

IS THERE ROOM FOR HERBS


and

Functional Nutrition in Renal Therapy?

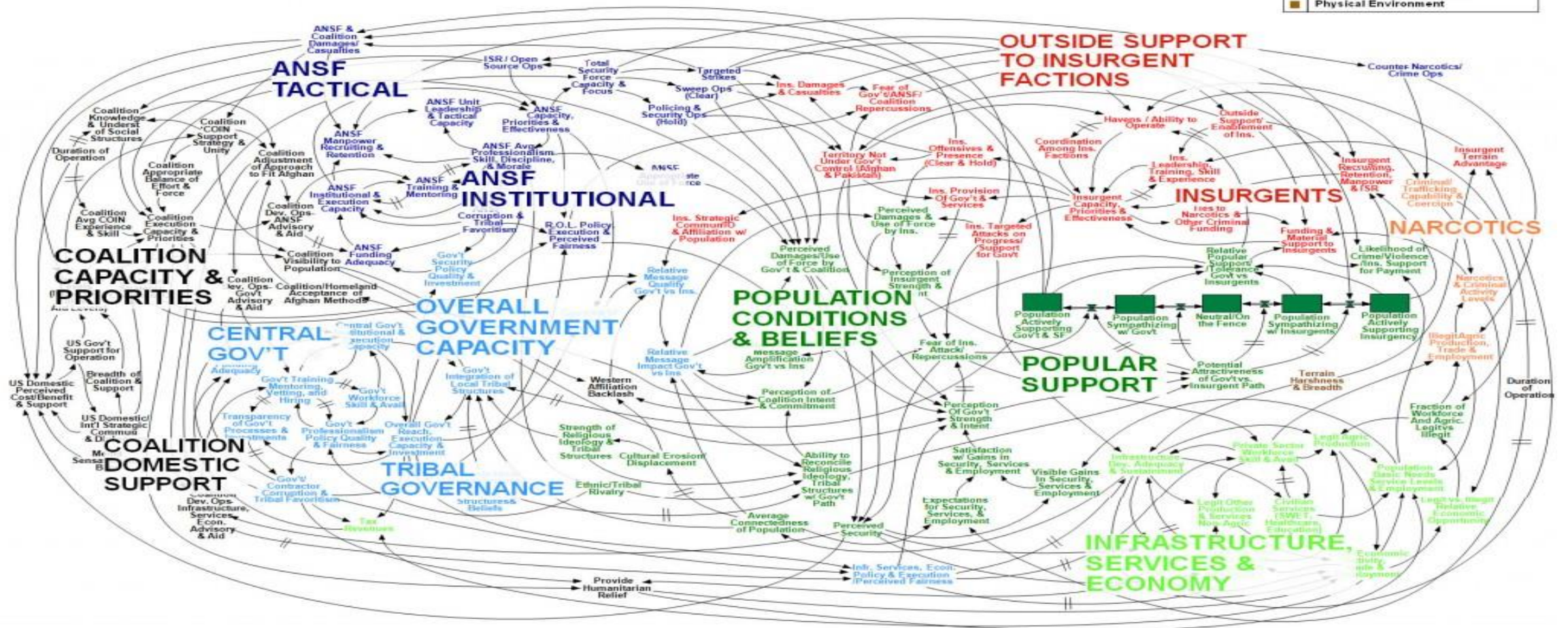
Njeri Kai Jarvis MS / RD / LDN



Afghanistan Stability / COIN Dynamics

 = Significant Delay

- Population/Popular Support
- Infrastructure, Economy, & Services
- Government
- Afghanistan Security Forces
- Insurgents
- Crime and Narcotics
- Coalition Forces & Actions
- Physical Environment



WORKING DRAFT - V3

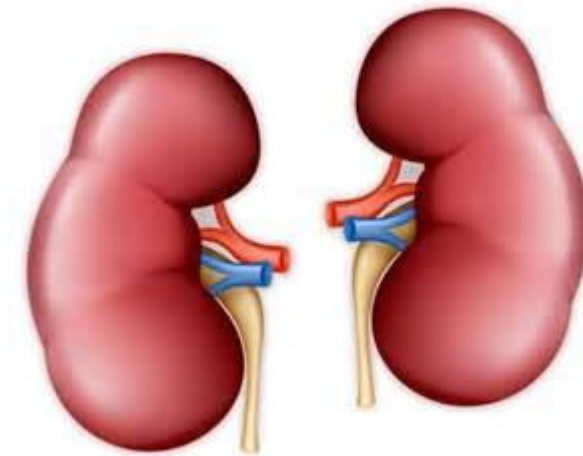
What We Know

- In the United States, 49 billion dollars was spent treating end stage renal disease ESRD / chronic kidney disease -CKD-5.
- This was eleven times more spent than in 1980.
- In 2003 , chronic kidney disease prevalence in the United States comprised about 11% of the population (19.2 million people)
 - 5.9 million had CKD 1
 - 5.3 million had CKD 2
 - 7.6 million had CKD 3
 - 400, 000 had CKD 4
 - 300, 000 had CKD 5 / ESRD



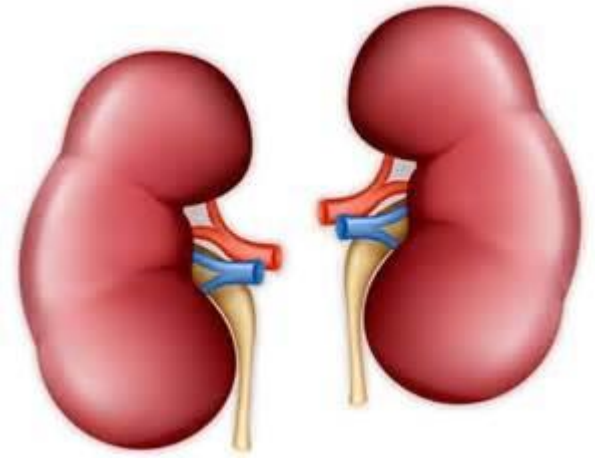
Kidney's Main Functions

- To keep the make up of the extracellular fluid constant with regards to its salts, acid, nutrient content
- Produce Hormones
 - Angiotensin
 - Erythropoietin
 - prostaglandins



What is Kidney Disease?

- Kidney failure is the loss of some but not all of the filtration capacity of the kidneys
- There are many different types of kidney diseases all of which cause a loss of filtration capacity



BIG PICTURE

Causes of Chronic Renal Failure

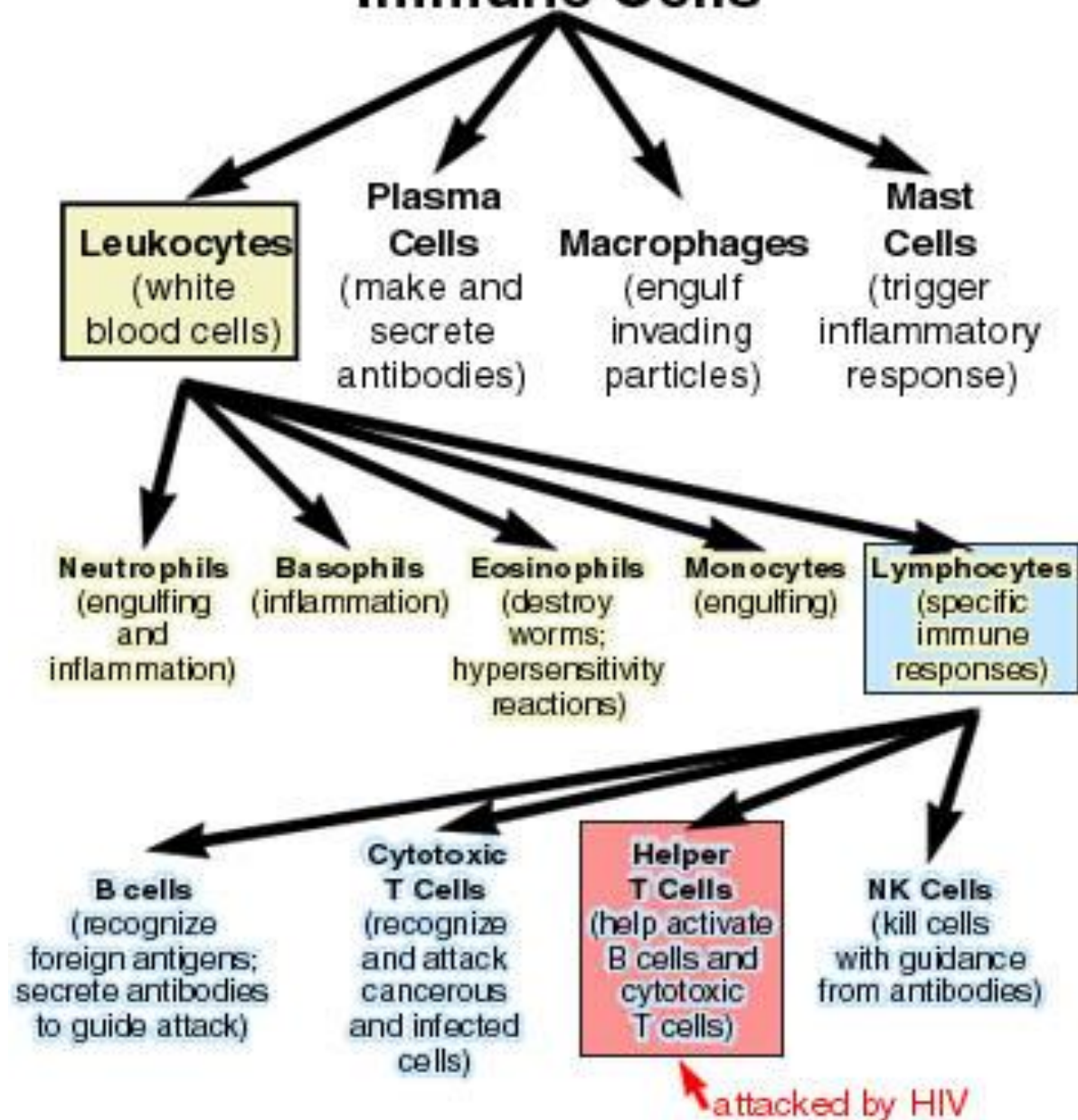
1. Primary glomerular disease
2. Primary tubular disease
3. Vascular Disease
4. Infections
5. Obstructive Disease
6. Collagen disease
7. Metabolic Renal disease
8. Congenital anomalies of kidney



Hypoxia – Common Path to Renal Failure

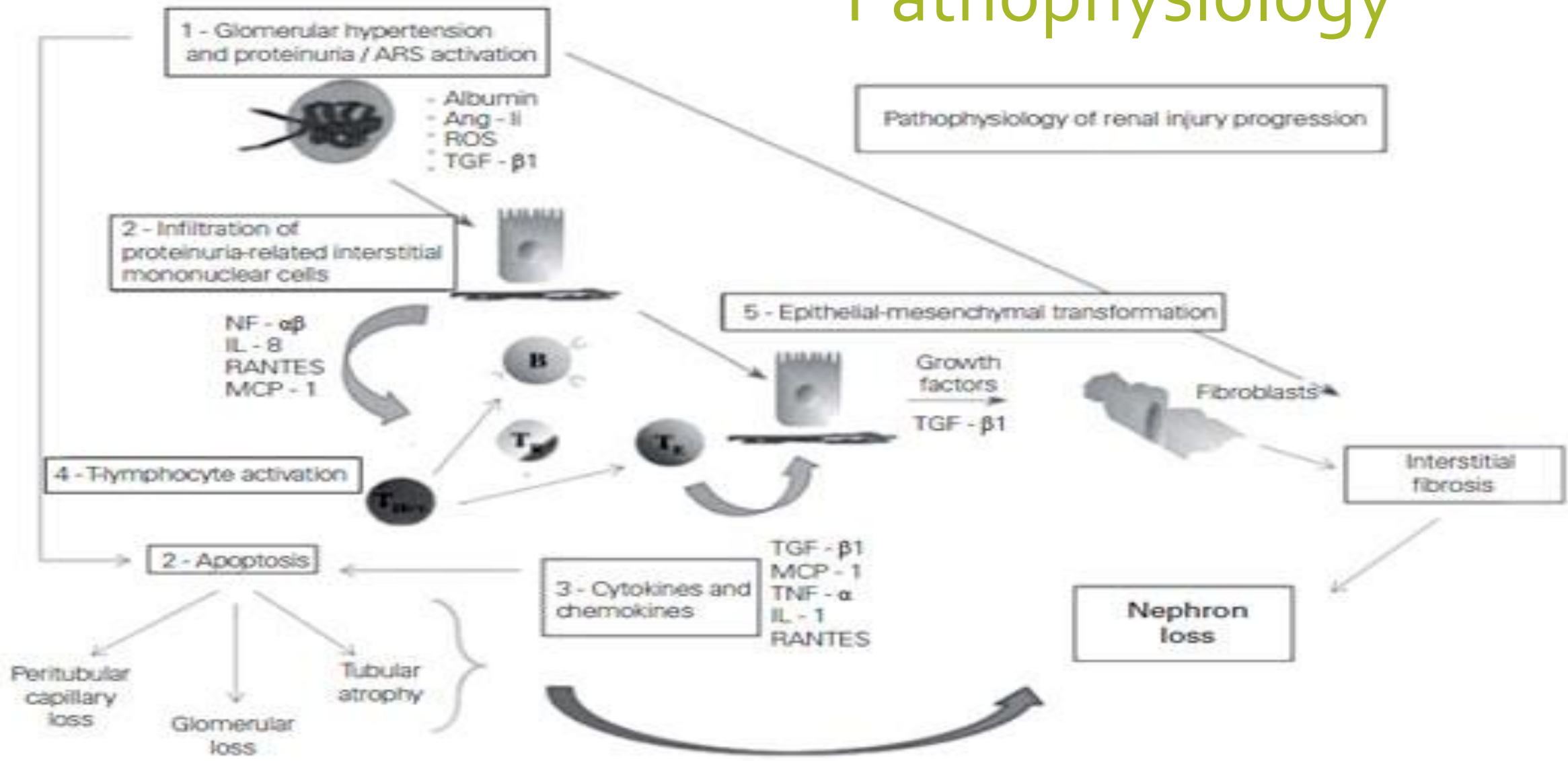
- A large body of evidence indicates that CKD is driven by renal tissue hypoxia and that chronic hypoxia is the final common pathway to end-stage renal failure.
- Numerous studies have demonstrated that one of the most potent means by which hypoxic conditions within the kidney produce CKD is by inducing a sustained inflammatory attack by infiltrating leukocytes.
- Consequently, targeting these transcriptional mechanisms would appear to represent a promising new therapeutic strategy. (Qiangwei, et al, 2016)

Immune Cells

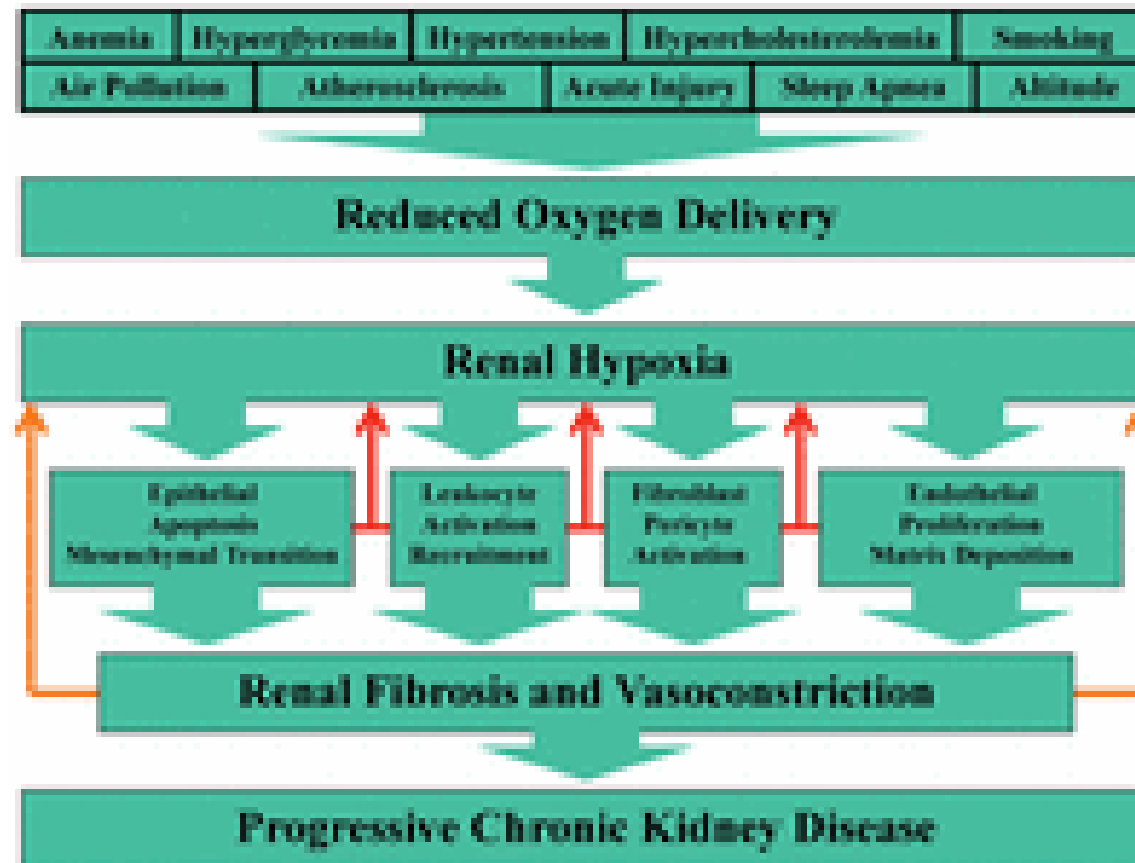


Pathophysiology

Pathophysiology of renal injury progression



The Hypoxia Cycle Driving Chronic Kidney Disease

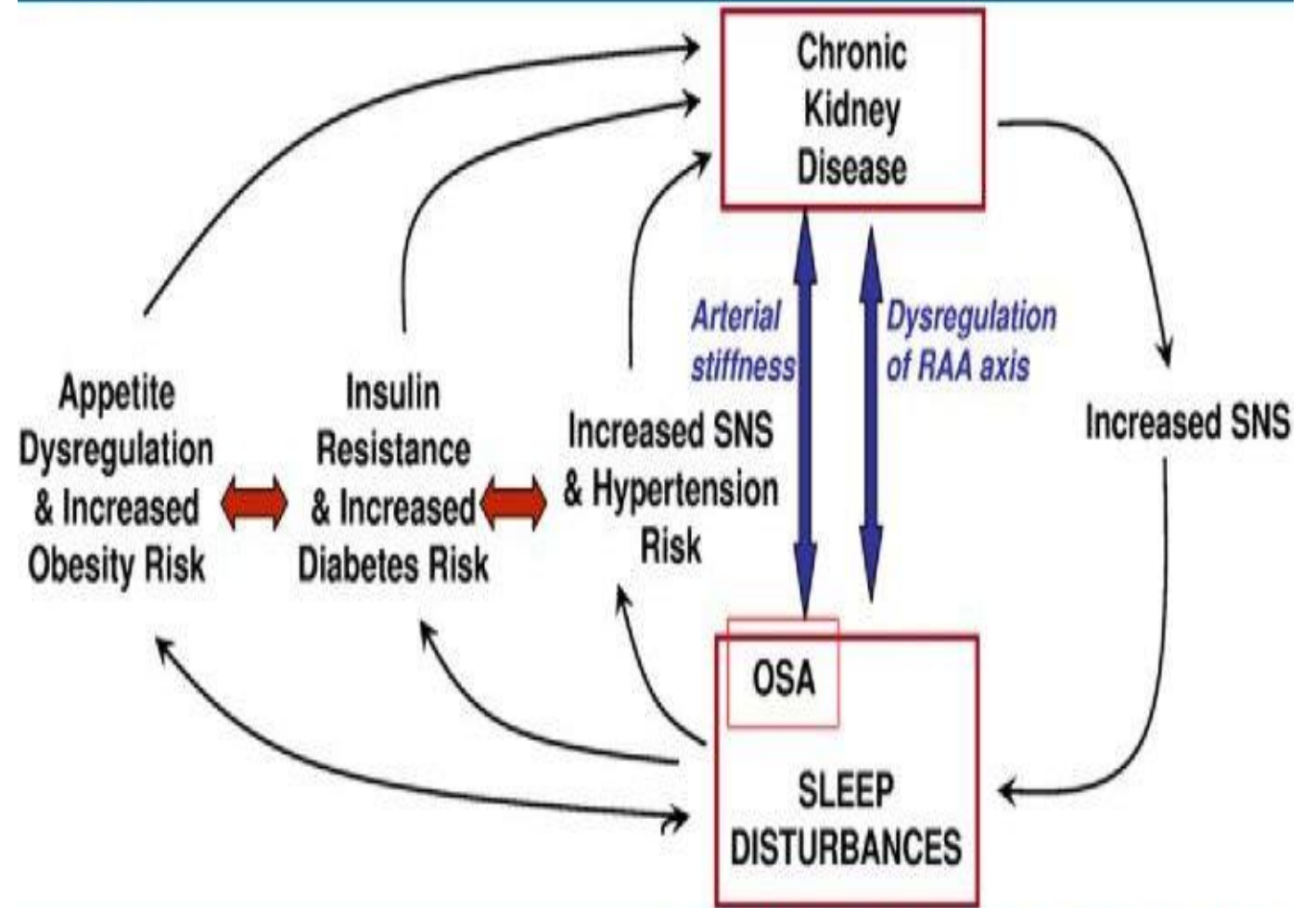


Consider This

Hypoxia and Inflammation from Sleep Apnea



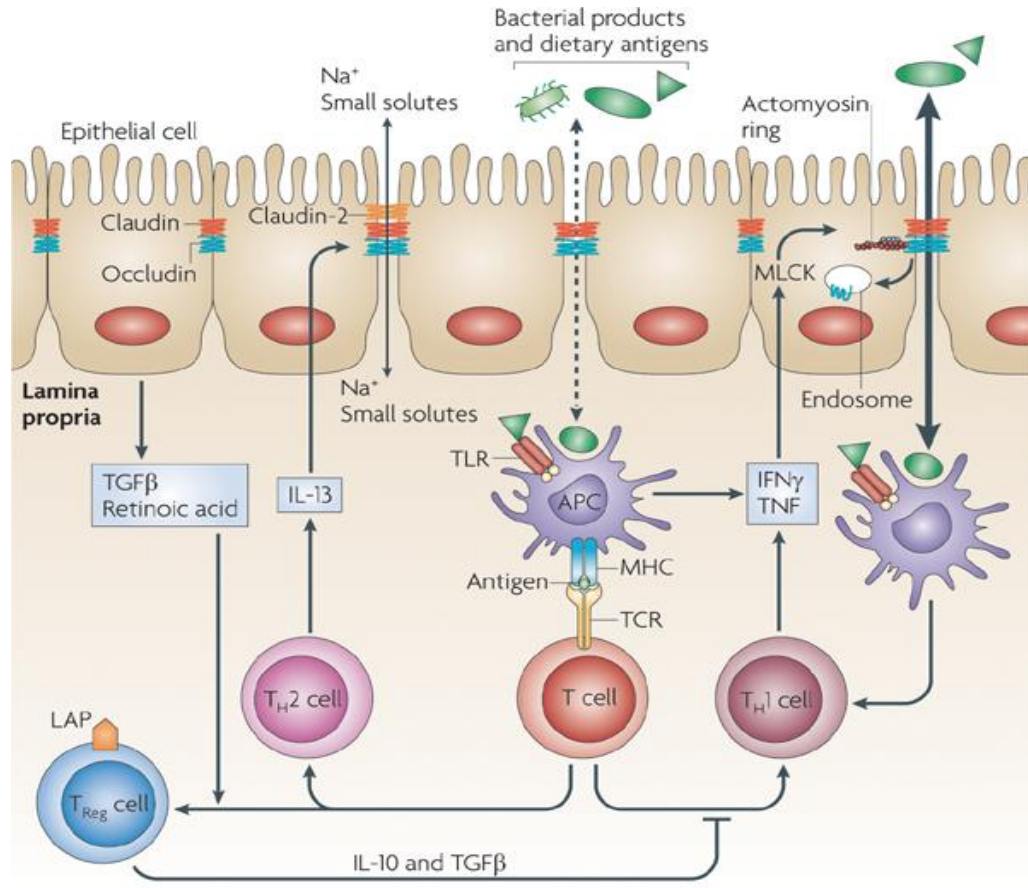
Medscape



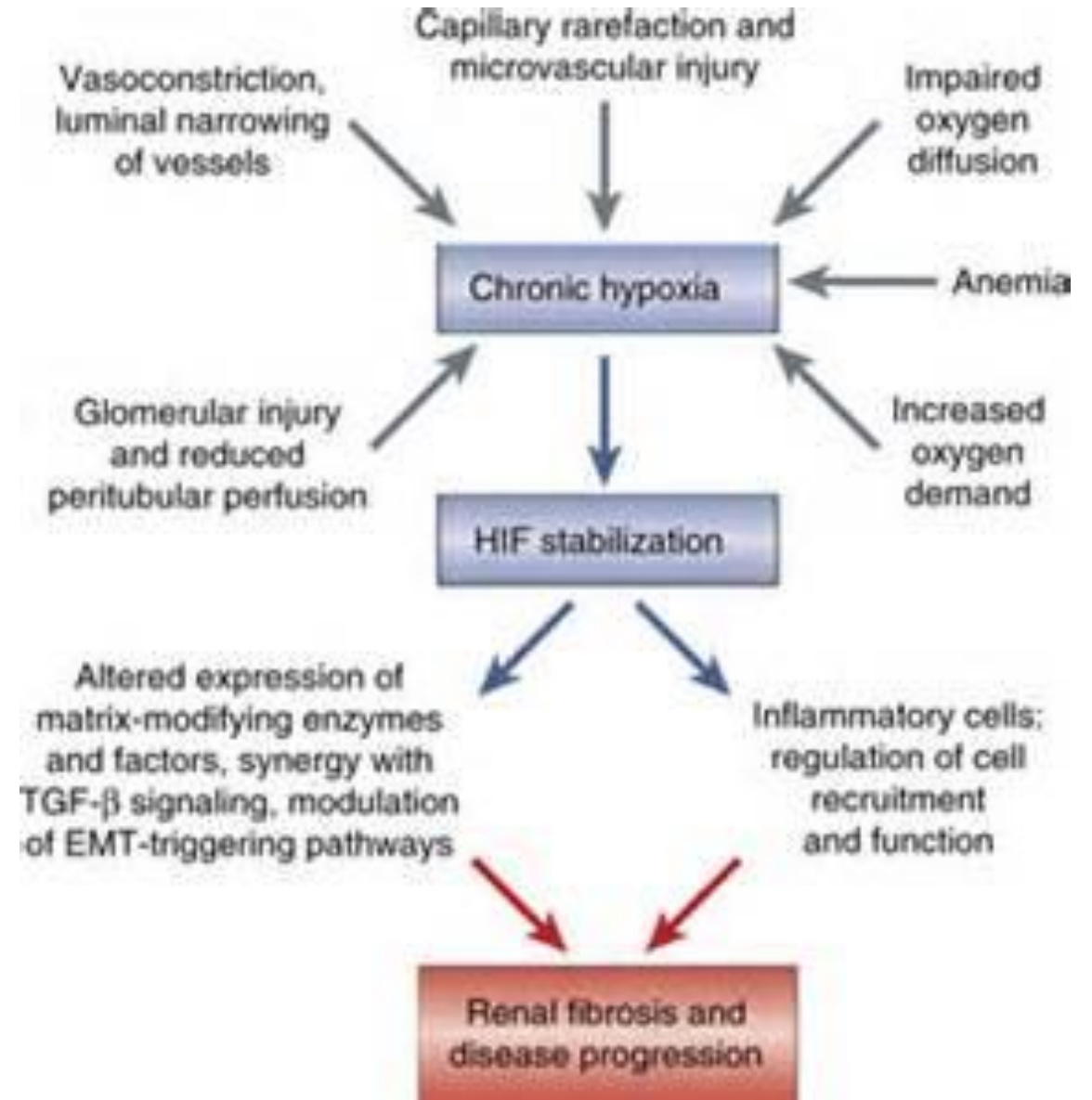
Source: Am J Kidney Dis © 2012 The National Kidney Foundation

Consider This

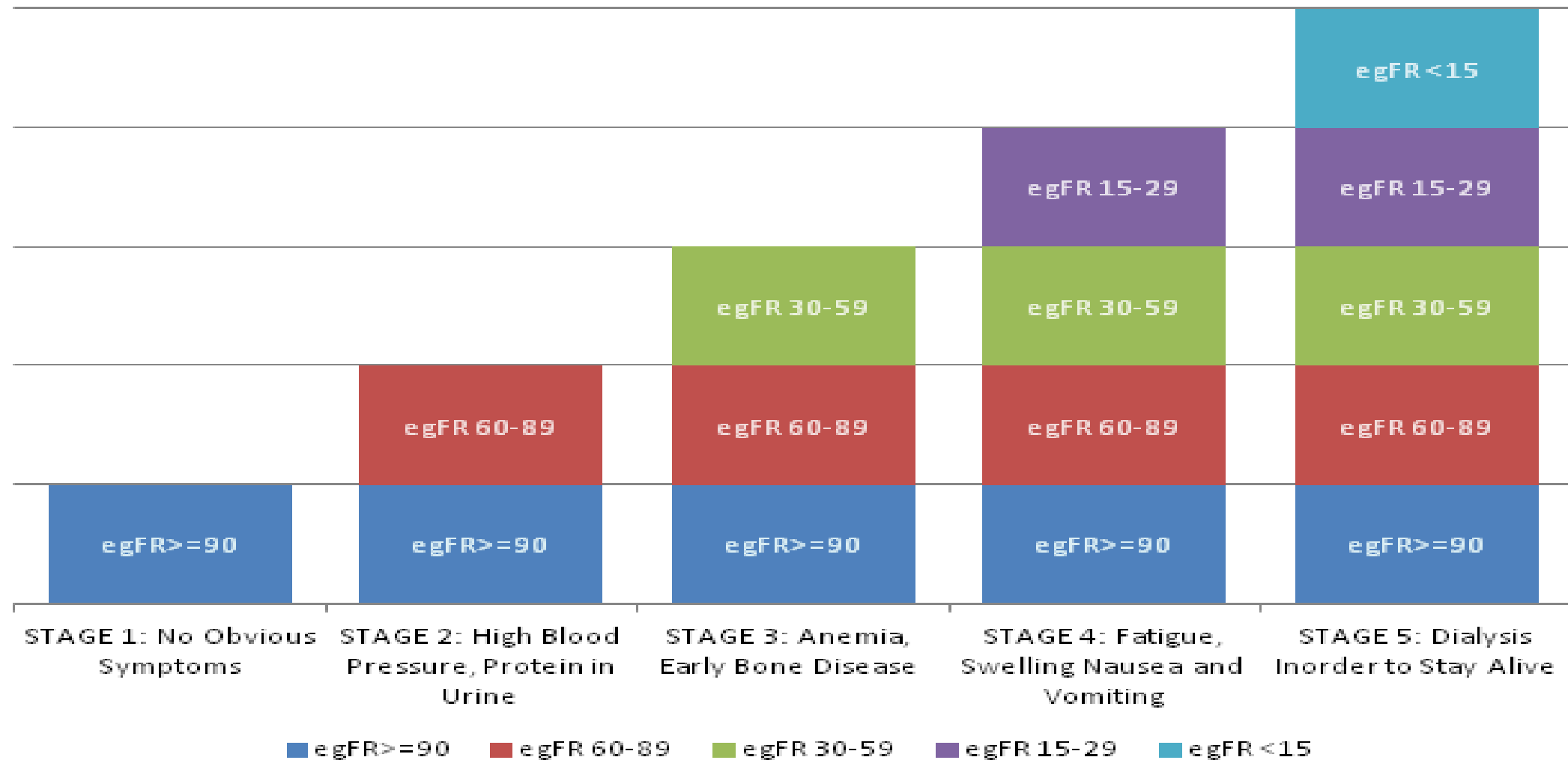
chronic inflammation from Failure of Tight Junctions



Nature Reviews | Immunology

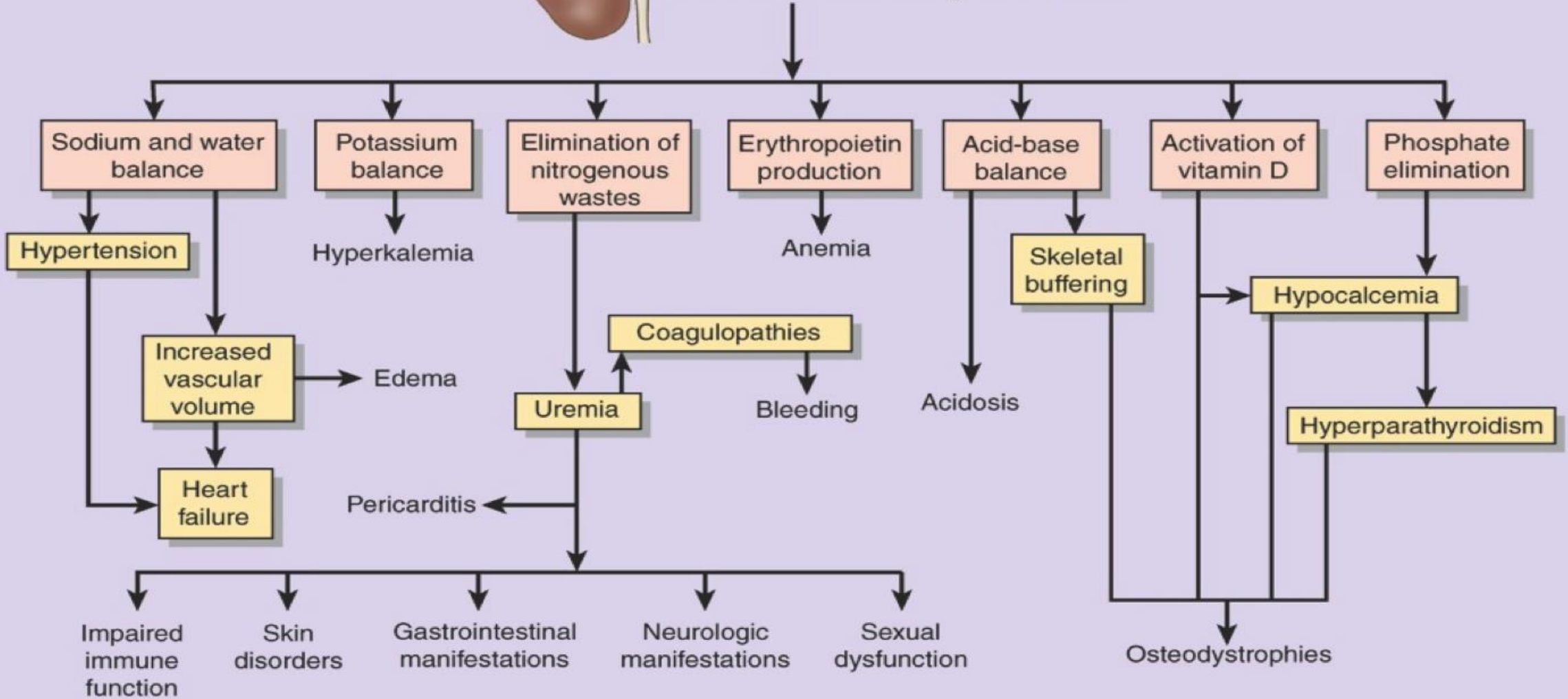


FIVE STAGES OF KIDNEY DISEASE





Chronic kidney disease



Consider the Research

- Many people start maintenance dialysis as a means of relieving symptoms rather than as a result of biochemical markers warranting it
- Controlling symptoms can delay the need for maintenance dialysis and can prevent further kidney damage
- The disconnect between biochemical markers and symptoms and symptoms and quality of life for patients
- Symptoms were correlated with protein intake.
- Lower intakes correlated with better sense of wellbeing

CHRONIC RENAL FAILURE (CRF)

- RENAL INSUFFICIENCY -



Chronic kidney disease symptoms

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Vomiting



Not feeling hungry



Weakness



Sleep problems



Changes in urine



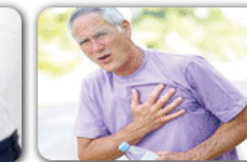
Hiccups



Swelling of feet



Itching



Chest pain



Shortness of breath



Why haven't we focused
more on Prevention in the
early stages of CKD?

The Gap

Causes for the Gap

- Modification of Diet in Renal Disease (MDRD) study
- Majority of medical care compensation comes at CKD 5 / ESRD and not as much before
- Inadequate public pressure
- Poorly allocated resources (Dietitians used at the end of the therapeutic loop mainly)



Qi Gong Break !



Feel Your Qi

Dance of the Pheonix

Is it time to consider New Paradigms?

- Preventing hypoxia

- Supporting tight junctions and inflammatory response issues
- Traditional herbs

- Greater use of Low Protein Diets and functional nutrition

- to decrease uremia and limit symptoms that may increase the need for maintenance dialysis.

- Greater use of Nutrition Professionals

- to support stages 1-4 CKD



Targeting Renal Hypoxia: Current and Future Treatments for chronic kidney disease

Hypoxia Pathology	Therapeutic strategy
Systemic Hypo-oxygenation	Erythropoiesis induction Continuous positive airway pressure (CPAP) Hyperbaric oxygen therapy (HBOT)
Vasoconstriction	Renal angioplasty and or stenting Vasopressin v2 receptor inhibition Renin inhibition / angiotensin inhibition
Microvascular rarefaction	Platelet-derived growth factor receptor beta inhibition
Oxidative Stress	Mitochondria protection Antioxidant administration
Leukocyte recruitment	Stem cell administration Herbal astragalus
Fibrosis	Aldosteron / angiotensin II inhibition Connective tissue growth factor inhibition
Destabalization of renal hypoxia-induced factor	Remote ischemic pre-conditioning



What's on the Horizon?

- **Indoxyl sulfate**
 - high levels of indoxyl sulfate are associated with higher risk of all cause mortality
 - Low protein diets have been shown to decrease indoxyl sulfate
- **Growing evidence** of the benefits of food components and dietary patterns for kidney health other than the traditional modifications of protein, sodium, potassium, phosphorus, fluid and fat
- **Research supports** diets promoting the following should be considered:
 - ❑ Alkali-inducing (vegetable and fruit rich) to help decrease markers of kidney injury
 - ❑ Mediterranean / Resistant starch rich diets to reduce inflammation
 - ❑ Potential benefits of adding Probiotics – decrease uremic toxins
 - ❑ Improving dyslipidemia
 - ❑ Dash Diet showed protections against declining GFR
 - ❑ Increasing evidence that some herbs may diminish and reverse renal interstitial fibrosis: Curcumin, polyglucoside of Tripterygium, tetramethylpyrazine /ligustrazine

Defining Herbs for use in Chronic Kidney Disease



- Shows strong in vivo evidence of protecting the kidney from toxic drugs or substances
- Those that have a strong renal anti-oxidant effect
- Herbs that have in vivo anticancer proliferative effects specific to the kidney
- Herbs that have in vivo beneficial effects in renal disease or kidney failures

(Wojcikowski, K. et al, 2004)

Herbs in Use Traditionally for CKD

- Multiple herbal medications are considered more effective than single herb agent
- Several herbs are usually combined in a prescription
- Prescribed formulas are usually a combination of several types of herbs or minerals
 - where one herb or a few herbs called the **“ruler drug”** provide the main effect.
 - Another group of herbs provided added effects to the ruler drug and are called the **“minister drugs”**
 - The remaining herbs are the **“assistant or messenger drugs”** help with delivery of the principal component.

The Herbal Approach for CKD:

- Replenish vital energy and nourish the blood
- Clear heat and eliminate dampness
- Coordinating balance in the body



Herbal Prescription Effects Promote

- Diuresis
- Reduction of proteinuria
- Improvement of renal function
- Anti-inflammation
- Anti-oxidant
- Anti-fibrosis
- Immune regulation
- Anti-coagulation
- Improved metabolic functioning.



Astragalus – *Astragalus membranaceus*





Cellular Mechanism	Animal studies	Human Studies
Regulates immune system	Reduction of proteinuria and kidney injury in 5/6 nephrectomy	Low to moderate level of evidence in diabetic nephropathy based on meta analysis and systemic review of multiple small clinical studies
Diuresis		
Antioxidant	Anti-fibrotic effects	
Anti-inflammatory		

Rhubarb – *Rheum officinalis*



Cellular mechanism	Animal studies	Human studies
Promotes waste product excretion	Reduction of proteinuria and improvement in renal function and histology in 5/6 nephrectomized rats and diabetic mice	Low level of evidence in CKD based on meta-analysis and systematic review of multiple small and low quality clinical studies
Regulates inflammation Immune response	Antioxidant effects	

Human Trials of the Most Commonly Used Herbs for CKD

Herb	Visual	Cellular mechanism	Animal studies	Human studies
Radix bupleuri	 <p>The visual section for Radix bupleuri contains two images. The left image shows a pile of dried, brown, fibrous roots, labeled 'Bupleurum Root'. The right image shows a green plant with yellow flowers, labeled 'Bupleurum painting'. A small copyright notice is visible at the bottom of the image area.</p>	<p>Anti-inflammation Immune modulation Anti-mesangial cell proliferative effects</p>	<p>Decreases urinary protein excretion and kidney injury Reduces proteinuria and extracellular deposition</p>	<p>Moderate level of evidence in patients with IgA nephropathy</p>
Triptolide	 <p>The visual section for Triptolide shows a photograph of a plant with green leaves and clusters of small yellow flowers, with a cluster of pink flowers visible in the background.</p>	<p>Immune suppression, modulation, anti-inflammatory and anti-oxidant</p>	<p>Reduction of proteinuria and improved renal function; inhibition of cyst growth in PKD mice; prevention of renal injury in Diabetes and lupus nephritis</p>	<p>Published clinical studies are only in Chinese medical journals A large clinical trial is ongoing currently in China</p>

Sage Root – *Salvia Militorrhiza* (*dan shen*)



- Used to treat angina and chronic glomerulonephritis
- It improves the flow of blood through coronary arteries and protects the heart from ischemia –induced derangements
- prevented Renal Interstitial Fibrosis progression by down-regulating TGF- β ₁ (transforming growth factor) and α -smooth muscle actin (α -SMA) expression in rats
- Properties:
 - Hypotensive
 - anti-microbial
 - Antioxidant
 - kidney protectant
 - heart tonic
 - inhibits platelet activity
 - Hepato-protective
 - antiarrhythmic

Cordyceps – *Cordyceps sinensis*



- ❑ Adaptogen traditionally used as a kidney tonic
- ❑ Contains polysaccharides that stimulate the immune system, amino acids, fatty acids, polyamines, ecdysterones
- ❑ Modern Herbal uses – treats imbalances of the kidney
- ❑ In vitro studies – anti-oxidant effects and Inhibits mesangial cell proliferation
- ❑ In vivo studies – antioxidant actions on acute renal injury in rats
- ❑ Human studies found:
 - Prevent immunosuppression and help restore normal macrophage and natural killer cell activity
 - 3 human trials (without blinding and no controls reported)
 - Groups receiving cordyceps developed less nephrotoxicity with lower Cr & BUN
 - Improved renal function

Tumeric - *Curcuma longa* - Curcumin



- ❑ curcumin is the active ingredient in the spice turmeric
- ❑ Can blunt the generation and action of inflammatory molecules to assist with CKD and its associated disorders
- ❑ Increased the expression of intestinal alkaline phosphatase and tight junction proteins to correct gut permeability
- ❑ Decreases the levels of circulatory inflammatory biochemical.

(Ghosh, et al 2014), (Sharaf, et al 2016)

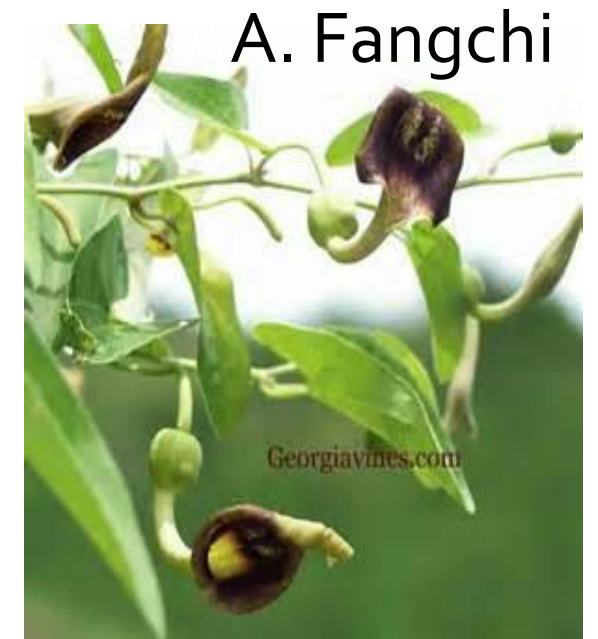
Herbs to AVOID in CKD

Aristolochia species refers to several members of the genus family Aristolochiaceae

- Aristolochia debilis
- Aristolochia contorta
- Aristalochia manshuriensis
- Aristalochia fangchi

All caused kidney damage,
leading to-

- rapidly progressive fibrosing interstitial nephritis.
- In animals, high doses administered orally or intravenously cause
 - severe necrosis of the renal tubules
 - atrophy of the spleen and thymus
 - ulceration of the forestomach,
 - hyperplasia and hyperkeratosis of the squamous epithelium



Edible plants associated with kidney injury

Plant species	Common name	Toxic compound	Manifestation
<i>Aristolochia</i> spp.		Aristolochic acid	Chronic interstitial nephritis, renal tubular defects, urothelial malignancies
<i>Larrea tridentata</i>	Chapparal	Nordihydroguaiareti acid	Renal cysts, renal cell carcinoma
<i>Ephedra sinica</i>	Ma-Huang, ephedra	Ephedrine	Nephrolithiasis, obstructive nephropathy
<i>Pithecolobium lobatum</i> , <i>P. jiringa</i>	Djengkol	Djenkolic acid	Nephrolithiasis, obstructive nephropathy
<i>Averrhoa carambola</i>	Star fruit	Oxalic acid	Nephrolithiasis, obstructive nephropathy
<i>Vaccinium macrocarpon</i>	Cranberry	Oxalic acid	Nephrolithiasis, obstructive nephropathy

Edible plants associated with kidney injury continued

Plant species	Common name	Toxic compound	Manifestation
<i>Glycyrrhiza glabra</i>	Licorice	Glycyrrhizin	Hypokalaemic nephropathy
<i>Salix daphnoides</i>	Willow bark	Salicin	Renal papillary necrosis
<i>Pausinystalia yohimbe</i>	Yohimbe	Yohimbine	Lupus nephritis
<i>Fucus vesiculosus</i>	Bladder wrack	Heavy metals (contaminant)	Chronic interstitial nephritis
<i>Rhizoma Rhei</i>	Rhubarb	Anthraquinone	Chronic interstitial nephritis
<i>Echinacea</i> spp.	Coneflower	Arabinogalactan	Renal tubular acidosis

Why haven't we used Herbal therapies more in the conventional healthcare community?



- ❑ It is currently not recommended based on the research
- ❑ Inadequate evidence to support herbal therapies in CKD based on current pooled meta analysis
- ❑ Suboptimal clinical studies
 - Most current clinical studies are published in Chinese with no translation
 - Prescription variation
 - Unstandardized dosing of herbal prescriptions
- ❑ Adverse effects of herb in clinical trials are underreported
- ❑ Increased rigorous testing of herbal therapies is needed to prevent renal damage due to potential:
 - Mistaken identification of herb
 - Impurities
 - Heavy metal toxicity
 - Other contaminants

What about Functional Nutrition?



Stop chasing symptoms and get to the root cause.



Putting it Altogether...with what we know now

❑ The Low Protein and Very low Protein Diet

- 0.6 – 0.8 grams of protein / kg body weight – 50% as High Biological value protein
- 21 grams of protein /day with use of supplemental amino acids

❑ Supporting a healthier microbiome

- Increasing resistance starch intake
- Consuming glutamine and glutamine rich foods and supplements
- Consider use of fermented foods, pre and probiotics

❑ Supporting improved digestion or inflammatory reduction

- Considering use of Bromelain and Enzymes
- Use of glutamine

❑ Should we be using the specific carbohydrate diet more?

- To limit inflammatory response by those sensitive to gluten, caseine and certain sugars

❑ Use of Promising Herbs

- Consult an herbalist, acupuncturist, naturopathic doctor for recommendations and consistent monitoring.
- Aged garlic for lowering blood pressure and cholesterol – as adjunct therapies



Lets consider an average 70 kg person

□ Low Protein diet:

- 0.6 – 0.8 grams of protein / kg / day (42 – 56 grams of protein)
- Aim for half of this protein as high biological value protein (21 – 28 grams of protein)

□ Very Low Protein diet

- 0.3 grams of protein / kg / day (21 grams per day)
- Supplemental amino acids – 10 grams per



(Walser, M. Et al, 2004)

What does 21 grams of high biological protein look like?

Choose 1 only



Sample Very Low Protein Diet Day for 70 kg person

Breakfast	Snacks	Lunch	Dinner
<ul style="list-style-type: none"> • ¼ teaspoon salt with dried herbs to put in a salt shaker to use throughout the day • 1 slice low protein bread, toasted • 2 Tbs unsalted butter • 1 Tbs jam • 1 apple • ½ cup cranberry juice <p>Supplements: 1 packet 3.5 grams nutramine T powder or tablets</p> <p>Renal vitamin</p>	<p>Morning : ½ cup rice dream</p> <p>Bedtime: 1 Homemade rice krispie treat made with natural marshmallows or 1 pear and Skullcap Tea or 3 Vanilla waffers</p>	<ul style="list-style-type: none"> • Sandwich on low protein bread / bagel or wrap • ¼ of an avocado • 1 slice low protein American cheese • 2 leaves iceberg lettuce • 1 oz potato chips unsalted • 1 medium peach • ½ cup apple juice <p>Supplements: 1 packet 3.5 grams nutramine T powder or tablets</p>	<ul style="list-style-type: none"> • 3 oz Shiitaki, Maitaki or Reishi mushrooms cooked • 2/3 cup cooked white rice • ½ cup green beans (fresh) • ½ cup honey glazed carrots • 1 slice low-protein bread • 1 baked Granny Smith apple with 5 raising and 1 Tbs brown sugar • ½ cup kumbucha or sparkling ginger beverage • 1 cup hawthorn berry tea or Lemon Verbena or Passion flower tea <p>Supplement: 1 packet 3.5 grams nutramine T powder or tablets</p>

Low Protein Resources



Low Protein Web Sites

- Cambrookefoods.com
- Dietspec.com
- Ener-g.com
- Lowprotein.com
- Med-diet.com
- Medicalfood.com
- Shsna.com

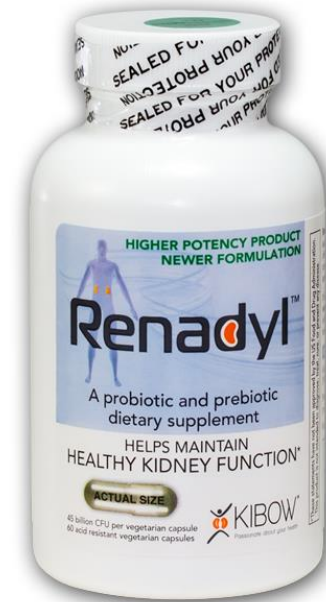
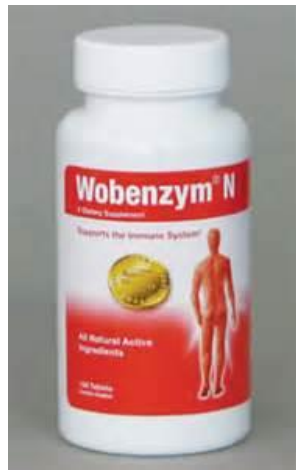


Amino Acid Supplements



**CALWOOD
NUTRITIONALS**
Nutramine

Consider these Supplements Enzyme with Bromelain



Some examples of Fermented foods

- microbiota help mitigate inflammation and oxidative stress
- properly controlled fermentation may often amplify the specific nutrient and phytochemical content of foods,
- furthermore, microbes (for example, *Lactobacillus* and *Bifidobacteria* species) help maintain tight junctions



Questions

