- Definition
  - NKF CKD Scheme (below) has some problems
    - (1) fails to incorporate other important prognostic parameters like proteinuria (eg. two with the same GFR but different degrees of proteinuria will have different prognosis)
    - (2) fails to recognize that pts some pts will have lower GFRs even though their kidney fxn is fine (eg. elderly, malnourished, certain racial groups, etc)

Stage	Prevalence	GFR and/or kidney damage based on UA/US x>3mo	
I	3%	>90 (nl ~120) and kidney damage	• Essentially asymptomatic • Determine cause w/ Bx and reverse if possible • Aggressively address comorbid conditions
II	3%	90-60 and kidney damage	• Assess how fast pt is progressing by what is found on UA
III	4%	60-30	• Treat complications
IV	0.2%	30-15	• Essentially symptomatic • Referral to nephrologist for prep for Stage V (remember that late referral appears to be a RF for progression to ESRD)
V (ESRD)	0.1%	<15	• Uremia • Renal Replacement Therapy (RRT) or Transplant

- Epidemiology
  - Susceptibility RFs: AA, FHx, older age, low kidney mass, low birth weight
  - Initiation RFs: DM, HTN, autoimmune disease, infection, obstruction, toxicity
  - Progression RFs: DM, HTN, proteinuria, smoking
  - End-Stage RFs: late referral, anemia
- A on CKD
  - Renal Vein Thrombosis
  - Cholesterol Embolization
  - RAS Atherosclerotic Rupture
  - Urinary Tract Obstruction w/ UTI
  - Drugs
  - Decreased Renal Perfusion
- Etiology
  - Pre-Renal & Post-Renal (15%)
  - Intra-Renal (85%)
    - Tubule-Interstitial Disease
      - **Chronic Tubulo-Interstitial Nephritis (CTIN) (5%)**
        - Repetitive Acute Tubulo-Interstitial Nephritis (ATIN)
        - Medications (Analgesics esp Phenacitin but possibly NSAIDs (esp in middle aged women w/ low socioeconomic class who often complain of HAs and have coincident psychiatric disease and thus chronically take large amounts of analgesics, use must be >3g/d, papillary necrosis is common), Cisplatin, Cyclosporin, Chinese Herbals containing Aristolocholic Acid)
        - Heavy Metals (Au, Li, Pb aka “Saturnine Gout”, Hg, Cadmium)
        - Electrolyes (Hypercalcemia, Hyperuricemia, Hyperoxaluria, Hyperphosphatemia, Hypokalemia)
        - Cancer (lymphoma)
        - Autoimmune (Sarcoidosis, SLE, Sjogren’s, Cryo)
        - Infection (TB, Fungal, Chronic Pyelo, HIV, BK Virus in transplant pts)
        - Chronic Allograft Rejection
        - SCD
    - Glomerular Disease

- **1° DM (45%)**
- **2° HTN (30%)**
- Other Chronic Glomerulonephritis

▪ Vascular Disease
- Vasculitis (rare)

▪ Other
- **PCKD (5%)**
- Vesicoureteral Reflux

- S/S/Complications & Tx
  - **Electrolyte/pH/Fluid Disturbances**
    - Decreased
      - **Na^+** (due to decreased reabsorption)
      - **Ca^+** (due to hyperPO4 and decreased VitD production)
        - Problem (chronic hypoCa causes osteoporosis and 2° hyperPTH)
        - Tx: refer below
    - Increased
      - **H_2O** (due to decreased UOP)
        - Problem (refer)
        - Tx: Fluid Restriction to <1.5L/d (~6cups), Na Restriction to <2gNa/d or <6gSalt/d (achieved by a no-added salt diet), Loop and Thiazides Diuretics to convert oliguric to non-oliguric renal failure if possible, be careful w/ in-pt IVF while pt is in-pt
      - **H^+** (due to decreased HCO3- reabsorption and decreased renal mass which results in decreased NH3+ production)
        - Problem (refer)
        - Tx: if on RRT then give $NaHCO_3$ 0.5-1mEq/kg/d or if not on RRT then give $NaHCO_3$ to keep HCO_3 >22, remember you are giving Na also so Na restrict more, try to avoid NaCitrate b/c even though citrate is converted into HCO_3 in the gut it enhances aluminum absorption leading to potential toxicity
      - **K^+** (due to decreased secretion/excretion)
        - Problem (refer)
        - Tx: chronic loop diuretics, 5g of Kayexalate w/ each meal, try to restrict K containing foods (bananas, melons, oranges, potatoes, tomatoes) to <2g/d
      - **Mg^+** (due to decreased secretion/excretion)
        - Problem (refer)
        - Tx: rarely do pts have clinically significant hyperMg that needs to be lowered medically just avoid magnesium containing compounds such as MOM, Mylanta, Fleets enema, etc, try to restrict Mg containing foods (nuts)
      - **PO_4^+** (due to decreased excretion)
        - Problem (chronic hyperPO4 is bad b/c it causes (1) 2° hyperPTH (2) large artery calcification w/ narrowing leading to organ ischemia esp of heart and systemic HTN, (3) valvular calcification, and (4) Calciphylaxis aka Calcific Uremic Arteriopathy = mechanism is unknown but there is Ca/PO4 deposits in small arteries causing fibrosis and thrombophilia with subseqent ischemic necrosis of skin and soft tissue, RFs: Coumadin (b/c Matrix G1a which is an endogenous protein that prevents soft tissue calcification requires vitk caboxylation to fxn), obese, female, etc, Dx: skin biopsy, bone scintography shows uptake in soft tissue, labs are variable but classically increased Ca, Phos, PTH, Tx: aggressive RRT, Na Thiosulfate (chelates Ca from tissue), wound care esp surgery/HBO, d/c Coumadin and consider heparin b/c thrombi form)
        - Tx: refer below
  - **Metabolic Bone Disease aka Renal Osteodystrophy** (there is a variety of bone dz therefore do a bone Bx if severe and cause unknown)
    - **Osteitis Fibrosa** (high PO4 + low Ca + low Calcitriol → 2° hyperPTH w/ hyperplasia → Osteitis Fibrosa (increased bone turnover w/ overall resorption = arthralgia/ostalgia, fractures, impaired growth, lytic bone lesions)
      - Tx: goal is to lower PTH w/ a target PTH (pg/mL) for CKD Stage 3/4/5 of 35-70/70-110/150-300pg/mL (follow Ca/PO4/VitD/PO4 Q12/3/1mo in Stage 3/4/5) by first correcting PO4/Ca/Calcitriol based on the Dialysis Outcomes Quality Initiative (DOQI) guidelines, problem is that correcting VitD and PO4 increases calcium to high levels causing calcification
        - 1^{st}: lower PO_4 to maintain level 2.7-4.6/?/3.5-5.5mg/dL in Stage 3/4/5 (refer)
        - 2^{nd}: raise VitD to ? (refer)
        - 3^{rd}: calcium is complicated so adjust Ca-PO4 product <55 and limit Ca <2000mg/d, raise Ca only after PO_4 is corrected and Ca is still low b/c after a CKD pt is being Tx for PO4 and VitD deficiency instead of hypocalcemia there is actually a high calcium load on the CKD body 2/2 phosphate binders and vitD intake, this high calcium does not go to bone b/c bone turnover in CKD pts is not normal but either high (there is actually release of

more calcium from bone) or low (bone cannot take up calcium) therefore the high calcium load deposits in extra-skeletal sites
        - 4th: address PTH directly b/c over time there is a decrease in VitD (VDR) and Calcium (CaR) receptors on the parathyroid gland causing resistance of the gland to VitD and Ca despite supplementation therefore the only way to decrease activity of parathyroid is by taking it out w/ parathyroidectomy or by increasing Ca/VitD receptor sensitivity on gland w/ cinacalcet (Sensipar)
    - **Adynamic Bone Disease** (2/2 aluminum toxicity, DM, steroid use, VitD supplementation when PTH is low = impaired osteoblastic/osteoclastic activity and mineralization = fractures, proximal muscle weakness, ostalgia, low PTH, nl-high calcium)
    - **Osteomalacia** (2/2 chronic VitD deficiency)
    - **Osteoporosis** (2/2 chronic hypoCa)
    - **β2-Microglobulin Amyloidosis** (2/2 β2-microglobulin accumulates in bone in pts who have been on RRT >10yrs = carpel tunnel syndrome, bone cysts, arthralgia, fractures)
- **Uremia** (retention of metabolic waste aka azotemia (increased Cr and BUN) that then leads to Sx)
    - General: fetor uremicus, metallic taste, decreased in growth (main problem in children) 2/2 decreased nutrition 2/2 anorexic effect of uremia, urea affects ILGF therefore decreased GH effect, bone problem, etc
    - CV: pericarditis (most serious problem requires emergent RRT), accelerated atherosclerosis (most common cause of death!!!)
    - GI: N/V, anorexia, cachexia, gastritis/duodenitis w/ significant GIB, colonic AVM
    - Neuro: "Uremic Encephalopathy", mixed (sensory/motor) peripheral (Leg>Arm) symmetric polyneuropathy, asterixis, autonomic neuropathy, restless leg syndrome
    - ID: dysfunction leading to infection (most common cause of death)
    - Heme: platelet dysfunction resulting in bleeding, anemia 2/2 decreased erythropoietin production b/c made by interstitial cells, BM suppression, Tx: DDAVP, estrogen
    - Derm: dryness w/ pruritis, Lindsey's nails (increased proximal lanulae with red/pink/brown distal nail bed), uremic frost (white urea crystals on skin)
    - Endo: decreased testosterone/estrogen, hyperprolactinemia, DL
- **Anemia**
    - Etiology: multifactorial including low erythropoietin, iron deficiency (why? hepcidin is produced by liver and excreted by kidney so in CKD there is increased hepcidin which acts to decrease iron GI absorption, because of this don't use PO iron rather use IV iron), bleeding b/c of platelet dysfunction, etc
    - Tx: keep Hgb 11-12mg/dL (no higher no lower), iron if IDA, erythropoietin if low epo levels, avoid transfusions b/c the resultant sensitization to HLA antigens makes kidney transplantation less successful, dDAVP/estrogens for bleeding from uremic platelet dysfunction
- **HTN**
    - Etiology: multifactorial including fluid retention, increased sympathetic activity and RAAS, etc
    - Tx: start w/ RAAS inhibition then add diuretic then add CCB/BB (NB more aggressive BP control w/ goal of <130/80)

- General Tx
    - Treat the underlying problem
    - Meds
        - Discontinue nephrotoxic meds
        - Avoid K/Mg/PO4 containing medications
        - Renal dose meds for decreased renal clearance (esp allopurinol, aminoglycosides, BB, digoxin, H2B, Li, Mg containing meds like antacids/laxatives, metformin/sulfonylureas, NSAIDs, sucralfate)
    - Diet
        - Strict I/O's
        - Nephrocaps 1 po qd (MVI used in CKD to replace water-soluble vitamins lost in HD)
        - In children stunted growth is such a problem that tube feeds and recombinant human growth hormone therapy has become the mainstay is almost universal
        - "renal diet" is actually bull shit as it tastes horrible, is physiologically inadequate, there are no studies showing its importance… the only important electrolyte to control is PO4 and Protein
            - Phos (normal diet is 1000mg/d, in CKD pts PO4 intake should be 600-700mg/d the problem is that the more protein has lots of PO4 and when pts are in ESRD they need protein supplementation and in doing so PO4 can never limited to recommended values by diet alone therefore you have to use PO4 binders)
            - Protein (the studies looking at protein restriction are controversial
                - CKD Stage I,II,III: normal diet (1.0g/kg/d)
                - CKD Stage IV: low protein diet (0.8g/kg/d)
                - CKD Stage V: supplement diet (1.2g/kg/d) b/c pts are uremic (a catabolic state and poor appetite) and it is found that low albumin is a very poor prognostic indicator (increased CV death) therefore these pts should actually get protein supplementation
    - Renal Protective Medications (even though you think that since AII increases GFR that it would be good it is actually bad) RAAS inhibition slows progression of every stage of CKD regardless of cause, Cooperate trial showed synergistic benefit of ACE-I and ARB, RAASI decrease BP/proteinuria/progression of kidney disease aside from its affect on BP and proteinuria

- avoid blood draws or IVs in one arm in anticipation for dialysis access and once placed check access sites for infection, stenosis, etc
- Avoid MRI Gadolinium Contrast b/c can cause Nephrogenic Systemic Fibrosis (NSF), similar systemic sclerosis, uniformly fatal