



E-ISSN: 2278-4136

P-ISSN: 2349-8234

www.phytojournal.com

JPP 2022; 11(4): 295-302

Received: 24-05-2022

Accepted: 27-06-2022

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Hypoxemia and hypercapnia: Its relation to joint diseases and the natural treatments for some joint diseases: A review

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DOI: <https://doi.org/10.22271/phyto.2022.v11.i4d.14474>

Abstract

The leading cause of disability worldwide is Arthritis. Arthritis can be either autoimmune joint disease or osteoarthritis. According to the Center for Disease Control (CDC), by 2040, 80 million U.S. adults will have some form of arthritis. The objective is to find the effect of Hypoxemia, hypercapnia and PH chemical imbalance of the blood on muscle loss and joint diseases, and to find natural remedies to treat these types of joint diseases. Three main types of joint diseases were found to be directly related to hypoxia (Low levels of oxygen in your body tissues), hypercapnia (Excess carbon dioxide build up), and blood PH imbalance: Rheumatoid Arthritis, Osteoarthritis, and gout joint diseases. The natural treatment of these joint diseases has been identified.

Keywords: blood on muscle, excess carbon

Introduction

The earth's atmosphere contains 21 percent oxygen ^[1]. A closed space has safe oxygen levels if readings are between 20.8-21%, while a space with readings of less than 19.5% are oxygen deficient according to OSHA guidelines ^[2]. Home air conditioners: split AC, window AC, and portable AC can't ventilate your room: doesn't have the capability to bring the outside air, it only circulates indoor air and cool it. Complex HVAC system used inside some hotels, office buildings, big malls, airports have the feature to ventilate the indoor area, and maintains freshness, humidity, and oxygen level. Some window ACs in the US can bring outside air and main the oxygen levels. Most of window ACs around the globe does not have this feature. Oxygen room level 19.5-23.5% is considered safe, oxygen levels between 14-16%, below the 19.5% is considered hazardous ^[3].

If while breathing out not enough carbon dioxide is expelled from the lungs, the increased carbon dioxide in the blood reduces the blood PH and makes the blood acidic causing raspatory acidosis. When your ability to breath is blocked by physical block limits, another condition, or a disease raspatory acidosis is caused. Raspatory acidosis can be either acute, chronic, or acute and chronic. The sudden arrival of CO₂ to the lungs is called Acute Respiratory Acidosis. The kidneys response of acute respiratory acidosis is so quick that it can happen within minutes. The causes may include cerebrovascular accidents like strokes, a group of diseases that interfere with gene's ability to make muscle and causes to steadily lose muscles causing Muscular dystrophy, voluntary muscles may become weak, or you lose control of them causing Myasthenia gravis, heart attack, a very rare neurological disorder where the immune system attacks itself and can cause problems from trouble eating to full body paralysis causing Guillain-Barre Syndrome, and/or block airways.

Chronic raspatory acidosis is more serious and it happens at slower rate and at a lesser degree than acute raspatory acidosis. The lower oxygen rate for the tissues to be fully supplied in the blood is known as hypoxemia The conditions may include pulmonary fibrosis or diseases that happens in the lung tissue/nerve or muscular diseases, sleep apnea, obesity, thoracic skeletal defects that causes pecs/rib cage/or sternum to be shaped in a way that it limits lung functioning or breathing, Asthma, and a group of airflow and breathing diseases including diseases like bronchitis and emphysema called Chronic obstructive pulmonary disease (COPD). Common treatments for raspatory acidosis are oxygen tubes, different medications, or other treatment to stop smoking, naloxone (for opioid overdose), anti-inflammatory medications to ease any constrictive swelling, and breathing machines like a CPAP or BiPAP.

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To prevent getting respiratory acidosis in general: lose weight if overweight, quit smoking, and don't drink alcohol while taking opioids, and strong pain medications [4]. A two-year study showed that there is adverse physical effect on medical staff when wearing an N 95 mask. Wearing an N 95 mask resulted in hypercapnia (Excessive CO₂ in the blood caused by inadequate respiration) and hypoxemia (Lack of oxygen in the blood) which reduced the ability to make correct decision and the working efficiency. Dizziness, short of breath, and headache were experienced by the medical staff wearing N95 masks [5].

If prolonged hypoventilation is accompanying respiratory acidosis, the condition becomes more severe, and it can cause the patient to have additional symptoms: myoclonus, seizures, and altered mental status. Hypercapnia (excessive amounts of carbon dioxide in the blood) can be caused by respiratory acidosis leading to cerebral vasodilation. Severe respiratory acidosis may cause papilledema and increased intracranial pressure increasing the risk of death and herniation. Chronic respiratory acidosis may cause impaired coordination, polycythemia, memory loss, heart failure, and pulmonary hypertension [6].

Dyspnea (difficult respiration) are commonly caused by chronic obstructive pulmonary disease (COPD), interstitial lung disease, heart failure, asthma, psychogenic problems that are usually linked to anxiety, and pneumonia. Chest X-rays and computed tomography (CT) images are used by doctors for its diagnosis. Spirometry tests can be used to measure airflow and the patient's lung capacity and to pinpoint the extent and the type of an individual's breathing problems. Other tests can be used to directly measure the blood capacity to carry oxygen and the level of oxygen in the blood. Treatment of dyspnea is dependent on its cause. If it's caused from having a bacterial pneumonia, antibiotics are prescribed. If it's caused from having asthma, bronchodilators and steroids are prescribed, other medications are also be effective (opiates, anti-anxiety drugs, and non-steroidal anti-inflammatory drugs (NSAIDs)). Special breathing techniques, such as breathing muscle strengthening exercises, and pursed-lip breathing can be used if the cause of dyspnea is caused by COPD. Supplemental oxygen may be prescribed if tests indicate low levels of oxygen in the blood [7].

A less well-known side effect of using nonsteroidal anti-inflammatory drugs (NSAIDs drugs) is the degradation of joint cartilages [8]. Nonsteroidal anti-inflammatory drugs include; Ibuprofen used in some drugs such as Motrin, Nuprin, and Advil; Piroxicam used in drugs such as Feldene; diclofenac used in drugs such as Voltaren; fenoprofen used in drugs such as Nalfon; indomethacin used in drugs such as Indocin; naproxen used in drugs such as Naprosyn; tolmetin used in drugs such as Tolectin; and sulindac used in drugs such as Clinoril. Other side effects of using nonsteroidal anti-inflammatory drugs are ulcer formation, dizziness, headaches, and gastrointestinal upset. Clinical studies had showed that nonsteroidal anti-inflammatory drugs usage have caused acceleration of osteoarthritis and increased joint destruction [9-12]. Common joint disease may include bursitis, osteoarthritis, gout, rheumatoid arthritis, spondyloarthritis, lupus, and juvenile idiopathic arthritis. Bursitis is caused by the inflammation of the small, fluid-filled sacs called bursae around the joints, tendons, muscles and bone. Overuse or sudden injury of joints such as the elbow, hip, and shoulder can lead to flare-ups. Bursitis can sometimes result from bacterial infections. Osteoarthritis is the wear-and-tear form that increases with age. Adults in their 50s and older are more

likely to develop this chronic and progressive disease. Women are more vulnerable to osteoarthritis than men. It's stiffness and pain with movement caused by breaks down of cartilages that cushions the joints. The flexibility decreases and walking becomes more difficult especially with knee and hip arthritis. The type of arthritis that affects the joint connecting the big toe to the rest of the foot is called gout. A waste product in the blood, uric acid would exist in excess and forms crystals in the joints. Flare-ups caused by gout are extremely painful and it would commonly strike in the night. Men are more vulnerable to gout disease, and women become more vulnerable to this disease after menopause.

The autoimmune condition affects the lining of the joints is called Rheumatoid arthritis. Immune system cells accumulate in large numbers in the joints. The interaction between joint cells and immune cells causes increasing inflammation leading to damage and destruction to of the bone and cartilage. Spondyloarthritis consists of certain other rheumatoid diseases including axial spondylitis, enteropathic arthritis, and psoriatic arthritis. The inflammation in the spine that can eventually lead to spinal fusion, or ankylosing spondylitis is called axial spondylitis. The complication of an inflammatory bowel diseases like ulcerative colitis, are called enteropathic arthritis. Psoriatic arthritis is associated with the skin condition psoriasis, and it tends to affect the joints of the hands and feet. The autoimmune condition affects various parts of the body, including internal organs, skin, brain, blood, bones and joints are called lupus. Lupus can cause an inflammation that would trigger arthritis, particularly in the knees, feet, hands, elbows, and shoulders. The most common chronic joint condition in kids is Juvenile idiopathic arthritis. The child's immune system attacks the body's own healthy tissue, and it's an autoimmune condition. The cause is unknown, and it may alter children's normal growth. This inflammation may affect the internal organs, eyes, muscles, joints, and ligaments [13].

Review and Discussion

The amount of oxygen circulating in the blood is the blood oxygen level. The normal reading using an oximeter is between 95 to 100 [14]. Forms of carbon dioxide carried in the blood are carbaminohemoglobin (CO₂ bound to hemoglobin), and the chemically modified bicarbonate (HCO₃⁻). The solubility of CO₂ in the blood is 0.07 mL CO₂/100 mL blood/mm Hg which would be almost 5% of the total CO₂ content of blood. The solubility of oxygen in the blood is 0.003 mL O₂/100 mL blood/mm Hg, which would be almost 2% of the total O₂ content of blood. The solubility of Carbon dioxide is 20 times more soluble in blood than oxygen. 15 According to Henry's law, the solubility of a gas is directly proportional to the partial pressure of that gas above the liquid. Increasing the pressure and decreasing the temperature would lead to increase the solubility of gaseous over a liquid. 16 Carbon dioxide gas has a lower ability to diffuse and exit the lungs compared to oxygen gas according to Graham's law 95 as it's denser than oxygen gas, the density of oxygen gas is 1.43 g/L compared to density of carbon dioxide gas 1.81 g/L. 96, 97.

The body normally maintains CO₂ in a range from 38 to 42 mm Hg by balancing its elimination and production. Ventilation is primarily initiated by the blood PH. PH of the blood is mainly regulated by the amount of CO₂ in the blood. The body produces more CO₂ than it can eliminate in case of hypoventilation causing a retention of CO₂. The increased CO₂ is what leads to an increase in blood acidity, due to

increase of hydrogen ion concentration, a slight increase in bicarbonate concentration, and the equilibrium would shift towards forming more hydrogen ions according to the following reaction:



A buffer system is created from the presence of the flowing molecules: HCO_3^- , CO_2 , and H_2CO_3 in equilibrium.

In the presence of excess hydroxide ions (OH^-), carbonic acid (H_2CO_3) would buffer a high PH, and in the presence of excess hydrogen ions (H^+), carbonate anion (HCO_3^-) would buffer a low PH which is the main mechanism behind respiratory acidolysis blood PH drop. In respiratory acidolysis the slight increase in bicarbonate act as a buffer for the increase in H^+ ions, which helps minimize the drop in PH blood value. Increase hydrogen ions (H^+) would lead to a slight decrease in the buffered blood PH, blood PH would be below 7.35. 17,18.

To evaluate patients with suspected respiratory acidosis, serum bicarbonate level and an arterial blood gas (ABG) are necessary. An elevated bicarbonate level HCO_3^- (>30 mmHg), an elevated PCO_2 (>45 mmHg), and decreased pH (<7.35) would show on an ABG test in case of respiratory acidolysis. Respiratory acidosis can be either chronic or acute based on the relative increase in HCO_3^- with respect to PCO_2 . A HCO_3^- will have increased by one mEq/L for every ten mmHg increase in PCO_2 over a few minutes in case of acute respiratory acidosis. A HCO_3^- will have increased by four mEq/L for every ten mmHg increase in PCO_2 over a time course of days in case of chronic respiratory acidosis. A mixed respiratory-metabolic disorder may be present if it

doesn't show either patterns of acute or chronic respiratory acidosis. A drug screen may also be warranted in a patient who show an unexplained respiratory acidosis^[19, 20].

The cause of respiratory acidosis must be treated once the diagnosis has been made. The rapid alkalization of the cerebrospinal fluid (CSF) may lead to seizures therefore the hypercapnia should be corrected gradually. To help improve ventilation, pharmacologic therapy may be used. Beta-agonists, anticholinergic drugs, and methylxanthines (Bronchodilators) may be used in treating patients with obstructive airway diseases. In case of patients who overdose on opioid use, Naloxone can be prescribed^[21, 22].

Acidolysis can be either respiratory or metabolic in origin depending on the measured pCO_2 . If pCO_2 is greater than 40 to 45, it's known to be due to decreased ventilation, and it's called respiratory acidosis. If the pCO_2 is less than 40 since it is not the cause of the primary acid-base disturbance it's called metabolic acidosis and it's confirmed by a measured decreased in bicarbonate (normal range 21 to 28 mEq/L)^[23].

In alkalosis, the fluids of the body are alkaline, the blood PH is high. When the blood has too little acid making it basic, the condition is called alkalosis, blood PH would be higher than the normal PH value of 7.45. There might be no noticeable symptoms for mild and chronic alkalosis. If there is a rapid PH increase, symptoms may include: confusion, nausea or vomiting, muscle twitching or spasms, numbness of the hands and feet, and/or dizziness or lightheadedness^[24].

Alkalosis can be either respiratory or metabolic depending on pCO_2 . If pCO_2 is greater than 45 mmHg, it's called metabolic alkalosis and the measured bicarbonate is greater than 29 mM. If pCO_2 is less than 32 mmHg, it's called respiratory alkalosis and the measured bicarbonate is less than 22 mM^[25].

	pH	pCO ₂	Total HCO ₃ ⁻
Metabolic acidosis	↓	N, then ↓	↓
Respiratory acidosis	↓	↑	N, then ↑
Metabolic alkalosis	↑	N, then ↑	↑
Respiratory alkalosis	↑	↓	N, then ↓

Reference values (arterial): pH: 7.35–7.45; pCO₂: male: 35–48 mm Hg, female: 32–45 mm Hg; total venous bicarbonate: 22–29 mM. N denotes normal; ↑ denotes a rising or increased value; and ↓ denotes a falling or decreased value.

Fig 1: Types of Blood Alkalosis and Acidosis. 26

A number of diseases, including rheumatoid arthritis (RA) are caused by alterations in tissue oxygen pressure. A condition known as hypoxia, low partial pressure of oxygen is involved in angiogenesis, apoptosis, cartilage degradation, inflammation, oxidative damage, and energy metabolism. Synovial hypoxia can be linked to pathogenic processes through indirect and direct effects on angiogenesis, oxidative damage, inflammation, cartilage damage, and bone resorption. Studies show that hypoxia and other promoters lead to inflammation in Rheumatoid Arthritis. The metabolic environment in the synovium is modified by hypoxia, and an autoimmune response is initiated by the presentation of the upregulated antigenic enzymes in the context of cellular stress. Hypoxia induces anaerobic glycolytic phenotype in the synovium.

Several of the enzymes induced by this metabolic shift may become antigenic once anaerobic glycolysis is established in the synovium^[27].

The abnormal biomechanics, attendant tissue-derived, and cell-derived factors causes Osteoarthritis (OA). The progression of Osteoarthritis is related to reactive oxygen species (ROS) and oxidative stress. It's a multifactorial and polygenic joint disease. Reactive oxygen species targets the complex oxidative stress signaling pathways as it regulates chondrocyte senescence and apoptosis, extracellular matrix synthesis and degradation, along with synovial inflammation and dysfunction of the subchondral bone, and intracellular signaling processes. Osteoarthritis progresses from silent cartilage destruction to painful presentation. Free radicals

mediate and amplify the sequence of joint degeneration in all tissues affected due to its chemical properties. Free radicals are the crucial factor involved in the inflammatory transformation of Osteoarthritis joints and all joint tissues disease development. 28 Both Osteoarthritis, and Rheumatoid arthritis is caused by reduced oxygen levels from increased consumption by inflammatory cells such as synoviocytes and the oxygen reduced delivery to synovial fluid [108-109].

Gout is a result of the presence of uric acid crystals build up in the joints. The production of uric acid in the joints is increased by the presence of excess carbon dioxide and the lack of presence of oxygen in the lungs [29, 30, 31]. While sleeping the produces less cortisone, an inflammation suppressant, the reduction of cortisone level might be contributing to gout disease [32, 33]. A person may have as much as 50% chance in getting gout disease if they suffer from sleep apnea. 5 Dehydration, loss of water in the body can contribute to the increase in the concentration of uric acid in joint fluids, enhancing the formation of uric acid crystals in the joints, causing gout attacks [32, 34]. Gout is a type of arthritis that is caused by uric acid concentration increase in the blood, it may cause debilitation due to uric acid deposit around tendons and joints. It's the most controllable metabolic disease [100, 101]. Gout is classified into primary and secondary. Primary gout causes are unknown. There are known genetic defects causing elevated uric acid. The increase of uric acid in primary gout can be due to reduced ability to excrete uric acid found in smaller group of patients (30%), increased formation of serum uric acid found in most patients or both which is found in minority of patients. [36].

Rheumatoid arthritis can't be cured by drugs, but it can be treated as it can/will come back. Treatment of rheumatoid arthritis includes using medications to slow the progression of the disease. Drugs including sulfasalazine (Azulfidine), methotrexate (Trexall), and other biologic drugs such as etanercept (Enbrel) and adalimumab (Humira) may be prescribed. Biologic drugs reduce the inflammation by targeting the immune system. Short-term treatment may include low-dose steroids [13]. Rheumatoid Arthritis is a multifactorial disease as both environmental and genetic factors contribute to the disease. Medical therapy is limited in most RA cases, it fails to address the causes of the disease. As in Osteoarthritis, the use of the NSAIDs drugs including aspirin is accompanied by the acceleration of factors that promote the disease process [35]. Examples of drugs currently in use are hydroxychloroquine, penicillamine, methotrexate, gold therapy, azathioprine, and cyclophosphamide. 36 A diet rich in vegetables, fiber, and whole foods, and low in meat, sugar, saturated fat, and refined carbohydrates (Western Diet) prevents the development of Rheumatoid Arthritis disease. Dietary therapy is to follow a vegetarian diet, eliminate food allergies, increase the intake of antioxidants, and alter the intake of fats and oils. Dietary therapy shows a tremendous promise in the treatment of Rheumatoid Arthritis. 37-39 Incomplete digestion may be a major factor in Rheumatoid Arthritis [40, 41]. Gamma-Linolenic acid (GLA) acts as a precursor to an anti-inflammatory prostaglandins' series 1. Studies show that some patients have responded to GLA treatment while others didn't. 42-44 Fish oil supplementation containing Omega-3 Fatty acid shows better and more positive response than GLA in the treatment of Rheumatoid Arthritis [43-50]. Due the neutralization of inflammation and support of collagen structure, dietary antioxidants such as Flavonoids is used in the treatment of Rheumatoid Arthritis. [53] Patients with Rheumatoid Arthritis have low levels of

selenium [54, 55]. Selenium combined with Vitamin E had a positive effect in the treatment of Rheumatoid Arthritis. 56 Zinc levels are commonly low in Rheumatoid Arthritis patients, treatments with zinc supplements in the form of sulfates showed a slight therapeutic effect [57, 58]. Patients with Rheumatoid Arthritis are deficient in manganese containing Superoxide dismutase. The injectable form of the enzyme (antioxidant enzyme Superoxide dismutase (Manganese SOD) available in Europe are effective in the treatment of Rheumatoid Arthritis [59]. Oral administration of SOD showed no effect. 60 Patients with Rheumatoid Arthritis are also deficient in vitamin C. 61 Supplements with vitamin C gives some anti-inflammatory action [62, 63]. Pantothenic acid in blood has shown to be lower in Rheumatoid Arthritis patients. 64 Patients who received 2 g of calcium Pantothenate daily showed improvement. 65 Arthritis patients showed a lower sulfur content of the fingernails. 80, using injectable sulfur alleviated pain and swelling [66, 67]. High dose of Niacinamide (900-4000 mg) has shown good results in the treatment of both Osteoarthritis and Rheumatoid Arthritis. 68,69 The administration of 500 mg of Pantothenic acid shown no effect on treatment of Rheumatoid Arthritis [70].

A vegetarian diet following short-term fasting showed reduction of Rheumatoid Arthritis disease activity [98-99].

Treatment of Osteoarthritis includes prescribing medications called bisphosphonates: risedronate (Actonel), and alendronate (Fosamax). In most Osteoarthritis cases drug treatment has shown to be ineffective and if the failure of nonsurgical treatment is consistent in at least three to six months, surgical replacement of large joints: knee replacement or hip replacement, is needed [13].

The therapeutic goal in the natural treatment of osteoarthritis is to enhance and repair collagen matrix and the regeneration of the connective tissues. It's recommended to lose excess weight causing increase stress on joints, the use of a healthy diet rich in complex carbohydrates and fiber, and to minimize and eliminate the consumption of nightshade vegetables [71]. Nightshade vegetables include potatoes, tomatoes, peppers, tobacco, and eggplants are known to contain alkaloids that promote the inflammatory degradation of the joints and inhibit the normal collagen repair. The high intake of antioxidants is shown to inhibit the progression of the disease and reduce the risk of cartilage loss [72]. As some people age, they lose their ability to manufacture sufficient levels of glucosamine. Glucosamine in form of glucosamine sulfate drug, is used to incorporate sulfur into the cartilages, and stimulate the manufacture of glycosaminoglycans [73, 74]. Chondroitin sulfate is drug that is composed of repeating units of derivatives of glucosamine sulfate attached to sugar molecules and is known to be a less effective drug than that of glucosamine sulfate due to its low absorption 0-13% compared to the solubility of glucosamine sulfate which is 90-98%. [75-77] High dose of Niacinamide (900-4000 mg) has shown good results in the treatment of both Osteoarthritis and Rheumatoid Arthritis. 78,79 Superoxide Dismutase (SOD) injections showed a significant effect in the treatment of osteoarthritis. 80,81 Vitamin E has the ability of stimulate the formation of new cartilage components, inhibit the breakdown of cartilages, and the administration of 600 IU showed significant benefits. 82,83 Vitamin C is like vitamin E, protects and enhances cartilages formation [83, 84, 85]. The administration of a little amount (12.5 mg) of Pantothenic acid is effective in relieving symptoms of Osteoarthritis [86, 87]. Joint degradation is accelerated by the deficiency of one of vitamins: A, B6, Zinc, Copper, and Boron, and

supplementation at appropriate level may promote cartilage synthesis and repair. 36 Niacinamide in high dosage of 900 to 4000 mg per day showed a promising result for the treatment of Osteoarthritis [89, 90].

Treatments of gout Joint disease includes prescribed medications, such as allopurinol and febuxostat [91]. Treatment of sleep apnea that would include continuous positive airway pressure (CPAP) machine or another treatment device to increase oxygen intake while sleeping are used to increased oxygen level and lower uric acid production and reduce the risk of a gout attacks [92]. Decrease the concentration of uric acid, by drinking fluids would increase blood volume lowers the risk of a gout attacks. Other lifestyle changes that may lower the risk of a gout attack include getting regular exercise, eating a plant-based diet that is low in purines and whole foods, and losing excess weight [93, 94]. The standard medical treatment for the disease is the administration of Colchicine, indomethacin, naproxen, fenoprofen or phenylbutazone. The dietary treatment involves fluid intake, low fat, low purine and low protein intake, consumption of complex carbohydrates, elimination of alcohol intake, and achieving the ideal body weight [101, 102, 103]. The natural treatment of gout disease includes the consumption of nutritional supplements: eicosapentaenic acid, vitamin E, folic acid, amino acids such as alanine, aspartic acid, glutamic acid, glycine, and niacin and vitamin C. Eicosapentaenic acid, omega-3 oils are found useful in the treatment of gout joint disease. Vitamin E, it acts as antioxidant and inhibits the formation of leukotrienes 104 Folic acid is known to inhibits the production of uric acid by inhibiting enzyme xanthine oxidase [105]. Alanine, aspartic acid, glutamic acid, glycine, these amino acids are shown to lower serum uric acid level by increasing uric acid excretion. 3 Niacin and Vitamin C, High doses of vitamin C and Niacin are used in the treatment of gout; niacin competes with uric acid in excretion and vitamin C increases the formation of uric acid in small group of people [106, 107].

Conclusion

It has been found that if the ability to breath is obstructed by a pulmonary condition or by physical block limits or by prolonged hypoventilation respiratory acidosis is caused. Three main types of joint diseases were found to be directly related to hypoxia (Low levels of oxygen in your body tissues), hypercapnia (Excessive amounts of carbon dioxide in the blood) and blood PH imbalance: Rheumatoid Arthritis, Osteoarthritis, and gout joint diseases.

Both Osteoarthritis, and Rheumatoid arthritis was found to be caused by reduced oxygen levels from increased consumption by inflammatory cells such as synoviocytes and the oxygen reduced delivery to synovial fluid. Rheumatoid arthritis was found to be directly caused by alterations in tissue oxygen pressure. Osteoarthritis was found to be directly related to aging, as the ability to synthesize and restoring cartilage structure decreases, and the progression of the disease was found to be directly related to the presence of reactive oxygen species and oxidative stress. Gout joint disease was found to be directly caused by the presence of uric acid crystals build up in the joints, and the crystal buildup increased by the presence of excess carbon dioxide.

The natural treatment of both rheumatoid arthritis, and osteoarthritis was found to include minimizing the consumption of nightshade vegetables, and eliminating the use of nonsteroidal anti-inflammatory drugs (NSAIDs drugs) as they cause the degradation of joint cartilages. High dose of

Niacinamide (900-4000 mg) has shown good results in the treatment of both Osteoarthritis and Rheumatoid Arthritis. Vitamin C is like vitamin E supplements has shown good results in the treatment of osteoarthritis and rheumatoid arthritis, and gout joint diseases. It's recommended to increase oxygen intake while sleeping and increase blood volume by drinking fluids to lower the risk of a gout attacks. It's recommended to lose excess weight and maintain a healthy body weight in the treatment of both Osteoarthritis and Gout joint diseases.

The dietary treatment of Rheumatoid Arthritis includes following a vegetarian diet, eliminate food allergies, increase the intake of antioxidants, and alter the intake of fats and oils, dietary treatment of Osteoarthritis includes the use of a healthy diet rich in complex carbohydrates and fiber, to minimize and eliminate the consumption of nightshade vegetables, and to intake antioxidants, and dietary treatment of Gout joint disease includes fluid intake, low fat, low purine and low protein intake, consumption of complex carbohydrates, and elimination of alcohol intake.

The natural treatment of gout joint disease includes the administration of nutritional supplements: eicosapentaenic acid, vitamin E, folic acid, amino acids such as alanine, aspartic acid, glutamic acid, glycine, and niacin and vitamin C, the natural treatment of rheumatoid arthritis disease includes the administration of some nutritional supplements: Omega-3 Fatty acid, Selenium combined with vitamin E, vitamin C, Niacinamide, and Pantothenic acid, and the natural treatment of osteoarthritis disease includes the administration of nutritional supplements: Glucosamine sulfate, Niacinamide, Vitamin E, Vitamin C, small amounts of Pantothenic acid, and Niacinamide.

References

1. Global Climate Change. 10 interesting things about air; c2016. www.climate.nasa.gov. Retrieved May 2022.
2. GDS Team. Understanding Safe Oxygen Levels as Outlined by OSHA in Confined Spaces; c2017. www.gdscorp.com. Retrieved May 2022.
3. Home Particle. How is Oxygen level maintained in Air-Conditioned Room; c2021. www.homeparticle.com. Retrieved May 2022.
4. Brennan D. What's Respiratory Acidosis?, www.webmd.com; c2021. Retrieved May 2022
5. US National Library of Medicine, The Physiological Impact of N95 Masks on Medical Staff; c2005. www.clinicaltrials.gov. Retrieved May 31, 2022.
6. Contreras M, Masterson C, Laffey JG. Permissive hypercapnia: what to remember. *Curr Opin Anaesthesiol*. 2015 Feb;28(1):26-37. [PubMed]
7. Error! Hyperlink reference not valid. What's dyspnea?, www.medicalnewstoday.com, Medical News Today, 2018. Retrieved May 2022.
8. Sheild MJ. Anti-Inflammatory Drugs and their Effects on Catilage Synthesis and Renal Function. *Eur J Rheumatol Inflamm*. 1993;13:7-16.
9. Brooks PM, Potter SR, Buchanan WW. NSAID and Osteoarthritis-Help or Hinderance. *J Rheumatol*. 1982;9:3-5.
10. Newman NM, Ling RSM. Acetabular Bone Destruction Related to Non-steroidal Anti-Inflammatory Drugs, *Lancet*. 1985;2:11-13.
11. Solomon L. Drug Induced Anthropology and Necrosis of the Femoral Head. *J Bone Joint Surg*. 1973;55B:246-51.

12. Ronningen H, Langeland N. Indomethacin Treatment in Osteoarthritis of Hip Joints, *Acta Orthop Scand*. 1979;50:169-74.
13. Lisa Esposito. A Patient's Guide to Bone and Joint Diseases, www.health.usnews.com, U.S. News, 2019. Retrieved May 2022.
14. Pristas A. Blood Oxygen Level: What's all the Hype about?, 2002. <https://www.hackensackmeridianhealth.org/> Retrieved May 2022.
15. Stanfield CL. Principles of Human Physiology 5th edition. Pearson, 2012.
16. Henry W. Experiments on the quantity of gases absorbed by water, at different temperatures, and under different pressures. *Phil. Trans. R. Soc. Lond*. 1803;93:29-43. doi:10.1098/rstl.1803.0004.
17. Brinkman JE, Toro F, Sharma S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Physiology, Respiratory Drive, 2021. [PubMed]
18. Kisaka T, Cox TA, Dumitrescu D, Wasserman K. CO₂ pulse and acid-base status during increasing work rate exercise in health and disease. *Respir Physiol Neurobiol*. 2015 Nov;218:46-56. [PubMed]
19. Katalinić L, Blaslov K, Pasini E, Kes P, Bašić-Jukić N. [Acid-base status in patients treated with peritoneal dialysis]. *Acta Med Croatica*. 2014 Apr;68(2):85-90. [PubMed]
20. Marhong J, Fan E. Carbon dioxide in the critically ill: too much or too little of a good thing? *Respir Care*. 2014 Oct;59(10):1597-605. [PubMed]
21. Cove ME, Federspiel WJ. Venovenous extracorporeal CO₂ removal for the treatment of severe respiratory acidosis. *Crit Care*. 2015 Apr 17;19:176. [PMC free article] [PubMed]
22. Sharma S, Hashmi MF, Burns B. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL); 2021 Aug 30. Alveolar Gas Equation. [PubMed]
23. MacKenzie Burger, Derek Schalle J. Metabolic Acidolysis, National Library of Medicine, www.ncbi.nlm.nih.gov, 2021. Retrieved May 2022.
24. Expert Board. Acidolysis and Alkalosis, www.testing.com, 2022. Retrieved May 2022.
25. Betts JG, Young KA, Wise JA, Johnson E, Poe B, Kruse DH, *et al.* Anatomy and Sociology, OpenStax, 2019. <http://cnx.org/contents/14fb4ad7-39a1-4eee-ab6e-3ef2482e3e22@15.5>.
26. Betts JG, Young KA, Wise JA, Johnson E, Poe B, Kruse DH, *et al.* Anatomy and Sociology, OpenStax, 2019. <http://cnx.org/contents/14fb4ad7-39a1-4eee-ab6e-3ef2482e3e22@15.5>.
27. Quiñonez-Flores CM, González-Chávez SA, Pacheco-Tena C. Hypoxia and its implication to Rheumatoid Arthritis, *J Biomed Sci*. 2016;23(1):62, Doi: 10.1186/s12929-016-0281-0
28. Zahan OM, Serban O, Gherman C, Fodor D. The evaluation oxidative stress in osteoarthritis, *Med Pharm Rep*. 2020 Jan; 93(1):12-22.
29. Neogi T, Chen C, Niu J, *et al.* Relation of temperature and humidity to the risk of recurrent gout attacks. *Am J Epidemiol*. 2014;180(4):372-377. DOI: 10.1093/aje/kwu147
30. Roddy E. Revisiting the pathogenesis of podagra: why does gout target the foot?. *J Foot Ankle Res*. 2011;4(1):13. Published 2011 May 13. PMID: 21569453 Doi:10.1186/1757-1146-4-13
31. Martillo MA, Nazzal L, Crittenden DB. The crystallization of monosodium urate. *Curr Rheumatol Rep*. 2014;16(2):400. PMID: 24357445 doi:10.1007/s11926-013-0400-9
32. Choi HK, Niu J, Neogi T, Chen CA, Chaisson C, Hunter D, *et al.* Nocturnal risk of gout attacks. *Arthritis Rheumatol*. 2015 Feb;67(2):555-62. PMID: 25436096 DOI: 10.1002/art.38917
33. Abhishek A, Valdes AM, Jenkins W, Zhang W, Doherty M. Triggers of acute attacks of gout, does age of gout onset matter? A primary care based cross-sectional study. *PLoS One*. 2017;12(10):e0186096. Published 2017 Oct 12. PMID: 29023487 doi:10.1371/journal.pone.0186096
34. Bouloukaki I, *et al.* Intensive versus standard follow-up to improve continuous positive airway pressure compliance. *European Respiratory Journal*. 2014;44(5):1262-1274. PMID: 24993911 DOI: 10.1183/09031936.00021314.
35. Jenkins R, Rooney P, Jones D, *et al.* Increased Intestinal Permeability for Patients with Rheumatoid Arthritis: A Side Effect of Oral Non-Steroidal Anti-Inflammatory Drug Therapy. *Br J Rheumatol*. 1987;26:103-7.
36. Murray M, Pizzorno J. Encyclopedia of Natural Medicine 2nd edition, 1998. ISBN: 978-0-7615-1157-1
37. Darlington LG, Ramsey NW. Clinical Review: Review of Dietary Therapy in Rheumatoid Arthritis. *Br J Rheumatol*. 1993;30:507-14.
38. Buchanan HM, Preston SJ, Brooks PM, *et al.* Is Diet Important in Rheumatoid Arthritis. *Br J Rheumatol*. 1991;30:125-34.
39. McCrae F, Veerapen K, Dieppe P. Diet and Arthritis, *Practitioner*. 1986;230:359-61.
40. De Witte TJ, *et al.*, Hypochlorhydria and Hypergastrinemia in Rheumatoid Arthritis, *Ann Rheu Dis*. 1979;38:14-17.
41. Henriksson K, *et al.* Gastrin, Gastric Acid Secretion, and Gastric Microflora in Patients with Rheumatoid Arthritis, *Ann Rheu Dis*. 1986;45:475-83.
42. Brzeski M, Madhok R, Capell HA. Evening Primrose Oil in Patients with Rheumatoid Arthritis and Side Effects on non-Steroidal Ant-Inflammatory Drugs. *Br J Rheumatol*. 1991;30:371-2.
43. Blech JF, *et al.*, Effects of Altering Dietary Essential Fatty Acids on Requirements for non-steroidal Anti-inflammatory Drugs in Patients with Rheumatoid Arthritis: A Double-Blinded Placebo Controlled Study. *Ann Rheu Dis*. 1988;47:96-104.
44. Levanthal LJ, *et al.* Treatment of Rheumatoid Arthritis with Gamma-Linolenic Acid, *Annals Int Med*. 1993;119:867-73.
45. Kremer JM, *et al.* Fish Oil Supplementation in Active Rheumatoid Arthritis: A Double-Blinded, Controlled Cross-Over Study, *Ann Intern Med*. 1987;106:497-502.
46. Sperling R, *et al.* Effects of Dietary Supplementation with Marine Fish Oil on Leukocyte Lipid Mediator Generation and Function in Rheumatoid Arthritis, *Arthritis Rheum*. 1987;30:988-97.
47. Cleland LG, *et al.* Clinical and Biochemical Effects of Dietary Fish Oil Supplementation in Rheumatoid Arthritis, *J Rheumatol*. 1988;15:1471-5.
48. Magaro M, *et al.* Influence of Diet with Different Lipid Composition on Neutrophil Chemiluminescence and Disease Activity in Patients with Rheumatoid Arthritis, *Ann Rheu Dis*. 1988;47:793-6.

49. Van H, Der Temple, *et al.* Effects of Fish Oil Supplementation in Rheumatoid Arthritis, *Ann Rheu Dis.* 1990;49:76-80.
50. Kremer JM, *et al.* Dietary Fish Oil and Olive Oil in Patients with Rheumatoid Arthritis, *Arth Rheum.* 1990;33:810-20.
51. Lau CS, *et al.* Maxepa on Non-Steroidal Anti-inflammatory Drug Usage in Patients with Mild Rheumatoid Arthritis. *Br J Rheumatol.* 1991;30:137.
52. Nielsen GL, *et al.* The Effects of Dietary Supplementation with N-3 Polysaturated Fatty Acids in Patients with Rheumatoid Arthritis, A Randomized double-blinded trial. *Eur J Clin Invest.* 1992;22:678-91.
53. Codey V, Middleton E, Harborne JB. *Plant Flavonoids in Biology and Medicine-Biochemical, Pharmacological, and Structure-Activity Relationships* (New York: Alan R. Liss, 1986); V. Codey, E. Middleton, J. B. Harborne, and A. Beretz, *Plant Flavonoids in Biology and Medicine II-Biochemical, Pharmacological, and Structure-Activity Relationships* New York: Alan R. Liss, 1988.
54. Tarp U, *et al.* Low Selenium Level in Severe Rheumatoid Arthritis. *Scandinavian Journal of Rheumatology.* 1985;14:97-101.
55. Munthe E, Aseth J. Treatment of Rheumatoid Arthritis with Selenium and Vitamin E. *Scandinavian Journal of Rheumatology.* 1984;53(suppl):103.
56. Pandley SP, Bhattacharya SK, Sundar S. Zinc in Rheumatoid Arthritis. *Indian Journal of Medical Research.* 1985;81:618-20.
57. Simkin PA. Treatment of Rheumatoid Arthritis with oral Zinc Sulfate. *Agents and Actions (Suppl.).* 1981;8:587-95.
58. Mattingly PC, Mowat AG. Zinc Sulfate in Rheumatoid Arthritis. *Annals of the Rheumatic Diseases.* 1982;41:456-7.
59. Menander-Huber KB. Orgotein in the Treatment of Rheumatoid Arthritis. *Europ J Rheum inflammation.* 1981;4:201-11.
60. Zidenberg-Cherr S, *et al.* Dietary Superoxide Dismutase Does not Affect Tissue Level. *Am J Clin Nutr.* 1983;37:5-7.
61. Mullen A, Wilson CWM. The Metabolism of Ascorbic Acid in Rheumatoid Arthritis, *Proc. Nutr. Sci.* 1976;35:8A-9A.
62. Subramanian N. Histamine Degradation Potential of Ascorbic Acid, *Agents and Actions.* 1978;8:484-7.
63. Levine M. New Concepts in Chemistry and Biochemistry of Ascorbic Acid. *New Engl J Med.* 1986;314:892-902.
64. Barton-Wright EC, Elliott WA. The Pantothenic Acid Metabolism of Rheumatoid Arthritis. *Lancet.* 1963;2:862-3.
65. General Practitioner Research Group. Pantothenic Acid in Rheumatoid Arthritis: Practitioner. 1980;224:208-11.
66. Senturia BD. Results of Treatment of Chronic Arthritis and Rheumatoid Conditions with Colloidal Sulfur, *J Bone Joint Surg.* 1935;16:185-8.
67. Wheeldon K. The Use of Colloidal Sulfur in the Treatment of Arthritis, *J Bone Joint Surg.* 1935;17:693-726.
68. Ransberger K. Enzyme Treatment of Immune Complex Diseases, *Arthritis Rheuma.* 1986;8:16-19.
69. Shapiro JA, *et al.* Diet and Rheumatoid Arthritis in Women: A Possible Protective Effects of Fish Consumption, *Epidemiology.* 1996;7:256-63.
70. Comstock GW, *et al.* Serum Concentrations of Alpha Tocopherol, Beta Carotene, and Retinol Preceding the Diagnosis of Rheumatoid Arthritis and Systematic Lupus Erythematosus, *Ann Rheum Dis.* 1997;56:323-5.
71. Childers NF, Russo GM. *The Nightshades and Health* Summerville NJ: Horticulture Publications, 1973.
72. McAlindon TE, *et al.* Do Antioxidant Micronutrients Protect against the Development and Progression of Knee Osteoarthritis?”, *Arthritis Rheumatism* 39 (1996):648-56.
73. K. Karzel, and R. Domenjoz, Effect of Hexosamine Derivatives and Uronic Acid Derivatives on Glycoaminoglycans Metabolism of Fibroblast Cultures”, *Pharmacology.* 1971;5:337-45.
74. Vidal RR, Plana Y, *et al.* Articular Cartilage Pharmacology: I. *In vitro* Studies on Glucosamine and Non-Steroidal Anti-inflammatory Drugs, *Pharmacol Res Comm.* 1978;10:557-69.
75. Setnikar I, *et al.* “Pharmacokinetic of Glucosamine in Man”, *Arzneim Forsch.* 1993;43(10):1109-13.
76. Biaci A, *et al.* Analysis of Glycoaminoglycans in Human Sera after Oral Administration of Chondroitin Sulfate”, *Rheumatol Int.* 1992;12:81-8.
77. Conte A, *et al.* Biochemical and Pharmacokinetic Aspect of Oral Treatment with Chondroitin Sulfate”, *Arzneim Forsch.* 1995;45:918-25.
78. Kaufman W. *The Common Form of Joint Dysfunction: Its Incidence and Treatment* (Brattleboro, VT: EL Hildreth Co, 1949.
79. Hoffer A. Treatment of Arthritis by Nicotinic Acid and Nicotinamide, *Can Med Assoc J.* 1959;81:235-9.
80. Lund-Olesen K, Menander KB. Orgotein: A new Anti-inflammatory Metalloprotein Drug: Preliminary Evaluation of Clinical Efficacy and Safety in Degenerative Joint Diseases. *Curr Ther Res.* 1974;16:706-17.
81. Huskisson EC, Scott J. Orgotein in Osteoarthritis of the Knee Joint. *Eur J Rheumatol Inflamm.* 1981;4:212.
82. Machtey I, Quaknine L. Toco-phenol in Osteoarthritis: A Controlled Pilot Study, *J Am Ger Soc.* 1978;26:328-30.
83. Schwartz ER. The Modulation of Osteoarthritic Development by Vitamin C and E. *Int J Vit Nutr Res Suppl.* 1984;26:141-46.
84. Bates CJ. Proline and Hydroxyproline and Vitamin C Status in Elderly Human Subjects. *Clin Sci Mol Med.* 1977;52:535-43.
85. Prins AP, Lipman JM, McDevitt CA, Sokoloff L. Effect of Purified Growth Factors on Rabbit Articular Chondrocytes in Monolayer Culture, *Arthr Rheum.* 1982;25:1228-32.
86. Anand JC. Osteoarthritis and Pantothenic Acid. *J Coll Gen Pract.* 1963;5:136-37.
87. Anand JC. Osteoarthritis and Pantothenic Acid. *Lancet.* 1963;2:1168.
88. Kaufman W. *The Common Form of Joint Dysfunction: Its Incidence and Treatment* (Brattleboro, VT: E.L. Hildreth Company, 1949.
89. Hoffer A. Treatment of Arthritis by Nicotinic Acid and Nicotinamide. *Canadian Medical Association Journal.* 1959;81:235-9.
90. Efthimiou Petros. *Absolute Rheumatology Review* 2020. 10.1007/978-3-030-23022-7.
91. Zhang Y, Peloquin CE, Dubreuil M, *et al.* Sleep Apnea and the Risk of Incident Gout: A Population-Based, Body Mass Index-Matched Cohort Study. *Arthritis Rheumatol.*

- 2015;67(12):3298-3302.
PMID: 26477891 doi:10.1002/art.39330
92. Giles TL, *et al.* Continuous positive airways pressure for obstructive sleep apnoea in adults. Cochrane Database of Systematic Reviews (3). PMID: 16437429. DOI: 10.1002/14651858.CD001106.pub2
93. Neogi T, Chen C, Niu J, *et al.* Relation of temperature and humidity to the risk of recurrent gout attacks. *Am J Epidemiol.* 2014;180(4):372-377. DOI: 10.1093/aje/kwu147
94. Ball D, Key J. *Introductory Chemistry 1st Canadian Edition*, 2014, ISBN: 978-1-77420-002-5.
95. Concoa Gas Controls, 2012, Oxygen (O₂), www.concoa.com. Retrieved May 2022.
96. Engineering Tool Box. Carbon dioxide - Density and Specific Weight vs. Temperature and Pressure, 2018. [online] Available at: https://www.engineeringtoolbox.com/carbon-dioxide-density-specific-weight-temperature-pressure-d_2018.html. Retrieved May 2022.
97. Skoldstam L, Larsson L, Lindstorm FD. Effects of Fasting and Lactovegetarian Diet on Rheumatoid Arthritis. *Scand J Rheumatol.* 1979;8:137-44.
98. Hafstrom I, *et al.* Effects of Fasting on Disease Activity, Neutrophil Function, Fatty Acid Composition, and Leukotriene Rheumatoid Arthritis, *Arthr Rheum.* 1988;31:585-92.
99. Petersdorf R, *et al.* eds., *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill, 1983.
100. Krause MV, Mahan LK. *Food, Nutrition, and Diet Therapy*, 7th edition, (Philadelphia: W.B Saunders, 1984, 677-9.
101. Nutrition Foundation, *Present Knowledge in Nutrition*, 5th edition (Washington D.C.: Nutrition Foundation, 1984, 740-56.
102. Pi-Sunyer FX. The Fattening of America, *JAMA.* 1994;272:238.
103. Panganamala RV, Cornwell DG. The Effect of Vitamin E on Arachidonic Acid Metabolism. *Ann NY Acad Sci.* 1982;393:376-91.
104. Lewis AS, Murphy L, McCalla C, *et al.* Inhibition of Mammalian Xanthine Oxidase by Folate Compounds and Amethopterin, *J Biol Chem.* 1984;259:15-5.
105. Bindoli A, Valentine M, Cavallini L. Inhibitory Action of Quercetin on Xanthine Oxidase and Xanthine Dehydrogenase Activity, *Pharm Res Comm.* 1985;17:831-9.
106. Gershon SL, Fox IH. Pharmacological Effects of Nicotinic Acid on Human Purine Metabolism, *J Lab Clin Med.* 1974;84:179-56.
107. Levick JR. Hypoxia and acidosis in chronic inflammatory arthritis; relation to vascular supply and dynamic effusion pressure. *J Rheum.* 1990;17(5):579-582.
108. Biniecka M, Kennedy A, Fearon U, Ng CT, Veale DJ, O'Sullivan JN. Oxidative damage in synovial tissue is associated with *in vivo* hypoxic status in the arthritic joint. *Ann Rheum Dis.* 2010;69(6):1172-1178.