



JANE WINANS, MA, received a master of arts in teaching from National-Louis University. She currently works for United Way. Jane lives in Manitowoc, Wisconsin, with her husband and three daughters. She and Dr. Norm Schwartz are establishing an organization to educate families and physicians on treatments for T21.



NORM SCHWARTZ, MD, is an integrative medicine specialist with over 30 years' experience and an extensive background in treating complex chronic health problems. Formerly medical director of Integrative Medicine for Wheaton Franciscan Healthcare in Milwaukee, Wisconsin, he is now in private practice, focusing on helping individuals and families who are dealing with ADHD and autism spectrum and neurodevelopmental disorders. As a practitioner with the network formerly known as Defeat Autism Now!, he approaches autism as a medical disorder that is treatable. Dr. Schwartz has a special interest in the application of ecological principles for the creation of a safer, more sustainable world for present and future generations.

In addition to his medical degree and residency training, Dr. Schwartz has received postgraduate training and education from the American Academy of Environmental Medicine, the Santa Fe Institute for Complex Studies, the Functional Medicine Institute, the International College of Integrative Medicine, and the American Academy for the Advancement of Medicine. He is a founding member of the American Society of Integrative Medical Practice and a Fellow of the Health Studies Collegium, a health policy and clinical outcomes research foundation.

HOW HYPERBARIC OXYGEN THERAPY HELPED MY DAUGHTER WITH DOWN SYNDROME

BY JANE WINANS, MA,
WITH CONTRIBUTIONS BY NORM SCHWARTZ, MD

I believe that Down syndrome is treatable, just like autism. For Down syndrome parents who share this belief, this can mean working with heavy metal chelation, vitamin supplements, methylation, oxidative stress, leaky gut, neurofeedback, and hyperbaric oxygen therapy (HBOT). (Your issues, my issues.) It might also mean Amy Yasko, S. Jill James, and doctors belonging to the network formerly known as Defeat Autism Now! (DAN!). (Your experts, my experts.) Again, Down syndrome is treatable.

My daughter Lydia is 9 and has Down syndrome. The medical name for her condition is trisomy 21 (T21). Dr. Norm Schwartz, Lydia's integrative medicine physician, describes the implications of T21 in this way:

Chromosome 21 is one of 23 human chromosomes. Normally, there are two copies of each chromosome: one from each parent. The addition of a third copy of the 21st chromosome, from either the mom or dad, is the usual cause of Down syndrome. In 2000, it was determined that chromosome 21 contains 1.5% of a cell's DNA, making it the chromosome with the smallest amount of DNA.¹ Of interest, this diminutive chromosome contains genes that code for enzymes and proteins with critical roles in cell physiology, including amyloid-beta precursor protein, cystathione beta-synthase, and superoxide dismutase that contribute to the pathophysiology of T21.

Exactly how the extra chromosome causes Down syndrome is still being researched. Possibilities include direct or indirect gene dysregulation or overexpression of genes on chromosome 21. And despite intensive medical research, how the complexity and variability of the genotype in T21 is involved in the phenotypic expression of Down syndrome is not fully understood.²⁻⁸ However,

*although generally not currently well appreciated, it is crucial that we increasingly begin to recognize the degree to which medical problems seen in T21 are the consequences of metabolic dysfunction from genetic alterations.*⁹⁻¹⁷

In any case, understanding how the *metabolic disruption in T21 creates multiple downstream consequences* that adversely affect cellular networks is the first step to treatment. Documented biochemical and physiological abnormalities in T21 include reduced energy production,¹⁸⁻²⁰ decreased glutathione,^{21,22} compromised mitochondrial function,²³⁻²⁷ increased oxidative stress,²⁸⁻³² neurotransmitter imbalances,^{15,33-35} altered redox regulation,^{4,36-39} abnormalities in the critical one-carbon methylation pathway,²¹ and faulty DNA repair.^{17,40} Knowledge of these biochemical and physiological abnormalities points the way to a rational, physiology-based treatment regimen to mitigate the adverse consequences of T21.

Down syndrome is treatable.



The enormity of that extra chromosome can still bring me to tears, even today when Lydia is in the third grade, reading Junie B. Jones books independently (these are beginning chapter books appropriate for up to third graders), going to basketball and dance class with her peers, calling friends on the phone to finagle sleepovers, and arguing her bedtime with me. How incredibly blessed we are. We have been able to get to this point because Lydia has consistently done well with targeted interventions. Her most dramatic improvements occurred in August 2011 after she began HBOT. To understand her progress with HBOT, however, it may help to first explain the other therapies that Lydia has used along the way.

LYDIA'S PATH TO HEALING

Lydia has been cared for with various therapies and interventions almost from birth. Throughout her first year, Lydia took omega-3 supplements and a multivitamin specific to people with T21. In addition, after being identified as hypothyroid at 2 months, Lydia began thyroid replacement that continues to the present day. Lydia also began receiving craniosacral therapy (CST) at a very young age to address cranial facial abnormalities that can otherwise inhibit brain function, respiration, and sleep. She continues to receive CST a number of times a year. At 5 months, Lydia had heart surgery for an atrial septal defect (congenital heart defect).

At 15 months, after a friend told me that children with autism and children with Down syndrome share some metabolic similarities, Lydia had her first appointment with a doctor

from what was formerly known as the DAN! network. Based on research and metabolic testing specific to Lydia, which revealed that her metabolic analysis profile was very dysfunctional, we began to systematically address her metabolic dysfunction. First, we implemented a gluten-free/casein-free (GF/CF) diet as well as more healthful food choices. We watched her carbohydrate and sugar intake to improve her digestive function. Many parent support networks have reported the benefits of this approach. A diet that decreases hard-to-digest and potentially allergenic and reactive foods can help with digestion, vitamin and mineral absorption, gut integrity, and balanced intestinal flora, all of which can benefit an individual with T21. In addition, gluten and casein, if not completely broken down, can have a negative effect on brain function. In T21, there is also an increased incidence of celiac disease, so eliminating gluten is an important proactive strategy since celiac disease often does not have intestinal symptoms and/or can be present for an extended period of time before it is diagnosed. Lydia began eating a high-protein, low-carbohydrate diet containing as much organic food as we could afford and nothing artificial. Lydia's doctor also recommended NAET (Nambudripad's Allergy Elimination Techniques) to eliminate Lydia's food and environmental sensitivities.

Lydia's testing pointed to vitamin insufficiency coupled with heavy metal overload, which affected almost every metabolic cycle and interrelationships among cycles. We addressed her high levels

of lead, mercury, and aluminum with both chelation and supplementation, devoting many appointments to determining what supplements to push and what metals to pull to allow her metabolic cycles to rotate as designed. Lydia's test results showed steady metabolic improvement as we adopted this healing strategy. Whenever Lydia failed to reach her therapy milestones, we focused on the metabolic function behind the targeted abilities. For example, low tone plagued Lydia for many years. "Snap practice" was arduous because the tone in her fingers simply wasn't strong enough to allow her to snap. One day, months after we had stopped snap practice and had begun to biomedically address building better muscle tone, Lydia got up, pulled on her jeans, and snapped without effort. This was one of many reminders that we have had along the way that T21 is treatable.

At just under 2 years of age, Lydia started a targeted neurodevelopment program (National Association for Child Development) which continued until she entered kindergarten.

ATTENTION AND COGNITIVE FUNCTION

In kindergarten, Lydia was able to read, do simple math, and learn fairly well alongside her peers. First grade was a different story, however, as Lydia's attention issues became glaringly apparent. Because Lydia did not qualify for learning disability (LD) or cognitive disability (CD) services, we heard that Lydia might not receive additional academic services. I pored over biomedical research and Lydia's lab results to try to qualify her for services under "Other Health Impairments." As I read research specific to T21 as well as descriptions of "precocious development of Alzheimer's disease" and "increased susceptibility to neuron apoptosis" (cellular suicide), often with tears streaming down my face and a breaking heart, I nevertheless refused to accept that others might be right—that I was simply in denial of all that Down syndrome implies. Although the extra chromosome will always exist, I became convinced that T21 is a treatable medical condition, and it is possible to increase functionality in many biochemical pathways to achieve improved cognition. Therefore, our concerted push to improve Lydia's attention and cognitive function began.

Research out of Stanford University has identified excessive GABA (gamma-aminobutyric acid) in people with

T21. GABA is the principal inhibitory neurotransmitter in the central nervous system. Our osteopath (DO), who was trained in Eastern medicine, prescribed Chinese memory herbs that included ginkgo, a GABA inhibitor. These helped tremendously. In addition, Lydia started taking other research-supported supplements specific to T21 abnormalities and brain function. These T21-specific interventions improved Lydia's memory, which was most clearly evidenced by her improved recall of math facts and dreams.

She also underwent auriculotherapy (stimulation of the auricle of the external ear) to enhance brain wave function and neurotransmitter levels and to achieve more fluid language production.^{41,42}

In October 2010, when Lydia was 8, we began neurofeedback to address her attention-deficit disorder (ADD) issues. Neurofeedback improved Lydia's language and focus somewhat, but daily charting of focus and attention by her teachers continued to show inconsistencies and deficits throughout second grade. As Lydia finished her second grade year, her timed math fact achievement was 10-17 per minute, and her words-read-per-minute score was low. However, it was clear to all concerned that focus rather than knowledge was the issue. With third grade looming, it became more urgent to find ways to improve both focus and cognition.

HYPERBARIC OXYGEN THERAPY

If neuron apoptosis was a feature of Down syndrome, I reasoned, then I wanted to find a way for Lydia to acquire more brain cells as well as new and healthier brain cells. In short, I wanted to find something that would stimulate neurogenesis. After I again turned to our experts, the consensus seemed to be that we should look into HBOT for Lydia.

Research has identified many ways that HBOT may benefit individuals with T21,⁴³ which are listed in Table 1. Knowing that Lydia had always responded well to mitochondrial support, our doctors saw good reason to believe that HBOT might produce comparable benefits for our daughter.

In the summer of 2011, we rented a hyperbaric chamber for a month to determine whether Lydia was a "responder" to HBOT. We used a soft chamber with a pressure of 1.3 atmospheres. Based on the recommendations of clinicians with extensive HBOT experience, we gradually increased the time Lydia was in the chamber to an hour and a half twice a day. For this month-long trial, we implemented a doable schedule that involved putting Lydia to sleep in the chamber and transferring her to her bed after one and a half hours. At 6:00 a.m., we carried her back to the chamber, where she again slept for one and a half hours.

The results of the month-long trial were amazing, with dramatic increases in Lydia's focus, attention, executive function, and language. There is no question that HBOT resulted in increased brain function. For example, there was a noticeable increase in Lydia's voice clarity on the phone, and she also began to use more sophisticated speech patterns. When retelling a story, Lydia now is able to describe the transitions characters in a book make from school to bus to home, whereas previously she related what happened without context. Lydia's math teacher, the same as last year, is awed by Lydia's improvement. Lydia's newfound focus is something her teachers could only dream of in second grade. Lydia now works independently and moves much more quickly through her work. The number of timed math facts that Lydia can complete in a minute has

increased by over half, and her words-read-per-minute also has increased significantly. For the first time, Lydia can remember and spell words consistently.

Best of all, Lydia now gets herself ready for school, getting up, getting dressed, and making her own lunch and snack in a very age-appropriate time frame. In other words, what we would expect a child of 9 to accomplish in 30 minutes actually takes 30 minutes, not 90. This has completely changed our lives. No more crabby mornings! Lydia is really excited about her newfound independence and responsibilities.

LOOKING AHEAD

As parents, none of us can afford to wait 10 or 15 years until the newest research enters into widespread medical practice. We must be advocates for our children here and now, seeking the best. As Lydia's advocate, what I have learned over the years is that, at least for my daughter, T21 is not a static condition. Clearly, the interventions we pursued for her were beneficial. As I gained greater understanding of T21 over time, I learned that the potential for treating T21 depends on understanding the metabolic consequences of chromosome 21 overexpression. Many practitioners have helped me shed light on Lydia's biochemical train wreck and have guided us through numerous interventions, some simple and easy, others more challenging and difficult.

During our month-long summer trial of HBOT, we made no changes to Lydia's neurofeedback regimen or supplements, other than a slight increase in vitamin C and coenzyme Q10 (CoQ10). Whereas in summers past we played school, read, wrote, and did math and unit studies, during our HBOT summer, I had a new job that meant we were lucky if we read a book every other day. The amount of television watched by Lydia over the summer definitely exceeded the suggested limit, as well. In short, the only meaningful change we made during that month was to add the hyperbaric oxygen therapy. Through HBOT, neurogenesis was achieved, confirming that Down syndrome is treatable. We love our happy mornings!

Table 1. Benefits of hyperbaric oxygen therapy for T21

Benefits of HBOT

1. Increases brain blood flow^{44,45}
2. Increases oxygen delivery to cells⁴⁶
3. Is anti-inflammatory^{47,48}
4. Reduces oxidative stress⁴⁹
5. Supports mitochondrial function⁴⁴
6. Mobilizes stem cells from bone marrow for self-healing⁵⁰
7. Promotes gastrointestinal healing⁵¹
8. Decreases neuroinflammation⁵²⁻⁵⁴

The results of the month-long trial were amazing, with dramatic increases in Lydia's focus, attention, executive function, and language. There is no question that HBOT resulted in increased brain function.

You can view Lydia reading at <http://www.youtube.com/user/jdwinans?ob=5#p/u/0/rnT-tKp7JMg> and hamming it up with diet talk and 3-digit math at <http://www.youtube.com/watch?v=UuWrqXvVIG8>

REFERENCES

1. Antonarakis SE, Lyle R, Deutsch S, Raymond A. Chromosome 21: a small land of fascinating disorders with unknown pathophysiology. *Int J Dev Biol*. 2002;46:89-96.
2. Coskun PE, Wyrembak J, Derbereva O, Melkonian G, Doran E, Lott IT, Head E, Cotman CW, Wallace DC. Systemic mitochondrial dysfunction and the etiology of Alzheimer's disease and down syndrome dementia. *J Alzheimers Dis*. 2010;20(Suppl 2):S293-S310.
3. Wiseman FK, Alford KA, Tybulewicz VL, Fisher EM. Down syndrome: recent progress and future prospects. *Hum Mol Genet*. 2009;18(R1):R75-R83.
4. Sawa A. Alteration of gene expression in Down's syndrome (DS) brains: its significance in neurodegeneration. *J Neural Transm Suppl*. 2001;61:361-71.
5. Reeves RH, Baxter LL, Richtsmeier JT. Too much of a good thing: mechanisms of gene action in Down syndrome. *Trends Genet*. 2001 Feb;17(2):83-8.
6. Reeves RH. Down's syndrome. A complicated genetic insult. *Lancet*. 2001 Dec;358 Suppl:S23.
7. Olson LE, Richtsmeier JT, Leszl J, Reeves RH. A chromosome 21 critical region does not cause specific Down syndrome phenotypes. *Science*. 2004 Oct;306(5696):687-90.
8. Olson LE, Roper RJ, Sengstaken CL, Peterson EA, Aquino V, Galdzicki Z, Siarey R, Pletnikov M, Moran TH, Reeves RH. Trisomy for the Down syndrome "critical region" is necessary but not sufficient for brain phenotypes of trisomic mice. *Hum Mol Genet*. 2007;16(7):774-82.
9. Lee M, Hyun D, Jenner P, Halliwell B. Effect of overexpression of wild-type and mutant Cu/Zn-superoxide dismutases on oxidative damage and antioxidant defences: relevance to Down's syndrome and familial amyotrophic lateral sclerosis. *J Neurochem*. 2001 Feb;76(4):957-65.
10. Galletti P, De Bonis ML, Sorrentino A, Raimo M, D'Angelo S, Scala I, Andria G, D'Aniello A, Ingrassio D, Zappia V. Accumulation of altered aspartyl residues in erythrocyte proteins from patients with Down's syndrome. *FEBS J*. 2007 Oct;274(20):5263-77.
11. Kim SH, Fountoulakis M, Dierssen M, Lubec G. Decreased protein levels of complex I 30-kDa subunit in fetal Down syndrome brains. *J Neural Transm Suppl*. 2001;61:109-16.
12. Griffin WS, Sheng JG, McKenzie JE, Royston MC, Gentleman SM, Brumback RA, Cork LC, Del Bigio MR, Roberts GW, Mrak RE. Life-long overexpression of S100beta in Down's syndrome: implications for Alzheimer pathogenesis. *Neurobiol Aging*. 1998 Sep-Oct;19(5):401-5.
13. Dowjat WK, Adayev T, Kuchna I, Nowicki K, Palmiello S, Hwang YW, Wegiel J. Trisomy-driven overexpression of DYRK1A kinase in the brain of subjects with Down syndrome. *Neurosci Lett*. 2007 Feb;413(1):77-81.
14. Gardiner K. Predicting pathway perturbations in Down syndrome. *J Neural Transm Suppl*. 2003;67:21-37.
15. Saran NG, Pletcher MT, Natale JE, Cheng Y, Reeves RH. Global disruption of the cerebellar transcriptome in a Down syndrome mouse model. *Hum Mol Genet*. 2003;12(16):2013-9.
16. Delabar JM, Theophile D, Rahmani Z, Chettouh Z, Blouin JL, Prieur M, Noel B, Sineit PM. Molecular mapping of twenty-four features of Down syndrome on chromosome 21. *Eur J Hum Genet*. 1993;1(2):114-24.
17. Korenberg JR, Chen XN, Schipper R, Sun Z, Gonsky R, Gerwehr S, Carpenter N, Daumer C, Dignan P, Disteche C, Graham JM Jr, Hudgins L, McGillivray B, Miyazaki K, Ogasawara N, Park JP, Pagon R, Pueschel S, Sack G, Say B, Schuffenhauer S, Soukup S, Yamanaka T. Down syndrome phenotypes: the consequences of chromosomal imbalance. *Proc Natl Acad Sci U S A*. 1994 May;91(11):4997-5001.
18. Dierssen M, Vallina IF, Baomonde C, Lumbieras MA, Martínez-Cué C, Catayud SG, Flórez J. Impaired cyclic AMP production in the hippocampus of a Down syndrome murine model. *Brain Res Dev Brain Res*. 1996 Aug;95(1):122-4.
19. Kim SH, Vlkolinsky R, Cairns N, Fountoulakis M, Lubec G. The reduction of NADH ubiquinone oxidoreductase 24- and 75-kDa subunits in brains of patients with Down syndrome and Alzheimer's disease. *Life Sci*. 2001 May;68(24):2741-50.
20. Miles MV, Patterson BJ, Chalfonte-Evans ML, Horn PS, Hickey FJ, Schapiro MB, Steele PE, Tang PH, Hotze SL. Coenzyme Q10 [ubiquinol-10] supplementation improves oxidative imbalance in children with trisomy 21. *Pediatr Neurol*. 2007 Dec;37(6):398-403.
21. Infantino V, Castegna A, Iacobazzi F, Spera I, Scala I, Andria G, Iacobazzi V. Impairment of methyl cycle affects mitochondrial methyl availability and glutathione level in Down's syndrome. *Mol Genet Metab*. 2011 Mar;102(3):378-82.
22. Schuchmann S, Heinemann U. Diminished glutathione levels cause spontaneous and mitochondria-mediated cell death in neurons from trisomy 16 mice: a model of Down's syndrome. *J Neurochem*. 2000;74:1205-14.
23. Conti A, Fabbri F, D'Agostino P, Negri R, Greco D, Genesio R, D'Armiato M, Olla C, Paladini D, Zannini M, Nitsch L. Altered expression of mitochondrial and extracellular matrix genes in the heart of human fetuses with chromosome 21 trisomy. *BMC Genomics*. 2007;8:268.
24. Shukkur EA, Shimohata A, Akagi T, Yu W, Yamaguchi M, Murayama M, Chui D, Takeuchi T, Amano K, Subramanyan KH, Hashikawa T, Sago H, Epstein CJ, Takashima A, Yamakawa K. Mitochondrial dysfunction and tau hyperphosphorylation in Ts1Cje, a mouse model for Down syndrome. *Hum Mol Genet*. 2006 Sep;15(18):2752-62.
25. Busciglio J, Pelsman A, Wong C, Pigino G, Yuan M, Mori H, Yankner BA. Altered metabolism of the amyloid beta precursor protein is associated with mitochondrial dysfunction in Down's syndrome. *Neuron*. 2002 Feb;33(5):677-88.
26. Arbuzova S, Hutchin T, Cuckle H. Mitochondrial dysfunction and Down's syndrome. *Bioessays*. 2002 Aug;24(8):681-4.
27. Valenti D, Manente GA, Moro L, Marra E, Vacca RA. Deficit of complex I activity in human skin fibroblasts with chromosome 21 trisomy and overproduction of reactive oxygen species by mitochondria: involvement of the cAMP/PKA signalling pathway. *Biochem J*. 2011 May;435(3):679-88.
28. de Haan JB, Susil B, Pritchard M, Kola I. An altered antioxidant balance occurs in Down syndrome fetal organs: implications for the "gene dosage effect" hypothesis. *J Neural Transm Suppl*. 2003;67:67-83.
29. Lott IT, Head E, Doran E, Busciglio J. Beta-amyloid, oxidative stress and Down syndrome. *Curr Alzheimer Res*. 2006 Dec;3(5):521-8.
30. Ishihara K, Amano K, Takaki E, Ebrahim AS, Shimohata A, Shibazaki N, Inoue I, Takaki M, Ueda Y, Sago H, Epstein CJ, Yamakawa K. Increased lipid peroxidation in Down's syndrome mouse models. *J Neurochem*. 2009 Sep;110(6):1965-76.
31. Brooksbank BW, Balazs R. Superoxide dismutase, glutathione peroxidase and lipoperoxidation in Down's syndrome fetal brain. *Brain Res*. 1984 Sep;318(1):37-44.
32. Garcez ME, Peres W, Salvador M. Oxidative stress and hematologic and biochemical parameters in individuals with Down syndrome. *Mayo Clin Proc*. 2005 Dec;80(12):1607-11.
33. Contestabile A, Fila T, Ceccarelli C, Bonasoni P, Bonapace L, Santini D, Bartesaghi R, Ciani E. Cell cycle alteration and decreased cell proliferation in the hippocampal dentate gyrus and in the neocortical germinal matrix of fetuses with Down syndrome and in Ts65Dn mice. *Hippocampus*. 2007;17(8):665-78.
34. Esposito G, Imitola J, Lu J, De Filippis D, Scuderi C, Ganesh VS, Folkert R, Hecht J, Shin S, Iuvone T, Chesnut J, Steardo L, Sheen V. Genomic and functional profiling of human Down syndrome neural progenitors implicates S100B and aquaporin 4 in cell injury. *Hum Mol Genet*. 2008 Feb;17(3):440-57.
35. Fuentes JJ, Genesca L, Kingsbury TJ, Cunningham KW, Perez-Riba M, Estivill X, de la Luna S. DSCR1, overexpressed in Down syndrome, is an inhibitor of calcineurin-mediated signaling pathways. *Hum Mol Genet*. 2000;9(11):1681-90.
36. Busciglio J, Yankner BA. Apoptosis and increased generation of reactive oxygen species in Down's syndrome neurons in vitro. *Nature*. 1995 Dec;378:776-9.
37. Canzonetta C, Mulligan C, Deutsch S, Ruf S, O'Doherty A, Lyle R, et al. DYRK1A-dosage imbalance perturbs NRSF/REST levels, deregulating pluripotency and embryonic stem cell fate in Down syndrome. *Am J Hum Genet*. 2008 Sep;83(3):388-400.
38. Carratelli M, Porcaro L, Ruscica M, De Simone E, Bertelli AA, Corsi MM. Reactive oxygen metabolites and prooxidant status in children with Down's syndrome. *Int J Clin Pharmacol Res*. 2001;21(2):79-84.
39. Kedziora J, Bartosz G. Down's syndrome: a pathology involving the lack of balance of reactive oxygen species. *Free Radic Biol Med*. 1988;4(5):317-30.
40. Morawiec Z, Janik K, Kowalski M, Stetkiewicz T, Szaflik J, Morawiec-Bajda A, Sobczuk A, Blasiak J. DNA damage and repair in children with Down's syndrome. *Mutat Res*. 2008 Jan;637(1-2):118-23.
41. Reshetniak VK, Chuvin BT. [Modulating effect of electric acupuncture stimulation on the bioelectrical activity of neurons of specific and nonspecific thalamic nuclei.] *Biull Eksp Biol Med*. 1986 May;101(5):515-7.
42. Reshetniak VK, Meizerov EE, Durinin RA. [Effect of electroacupuncture on the integration of nociceptor and non-nociceptor afferent pathways in the second somatosensory cortex of the cerebral hemisphere.] *Biull Eksp Biol Med*. 1982 Mar;93(3):11-3.
43. Buckley JA. How mild hyperbaric oxygen therapy works and why it is good for our children. *Medical Veritas*. 2005;2:647.
44. Rossignol DA. Hyperbaric oxygen therapy might improve certain pathophysiological findings in autism. *Med Hypotheses*. 2007;68(6):1208-27.
45. Neubauer RA, James P. Cerebral oxygenation and the recoverable brain. *Neural Res*. 1998;20(Suppl 1):S33-36.
46. Hutchison JH, Kerr MM, Williams KG, Hopkinson WI. Hyperbaric oxygen in the resuscitation of the newborn. *Lancet*. 1963 Nov 16;2(7316):1019-22.
47. Veltkamp R, Siebing DA, Heiland S, Schoenfeldt-Varas P, Veltkamp C, Schwanninger M, Schwab S. Hyperbaric oxygen induces rapid protection against focal cerebral ischemia. *Brain Res*. 2005 Mar;1037(1-2):134-8.
48. Al-Waili NS, Butler GJ. Effects of hyperbaric oxygen on inflammatory response to wound and trauma: possible mechanism of action. *Scientific World Journal*. 2006 Apr;6:425-41.
49. Saito K, Tanaka Y, Ota T, Eto S, Yamashita U. Suppressive effect of hyperbaric oxygenation on immune responses of normal and autoimmune mice. *Clin Exp Immunol*. 1991 Nov;86(2):322-7.
50. Thom SR, Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol*. 2006 Apr;290(4):H1378-86.
51. Akin ML, Gulluoglu BM, Uluutku H, Erenoglu C, Elbuken E, Yildirim S, Celenk T. Hyperbaric oxygen improves healing in experimental rat colitis. *Undersea Hyperb Med*. 2002;29(4):279-85.
52. Shyu WC, Lin SZ, Saeki K, Kubosaki A, Matsumoto Y, Onodera T, Chiang MF, Thajeb P, Li H. Hyperbaric oxygen enhances the expression of prion protein and heat shock protein 70 in a mouse neuroblastoma cell line. *Cell Mol Neurobiol*. 2004 Apr;24(2):257-68.
53. Harch PG, Neubauer RA. Hyperbaric oxygen therapy in global cerebral ischemia/anoxia and coma. In KK Jain (Ed.), *Textbook of Hyperbaric Medicine*, 3rd revised edition (pp. 319-349). Seattle: Hogrefe & Huber Publishers, 1999.
54. Stoller KP. Quantification of neurocognitive changes before, during, and after hyperbaric oxygen therapy in a case of fetal alcohol syndrome. *Pediatrics*. 2005 Oct;116(4):e586-91.