Systemic Complications of CKD IV and End Stage Renal Disease

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Four Stages of Progressive Renal Dysfunction (Continued)

- **Stage IV**
  - GFR < 30, normocytic normochromic anemia, and electrolyte compensatory mechanisms no longer adequate
  - Hyperparathyroidism/Hyperphosphatemia is often apparent

- **Stage V, Uremic symptoms**
  - Symptoms are characterized by nausea, emesis, fatigue, malaise, pruritus, mental lassitude, dysgeusia, poor concentration, myoclonus, and bad breath
  - Fluid, electrolyte and acid-base complications and disorders of metabolism and organ dysfunction predominate

Fluid, Electrolyte, & Acid-Base Complications

- Volume Overload
- Volume Depletion
- Water Overload (Hyponatremia)
- Water Depletion (Hypernatremia)
- Hyperkalemia
- Hypocalcemia
- Hyperphosphatemia
- Metabolic Acidosis
- Metabolic Alkalosis
- Hypokalemia

Disorders of Metabolism and Organ System Function

- Hypertension
- Renal Osteodystrophy
- Anemia
- Dyslipidemia
- Coagulopathy
- Pericarditis
- Gastrointestinal Disorders
- Neuropathy and Encephalopathy
- Sleep Disorders
- Sexual Dysfunction
- Psychologic Disorders
- Immune Disorders
- Dermatologic Complications

CKD 4 Management

- All the same methods to limit the progression of stage 1–3, also apply in stage 4
- New focus is on dietary restrictions, dealing with electrolyte problems, endocrine issues, and other medical issues that may arise
- Discussing renal replacement therapy including a vascular access
- Fistulas take 10–12 weeks to mature

Definition of CKD IV–V

- GFR between 15–30cc/min stage 4
- GFR below 15cc/min stage 5
- Stage 5 is when dialysis is usually initiated
- These patients need to be seen frequently, since problems arise on a frequent basis.
- Their level of renal function should be monitored and the rate of decline followed.
- The complications of the uremic state need to be monitored and dealt with.
Discussing Options

- Stage IV is the time to discuss the patients options for renal replacement if they progress to Stage V
- In Kaiser in all areas we have a “Choices Class”
- Open enrollment
- The different modalities of transplant, peritoneal dialysis, hemodialysis, home hemodialysis, and no renal replacement are discussed.
- We attempt to have “optimal starts”
- We attempt to avoid “crash starts”

Kaiser excels in this education

- Approximately 65–70% of Kaiser patients start dialysis with an optimal start.
- Much higher percentage than in the community
- Advantages of peritoneal dialysis (stay at home, flexible schedule, in Kaiser mortality benefit, less dietary restrictions)
- Advantages of hemodialysis (no self care, 3x a week, diabetic control)
- Advantages of home hemodialysis (most closely resembles non uremic gfr, patients feel better)
- Transplant (No dialysis treatments, best mortality option)

No renal replacement option

- Should be considered if a comorbid condition that confers a limited life expectancy that dialysis is unlikely to prolong in a meaningful way.
- Acute kidney injury (AKI) patients typically die within days if dialysis is not initiated.
- CKD may survive for weeks or months after a decision is made to forego chronic dialysis.
- 122 older patients treated with supportive nondialytic care reported a median survival time of 16 months; 32 percent of patients survived >12 months after eGFR decreased <10
- Age of 85

Arterial Venous Graft

Peritoneal Dialysis Catheter

Central Venous Catheters
**Things to know about dialysis access**

- Do not aspirate fluid from PD catheter, let the PD nurse manipulate the catheter.
- Ascites/Free Air on CT scan in PD patients is a normal finding.
- Steal syndrome can present with cool hand, numbness, and ischemic lesion on digits.
- Save the veins in selected access arm (Avoid PIC lines).
- Do not cannulate, take blood pressures, or do IV in access arm.

**Volume Overload & Edema**

- Sodium & Intravascular Volume is maintained usually until GFR falls below 20–30ml/min.
- Patients with mild–moderate CRI are prone to volume overload.
- Much more severe problem with nephrotic syndrome.
- Manifested as peripheral edema and/or pulmonary edema, ascites, testicular edema.
- Typically treated with loop diuretics and dietary sodium restriction.

**Diuretic Dose**

- Once Daily Dosing Better than BID dosing in producing Diuresis due to Loop Diuretic Dose Response Curve. This is initial approach.
- Furosemide: Bumetanide = 20:1 in chronic renal failure and 40:1 otherwise.
- Moderate Renal Insufficiency: 80–160mg/day Lasix or 2–4mg of Bumetanide respectively.
- Severe Renal Insufficiency: may require up to 240 to 480mg of furosemide or 8–10mg of Bumex.
- Thiazides are usually not effective at this level of GFR.
- Aldactone and K issue.
- Furosemide IV to PO conversion is 1:2.

**Diuretics Effect of Electrolytes**

- Sodium: Can see either Hyper or Hyponatremia (Thiazides much more likely to cause hyponatremia).
- Calcium: Thiazides will increase calcium, loop diuretics will decrease the calcium.
- Potassium: Amloride, Triamterene, Aldactone will increase K. Loops, Thiazide will lower.
- Maxzide.
- Bicarb: Acetazolamide will cause acidosis, and others will generally increase bicarb.
Case

- 65 yr old with CHF, and CKD 4
- Medications include Lasix 40mg, and Lisinopril, Asa, and diabetes medications
- Pt c/o edema
- Lasix increased to BID, f/u labs show creatinine increased from 3.0–3.9mg/dl but edema is much better
- What is next step?

Modalities Choices to treat volume overload in dialysis patients

- Diuretics in dialysis patient
- Nocturnal dialysis
- Short daily hemodialysis
- Peritoneal dialysis
- Isolated ultrafiltration
- Fluid and Sodium restriction

Coumadin and dialysis patients

- Dialysis patients have higher risk for bleeding, and higher risk for stroke.
- High risk of falls, and are systemically anticoagulated three times a week, significant problems with orthostatic hypotension
- Most AF patients on dialysis, no anticoagulation
- For dialysis patients with very high-risk predictors atrial thrombus, valvular/rheumatic valve disease, a previous TIA or stroke anticoagluate with warfarin
- Insufficient data to support the use of NOAC in this patient population
- Problems with calciphylaxis

Hyperkalemia

- Potassium excretion is preserved until late in course of chronic renal disease but usually presents in late stage IV.
- It can present earlier.
- Earlier presentations of hyperkalemia include:
  - Hyporeninemic Hypoaldosteronism (Type IV RTA) frequently seen in Diabetic Nephropathy & Interstitial Nephritis
  - Volume Depletion and Sodium Restriction induced reduction of GFR
  - Constipation, Dietary Indiscretion, & Drugs (ie. NSAIDS, ACE-, K+ sparing diuretics, non selective B-blockers, Septra/Bactrim, lactic acidotic states, hyperglycemia.

Hyperkalemia

- Symptoms are related to impaired neuromuscular transmission manifested clinically by impaired cardiac conduction, muscle weakness or paralysis. The most common manifestations you will see are fatigue, weakness, bradycardia, parasthesias.
- Severe symptoms usually occur at levels > 7meg/L. The more acute the rise in K, the more likely there will be symptoms.
- There is however interpatient variability depending on rate of increase in plasma concentration, hypocalcemia, and metabolic acidosis.

Indications for urgent treatment include peripheral neuromuscular abnormalities and electrocardiographic changes regardless of the degree of hyperkalemia. So check EKG if the K is high.
- If K is 6.5, the patient needs an EKG
- Asymptomatic patients with a plasma concentration of 6.5 meq/L can be treated with Kayexalate & a low K+ diet.
- Asymptomatic patients with a plasma concentration’s of 6 meq/L or less may be placed on Diuretics & low K+ Diet.
- Consider NaHCO3 if pt is acidic
- Eliminate high K medications
Hyperkalemia (Treatment)

- Calcium Gluconate -- indicated when p waves are lost or QRS complex widened (not necessary for peaked T-waves only)
  - Temporizing Measure, works immediately
  - Contraindicated in Digitalis toxicity
  - The effect only last temporarily

- Glucose & Insulin
  - Dose: 1 amp D50 & 10u of IV Regular Insulin followed by D5W infusion to prevent hypoglycemia
  - Onset of Action: 15 minutes (peaks at 60 minutes and lasts several hours)
  - Decreases K+ by 0.5 to 1.5 meq/L
  - Follow fingersticks (hyperglycemia can worsen hyperkalemia by osmotic effect on cells)

- B2 Adrenergic Agonists
  - Albuterol given 10–20 mg in 4cc of NS by nasal inhalation over 10 minutes
  - Can lower K+ by 0.5 to 1.5 meq/L
  - Should be avoided in patients with known or at high risk for ASCAD (can cause ischemia by increasing heart rate and thus double product)

- Mushrooms
- Dried Apricots
- White beans
- Dairy
- Dark Greens
- Avocado
- Orange Juice
- Tomato Juice
- Pumpkin, Acorn Squash
- Raisins

Case

- 65 yr old, with diabetic nephrotic syndrome
- Has 4.5 gms of protein, and creatinine of 2
- His K is 5.8, he is on 20 of Lisinopril
- How do you treat proteinuria and K?

Metabolic Acidosis

- Non Anion Gap – due to reduction in titratable acid excretion (ie. decreased ammonium NH4 genesis and thus excretion)
- Anion Gap – due to retention of phosphate, sulfate, urate & hippurate.
- Very common problem in CKD 4
When & Why to treat Metabolic Acidosis

- **When:** $\text{HCO}_3^- < 24 \text{ meq/L or pH } < 7.25$
- **Why:**
  - Excess hydrogen ions are buffered by bone with release of calcium phosphate.
  - One study which maintained bicarb at 24 with treatment vs a bicarb level of 16 in a control group prevented progression of osteopenia and hyperparathyroidism related bone disease.
  - Another study showed that maintaining a normal pH with treatment resulted in increased sensitivity of the parathyroid gland to ionized calcium.

Why to treat Metabolic Acidosis (Continued)

- Uremic acidosis causes a catabolic state characterized by reduced albumin synthesis and muscle breakdown and resultant weakness.
  - This catabolic state can be reversed by normalizing the serum $\text{HCO}_3^-$.  
- Animal studies showed that normalization of serum $\text{HCO}_3^-$ slowed progression of renal dysfunction.
- Pt may become symptomatic from acidosis and it can worsen K

How To Treat Metabolic Acidosis in Chronic Renal Insufficiency

- **Goal:** maintain above 22–24meq/L.
- **NaHCO3** (650mg = 8meq) at a daily dose of 0.5 to 1meq/Kg/day is agent of choice (35–70 meq/daily = 2 tab bid to qid)
- One problems with NaHCO3 is the Na+
  - NaCitrate as an alternative may reduce intestinal bloating associated with NaHCO3–.
    - Should be avoided in patients on Al containing phosphorous binders due to increased absorption of Al & associated toxicity. It also contains K.
  - CaCO3 may also be a useful alternative.

Case

- Your pt with GFR of 25cc/min
- Has a bicarb of 18
- You start them on NaHCO3 650 2 tabs BID
- Besides bicarb, what other labs should you check at follow-up?

Hyperphosphatemia (HP)

- Phosphate retention begins early in renal disease (GFR 40–50) and is intimately related to secondary hyperparathyroidism and renal osteodystrophy.
- Retention causes:
  - Hypersecretion of PTH thereby increasing excretion of phosphate and increasing calcium phosphate release from bone
  - Reduction in $1\text{-alpha}$-hydroxylation of 25-$\text{hydroxyvitamin D}$
- HP not seen until GFR < 25 to 30 ml/min (due to secondary hyperparathyroidism)
- Dietary intake
- Bottom line is phosphorous levels increase as gfr declines

How to Prevent Hyperphosphatemia

- Recent studies have shown that placing person on low phos diet early in course of renal disease will limit rise in pth. Goal for CKD 4 is 4.5
- So, likely we should start around a gfr of 25cc/min
- So why don’t we just restrict diets, and forget the binders?
- Because in advanced kidney disease, dietary restriction will not reduce phos to normal
- Pt starting dialysis will likely only excrete about 15% of phos they intake.
Besides secondary hyperparathyroidism and renal osteodystrophy, why treat HP?

- 2 studies showed hemodialysis patients with phos > 6.5 had increased relative risk of mortality of 1.27 versus controls with lower phos.
- Or in other words this will cause an earlier death
- Increase in death by 23% for every 1mg/dl elevation in serum phos
- Calcium phosphate product > 70
  - May cause precipitation of calcium phosphate in arteries, joints, soft tissues, and viscera in a process called metastatic calcification.
  - When very severe may cause tissue ischemia called "Calciphylaxis"

Tissue deposition in cardiac vessels will lead to coronary calcifications

- This leads to increase risk of coronary events
- This change is even seen in very young dialysis patients
- There are calcifications commonly seen in aorta, and ileofemoral vessels, leading to increase aspvad
- There is an increase in vascular calcifications in dialysis patients

This is likely related to increase calcium intake

- Likely from calcium containing binders
- So sevalamer should likely be first choice in binder. It also lowers LDL
- Dialysis patients have stiffened arterial walls vs ruptured plaque
- What about vitamin D?

Best option is to limit dietary phosphorous so phos level is below 5.5 at dialysis, and 4.5 in CKD 4

- Renvela is preferable if patients have known calcium deposits in vessels
- New focus will likely be to limit serum calcium levels to less than 10.2
- Other potential beneficial drugs include statins, thiosulfate
- Benefit of longer dialysis, home dialysis

Processed food often has a lot of phosphorous that allow preservation

- "The longer the food has been dead the higher the phosphorous"
- The phosphorous in processed food is absorbed very quickly vs plant placed phosphorous
Phosphate Binders
- Required by most patients with CRI and all patients on hemodialysis.
- Calcium Carbonate (OsCal—requires acid environment to dissolve)
- Calcium Acetate (PhosLo—dissolves better in setting of achlorhydria, PPI, or H2 blockers)
- Can lead to hypercalcemia when given with calcitriol or when patients have decreased bone turnover due to osteomalacia or adynamic bone disease.
- Renvela
- Fosrenol
- Magnabind
- Nicotinamide
- Iron based binders Velphoro
- Binders need to be taken with meals

Parathyroidectomy
- In cases of recalcitrant hyperphosphatemia and secondary hyperparathyroidism

Extended Nocturnal Hemodialysis
- 8–10 hours 6–7 nights per week
- Patients normalized phosphate and were taken off oral phosphate binders.
- Sinacalcet

RD refers to several bone diseases that occur as a result of CRI. These diseases may occur simultaneously.

Classified as:
- High Turnover
  - Secondary Hyperparathyroidism (Osteitis Fibrosa Cystica)
- Low Turnover
  - Osteomalacia (Calcitriol Deficiency/Metabolic Acidosis/Aluminum Toxicity)
  - Adynamic Bone Disease (Peritoneal Dialysis, Diabetes Mellitus, Advanced age)

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Osteomalacia has two important causes:
- Calcitriol Deficiency
- Aluminum intoxication with Al hydroxide containing phosphate binders, ie., Amphojel & Carafate (most common cause in Dialysis patients)
- Al absorption is markedly increased with concomitant use of Citrate (ie CaCitrate, Shohl’s Solution)
- ABC’s of Al Toxicity
  - Anemia (normochromic/normocytic)
  - Bone Disease (osteomalacia)
  - Central Nervous System (encephalopathy)

46 yr old has a PTH of 251
Phos is 5.9, and vitamin D level is 19, calcium is 8.6?
What should be your initial therapy?
What labs change with rocaltril therapy?
Avoid Fleets enema, po in these patients
High risk for metastatic calcifications
Magnesium containing solutions also a risk (MOM, Maalox)
Prune Juice (High in K)
Kayexalate
No problem with tap water enema, or soap suds enema.

Increased GERD in PD patients
Increase incidents of gastroparesis esp in PD, DM gastroparesis does not improve with HD
No increase in PUD, however cannot use carafate, MOM, or bismuth. H2 blockers dosed reduced due to confusion issues
Amylase and Lipase elevations
Kayexalate causes colonic necrosis (enema)
Increased incidence of GI Bleeding, angiodysplasia, heparin, platelet dysfunction.

Causes of anemia:
- Erythropoietin deficiency
- Microvascular trauma (severe hypertension & diabetes)
- Frequent blood draws (dialysis)
- GI Bleed (Angiodysplasia & PUD)
- Increased Oxidative Stress

Functional Iron Deficiency
- Occurs when patient on erythropoietin and RBC’s are produced faster than transferrin can carry iron to bone marrow.
- Defined by a reticulocytosis after given IV iron and a decrease in erythropoietin.
- IV iron has been shown to decrease erythropoietin requirements by 30-35%.
- Iron saturation above 30%

Treatment:
- Erythropoietin 30u/kg SQ TIW or 50u/kg SQ BIW
- SQ vs. IV
- Target Hgb 10-11.5 based on National Kidney Foundation’s Dialysis Outcomes Quality Initiative (DOQI)
  - Demonstrated improved functional and cognitive status, improved quality of life, regression of LVH and decreased morbidity and mortality.
  - Prolongs life after initiation of dialysis
  - Procrit may worsen hypertension
  - Can cause thrombotic events if Hgb is too high, studies have had significant elderly population.
  - Problematic in patients with metastatic cancer, or on chemo
  - No cookie cutter solutions

You see a patient with gfr of 20cc/min
They have a Hgb of 9.9
They ask if they should start Procrit?
What do you do next?
Abnormalities in Sexual Function

- **Men**
  - Low Testosterone & Hypogonadism Common
  - Erectile dysfunction & decreased libido seen in > 50% of men with advanced renal disease

- **Women**
  - Hyperprolactinemia & Hypogonadism
  - Dysfunctional Uterine Bleeding or Amenorrhea

- **Pregnancy**
  - In women with ESRD spontaneous abortions are the rule (uncommon to carry to term with Cr > 3)
  - Fertility may be restored with renal transplant

Gout in CKD

- Very common problem
- Treatment options are limited by renal disease
- Indocin is contraindicated in acute flares
- Allopurinol should be dosed reduced
- Colcicine is commonly used in renal patients, needs to be dose reduced
- Uloric has not been studied in CKD 4/5

Malnutrition and ESRD

- Why is nutrition important?
  - U.S. Renal Data Systems analysis showed that patients who initiated dialysis when they were hypoalbuminemic had poorer outcomes
  - may or may not be related to malnutrition
- Why is malnutrition so common among these patients?
  - Decreased food intake
    - from uremic symptoms (nausea, emesis, anorexia)
    - decreased intestinal absorption
    - metabolic acidosis

Malnutrition and ESRD

- Management:
  - Monitor serial weight, albumin & Cr in patients with CRI & ESRD q3mos.
  - Expect increasing Cr, if a stable or declining Cr is noted with an increasing BUN consider malnutrition.
  - Maintaining adequate nutrition competes with desire to slow progression of renal dysfunction with the use of a low protein diet.
    - Reasonable to restrict protein to 1.0g/kg/day to slow progression of renal disease prevent malnutrition.

Uremic Platelet Dysfunction & Bleeding

- **Pathogenesis (likely multiple factors)**
  - Uremic Toxins
    - Dialysis improves platelet dysfunction
    - Individuals with diet manipulated to increase BUN from 60 to 120 mg/dL will diminish platelet adhesiveness and increase bleeding time
    - BUN is not the only culprit and other toxins are present in the uremic milieu which cause platelet dysfunction
    - Binding of GPIIb–IIIa is interfered with when uremic serum incubated with normal platelets.

Uremic Platelet Dysfunction & Bleeding

- **Pathogenesis (continued)**
  - Anemia
    - degree of anemia correlates with bleeding time
    - at HCT > 30% RBC’s occupy center of vessel and platelets skim along endothelial surface
    - at low HCT platelets mix with RBC’s and less are present to form platelet plug when endothelial injury occurs.
  - Nitric Oxide
    - uremic plasma stimulates NO production in platelets and endothelial cells
    - NO inhibits platelet aggregation
Uremic Platelet Dysfunction & Bleeding

- Treatment (indicated in bleeding and preoperatively)
  - Estrogens
  - Cryoprecipitate
  - Correction of Anemia
    - transfuse PRBC to HCT of 30
  - dDAVP (synthetic ADH, aka vasopressin)
    - effective in apx. 50% of uremic patients
    - 0.3ug/kg in 50cc NS IV/SQ over 15 minutes
    - 3ug intranasally also effective
    - tachyphylaxis occurs after second dose

Uremic Neuropathy & Encephalopathy & Dialysis Related Neurologic Complications

- Uremic Neuropathy
  - Symptoms: include Restless Leg Syndrome, burning Feet, complaints of crawling, pricking or pruritus, orthostatic symptoms.
  - Signs: include decreased tendon reflexes and muscle wasting as well as loss of pain, light touch, vibration, and pressure, postural hypotension.
  - Toxic symmetrical mixed sensorimotor polyneuropathy: Usually occurs in 'glove and stocking pattern' (indistinguishable from polyneuropathy of diabetes mellitus or chronic alcohol abuse). Autonomic insufficiency also common.
  - Problems with gabapentin

- Depressed Intellectual Function in Dialysis Patients
  - frequently recognized complication with one study showing IQ lower than general population
- Dialysis Dementia: progressive frequently fatal neurological disease seen almost exclusively in patients treated with chronic HD.
- 30% of dialysis patients show some cognitive dysfunction

Pericardial Disease

- Large Pericardial Effusions
  - CRI accounted for 20% of effusions in population of men with this disorder
- Uremic Pericarditis
  - occurs in 6–10% of patients with advanced renal failure (acute or chronic)
  - rough correlation with degree of azotemia and development of pericarditis
- Dialysis Associated Pericarditis
  - occurs in 13% of patients undergoing chronic HD and occasionally in PD

- Treatment of Uremic Pericarditis
  - An indication for dialysis if patient does not have tamponade
  - If tamponade present must do pericardiocentesis first (intravascular volume removal will cause circulatory collapse)
  - Heparin free HD or PD due to possibility of hemorrhage into pericardial space
- Treatment for Dialysis Associated Pericarditis
  - Increased intensity of dialysis if hemodynamically stable.
  - May be switched to PD to avoid anticoagulation associated with HD.

Hyperlipidemia

- Treatment of Hyperlipidemia of Nephrotic Syndrome:
  - treat underlying problem
  - HMG CoA reductase inhibitor ("statin") is treatment of choice for LDL. While Fibric acid derivative Gemfibrozil is choice for TG.
  - Incidence of myositis with statin is 0.1 to 0.2% but may be increased to as high as 6% with concomitant use with fibric acid derivative or cyclosporine.
Hyperlipidemia

- **Chronic Renal Dysfunction & Dialysis**
  - Hypertriglyceridemia is primary finding
    - decreased catabolism but by different method than nephrotic syndrome
    - decreased activity of lipoprotein lipase and hepatic lipase TG lipase
    - perhaps due to increased deposition of calcium in liver & adipose tissue cells
    - parathyroidectomy or the administration of verapamil normalized TG levels and improves activity of lipoprotein lipase in animal models.

Case

- 46 yr old diabetic with CKD 4, nephrotic syndrome, and mixed lipidemia? He is on zocor 80mg a day.
- LDL is 121
- Trig 460
- What is you next move?

Hypertension In Dialysis Patients

- **Epidemiology**
  - 80% of patients are hypertensive prior to initiating dialysis
  - 50–60% of patients on chronic HD and 30% of patients on chronic PD are hypertensive
  - Improvement based on better volume control
- **Cardiovascular Risk**
  - enhanced mortality seen in HD patients with lowest blood pressures followed for one year
  - improved survival due to adequate blood pressure demonstrated in trials with long followup

Hypertension In Dialysis Patients

- **Pathogenesis is multifactorial**
  - Sodium & volume excess
    - major factor in development of htn in this patient population
    - removal of excess sodium and attainment of "dry weight" normalizes BP in 60% of patients
    - absence of edema does not rule out hypervolemia
  - Increased sympathetic nervous system activity
    - in the presence of uremic metabolites activates chemoreceptors within the kidney producing an afferent signal to the brain which increased sympathetic tone.
    - absent in patients who are anephric.

HTN Rx in a dialysis patient

- Best if left to the Nephrologist since the dialysis Rx is key factor in control
- Otherwise minimal difference
- Careful use of Atenolol
- Clonidine will often cause bradycardia in renal patients
- The concept of the dry weight

Coronary Heart Disease in Renal Dysfunction

- Cardiovascular disease accounts for >50% of deaths in patients with ESRD and is single best predictor of mortality.
- HD patients profile and risk factors
  - 1/3 have diabetes mellitus
  - average age > 60 years old
  - 30–50% with hypertension
  - LVH and Myocardial Dysfunction
Coronary Heart Disease in Renal Dysfunction

- **HD patients profile and risk factors**
  - Abnormal lipid metabolism
  - Angina during dialysis is a common clinical manifestation of ASCAD due to hypotension
  - Increased plasma homocysteine levels
    - common in ESRD patients with vascular disease
    - patients in upper 2 quintiles of highest homocysteine levels had 2.9 times the risk of having a thrombotic or atherosclerotic event compared to lowest 3 quintiles.
    - Homocysteine is marker for disease but unclear if lowering levels with folate and B-complex vitamins improves outcomes (although it does improve endothelial dysfunction)

- **Increased levels of cytokines and complement increases oxidative stress and increases inflammation leading to more endothelial dysfunction**
  - one randomized study of 200 HD patients who took 800u of Vit E vs placebo showed a 50% reduction in MI, Ischemic CVA, PVD, and Unstable Angina.
  - Increased intake of calcium may enhance coronary artery calcification which may enhance atherosclerosis
  - Compared to age matched controls the detection of coronary artery calcification using CT was markedly higher in those undergoing HD (88% vs. 5%)

- **Diagnosis**
  - Dipi GXT thallium was evaluated in 60 chronic HD patients followed by coronary angiography
    - sensitivity 92%, specificity 89%, PPV 71%, NPV 98%, accuracy 90%
  - In a prospective study of 56 patients with renal failure and suspected recent MI
    - Troponin I > 0.8 had sensitivity 94%, specificity 100%
    - CK-MB > 5% had sensitivity of 44%, specificity 56%

Myocardial Dysfunction

- **LVH**
  - risk factors include htn, advanced age, anemia, av fistula
  - a major risk factor for morbidity & mortality in patients with ESRD
  - 2/3 die from CHF or sudden death
  - 1/3 die from noncardiovascular cause
  - regression can be achieved by bp control, & correction of anemia
  - ACE- & CCB have greatest utility in reducing LV mass
  - correction of anemia with erythropoietin decreases cardiac work and may reduced LV mass index by 10 to 30%

- **Atrial Fibrillation**
  - of 190 patients on chronic HD 14% percent experienced episodes of atrial fibrillation with another 9% having sustained atrial fibrillation.
  - Newer studies are questioning the need for anticoagulation in this population
Dermatologic Problems in CKD/ESRD

- Calciphylaxis
- Nephrogenic Systemic Fibrosis
- Uremic pruritus

Calciphylaxis

- Calciphylaxis is a rare and serious disorder characterized by systemic medial calcification of the arterioles that leads to ischemia and subcutaneous necrosis
- Risk factors include high PTH, high calcium x phos double product, the use of vitamin D analogs, Coumadin, previous transplant, and CHF
- Treatment includes removal of offending agents, thiosulfate, wound care, hyperbaric chambers, increasing dialysis

Nephrogenic Systemic Fibrosis

- Nephrogenic systemic fibrosis (NSF) is a recently identified fibrosing disorder seen only in patients with kidney failure. It is characterized by two primary features
  - Thickened, hardened skin over ext and trunk
  - Marked expansion and fibrosis of dermis
- Association with Gadolinium
- CKD 4/5/ESRD should avoid MRI with gadolinium
- Association with Epogen

Uremic pruritus

- Risk factors: Inadequate dialysis, high ca/phos double product, high pth, high levels of mg, and aluminum
- Worse with heat and stress, better with showers, cool temperature, +/- with dialysis
- Treatments include optimizing dialysis treatments
  - Correct pth, phos, ca
  - Emollients and topical analgesics
  - Oral antihistamines, gabapentin
  - Zoloft
  - UVB therapy

Early and Late Calciphylaxis Lesions

Nephrogenic Systemic Fibrosis
Hemodialysis

- Heparinized blood pumped through a circuit
- Pressure driven, usually > 250cc/min
- Special vascular access needed
- 3 times per wk, 3.5 – 5.0 hours per treatment

Dialysis Access

- Usually placed at GFR 15–25cc/min
- Should avoid lab draws, blood pressure measurement, and IV in the access arm
- Should avoid lab draws and IV in non-dominant arm when GFR is less than 30
- Types: graft, fistulas

Peritoneal Dialysis

- Sterile dialysate infused into the peritoneum through surgically placed catheter.
- CAPD typically 4 exchanges/day
- Dwell time is 4 – 8 hours
- Osmotic forces remove excess fluid
- CCPD is a nighttime modality involving a cycler machine that performs the exchanges

PD

- Dialysate in Peritoneum
- Blood
- K
- Na
- Bicarb

Dialysate Content

- Sodium 132 Meq/L
- Potassium 0
- Magnesium 1.5
- Calcium 3.5
- Chloride 102
- Lactate 35–40
- Dextrose 1.5–4.25%
Problem: These pts have problems----

Life expectancy:

<table>
<thead>
<tr>
<th>Age</th>
<th>ESRD pt</th>
<th>vs</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>@ age 49:</td>
<td>6yrs</td>
<td></td>
<td>29yrs</td>
</tr>
<tr>
<td>@ age 59:</td>
<td>4yrs</td>
<td></td>
<td>21yrs</td>
</tr>
</tbody>
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Indications for Chronic Dialysis

Non-diabetics: GFR 10cc/min
Diabetics: GFR 15cc/min
Uncontrollable metabolic problems
Malnutrition
Difficult to control CHF/vol overload

The concept of KT/V

- Calculation of the adequacy of the dialysis prescription
- Time on dialysis, blood flow rates into the machine, the size of the artificial kidney, the rate of dialysate flow all contribute to this factor
- Determines how often and how long a patient stays on the machine

Medications to avoid in this stage of CKD

- Magnesium containing medications (Maalox, MOM, Magnesium Citrate)
- Phos containing medications (Fleets)
- Gabapentin dosing
- Insulin, and antiglycemics
- Allopurinol needs to be dosed reduced
- Avoid Septra, Zyrtec
- Antibiotics need to be dosed for renal function

Lab Abnormalities

- Amylase, Lipase are 3–4x elevated in CKD stage 4–5
- Think twice abt the pancreatitis diagnosis
- ESR, often increase by 10 for every gram of protein the patient has
- Post dialysis labs are notoriously inaccurate
- Wait at least 4 hr post HD to draw labs
- PT/PTT drawn at dialysis

Radiologic issues

- CT contrast can often cause ARF
- The risk of a contrast study can be minimized with mucomyst and bicarb therapy
- MRI, gad has been associated with Nephrogenic Fibrosing Dermopathy
Long term dialysis issues

- Acquired renal cystic disease
- Risk factor for renal cell carcinoma
- B-2 microglobulin/Amyloid deposits disease
- Usual manifestation is carpal tunnel syndrome
- Blood transfusions