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REPORT

Innovative Strategies to Combat Kidney Disease

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You may be surprised to learn that until **2002**, no standard definition for **chronic kidney disease** (CKD) existed within the medical community.¹ Before then, conflicting classifications had created a state of confusion as to how many Americans were afflicted with this progressive, life-threatening condition.

Once proper categorization of the various phases of CKD was established, the stark and daunting scale of this **modern epidemic** emerged.

We now know that as many as **26 million** Americans currently suffer from some form of chronic kidney disease.^{2,3} Aging individuals are especially vulnerable.⁴

Yet public awareness of the threat remains low. When you consider that the risk of cardiovascular *mortality* in CKD sufferers is **30 times** that of the general population,⁵ the steady increase in kidney disease rates seen today amounts to a public health disaster hidden in plain sight.

Life Extension® has long emphasized the need for vigilance through **regular testing** (at least once a year) to monitor kidney health. In addition to the standard tests for **creatinine**, **albumin**, and **BUN/creatinine ratio**, certain individuals should insist their doctor test for **cystatin-C**, a largely overlooked blood marker which provides a far more precise measure of renal function. Optimal levels are less than **.91 mg/L**.

Individuals should also keep a record of their test results. Once any sign of disease is detected (such as an increase in creatinine), it is imperative that immediate steps be taken to halt its progress, as kidney function can decline precipitously and may be irreversible. Fortunately, many **Life Extension®** members are already taking a variety of nutrients that support kidney health.

In this article, you will discover the most recent scientific advances in our understanding of how CKD unfolds, the specific risk factors that contribute to its progress, and how you can bring them under control.

You will also learn of **safe, low-cost, natural interventions** that have been shown to stop CKD in its tracks, long before end-stage renal disease (ESRD) renders dialysis or kidney transplant the only option.

PYRIDOXAMINE OR PYRIDOXAL-5-PHOSPHATE: POTENT KIDNEY DEFENSE

Since the formation of *advanced glycation end-products* (AGEs) is such a well-established factor in the onset and progression of kidney disease, nutrients that have been conclusively shown to mitigate the effects of these lethal agents constitute a front line, low-cost intervention.

A *formidable* AGE antagonist is the vitamin B6 compound **pyridoxamine**. A plethora of research confirms its power to halt formation of AGEs.⁶⁻⁸ Evidence has also emerged that pyridoxamine drastically limits formation of equally deadly *advanced lipoxidation end products* (ALEs)—another deadly catalyst for kidney disease.⁹⁻¹¹

A team of biochemists at the University of South Carolina were able to show that pyridoxamine *traps* the reactive molecules formed during lipid (fat) peroxidation and helps to “chaperone” them harmlessly into the urine.^{10,12}



Their colleagues subsequently found that neutralizing AGEs and ALEs can prevent kidney disease and lipid profile abnormalities in diabetic rats.¹³ They found that rats supplemented with pyridoxamine had lower levels of albumin (protein) in their urine, lower plasma levels of the waste product creatinine, and less dramatically elevated blood lipids than the placebo treated animals, all directly related to the reduction of AGE/ALEs.

They subsequently examined whether similar results could be obtained in obese animals that had *not yet developed diabetes*.¹⁴ Three groups of animals were studied:

1. lean (healthy) rats
2. obese rats without treatment
3. obese rats treated with pyridoxamine.

As expected, AGE and ALE formation underwent a **two- to threefold increase** in obese untreated rats compared to lean animals. Conversely, those increases were entirely absent in obese animals treated with pyridoxamine. Treated animals also experienced a smaller increase in plasma triglycerides, cholesterol, and creatinine levels, compared with the obese untreated rats.¹⁴



In an equally compelling development, hypertension in animals treated with pyridoxamine also resolved, as did thickening of blood vessel walls. Untreated animals displayed urinary evidence of renal disease (albuminuria) that in contrast had been nearly normalized in supplemented animals. This provides powerful evidence of pyridoxamine's **multi-targeted** protective effect against CKD.¹⁴

In 2004, the same research team made a landmark discovery: while studying the relative effects of pyridoxamine along with a variety of additional natural antioxidants on the progression of kidney disease in diabetic rats, they decided to examine how these natural compounds stacked up against enalapril, a standard pharmaceutical intervention used to prevent CKD.⁹ Enalapril is an ACE inhibitor, one of a class of drugs commonly used to control blood pressure and kidney disease.

They found that pyridoxamine therapy was the *most effective* at preventing progression of kidney disease, followed by vitamin E and lipoic acid. Enalapril, the prescription drug, proved to be the least effective intervention. Pyridoxamine also limited lipid profile abnormalities and formation of AGEs and ALEs, offering a far broader spectrum of preventive effects than enalapril.⁹

Researchers at the University of Miami advanced these findings by treating diabetic mice with both pyridoxamine and enalapril.¹⁵ Again they found that pyridoxamine alone provided substantial benefit, cutting albuminuria and damage to the glomeruli. Combining enalapril with pyridoxamine reduced kidney disease mortality in these animals as well, leading the researchers to suggest that the ACE-inhibitor (enalapril)/pyridoxamine combination might be useful.

A convincing body of research on pyridoxamine therapy in *humans* with CKD has also emerged in recent years. In 2007, a team of researchers at Harvard set out to determine optimal interventions to halt the progression of kidney disease in diabetics.¹⁶ They conducted two 24-week multicenter placebo-controlled trials in patients with known **diabetic nephropathy**—treatment of which is known to delay the onset of end-stage renal disease in diabetics. Doses of pyridoxamine ranged from **50 to 250 mg** twice daily.

Pyridoxamine significantly inhibited the rise in blood levels of the waste product creatinine, one of the key biomarkers of kidney dysfunction and a predictor of kidney failure. Urinary levels of inflammatory cytokines were also significantly lower in the treated group compared to controls.

Pyridoxamine has been firmly established as a front line, safe, low-cost intervention in CKD caused or exacerbated by AGEs and ALEs. Further, this natural vitamin B6 compound has been shown to significantly improve outcomes of experimental kidney transplants and other forms of kidney disease.¹⁷⁻¹⁹

It therefore borders on the *criminal* that in January of 2009, the FDA classified this potent, entirely safe CKD therapeutic as a drug, putting it out of reach for many Americans suffering from this deadly condition. No one should be forced to bear the *outrageous* burden of costly pharmaceuticals and their toxic side effects when a perfectly safe alternative exists.

Fortunately, there is another equally safe option available—another form of **vitamin B6** known as **pyridoxal-5-phosphate (P5P)** that also exerts potent anti-AGE effects. It has been shown to prevent the progression of diabetic kidney disease in pre-clinical models.²⁰ In fact, as far back as 1988, P5P was used by a German research group to reduce blood lipids in humans with chronic kidney disease.²¹

Coenzyme Q10

Because of the tremendous blood flow and high concentration of metabolic toxins continuously circulating through the kidneys, they are the site of extraordinary oxidative stress, which is known to contribute to progressive kidney damage and its complications, such as high LDL and increased cardiovascular disease risk.²²

Coenzyme Q10 (CoQ10) fortifies the body's natural antioxidant capacity and reduces levels of oxygen free radicals, indicating its important defense against CKD. As it happens, CoQ10 has been used experimentally to control hypertension and kidney disease in laboratory animals *since the early 1970s*.^{23,24}

Human studies have shown that CoQ10 levels substantially decline, while markers of oxidation such as malondialdehyde are dramatically *elevated*, in kidney disease patients with even mild renal dysfunction.⁴¹ These decreased CoQ10 levels also make circulating **lipoproteins** (such as LDL) more vulnerable to oxidative damage, which in turn increases risk for further cardiovascular damage, adding to the renal burden and substantially increasing the risk of kidney disease.²⁵

A team of European researchers published compelling evidence in 2001 of how effective such a nutritional intervention can be, studying a group of patients with established kidney disease.²⁶ Subjects received antioxidant therapy with vitamin C, E, and riboflavin (vitamin B2) for one month before the addition of 2 months of CoQ10 therapy. Prior to supplementation, CoQ10 values in blood were just one-quarter of normal levels; they increased to nearly **four times** the reference level following supplementation. The study was too brief to demonstrate any change in kidney function, but evidence from animal trials that same year showed that when CoQ10 levels were increased in tissues of diabetic rats, a reversal of markers of oxidative stress in kidney, heart, and liver resulted.²⁷

WHAT YOU NEED TO KNOW: STRATEGIES TO COMBAT KIDNEY DISEASE

- It is imperative that aging individuals receive regular **blood tests** to monitor kidney health. In addition to standard **creatinine, albumin, and BUN/creatinine ratio** testing, **cystatin-C** levels should also be measured, as this constitutes a far more accurate biomarker of renal function.
- The high-pressure and toxin-rich environment involved in renal function renders these delicate, highly complex organs especially vulnerable to damage, dysfunction, and disease.
- **High blood pressure, elevated blood sugar, NSAIDs, certain medications, and high-protein diets** are the most common threats to kidney health.
- Nutrients such as **pyridoxal-5-phosphate (P5P)** fight AGEs and ALEs.
- **CoQ10, silymarin, resveratrol, and lipoic acid** are also clinically supported, potent interventions.
- Omega-3 fatty acids help quell inflammation, contributing to enhanced kidney health.
- A host of additional nutrients complement these actions, including folic acid (folate) and vitamins C and E.

By 2004, definitive demonstration of CoQ10 in human kidney disease patients was demonstrated by researchers working with transplant recipients.²⁸ Such individuals undergo tremendous oxidative stress and typically have marked disturbances in lipid profiles as a result. The European group provided their patients with CoQ10 supplements of **30 mg** three times per day for four weeks, and monitored levels of oxidation factors (such as *malondialdehyde*), levels of natural antioxidant enzymes in the body, and lipid profiles.²⁸

Significant improvements were seen after just four weeks, with reduction in LDL, increase in beneficial HDL, and a decrease in presence of inflammatory cells. These results suggest a potentially dramatic improvement in both quality of life and survival rates for patients whose disease has progressed to the point of kidney failure requiring transplantation or dialysis. They also bode well for those with early-stage kidney disease.

Animal studies have also shown that CoQ10 can protect kidney tissue from numerous **nephrotoxic drugs**, including **gentamicin**, a powerful antibiotic with a notorious propensity for causing kidney damage.^{33,34} These findings are significant both because they offer protection in patients who might be exposed to such drugs, and because of what they teach us about CoQ10's potent ability to combat the extreme oxidant stress that the kidney faces as it deals with a variety of foreign chemicals.

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