

Home &gt; Journals &gt; Medicine &amp; Healthcare &gt; IJCM

Articles Archive Indexing Aims &amp; Scope Editorial Board For Authors Publication Fees

IJCM &gt; Vol.7 No.1, January 2016

21

Open Access

## Clinical Effects of Hydrogen Administration: From Animal and Human Diseases to Exercise Medicine

 [Download as PDF](#) (Size:1597KB)   PP. 32-76
DOI: [10.4236/ijcm.2016.71005](https://doi.org/10.4236/ijcm.2016.71005) 6,628 Downloads 13,037 Views**Author(s)** [Leave a comment](#)

Garth L. Nicolson<sup>1\*</sup>, Gonzalo Ferreira de Mattos<sup>2</sup>, Robert Settineri<sup>3</sup>, Carlos Costa<sup>2</sup>, Rita Ellithorpe<sup>4</sup>, Steven Rosenblatt<sup>5</sup>, James La Valle<sup>6</sup>, Antonio Jimenez<sup>7</sup>, Shigeo Ohta<sup>8</sup>

**Affiliation(s)**<sup>1</sup>Department of Molecular Pathology, The Institute for Molecular Medicine, Huntington Beach, USA.<sup>2</sup>Laboratory of Ion Channels, School of Medicine, Universidad de la República, Montevideo, Uruguay.<sup>3</sup>Sierra Research, Irvine, USA.<sup>4</sup>Tustin Longevity Center, Tustin, USA.<sup>5</sup>Saint John's Health Center, Santa Monica, USA.<sup>6</sup>Progressive Medical Center, Orange, USA.<sup>7</sup>Hope Cancer Institute, Playas de Tijuana, Mexico.<sup>8</sup>Department of Biochemistry and Cell Biology, Graduate School of Medicine, Nippon Medical School, Kawasaki, Japan.**ABSTRACT**

Here we review the literature on the effects of molecular hydrogen ( $H_2$ ) on normal human subjects and patients with a variety of diagnoses, such as metabolic, rheumatic, cardiovascular and neurodegenerative and other diseases, infections and physical and radiation damage as well as effects on aging and exercise. Although the effects of  $H_2$  have been studied in multiple animal models of human disease, such studies will not be reviewed in depth here.  $H_2$  can be administered as a gas, in saline implants or infusions, as topical solutions or baths or by drinking  $H_2$ -enriched water. This latter method is the easiest and least costly method of administration. There are no safety issues with hydrogen; it has been used for years in gas mixtures for deep diving and in numerous clinical trials without adverse events, and there are no warnings in the literature of its toxicity or long-term exposure effects. Molecular hydrogen has proven useful and convenient as a novel antioxidant and modifier of gene expression in many conditions where oxidative stress and changes in gene expression result in cellular damage.

**KEYWORDS**

Anti-Oxidant, Hydrogen Therapy, Gene Regulation, Gamates, Inflammatory Disease, Neurodegenerative Disease, Rheumatic Disease, Infections, Aging, Exercise, Metabolic Disease, Ischemia, Cardiovascular Disease, Neuromuscular Disease, Radiation, Skin, Sepsis

**Cite this paper**

Nicolson, G. , de Mattos, G. , Settineri, R. , Costa, C. , Ellithorpe, R. , Rosenblatt, S. , La Valle, J. , Jimenez, A. and Ohta, S. (2016) Clinical Effects of Hydrogen Administration: From Animal and Human Diseases to Exercise Medicine. *International Journal of Clinical Medicine*, **7**, 32-76. doi: [10.4236/ijcm.2016.71005](https://doi.org/10.4236/ijcm.2016.71005).

**References**

- [1] Ohta, S. (2015) Molecular Hydrogen as a Novel Antioxidant: Overview of the Advantages of Hydrogen for Medical Applications. *Methods in Enzymology*, **555**, 289-317.  
<http://dx.doi.org/10.1016/bs.mie.2014.11.038>
- [2] Ohta, S. (2014) Molecular Oxygen as a Preventive and Therapeutic Medical Gas: Initiation, Development and Potential of Hydrogen Medicine. *Pharmacology and Therapeutics*, **144**, 1-11.

**• Open Special Issues****• Published Special Issues****• Special Issues Guideline**[IJCM Subscription](#)**E-Mail Alert**[IJCM Most popular papers](#)[Publication Ethics & OA Statement](#)[IJCM News](#)[Frequently Asked Questions](#)[Recommend to Peers](#)[Recommend to Library](#)[Contact Us](#)

Downloads: 1,469,596

Visits: 2,267,490

**Related Articles >>**

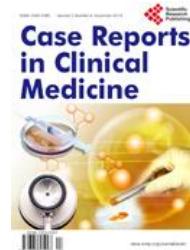
- Effects of Levosimendan on Hydrogen Peroxide Induced Contraction in Human Saphenous Vein
- Studies on the effects of pretreatment on production hydrogen from municipal sludge anaerobic fermentation
- Effects of flu vaccine, solely or accompanied by pneumovax-23 vaccine on clinical consequences of the respiratory diseases among Iranian pilgrims in Hajj
- Alternative Medicine and Molecular Mechanisms in Chronic Degenerative Diseases
- Vasoactive Effects of Oxidative Stress Elicited by Hydrogen Peroxide in the Human Umbilical Artery: An *in Vitro* Study

**Sponsors, Associates, and Links >>**

<http://dx.doi.org/10.1016/j.pharmthera.2014.04.006>

- [3] Zhai, X., Chen, X., Ohta, S. and Sun, X. (2014) Review and Prospect of the Biomedical Effects of Hydrogen. *Medical Gas Research*, 4, Article 19.  
<http://dx.doi.org/10.1186/s13618-014-0019-6>
- [4] Pilcher, J.E. (1888) On the Diagnosis of Gastrointestinal Perforation by the Rectal Insufflation of Hydrogen Gas. *Annals of Surgery*, 8, 190-204.  
<http://dx.doi.org/10.1097/00000658-188807000-00087>
- [5] Ohsawa, I., Ishikawa, M., Takahashi, K., Watanabe, M., Nishimaki, K., Yamagata, K., Katsura, K., Katayama, Y., Asoh, S. and Ohta, S. (2007) Hydrogen Acts as a Therapeutic Antioxidant by Selectively Reducing Cytotoxic Oxygen Radicals. *Nature Medicine*, 13, 688-694.  
<http://dx.doi.org/10.1038/nm1577>
- [6] Christensen, H. and Sehested, K. (1983) Reaction of Hydroxyl Radicals with Hydrogen at Elevated Temperatures. *Journal of Physical Chemistry*, 87, 118-120.  
<http://dx.doi.org/10.1021/j100224a027>
- [7] Indo, H.P., Yen, H.C., Nakanishi, I., Matsumoto, K., Tamura, M., et al. (2015) A Mitochondrial Superoxide Theory for Oxidative Stress Diseases and Aging. *Journal of Clinical Biochemistry and Nutrition*, 56, 1-7.  
<http://dx.doi.org/10.3164/jcbn.14-42>
- [8] Andersen, K. (2004) Oxidative Stress in Neurodegeneration: Cause or Consequence? *Nature Medicine*, 10, S18-S25.  
<http://dx.doi.org/10.1038/nrn1434>
- [9] Maise, K. (2015) New Insights for Oxidative Stress and Diabetes Mellitus. *Oxidative Medicine and Cellular Longevity*, 2015, Article ID: 875961.  
<http://dx.doi.org/10.1155/2015/875961>
- [10] Vendemiale, G., Grattagliano, I. and Altomare, E. (1999) An Update on the Role of Free Radicals and Antioxidant Defense in Human Disease. *International Journal of Clinical Laboratory Research*, 29, 49-55.  
<http://dx.doi.org/10.1007/s005990050063>
- [11] Bonomini, F., Rodella, L.F. and Rezzani, R. (2015) Metabolic Syndrome, Aging and Involvement of Oxidative Stress. *Aging and Disease*, 6, 109-120.  
<http://dx.doi.org/10.14336/AD.2014.0305>
- [12] Harman, D. (1972) The Biologic Clock: The Mitochondria? *Journal of American Geriatric Society*, 20, 145-147.  
<http://dx.doi.org/10.1111/j.1532-5415.1972.tb00787.x>
- [13] Miquel J., Economos, A.C., Fleming, J. and Johnson Jr, J.E. (1980) Mitochondrial Role in Cell Aging. *Experimental Gerontology*, 15, 575-591.  
[http://dx.doi.org/10.1016/0531-5565\(80\)90010-8](http://dx.doi.org/10.1016/0531-5565(80)90010-8)
- [14] Turrens, J.F. (2003) Mitochondrial Formation of Reactive Oxygen Species. *Journal of Physiology*, 552, 335-344.  
<http://dx.doi.org/10.1113/jphysiol.2003.049478>
- [15] Lipinski, B. (2011) Hydroxyl Radical and Its Scavengers in Health and Disease. *Oxidative Medicine and Cell Longevity*, 2011, Article ID: 809696.  
<http://dx.doi.org/10.1155/2011/809696>
- [16] Harish, G., Mahadevan, A., Pruthi, N., Sreenivasamurthy, A.K., Putta-mallesh, V.N., et al. (2015) Characterization of Traumatic Brain Injury in Human Brains Reveals Distinct Cellular and Molecular Changes in Contusion and Pericontusion. *Journal of Neurochemistry*, 134, 156-172.  
<http://dx.doi.org/10.1111/jnc.13082>
- [17] Carri, M.T., Valle, C., Bozzo, F. and Cozzolino, M. (2015) Oxidative Stress and Mitochondrial Damage: Importance in Non-SOD1 ALS. *Frontiers in Cellular Neuroscience*, 9, Article 41.  
<http://dx.doi.org/10.3389/fncel.2015.00041>
- [18] Wei, Y.H. (1992) Mitochondrial DNA Alterations as Ageing-Associated Molecular Events. *Mutation Research*, 275, 145-155.  
[http://dx.doi.org/10.1016/0921-8734\(92\)90019-L](http://dx.doi.org/10.1016/0921-8734(92)90019-L)
- [19] Pak, J.W., Herbst, A., Bua, E., Gokey, N., McKenzie, D. and Aiken, J.M. (2003) Mitochondrial DNA Mutations as a Fundamental Mechanism in Physiological Declines Associated with Aging. *Aging Cell*, 2, 1-7.

• Case Reports in Clinical Medicine



• Health



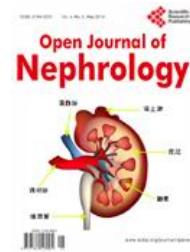
• International Journal of Medical Physics, Clinical Engineering and Radiation Oncology



• Neuroscience & Medicine



• Open Journal of Nephro



• Journal of Biosciences and Medicines



• Open Journal of Clinical Diagnostics

<http://dx.doi.org/10.1046/j.1474-9728.2003.00034.x>

- [20] Reddy, P.H. (2008) Mitochondrial Medicine for Aging and Neurodegenerative Diseases. *Neuromolecular Medicine*, 10, 291-315.  
<http://dx.doi.org/10.1007/s12017-008-8044-z>
- [21] Karowski, M. and Neutzner, A. (2011) Neurodegeneration as a Consequence of Failed Mitochondrial Maintenance. *Acta Neuropathologica*, 123, 157-171.  
<http://dx.doi.org/10.1007/s00401-011-0921-0>
- [22] Nicolson, G.L. (2014) Mitochondrial Dysfunction and Chronic Disease: Treatment with Natural Supplements. *Alternative Therapies for Health and Medicine*, 20, 18-25.
- [23] Maiiese, K., Chong, Z.Z., Shang, Y.C. and Wang, S. (2012) Targeting Disease through Novel Pathways of Apoptosis and Autophagy. *Expert Opinions in Therapeutic Targets*, 16, 1203-1214.  
<http://dx.doi.org/10.1517/14728222.2012.719499>
- [24] Suzen, S., Cihaner, S.S. and Coban, T. (2012) Synthesis and Comparison of Antioxidant Properties of Indole-Based Metatonin Analogue Indole Amino Acid Derivatives. *Chemical and Biological Drug Design*, 79, 76-83.  
<http://dx.doi.org/10.1111/j.1747-0285.2011.01216.x>
- [25] Schoenfeld, M.P., Ansari, R.R., Nakao, A. and Wink, D. (2012) A Hypothesis on Biological Protection from Space Radiation through the Use of New Therapeutic Gases as Medical Counter Measures. *Medical Gas Research*, 2, Article 8.
- [26] Grassi, D., Desideri, G., Ferri, L., Aggio, A., Tiberti, S. and Ferri, C. (2010) Oxidative Stress and Endothelial Dysfunction: Say No to Cigarette Smoking! *Current Pharmaceutical Design*, 16, 2539-2550.  
<http://dx.doi.org/10.2174/138161210792062867>
- [27] Harma, M.I., Harma, M. and Erel, O. (2006) Measuring Plasma Oxidative Stress Biomarkers in Sport Medicine. *European Journal of Applied Physiology*, 97, 505-508.  
<http://dx.doi.org/10.1007/s00421-006-0202-0>
- [28] Aukland, K., Bower, B.F. and Berliner, R.W. (1964) Measurement of Local Blood Flow with Hydrogen Gas. *Circulation Research*, 14, 164-187.  
<http://dx.doi.org/10.1161/01.RES.14.2.164>
- [29] Ohta, S. (2011) Recent Progress toward Understanding Hydrogen Medicine: Potential of Molecular Hydrogen for Preventive and Therapeutic Applications. *Current Pharmaceutical Design*, 17, 2241-2252.  
<http://dx.doi.org/10.2174/138161211797052664>
- [30] Schieber, M. and Chandel, N.S. (2014) ROS Function in Redox Signaling and Oxidative Stress. *Current Biology*, 24, R453-R462. <http://dx.doi.org/10.1016/j.cub.2014.03.034>
- [31] Fenkel, T. (1998) Oxygen Radicals and Signaling. *Current Opinion in Cell Biology*, 10, 248-253.  
[http://dx.doi.org/10.1016/S0955-0674\(98\)80147-6](http://dx.doi.org/10.1016/S0955-0674(98)80147-6)
- [32] Collins, Y., Chouchani, E.T., James, A.M., Menger, K.E., Cocheme, H.M. and Murphy, M.P. (2012) Mitochondrial Redox Signaling at a Glance. *Journal of Cell Science*, 125, 801-816.  
<http://dx.doi.org/10.1242/jcs.098475>
- [33] Chandel, N.S., Vander Heiden, M.G., Thompson, C.B. and Schumacker, P.T. (2000) Redox Regulation of p53 during Hypoxia. *Oncogene*, 19, 3840-3848.  
<http://dx.doi.org/10.1038/sj.onc.1203727>
- [34] Liu, H., Colavitti, R., Rovira, I.I. and Finkel, T. (2005) Redox-Dependent Transcriptional Regulation. *Circulation Research*, 97, 967-974.  
<http://dx.doi.org/10.1161/01.RES.0000188210.72062.10>
- [35] Nakai, Y., Sato, B., Ushijima, S., Okada, S., Abe, K. and Arai, S. (2011) Hepatic Oxidoreduction-Related Genes Are Upregulated by Administration of Hydrogen-Saturated Drinking Water. *Bioscience Biotechnology and Biochemistry*, 75, 774-776.  
<http://dx.doi.org/10.1271/bbb.100819>
- [36] Chandel, N.S., Trzyna, W.C. and McClintock, D.S. (2000) Role of Oxidants in NF-Kappa B Activation and TNF-Alpha Gene Transcription Induced by Hypoxia and Endotoxin. *Journal of Immunology*, 165, 1013-1021.  
<http://dx.doi.org/10.4049/jimmunol.165.2.1013>
- [37] Murphy, M.P. and Smith, R.A. (2000) Drug Delivery to Mitochondria: The Key to Mitochondrial Medicine. *Advances in Drug Delivery Reviews*, 41, 235-250.



- [Open Journal of Preventive Medicine](#)



- [The 3rd Conference on Laboratory Medicine and Clinical Research \(CLMCR 2017\)](#)



[http://dx.doi.org/10.1016/S0169-409X\(99\)00069-1](http://dx.doi.org/10.1016/S0169-409X(99)00069-1)

- [38] Smith, R.A. and Murphy, M.P. (2011) Mitochondria-Targeted Antioxidants as Therapies. *Discovery Medicine*, 11, 106-114.
- [39] Hayashida, K., Sano, M., Kamimura, N., Yokota, T., Suzuki, M., et al. (2012) H<sub>2</sub> Gas Improves Functional Outcome after Cardiac Arrest to an Extent Comparable to Therapeutic Hypothermia in a Rat Model. *Journal of the American Heart Association*, 1, e003459.  
<http://dx.doi.org/10.1161/jaha.112.003459>
- [40] Hayashida, K., Sano, M., Ohsawa, I., Shinmura, K., Tamaki, K., et al. (2008) Inhalation of Hydrogen Gas Reduces Infarct Size in the Rat Model of Myocardial Ischemia-Reperfusion Injury. *Biochemical and Biomedical Research Communications*, 373, 30-35.  
<http://dx.doi.org/10.1016/j.bbrc.2008.05.165>
- [41] Kawamura, T., Huang, C.S., Tochigi, N., Lee, S., Shigemura, N., et al. (2010) Inhaled Hydrogen Gas Therapy for Prevention of Lung Transplant-Induced Ischemia/Reperfusion Injury in Rats. *Transplantation*, 90, 1334-1351.
- [42] Xie, K.L., Yu, Y.H., Pei, Y.P., et al. (2010) Protective Effects of Hydrogen Gas on Murine Polymicrobial Sepsis via Reducing Oxidative Stress and HMGB1 Release. *Shock*, 34, 90-97.  
<http://dx.doi.org/10.1097/SHK.0b013e3181cdc4ae>
- [43] Xie, K., Yu, Y., Zhang, Z., Liu, W., Pei, Y., Xiong, L., Hou, L. and Wang, G. (2010) Hydrogen Gas Improves Survival Rate and Organ Damage in Zymosan-Induced Generalized Inflammation Model. *Shock*, 34, 495-501.  
<http://dx.doi.org/10.1097/SHK.0b013e3181def9aa>
- [44] Cai, J.M., Kang, Z.M., Liu, K., et al. (2009) Neuroprotective Effects of Hydrogen Saline in Neonatal Hypoxia-Ischemia Rat Model. *Brain Research*, 1256, 129-137.  
<http://dx.doi.org/10.1016/j.brainres.2008.11.048>
- [45] Li, J., Wang, C., Zhang, J.H., Cai, J.M., Cao, Y.P. and Sun, X.J. (2010) Hydrogen-Rich Saline Improves Memory Function in a Rat Model of Amyloid-Beta-Induced Alzheimer's Disease by Reduction of Oxidative Stress. *Brain Research*, 1328, 152-161.  
<http://dx.doi.org/10.1016/j.brainres.2010.02.046>
- [46] Nagata, K., Nakashima-Kamimura, N., Mikami, T., Ohsawa, I. and Ohta, S. (2009) Consumption of Molecular Hydrogen Prevents the Stress-Induced Impairments in Hippocampus-Dependent Learning Tasks during Chronic Physical Restraint in Mice. *Neuropharmacology*, 34, 501-508.  
<http://dx.doi.org/10.1038/npp.2008.95>
- [47] Nakashima-Kamimura, N., Mori, T., Ohsawa, I., Asoh, S. and Ohta, S. (2009) Molecular Hydrogen Alleviates Nephrotoxicity Induced by an Anti-Cancer Drug Cisplatin without Comproosing An-ti-Tumor Activity in Mice. *Cancer Chemotherapy and Pharmacology*, 64, 753-761.  
<http://dx.doi.org/10.1007/s00280-008-0924-2>
- [48] Fontanari, P., Badier, M., Guillot, C., Tomei, C., Burnet, H., Gardette, B., et al. (2000) Changes in Maximal Performance in Inspiratory and Skeletal Muscles during and after the 7.1-MPa Hydra 10 Record Human Dive. *European Journal of Applied Physiology*, 81, 325-328.  
<http://dx.doi.org/10.1007/s004210050050>
- [49] Lillo, R.S., Parker, E.C. and Porter, W.R. (1997) Decompression Comparison of Helium and Hydrogen in Rats. *Journal of Applied Physiology*, 82, 892-901.
- [50] Lillo, R.S. and Parker, E.C. (2000) Mixed-Gas Model for Predicting Decompression Sickness in Rats. *Journal of Applied Physiology*, 89, 2107-2116.
- [51] Abraini, J.H., Gardette-Chauffour, M.C., Martinez, E., Rostain, J.C. and Lemaire, C. (1994) Psychophysiological Reactions in Humans during an Open Sea Dive to 500 m with a Hydrogen-Helium-Oxygen Mixture. *Journal of Applied Physiology*, 76, 1113-1118.
- [52] Lafay, V., Barthelemy, P., Comet, B., Frances, Y. and Jammes, Y. (1995) ECG Changes during the Experimental Human Dive HYDRA 10 (71 ATM/7,200 kPa). *Undersea Hyperbaric Medicine*, 22, 51-60.
- [53] Tomofugi, T., Kawabata, Y., Kasuyama, K., Endo, Y., Yoneda, T., Yamane, M., et al. (2014) Effects of Hydrogen-Rich Water on Aging Periodontal Tissue in Rats. *Scientific Reports*, 4, Article 5534.  
<http://dx.doi.org/10.1038/srep05534>
- [54] Huang, C.S., Kawamura, T., Toyoda, Y. and Nakao, A. (2010) Recent Advances in Hydrogen Research as a Therapeutic Medical Gas. *Free Radical Research*, 44, 971-982.

<http://dx.doi.org/10.3109/10715762.2010.500328>

- [55] Ohno, K., Ito, M., Ichihara, M. and Ito, M. (2012) Molecular Hydrogen as an Emerging Therapeutic Medical Gas for Neurodegenerative and Other Diseases. *Oxidative Medicine and Cellular Longevity*, 2012, Article ID: 353152.  
<http://dx.doi.org/10.1155/2012/353152>
- [56] Shen, M., Zhang, H., Yu, C., Wang, F. and Sun, X. (2014) A Review of Experimental Studies of Hydrogen as a New Therapeutic Agent in Emergency and Critical Care Medicine. *Medical Gas Research*, 4, Article 17.  
<http://dx.doi.org/10.1186/2045-9912-4-17>
- [57] Oharazawa, H., Igarashi, T., Yokota, T., Fujii, H., Suzuki, H., Machide, M., et al. (2010) Protection of the Retina by Rapid Diffusion of Hydrogen: Administration of Hydrogen-Loaded Eye Drops in Retinal Ischemia-Reperfusion Injury. *Investigative Ophthalmology and Vision Science*, 51, 487-492.  
<http://dx.doi.org/10.1167/iovs.09-4089>
- [58] Noda, K., Shigemura, N., Tanaka, Y., Kawamura, T., Hyun Lim, S., et al. (2013) A Novel Method of Preserving Cardiac Grafts Using a Hydrogen-Rich Water Bath. *Journal of Heart and Lung Transplantation*, 32, 241-250.  
<http://dx.doi.org/10.1016/j.healun.2012.11.004>
- [59] Gaffron, H. (1939) Reduction of Carbon Dioxide with Molecular Hydrogen in Green Algae. *Nature*, 143, 204-205.  
<http://dx.doi.org/10.1038/143204a0>
- [60] Melis, A. and Melnicki, M.R. (2006) Integrated Biological Hydrogen Production. *International Journal of Hydrogen Energy*, 31, 1563-1573.  
<http://dx.doi.org/10.1016/j.ijhydene.2006.06.038>
- [61] Zeng, J., Zhang, M. and Sun, X. (2013) Molecular Hydrogen Is Involved in Phytohormone Signaling and Stress Responses in Plants. *PLoS ONE*, 8, e71038.  
<http://dx.doi.org/10.1371/journal.pone.0071038>
- [62] Zeng, J., Ye, Z. and Sun, X. (2013) Progress in the Study of Biological Effects of Hydrogen on Higher Plants and Its Promising Application in Agriculture. *Medical Gas Research*, 4, Article 15.
- [63] Vilahur, G. and Badimon, L. (2014) Ischemia/Reperfusion Activates Myocardial Innate Immune Responses: The Key Role of the Toll-Like Receptor. *Frontiers in Physiology*, 5, e00497.  
<http://dx.doi.org/10.3389/fphys.2014.00497>
- [64] Dorweiler, B., Pruefer, D., Andras, T.B., Maksan, S.M., Schmiedt, W., Neufang, A. and Vahl, C.F. (2007) Ischemia-Reperfusion Injury. *European Journal of Trauma and Emergency Surgery*, 33, 600-612.  
<http://dx.doi.org/10.1007/s00068-007-7152-z>
- [65] Carden, D.L. and Granger, D.N. (2000) Pathophysiology of Ischaemia-Reperfusion Injury. *Journal of Pathology*, 190, 255-266.  
[http://dx.doi.org/10.1002/\(SICI\)1096-9896\(200002\)190:3<255::AID-PATH526>3.0.CO;2-6](http://dx.doi.org/10.1002/(SICI)1096-9896(200002)190:3<255::AID-PATH526>3.0.CO;2-6)
- [66] Granger, D.N. (1988) Role of Xanthine Oxidase and Granulocytes in Ischemia-Reperfusion Injury. *American Journal of Physiology*, 255, H1269-H1275.
- [67] Di Lisa, F. and Bernardi, P. (2006) Mitochondria and Ischemia-Reperfusion Injury of the Heart: Fixing a Hole. *Cardiovascular Research*, 70, 191-199.  
<http://dx.doi.org/10.1016/j.cardiores.2006.01.016>
- [68] Thapalia, B.A., Zhou, Z. and Lin, X. (2014) Autophagy, a Process within Reperfusion Injury: An Update. *International Journal of Clinical and Experimental Pathology*, 7, 8322-8341.
- [69] Ostojic, S.M. (2015) Targeting Molecular Hydrogen to Mitochondria: Barriers and Gateways. *Pharmacological Research*, 94, 51-53.  
<http://dx.doi.org/10.1016/j.phrs.2015.02.004>
- [70] Sobue, S., Yamai, K., Ito, M., Ohno, K., Ito, M., et al. (2015) Simultaneous Oral and Inhalational Intake of Molecular Hydrogen Additively Suppresses Signaling Pathways in Rodents. *Molecular and Cellular Biochemistry*, 403, 231-241.  
<http://dx.doi.org/10.1007/s11010-015-2353-y>
- [71] Boyle, E.M., Pohlman, T.H., Cornejo, C.J. and Verrier, E.D. (1997) Ischemia-Reperfusion Injury. *The Annals of Thoracic Surgery*, 64, S24-S30.  
[http://dx.doi.org/10.1016/s0003-4975\(97\)00958-2](http://dx.doi.org/10.1016/s0003-4975(97)00958-2)

- [72] Anaya-Prado, R., Toledo-Pereyra, L.H., Lentsch, A.B. and Ward, P.A. (2002) Ischemia/Reperfusion Injury. *The Journal of Surgical Research*, 105, 248-258.  
<http://dx.doi.org/10.1006/jssr.2002.6385>
- [73] Ohta, S. (2012) Molecular Hydrogen Is a Novel Antioxidant to Efficiently Reduce Oxidative Stress with Potential for the Improvement of Mitochondrial Diseases. *Biochimica et Biophysica Acta*, 1820, 586-594.  
<http://dx.doi.org/10.1016/j.bbagen.2011.05.006>
- [74] Casillas-Ramirez, A., Mosbah, I.B., Ramalho, F., Rosello-Catafau, J. and Peralta, C. (2006) Past and Future Approaches to Ischemia-Reperfusion Lesion Associated with Liver Transplantation. *Life Sciences*, 79, 1881-1894.  
<http://dx.doi.org/10.1016/j.lfs.2006.06.024>
- [75] Gok, M.A., Shenton, B.K., Pelsers, M., Whitwood, A., Mantle, D., et al. (2006) Ischemia-Reperfusion Injury in Cadaveric Nonheart Beating, Cadaveric Heart Beating and Live Donor Renal Transplants. *The Journal of Urology*, 175, 641-647.  
[http://dx.doi.org/10.1016/S0022-5347\(05\)00170-9](http://dx.doi.org/10.1016/S0022-5347(05)00170-9)
- [76] Kosieradzki, M. and Rowinski, W. (2008) Ischemia/Reperfusion Injury in Kidney Transplantation: Mechanisms and Prevention. *Transplantation Proceedings*, 40, 3279-3288.  
<http://dx.doi.org/10.1016/j.transproceed.2008.10.004>
- [77] Hong, Y., Chen, S. and Zhang, J.M. (2010) Hydrogen as a Selective Antioxidant: A Review of Clinical and Experimental Studies. *Journal of International Medical Research*, 38, 1893-1903.  
<http://dx.doi.org/10.1177/147323001003800602>
- [78] Ohta, S., Nakao, A. and Ohno, K. (2011) The 2011 Medical Molecular Hydrogen Symposium: An Inaugural Symposium of the Journal Medical Gas Research. *Medical Gas Research*, 1, Article 10.  
<http://dx.doi.org/10.1186/2045-9912-1-10>
- [79] Ostojic, S.M. (2015) Molecular Hydrogen: An Inert Gas Turns Clinically Effective. *Annals of Medicine*, 47, 301-314.  
<http://dx.doi.org/10.3109/07853890.2015.1034765>
- [80] Shen, M., Zhang, H., Yu, C., Wang, F. and Sun, X. (2014) A Review of Experimental Studies of Hydrogen as a New Therapeutic Agent in Emergency and Critical Care Medicine. *Medical Gas Research*, 4, Article 17.  
<http://dx.doi.org/10.1186/2045-9912-4-17>
- [81] Sun, Q., Kang, Z., Cai, J., Liu, W., Liu, Y., et al. (2009) Hydrogen-Rich Saline Protects Myocardium against Ischemia/ Reperfusion Injury in Rats. *Experimental Biology and Medicine*, 234, 1212-1219.  
<http://dx.doi.org/10.3181/0812-RM-349>
- [82] Zhang, Y., Sun, Q., He, B., Xiao, J., Wang, Z. and Sun, X. (2011) Anti-Inflammatory Effect of Hydrogen-Rich Saline in a Rat Model of Regional Myocardial Ischemia and Reperfusion. *International Journal of Cardiology*, 148, 91-95.  
<http://dx.doi.org/10.1016/j.ijcard.2010.08.058>
- [83] Wu, S., Zhu, L., Yang, J., Fan, Z., Dong, Y., et al. (2014) Hydrogen-Containing Saline Attenuates Doxorubicin-Induced Heart Failure in Rats. *Die Pharmazie*, 69, 633-636.
- [84] Shinbo, T., Kokubo, K., Sato, Y., Hagiri, S., Hataishi, R., et al. (2013) Breathing Nitric Oxide plus Hydrogen Gas Reduces Ischemia-Reperfusion Injury and Nitrotyrosine Production in Murine Heart. *American Journal of Physiology, Heart and Circulatory Physiology*, 305, H542-H550.  
<http://dx.doi.org/10.1152/ajpheart.00844.2012>
- [85] Vander Heide, R.S. and Steenbergen, C. (2013) Cardioprotection and Myocardial Reperfusion: Pitfalls to Clinical Application. *Circulation Research*, 113, 464-477.  
<http://dx.doi.org/10.1161/CIRCRESAHA.113.300765>
- [86] Kubler, W. and Haass, M. (1996) Cardioprotection: Definition, Classification, and Fundamental Principles. *Heart*, 75, 330-333.  
<http://dx.doi.org/10.1136/hrt.75.4.330>
- [87] Murry, C.E., Jennings, R.B. and Reimer, K.A. (1986) Preconditioning with Ischemia: A Delay of Lethal Cell Injury in Ischemic Myocardium. *Circulation*, 74, 1124-1136.  
<http://dx.doi.org/10.1161/01.CIR.74.5.1124>
- [88] Zhao, Z.Q., Corvera, J.S., Halkos, M.E., Kerendi, F., Wang, N.P., Guyton, R.A. and Vinten-Johansen, J. (2003) Inhibition of Myocardial Injury by Ischemic Postconditioning during Reperfusion: Comparison with Ischemic Preconditioning. *American Journal of Physiology, Heart and Circulatory Physiology*, 285, H579-

H588.

<http://dx.doi.org/10.1152/ajpheart.01064.2002>

- [89] Piot, C., Croisille, P., Staat, P., Thibault, H., Rioufol, G., et al. (2008) Effect of Cyclosporine on Reperfusion Injury in Acute Myocardial Infarction. *The New England Journal of Medicine*, 359, 473-481.  
<http://dx.doi.org/10.1056/NEJMoa071142>
- [90] Rajesh, K.G., Sasaguri, S., Suzuki, R., Xing, Y. and Maeda, H. (2004) Ischemic Preconditioning Prevents Reperfusion Heart Injury in Cardiac Hypertrophy by Activation of Mitochondrial KATP Channels. *International Journal of Cardiology*, 96, 41-49.  
<http://dx.doi.org/10.1016/j.ijcard.2003.06.010>
- [91] Qian, L., Cao, F., Cui, J., Wang, Y., Huang, Y., Chuai, Y., et al. (2010) The Potential Cardioprotective Effects of Hydrogen in Irradiated Mice. *Journal of Radiation Research*, 51, 741-747.  
<http://dx.doi.org/10.1269/jrr.10093>
- [92] Sakai, K., Cho, S., Shibata, I., Yoshitomi, O., Maekawa, T. and Sumikawa, K. (2012) Inhalation of Hydrogen Gas Protects against Myocardial Stunning and Infarction in Swine. *Scandinavian Cardiovascular Journal*, 46, 183-189.  
<http://dx.doi.org/10.3109/14017431.2012.659676>
- [93] Yoshida, A., Asanuma, H., Sasaki, H., Sanada, S., Yamazaki, S., et al. (2012) H(2) Mediates Cardioprotection via Involvements of K(ATP) Channels and Permeability Transition Pores of Mitochondria in Dogs. *Cardiovascular Drugs and Therapy*, 26, 217-226.  
<http://dx.doi.org/10.1007/s10557-012-6381-5>
- [94] Xie, Q., Li, X., Zhang, P., Li, J.C., Cheng, Y., et al. (2014) Hydrogen Gas Protects against Serum and Glucose Deprivation Induced Myocardial Injury in H9c2 Cells through Activation of the NFE2 Related Factor 2/Heme Oxygenase 1 Signaling Pathway. *Molecular Medicine Reports*, 10, 1143-1149.
- [95] Nakao, A., Kaczorowski, D.J., Wang, Y., Cardinal, J.S., Buchholz, B.M., et al. (2010) Amelioration of Rat Cardiac Cold Ischemia/Reperfusion Injury with Inhaled Hydrogen or Carbon Monoxide, or Both. *The Journal of Heart and Lung Transplantation*, 29, 544-553.  
<http://dx.doi.org/10.1016/j.healun.2009.10.011>
- [96] Noda, K., Tanaka, Y., Shigemura, N., Kawamura, T., Wang, Y., et al. (2012) Hydrogen-Supplemented Drinking Water Protects Cardiac Allografts from Inflammation-Associated Deterioration. *Transplant International*, 25, 1213-1222.  
<http://dx.doi.org/10.1111/j.1432-2277.2012.01542.x>
- [97] Tan, M., Sun, X., Guo, L., Su, C., Sun, X. and Xu, Z. (2013) Hydrogen as Additive of HTK Solution Fortifies Myocardial Preservation in Grafts with Prolonged Cold Ischemia. *International Journal of Cardiology*, 167, 383-390.  
<http://dx.doi.org/10.1016/j.ijcard.2011.12.109>
- [98] Buchholz, B.M., Kaczorowski, D.J., Sugimoto, R., Yang, R., Wang, Y., Billiar, T.R., McCurry, K.R., Bauer, A.J. and Nakao, A. (2008) Hydrogen Inhalation Ameliorates Oxidative Stress in Transplantation Induced Intestinal Graft Injury. *American Journal of Transplantation*, 8, 2015-2024.  
<http://dx.doi.org/10.1111/j.1600-6143.2008.02359.x>
- [99] Salehi, P., Bigam, D.L., Ewaschuk, J.B., Madsen, K.L., Sigurdson, G.T., Jewell, L.D. and Churchill, T.A. (2008) Alleviating Intestinal Ischemia-Reperfusion Injury in an in Vivo Large Animal Model: Developing an Organ-Specific Preservation Solution. *Transplantation*, 85, 878-884.  
<http://dx.doi.org/10.1097/TP.0b013e318166a42f>
- [100] Zheng, X., Mao, Y., Cai, J., Li, Y., Liu, W., Sun, P., Zhang, J.H., Sun, X. and Yuan, H. (2009) Hydrogen-Rich Saline Protects against Intestinal Ischemia/Reperfusion Injury in Rats. *Free Radical Research*, 43, 478-484.  
<http://dx.doi.org/10.1080/10715760902870603>
- [101] Buchholz, B.M., Masutani, K., Kawamura, T., Peng, X., Toyoda, Y., Billiar, T.R., Bauer, A.J. and Nakao, A. (2011) Hydrogen-Enriched Preservation Protects the Isogeneic Intestinal Graft and Amends Recipient Gastric Function during Transplantation. *Transplantation*, 92, 985-992.  
<http://dx.doi.org/10.1097/tp.0b013e318230159d>
- [102] Shigeta, T., Sakamoto, S., Li, X.K., Cai, S., Liu, C., Kurokawa, R., Nakazawa, A., Kasahara, M. and Uemoto, S. (2015) Luminal Injection of Hydrogen-Rich Solution Attenuates Intestinal Ischemia-Reperfusion Injury in Rats. *Transplantation*, 99, 500-507.  
<http://dx.doi.org/10.1097/TP.0000000000000050>
- [103] Mao, Y.F., Zheng, X.F., Cai, J.M., You, X.M., Deng, X.M., Zhang, J.H., Jiang, L. and Sun, X.J. (2009)

- Hydrogen-Rich Saline Reduces Lung Injury Induced by Intestinal Ische-mia/Reperfusion in Rats. Biochemical and Biophysical Research Communications, 381, 602-605.  
<http://dx.doi.org/10.1016/j.bbrc.2009.02.105>
- [104] den Hengst, W.A., Gielis, J.F., Lin, J.Y., Van Schil, P.E., De Windt, L.J. and Moens, A.L. (2010) Lung Ischemia-Reperfusion Injury: A Molecular and Clinical View on a Complex Pathophysiological Process. American Journal of Physiology, Heart and Circulatory Physiology, 299, H1283-H1299.  
<http://dx.doi.org/10.1152/ajpheart.00251.2010>
- [105] Gennai, S., Pison, C. and Briot, R. (2014) [Ischemia-Reperfusion Injury after Lung Transplantation]. Presse Medicine, 43, 921-930.  
<http://dx.doi.org/10.1016/j.lpm.2014.01.018>
- [106] Dark, J. (2014) Hydrogen in Lung Reconditioning-More than Just Inflation. Transplantation, 98, 497-498.  
<http://dx.doi.org/10.1097/TP.0000000000000311>
- [107] Tanaka, Y., Shigemura, N., Kawamura, T., Noda, K., Isse, K., Stoltz, D.B., Billiar, T.R., Toyoda, Y., Bermudez, C.A., Lyons-Weiler, J. and Nakao, A. (2012) Profiling Molecular Changes Induced by Hydrogen Treatment of Lung Allografts Prior to Procurement. Biochemical and Biophysical Research Communications, 425, 873-879.  
<http://dx.doi.org/10.1016/j.bbrc.2012.08.005>
- [108] Zhou, H., Fu, Z., Wei, Y., Liu, J., Cui, X., Yang, W., Ding, W., Pan, P. and Li, W. (2013) Hydrogen Inhalation Decreases Lung Graft Injury in Brain-Dead Donor Rats. Journal of Heart and Lung Transplantation, 32, 251-258.  
<http://dx.doi.org/10.1016/j.healun.2012.11.007>
- [109] Fang, Y., Fu, X.J., Gu, C., Xu, P., Wang, Y., Yu, W.R., Sun, Q., Sun, X.J. and Yao, M. (2011) Hydrogen-Rich Saline Protects against Acute Lung Injury Induced by Extensive Burn in Rat Model. Journal of Burn Care Research, 32, e82-e91.  
<http://dx.doi.org/10.1097/bcr.0b013e318217f84f>
- [110] Noda, K., Shigemura, N., Tanaka, Y., Bhama, J., D'Cunha, J., Kobayashi, H., Luketich, J.D. and Bermudez, C.A. (2014) Hydrogen Preconditioning during ex Vivo Lung Perfusion Improves the Quality of Lung Grafts in Rats. Transplantation, 98, 499-506.  
<http://dx.doi.org/10.1097/TP.0000000000000254>
- [111] Terasaki, Y., Ohsawa, I., Terasaki, M., Takahashi, M., Kunugi, S., Dedong, K., Urushiyama, H., Amenomori, S., Kaneko-Togashi, M., Kuwahara, N., Ishikawa, A., Kamimura, N., Ohta, S. and Fukuda, Y. (2011) Hydrogen Therapy Attenuates Irradiation-Induced Lung Damage by Reducing Oxidative Stress. American Journal of Physiology, Lung Cellular and Molecular Physiology, 301, L415-L426.  
<http://dx.doi.org/10.1152/ajplung.00008.2011>
- [112] Hattori, Y., Kotani, T., Tsuda, H., Mano, Y., Tu, L., Li, H., Hirako, S., Ushida, T., Imai, K., Nakano, T., Sato, Y., Miki, R., Sumigama, S., Iwase, A., Toyokuni, S. and Kikkawa, F. (2015) Maternal Molecular Hydrogen Treatment Attenuates Lipopolysaccharide-Induced Rat Fetal Lung Injury. Free Radical Research, 49, 1026-1037.  
<http://dx.doi.org/10.3109/10715762.2015.1038257>
- [113] Xie, K., Yu, Y., Huang, Y., Zheng, L., Li, J., Chen, H., Han, H., Hou, L., Gong, G. and Wang, G. (2012) Molecular Hydrogen Ameliorates Lipopolysaccharide-Induced Acute Lung Injury in Mice through Reducing Inflammation and Apoptosis. Shock, 37, 548-555.  
<http://dx.doi.org/10.1097/shk.0b013e31824ddc81>
- [114] Liu, H., Liang, X., Wang, D., Zhang, H., Liu, L., Chen, H., Li, Y., Duan, Q. and Xie, K. (2015) Combination Therapy with Nitric Oxide and Molecular Hydrogen in a Murine Model of Acute Lung Injury. Shock, 43, 504-511.  
<http://dx.doi.org/10.1097/SHK.0000000000000316>
- [115] Bringmann, A., Uckermann, O., Pannicke, T., Iandiev, I., Reichenbach, A. and Wiedemann, P. (2005) Neuronal versus Glial Cell Swelling in the Ischaemic Retina. Acta Ophthalmologica Scandinavia, 83, 528-538.  
<http://dx.doi.org/10.1111/j.1600-0420.2005.00565.x>
- [116] Sun, M.H., Pang, J.H., Chen, S.L., Han, W.H., Ho, T.C., Chen, K.J., Kao, L.Y., Lin, K.K. and Tsao, Y.P. (2010) Retinal Protection from Acute Glaucoma-Induced Ischemia-Reperfusion Injury through Pharmacologic Induction of Heme Oxygenase-1. Investigative Ophthalmology and Vision Science, 51, 4798-4808.  
<http://dx.doi.org/10.1167/iovs.09-4086>

- [117] Makita, J., Hosoya, K., Zhang, P. and Kador, P.F. (2011) Response of Rat Retinal Capillary Pericytes and Endothelial Cells to Glucose. *Journal of Ocular Pharmacology and Therapeutics*, 27, 7-15.  
<http://dx.doi.org/10.1089/jop.2010.0051>
- [118] Liu, Y., Tang, L. and Chen, B. (2012) Effects of Antioxidant Gene Therapy on Retinal Neurons and Oxidative Stress in a Model of Retinal Ischemia/Reperfusion. *Free Radical Biology and Medicine*, 52, 909-915.  
<http://dx.doi.org/10.1016/j.freeradbiomed.2011.12.013>
- [119] Pazdro, R. and Burgess, J.R. (2012) Differential Effects of Alpha-Tocopherol and N-Acetyl-Cysteine on Advanced Glycation End Product-Induced Oxidative Damage and Neurite Degeneration in SH-SY5Y Cells. *Biochimica et Biophysica Acta*, 1822, 550-556.  
<http://dx.doi.org/10.1016/j.bbadi.2012.01.003>
- [120] Varnum, M.D., Black, K.D. and Zagotta, W.N. (1995) Molecular Mechanism for Ligand Discrimination of Cyclic Nucleotide-Gated Channels. *Neuron*, 15, 619-625.  
[http://dx.doi.org/10.1016/0896-6273\(95\)90150-7](http://dx.doi.org/10.1016/0896-6273(95)90150-7)
- [121] Liu, G.D., Zhang, H., Wang, L., Han, Q., Zhou, S.F. and Liu, P. (2013) Molecular Hydrogen Regulates the Expression of miR-9, miR-21 and miR-199 in LPS-Activated Retinal Microglia Cells. *International Journal of Ophthalmology*, 6, 280-285.
- [122] Yokota, T., Kamimura, N., Igarashi, T., Takahashi, H., Ohta, S. and Ohara, H. (2015) Protective Effect of Molecular Hydrogen against Oxidative Stress Caused by Peroxynitrite Derived from Nitric Oxide in Rat Retina. *Clinical and Experimental Ophthalmology*, 43, 568-577.  
<http://dx.doi.org/10.1111/ceo.12525>
- [123] Liu, H., Hua, N., Xie, K., Zhao, T. and Yu, Y. (2015) Hydrogen-Rich Saline Reduces Cell Death through Inhibition of DNA Oxidative Stress and Overactivation of Poly (ADP-Ribose) Polymerase-1 in Retinal Ischemia-Reperfusion Injury. *Molecular Medicine Reports*, 12, 2495-2502.  
<http://dx.doi.org/10.3892/mmr.2015.3731>
- [124] Sanderson, T.H., Reynolds, C.A., Kumar, R., Przyklenk, K. and Huttemann, M. (2013) Molecular Mechanisms of Ischemia-Reperfusion Injury in Brain: Pivotal Role of the Mitochondrial Membrane Potential in Reactive Oxygen Species Generation. *Molecular Neurobiology*, 47, 9-23.  
<http://dx.doi.org/10.1007/s12035-012-8344-z>
- [125] Pan, J., Konstas, A.A., Bateman, B., Ortolano, G.A. and Pile-Spellman, J. (2007) Reperfusion Injury Following Cerebral Ischemia: Pathophysiology, MR Imaging, and Potential Therapies. *Neuroradiology*, 49, 93-102.  
<http://dx.doi.org/10.1007/s00234-006-0183-z>
- [126] Ji, X., Liu, W., Xie, K., Liu, W., Qu, Y., Chao, X., Chen, T., Zhou, J. and Fei, Z. (2010) Beneficial Effects of Hydrogen Gas in a Rat Model of Traumatic Brain Injury via Reducing Oxidative Stress. *Brain Research*, 1354, 196-205.  
<http://dx.doi.org/10.1016/j.brainres.2010.07.038>
- [127] Ji, X., Tian, Y., Xie, K., Liu, W., Qu, Y. and Fei, Z. (2012) Protective Effects of Hydrogen-Rich Saline in a Rat Model of Traumatic Brain Injury via Reducing Oxidative Stress. *Journal of Surgical Research*, 178, e9-e16.  
<http://dx.doi.org/10.1016/j.jss.2011.12.038>
- [128] Huo, T.T., Zeng, Y., Liu, X.N., Sun, L., Han, H.Z., Chen, H.G., Lu, Z.H., Huang, Y., Nie, H., Dong, H.L., Xie, K.L. and Xiong, L.Z. (2014) Hydrogen-Rich Saline Improves Survival and Neurological Outcome after Cardiac Arrest and Cardiopulmonary Resuscitation in Rats. *Anesthesiology and Analgesiology*, 119, 368-380.  
<http://dx.doi.org/10.1213/ANE.0000000000000303>
- [129] Ji, Q., Hui, K., Zhang, L., Sun, X., Li, W. and Duan, M. (2011) The Effect of Hydrogen-Rich Saline on the Brain of Rats with Transient Ischemia. *Journal of Surgical Research*, 168, e95-e101.  
<http://dx.doi.org/10.1016/j.jss.2011.01.057>
- [130] Liu, L., Xie, K., Chen, H., Dong, X., Li, Y., Yu, Y., Wang, G. and Yu, Y. (2014) Inhalation of Hydrogen Gas Attenuates Brain Injury in Mice with Cecal Ligation and Puncture via Inhibiting Neuroinflammation, Oxidative Stress and Neuronal Apoptosis. *Brain Research*, 1589, 78-92.  
<http://dx.doi.org/10.1016/j.brainres.2014.09.030>
- [131] Ono, H., Nishijima, Y., Adachi, N., Sakamoto, M., Kudo, Y., Kaneko, K., Nakao, A. and Imaoka, T. (2012) A Basic Study on Molecular Hydrogen (H<sub>2</sub>) Inhalation in Acute Cerebral Ischemia Patients for Safety Check with Physiological Parameters and Measurement of Blood H<sub>2</sub> Level. *Medical Gas Research*, 2, Article 21.

<http://dx.doi.org/10.1186/2045-9912-2-21>

- [132] Eckel, R.H., Grundy, S.M. and Zimmet, P.Z. (2005) The Metabolic Syndrome. *Lancet*, 365, 1415-1428.  
[http://dx.doi.org/10.1016/S0140-6736\(05\)66378-7](http://dx.doi.org/10.1016/S0140-6736(05)66378-7)
- [133] Grundy, S.M., Cleeman, J.L., Daniels, S.R., Donato, K.A., Eckel, R.H., Franklin, B.A., Gordon, D.J., Krauss, R.M., Savage, P.J., Smith Jr., S.C., Spertus, J.A. and Costa, F. (2005) Diagnosis and Management of the Metabolic Syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 112, 2735-2752.  
<http://dx.doi.org/10.1161/CIRCULATIONAHA.105.169404>
- [134] Alberti, K.G., Zimmet, P. and Shaw, J., IDF Epidemiology Task Force Consensus Group (2005) The Metabolic Syndrome—A New Worldwide Definition. *Lancet*, 366, 1059-1062.  
[http://dx.doi.org/10.1016/S0140-6736\(05\)67402-8](http://dx.doi.org/10.1016/S0140-6736(05)67402-8)
- [135] Eckel, R.H., Alberti, K.G., Grundy, S.M. and Zimmet, P.Z. (2010) The Metabolic Syndrome. *Lancet*, 375, 181-183.  
[http://dx.doi.org/10.1016/S0140-6736\(09\)61794-3](http://dx.doi.org/10.1016/S0140-6736(09)61794-3)
- [136] Reaven, G.M. (1988) Banting Lecture 1988. Role of Insulin Resistance in Human Disease. *Diabetes*, 37, 1595-1607.  
<http://dx.doi.org/10.2337/diab.37.12.1595>
- [137] Reaven, G.M. (1988) Dietary Therapy for Non-Insulin-Dependent Diabetes Mellitus. *New England Journal of Medicine*, 319, 862-864.  
<http://dx.doi.org/10.1056/NEJM198809293191310>
- [138] Kylin, E. (1923) Studien ueber das hypertonie-hyperglykamie-hyperurikamiesyndrom. *Zentralblatt für innere Medizin*, 44, 105-127.
- [139] Rosales-Corral, S., Tan, D.X., Manchester, L. and Reiter, R.J. (2015) Diabetes and Alzheimer Disease, Two Overlapping Pathologies with the Same Background: Oxidative Stress. *Oxidative Medicine and Cellular Longevity*, 2015, Article ID: 985845.  
<http://dx.doi.org/10.1155/2015/985845>
- [140] Muller, M., Grobbee, D.E., den Tonkelaar, I., Lamberts, S.W. and van der Schouw, Y.T. (2005) Endogenous Sex Hormones and Metabolic Syndrome in Aging Men. *Journal of Clinical Endocrinology and Metabolism*, 90, 2618-2623.  
<http://dx.doi.org/10.1210/jc.2004-1158>
- [141] Tangarasittichai, S. (2015) Oxidative Stress, Insulin Resistance, Dyslipidemia and Type 2 Diabetes Mellitus. *World Journal of Diabetes*, 6, 456-480.  
<http://dx.doi.org/10.4239/wjd.v6.i3.456>
- [142] Yubero-Serrano, E.M., Delgado-Lista, J., Pena-Orihuela, P., Perez-Martinez, P., Fuentes, F., Marin, C., Tunex, I., Tinahones, F.J., Perez-Jimenez, F., Roche, H.M. and Lopez-Miranda, J. (2013) Oxidative Stress Is Associated with the Number of Components of Metabolic Syndrome: LIPGENE Study. *Experimental Molecular Medicine*, 45, e28.  
<http://dx.doi.org/10.1038/emm.2013.53>
- [143] Vincent, H.K. and Taylor, A.G. (2006) Biomarkers and Potential Mechanisms of Obesity-Induced Oxidant Stress in Humans. *International Journal of Obesity (London)*, 30, 400-418.  
<http://dx.doi.org/10.1038/sj.ijo.0803177>
- [144] Kopprasch, S., Srirangan, D., Bergmann, S., Graessler, J., Schwarz, P.E. and Bornstein, S.R. (2015) Association between Systemic Oxidative Stress and Insulin Resistance/Sensitivity Indices—The PREDIAS Study. *Clinical Endocrinology*, 84, 48-54.  
<http://dx.doi.org/10.1111/cen.12811>
- [145] Freeman, B.A. and Crapo, J.D. (1982) Biology of Disease: Free Radicals and Tissue Injury. *Laboratory Investigation*, 47, 412-426.
- [146] Slater, T.F. (1984) Free-Radical Mechanisms in Tissue Injury. *Biochemical Journal*, 222, 1-15.  
<http://dx.doi.org/10.1042/bj2220001>
- [147] Dobrian, A.D., Davies, M.J., Schriver, S.D., Lauterio, T.J. and Prewitt, R.L. (2001) Oxidative Stress in a Rat Model of Obesity-Induced Hypertension. *Hypertension*, 37, 554-560.  
<http://dx.doi.org/10.1161/01.HYP.37.2.554>
- [148] Nicolson, G.L. (2007) Metabolic Syndrome and Mitochondrial Function: Molecular Replacement and Antioxidant Supplements to Prevent Membrane Peroxidation and Restore Mitochondrial Function. *Journal*

- of Cellular Biochemistry, 100, 1352-1369.  
<http://dx.doi.org/10.1002/jcb.21247>
- [149] Hashimoto, M., Katakura, M., Nabika, T., Tanabe, Y., Hossain, S., Tsuchikura, S. and Shido, O. (2011) Effects of Hydrogen-Rich Water on Abnormalities in a SHR.Cg-Leprcp/NDmcr Rat—A Metabolic Syndrome Rat Model. *Medical Gas Research*, 1, Article 26.  
<http://dx.doi.org/10.1186/2045-9912-1-26>
- [150] Shirahata, S., Hamasaki, T., Haramaki, K., Nakamura, T., Abe, M., Yan, H., Kinjo, T., Nakamichi, N., Kabayama, S. and Teruya, K. (2011) Anti-Diabetes Effect of Water Containing Hydrogen Molecule and Pt Nanoparticles. *BMC Proceedings*, 5, P18.  
<http://dx.doi.org/10.1186/1753-6561-5-S8-P18>
- [151] Haslam, D.W. and James, W.P. (2005) Obesity. *Lancet*, 366, 1197-1209.  
[http://dx.doi.org/10.1016/S0140-6736\(05\)67483-1](http://dx.doi.org/10.1016/S0140-6736(05)67483-1)
- [152] Furukawa, S., Fujita, T., Shimabukuro, M., Iwaki, M., Yamada, Y., Nakajima, Y., Nakayama, O., Makishima, M., Matsuda, M. and Shimomura, I. (2004) Increased Oxidative Stress in Obesity and Its Impact on Metabolic Syndrome. *Journal of Clinical Investigation*, 114, 1752.  
<http://dx.doi.org/10.1172/JCI21625>
- [153] Kamimura, N., Nishimaki, K., Ohsawa, I. and Ohta, S. (2011) Molecular Hydrogen Improves Obesity and Diabetes by Inducing Hepatic FGF21 and Stimulating Energy Metabolism in db/db Mice. *Obesity*, 19, 1396-1403.  
<http://dx.doi.org/10.1038/oby.2011.6>
- [154] Nakao, A., Toyoda, Y., Sharma, P., Evans, M. and Guthrie, N. (2010) Effectiveness of Hydrogen Rich Water on Antioxidant Status of Subjects with Potential Metabolic Syndrome—An Open Label Pilot Study. *Journal of Clinical Biochemistry and Nutrition*, 46, 140-149.  
<http://dx.doi.org/10.3164/jcbn.09-100>
- [155] Song, G., Li, M., Sang, H., Zhang, L., Li, X., Yao, S., Yu, Y., Zong, C., Xue, Y. and Qin, S. (2013) Hydrogen-Rich Water Decreases Serum LDL-Cholesterol Levels and Improves HDL Function in Patients with Potential Metabolic Syndrome. *Journal of Lipid Research*, 54, 1884-1893.  
<http://dx.doi.org/10.1194/jlr.M036640>
- [156] Iio, A., Ito, M., Itoh, T., Terazawa, R., Fujita, Y., Nozawa, Y., Ohsawa, I., Ohno, K. and Ito, M. (2013) Molecular Hydrogen Attenuates Fatty Acid Uptake and Lipid Accumulation through Downregulating CD36 Expression in HepG2 Cells. *Medical Gas Research*, 3, Article 6.
- [157] Ekuni, D., Tomofuji, T., Endo, Y., Kasuyama, K., Irie, K., Azuma, T., Tamaki, N., Mizutani, S., Kojima, A. and Morita, M. (2012) Hydrogen-Rich Water Prevents Lipid Deposition in the Descending Aorta in a Rat Periodontitis Model. *Archives of Oral Biology*, 57, 1615-1622.  
<http://dx.doi.org/10.1016/j.archoralbio.2012.04.013>
- [158] Zong, C., Song, G., Yao, S., Li, L., Yu, Y., Feng, L., Guo, S., Luo, T. and Qin, S. (2012) Administration of Hydrogen-Saturated Saline Decreases Plasma Low-Density Lipoprotein Cholesterol Levels and Improves High-Density Lipoprotein Function in High-Fat Diet-Fed hamsters. *Metabolism*, 61, 794-800.  
<http://dx.doi.org/10.1016/j.metabol.2011.10.014>
- [159] Brooks-Wilson, A., Marcil, M., Clee, S.M., Zhang, L.H., Roomp, K., van Dam, M., Yu, L., Brewer, C., et al. (1999) Mutations in ABC1 in Tangier Disease and Familial High-Density Lipoprotein Deficiency. *Nature Genetics*, 22, 336-345.  
<http://dx.doi.org/10.1038/11905>
- [160] Song, G., Lin, Q., Zhao, H., Liu, M., Ye, F., Sun, Y., Yu, Y., Guo, S., Jiao, P., Wu, Y., Ding, G., Xiao, Q. and Qin, S. (2015) Hydrogen Activates ATP-Binding Cassette Transporter A1-Dependent Efflux ex Vivo and Improves High-Density Lipoprotein Function in Patients with Hypercholesterolemia: A Double-Blinded, Randomized, and Placebo-Controlled Trial. *Journal of Clinical Endocrinology and Metabolism*, 100, 2724-2733.  
<http://dx.doi.org/10.1210/jc.2015-1321>
- [161] Reaven, G.M., Hollenbeck, C., Jeng, C.Y., Wu, M.S. and Chen, Y.D. (1988) Measurement of Plasma Glucose, Free Fatty Acid, Lactate, and Insulin for 24 h in Patients with NIDDM. *Diabetes*, 37, 1020-1024.  
<http://dx.doi.org/10.2337/diab.37.8.1020>
- [162] Shirahata, S., Nishimura, T., Kabayama, S., Aki, D., Teruya, K., Otsubo, K., Morisawa, S., Ishii, Y., et al. (2008) Supplementation of Hydrogen-Rich Water Improves Lipid and Glucose Metabolism in Patients with Type 2 Diabetes or Impaired Glucose Tolerance. *Nutrition Research*, 28, 137-143.  
<http://dx.doi.org/10.1016/j.nutres.2008.01.008>

- [163] Amitani, H., Asakawa, A., Cheng, K., Amitani, M., Kaimoto, K., Nakano, M., Ushikai, M., Li, Y., Tsai, M., Li, J.B., Terashi, M., Chaolu, H., Kamimura, R. and Inui, A. (2013) Hydrogen Improves Glycemic Control in Type1 Diabetic Animal Model by Promoting Glucose Uptake into Skeletal Muscle. *PLoS ONE*, 8, e53913. <http://dx.doi.org/10.1371/journal.pone.0053913>
- [164] Song, G., Tian, H., Qin, S., Sun, X., Yao, S., Zong, C., Luo, Y., Liu, J., Yu, Y., Sang, H. and Wang, X. (2012) Hydrogen Decreases Athero-Susceptibility in Apolipoprotein B-Containing Lipoproteins and Aorta of Apolipoprotein E Knockout Mice. *Atherosclerosis*, 221, 55-65. <http://dx.doi.org/10.1016/j.atherosclerosis.2011.11.043>
- [165] Jiang, H., Yu, P., Qian, D.H., Qin, Z.X., Sun, X.J., Yu, J. and Huang, L. (2013) Hydrogen-Rich Medium Suppresses the Generation of Reactive Oxygen Species, Elevates the Bcl-2/Bax Ratio and Inhibits Advanced Glycation End Product-Induced Apoptosis. *International Journal of Molecular Medicine*, 31, 1381-1387.
- [166] Chen, Y., Jiang, J., Miao, H., Chen, X., Sun, X. and Li, Y. (2013) Hydrogen-Rich Saline Attenuates Vascular Smooth Muscle Cell Proliferation and Neointimal Hyperplasia by Inhibiting Reactive Oxygen Species Production and Inactivating the Ras-ERK1/2-MEK1/2 and Akt Pathways. *International Journal of Molecular Medicine*, 31, 597-606.
- [167] Song, G., Tian, H., Liu, J., Zhang, H., Sun, X. and Qin, S. (2011) H2 Inhibits TNF-Alpha-Induced Lectin-Like Oxidized LDL Receptor-1 Expression by Inhibiting Nuclear Factor KappaB Activation in Endothelial Cells. *Biotechnology Letters*, 33, 1715-1722. <http://dx.doi.org/10.1007/s10529-011-0630-8>
- [168] McGill, H.C., McMahan, C.A. and Gidding, S.S. (2008) Preventing Heart Disease in the 21st Century: Implications of the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Study. *Circulation*, 117, 1216-1227. <http://dx.doi.org/10.1161/CIRCULATIONAHA.107.717033>
- [169] Colbourne, F. and Corbett, D. (1994) Delayed and Prolonged Post-Ischemic Hypothermia Is Neuroprotective in the Gerbil. *Brain Research*, 654, 265-272. [http://dx.doi.org/10.1016/0006-8993\(94\)90488-X](http://dx.doi.org/10.1016/0006-8993(94)90488-X)
- [170] Gisvold, S.E., Sterz, F., Abramson, N.S., Bar-Joseph, G., Ebmeyer, U., et al. (1996) Cerebral Resuscitation from Cardiac Arrest: Treatment Potentials. *Critical Care Medicine*, 24, S69-S80.
- [171] Hickey, R.W., Ferimer, H., Alexander, H.L., Garman, R.H., Callaway, C.W., et al. (2000) Delayed, Spontaneous Hypothermia Reduces Neuronal Damage after Asphyxia Cardiac Arrest in Rats. *Critical Care Medicine*, 28, 3511-3516. <http://dx.doi.org/10.1097/00003246-200010000-00027>
- [172] Ye, S., Weng, Y., Sun, S., Chen, W., Wu, X., et al. (2012) Comparison of the Durations of Mild Therapeutic Hypothermia on Outcome after Cardiopulmonary Resuscitation in the Rat. *Circulation*, 125, 123-129. <http://dx.doi.org/10.1161/CIRCULATIONAHA.111.062257>
- [173] Hayashida, K., Sano, M., Kamimura, N., Yokota, T., Suzuki, M., et al. (2014) Hydrogen Inhalation during Normoxic Resuscitation Improves Neurological Outcome in a Rat Model of Cardiac Arrest Independently of Targeted Temperature Management. *Circulation*, 130, 2173-2180. <http://dx.doi.org/10.1161/CIRCULATIONAHA.114.011848>
- [174] Neumar, R.W., Bircher, N.G., Sim, K.M., Xiao, F., Zadach, K.S., et al. (1995) Epinephrine and Sodium Bicarbonate during CPR Following Asphyxia Cardiac Arrest in Rats. *Resuscitation*, 29, 249-263. [http://dx.doi.org/10.1016/0300-9572\(94\)00827-3](http://dx.doi.org/10.1016/0300-9572(94)00827-3)
- [175] Ohsawa, I., Nishimaki, K., Yamagata, K., Ishikawa, M. and Ohta, S. (2008) Consumption of Hydrogen Water Prevents Atherosclerosis in Apolipoprotein E Knockout Mice. *Biochemical and Biophysical Research Communications*, 377, 1195-1198. <http://dx.doi.org/10.1016/j.bbrc.2008.10.156>
- [176] He, B., Zhang, Y., Kang, B., Xiao, J., Xie, B. and Wang, Z. (2013) Protection of Oral Hydrogen Water as an Antioxidant on Pulmonary Hypertension. *Molecular Biology Reports*, 40, 5513-5521. <http://dx.doi.org/10.1007/s11033-013-2653-9>
- [177] Sakai, T., Sato, B., Hara, K., Hara, Y., Naritomi, Y., et al. (2014) Consumption of Water Containing over 3.5 mg of Dissolved Hydrogen Could Improve Vascular Endothelial Function. *Vascular Health and Risk Management*, 10, 591-597.
- [178] Harris, R.A., Nishiyama, S.K., Wray, D.W. and Richardson, R.S. (2010) Ultrasound Assessment of Flow-Mediated Dilation. *Hypertension*, 55, 1075-1085.

<http://dx.doi.org/10.1161/HYPERTENSIONAHA.110.150821>

- [179] Thompson, L.M. (2008) Neurodegeneration: A Question of Balance. *Nature*, 452, 707-708.  
<http://dx.doi.org/10.1038/452707a>
- [180] Lin, M.T. and Beal, M.F. (2006) Mitochondrial Dysfunction and Oxidative Stress in Neurodegenerative Diseases. *Nature*, 443, 787-795.  
<http://dx.doi.org/10.1038/nature05292>
- [181] Vila, M. and Przedbroski, S. (2003) Targeting Programmed Cell Death in Neurodegenerative Diseases. *Nature Reviews*, 4, 1-11.  
<http://dx.doi.org/10.1038/nrn1100>
- [182] Pagano, G., Talamanca, A.A., Castello, G., Cordero, M.D., d'Ischia, M., et al. (2014) Oxidative Stress and Mitochondrial Dysfunction across Broad-Ranging Pathologies: Toward Mitochondria-Targeted Clinical Strategies. *Oxidative Medicine and Cellular Longevity*, 2014, Article ID: 541230.  
<http://dx.doi.org/10.1155/2014/541230>
- [183] Moosmann, B. and Behl, C. (2002) Antioxidants as Treatment for Neurodegenerative Disorders. *Expert Opinions on Investigative Drugs*, 11, 1407-1435.  
<http://dx.doi.org/10.1517/13543784.11.10.1407>
- [184] Dania, C.C. and Piplani, P. (2014) The Discovery and Development of New Potential Antioxidant Agents for the Treatment of Neurodegenerative Diseases. *Expert Opinions in Drug Discovery*, 9, 1205-1222.  
<http://dx.doi.org/10.1517/17460441.2014.942218>
- [185] Camilleri, A. and Vassallo, N. (2014) The Centrality of Mitochondria in the Pathogenesis and Treatment of Parkinson's Disease. *CNS Neuroscience and Therapy*, 20, 591-602.  
<http://dx.doi.org/10.1111/cns.12264>
- [186] Moon, H.E. and Paek, S.H. (2015) Mitochondrial Dysfunction in Parkinson's Disease. *Experimental Neurobiology*, 24, 103-116.  
<http://dx.doi.org/10.5607/en.2015.24.2.103>
- [187] Abrous, D.N., Koehl, M. and Le Moal, M. (2003) Adult Neurogenesis: From Precursors to Network and Physiology. *Physiology Reviews*, 85, 523-569.  
<http://dx.doi.org/10.1152/physrev.00055.2003>
- [188] Trancikova, A., Tsika, E. and Moore, D.J. (2012) Mitochondrial Dysfunction in Genetic Animal Models of Parkinson's Disease. *Antioxidants and Redox Signaling*, 16, 896-919.  
<http://dx.doi.org/10.1089/ars.2011.4200>
- [189] Montaron, M.F., Koehl, M., Lemaire, V., Drapeau, E., Abrous, D.N. and Le Moal, M. (2004) Environmentally Induced Long-Term Structural Changes: Cues for Functional Orientation and Vulnerabilities. *Neurotoxin Research*, 6, 571-580.  
<http://dx.doi.org/10.1007/BF03033453>
- [190] Schapira, A.H. (2008) Mitochondria in the Aetiology and Pathogenesis of Parkinson's Disease. *Lancet Neurology*, 7, 97-109.  
[http://dx.doi.org/10.1016/S1474-4422\(07\)70327-7](http://dx.doi.org/10.1016/S1474-4422(07)70327-7)
- [191] Fu, Y., Ito, M., Fujita, Y., Ichihara, M., Masuda, A., Suzuki, A., et al. (2009) Molecular Hydrogen Is Protective against 6-Hydroxydopamine-Induced Nigrostriatal Degeneration in a Rat Model of Parkinson's Disease. *Neuroscience Letters*, 453, 81-85.  
<http://dx.doi.org/10.1016/j.neulet.2009.02.016>
- [192] Daur, W. and Przedborski, S. (2003) Parkinson's Disease: Mechanisms and Models. *Neuron*, 39, 889-909.  
[http://dx.doi.org/10.1016/S0896-6273\(03\)00568-3](http://dx.doi.org/10.1016/S0896-6273(03)00568-3)
- [193] Fujita, K., Seike, K., Yutsudo, N., Ohno, M., Yamada, H., Yamaguchi, H., et al. (2009) Hydrogen in the Drinking Water Reduces Dopaminergic Neuronal Loss in the 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine Mouse Model of Parkinson's Disease. *PLoS ONE*, 4, e7247.  
<http://dx.doi.org/10.1371/journal.pone.0007247>
- [194] Yoritaka, A., Takanashi, M., Hirayama, M., Nakahara, T., Ohta, S. and Hattori, N. (2013) Pilot Study of H2 Therapy in Parkinson's Disease: A Randomized Double-Blind Placebo-Controlled Trial. *Movement Disorders*, 28, 836-839.  
<http://dx.doi.org/10.1002/mds.25375>
- [195] Gintjee, J.J., Magh, A.S.H. and Bertoni, C. (2014) High Throughput Screening in Duchenne Muscular Dystrophy: From Drug Discovery to Functional Genomics. *Biology*, 3, 752-780.

<http://dx.doi.org/10.3390/biology3040752>

- [196] Rauroux, B. and Khirani, S. (2014) Neuromuscular Disease and Respiratory Physiology in Children: Putting Lung Function into Perspective. *Respirology*, 19, 782-791.  
<http://dx.doi.org/10.1111/resp.12330>
- [197] Rahimov, F. and Kunkel, L.M. (2013) The Cell Biology of Disease: Cellular and Molecular Mechanisms Underlying Muscular Dystrophy. *Journal of Cell Biology*, 201, 499-510.  
<http://dx.doi.org/10.1083/jcb.201212142>
- [198] Vaquer, G., Riviere, F., Mavris, M., Bignami, F., Linares-Garcia, J., Westemark, K. and Sepodes, B. (2013) Animal Models for Metabolic, Neuromuscular and Ophthalmological Rare Diseases. *Nature Reviews on Drug Discovery*, 12, 287-305.  
<http://dx.doi.org/10.1038/nrd3831>
- [199] Whitmore, C. and Morgan, J. (2014) What Do Mouse Models of Muscular Dystrophy Tell Us about the DAPC and Its Components? *International Journal of Experimental Pathology*, 95, 365-377.  
<http://dx.doi.org/10.1111/iep.12095>
- [200] Ito, M., Ibi, T., Sahashi, K., Ichihara, M., Ito, M. and Ohno, K. (2011) Open-Label Trial and Randomized, Double-Blind, Placebo-Controlled Crossover Trial of Hydrogen-Enriched Water for Mitochondrial and Inflammatory Myopathies. *Medical Gas Research*, 1, Article 24.  
<http://dx.doi.org/10.1186/2045-9912-1-24>
- [201] Kojic, D., Siegler, B.H., Uhle, F., Lichtenstern, C., Nawroth, P.P., Weigand, M.A., Hofer, S. and Brenner, T. (2015) Are There New Approaches for Diagnosis, Therapy Guidance and Outcome Prediction of Sepsis? *World Journal of Experimental Medicine*, 5, 50-63.  
<http://dx.doi.org/10.5493/wjem.v5.i2.50>
- [202] Levy, M.M., Fink, M.P., Marshall, J.C., Abraham, E., Angus, D., et al. (2001) SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Intensive Care Medicine*, 29, 530-538.  
<http://dx.doi.org/10.1007/s00134-003-1662-x>
- [203] Rittirsch, D., Flierl, M.A. and Ward, P.A. (2008) Harmful Molecular Mechanisms in Sepsis. *Nature Reviews in Immunology*, 8, 776-787.  
<http://dx.doi.org/10.1038/nri2402>
- [204] Duran-Bedolla, J., Montes de Oca-Sandoval, M.A., Saldaña-Navor, V., Villalobos-Silva, J.A., Rodriguez, M.C. and Rivas-Arancibia, S. (2014) Sepsis, Mitochondrial Failure and Multiple Organ Dysfunction. *Clinical Investigative Medicine*, 37, E58-E69.
- [205] Xie, K., Liu, L., Yu, Y. and Wang, G. (2014) Hydrogen Gas Presents a Promising Therapeutic Strategy for Sepsis. *Biomed Research International*, 2014, Article ID: 807635.  
<http://dx.doi.org/10.1155/2014/807635>
- [206] Xie, K., Fu, W., Xing, W., Li, A., Chen, H., Han, H., Yu, Y. and Wang, G. (2012) Combination Therapy with Molecular Hydrogen and Hyperoxia in a Murine Model of Polymicrobial Sepsis. *Shock*, 38, 656-663.
- [207] Li, Y., Xie, K., Chen, H., Wang, G. and Yu, Y. (2015) Hydrogen Has Inhibits High-Mobility Group Box 1 Release in Septic Mice by Upregulation of Heme Oxygenase 1. *Journal of Surgical Research*, 196, 136-148.  
<http://dx.doi.org/10.1016/j.jss.2015.02.042>
- [208] Zhou, J., Chen, Y., Huang, G.Q., Li, J., Wu, G.M., Liu, L., Bai, Y.P. and Wang, J. (2012) Hydrogen-Rich Saline Reverses Oxidative Stress, Cognitive Impairment and Mortality in Rats Submitted to Sepsis by Cecal Ligation and Puncture. *Journal of Surgical Research*, 178, 390-400.  
<http://dx.doi.org/10.1016/j.jss.2012.01.041>
- [209] Zhai, Y., Zhou, X., Dai, Q., Fan, Y. and Huang, X. (2015) Hydrogen-Rich Saline Ameliorates Lung Injury Associated with Cecal Ligation and Puncture-Induced Sepsis in Rats. *Experimental and Molecular Pathology*, 98, 268-276.  
<http://dx.doi.org/10.1016/j.yexmp.2015.03.005>
- [210] Xia, C., Liu, W., Zeng, D., Zhu, L., Sun, X. and Sun, X. (2013) Effect of Hydrogen-Rich Water on Oxidative Stress, Liver Function and Viral Load in Patients with Chronic Hepatitis B. *Clinical and Translational Science*, 6, 372-375.  
<http://dx.doi.org/10.1111/cts.12076>
- [211] Seronello, S., Sheikh, M.Y. and Choi, J. (2007) Redox Regulation of Hepatitis C in Nonalcoholic and Alcoholic Liver. *Free Radical Biology and Medicine*, 43, 869-882.  
<http://dx.doi.org/10.1016/j.freeradbiomed.2007.05.036>

- [212] Qian, L., Shen, J., Chuai, Y. and Cai, J. (2013) Hydrogen as a New Class of Radioprotective Agent. *International Journal of Biological Science*, 9, 887-894.  
<http://dx.doi.org/10.7150/ijbs.7220>
- [213] Ward, J.F. (1988) DNA Damage Produced by Ionizing Radiation in Mammalian Cells: Identities, Mechanisms of Formation, and Reparability. *Progress in Nucleic Acid Research and Molecular Biology*, 35, 95-125.  
[http://dx.doi.org/10.1016/S0079-6603\(08\)60611-X](http://dx.doi.org/10.1016/S0079-6603(08)60611-X)
- [214] Fan, X. (2003) Ionizing Radiation Induces Formation of Malondialdehyde, Formaldehyde and Acetaldehyde from Carbohydrates and Organic Acid. *Journal of Agriculture and Food Chemistry*, 51, 5946-5949.  
<http://dx.doi.org/10.1021/jf0344340>
- [215] Marnett, L.J. (2000) Oxyradicals and DNA Damage. *Carcinogenesis*, 21, 361-370.  
<http://dx.doi.org/10.1093/carcin/21.3.361>
- [216] Qian, L., Cao, F., Cul, J., Huang, Y., Zhou, X., Liu, S. and Cai, J. (2010) Radioprotective Effect of Hydrogen in Cultured Cells and Mice. *Free Radical Research*, 44, 275-282.  
<http://dx.doi.org/10.3109/10715760903468758>
- [217] Liu, C., Cui, J., Sun, Q. and Cai, J. (2010) Hydrogen Therapy May Be an Effective and Specific Novel Treatment for Acute Radiation Syndrome. *Medical Hypotheses*, 74, 145-146.  
<http://dx.doi.org/10.1016/j.mehy.2009.07.017>
- [218] Chuai, Y., Gao, F., Li, B., Zhao, L., Qian, L., Cao, F., et al. (2012) Hydrogen-Rich Saline Attenuates Radiation-Induced Male Germ Cell Loss in Mice through Reducing Hydroxyl Radicals. *Biochemical Journal*, 442, 49-56.  
<http://dx.doi.org/10.1042/BJ20111786>
- [219] Guo, Z., Zhou, B., Li, W., Sun, X. and Luo, D. (2012) Hydrogen-Rich Saline Protects against Ultraviolet B Radiation Injury in Rats. *Journal of Biomedical Research*, 26, 365-371.  
<http://dx.doi.org/10.7555/JBR.26.20110037>
- [220] Mei, K., Zhao, S., Qian, L., Li, B., Ni, J. and Cai, J. (2013) Hydrogen Protects Rats from Dermatitis Caused by Local Irradiation. *Journal of Dermatology Treatment*, 25, 182-188.  
<http://dx.doi.org/10.3109/09546634.2012.762639>
- [221] Ignacio, R.M., Yoon, Y.-S., Sajo, M.E.J., Kim, C.-S., Kim, D.-H., Kim, S.-K., et al. (2013) The Balneotherapy Effect of Hydrogen Reduced Water on UVB-Mediated Skin Injury in Hairless Mice. *Molecular and Cellular Toxicology*, 9, 15-21.  
<http://dx.doi.org/10.1007/s13273-013-0003-6>
- [222] Huo, H.-M., Yang, S., Chen, L.-S., Lu, H.-J., Wang, A.-D. and Zhang, L.-Y. (2012) Hydrogen-Rich Saline Alleviation of the Oxidative Stress and Early-Phase Radiation-Induced Brain Injury in Rats. *Chinese Journal of Radiological Medicine and Protection*, 32, 485-487.
- [223] Yuan, L., Chen, X., Shen, J. and Cai, J. (2015) Administration of Hydrogen-Rich Saline in Mice with Allegeneic Hematopoietic Stem-Cell Transplantation. *Medical Science Monitor*, 21, 749-754.  
<http://dx.doi.org/10.12659/MSM.891338>
- [224] Qian, L., Li, B., Cao, F., Huang, Y., Liu, S., Cai, J., et al. (2010) Hydrogen-Rich PBS Protects Cultured Human Cells from Ionizing Radiation-Induced Cellular Damage. *Nuclear Technology and Radiation Protection*, 25, 23-29.  
<http://dx.doi.org/10.2298/NTRP1001023Q>
- [225] Dole, M., Wilson, F.R. and Fife, W.P. (1975) Hyperbaric Hydrogen Therapy: A Possible Treatment for Cancer. *Science*, 190, 152-154.  
<http://dx.doi.org/10.1126/science.1166304>
- [226] Roberts, B.J., Fife, W.P., Corbett, T.H. and Schabel Jr., F.M. (1978) Response of Five Established Solid Transplantable Mouse Tumors and One Mouse Leukemia to Hyperbaric Hydrogen. *Cancer Treatment Reports*, 62, 1077-1099.
- [227] Kang, K.-M., Kang, Y.-N., Choi, I.-B., Gu, Y., Kawamura, T., Toyoda, Y. and Nakao, A. (2011) Effects of Drinking Hydrogen-Rich Water on the Quality of Life of Patients Treated with Radiotherapy for Liver Tumors. *Medical Gas Research*, 1, Article 11.  
<http://dx.doi.org/10.1186/2045-9912-1-11>
- [228] Citrin, D., Cotrim, A.P., Hyodo, F., Baum, B.J., Krishna, M.C. and Mitchell, J.B. (2010) Radioprotectors and Mitigators of Radiation-Induced Normal Tissue Injury. *Oncologist*, 15, 360-371.

<http://dx.doi.org/10.1634/theoncologist.2009-S104>

- [229] Shin, M.H., Park, R., Nojima, H., Kim, H.-C., Kim, Y.K., et al. (2013) Atomic Hydrogen Surrounded by Water Molecules, H(H<sub>2</sub>O)m, Modulates Basal and UV-Induced Gene Expression in Human Skin in Vivo. *PLoS ONE*, 8, e61696.  
<http://dx.doi.org/10.1371/journal.pone.0061696>
- [230] Qian, L. and Shen, J. (2013) Hydrogen Therapy May Be an Effective and Specific Novel Treatment for Acute Graft-versus-Host Disease (GvHD). *Journal of Cellular and Molecular Medicine*, 17, 1059-1063.  
<http://dx.doi.org/10.1111/jcmm.12081>
- [231] Barrett, A.J. and Ito, S. (2015) The Role of Stem Cell Transplantation for Chronic Myelogenous Leukemia in the 21st Century. *Blood*, 125, 3230-3235.  
<http://dx.doi.org/10.1182/blood-2014-10-567784>
- [232] Scarci, F. and Mailland, F. (2014) In Vitro Evaluations for a New Topical Anti-Aging Formulation. *Journal of Cosmetics, Dermatological Sciences and Applications*, 4, 316-322.  
<http://dx.doi.org/10.4236/jcdsa.2014.45041>
- [233] Rinnerhaler, M., Bischof, J., Streubel, M.K., Trost, A. and Richter, K. (2015) Oxidative Stress in Aging Human Skin. *Biomolecules*, 5, 545-589.  
<http://dx.doi.org/10.3390/biom5020545>
- [234] Vedamurthy, M. (2006) Antiaging Therapies. *Indian Journal of Dermatology, Venereology and Leprology*, 72, 183-186.  
<http://dx.doi.org/10.4103/0378-6323.25776>
- [235] Kato, S., Saitoh, Y., Iwai, K. and Miwa, N. (2012) Hydrogen-Rich Electrolyzed Warm Water Represses Wrinkle Formation against UVA Ray Together with Type-1 Collagen Production and Oxidative Stress Dimishment in Fibroblasts and Cell-Injury Prevention in Keratinocytes. *Journal of Photochemistry and Photobiology B*, 106, 24-33.  
<http://dx.doi.org/10.1016/j.jphotobiol.2011.09.006>
- [236] Tomofuji, T., Kawabata, Y., Kasuyama, K., Endo, Y., et al. (2014) Effects of Hydrogen-Rich Water on Aging Periodontal Tissues in Rats. *Scientific Reports*, 4, 5534.  
<http://dx.doi.org/10.1038/srep05534>
- [237] Guo, S.X., Jin, Y.Y., Fang, Q., You, C.G., et al. (2015) Beneficial Effects of Hydrogen-Rich Saline on Early Burn-Wound Progression in Rats. *PLoS ONE*, 10, e0124897.  
<http://dx.doi.org/10.1371/journal.pone.0124897>
- [238] Li, Q., Kato, S., Matsuoka, D., Tanaka, H. and Miwa, H. (2013) Hydrogen Water Intake via Tube-Feeding for Patients with Pressure Ulcers and Its Reconstructive Effects on Normal Human Skin Cells in Vitro. *Medical Gas Research*, 3, Article 2.
- [239] Miesel, R., Drzejczak, P.J. and Kurpisz, M. (1993) Oxidative Stress during the Interaction of Gametes. *Biology of Reproduction*, 49, 918-923.  
<http://dx.doi.org/10.1095/biolreprod49.5.918>
- [240] Lane, M., McPherson, N.O., Fullston, T., Spillane, M., Sandeman, L., Kang, W.X. and Zander-Fox, D.L. (2014) Oxidative Stress in Mouse Sperm Impairs Embryo Development, Fetal Growth and Alters Adiposity and Glucose Regulation in Female Offspring. *PLoS ONE*, 9, e100832.  
<http://dx.doi.org/10.1371/journal.pone.0100832>
- [241] Tamura, H., Takasaki, A., Miwa, I., Taniguchi, K., Maekawa, R., Asada, H., Taketani, T., Matsuoka, A., Yamagata, Y., Shimamura, K., Morioka, H., Ishikawa, H., Reiter, R.J. and Sugino, N. (2008) Oxidative Stress Impairs Oocyte Quality and Melatonin Protects Oocytes from Free Radical Damage and Improves Fertilization Rate. *Journal of Pineal Research*, 44, 280-287.  
<http://dx.doi.org/10.1111/j.1600-079X.2007.00524.x>
- [242] Armstrong, J.S., Rajasekaran, M., Chamulitrat, W., et al. (1999) Characterization of Reactive Oxygen Species Induced Effects on Human Spermatozoa Movement and Energy Metabolism. *Free Radical Biology and Medicine*, 26, 869-880.  
[http://dx.doi.org/10.1016/S0891-5849\(98\)00275-5](http://dx.doi.org/10.1016/S0891-5849(98)00275-5)
- [243] Gavrilouk, D. and Aitken, R.J. (2015) Damage to Sperm DNA Mediated by Reactive Oxygen Species: Its Impact on Human Reproduction and the Health Trajectory of Offspring. *Advances in Experimental Medicine and Biology*, 868, 23-47.  
[http://dx.doi.org/10.1007/978-3-319-18881-2\\_2](http://dx.doi.org/10.1007/978-3-319-18881-2_2)
- [244] Jiang, D., Wu, D., Zhang, Y., Xu, B., Sun, X. and Li, Z. (2012) Protective Effects of Hydrogen Rich Saline

- Solution on Experimental Testicular Ischemia-Reperfusion Injury in Rats. *Journal of Urology*, 187, 2249-2253.  
<http://dx.doi.org/10.1016/j.juro.2012.01.029>
- [245] Oyeyipo, I.P., Raji, Y., Emikpe, B.O. and Bolarinwa, A.F. (2011) Effects of Nicotine on Sperm Characteristics and Fertility Profile in Adult Male Rats: A Possible Role of Cessation. *Journal of Reproduction and Infertility*, 12, 201-207.
- [246] Vijayalaxmi, Reiter, R.J., Tan, D.X., Herman, T.S. and Thomas Jr., C.R. (2004) Melatonin as a Radioprotective Agent: A Review. *International Journal of Radiation, Oncology and Biological Physics*, 59, 639-653.  
<http://dx.doi.org/10.1016/j.ijrobp.2004.02.006>
- [247] Chuai, Y., Gao, F., Li, B., Zhao, L., Qian, L., Cao, F., Wang, L., Sun, X., Cui, J. and Cai, J. (2012) Hydrogen-Rich Saline Attenuates Radiation-Induced Male Germ Cell Loss in Mice through Reducing Hydroxyl Radicals. *Biochemical Journal*, 442, 49-56.  
<http://dx.doi.org/10.1042/BJ20111786>
- [248] Matzuk, M.M. and Lamb, D.J. (2008) The Biology of Infertility: Research Advances and Clinical Challenges. *Nature Medicine*, 14, 1197-1213.  
<http://dx.doi.org/10.1038/nm.f.1895>
- [249] Ruiz-Pesini, E., Lapena, A.C., Diez-Sanchez, C., Perez-Martos, A., Montoya, J., Alvarez, E., Diaz, M., Urries, A., Montoro, L., Lopez-Perez, M.J. and Enriquez, J.A. (2000) Human mtDNA Haplogroups Associated with High or Reduced Spermatozoa Motility. *American Journal of Human Genetics*, 67, 682-696.  
<http://dx.doi.org/10.1086/303040>
- [250] Gharagozloo, P. and Aitken, R.J. (2011) The Role of Sperm Oxidative Stress in Male Infertility and the Significance of Oral Antioxidant Therapy. *Human Reproduction*, 26, 1628-1640.  
<http://dx.doi.org/10.1093/humrep/der132>
- [251] El-Taieb, M.A., Herwig, R., Nada, E.A., Greilberger, J. and Marberger, M. (2009) Oxidative Stress and Epididymal Sperm Transport, Motility and Morphological Defects. *European Journal of Obstetrics, Gynecology and Reproductive Biology*, 144, S199-S203.  
<http://dx.doi.org/10.1016/j.ejogrb.2009.02.018>
- [252] Nakata, K., Yamashita, N., Noda, Y. and Ohsawa, I. (2015) Stimulation of Human Damaged Sperm Motility with Hydrogen Molecule. *Medical Gas Research*, 5, Article 2.
- [253] Guerin, P., El Mouatassim, S. and Menezo, Y. (2001) Oxidative Stress and Protection against Reactive Oxygen Species in the Pre-Implantation Embryo and Its Surroundings. *Human Reproduction Update*, 7, 175-189.  
<http://dx.doi.org/10.1093/humupd/7.2.175>
- [254] Menezo, Y. and Guerin, P. (2005) Gamete and Embryo Protection against Oxidative Stress during Medically Assisted Reproduction. *Bulletin of Academy of National Medicine*, 189, 715-726.
- [255] Guan, Z., Li, H.F., Guo, L.L. and Yang, X. (2015) Effects of Vitamin C, Vitamin E, and Molecular Hydrogen on the Placental Function in Trophoblast Cells. *Archives of Gynecology and Obstetrics*, 292, 337-342.  
<http://dx.doi.org/10.1007/s00404-015-3647-8>
- [256] Mano, Y., Kotani, T., Ito, M., Nagai, T., Ichinohashi, Y., Yamada, K., Ohno, K., Kikkawa, F. and Toyokuni, S. (2014) Maternal Molecular Hydrogen Administration Ameliorates Rat Fetal Hippocampal Damage Caused by In Utero Ischemia-Reperfusion. *Free Radical Biology and Medicine*, 69, 324-330.  
<http://dx.doi.org/10.1016/j.freeradbiomed.2014.01.037>
- [257] Saugstad, O.D. (2005) Oxidative Stress in the Newborn—A 30-Year Perspective. *Neonatology*, 88, 228-236.  
<http://dx.doi.org/10.1159/000087586>
- [258] Matchett, G.A., Fathali, N., Hasegawa, Y., Jadhav, V., Ostrowski, R.P., Martin, R.D., Dorotta, I.R., Sun, X. and Zhang, J.H. (2009) Hydrogen Gas Is Ineffective in Moderate and Severe Neonatal Hypoxia-Ischemia Rat Models. *Brain Research*, 1259, 90-97.  
<http://dx.doi.org/10.1016/j.brainres.2008.12.066>
- [259] Olah, O., Toth-Szuki, V., Temesvari, P., Bari, F. and Domoki, F. (2013) Delayed Neurovascular Dysfunction Is Alleviated by Hydrogen in Asphyxiated Newborn Pigs. *Neonatology*, 104, 79-86.  
<http://dx.doi.org/10.1159/000348445>
- [260] Papile, L.-A., Burstein, J., Burstein, R. and Koffler, H. (1978) Incidence and Evolution of Subependymal

- and Intraventricular Hemorrhage: A Study of Infants with Birth Weights Less than 1,500 gm. *Journal of Pediatrics*, 92, 529-534.  
[http://dx.doi.org/10.1016/S0022-3476\(78\)80282-0](http://dx.doi.org/10.1016/S0022-3476(78)80282-0)
- [261] Salafia, C.M., Minior, V.K., Rosenkrantz, T.S., Pezzullo, J.C., Popek, E.J., Cusick, W. and Vintzileos, A.M. (1995) Maternal, Placental, and Neonatal Associations with Early Germinal Matrix/Intraventricular Hemorrhage in Infants Born before 32 Weeks' Gestation. *American Journal of Perinatology*, 12, 429-436.  
<http://dx.doi.org/10.1055/s-2007-994514>
- [262] Zia, M.T., Csiszar, A., Labinsky, N., Hu, F., Vinukonda, G., LaGamma, E.F., Ungvari, Z. and Ballabh, P. (2009) Oxidative-Nitrosative Stress in a Rabbit Pup Model of Germinal Matrix Hemorrhage Role of NAD (P) H Oxidase. *Stroke*, 40, 2191-2198.  
<http://dx.doi.org/10.1161/STROKEAHA.108.544759>
- [263] Lekic, T., Manaenko, A., Rolland, W., Fathali, N., Peterson, M., Tang, J. and Zhang, J.H. (2011) Protective Effect of Hydrogen Gas Therapy after Germinal Matrix Hemorrhage in Neonatal Rats. *Acta Neurochirurgica*, 111, 237-241.  
[http://dx.doi.org/10.1007/978-3-7091-0693-8\\_40](http://dx.doi.org/10.1007/978-3-7091-0693-8_40)
- [264] Holman, R.C., Stoll, B.J., Clarke, M.J. and Glass, R.I. (1997) The Epidemiology of Necrotizing Enterocolitis Infant Mortality in the United States. *American Journal of Public Health*, 87, 2026-2031.  
<http://dx.doi.org/10.2105/AJPH.87.12.2026>
- [265] Sheng, Q., Lv, Z., Cai, W., Song, H., Qian, L. and Wang, X. (2013) Protective Effects of Hydrogen-Rich Saline on Necrotizing Enterocolitis in Neonatal Rats. *Journal of Pediatric Surgery*, 48, 1697-1706.  
<http://dx.doi.org/10.1016/j.jpedsurg.2012.11.038>
- [266] Serhan, C.N., Ward, P.A. and Gilroy, D.W. (2010) Fundamentals of Inflammation. Cambridge University Press, Cambridge.  
<http://dx.doi.org/10.1017/CBO9781139195737>
- [267] Lei, Y., Wang, K., Deng, L., Chen, Y., Nice, E.C. and Huang, C. (2015) Redox Regulation of Inflammation: Old Elements, a New Story. *Medical Research Reviews*, 35, 306-340.  
<http://dx.doi.org/10.1002/med.21330>
- [268] Maccarrone, M. and Brune, B. (2009) Redox Regulation in Acute and Chronic Inflammation. *Cell Death and Differentiation*, 16, 1184-1186.  
<http://dx.doi.org/10.1038/cdd.2009.65>
- [269] Li, G.M., Ji, M.H., Sun, X.J., Zeng, Q.T., Tian, M., Fan, Y.X., Li, W.Y., Li, N. and Yang, J.J. (2013) Effects of Hydrogen-Rich Saline Treatment on Polymicrobial Sepsis. *Journal of Surgical Research*, 181, 279-286.  
<http://dx.doi.org/10.1016/j.jss.2012.06.058>
- [270] Qian, L., Mei, K., Shen, J. and Cai, J. (2013) Administration of Hydrogen-Rich Saline Protects Mice from Lethal Acute Graft-Versus-Host Disease (aGvHD). *Transplantation*, 95, 658-662.  
<http://dx.doi.org/10.1097/TP.0b013e31827e6b23>
- [271] Rose, N.R. and Mackay, I.R. (2006) The Autoimmune Diseases. Elsevier Academic Press.
- [272] Mackay, I.R. and Rose, N.R. (2013) The Autoimmune Diseases. Elsevier Science.
- [273] Clair, E.W.S., Pisetsky, D.S. and Haynes, B.F. (2004) Rheumatoid Arthritis. Lippincott Williams & Wilkins.
- [274] Ishibashi, T. (2013) Molecular Hydrogen: New Antioxidant and Anti-Inflammatory Therapy for Rheumatoid Arthritis and Related Diseases. *Current Pharmaceutical Design*, 19, 6375-6381.  
<http://dx.doi.org/10.2174/13816128113199990507>
- [275] Ishibashi, T., Sato, B., Rikitake, M., Seo, T., Kurokawa, R., Hara, Y., Naritomi, Y., Hara, H. and Nagao, T. (2012) Consumption of Water Containing a High Concentration of Molecular Hydrogen Reduces Oxidative Stress and Disease Activity in Patients with Rheumatoid Arthritis: An Open-Label Pilot Study. *Medical Gas Research*, 2, Article 27.  
<http://dx.doi.org/10.1186/2045-9912-2-27>
- [276] Ishibashi, T., Sato, B., Shibata, S., Sakai, T., Hara, Y., Naritomi, Y., Koyanagi, S., Hara, H. and Nagao, T. (2014) Therapeutic Efficacy of Infused Molecular Hydrogen in Saline on Rheumatoid Arthritis: A Randomized, Double-Blind, Placebo-Controlled Pilot Study. *International Immunopharmacology*, 21, 468-473.  
<http://dx.doi.org/10.1016/j.intimp.2014.06.001>
- [277] Ishibashi, T., Ichikawa, M., Sato, B., Shibata, S., Hara, Y., Naritomi, Y., Okazaki, K., Nakashima, Y., Iwamoto, Y., Koyanagi, S., Hara, H. and Nagao, T. (2015) Improvement of Psoriasis-Associated Arthritis

and Skin Lesions by Treatment with Molecular Hydrogen: A Report of Three Cases. *Molecular Medicine Reports*, 12, 2757-2764.

<http://dx.doi.org/10.3892/mmr.2015.3707>

- [278] Itoh, T., Hamada, N., Terazawa, R., Ito, M., Ohno, K., Ichihara, M., Nozawa, Y. and Ito, M. (2011) Molecular Hydrogen Inhibits Lipopolysaccharide/Interferon Gamma-Induced Nitric Oxide Production through Modulation of Signal Transduction in Macrophages. *Biochemical Biophysical Research Communications*, 411, 143-149.  
<http://dx.doi.org/10.1016/j.bbrc.2011.06.116>
- [279] Xu, Z., Zhou, J., Cai, J., Zhu, Z., Sun, X. and Jiang, C. (2012) Anti-Inflammation Effects of Hydrogen Saline in LPS Activated Macrophages and Carrageenan Induced Paw Oedema. *Journal of Inflammation (London)*, 9, 2.  
<http://dx.doi.org/10.1186/1476-9255-9-2>
- [280] Spulber, S., Edoff, K., Hong, L., Morisawa, S., Shirahata, S. and Ceccatelli, S. (2012) Molecular Hydrogen Reduces LPS-Induced Neuroinflammation and Promotes Recovery from Sickness Behaviour in Mice. *PLoS ONE*, 7, e42078.  
<http://dx.doi.org/10.1371/journal.pone.0042078>
- [281] Chen, H.G., Xie, K.L., Han, H.Z., Wang, W.N., Liu, D.Q., Wang, G.L. and Yu, Y.H. (2013) Heme Oxygenase-1 Mediates the Anti-Inflammatory Effect of Molecular Hydrogen in LPS-Stimulated RAW 264.7 Macrophages. *International Journal of Surgery*, 11, 1060-1066.  
<http://dx.doi.org/10.1016/j.ijsu.2013.10.007>
- [282] Yu, Y., Wang, W.N., Han, H.Z., Xie, K.L., Wang, G.L. and Yu, Y.H. (2015) Protective Effects of Hydrogen-Rich Medium on Lipopolysaccharide-Induced Monocytic Adhesion and Vascular Endothelial Permeability through Regulation of Vascular Endothelial Cadherin. *Genetic and Molecular Research*, 14, 6202-6212.  
<http://dx.doi.org/10.4238/2015.June.9.6>
- [283] Xie, K., Wang, W., Chen, H., Han, H., Liu, D., Wang, G. and Yu, Y. (2015) Hydrogen-Rich Medium Attenuated Lipopolysaccharide-Induced Monocyte-Endothelial Cell Adhesion and Vascular Endothelial Permeability via Rho-Associated Coiled-Coil Protein Kinase. *Shock*, 44, 58-64.  
<http://dx.doi.org/10.1097/SHK.0000000000000365>
- [284] He, J., Xiong, S., Zhang, J., Wang, J., Sun, A., Mei, X., Sun, X., Zhang, C. and Wang, Q. (2013) Protective Effects of Hydrogen-Rich Saline on Ulcerative Colitis Rat Model. *Journal of Surgical Research*, 185, 174-181.  
<http://dx.doi.org/10.1016/j.jss.2013.05.047>
- [285] Zhang, J.Y., Wu, Q.F., Wan, Y., Song, S.D., Xu, J., Xu, X.S., Chang, H.L., Tai, M.H., Dong, Y.F. and Liu, C. (2014) Protective Role of Hydrogen-Rich Water on Aspirin-Induced Gastric Mucosal Damage in Rats. *World Journal of Gastroenterology*, 20, 1614-1622. <http://dx.doi.org/10.3748/wjg.v20.i6.1614>
- [286] Zhang, J., Wu, Q., Song, S., Wan, Y., Zhang, R., Tai, M. and Liu, C. (2014) Effect of Hydrogen-Rich Water on Acute Peritonitis of Rat Models. *International Immunopharmacology*, 21, 94-101.  
<http://dx.doi.org/10.1016/j.intimp.2014.04.011>
- [287] Esrefoglu, M. (2012) Oxidative Stress and Benefits of Antioxidant Agents in Acute and Chronic Hepatitis. *Hepatitis Monthly*, 12, 160-167.  
<http://dx.doi.org/10.5812/hepatmon.5090>
- [288] Xia, C., Liu, W., Zeng, D., Zhu, L., Sun, X. and Sun, X. (2013) Effect of Hydrogen-Rich Water on Oxidative Stress, Liver Function, and Viral Load in Patients with Chronic Hepatitis B. *Clinical and Translational Science*, 6, 372-375.  
<http://dx.doi.org/10.1111/cts.12076>
- [289] Zhang, D.Q., Feng, H. and Chen, W.C. (2013) Effects of Hydrogen-Rich Saline on Taurocholate-Induced Acute Pancreatitis in Rat. *Evidence-Based Complementary and Alternative Medicine*, 2013, Article ID: 731932.
- [290] Ren, J.D., Ma, J., Hou, J., Xiao, W.J., Jin, W.H., Wu, J. and Fan, K.H. (2014) Hydrogen-Rich Saline Inhibits NLRP3 Inflammasome Activation and Attenuates Experimental Acute Pancreatitis in Mice. *Mediators of Inflammation*, 2014, Article ID: 930894.  
<http://dx.doi.org/10.1155/2014/930894>
- [291] Wang, X., Yu, P., Yang, Y., Liu, X., Jiang, J., Liu, D. and Xue, G. (2015) Hydrogen-Rich Saline Resuscitation Alleviates Inflammation Induced by Severe Burn with Delayed Resuscitation. *Burns*, 41, 379-385.  
<http://dx.doi.org/10.1016/j.burns.2014.07.012>

- [292] Liu, S.L., Liu, K., Sun, Q., Liu, W.W., Tao, H.Y. and Sun, X.J. (2011) Hydrogen Therapy May Be a Novel and Effective Treatment for COPD. *Frontiers in Pharmacology*, 2, 19.  
<http://dx.doi.org/10.3389/fphar.2011.00019>
- [293] Xiao, M., Zhu, T., Wang, T. and Wen, F.Q. (2013) Hydrogen-Rich Saline Reduces Airway Remodeling via Inactivation of NF-KappaB in a Murine Model of Asthma. *European Review for Medical and Pharmacological Science*, 17, 1033-1043.
- [294] Matsumoto, S., Ueda, T. and Kakizaki, H. (2013) Effect of Supplementation with Hydrogen-Rich Water in Patients with Interstitial Cystitis/Painful Bladder Syndrome. *Urology*, 81, 226-230.  
<http://dx.doi.org/10.1016/j.urology.2012.10.026>
- [295] Zhao, S., Yang, Y., Liu, W., Xuan, Z., Wu, S., Yu, S., Mei, K., Huang, Y., Zhang, P., Cai, J., Ni, J. and Zhao, Y. (2014) Protective Effect of Hydrogen-Rich Saline against Radiation-Induced Immune Dysfunction. *Journal of Cell and Molecular Medicine*, 18, 938-946.  
<http://dx.doi.org/10.1111/jcmm.12245>
- [296] Page, D.W. (2006) Body Trauma: A Writer's Guide to Wounds and Injuries. Vol. 978, No. 1-933042, Behler Publications.
- [297] Dohi, K., Kraemer, B.C., Erickson, M.A., McMillan, P.J., Kovac, A., Flachbartova, Z., Hansen, K.M., Shah, G.N., Sheibani, N., Salameh, T. and Banks, W.A. (2014) Molecular Hydrogen in Drinking Water Protects against Neurodegenerative Changes Induced by Traumatic Brain Injury. *PLoS ONE*, 9, e108034.  
<http://dx.doi.org/10.1371/journal.pone.0108034>
- [298] Zhuang, Z., Sun, X.J., Zhang, X., Liu, H.D., You, W.C., Ma, C.Y., Zhu, L., Zhou, M.L. and Shi, J.X. (2013) Nuclear Factor-KappaB/Bcl-XL Pathway Is Involved in the Protective Effect of Hydrogen-Rich Saline on the Brain Following Experimental Subarachnoid Hemorrhage in Rabbits. *Journal of Neuroscience Research*, 91, 1599-1608.  
<http://dx.doi.org/10.1002/jnr.23281>
- [299] Hong, Y., Shao, A., Wang, J., Chen, S., Wu, H., McBride, D.W., Wu, Q., Sun, X. and Zhang, J. (2014) Neuroprotective Effect of Hydrogen-Rich Saline against Neurologic Damage and Apoptosis in Early Brain Injury Following Subarachnoid Hemorrhage: Possible Role of the Akt/GSK3beta Signaling Pathway. *PLoS ONE*, 9, e96212.  
<http://dx.doi.org/10.1371/journal.pone.0096212>
- [300] Shao, A., Wu, H., Hong, Y., Tu, S., Sun, X., Wu, Q., Zhao, Q., Zhang, J. and Sheng, J. (2015) Hydrogen-Rich Saline Attenuated Subarachnoid Hemorrhage-Induced Early Brain Injury in Rats by Suppressing Inflammatory Response: Possible Involvement of NF-KappaB Pathway and NLRP3 Inflammasome. *Molecular Neurobiology*, 1-15.  
<http://dx.doi.org/10.1007/s12035-015-9242-y>
- [301] Sun, J.C., Xu, T., Zuo, Q., Wang, R.B., Qi, A.Q., Cao, W.L., Sun, A.J., Sun, X.J. and Xu, J. (2014) Hydrogen-Rich Saline Promotes Survival of Retinal Ganglion Cells in a Rat Model of Optic Nerve Crush. *PLoS ONE*, 9, e99299.  
<http://dx.doi.org/10.1371/journal.pone.0099299>
- [302] Zhai, Y., Zhou, X., Dai, Q., Fan, Y. and Huang, X. (2015) Hydrogen-Rich Saline Ameliorates Lung Injury Associated with Cecal Ligation and Puncture-Induced Sepsis in Rats. *Experimental and Molecular Pathology*, 98, 268-276.  
<http://dx.doi.org/10.1016/j.yexmp.2015.03.005>
- [303] Liu, W., Shan, L.P., Dong, X.S., Liu, X.W., Ma, T. and Liu, Z. (2013) Combined Early Fluid Resuscitation and Hydrogen Inhalation Attenuates Lung and Intestine Injury. *World Journal of Gastroenterology*, 19, 492-502.  
<http://dx.doi.org/10.3748/wjg.v19.i4.492>
- [304] Ning, Y., Shang, Y., Huang, H., Zhang, J., Dong, Y., Xu, W. and Li, Q. (2013) Attenuation of Cigarette Smoke-Induced Airway Mucus Production by Hydrogen-Rich Saline in Rats. *PLoS ONE*, 8, e83429.  
<http://dx.doi.org/10.1371/journal.pone.0083429>
- [305] Chen, X., Liu, Q., Wang, D., Feng, S., Zhao, Y., Shi, Y. and Liu, Q. (2015) Protective Effects of Hydrogen-Rich Saline on Rats with Smoke Inhalation Injury. *Oxidative Medicine and Cell Longevity*, 2015, Article ID: 106836.  
<http://dx.doi.org/10.1155/2015/106836>
- [306] Lucas, K. and Maes, M. (2013) Molecular Mechanisms Underpinning Laser Printer and Photocopier Induced Symptoms, including Chronic Fatigue Syndrome and Respiratory Tract Hyperresponsiveness: Pharmacological Treatment with Cinnamon and Hydrogen. *Neuroendocrinology Letters*, 34, 723-737.

- [307] Li, F.Y., Zhu, S.X., Wang, Z.P., Wang, H., Zhao, Y. and Chen, G.P. (2013) Consumption of Hydrogen-Rich Water Protects against Ferric Nitrilotriacetate-Induced Nephrotoxicity and Early Tumor Promotional Events in Rats. *Food and Chemical Toxicology*, 61, 248-254.  
<http://dx.doi.org/10.1016/j.fct.2013.10.004>
- [308] Xu, B., Zhang, Y.B., Li, Z.Z., Yang, M.W., Wang, S. and Jiang, D.P. (2013) Hydrogen-Rich Saline Ameliorates Renal Injury Induced by Unilateral Ureteral Obstruction in Rats. *International Immunopharmacology*, 17, 447-452.  
<http://dx.doi.org/10.1016/j.intimp.2013.06.033>
- [309] Xin, H.G., Zhang, B.B., Wu, Z.Q., Hang, X.F., Xu, W.S., Ni, W., Zhang, R.Q. and Miao, X.H. (2014) Consumption of Hydrogen-Rich Water Alleviates Renal Injury in Spontaneous Hypertensive Rats. *Molecular and Cellular Biochemistry*, 392, 117-124.  
<http://dx.doi.org/10.1007/s11010-014-2024-4>
- [310] Gu, H., Yang, M., Zhao, X., Zhao, B., Sun, X. and Gao, X. (2014) Pretreatment with Hydrogen-Rich Saline Reduces the Damage Caused by Glycerol-Induced Rhabdomyolysis and Acute Kidney Injury in Rats. *Journal of Surgical Research*, 188, 243-249.  
<http://dx.doi.org/10.1016/j.jss.2013.12.007>
- [311] Guo, S.X., Fang, Q., You, C.G., Jin, Y.Y., Wang, X.G., Hu, X.L. and Han, C.M. (2015) Effects of Hydrogen-Rich Saline on Early Acute Kidney Injury in Severely Burned Rats by Suppressing Oxidative Stress Induced Apoptosis and Inflammation. *Journal of Translational Medicine*, 13, 183.  
<http://dx.doi.org/10.1186/s12967-015-0548-3>
- [312] Homma, K., Yoshida, T., Yamashita, M., Hayashida, K., Hayashi, M. and Hori, S. (2014) Inhalation of Hydrogen Gas Is Beneficial for Preventing Contrast-Induced Acute Kidney Injury in Rats. *Nephron Experimental Nephrology*, 128, 116-122.  
<http://dx.doi.org/10.1159/000369068>
- [313] Shi, Q., Liao, K.S., Zhao, K.L., Wang, W.X., Zuo, T., Deng, W.H., Chen, C., Yu, J., Guo, W.Y., He, X.B., Abiliz, A., Wang, P. and Zhao, L. (2015) Hydrogen-Rich Saline Attenuates Acute Renal Injury in Sodium Taurocholate-Induced Severe Acute Pancreatitis by Inhibiting ROS and NF-KappaB Pathway. *Mediators of Inflammation*, 2015, Article ID: 685043.  
<http://dx.doi.org/10.1155/2015/685043>
- [314] Eye Diseases Prevalence Research Group (2004) The Prevalence of Diabetic Retinopathy among Adults in the United States. *Archives of Ophthalmology*, 122, 552.  
<http://dx.doi.org/10.1001/archoph.122.4.552>
- [315] Xiao, X., Cai, J., Xu, J., Wang, R., Cai, J., Liu, Y., Xu, W., Sun, X. and Li, R. (2012) Protective Effects of Hydrogen Saline on Diabetic Retinopathy in a Streptozotocin-Induced Diabetic Rat Model. *Journal of Ocular Pharmacology and Therapeutics*, 28, 76-82.  
<http://dx.doi.org/10.1089/jop.2010.0129>
- [316] Tian, L., Zhang, L., Xia, F., An, J., Sugita, Y. and Zhang, Z. (2013) Hydrogen-Rich Saline Ameliorates the Retina against Light-Induced Damage in Rats. *Medical Gas Research*, 3, Article 19.  
<http://dx.doi.org/10.1186/2045-9912-3-19>
- [317] Zhang, J.Y., Song, S.D., Pang, Q., Zhang, R.Y., Wan, Y., Yuan, D.W., Wu, Q.F. and Liu, C. (2015) Hydrogen-Rich Water Protects against Acetaminophen-Induced Hepatotoxicity in Mice. *World Journal of Gastroenterology*, 21, 4195-4209.  
<http://dx.doi.org/10.3748/wjg.v21.i14.4195>
- [318] Ren, J., Luo, Z., Tian, F., Wang, Q., Li, K. and Wang, C. (2012) Hydrogen-Rich Saline Reduces the Oxidative Stress and Relieves the Severity of Trauma-Induced Acute Pancreatitis in Rats. *Journal of Trauma and Acute Care Surgery*, 72, 1555-1561.  
<http://dx.doi.org/10.1097/TA.0b013e31824a7913>
- [319] Xie, Q., Li, X.X., Zhang, P., Li, J.C., Cheng, Y., Feng, Y.L., Huang, B.S., Zhuo, Y.F. and Xu, G.H. (2014) Hydrogen Gas Protects against Serum and Glucose Deprivation Induced Myocardial Injury in H9c2 Cells through Activation of the NFE2 Related Factor 2/Heme Oxygenase 1 Signaling Pathway. *Molecular Medicine Reports*, 10, 1143-1149.
- [320] Steinbacher, P. and Eckl, P. (2015) Impact of Oxidative Stress on Exercising Skeletal Muscle. *Biomolecules*, 5, 356-377.  
<http://dx.doi.org/10.3390/biom5020356>
- [321] Niess, A.M. and Simon, P. (2007) Response and Adaptation of Skeletal Muscle to Exercise—The Role of Reactive Oxygen Species. *Frontiers in Bioscience*, 12, 4826-4838.

<http://dx.doi.org/10.2741/2431>

- [322] Huang, T., Wang, W., Tu, C., Yang, Z., Bramwell, D. and Sun, X. (2015) Hydrogen-Rich Saline Attenuates Ischemia-Reperfusion Injury in Skeletal Muscle. *Journal of Surgical Research*, 194, 471-480.  
<http://dx.doi.org/10.1016/j.jss.2014.12.016>
- [323] Tsubone, H., Hanafusa, M., Endo, M., Manabe, N., et al. (2013) Effect of Treadmill Exercise and Hydrogen-Rich Water Intake on Serum Oxidative and Anti-Oxidative Metabolites in Serum of Thoroughbred Horses. *Journal of Equine Science*, 24, 1-8.  
<http://dx.doi.org/10.1294/jes.24.1>
- [324] Ostoic, S.M., Vukomanovic, B., Calleja-Gonzalez, J. and Hoffman, J.R. (2014) Effectiveness of Oral and Topical Hydrogen for Sports-Related Soft Tissue Injuries. *Postgraduate Medicine*, 126, 187-195.  
<http://dx.doi.org/10.3810/pgm.2014.09.2813>
- [325] Aoki, K., Nakao, A., Adachi, T., et al. (2012) Pilot Study: Effects of Drinking Hydrogen-Rich Water on Muscle Fatigue Caused by Acute Exercise in Elite Athletes. *Medical Gas Research*, 2, Article 12.  
<http://dx.doi.org/10.1186/2045-9912-2-12>
- [326] Ge, Y., Wu, F., Sun, X., Xiang, Z., Yang, L., Huang, S., Lu, Z., Sun, Y. and Yu, W.-F. (2014) Intrathecal Infusion of Hydrogen-Rich Normal Saline Attenuates Neuropathic Pain via Inhibition of Activation of Spinal Astrocytes and Microglia in Rats. *PLoS ONE*, 9, e97436.  
<http://dx.doi.org/10.1371/journal.pone.0097436>
- [327] Kawaguchi, M., Satoh, Y., Otsubo, Y. and Kazama, T. (2014) Molecular Hydrogen Attenuates Neuropathic Pain in Mice. *PLoS ONE*, 9, e100352.  
<http://dx.doi.org/10.1371/journal.pone.0100352>
- [328] Zhang, L., Shu, R., Wang, H., Yu, Y., Wang, C., Yang, M. and Wang, G. (2014) Hydrogen-Rich Saline Prevents Remifentanil-Induced Hyperalgesia and Inhibits MnSOD Nitration via Regulation of NR2B-Containing NMDA Receptor in Rats. *Neuroscience*, 280, 171-180.  
<http://dx.doi.org/10.1016/j.neuroscience.2014.09.024>
- [329] Wang, C., Li, Y., Wang, H., Xie, K., Shu, R., Zhang, L., Hu, N., Yu, Y. and Wang, G. (2015) Inhibition of DOR Prevents Remifentanil-Induced Postoperative Hyperalgesia through Regulating the Trafficking and Function of Spinal NMDA Receptors in Vivo and in Vitro. *Brain Research Bulletin*, 110, 30-39.  
<http://dx.doi.org/10.1016/j.brainresbull.2014.12.001>
- [330] Shen, M., He, J., Cai, J., Sun, Q. and Huo, Z. (2010) Hydrogen as a Novel and Effective Treatment of Acute Carbon Monoxide Poisoning. *Medical Hypotheses*, 75, 235-237.  
<http://dx.doi.org/10.1016/j.mehy.2010.02.029>
- [331] Yu, Y.P., Li, Z.G., Wang, D.Z., Zhan, X. and Shao, J.H. (2011) Hydrogen Sulfide as an Effective and Specific Novel Therapy for Acute Carbon Monoxide Poisoning. *Biochemical and Biophysical Research Communications*, 404, 6-9.  
<http://dx.doi.org/10.1016/j.bbrc.2010.11.113>
- [332] Sun, Q., Cai, J., Zhou, J., Zhang, J.H., Zhang, W. and Sun, X.J. (2011) Hydrogen-Rich Saline Reduces Delayed Neurological Sequelae in Experimental Carbon Monoxide Toxicity. *Critical Care Medicine*, 39, 765-769.  
<http://dx.doi.org/10.1097/CCM.0b013e318206bf44>
- [333] Shen, M.-H., Cai, J.-M., Sun, Q., Zhang, D.-W., Zheng, L.H., He, J. and Sun, X.J. (2013) Neuroprotective Effect of Hydrogen-Rich Saline in Acute Carbon Monoxide Poisoning. *CNS Neuroscience and Therapeutics*, 19, 361-363.  
<http://dx.doi.org/10.1111/cns.12094>
- [334] Du, Z., Jia, H., Liu, J., Zhao, X., Wang, Y. and Sun, X. (2014) Protective Effects of Hydrogen-Rich Saline in Uncontrolled Hemorrhagic Shock. *Experimental and Therapeutic Medicine*, 7, 1253-1258.
- [335] Du, Z., Jia, H., Liu, J., Zhao, X. and Xu, W. (2015) Effects of Three Hydrogen-Rich Liquids on Hemorrhagic Shock in Rats. *Journal of Surgical Research*, 193, 377-382.  
<http://dx.doi.org/10.1016/j.jss.2014.06.051>
- [336] Bien, A., Seidenbecher, C.I., Bockers, T.M., Sabel, B.A. and Kreutz, M.R. (1999) Apoptotic versus Necrotic Characteristics of Retinal Ganglion Cell Death after Partial Optic Nerve Injury. *Journal of Neurotrauma*, 16, 153-163.  
<http://dx.doi.org/10.1089/neu.1999.16.153>
- [337] Organisciak, D.T. and Vaughan, D.K. (2010) Retinal Light Damage: Mechanisms and Protection. *Progress in Retinal and Eye Research*, 29, 113-134.

<http://dx.doi.org/10.1016/j.preteyeres.2009.11.004>

- [338] Ghanizadeh, A. and Berk, M. (2013) Molecular Hydrogen: An Overview of Its Neurobiological Effects and Therapeutic Potential for Bipolar Disorder and Schizophrenia. *Medical Gas Research*, 3, Article 11.  
<http://dx.doi.org/10.1186/2045-9912-3-11>

0 Comments Scientific Research Publishing

 1 Login ▾

 Recommend

 Share

Sort by Best ▾



Start the discussion...

Be the first to comment.

#### ALSO ON SCIENTIFIC RESEARCH PUBLISHING

#### A Conservative's View from the Academic Trenches: Reply to Duarte, Crawford, ...

1 comment • 2 months ago

scottrose — When Walter Schumm published a commentary on Regnerus's junk science paper, he failed to disclose that he was a ...

#### Evaluation of Physical and Mental Quality of Life of Motorcycle Taxi Drivers

1 comment • 2 months ago

Jules Ramon — Parabéns pelo estudo desenvolvido. Sou Jules Teixeira, autor de duas referências utilizadas no estudo. Os ...

#### Excess Alcohol Use and Death among Tuberculosis Patients in the United ...

1 comment • 3 months ago

TB Doctor — These guys are awesome!

#### Wave Particle Duality & Interference Explained

1 comment • 4 months ago

N S Agarwal — True Mass of Photon, a new term introduced here, is the actual mass of Photon and always remains constant under ...

 Subscribe

 Add Disqus to your site Add Disqus Add

 Privacy

Copyright © 2016 by authors and Scientific Research Publishing Inc.



This work and the related PDF file are licensed under a [Creative Commons Attribution 4.0 International License](#).

[Home](#) | [About SCIRP](#) | [Sitemap](#) | [News](#) | [Jobs](#)

Copyright © 2006-2016 Scientific Research Publishing Inc. All Rights Reserved.