



## Benefits of H<sub>2</sub> Elite (Molecular Hydrogen Water)

*Especially Beneficial When Used with Hyperbaric Treatment*

Dr. Baker emphatically recommends the use of molecular hydrogen water to ALL of his patients. Particularly those that are recovering from injuries, sickness, or may be pregnant. Studies show the use of molecular hydrogen water has huge potential health benefits. Below is a very brief summary of the potential health benefits of molecular hydrogen water and some research that explains it.

### **Benefits of Molecular Hydrogen Water:**

- Hydrogen acts as an antioxidant preventing organ and cell damage. It will also support and strengthen your natural antioxidant system
- Hydrogen acts as an anti-inflammatory
- Decreases pain (especially in joints)
- Protects your muscles and improves effectiveness of exercise
- Helps speed recovery after exercise
- Promotes better PH Balance in your blood
- Helps to combat diabetes, obesity, and metabolic syndrome
- Protects DNA against radiation damage
- Provides protection against cancer and reduces the side effects of chemotherapy in some patients
- Calms mild allergic reactions
- Improves immune system to fight infections and decrease cancer risks Helps every cell and organ in the body function at a higher level of efficiency. From eyes to kidneys, brain, heart, sex organs, liver, adrenal glands, ears, lungs, bones, joints etc.
- Helps in weight loss and to decrease hunger
- Helps mood disorders
- Helps to heal wounds
- Helps to decrease arthritis in joints
- Helps in brain healing from traumatic injuries and dementia
- Prevents aging skin and tissues
- In pregnancy it can decrease toxemia/pre-eclampsia and improve fetal brain development and decrease autism and cognitive disorders in children

There are no side effects of molecular hydrogen and new research continues to support its huge potential in the body's desire to heal. It assists in this effort down to the mitochondrial, microscopic cellular level and thus improves most everything that is out of balance.

Dr. Baker feels it is one of the most cost effective and beneficial supplements for helping the body stay healthy, young, and vital. Use it daily during pregnancy or anytime during your life that you want to feel healthy and lively.

**How it Works:**

A military grade tablet of magnesium is dropped into a glass of water causing thousands of tiny hydrogen gas bubbles to form and bubble to the surface and gather in the water. As hydrogen gas is inhaled at low concentrations, or swallowed from the gas bubbles in the water, it can have huge health benefits. Drop one tablet in a 6-8oz glass of water and inhale the gas being released from the top of the water to maximize its benefits. Once the tablet has risen to the top of the water and totally dissolved, drink all contents in the glass.

This does not replace the common-sense decisions of proper nutrition, healthy eating, rest, exercise and stress reduction but it will aid you in entering a new level of health and vitality. Life is all about a healthy balance.

**For those interested in a more technical explanation of how hydrogen molecular water aids the body, please read the attached articles:**

# Anti-inflammatory and antitumor action of hydrogen via reactive oxygen species (Review)

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**Abstract.** Hydrogen ( $H_2$ ) has advantages that lead it to be used as a novel antioxidant in preventive and therapeutic applications.  $H_2$  can permeate into biomembranes, cytosol, mitochondria and nuclei, and can be dissolved in water or saline to produce  $H_2$  water or  $H_2$ -rich saline.  $H_2$  selectively reduces oxidants of the detrimental reactive oxygen species (ROS), including hydroxyl radicals ( $\cdot OH$ ) and peroxynitrite ( $ONOO^-$ ), which serve a causative role in the promotion of tumor cell proliferation, invasion and metastasis, but do not disturb metabolic oxidation-reduction reactions in cell signaling. Compared with traditional antioxidants,  $H_2$  is a small molecule that can easily dissipate throughout the body and cells; thus, it may be a safe and effective antioxidant for inflammatory diseases and cancer, since ROS usually initiates tumor progression. Treatment with  $H_2$  may involve correction of the oxidative/anti-oxidative imbalance and suppression of inflammatory mediators. Therefore the present review will discuss the anti-inflammatory and anti-tumorigenic action of  $H_2$  via ROS.

## Contents

1. Introduction
2.  $H_2$  usage method
3. ROS in inflammatory disease and cancer
4. Anti-oxidative characteristic of  $H_2$

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## 1. Introduction

Hydrogen ( $H_2$ ) occurs safely in the air with a concentration of <4.7%, and can be used as an inert gas at body temperature.  $H_2$  selectively quenches detrimental reactive oxygen species (ROS), and it has become a novel anti-oxidant due to its anti-apoptotic, antioxidant, anti-inflammatory and anti-allergy effects (1,2). ROS increase cell migration and enhance tumor invasion and metastasis (3). Antioxidants have been demonstrated to effectively protect against cell damage, and  $H_2$  effectively decreases radicals ( $\cdot OH$ ) and peroxynitrite ( $ONOO^-$ ) in living cells without disrupting the ROS that are involved in normal metabolic oxidation reduction reactions in cell signaling. Therefore,  $H_2$  can be used as an anti-inflammatory and anti-tumorigenic agent in clinical practice. The present review focuses on the association between  $H_2$  and ROS in inflammatory disease and cancer.

## 2. $H_2$ usage method

*Inhalation.*  $H_2$  has capability to penetrate biomembranes and diffuse into the cytosol, mitochondria and nuclei due to its distribution characteristics, including being able to rapidly penetrate vessel walls and being able to dissolve in water or saline (Fig. 1) (4,5). By contrast, the majority of hydrophilic antioxidants cannot penetrate biomembranes and remain on the surface. Inhalation of  $H_2$  or the administration of  $H_2$  water can increase the concentration of  $H_2$  in arterial and venous blood (6).

*Oral administration.* There are several methods to produce  $H_2$  water, including infusing  $H_2$  gas into water up to 0.8 mM (1.6 ppm) under atmospheric pressure or dissolving electrolyzed  $H_2$  into pure water to form  $H_2$  bubbled water.  $H_2$  rapidly penetrates the glass and plastic walls of any vessels, but has a half-time of

0-2 h and almost disappears after 8 h, so aluminum containers with no dead volume are usually used to reserve H<sub>2</sub> gas (7).

*Intravenous drip.* In contrast to H<sub>2</sub> gas, H<sub>2</sub> saturated in saline (HS) is easy to administer by dissolving H<sub>2</sub> in physiological saline for 6 h under 0.4 MPa pressure to a supersaturated level (8). HS can be stored in an aluminum bag under atmospheric pressure at 4°C, with a >0.6 mmol/l concentration of H<sub>2</sub> (8). HS can be infused into the stomachs of rats for experimental and clinical treatments (8,9).

Clinical application of H<sub>2</sub>-enriched glucose-electrolyte solution can be used for acute cerebral infarction and in patients treated with t-PA (9). The solution can be produced at 1.6 ppm H<sub>2</sub> concentrations using H<sub>2</sub> adding equipment. Administration of 500 ml intravenous H<sub>2</sub>-enriched fluid over 30 min for >3 days could relieve the associated symptoms of fever and pain in patients with acute erythematous skin diseases, but does not change physiological parameters in the blood (10).

*External use.* H<sub>2</sub> penetrates the skin easily and is distributed throughout the whole body via the blood in 10 min, as measured by H<sub>2</sub> gas content in expired breath. Submersion in a warm water bath with dissolved H<sub>2</sub> is a method of absorbing H<sub>2</sub> into the body in daily life. Hydrogen-water bathing therapy (hydrogen-water was provided by Shanghai Yiquan Investment Limited Partnership Company, Shanghai, China) has a significant and rapid improvement on disease severity and the quality of life for patients with psoriasis and parapsoriasis en plaques (11). Additionally, H<sub>2</sub>-loaded eye drops can be made by dissolving H<sub>2</sub> in saline and can be directly dropped onto the ocular surface (12,13).

### **3. ROS in inflammatory disease and cancer**

Cancer is a multi-stage process defined by initiation, promotion and progression (14-16), and oxidative stress interacts with all three stages of this process. ROS can increase tumor cell proliferation, survival and cellular migration in animal models and humans by inducing cellular signal transduction pathways (17,18).

*What are ROS?* ROS are formed as a result of an imbalance between free radical and reactive metabolite production, and can potentially exhibit a negative impact on the organism (19). ROS are products of oxygen-derived small molecules involved in normal cellular metabolism, including oxygen radicals such as superoxide anion (O<sub>2</sub><sup>•-</sup>), hydroxyl (·OH), peroxy (RO<sub>2</sub><sup>•</sup>), and alkoxyl (RO<sup>•</sup>), as well as non-radicals, which can be converted to radicals or function as oxidizing agents, including H<sub>2</sub> peroxide (H<sub>2</sub>O<sub>2</sub>), hypochlorous acid (HOCl), ozone (O<sub>3</sub>) and singlet oxygen (<sup>1</sup>O<sub>2</sub>). ROS promote DNA synthesis, cell proliferation, cell survival, cellular migration and invasion, tumor metastasis and angiogenesis (20). Aerobic cells produce ROS, including O<sub>2</sub><sup>•-</sup>, H<sub>2</sub>O<sub>2</sub> and ·OH, in endogenous metabolic reactions (21).

Mitochondria are constantly exposed to high levels of ROS, which cause mitochondrial DNA damage and increase O and ·OH levels in cellular apoptosis (2).

Reactive nitrogen species (RNS) are formed from nitrogen-containing oxidants such as nitric oxide (NO). The mitochondrial respiratory chain can generate RNS under hypoxic conditions, while RNS can further generate other reactive species (22), and continuous cellular ROS and RNS generation is now known to be a consequence of numerous factors, including carcinogen exposure, inflammation and mitochondrial respiration (23).

*ROS initiate tumor progression.* Tumor cells generate ROS more abundantly than normal cells and cause elevated oxidative stress (24). Damage to DNA by ROS is involved in chronic inflammatory diseases and in a wide variety of cancer types, including bladder cancer (25), brain tumors (26), breast cancer (27), cervical cancer (28), gastric cancer (29), liver cancer (30), lung cancer (31), melanoma (32), multiple myeloma (33), leukemia (34), lymphoma (35), oral cancer (36), ovarian cancer (37), pancreatic cancer (38), prostate cancer (39) and sarcoma (40).

ROS can initiate tumorigenicity and subsequent tumor progression by inducing DNA damage (41). Oxidative stress interacts with the initiation, promotion and progression of cancer. During the initiation stage, ROS introduce gene mutations and structural alterations into the DNA and produce DNA damage. In the promotion stage, ROS increase cell proliferation or decrease apoptosis of the initiated cell population by causing abnormal gene expression, blocking cell communication and modifying second-messenger systems. Finally, oxidative stress may add DNA alterations to the initiated cell population and promote cancer progression (42).

*Impact of ROS on cancer by regulation of gene expression.* ROS serve vital roles in stimulating cell signaling pathways in intra- and extracellular environmental conditions (43), regulating gene mutations, and balancing cell proliferation and apoptosis (3,44). Cancer signaling starts from the hypoxic microenvironment of the autocrine and paracrine elements, including vascular endothelial growth factor, hepatocyte growth factor, hypoxia-inducible factor-1α (HIF-1α), NO and H<sub>2</sub>O<sub>2</sub>, which generate a positive feedback loop to hyper-activate the protein kinase B (Akt) locus. Oxidative stress can activate several transcription factors, including nuclear factor (NF)-KB, activator protein 1, p53, HIF-1α, matrix metalloproteinases, peroxisome proliferator-activated receptor-γ, β-catenin/Wnt and nuclear factor erythroid 2-related factor 2 (Nrf2). These effector molecules are activated under prolonged ROS-related chronic inflammation and alter the malignant transformation and the expression of genes involved in immune, inflammatory responses, carcinogenesis and metastasis.

#### 4. Anti-oxidative characteristic of H<sub>2</sub>

It has been demonstrated that a number of factors, including intense exercise, cardiac infarction (45), cessation of blood flow, organ transplantation and inflammation (46), can cause acute oxidative stress. H<sub>2</sub> is able to reduce the risk of life style-related diseases and cancer (7,47-49), and thus can be used to treat various diseases using its characteristic of protecting nuclear DNA and mitochondria.

*H<sub>2</sub> reduces oxidants in ROS.* H<sub>2</sub> dissolved in culture medium selectively reduces the strongest oxidants, such as OH and ONOO<sup>-</sup>, in cell signaling, but does not disturb the cellular levels of ·O<sub>2</sub>, NO· or H<sub>2</sub>O<sub>2</sub>, as well as ROS involved in metabolic oxidation-reduction reactions in cell-free systems (Fig. 2). As ·OH is strong enough to react with H<sub>2</sub>, it can be a marker of the oxidative strength of ROS. It was previously reported that H<sub>2</sub> treatment significantly reduced ·OH produced by radiolysis or photolysis of water and decreased the levels of ·OH in cultured cells, thus protecting the mitochondria from OH (1). Since H<sub>2</sub> penetrates biomembranes and diffuses into organelles, it can decrease cellular levels of ATP synthesized in the mitochondria and nucleus (1). Ren *et al* (50) demonstrated that treatment with 5% H<sub>2</sub>-rich water led to a significant decrease in the level of ROS, maintained the biomass and polar growth morphology of the mycelium, and decreased the secondary metabolism under acetic acid-induced oxidative stress (50). H<sub>2</sub> also decreased the levels of ROS and promoted the chronic ultraviolet exposure-induced expression of phosphoinositide 3-kinase, Akt and Nrf2 in HaCaT cells (51). Since H<sub>2</sub> treatment exhibited anti-oxidant and anti-inflammatory neuroprotective effects, it essentially decreased cyclooxygenase-2 (oxidative stress markers) in immune-positive neurons (52).

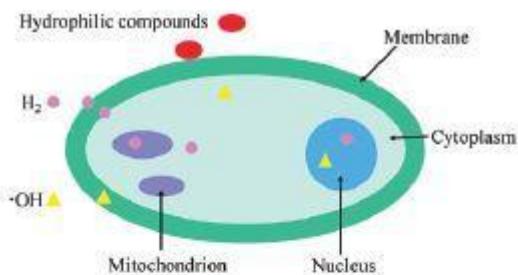


Figure 1. Illustration of H<sub>2</sub> diffusion in a cell. The majority of hydrophilic compounds cannot reach the cytosol and remain at the membranes, but H<sub>2</sub> can rapidly distribute into the cytosol and organelles. H<sub>2</sub>, hydrogen.

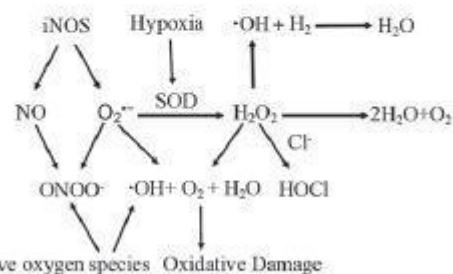


Figure 2. Impact of key oxidants of H<sub>2</sub> in cancer: ·OH and ONOO<sup>-</sup> are highly reactive to damaged cells, while ·O<sub>2</sub>, NO· and H<sub>2</sub>O<sub>2</sub> have physiological roles as signaling molecules. H<sub>2</sub>, hydrogen; OH, hydroxyl radicals; ONOO<sup>-</sup>, peroxynitrite; ·O<sub>2</sub>, superoxide anion; NO, nitric oxide; H<sub>2</sub>O<sub>2</sub>, H<sub>2</sub> peroxide; Cl<sup>-</sup>, chloride; H<sub>2</sub>O, water; iNOS, inducible nitric oxide synthase; SOD, superoxide dismutase.

Table I. Summary of various preventive and therapeutic effects of hydrogen by clinical examinations or by animal experiments.

Category	Disease/condition	Preventive treatment (Refs.)
Metabolic syndrome	Diabetes	Improve the impaired sugar tolerance abilities of obese insulin-resistant type 2 diabetic mice. (47)
Ischemia-reperfusion injuries	Hypertension and dyslipidaemia	Increase the level of antioxidant enzyme SOD and decrease total cholesterol/HDL-cholesterol level. (7)
	Cerebral infarction	Protect brain ischemia and reperfusion injuries against inflammation and oxidative stress. (1)
	Liver cirrhosis	Prevent ROS-induced cell death and inflammation in the liver. (53)
	Myocardial infarction	Reduce infarct size in the rat model of myocardial ischemia-reperfusion injury. (45)
	Organ transplantation	Reduce ischemia-reperfusion injury in the intestinal graft injury. (46)
	Parkinson's disease	Reduce dopaminergic neuronal loss in L-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in Parkinson's disease. (60)
Neuroprotection	Cognitive impairment	Ameliorate cognitive impairment in senescence-accelerated mice. (59)
	Septic appendicitis	Reduce early and late pro-inflammatory cytokine levels in the serum and tissues of appendicitis rats. (57)
	Intestine disease	Reduce ischemia-reperfusion injury in the intestinal graft injury. (61)
	Fibrosarcoma	Inhibit tumor invasion of human fibrosarcoma cells. (48)
	Tongue carcinoma	Inhibit clonal growth of human tongue carcinoma cells. (48)
	Ehrlich ascites tumor	Erase the ROS in Ehrlich ascites tumor types. (49)
Cancer therapy		

SOD, superoxide dismutase; HDL, high-density lipoprotein; ROS, reactive oxygen species.

#### *Anti-inflammatory and antitumor activity of H<sub>2</sub>.*

H<sub>2</sub> anti-inflammatory and anti-allergic features that function via the induction of inflammatory cytokines and the inhibition of cell signal factors. H<sub>2</sub> has been shown to decrease the expression of a number of pro-inflammatory factors, including tumor necrosis factor-α (TNF-α), interleukin (IL)-6, IL-1β, IL-10, IL-12, chemokine ligand 2 (CCL2), intercellular adhesion molecule 1, NF-κB, high mobility group box 1 protein and prostaglandin E2. Furthermore, H<sub>2</sub>-rich saline reduced serum diamine oxidase, TNF-α, IL-1β, IL-6, tissue malondialdehyde, protein carbonyl and myeloperoxidase activity, and also inhibited pro-apoptotic players, including JNK and caspase-3 (53,54).

In a previous study, H<sub>2</sub> gas inhalation significantly reduced the number of total cells, eosinophils and lymphocytes in the bronchial alveolar lavage fluid, and increased the level of IL-4, IL-13, TNF-α and chemokine (C-X-C motif) ligand 15. The IL-4 serum level was significantly decreased following inhalation. H<sub>2</sub> gas inhalation markedly upregulated the activity of superoxide dismutase and significantly attenuated the increased level of malondialdehyde and myeloperoxidase in allergic asthmatic mice (55).

H<sub>2</sub> can function as an anti-tumorigenic agent due to its preventive effect against tumor progression and invasion. Accordingly, neutral pH H<sub>2</sub>-enriched electrolyzed (NHE) water as an anti-oxidant was previously shown to counteract ROS, inhibiting tumor cell proliferation and invasion together with scavenging of intracellular oxidants. NHE water preferentially inhibited clonal growth of human tongue carcinoma cells, inhibited tumor invasion of human fibrosarcoma cells concurrently with intracellular oxidant repression, and scavenged intracellular oxidant H<sub>2</sub> peroxides (48). Additionally, nano-bubble H<sub>2</sub> water with platinum colloid is more attractive as a novel antitumor regimen, as it reduces the side effects in normal tissues; it was reported that decreased cell numbers, cell shrinkage, cell apoptosis, cell deformation and microvilli on the membrane surface were observed in Ehrlich ascites tumors, as H<sub>2</sub> water erased the ROS that were indispensable for cell growth. These antitumor effects were promoted by combination with hyperthermia at 42°C (49) (Table I).

***H<sub>2</sub> treats disease via an antioxidant effect.*** In previous studies, the beneficial effects of treatment with H<sub>2</sub> on organ damage were associated with decreased oxidative product levels, increased antioxidant enzyme activities, and reduced early and late pro-inflammatory cytokine levels in the serum and tissue. Brain damage followed by cerebral ischemia/reperfusion (I/R) injuries generated ROS, while the antioxidant effect of H<sub>2</sub> gas inhalation was able to reduce brain, liver and heart ischemia-reperfusion injury, and intestinal graft injury (1,45,46,56). H<sub>2</sub> protected neurons from ischemia and reperfusion, and was efficacious for cerebral infarction. Furthermore, H<sub>2</sub> gas suppressed the progression of hepatic ischemia and reperfusion injury (1). Inhalation of H<sub>2</sub> gas

significantly lessened the damage to the organs of septic mice with moderate or severe appendicitis by reducing early and late pro-inflammatory cytokine levels in the serum and tissues, thus increasing the survival rate (57).

Ingestion of H<sub>2</sub> water can eliminate ROS and confer antitumor activity (48); it represents a novel method of H<sub>2</sub> administration and has greater advantages over other forms of antioxidant therapy. Consumption of H<sub>2</sub>-enriched water has beneficial effects in clinical practice, including the treatment of atherosclerosis, metabolic syndrome, type 2 diabetes, and cognitive impairment during aging and Parkinson's disease (7,47,58-60).

It was previously reported that HS protected brain ischemia and reperfusion injuries against inflammation and oxidative stress, as well as improving function in a neonatal hypoxia- ischemia rat model (59). HS prevented early pathological changes in acute hepatic injury and was able to prevent ROS-induced cell death and inflammation in the liver by inhibiting the processes of liver cirrhosis and hepatocyte compensatory proliferation (53). Additionally, HS has protective effects on small intestine ischemia/reperfusion injuries (8). These advantages of HS elucidate the clinical potential for preventive and therapeutic anti-oxidative applications (Table I).

*Therapeutic and protective function of H<sub>2</sub> in chemotherapy and radiotherapy.* Radiotherapy and chemotherapy are major treatment types for cancer. H<sub>2</sub> diffuses rapidly to reduce cytotoxic radicals and inflammation in tissues. H<sub>2</sub> gas or H<sub>2</sub> water has been shown to improve the quality of life (QOL) of patients during chemotherapy via its antioxidant properties.

Inhalation of 1% H<sub>2</sub> gas or drinking H<sub>2</sub> water alleviated the nephrotoxicity, mortality and body-weight loss caused by cisplatin. Drinking H<sub>2</sub> water also decreased the level of apoptosis in the kidney. Despite possessing protective effects against cisplatin-induced toxicity, H<sub>2</sub> did not compromise the antitumor effects of cisplatin against cancer cell lines in vitro and in tumor-bearing mice in vivo (4,61).

It was hypothesized that the majority of radiation-induced symptoms associated with increased ROS and inflammation during radiotherapy would significantly affect the patient's QOL (62). The biological reaction to radiation-induced oxidative stress is reduced by the consumption of H<sub>2</sub>-rich water, without antitumor activities being impaired. In one study, consumption of H<sub>2</sub>-rich water for 6 weeks during radiotherapy significantly improved the QOL scores of patients with malignant liver tumors, and the levels of reactive oxygen metabolites in the blood were reduced (63). Overall, H<sub>2</sub> reduces the risk of life style-related oxidative stress by reacting with strong reactive oxygen/nitrogen species in cell-free reactions. It is easily to apply H<sub>2</sub> in cases of oxidative stress, inflammation and tumors. Due to the lack of adverse effects and the high efficacy for the majority of pathogenic statuses involved, H<sub>2</sub> gas, H<sub>2</sub> water and HS are increasingly being accepted as promising candidates for therapeutic approaches. We hypothesize that H<sub>2</sub> gas inhalation and oral administration of H<sub>2</sub> water could protect against inflammation in oxidative stress-related cancer, and thus improve the antitumor effect in the clinical management of cancer.



## Dr. Otto Heinrich Warburg

### Nobel Prize Winner

#### The Root Cause of Cancer



Biochemist Otto Heinrich Warburg, one of the twentieth century's leading cell biologists, discovered that the root cause of cancer is too much acidity in the body, meaning that the pH, potential hydrogen, in the body is below the normal level of 7.365, which constitutes an "acidic" state. Warburg investigated the metabolism of tumors and the respiration of cells and discovered that cancer cells maintain and thrive in a lower pH, as low as 6.0, due to lactic acid production and elevated CO<sub>2</sub>. He firmly believed that there was a direct relationship between pH and oxygen. Higher pH, which is Alkaline, means higher concentration of oxygen molecules, while lower pH, which is acidic, means lower concentrations of oxygen...the same oxygen that is needed to maintain healthy cells.

In 1931 he was awarded the Nobel Prize in Medicine for this important discovery. Dr. Warburg was director of the Kaiser Wilhelm Institute (now Max Planck Institute) for cell physiology at Berlin. He investigated the metabolism of tumors and the respiration of cells, particularly cancer cells. Below are some direct quotes by Dr. Warburg during medical lectures where he was the keynote speaker:

"Cancerous tissues are acidic, whereas healthy tissues are alkaline. Water splits into H+ and OH- ions, if there is an excess of H+, it is acidic; if there is an excess of OH- ions, then it is alkaline."

In his work *The Metabolism of Tumours* Warburg demonstrated that all forms of cancer are characterized by two basic conditions: acidosis and hypoxia (lack of oxygen). "Lack of oxygen and acidosis are two sides of the same coin: where you have one, you have the other."

"All normal cells have an absolute requirement for oxygen, but cancer cells can live without oxygen - a rule without exception."

"Deprive a cell 35% of its oxygen for 48 hours and it may become cancerous."

Dr. Warburg has made it clear that the root cause of cancer is oxygen deficiency, which creates an acidic state in the human body. Dr. Warburg also discovered that cancer cells are anaerobic (do not breathe oxygen) and cannot survive in the presence of high levels of oxygen, as found in an alkaline state.