

Slide #1

- The goal of this presentation is to shed some light on ways to address digestion and assimilation in the CKD population via supplements and herbs and to review some of the causes of poor digestion and assimilation. Finally, to provide some additional information on supplemental and herbal support for other comorbidities associated with CKD.
- Poor digestion and assimilation is a topic that is often overlooked in not just the CKD population but in nutrition therapy in general.
- Herbal Medicine is uniquely suited to treat digestive system illness as there are numerous herbs that address inflammation, stimulate gastric juices, bile and pancreatic enzymes, act as antimicrobials as well as have vasodilating, anti-hypertensive actions.

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Lets first explore this. *How many people hear complaints about GI issues in their clinic? What are you hearing?*

Often times the things that matter most to patients regarding their outlook on dialysis and life is based on how they feel. Many times the outcomes that are important to us as clinicians due to there importance to current paradigms of what counts for payment in dialysis is not even on the patients radar (P, Ca, PTH and alb). With the exception of P and its correlation to itching, patients often don't feel the affects immediately.

These are the common complaints and issue I hear on a monthly basis. Often these are the issues affecting intake and even attendance. However, these are the issues that I believe we have least amount of tangible tools to use beyond band-aid over the counter fixes. Due to Uremia these may never be able to be resolved however, we will explore additional tools that we may be able to put in our tool kit.

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- CKD patients have a difficult time with digestion and assimilation due to the uremic process that results from diminished kidney function.
- The uremic syndrome is characterized by the retention of various solutes that would normally be excreted by the kidneys. The substances that interact negatively with biologic functions are called uremic toxins.
- Chronic kidney disease (CKD) affects gastrointestinal (GI) function in many maladaptive ways. It disrupts the colonic microbiome, this disruption leads to the loss of gut barrier integrity and it increases the production of uremic toxins, Grant et al 2017.
- Grant et al studied upper GI function in those with advanced renal impairment and found that CKD was associated with dysmotility and reduced fasting and post-prandial small bowel water, reflecting abnormal digestive secretion and absorption. They found that this was related to the degree of endotoxemia

- Duranton et al 2012 performed a literature search and found 621 articles about uremic toxicity published after 2003. These records described 32 previously known uremic toxins and 56 newly reported solutes. The articles most frequently reported concentrations of β 2-microglobulin, indoxyl sulfate, homocysteine, uric acid, and parathyroid hormone.

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- Many uremic solutes have been shown to be associated with mortality or morbidity in epidemiologic studies
- Randomized clinical trials of retention solute removal on hard outcomes such as mortality are scarce, and results are not always supportive of improved survival, Duranton et al 2012.
- Recently, the strong vasoconstrictor **uridine adenosine tetraphosphate (Up₄A)** was described as a uremic toxin. CKD patients had, on average, a 5.2-fold higher Up₄A plasma concentration compared with healthy subjects, and this increased Up₄A concentration may influence blood pressure, proliferation rate of vascular smooth muscle cells, and calcification processes in CKD patients
- several large acute phase proteins (**α 2-macroglobulin, fibrinogen, myeloperoxidase, and IL-12**)^{56,95-97} and endothelium-related proteins (**vascular cell adhesion molecule 1, vascular endothelial growth factor 1, and soluble vascular endothelial growth factor receptor**)^{45,70} were increased in CKD, and they could have a significant diagnostic and pathophysiologic value

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- On the reverse end, Uremia reduces some of the beneficial substances that act as anti-oxidants, anti-inflammatories and vasodilating properties.
- Duranton et al 2012 identified molecules that were also reduced in uremia (**bilirubin, reduced glutathione, α 1-antitrypsine, arginine, and homoarginine**).^{10,35,81,100}
- Because these solutes are associated with **antioxidant, anti-inflammatory, and vasodilating properties**, their reduced concentration could be involved in additional adverse effects of uremia.

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Let's do a **brief review** of all of the steps needed for digestion and absorption:

- The digestive tract extends from the mouth to the anus
- We need good acid base balance in the GI tract for proper pH, adequate smooth muscle tone for moving materials down the digestive tract, proper acid secretion in the stomach, sufficient pancreatic digestive enzyme secretion into the intestine, sufficient bile secretion for fat absorption, and integrity of the gastrointestinal mucosa for protection and nutrient absorptions, (Liska, et al 2004)
- It needs all of these steps to break down large protein, carbohydrate and fat molecules in foods into smaller substances that can be absorbed into the blood by the brush border cells of the intestinal mucosa.
- In this process, vitamins and minerals are released from food material in order to be absorbed by the body.
- **Chewing** food properly starts the process and affects the end product. One rule of thumb is if you still identify the food in the mouth based on texture, then you haven't chewed it enough. (Liska, et al 2004)
- **Hypochlorhydria** – inadequate secretion of gastric acid by parietal cells in the stomach wall in general and exacerbated by H-2 blocking antacids and proton pump inhibitors. Research suggests that low gastric acidity may influence the development of diseases such as food allergies, rheumatoid arthritis, acne, rosacea, asthma; gastric acid decreases as we age and most people over the age of 60 have insufficient secretory abilities. **Chronic inflammation can increase hypochlorhydria.** Hypochlorhydria invites bacterial overgrowth in the small intestine since elevated pH values allow greater numbers of small intestine microflora to proliferate. This overgrowth compromises digestion and absorption particularly for the B-complex vitamins (especially folate, B6 and B12) and minerals iron and calcium. So a renal vitamin is key but use of a liquid or sublingual may be better as is it really reaching the patient in tablet form? Due to so much dysbiosis in the first place?
- Chronic **hyposcretion of pancreatic enzymes** not only leads to fat and protein maldigestion and malabsorption but also to micronutrient deficiencies. Pancreatic insufficiency directly causes B12 deficiency. (Liska, et al 2004) **My additional synopsis / RECAP:** Remember the stomach also produces intrinsic factor needed to absorb vitamin B12 from the small intestine; the chief cells produce protein digesting enzymes (pepsinogens) which are converted to the active form of pepsin by the hydrochloric acid produced by the parietal cells.
- **Bile** – manufacture in the liver and stored in the gallbladder helps to break up fat into smaller globules for better absorption of fat. Insufficient amounts reduce fat and fat soluble vitamin absorption.
Let's consider some stomach cells produce intrinsic factor which is needed to absorb vitamin B 12 from the small intestine
- Chief cells produce protein-digesting enzymes, mostly pepsinogens
- Parietal cells produce hydrochloric acid which makes the stomach contents acidic and activates the enzymes, example: converts pepsinogen to pepsin
- Entero-endocrine cells produce gastrin.

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- In recent years, the gastrointestinal tract has emerged as a major instigator of systemic inflammation in CKD.
 - Postmortem studies previously discovered gut wall inflammation throughout the digestive tract in chronic dialysis patients.
- In CKD animals, colon wall inflammation is associated with breakdown of the epithelial tight junction barrier ('leaky gut') and translocation of bacterial DNA and endotoxin into the bloodstream.
 - Gut bacterial DNA and endotoxin have also been detected in the serum from CKD and dialysis patients,
 - whereby endotoxin levels increase with the CKD stage
 - and correlate with the severity of systemic inflammation in the dialysis population.
- The CKD diet that is low in plant fiber and symbiotic organisms (in adherence with low potassium, low phosphorus intake)
 - can alter the normal gut microbiome,
 - leading to overgrowth of bacteria that produce uremic toxins such as **cresyl** and **indoxyl** molecules.
- The translocation of these toxins from the 'leaky gut' into the bloodstream further promotes
 - systemic inflammation,
 - adverse cardiovascular outcomes
 - and CKD progression.
- Data are lacking on optimal fiber and yogurt consumption in CKD that would favor growth of a more symbiotic microbiome while avoiding potassium and phosphorus overload.
- Prebiotic and probiotic formulations have shown promise in small clinical trials, in terms of lowering serum levels of uremic toxins and improving quality of life.
- The evidence points to a strong relationship between intestinal inflammation and adverse outcomes in CKD, and more trials investigating gut-targeted therapeutics are needed, (Lau et al 2015).

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- Montemurno et al 2014, indicate that for the CKD population the role of gut microbiota is the missing link between food and health. Microbiota are the microbial community found in the large intestine. It is considered a symbiotic "supplementary organ", contributing to digestion, mainly through two catabolic pathways: saccharolytic (fermentation) or proteolytic (putrefaction).
- It also interacts with host influencing immunity, metabolism, and general health status (mood, memory and more).

- It is believed that a **balanced healthy microbiota is primarily saccharolytic** and diet has a deep effect on its composition.
- **Mediterranean Diet** they note that there is a high supply of fiber and antioxidants in the Mediterranean Diet and that it favours the prevalence of saccharolytic species, while the typical Western Diet that many of our patients follow, promotes the shift towards a proteolytic profile and dysbiosis.
- In CKD a vicious cycle exists, in which proteolytic-derived microbial metabolites (p-cresol and indoxyl sulphate), represent the main circulating uremic toxins: their accumulation worsens dysbiosis and promotes CKD progression.
- Felizardo et al 2016 note that not only is the westernized diet altering the gut microbiota in a way that directly correlates with increased incidences of diabetes and hypertension, leading causes of CKD, **data is also showing that the progression of CKD is strictly related to the composition of microbiota.**
- They note that these alterations intensify renal injury and may also contribute to comorbidities such as cardiovascular diseases and insulin resistance. They further note that increased progression of CKD further modifies the diversity and abundance of the microbiota, further intensifying the progression of CKD, creating a vicious Cycle (March et al).

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Is it time to rethink the Renal Diet?

- The great news is that the renal diet has changed for the better already. Greater use of whole grains and more liberal use of vegetables and fruits and greater avoidance of processed foods that used to be encouraged like marshmallows.
- *Gut microbiota shaping through non-pharmacologic nutritional treatments, based on Mediterranean Diet,*
- Considering greater use of a Mediterranean diet represents an innovative approach in CKD, potentially restoring microbiota balance, ameliorating CKD conditions and slowing down disease progression, Montemurno et al 2014.
- March et al 2017 note there is accumulating evidence that the intestinal barrier and the microbiota may also play a role in the systemic inflammation present in Hemo-Dialysis patients and more research is needed in this area.
- A Chinese Study conducted by Han et al 2017 indicate that the gut microbiota dysbiosis is one of the risk factors in the progression from the advanced chronic kidney disease (CKD) to uremia and it is characterized by the reduction of probiotics and the increase of opportunistic pathogens including urease-related microbes, endotoxin-related microbes and toxin-related microbes, which can produce uremic toxins.
- It is thought that gut microbiota dysbiosis aggravates renal damage by accumulating uremic toxins and inducing the systemic micro-inflammation.
- Preliminary clinical trials and animal experiments show that the
 - **probiotics biologicals from Lactobacillus acidophilus or Bifidobacterium,**
 - and the **prebiotics including inulin and galactooligosaccharides,**

- as well as **lubiprostone** (used for idiopathic constipation / opioid constipation) and **activated carbon adsorbents** Vaziri et al 2013 found that CKD animals had Tight Junction failure due systemic inflammation, oxidative stress and endotoxemia. They administered AST-120 and Activated Carbon Absorbant / Activated Charcoal and it decreased uremia induced disruption of colonic epithelial tight junctions and associated endotoxemia, oxidative stress and inflammation.
- These can all be used for improving dysfunction of CKD patients with the gut microbiota dysbiosis via reducing uremic toxins and inhibiting the systemic micro-inflammation.
- They note that oral or enema administration can also regulate the gut microbiota dysbiosis, protect the intestinal epithelial barrier, reduce uremic toxins accumulation, inhibiting micro-inflammation and delay CKD progression.
- **FUTURE STUDY** - Based on these results, they note that interventional studies targeting the gut microbiota-related pathological factors such as tight junction proteins, helper T cells and regulatory T cells in the intestinal tract of the advanced CKD patients will become one of the key development directions in the future.

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- Herbal Medicine is uniquely suited to treat digestive system illness.

Terms

- Anti-inflammatory – helps the body combat inflammation
- Antimicrobial – help the body destroy or resist pathogenic microorganisms in some way (bacteria, fungi, viruses)
- Antispasmodic – prevents cramps or eases spasms
- Astringent – helps to tighten tissue which can help stop bleeding –in the gut they help reduce inflammation
- Demulcent – soothe and protect irritated or inflamed internal tissue
- Bitters – assist digestion and stimulate gastric and pancreatic juices
- Nervine – herbs that strengthen and nourish the nervous system
- Hypnotics – nervines that help induce a deep and healing state of sleep

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- There is ongoing interest in the development of pharmacological approaches targeting the reduction of intestinal permeability.
 - corticosteroids, aminosaliclates and anti-tumor necrosis factor- α (TNF- α), which act by reducing inflammation;
 - probiotics, which modulate the production of mucin and epithelial tight junction proteins;
 - and mucoprotectants, which form a protective film over the epithelium.

- such as gelatin tannate
- and xyloglucan

Recently, preclinical and clinical data highlight, the ability of new mucoprotectants, such as gelatin tannate and xyloglucan, to protect the intestinal mucosa and to exert anti-diarrheal effects.

In the future the ability of these substances to enhance the intestinal barrier may extend their use in the management of a variety of gastro-intestinal diseases associated with 'leaky gut' (Eutamene et al 2017).

- **Glutamine** (Braun and Cohen 2008) – a conditionally essential amino acid found in all life forms and the most abundant amino acid in the human body. During conditions of metabolic stress the body is unable to synthesise L-Gln in sufficient quantities to meet biological needs and it becomes essential to have an exogenous intake (543)
- Glutamine is vital for maintain the integrity of the intestinal lining and preventing the translocation of microbes and endotoxins into the body

Among the various tissues using glutamine at high rates, the intestine utilizes about 30% of total glutamine [15], indicating that it is a key nutrient for the intestine.

- Tight junctions maintain intestinal integrity, which prevents pathogens and toxins from entering the intestinal lumen [36]. There are four types of transmembrane components of tight junctions, including claudins, occludin, tricellulin, and junctional adhesion molecules
- Restriction of glutamine in cell culture media significantly increased epithelial cell permeability in Caco-2 cells.
- The addition of glutamine in glutamine-deprived cells rescued the impaired barrier functions. These studies suggest that glutamine supplementation may be beneficial for individuals with an impaired gut permeability by enhancing the expression of tight junction proteins.
- Nitric oxide (NO) is synthesized by multiple cells and modulates a variety of cellular signaling pathways, including inflammatory responses [69]. During intestinal inflammation, NO may play a dichotomous role, as both beneficial and harmful effects of NO have been observed [70]. Glutamine is an important regulator of NO synthesis.
- Therefore, based on the in vitro and in vivo studies mentioned above, glutamine supplementation could be one promising candidate for treating intestinal inflammatory disorders by inhibiting activation of NF- κ B and STAT, and suppressing expression of inflammatory cytokines such as IL-6, TNF- α , and IL-8, and inflammatory enzyme inducible NO synthase, Kim et al 2017.
- **Butyric Acid** - a small 4 carbon nonessential short-chain fatty acid that functions the large intestine similarly to glutamine in the small intestine as the fuel of choice. 75% of all dietary carbohydrate that reaches the colon (mainly as undigested fiber) can be converted by colonic bacteria into short chain fatty acids, including butyrate. Supplementation may be beneficial (Liska et al 2004).
- **Fermented Foods** – provide acid to stimulate the stomachs natural acids, enzymes and prebiotics and probiotics

- **Colostrum** – is the milk produced by female mammals towards the end of pregnancy and is secreted from the mammary gland in the first 2 days after giving birth. It imparts passive immunity to the neonate and also improves gut permeability.
- Bovine Colostrum contains nutrients, antibodies, growth factors, vitamins and minerals and has a variety of effects on the gastrointestinal tract, immune function and the ability to fight some infections and may possibly reduce muscle catabolism. Improvements in gut permeability are usually seen in about 5 days. It should be avoided by those with lactose intolerance. Braun and Cohen

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Garlic

- Is an antimicrobial, hypotensive, antispasmodic. It acts as a broad spectrum antibiotic, antifungal, antiviral and anti-parasitic. It has known chemopreventive and anticancer, antioxidant and immunostimulant properties. The organosulfur constituents (alliin, gamma-L-glutamyl peptides) whose mechanisms are not completely known and, flavanoids and saponins. **Interactions:** has anti-platelet activity and must be used with care with warfarin. High doses may irritate the intestinal mucosa causing nausea, diarrhea, vomiting and burning of the mouth. Garlic reduces serum cholesterol and triglycerides while raising levels of high density lipoproteins. During acute infections 1 clove 3 times daily can be used or even enteric coated garlic supplements. Garlic cooked loses its antimicrobial abilities but retains its anti-hypertensive and cholesterol lowering abilities. Combined with onion oil packs a bigger punch. Consider encouraging patients and yourself to eat 1 clove of garlic daily with meals. Garlic has large consensus as a treatment as a hypolipidemic, antiatherosclerotic, hypotensive, antiplatelet, and fibrinolytic agent.

Thyme

- Is a Carminative and an antimicrobial, antispasmodic, astringent and expectorant.
- Has a lot of volatile oils, and is good for dyspepsia and sluggish digestion. Can be used as a gargle for laryngitis and tonsillitis, eases sore throats and coughs.
- does not have many human studies but constituent knowledge (phenolics, saponin, tannins, Thymol and eugenol). Thymol and eugenol have antifungal activity with their ability to alter the cell wall and membrane of the yeasts *Saccharomyces cerevisiae* and *Candida albicans*; they also are antibacterial, antiviral, antioxidant, astringent, and anti-inflammatory. Traditionally it has been used to treat respiratory tract infections. It has invitro activity against *E. coli*, *Listeria monocytogenes*, *Streptococcus mutans* and *Salmonella enterica* (Braun and Cohen 2010).
- How to use – fresh chopped or as an infusion 1 cup boiling water over 2 teaspoons of dried herb and infuse in covered container for 10 minutes. Drink 3 times daily.

Myrrh

- Is a gum resin antimicrobial, astringent, carminative, expectorant, vulnerary that has been shown to stimulate the production of white blood cells and it has direct

antimicrobial effects. It is good for mouth infections and mouth ulcers, gingivitis, pyorrhea, pharyngitis and sinusitis. It is also a hypoglycemic.

- Theoretically it may interfere with antidiabetic therapy since it has hypoglycemic properties. Undiluted tincture in the mouth can burn or irritate the palate.
- How to use – as a mouth rinse or gargle add 5 to 10 drops of tincture to a glass of water. Dental powders should contain 10% powdered resin.

Sage

- Carminative, antispasmodic, antimicrobial, anti-inflammatory. It has soothing actions on the mucous membranes. It helps with inflammations of the mouth, throat and tonsils and may be used as a mouthwash to treat gingivitis, glossitis, stomatitis. It helps with dyspepsia.
- Safety / Considerations – adverse reactions are likely only with overdoses more than 15 g = 7.5 Tablespoons sage leaf per dose or prolonged use of red sage. The toxic constituents of the essential oil thujone, causes symptoms such as tachycardia, hot flashes, convulsions and dizziness. Avoid during pregnancy.
- Infusion – pour 1 cup of boiling water over 1-2 teaspoons of leaf and infuse covered for 10 minutes. Three times daily. Mouthwash – place 2 teaspoons of leaf in a pint of water bring to a boil and let stand, covered for 15 minutes. Gargle deeply with the hot infusion several times a day, (Hoffmann, 2003)

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ACTIVITY

Pass Out Sample

Kombucha
Sauerkraut
Salad Dressing with Lettuce etc
Ginger Chews

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Marshmallow

- because of its mucilaginous nature it is a great demulcent (soothes and protects irritated or inflamed internal tissue, particularly on the lining of the intestines where it soothes and reduces irritation by direct contact). Can be used internally or externally.
- Safety Considerations – may delay absorption of other drugs taken at the same time.
- Should be in tincture 3 times daily or via a cold infusion 2-4 grams of root in 1 cup of water for a goal of 6 grams daily

2 grams tea leaves = 1 Tablespoon

Calendula

- Externally it soothes inflamed skin; internally it acts as an anti-inflammatory in the digestive system; it relieves gallbladder problems and many vague digestive complaints known as indigestion. It also combats fungal infections.
- Safety considerations – possible allergen (Asteraceae family for those allergic). Non-toxic, no current reports of adverse issues.
- How to use: make an infusion 1-2 teaspoons of flowers in 8 oz water and infuse for 10-15 minutes. Drink 3 times daily.

German Chamomile

- Is a nervine, antispasmodic, carminative, anti-inflammatory, anti-microbial, bitter, vulnerary
- Helps with insomnia, anxiety, menopausal depression, loss of appetite, dyspepsia, gastric ulcers, diarrhea, colic aches and pains of flu, migraine, neuralgia, teething, vertigo, motion sickness, conjunctivitis, inflamed skin, urticaria and many others.
- Most widely used nervine herb in the West
- It has a wide safety range.
- Safety / Precautions - May cause allergic reactions in people sensitive to plants in the Asteraceae family. Reactions are noted to be extremely rare.
- Infusion – 2-3 teaspoons of herb in 1 cup of boiling water for 10 minutes in a covered container and drink 3-4 times a day. ora tincture 1-4 ml three times daily.

Peppermint

- Is a carminative (ease discomfort caused by flatulence) with relaxing effects on the muscles of the digestive system. It combats flatulence, dyspepsia, intestinal colic, stimulates the flow of bile and digestive juices. The volatile oil acts as a mild anaesthetic to the stomach wall, decreasing feelings of nausea and the desire to vomit. Helps relieve nausea and vomiting related to pregnancy and motion sickness. It is also an anti-inflammatory, antispasmodic, nervine, antimicrobial, analgesic.
- Safety Considerations – no side effects or drug interactions

Gentian

- Is a bitter (remedies that have bitter tastes that trigger a sensory response in the mouth that is directed by the nerves to the central nervous system and sends a message to the gut to give rise to the release of the digestive hormone gastrin which triggers and supports the digestive cascade).
- Bitters stimulate appetite and digestion via general stimulation of digestive juices, stimulating saliva, gastric juices, and bile. Aids the liver in detox, helps regulate the secretion of pancreatic hormones that regulate sugar, insulin and glucagon; helps stimulate self-repair mechanism of the gut and more.
- It accelerates the emptying of the stomach. It is indicated for slow digestion and loss of appetite, dyspepsia and flatulence.
- Safety Considerations: may cause headaches in predisposed persons. It is contraindicated during pregnancy and for those with gastric or duodenal ulcers; avoid with hiatal hernia, gallbladder disease, kidney stones, dysmenorrhea, GERD.
- How to use – take tincture 1-2 ml (30 – 60 drops) 15 – 30 minutes before meals or any time acute stomach pains are associated with a feeling of fullness. Decoct ½ teaspoon of shredded root in 1 cup of water and boil for 5 minutes.

Valerian

- Is a Nervine (a plant remedy with some type of beneficial effect upon the nervous system – in cases of shock, stress, nervous debility, anxiety). It is also a hypnotic, antispasmodic, carminative, hypotensive and emmenagogue (herbs that treat women's reproductive organs). It has a wide range of uses but is mainly used for anxiety, nervous sleeplessness and bodily symptoms of tension, such as muscle cramping and indigestion.
- Safety Considerations – Valerian may increase the effects of sedatives and for a small few it may cause a stimulating affect.
- How to use – must be used at a sufficiently high dosage to be effective; Tincture is most widely used 2.5 – 5 ml (75 drops – 150 drops = ½ - 1 teaspoon) up to 10 ml per dose at one time. Infusion – use 2 teaspoons of dried herb per 1 cup of boiling water. Prepare in a closed vessel to ensure no loss of volatile oils. Or, a cold infusion can be made by pouring 1 cup of cold water over 2 teaspoons of root and let stand 8-10 hours. Gastritis is the same but replace calendula with Filipendula umaria (meadow sweet); 3 part Althea and 1 part Filipendula and Matricaria

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Ginger

- contains an essential oil and resin known collectively at oleoresin. It has demonstrated anti-emetic activity in both experimental models and human studies. It also inhibits serotonin –induced diarrhea and acts as an antispasmodic on visceral and vascular smooth muscle. It blunts gastric dysrhythmia and nausea evoked by acute hyperglycemia.
- Exerts several effects in the gastrointestinal tract, which leads to improvements in gastrointestinal symptoms.
- Stimulates the flow of saliva, bile and gastric secretions
- Increases GI motility in several animal models
- Appetite Stimulant since it accelerates gastric emptying and stimulates antral contractions in a randomized double blind study.
- Eases GI discomfort, colic, diarrhea, bloating
- Effective in inhibiting H.pylori
- Prevented the decline in renal antioxidant status by increasing glutathione-s-transferase activity in an experimental model of nephrotoxicity
- Nausea treatment (post operatively, pregnancy, motion sickness, chemotherapy induced) – however with pregnancy the German Commission E ginger should not be used to alleviate morning sickness in pregnancy; however there is tradition use of it in pregnancy. TCM says don't use more than 2 g of dried ginger daily during pregnancy .
- Can help treat Migraine as it inhibits thromboxane A2 and exert antihistamine, anti-inflammatory and gastric actions
- Can be taken in many forms (cooked, fresh, tea, pickled, glazed, candy, ethanol extracts)

- Theoretical risk with warfarin since it has anti-platelet effects but there is not evidence of an interaction with warfarin at the usual dietary and therapeutic intakes. Has been shown not to alter prothrombin times,
- People with gall stones, gastric ulcer and reflux should use ginger with caution, Braun and Cohen 2008.

Ginger Dose –

- Tincture dose 1.5 – 5 ml three times daily
- Fluid Extract – 0.25 to 1 ml three time daily
- Infusion – pour 1 cup boiling water over 1 teaspoon of fresh root and infuse ofr 5 minutes – drink as needed.

Fennel:

- An excellent stomach and intestinal remedy that relieves flatulence and colic while stimulating digestion and appetite .
- Can be used as a compress to treat conjunctivitis and blepharitis (inflammation of the eyelids)
- Increases milk flow in nursing mothers
- And calms coughs in bronchitis and other colds
- No side effects or drug interactions have been reported.

Fennel Dose and Preparation:

- For infusion pour 1 cup of boiling water over 1 to 2 teaspoons of slightly crushed seeds and infuse in a covered container for 10 minutes. Drink three times daily
- To ease gas and flatulence take a cup 30 minutes before meals., (Hoffman 2003)

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- Ali-Hasan et al 2016 in a systematic review with meta-analysis found that overall, antioxidants such as **N-acetyl cysteine NAC, vitamin C, and vitamin E** can reduce the incidence of Contrast induced nephropathy, while only NAC might be able to significantly lower serum creatinine levels. There is no impact of Antioxidant supplementation on mortality.
- There is increased evidence that **magnesium** can inhibit vascular calcification, which is a common risk factor that occurs in CKD. Cohort studies in patients receiving dialysis have shown a lower serum magnesium level as a significant risk for cardiovascular mortality. Also, the cardiovascular mortality risk associated with hyperphosphatemia is alleviated among those with high serum magnesium levels. It was also found that one of the harmful effects of high phosphate on the progression of CKD is also reduced among those with high serum magnesium levels. The potential usefulness of magnesium as a remedy for phosphate toxicity should be further explored by future intervention studies. Sakaguchi et al 2017.

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- Omega 3 Fatty acids are one of 2 essential fatty acids that humans cannot make on our own. Our bodies cannot insert the double bond needed in the 3 and 6 position. So we must get it via diet.
- Alpha-linolenic acid (ALA) is the source of EPA and DHA.
- Fish oil (ALA) provides it in a pre-formed state that requires no conversion vs Non fish oil derived (ALA) which must be converted.
- Non fish ALA is found in canola, linseed, soybean, flaxseed, pumpkin and walnuts – research doesn't show that same beneficial results with non fish ALA as with fish ALA possibly due to inefficient conversion of ALA into EPA and DHA. In this conversion we usually only get 5-10% of ALA converts to EPA and 2-5% of ALA converts to DHA.
- **Omega 3 Fatty Acids** - Many CKD patients complain of pruritus or itching even when there Phosphorus is well controlled. There is greater interest looking into the reasons why. Essential Fatty Acid deficiency is starting to be considered more closely. Panahi et al 2016 conducted a literature review of omega 3 fatty acids on uremic pruritus and found four small studies with 3 having small randomized controlled trials that showed a significant improvement in pruritus symptoms (evaluated by questionnaire) in CKD patients who took omega-3 supplements compared to omega 6, omega 9 and placebo. They noted numerous limitations of the studies but still self reported feelings of improvements with itching.
- Signs of deficiency: cardiovascular disease, inflammatory disorders, rheumatoid arthritis, unipolar depression, senile dementia, asthma, atopic dermatitis.
- EFA's help to prevent cardiac arrhythmias and associated sudden death, protects against ventricular fibrillation and ischemia and reperfusion (restoring blood flow back to the heart after heart attack)
- 3 oz of cold water fish provides about 1000 mg omega 3 EFA
- People with fat malabsorption syndrome are at risk for developing deficiency (elderly, diabetics and people with a variety of metabolic disorders, alcoholics(Brauhn and Cohen 2010)
- **ALSO CONSIDER** : fish oil may decrease immunological renal injury in patient with IgA Nephropathy and slow the decline in renal function – although the research is limited and the findings are mixed. Fish oil taken with Selective serotonin reuptake inhibitors may enhance therapeutic activity of antidepressant. Fish oil may improve vascular health but in the presence of statins may increase LDL level and decrease glycemic control , Stargrove et al 2008.
- The literature suggests 1 – 10 g per day but it will vary depending on the pathophysiology and the level of health of the individual. The practitioners I have worked with and myself note 3000 mg daily is the baseline therapeutic dose and 5000 mg may be needed during acute inflammatory issues, Stargrove et al 2008.
- Docosahexaenoic acid (DHA)
- Eicosapentaenoic acid (EPA)
- **Another more comprehensive look at omega 3 EFA** and hemodialysis was research published in BMC Nephrology in 2015. Bessell et al 2015 took components of the

Mediterranean diet due to its known protections for cardiovascular disease in the general population and trialled it in hemodialysis patients with the aim of reducing the risk of cardiovascular disease and improving associated risk factors.

- Components include fish, fruit and vegetables in the form of fish oil supplements and vitamin and antioxidant supplements.
- They conducted a narrative review where they looked at observational studies, and interventional and randomized controlled trials.
- In the literature they found that risk of mortality is reduced in patients with a higher fish intake and those with higher serum omega-3 fatty acid levels. However, the pathways by which risk of mortality is reduced have not been fully extrapolated.
- The few studies that examined the effect of **vitamin B** supplementation in hemodialysis patients, these studies suggest that supplementation alone does not reduce the risk of mortality.
- Finally, studies examining **vitamin E** supplementation have drawn inconsistent conclusions regarding its pro-oxidant or antioxidant effects.
- They further note that dietary supplementation in hemodialysis patients is an area which requires larger, more methodologically robust randomised controlled trials to determine if risk of cardiovascular outcomes can be improved.

Slide #18

- **Garlic** - Consider encouraging patients and yourself to eat 1 clove of garlic daily with meals. Garlic has large consensus as a treatment as a hypolipidemic, antiatherosclerotic, hypotensive, antiplatelet, and fibrinolytic agent. It acts as a broad spectrum antibiotic, antifungal, antiviral and anti-parasitic. It has known chemopreventive and anticancer, antioxidant and immunostimulant properties. The organosulfur constituents (alliin, gamma -L-glutamyl peptides) whose mechanisms are not completely known and, flavonoids and saponins. Interactions: has anti-platelet activity and must be used with care with warfarin. High doses may irritate the intestinal mucosa causing nausea, diarrhea, vomiting and burning of the mouth Garlic reduces serum cholesterol and triglycerides while raising levels of high density lipoproteins. During acute infections 1 clove 3times daily can be used.or even enteric coated garlic supplements. Garlic cooked loses its antimicrobial abilities but retains its anti-hypertensive and cholesterol lowering abilities. Combined with onion oil packs a bigger punch.
- **Cayenne** – Avoid if using ace inhibitors as I may induce ACE inhibitor (lisinopril) induced cough during early co-administration. Can use internally or topically as an anti-arthritis (Stargrove et al 2008). Research indicates that topically capsaicin blocks the transmission of pain and itching by nerve fibers in the skin (depletes local supplies of a neurotransmitter called substance P, which transmits pain and itching signals from the nerve in the skin to the spinal cord, Hoffmann 2003. It is most useful as a systemic stimulant for circulation, stimulation blood flow and strengthening the heart, arteries,

capillaries and nerves. It is known for toning the circulatory system and digestive system, Hoffman 2003.

- These herbs are helpful with hypertension, congestive heart failure, Angina
- **Hawthorn** – is considered to be an all around cardiovascular wellness remedy and the most significant herb for ischemic heart disease. It is considered a cardiotonic. It contains (flavonoids, glycosides – rutin and quercetin being some of them, anthocyanidins, oligomeric proanthocyanidins. It is recommended by Stargrove et al 2008 indicated it should be used with caution in the elderly on multiple medications with psychiatric medications. They also note that Pittler et al conducted a meta analysis of clinical trials using Hawthorn extract for the treatment of chronic heart failure 8 of 13 of the studies allow concomitant meds for CHF, ACE inhibitors, diuretics, calcium channel blockers and it concluded there was a better than placebo effect on the endpoints (max workload, pressure – heart rate product, left ventricular ejection fraction. Also Quality of Life was tested in a smaller trial via questionnaire and had significant improvements over the placebo groups (Braun & Cohen 2008)
- CanCombine the 5 herbs together to make a tea with 2 part of Hawthorn and 1 part everything else.

Slide #19

- There are numerous herbs that can be used for cough, upper respiratory issues and bronchitis. However, they may not be the safest for CKD patients as some have some liver toxicity with prolonged use or in large amounts and some interfere with anticoagulant medications.
- Hyssop, Mullein and Thyme are 3 herbs that are effective and have no side effects or reports of drug interactions. on the other hand has a very high safety range.
- Hyssop -
- **Mullein** – has not been significantly studied in clinical trials so most of the information we have for it is traditional uses over centuries internally and externally. Also invitro, phytochemical and pharmacological information based on its constituent parts (mucilaginous polysaccharides, flavonoids, caffeic acid, triterpene saponins and sterols) most of the information (Braun & Cohen 2010). It has been used traditionally for dry cough in conjunction with (licorice, coltsfoot and marshmallow). IT reduces inflammation while stimulating fluid production, thus facilitating expectoration. It has been used for a hard dry cough with soreness and for inflammation of the trachea (Hoffman 2003).
- **Thyme** – does not have many human studies but constituent knowledge (phenolics, saponin, tannins, Thymol and eugenol). Thymol and eugenol have antifungal activity with their ability to alter the cell wall and membrane of the yeasts *saccharomyces cervasiae* and *candida albicans*; they also are antibacterial, antiviral, antioxidant, astringent, and anti-inflammatory. Traditionally it has been used to treat respiratory tract infections. It has invitro activity against *E. coli*, *Listeria monocytogenes*, *Streptococcus mutans* and *Salmonella enterica* (Braun and Cohen 2010).

- **Horehound** – used for unproductive cough and bronchitis. It helps to relax the smooth muscles of the bronchus while promoting mucus production and expectoration. It stimulates the laryngeal and bronchial mucous membranes. In syrup form it is also used for asthma, hoarseness, some forms of dyspepsia and pulmonary affections.
- The General Infusion would be 2 teaspoons of dry herb combined in 1 cup of boiling water for 20 minutes. Drink hot three times a day.
- For renal we would increase the concentration to 3 teaspoons of dry herb in less water 5 oz of boiling water – three times daily for a total of 15 oz rather than 24 oz.
- Other herbs to add are garlic and sage; consider cooking with these. Garlic should be chopped and let to stand in the open air for at least 7 minutes to activate its medicinal qualities.