Evidence Based Herbal Medicine

Dr. Jenna Henderson
drhenderson@holistic-kidney.com
www.holistic-kidney.com
Disclaimer

• The KDIGO CKD guideline 4.4.5 states: We recommend not using herbal remedies in people with CKD. (Level of evidence: 1B)
• Patients often chose alternative medicine either with self medication or working with an alternative practitioner.
• Beneficial to understanding what the patients are encountering.
Patients and family often looking for alternatives to mainstream medicine for a variety of reasons:

- Side effects of medications, particularly prednisone and other immune suppressants.
- Medications often not successful at bringing remission.
- Cost of medications can be prohibitive for many families.
- Personal preferences toward natural remedies.
- Fear of dialysis and a willingness to do anything that may help them avoid it.
Objectives

• Understanding of what professionals might recommend herbal medicine.
• What herbs are commonly used by kidney patients when they self medicate.
• Awareness of research in the field of botanical medicine as it pertains to nephrology.
• Some herbs that show potential in research for treating specific kidney conditions.
• Red flags of when to be concerned about patient safety.
Nephrology and alternative medicine often worlds apart

• Completely different terminology.
• Nephrologists are not trained in herbal medicine.
• Alternative practitioners usually have a limited understanding of nephrology, especially advanced kidney disease, dialysis and transplantation.
• Many patients self-medicate with herbs and don’t tell their MD.
• Many patients take advice from individuals who are not qualified, especially online.
There are many professions in which there is some formal training with botanical medicine.

- American Herbalists Guild (AHG) recommends many different training programs.
- Acupuncturists (Lac) or Doctor of Oriental Medicine (DOM) will have training with traditional Chinese botanicals.
- Programs to study traditional Indian herbs (Ayurveda)
- Naturopathic doctors (ND) are the only professionals trained with both mainstream medicine and herbal medicine. Core curriculum includes botanical medicine and pharmacology.
- Not all who call themselves naturopathic doctors are in fact doctors. Unaccredited programs exist in unlicensed states. Often referred to as “un-Ds”.
Bio

• Dr. Henderson has been a kidney patient since 1993.
• Has gone through renal failure, dialysis and transplantation.
• Attended an accredited 4-year doctoral program.
• Wrote doctoral thesis on Botanical Medicine as Adjunctive Therapy for the Transplant Patient.
• Licensed by the state of Connecticut.
• Has the largest naturopathic practice exclusively for renal patients, with consultations from around the world.
Does this alternative practitioner understand kidneys disease? Be alert to red flags:

• They don’t understand the difference between kidney failure and chronic kidney disease.
• All kidney advice lumped together, whether diabetic nephropathy, nephrotic syndrome, polycystic kidneys, kidney stones or kidney infection.
• Claiming that the body is too acidic based on the pH of the urine.
• Extreme diets or overblown claims-- macrobiotics, raw juice fasting, etc.
Don’t walk-- run!

- Willingness to give off-the-cuff advice without reviewing labs or history.
- A more is better approach to drinking water.
- Practitioners who want patients to abruptly stop all medications.
- Practitioners who encourage patients to stop seeing a nephrologist.
- Practitioners who discourage dialysis when the patient is clearly in kidney failure.
What resources exist to learn about peer reviewed research into herbal medicine?

• NIH website http://www.ncbi.nlm.nih.gov/pubmed

• Guidebook published by the German government equivalent of the FDA translated into English: *Herbal Medicine: Expanded Commission E Monographs*. Considered by many to be a definite guidebook. (Note info. on transplant medicine safety is lacking.)

• *Nutritional Herbology: A Reference Guide to Herbs* by Mark Pedersen. Useful information on potassium and phosphorus content.
Additional resources:

- *Natural Medicine Journal* the official journal of the American Association of Naturopathic Physicians.
- *HerbalGram* the journal of the American Botanical Council.
- [www.herbalgram.org](http://www.herbalgram.org) has online herbal library.
- *NDNR* Naturopathic Doctors News & Reviews
- Townsend Letter: The Examiner of Alternative Medicine
Understanding what kidney patients encounter when they look to natural medicine.

• What are the most common herbs/ remedies on the market?
• Herbs to approach with caution for all kidney patients
• Herbs marketed for kidney problems-- what they think is going to help
• Culinary herbs-- very familiar but are they safe?
• Herb/drug interactions
• Beneficial herbs for CKD
• Herbs for dialysis patients
• Herbs and the transplant patient
Top ten best selling herbs. Note that kidney patients often self-medicate for concerns other than their kidneys. Good to be aware of what they might take.

- Cranberry
- Saw palmetto
- Soy
- Garlic
- Gingko
- Echinacea
- Milk thistle
- Black cohosh
- St. John's Wort
- Ginseng
Cranberry

- Use by many kidney patients for all types of ailments.
- Inhibits E-Coli, Proteus and Strep infections. Useful for UTI and some kidney stones.
- High antioxidant
- Juice is low (K+) and phosphorus (P). Dried or concentrated may be high.
Saw Palmetto

- Common herb used by older men.
- Used primarily for prostate health.
- May also be used for polycystic ovarian syndrome.
- Inhibits conversion of testosterone to dihydrotosterone.
- Relatively high K+ and P.
Soy

- Used for menopausal symptoms.
- Used as a meat alternative.
- Relatively high in K+ and P.
- High in phytates
- Also high in aluminum and manganese.
Garlic

- Reduces cholesterol around 10%
- Antibacterial, antiviral, antifungal.
- Can help mildly elevated blood pressure.
- Sulfur based antioxidants.
- Relatively low K+ Medium P.
Ginkgo biloba

- Blood thinner
- Very high antioxidant content.
- Evidence of usefulness for fibrosis of kidney with diabetic nephropathy
- May protect the kidney from glyphosate (Roundup) toxicity.
- Medium level K+ and P.
Echinacea

- Used against colds, flus and viral infections.
- Increases cell mediated immunity, IL-2
- Increases production of leukocytes
- Should be approached cautiously with autoimmune conditions.
- Low K+ and P.
Milk thistle

- Used for all types of liver problems-- fatty liver, hepatitis, alcoholic damage, jaundice.
- Evidence that it helps protect the kidneys from diabetic damage.
- Low in K+. Relatively high in P.
Black cohosh

- Used primarily for menopause.
- Also used for dysmenorrhea.
- In large doses can irritate the stomach.
- Relatively low in K+ and P.
St. John’s Wort

- Traditionally used topically for nerve pain.
- Relatively new use for depression.
- Useful for mild to moderate depression.
- Interacts with many medications.
Ginseng

- American, Chinese, Korean and Siberian varieties.
- Much American ginseng imported to China.
- Classified as an adaptagen herb; increases the amount of physiologic stress one can handle.
- Often used for fatigue.
- Some evidence of protective effect on kidneys.
Herbs often perceived as being less dangerous than prescription medications.

- Large number of prescription medications are synthetic forms of compounds originally discovered in plants.
- Prescription medications are a large dose of a single chemical compound.
- Herbal preparations contain the active constituent plus a myriad of cofactors which often mitigate side effects.
- Low dose of any one compound makes it harder to isolate a single factor. Usually combined effect of many chemically naturally occurring in the plant.
The good and the bad

- Often fewer side effects. Compare white willow to aspirin or Cyclosporine to Cordyceps mushroom.
- Far fewer fatalities from herbal medicine.
- Harder to quantify the active chemical components.
- Herbs cannot be patented. Therefore far less financial incentive to study.
- Many animal studies. Fewer human studies.
- Herbs with extensive histories usually classified as GRAS—generally recognized as safe.
Do dosages of herbs need to be adjusted with decreased kidney clearance?

• Herbs generally contain a low dose of any one constituent and a variety of related compounds.

• Most herbs would require an extremely high intake to be toxic.

• With patients who are frail or especially sensitive, good to start on a low dose and increase as tolerated.
Herbs/ remedies for kidney patients to avoid or use with caution with advice of qualified practitioner.

• **Stimulants that can raise blood pressure:**
  – Yohimbe. Commonly added to “male enhancement formulas”. Note that testosterone raises blood pressure.
  – Ma Huang (Ephedra). Traditional in Chinese respiratory formulas.

• **Licorice**—increases aldosterone and water retention.
Herbs/ remedies for kidney patients to avoid or use with caution with advice of qualified practitioner.

- Strong laxatives like senna and cascara segrada.
- Essential oils/ aromatherapy
- Colloidal silver
- Be suspicious of very inexpensive supplements.
- Phosphorus (P) additives. Phosphatidylserine, phosphatidylcholine
Caution-- Immune stimulants

• Best to avoid with autoimmune nephritis: Minimal Change, IgA nephropathy, FSGS, lupus nephritis.
• This includes: echinacea, elderberry (Sambucol), maitake, andrographis. Herbs used for cold/flu. Also bovine colostrum.
• Caution with herbs classified as Adaptogens-- Panax ginseng, American ginseng, Ashwagandha, Eleuthero and Rhodiola. Used as stimulants for energy.
• Absolutely contraindicated post-transplant.
Herbs commonly marketed to kidney patients

- Generally oriented toward UTI or kidney stones. Very little aimed toward chronic kidney disease.
- Botanical medicine kidney formulas will usually includes 1 or more of the following:
  - Diuretic
  - Demulcent
  - Antibacterial agent
Herbal diuretics-- do the kidneys really need to be cleansed?

- Often sold in health food stores often as detox teas. These include uva ursi, juniper, buchu, goldenrod, dandelion, parsley.
- Diuretics push the kidneys to work harder. They don’t “build the kidneys” or do anything to protect kidney tissue from the damage of chronic kidney disease.
- Lasix is still best bet for water retention issues.
Demulcent herbs

- Soothing to irritated membranes.
- Often a gummy texture due to mucopolysaccharides.
- Aloe vera topically for burns is an example of a demulcent.
- For kidneys-- slippery elm, marshmallow tea, corn silk or aloe vera juice.
- Soothing to kidney membrane.
- Clinically useful with nephritis or hematuria.
- NOT safe post-transplant
Antibacterial agents

- Cranberry or blueberry. Fruit, fruit juice or encapsulated extract.
- Inhibits bacteria from adhering to lining of urinary tract.
- Cranberry is acidic. Blueberry is alkaline.
- Good for UTI.
- Good antioxidants and low potassium. But otherwise not targeted for chronic kidney disease.
Culinary herbs that can effect the kidneys

- Garlic
- Cinnamon
- Curry/ turmeric
- Ginger
- Tea (Camilla sinensis) includes black tea, green tea and white tea.
Garlic (Allium sativum)

• Mildly anti-hypertensive
• Evidence that it protects the kidneys from toxicity of medications including Methotrexate, Gentamicin and Cisplatin.
• Antifungal, antibacterial, antiviral. Potentially beneficially for the immune compromised.
• Reduces the nephrotoxicity of medications like Cyclosporine.
• One of the very few herbs safe post-transplant.
Cinnamon (Cinnamomum cassia)

- Decreases blood sugar
- Increases insulin sensitivity
- Some evidence that it helps nephritis
- Reduces LDL cholesterol and triglycerides
- Maybe toxic at large doses.
- Appears safe post-transplant but definitive studies are lacking
Curry/ turmeric (Curcuma longa)

- Curcumin is the most active constituent of the curry spice turmeric.
- Reduces inflammation/proteinuria
- Supports kidney function
- Improves bone density
- Reduces pain. May help decrease reliance on pain medication.
- Helps blood sugar
- Helps blood pressure
Ginger (Zingiber officinalis)

- Botanically similar to turmeric.
- More than 300 active constituents of ginger identified.
- Possibly more medicinal uses than any other herb. One of the best researched plants on earth.
- Reduces inflammation in the kidneys
- Anti-platelet activity. Benefits of aspirin without the side effects.
- Reduces nephrotoxicity of antibiotics.
Tea (Camilla sinensis)

- Black tea, green tea and white tea all come from the same plant.
- Highest food source of antioxidant quercetin.
- Reduces inflammation/proteinuria.
- Reduces blood pressure in spite of small amount of caffeine.
- Prevents cardiac hypertrophy of CKD.
- Protects the kidney from contrast induced nephropathy.
- Reports of liver toxicity only with capsules in very concentrated form. Not toxic when used traditionally as a beverage.
Herb/prescription drug interactions

• Good to look up case by case.
• Don’t mix herbs with prescription drugs that have opposite effects—i.e. Herbs that raise immunity by increasing Il-2 along with prescription medications that lower Il-2.
• Some herbs can effect the rate of metabolism of medications. If you’re consistent, dosages can be adjusted. Don’t take sporadically.
Herbs that ameliorate specific conditions of the kidney

- IgA nephropathy -- Astragalus membranaceus
- FSGS -- Ganoderma lucindum
- Lupus nephritis -- Cordyceps, Artemisia
- Membranous glomerulonephritis (MGN) -- Arctium lappa
- Minimal Change Nephrotic Syndrome (MCNS) -- Bromelain
- Polycystic kidney disease (PKD) -- Curcumin, betaine
Advanced kidney disease

- Creatinine high/ most of the kidney tissue too damaged to work.
- Specific herbs can help support kidney function.
- Patient may be able to delay end stage renal disease.
- Many of these herbs are not well known.
Herbs for advanced kidney disease—evidence with the 5/6 nephrectomy model.

• With advanced kidney disease most of the nephrons are too damaged to work.
• Remaining nephrons working overtime to keep up with the demands of the body. State of hyperfiltration.
• Animal model to simulate progressed kidney disease involved removing 1 kidney and 2/3 of the other kidney. Resulting in reduced kidney mass, struggling to keep up with demands.
Herbs that show promise with the 5/6 nephrectomy model

- Cordyceps mushroom
- Curcumin
- Red propolis
- Astragalus membranaceus in combination with Angelica sinesis
- Epimedium sagittum
- Salvia miltiorrhiza
- Hibiscus
- Green tea
- Rehmannia glutinosa
- Rutin
Cordyceps mushroom

• Very long history of use for kidney ailments in China.
• Cyclosporine comes from the Cordyceps mushroom.
• 5/6 nephrectomy model shows less tissue damage and improved markers of kidney function.

[Effect of Cordyceps sinensis powder on renal oxidative stress and mitochondria functions in 5/6 nephrectomized rats]. PMID 26043568
Curcumin

- Associated with improved renal blood flow, antioxidant status and preservation of renal function in 5/6 nephrectomy model.
  PMID 27801955

- Comparable results to prescription medication Mycophenolate mofetil (Cellcept).
  PMID 27050624
Brazilian red propolis

• Bee product similar to honey traditionally used for a wide variety of ailments.

• 5/6 nephrectomy model showed significant reduction of hypertension, proteinuria, serum creatinine, glomerulosclerosis, renal macrophage infiltration and oxidative stress.

PMID 25607548
Astragalus membranaceus and Angelica sinensis

• Common to use in combination in traditional Chinese medicine.
• Showed improved renal microvasculature, reduced fibrosis, reduced proteinuria in 5/6 nephrectomy model.

PMID 19563735
Icariin, constituent of *Epimedium sagittum*

- *Epimedium sagittum*, commonly called “horny goat weed” is a common in male enhancement formulas. Can be used by women as well.
- Icariin significantly reduced serum creatinine, BUN and uric acid in 5/6 nephrectomy model. It also increased renal stem cells.

PMID 26490949
Tanshinone IIA, an active component of Salvia miltiorrhiza

- Salvia miltiorrhiza is a common herb in China, considered a heart tonic.
- Also known as Danshen, tan shen or red sage
- Reduced serum creatinine and proteinuria in 5/6 nephrectomy model.
PMID 21043035
Hibiscus

• Typically used as an herbal tea
• Often mixed with berries. 1st ingredient in common tea “red zinger”.
• Treatment with hibiscus showed fewer renal injuries as measured by blood urea nitrogen, serum creatinine, creatinine clearance, and renal pathology.

PMID 23157715
Green tea

• Multiple benefits for kidney patients including reduced blood pressure and improved bone density.

• Green tea showed protection from cardiac hypertrophy secondary to renal failure in 5/6 nephrectomy model.

PMID 12675854
Rehmannia glutinosa

- Widely used in Asian countries for kidney disease.
- Popular formula called Rehmannia 8 used as general tonic for fatigue.
- Rehmannia reduced serum creatinine, blood pressure and proteinuria in 5/6 nephrectomy model.

PMID 19146934
Rutin

• Food in foods—buckwheat, apple (skins), figs and rooibos tea.
• Can be taken as a supplement
• Rutin may reduce creatinine, BUN and proteinuria. Also helps reduce sclerosis and tubular injuries to the kidney.
PMID 26191162
Ongoing support for cardiovascular health in dialysis patients.

- Serum coenzyme Q10 levels are associated with coronary flow reserve in hemodialysis patients. PMID 23185999
- Coenzyme Q10 helps with coronary artery stenosis.
- Anecdotal evidence it helps with muscle cramps that are common during dialysis treatment.
Pomegranate juice for dialysis patients

• One year of pomegranate juice intake decreases oxidative stress, inflammation, and incidence of infections in hemodialysis patients: a randomized placebo-controlled trial. PMID 22609423

• A medium potassium food. Drink 1 or 2 oz. only. Not 8 oz. glass. Stay within daily limitations for potassium.
Epimedium sagittum improves quality of life for men on dialysis.

- Also increased immunity as measured by peripheral blood monocytes and IL-2.

PMID 7647539

- NOT SAFE POST-TRANSPLANT
Issues with clotting while on hemodialysis

- Heparin used during treatment but some patients still prone to clotting.
- Clotting during treatment can lead to reduced time on machine.
- Natural blood thinners: green tea, ginger, ginkgo biloba and vitamin E (mixed tocopherols).
- Discontinue or reduce dose if bleeding while coming off dialysis is an issue.
Herbal medicine and transplantation

- Widespread transplantation was made possible by the Cordyceps mushroom.
- Cordyceps is a medicinal mushroom from China with a very long history of use.
- Cyclosporine came from Tolypocladium inflatum, which is the asexual form of the Cordyceps mushroom.
All transplant medications suppress a particular immune signal.

- Interleukin2 (Il-2) is a chemical signal which turns on the immune response.
- All anti-rejection medications suppress Il-2.
- Many botanical medicines and medicinal mushrooms increase Il-2 and would therefore be contraindicated.
- **Traditional herbal folklore cannot be used with transplant medicine, only controlled studies.**
Partial list of herbs contraindicated with a transplant

- Aloe vera (internal use)
- Andrographis
- Angelica sinensis
- Ashwagandha
- Astragalus
- Corn silk
- Echinacea
- Emblica
- Epimedium
- Ginseng (all types)
- Licorice
- Milk thistle
- Maitake mushrooms
- Momordica charantia
- Rauwolfia serpentina
- Rehmannia glutinosa
- Reishi mushrooms
- Rhodiola
- Shiitake mushrooms
- Slippery elm
- St. John’s Wort
- Viscum album (Mistletoe)
Why do transplant patients look to herbal medicine?

- Estimated 30% of all transplant patients take some natural supplement.
- Perception that natural = safe.
- Difficulty living with immune suppression.
- Increased cancer rates.
- Increased infections-- virus, bacterial and fungal
- Gastrointestinal distress
- Graft loss, decreased function
- Nephrotoxicity of immune suppressants.
Herbs that are safe with transplants

• Camilla sinensis (black and green tea)
• Cordyceps mushroom
• Garlic
• Ginkgo biloba
• Salvia miltiorrhiza (Dan shen)
• Turmeric (Curcumin)
Some benefits of botanical medicine with transplants

• Cancer prevention-- melanoma and lymphoma
• Preventing infections
• Reducing nephrotoxicity
• Reducing cardiovascular stress
• Reducing gastrointestinal distress
• Better blood sugar, reduced post-transplant diabetes
• Extending graft survival.
Green tea and transplantation

• Often perceived as stimulating the immune system. This is incorrect.

• In an animal model, green tea increased graft survival and decreased reaction with mismatched donors. PMID 14962801

• Helps prevent skin cancer, the #1 cancer among the transplant population.

• Improves glycemic control.
Black tea and transplantation

• Black tea improves cardiovascular markers and vasodilation in renal transplant recipients.
• Measured in kidney recipients who were approximately 2 years post-transplant.
• Measurements taken at baseline and 2 hours after black tea consumption.

PMID 17524915
Cordyceps mushroom and transplantation

- Toxicity of Cyclosporine is an issue for many transplant patients. Nephrotoxicity of calcineurin inhibitors raise creatinine and can even lead to renal failure.
- Use of Cordyceps mushroom allowed for a reduced dose of Cyclosporine without changing immune compromised status.

PMID 21196310
Garlic

- Garlic reduced serum creatinine in renal transplant recipients. This effect was attributed to reduced nephrotoxicity of anti-rejection medication.
  PMID 15943877
- Garlic reduced Cyclosporine induced high cholesterol.
  PMID 17602419
- Garlic is antiviral, antifungal and antibacterial which is important when immune suppressed.
Ginkgo biloba and transplantation

• Ginkgo has been demonstrated to reduce cyclosporine toxicity. Study found a reduction in tubular and interstitial damage without interference of immunosuppressive effects.
PMID 3388505

Must be used cautiously if patient on blood thinners.
Salvia miltiorrhiza and transplantation

• Improves microcirculation to grafted kidney. PMID: 15957830
• Protects the kidney from injury: Danshen protects kidney grafts from ischemia/reperfusion injury after experimental transplantation. PMID: 18954374
Curcumin and transplantation

• Combined with quercitin, curcumin improved delayed graft function, lowered serum creatinine and prevented rejection.

PMID 16371925

• Helps prevent lymphoma, the #2 most common cancer post-transplant.

• Can improved bone density.

• Helps with gastrointestinal distress

• Improves blood sugar.
In Conclusion. Safe herbal medicine available to:

- Target specific kidney problems
- Protect the functional tissue of the kidney
- Support kidney function
- Potentially delay the need for dialysis
- Improve quality of life on dialysis.
- Protect from secondary heart disease
- Improve outcome with renal transplants
Some barriers to the safe use of botanical medicine for renal patients

- Perception that botanical medicine does not have research behind it. People don’t know that good research exists from reputable medical journals.
- Difficulty finding a qualified practitioner.
- Lack of communication between nephrology and alternative medicine.
- Misinformation on the web.
Integrative medicine of the future

• Model of China using prescription medications and traditional herbal remedies side by side.
• Increasing acceptance of herbal medicine in past few decades.
• Well informed patients increasing demand all options to be available.