



Case Study

Chronic Kidney Disease Reversal: Case Study

Rainey JT*, Vander Stoep C and Holley M

Texas Institute for Advanced Dental Studies, Mouth Matters Book, International Hyperbaric Medical Foundation, USA

Received: 26 October, 2024

Accepted: 18 November, 2024

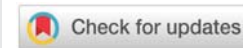
Published: 19 November, 2024

*Corresponding author: Rainey JT, Texas Institute for Advanced Dental Studies, Mouth Matters Book, International Hyperbaric Medical Foundation, USA, E-mail: drainey@jtimrainey.com

ORCID: <https://orcid.org/0000-0002-6098-1387>

Keywords: Chronic Kidney Disease (CKD); Cardiovascular Disease (CVD); Systemic ozone therapies; Malignant hypertension; Kidney dysfunction

Copyright License: © 2024 Rainey JT, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

<https://www.organsciengroup.com>

Abstract

Chronic Kidney Disease (CKD) and its primary cause, Cardiovascular Disease (CVD) with its multiple risk factors, are not necessarily the irreversible diseases most medical practitioners claim they are. By implementing an anti-inflammatory lifestyle, in particular, a diet tweaked by close observation, and then introducing routine systemic ozone therapies plus ingestion of C₆₀ chased by supersaturated hydrogen water daily, this case study follows the treatment plan in a 79-year-old male to illustrate how the glomeruli filters of the kidney will begin to improve their performance along with control of CVD. Nocturnal Fluctuating Blood Pressure is a classic presentation of Malignant Hypertension, characterized by systolic blood pressure >180 mm Hg and diastolic blood pressure > 120 mm Hg in hypertensive crisis. By careful real-time monitoring and feedback, the triggers of nocturnal blood pressure spikes were identified and when the triggers were avoided, the hypertension-induced arterial wall hypertrophy contributing to the high blood pressure decreased. This technique resulted in the normalization of blood pressure to low normal ranges over diurnal cycles, minimizing a key threat contributing to kidney dysfunction.

Introduction

Prevention is primary for health maintenance but, irrespective of events of the past, it is never too late to intercede by making better health choices and initiating proactive steps to improve outcomes. Once a health challenge is recognized, the first step in mitigation is to sort out the etiologies and then to moderate or eliminate causality. Many of these steps are logical and well-known, such as alcohol avoidance, daily exercise, a clean and thoughtful anti-inflammatory diet that controls weight and supports health, restful sleep, and avoidance of exogenous chemical exposures. Changing predictable and inevitable negative health consequences of a status quo lifestyle and typical diets always involves a commitment to not just changing habits we know are harmful, but also to discovering and embracing consequential and emerging information that challenge existing paradigms.

By focusing on the mitigation and reversal of a disease state that one initiated, has long been deemed irreversible, with a continual decline in kidney function to inevitable failure, and that proper pharmacological control of CKD can, at best, slow the inevitable decline. As with all diseases, a plethora of etiologies and pathophysiologies can contribute to kidney failure. Sometimes physical trauma to the kidneys, polycystic kidney disease, and/or genetics initiate renal dysfunction. The traditional risk factors of cardiovascular disease in CKD, high blood pressure, atherosclerosis, and diabetes are the most common factors. Later in the kidney degenerative process, inflammation, oxidative stress, uremia, anemia and non-atherosclerotic cardiovascular events like arrhythmias, hemorrhagic stroke, and left-ventricular hypertrophy play increasingly larger roles.

The interplay between cardiovascular disease, multi-



system inflammation, obesity, diabetes, periodontal infections, and commonly used nephrotoxic drugs, such as NSAIDs, are intricately intertwined, leading to decreased Glomerular Filtration Rate (GFR) by causing immune-mediated and/or hemodynamically-mediated acute kidney injury. An example of immune-mediated injury is caused by reduced renal plasma flow. An acute bacterial, fungal, or viral infection can trigger Acute Tubulo-Interstitial Nephritis, such as the well-documented cytokine storm from SARSCoV-2, initiating immune-mediated acute kidney injury. Long-term use of NSAIDs can modify this dynamic from Acute Kidney Disease (AKD) to CKD [1,2].

The first step in controlling any disease is to identify the underlying etiologies. Knowing one marker for CKD, a rise in creatinine blood levels, and then choosing to treat the symptoms of the lower eGFR% numbers it portends with drugs will not reverse the disease. For success, it is important to identify all of the threats and remove them while also upregulating all the biological systems that define health. Yes, hypertension drives many metabolic byproducts that block the kidneys' glomeruli and yes, Reactive Oxidative Species (ROS) and Reactive Nitrogen Species (RNS) are contributing factors. Weekly administration of systemic ozone therapy and eventual daily ingestion of buckminsterfullerene, an allotrope of carbon called C₆₀, in conjunction with a supersaturated cocktail of hydrogen water was chosen to test the hypothesis that, by judiciously administering these carefully selected agents in combination, recalcitrant eGFR% would increase significantly. C₆₀ exponentially increases the antioxidant potential of the hydrogen water.

A blood test included in commonly ordered Complete Metabolic Panels offers an accurate kidney function report shown as a percentage of function. It is called the, "estimated Glomerular Filtration Rate," given as a percentage (eGFR%), though in lab reports the "percent" sign seldom follows the number. If it did, perhaps more people would realize the significance of the number and take positive steps to reverse the function of their kidneys. This scale is titrated with 100 being the full 100 percent function most persons are born with, but which declines with age as do all other human systems. An eGFR% of 0 means complete kidney failure. In 2021, the nephrology industry adopted guidelines redefining the various stages of CKD. At that time, a 42 eGFR% (current Stage 3B or moderate CKD) was the trigger for diagnosing CKD. Unfortunately, this deprived most CKD sufferers of an awareness that their kidneys were already in serious decline.

In fact, this lack of awareness heightens the morbidity and mortality of CKD because, as a function of the longer the time spent in each stage of CKD before commencing dialysis, the longer the exposure to the risk factors, therefore the greater accumulated damage and overall risk. The cardiovascular system and the kidneys are inextricably linked. CVD mortality risk doubles and triples in CKD Stages 3 and 4, respectively.

Specific to this case study, it is important to catch CKD in the early stages when atherosclerosis and its accompanying hypertrophy of blood vessel walls is the major contributor to

CKD advancement. As CKD progresses, non-atherosclerotic causes contribute more than the atherosclerotic cause. In late-stage disease, uremia, anemia, inflammation, and oxidative stress emerge as the greater renal stressors.

CVD and CKD are silent epidemics in their early stages of development, CDC statistics show an alarming number of people in the US, both diagnosed and undiagnosed. In the United States in 2021:

- More than 1 in 7 US adults, about 37 million people or 15%, are estimated to have CKD.
- As many as 90% of adults with CKD do not know they have it.
- About 33% of adults with severe CKD do not know they have it.

These numbers increase annually. Many other countries have significantly higher rates of CKD. CKD contributes to statistically shortening the life expectancy of males throughout the Third World.

Chronic Kidney Diseases are described by gradual kidney function loss; the kidneys become less and less capable of filtering toxic wastes from blood or removing excess fluids, both essential life functions (Table 1).

As noted, conventional medicine generally holds that damage from CKD cannot be undone and that it is progressive and terminal, culminating in end-stage kidney disease which requires dialysis, that is, artificial blood filtering, typically three times a week until (or if) a donor's kidney is successfully transplanted. Regardless, life expectancy is shortened by CKD by varying amounts.

Kidneys, in function or disease, are illustrative of just how integrated our bodies are. No singular physiological system is separate from the other systems. Neither CKD nor any other of the inflammatory diseases has to be a life sentence. High blood pressure, inflammation, oxidative stress, and the resulting cascade of diseases they cause can be reversible, including CKD and CVD. Normalizing bodily systems to baseline is key to solving underlying causes of inflammatory diseases. Normalizing them occurs concurrently via their common underlying repair mechanisms, i.e., each person must regulate grouped biological systems simultaneously, *not* sequentially.

Table 1: The estimated GFR for the five stages of Chronic Kidney Disease (CKD).

Stages OF CKD based on estimated GFR		
GFR		Stage of Kidney Disease
90 ml/min above	and	Stage 1 Kidney Disease with normal or high GFR
60-89 ml/min		Stage 2 Kidney Disease (mild)
45-59 ml/min		Stage 3A Kidney Disease (Moderate)
31-44 ml/min		Stage 3B Kidney Disease (Moderate)
15-29 ml/min		Stage 4 Kidney Disease (Severe)
Less than ml/min	15	Stage 5 Kidney disease (End Stage renal Disease – ESRD)



The biological systems are:

- 1) Adrenal glands (neuroendocrine feedback loops, primary hyperaldosteronism)
- 2) Liver
- 3) Kidneys
- 4) Nerve/brain complex (neurological system)
- 5) Immune system including the lymphatic system
- 6) Digestive tract
- 7) Metabolism (the sum of all body processes)
- 8) Hormones
- 9) Musculoskeletal

Many powerful bioregulation therapies are available to normalize biological systems. What's more, these healing therapies are simpler, nontoxic, less invasive, and far more cost-effective than traditional medical solutions that are expensive, toxic, more invasive, and geared towards ameliorating symptoms but do little to eliminate root causes.

First and foremost, excellent sleep hygiene, including effective treatment for sleep apnea if present, is a critical pillar of reversing inflammation. Without uninterrupted sleep, healing of any sort is almost impossible, like rolling a boulder uphill. This is true even when a person employs good stress relief strategies, excellent physical fitness regimens, and a proper diet. As a fundamental pillar of health, neurometabolic waste byproducts are drained via the glymphatic system, apoptosis eliminates improperly functioning and improperly transcribed cells, autophagy breaks down and recycles nutrients, and cell regeneration occurs primarily during sleep, especially Stages III and IV slow-wave sleep. Without restful sleep, these accumulate in the organs, causing neurotoxic and cytotoxic compounds, literally poisoning the body. Four critical downsides to interrupted sleep that directly affect kidney function are:

- 1) Every awakening prompts a surge of cortisol, the ultimate stress hormone, the secretion of which spikes blood sugar, increases heart rate and elevates blood pressure. Chronic hypertension is the second leading contributor to kidney disease, but it does not occur in a vacuum.
- 2) Frequent awakenings block Antidiuretic Hormone (ADH) production. ADH helps regulate body fluids and minerals by controlling the amount of water kidneys reabsorb or flush out in urine as they filter waste from the blood which is associated with kidney health. Inhibition of ADH flushes minerals from the body, resulting in electrolyte imbalances, dehydration, and dysregulation of ion channels.
- 3) Sleep disorders, especially obstructive sleep apnea, can contribute to CKD through a direct effect of intrarenal

hypoxia on the kidney and activation of the intrarenal Renin-Angiotensin System (RAS). Intrarenal RAS is activated by high blood pressure. It amplifies the Ang II peptide that perpetuates vasoconstriction, antinatriuresis, and chronic hypertension. Secretion of Atrial Natriuretic Peptide (ANP), insulin, and NSAIDs, provoke antinatriuresis, or sodium retention, causing edema (tissue swelling) and elevating blood pressure.

- 4) As insomnia and renal disease often go hand in hand, melatonin production is severely impaired when a person has advanced renal disease. A 2007 experiment in rats with reduced renal mass showed that melatonin not only reduced proteinuria and creatinine (a marker for kidney disease) but significantly slowed kidney deterioration that happens because of glomerulosclerosis and tubular damage from Reactive Oxygen Species (ROS). The pineal gland begins secreting melatonin when the environment becomes dark and peaks between 2-4 AM as long as a person experiences uninterrupted sleep in a completely darkened environment. One of melatonin's functions is to initiate and maintain sleep. It also exerts strong antioxidant effects through direct and indirect mechanisms that make it a powerful protector against highly toxic oxygen-derived and nitrogen-derived free radicals whose reduction is especially important for those with CKD, therefore a solid 7-8 hours of uninterrupted sleep while nasal breathing is a primary key to normalizing body functions, especially those with CKD.
- 5) Studies show that nocturnal dips and spikes in cortisol levels cause corresponding dips and elevations in nocturnal blood pressure [3].

Other bioregulation strategies revolve around various ways to increase cellular mitochondrial numbers and Adenosine Triphosphate (ATP), a nucleoside triphosphate, output while avoiding excessive oxidative stress. Optimal health depends on the ability of cellular mitochondria to make, store, and release energy as flows of ions across cell membranes the body needs to power neuromusculoskeletal processes and metabolic functions. Sick people have a low energy output, often as low as two ATP energy units per mitochondria, compared to healthy people who have a robust energy output of up to thirty-six units per mitochondria. Reverting to anaerobic glycolysis, even in the presence of oxygen, is a metabolic process that produces lactate, which produces only 2 molecules of ATP per molecule of glucose, in stark contrast to aerobic respiration which produces 34 molecules of ATP per molecule of glucose. This is referred to as the Warburg Effect, a classic hallmark of cancers [4]. Altered metabolism results in the excess production and flood of free radicals. Even worse, excessive ROS in the presence of highly inflammatory Inducible Nitric Oxide Synthase (iNOS) results in the formation of Reactive Nitrogen Species (RNS), especially the cytotoxic ONOO⁻, with increased formation under hyperglycemic conditions and/or endothelial dysfunction. iNOS expression is increased by inflammatory signaling and epigenetic dysregulation [5]. Lifestyle-acquired



diabetes is a classic case of an acquired mitochondrial disorder, hence metabolic syndrome.

Cellular energy is essential for a body's self-repair mechanisms. This is why energy medicine is a critical health component. The nervous system, every cell's transport system, circulatory system, and muscles are examples of electrically-driven sub-systems operating within a bioelectrical body. Examples of energy medicine are pulsed electromagnetic field therapy; near-infrared saunas; far-infrared saunas; and, red light therapies of various wavelengths within the spectrum.

Oxygen therapies are other pH-related tools used to regularize body systems and health. Oxygen therapy is an umbrella term for multiple types of closely related leading-edge therapies that promote healing by flooding the body with oxygen. The focus of this case study demonstrate the effectiveness of ozone therapy in reversing CKD. Ozone therapy is the most highly oxidative oxygen therapy, having an oxidation potential of 2.076v. Ozone reacts with water to form hydroxyl ions, whose rate increases as pH increases in alkalinity, possessing an even higher potential energy of 2.7v. Because of its efficacy and the applied therapy being much more economical; ozone therapy was eventually chosen as one of the main modulators of kidney disease in this case study.

These therapies are seldom discussed in the US because they are not profitable for the pharmaceutical industry, an industry that dominates mainstream medicine in the United States. Nonetheless, ozone is part of the established healthcare system in many parts of the world. Cuban doctors use it to treat at least fifty different disorders and in Germany, health insurance covers ozone therapies. In one of many US medical practices focusing on ozone therapy, stunning successes were demonstrated in treating COVID and other maladies, with some 300 high-risk COVID cases treated in a row with zero fatalities. Initial statistical COVID death rates were approximately 15%, varying by age and comorbidities. Without prompt and effective treatment, some 45 of these 300 people may have died.

There is a logical reason why ozone therapies can treat deep-seated lung diseases like Covid, mycoplasma, tuberculosis, and both viral, bacterial, and fungal pneumonia, being especially effective in controlling antimicrobial-resistant organisms [6]. Systemic modes of ozone therapy, such as Major Autohemotherapy (MAH) and direct intravenous ozone (DIV O₃), are accompanied by some off-gassing of ozone into the alveoli, killing any pathogens blocking the proper function of the alveoli and regulating ROS there, thereby preventing death from COVID-related latent pulmonary bacterial infections. Meanwhile, the FDA continues to state on its website, "There is no known medical use for Ozone," despite nearly 200 peer-reviewed articles and widespread acceptance and common usage in many European nations.

The constellation of interrelated chronic inflammatory diseases discussed in this paper is characterized by oxidative stress and body function dysregulation. As one example, cells produce energy by burning sugar in the presence of oxygen.

The waste products are carbon dioxide and water. If cells are deficient in oxygen, the reaction is incomplete, forming carbon monoxide and lactic acid. Carbon monoxide poisoning can cause death because carbon monoxide bonds covalently with hemoglobin to form methemoglobin, causing tissue hypoxia across the entire body. Organs and fluids within and in between cells are oxygen-starved. Everything becomes clogged like a clogged oil filter. It is a downward spiral because of course, more oxygen is needed to oxidize these toxins that build up yet prevent its delivery. This is partly how kidney glomeruli become sludgy and clogged as lymph and blood become dirtier and dirtier.

Eventually, toxins are deposited in the fat, and weight increases. Free radicals proliferate as toxins interfering with the normal neutralizing enzyme mechanisms. When tissues and organs are hypo-oxygenated, kidney disease and cancer are just two of the resultant disease outcomes.

As Dr. Stephen Levine, renowned molecular biologist and author of *Oxygen Deficiency: A Concomitant to All Degenerative Illness* says:

"In all serious disease states, we find a concomitant low oxygen state ... Low oxygen in the body tissues is a sure indicator for disease... Hypoxia, or lack of oxygen in the tissues, is the fundamental cause for all degenerative disease".

Background: Oxygen therapy and rationale for its use in this study

The following extensive, yet incomplete list of ozone's health benefits is taken from Vander Stoep's book *Primal Dentistry: Less Is More* in 2018 [7]. It illustrates how ozone therapies address the many underlying causes of CKD and other inflammatory diseases and why ozone therapy was chosen for CKD treatment for this patient:

- 1) Ozone helps the biological system repair faster because it normalizes NAD to NADH ratios. NAD (nicotinamide adenine dinucleotide) is a linchpin of energy metabolism. It has been called the "Fountain of Youth" gene. NAD and NADH control nearly every aspect of metabolism. Blood sugars can't enter mitochondria to produce energy without NAD. If a person has plenty of it, they have boundless energy. If too much NADH is present, that person slows down. The optimum ratio of NAD/ NADH is 700/1. The ratios should be optimal or various body systems start falling apart. The older a person is, the more this ratio is skewed, and the harder they have to work to change their NAD/NADH ratio.
- 2) Ozone reduces lactic acid build-up, which changes a body's NAD/NADH ratio. It is the kidney's job to remove excess lactic acid, but if there are excessive levels, the organs are impaired, or both, they can't keep up, and lactic acid builds in the blood and tissues. It is more serious when the body persistently produces too much lactic acid, or the liver and kidneys are consistently functioning too poorly to process lactic acid. As blood



lactate levels continue to rise and pH levels fall, cardiac output is increasingly suppressed. This can lead to organ failure and death.

- 3) Related to lactic acid build-up, ozone increases the efficiency of the antioxidant enzyme system, which scavenges excess free radicals in the body including the kidneys, while at the same time it conquers oxidative stress. This ability is also key when detoxing heavy metals like mercury, another contributor to CKD. A small, acute oxidative stress provokes a strong antioxidant response. This is important for everyone, but diabetics should take special note, since diabetes is a classic scenario of excessive oxidative stress and is the primary cause of CKD. An example is the enzyme Superoxide Dismutase (SOD). SOD and other antioxidant enzymes recycle antioxidants so a person receives greater benefit from their diet and nutrition. SOD normalizes organic peroxide (-O-O-) levels, which directly affect blood sugar levels. Increasing SOD enzyme levels also improve tissue and cell oxygenation because SOD decreases lactic acid via accelerated oxidative mitochondrial phosphorylation. SOD also helps control the elevated lactic acid levels that occur with impaired liver and kidney function. Ozone upregulates other antioxidant enzymes, among them, glutathione peroxidase, and catalase. This protective balance provides the key to why healthy human cell walls do not oxidize in the presence of ozone and why ozone protocols benefit healthy cells instead of harming them. It is no different from that which we know of exercise.
- 4) Kidney disease is associated with inflammation and oxidative stress, but also Nitric Oxide (NO) and Glutathione (GSH) deficiencies. Glutathione benefits health in multiple ways. In and of itself, it is the body's master antioxidant, regulating other antioxidants to perform at peak efficiency. Proper antioxidant activity is critical to all tissues and organs, but especially the kidneys and liver since they are the sites for clearing most waste and toxins from the body. Numerous studies show low GSH levels in the kidneys of patients with acute kidney failure. These low levels of GSH allow excessive oxidative stress, leading to kidney failure. Low GSH levels are also associated with other chronic pro-inflammatory conditions, such as metabolic syndromes, CVD, liver disease, neurodegenerative syndromes, and autoimmune diseases. GSH regulates the receptors of various amino acids, such as vitamins D, E and C, and detoxifies drugs and other toxins. It binds directly to toxins like organic and inorganic cancer-causing agents, mold toxins, and heavy metals, physiologically chelating them for elimination via urine and bile. For example, two glutathione molecules remove one atom of mercury, which requires both Phase I and Phase II of the detoxification for which the liver is responsible.
- 5) Glutathione plays a direct protective role in mitochondrial metabolism by neutralizing the free

radicals (ROS) formed during the Electron Transport Cycle (ETC) of ATP generation. Glutathione peroxidase reduces inflammatory mediators. For instance, GPX7 can reduce oxidative stress generated from polyunsaturated fatty acid metabolism. Lipid peroxidation of fats leads to decreased ATP production and lipid deposition which in turn contributes to chronic kidney disease development and ultimately, renal failure.

- 6) Kidneys are at risk when the body carries an excessive heavy metal load, which the kidneys and liver help expel. Ozone therapy is a perfect adjunct for heavy metal detoxing for healthier kidneys. The liver and kidneys work together and can be thought of as the body's "oil filters". Ozone oxidizes heavy metals, such as arsenic, lead, and mercury, making them easier to eliminate. When detoxing mercury or other heavy metals, ozone therapy helps maintain the integrity of these two critical organs. Ozone neutralizes many other toxins in these organs as well. Mercury inactivates critical sulfur-containing antioxidants like NAC, Alpha-Lipoic Acid (ALA), and Glutathione, seriously curtailing antioxidant defense systems and increasing body-wide oxidation and inflammation.
- 7) Ozone enhances the oxidative carboxylation of pyruvate to activate the Krebs cycle, resulting in a greater amount of energy production from mitochondrial respiration.
- 8) Ozone is an adaptogen, balancing the immune system's proinflammatory/antiinflammatory responses by either suppressing or encouraging the response, seeking homeostasis. In other words, where tissues are unnecessarily inflamed, ozone will dampen inflammation to allow healing. Where the immune system response is too weak, such as in cancer, AIDS, or chronic infections, ozone can help improve immunological response to facilitate healing.
- 9) Ozone enhances tissue oxygenation because it improves oxygen transport mechanisms, increasing the ability of red blood cells to release oxygen near tissues that need it most via 2,3-Diphosphoglyceric Acid up-regulation. If red blood cells cling too tightly to their oxygen payload and fail to fully and timely release the oxygen, tissues will be hypoxic irrespective of blood serum levels of oxygen.
- 10) Ozone improves blood flow because it increases red blood cell flexibility. Red blood cells (RBC) have to flex to get through the capillaries that are smaller than they are. When ozonated, they carry a higher negative electrical charge, so they repel each other (higher zeta potential) instead of stacking together like a stack of coins, called Rouleaux formation. Stacking means blood is sticky and thick and is more prone to clotting. Not only does ozone help to control Rouleaux formation, but also confers better oxygen-carrying capacity to the RBC.
- 11) Ozone helps blood flow better also because it dilates blood vessels by inducing the synthesis and



secretion of prostacycline, relieving angina pain via a cyclooxygenase-2 dependent mechanism [8].

- 12) Ozone promotes white blood cell production, increasing the rate of healing and fighting infections [9].
- 13) Ozone activates Nuclear Factor Erythroid 2 (NRF2), a basic leucine zipper protein that elicits a strong antioxidant response. The NRF2 pathway is the body's primary cellular defense against oxidative stress, guarding against inflammatory diseases. NRF2 regulates an entire family of detoxification and chemical protection genes.
- 14) Ozone mobilizes stem cells by inducing Nitric Oxide (NO) synthase, which promotes tissue regeneration.

One of the most important principles when treating disease with ozone (O₃) gas is paying close attention to the strong dose-dependent pharmacological curve to determine maximum efficacy for the target condition. In a study intending to demonstrate ozone therapy benefits for those with Rheumatoid Arthritis (RA), a highly inflammatory autoimmune disease, ozone gas was administered in concentrations of 60–80 µg/mL. Rather than regulating the immune system and increasing SOD, NRF2, GSH, and decreasing inflammatory cytokines, a biphasic role was found, but high doses blocked the bioregulation. Ozone therapy to treat RA was abandoned until further studies showed low-dose ozone ranges were effective, demonstrating hormesis. More study on dosing is needed to define maximum efficacy for each target condition.

In 2021, Renate Viebahn-Haensler and Olga Sonia Leon Fernandez undertook another experiment in line with a lower dose protocol that demonstrated a highly effective low dose range of 20–30 µg/mL, but with a maximum of 40 µg/mL using two routes of administration:

- Major Autohemotherapy (MAH) at a dose of 1000–1500 µg, maximum of 2000 µg per treatment
- Rectal insufflation 5 times per week with a volume of 150–300 mL, scaled up 5µg/mL increments per week from 25–40 µg/mL for a total of 20 weeks [10].

The authors clearly elucidate ozone's role in bioregulation as they demonstrate ozone therapy's powerful effect once again on a classic model of chronic inflammation, (RA). RA, in preclinical and clinical trials, reflects the pharmacology of ozone in a typical manner:

- Ozone peroxides restore redox signaling and improve antioxidant capacity. SOD (superoxide dismutase), CAT (catalase), and finally GSH (reduced glutathione) increase, followed by a significant reduction of oxidative stress as antioxidants are upregulated and inflammatory cytokines are downregulated.
- Used systemically, “ozone peroxide” is directly reduced by the glutathione system, acting as a signaling molecule for nuclear factors to start the regulation. The

GSH/GSSG balance outlines the ozone dose and tissue concentration as the limiting factor. Accordingly, the clinical status improves with judicious dosing [10].

The pharmacological background of ozone therapies has been investigated in a remarkable number of cell experiments, preclinical and clinical trials and is well documented and published in internationally peer-reviewed journals [10]. An excellent article published in 2007 by Irfan Rahman, et al. [11] discusses how systemic system ozone therapies upregulate pathways via antioxidant enzyme recycling:

“In systemic [ozone] treatments, the indirect, ionic mechanism is to be discussed: “ozone peroxide” will be directly reduced by the glutathione [GSH] system, informing the nuclear factors to start the regulation. The GSH/GSSG balance outlines the ozone dose and concentration limiting factor. Antioxidants are regulated, and in the case of inflammatory diseases upregulated; cytokines are modulated, here downregulated. Rheumatoid arthritis RA as a model for chronic inflammation: RA, in preclinical and clinical trials, reflects the pharmacology of ozone in a typical manner: SOD (superoxide dismutase), CAT (catalase) and finally GSH (reduced glutathione) increase, followed by a significant reduction of oxidative stress. Inflammatory cytokines are downregulated. Accordingly, the clinical status improves. The pharmacological background investigated in a remarkable number of cell experiments, preclinical and clinical trials is well documented and published in internationally peer reviewed journals. This should encourage clinicians to set up clinical trials with chronic inflammatory diseases integrating medical ozone as a complement.

Medical ozone at low concentration and dosage in the form of “ozone peroxide” replaces the biological redox and immune regulation of hydrogen peroxide. This is of special interest in chronic inflammatory diseases with high oxidative stress, antioxidant deficiency, and immune imbalance, a condition in which biological regulation is largely disrupted.”

“*The Protective Role of Ozone Therapy in Kidney Disease: A Review*, by Life,” [12] in 2023 was the first to report that ozone therapy could improve chronic tubulointerstitial injury and exert renoprotection effect by restoring impaired NRF2 activation and down-regulating NF-κB activation in rats with adenine-induced CKD. This also applies to generalized inflammation including damage to blood vessel walls.

As the study reported, “Therapeutic effects commonly observed in the kidney after the administration of O₃ administration include amelioration of renal function, measured through plasma clearance of endogenous metabolites, blood urea nitrogen (BUN), and serum creatinine (SCr)”. Further:

- 1) O₃ therapy has been reported to decrease morphological damage mainly evidenced under photon microscopy, including medullary hemorrhage, tubular necrosis, glomerular damage, collagen deposition, and fibrosis markers, such as α-smooth muscle actin (αSMA) and TGF.



- 2) O₃ therapy reduces inflammation, as evidenced by a diminished expression of cytokines, such as IL, TNF- α , monocyte chemoattractant protein-1 (MCP-1), and intercellular adhesion molecule-1 (ICAM-1), as well as the toll Like receptor 4 (TLR 4)-NF κ B pathway.
- 3) Another therapeutic effect is the diminishment of lipid peroxidation, which represents the oxidative stress induced by polyunsaturated fatty acids. A useful marker to quantify this is via malondialdehyde (MDA), which diminishes its renal expression when treated with O₃.
- 4) Studies revealed that impaired NRF2 activation, which results in a diseased antioxidative system and oxidation-mediated injury, is one of the critical causes that lead to chronic tubulointerstitial injury in CKD.

Case presentation

The male subject in the instant case study was 79 years old when first diagnosed on September 28, 2022, with CKD Stage 3A, mild to moderate kidney disease with eGFRs% between 45% - 59%. At that time his eGFR% was 53 and dropped into the low 40's immediately after diagnosis. Earlier labs showed his eGFR% had been in the 50-59 range since a lab report dated 08/2014. The normal range for a 77 yo male is 75-85 eGFR%. Throughout that time subject's albumin/globulin ratio ranged between 1.68-1.98, with 1.0 to 2.0 being the normal range.

Comorbidities were malignant hypertension that was recorded as high as 225/132, mild prediabetes with blood sugar control over time showing HbA1c of 5.6-6.2, and chronic sleep maintenance difficulties. The subject reported a lifelong pattern of awakening at 2 AM. He would often work for a time on a computer screen before going back to sleep, noting that his blood pressure spiked \sim 160/ $>$ 100 and most of the spikes were observed to be nocturnal. Further complications that contributed to his CKD were at least two incidents of atrial fibrillation and three episodes of deep vein thrombosis.

Creatinine levels tended towards elevation and inversely mirrored eGFR as is common in CKD. Anything impairing kidney function usually raises creatine blood levels. Normal levels for men over age 16 are 0.8-1.3 mg/dL. Since 2014, the patient's creatinine levels have usually been out of the normal range from 1.4 to 2.1.

Upon diagnosis of Stage 3 CKD, the subject immediately cleaned up his diet and despite conflicting recommendations from his medical specialists, continued to experiment with his Blood Pressure (BP) medications. Being a medical professional, the subject understood the risks and ramifications of this diagnosis. Monitoring BP during his nocturnal awakenings, the subject realized one of the culprits of his CKD might be nocturnal idiopathic blood pressure spiking to \sim 223/135 although daytime BP was typically in the 145/85 range, even during stressful workloads. BP at this range is well documented to cause kidney damage, and in more immediate threat, carries a high risk of stroke or ruptured aneurism. He was prescribed the potent, antihypertensive drug, Clonidine 0.1 mg 3X daily.

In 1998, the subject was diagnosed with Deep Vein Thrombosis (DVT) and prescribed 20 mg daily Altace® (Ramipril) every morning to decrease daytime BP, it is a proven powerful antioxidant. In addition to Clonidine 3x per day, he was advised to radically change his lifestyle and to lose 23 pounds. He declined the suggested pharmaceutical drug Farxiga.

After the 2022 CKD diagnosis, he increased over-the-counter Nitric Oxide tablets (Berkeley Life natural vasodilator, 250 mg) to 4 or more times daily [13]. His nocturnal BP spikes were relentless, necessitating adding the prescription drugs:

- 1) Hydralazine, a vasodilator: 25 mg 2X daily
- 2) Diltiazem, a calcium channel blocker: 30 MG nightly, at 11 PM
- 3) Tadalafil (Cialis), prostate hypertrophy Rx; also a mild vasodilator with minimal blood pressure effects, especially at the 5 mg dose prescribed for hypertrophy rather than the recommended $>$ 20 mg dose prescribed for erectile dysfunction. Tadalafil has a uniquely long half-life of 17.5 hours compared to that of the other PDE5 Inhibitor drugs like Sildenafil, whose half-life is about four hours [14,15]: 5 mg at 8 PM
- 4) Sildenafil, (Viagra) a mild vasodilator [14]: 100 mgs nightly at 11 pm

These drugs are proven to lower BP when taken at night paralleling the sleep cycle of the circadian rhythm. The subject had already become serious about avoiding processed foods and losing weight as he realized the multiple repercussions of his malignant hypertension. At that time prices for accurate automatic BP recording devices prices dropped radically. He found the OMRON upper arm blood pressure cuff with Bluetooth connectivity which allowed him to track his BP as it is affected by the circadian rhythm. He understood that automatic BP recording would help his collaborative team of practitioners and him to design a successful, personalized medication regimen.

The subject knew there had to also be food triggers for his high blood pressure and set out, as everyone must do to be successful, to figure out what those were for him in particular. He undertook food allergy testing but also took careful notes of his diet and BP spike times. BP food triggers are highly individualized, so each person is responsible for figuring out their own. Several of the subject's triggers were fairly typical; some were not. But they are a starting point for those trying to figure out their own high blood pressure triggers. His are:

- 1) Caffeine. A sympathetic nervous system stimulant and a natural ingredient present in coffee, tea, and chocolate. The source may make a difference. For instance, green tea contains abundant polyphenols that carry antioxidant and anti-inflammatory benefits that help counteract cardiovascular disease from its caffeine content. Recent recommendations are that people with extremely high blood pressure drink no more than one



cup of coffee daily. Two cups daily seem to double the heart attack risk. In a review of 34 studies, 200–300 mg of caffeine from coffee— approximately the amount one would consume in 1.5–2 cups — resulted in an average increase of 8 mm Hg and 6 mm Hg in systolic and diastolic blood pressure, respectively [16,17].

- 2) Salts, Sodium, including nitrates, nitrites, and in particular MSG. A controversial flavor enhancer found especially in fast foods and Chinese foods in the US, MSG is banned in more than 40 countries but allowed in US foods with unseen and often unrealized consumer consequences. While MSG only affects a small percentage of the population, some individuals do experience a brief blood pressure spike after consumption, often linked to headaches and asthma induced by the Chinese Restaurant Syndrome [18]. For most people to experience this, the MSG intake must be much higher than that typically consumed in a meal [19]. It takes at least 24 hours to clear the body. Know that MSG also occurs naturally in carrots, tomatoes, potatoes, onions, cabbages, soy sauce, anchovies, and shrimp. Because it contains gluten, MSG may also trigger food sensitivities in some people.
- 3) Alcohol's effects on people's blood pressure vary widely. Low occasional doses rarely cause permanent blood pressure problems. The occasional binge is also not likely to cause a permanent health effect in those without a history of drinking. However, there are many mechanisms involved in even the short time increases in blood pressure. Alcohol happened to be a major trigger for the subject. During this experiment, the subject cheated once and imbibed two, 4 oz glasses of wine two hours apart after which his blood pressure quickly spiked.
 - a) Alcohol reduces levels of the antidiuretic hormone, vasopressin, the reason alcohol creates a need to urinate frequently, which leads to dehydration. This would seemingly lower blood pressure.
 - b) On the other hand, the kidneys control a system called the Renin–Angiotensin–Aldosterone System (RAAS). Alcohol increases renin hormone levels causing blood vessels to constrict, raising the BP. Renin exerts an opposite effect of that of vasopressin. It *decreases* how much fluid is eliminated by the kidneys as urine.
 - c) Alcohol increases calcium-binding to blood vessel walls, which increases their sensitivity to compounds that constrict them leading to high blood pressure [20,21]
 - d) Alcohol raises levels of the stress hormone, cortisol, causing it to release catecholamines. Catecholamines act as renin does, restricting fluid excretion and increasing BP [21].
 - e) Alcohol decreases both high- and low- baroreceptor sensitivity. The result is the baroreceptors fail to signal

blood vessel walls to stretch as necessary, increasing blood pressure.

- 4) Nuts. Typically nuts tend to lower people's blood pressure [22], but a nut allergy conceivably can have the opposite effect, especially indirectly if taking a compound to alleviate symptoms. Pseudoephedrine and phenylephrine constrict blood vessels body-wide, not just in the nose. Allergy testing will identify this trigger. Even though peanuts are a legume, there is frequently a cross-reaction between it and nuts. The small amount of peanut butter in one Reese's Peanut Butter Cup seriously spiked the subject's blood pressure.

Encouraged by his naturopathic doctor in 2023, the subject learned how to administer various O₃ therapies. At first he “bagged” his body with O₃ several times weekly and consumed at least 1500 ml of 8 PPM Hydrogen-infused water, both for its antioxidant properties and to upregulate his immune system “T” cells. 2023 was dedicated to the Western Medicine regimens outlined above, along with some seemingly nonproductive “naturopathic” regimens and the lifestyle changes previously outlined. His eGFR% remained in the survivable ± 40 range with no improvement, but he experienced no further decline.

In 2024, the subject developed a theory that Malignant Hypertension, a failure to maintain normal blood pressure [23], was a myth. He believes “Malignant Hypertension” actually refers to the lack of medical resources to maintain BP control. By relentlessly doing the granular work necessary for his own individual health journey, as the subject recorded his own BP numerous times day and night, the pattern of unexplained nocturnal spikes emerged. He realized there was an obvious need for an entirely different medication regimen at night to accommodate the circadian rhythm pattern of highs and lows of BP into dangerous hypertensive nighttime levels.

The conventional wisdom regarding nocturnal blood pressure control [23] is to check for sleep apnea. The subject had long ago controlled sleep apnea with a custom TAP dental sleep appliance plus routine CPAP use while sleeping, even during short daytime naps. The effectiveness of his regimen was verified by various sleep studies in a clinical sleep lab. The subject had taken two 10 mg of Ramipril once daily, which successfully controlled daytime BP for years. Later, he modified this regimen to Ramipril, 10 mg twice a day at 8 AM and 8 PM along with 5 mg Tadalafil once a day at 8 PM (initially for successful treatment of prostate enlargement) and lowering BP. Even with this change, he experienced recalcitrant nocturnal spikes in blood pressure, so he adjusted his medication regimen further to address this issue by settling on the following prescription drug regimen:

- 1) Clonidine 0.1 mg, four times daily, at 6 AM and PM and 12 AM and PM,
- 2) Hydrochlorothiazide (a vasodilator) 25 mg at midnight
- 3) Diltiazem (a calcium channel blocker) 30 mg at midnight
- 4) Sildenafil Citrate 100mg was the final addition that



filled out the successful PM regimen that eliminated nocturnal spikes. In this case, it was repurposed back to its original intent, it was designed to modulate high BP by vasodilation.

Though seldom discussed, high BP contributes to even higher BP due to the physiologic response of any muscle, whether striated or smooth, when loaded. Muscle will hypertrophy when taxed as any weightlifter will tell you. Smooth muscle in the inner wall of the outgoing circulatory venous blood supply hypertrophies to accommodate resistance to outgoing BP. As the lumen decreases in size, the BP rises in response, thus high BP precipitates higher BP in a positive feedback loop.

In this oversimplification, one can draw a good analogy from the physiologic response of veins used in cardiac bypass. Arteries are difficult to harvest, and even more difficult to anastomose in cardiac bypass surgery. Within a very short time into the animal trials used to develop the bypass surgery techniques, veins were substituted for clogged arteries in bypass surgery. The veins responded to the outgoing blood pressures by hypertrophy just like any other taxed muscle would and began to perform as arteries due to the buildup of non-striated smooth muscle mass in the venous lumen, resisting the pressures of cardiac function.

The subject decided to manually monitor his BP every single hour over a week and identified a persistent nocturnal BP spike. He did this to prove his theory that uncontrolled BP leads to a buildup of smooth muscle in the venous system, which in turn narrows the lumen, thereby increasing the diastolic pressure of the returning venous blood. With meticulous monitoring and adjustment of the prescription drugs, he found he could help maintain BP within “normal limits”. He theorized that it would allow dystrophy of the venous smooth muscle that had hypertrophied in response to chronic hypertension. Over time, he reasoned he would be able to naturally return BP back to “normal”. With all his careful lifestyle changes, his expectation was that through this process, he would either be able to reduce or eliminate his dependence on prescription drugs. He particularly detested Clonidine, which carries a host of undesirable side effects, most particularly an unbalanced gait, yet remains the most effective antihypertensive in many people’s regimens, including his.

The journey expands : December 4, 2023 to – present

After one year of traditional Western medical intervention with little movement in eGFR%, the subject was frustrated. He realized for instance, that if he had adhered to one of his physician’s advice to “Drop the Clonidine 0.1 mg three times a day to one a day since it tends to make people feel bad”, he probably would have died of the malignant hypertension he was supposed to be treating. He also realized that would probably have caused a severe decline in his eGFR% numbers and he would be guaranteed a need for dialysis soon.

Though disparaged by the FDA and traditional Western-trained physicians, at that point subject wanted to radically

switch to certain treatments, so in December 2023, he thought he could do more and requested his doctor help him lay out more advanced ideas to help him reverse his CKD.

His doctor recommended he begin more effective ozone therapies. As already noted, ozone upregulates many critical biological systems. Starting December 3, 2023, he went for weekly Major Autohemotherapy (MAH) sessions. After four sessions, each requiring at least a four-hour commitment, he switched to a less time-consuming and easier regimen of inexpensive Direct Intravenous Ozone (DIV O₃). DIV O₃ takes less than 30 minutes and can be transported throughout the world at the cost of an insulin syringe and a little more for treatment. A recommended dose is 1.1 mg per kilogram bodyweight. For the purposes of this paper, both MAH and DIV O₃ are considered systemic ozone therapies, each requiring different dose levels as noted in the introduction. The recommended dosage for DIV O₃ ozone therapy is a volume of 150 – 300 mL at 10 – 25 µg ozone/mL oxygen gas mixture administered. The chosen DIV dose was 30–50cc at 53.7µg/mL concentration. (86.2 kilograms X 1.1 = 94.8 ml gas).

Rectal Insufflation (RI) is a valid alternative to MAH and DIV O₃ therapies, particularly for elderly patients presenting with unfavorable vein conditions often due to chronic inflammatory diseases. Inflammatory diseases like heart disease, diabetes, gum diseases, and other oral infections usually render blood vessel walls throughout the body friable, so this would not be uncommon for those suffering from CKD.

The eGFR% of the subject was unaffected by the first month of treatments, so in February 2024, one teaspoon of oil-based Carbon 60 (C₆₀) chased by 500 CCs (~17 ounces) of 8PPM hydrogen water (H₂+H₂O), made with Magnesium tablets, was added every Monday, Wednesday, and Friday. Hydrogen water is known to be a powerful antioxidant that reduces ROSs in the body and also upregulates the immune system’s “T” cells, an important subset of white blood cells. “T” cells are the primary guardians of the immune system, proven to upregulate over 170 immune functions in response to H₂ stimulation. Normalization of BP, a super-clean anti-inflammatory diet, routine frequent DIV O₃ therapy plus the C₆₀ plus hydrogen water was anticipated to finally start unclogging and repairing his kidney’s glomeruli.

Choosing an arbitrary set point, as BP dropped to < 120/70 and was maintained in that range, on a monthly basis starting on March 1, 2024, then April 1, 2024, and May 1, 2024, dosage was reduced by one Clonidine .1 mg tablet each month, and discontinued the Clonidine weekly transdermal patch of 0.3 mg daily to a weekly Clonidine transdermal patch of 0.2 mg daily, going from a daily dose of 0.7 mg to a comfortable 0.3 mg daily. By June 2024, he not only dropped a single Clonidine 0.1 mg tablet per day but substituted a Clonidine 0.1 mg 12 hr. time release tablet taken near midnight to accommodate his circadian rhythm. In this manner, the dangerous instability that accompanies higher doses of Clonidine was circumvented. He postulated that this new regimen reflected the decrease of

the hypertrophied smooth muscle in response to meticulous maintenance of blood pressures in low normal ranges, proving that the “Malignant Hypertension Theory,” was a myth and that the goal of his experimentation had been accomplished. To reiterate, the subject proved that malignant hypertension is the result of the inability to maintain consistent control of blood pressure in low normal ranges throughout the entire daily cycle of hours, thus allowing the venous system to dystrophy to normal lumen size.

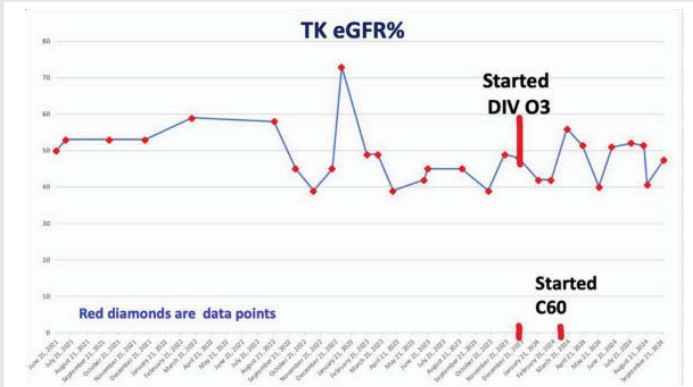
From February 2024 through April 2024, the subject’s eGFR rose once again to the low 50’s range, debunking the myth that CKD cannot be reversed. The following chart shows the progress over time. While it shows eGFR% scores improved, the truce is fragile due to a complicated health profile. Note the drop in eGFR% score to the low 40s following the stress of a tragic death on May 10, 2024, taking two long airplane trips in quick succession, eating airport junk food, and the surgical removal of a small cyst. Once diet and stress were again regulated, eGFR% bounced back to < 50 by June 14, 2024.

Progress was halted once again when he contracted COVID on August 5, 2024. On August 16, 2024, his GFR% showed no negative effects. On August 17, 2024, he was bitten by a notoriously poisonous brown recluse spider, and by August 23, his eGFR% showed a dip of ten points (40.75) Once again, with meticulous control of all controllable factors, his eGFR% had somewhat recovered by the September 16, 2024 CMP to an eGFR% of 47.35.

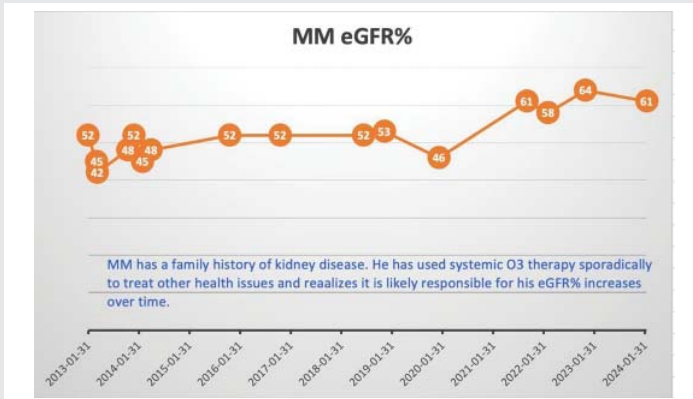
The following chart demonstrates how his eGFR bounced around due to various life and health events (Graph 1). While we can’t extrapolate from the data what his eGFR% would be had not all these complications arisen, we can certainly surmise his percent kidney function would likely have plummeted had he not taken these proactive steps to upregulate his biological systems and to significantly reduce inflammation and BP.

Other related experiences with ozone and kidney glomeruli clearing

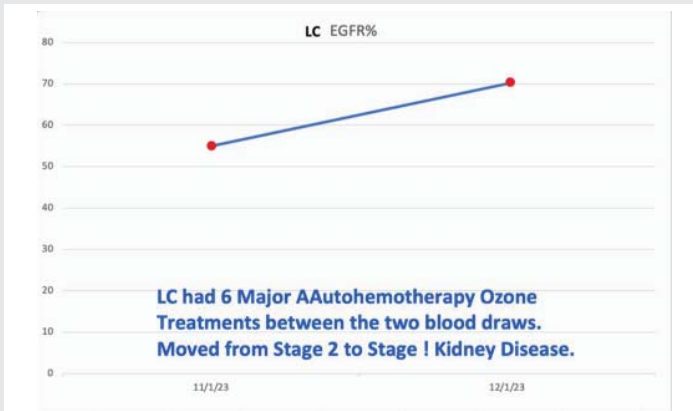
- 1) Despite an unexplained family history of kidney failure in the adult males of his bloodline, MM was able to raise his eGFR% from the high 30s in 2012 to a current comfortable eGFR in the 60s by mid-2024. There is no hereditary component of hypertension or diabetes. His declining eGFR% was apparently in response to the clogging of the glomeruli apparatus of the kidneys by ROS. His exposure to IV O3 has been sporadic, self-administered when an immune challenge presented, not realizing he’d experience the unexpected serendipitous side effect of a consistent rise in eGFR% over the ensuing decade (Graphs 2-5).
- 2) Rainey’s patient, LC:
- 3) Rainey’s patient CA
- 4) Rainey’s patient, WM



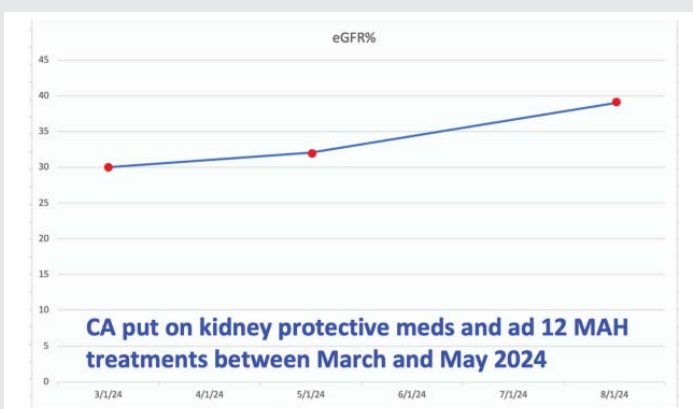
Graph 1: Patient TK’s eGFR% from June 2021 to September 2024.



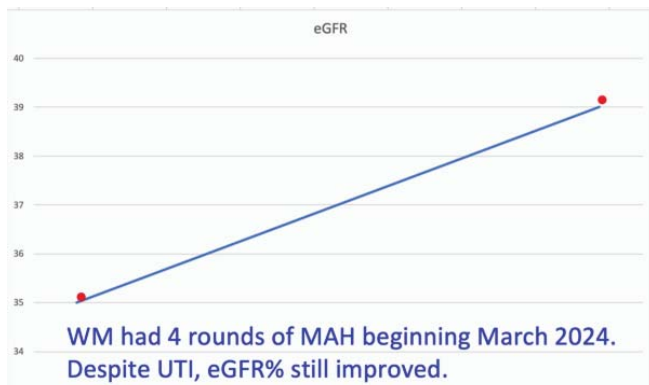
Graph 2: Patient MM’s eGFR% from 2013-2024.



Graph 3: Patient LC’s eGFR% in November and December of 2023.



Graph 4: Patient CA’s eGFR% from March to August 2024.



Graph 5: Patient WM's eGFR% in February and August 2024.

Discussion

It is clear that loss of kidney function is most often a sign of runaway loss of autologous bioregulation, whether caused by poor sleep or inflammatory lifestyle choices, which is difficult to avoid in large swaths of the world today, and eventually results in cardiovascular disease, diabetes, acquired mitochondrial disorder, plus nitric oxide and glutathione deficiencies. A component of all of these is excessive Reactive Oxygen Species (ROS) or oxidizers, responsible for inflammation. Because the subject desired an integrative approach to reregulate all his biological systems, together with Dr. Rainey chose the following strategies, tweaking them along the way as necessary:

- 1) Ozone therapy as a master re-regulator
- 2) Hydrogen water, thought to have many health-enhancing properties including renal function improvement possible via its anti-inflammatory and antioxidant properties and effects on mitochondrial ATP output
- 3) C₆₀ to multiply hydrogen water benefits. Two other important components of bioregulation—liposomal glutathione and nitric oxide
- 4) Discover his malignant high BP triggers so he can reverse this disease concurrently.

In years past, the subject had already confirmed his sleep apnea treatment was effective via sleep labs and took daily doses of liposomal glutathione and nitric oxide to augment these strategies, so Dr. Rainey thought he would be compliant and was willing to show him how to accomplish DIV O₃ at home.

The subject was fairly compliant and always ready to try new modalities as the eGFR numbers reflected his successes and failures. Certainly, he stumbled from time to time as he accepted an occasional glass of wine or a restaurant meal, but he quickly learned from how he felt and from eGFR% responses that he could no longer tolerate these lifestyle lapses. He now knows that starting at the inexcusable low % function he did because his lab results were not called out by his doctor until very late stages, negative life events will take their toll more intensely than had he started to look for

answers before significant damage already occurred during an earlier stage of kidney function decline. He also knows he will have to rigorously monitor and continue to tweak both lifestyle and therapies, however, he realizes his kidney health is an important barometer of how healthy all his biological systems are.

Being able to heal his blood vessel walls as part of his journey to lower his blood pressure without relying as heavily on prescriptions and their serious side effects was empowering. His formulas for success are science-based and should be a starting blueprint for everyone's journey to better health.

The subject was particularly compliant and motivated to keep collecting copious data and following through on new ideas. There is also more available information regarding various roadblocks to improvement, but these observations make the case study even more useful, as it shows how fragile the road back to health can be.

Nonetheless, the opportunity to add even minimal data from four other people experiencing kidney failure from whatever cause(es) to some degree or another bolster the theory that CKD can be reversed with attention to lifestyle and employing the strategies discussed.

Conclusion

Subject's quest to improve his GFR scores in conjunction with a trusted health care professional, Dr. Tim Rainey, launched their mission to expose the myths perpetuated by conventional US medical practitioners, that CKD could only be slowed down but would eventually deteriorate into dialysis or worse and similarly, that malignant hypertension could be cured. Contrast the results of treatment outcomes between 2023 when only regimented administration of conventional prescription drugs along with his patient's attempts to control inflammation through diet and sleep apnea treatment to treat his, "Malignant Hypertension", high BP, and CKD, with the results shown in 2024 after adding the more potent oxidant/antioxidant ozone therapies of Major Autohemotherapy and then DIV ozone, as well as hydrogen water and C₆₀, to exponentially increase antioxidant potential. There is a clear differential.

It is clearly apparent that kidney function can be upregulated, at least in part by downregulating hypertension to normal ranges in those persons suffering CKD caused by hypertension. With meticulous attention to maintaining blood pressure in a normal range, the smooth muscle of the vascular walls that have hypertrophied to accommodate higher blood pressures will atrophy back to normal. In any case of ROS-related kidney decline, it appears that using ozone, an oxidative species, via IV infusion, will react with the Reactive Oxidative Species and other byproducts of metabolism clogging the glomeruli regardless of the cause of their presence, and upregulating kidney function. We now have algorithms under development that will work in conjunction with automatic recordings of BP to guide professional caregivers in their medication regimens that can be altered in real time to respond to the patient's changing needs. Meanwhile, time waits for no



man. Any individual motivated by their own drop in eGFR% can follow these guidelines and restore their BP into a normal range for age and gender while benefiting from the concurrent DIV O₃ treatments to unclog the glomeruli. The alternative choice is to live with CKD and declining kidney function while hoping that these crucial adjuncts will be developed in time to save whatever kidney response is possible.

This is a case study and as such, is limited in sample size. There is a need for more rigorous, long-term studies.

References

- Drozdal S, Lechowicz K, Szostak B, Rosik J, Kotfis K, Machoy-Mokrzyńska A, et al. Kidney damage from nonsteroidal anti-inflammatory drugs—Myth or truth? Review of selected literature. *Pharmacol Res Perspect*. 2021;9(4):e00817. Available from: <https://doi.org/10.1002/prp2.817>
- Wan EYF, Yu EYT, Chan L, Mok AHY, Wang Y, Chan EWY, et al. Comparative Risks of Nonsteroidal Anti-Inflammatory Drugs on CKD. *Clin J Am Soc Nephrol*. 2021;16(6):898-907. Available from: <https://doi.org/10.2215/CJN.18501120>
- Holt-Lunstad J, Steffen PR. Diurnal cortisol variation is associated with nocturnal blood pressure dipping. *Psychosom Med*. 2007;69(4):339-343. Available from: <https://doi.org/10.1097/psy.0b013e318050d6cc>
- Bouillaud F, Hammad N, Schwartz L. Warburg Effect, Glutamine, Succinate, Alanine, When Oxygen Matters. *Biology (Basel)*. 2021;10(10):1000. Available from: <https://doi.org/10.3390/biology10101000>
- Pérez-Torres I, Manzano-Pech L, Rubio-Ruiz ME, Soto ME, Guarner-Lans V. Nitrosative Stress and Its Association with Cardiometabolic Disorders. *Molecules*. 2020;25(11):2555. Available from: <https://doi.org/10.3390/molecules25112555>
- Lunov O, Zablotskii V, Churpita O, Chánová E, Syková E, Dejnek A, Kubinová Š. Cell death induced by ozone and various non-thermal plasmas: therapeutic perspectives and limitations. *Sci Rep*. 2014 Nov 20;4(1):7129. Available from: <https://doi.org/10.1038/srep07129>
- Vander Stoep C. *Primal Dentistry: Less Is More*. 1st ed. Iana Publishing; 2018;136-144.
- Schulz S, Ninke S, Watzel B, Nüsing RM. Ozone induces synthesis of systemic prostacyclin by cyclooxygenase-2 dependent mechanism in vivo. *Biochem Pharmacol*. 2012;83(4):506-513. Available from: <https://doi.org/10.1016/j.bcp.2011.11.025>
- Inci H, İnci F. Effect of ozone therapy on neutrophil/lymphocyte, platelet/lymphocyte ratios, and disease activity in ankylosing spondylitis: a self-controlled randomized study. *Med Gas Res*. 2023;13(2):53-58. Available from: <https://doi.org/10.4103/2045-9912.344981>
- Viebahn-Haensler R, León Fernández OS. Ozone in Medicine. The Low-Dose Ozone Concept and Its Basic Biochemical Mechanisms of Action in Chronic Inflammatory Diseases. *Int J Mol Sci*. 2021;22(15):7890. Available from: <https://doi.org/10.3390/ijms22157890>
- Rahman I, Kode A, Biswas SK. Assay for quantitative determination of glutathione and glutathione disulfide levels using enzymatic recycling method. *Nat Protoc*. 2006;1(6):3159-3165. Available from: <https://doi.org/10.1038/nprot.2006.378>
- Delgado-Valero LF, Hernández-Cruz EY, Pedraza-Chaverri J. The Protective Role of Ozone Therapy in Kidney Disease: A Review. *Life (Basel)*. 2023;13(3):752. Available from: <https://doi.org/10.3390/life13030752>
- McNally B, Griffin JL, Roberts LD. Dietary inorganic nitrate: From villain to hero in metabolic disease? *Mol Nutr Food Res*. 2016;60(1):67-78. Available from: <https://doi.org/10.1002/mnfr.201500153>
- Kloner RA, Mitchell M, Emmick JT. Cardiovascular effects of tadalafil. *Am J Cardiol*. 2003;92(9a):37m-46m. Available from: [https://doi.org/10.1016/s0002-9149\(03\)00074-2](https://doi.org/10.1016/s0002-9149(03)00074-2)
- Kloner RA. Cardiovascular effects of the 3 phosphodiesterase-5 inhibitors approved for the treatment of erectile dysfunction. *Circulation*. 2004;110(19):3149-55. Available from: <https://doi.org/10.1161/01.cir.0000146906.42375.d3>
- Teramoto M, Yamagishi K, Muraki I, Tamakoshi A, Iso H. Coffee and Green Tea Consumption and Cardiovascular Disease Mortality Among People With and Without Hypertension. *J Am Heart Assoc*. 2023;12(2). Available from: <https://doi.org/10.1161/jaha.122.026477>
- Chrysant SG. The impact of coffee consumption on blood pressure, cardiovascular disease and diabetes mellitus. *Expert Rev Cardiovasc Ther*. 2017;15(3):151-6. Available from: <https://doi.org/10.1080/14779072.2017.1287563>
- Assarzagdegan F, Asadollahi M, Hesami O, Aryani O, Mansouri B, Beladi Moghadam N. Secondary headaches attributed to arterial hypertension. *Iran J Neurol*. 2013;12(3):106-10. Available from: <https://pubmed.ncbi.nlm.nih.gov/24250915/>
- Shimada A, Cairns BE, Vad N, Ulriksen K, Pedersen AM, Svensson P, et al. Headache and mechanical sensitization of human pericranial muscles after repeated intake of monosodium glutamate (MSG). *J Headache Pain*. 2013;14(1):2. Available from: <https://doi.org/10.1186/1129-2377-14-2>
- Husain K, Ansari RA, Ferder L. Alcohol-induced hypertension: Mechanism and prevention. *World J Cardiol*. 2014;6(5):245-252. Available from: <https://doi.org/10.4330/wjc.v6.i5.245>
- Tasnim S, Tang C, Musini VM, Wright JM. Effect of alcohol on blood pressure. *Cochrane Database Syst Rev*. 2020;7(7):CD012787. Available from: <https://doi.org/10.1002/14651858.cd012787.pub2>
- Glenn AJ, Aune D, Freisling H, Mohammadifard N, Kendall CWC, Salas-Salvadó J, et al. Nuts and Cardiovascular Disease Outcomes: A Review of the Evidence and Future Directions. *Nutrients*. 2023;15(4):911. Available from: <https://doi.org/10.3390/nu15040911>
- Naranjo M, Chauhan S, Paul M. Malignant Hypertension. *StatPearls*. Treasure Island (FL): StatPearls Publishing, Copyright © 2024, StatPearls Publishing LLC.; 2024. Available from: <https://pubmed.ncbi.nlm.nih.gov/29939523/>

Discover a bigger Impact and Visibility of your article publication with Peertechz Publications

Highlights

- ❖ Signatory publisher of ORCID
- ❖ Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- ❖ Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TDNet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- ❖ Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- ❖ OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- ❖ Dedicated Editorial Board for every journal
- ❖ Accurate and rapid peer-review process
- ❖ Increased citations of published articles through promotions
- ❖ Reduced timeline for article publication

Submit your articles and experience a new surge in publication services
<https://www.peertechzpublications.org/submit>

Peertechz journals wishes everlasting success in your every endeavours.