Cystic Fibrosis: Defeated With Natural Self-Oxygenation Methods

Discover the most effective and successful natural methods that increase body O2 content, defeat major symptoms of cystic fibrosis, and guarantee excellent health

Artour Rakhimov (PhD)

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Preface

In this groundbreaking book on cystic fibrosis, Dr. Artour Rakhimov analyzes dozens of western medical research studies related to causes of cystic fibrosis, effects of low body oxygen content on the human body, breathing parameters in people with cystic fibrosis, oxygen transport in people with cystic fibrosis, and successful clinical experience of Soviet and Russian medical doctors in dealing with cystic fibrosis.

Dr. Artour Rakhimov provides a blueprint and his own fascinating experience related to successful elimination of major symptoms of cystic fibrosis in his students using natural self-oxygenation methods based on breathing normalization or breathing in accordance with medical norms.

This medical program is largely developed by Russian and Soviet Buteyko breathing doctors, and it is based on a simple DIY body oxygen test. The suggested therapies address all those lifestyle factors that influence body oxygenation and suggest breathing exercises that increase body oxygenation.

Introduction: hypoxia, cystic fibrosis, and chronic diseases

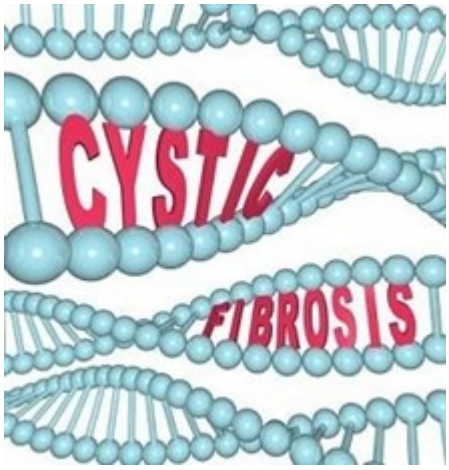
*"**All chronic pain, suffering and diseases are caused from a lack of oxygen at the cell level."***

*Professor AC Guyton, MD, Textbook of Medical Physiology**

* World's most widely used medical textbook of any kind * World's best-selling physiology book

With the advance of any chronic disease, cystic fibrosis included, oxygen content in body and brain cells progressively decreases. Sometimes low cellular oxygen content is the proven driving force of major symptoms and features of diseases (e.g., as in cases of cancer, asthma, bronchitis, and heart disease). For other conditions, tissue hypoxia or low body O2 is an acknowledged accompanying factor. Indeed, for advanced stages of many chronic diseases, cell oxygenation becomes so low that providing pure oxygen is a common mainstream medical treatment to prolong one's life. CF (cystic fibrosis) is no exception.

1. Hypoxia controls cystic fibrosis transmembrane conductance regulator (CFTR)



As we learned above, hyperventilation and resultant cell hypoxia are normal in people with CF. Tissue hypoxia leads to overexpression of hypoxia inducible factor-1 (HIF-1), an oxygen-sensitive transcriptional activator, which plays a crucial role in cellular adaptation to reduced oxygen availability. Microbiological studies suggest that HIF-1 (representing oxygen availability) controls the expression of cystic fibrosis transmembrane conductance regulator (CFTR). This conclusion was found in the following articles.

American scientists from the Department of Medicine at the University of Alabama (Birmingham) tested the effects of cell oxygenation on CFTR in vitro. The title of their article in the *American Journal of Physiology and Cell Physiology*, states that *Improved oxygenation promotes CFTR maturation and trafficking in MDCK monolayers* (Bebök et al, 2001). In their abstract, the researchers wrote, "*Together, our data indicate that improved cellular oxygenation can increase endogenous CFTR maturation and/or trafficking*".

Another group of US scientists from Alabama (Department of Genetics, Fleming James Cystic Fibrosis Research Center, University of Alabama at Birmingham) was concerned about the *Role of oxygen availability in CFTR expression and function* (Guimbellot et al, 2008). Their abstract suggests, "*... In the present study, we investigated regulation of CFTR mRNA during oxygen restriction, examined effects of hypoxic signaling on chloride transport across cell monolayers, and related these findings to a possible role in the pathogenesis of chronic hypoxic lung disease. CFTR mRNA, protein, and function were robustly and reversibly altered in human cells in relation to hypoxia. In mice subjected to low oxygen in vivo, CFTR mRNA expression in airways, gastrointestinal tissues, and liver was repressed. CFTR mRNA expression was also diminished in pulmonary tissues taken from hypoxemic subjects at the time of lung transplantation. Environmental factors that induce hypoxic signaling regulate CFTR mRNA and epithelial Cl(-) transport in vitro and in vivo.*"

One year later, in 2009, German scientists from the Hanover Medical High School also supported the idea that *Hypoxia inducible factor-1 (HIF-1)-mediated repression of cystic fibrosis transmembrane conductance regulator (CFTR) in the intestinal epithelium* (Zheng et al, 2009). They wrote, " *... Consequently, HIF-1 overexpressing cells exhibited significantly reduced transport capacity in colorimetric Cl(-) efflux studies, altered short circuit measurements, and changes in transepithelial fluid movement. Whole-body hypoxia in wild-type mice resulted in significantly reduced small intestinal fluid and HCO(3)(-) secretory responses to forskolin. Experiments performed in Cftr(-/-) and Nkcc1(-/-) mice underlined the role of altered CFTR expression for these functional changes, and work in conditional HIF-1 mutant mice verified HIF-1-dependent CFTR regulation in vivo. In summary, our study clarifies CFTR regulation and introduces the concept of a HIF-1-orchestrated response designed to regulate ion and fluid movement across hypoxic intestinal epithelia*".

Therefore, we can now state that reduced oxygen availability in body cells plays the central role in abnormal work of the CFTR protein that causes formation of salty viscous mucus (due to abnormal transport of chloride and sodium ions and water caused by the CFTR mutation protein). This leads to the development and pathogenesis of CF, where dysfunctional mucus harbors pathogens and promotes respiratory infections and pathological gastrointestinal flora.

Conclusions. Abnormal work of ionic pumps that took place in people with developing cystic fibrosis can take place only due to low oxygen levels in tissues. While all people experience more problems with these tiny pumps to transport sodium, chloride and other ions, people with cystic fibrosis have an additional genetic component that worsens transfer of ions across the epithelial layers in the lungs and GI tract.

In short, if you have reduced body O2 and the CFTR gene, you will develop cystic fibrosis since pumping ions requires normal cell oxygenation. If your body O2 stores are normal or high, you will not suffer from effects of the defective cystic fibrosis gene.

Now let us focus on the causes of reduced oxygen levels in people with CF.

2. Oxygen Transport in Cystic Fibrosis

Oxygen is delivered to body cells via breathing. Hence, we have to analyze the respiratory parameters and breathing patterns in people with CF. What is wrong with breathing in people with cystic fibrosis?

2.1 Minute ventilation in cystic fibrosis patients at rest

This Table summarizes the results of 14 studies performed on healthy subjects and 8 studies related to minute ventilation in cystic fibrosis.

Condition	Minute ventilation	Number of patients	References
Normal breathing	6 L/min	-	Medical textbooks
Healthy subjects	6-7 L/min	>400	Normal Minute Ventilation
Cystic fibrosis	15 L/min	15	Fauroux et a, 2006
Cystic fibrosis*	13 (±2) L/min	10	Bell et al, 1996
Cystic fibrosis	10 L/min	11	Browning et al, 1990
Cystic fibrosis	11-14 L/min	6	Tepper et al, 1983
Cystic fibrosis*	10 L/min	10	Ward et al, 1999
CF and diabetes*	10 L/min	7	Ward et al, 1999
Cystic fibrosis	16 L/min	7	Dodd et al, 2006
Cystic fibrosis	18 L/min	9	McKone et al, 2005

** Some studies indicated the abnormal average weight of their subjects. As a result, minute ventilation for 2 studies (Bell et al, 1996) and (Ward et al, 1999) was adjusted to normal weight (70 kg).*

Available medical research suggests that a typical person with mild CF breathes at rest from about 10 to 18 liters of air per minute instead of 6 L/min (the medical norm). Therefore, they suffer from chronic hyperventilation (or breathing more than the medical norm). Note that numerous studies have found that modern healthy people have light and easy breathing at rest, with only about 6-7 L/min for their minute ventilation.

2.2 Breathing frequency in cystic fibrosis

Furthermore, many medical professionals have noticed that breathing frequency or respiratory rate is abnormally high in cystic fibrosis. This is reflected in the title of the publication by American doctors from the Department of Medicine of the University of Texas Health Science Center in Houston, Texas in the Chest magazine *Importance of respiratory rate as an indicator of respiratory dysfunction in patients with cystic fibrosis*. The title suggests respiratory frequency in cystic fibrosis correlates with the degree of pathological changes in the lungs. (Note that up to 80% of people with CF die due to respiratory failure.)

Even infants with CF have higher respiratory frequency in comparison with matched healthy infants. While comparing 95 healthy infants with 47 infants with CF of similar age (39-40 weeks gestational age), sex, ethnicity and proportion exposed to maternal smoking, it was found that CF infants had a significantly greater respiratory rate (almost 6 more breaths per minute) and elevated minute ventilation as well: 424 ml/kg for infants with CF and 313 ml/kg for healthy infants (Ranganathan et al, 2003).

These measurements suggest that abnormal respiratory parameters, related to chronic hyperventilation with elevated respiratory frequency, appear in people with the CF gene at an early age. Clinical observations also reveal that increased breathing frequency contributes to increased rib cage - abdominal muscular discoordination (upper chest breathing), as is common in CF (see references below).

Chronic hyperventilation found in CF occurs because of increased respiratory frequency and tidal volume. In other words, people with CF breathe faster and deeper than the medical norms. Since metabolic rate and CO2 production rates are relatively fixed parameters, there is one immediate effect of alveolar hyperventilation in people with CF: alveolar hypocapnia or low levels of CO2 in the airways and lungs.

3. Effects of chronic hyperventilation on oxygen transport

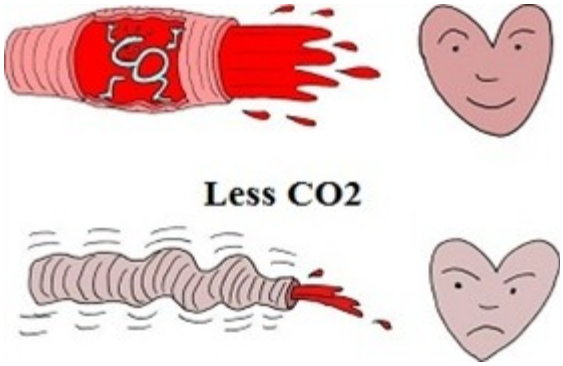
Let us consider the range of immediate and long-term effects caused by chronic hyperventilation in an otherwise healthy person who has previously had normal breathing parameters.

Chronic hyperventilation (overbreathing) suppresses the oxygen content in cells. There are two different mechanisms of suppression that depend on the transport of oxygen in the lungs or ventilation-perfusion ratio.

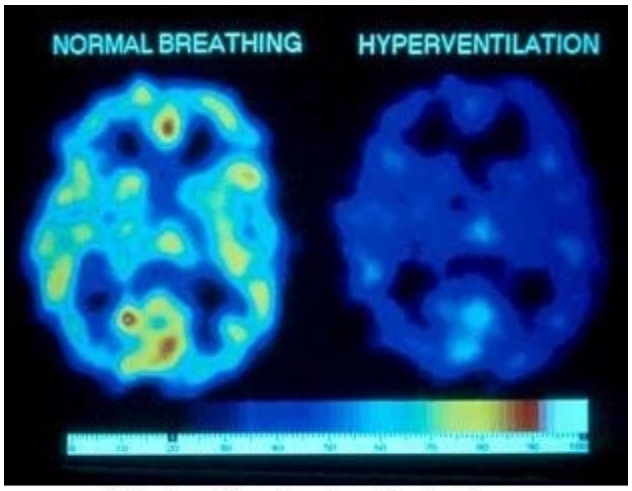
3.1 Hyperventilation with normal lungs

The most common mechanism of reduced oxygen delivery occurs when there are no problems with the lungs, as in typical cases of heart disease, cancer, diabetes, and light forms of CF. In this case (normal lungs), hyperventilation leads to arterial hypocapnia (reduced CO2), which results in two effects:

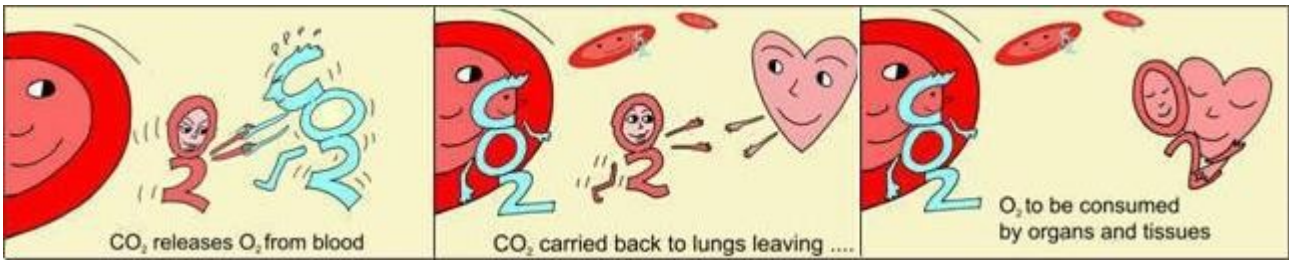
A. **Heavy breathing and low CO2 leads to vasoconstriction** or spasm of smooth muscles in arteries and arterioles that causes reduced blood flow or perfusion of all vital organs.



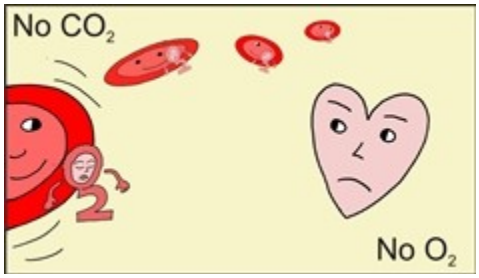
There are numerous studies that proved this effect on:- brain (Fortune et al, 1995; Karlsson et al, 1994; Liem et al, 1995; Macey et al, 2007; Santiago & Edelman, 1986; Starling & Evans, 1968; Tsuda et al, 1987)- heart (Coetzee et al, 1984; Foëx et al, 1979; Karlsson et al, 1994; Okazaki et al, 1991; 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).



Effects of 1 minute of voluntary hyperventilation on brain oxygen levels (vasoconstriction due to lack of CO2)



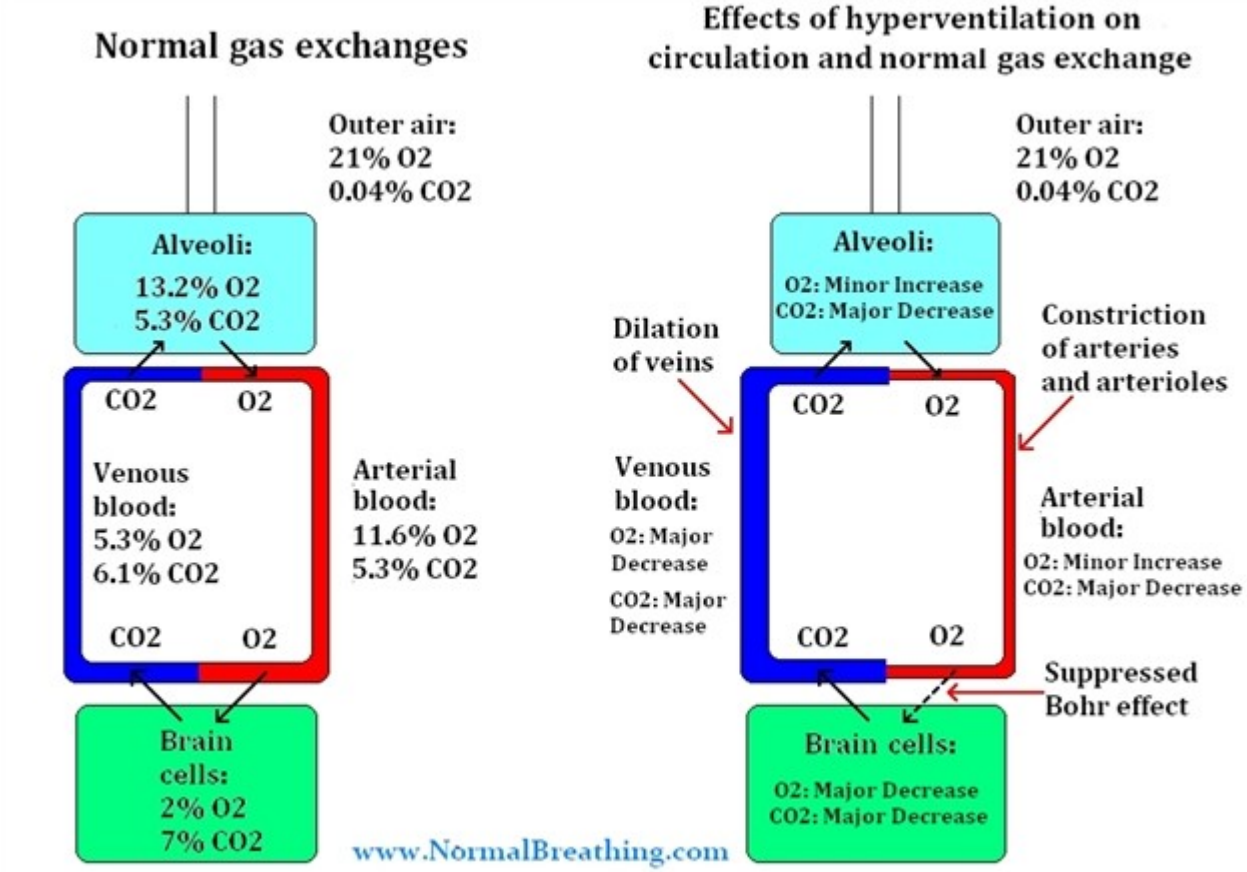
B. The suppressed Bohr effect - low CO2 causes the increased affinity between hemoglobin and oxygen molecules that hampers release of oxygen in tissues (Carter & Grønlund, 1983; diBella et al, 1996; Dzhagarov & Kruk, 1996; Grant, 1982; Jensen, 2004; Kister et al, 1998; Lapennas, 1983; Tyuma, 1984).



These two effects are independent from each other, but both reduce oxygen transport to cells. As a result, it is a proven fact that hyperventilation reduces cell oxygen level in vital organs of the human body, including:- brain (Brown, 1953; Kennealy et al, 1980; Liem et al, 1995; Lum, 1975; Lum, 1982; Macey et al, 2007; Litchfield, 2003; Santiago & Edelman, 1986; Skippen et al, 1997; Starling & Evans, 1968; Tsuda et al, 1987)- heart (Foëx et al, 1979; Karlsson et al, 1994; Okazaki et al, 1991; Okazaki et al, 1992; Wexels et al, 1985)- liver (Fujita et al, 1989; Hughes et al, 1979; Okazaki, 1989)- kidneys (Karlsson et al, 1994; Okazaki, 1989)- spleen (Karlsson et al,

1994)- colon (Guzman et al, 1999)- systemic or body tissues in general (Laffey & Kavanagh, 2002; Nunn, 1987).

Summary of the effects of hyperventilation and hypocapnia (low CO2) on oxygen transport

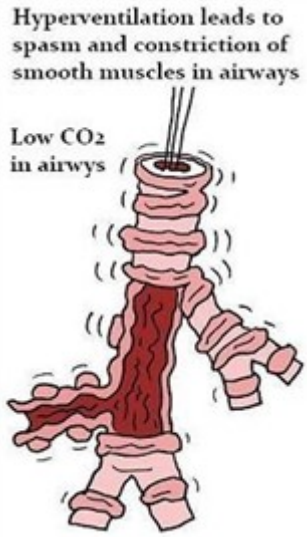


Note that hyperventilation may not result in hypocapnia (advanced stages of cystic fibrosis, asthma, COPD, etc.) due to ventilation-perfusion mismatch and too high CO2 in the arterial blood (hypercapnia), but the main driving force for cell hypoxia and destructions of the lungs remains the same: alveolar hyperventilation or too low CO2 in the lungs.

3.2 Hyperventilation causes problems with ventilation-perfusion

Modern research suggests that alveolar hypocapnia (low CO2 in the lungs) causes various negative effects on the respiratory system, airways and lungs of normal subjects and people with cystic fibrosis. The adverse effects include:

A. Bronchoconstriction, which is a normal physiological reaction to alveolar hyperventilation present in all people (Jamison et al, 1987; O'Cain et al, 1979; Sterling, 1968). However, when hypocapnic bronchoconstriction is combined with chronic tissue hypoxia, the effects are different. Chronic hypoxia leads to anaerobic cellular respiration in mitochondria that causes the production of reactive oxygen species (free radicals) and chronic inflammation.



B. Chronic inflammation, according to medical cystic fibrosis research, is the pivotal point that exacerbates this disease because inflammatory mechanisms in CF airways lead to pulmonary complications which are the most serious complications in cystic fibrosis (e.g., Döring & Worlitzsch, 2000). According to recent biomedical research, chronic inflammation is either associated with or even caused by tissue hypoxia. Medical biologists have finally been able to pinpoint the mechanism. Among the key driving forces of chronic inflammation, according to recent research studies, are pro-inflammatory transcription factors, such as nuclear factor kappa B (NF-kappaB) and activator protein (AP)-1 (Safronova & Morita, 2010; Ryan et al, 2009), and hypoxia-inducible factor 1 (Imtiyaz & Simon, 2010; Sumbayev & Nicholas, 2010). The link between tissue hypoxia and chronic inflammation is so strong, that there are dozens of recent research publications that use the term “hypoxic inflammation”.

C. Immunosuppression is a normal result of chronic hypoxia (Sitkovsky, 2009; Hatfield et al, 2009). Here is a part of the recent abstract from one of these studies, "*... Here, we attract attention to the possibility of iatrogenic exacerbation of immune-mediated tissue damage as a result of the unintended weakening of the tissue-protecting, hypoxia-adenosinergic pathway. These immunosuppressive, anti-inflammatory pathways play a critical and nonredundant role in the protection of normal tissues from collateral damage during an inflammatory response. We believe that it is the tissue hypoxia associated with inflammatory damage that leads to local inhibition of overactive immune cells by activating A2AR and A2BR and stabilizing HIF-1alpha. We show in an animal model of acute lung injury that oxygenation (i.e., inspiring supplemental oxygen) reverses tissue hypoxia and exacerbates ongoing inflammatory lung tissue damage...*" (Hatfield et al, 2009).

D. Lung injury, according to Canadian biomedical researchers, is proportional to the degree of alveolar hypocapnia (Laffey et al, 2000; Laffey et al, 2003). Another medical study suggested, according to its title, that *Airway hypocapnia increases microvascular leakage in the guinea pig trachea* (Reynolds et al, 1992) worsening airway injury. While evaluating effects of alveolar hypocapnia on ventilation-perfusion heterogeneity, it was found that "*Hypocapnia worsens arterial blood oxygenation and increases VA/Q heterogeneity in canine pulmonary edema*" (Domino et al, 1993), where VA/Q is the ventilation-perfusion ratio.

What are the possible solutions? "Deliberate elevation of PaCO2 (therapeutic hypercapnia) protects against lung injury induced by lung reperfusion and severe lung stretch" (Laffey et al, 2003). Note that, according to many studies, breathing CO2-rich air does not improve blood oxygenation and ventilation-perfusion ratio because CO2 is a powerful respiratory stimulant causing increased minute ventilation that can mechanically worsen existing inflammation and lung injury. In order to be effective, higher alveolar CO2 content should not be accompanied by excessive mechanical stress.

Hence, even when the lungs are not involved, chronic hyperventilation naturally leads to systemic cell hypoxia, bronchoconstriction, chronic inflammation, immunosuppression, frequent

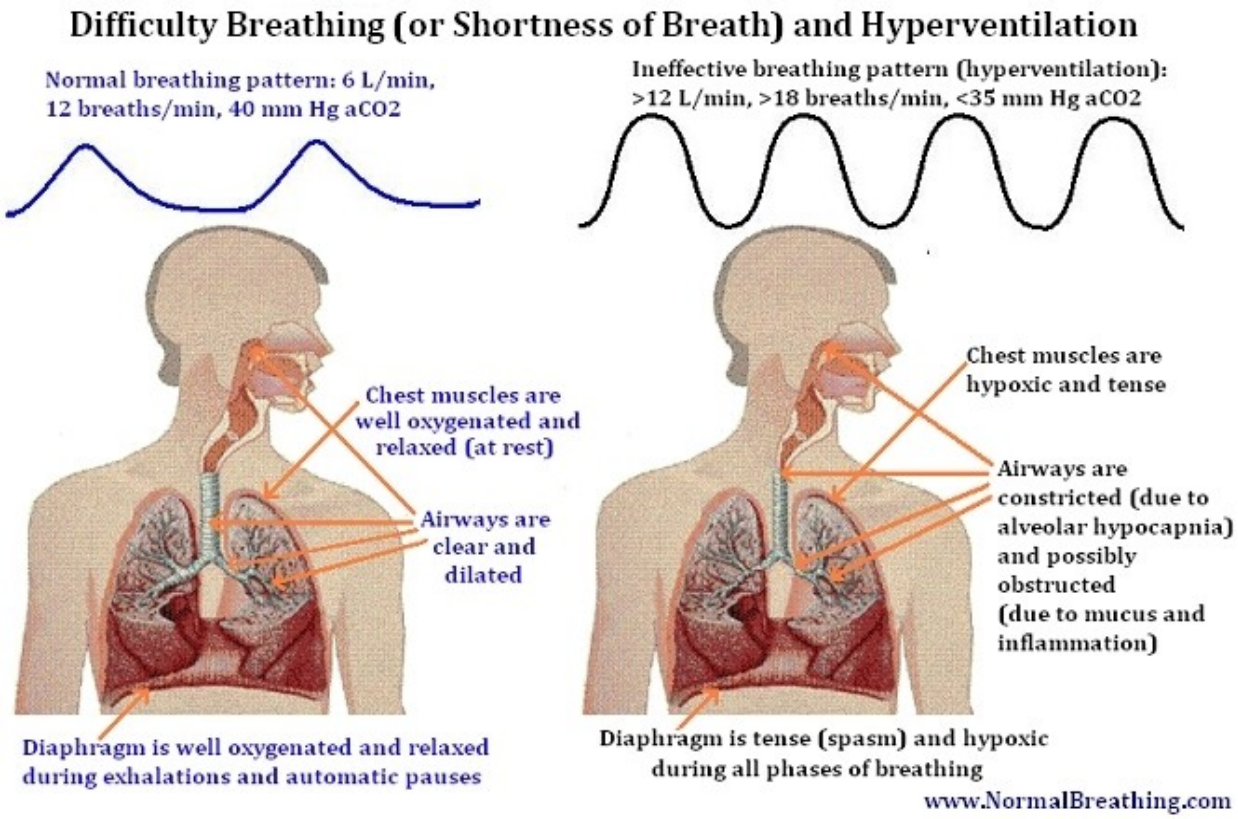
respiratory infections and other pathological processes in the lungs that can worsen oxygen transport and increase CO2 retention.

E. Impairment of thoraco-abdominal mechanics (or predominantly upper chest breathing) is a normal result of worsening cell oxygenation, chronic inflammation of airways, and reduced ventilation-perfusion ratio. This effect is common for obstructive lung diseases, while some studies found that this contribution of chest breathing correlates with a higher degree of symptoms of CF (Szeinberg et al, 1985; Pinet et al, 2003; Hart et al, 2004).

Probably, the presence of the faulty CFTR gene makes the situation with diaphragmatic breathing worse, as the title of a recent study suggests *Lack of CFTR in skeletal muscle predisposes to muscle wasting and diaphragm muscle pump failure in cystic fibrosis mice* (Divangahi et al, 2009). The main reason for the diaphragmatic weakness is the hypoxic inflammatory environment for muscle cells of the diaphragm.

These observations suggest that development and maintenance of diaphragmatic breathing 24/7 should be a part of any rehabilitative therapy for any stage of CF, while children with CF must learn simple diaphragmatic breathing techniques (preferably, the Buteyko reduced breathing exercise) as early as possible.

Summary: Effects of chronic hyperventilation on normal lungs



Due to a variety of adverse effects on lung tissue, chronic hyperventilation can result in development of lung pathologies (severe asthma, bronchitis, emphysema, bronchiectasis, bronchiolitis, tuberculosis, and so forth), mild and more advanced forms of CF included. Hampered gas exchange in the lungs (due to airway collapse, modification and destruction of alveoli, chronic inflammation, mucus and liquid in airways and lungs and other abnormalities) leads to lower O2 and higher CO2 tensions in the arterial blood (hypoxemia and hypercapnia or CO2 retention). Worsened ventilation-perfusion ratio immediately causes tissue hypoxia. It is, therefore, common that people with advanced stages of these lung pathologies are candidates for supplemental oxygen. Bear in mind that oxygen therapies work mostly due to the greatly increased amount of oxygen freely dissolved in blood plasma.

Note about breathing pure oxygen. In normal conditions, up to about 98% of all oxygen is combined with red blood cells, while only about 2% of O2 is freely dissolved in plasma. Breathing pure oxygen increases the amount of free oxygen about 5 times, thus, saving the lives of people, but providing mild chronic stress for the lungs due to oxidative stress or the generation of reactive oxygen species (free radicals). Leading respiratory specialists share the same (negative) opinion in relation to pure oxygen therapies and hyperbaric oxygen therapies which may increase oxygenation in under-ventilated portions of the lungs, but are destructive in relation to the functioning parts of the lungs.

3.3 Additional effects of mouth breathing and hyperventilation on airways and mucus formation in cystic fibrosis

Mouth breathing in cystic fibrosis

Oral breathing is very common in children and adults with cystic fibrosis (Fernald et al, 1990; Brihaye et al, 1997). The problem appears at a very young age. As it was found by Ramsey & Richardson (1992), " *... the vast majority of patients with cystic fibrosis develop sinus disease with panopacification of the sinuses present in 90% to 100% of patients older than 8 months of age.*" The common effects of mouth breathing and chronic sinusitis are a loss of the sense of smell, deformities of the external nasal skeleton, and headaches, while up to 20% of patients eventually require surgical treatment of their sinuses (Ramsey & Richardson, 1992).

A group of Italian researchers in their article *Orocraniofacial changes in young subjects with cystic fibrosis* suggested that orofacial changes were linked with habitual mouth breathing of young cystic fibrosis people: "…Even if causes can be hardly distinguished from effects, the role of the juvenile oral breathing in these cases seems to be any way undeniable with statistically significant results" (Gola et al, 1989).

A group of Swedish orthodontists in their study *Craniofacial morphology in children with cystic fibrosis* noted that, "… The cystic fibrosis group showed open bite, decreased posterior facial height, increased mandibular and craniocervical inclination" (Hellsing et al, 1992).

Mouth breathing causes drying of airways

What are the effects of habitual hyperventilation through the mouth? A study conducted in the Department of Pediatrics at Case Western Reserve University (Cleveland, Ohio) measured effects of the breathing route on humidity and surface temperature in airways of normal and CF subjects. During nose breathing, the nasal passages are designed to humidify and warm up the incoming flow of air. Mouth breathing leads to drying and cooling of bronchi and bronchioles. For example, during inhalation, the relative humidity at the pharynx for nose breathing was about 95%, while for mouth breathing it was only 75% (Primiano et al, 1988). Hence, mouth breathing requires about 5 times more water from bronchi and bronchioles in order to achieve 100% humidity. (It is unlikely that alveoli significantly contribute to humidification of inhaled air.) These doctors observed that, "... *These data suggest that when the rate of evaporation is sufficiently high, the rate-limiting step may be water transport through the mucosal tissue and/or secretions. At least for the upper airways, this rate limitation is more evident for CF patients than for normal subjects.*"

Hyperventilation and mouth breathing causes overcooling of airways

An additional effect of chronic hyperventilation relates to overcooling of airways, especially in cases of oral breathing. While measuring temperature of airways during pulmonary and hyperventilation tests, a group of Italian doctors discovered that hyperventilation induced a significant temperature loss (Vitacca et al, 1994). The aim of their study was to test the usefulness of hygroscopic condenser humidifiers on secretion and on inspired gas temperature in tracheostomized patients. These Italian doctors found that hygroscopic condenser humidifiers have positive effects of thickness and coloring of mucosal secretions: "*Statistically significant differences were found in thickness and coloring of secretions between the two groups during the period of 10 days. Group 2 showed a significantly greater trend in number of bacteria than Group 1. The group with the hygroscopic condenser humidifier showed respiratory function improvement over time for forced expiratory volume in one second (FEV1) and tidal volume (VT), maximal inspiratory pressure (MIP), and maximal voluntary ventilation (MVV) in comparison to the control group, who did not." In conclusion, they write that hygroscopic condenser humidifiers can be useful, among other things, to "heat inspiratory airflow, possibly protecting against temperature loss during a hyperventilation test*".

These results suggest that hyperventilation in cystic fibrosis also leads to overcooling of airways. It is known that even a slight drop in temperatures of airways can lead to immune dysfunction and possible infections. Overcooling may also contribute to thickness and coloring of sputum, as the above study suggested.

Effects of hyperventilation and mouth breathing on nitric oxide absorption

Nitric oxide (NO) is an exceptionally important compound with extensive respiratory functions, ranging from bronchial and vascular dilation (similar to CO2 in airways) to ciliary motion and antibacterial defense. From a biochemical viewpoint, NO can be a key chemical that suppresses pathogens in alveoli and airways.

Nasal and sinus cavities are the known major sites of NO production, followed by airway and alveolar compartments (Rolla et al, 2005). However, while many lung pathologies are characterized by increased levels of NO in exhaled air and airways, concentrations of NO are decreased in the airways of patients with cystic fibrosis (e.g., Grasemann et al, 2000; Grasemann & Ratjen, 2002; Keen et al, 2010). Furthermore, as the title of one medical study claims, "*Impaired lung diffusing capacity for nitric oxide and alveolar-capillary membrane conductance results in oxygen desaturation during exercise in patients with cystic fibrosis"* (Wheatley et al, 2011).

Hyperventilation, mouth breathing and tissue hypoxia are known factors that disrupt normal synthesis and absorption of nitric oxide. Let us consider the contributions of these effects.

The generation and absorption of increased levels of NO explains some of the benefits of nose breathing rather than mouth breathing (Scadding et al, 2007). Hence, habitual mouth breathing, or mouth breathing during sleep, is a factor that leads to reduced NO levels in the airways and arterial blood. This causes problems with infections in airways and reduced oxygen transport in the cardiovascular system.

Hyperventilation, apart from biochemical effects related to synthesis of NO, causes changes in the breathing patterns of people. During normal breathing at rest, healthy people have a natural period of no breathing (an automatic pause), after each exhalation. This pause is followed by relatively short and fast diaphragmatic inhalation that creates turbulent air flow allowing better absorption of NO generated in sinuses. The exhalation, immediately after this inhalation, is passive, slow and relaxed - allowing generation of nitric oxide in sinuses. Therefore, a normal breathing pattern favors generation and effective utilization of nasal NO, and nasal NO output in the healthy subjects is four-fold greater during inhalation when compared to exhalation (Törnberg et al, 2002).

In contrast, hyperventilation is characterized by an absence of the automatic pause and forceful exhalations that have turbulent air flow so it blows off most of the nitric oxide generated in the sinuses.

Important note about airway clearance techniques for cystic fibrosis

Conventional chest physiotherapy often includes forceful high-velocity coughing through the mouth with inhalations through the mouth. Such therapy involves losses in alveolar CO2, reduced nasal nitric oxide absorption, and overcooling and drying of airways due to large flow of air (hyperventilation). Russian medical doctors practicing the Buteyko method suggest that all coughing should be done through the nose, while mucus or sputum should be gently removed when it comes out naturally and is located inside the mouth. The most effective methods to

encourage airway clearance are correct breathing exercises and physical activity with strictly nasal breathing because they lead to higher levels of alveolar CO2. Increased CO2 improves oxygenation and perfusion of hypoxic cilia cells naturally, leading to the restoration of their primary functions. Furthermore, this approach does not cause production of new sputum due to adverse effects of overbreathing.

Humming and nitric oxide

Nasal levels of NO can be increased 15-fold during humming compared with quiet exhalation (e.g., Weitzberg & Lundberg, 2002). Furthermore, clinical evidence suggests, according to the title of one study, that "*Strong humming for one hour daily to terminate chronic rhinosinusitis in four days: a case report and hypothesis for action by stimulation of endogenous nasal nitric oxide production"* (Eby et al 2006). In this report, it was found that the morning after the first 1 hour humming session, "*the subject awoke with a clear nose and found himself breathing easily through his nose for the first time in over 1 month. During the following 4 days, CRS [chronic rhinosinusitis] symptoms slightly reoccurred, but with much less intensity each day. By humming 60-120 times four times per day (with a session at bedtime), CRS symptoms were essentially eliminated in 4 days.*"

Leading Soviet physiologist Konstantin Buteyko, MD, PhD also suggested that humming has some health benefits. Note that humming during breathing retraining can have either positive or negative effects on alveolar CO2 levels depending on the current breathing parameters and other factors, e.g., after meals versus on an empty stomach, posture, metabolic rate (exercise), and some others.

3.4 Nocturnal hypoxemia or nocturnal oxygen desaturation

Another practical aspect related to breathing and cystic fibrosis is that for the overwhelming majority of CF patients, their worst hypoxemia (low blood oxygen saturation) and lowest body oxygenation take place during early morning hours or the last portion of the night sleep (Dancey et al, 2002; Frangolias & Wilcox, 2001; Salvatore & D'Andria, 2002; Young et al, 2011).

This effect is common in the sick, since early morning hours from about 4 to 7 am (as numerous medical studies have identified) have the highest mortality rates due to strokes, coronary artery

spasms, acute asthma attacks, seizures and other exacerbations. Note that this effect of oxygen desaturation is even present in infants with cystic fibrosis (Villa et al, 2001).

While some researchers suggest that hypoventilation could be a factor that makes nocturnal oxygen desaturation possible, those studies that measured respiratory frequencies in CF patients reported their higher breathing rates. For example, the study conducted on infants (Villa et al, 2001) found that the average respiratory rate in infants with CF was 10 breaths/min higher than in normal infants. Furthermore, the authors suggested that, "*... Another predisposing factor for nocturnal desaturation was a high respiratory rate, an expression of possible lung impairment. Accordingly, subjects who had higher respiratory rates also had lower SaO2 values during sleep*" (Villa et al, 2001).

Hence, thoracic (or upper chest) breathing, when combined with hypoventilation and high respiratory rates, leads to abnormally low blood oxygenation values. These clinical findings indicate that abdominal breathing and slowing down the respiratory rates should be essential parts of breathing retraining in CF.

4. Can automatic breathing be retrained?

Chronic hyperventilation in CF at rest can have two explanations.

1. Chronic overbreathing can be the result of the disease and then we can declare that abnormal breathing has nothing to do with CF. Then we also need to assume that it is hard or impossible to change one's automatic breathing pattern back to the medical norm, and we are going to try to find other methods and techniques, apart from breathing retraining, to address the symptoms of CF.

2. The second approach is to assume that heavy breathing causes tissue hypoxia, CFTR expression and development of CF. Then we can apply all known therapies for cystic fibrosis

(medication, digestive enzymes, physiotherapy, lifestyle changes related to diet, exercise, and so forth) and use breathing retraining as an additional or supplementary technique with the goal to change or normalize automatic or basal breathing in people with cystic fibrosis.

Which way to choose? Consider supporting medical evidence.

4.1 Hyperventilation provocation test

It is well known that the hyperventilation provocation test is a 100% specific test that readily provokes the main symptoms of angina pain, asthma, epilepsy, and panic attacks. For example, voluntary over-breathing in people with hypertension causes the heart attack, in asthmatics – the asthma attack, in epileptics – epilepsy seizures, etc. Here is a summary of some medical studies regarding different health conditions, number of patients investigated, and the percentage of patients who reproduced their specific health problem:- coronary artery spasms (Nakao et al, 1997) 206 patients, 100% specific;- bronchial asthma (Mojsoski & Pavicic, 1990) 90 patients, 100% specific;- panic attacks (Bonn et al, 1984; Holt & Andrews, 1989; Nardi et al, 2000), 95% specific;- epileptic absence seizures (Esquivel, 1991; Wirrel, 1996).

All these symptoms (chest pain, wheezing, seizures, etc.) can be expected since they are based on known laws of physiology related to oxygen and carbon dioxide changes (considered above).

It is also known that symptomatic application of reduced breathing decreases the severity of symptoms. For example, clinical experience of Russian Buteyko doctors testifies that most asthmatics can stop acute asthma attacks using a simple breathing exercise instead of using ventolin or other medication (Buteyko et al, 1968; Genina, 1982). The same breathing exercise can unblock the nose for people with sinusitis. Reduced breathing can stop most coronary artery spasms as well (Buteyko et al, 1965).

So we see from two different perspectives - hyperventilation provocation and intentionally reduced breathing - that purposeful, short-term changes in breathing patterns can have dramatic physiological effects. This raises the question "Can systematic breathing retraining permanently alter automatic breathing patterns to produce long-term positive effects"?

4.2 What are the effects of breathing training on people with CF?

Clinical trials of various breathing training techniques have so far been limited to the application of biofeedback assisted breathing retraining. The purpose has been to develop *diaphragmatic breathing using the pursed-lip breathing technique* (Delk et al, 1994) and *inspiratory muscle training* (e.g., de Jong et al, 2001; Enright et al, 2004).

During the first such study, the experimental subjects "*underwent eight sessions of pneumographic or strain-gauge feedback from the abdominal muscles and electromyogram feedback from accessory respiratory muscles to assist in learning diaphragmatic and pursed-lips breathing maneuvers*" (Delk et al, 1994). They experienced a 38 percent (clinically significant)

increase in FEF25; 50; and 75% after 4 weeks of diaphragmatic breathing. There were no significant changes (3%) in the control group. There was also a 29% improvement in FVC (significant) for the experimental group. The FVC percent change in the control group was 8% (insignificant).

One clinical trial of *inspiratory muscle training* found that low-intensity inspiratory-threshold loading (at the level of 40% of maximum inspiratory pressure) produced an increased inspiratory-muscle endurance in patients with CF (de Jong et al, 2001). However, since this trial did not intend to address problems with chest breathing and low alveolar CO2, there were no changes in pulmonary function tests.

Another inspiratory muscle training trial found improved lung function and exercise capacity in adults with cystic fibrosis (Enright et al, 2004). The effect was probably due to two factors: higher training intensity (80% of maximal inspiratory effort) and improved basal breathing patterns. This may be because the instructions for all respiratory trainers (Powerbreathe, Ultrabreathe, etc.) suggest that exhalations should be slow and relaxed. It is very likely that if the inhaled air has higher CO2 content, as is the case with some breathing devices, breathing training can provide double benefits: improved strength of respiratory muscles; and improved automatic breathing patterns after the breathing session. This would lead to lasting biochemical effects related to improved cell oxygenation.

4.3 Clinical trials of the Buteyko breathing technique

The Buteyko breathing method is (also known as the Buteyko method or Buteyko breathing technique) is a system of activities that include breathing exercises and lifestyle changes. The program of lifestyle changes in the Buteyko method is similar to hatha yoga, but it has more science behind it. The goal of the technique is to normalize one's automatic or unconscious breathing pattern (learn how to breathe in accordance with medical norms 24/7). This method was created by Doctor Konstantin Buteyko.

There were 6 Western randomized clinical trials of the Buteyko breathing technique on subjects with asthma - another health condition that involves pathological changes in the lungs. All these trials found that the control groups could significantly reduce their short-term bronchodilator use by up to 70-90% and steroid use by about 50% in 3-6 months. But there were no changes in abnormal lung function results.

Furthermore, while most subjects with asthma had improvements in various tested parameters (less medication, better quality of life, reduced symptom score, and reduced frequency of infections), there were a few people who got worse at the end of these trials. This fact indicates that there are certain hidden factors that can also influence automatic breathing patterns, and, for some people, these hidden factors can play a crucial role in their long-term respiratory changes.

The central question, however, in relation to all these trials of the Buteyko method is this: Did the control group achieve **normal breathing parameters**? This question is very important because Dr. Konstantin Buteyko made 2 essential physiological claims in relation to many chronic diseases, asthma and CF included:1). Sick people suffer from alveolar hypocapnia (lack of CO2) caused by chronic hyperventilation at rest2) If they normalize their breathing, their symptoms and diseases are going to disappear.

Available data suggests that the control groups during these 6 clinical trials did not achieve the medical norm (6 L/min, 10-12 breaths/min, 500-600 ml for tidal volume, 40 mm Hg for alveolar CO2m and so forth). What were the final breathing parameters in these 6 Western trials? The asthmatics with the best results started with about 12 L/min and finished with about 9 L/min. Hence, they got only half way to the medical norm.

But Dr. Buteyko did not claim that partial breathing normalization can cure asthma. Furthermore, doctor Buteyko established different norms for breathing, such as 4 L/min, 8 breaths/min, 500 ml for tidal volume (amount of air for one breath), and about 46 mm Hg for alveolar CO2. His physiological requirement to cure asthma is to slow breathing down to about 4 L/min for minute ventilation and 46 mm Hg for alveolar CO2 pressure.

Therefore, we can conclude that these clinical trials tested the abilities of Buteyko breathing practitioners to reduce symptoms and medication in asthma. Meanwhile, the trials did not address the key physiological statements proposed by Dr. Buteyko in relation to asthma.

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