Release of interleukin-10 and neurotrophic factors in the choroid plexus: possible inducers of neurogenesis following copolymer-1 immunization after cerebral ischemia.

[Acta Cir Bras.](#) 2018 Jun;33(6):491-498. doi: 10.1590/s0102-865020180060000003.

Interleukin-4 protects from chemotherapy-induced peripheral neuropathy in mice modal via the stimulation of IL-4/STAT6 signaling.

IL10 – potent anti inflammatory coupled with IL13

0031-6997/03/5502-241-269\$7.00

PHARMACOLOGICAL REVIEWS

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Pharmacol Rev 55:241–269, 2003

Vol. 55, No. 2

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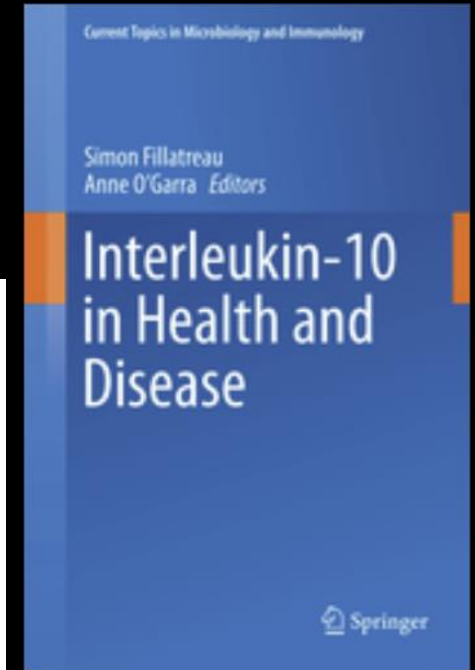
Printed in U.S.A.

Interleukin-10 Therapy—Review of a New Approach

- Potent anti-inflammatory TH2 cytokine that has a critical role in **limiting the immune response to pathogens** to prevent host damage.
- **Strong inhibitor of inflammation.**
- Elevated levels in **parasitic infection**, high expression levels of IL10 are also found in **retroviral infections inducing immunodeficiency**.
- The **immunosuppressive properties** of IL10 suggest a possible clinical use in **suppressing rejections of grafts after organ transplantations**.
- Patients with **Crohn's disease** react favourably to treatment with bacteria producing recombinant IL10.
- Pre conditioning elevation of IL10 induces a **resistance of the brain cells to ischemia-evoked damages**.
- This protective effect in cultured hippocampal cells is developed rapidly after application of IL10, capable to exert the **rapid neuroprotective effects** through transcription-independent modulation of ischemia-induced intracellular Ca(2+) responses in the brain cells.
- IL10 **upregulates BDNF** production.

[Int J Mol Sci.](#) 2018 Aug 28;19(9). pii: E2550. doi: 10.3390/ijms19092550.

Schwann Cell Transplantation Subdues the Pro-Inflammatory Innate Immune Cell Response after Spinal Cord Injury.



OXYMED

IL10 – chronic pain syndromes, neurodegenerative disorders

[Neural Regen Res.](#) 2018 Sep;13(9):1650-1656. doi: 10.4103/1673-5374.237139.

Saikosaponin a increases interleukin-10 expression and inhibits scar formation after sciatic nerve injury.

[J Stroke Cerebrovasc Dis.](#) 2018 Aug 14. pii: S1052-3057(18)30399-9. doi: 10.1016/j.jstrokecerebrovasdis.2018.07.030. [Epub ahead of print]

The Effects of Mouse Recombinant Resistin on mRNA Expression of Proinflammatory and Anti-Inflammatory Cytokines and Heat Shock Protein-70 in Experimental Stroke Model.

[Neurosci Lett.](#) 2018 Sep 14;683:181-184. doi: 10.1016/j.neulet.2018.07.027. Epub 2018 Jul 29.

Association of Parkinson's disease-related pain with plasma interleukin-1, interleukin-6, interleukin-10, and tumour necrosis factor- α .

Abstract

OBJECTIVE: To study the association between Parkinson's disease (PD)-related pain and plasma interleukin (IL)-1, IL-6, IL-10, and tumour necrosis factor (TNF)- α levels.

METHODS: Sixty-seven participants were enrolled. Plasma inflammatory cytokine levels of IL-1, IL-6, IL-10, and TNF- α were measured with enzyme-linked immunosorbent assay. We additionally administered the third part of the Unified Parkinson's Disease Rating Scale (UPDRS III) and Hoehn and Yahr (H-Y) scale stage and recorded the course of the disease, the type and location of the pain, and the use of drugs.

[Neuropsychopharmacology.](#) 2018 Jul 16. doi: 10.1038/s41386-018-0154-1. [Epub ahead of print]

Resolution of inflammation-induced depression requires T lymphocytes and endogenous brain interleukin-10 signaling.



CHIMERIC ANTIGEN RECEPTOR (CAR)

CHIMERIC ANTIGEN RECEPTOR & HYPERBARIC OXYGEN THERAPY

Hyperbaric Oxygen Therapy is a form of "Chimeric Antigen Receptor Therapy" in that HBOT modulates "gene expressions".

* HBOT impacts cytokine gene expressions and may work by 're-setting' or 're-booting' the immune system. HBOT reduces pro-inflammatory cytokine gene expressions including chronic inflammatory cascades, which in turn may lead to improvement in damaged organs and tissues.

Hemopoietic stem cells work best if chronic inflammation can be "switched off".

** Hyperbaric Oxygen mobilises and elevates both the production and circulation of pluripotent bone marrow stem cells which activates other circulating stem cells unique to the body speeding up healing and regeneration (Thoms 2005).

Chimeric Antigen Receptor - next generation, is referred to as **TRUCKS - T cell Redirected for Universal Cytokine-mediated Killing** in cancer immunotherapy and how to "best augment the antitumor potency using cytokines to safely improve treatment outcomes in patients with advanced blood or solid tumors".

[Fueling Cancer Immunotherapy With Common Gamma Chain Cytokines. Front. Immunol., 20 February 2019 | https://doi.org/10.3389/fimmu.2019.00263](https://doi.org/10.3389/fimmu.2019.00263)

Herald Sun Newspaper, 3 August 2019



Lifesaving therapy now available in Melbourne

MELBOURNE will be home to the next frontier in cancer treatment, giving new hope to the nation's youngest cancer patients.

Many people fighting blood cancer had been forced to travel overseas for lifesaving treatment.

But revolutionary cancer therapy — which supercharges the immune system — will now be available at two Melbourne hospitals.

The federal and state governments will today confirm a partnership to bring the cancer-killing chimeric antigen receptor T-cell therapy to Australia.

Federal Health Minister Greg Hunt told the *Sunday Herald Sun* the first patients had already received free treatments.

"Our governments have worked together to make this lifesaving treatment available as soon as possible," Mr Hunt said.

The Royal Children's Hospital and Peter MacCallum Cancer Centre will offer the treatment.

ANNIKA SMETHURST

State Health Minister Jenny Mikakos said the therapy would "make a world of difference for some of our sickest children and young people".

Patients battling acute lymphoblastic leukaemia have needed to find a local clinical trial or travel to the US for the lifesaving treatment, which costs more than \$500,000.

In 2017, there were 105 new diagnoses of the blood cancer. Sixty were children or young adults.

The treatment has been available in the US since 2017 and was approved for use in the UK and Canada last year.

Global trials found more than 60 per cent of young patients were cancer-free two years after treatment.

The therapy, known commercially as Kymriah, was approved for use in Australia late last year and is now being given to patients for free after the federal and state governments agreed to a funding deal.

Violet Uhi, 8, is cancer-free after receiving the treatment in Seattle last year.

The Malvern East youngster was four when she was diagnosed with blood cancer after seeing five different GPs over seven weeks who sent her away with antibiotics.

Since then she has twice relapsed with leukaemia affecting her central nervous system, not her bone marrow, limiting her treatment options in Australia.

Last September the family of four moved to the US for three months while Violet received the immunotherapy treatment, which has seen her return to school and join the choir.

"She is incredibly resilient, she has a fire in her belly nobody can put out," mum Tess Uhi said.

"It's amazing Australia has a licence to practise this treatment. For Violet, it was like being reborn again, you are getting this whole new opportunity."

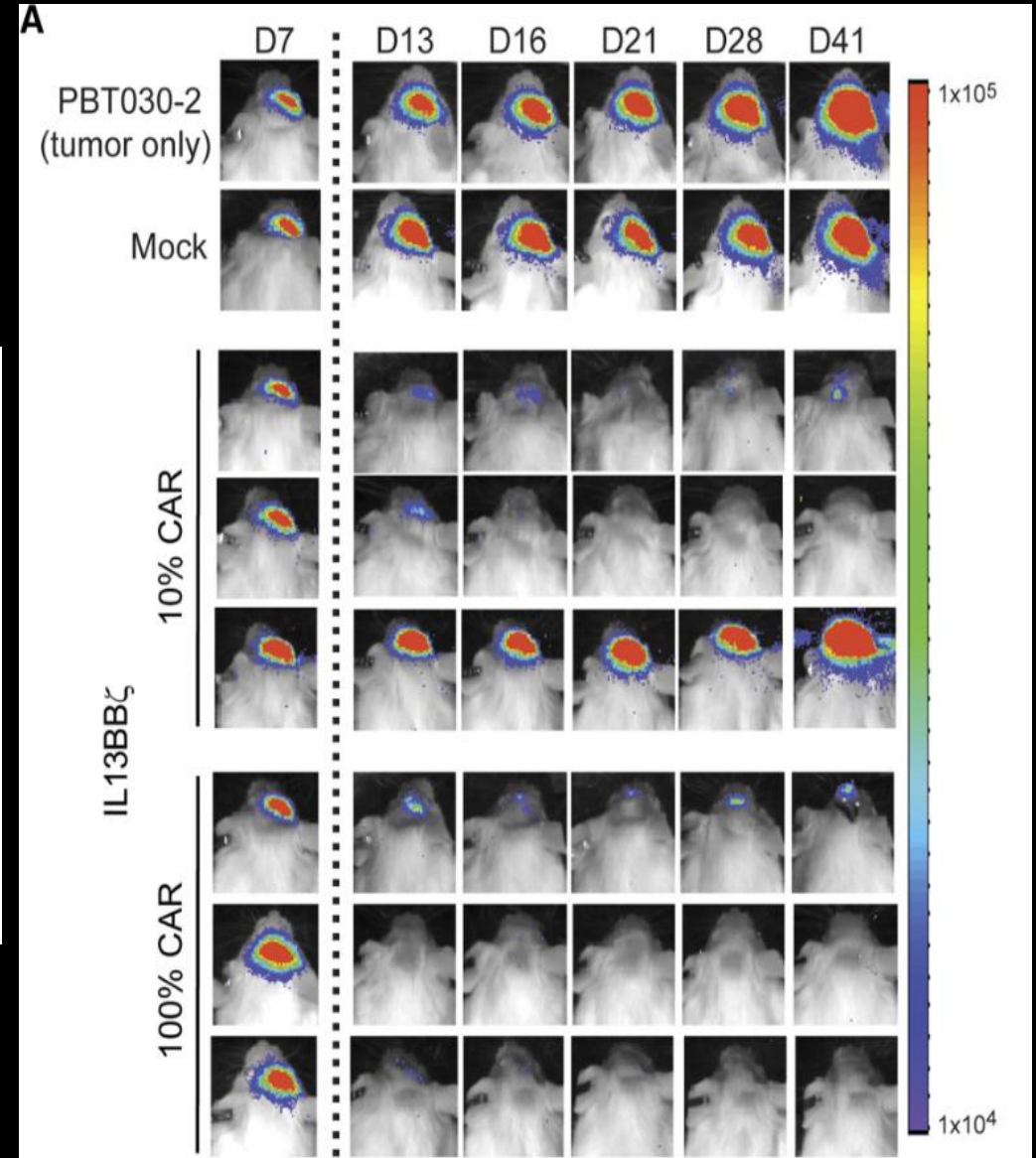
annika.smethurst@news.com.au

IL13 - T Cell Immunotherapy

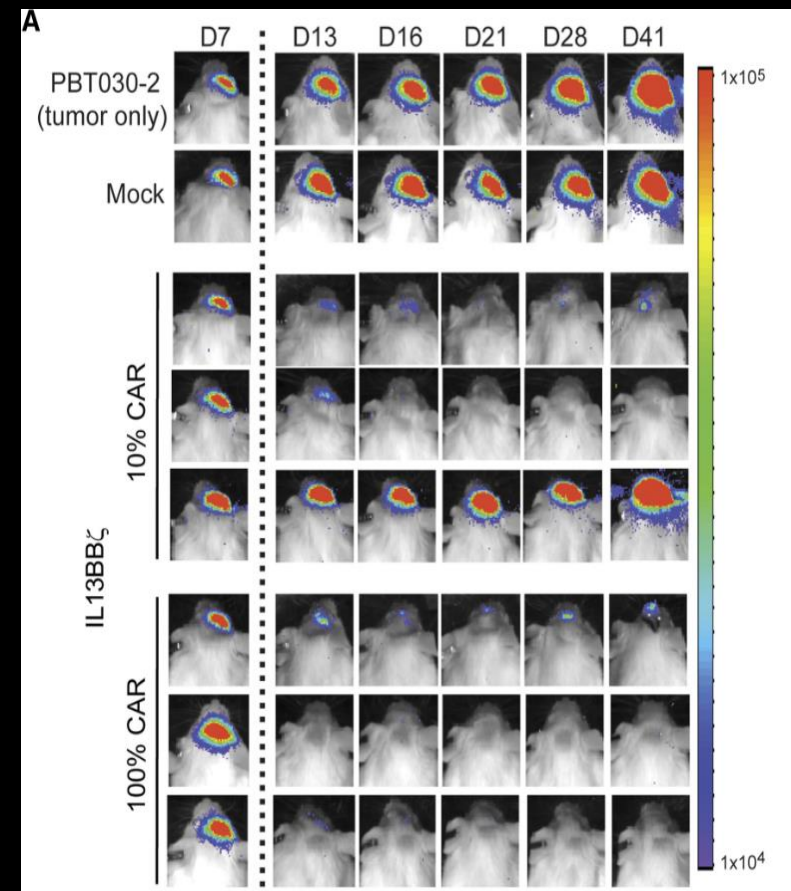
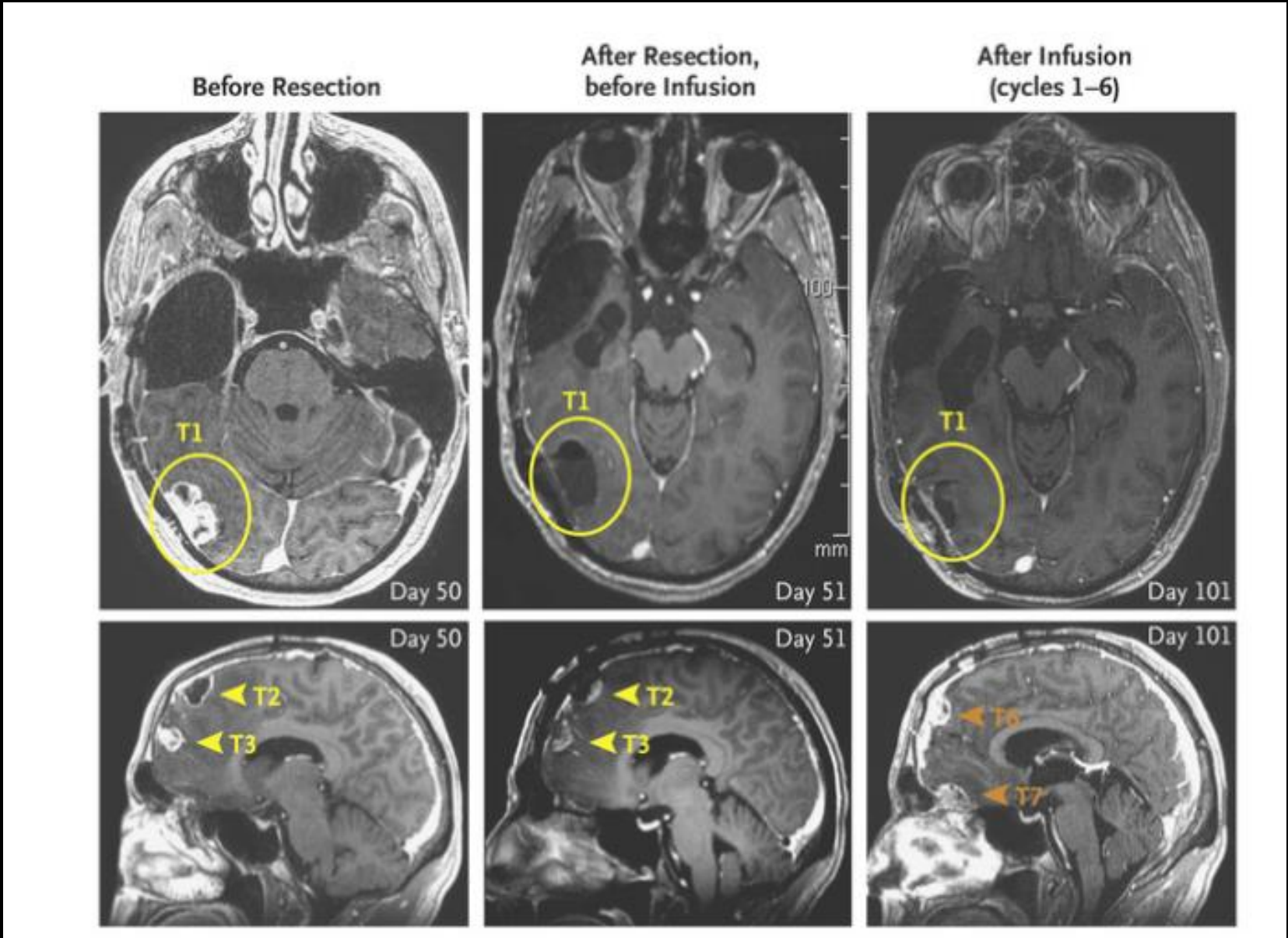
ORIGINAL ARTICLE | VOLUME 26, ISSUE 1, P31-44, JANUARY 03, 2018

Optimization of IL13R α 2-Targeted Chimeric Antigen Receptor T Cells for Improved Anti-tumor Efficacy against Glioblastoma

- IL13 based T cell immunotherapy is emerging as a powerful strategy to treat cancer and may improve outcomes for patients with glioblastoma (GBM).
- Chimeric Antigen Receptor (CAR) T cell immunotherapy targeting IL-13 receptor α 2 (IL13R α 2) for the treatment of GBM. The general premise of CAR-T cells is to artificially generate T-cells targeted to markers found on cancer cells. Scientists can remove T-cells from a person, genetically alter them, and put them back into the patient to attack the cancer cells.
- Intracranial delivery of CAR T cells elicits superior anti-tumor efficacy as compared to intravenous administration, with intraventricular infusions exhibiting possible benefit over intracranial tumor infusions.





IL13CAR - Glioblastoma



Hyperbaric Oxygenation of Hypoxic Glioblastoma Multiforme Cells Potentiates the Killing Effect of an Interleukin-13-Based Cytotoxin

- IL13 has anti-tumour effects and when combined with HBO enhances the killing effects of Glioblastoma and other cancers.
- Interleukin-13 receptor-targeted cytotoxin (IL13-PE38) is highly cytotoxic to human glioblastoma (GBM) cells.

Combined effects of radiation and interleukin-13 receptor-targeted cytotoxin on glioblastoma cell lines

Koji Kawakami, M.D., Ph.D., Mariko Kawakami, M.D., Ph.D., Qi Liu, M.D., Ph.D., Raj K. Puri, M.D., Ph.D.  

Laboratory of Molecular Tumor Biology, Division of Cellular and Gene Therapies, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD

Received: November 18, 2004; Received in revised form: May 9, 2005; Accepted: May 10, 2005;



DOI: <http://dx.doi.org/10.1016/j.ijrobp.2005.05.017>

Article Info

Abstract Full Text Images References

Purpose: Interleukin-13 receptor-targeted cytotoxin (IL13-PE38) is highly cytotoxic to human glioblastoma (GBM) cells. Although this molecule is being tested in a multicenter Phase III clinical trial (PRECISE Study) in patients with recurrent disease, the activity of IL13-PE38 when combined with radiation therapy has not been investigated.

Methods and Materials: Cytotoxicity of IL13-PE38 to GBM cell lines was assessed by protein synthesis inhibition and clonogenic assays, and the growth of GBM cells receiving radiation was assessed by thymidine uptake assays. Expression of IL-13 receptor $\alpha 2$ (IL-13R $\alpha 2$) messenger ribonucleic acid (mRNA) in GBM cells exposed to radiation was assessed by quantitative reverse transcriptase/polymerase chain reaction (RT-PCR) and IL-13R density by radiolabeled IL-13 binding assays.

Results: Prior irradiation of GBM cell lines followed by IL13-PE38 treatment did not enhance cytotoxicity; however, concomitant 5 Gy irradiation and IL13-PE38 treatment was highly cytotoxic to T98G, M059K, A172, and LN-229 cell lines as determined by cell viability assays. There was a statistically significant decrease in number of viable cells in IL13-PE38 and irradiated cells compared with irradiated cells alone ($p < 0.05$) or IL13-PE38 treated cells alone ($p < 0.05$). In contrast, U251, SN19, and U87MG cell lines did not show any combined effect. These results were confirmed by clonogenic assays. Although three GBM cell lines—U251, SN19, and A172—showed 2.8- to 13.9-fold upregulation of IL-13R $\alpha 2$ mRNA expression at 6–24 h after exposure to 5 Gy radiation, specific binding of radiolabeled IL-13 to these cell lines did not improve.

Conclusions: Our results suggest that concomitant radiation therapy and IL13-PE38 treatment may be beneficial for the treatment of patients with GBM. This strategy may be worth exploring in animal models of human glioma.

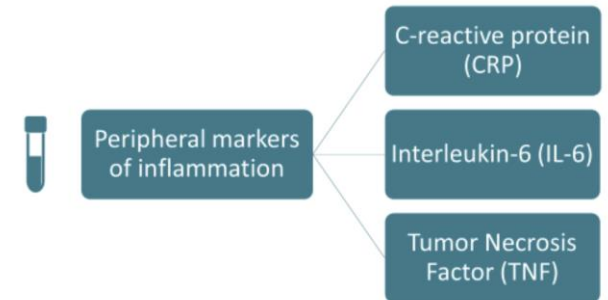
IL13 – anti tumour, neuroprotection, anti parasites

Reoxygenation of Hypoxic Glioblastoma Multiforme Cells Potentiates the Killing Effect of an Interleukin-13-Based Cytotoxin

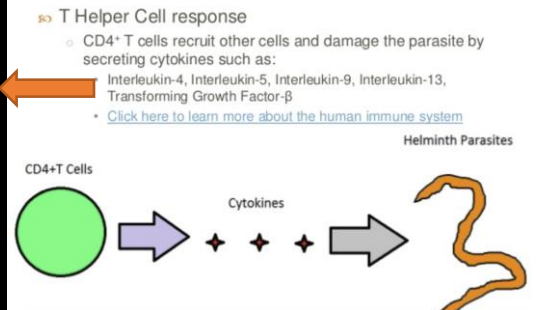
Tie Fu Liu,^{1,2} Jiaozhong Cai,² Denise M. Gibo,¹ and Waldemar Debinski¹

- IL13 has **anti-tumour effects** and when **combined with HBO** enhances the killing effects of **Glioblastoma and other cancers**.
- Interleukin-13 receptor-targeted cytotoxin (IL13-PE38) is **highly cytotoxic to human glioblastoma (GBM) cells**.
- IL13 is a cytokine found to **powerfully inhibits proinflammatory cytokines**.
- Elevated IL13 levels in the CSF are reported to have **neuroprotective effects in multiple neurodegenerative disorders including Multiple Sclerosis**.
- IL13 enhances **neuronal integrity and synaptic function in neurodegenerative disorders including MS**.
- IL13 specifically **induces physiological changes in parasitized organs** that are required to expel the **offending organisms or their products**. For example, **expulsion from the gut** of a variety of mouse helminths requires IL13.
- IL-13 induces several changes in the gut that **create an environment hostile to the parasite**, including enhanced contractions and glycoprotein hyper-secretion from gut epithelial cells, that ultimately lead to **detachment of the organism from the gut wall and their removal**.

Anti-inflammatory agents



Human response to Parasites

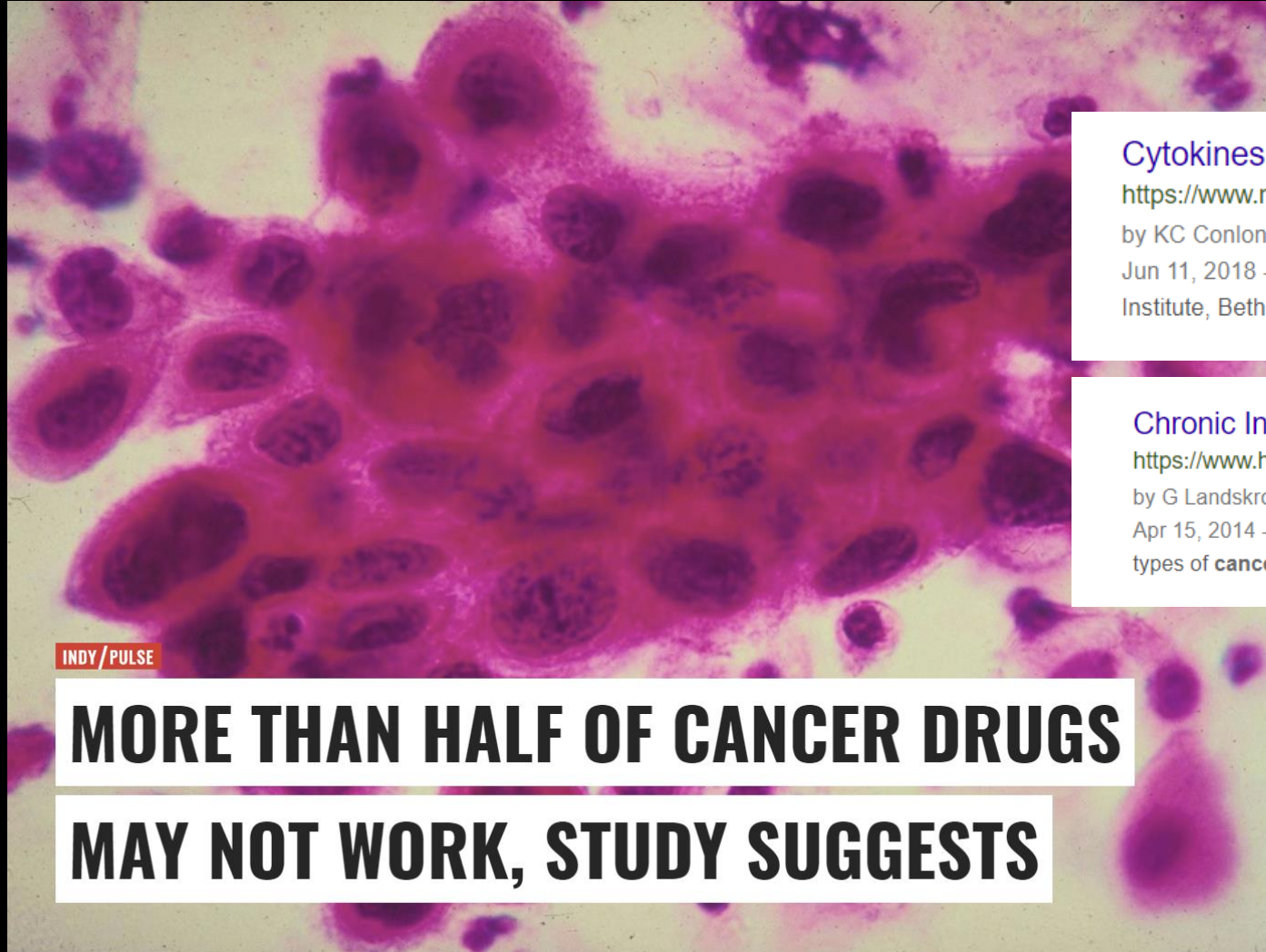


PLoS One. 2018 Apr 5;13(4):e0193565. doi: 10.1371/journal.pone.0193565. eCollection 2018.

IL-13 receptors as possible therapeutic targets in diffuse intrinsic pontine glioma.

OXYMED

Cytokines & Cancer



INDY/PULSE

**MORE THAN HALF OF CANCER DRUGS
MAY NOT WORK, STUDY SUGGESTS**

Cytokines in the Treatment of Cancer. - NCBI

<https://www.ncbi.nlm.nih.gov/pubmed/29889594>

by KC Conlon - 2019 - Cited by 13 - Related articles

Jun 11, 2018 - (1)Lymphoid Malignancies Branch, Center for **Cancer** Research, National **Cancer** Institute, Bethesda, Maryland. **Cytokines** are major regulators ...

Chronic Inflammation and Cytokines in the Tumor Microenvironment

<https://www.hindawi.com/journals/jir/2014/149185/> ▼

by G Landskron - 2014 - Cited by 702 - Related articles

Apr 15, 2014 - Finally, we will provide an in-depth analysis of the participation of these **cytokines** in two types of **cancer** attributable to chronic inflammatory ...

More than half of cancer drugs may be ineffective

Researchers found certain drugs on the market don't have proven benefits

London: According to a recent study, half of the cancer drugs that have recently arrived on the market have come with little evidence that they boost the survival or wellbeing of patients.

The researchers found that of cancer drugs approved by the European Medicines Agency (EMA) between 2009 and 2013, 57 per cent (39 out of 68) had no supporting evidence of better survival or quality

of life when they entered the market.

After an average of five years of follow up, only half of the drugs had shown a survival or quality of life gain in patients over existing treatments or placebo.

For the remaining 33 (49 per cent), uncertainty remains over whether the drugs extend survival or improve quality of life, according to the authors of the study from King's College London and the London School of Economics and Political Science (LSE).

DRUGS OR SCAMS?

- Of drugs approved by the EMA between 2009 and 2013, 57 per cent had no supporting evidence of better survival.

- With 49 per cent of the drugs, uncertainty remains over their benefits.

- Of the 23 drugs with a survival benefit, only 48 per cent were judged to offer a clinically meaningful benefit.

Of the 23 drugs with a survival benefit that could be scored with a validated tool, only 11 (48 per cent) were judged to offer a clinically meaningful benefit, they added.

Author Huseyin Naci, assistant professor in LSE's Department of Health Policy, said, "It is remarkable that so few cancer drugs enter the European market without any clear data on outcomes that matter to patients and their doctors: longer survival and better quality of life. There is a clear need to raise the bar for approving new cancer drugs."

Dr Courtney Davis, a medical and political sociologist in the Department of Global Health and Social Medicine at King's, added, "We evaluated the evidence base for all new drugs entering the market over a five year period and found that the majority came onto the market without clear evidence that they improved patients' survival or quality of life."

The study was published in *The British Medical Journal*. — Agencies



THINKSTOCK

Australia leading the way?

The Contribution of Cytotoxic Chemotherapy to 5-year Survival in Adult Malignancies

- The overall contribution of curative and adjuvant cytotoxic chemotherapy to 5-year survival in adults was estimated to be **2.3% in Australia and 2.1% in the USA.**
- "As the 5-year relative survival rate for cancer in Australia is now over 60%, **it is clear that cytotoxic chemotherapy only makes a minor contribution to cancer survival.** To justify the continued funding and availability of drugs used in cytotoxic chemotherapy, a rigorous evaluation of the cost-effectiveness and impact on quality of life is urgently required."

Clinical Oncology (2004) 16: 549–560
doi:10.1016/j.clon.2004.06.007

Overview

The Contribution of Cytotoxic Chemotherapy to 5-year Survival in Adult Malignancies

Graeme Morgan*, Robyn Ward†, Michael Barton‡

*Department of Radiation Oncology, Northern Sydney Cancer Centre, Royal North Shore Hospital, Sydney, NSW; †Department of Medical Oncology, St Vincent's Hospital, Sydney, NSW; ‡Collaboration for Cancer Outcomes Research and Evaluation, Liverpool Health Service, Sydney, NSW, Australia

Our history | Peter MacCallum Cancer Centre

<https://www.petermac.org/about/our-history> ▼

In June 2016, Peter Mac moved into its new home within the \$1 billion purpose-built Victorian Comprehensive Cancer Centre building, located at the entrance to ...



Cancer – A Metabolic Disease: “You are N of 1”

Carcinogenesis vol.35 no.3 pp.515–527, 2014
doi:10.1093/carcin/bgt480
Advance Access publication December 16, 2013

REVIEW

Cancer as a metabolic disease: implications

Thomas N.Seyfried*, Roberto E.Flores, Angela M.Poff¹ and Dominic P.D'Agostino¹

Biology Department, Boston College, Chestnut Hill, MA 02467, USA and
¹Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, FL 33612, USA

*To whom correspondence should be addressed. Tel: +1 617 552 3563;
Fax: +1 617 552 2011;
Email: thomas.seyfried@bc.edu

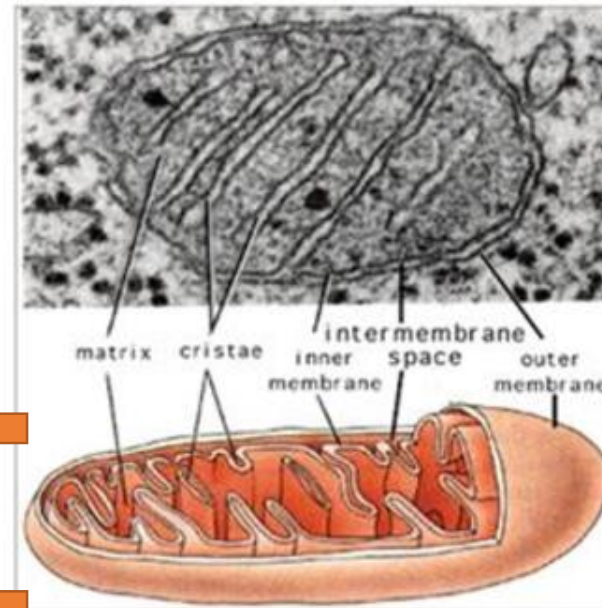
Emerging evidence indicates that cancer is primarily a metabolic disease involving disturbances in energy production through respiration and fermentation. The genomic instability observed in tumor cells and all other recognized hallmarks of cancer are considered downstream epiphenomena of the initial disturbance of cellular energy metabolism. The disturbances in tumor cell energy metabolism can be linked to abnormalities in the structure and function of the mitochondria. When viewed as a mitochondrial metabolic disease, the evolutionary theory of Lamarck can better explain cancer progression than can the evolutionary theory of Darwin. Cancer growth and progression can be managed following a whole body transition from fermentable metabolites, primarily glucose and glutamine, to respiratory metabolites, primarily ketone bodies. As each individual is a unique metabolic entity, personalization of metabolic therapy as a broad-based cancer treatment strategy will require fine-tuning to match the therapy to an individual's unique physiology.

Cancer as a metabolic disease: implications for novel therapeutics

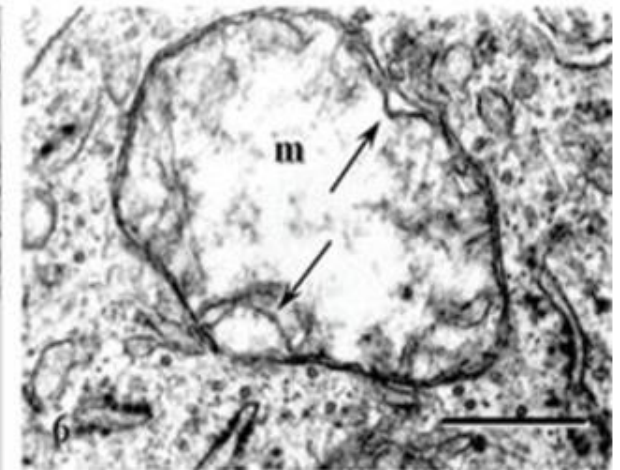
Thomas N. Seyfried ✉, Roberto E. Flores, Angela M. Poff, Dominic P. D'Agostino

Carcinogenesis, Volume 35, Issue 3, 1 March 2014, Pages 515–527,

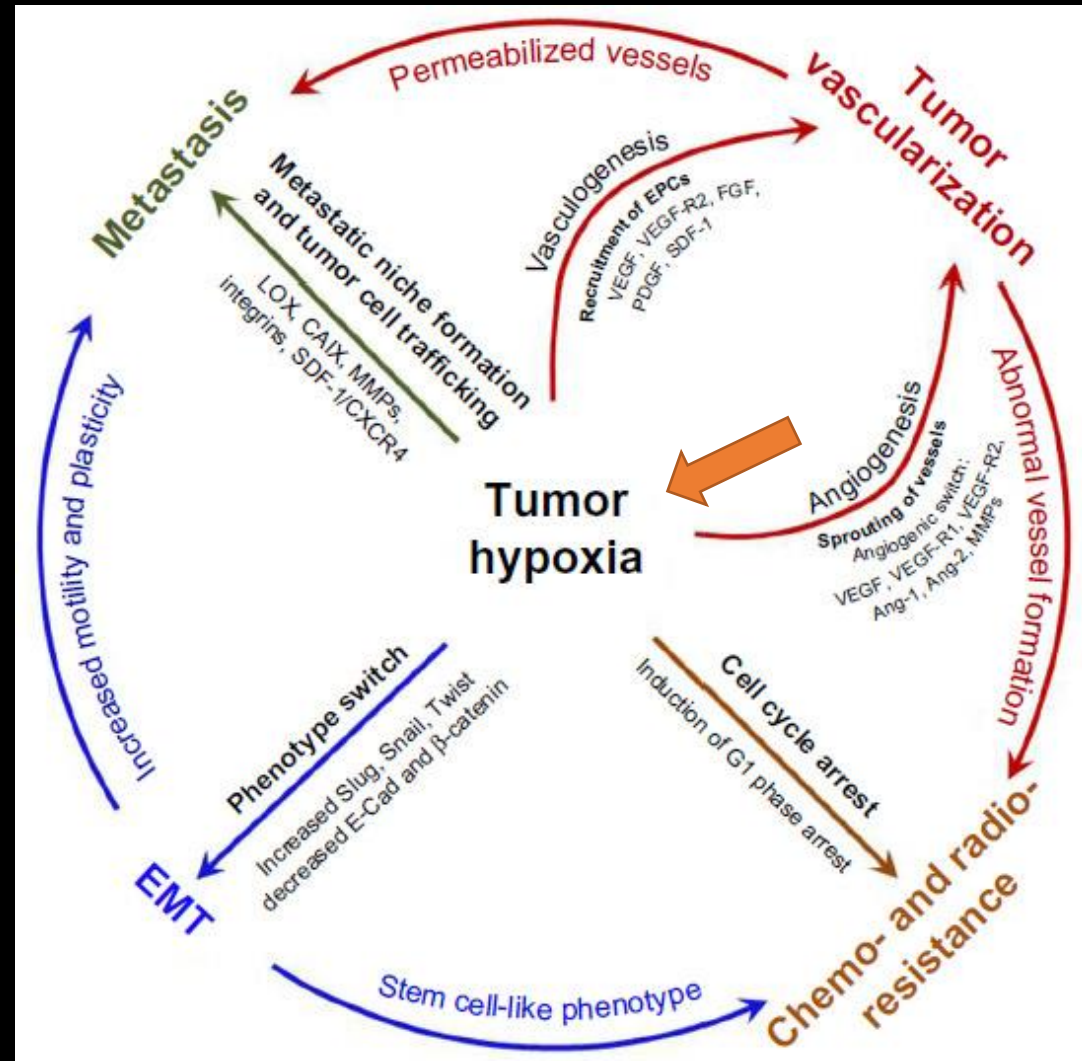
Normal Mitochondria



GBM Mitochondria



Hypoxia drives Cancer mutations



Dominic D'Agostino: Metabolic Therapies: Therapeutic Implications and Practical Application

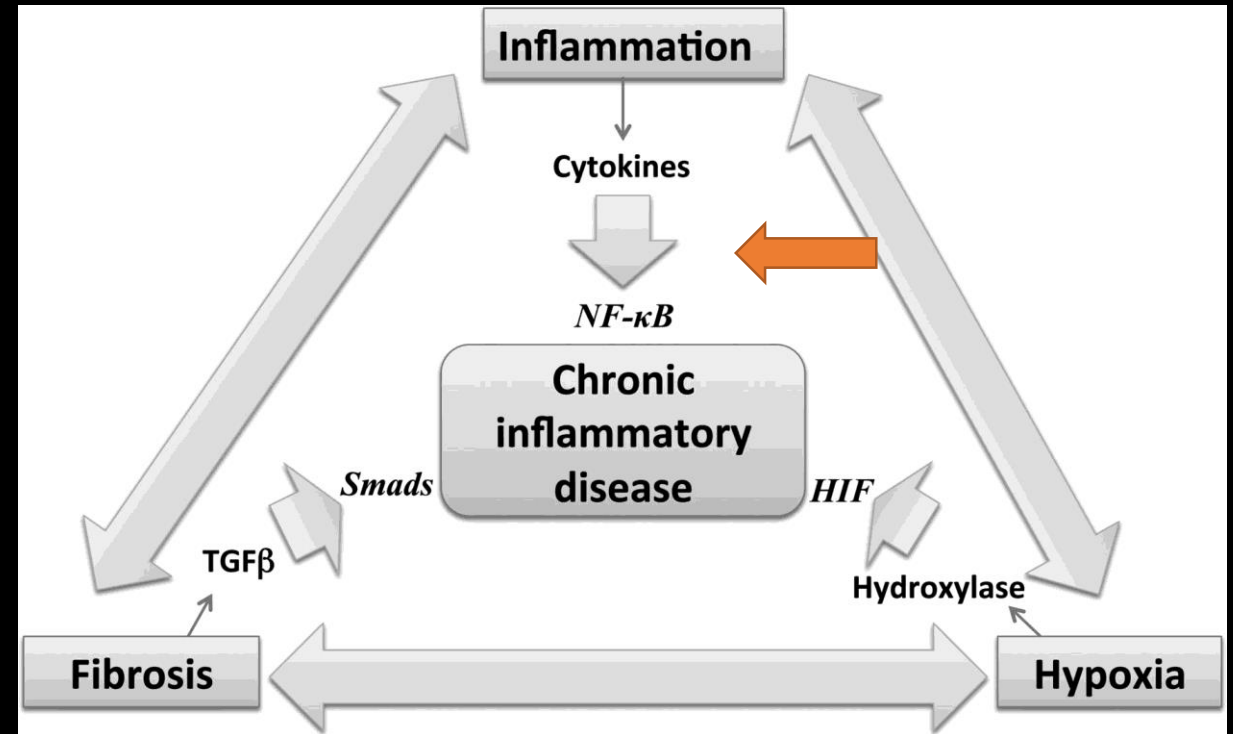
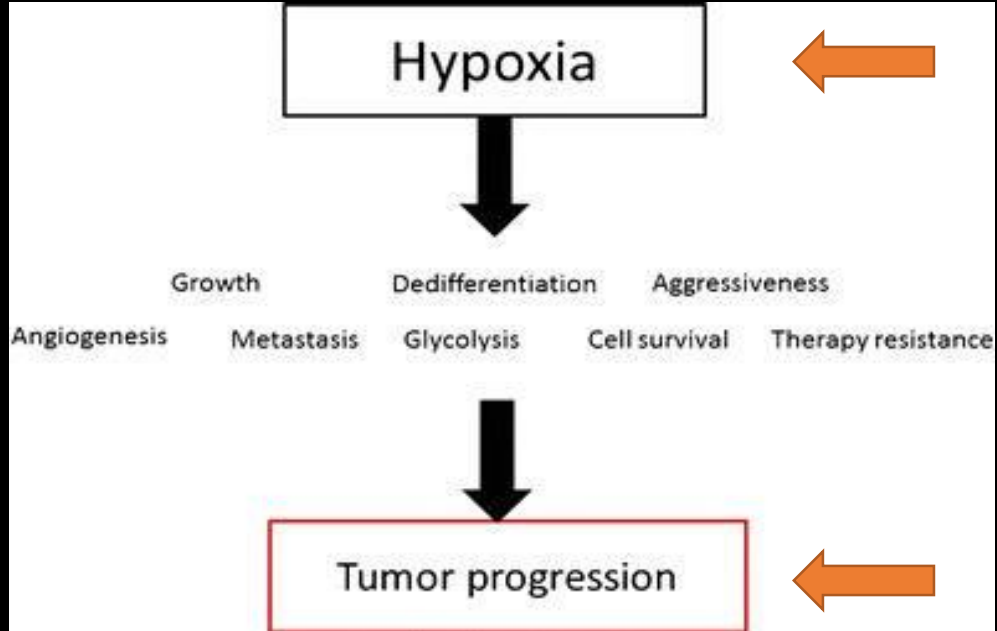
Hypoxia – Feldmeier 2003

Hyperbaric Oxygen: Does it promote growth or recurrence of malignancy?

J. FELDMEIER¹, U. CARL², K. HARTMANN³, P. SMINIA⁴.

¹Radiation Oncology Department, Medical College of Ohio, Toledo, OH, USA; ²Department of Radiation Oncology and Nuclear Medicine, Dinkontekrankenhaus Rotenberg, Germany; ³Department of Radiation Oncology, Heinrich Heine University, Dueseldorf, Germany; ⁴Department of Radiation Oncology, VU University Medical Center, The Netherlands

- iii. Interleukin-8 release is increased by hypoxia⁶⁸ This has been demonstrated in human glioblastoma cells in culture. IL-8 has been shown to have angiogenic properties in this model. The work of Shi and associates⁶⁹ confirms an increase in IL-8 by hypoxia and acidosis and suggest this contributes significantly to the aggressive biology of pancreatic cancer.



Prof Dominic D'Agostino – Starving Cancer – Ketogenic Diet, intermittent fasting



Ketogenic Diet & HBOT – 78% increase in survival

The Ketogenic Diet and Hyperbaric Oxygen Therapy Prolong Survival in Mice with Systemic Metastatic Cancer

Angela M. Poff^{1*}, Csilla Ari¹, Thomas N. Seyfried², Dominic P. D'Agostino¹

¹ Department of Molecular Pharmacology and Physiology, University of South Florida, Tampa, Florida, United States of America, ² Department of Biology, Boston College, Chestnut Hill, Massachusetts, United States of America

Abstract

Introduction: Abnormal cancer metabolism creates a glycolytic-dependency which can be exploited by lowering glucose availability to the tumor. The ketogenic diet (KD) is a low carbohydrate, high fat diet which decreases blood glucose and elevates blood ketones and has been shown to slow cancer progression in animals and humans. Abnormal tumor vasculature creates hypoxic pockets which promote cancer progression and further increase the glycolytic-dependency of cancers. Hyperbaric oxygen therapy (HBO₂T) saturates tumors with oxygen, reversing the cancer promoting effects of tumor hypoxia. Since these non-toxic therapies exploit overlapping metabolic deficiencies of cancer, we tested their combined effects on cancer progression in a natural model of metastatic disease.

Methods: We used the firefly luciferase-tagged VM-M3 mouse model of metastatic cancer to compare tumor progression and survival in mice fed standard or KD *ad libitum* with or without HBO₂T (2.5 ATM absolute, 90 min, 3x/week). Tumor growth was monitored by *in vivo* bioluminescent imaging.

Results: KD alone significantly decreased blood glucose, slowed tumor growth, and increased mean survival time by 56.7% in mice with systemic metastatic cancer. While HBO₂T alone did not influence cancer progression, combining the KD with HBO₂T elicited a significant decrease in blood glucose, tumor growth rate, and 77.9% increase in mean survival time compared to controls.

Conclusions: KD and HBO₂T produce significant anti-cancer effects when combined in a natural model of systemic metastatic cancer. Our evidence suggests that these therapies should be further investigated as potential non-toxic treatments or adjuvant therapies to standard care for patients with systemic metastatic disease.

Citation: Poff AM, Ari C, Seyfried TN, D'Agostino DP (2013) The Ketogenic Diet and Hyperbaric Oxygen Therapy Prolong Survival in Mice with Systemic Metastatic Cancer. PLoS ONE 8(6): e65522. doi:10.1371/journal.pone.0065522

Editor: Chih-Hsin Tang, China Medical University, Taiwan

Received: December 20, 2012; **Accepted:** May 2, 2013; **Published:** June 5, 2013

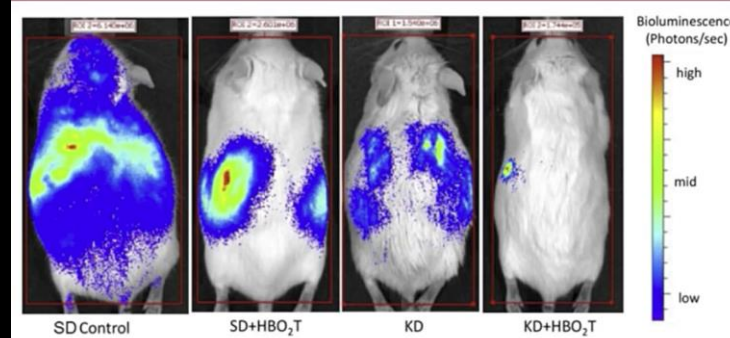
Copyright: © 2013 Poff et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: This work was supported by the Office of Naval Research, ONR grant N000140610105 and ONR-DURIP equipment grant N000140210643 (<http://www.onr.navy.mil/>). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: abennett@health.usf.edu

Press-Pulse therapy using the KD with hyperbaric oxygen for managing systemic metastatic cancer in VM mice



Poff, A., C. Ari, T. N. Seyfried, and D. P. D'Agostino (PLoS One, 2013)

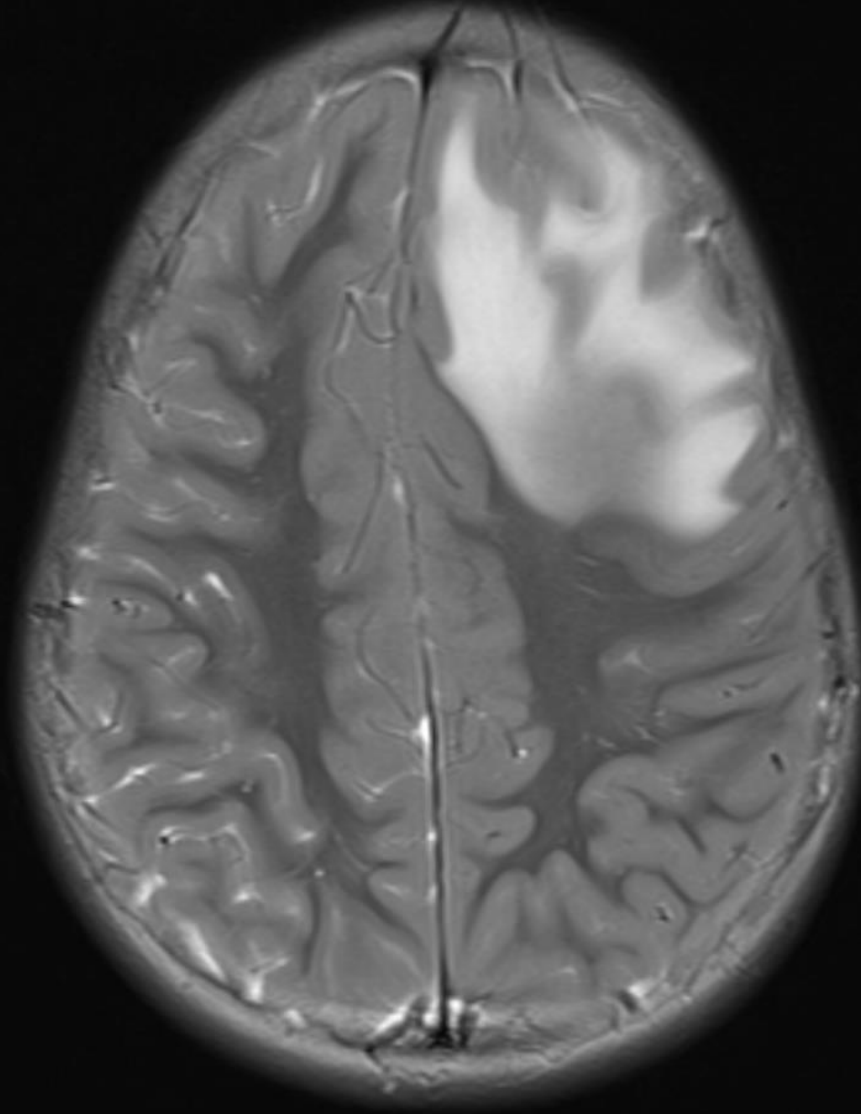
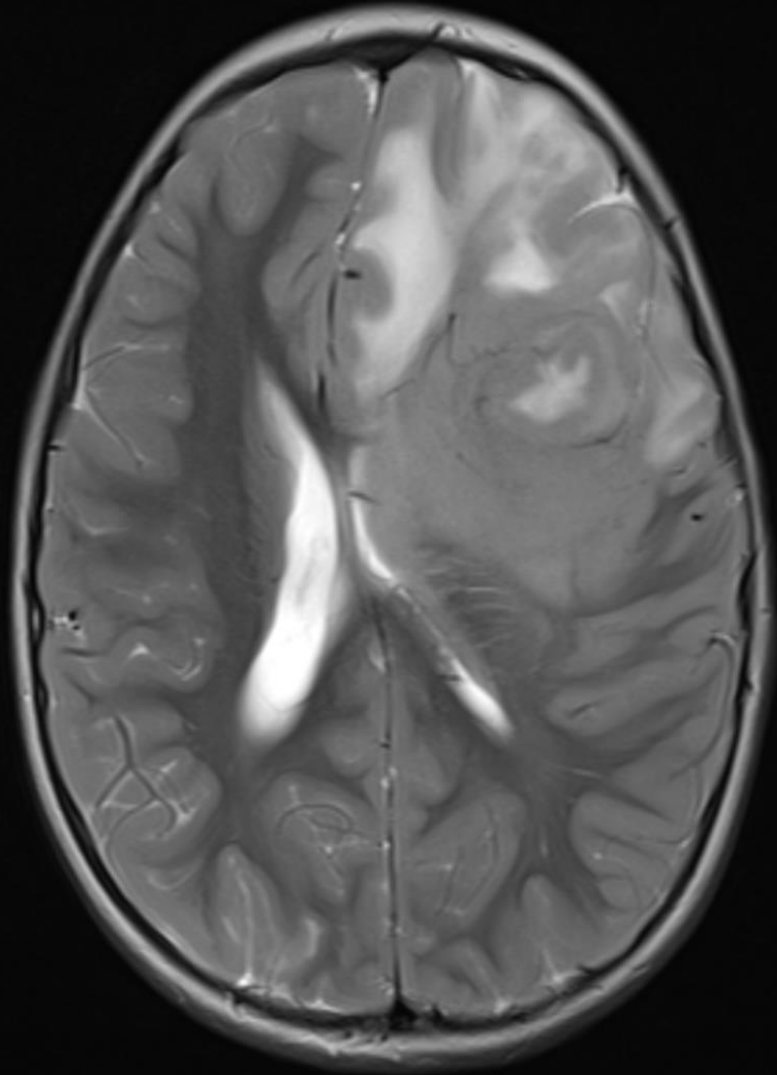
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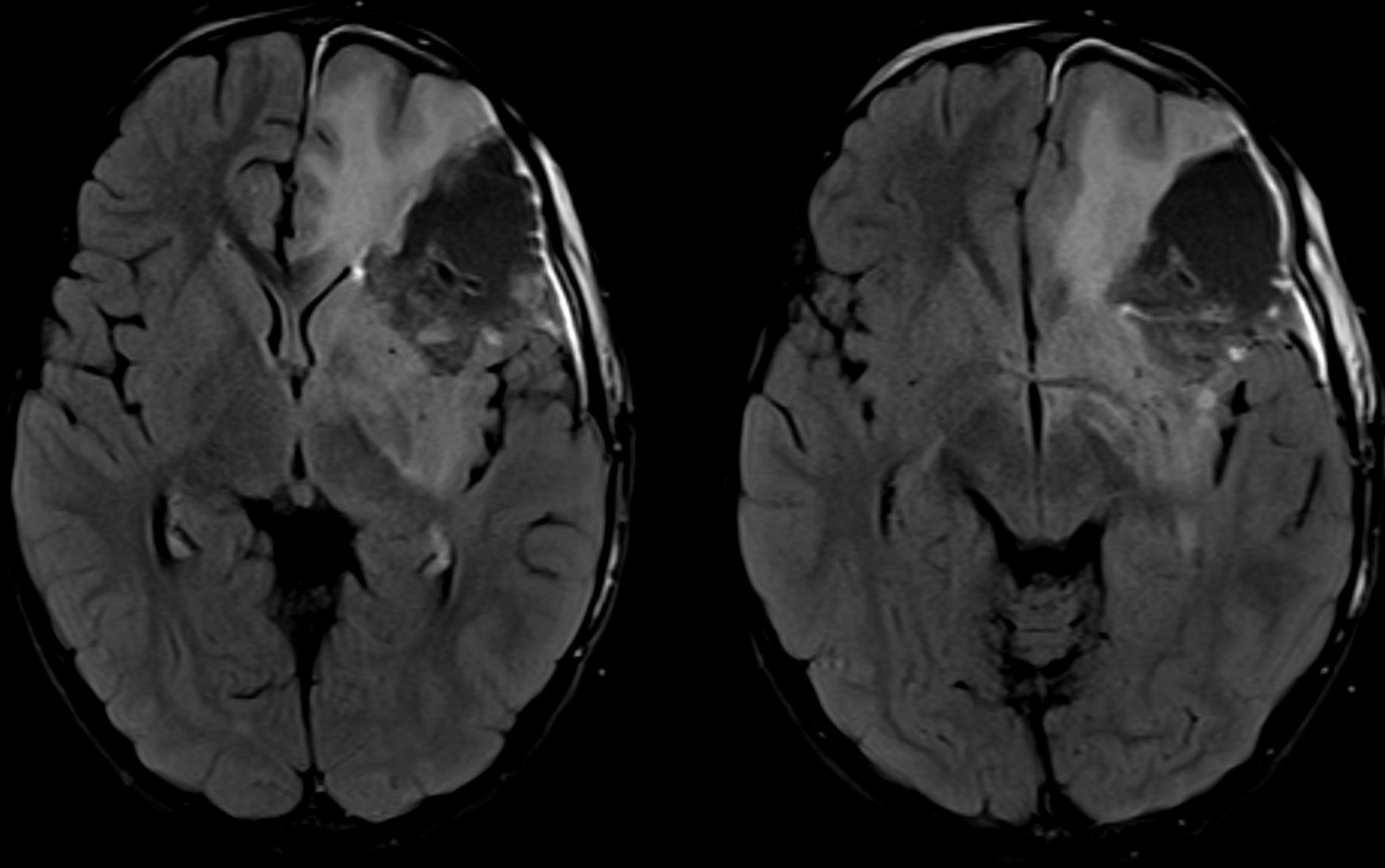
Thomas Seyfried: Cancer: A Metabolic Disease With Metabolic Solutions

OXYMED

Case Study – Glioblastoma Multiforme, age 7



Surgical resection, Radiotherapy



Cytokine Profile – Before HBOT



Date of Birth : 21-Oct-2009
Sex : M
Collected : 01-Mar-2017

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Lab id: UR#:

INTEGRATIVE MEDICINE

BLOOD - SERUM

CYTOKINES, Extensive Panel

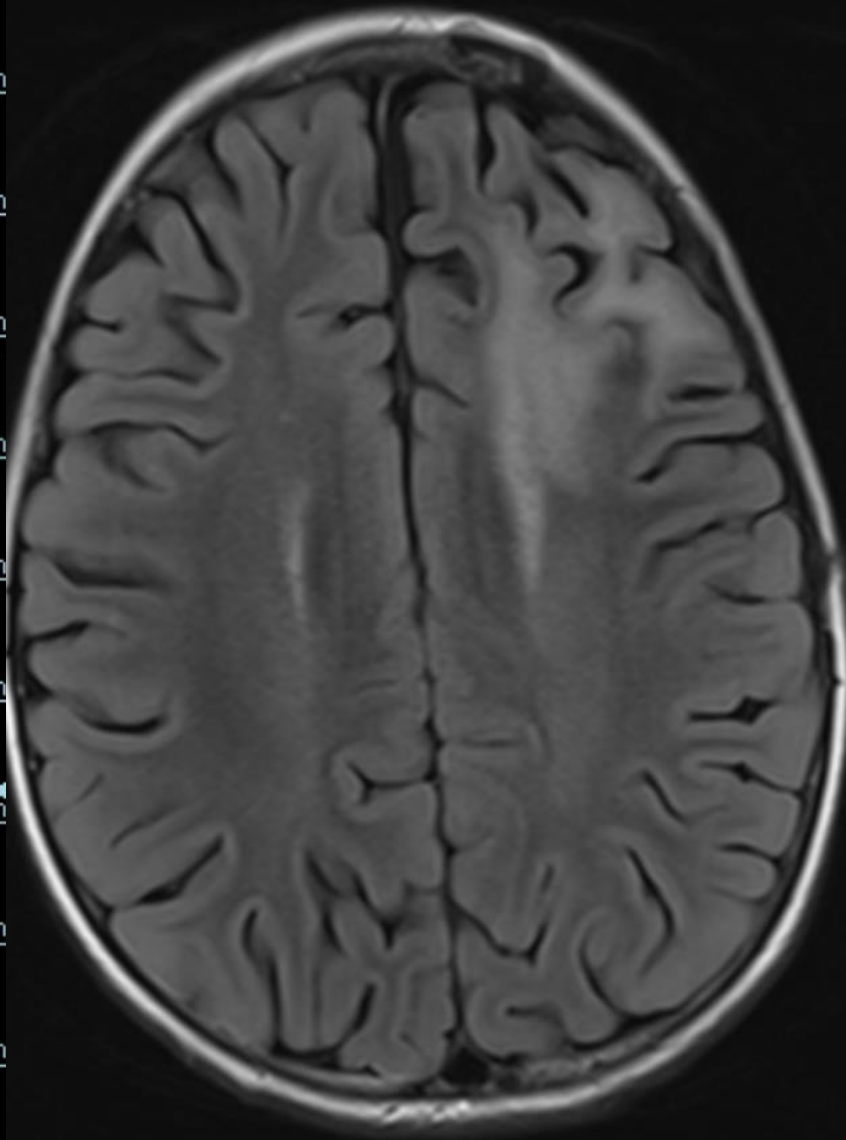
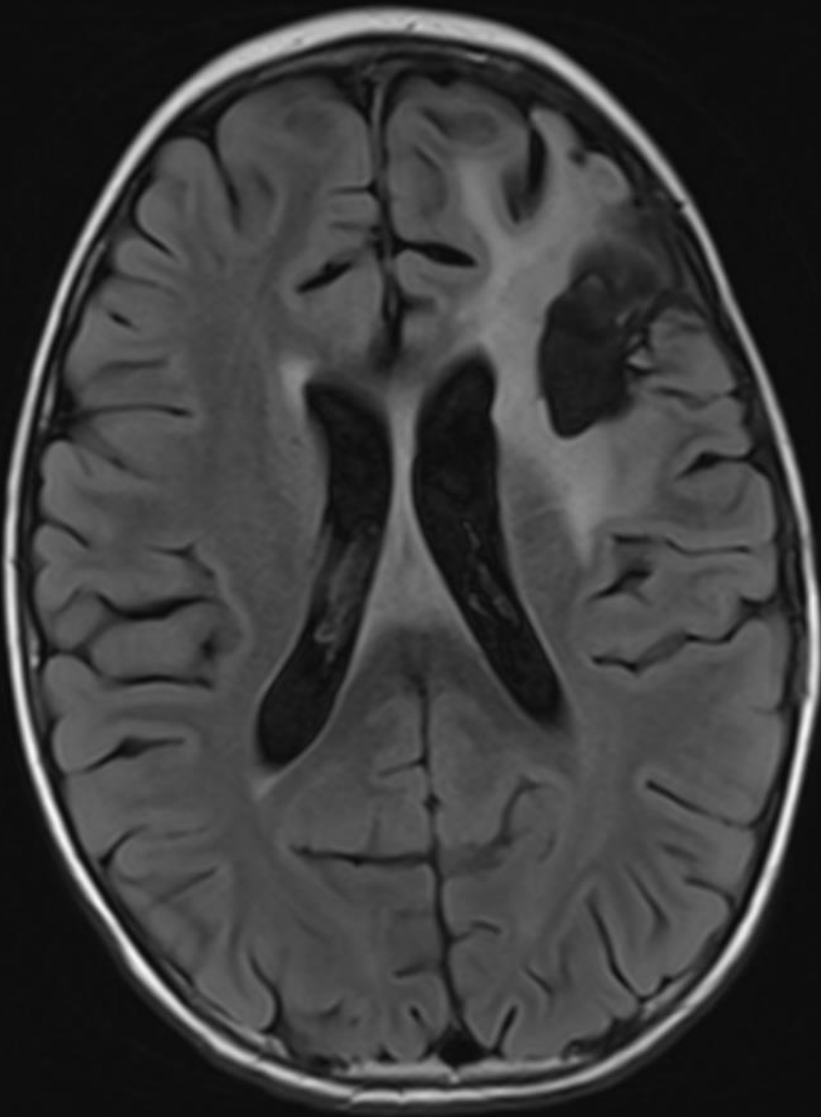
ProInflammatory Cytokines (TH1)

	Result	Range	Units	
Interleukin 1	3463.0 *H	0.0 - 2.8	pg/mL	
Interleukin 6	1252.0 *H	0.0 - 11.0	pg/mL	
Interleukin 7	67.8 *H	0.0 - 16.0	pg/mL	
Interleukin 8	>2500.0 *H	0.0 - 28.0	pg/mL	
Interleukin 17	10.4	< 13.0	pg/mL	
TNFa	816.00 *H	0.00 - 13.00	pg/mL	
TNFb	164.0 *H	0.0 - 156.0	pg/mL	
S100B	151.8 *H	60.0 - 100.0	pg/mL	

AntiInflammatory Cytokines (TH2)

GM-CSF	1620.0 *H	0.0 - 80.0	pg/mL	
Interleukin 2	7.4	0.0 - 10.0	pg/mL	
Interleukin 3	<3.2	< 5.0	pg/mL	
Interleukin 4	127.2 *H	0.0 - 19.0	pg/mL	
Interleukin 5	3.8	0.0 - 13.0	pg/mL	
Interleukin 10	99.7 *H	0.0 - 7.0	pg/mL	
Interleukin 12	7.9	0.0 - 14.0	pg/mL	
Interleukin 13	21.7 *H	0.0 - 6.0	pg/mL	
INFg	25.8	0.0 - 28.0	pg/mL	
TGFb	57.7	28.0 - 64.0	pg/mL	
Brain Derived Neurotrophic Factor BDNF	33.2	20.0 - 50.0	ng/mL	

HBOT 84 hours



Cytokine Profile – Before and After HBOT (106 hours)



Date of Birth : 21-Oct-2009
Sex : M
Collected : 01-Mar-2017
02-May-2017

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SOUTH YARRA VIC 3141

Lab id: UR#:

INTEGRATIVE MEDICINE

BLOOD - SERUM

CYTOKINES, Extensive Panel

ProInflammatory Cytokines (TH1)

	Result	Hours		
	0	106.0		
Interleukin 1	3463.0 *H	1.9	0.0 - 2.8	pg/mL
Interleukin 6	1252.0 *H	4.9	0.0 - 11.0	pg/mL
Interleukin 7	67.8 *H	24.8 *H	0.0 - 16.0	pg/mL
Interleukin 8	>2500.0 *H	48.4 *H	0.0 - 28.0	pg/mL
Interleukin 17	10.4	7.8	< 13.0	pg/mL
TNFa	816.00 *H	10.80	0.00 - 13.00	pg/mL
TNFb	164.0 *H	144.0	0.0 - 156.0	pg/mL
S100B	151.8 *H	13.6 *L	60.0 - 100.0	pg/mL

AntiInflammatory Cytokines (TH2)

GM-CSF	1620.0 *H	1510.3 *H	0.0 - 80.0	pg/mL
Interleukin 2	7.4	3.6	0.0 - 10.0	pg/mL
Interleukin 3	<3.2	<3.0	< 5.0	pg/mL
Interleukin 4	127.2 *H	44.4 *H	0.0 - 19.0	pg/mL
Interleukin 5	3.8	1.8	0.0 - 13.0	pg/mL
Interleukin 10	99.7 *H	14.8 *H	0.0 - 7.0	pg/mL
Interleukin 12	7.9	2.4	0.0 - 14.0	pg/mL
Interleukin 13	21.7 *H	7.1 *H	0.0 - 6.0	pg/mL
INFg	25.8	17.7	0.0 - 28.0	pg/mL
TGFb	57.7	50.2	28.0 - 64.0	pg/mL
Brain Derived Neurotrophic Factor BDNF	33.2	382.0 *H	20.0 - 50.0	ng/mL

HBOT & Glioblastoma Multiforme

Med Gas Res.


2018 Apr 18;8(1):24-28. doi: 10.4103/2045-9912.229600. eCollection 2018 Jan-Mar.

Hyperbaric Oxygen Therapy as adjunctive strategy in treatment of glioblastoma multiforme.

- Glioblastoma multiforme (GBM) is the most common type of malignant intracranial tumor in adults. Tumor tissue hypoxia, high mitotic rate, and rapid tumor spread account for its poor prognosis. **Hyperbaric oxygen therapy (HBOT) may improve the sensitivity of radio-chemotherapy by increasing oxygen tension within the hypoxic regions of the neoplastic tissue.** This review summarizes the research of HBOT applications within the context of experimental and clinical GBM.
- Limited clinical trials and preclinical studies suggest that radiotherapy immediately after **HBOT enhances the effects of radiotherapy** in some aspects.
- **HBOT also is able to strengthen the anti-tumor effect of chemotherapy when applied together.**
- Overall, HBOT is well tolerated in the GBM patients and does not significantly increase toxicity. However, HBOT applied by itself as curative strategy against GBM is controversial in preclinical studies and has not been evaluated rigorously in GBM patients. In addition to HBOT favorably managing the therapeutic resistance of GBM, future research needs to focus on the multimodal or cocktail approaches to treatment, as well as molecular strategies targeting GBM stem cells.




HBOT combined with DOXIL – ‘tumour inhibition rate of 91.5%’

"As a result, the combination treatment (DOX-loaded liposome (Doxil) is coadministered with HBO) synergistically inhibits tumor growth, with a tumor inhibition rate of 91.5%." 


Adv Sci (Weinh). 2018 Jun 25;5(8):1700859. doi: 10.1002/advs.201700859. eCollection 2018 Aug.


Hyperbaric Oxygen Potentiates Doxil Antitumor Efficacy by Promoting Tumor Penetration and Sensitizing Cancer Cells.

- Hypoxia plays a central role in tumor biology,[1] as it not only fuels tumor development, progression, and metastasis, but also induces chemotherapy resistance both in pharmacokinetics and pharmacodynamics.[2] Hypoxia upregulates hypoxia induced factor 1 α (HIF-1 α)[3] and collagen,[4] which builds up a dense extracellular matrix (ECM) and severely limits drug delivery efficiency and antitumor efficacy.[5] Moreover, tumor cells under hypoxic condition are often caught in an inactive state and are insensitive to chemotherapeutic agents.[6] 

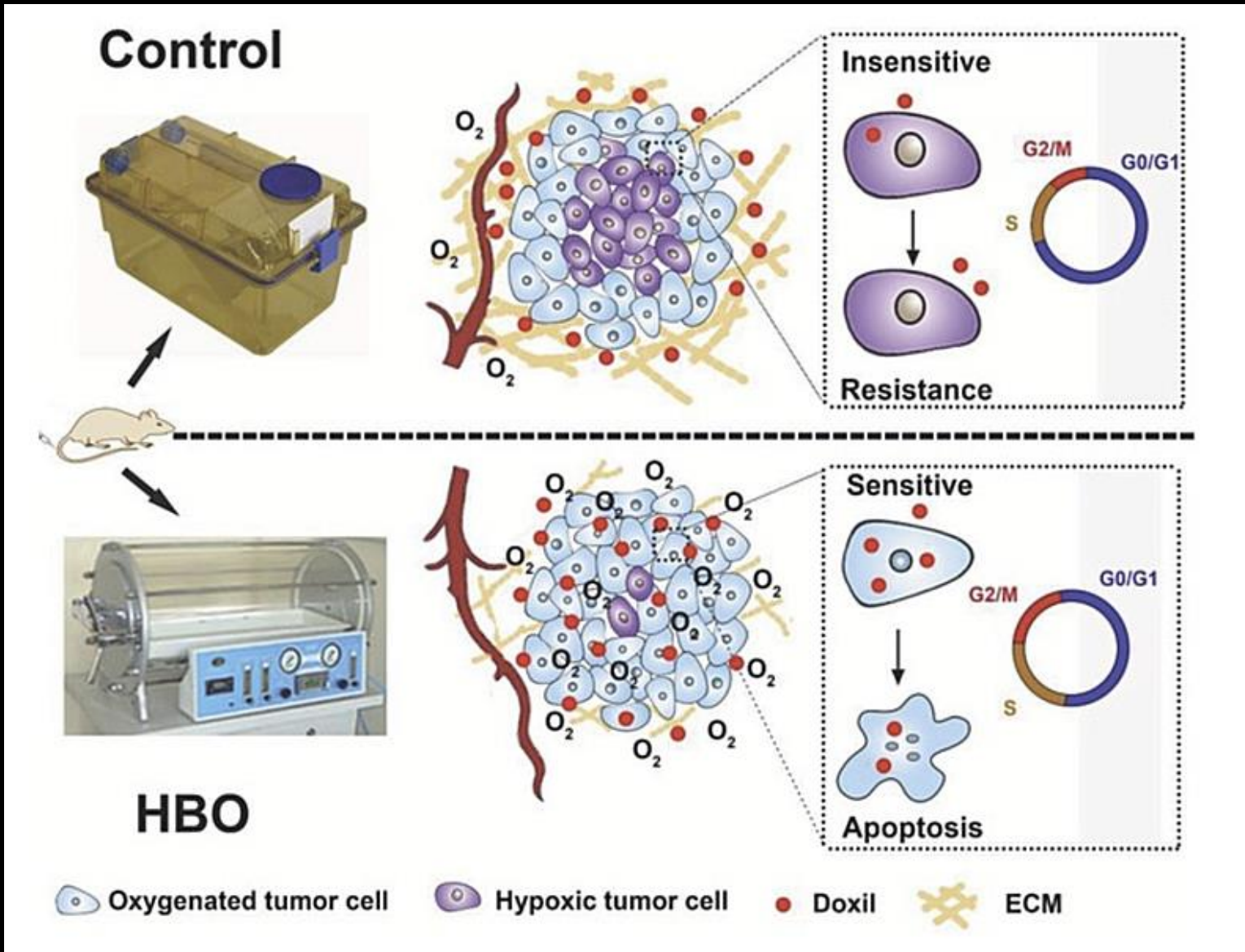
- Therefore, overcoming hypoxia can significantly potentiate chemotherapy. To that end, various systems aiming at raising oxygen tension at hypoxic solid tumors have been urgently pursued.[7]. Hyperbaric oxygen (HBO) therapy can overcome tumor hypoxia and has been routinely utilized in clinics for many years.[8] Operating at elevated pressure, typically 2–3 atmosphere absolute (ATA), HBO increases the oxygen concentration in the plasma and therefore facilitates oxygen delivery directly. HBO is considered a safe clinical treatment and has been used for ischemia, acute carbon monoxide poisoning, nonhealing wounds, and late radiation injury.[9] As an effective approach in elevating oxygen content, HBO has already been combined with radiotherapy and photodynamic therapy for hypoxic solid tumor treatment.[10]

- HBO therapy reduced the deposition of collagen in tumor ECM. These results are aligned with published work which has shown that the number of collagen fibril per μm^2 in tumor tissue decreased 66.7% after HBO therapy.[16] Combined with the immunohistochemistry and western blotting results of HIF-1 α , the results showed in Figure 2 demonstrate that HBO therapy decreases collagen fibril deposition through the regulation of HIF-1 α /CTGF/collagen I pathway. Decreased collagen I deposition in tumor ECM is expected to boost Doxil deep penetration and accumulation in tumor tissue.[5a,15c,32] These findings (Figures 2 and 3) clearly demonstrate that HBO opens up the dense ECM in hypoxic solid tumors and selectively benefits Doxil rather than DOX.

- To the best of our knowledge, this is the first report in which HBO therapy acts as a facilitative therapy for deep penetration of nanotherapeutics. A variety of methods have also been developed to bolster penetration of nanotherapeutics,[37] and many of these focus on degradation of tumor ECM by delivering small molecular drugs or enzymes. 

- Compared with these methods, HBO uses oxygen as a drug to oxygenate hypoxic tumors and modulate ECM. Oxygen has the advantage of higher delivery and penetration efficiencies under HBO situations. Moreover, the drugs and enzymes used to degrade ECM in those methods have safety concerns that must be alleviated with clinical trials, whereas HBO has been used for many years with a proven safety profile. Collectively, our results show that HBO therapy reinforces Doxil penetration and enhances DOX accumulation at tumor tissue. These actions are beneficial for in vivo antitumor efficacy 

HBOT & Liposomal DOXIL



Normobaric Oxygen combined with Chemotherapy - Carboplatin

"Intermittent normobaric hyperoxia combined with chemotherapy reduced the tumor number by 59% and the load by 72% compared with the control"

Korean J Intern Med. 2018 May;33(3):541-551. doi: 10.3904/kjim.2016.334. Epub 2017 Dec 15.

Combination of carboplatin and intermittent normobaric hyperoxia synergistically suppresses benzo[a]pyrene-induced lung cancer.

We explored the effects of intermittent normobaric hyperoxia alone or combined with chemotherapy on the growth, general morphology, oxidative stress, and apoptosis of benzo[a]pyrene (B[a]P)-induced lung tumors in mice.

METHODS:

Female A/J mice were given a single dose of B[a]P and randomized into four groups: control, carboplatin (50 mg/kg intraperitoneally), hyperoxia (95% fraction of inspired oxygen), and carboplatin and hyperoxia. Normobaric hyperoxia (95%) was applied for 3 hours each day from weeks 21 to 28. Tumor load was determined as the average total tumor numbers and volumes. Several markers of oxidative stress and apoptosis were evaluated.

RESULTS:

Intermittent normobaric hyperoxia combined with chemotherapy reduced the tumor number by 59% and the load by 72% compared with the control B[a]P group. Intermittent normobaric hyperoxia, either alone or combined with chemotherapy, decreased the levels of superoxide dismutase and glutathione and increased the levels of catalase and 8-hydroxydeoxyguanosine. The Bax/Bcl-2 mRNA ratio, caspase 3 level, and number of transferase-mediated dUTP nick end-labeling positive cells increased following treatment with hyperoxia with or without chemotherapy.

CONCLUSIONS:

Intermittent normobaric hyperoxia was found to be tumoricidal and thus may serve as an adjuvant therapy for lung cancer. Oxidative stress and its effects on DNA are increased following exposure to hyperoxia and even more with chemotherapy, and this may lead to apoptosis of lung tumors.



OXYMED

Case Study – Autism

Case Study DC age 7 Autism

Cytokine Testing pre-HBOT, then again at 70-hours HBOT and final test at 120 hours HBOT.

- High functional autism, non-social, non-verbal.
- Typically between 50-70 hours of HBOT, there is a 'washout of inflammatory cytokines' followed by reduction of the inflammatory markers corresponding with notable elevation of the anti-inflammatory cytokines including BDNF (Brain Derived Neurotrophic Factor).
- After 120-hours of HBOT, young DC has significant improvements including global executive functioning, talking, instructional responsive, social interactions, drawing and reading.



Autism Case Study DC – before HBOT



Date of Birth : 20-Nov-2013
Sex : M
Collected : 16-Jan-2018

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Lab id: UR#:

INTEGRATIVE MEDICINE

BLOOD - SERUM

CYTOKINES, Extensive Panel

ProInflammatory Cytokines (TH1)

	Result	Range	Units	
Interleukin 1	6.2 *H	0.0 - 2.8	pg/mL	
Interleukin 6	6.7	0.0 - 11.0	pg/mL	
Interleukin 7	22.7 *H	0.0 - 16.0	pg/mL	
Interleukin 8	106.3 *H	0.0 - 28.0	pg/mL	
Interleukin 17	26.7 *H	< 13.0	pg/mL	
TNFa	21.60 *H	0.00 - 13.00	pg/mL	
TNFb	98.0	0.0 - 156.0	pg/mL	
S100B	>5000.0 *H	60.0 - 100.0	pg/mL	

AntiInflammatory Cytokines (TH2)

GM-CSF	1217.7 *H	0.0 - 80.0	pg/mL	
Interleukin 2	7.3	0.0 - 10.0	pg/mL	
Interleukin 3	9.6 *H	< 5.0	pg/mL	
Interleukin 4	30.6 *H	0.0 - 19.0	pg/mL	
Interleukin 5	5.4	0.0 - 13.0	pg/mL	
Interleukin 10	35.3 *H	0.0 - 7.0	pg/mL	
Interleukin 12	15.6 *H	0.0 - 14.0	pg/mL	
Interleukin 13	24.0 *H	0.0 - 6.0	pg/mL	
INFg	18.5	0.0 - 28.0	pg/mL	
TGFb	36.4	28.0 - 64.0	pg/mL	
Brain Derived Neurotrophic Factor BDNF	47.0	20.0 - 50.0	ng/mL	

Autism Case Study DC – Before and After HBOT (120 hours)



Date of Birth : 20-Nov-2013
Sex : M
Collected : 16-Jan-2018

OXYMED, 643 CHAPEL STREET
SOUTH YARRA VIC 3141

Lab id: UR#:

INTEGRATIVE MEDICINE

BLOOD - SERUM

CYTOKINES, Extensive Panel

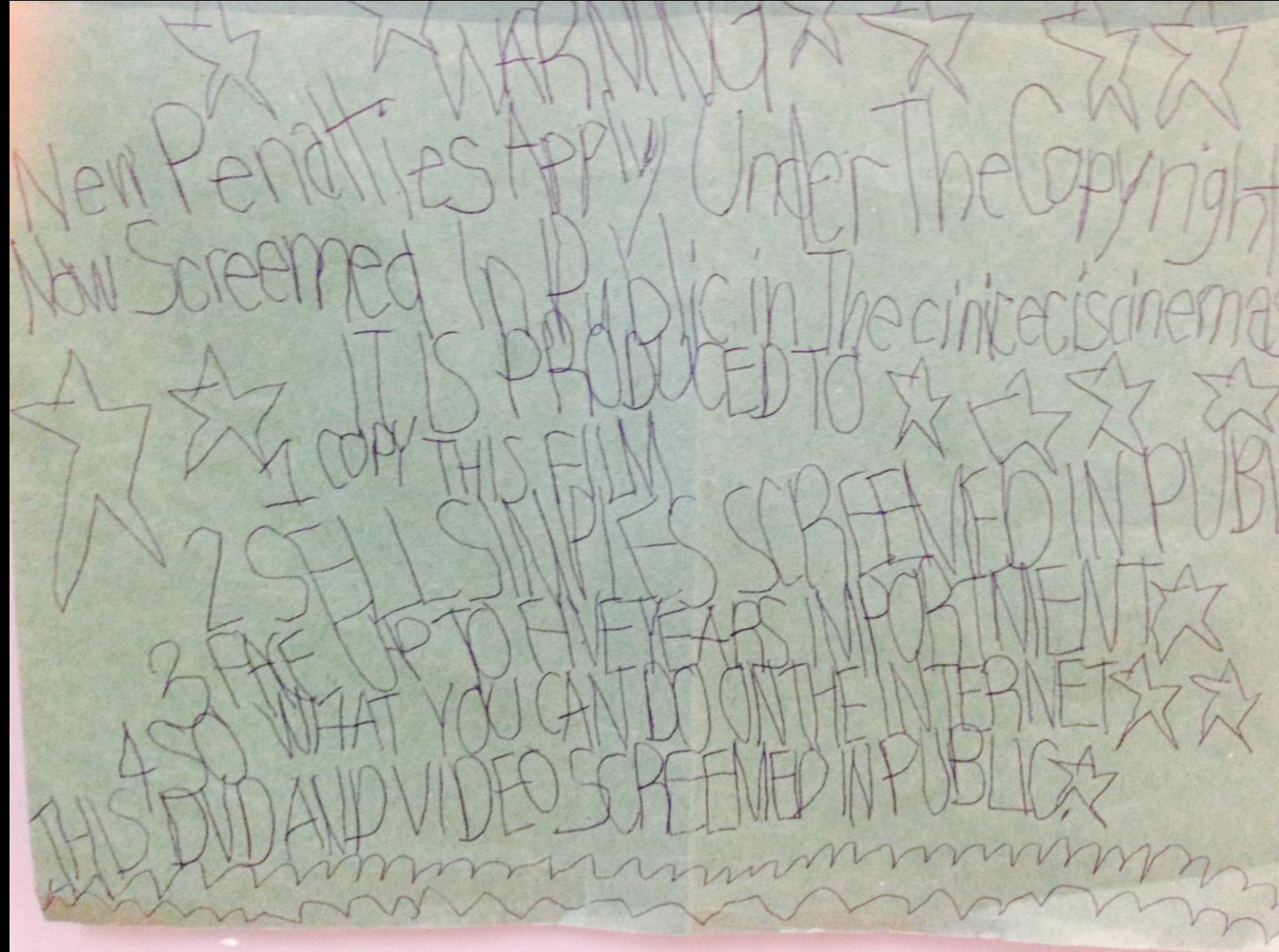
ProInflammatory Cytokines (TH1)

	Result	70.0	120.0	
Interleukin 1	6.2 *H	945.6 *H	9.6 *H	0.0 - 2.8
Interleukin 6	6.7	<0.4	7.2	0.0 - 11.0
Interleukin 7	22.7 *H	43.9 *H	34.3 *H	0.0 - 16.0
Interleukin 8	106.3 *H	>2500.0 *H	317.9 *H	0.0 - 28.0
Interleukin 17	26.7 *H	16.6 *H	33.0 *H	< 13.0
TNFA	21.60 *H	213.90 *H	33.40 *H	0.00 - 13.00
TNFb	98.0	123.0	93.0	0.0 - 156.0
S100B	>5000.0 *H	639.0 *H	<10.0 *L	60.0 - 100.0

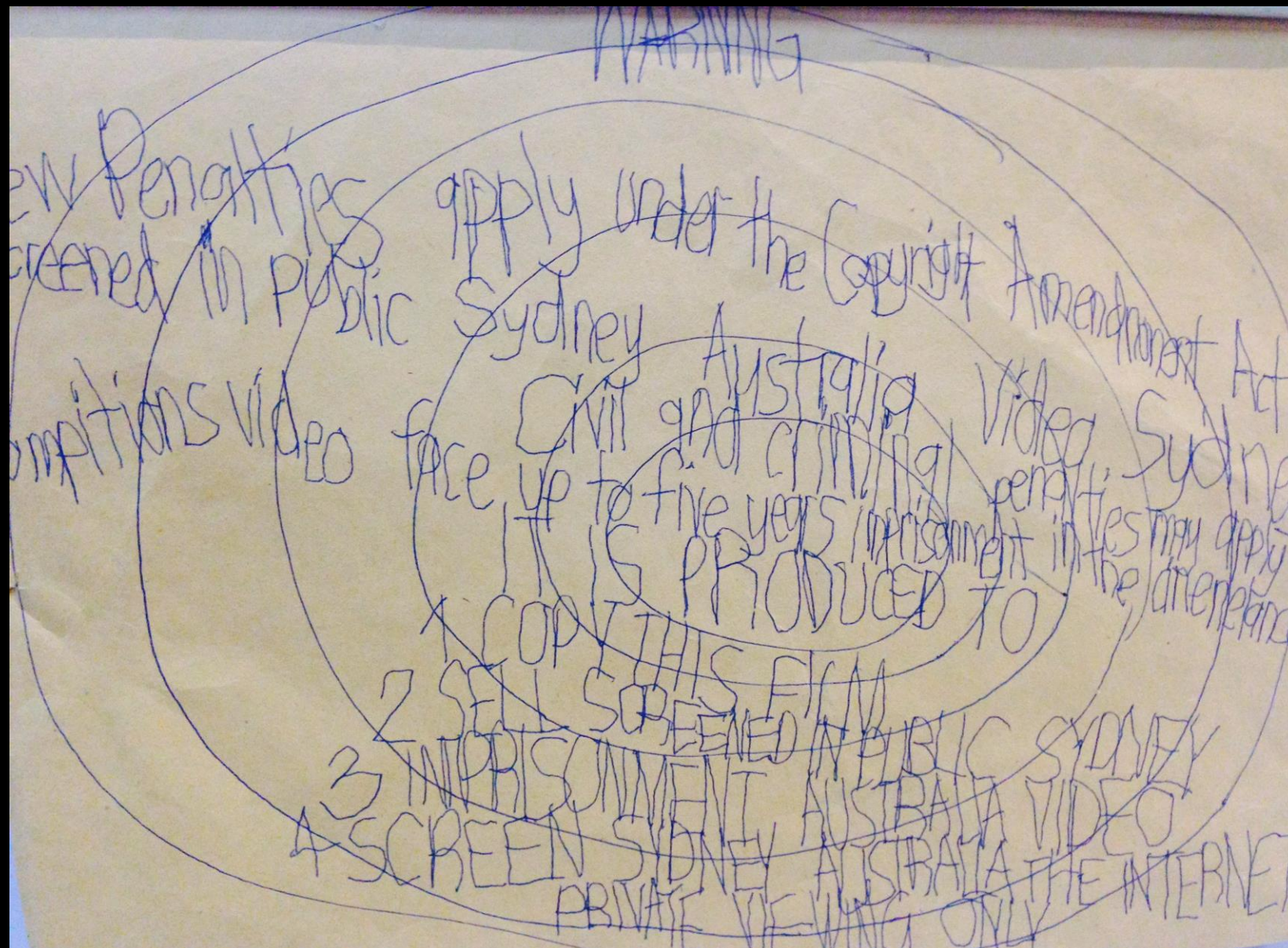
AntiInflammatory Cytokines (TH2)

GM-CSF	1217.7 *H	1710.3 *H	514.0 *H	0.0 - 80.0
Interleukin 2	7.3	9.8	9.6	0.0 - 10.0
Interleukin 3	9.6 *H	1.3	<1.0	< 5.0
Interleukin 4	30.6 *H	34.7 *H	61.3 *H	0.0 - 19.0
Interleukin 5	5.4	4.7	5.2	0.0 - 13.0
Interleukin 10	35.3 *H	56.9 *H	34.0 *H	0.0 - 7.0
Interleukin 12	15.6 *H	18.2 *H	13.1	0.0 - 14.0
Interleukin 13	24.0 *H	30.0 *H	37.3 *H	0.0 - 6.0
INFg	18.5	23.1	28.0	0.0 - 28.0
TGFb	36.4	33.0	37.0	28.0 - 64.0
Brain Derived Neurotrophic Factor BDNF	47.0	39.0	52.0 *H	20.0 - 50.0

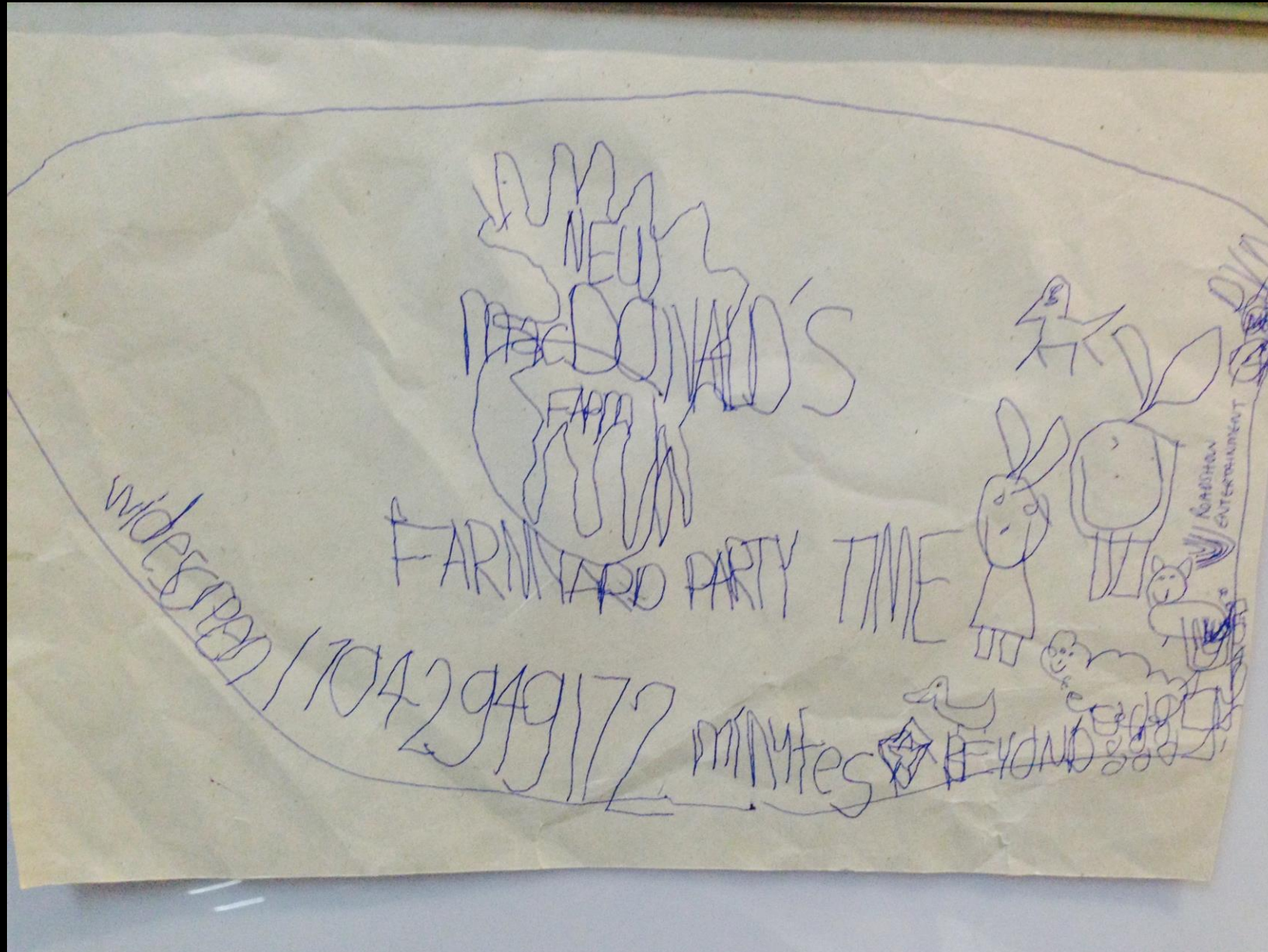
Autism ADHD - Case Study JP – after 45 hours HBOT



Case Study JP – after 45 hours HBOT



Case Study JP – after 45 hours HBOT



Brain Derived Neurotrophic Factor (BDNF)

[Int J Geriatr Psychiatry](#). 2018 Aug 29. doi: 10.1002/gps.4962. [Epub ahead of print]

Role of physical activity in ameliorating neuropsychiatric symptoms in Alzheimer disease: A narrative review.

[J Stroke Cerebrovasc Dis](#). 2018 Aug 24. pii: S1052-3057(18)30356-2. doi: 10.1016/j.jstrokecerebrovasdis.2018.06.032. [Epub ahead of print]

Brain-Derived Neurotrophic Factor Levels are Lower in Chronic Stroke Patients: A Relation with Manganese-dependent Superoxide Dismutase ALA16VAL Single Nucleotide Polymorphism through Tumor Necrosis Factor- α and Caspases Pathways.

[Med Sci Monit](#). 2018 Aug 26;24:5943-5950. doi: 10.12659/MSM.909449.

Diagnostic Significance of Serum Levels of Nerve Growth Factor and Brain Derived Neurotrophic Factor in Diabetic Peripheral Neuropathy.

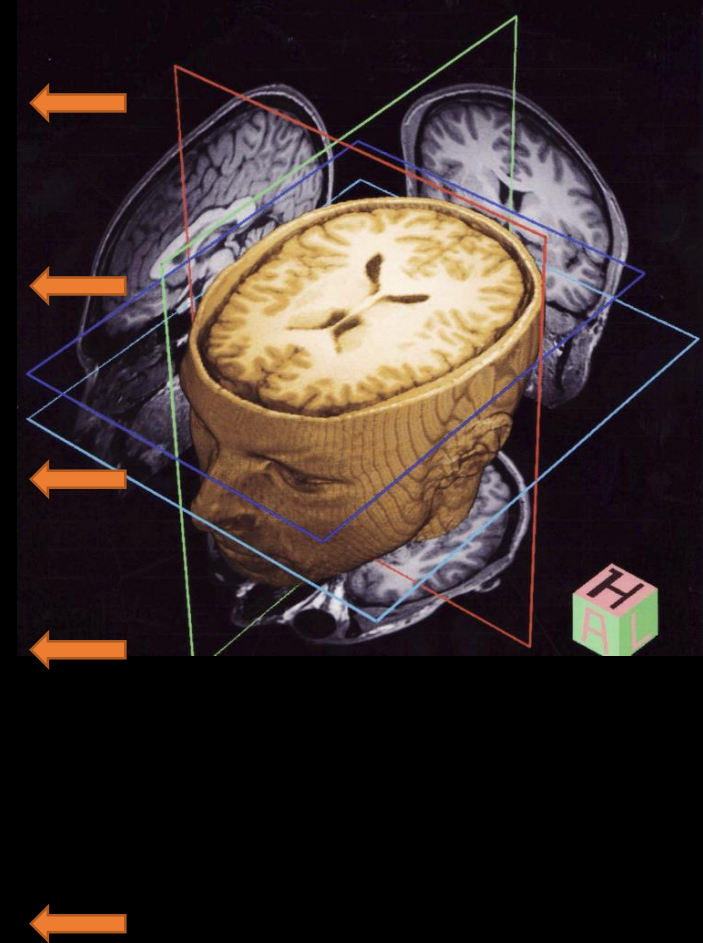
[Psychiatry Res](#). 2018 Jul 26;268:478-483. doi: 10.1016/j.psychres.2018.07.013. [Epub ahead of print]

Altered levels of brain-derived neurotrophic factor, proBDNF and tissue plasminogen activator in children with posttraumatic stress disorder.

[Zh Nevrol Psikiatr Im S S Korsakova](#). 2018;118(5. Vyp. 2):51-56. doi: 10.17116/jnevro20181185251.

[A neuroprotective approach to optimizing treatment and correction activities in children with autism spectrum disorders].

RESULTS AND CONCLUSION: There was a decrease in NGF, BDNF, Hsp27, Hsp70 in the total group and in boys with severe ASD. These changes reflect the deterioration of neuroprotective processes in the brain in children with ASD that demands further research and development of treatment procedures.



Cerebrolysin (BDNF)

- Cerebrolysin – brain derived neurotrophic factor (BDNF), glial derived neurotrophic factor (GDNF), nerve growth factor (NGF), ciliary neurotrophic factor (CNTF) and other peptide fragments.
- **Improves cognitive performance and global function** in neurodegenerative disorders with 'increased daily quality living'. CL activates cerebral mechanisms related to attention and memory processes.
- CL improvements reported in **mild to moderate progressive neurodegenerative disease** - multiple sclerosis, Parkinson's disease, Alzheimer's disease, dementia, acute and chronic Stroke, acute traumatic brain injury, childhood autism (89%) and cerebral palsy.
- Attenuates **motor neuron damage in spinal cord** with significant motor recovery. reducing chronic nerve cell inflammation in both acute and chronic neurodegenerative diseases.
- Neuroprotective and neurorestorative properties, demonstrates '**anti-aging**' with benefits '**improving cognition, memory function, brain metabolism with capacity.**
- **Reduces brain A β deposition**, and tau-related neuropathology. Modulates neuroinflammation, attenuating microglia activation and IL-1 β release, reducing the elevated serum levels of TNF- α and TNF receptor-1 in AD patients.
- **Neurotrophic-like actions** on neuronal survival and outgrowth, increases circulating IGF-1 and BDNF levels in humans. Enhances the supply of glucose to the brain and **ameliorates the slowing of brain bioelectrical activity.**
- Promotes **neural plasticity, neurogenesis and neuronal survival** protecting from apoptosis and degeneration.



Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial

Rahav Boussi-Gross^{1,3}, Haim Golan^{3,4,5}, Gregori Fishlev¹, Yair Bechor¹, Olga Volkov^{3,4}, Jacob Bergan¹, Mony Friedman¹, Dan Hoofien^{6,7}, Nathan Shlamkovitch⁸, Eshel Ben-Jacob^{2,5,9,10*}, Shai Efrati^{1,2,3,10*}

¹ The Institute of Hyperbaric Medicine, Assaf Harofeh Medical Center, Zerifin, Israel, ² Research and Development Unit, Assaf Harofeh Medical Center, Zerifin, Israel, ³ Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel, ⁴ Nuclear Medicine Institute, Assaf Harofeh Medical Center, Zerifin, Israel, ⁵ The Raymond and Beverly Sackler Faculty of Exact Sciences, School of Physics and Astronomy, Tel-Aviv University, Tel-Aviv, Israel, ⁶ Department of Psychology, The Hebrew University of Jerusalem, Jerusalem, Israel, ⁷ The National Institute for the Rehabilitation of the Brain Injured, Tel-Aviv, Israel, ⁸ Otolaryngology, Head & Neck Surgery, Assaf-Harofeh Medical Center, Zerifin, Israel, ⁹ Center for Theoretical Biological Physics, Rice University, Houston, Texas, United States of America, ¹⁰ Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

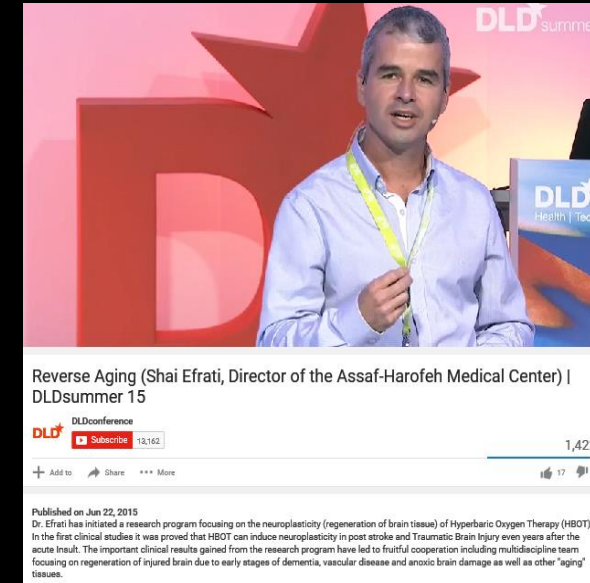
Abstract

Background: Traumatic brain injury (TBI) is the leading cause of death and disability in the US. Approximately 70-90% of the TBI cases are classified as mild, and up to 25% of them will not recover and suffer chronic neurocognitive impairments. The main pathology in these cases involves diffuse brain injuries, which are hard to detect by anatomical imaging yet noticeable in metabolic imaging. The current study tested the effectiveness of Hyperbaric Oxygen Therapy (HBOT) in improving brain function and quality of life in mTBI patients suffering chronic neurocognitive impairments.

Methods and Findings: The trial population included 56 mTBI patients 1–5 years after injury with prolonged post-concussion syndrome (PCS). The HBOT effect was evaluated by means of prospective, randomized, crossover controlled trial: the patients were randomly assigned to treated or crossover groups. Patients in the treated group were evaluated at baseline and following 40 HBOT sessions; patients in the crossover group were evaluated three times: at baseline, following a 2-month control period of no treatment, and following subsequent 2-months of 40 HBOT sessions. The HBOT protocol included 40 treatment sessions (5 days/week), 60 minutes each, with 100% oxygen at 1.5 ATA. "Mindstreams" was used for cognitive evaluations, quality of life (QOL) was evaluated by the EQ-5D, and changes in brain activity were assessed by SPECT imaging. Significant improvements were demonstrated in cognitive function and QOL in both groups following HBOT but no significant improvement was observed following the control period. SPECT imaging revealed elevated brain activity in good agreement with the cognitive improvements.

Conclusions: HBOT can induce neuroplasticity leading to repair of chronically impaired brain functions and improved quality of life in mTBI patients with prolonged PCS at late chronic stage.

Trial Registration: ClinicalTrials.gov NCT00715052



Hyperbaric Oxygen Induces Late Neuroplasticity in Post Stroke Patients - Randomized, Prospective Trial

Shai Efrati^{1,2,3*}, Gregori Fishlev¹, Yair Bechor¹, Olga Volkov^{3,4}, Jacob Bergan¹, Kostantin Kliakhandler⁵, Izhak Kamiager^{3,6}, Nachum Gal¹, Mony Friedman¹, Eshel Ben-Jacob^{2,5,7}, Haim Golan^{3,4}

1 The Institute of Hyperbaric Medicine, Assaf Harofeh Medical Center, Zerifin, Israel, **2** Research and Development Unit, Assaf Harofeh Medical Center, Zerifin, Israel, **3** Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel, **4** Nuclear Medicine Institute, Assaf Harofeh Medical Center, Zerifin, Israel, **5** School of Physics and Astronomy, The Raymond and Beverly Sackler Faculty of Exact Sciences, Tel-Aviv University, Tel-Aviv, Israel, **6** Neurology Department, Assaf Harofeh Medical Center, Zerifin, Israel, **7** Center for Theoretical Biological Physics, Rice University, Houston, Texas, United States of America

Abstract

Background: Recovery after stroke correlates with non-active (stunned) brain regions, which may persist for years. The current study aimed to evaluate whether increasing the level of dissolved oxygen by Hyperbaric Oxygen Therapy (HBOT) could activate neuroplasticity in patients with chronic neurologic deficiencies due to stroke.

Methods and Findings: A prospective, randomized, controlled trial including 74 patients (15 were excluded). All participants suffered a stroke 6–36 months prior to inclusion and had at least one motor dysfunction. After inclusion, patients were randomly assigned to "treated" or "cross" groups. Brain activity was assessed by SPECT imaging; neurologic functions were evaluated by NIHSS, ADL, and life quality. Patients in the treated group were evaluated twice: at baseline and after 40 HBOT sessions. Patients in the cross group were evaluated three times: at baseline, after a 2-month control period of no treatment, and after subsequent 2-months of 40 HBOT sessions. HBOT protocol: Two months of 40 sessions (5 days/week), 90 minutes each, 100% oxygen at 2 ATA. We found that the neurological functions and life quality of all patients in both groups were significantly improved following the HBOT sessions while no improvement was found during the control period of the patients in the cross group. Results of SPECT imaging were well correlated with clinical improvement. Elevated brain activity was detected mostly in regions of live cells (as confirmed by CT) with low activity (based on SPECT) – regions of noticeable discrepancy between anatomy and physiology.

Conclusions: The results indicate that HBOT can lead to significant neurological improvements in post stroke patients even at chronic late stages. The observed clinical improvements imply that neuroplasticity can still be activated long after damage onset in regions where there is a brain SPECT/CT (anatomy/physiology) mismatch.

Trial Registration: ClinicalTrials.gov NCT00715897

HBOT neuroprotection elevating (hippocampus) brain stem cells

A Dual Role for Hyperbaric Oxygen in Stroke Neuroprotection: Preconditioning of the Brain and Stem Cells

[Grant M. Liska](#), [Trenton Lippert](#), [Eleonora Russo](#), [Norton Nieves](#), and [Cesar V. Borlongan](#)¹

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The publisher's final edited version of this article is available at [Cond Med](#)

Abstract

Go to: 

Stroke continues to be an extremely prevalent disease and poses a great challenge in developing safe and effective therapeutic options. Hyperbaric oxygen therapy (HBOT) has demonstrated significant pre-clinical effectiveness for the treatment of acute ischemic stroke, and limited potential in treating chronic neurological deficits. Reported benefits include reductions in oxidative stress, inflammation, neural apoptosis, and improved physiological metrics such as edema and oxygen perfusion, all of which contribute to improved functional recovery. This pre-clinical evidence has failed to translate into an effective evidence-based therapy, however, due in large part to significant inconsistencies in treatment protocols and design of clinical studies. While the medical community works to standardize clinical protocols in an effort to advance HBOT for acute stroke, pre-clinical investigations continue to probe novel applications of HBOT in an effort to optimize stroke neuroprotection. One such promising strategy is HBOT preconditioning. Based upon the premise of mild oxidative stress priming the brain for tolerating the full-blown oxidative stress inherent in stroke, HBOT preconditioning has displayed extensive efficacy. Here, we first review the pre-clinical and clinical evidence supporting HBOT delivery following ischemic stroke and then discuss the scientific basis for HBOT preconditioning as a neuroprotective strategy. Finally, we propose the innovative concept of stem cell preconditioning, in tandem with brain preconditioning, as a promising regenerative pathway for maximizing the application of HBOT for ischemic stroke treatment.

HBOT Erectile Dysfunction

Int J Impot Res. 2018 May 18. doi: 10.1038/s41443-018-0023-9. [Epub ahead of print]

Hyperbaric oxygen can induce angiogenesis and recover erectile function.

Hadanny A1,2,3, Lang E4,5,6, Copel L5,7, Meir O4, Bechor Y4, Fishlev G4,5, Bergan J4,5, Zisman A5,6, Efrati S4,5,8,9.

Author information

Erratum in

- Correction: *Hyperbaric oxygen can induce angiogenesis and recover erectile function.* [Int J Impot Res. 2018]

Abstract

Erectile dysfunction (ED) is caused by microvascular or macrovascular insufficiency in the majority of patients. Recent studies have shown that hyperbaric oxygen therapy (HBOT) can induce angiogenesis in different body organs. The effect of HBOT on the non-surgery-related ED has not been investigated yet. The aim of the current study was to evaluate the effects of HBOT on sexual function and penile vascular bed in non-surgical ED patients. A prospective analysis of patients suffering from chronic ED treated with 40 daily HBOT sessions (80-hours HBO 2 ATA 100% O₂).

Clinical efficacy was assessed using the International Index of Erectile Function questionnaire (IIEF) and a global efficacy question (GEQ). The effect on the penile vascular bed was evaluated by perfusion MRI.

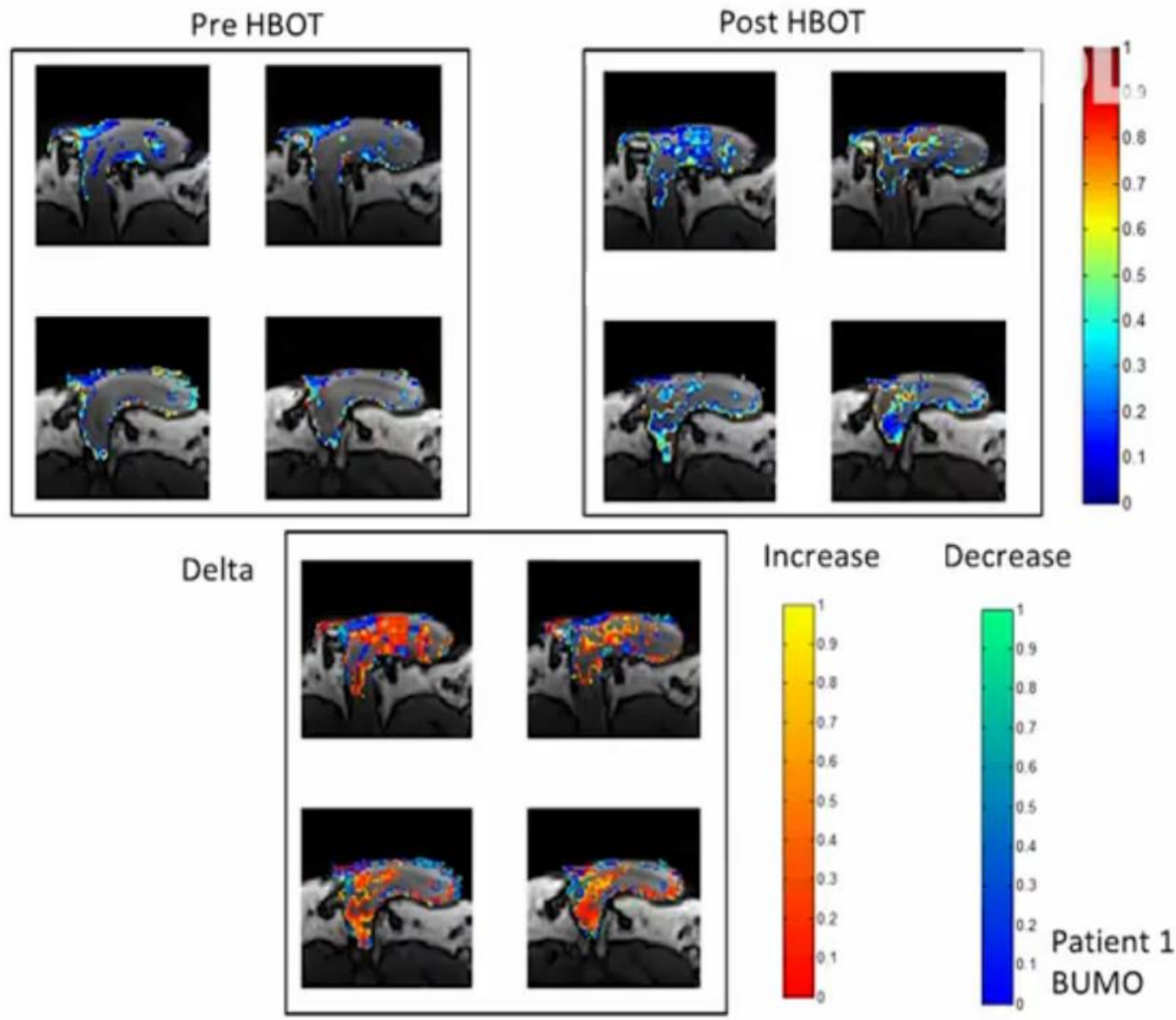
Thirty men (mean age of 59.2 ± 1.4) suffering from ED for 4.2 ± 0.6 years completed the protocol. HBOT significantly improved all IIEF domains by 15-88% ($p < 0.01$). Erectile function improved by 88% ($p < 0.0001$) and 80% of the patients reported positive outcome according to the GEQ.

Angiogenesis was indicated by perfusion MRI that showed a significant increase by $153.3 \pm 43.2\%$ of K-trans values in the corpus cavernous ($p < 0.0001$).

- HBOT can induce penile angiogenesis and improve erectile function in men suffering from EcD. HBOT reverses the basic common pathophysiology, atherosclerosis and decreased penile perfusion, responsible for most cases of ED.



Blood flow changes



OXYGEN is “OXYGENE” Therapy



OXYMED

Hyperbaric Oxygen impacts the Cellular landscape

- Hyperbaric Oxygen is breathing 100 per cent oxygen at pressures greater than normal. HBOT increases dissolved oxygen into the into the damaged regions of the body. HBO increases blood plasma by 10-15 fold (1000-1500 per cent). The normal blood plasma carry only 1-2 per cent oxygen with red blood cells carrying approximately 98 per cent oxygen.
- *"Hyperbaric Oxygen Therapy creates a 'fertile neurovascular platform' for emerging stem cell, immunotherapies and nanotechnology techniques. The impact and success of these and future procedures are dependent on the integrity of the underlying supporting neurovascular bed."* (Hooper 2005).
- HBO acts as a 'catalyst' promoting immune modulation. HBO results in increased blood flow by fostering the formation of **existing and new capillary dynamics** (neovascularization) activating damaged and dormant nerve cells ('penumbra state'). HBO accelerates neuroplasticity.
- Approximately 20 to 30 percent of the body's consumption of Oxygen occurs within three to five per cent of the body mass – the brain and spinal cord. These structures are extremely sensitive to Oxygen deficiency and the use of HBO.
- Increased Oxygenation accelerates the rate of healing, stabilization and repair through numerous immune modulating effects, providing upregulation of anti-inflammatory cytokines, including: Granulocyte Macrophage Colony Stimulating Factor (GM-CSF), Interleukin-3 (IL3), Interleukin-4 (IL4), Interleukin10 (IL10), Interleukin-13 (IL13), Interleukin-21 (IL21), Brain Derived Neural Growth Factors (BDNF, GDNF), Vascular Growth Factors (VEGF), TGFβ1 Signaling and IGF1.
- In chronic injuries, the microenvironment is in a constant **smoldering "cytokine storm" state**. Pro-inflammatory cytokines are important in mobilizing the reparative and regenerative responses when 'attacked', but chronic over-expression leads to immune confusion and autoimmune degradation. Over-expressions of pro-inflammatory cytokines can affect synaptic strength and synaptic plasticity, and excess contributes to maladaptive plasticity and chronic pain syndromes.



Hyperbaric Oxygen 'Epigenetic Therapy' (Harch 2015)

- In essence, hyperbaric therapy physicians are playing a symphony with patients' gene expression, the music of which is determined by the various pressures and amounts of hyperoxia to which the patient is exposed.
- Tissue growth requires replication of DNA. **HBOT is a DNA signaling agent.**
- A single HBOT, at the pressure used for diabetic foot wounds and radiation wounds up or downregulated the expression of **8,101 genes** (nearly 50%) of the known 19-20,000 protein-coding genes in the human genome.
- Clusters of neuronal genes are affected by 'different pressures' and 'different amounts of hyperoxia'.
- Upregulated genes are primarily growth and repair hormones and anti-inflammatory genes.
- Downregulated genes are the pro-inflammatory and apoptotic genes.
- HBO 'expands the therapeutic window' reducing continuing neurovascular deterioration. HBO upregulates the patient's own **target specific Stem Cells** (with an 8-fold or 800 percent increase in circulating CD34+).
- HBO enhances **Mitochondrial respiration.**
- HBO proliferates Granulocyte Macrophage Colony Stimulating Factor (GM-CSF), Interleukin-3 (IL3), Interleukin-4 (IL4), Interleukin-10 (IL10), Interleukin-13 (IL13), Interleukin-21 (IL21), Brain Derived Neural Growth Factors (BDNF, GDNF), Vascular Growth Factors (VEGF), TGFβ Signalling, IGF1.
- HBO reduces **Telomere degeneration.**
- HBO down regulates toxic intra and extra cellular inflammatory Cytokines (IL1, 2, 6, 7, 8, 17), Tumour Necrosis Factor Alpha (TNFα), GlycA, S100B.
- HBO inhibits opportunistic infections (MRSA, viral, bacterial, parasitic), cell sepsis and more.

Harch Medical Gas Research (2015) 5:9
DOI 10.1186/s13618-015-0030-6



COMMENTARY

Open Access

Hyperbaric oxygen in chronic traumatic brain injury: oxygen, pressure, and gene therapy

Paul G. Harch



OXYMED

President Trump – “Heal The Warriors”

New law gives veterans option to seek oxygen-based therapy for PTSD



Julie Havlak
in CJ Exclusives

July 30, 2019
2:19PM



Healing technology for Hoosier veterans Norton Fort Wayne Journal Gazette - 24 Dec. 2016

We need \$2 million in funding for a world-class **hyperbaric oxygen** therapy treatment program, conducted in existing Indiana clinics.



HEAL THE WARRIORS

Traumatic Brain Injury (TBI) | Post-Concussion Syndrome (PCS)
Post-Traumatic Stress Disorder (PTSD)
Hyperbaric Oxygen Therapy - Fighting to treat the effects of TBI and PTSD

Veterans study reports reduction in suicide ideation after HBOT

<https://medicalxpress.com> > Psychology & Psychiatry ▼

Oct 19, 2017 - The improvements, including a discontinuation or decreased dosage of ... Hyperbaric oxygen therapy is the use of increased atmospheric pressure ... ideation prior to the HBOT did not express suicidal thoughts after treatment.

PTSD Symptoms, Suicidal Ideation Reduced by Oxygen Therapy ...

<https://www.psychiatryadvisor.com> > ... > Anxiety > PTSD trauma and stressor-related ▼

Oct 25, 2017 - Hyperbaric oxygen therapy (HBOT) demonstrated a significant drop in post-traumatic stress disorder (PTSD) symptoms and suicidal ideation in ...

China – over 5000 Chambers in use with over ‘60-conditions’ approved.



Large-scale medical oxygen chamber group

 Yantai Hongyuan Oxygen Industrial Inc.



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 31

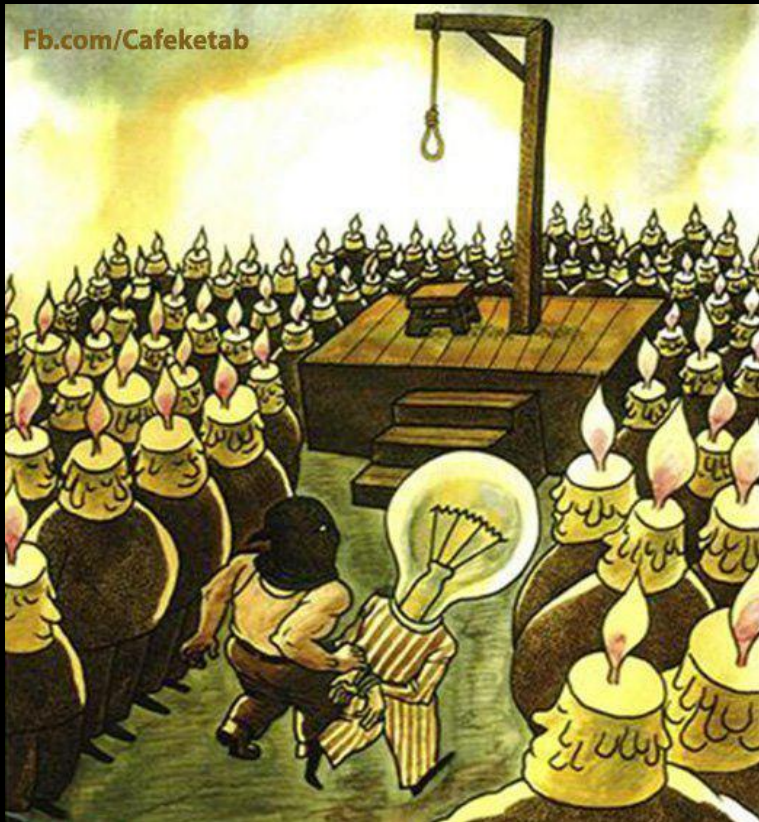
 3 Comments

 129 Shares

AHPRA v DR MALCOLM R HOOPER (2009-2013)

- [AHPRA vs Dr Malcolm R. Hooper \(2009-2013\)](#)

* AHPRA in its media releases FAILS to acknowledge that the treatment challenged under the National Law were in relationship to **Hyperbaric Oxygen Therapy** for [71 listed conditions](#) (as listed from P76 Jain TextBook - Summary of International Conditions Treated using HBOT) and **LOKOMAT Robotic Gait Assisted Walking** (now covered at several Australian Hospitals and also under the NDIS program).



Australian **Health Practitioner** Regulation Agency

G.P.O. Box 9958 | Melbourne VIC 3001 | www.ahpra.gov.au

1

In this case, the Chiropractic Board of Australia used its full powers under the National Law and laid a complaint against Malcolm Hooper in the Victorian Civil and Administrative Tribunal, in one of the most protracted legal actions in health practitioner regulation in Australia.

The Tribunal found that Dr Hooper's claims on his website about hyperbaric oxygen treatment were misleading and deceptive because he did not present a balanced view about the effectiveness of hyperbaric oxygen treatment for specified conditions, including that such treatment was not conventionally used in Australia and in western countries with a comparable health service culture and was not supported by medical and scientific evidence.

As a result of the action taken by the Chiropractic Board of Australia and the tribunal decision, his registration was cancelled and his name was removed from the public register of registered practitioners on 30 August 2013. Malcolm Hooper is now listed on the [List of cancelled practitioners](#).



MALCOLM R. HOOPER

