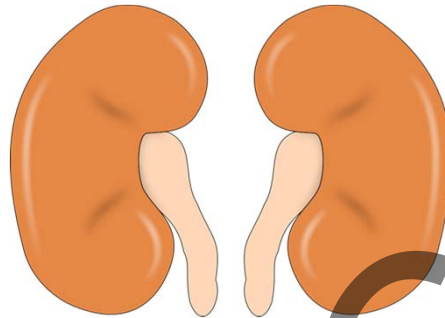


## Complementary Medicine and Lifestyle Modifications for Kidney Health: Highlighting Samueli Center



Susan Samueli Integrative Health Institute



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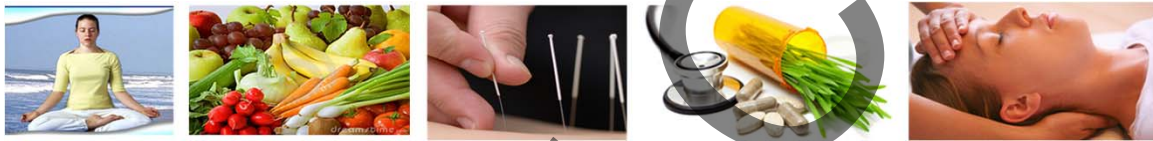
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## Disclosures

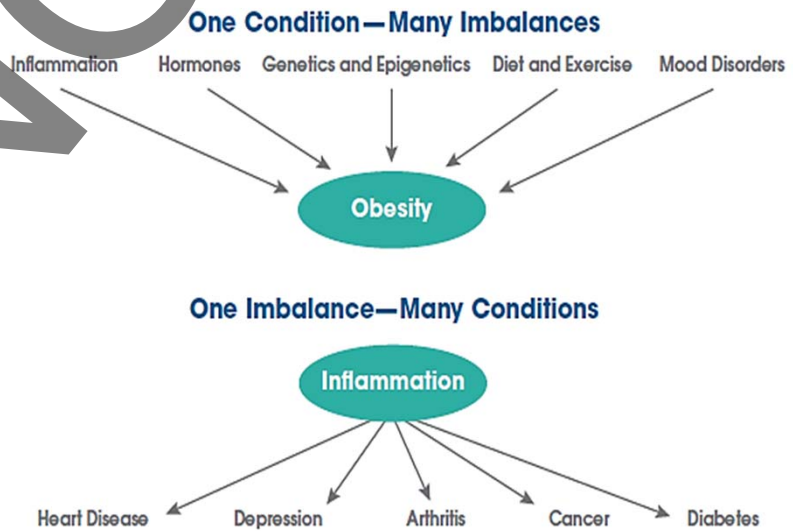
I have no financial disclosures or conflicts of interest to report.

## Complementary & Integrative Health

- Focuses on **health promotion, disease prevention, and the integrative approach to delivering patient care**
- Emphasizes a **whole-person and functional approach** to evaluating and treating patients
- Recognizes the **interconnectedness of systems**
- Identifies and addresses **underlying mechanisms** → downstream symptoms & complications



*Integrative doctors recognize that disease and imbalance are not the same thing*





## Integrative Approach to CKD

### Whole-Person Care

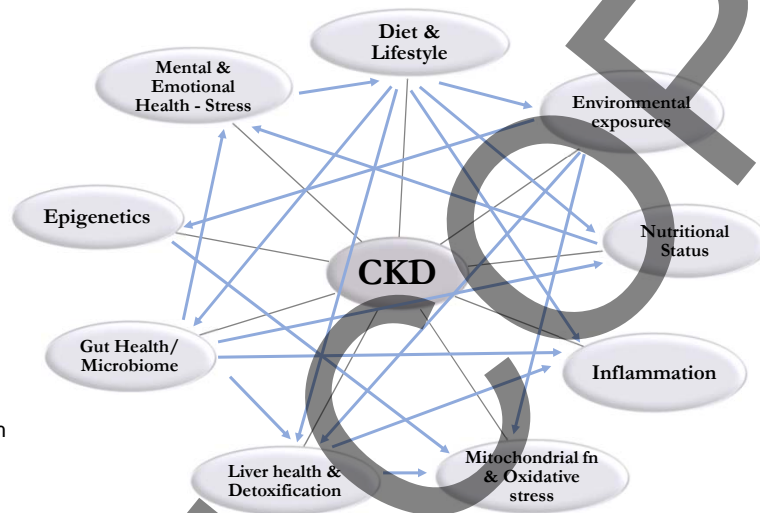
consider multiple influences that impact health

### Focus on underlying mechanisms

What is driving the disease process? inflammation, vascular changes, oxidative stress, mitochondrial damage/insufficiency, etc.

### Complex relationships, Systems-Based

The kidneys don't exist in isolation from other organs and systems – e.g. GI Health, Liver health



## What is our goal?

The over-arching goal is **to decrease the progression of kidney disease and delay the need for dialysis and transplant**

*Secondary goals and outcomes:*

- Improvement in all aspects of patient's health
- Improved quality of life and general outlook for patients
- Reduction of the cost of care associated with CKD, leading to economically favorable models of care



Rate of progression of CKD varies from patient to patient!

According to the National Kidney Foundation, average life expectancy on dialysis is 5 to 10 years, but the foundation also indicates that some patients can live well for 20 or even 30 years.

*What accounts for this?*



## CKD is a “Lifestyle Disease”

- Studies have demonstrated that **kidney disease is directly related to lifestyle and diet variables—so much that CKD can be called a “lifestyle disease.”**

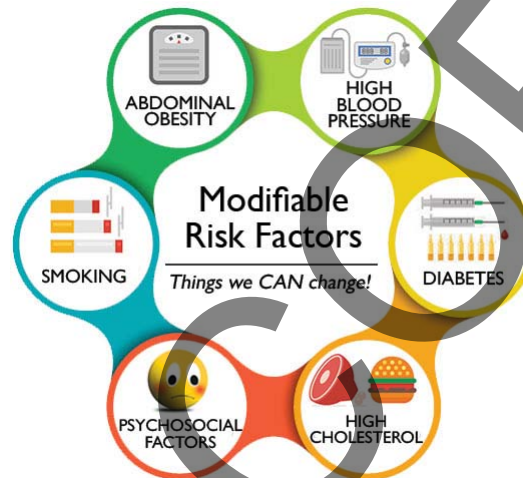
- Foster MC, Hwang SJ, Massaro JM, Jacques PF, Fox CS, Chu AY. Lifestyle factors and indices of kidney function in the Framingham Heart Study. *Am J Nephrol.* 2015;41(4–5):267–274.
- Teng HL, Yen M, Fetzter S, Sung JM, Hung SY. Effects of targeted interventions on lifestyle modifications of chronic kidney disease patients: Randomized controlled trial. *West J Nurs Res.* 2013;35(9):1107–1127.
- Robinson-Cohen C, Littman AJ, Duncan GE, et al. Physical activity and change in estimated GFR among persons with CKD. *J Am Soc Nephrol.* 2014;25(2):399–406.

- In studies that looked at twins, it was found that **lifestyle, diet, and environmental factors were the most significant contributors to the disease.**

- Luttrupp K, Lindholm B, Carrero JJ, Glorieux G, Schepers E. Genetics/genomics in chronic kidney disease: Towards personalized medicine. *Semin Dial.* 2009;22(4):417–422.
- Tarnoki DL, Tarnoki LD, Littvay L, et al. Genetic and environmental variance of renal parenchymal thickness: A twin study. *Croat Med J.* 2013;54(6):550–554.



Many of these risk factors are **modifiable and preventable**. For example, **diabetes** and **hypertension** account for about 44% and 28%, respectively, of all ESRD cases in the United States



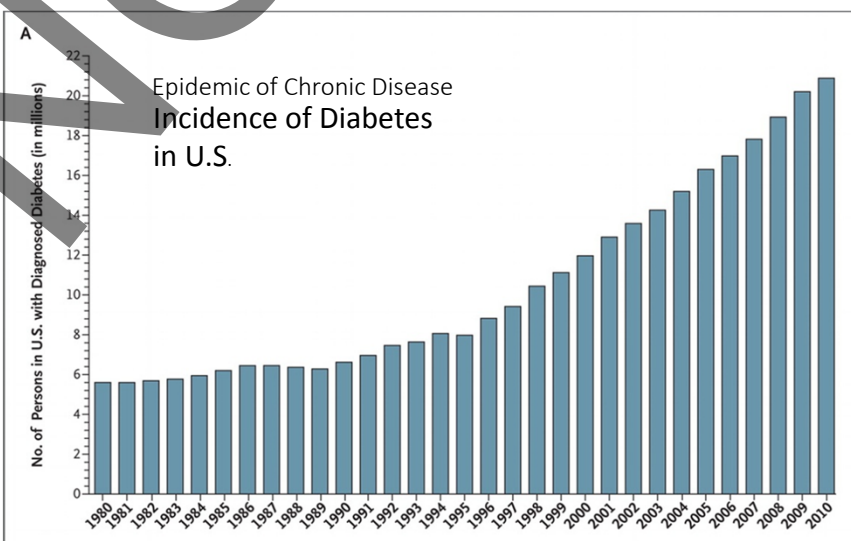
## Closer look at Diabetes:

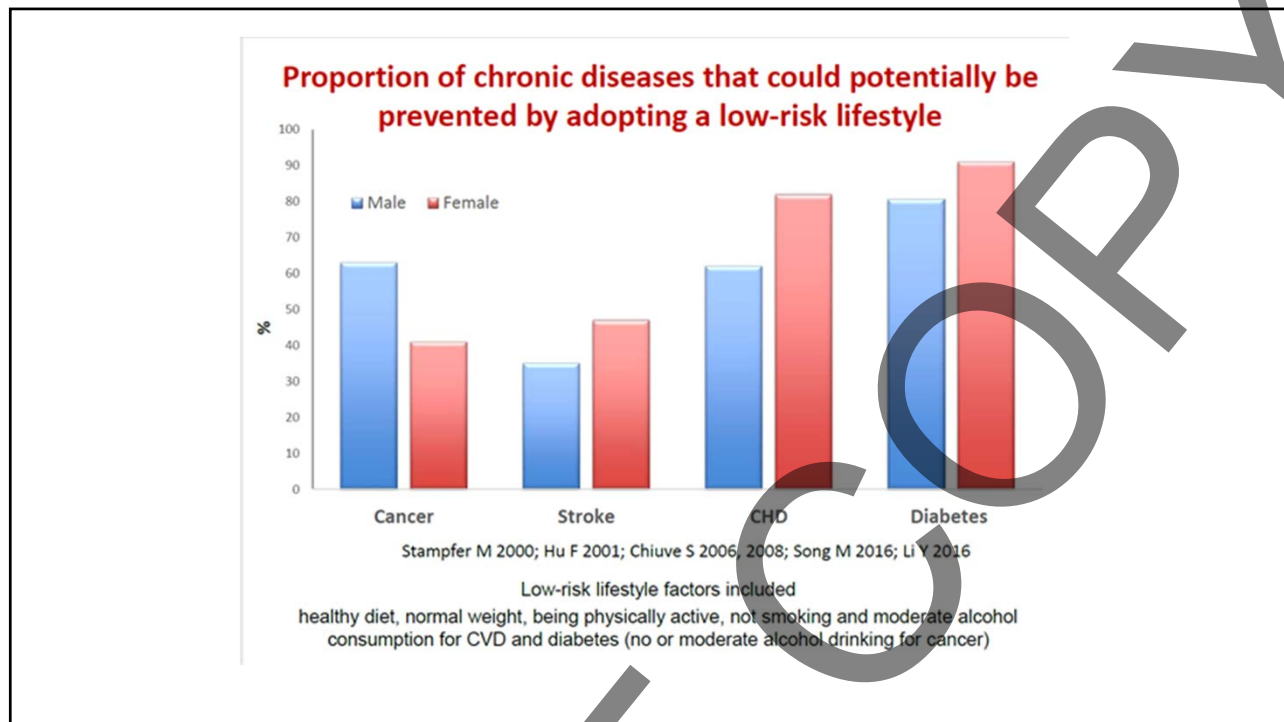
### Diabetes –

- 29 million Americans
- 8.3% U.S. population

### Pre-diabetes:

- 86 million Americans
  - 35% of all adults
  - 50% of adults >65
- Progression to diabetes 5 – 15% per year





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## Where do we start?

We start by creating a **healthy foundation** to support better outcomes – **diet, lifestyle, patient education, medication management, organ and system function optimization, psychosocial determinants**

- **Improve baseline nutritional status** → slow disease progression; ↓ complications
- ↓ smoking, alcohol consumption, poor diet, stress
- ↑ physical activity, social support
- **Optimize diet** - lower protein, low glycemic load, primarily plant-based, clean and green!



### Ref.

- Dunkler D, Kohl M, Heinze G, et al. Modifiable lifestyle and social factors affect chronic kidney disease in high-risk individuals with type 2 diabetes mellitus. *Kidney Int.* 2015;87(4):784–791.
- Galbraith L, Hemmelgarn B, Manns B, et al. *Can J Kidney Health Dis.* 2016;3:35.
- Collister D, Ferguson T, Komenda P, Tangri N. The patterns, risk factors, and prediction of progression in chronic kidney disease: A narrative review. *Semin Nephrol.* 2016;36(4):273–282.
- Morales E, Praga M. The effect of weight loss in obesity and chronic kidney disease. *Curr Hypertens Rep.* 2012;14(2):170–176.
- Steinman TI. Kidney protection: How to prevent or delay chronic renal failure. *Geriatrics.* 1996;51(8):28–35.

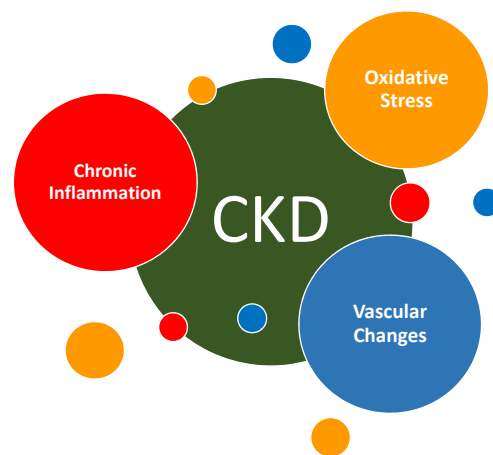


In addition to foundational support and improvements in diet and lifestyle, integrative health uses targeted treatments and therapies to:

- control *hypertension, diabetes, and hyperlipidemia*
- address underlying mechanisms that contribute to disease progression
- protect the kidneys from damage



**Vascular changes, chronic inflammation, and oxidative stress** are the main mechanisms demonstrated to contribute to the progression of CKD regardless of *etiology!*

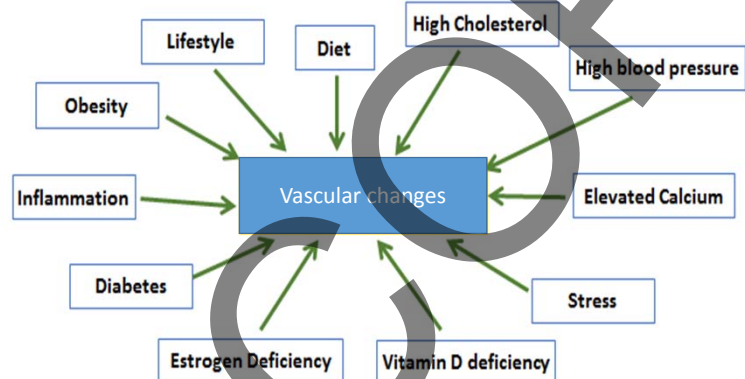




## Vascular Changes

- Endothelial dysfunction
  - Nitric oxide-mediated
- Microvascular disease
- Vascular calcification
- Atherosclerosis

### Preventable risk factors...



## Chronic Inflammation

- Inflammation is common in patients with CKD
- Contributing factors include:
  - **Increased production of proinflammatory cytokines**
  - **Oxidative stress**
  - **Immune dysfunction → infections**
  - **Altered metabolism/acidosis**
  - **Altered microbiome (Dysbiosis)**
- Other factors include: **diet, stress, lack of sleep, diabetes, obesity, environmental toxicants, myco- and bio-toxins**

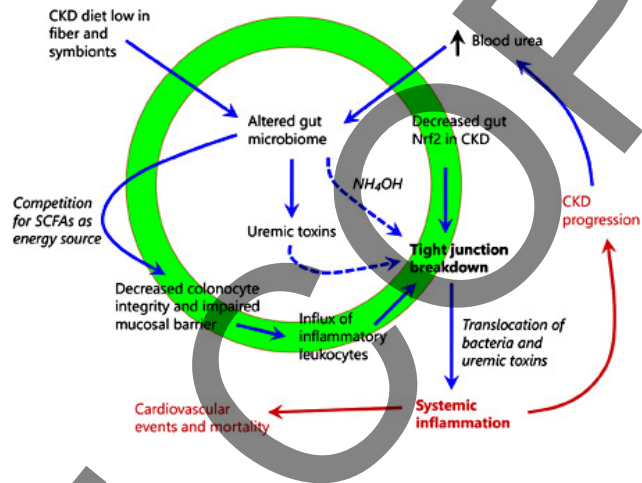
Mohsen Agharazii, Ronald St-Louis, Alexandra Gautier-Bastien, Roth-Visal Ung, Sophie Mokas, Richard Larivière, Darren E. Richard, *Inflammatory Cytokines and Reactive Oxygen Species as Mediators of Chronic Kidney Disease-Related Vascular Calcification*, American Journal of Hypertension, Volume 28, Issue 6, June 2015, Pages 746–755





## The Gut as a Source of Chronic Inflammation

- Dysbiosis associated with breakdown of intestinal barrier → hyper-permeability (leaky gut) → **translocation of gut bacterial DNA and uremic toxins** → **systemic inflammation**
- Altered microflora can also result in deactivation of certain toxic metabolites, increasing systemic toxic burden → oxidative stress & inflammation
- Additionally, altered microflora can affect nitric oxide availability and alter endothelial function



Lau W, L, Kalantar-Zadeh K, Vaziri N, D: *The Gut as a Source of Inflammation in Chronic Kidney Disease*. *Nephron* 2015;130:92-98.



## Oxidative Stress

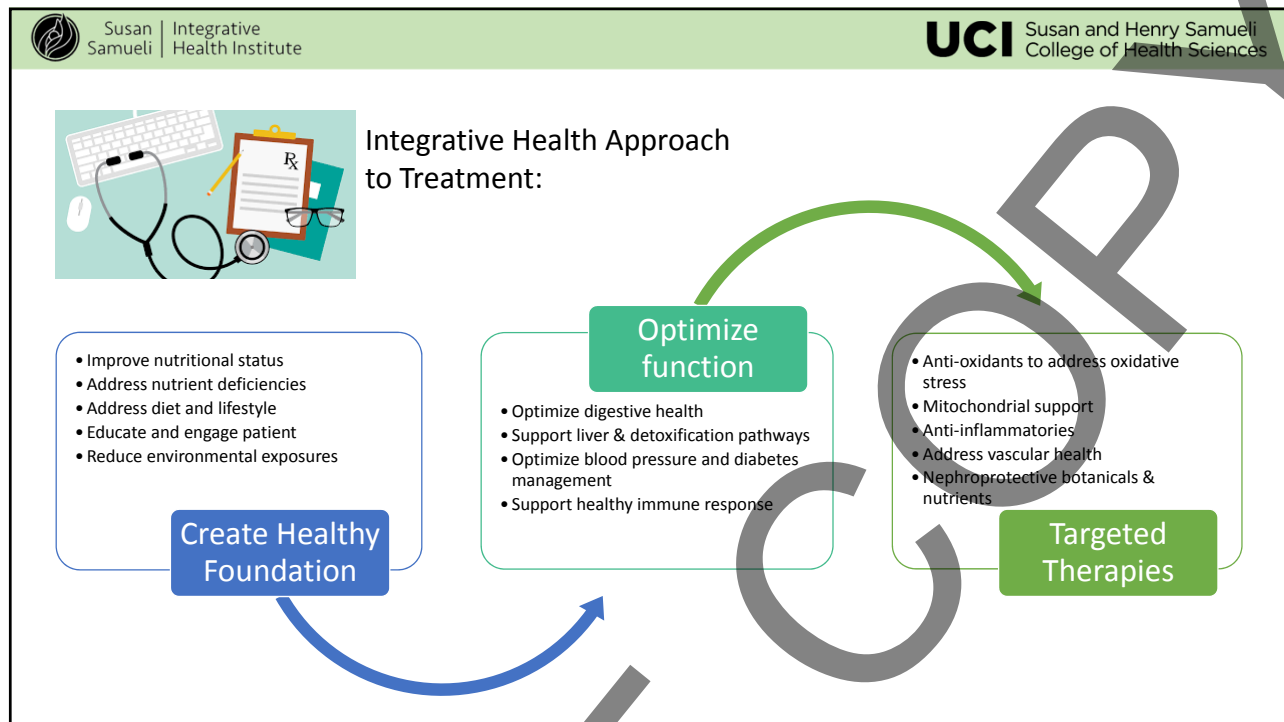
- **Oxidative stress occurs early in the course of CKD and is amplified as the disease progresses**

- Himmelfarb J. Linking oxidative stress, and inflammation in kidney disease: which is the chicken and which is the egg? *Semin Dial* 17: 449–454, 2004.
- Oberg BP, McMenamin E, Lucas FL, McMonagle E, Morrow J, Ikizler TA, Himmelfarb J. Increased prevalence of oxidant stress, and inflammation in patients with moderate to severe chronic kidney disease. *Kidney Int* 65: 1009–1016, 2004.

- **Oxidative stress → ↓NO bioavailability → renal hypoxia → inefficient use of oxygen within renal mitochondria**

- Singh P, Ricksten SE, Bragadottir G, Redfors B, Nordquist L. Renal oxygenation and haemodynamics in acute kidney injury and chronic kidney disease. *Clin Exp Pharmacol Physiol* 2013;40:138–147







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**If evaluation reveals:**

- **Poor nutritional status** → medical foods/ supplemental nutrients used to correct nutrient deficiencies and increase functional reserves
- **Poor digestive health** → improve digestion including biliary function, optimize breakdown and absorption of food & nutrients, decrease gut inflammation, improve elimination – may use combination of anti-inflammatories, digestive enzymes, bitters, pre- and pro-biotics, fiber, etc.
- **Increased toxin burden** → maybe due to poor liver health, increased environmental exposures, medication, epigenetic variants affecting detox pathways, etc. Select botanicals and nutrients to enhance metabolism of toxicants - e.g. Glutathione, NAC, Probiotics, Methionine, Glycine, B vitamins



## Dietary supplements may be selected based on:



### Anti-inflammatory properties:

- Curcumin
- EGCG
- Quercetin
- Fish oils
- Bromelain
- Boswellia

### Ability to improve vascular health:

- Vitamin D
- Vitamin E
- L-Carnitine
- L-arginine
- L-citrulline

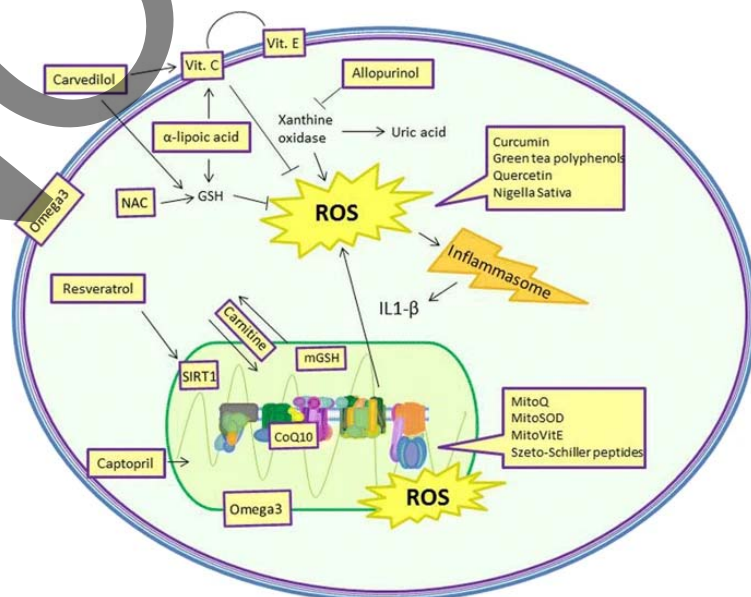
### Anti-oxidant & Mitochondrial support properties:

- Alpha lipoic acid
- Co-Enzyme Q10
- Vitamin E
- Resveratrol
- D-ribose
- L-Carnitine
- Taurine
- Magnesium
- NAC/Glutathione

### Botanical Medicine

- Evidence is encouraging but weak – Need for more research
- Based on several key herbs used in traditional Chinese medicine
- Most promising herbs: **Cordyceps** and **Astragalus** shown to have immunomodulating and nephroprotective properties

## Target sites of major anti-oxidants agents



Granata S, Dalla Gassa A, Tomei P, Lupo A, Zaza G. Mitochondria: a new therapeutic target in chronic kidney disease. *Nutr Metab (Lond)*. 2015 Nov 25;12:49

## Botanical Medicine



### Astragalus (a traditional Chinese medicine) for treating chronic kidney disease (Review)

Zhang HW, Lin ZX, Xu C, Leung C, Chan LS

Results concerning the effects of Astragalus on kidney function were inconsistent. Astragalus significantly increased CrCl at end of treatment (4 studies, 306 participants; MD 5.75 mL/min, 95% CI 3.16 to 8.34;  $I^2 = 0\%$ ), decreased SCr (13 studies, 775 participants; MD -21.39  $\mu\text{mol/L}$ , 95% CI -34.78 to -8;  $I^2 = 70\%$ ) and especially in those whose baseline SCr was  $< 133 \mu\text{mol/L}$  in particular (3 studies, 187 participants; MD -2.52  $\mu\text{mol/L}$ , 95% CI -8.47 to 3.42;  $I^2 = 0\%$ ). Astragalus significantly decreased 24 hour proteinuria at end of treatment (10 studies, 640 participants; MD -0.53 g/24 h, 95% CI -0.79 to -0.26;  $I^2 = 90\%$ ); significantly increased haemoglobin levels overall (4 studies, 222 participants); MD 9.51 g/L, 95% CI 4.90 to 14.11;  $I^2 = 0\%$  and in haemodialysis patients in particular (3 studies, 142 participants; MD 11.20 g/L, 95% CI 5.81 to 16.59;  $I^2 = 0\%$ ). Astragalus significantly increased serum albumin (9 studies, 522 participants; MD 3.55 g/L, 95% CI 2.33 to 4.78;  $I^2 = 65\%$ ). This significant increase was seen in both dialysis (3 studies, 152 participants); MD 4.04 g/L, 95% CI 1.91 to 6.16;  $I^2 = 72\%$ ) and non-dialysis patients (6 studies, 370 participants; MD 3.24 g/L, 95% CI 1.70 to 4.77;  $I^2 = 61\%$ ). Astragalus significantly decreased systolic blood pressure (2 studies, 77 participants; MD -16.65 mm Hg, 95% CI -28.83 to -4.47;  $I^2 = 50\%$ ), and diastolic blood pressure (2 studies, 77 participants; MD -6.02 mm Hg, 95% CI -10.59 to -1.46;  $I^2 = 0\%$ ).

Six of 22 included studies reported no adverse effects were observed, while the remaining 16 studies did not report adverse effects.

#### Authors' conclusions

Although Astragalus as an adjunctive treatment to conventional therapies was found to offer some promising effects in reducing proteinuria and increasing haemoglobin and serum albumin, suboptimal methodological quality and poor reporting meant that definitive conclusions could not be made based on available evidence.



### Cordyceps sinensis (a traditional Chinese medicine) for treating chronic kidney disease (Review)

Zhang HW, Lin ZX, Tung YS, Kwan TH, Mok CK, Leung C, Chan LS

#### Main results

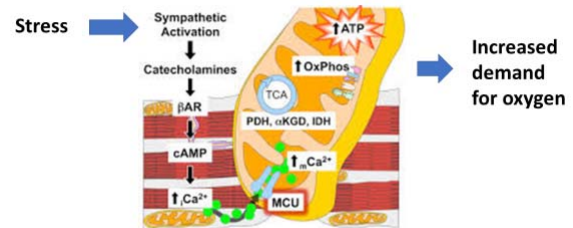
We included 22 studies that involved 1746 participants. Among people with CKD who were not receiving dialysis, Cordyceps preparations were found to significantly decrease serum creatinine (14 studies, 987 participants); MD -60.76  $\mu\text{mol/L}$ , 95% CI -85.82 to -35.71; increase creatinine clearance (6 studies, 362 participants); MD 9.21 mL/min, 95% CI 3.10 to 15.34 and reduce 24-hour proteinuria (4 studies, 211 participants; MD -0.15 g/24 h, 95% CI -0.24 to -0.05). However, suboptimal reporting and flawed methodological approaches meant that risk of bias was assessed as high in four studies and unclear in 18 studies, and hence, these results need to be interpreted with caution.

#### Authors' conclusions

We found that Cordyceps preparation, as an adjunctive therapy to conventional medicine, showed potential promise to decrease serum creatinine, increase creatinine clearance, reduce proteinuria and alleviate CKD-associated complications, such as increased haemoglobin and serum albumin. However, definitive conclusions could not be made because of the low quality of evidence.

## The role of Stress

- ✓ Stress increases heart rate, causes us to breathe more rapidly, makes us feel physically and mentally tense, and raises our blood pressure
- ✓ Stress causes increased oxidative damage to blood vessels
- ✓ Stress can weaken the immune system → more illnesses and longer duration
- ✓ Stress can lead to digestive issues i.e., malnutrition, diarrhea/constipation, malabsorption of nutrients, inflammation, bloating, and discomfort.
- ✓ Stress can affect our brain – our mood, memory, and ability to focus.





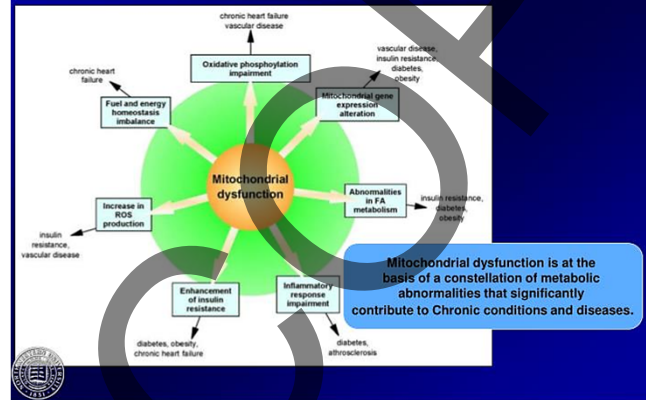
## Is it Time for “Metabolic Nephrology”?

- Dr. Steven Sinatra introduced us to *Metabolic Cardiology* as “a vital therapeutic strategy utilizing nutritional biochemical interventions that preserve and promote adenosine triphosphate (ATP) production”
- Integrative doctors apply this concept to most chronic diseases – improving tissue and organ resilience and protect them from damage and progressive failure - common conditions include heart disease, neurodegenerative disease, liver disease, and kidney disease
- Resilience is the key to “metabolic nephrology”!
- **Mitochondria** play an important role in – *Mitochondrial dysfunction* may occur as a result of the adverse effects of drugs, infections, environmental toxin exposure, a poor diet, or the body’s decreased capacity to handle stress!

Are you calling me dysfunctional?



### Translating the Basic Knowledge of Mitochondrial Functions to Metabolic Therapy



Mihai Gheorghide MD, FACC Professor of Medicine and Surgery Director of Experimental Therapeutics Center for Cardiovascular Innovation Northwestern University Feinberg School of Medicine. Mitochondria as a Therapeutic Target to Promote Cardio Vascular Health and Micronutrients.



## What does all this mean:

- Integrative approaches offer additional resources and options for patients with chronic kidney disease
- Exciting opportunities exist for collaboration and the development of clinical initiatives that combine integrative treatments and therapies to enhance patient outcomes
- There is a need for quality research examining the efficacy and impact of an integrative approach to managing patients with CKD – clinical outcome and QOL studies
- There is a need for further research to evaluate the benefits of individual botanicals and/or nutrients on kidney function and progression of kidney disease
- There is a need to identify novel measures to evaluate risk and progression of CKD, allowing for more individualized treatments

Thank you!

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