WATER

Brown's Gas for Health: Background, Observations and Medical Data

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Abstract

Intensive research on the therapeutic effects of hydrogen has already been undertaken for years. In some of these studies, however, instead of pure molecular hydrogen, a special gas mixture known as BG (Brown's Gas) is used, which is produced by the electrolysis of water and contains 67 % hydrogen, 33 % oxygen and an energy-rich gas component defined as "ExW," which is to be investigated in more detail in the future. The special properties of this gas and its therapeutic effects are described on the basis of the advanced hydrogen research and its benefits are discussed in the context of the underlying mechanisms of chronic diseases and aging. After explaining the individual stages of the development of chronic diseases, possible applications of BG are presented as examples of successful application. The promotion of clinical studies on the use of this gas for treatment of acute and chronic diseases in humans is recommended. Comparative studies of BG and molecular hydrogen from the storage bottle are necessary to determine a possible superiority of BG over pure molecular hydrogen. BG is considered to be an inexpensive, flexible and effective therapy which, due to its production using water electrolysis compared to molecular hydrogen from a purified source, may be used "on demand" for many diseases in hospitals and outpatient departments.

Introduction

Though medical research has made immense progress in recent decades, it is often a slow process involving skepticism until the research studies are there to support health claims. This is especially true when the medicine or treatment claims to successfully treat many different diseases.

This initial skepticism is often appropriate, as there are many examples in the medical literature that show that the initial enthusiasm for a treatment approach proved to be unsustainable in studies. Many claims for a medicine or treatment or drug have shown to be limited in their effects or even harmful, such as with certain vitamins. Some vitamins are said to have omnipotent, positive effects, yet studies may fail to show these results. An example is vitamin E, in which its reported efficacy proved unsustainable in medical studies (Brigelius-Flohé, 2007).

One such area of exploration that may have health benefits is provided by the study of Brown's Gas (BG), which is produced by the electrolysis of water. Claims about the benefits of BG have been reported for several kinds of diseases. In Asia, this gas, or hydrogen alone, has been used therapeutically for some time in the treatment of diseases as will be shown below.

In the pursuit of personal healing the first author engaged herself in researching the scientific literature for the medical benefits of BG and acquired experience with a BG electrolyzer in its application.

This article presents the use of BG for health purposes and gives a general overview of the current status of studies and related topics on the use of hydrogen in medical applications.

Brown's Gas and its Components

The name, "Brown's Gas" (BG), is derived from the research of *Ilya Velbov*, a Bulgarian engineer who emigrated to Australia and there changed his name to *Yull Brown*. He dedicated 30 years of his life to the development of this specific water electrolysis technology. In recognition of his work, this gas was posthumously named after him – in the scientific literature, BG is also termed HHO (Santilli, 2006; Calo, 2007; Cloonan, 2008) and HydrOxy. The discovery of BG was made by *William Rhodes*, who received a patent for the "single-ducted" electrolysis technology in 1967 (Rhodes, 1967).

The production of BG involves electrolysis. In this process, water is separated into its components hydrogen and oxygen by using a "single line electrolyzer." Electrolysis splits water into hydrogen and oxygen by inserting two electrodes into a solution containing a catalyst and water, then running direct current through the solution:

Classical stoichiometry of electrolysis:

$$2(H\text{-}O\text{-}H) \rightarrow 2(H\text{-}H) + O\text{-}O$$

Santilli's interpretation of electrolysis:

$$n(H\text{-}O\text{-}H) \rightarrow H\text{-}H + (H\text{-}H)\times(H\text{-}H) + (H\text{-}H)\times H\times H + H\times H\times H\times H + O\text{-}H\cdot + H\times O + O + (O\text{-}O)\times H + O\text{-}O + (H\text{-}O)\times O + H\times O\times O + (H\text{-}H)\times(O\text{-}O)\times(H\text{-}H)\times H + (O\text{-}O)\times(H\text{-}H)\times(H\text{-}H)\times H + O\times O\times O + (O\text{-}O)\times O$$

Hydrogen develops from the negative electrode (cathode) and oxygen evolves from the positive electrode (anode). The difference between conventional and Brown's Gas (BG) electrolyzers is that the former utilizes a "membrane" in the solution between the cathode and anode. This membrane separates the hydrogen and oxygen into two separate compartments. BG electrolyzers do not make use of such a membrane, thus all gasses produced in the process exit from the same tube. For further details see Wiseman (2019a).

In the scientific literature, BG is also known as HHO; it should be mentioned though that this terminology is controversial and still disputed (see Calo, 2007). Nonetheless not all of Santilli's claims could be rejected (Cloonan, 2008), indicating that the transition from the conventional H–O–H species to the new (H×H)–O species (x, denoting magnecule) indeed may be regarded as a change of the electric polarization of water caused by the electrolyzer (for further details, see Santilli, 2006).

BG has been primarily used for welding torches, and to improve the efficiency of fuels. Because of its extraordinary energetic properties, there are many amazing technical applications for this gas. BG consists of hydrogen and oxygen in the stoichiometric

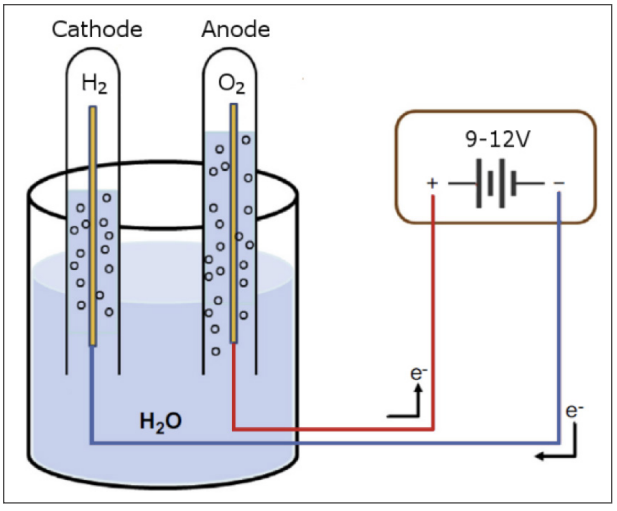

Figure 1: *Schematic principle of electrolysis displaying conventional products of electrolysis.*

ratio of water, which is two to one. Most of the hydrogen and oxygen is molecular, as the more stable form, where two atoms are connected by atomic bonding (H_2 and O_2). H_2O as water vapor is also present. Due to the process of electrolysis, and as shown above, BG also contains fewer stable forms, such as positively charged hydrogen ions (H^+) and negatively charged oxygen ions (O^-) (Wiseman, 2019b). It is assumed that it also contains negatively charged hydrogen, hydride ions (H^-), OH_2, H_2OH_2 and OH_2O-species. Yet, these less stable monatomic parts of the gas remain stable only for a very short time (Kadeisvili, 2008).

BG is also comprised of an additional constituent known as "electrically expanded water" (ExW) (Wiseman, 2019b). *George Wiseman*, the leading BG researcher in North America today, has detected ExW as a fraction of gas that forms in the fluid between the electrodes during elecytrolysis. ExW remains stable in the gaseous state and does not condense on cooling. *Wiseman* calls it a "plasma form of water," a fourth state of matter. He describes the gas according to its special features: it is lighter than air, heavier than hydrogen and it implodes when ignited. It is possible to detect this portion of gas through chromatographic analysis (Wiseman, 2019b).

It seems that this high-energy, electron-containing gas fraction is the cause of BG's extraordinary effects for technical purposes. *Chris Eckman* describes it as linear water molecules that expand to gain electrons in the d orbital sub-shell, one of the orbital subshells where electrons may be found in the atom. The additional electrons are responsible for the special effects of BG (Eckmann. 2010). It is common knowledge to anyone who understands the basics of chemistry that a combination of hydrogen and oxygen can be explosive. For an air-gas mixture to be considered combustible, it must contain more than 4.7 vol% hydrogen.

Components

Oxygen: If BG were to be used in a medical application involving inhalation, the oxygen component would be a relatively low dose. *Wiseman* recommends a gas flow of 18-20 L/h for the inhalation of BG for a normal-weight adult (Wiseman, 2019b). Here there is a net increase of inhaled oxygen in the BG-air mixture increases from 21 to 23 vol%, as it is presumed that the BG contains 33 vol% oxygen (while in ambient air the volumetric concentration amounts to 21 %).

Hydrogen: For inhalation purposes, the hydrogen content is kept below 4 vol%, which is the safe value used in a BG inhalation system. Hydrogen is the majority of BG. The human body is comprised of hydrogen at an estimated 10 % by weight and 63 % in volume (Helmenstine, 2019; Wikipedia, 2020).

All organic compounds contain hydrogen as the predominant element. It is through eating and absorption of nutrients that we ingest organic compounds and therefore, bound hydrogen. It is then used by the body in many ways, such as through oxidation to support energy. Intestinal bacteria produce hydrogen as molecular hydrogen by splitting up indigestible hydrocarbons, which are then absorbed into the body (Ross *et*

al., 2014).

Hydrogen, the element with atomic number one, has the lowest atomic mass of all elements in the periodic table. The molecular weight of molecular hydrogen is, for example, only 1/88 of the molecular weight of vitamin C. By comparison, molecular hydrogen is able to pass through all cell membranes, even reaching the mitochondria and the nucleus. The molecule also crosses the blood-brain barrier and the blood-testicle barrier. The ability of molecular hydrogen to move through these cell membranes on the one hand is due to its small size and on the other hand to its neutral charge. Depending on the charge of the cell membrane, polar molecules from the outside are attracted or attached. The charge of the cell membrane has no influence on hydrogen, since it is a non-polar or neutral molecule. Because hydrogen has good tissue distribution properties, it only needs a short time to spread within the body. Hydrogen-dissolved water spreads across the entire body within 10 minutes after drinking (Lim & Kim, 2015).

Hydrogen has a low level of solubility in water as compared to oxygen, which has a much higher rate of solubility, dissolving in water at room temperature at 40 mg/L. Comparatively, the saturation limit of hydrogen is only 1.6 mg/L of water at room temperature (ETB, 2020). In the air of our atmosphere, molecular hydrogen exists at only 0.000055 %, a very small amount.

Nevertheless, hydrogen has been used for many years by humans for inhalation under extreme conditions, such as its application as a gas used in technical diving. In 1988, for example, using the gas mixture "Hydreliox," in which helium (50 %) is added to the hydrogen (49 %) and oxygen (1 %), maximum diving depths of up to 534 m were achieved, resulting in the world record for the deepest diving in free water. In these applications, no harmful effects of hydrogen on health were found, although deep diving is an extreme strain on the human body. It has also been used to prevent decompression sickness and nitrogen narcosis under deep sea diving conditions (Abraini *et al.*, 1994). Another hydrogen-oxygen gas mixture named "Hydrox" is also used for deep diving.

A study by Oshawa *et al.* (2007), considered a medical breakthrough at the time, provided inspiration for the health-promoting properties of hydrogen. Until 2007, there were only about 50 studies on the use of hydrogen in medicine; the number has now risen to more than 1,500. Most of them are research projects from Asia, most notably Japan, South Korea and China (Ichihara *et al.*, 2015), where research work on hydrogen is already well advanced.

In Asia, hydrogen is traditionally widely used as a prophylactic agent. At the beginning of the 20th century, devices were introduced in Japan that produced hydrogen-enriched water, which were well accepted by the general population. Today you can inhale hydrogen for rejuvenation, to reduce wrinkles and for maintaining health in wellness centers there. This development is certainly due to the traditional understanding of medicine in Asia, where prophylactic treatment has a high priority.

Hydrogen and Theories of Aging

Free Radical Theory of Aging

Among the theories of aging is the "**Free Radical Theory of Aging**," a model that explains both aging and the development of chronic diseases in human organisms. It is based upon the assumption that free radicals, or reactive oxygen species (ROS), play an important role in these processes. This concept may be helpful when defining the contribution that oxidative damage plays in the aging process, though it should not be considered in isolation (Gladyshev, 2014).

How ROS as by-products of chemical processes contribute to aging is determined by the metabolic organization of the cell, its protective systems and genotype. These factors have been influenced by natural selection and affect the composition of the cumulative damage. Although ROS are not the sole cause of aging, it is important at this point to consider their effects separately (Gladyshev, 2014).

Free radicals include not only ROS but also nitrogen species that are "searching" for a free electron to stabilize their own energy state. They are very reactive and able to "steal" an electron from other molecular compounds and thereby destabilize cell membranes or other cell components, even DNA. Of course, it should be mentioned that free radicals also act as signaling molecules in special situations and thereby stimulate metabolic processes (Voiekov & Del Giudice, 2009).

In a healthy organism ROS are constantly being generated by oxidative metabolic processes. These energy supplying processes are prerequisites for the life of the human organism in general. They take place in the mitochondria. Free radicals are formed as by-products of these oxidative processes. Harmful ROS are regularly removed by the body's own antioxidants. On the other hand, some ROS are also signal molecules that activate the body's own defense mechanisms and some, such as nitric oxide, are needed for healthy cardiovascular function.

It is only when the body's own redox systems are overloaded by external influences that the elimination of these free radicals no longer can be managed adequately. Such a xenobiotic influence was document in a Europe-wide study which investigated the influence of nine common environmental stressors (chemical agents like benzene, dioxins including furans and dioxin-like PCBs, secondhand smoke, formaldehyde, lead, ozone, particulate matter, radon and one physical agent such as noise) known to cause 3 - 7 % of the annual burden of disease (Hanninen *et al.*, 2014).

In addition, another, purely physical environmental factor affecting health was re-investigated and re-evaluated: the increasing exposure of the population to non-ionizing radiation. This in particular concerns both low- as well high-frequency electromagnetic fields (EMF) and includes exposure to THz-radiation (Alexandrov *et al.*, 2011), radiofrequency (RF) radiation (Lai & Singh, 1997a; Nasim & Kim, 2017), exposure to electric fields (Pethig, 2017), and extremely low frequency (Lai & Singh, 1997b; Wertheimer & Leeper, 1979) as well low-intensity magnetic fields (Barnothy, 1969; ,Ho *et al.*, 1994; Adey, 2004; Medinger, 2005). Therein especially the non-thermal effects and potential long-term effects of low-dose field exposure have been shown to be a major cause of concern (Belyaev *et al.*, 2016).

There is strong evidence that long-term exposure to certain EMFs is a risk factor for diseases, including certain types of cancer (Milham, 2010) and Alzheimer's (Santibáñez *et al.*, 2007). Furthermore, the growing incidence of electromagnetic hypersensitivity (EHS) (Hallberg O, Oberfeld, 2006), has finally been recognized by health authorities. They noted that some patients with EHS suffer from mitochondrial dysfunction (Belyaev *et al.*, 2016; Herbert & Sage, 2013; Pokorný, 2011; Kaplan *et al.*, 2016).

A plausible mechanism may occur at the intracellular level, where the formation of free radicals or oxidative and nitrosative stress develops. It has been shown that "reactive oxygen species (ROS) may be involved in radical pair reactions; thus, radical pairs may be considered as one of the mechanisms of transduction able to initiate EMF-induced oxidative stress" (Belyaev *et al.*, 2016). It has also been said that, "Even small effects on radical concentration could potentially affect multiple biological functions" (IARC, 2013).

If the body's own detoxification and repair functions are disturbed, cellular and extracellular macromolecules will be damaged. First, ROS damage the mitochondria, the "power plants" of the cell. This deprives the cell of its energetic basis. It may subsequently lead to the development of illnesses and premature aging. To a certain extent, the administration of an antioxidant, such as vitamin C, can improve this situation by initiating the necessary redox reaction, but will be oxidized itself. That begs the question: What actually happens to the oxidized antioxidant? That is indeed a pressing issue as the resulting compounds can also damage the DNA. Further chain reactions are necessary until these molecules are rendered harmless.

This is where hydrogen comes into play. In the previously discussed study, the antioxidant properties of hydrogen were mentioned (Oshawa *et al.*, 2007). Therein, it has been postulated that, when an electron is pulled out of the hydrogen for neutralizing a hydroxyl radical (OH·), which is considered the most harmful free radical in the human body, no harmful compounds remain. In fact, in a previous study, successfully treating tumors in mice under a hyperbaric hydrogen-rich atmosphere, it was claimed that no harmful by-products were observed in this process (Dole *et al.*, 1975).

In the previously mentioned study by *Oshawa, Otha et al.* (2007), the remarkable antioxidative effect of hydrogen derives from its ability to act in the direct neutralization of free radicals, such as oxygen radicals (hydroxyl radicals = OH·) and nitrogen radicals (peroxynitrite anions = $ONOO^-$) (Oshawa *et al.*, 2007). The researchers used several methods to prove this, including through an animal model in which they induced local cerebral ischemia (reduced cerebral blood flow). Damage occurs from oxidative stress during reperfusion or reoxygenation of the affected tissues. When the animals inhaled hydrogen gas, there was significant reduction in brain damage that occurred by the reduction of oxidative tissue damage. By the time of its publication, this study was considered a medical breakthrough. To date, many other studies have been performed, many of which used animal models, like mice and rats and, to a lesser extent, rabbits and pigs (Ichihara *et al.*, 2015; Nicolson *et al.*, 2016).

The pleiotropic effects of hydrogen could be explained by its ability to affect the signaling pathways via modulation of the expression/activity of different molecules, gene expression and microRNA, in addition to its proposed direct extinctions of the hydroxyl radical and peroxynitrite.

The transcription factor, Nuclear Factor (erythroid-derived 2)-similar 2, NrF2, is the "main regulator" of cellular antioxidant defense. Nrf2 regulates a wide range of cytoprotective responses and helps to attenuate age-related diseases. This mediator switches genes on and off to ensure that the right genetic information for the synthesis of proteins is available at the right time, in the right place and in the right quantity. Its activity is positively linked to the life potential of the species. It seems that hydrogen indirectly modulates the signal transduction, protein phosphorylation, and gene expression in this process. As a part of this action, it can increase the amounts of antioxidants and antioxidant enzymes inside cells (Brun *et al.*, 2015). It has been found that Nrf2 is upregulated by ingestion of hydrogen-rich water. The researchers found an "increased Nrf2 activation response" (Settineri *et al.*, 2018).

Hydrogen's antioxidant potential may also make it a promising option for the treatment and prophylaxis of EMF-related disorders (Belyaev *et al.*, 2016).

For the explanation of the antioxidative effect of hydrogen, both the direct and the indirect mechanism seem be applicable. Based on the assumption that electrons for

a reduction reaction are generated in the electrolysis process, the direct effect is most likely to be possible if hydrogen is produced via electrolysis. As for the indirect effect at the cellular level, molecular hydrogen, which is delivered from a storage bottle, seems to be appropriate. All these issues require in-depth studies and should be addressed in future research.

Phenotype Expression of Aging

Another theory of aging to mention is the theory of "**Phenotype Expression Aging.**"

Aging is a complex process of progressive decline in the biological function and a change in phenotypic characteristics of an organism. This can lead to an increased likelihood of developing diseases and ultimately to the death of the organism. Many of these traits, such as genome instability, epigenetic alterations, loss of proteostasis (the maintenance of protein homeostasis) and telomere attrition, are associated with changes in gene expression. This means genes can be expressed differently and this determines the type of aging. It has been shown that the expression of up to 75 % of genes can be associated with aging. These modifications can occur by the splicing of the produced mRNA or by an altered regulation of the gene expression (Viñuela *et al.*, 2018).

From the previous section it should be evident by now that genes can also be up- or down-regulated via EMF-exposure. Aging is no exception, yet in particular skin aging seems to respond intriguingly to low-intensity fractal EMF-signals (Madl *et al.*, 2020).

Age-related epigenetic changes can also be reversed, for example, through interventions such as the cyclic expression of Yamanaka reprogramming factors (Kane & Sinclair, 2019). This means that there are factors that can slow down the aging process and consequently prolong life expectancy. Initial investigations have already been undertaken to see if hydrogen could be such a substance, as in a study by Kamimura *et al*, (2016), which examined the effects of drinking hydrogen-rich water on life span.

Moreover, hydrogen has one very special property: it only neutralizes the dangerous free radicals, i.e., it works as a selective antioxidant. It does not interact with the vital oxidation processes of the body or affect vital substances (Oshawa *et al.*, 2007; Ichihara *et al.*, 2015; Nicolson *et al.*, 2016). Another interesting fact is that some immune cells of the human body also use oxidants to defend against pathogens. Special oxidants, such as hydrogen peroxide, are needed for the body's own defense and are important for survival (Oshawa *et al.*, 2007). The first breast milk produced, for example, known as colostrum, contains a high content of hydrogen peroxide (Gartz, 2014).

Because no negative side effects from consuming pure molecular hydrogen have been found and because it is impossible to overdose, the time seems right to prioritize in-depth clinical studies with humans. To quote *Prof. Garth Nicolson*, "it is now time to shift the focus of research to patients with acute or chronic clinical conditions" (Nicolson *et al.*, 2016).

Hydrogen for Health Research

This section contains research work on the medical effects of hydrogen. Some overview studies have been published, including studies involving animal models as well as clinical studies with patients.

A study by *Ichihara et al.* from 2015 summarized the results of 321 studies (Ichihara *et al.*, 2015). Many diseases that were treated with hydrogen through animal models were described in this study. Another review study was published by Nicolson *et al.* (2016), whereby a total of 338 studies on the effects of hydrogen applications

were included. Both overview studies have shown that hydrogen is not only beneficial for the treatment of acute and chronic diseases, but can also improve physical performance, slow the aging process and promote health.

Accordingly, hydrogen has a pronounced antioxidant potential and therefore can act as an anti-apoptotic (preventing cell death), cytoprotective, anti-inflammatory, and anti-allergic agent. Future studies will need to focus on the cellular receptors of hydrogen and investigate the function of hydrogen at the level of the cell membrane, enzyme synthesis, protein biosynthesis, and gene regulation.

Hydrogen also has a positive effect at a reduced perfusion due to its good diffusibility. Studies show hydrogen applications to be safe, cost-effective, easy to perform and thus promising for medical applications.

Beside its stated antioxidative potential, hydrogen is also able to reduce inflammatory mediators in cases of inflammation. These inflammatory mediators include interleukin-6, interleukin-1, tumor necrosis factor alpha, and others that maintain the inflammatory process. According to the studies hydrogen contributes to an elimination of these substances (Ichihara *et al.*, 2015; Nicolson *et al.*, 2016).

Based on the scientific literature available, a bulk of scientific and clinical studies is at hand that justify the use of hydrogen as a primary or supporting component of clinical care. However, further studies will be needed to find the right dose for the various forms of application of hydrogen (gas inhalation, hydrogen-enriched water, infusion).

Studies about Hydrogen Applications for Health

In this next section, a selection of the many studies involving hydrogen applications will be presented.

Circulatory Disorders and Cardiovascular Diseases

If an acute circulatory disorder develops, then damage to the tissues follows. After reperfusion of this area, ROS (hydroxyl radicals) and reactive nitrogen species (peroxynitrites) are released and constitute the primary cause of organ dysfunction. The inflammatory processes that follow that are accompanied by water retention (edema) and other symptoms are known as reperfusion injury. The body can only repair this to a limited extent by itself; the initial state is usually not attainable. Permanent structural damage and functional disorders are the result.

Reperfusion damage of this kind can occur in heart attack, stroke, and acute ischemia in organs such as the liver, kidneys, gastrointestinal tract, and retina, as well as in the extremities. In various animal models, hydrogen administered through inhalation or injection of hydrogen-enriched saline solutions was found to reduce reperfusion damage in all these situations.

During a heart attack, hydrogen treatment was found to significantly reduce the area of damaged heart muscle. On pigs it was observed that the left ventricular function was improved and resulted in a positive effect on the remodeling. Remodeling is a structural change of the entire left ventricle after a prolonged myocardial infarction (Hayashi *et al.*, 2011). The positive effects were explained by expression of antioxidant enzymes in the mitochondria.

In the case of organ transplants, the administration of hydrogen led to a reduced rejection reaction and an increase in the survival rate in animal experiments.

In a clinical trial from 2017, 50 patients with stroke were divided into two groups. One of these groups received a conventional medical therapy and the other received dai-

ly 3% hydrogen inhalations in addition to the conventional treatment. Regular MRI studies have shown a significant reduction in infarct size and a faster normalization of tissue morphology in the hydrogen group. Patients were assessed using the Barthel index, a scoring method comprised of a set of variables used to assess their mobility and their ability to perform activities of daily living. The index showed significantly better results in the hydrogen-treated patients when compared to the control group (Ono *et al.*, 2017).

Further studies performed on animals have shown the following results:

Following cardiopulmonary bypass surgery, there was a better outcome from treatment when using hydrogen (Fujii *et al.*, 2013).

In studies of glaucoma and diabetic retinopathy, the ischemic damage to the retina could be reduced by application of hydrogen-enriched eye drops (Nicolson *et al.*, 2016).

After cardiac arrest, the brain, which is the most oxygen-dependent organ of our body, can be damaged. Studies have shown that this can be diminished by using hydrogen (Nicolson *et al.*, 2016).

The development of pulmonary hypertension has been reduced by using hydrogen (Nicolson *et al.*, 2016).

When hydrogen-enriched water was administered to animals with risk factors for the development of atherosclerosis for six months, the development of this disease was reduced compared to a control group without hydrogen but with the same risk factors (Nicolson *et al.*, 2016).

Recently, a multi-center clinical study known as the "HYBRID II Study" was initiated. This study includes 360 patients who had suffered cardiac arrest and had to be resuscitated. Cardiac resuscitation can lead to varying degrees of brain damage. Researchers are now investigating whether the administration of 2 % hydrogen mixed with 24-50% oxygen via mechanical ventilation has an effect on the survival time and the remaining neurological symptoms in these patients. The first results from this study are expected within a year or two (Tamura *et al.*, 2017).

Lung Diseases

The lung damage caused by ventilation as a complication of artificial respiration was reduced in an animal model by adding hydrogen to the supplied air. Pulmonary edema did not occur as frequently as it does without hydrogen (Huang *et al.*, 2011).

Chronic obstructive pulmonary disease (COPD) is associated with excessive activation of specific inflammatory cells, such as macrophages, T-lymphocytes and fibroblasts in the lung tissue. It is brought on by oxidative stress, which can be triggered by smoking, and is accompanied by chronic inflammation. In animal models, researchers found evidence that the inhalation of hydrogen could be an effective treatment for this disease (Liu *et al*, 2011).

Diseases of the Gastrointestinal Tract

The chronic inflammation that occurs in ulcerative colitis could be diminished by giving hydrogen-enriched water to rats for drinking. Symptoms like diarrhea and weight loss were reduced in a 2013 study (He *et al.*, 2013). Decreases occurred in the liver enzymes, ALT and AST, and there was a general cytoprotective effect provided by a hydrogen supply in this trial (Liu *et al.*, 2010).

Further animal studies have shown that hydrogen can effectively counteract contrast agent-induced kidney damage and damage induced by cytostatics such as Cisplatin. In other animal experiments, the kidney damage caused by arterial hypertension were diminished when hydrogen was adminis-

tered. The same thing was observed following kidney damage caused by rhabdomyolysis (an increased myoglobin content in the blood due to extensive muscle trauma). Injection of hydrogen saline reduced the inflammation from acute pancreatitis in rats in another study (Nicolson *et al.*, 2016).

Brain and Nerve Diseases

Results of animal studies suggest hydrogen may be successfully used to treat Parkinson's disease, Alzheimer's disease, ALS, traumatic nerve injuries, and bipolar disorders (Nicolson *et al.*, 2016). A recently published study has shown cell-protective effects by hydrogen administration in central nervous system diseases caused by oxidative stress. The researchers have found an increase in glutathione synthesis caused by hydrogen-mediated gene expression (Settineri *et al.*, 2018).

A randomized placebo-controlled Asian clinical study conducted in 2013 is worth mentioning. In this study, 48 patients with Parkinson's disease being treated with levodopa were divided into two groups. One group drank one liter of hydrogen-enriched water per day and the other group served as the control group, drinking normal water. After 48 weeks, the researchers found worsening symptoms in the control group, while the symptoms in the hydrogen group improved significantly. The clinical assessment was made by the UPDRS (Unified Parkinson's Disease Rating Scale) score, an indicator used to assess both motor and non-motor symptoms associated with Parkinson's patients (Yoritaka *et al.*, 2013). There is also a YouTube video in which a patient describes rapid improvement of his tremor in both hands following inhalation of BG (EETC, 2015). In a small study, researchers noted improvement of mood and anxiety after study participants drank 600 ml of hydrogen-enriched water per day (Mizuno *et al.*, 2018).

Metabolic Diseases

Reactive oxygen species also play a role in diseases such as *diabetes mellitus*. Damage to mitochondrial function and other inflammatory processes lead to *diabetic sequelae*. Animal experiments have shown that the application of hydrogen-enriched water for drinking reduces oxidative stress in the liver, resulting in reduced fat retention. Dyslipoproteinemy (fat metabolism disorder) could also be positively influenced here: HDL is increased and the LDL fraction is decreased, reducing the risk of development of arteriosclerosis in the future (Nicolson *et al.*, 2016).

Hydrogen water also improved blood sugar levels in studies. In a clinical study involving 30 type 2 diabetes patients, study participants drank one liter of hydrogen-enriched water per day for eight weeks. It was found that biomarkers for oxidative stress, insulin resistance and glucose metabolism were improved. In addition, a significant improvement in the LDL fraction and improvement in insulin production (56 %) was observed in this trial (Kajiyama *et al.*, 2008).

Type 1 diabetes was induced in an animal study. The glucose uptake into muscle cells was improved by stimulating a special glucose transport protein called GLUT-4 by adding hydrogen (Amitani *et al.*, 2013).

Diabetic sequelae, such as diabetic retinopathy, could be influenced positively by hydrogen administration as demonstrated in an animal model (Xiao *et al.*, 2012).

Erectile dysfunction as a complication of diabetes could also be improved by hydrogen. This has been shown in a rat model (Fan *et al.*, 2013).

Other Diseases

It is almost impossible to list all the diseases that have been investigated in studies and shown positive results with hydrogen

therapy. Some of these are discussed in this section.

In the study of Ichihara *et al.* there is a comprehensive table of all diseases in which the effect of hydrogen was investigated (Ichihara *et al.*, 2015).

Animal studies of the antioxidative effects of hydrogen have shown positive results, especially in the case of allergies, atopic dermatitis and asthma (Nicolson *et al.*, 2016; Ignacio *et al.*, 2013).

A study of patients with psoriatic arthritis and skin lesions used hydrogen as hydrogen-enriched water, as gas inhalation or as infusion over a period of four weeks. There was a significant improvement in the symptoms of psoriasis, with the skin symptoms almost disappearing (Ishibashi *et al.*, 2015).

Hydrogen therapy also has found its way into cancer research, focusing mainly on animal models so far. Positive results were found in the treatment of tongue carcinoma, colon carcinoma, liver tumors, thymus lymphoma, leukemia, and others. In studies researchers found that tumor cell growth was suppressed by hydrogen therapy. In addition, hydrogen therapy can reduce the side effects of cytostatic therapies and radiation (Nicolson *et al.*, 2016).

In a study of 49 patients with malignant liver tumors (hepatocellular carcinoma) who also received radiation therapy, the patients who drank 1.5 to 2 L of hydrogen-enriched water daily during a period of seven to eight weeks showed significantly fewer radiotherapy-related side effects, such as loss of appetite and loss of taste, as compared to the control group. The effectiveness of radiotherapy was unchanged in these cases. Researchers attribute the mechanism of action to be the antioxidative property of hydrogen on the hydroxyl radicals formed more often under irradiation. It is important to mention that additional hydrogen therapy did not influence the success of anti-tumor chemotherapy or radiation therapy (Qian *et al.*, 2013).

Hydrogen has also proved to be helpful in autoimmune diseases such as rheumatoid arthritis (RA). There is a clinical study of 20 Japanese patients who consumed 530 mL of hydrogen-enriched water daily for eight weeks. A significant reduction of inflammatory biomarkers such as C-reactive protein (CRP) was found in this trial. Five of the 20 patients had an early manifestation of RA; four of them showed a complete remission of the disease, becoming symptom-free with no further elevation in biomarkers of this disease. Researchers considered the possible mechanism of action to be an anti-inflammatory effect of hydrogen on osteoblasts (Ishibashi *et al.*, 2012).

In another Japanese study, 22 elderly bedridden patients with pressure ulcers were divided into two groups. The patients in one group were given 600 mL of hydrogen-enriched water per day for drinking; the other group was the control group and they did not drink hydrogen-enriched water. A significant reduction in hospitalization time was found in the group treated with hydrogen. The group drinking the hydrogen-enriched water experienced a 94.4 % reduction in pressure ulcer size, which was significant as compared to the control group, which only experienced a 48.6 % improvement (Nicolson *et al.*, 2016).

Hydrogen is also supposed to have an analgesic effect. A rat model has shown that treatment with hydrogen can reduce neuropathic symptoms. It is known that reactive oxygen and nitrogen species are key molecules in the triggering and regulation of pain. The antioxidative potential of hydrogen is the main mechanism of action in this case too. A direct effect on the activation of astrocytes and microglia was also discussed (Chen *et al.*, 2013; Chen *et al.*, 2015).

The Life-Prolonging and Performance-Enhancing Effects of Hydrogen

Japan is known as a nation with a longer life expectancy. Hydrogen already plays a traditional role in the Japanese way of life; for many years, Japanese have bathed in natural water reservoirs containing molecular hydrogen and they drink hydrogen-enriched water. It may not be surprising that hydrogen can support longevity, since it may have anti-inflammatory and antioxidant effects.

The cosmetic industry is using the skin-image-improving effect of hydrogen. The wrinkling of the skin, which occurs during aging, can be reduced by hydrogen. This effect has been examined in a Japanese study in which Japanese women took a daily bath in hydrogen-enriched water (0.2-0.4 ppm H_2) for three months. Within two to five days of starting the study, type 1 collagen synthesis was doubled with an increased fibroblast activity in this group as compared to a control group without hydrogen treatment. Neck wrinkles were significantly reduced at the end of this 90-day bath treatment (Kato *et al.*, 2012).

It is well known that intensive physical activity increases the concentration of reactive oxygen and nitrogen radicals in the skeletal muscles. This can lead to muscular weakness and fatigue, but also muscle damage and inflammation. The effects of hydrogen in situations of physical stress have been studied in rats and in horses. Researchers found there was a reduction in muscular damage, which may be explained by an increased synthesis of antioxidant enzymes such as superoxide dismutase, myeloperoxidase and other substances (Tsubone *et al.*, 2013).

In a study of male professional athletes who had suffered sports accidents to the extremities, study participants received hydrogen-enriched water and hydrogen was also used locally. With these treatments, athletes more quickly returned to normal joint mobility. The researchers also found that the group treated with hydrogen had a reduced plasma viscosity as compared to the control group (Ostojic *et al.*, 2014).

Another investigation showed that the oral uptake of hydrogen-enriched water led to a significantly lower increase in lactate level build-up in muscles after excessive physical activity as compared to a control group without hydrogen. The hydrogen treatment also improved the training-related decline in muscle function. The researchers concluded that hydrogen can increase muscular performance (Aoki *et al.*, 2012).

Technical Requirements for BG Applications

There are some BG devices for health available on the market, which vary according to use and price.

A commonly available device from the U.S. is the *AquaCure,* designed by *George Wiseman/Eagle Research*. With this device, unlike most others, different protocols for BG application are possible.

The produced gas can be used for inhalation as well as application of the gas directly to the skin by using a spot applicator (a flexible funnel placed on the skin). Another way to apply the gas to the skin is to pull a plastic bag over an extremity into which you direct the gas.

One can make BG bubbled water by using a special bubbler that is supplied with the device. It is also possible to make a bath with BG bubbled water. By increasing the amount of gas produced by the machine, it is possible to infuse the water with BG more quickly (Wiseman, 2019c).

When using a water electrolyzer, one needs to pay extra attention to safety standards

that are installed in your device. It should have a low-fill automatic stop function, which is activated when the water level inside the machine has dropped below a certain point. This would happen if you failed to refill distilled water into the machine according to the water level indicator. Low water level is dangerous because of a possible internal explosion. In this case, *AquaCure* turns itself off and prompts an alarm. Furthermore, overpressure protection devices are included. This is useful in case hoses are accidentally kinked by the user during gas production. If not remedied, the expanding gas volume would lead to overpressure in the machine with possible explosive consequences (Wiseman, 2019d).

When using BG, it is advisable to avoid static electrical sparks that may be caused by clothing made of synthetic materials in low humidity environments. It´s better to use fabrics made of natural materials such as cotton, wool and silk. A static spark outside a hose or container containing BG can ignite the gas inside by capacitive reactance. Obviously, one should not handle open flame or lighted cigarettes near BG applications. For your safety you should carefully and conscientiously follow the instructions in the operating manual of the device.

Practical Implementation of BG Applications

It can be assumed that the positive effects of hydrogen described above can be transferred to the application of BG, since two-thirds of BG consists of hydrogen.

Among the kinds of hydrogen applications available, inhalation seems to be the most effective. In an animal study from 2016, the possible applications of hydrogen (inhalation, drinking of hydrogen-enriched water, intravenous administration of hydrogen-enriched saline and its intraperitoneal application) were compared. For practical reasons, only drinking and inhalation are considered here. When comparing these two forms of application, some specific results were obtained. Five minutes after oral ingestion, peak hydrogen concentration occurred in the blood. In comparison, after inhalation, the hydrogen concentration in the blood only reached its peak after 30 minutes, but it was higher than after oral ingestion and remained at this level for about 60 minutes. In addition, after inhalation of hydrogen, a significantly higher concentration was observed in the muscles, followed by the brain. These concentrations were higher as compared to other forms of application. An overdose of hydrogen was not possible because excess hydrogen is exhaled via the lungs (Liu *et al.*, 2014).

For treatment involving **inhalation,** a BG flow that results in 2 % to 4 % hydrogen in the inhaled air is recommended. For a 60 kg person, this would be about 18 L/min.

For beginners of inhalation therapy with BG, it is recommended to initiate carefully; i.e., one should constantly practice self-observation and not inhale the gas any longer than five to ten minutes (using a nasal cannula). After several sessions, the inhalation time can then be gradually increased to 20 -30 minutes according to personal sensation and compatibility. However, one is advised not to engage in continuous BG inhalation for hours. This also has been shown in an animal study examining the effects of hydrogen inhalation in Parkinson's disease. Intermittent inhalation proved to be most effective (Ito *et al.*, 2012). How this finding can be explained has not yet been investigated. It is possible that there is a kind of tolerance or habituation by reduced endogenous enzyme production, as known from drugs or active ingredients, where the effects are reduced by repeated or chronic use over a period of time. It seems to be important to investigate it in dose-response studies. There are anecdotal examples that

show 20 minutes of inhalation two-to-three times a day have achieved good results.

Caution should be used if BG were to be considered for patients with chronic pulmonary disease (COPD). In COPD and other advanced chronic lung diseases, patients mostly have a chronic oxygen deficiency. Normally, the respiratory drive in the human physiology is regulated by an increase in the carbon dioxide partial pressure in the blood. To a lesser extent, a decreasing oxygen partial pressure contributes to the respiratory drive. In patients with lung diseases, there is normally found a permanently increased carbon dioxide content in the blood. When adapted to this state, the respiratory drive can no longer be controlled by an increased carbon dioxide content of the blood, so this is done by decreasing the oxygen content. An uncontrolled oxygen supply leads to an increase in the oxygen partial pressure in the blood and may lead to a lower respiratory drive and consequently to hypoxemia. Patients with these conditions must therefore be careful with external oxygenation. Provided the above-mentioned gas flow is maintained, BG inhalation should not cause any of these problems, as the oxygen content of the inhaled gas mixture is only slightly higher than in normal air. For beginners it is recommend to reduce inhalation times with BG to a few minutes with simultaneous observation of the respiratory drive during inhalation. In addition it is suggested that any extension of the exposure window is supervised by a pulmonologist.

To enrich water with BG **for drinking**, it is only necessary to bubble the gas in the water for a certain time (depends on the gas flow and the amount of water). It is recommended to use deionized water, distilled or spring water for this purpose. BG bubbled water has already been used for **topical applications** (superficial wounds, rashes, age spots, etc.) with good results.

Studies with humans have also been done based on inhalation mixtures with 2-4 % hydrogen (Ichihara *et al.*, 2015; Nicolson *et al.*, 2016; Ono *et al.*, 2017). There is one case report where even 50 % of the breathing volume was replaced by BG under clinical conditions (Chen *et al.*, 2019).

Some studies in humans have also been done using hydrogen-enriched water (Ichihara *et al.*, 2015; Nicolson *et al.*, 2016; Yoritaka *et al.*, 2013).

Development of Chronic Disease

Today most diseases can be considered chronic diseases. It´s interesting to take a look at their development from the perspective of naturopathy.

Today high demands are made on medical therapies in general. The progress achieved in medicine may suggest that "*restitutio ad integrum*" or the complete restoration of organ function, can be achieved through these therapies. In many cases, modern medicine already comes quite close to this and in many other cases it is impossible due to disease progression.

It is, therefore, best to intervene at an early stage in the development of disorders and thus stop or prevent the development of a chronic diseases. In naturopathy there is an interesting model for this development, as explained below.

In the 1940s, the German physician, *H.H. Reckeweg*, developed a system that consists of 6 stages to describe the dynamic development of diseases. This system assumes that the body is brought out of balance by pathogenic influences and can subsequently go through various phases of disease development (DocMedicus, 2020).

If the body is exposed to pathogenic influences and/or physical or psychological stress, it first tries to free itself from toxins via an increased excretion. This stage is called the **excretion phase.** During this stage, you can notice, for example, an in-

creased mucus secretion or urine volume. It´s also possible, that the body sends out intermittent signals as stomach, heart or other pain. If the individual does not react to these signs, the body itself takes over.

The permanent strain from the excretion phase leads to the next stage, or **inflammatory processes.** Examples might include epicondylitis, gastritis or myogelosis. If still nothing is changed, we come to a kind of fixation where the body tries to cope with the disturbances by itself through modifications or deposits.

In this **deposition phase** we might find, for instance, uric acid crystal deposits, which can lead to gout attacks, arteriosclerosis, urinary calculus formation, exostoses in the joints, struma and in other areas of the body. If these changes are occurring in the initial stages of development of disease, all of these changes can still be reversed. Even atherosclerosis is reversible at the beginning stages (!), as demonstrated by studies (Ohsawa *et al.*, 2008).

If nothing changes, this process becomes chronic. *Reckeweg*, the founder of antihomotoxic therapy, who created the 6-phase table of disease development, called this the "biological cut" to point out an incision in the progression of diseases, which means that at this point functional disorders turn into structural changes. The states prior to the biological cut can still be eliminated by stimulating the self-healing capacities of the organism, after which it is usually not possible anymore.

The next stage is the **impregnation phase**, which later can go into a **degeneration phase**. Examples of this can include cartilage loss in arthritis, destruction of tissue structures in liver cirrhosis or lung emphysema, nerve cell degeneration in Alzheimer's disease or Parkinson's disease, and in many other states. Uncontrolled cell division may occur in the **differentiation phase**, which is characteristic for cancer development (DocMedicus, 2020).

Unfortunately, the initial processes involved in the development of chronic disease that occur before reaching the biological cut often cannot be observed by the patient. It is these stages, however, that are probably best managed therapeutically by hydrogen and BG. In the first author's opinion, the greatest success to be achieved when using BG is obtained when a patient finds her/himself within these first three stages of the disease progression, as the stimulation of the self-healing capacity of the body should even make a "*restitutio ad integrum*" possible. This assumption should be examined in more details in future investigations.

Anecdotal Personal Experiences with BG in Different Phases of Diseases

There are a lot of anecdotal case reports on the use of BG for special health problems. An overview of individual case reports and testimonials can be found on *George Wiseman's* website (Wiseman, 2019e).

The first author of this paper personally has gained some anecdotal experiences with the use of BG, both via inhalation and drinking of BG bubbled water, for various health disorders. As these testimonials would never meet the criteria of a study, they will only be mentioned here as empirical examples:

1. Chronic eyelid inflammation (improvement after 3 topical BG applications for 20 minutes each).
2. Depression (improvement in mood after BG inhalation with reduction of anxiety symptoms).
3. Peripheral sensitive polyneuropathy (improvement of symptoms after 3 BG inhalation sessions for 20 minutes each).
4. Multiple sclerosis related neurogenic symptoms of the bladder (reduction in

muscular spasticity after 4 BG inhalation sessions for 20 minutes each).

5. Insomnia (reduction of sleep disturbance after BG inhalation sessions for 20 minutes each).

6. Alleviated weight reduction during a diet by regular drinking of BG bubbled water.

7. Extended sun exposure time without sunburn after inhalation of BG.

Scientific studies of the effects of BG on these health concerns would be desirable, as well as BG's impact depending on the stage of disease development.

BG versus hydrogen

Unfortunately, there are no studies comparing the effects of BG with those of pure molecular hydrogen from a storage reservoir so far. This would be an interesting approach in research.

In Asia, devices are being built that produce hydrogen and oxygen in a two-channel system separately and then these gases are supplied to the patient for inhalation via a Y-shaped-piece. This is not BG, since BG only can be produced in a single line electrolyzer an electrolyzer without a membrane. There are some studies where a "hydrogen-oxygen mixture," containing 67 % hydrogen and 33 % oxygen, was used. It was not specified whether the gas mixture was produced in a single-channel system (BG) or if hydrogen and oxygen were produced separately as described above.

However, the scientific literature on hydrogen might already contain studies in which BG was used instead of purely molecular hydrogen, as it has been described as a gas produced by electrolysis, containing 67 % hydrogen and 33 % oxygen. If BG was used instead, it is remarkable and, at the same time, astonishing that the researchers in these studies were focused mostly only on hydrogen, not knowing that there is a difference between pure hydrogen and BG, as a gas mixture that additionally contains energy-rich "water plasma" and oxygen. It is therefore possible that researchers could draw incorrect conclusions if they believe that the positive results were achieved exclusively by hydrogen.

In 2018, an animal study using an inhalation of an "oxygen-hydrogen mixture" for ovarian cancer was published in which researchers reported an astonishing result. They reported that, "The *in vivo* study demonstrated that 6 weeks of hydrogen inhalation significantly inhibited tumor growth, as evidenced by decreased mean tumor volume (32.30 %) and Ki67 expression (30.00 %)" (Shang *et al.*, 2018).

A case report of a 72-year-old female patient with gallbladder cancer (GBC) was published in 2019. After surgery and subsequent chemotherapy, she developed *in situ* recurrence and liver metastases. The patient had severe anemia, which required blood transfusions every week. The gallbladder tumor invaded the descending part of the duodenum, causing intestinal leakage and hepatic colonic adhesion. The patient refused other treatments and began daily inhalation with a "hydrogen-oxygen-mixture" that represented about 50 % of her respiratory volume (3 L/ min = 180 L/h, 3 to 6 hours per day). After the inhalation therapy and symptomatic treatment such as intravenous nutritional support, the intestinal obstruction was gradually removed. Three months later, metastases in the abdominal cavity gradually decreased, her anemia and hypoalbuminemia were corrected, lymphocyte and tumor marker levels returned to normal levels, and the patient was discharged from the hospital, able to resume her normal life (Chen *et al.*, 2019).

One usually hears about such impressive cases only in the context of so-called "miracle cures." As the authors did not

specify whether they had used BG explicitly, one can only speculate about the miraculous nature. On the other hand, if BG was used intentionally to treat this serious disease, this alone would legitimize a clinical trial in a larger group of patients, in which the effects of BG are compared with separately produced hydrogen-oxygen mixtures. Unfortunately, the studies presented did not provide more detailed information on the technical details of the devices.

In a study made with sanitation workers exposed to air pollution, inhalation of a hydrogen-oxygen mixture (described as $H_2:O_2$ mixture: 66.67 %:33.33 %) reduced airway inflammation and oxidative stress. The researchers attributed this result only to hydrogen and wrote: "Inhalation of hydrogen gas could alleviate airway inflammation and oxidative stress of sanitation workers exposed to air pollution. There was even a significant inhibitory effect on the level of systemic inflammatory response. Importantly, inhalation of hydrogen could improve respiratory symptoms such as cough" (Gong *et al.*, 2016).

In view of current health problems in the world, it is also important to mention that a hydrogen-oxygen-mixture has been successfully used to treat pneumonia in COVID-19 patients in China. *Prof. Nashan Zhong* mentioned this treatment in his lecture about "Perspectives of the management of COVID 19 infection in China," that can be watched on the Internet (timestamp: 34th minute). In his lecture he emphasized the "neutralization of excessive free radicals, the anti-inflammatory and anti-apoptosis effects" and described an "improvement of the respiratory exertion of the patients by hydrogen" (Zhong, 2020).

Treatment with hydrogen-oxygen-mixture is already mentioned in the "Strategies of prevention and management of Coronavirus disease 2019" (Guan *et al.*, 2020). To quote the Chinese National Health Commission, "In light of the significantly decreased airway resistance and safety, inhalation of hydrogen and oxygen mixed gas which is generated through water electrolysis has been applied in clinical practice. Hydrogen/oxygen mixed gas inhalation resulted in a major amelioration of dyspnea in most patients with COVID-19 in a pilot investigation, and has therefore been endorsed by the latest *Recommendation for the Diagnosis and Management of COVID-19* document" (NHC, 2020; LeBaron, 2020).

In a study carried out in 2017 involving hydrogen, researchers wrote that, because most virally induced tissue damage and discomfort are caused by an inflammatory cytokine storm and oxidative stress rather than by virus itself, suppression of the cytokine storm and a reduction of oxidative stress could significantly alleviate the symptoms of influenza and other severe viral infectious diseases. The researchers suspect that hydrogen could be effective in the treatment of multiple organ dysfunction syndromes caused by influenza and other viral infections, making it a promising new protective agent against influenza and other serious viral infections. It could thus be help against the global problems caused by virus pandemics, the researchers stated (Hu *et al.* 2017). The good results achieved so far with hydrogen-oxygen-mixture in the treatment of COVID-19 may be a confirmation of these researchers' findings in case of hydrogen.

The possible underlying mechanisms of hydrogen are explained in detail in a video (LeBaron, 2020; MERCOLA, 2020). One mechanism contributing to its effect is its influence on cytokine production by affecting the transcription factors NFkB, NFAT and STAT1,3. NFkB for instance is involved in cellular responses on stress, cytokines, free radicals, heavy metals, ultraviolet irradiation, oxidized LDL, and bacterial or viral antigens and controls transcription of DNA, cytokine production and cell survival in almost all animal cell types. It remains

to be seen what the results may be from the use of a hydrogen-oxygen-mixture as a treatment in cases of COVID-19 and other diseases in ongoing studies in China.

We do not know whether and to what extent the other components of BG provide a benefit in conjunction with hydrogen, an area that would be interesting to investigate. It only can be speculated to what extent the ExW in BG causes or contributes to positive results. It could be assumed that the provided electrons can be used in the energy metabolism of the body. On the one hand, there may be a positive influence on the electron transport chain (respiratory chain) within the mitochondria and thus an increased ATP production. On the other hand, an improvement in the structuring of cell and tissue water with the help of the supplied energy could be possible, which would have a positive influence on all metabolic processes. Further research on how BG affects the interaction between water molecules and hydrophilic surfaces is awaited and may bring to light exciting insights into how BG works in biological organisms.

It is advantageous that the use of hydrogen has been shown not to interfere with conventional medical therapy (Nicolson *et al.*, 2016). Provided that this also applies to BG, it could be used as a complementary treatment in addition to conventional medicine. It might shorten treatment time in hospitals, which would be of great health and economic benefit.

BG may also have a potential use in emergency medicine. Recent studies suggest negative effects of pure oxygen administration occur, because, as the oxygen partial pressure in the blood increases, more reactive oxygen radicals are released and have a negative influence on the healing process. In cases of myocardial infarction, this leads to reinfarction and rhythm disturbances, higher infarct sizes and increased mortality (Grensemann *et al.*, 2018). In these situations, the additional use of hydrogen with its antioxidant effect could compensate for the negative effects of pure oxygen administration.

Conclusions

A large number of studies show strong evidence for the positive effects of hydrogen for the benefit of health, some of which have been discussed in this article. Human studies are increasingly being conducted for both hydrogen and BG. Negative side effects have not been found according to the current state of research so far. Since BG consists of two-thirds hydrogen, it can be assumed that the positive results found in hydrogen studies also apply to BG.

In addition to being comprised of one-third oxygen, BG contains a special gaseous component (ExW) that is currently being investigated in more detail and to which additional biological effects may possibly be attributed. Further studies will be necessary to access this assumption.

It would also be advisable to initiate studies directly comparing BG and pure hydrogen to have an evaluation of the benefits of both gases. It is also important to clarify the best modality of BG administration and the optimal BG dose for each disease model in specific patient populations through clinical trials.

BG may have practical applications in both hospital and outpatient medicine because of its availability, since it can be made on demand via water electrolysis using appropriate equipment.

When using BG, safety standards must be observed; in particular, for individual inhalation, it is recommended that the inhaled hydrogen content of the gas mixture remains below 4 %. If further clinical studies would show that higher BG quantities are associated with more benefits, a higher

BG content could be used for inhalations under hospital conditions. In this case, strict safety precautions would have to be taken under clinical conditions (similar to the regular use of the relatively dangerous X-rays and gamma rays in hospitals).

Based on the study results mentioned above (Chen *et al.*, 2019; Shang *et al.*, 2018; Gong *et al.*, 2016) and throughout this article and to the first author's own experience, it can be assumed that BG is a safe and promising therapy, provided that the safety precautions are carefully observed.

This fascinating therapeutic agent deserves to be given more attention through clinical research. BG is a safe, inexpensive and versatile gas that should find its way to outpatient clinics and hospitals for use in various medical disciplines as soon as possible.

Disclaimer

There are relatively few broad-based, evidence-based clinical trials specifically for BG. Please be aware that the individual use of BG for health is still experimental; this means that the user must take responsibility for this use as its efficacy and safety for use has not been sufficiently clinically evaluated. The experiences presented in this article are for information only; they are subject to your own judgment and have yet to be proven by further studies. They do not replace medical diagnostics, consultations or conventional medical assessment or evaluation. Neither the author nor the publisher are liable for damages resulting from the use of BG in humans.

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