



*Diabetes, HTN & Chronic
Kidney Disease*



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Objectives



- ★ Understand the epidemiology of CKD
- ★ Understand the pathology of diabetic kidney disease
- ★ Learn how to prevent CKD
- ★ Learn how to treat CKD
- ★ Identify proteinuria and treatment
- ★ Identify appropriate time for nephrology referral
- ★ How to identify and treat Conn's and Liddle's





Chronic Kidney Disease (CKD)

- ★ 20 million Americans have CKD (1 out of 9 persons)
- ★ Higher morbidity and mortality on dialysis
 - Diabetic life expectancy is 2 years (25% death rate/yr)
 - Non-diabetic is 5 years (10% death rate/yr)
 - Worse than breast CA



Table 6.4 Expected remaining lifetime (years) by age, sex, and treatment modality of prevalent dialysis patients, prevalent transplant patients, and the general U.S. population (2012), based on USRDS data and the National Vital Statistics Report (2013)

Age	ESRD patients, 2013				General U.S. population, 2012	
	Dialysis		Transplant		Male	Female
	Male	Female	Male	Female		
0-14	24.1	22.4	59.2	61.2	70.7	75.4
15-19	20.9	19.3	46.8	48.6	59.7	64.4
20-24	18.1	16.5	42.5	44.2	55.0	59.5
25-29	15.8	14.3	38.6	40.2	50.3	54.6
30-34	14.1	13.0	34.7	36.4	45.7	49.7
35-39	12.5	11.7	30.8	32.4	41.0	45.0
40-44	10.8	10.3	26.9	28.6	36.4	40.3
45-49	9.1	8.8	23.2	24.8	31.9	35.6
50-54	7.7	7.7	19.8	21.3	27.7	31.1
55-59	6.5	6.6	16.6	18.1	23.7	26.8
60-64	5.5	5.7	13.8	15.2	19.8	22.6
65-69	4.5	4.8	11.4	12.7	16.2	18.5
70-74	3.8	4.0	9.4	10.4	12.8	14.7
75-79	3.2	3.5	7.7a	8.6a	9.8	11.3
80-84	2.6	2.9			7.1	8.4
85+	2.1	2.4			4.9	5.8



Costs of CKD in 2013 dollars

USRDS report



★ 469,950 pts ESRD (10,000 pts 1972)

★ 17,600 transplanted patients 2013

★ CKD 10% medicare pop., 20% cost

★ ESRD 1% medicare pop., 7 % cost

★ ESRD \$84,550/yr Hemodialysis

★ ESRD \$69,919/yr Peritoneal dialysis

★ Transplant \$29,920/yr/\$75,000-150,000 for actual transplant and 3 months of followup





CKD Stages by Glomerular Filtration Rate & Proteinuria



★ Normal GFR 100-125 ml/min

★ Stage 1- GFR \geq 90 ml/min & proteinuria

★ Stage 2- GFR = 60-89 ml/min



★ Stage 3- GFR = 30-59 ml/min

★ Stage 4- GFR = 15-29 ml/min

★ Stage 5- GFR < 15 ml/min or dialysis



★ GFR equivalent = creatinine clearance

★ I give patients percent of function



Diabetic Nephropathy

- ★ Clinical syndrome
- ★ Albuminuria >30 mg/ 24 hrs
- ★ Proteinuria >500 mg/24 hrs (I've seen 16 gms a day)
- ★ Hypertension develops
- ★ Progressive increase in proteinuria
- ★ Progressive decline in glomerular filtration rate





Hypertension



- ★ Just having HTN can cause proteinuria
- ★ Usually more like 1-2 gms of protein a day
- ★ I treat them like a diabetic with ACEI and ARBS and tight blood pressure control



Mortality

- ★ After 40 yrs of DM
 - 10% alive if proteinuria is present
 - 70% alive if proteinuria is absent
- ★ Heart Disease is 15 times higher risk in those with proteinuria
- ★ Proteinuria = death in this population





Predictors CKD: GENETICS

- ★ Higher rates in AA, American Indians and Hispanics versus caucasians
- ★ Siblings with DN
- ★ Higher values in ambulatory BP
- ★ Diabetic Retinopathy 9 x higher risk of DN
- ★ Smoking-increase thickness of glomerular basement membranes





Blood pressure & A1c effects

- ★ Type 1 DM-if SBP <115 mmHg then 1.4 fold reduction in proteinuria
- ★ Type 2 DM-if SBP <129 then reduction of proteinuria can occur
- ★ Hgb A1c <6.95 has best chance to revert to normal albuminuria
- ★ JNC 8- goal <130/80 with CKD





Stages of DM Nephropathy (Different than 5 CKD levels)



★ Stage 1-GFR elevated 20-40% and urinary albumin excretion rate rises



★ Stage 2-high GFR-pathology changes

★ Stage 3-Alb 30-300 mg/24 hrs, HTN

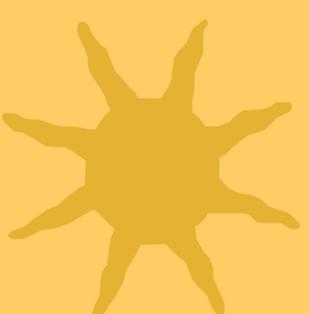
★ Stage 4-GFR decreases/hematuria occurs



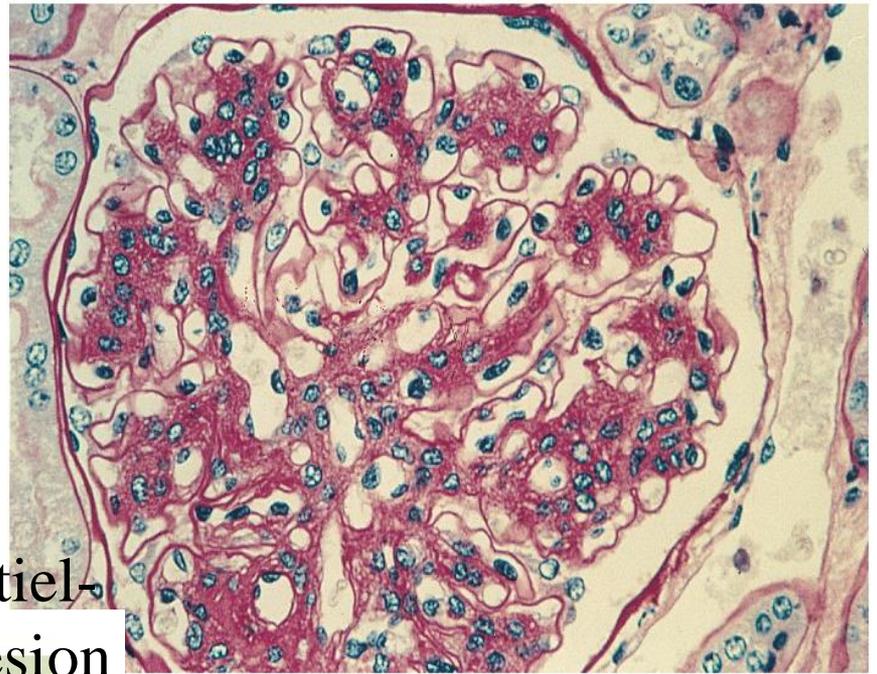
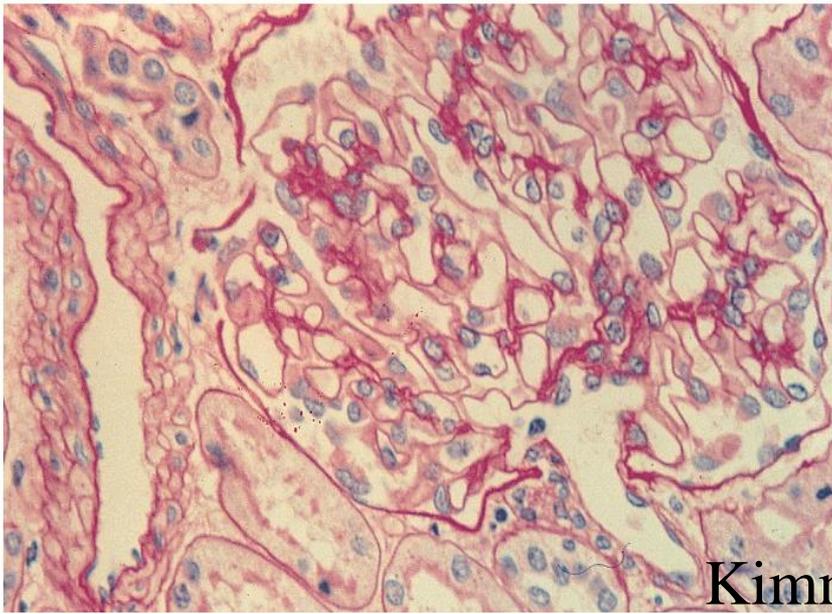
★ Stage 5-ESRD (average time is 7 yrs to start dialysis with no treatment at all)



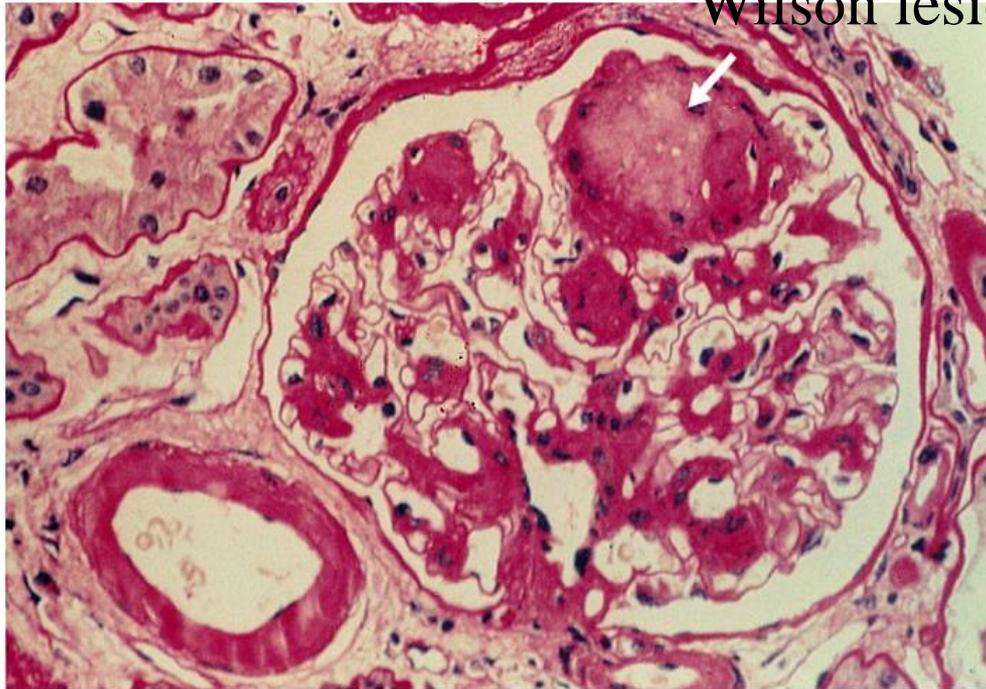
Pathology



- ★ Average kidney size is larger than normal
normal renal size is 10 cm
diabetics can be 11-13 cm in length, HTN
& RAS small kidneys <9 cm
- ★ Thickening of basement membranes
- ★ Thickening of support tissue
- ★ Blockage of capillaries and arteries
- ★ Scarring of interstitial support tissue



Kimmelstiel-
Wilson lesion



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Pathology
Changes in
Diabetes



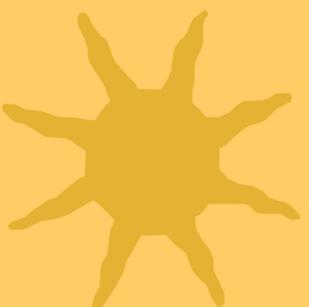
Cellular Level activation of inflammatory cytokines



★ Monocytes/macrophages-create nitric oxide, IL-1, TNF alpha, TGF Beta, complement



★ T lymphocytes-IFN gamma, TNF alpha (also seen in renal transplant rejection)



★ Neutrophils-Mac 1-converts to hydrogen peroxide. (also seen in pyelonephritis)



Appropriate Screening of DM and HTN

- ★ All Type 1 DM at diagnosis & q 3-12 mon
- ★ All Type 2 DM at diagnosis & q 3-12 mon
- ★ Measure microalb/creatinine ratio.
Abnormal >30 mcg/ml
- ★ Or Total protein/creatinine ratio, when
microalbumin is too high to measure.
0.5 mg/dl is proportionate to 500 mg
protein/24 hrs.
- ★ You DON'T have to do 24 hr urines



Basic Screening



- ★ BP
- ★ Serum Creatinine
- ★ Cockcroft-Gault Formula for GFR
$$\frac{(140 - \text{age}) \times (\text{wgt kg})}{(72) \times (\text{serum creat mg/dl})} \times .85 \text{women}$$
- ★ MDRD equation www.MDRD.com
- ★ Schwartz formula for children
<http://www.clinicalcalculator.com>



Screening Continued

- ★ Urine protein/creatinine ratio- should be < 0.5 mg/dl (< 500 mg/day)
- ★ UA for protein and hematuria screen-need RBC eval for bladder cancer. May have GN
- ★ Glucose/hgb A1c
- ★ When CKD level 3,4,5-then do PTH intact, CBC, lipids, 25-OH vitamin D levels, & uric acid, UA with micro, prot/creat, cmp, phos





Medicine caution



★ Hold metformin when gfr <35 ml/min

★ GFR <50 ml/min should alert to check all doses of meds



★ No bisphosphanates <35 ml/min

★ No NSAIDS/cox 2 inhibitors <60 ml/min

★ Atenolol –renal excretion



★ BACTRIM!!!! A lot of AKI!!!

★ Insulin renally excreted-low sugars? Ck gfr



Medicine caution



★ Lovenox-use subcut heparin

★ Apixiban



★ Dabigatran

★ Rivaroxiban

★ Lithium



★ GABAPENTIN



Loss of GFR

- ★ Normal GFR is 100-125 ml/min
- ★ Normal GFR loss is .5-.75ml/min/year after age 40
 - 80 yr old should lose (80 - 40 years)X .5-.75. So the loss is 40 X .5- .75 or 20-30ml/min. Normal aging GFR for this 80 yr old should be: 100-125ml/min minus 20-30 ml/min = 70-95 ml/min (which is CKD level 2 even with normal aging)
- ★ DM nephropathy may lose 2-20ml/min/year



Causes of ESRD

- ★ Diabetes accounts for 50% of dialysis patients by USRDS data
- ★ Hypertension is 27% of ESRD
- ★ Polycystic Kidney disease
- ★ Glomerulonephritis
- ★ Reflux (re-implant ureters at age 4 to 5 yrs old to prevent ESRD in the 20 yr olds)
- ★ Nephrolithiasis





Other Renal Diseases



- ★ Glomerulonephritis
(Wegener's/Goodpasture's/Lupus)
- ★ Membranous nephropathy (Hep B, C, Cancer)
- ★ Renal papillary necrosis (rare)
- ★ Renovascular disease (very common)
- ★ Autonomic neuropathy of the bladder
- ★ Urinary tract infection
- ★ Pyelonephritis
- ★ Contrast Nephropathy (from Dye)





Renal Artery Stenosis



★ Lisinopril 10 mg if creat rises $>.3$ or potassium rises >5.0 suspect RAS



★ DX: captopril renal scan, CTA, MRA, renal angiogram+ poss stents.



★ Occasional need for stents if dropping GFR uncontrolled HTN

★ Medical management is standard of care



Prevention of Contrast damage, Also for surgery ATN prevention



★ IV Saline drip (1 liter bolus if emergency)

★ Mucomyst 600 mg BID day prior to procedure and day of procedure



★ Bicarb protocol-1L D5W, 3 amps bicarb, start 3ml/kg/hr 1 hr prior to procedure, then at 2nd hr change to 1ml/kg/hr for 3-9 hours depending on volume of contrast.



★ Hold ACEI, ARBS, Diuretics, KCL day of test and day prior to test if possible (also hold for surgery)



DM and Pregnancy



★ Proteinuria high in 1st , 2nd , trimester and highest in 3rd trimester

★ HTN is worse (BP normally is lower)



★ Small for gestational age

★ Large for gestational age

★ Use insulin



★ No ACE inhibitors or ARB's for HTN-they cause fetal abnormalities in kidneys



Renoprotective effect of ACE I



★ Lower systemic BP

★ Lower glomerular pressure

★ Increase renal bloodflow



★ Reduce proteinuria

★ Natriuretic (salt excretion)

★ Decrease in Aldosterone production



★ Inhibit angiotensin II, cytokines, growth factors and macrophages



Prevention and Treatment of CKD



- ★ Blood pressure goal <130/80
- ★ ACE Inhibitors to max dose-may not improve blood pressure after moderate dose but will improve proteinuria. Then add ARB. Monitor K⁺ closely
- ★ Hemoglobin A1c <7.0 (6.5 is better)
- ★ No NSAIDS/COX-2 inhibitors
- ★ Tylenol or narcotics for pain.
- ★ Aspirin one daily is ok for heart prevention-I usually give 81 mg



Treat to Goal



- ★ Phosphorus binders when phos >5.5
- ★ Goal for protein/creatinine ratio is <0.5 mg/dl or total protein to <500 mg/day.
- ★ LDL cholesterol <70
- ★ Smoking Cessation





HTN--Collecting Ducts

- ★ Aldosterone Receptor binds Aldosterone
- ★ Causes Na & H₂O reabsorption and potassium loss
- ★ Conns Syndrome is high aldosterone
- ★ BP high systolic and diastolic and low potassium
- ★ Ex: 180/100, Potassium 2-3.5
- ★ Aldosterone/Renin level >20-30 likely Conns
- ★ Get CT scan abd and pelvis IV contrast thin cuts through adrenals. Remove adrenal if mass >4cm





Conn's & Liddle's Tx



★ High aldo/renin –use spironolactone or eplerenone and titrate up on dose



★ Aldo/renin normal: then try amiloride or triamterene and titrate up on dose



★ Dose maxed if bp normal or K up to 5.5 then add other agents.



Case Example

- ★ 44 yo WM. HTN 4 yrs 154/102
- ★ Amlodipine 10 mg daily
- ★ Atenolol 100 mg daily
- ★ Atacand 32 mg daily
- ★ HCTZ 25 mg daily
- ★ Terazosin 2 mg daily
- ★ Potassium 2.8
- ★ Microalbumin/creat =32 mg





Case Evaluation



★ Aldosterone 25.9/Renin <0.15=ratio 172

★ Renal sono: R 11.7 cm, L 11.6 cm



★ CT abd –nodular thickening of bilateral adrenal glands.





Case Treatment



★ Spironolactone 25 mg, 50, 75, 100 mg daily



★ Stopped HCTZ, amlodipine, terazosin, atenolol



★ Kept the atacand for microalbuminuria- could have used an ACE inhibitor also.

★ BP 109/59

★ Potassium 4.3



Statins-

Renoprotective?/Controversy

- ★ HMG-CoA reductase inhibitors (statins) in high doses can cause proteinuria
- ★ Associated with less inflammation, endothelial dysfunction, and scarring in the kidney because they also block inflammatory cytokines
- ★ I choose to use statins if CAD/PVD
- ★ Zetia & Niacin-no proof they help





Hyperuricemia levels & CKD

- ★ <4.41- 7% CKD 1.0 CKD progression
- ★ 4.41-5.2- 14% CKD .88 progression
- ★ 5.21-5.90- 12% CKD 1.23 progression
- ★ 5.91-6.9 25% CKD 1.47 progression
- ★ >6.9 42% CKD 1.49 progression
- ★ My current goal is Uric acid level <5.0 with use of allopurinol max dose is 900 mg/day, Uloric 80 mg also can be used

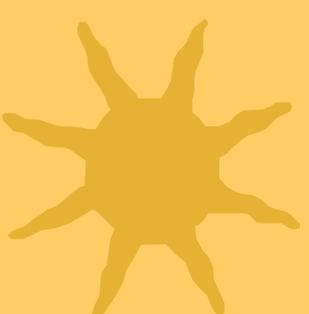




Vitamin D deficiency



★ Associated with secondary hyperparathyroidism



★ Associated with increases in albuminuria

★ 25, OH vit d goal >30

★ PTH intact goal <100 ckd 3 & 4



★ Calcitriol .25 mcg mwf, or daily



Metabolic Acidosis



★ Goal CO₂ 22-26

★ Sodium Bicarb 650 1-2 bid to tid



★ Bicitra 30 ml daily to bid

★ Potassium Citrate 15 meq 2 po bid





Anemia of CKD

- ★ To use ESA: hgb <10
- ★ Iron sat >20%, Ferritin >100
- ★ Keep b12 >400
- ★ Lab q 2 weeks to titrate med
- ★ Epo, procrit, aranesp, mircera options



CKD and CHF

- ★ I push up diuretics to keep lungs dry and sacrifice some renal function to do so
- ★ Push BUN up to around 80
- ★ Push Creat up to eGFR 15 ml/min
- ★ GFR <30 usually Bumex 2 mg bid and metolazone 5 mg daily or qod or 2-3 times a week.





Refer to Nephrology



- ★ When creatinine clearance less than 60 ml/min is recommended. (Tell the pt their GFR)
- ★ GFR <30 ml/min definite referral
- ★ Greater than 500 mg/protein in urine
- ★ Accelerated HTN
- ★ Uncontrolled HTN
- ★ Hematuria (could be bladder cancer also)-I send for cystoscopy



Complications of CrCl <30 ml/min



- ★ Anemia-epo deficiency, iron, folate & B12
- ★ Hypocalcemia-secondary to low Vit D
- ★ Acidosis-bone will act as buffer & dump calcium
- ★ Osteomalacia/osteopenia/osteoporosis
- ★ Secondary hyperparathyroidism from Vit D deficiency & hyperphosphatemia
- ★ Malnutrition-Alb <3.8 increases mortality in ESRD due to low immunoglobulin production
- ★ Fluid control-thiazide diuretics are ineffective with creatinine clearance <30 ml/min, use loop diuretics ± metolazone



Treatment Plan Cr Cl <30 ml/min



★ Save non-dominant arm from IV site, PICC lines, needles to save veins for future graft or fistula. Also avoid subclavian lines. These all cause stenosis in veins



★ Improve nutrition (no protein restriction) protein intake 1.2gm/kg

★ Pre-ESRD training/class

★ Placement of fistula/graft/peritoneal dialysis catheter gfr around 11-20 ml/min



★ Transplant evaluation/transplant <20 ml/min (dialysis is not necessary first)

★ Dialysis at 10-15 ml/min



Kidney-Pancreas transplant



- ★ Type 1 diabetics can choose pancreas only transplant prior to development of end-organ damage from diabetes
- ★ Pancreas after kidney transplant is an option
- ★ Simultaneous pancreas and kidney transplant is best for Type 1 diabetes with ESRD
- ★ LRD (living related) donor is done first to get the patient off of dialysis, then can list for CAD (cadaver) pancreas



How Do I Do All This?



- ★ BP and med titration every 3-4 weeks
- ★ Cholesterol and med adjust every 6 weeks use Code Z79.899 the med monitoring code to bill
- ★ Proteinuria check every 3 months then Q 6-12 months
- ★ PTH intact every 3 months until stable then 1 x year
- ★ Vitamin D level once a year, repeat in 3 mon if low
- ★ Patients call in sugars and insulin doses every 3-4 days to adjust insulin
- ★ Intensive patient education-I TELL them their life expectancy!!
- ★ Even with all this—I still have non-compliant pts.



Summary



- ★ Screen all diabetics and HTN, Fam Hx
- ★ Aggressive control of HTN, Diabetes, Lipids
- ★ Use of ACE inhibitor &/or ARB
- ★ Prevent progression to ESRD
- ★ Appropriate Nephrology referral
- ★ Prepare for dialysis, transplant, hospice
- ★ Phone your friend the nephrologist if needed



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