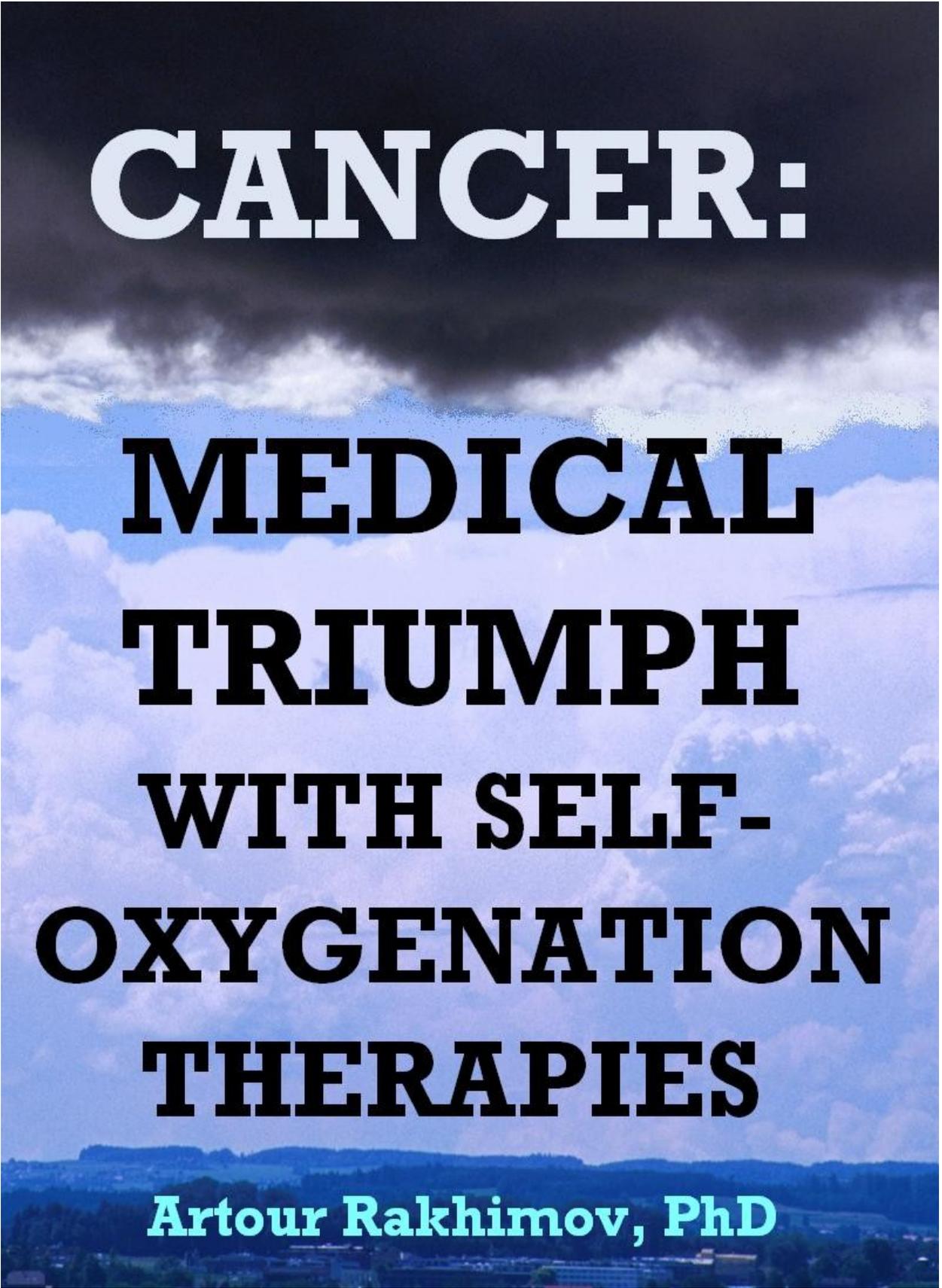


**CANCER:  
MEDICAL  
TRIUMPH  
WITH SELF-  
OXYGENATION  
THERAPIES**

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# ***Cancer: Medical Triumph With Self-Oxygenation Therapies***

*Artour Rakhimov (PhD)*

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## **Introduction**

This book does not claim that all metastasized cancers can be reversed. However, the initial stages of metastasis or spread of malignant cells to neighboring lymph nodes can be successfully addressed with those therapies that increase body oxygenation naturally 24/7. Russian and Ukrainian medical doctors applied their methods on hundreds of people with cancer and even had a published clinical trial on women with metastasized breast cancer. This trial was not an application of totally new techniques and methods for people with metastasized. Their protocol involved the application of additional therapies together with standard medical treatments such as surgery and radiation or chemotherapy. This trial clearly demonstrated the power of natural self-oxygenation methods, as well as dangerously low oxygen content in the participants of this trial before they applied those powerful self-oxygenation techniques. Cancer cannot exist in people with normal body O<sub>2</sub> content.

Oxygen concentrations in cells of the body and within tumors is a known key factor that predicts appearance and aggressiveness of tumors and even chances of survival for last

stages of cancer. There are hundreds of recent medical studies that again and again claim the leading role of tissue hypoxia or low body oxygenation in development of cancer. These researchers and doctors work on a cell level using very sophisticated techniques and methods to measure effects of oxygen deprivation on malignant cells. They openly claim that they have no clue about the causes of tissue hypoxia which is found in every and each person with cancer.

However, the cause of low body oxygenation in people with cancers is their abnormal breathing that has been discovered so far in each tested individual. What should happen if some physiological parameter is about 2 or more times away from the physiological standard? Imagine that one's heart rate or blood pressure twice larger than normal. Should it be a concern for medical community and people who are involved in health care and treatment of diseases? Or assume that some people have some blood parameters that are 2 or more times lower or higher than the norms. Would it be smart to address such deviations?

Oxygen does not appear in cells by itself or due to diffusion. The human respiratory system delivers oxygen to the lungs, then to blood and finally to tissues of the human body. If any transportation system is slightly ineffective, even to a slightest degree (by for example bringing only 1% less oxygen per minute), then after a certain time, the whole body starts to suffer from tissue hypoxia.

Cell hypoxia immediately generates a cascade of abnormal effects. Anaerobic respiration in cells elevates levels of lactic acid in blood, causes increased production of free radicals, promotes existing chronic inflammation, and leads to suppression of the immune system.

## 1. Body oxygen: the key health factor



***"All chronic pain, suffering and diseases are caused from a lack of oxygen at the cell level"***

**Guyton AC, The Textbook of Medical Physiology\*, Fifth Edition**

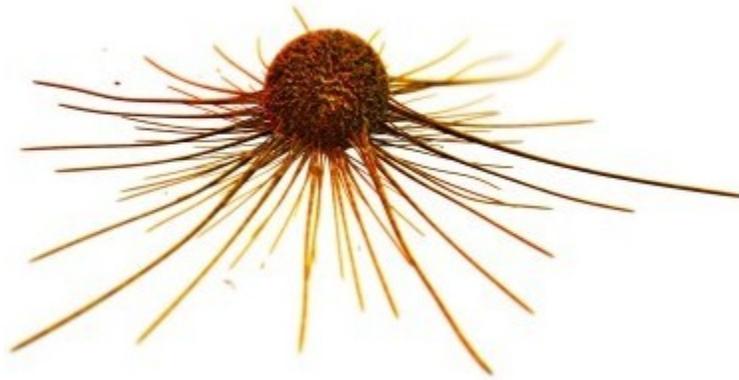
*\* World's most widely used medical textbook of any kind*

*\* World's best-selling physiology book*

Professor Guyton was the Dean of the University of Mississippi Medical School. This Guyton's quote suggests that chronic diseases require low body oxygenation. One cannot

have normal body O<sub>2</sub> concentrations and any chronic degenerative health problem. Let us consider the role of tissue hypoxia in case of cancer.

## 1.1 Low body O<sub>2</sub>: the crucial factor in development of cancer



Nobel Laureate, Dr. Otto Warburg, in his Nobel Prize speech “The Prime Cause and Prevention of Cancer” (1966) stated, *"The prime cause of cancer is the replacement of the respiration of oxygen (oxidation of sugar) in normal body cells by fermentation of sugar... In every case, during the cancer development, the oxygen respiration always falls"*. Dr. Otto Warburg investigated the metabolism of tumors and the types of respiration of cells, particularly malignant cells. In 1931 he was awarded the Nobel Prize in Physiology and Medicine for his discovery of the *"nature and mode of action of the respiratory enzyme"*.

While Dr. Warburg only started the new era in molecular effects or micro causes of cancer (what is going on a cell level), there are numerous modern studies related to cellular causes of cancer. Many alternative therapy people suggest that cancer tumors appear and grow due to too acidic pH within cells of the human body. This acidic environment, as they assert, is created due to environmental influences where abnormal diet with too much animal proteins and too little vegetables and grains plays the crucial role. While this idea of acidic dietary influences has some rational foundation, the real negative effects of excessive protein consumption are very different. We are going to explore this acidic pH idea and effects of diets in more detail later in this book. At the moment, let us focus on recent studies that explain the origins and cause of cancer.

### **First groups of cancer cells can appear only at low body O<sub>2</sub>**

Why do first cancer cells appear? A group of microbiologists from the University of California in San Diego had the following title for their article: *"The hypoxia inducible factor-1 gene is required for embryogenesis and solid tumor formation"* (Ryan et al, 1998). As we can see from this title, tumors do not appear out of nowhere. They require low body oxygenation that is expressed in the hypoxia-inducible factor-1 that is the marker of low body oxygenation and a necessary factor for any first cancer cells to multiply and form a malignant tumor.

### **Cancer cells enjoy tissue hypoxia**

Under normal conditions, even a group of hypoxic cells is going to die or will be easily destroyed by the immune system. What about cells in malignant tumors? Researchers from the Gray Laboratory Cancer Research Trust located in Mount Vernon Hospital, Northwood, Middlesex, the UK concluded, “*Cells undergo a variety of biological responses when placed in hypoxic conditions, including activation of signaling pathways that regulate proliferation, angiogenesis and death. Cancer cells have adapted these pathways, allowing tumors to survive and even grow under hypoxic conditions...*” (Chaplin et al, 1986). These scientists say that cancer tumors like tissue hypoxia.

Here is another quote from a study done in the Yale University School of Medicine (USA). Dr Rockwell studied malignant changes on the cellular level and wrote, “*The physiological effects of hypoxia and the associated micro environmental inadequacies increase mutation rates, select for cells deficient in normal pathways of programmed cell death, and contribute to the development of an increasingly invasive, metastatic phenotype*” (Rockwell, 1997). The title of his publication is “*Oxygen delivery: implications for the biology and therapy of solid tumors*”.

### **Low O<sub>2</sub> is the crucial factor in cancer metastasis**

When the solid tumor is large enough, while the body oxygenation becomes critically low, malignant cells start to invade neighboring lymph nodes and later other organs and tissues. This process is called metastasis. What is the role of low oxygenation in this process?

Dozens of medical and physiological studies confirmed that low O<sub>2</sub> concentrations in tumors and body cells control spread of malignant cells to other organs and tissues. Here is one title that claims, “*Tumor oxygenation predicts for the likelihood of distant metastases in human soft tissue sarcoma*” (Brizel et al, 1996).

German researchers from the the University of Leipzig and University of Rostock concluded, “*...Therefore, tissue hypoxia has been regarded as a central factor for tumor aggressiveness and metastasis*” (Kunz & Ibrahim, 2003).

Canadian doctors from the Ontario Cancer Institute at the Princess Margaret Hospital (University of Toronto) even measured the effects of low body O<sub>2</sub> values in chances of tumors to metastasize. These doctors found, “*In our studies of carcinoma of the cervix, nodal metastases were 1.5 times more likely at diagnosis in patients with more hypoxic tumours relative to those with less hypoxic tumours...*” (Hill et al, 2001)

### **Hypoxia and chances of survival**

“*Clinical evidence shows that tumor hypoxia is an independent prognostic indicator of poor patient outcome. Hypoxic tumors have altered physiologic processes, including increased regions of angiogenesis, increased local invasion, increased distant metastasis and altered apoptotic programs*” (Denko et al, 2003).

### **Low O<sub>2</sub> is a key parameter in treatment resistance**

There are many therapies used by modern oncologists to treat cancers. Apart from radical treatment methods (or different forms of surgeries), there are other methods that include common conservative methods that include radiation therapy and chemotherapy. Obviously, medical professionals are trying to improve efficiency of these methods and

find out causes of their low success rates. Low cell O<sub>2</sub> is one of the main factors that reduces success rates for chemotherapy and radiation therapy.

American scientists from Harvard Medical School noted "... *Hypoxia may thus produce both treatment resistance and a growth advantage*" (Schmaltz et al, 1998).

In their article published in Cancer Letters, Dr. Evans and Dr. Koch observed, "*Low tissue oxygen concentration has been shown to be important in the response of human tumors to radiation therapy, chemotherapy and other treatment modalities. Hypoxia is also known to be a prognostic indicator, as hypoxic human tumors are more biologically aggressive and are more likely to recur locally and metastasize*" (Evans & Koch, 2003).

### **Low O<sub>2</sub> is the central factor in cancer dynamics**

Growth of tumors and progression of any cancer is a dynamic process with changes that can take place within 5-10 minutes in both directions. We are going to provide practical examples related to this dynamic nature of cancer later. At the present moment, let us review relevant conclusions from recent medical and oncological research.

German biologists from the Edinger Institute at the Johann Wolfgang Goethe University in Frankfurt directly claim, "*Thus mounting evidence suggests that the HIF [hypoxia-inducible factor] system plays a decisive role in tumor physiology and progression*" in their study "*A role for hypoxia and hypoxia-inducible transcription factors in tumor physiology*" (Acker & Plate, 2002).

French oncologists from the Institute of Signaling, Developmental Biology and Cancer Research at the University of Nice also reviewed the role of cell hypoxia in cancer dynamics. They wrote, "*Hypoxia is a common characteristic of the microenvironment of solid tumors and, through activation of the hypoxia-inducible factor, is at the center of the growth dynamics of tumor cells*" (Dayan et al, 2008).

There is so much professional evidence about the fast growth of tumors when the condition of hypoxia is present that a large group of Californian researchers recently wrote a paper "*Hypoxia - inducible factor-1 is a positive factor in solid tumor growth*" (Ryan et al, 2000).

Echoing their paper, a British oncologist Dr. Harris from the Weatherhill Institute of Molecular Medicine (Oxford) went further with the manuscript "*Hypoxia - a key regulatory factor in tumor growth*" (Harris, 2002).

### **Conclusions**

As we see from all these quoted studies, all stages of cancer from its birth and up to its death (and/or death of the owner) are tightly linked to O<sub>2</sub> content in tumors and body cells. Note that I put these phrases together since body oxygenation and tumor oxygenation correlate with each other. When tumors grow, its low oxygenation exist on the background of whole body hypoxia that is an equal driving force for cancer development. If body oxygenation improves, due to some smart things that we can do, the tumor O<sub>2</sub> content may not remain unaffected. Indeed, as we reviewed above, appearance of very first groups of cancer cells requires hypoxia that exist in normal (not malignant yet) cells.

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## **1.2 Acidic cellular pH or low body O<sub>2</sub>: what causes what?**

As it was mentioned above, many alternative people believe that cellular pH is the main factor that causes cancer tumors. Indeed, there are numerous studies that found that tumor acidity is a significant factor that prevents success of conservative cancer treatment methods, such as chemotherapy and radiation. Therefore, there are numerous websites and books who promote this idea and even offers treatment protocols to fight cancers. In

this section of the book, we are going to review scientific evidence related to this topic: What is the primary factor in cancer growth: tissue hypoxia or acidic cellular pH?

This question of cancer origins was analyzed in numerous published studies on cancer. A group of American doctors from the Department of Medicine and the Cancer Center at the University of California in La Jolla in their conclusions wrote, "*These results indicate that hypoxia and its accompanying low pH enrich for MMR-deficient cells and that loss of MMR renders human colon carcinoma cells hypersensitive to the ability of hypoxia to induce microsatellite instability and generate highly drug-resistant clones in the surviving population*" (Kondo et al, 2001).

A team of scientists from the Cancer Research Institute at the University of Nice in France devoted their publication to the following topic, "*A dialogue between the hypoxia-inducible factor and the tumor microenvironment*" (Dayan et al, 2008). In their abstract, they wrote, "*Hypoxia is a common characteristic of the microenvironment of solid tumors and, through activation of the hypoxia-inducible factor, is at the center of the growth dynamics of tumor cells. Not only does the microenvironment impact on the hypoxia-inducible factor but this factor impacts on microenvironmental features, such as pH, nutrient availability, metabolism and the extracellular matrix.*" We can see here that the answer is simple. Low cellular O<sub>2</sub> causes abnormal pH changes.

Californian researcher Dr. Payne from the Steenblock Research Institute suggested the exact mechanism how tissue hypoxia causes low intracellular pH. "*Chemo- and radio-resistant cancer cells within solid tumors undermine the effectiveness of these approaches to achieving oncolysis. These resistant cells and clusters of cells typically thrive at low oxygen tensions and are reliant on anaerobic metabolic pathways that churn out lactate. This hypoxic state is one that can be exploited and in this paper a novel method is advanced involving tumor cell infiltration by bifidobacterium species which should bring about prodigious lactate synthesis; concomitant blocking of its enzymatic degradation by urea as well as export (from the cell) by use of quercetin; depletion of ATP using exogenous thyroid; and compromised oxidative catabolism of free fatty acids and amino acids via oral intake of l-hydroxycitrate, melatonin and nontoxic NDGA. This "anaerobic pathway cocktail", it is hypothesized, will bring about a profound reduction in intracellular pH and a compromised state of cellular energetics sufficient to effect oncolysis*" (Payne, 2007).

Italian scientists from Rome were also interested, according to the title of their article in "*Tumor acidity, chemoresistance and proton pump inhibitors*". They wrote, "*An important determinant of tumor acidity is the anaerobic metabolism that allows selection of cells able to survive in an hypoxic-anoxic environment with the generation of lactate*" (De Milito & Fais, 2005). As we see, they also suggest that anaerobic respiration of cells causes acidity in tumors.

British Oxford researchers from the Imperial Cancer Research Fund at the University of Oxford (Institute of Molecular Medicine) pinpointed the key trigger of pathological events leading to advance of cancers. "*Hypoxia, a common consequence of solid tumor growth in breast cancer and other cancers, serves to propagate a cascade of molecular pathways which include angiogenesis, glycolysis, and alterations in microenvironmental pH...*" (Goonewardene et al, 2002).

A study by German oncologists published in the Journal of Molecular Medicine confirmed the same conclusion about the primary driving force of cancers. The researchers wrote, "*The HIF system induces adaptive responses including angiogenesis, glycolysis, and pH regulation which confer increased resistance towards the hostile tumor microenvironment*" (Acker & Plate, 2002).

To my knowledge, there are no studies that suggested or confirmed the leading role of cellular pH in creation of cell hypoxia or in cancer dynamics. There are indeed numerous studies claiming that low pH or acidic environment of tumors is a very potent negative factor that makes acidic tumors very resistant to all types of conservative treatments.

Many alternative people promote an idea that cancer is caused by poor diet with too many acidic foods that makes cells acidic and leads to growth of tumors, the influence of acidic diets (or diets that are based on animal proteins and junk foods). However, these effects are not due to this nearly mechanical hypothetical relationship: you eat more amino acids and less foods with minerals, therefore you get acidic body cells. The negative mechanism due to excessive dietary proteins, especially animal proteins in comparison with vegetables, fruits and other foods that have less amino acids but more minerals and other nutrients, is very different. There is some rationality in having vegetarian diets provided that all required nutrients are provided. Medical research showed that diets based on animal proteins make breathing heavier in comparison with vegetarian diets. Heavy breathing, as we are going to learn later, reduces body and tumor oxygenation.

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## 1.3 Chronic inflammation and cancer

When we consider only appearance of inflamed tissues, we can immediately suspect that these swollen inflamed cells have some features that make them similar to malignant cells. Rudolph Carl Virchow (1821 – 1902) was a famous German doctor, anthropologist, pathologist, and biologist who was probably the first doctor who in 1863 suggested the link between chronic inflammation and cancer. He demonstrated leucocytes in neoplastic tissue. Dr. Virchow is often referred to as "the father of modern pathology" and considered one of the founders of social medicine.

Recent modern oncological studies have also confirmed the link using a more detailed description of events leading to chronic inflammation and appearance of malignant tumors. There are several common key chemicals that are parts of chronic inflammatory and developing malignant processes. Furthermore, many researchers found that having inflammatory health problems increase chances of cancer. Many oncologists suggested that chronic inflammation is even one the key factors causing cancer.

For example, doctors from the The Sidney Kimmel Comprehensive Cancer Center in Baltimore, MD wrote, "*Chronic inflammation is now known to contribute to several forms of human cancer, with an estimated 20% of adult cancers attributable to chronic inflammatory conditions caused by infectious agents, chronic non-infectious inflammatory diseases and/or other environmental factors. Indeed, chronic inflammation is now regarded as an 'enabling characteristic' of human cancer*" (Sfanos & De Marzo, 2012).

Australian scientists from Melbourne (Peter MacCallum Cancer Centre and Department of Oncology at the University of Melbourne) also observed, "*Chronic inflammation is a risk factor for tumor development*" (Chow et al, 2012).

Dr. Morrison provided several common chemicals that explain why chronic inflammation promotes growth of cancers, "... *chronic inflammation and associated reactive free radical overload and some types of bacterial, viral, and parasite infections that cause inflammation were recognized as important risk factors for cancer development and account for one in four of all human cancers worldwide. Even viruses that do not directly cause inflammation can cause cancer when they act in conjunction with proinflammatory cofactors or when they initiate or promote cancer via the same signaling pathways utilized in inflammation. Whatever its origin, inflammation in the tumor microenvironment has many cancer-promoting effects and aids in the proliferation and survival of malignant cells and promotes angiogenesis and metastasis. Mediators of inflammation such as cytokines, free radicals, prostaglandins, and growth factors can induce DNA damage in tumor suppressor genes and post-translational modifications of proteins involved in essential cellular processes including apoptosis, DNA repair, and cell cycle checkpoints that can lead to initiation and progression of cancer*" (Morrison, 2012).

Korean oncologists from the Cancer Research Institute at the Seoul National University devoted their review, according to the title of their recent article to "*Inflammation: gearing the journey to cancer*" (Kundu & Surh, 2008). In their summary, they wrote, "*Many of proinflammatory mediators, especially cytokines, chemokines and prostaglandins, turn on the angiogenic switches mainly controlled by vascular endothelial growth factor, thereby inducing inflammatory angiogenesis and tumor cell-stroma communication. This will end up with tumor angiogenesis, metastasis and invasion. Moreover, cellular microRNAs are emerging as a potential link between inflammation and cancer*".

Another title of the research paper written by researchers from the Department of Molecular and Biomedical Pharmacology at University of Kentucky School of Medicine in Lexington also suggests the same story "*Inflammation: a driving force speeds cancer metastasis*" (Wu & Zhou, 2009).

Drs. Hofseth and Wargovich from the Department of Basic Pharmaceutical Sciences at the South Carolina College of Pharmacy also specified key chemicals that participate in promotion of chronic inflammation and development of cancer. *"At the molecular level, free radicals and aldehydes, produced during chronic inflammation, can induce deleterious gene mutation and posttranslational modifications of key cancer-related proteins. Other products of inflammation, including cytokines, growth factors, and transcription factors such as nuclear factor kappaB, control the expression of cancer genes (e.g., suppressor genes and oncogenes) and key inflammatory enzymes such as inducible nitric oxide synthase and cyclooxygenase-2. These enzymes in turn directly influence reactive oxygen species and eicosanoid levels. The procancerous outcome of chronic inflammation is increased DNA damage, increased DNA synthesis, cellular proliferation, disruption of DNA repair pathways and cellular milieu, inhibition of apoptosis, and promotion of angiogenesis and invasion. Chronic inflammation is also associated with immunosuppression, which is a risk factor for cancer"* (Hofseth & Wargovich, 2007)

There are so many similarities between chronic inflammation and cancer, that many teams of scientists are even trying the same medical drugs and natural extracts or substances to combat both these conditions. This relates to application of:

- andrographolide and its analogues (Lim et al, 2012)
  - curcumin (Schaffer et al, 2011)
  - folic acid that is also known as vitamin B9 (Yang et al, 2012),
  - tocotrienols, the potent isoforms of vitamin E (Nesaretnam & Meganathan, 2011)
  - thymoquinone, an active ingredient isolated from *Nigella sativa* (Woo et al, 2012)
  - unstable naturally derived hepoxilins, metabolites of arachidonic acid (Pace-Asciak, 2011)
  - group of autacoid mediators that are the products of arachidonic acid metabolism include: the prostaglandins, leukotrienes, lipoxins and cytochrome P450 (CYP) derived bioactive products, which are all collectively referred to as eicosanoids (Greene et al, 2011)
  - resveratrol (trans-3,4',5-trihydroxystilbene), a natural polyphenol with antioxidant, anti-inflammatory, and anticancer properties (Tili & Michaille, 2011)
- and some other substances.

While application of these products may have certain beneficial chemical reactions, without removal of the key cause of low body O<sub>2</sub> levels, their overall efficiency will be very low. Note that there are often true stories of people testifying about their magic recovery following use of some special protocols. However, when other people with cancer apply to the same substances using the same dosages, very few of them are able to achieve the same results. The effects of various positive substances and functional foods depends on body oxygen levels that can be easily measured using the body oxygen test described below.

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## 1.4 Inflammatory disorders are also based on low O<sub>2</sub>

As numerous very recent studies claim, chronic inflammatory conditions, on a cell level, are also controlled by tissue hypoxia or low oxygen content in cells. Among the key driving forces of chronic inflammation are pro-inflammatory transcription factors, such as nuclear factor kappa B (NF-kappaB), activator protein (AP)-1 (Safronova & Morita, 2010; Ryan et al, 2009), and *hypoxia-inducible factor 1* (Imtiyaz & Simon, 2010; Sumbayev & Nicholas, 2010), the same substance that is the key factor in cancer (see Part 1.1).



Both effects, chronic inflammation and low oxygen levels in cells, are common in people with many chronic diseases, such as:

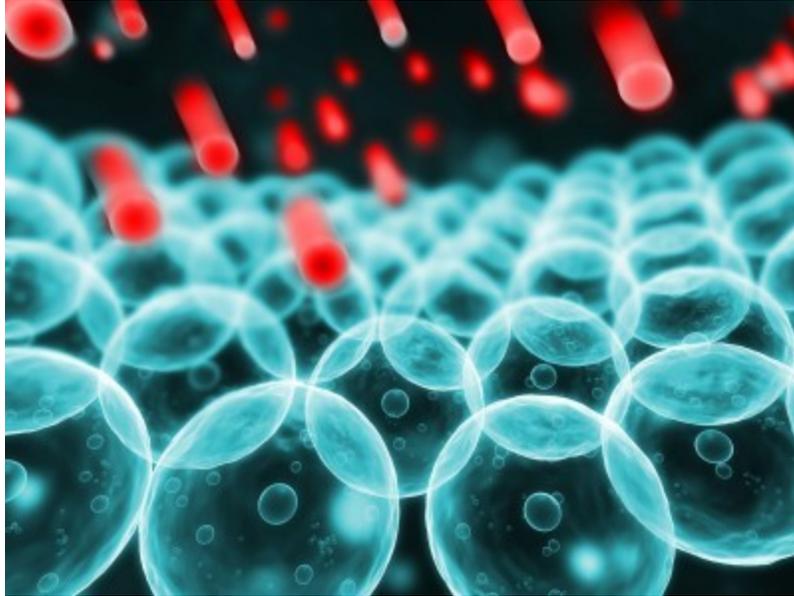
- arthritic conditions
- Alzheimer's disease
- asthma
- autoimmune diseases
- acne
- allergic reactions
- atherosclerosis
- chronic prostatitis
- Crohn's disease
- COPD
- dermatitis
- hepatitis
- hypersensitivities and allergic reactions
- insulin resistance (diabetes)
- irritable bowel syndrome (IBS) of the intestinal tract
- inflammatory bowel diseases (IBD)
- lupus
- nephritis
- obesity
- cachexia
- gastrointestinal ischemia
- osteoarthritis
- pelvic inflammatory disease
- Parkinson's disease
- sarcoidosis
- sleep apnea
- transplant rejection
- and ulcerative colitis.

Symptoms of these chronic diseases include inflammation, possible fatigue due to exhausted cortisol reserves, likely pain, and other symptoms. Several other chronic diseases (including atherosclerosis, and ischemic heart disease) also have their origins in chronic inflammatory processes. The same is true for cancer as we discussed above. There are hundreds of research studies that either mentioned or proved the facts provided above. Some of these studies are listed below.

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## 1.5 Cell hypoxia causes oxidative stress and generation of free radicals



When oxygen supply is restricted, but it is necessary for various bodily processes and reactions to take place in cells and organs (even for a survival of the organism), there are various protective but damaging mechanisms and solutions that maintain these vital functions in various parts of the human body. These adaptations to cell hypoxia are different in various organs of the human body and, in addition, are specific in duration. These were the conclusions of the study titled "*Intermittent hypoxia has organ-specific effects on oxidative stress*" (Jun J, Savransky et al, 2008) and conducted in the Division of Pulmonary and Critical Care Medicine at Johns Hopkins Asthma and Allergy Center in Baltimore, MD, USA. Furthermore, hypoxia-induced chemicals can be generated in some areas and parts of the human body, but cause problems for, for example, the brain and heart.

However, there are common mechanisms related to effects of tissue hypoxia. You have probably heard about antioxidants and free radicals. Free radicals are also called "reactive oxygen species" (those powerful chemicals that can cause damage to hundreds or thousands of other cells due to their inherent destructive power). They create so called "oxygen stress". Maybe you even take supplements that contain such known and popular antioxidants as vitamin C, zinc, vitamin A, selenium and some others. However, it is very likely that you generate free radicals in your body cells due to your ineffective or abnormal breathing.

Why do researchers call it "oxygen stress"? Normal air has only about 20% of oxygen, while the main remaining part is neutral nitrogen that is an inert gas. Pure oxygen (or 100% oxygen), as any respirologist can tell you, is toxic due to its powerful abilities to react with tissues. The damage due to breathing pure oxygen and especially hyperbaric breathing starts in the lungs. Right oxygen is bound with red blood cells (or hemoglobin cells). It is released in tissues and safely transported to required cells and parts of the cell. Obviously, any attempts to consume oxygenated drinks, oxygenated bars, or even breathing hyperoxic air (more than 20% at normal pressure) can be life-saving for critically ill people, but always leads to worse health in a long run.

Let us now consider other well-proven effects of hypoxia related to generation of free radicals. Abnormally low oxygen delivery leads to anaerobic (i.e., without participation of oxygen) cellular respiration, generation of lactic acid and free radicals. There are hundreds of research studies that claim that generation of free radicals is a normal and known outcome of cell hypoxia. (Note that some studies simulated cell hypoxia by reducing oxygen content in the inspired air, but breathing abnormalities present in most people cause exactly the same effect: low body O<sub>2</sub> content.) There are only some references that are provided below. Their titles clearly highlight the role of hypoxia in generation of free radicals.

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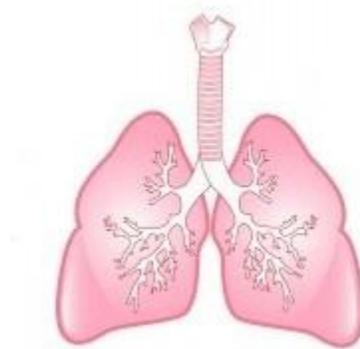
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## **2. Breathing norms vs. breathing in people with cancer**

Each and every person with cancer has ineffective or abnormal breathing pattern that reduces their body oxygenation. We can make this conclusion from all studies that measured automatic breathing patterns in people with cancer, as well as from clinical experience of medical doctors and health practitioners who measured breathing in their patients and clients.

In order to investigate and understand what is wrong with breathing in people with cancers, let us start with analysis of medical norms for breathing at rest, as well as typical respiratory parameters in healthy and ordinary people. Later, we are going to consider those studies that measured various breathing parameters in people with cancer.

### **2.1 Physiological norms for breathing at rest**

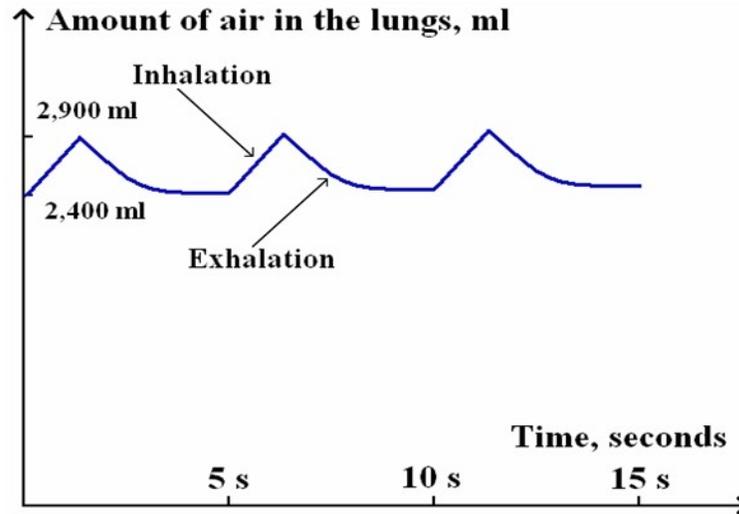


Normal breathing is strictly nasal (in and out), predominantly diaphragmatic (i.e., abdominal), very slow in frequency (see the numbers below) and imperceptible (no feelings or sensation about one's own breathing at rest; see the explanation below). The physiological norm for minute ventilation at rest is 6 liters of air for one minute for a 70 kg man, as numerous physiological textbooks indicate (e.g., Guyton, 1984; Ganong, 1995; and Straub, 1998). These medical textbooks also provide the following parameters

for normal breathing:

- normal breathing frequency is 12 breaths per minute
- normal tidal volume (air volume breathed in during a single breath) is 500 ml
- normal inspiration is about 2 seconds
- normal exhalation is about 3 seconds.

To be more accurate, the normal inhalation is little bit shorter or about 1.5 seconds, while the exhalation is longer or nearly 3.5 seconds. The following graph represents the normal breathing pattern at rest or the dynamic of the air volume in the lungs as a function of time:



If a person with normal breathing is asked about what they feel or their breathing sensations, they will testify that they do not feel their breathing at all (unless their practice yoga breathing or some other breathing exercises). Why is this so? Normal tidal volume is only 500 ml or about 0.6 g of air, which is inhaled during one inspiration. Hence, normal breathing is slow in frequency and very small in amplitude.

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### 3.2 Other parameters of normal breathing

“If a person breath-holds after a normal exhalation, it takes about 40 seconds before breathing commences” (McArdle et al, 2000). This 40 seconds indicate normal oxygenation of tissues. Note that the breath holding test is done after usual exhalation.

The current medical norm for CO<sub>2</sub> content in the alveoli of the lungs and the arterial blood is 40 mm Hg CO<sub>2</sub>. This number was established during the first decade of the 20th century by famous British physiologists Charles G. Douglas and John S. Haldane from Oxford University. Their results were published in 1909 article "*The regulation of normal breathing*" by the Journal of Physiology (Douglas & Haldane, 1909). This corresponds to about 5.3% (at sea level). You do not need to remember all these numbers. They are going to be used only to show that cancer patients never have these norms.

Let me note here that normal CO<sub>2</sub> in the arterial blood is absolutely necessary for normal transport of oxygen to cells. We are going to discuss the reasons later.

Normal breathing is regular, invisible (no chest or belly movements), mainly diaphragmatic, and inaudible (no panting, no wheezing, no sighing, no yawning, no sneezing, no coughing, no deep inhalations or exhalations).

**According to numerous medical textbooks, this very small and slow normal diaphragmatic breathing leads to nearly ideal oxygenation of the arterial blood: about 98-99%.** This conclusion is important for future since many people believe in a myth that deep breathing or breathing more air helps to increase blood oxygenation. In reality, one can breathe 3-5 times more than the norm, but blood oxygenation will not be improved to any essential degree. In fact, since chronic automatic overbreathing leads to chest breathing, while lower parts of the lungs get about 5-6 times more blood due to gravity, **overbreathing usually reduces blood oxygenation.**

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### 3.3 Dr. Buteyko norms for breathing

During the 1960's for nearly the whole decade, Soviet Dr. Konstantin Buteyko (born in Ukraine) was the manager of the respiratory laboratory in Novosibirsk (USSR). Based on his studies of thousands of healthy and sick people in this laboratory, he suggested different norms for breathing (e.g., Buteyko, 1991) that guarantee excellent health and absence of nearly all chronic degenerative diseases cancer included. What are his medical norms? For example, his normal respiratory rate is only 8 breaths/min instead of 12. Here are his numbers for normal breathing:

- normal minute ventilation is 4 l/min;
- normal tidal volume (air volume breathed in during a single breath) is 500 ml;
- normal breathing rate or respiratory frequency is 8 breaths per minute;
- inspiration is about 1.5 seconds;
- exhalation is 2 seconds;
- automatic pause (or period of no breathing after exhalation) is 4 seconds;
- breath holding time (after usual exhalation and without any stress at the end of the test) is 60 seconds;

- CO<sub>2</sub> concentrations in the alveoli or arterial blood is 6.5% or about 46 mm Hg (at sea level).

As we are going to study later, such easy and slow automatic breathing at rest delivers more oxygen to tissues of the human body than the current official medical norm accepted all over the world.

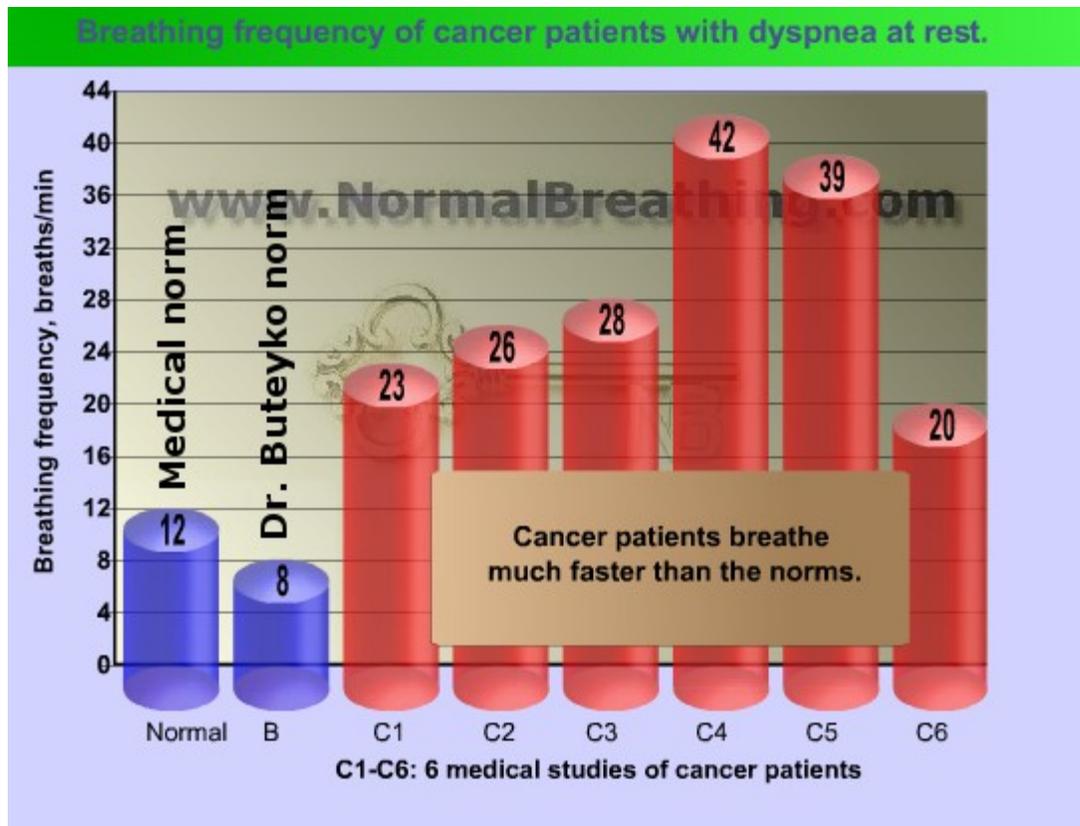
### **3.4 Breathing parameters in people with cancer**

All available medical literature clearly demonstrates that virtually all people with cancer have ineffective or abnormal breathing. In one study conducted by the Division of Respiratory and Critical Care Medicine at the Department of Medicine of the Queen's University in Kingston (Ontario, Canada), researchers measured minute ventilation in people with cancer (Travers et al, 2008). The scientists were actually interested in respiratory differences related to presence of dyspnea that is one of the symptoms in cancer patients. However, minute ventilation in participants of this study was the same regardless the presence of dyspnea. Both cancer groups (40 participants in total) had about 12±2 liters of air per minute at rest, while the medical norm for adults is about 6 liters per minute. All these cancer patients also had elevated breathing frequency of about 19-20 breaths/min instead of normal 12 breaths/min.

Obviously, when one breathes or ventilates much more than the physiological norm, it is called "hyperventilation". It would be logical to expect that their overbreathing caused low CO<sub>2</sub> levels in the airways and the arterial blood.

This Canadian study allows us to calculate the amount of air per one breath in people with cancer. Since the participants had about 12 liters per minute with nearly 20 breaths per minute, we can divide 12 by 20 and get 0.6 liters for one breath or 600 ml of air for their tidal volume. The normal value is 500 ml. Therefore, we see that this group of cancer patients had deep breathing at rest. Their breathing was faster and deeper than the medical norms.

Several other studies measured respiratory frequency at rest in patients with cancer who experienced dyspnea. All the results of these studies are summarized in this graph.



The same results for Rf (respiratory frequency) are provided in this table.

Condition	N.of people	Rf	References
Medical norm	-	<b>12</b>	Medical textbooks
Dr. Buteyko norm	-	<b>8</b>	Buteyko, 1991
Cancer with dyspnea	10	<b>23</b>	Bruera et al, 1993
Cancer with dyspnea	9	<b>26</b>	Mazzocato et al, 1999
Cancer with dyspnea	20	<b>28</b>	Coyne et al, 2002
Cancer with dyspnea	11	<b>42</b>	Clemens et al, 2007
Cancer with dyspnea	14	<b>39</b>	Clemens et al, 2008
Cancer with dyspnea	20	<b>20</b>	Travers et al, 2008
Cancer	20	<b>19</b>	Travers et al, 2008

Note that some of these studies investigated patients with metastasized cancer and terminally sick cancer patients who are often given morphine during last weeks of their lives in order to reduce pain and suffering. Morphine is a powerful respiratory suppressant and can dramatically reduce minute ventilation and Rf. These factors make results for cancer patients different, but in each and every case we observe that they have very fast breathing up to about 2-3 times faster than the official medical norm.

Ukrainian medical doctor Sergey Paschenko measured CO<sub>2</sub> content in the expired air or so called end-tidal CO<sub>2</sub> in 120 women with metastasized breast cancer (Paschenko, 2001). End-tidal CO<sub>2</sub> concentrations are generally very close to the arterial CO<sub>2</sub> concentrations. The average value for end-tidal CO<sub>2</sub> in these cancer patients was about 2.9%, while the official medical norm is about 5.3% that corresponds to 40 mm Hg at sea level.

This study directly confirmed the results of all previous studies: **People with cancer have abnormally low CO<sub>2</sub> levels in their lungs and arterial blood due to too heavy breathing at rest.**

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## 4. Effects of overbreathing (hyperventilation)

We found that people with cancer breathe too much air at rest. Are there any problems with overbreathing? While most people assume that deep breathing or breathing more air is beneficial for health and more O<sub>2</sub> in body cells, hundreds of medical research studies found that hyperventilation causes many adverse reactions and no benefits. First of all, as we discussed above, breathing more air does not increase blood oxygenation in any significant degree. Let us consider other effects of chronic overbreathing (or chronic hyperventilation) on the human organism.

If a healthy person with normal breathing starts to breathe more or deeper than the norms, what are the initial effects? There are following consequences:

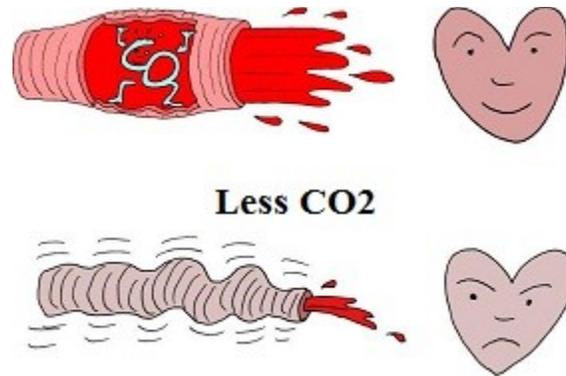
- More CO<sub>2</sub> is removed from the lungs with each breath and therefore the level of CO<sub>2</sub> in the airways and lungs immediately decreases.
- In 1-2 minutes, the CO<sub>2</sub> level falls below the norm in the arterial blood.
- In 3-5 minutes, due to CO<sub>2</sub> diffusion from tissues, most cells of the body (including vital organs and muscles) experience lowered CO<sub>2</sub> concentrations.
- In 15-20 minutes, the CO<sub>2</sub> level in the brain is below the norm due to a slower diffusion rate caused by the blood-brain barrier.

#### **4.1 Vasoconstriction and reduced blood flow are caused by low CO<sub>2</sub> in the arterial blood**

As dozens of independent physiological studies found, hypocapnia (low CO<sub>2</sub> concentration in the arterial blood) decreased blood flow of circulation for the following organs:

- brain (Fortune et al, 1995; Karlsson et al, 1994; Liem et al, 1995; Macey et al, 2007; Santiago & Edelman, 1986; Starling & Evans, 1968; Tsuda et al, 1987)
- heart (Coetzee et al, 1984; Foëx et al, 1979; Karlsson et al, 1994; Okazaki et al, 1991; Okazaki et al, 1992; Wexels et al, 1985)
- liver (Dutton et al, 1976; Fujita et al, 1989; Hughes et al, 1979; Okazaki, 1989)
- kidneys (Karlsson et al, 1994; Okazaki, 1989)
- spleen (Karlsson et al, 1994)
- colon (Gilmour et al, 1980).

What is the physiological mechanism of the reduced blood flow to vital organs? CO<sub>2</sub> is a dilator of blood vessels (arteries and arterioles). Arteries and arterioles have their own tiny smooth muscles that can constrict or dilate (relax) depending on CO<sub>2</sub> concentrations. When we breathe more, CO<sub>2</sub> level in the arterial blood decreases, blood vessels constrict and vital organs (like the brain, heart, kidneys, liver, stomach, spleen, colon, etc.) get less blood supply.



This effect of vasoconstriction is noticeable or detectable even for very small decrease in arterial CO<sub>2</sub>. This because CO<sub>2</sub> is a very potent vasodilator, Some studies claim that CO<sub>2</sub> is a more powerful vasodilator than any chemical drug. For example, medical doctors from the Department of Anesthesia, Armed Forces Hospital, in Riyadh (Saudi Arabia) suggested that "*Carbon dioxide, a most potent cerebral vasodilator...*" (Djurberg et al, 1998).

**Dilation of blood vessels means more O<sub>2</sub>, glucose, and other vital nutrients and chemicals for all organs, cells and tissues of the human body. Breathing more air causes constriction of blood vessels. This slows down delivery of all these key chemicals to all organs and tissues of the body.**

Since all people with cancer are heavy breathers, they naturally have reduced blood flow and reduced oxygen delivery to all vital organs and tissues.

### **Low CO<sub>2</sub> increases pulse**

Numerous studies have found that when cancer advances, it is very common for sufferers to have elevated heart rates or pulse. There are even statistical data claiming that lower hear rates and lower respiratory rates in people with advanced forms of cancer are predictors of their better survival. However, we can show that these two parameters relate to each other. In fact, the respiratory and cardiovascular systems were not divided during first decades of the 20th century. Indeed, the leading physiologists and main medical textbooks were studying the cardiorespiratory system due to the intimate links between these two systems.

How are they linked? While the effects and interactions between them are numerous, there is one main relationship that is based on effects of CO<sub>2</sub> to dilate blood vessels. The state of arteries and arterioles controls the total resistance to the systemic blood flow in the human body. Hence, when the arterial CO<sub>2</sub> is normal or high, the arteries and arterioles are dilated, and it is easy for the heart to push blood for the total circulation. However, low CO<sub>2</sub> or hypocapnia increases total resistance and the strain on the heart. Therefore, breathing patterns directly participate in regulation of the heart rate.

The father of cardiorespiratory physiology, Yale University Professor Yandell Henderson (1873-1944) was the author of first medical textbooks on respiration. He knew about this CO<sub>2</sub> effect on the heart rate. During one of his physiological projects, he performed experiments with anaesthetized dogs on mechanical ventilation. The results were described in his article "*Acapnia and shock. - I. Carbon dioxide as a factor in the*

*regulation of the heart rate". In this 1908 article, published in the American Journal of Physiology, he noticed, "... we were enabled to regulate the heart to any desired rate from 40 or fewer up to 200 or more beats per minute. The method was very simple. It depended on the manipulation of the hand bellows with which artificial respiration was administered... As the pulmonary ventilation increased or diminished the heart rate was correspondingly accelerated or retarded" (p.127, Henderson, 1908).*

Note that the effects of changes in breathing on heart rate, as well as blood pressure, are individual in a short run. However, when there are chronic changes in automatic breathing patterns in the direction of hyperventilation, nearly all people develop higher pulse. Is there any significance in these variables for cancer patients?

Generally, when doctors try to identify the key factors that predict survival of cancer patients, they choose various blood parameters that require special laboratory testing, dyspnea score, presence of edema, delirium, loss of appetite, and some other variables. However, in one study conducted by Spanish researchers, they decided to use those factors that can be easily measured. The title of their study was "*Palliative performance status, heart rate and respiratory rate as predictive factors of survival time in terminally ill cancer patients*" (Sánchez et al, 2006). They tested 98 patients and in the conclusions wrote, "*The median survival was 32 days. In the multivariate analysis, three independent variables were identified: Palliative Performance Score of 50 or under, heart rate of 100/minute or more, and respiratory rate of 24/minute or more. The variables that were found to be prognostic in our study are objective, easy, and quick to measure, and do not require that the professional have special training or experience*".

Therefore, it is logical to expect that if people with cancer slow down their breathing closer or back to the medical norms, they can expect reduced average respiratory frequencies (slower breathing) and decreased heart rates, at the same time. Furthermore, these numbers for the heart rate and breathing frequency are in complete agreement with parameters for the terminally sick people that are provided by the Buteyko Table of Health Zones.

Dr. Buteyko, after analyzing hundreds of sick, severely sick and healthy subjects, suggested 12 health zones and average cardiorespiratory parameters corresponding to each of these health zones. Having heart rate more than 100 beats/min and over 24 breaths/min for the respiratory rate are in complete agreement with the last zone (terminally sick patients) of the Buteyko Table of Health Zones. We are going to consider it below.

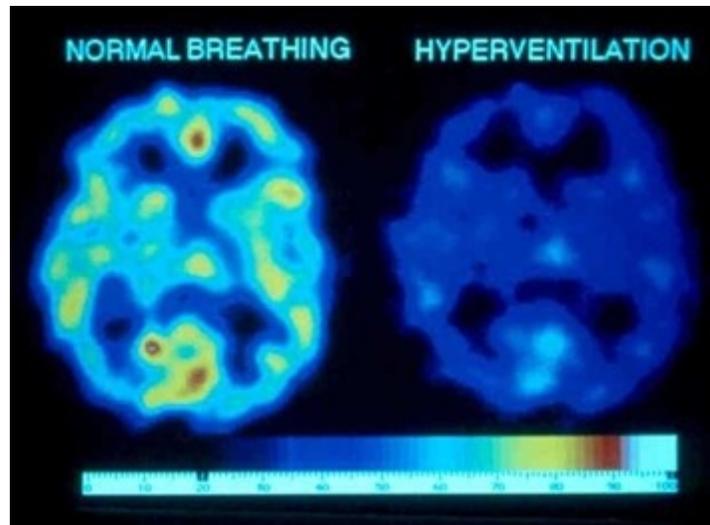
We can now conclude that since both breathing frequency and pulse are factors for survival, easier breathing is something that each every cancer patient needs.

### **Effects of overbreathing on the brain**

Advancing cancer has a profound effect on emotional, mental, and spiritual lives of patients. Depression, anxiety, confusion, insomnia, delirium, and many other problems become more and more common in people with advancing cancer. Can we anticipate all these problems? Yes, if we know that they breathing becomes faster and heavier. If a healthy person starts to hyperventilate or breathe very heavy and fast at rest, what are the

effects on the brain? As a result of voluntary hyperventilation, this person would feel dizzy and could easily faint or pass out in about 2-3 minutes.

What are the causes? Many people believe that this is due to too much oxygen in the brain, but we already know that during very small and slow normal breathing we have nearly ideal oxygenation of the arterial blood. You cannot increase blood oxygenation by taking a deep breath or many deep breaths. This scan below shows brain oxygenation in two conditions: during normal breathing and after 1 minute of voluntary hyperventilation. The red color represents the most O<sub>2</sub>, dark blue the least. Brain oxygenation for overbreathing is reduced by about 40% or nearly 2 times (Litchfield, 2003).



This result is quoted in medical textbooks (e.g., Starling & Evans, 1968) since the effect is well documented and has been confirmed by dozens of professional medical experiments. According to the Handbook of Physiology (Santiago & Edelman, 1986), cerebral blood flow decreases by about 2% for every mm Hg decrease in CO<sub>2</sub> pressure.

Since cancer patients have heavy breathing 24/7, it is sensible that they suffer from reduced brain oxygenation. In addition, there are negative effects of low CO<sub>2</sub> on nerve cells that we are going to discuss below.

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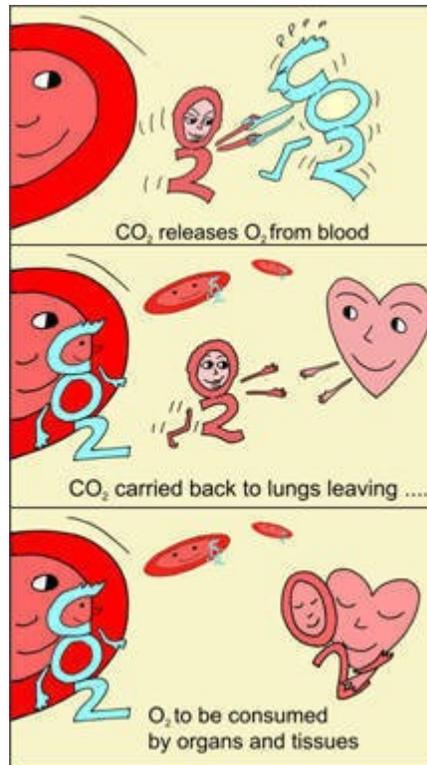
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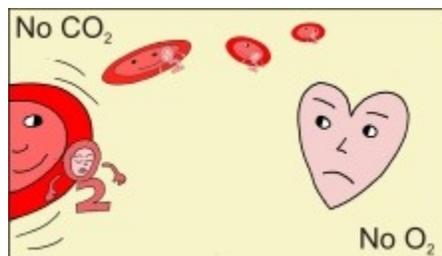
### **3.2 Low CO<sub>2</sub> causes the suppressed Bohr effect**

There is an additional negative effect of low CO<sub>2</sub> on oxygen delivery. Now we know that hypocapnia decreases blood supply to all vital organs. But why do hemoglobin cells or red blood cells release oxygen in the tissues, not in the arteries, or arterioles, or veins? Why is more O<sub>2</sub> released in those tissues of the human body that generate more energy? For example, the heart, due to its constant work, gets more O<sub>2</sub> than those muscles that are at rest. The answer is in the Bohr law (or Bohr effect). The Bohr effect was first described in 1904 by the Danish physiologist Christian Bohr. He was the father of famous physicist Niels Bohr. Christian Bohr discovered that due to higher CO<sub>2</sub> content in tissues and capillaries (more acidic environment than in arteries and arterioles), hemoglobin is bound to oxygen with less affinity. Hence, oxygen is released in tissues due to higher CO<sub>2</sub> levels in those tissues.



There are many modern professional investigations devoted to various aspects of the Bohr effect (e.g., Braumann et al, 1982; Böning et al, 1975; Bucci et al, 1985; Carter et al, 1985; diBella et al, 1986; Dzhagarov et al, 1996; Grant et al, 1982; Grubb et al, 1979; Gersonde et al, 1986; Hlastala & Woodson, 1983; Jensen, 2004; Kister et al, 1988; Kobayashi et al, 1989; Lapennas, 1983; Matthew et al, 1979; Meyer et al, 1978; Tyuma, 1984; Winslow et al, 1985).

Hyperventilation causes reduced CO<sub>2</sub> tissue tension, and this leads to reduced O<sub>2</sub> release and reduced oxygen tension in tissues (Aarnoudse et al, 1981; Monday & Tétreault, 1980; Gottstein et al, 1976). In simple terms, low absolute CO<sub>2</sub> values prevent effective release of oxygen by red blood cells in tissues of the human body. And the blood carries oxygen away from tissues when there are no CO<sub>2</sub>.



In order to improve the release of oxygen by red blood cells in tissues, cancer patients require normal (or even slightly above the norm) arterial CO<sub>2</sub> values.

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- \* Former captain of the ski-O varsity team and member of the cross-country skiing varsity team of the Moscow State University, best student teams of the USSR
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- \* Total distance covered by running, cross country skiing, and swimming: over 100,000 km or over 2.5 loops around the Earth
- \* Author of the publication which won Russian National 1998 Contest of scientific and methodological sport papers
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  - “[Cancer: Medical Triumph with Self-Oxygenation Therapies](#)” 2012 - Amazon Kindle book; ASIN: B0071ZZ4AQ
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