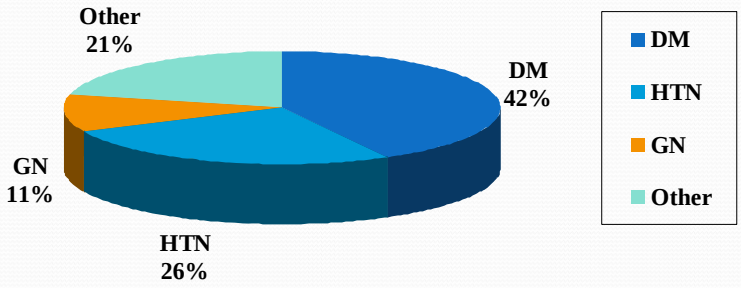
The Primary Care Physician's Role in Preventing the Progression of CKD

Early Treatment is the Key

Stages of Chronic Kidney Disease (CKD)

Stage	*Description*	*GFR (ml/min/1.73 m^2)*
1	Kidney damage with normal or ↑ GFR	>90
2	Mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney Failure	<15 or Dialysis

Causes of ESRD



What can be done?

- Control blood pressure
- Control blood sugar
- Detect and treat microalbuminuria
- Decrease proteinuria
- Protein restriction
- Statin therapy
- Smoking cessation
- Treat metabolic acidosis
- Treat reversible causes
- Refer to nephrologist

Control Blood Pressure

- Single most effective intervention to prevent CKD progression
- Frequently volume driven in CKD patients – diuretic required
- JNC VIII recommendations less stringent than previous
  - All CKD patients should have systolic < 140 and diastolic <90
  - All patients with microalbuminuria or proteinuria of any amount should have systolic <140 and diastolic <90
  - All diabetics should have systolic BP <140 and diastolic <90
  - All CKD* and diabetic patients with hypertension should be treated with ACE or ARB as part of the regimen

*Patients with proteinuria of any degree have a least CKD Stage 1

Fluid Excess (Edema)

Sodium is the "Devil" in CKD

- Usually due to glomerular disease (diabetes a cause) – sodium retention
- Tubulointerstitial disease – sodium loss until late
- Treatment – critical if hypertensive
  - Salt restriction – key to volume regulation in CKD
  - Loop diuretics – thiazides ineffective if GFR < 30
  - Monitor weight
  - Fluid restriction only occasionally – for hyponatremia
- Edema of nephrotic syndrome
  - Treat cautiously if normotensive
- **BEWARE** – excessive sodium restriction or diuretics will worsen renal function rapidly. "I feel dizzy when I stand."

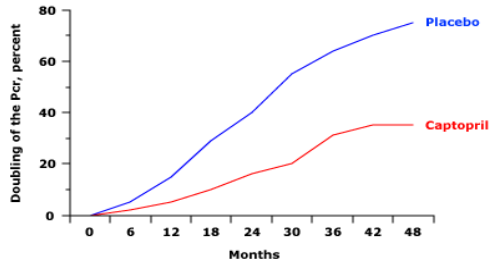
Hypertension in CKD

- Both cause and result of CKD
- **Most important factor in progression to ESRD**
- Usually volume related in CKD patients – 80%
  - Sodium restriction essential
  - Fluid restriction not beneficial
- Drugs:
  - ACE inhibitor or ARB (may worsen renal function)
  - Diuretic (loop or metolazone)
  - Calcium channel blocker
- **Always** treat

Blood pressure goals

- CKD with proteinuria < 200 mg/day – <140/90
- CKD with proteinuria > 500 mg/day –
  < **130/80** including diabetics (some still advocate < 120/75)
- Diastolic should remain > 65 in patients with CAD
- Diffuse atherosclerotic disease reduces blood flow to all organs. Need to be practical about BP control and allow higher pressures if renal function worsening.

ACE inhibitor slows progression of diabetic nephropathy



The effect of the administration of placebo or captopril to patients with type 1 diabetes with overt proteinuria and a Pcr equal to or greater than 1.5 mg/dL (132 µmol/L). The likelihood of a doubling of the Pcr was reduced by more than 50 percent in the captopril group.

ACE: angiotensin-converting enzyme; Pcr: plasma creatinine concentration.

Data from: Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. N Engl J Med 1993; 329:1456.

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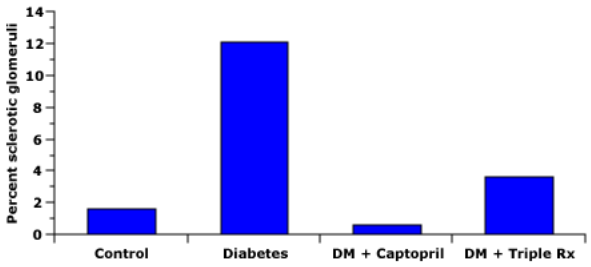
ACE inhibitor is more effective than triple therapy in protecting against experimental diabetic nephropathy



Efficacy of antihypertensive therapy in diabetic rats in reducing the number of sclerotic glomeruli at 70 weeks. Triple therapy with hydrochlorothiazide, hydralazine, and reserpine was partially protective, but captopril was completely protective, with the degree of glomerulosclerosis being less than that in control (normal) rats (left column). Captopril also normalized the intraglomerular pressure (46 mmHg) versus 64 mmHg in untreated diabetic animals and 56 mmHg with triple therapy.

Data from Anderson S, Rennke HG, Garcia DL, et al. Kidney Int 1989; 36:526.

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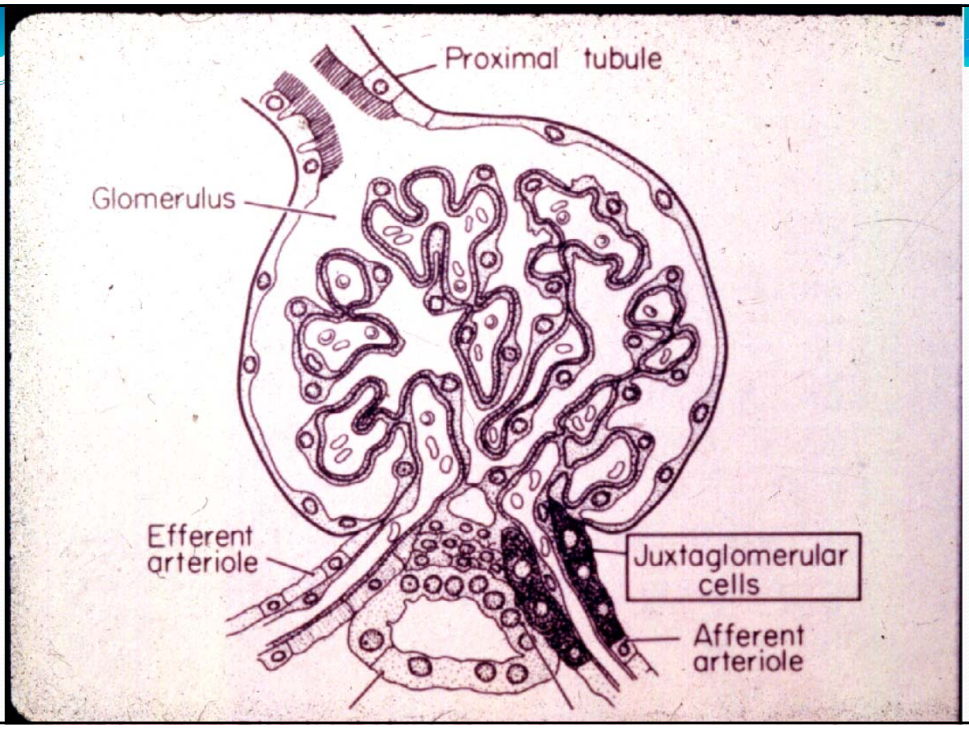
Effects of Angiotensin II

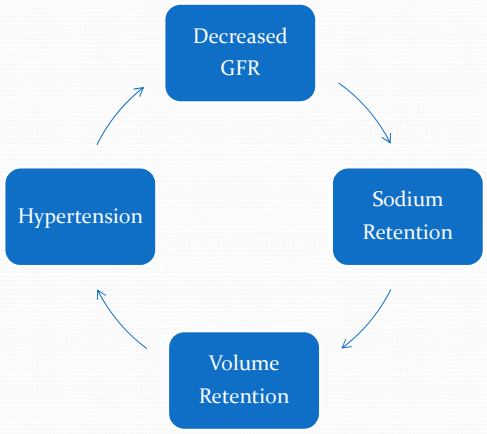
- General vasoconstriction
- Increase aldosterone production
- Enhanced vasoconstriction of efferent arterial greater than afferent arterial
- Net effect is increased BP (MAP = SVR x CO)
  - Increased systemic vascular resistance
  - Increased intravascular volume
- ACE inhibitor decreases AG-II by preventing conversion of AG-I to AG-II
- ARB prevents effect of A-II by blocking receptor
- Decreasing AG-II decreases proteinuria



When **Not** to Use an ACE or ARB

- Hyperkalemia – potassium > 5.5 and following corrected:
  - Metabolic acidosis
  - Taking other potassium retaining drug
  - Not on low potassium diet
- Bilateral renal artery stenosis
- Near starting dialysis

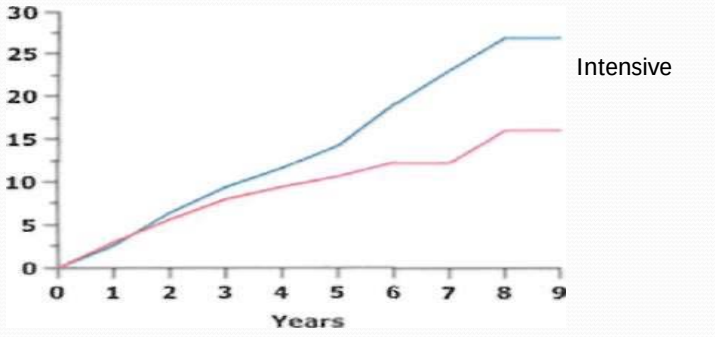
The Cycle of ***No*** Life



Treatment of Type 2 DM in CKD

- Preferred sulfonylurea is glipizide (Glucotrol)
  - Shorter half life
  - 2.5 – 10 mg daily
- Rapaglinide (Prandin) may be used instead of glipizide
  - Start with 0.5 mg 30 minutes before meals
  - Max 16 mg per day
- Metformin use with caution in CKD
  - Do not use if GFR <30 ml/min
  - May use if GFR >45 ml/min
  - GFR 30 – 44 ml/min not defined, but probably okay
  - 500 mg bid to 1000 mg bid
- Sitagliptin (Januvia)
  - GFR 30 – 49 ml/min 50 mg per day
  - GFR <30 ml/min 25 mg/day
- Insulin usually required

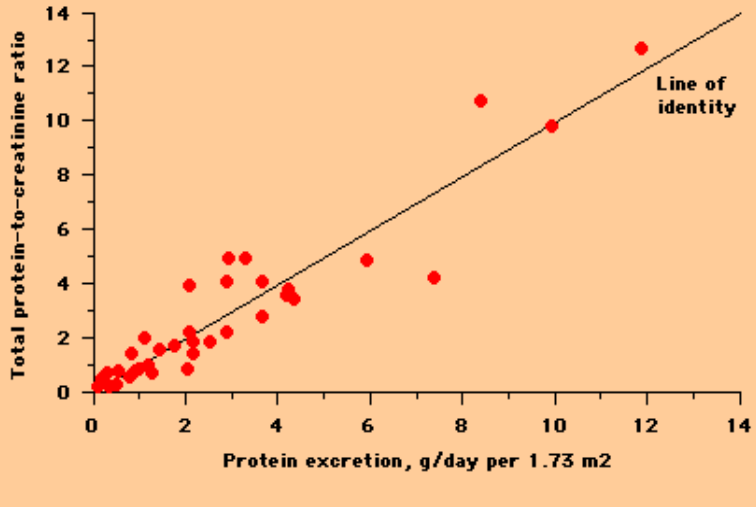
Intensive vs. Conventional Control of Type I DM



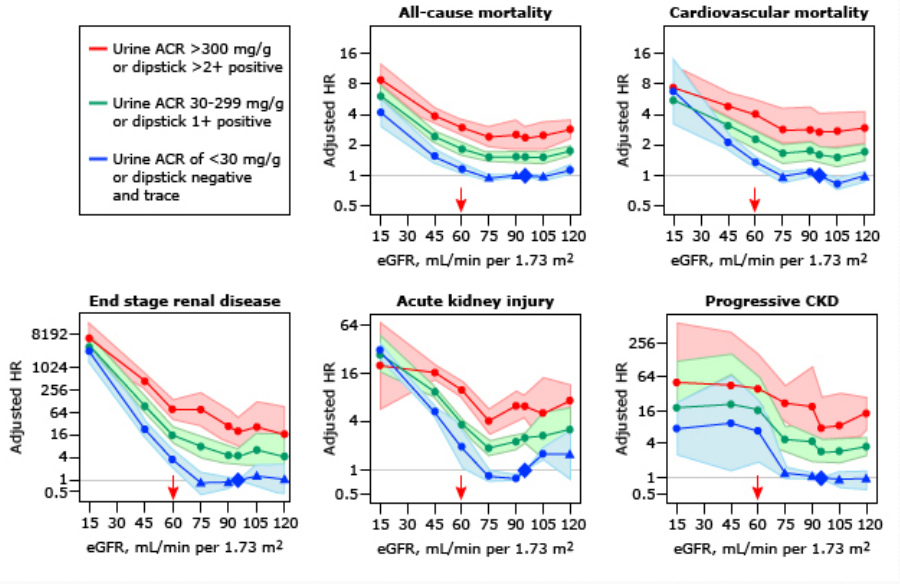
Incidence of microalbuminuria over 9 years (p <0.04)

Protein in the Urine

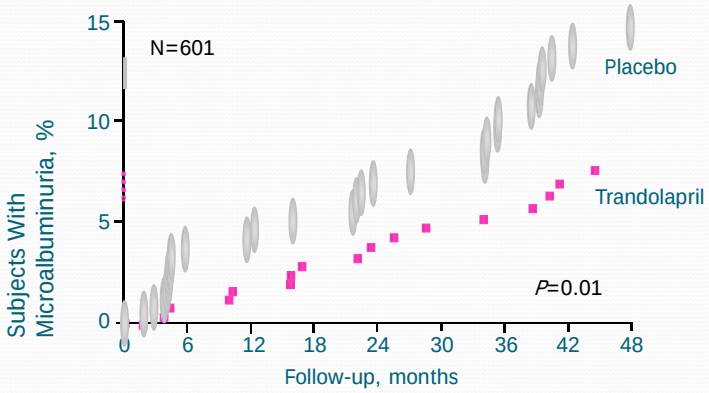
- Proteinuria = >200 mg/day
- Microalbuminuria (now moderate albuminuria) 30 – 300 mg/day
- Macroalbuminuria (now severe albuminuria) >300 mg/day
- Dipstick records albumin levels only above 300 mg/day
- ACE inhibitors and ARBs drugs of choice
- Decreasing proteinuria decreases rate of progression of CKD



Protein-creatinine ratio to estimate protein excretion This graph illustrates the close relation between total daily urinary protein excretion and the total protein-to-creatinine ratio (mg/mg) determined on a random urine specimen. (Data from Ginsberg, JM, Chang, BS, Matarese, RA, Garella, S. N Engl J Med 1983; 309:1543.)



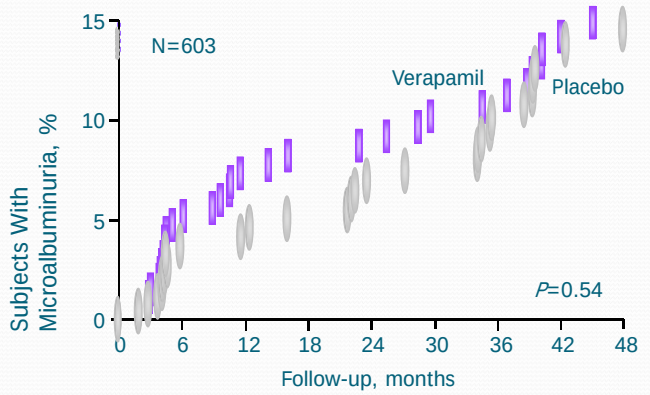
RAAS Blockade Delayed the Onset of Microalbuminuria by a Factor of 2.1 vs Placebo in Type 2 Diabetes



Bergamo Nephrologic Diabetes Complications Trial (BENEDICT)

Ruggenenti P et al. *N Engl J Med.* 2004;351:1941–1951.

Verapamil Does Not Delay the Onset of Microalbuminuria in Type 2 Diabetes



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Nutrition

- Goal serum albumin at least 4 g%
- Use prealbumin for earlier diagnosis
- Less than 10:1 BUN/Creatinine ratio - clue that patient is malnourished
- Protein restriction beneficial in glomerular disease especially diabetic nephropathy – about 0.8 grams/kg per day
  - Do not restrict to <0.6 grams/kg per day
  - Plant proteins superior
- Treatment of CKD with protein restriction may be a contributing factor to hypoalbuminemia

Statin Therapy
Smoking Cessation

- Controversial whether they benefit renal function
- More pressing reasons to implement than for renal function

Metabolic Acidosis

- Goal bicarbonate 23-29 mM/L
- Anion gap usually present
- Renal Tubular Acidosis may be aggravating factor
  - Normal or small anion gap
  - Type I and II seen with interstitial disease
  - Type IV in diabetics
- Treatment
  - Arm & Hammer baking soda 1 level tsp daily
  - $NaHCO_3$ tabs - 650 mg tab = about 7.75 meq)
  - Give 0.5 to 2 meq/kg/day
  - Phosphate binders also increase serum bicarbonate
    - PhosLo (calcium acetate)
    - TUMS (calcium carbonate)

CKD vs. CKD with Acute Exacerbation

- History -- more rapid progression than expected
- Presence or absence of reversible causes of acute exacerbation of chronic kidney disease

Reversible Factors for Renal Function Deterioration

- Volume depletion
- Infection
- Urinary tract obstruction
- Volume excess and CHF
- Nephrotoxic agents
- Severe hypertension
- Pericardial tamponade
- Hypercalcemia
- Hyperuricemia
- Renal artery stenosis

When to Refer to Nephrologist

- When eGFR <45 – preferred time first referral
- Urine albumin-to-creatinine ratio (ACR) > 300 mg/g
- Hematuria not secondary to urological condition
- eGFR decline of > 30% in < 4 months
- Significant anemia (Hgb <10 g)
- Persistent hyperkalemia (> 5.5 meq/L)
- Resistant hypertension
- Hyperphosphatemia (> 5.5 meq/L)
- Metabolic acidosis (bicarbonate < 15 mM/L)