

Changes in Acute and Chronic Kidney Disease and Staging of Kidney Disease

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Review and Reunion

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Pre Test Question:

Regarding CKD:

Which of the following is FALSE:

1. Pt with advanced CKD has same risk as if they have already had their first MI.
2. Should be on B-Blocker, ASA, Statin, and ACE or ARB if tolerated.
3. May need to stop the ACE/ARB as renal function declines
4. MRI contrast is safe in patients with CKD even if GFR is less than 40.

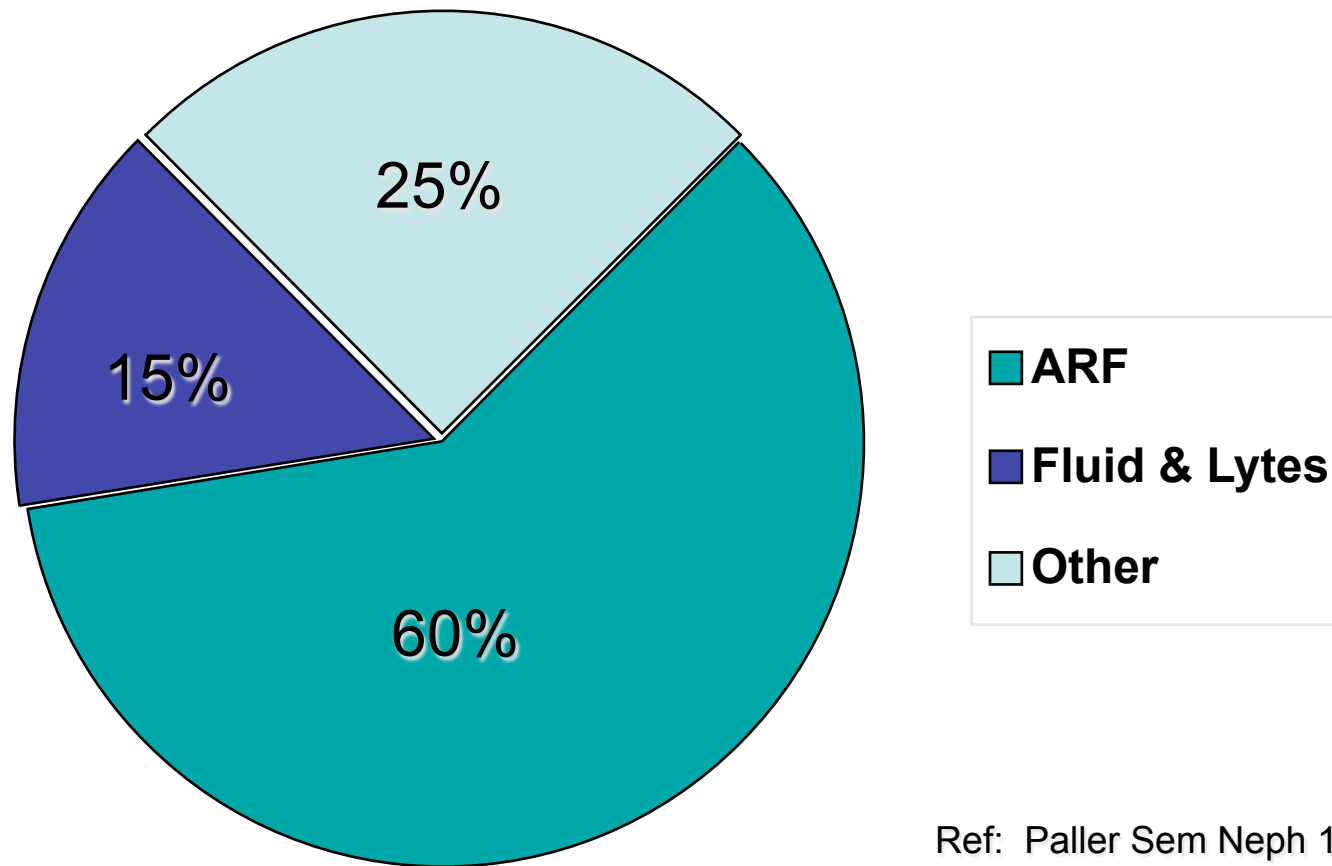
Summary ARF

- Acute Renal Failure
 - Differential
- Initial treatment of ARF
- RIFLE Criteria for staging of ARF
- New markers for Acute renal Injury
- How to differentiate Acute from Chronic kidney disease

Summary for CKD

- Prevalence of CKD
- Stages of CKD
- Progression of CKD
- Cardiovascular and All cause mortality in CKD – How can we Help our patients?

Reason for Nephrology Consultation



Ref: Paller Sem Neph 1998, 18(5), 524.

Approach to ARF

- Pseudo-ARF
- Pre-Renal
- Intra-Renal
- Post- Renal

Approach to ARF

- Pseudo-ARF
 - Pt hosp for liver lac, allowed to go home on weekends. Normal renal function.
 - First weekend, creat bumped to 1.5, not noticed
 - 2nd weekend, creat up to 1.8, hydrated and came down.
 - 3rd weekend, creat over 2.0, so we were consulted.
 - What was happening?

Approach to ARF

- Pseudo-ARF
 - Pt was eating steak dinners at home/restaurant
 - Texan so steak was WELL done
 - Creatine in muscle converted to Creatinine.
- Creatinine production also much higher in Rhabdomyolysis, so BUN / Creat ratio may be less than 10.

Approach to ARF

- Pre-Renal
 - Most common
 - Due to NPO, Diuretics, ACE inhibitors, NSAIDS
 - Due to renal artery disease, CHF with poor EF.
 - Usually BUN / creat ratio over 20.
 - Usually creat < 2.5

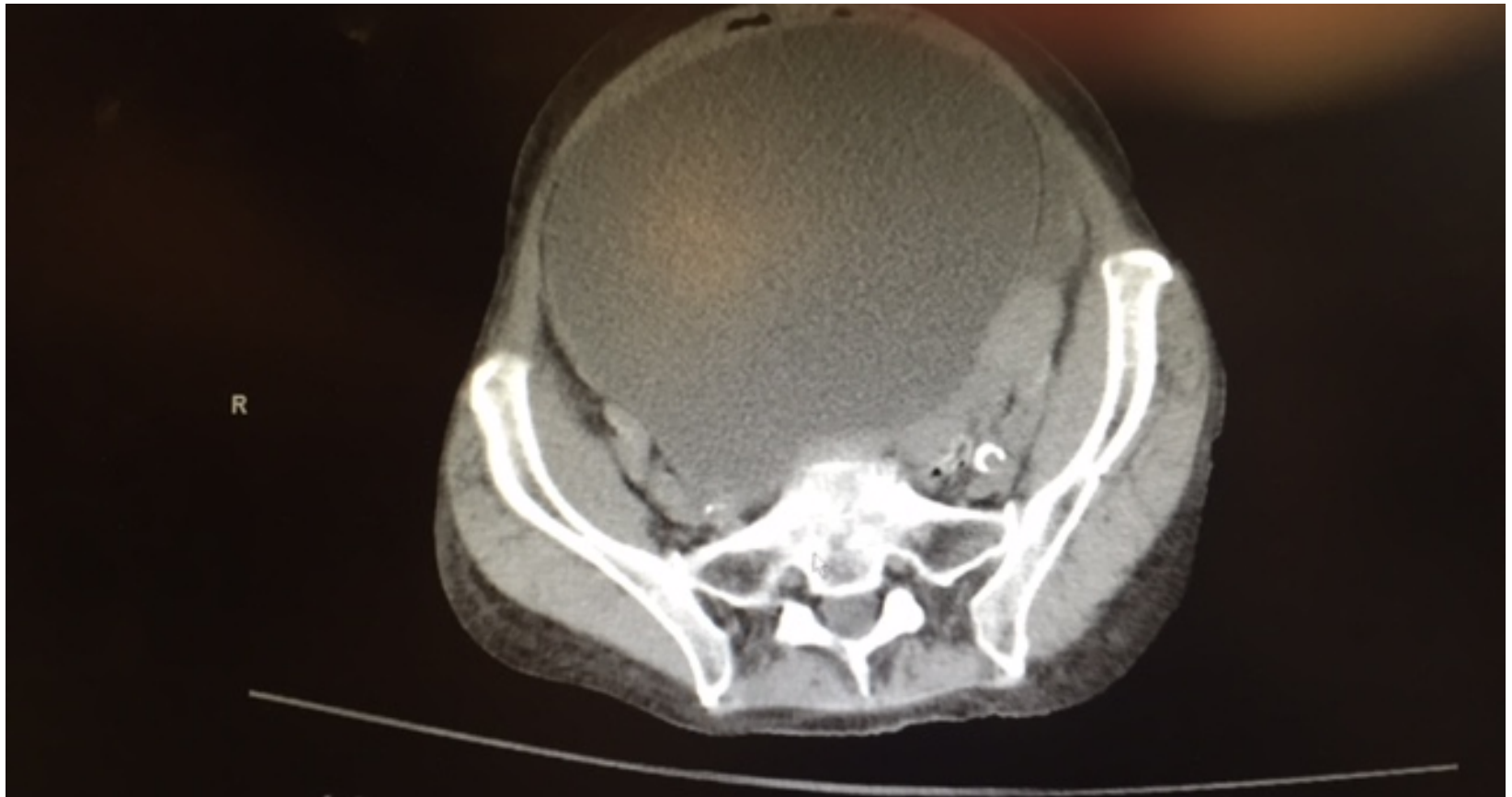
Approach to ARF

- Intra-Renal
 - Most commonly pre-renal tipping over into true renal injury.
 - Acute Tubular Necrosis is result (70%)
 - Tubulo-Interstitial Nephritis (20%)
 - Acute vasculitis/GN rare (5-10 %)

Approach to ARF

- Post- Renal
 - Most commonly due to obstruction at bladder outlet
 - Prostate problems
 - Neurogenic bladder
 - Stone
 - Urethral stricture (esp after CABG)

Post Renal ARF



Distribution of ARF Cause

Distribution of causes:

<u>Pre-renal</u>	<u>Intra-renal</u>	<u>Post-renal</u>
CHF	ATN (70%)	Obstruction @
Nausea/vomiting	Interstitial Nephritis (15-20%)	Bladder Outlet
NPO status	Glomerulonephritis (5%)	most commonly
Medications (diuretics, ACE, NSAIDS)	Vasculitis (1%)	

Initial Treatment of ARF

- Goal Directed Fluid Resuscitation
- Always place Foley Catheter
- Stop offending agents
 - NSAIDS, Contrast, ACE/ARB, potassium
- Watch labs
- Consider diuretics/Natreacor

Diuretic use in ARF

First get volume repleted
then give big enough dose of diuretic – see Below



Indications for Dialysis

- A acidosis
- E electrolyte abnormalities
- I intoxication/poisoning
- O fluid overload
- U uremia symptoms/complications

Choice of Dialysis Modality

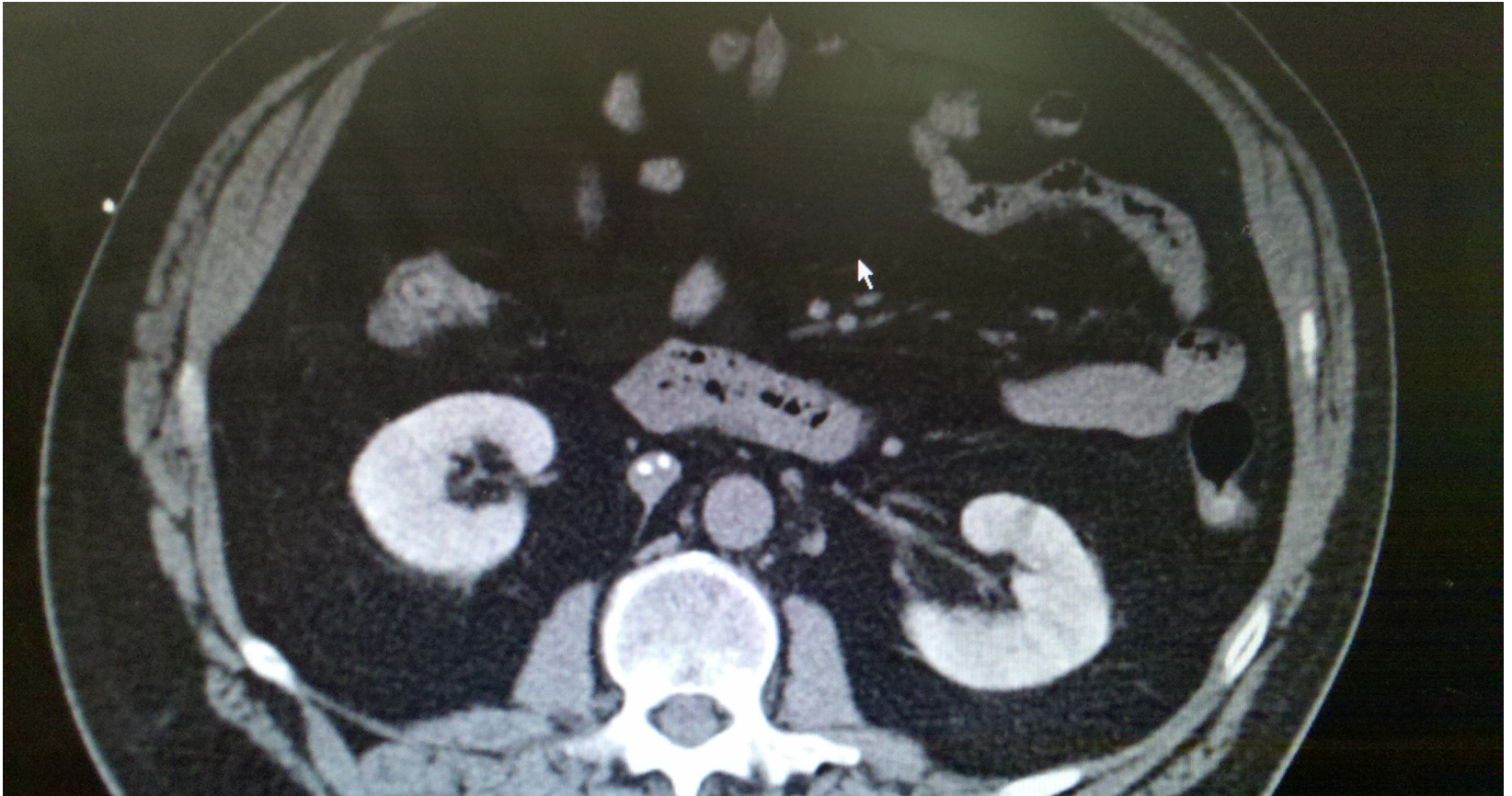
- Standard Hemodialysis - The gold standard, able to clear the most toxins quickest, requires stable patient
- Acute Peritoneal Dialysis - good for fluid and uremic waste product removal, avoids need for vascular access. Requires a closed abdomen, not good for poisonings
- CVVHD - useful for unstable/hypotensive patients.

ARF Case:

Basic 2: 63 y.o. male admitted with persistent nausea and vomiting, 2 weeks after cardiac cath for chest pain. Creatinine pre-cath was 1.8, no new medications given. Has history of diabetes mellitus and urinalysis shows proteinuria 3+. Your next test would be:

- a. Upper endoscopy
- b. CT scan of abdomen
- c. Basic metabolic profile (lytes BUN, Creat)
- d. Renal ultrasound .

CT abdomen



Risk Factors for Contrast Nephropathy

- Age over 60
- Diabetes
- Pre-Renal States
 - CHF
 - NSAIDS, ACE Inhibitors, Diuretics
- Proteinuria Includes, but not limited to Myeloma.
- Pre-existing Renal Disease

Etiology of Contrast induced AKI

Two phases of injury:

- Immediate phase:
 - Contrast load (similar to Gentamicin or Amphotericin) causes intense renal vasoconstriction with immediate oliguria
 - Fluid shifts into vascular space, so patients can go into flash pulmonary edema
 - Can be treated with dialysis
 - Prevented by giving any sodium containing fluid – bicarb is not magical

Etiology of Contrast induced AKI

Two phases of injury:

- Delayed/ secondary phase
 - Occurs at the time of the contrast infusion, but creatinine starts climbing 3-7 days after the contrast exposure
 - Due to direct tubular toxicity of the contrast (or gent/ Amphotericin)
 - Due to reactive oxygen radicals
 - Prevented by mucomyst

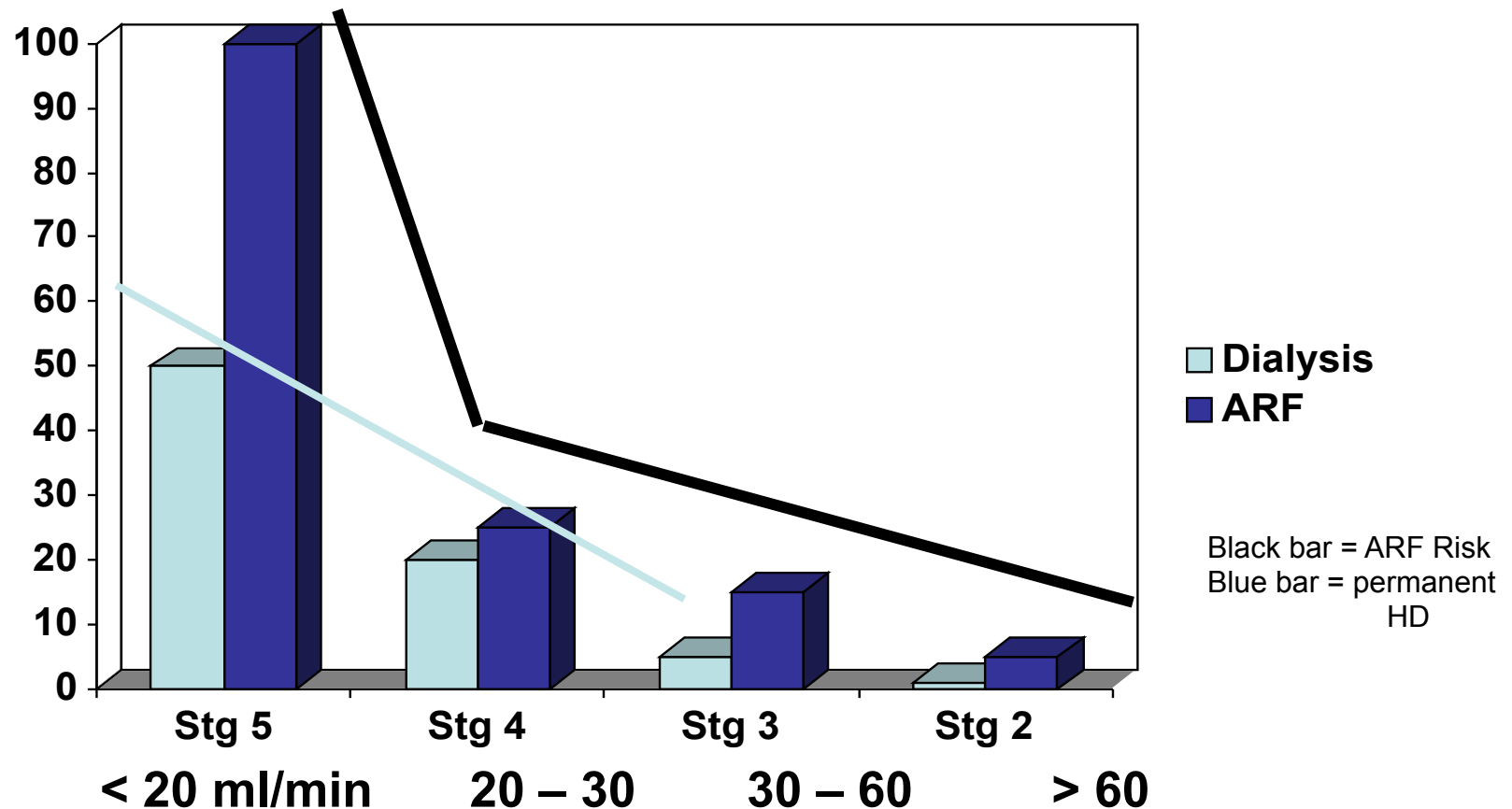
Etiology of Contrast induced AKI

Two phases of injury:

- Delayed/ secondary phase
 - Prevented by mucomyst
 - Mucomyst provides sulfhydryl groups to the Pentose Phosphate shunt, which makes NADP and other free oxygen scavengers
 - PPS runs concurrently with the Krebs cycle, which is producing ATP and a lot of free oxygen radicals.

Risk of CN By Stage of CKD

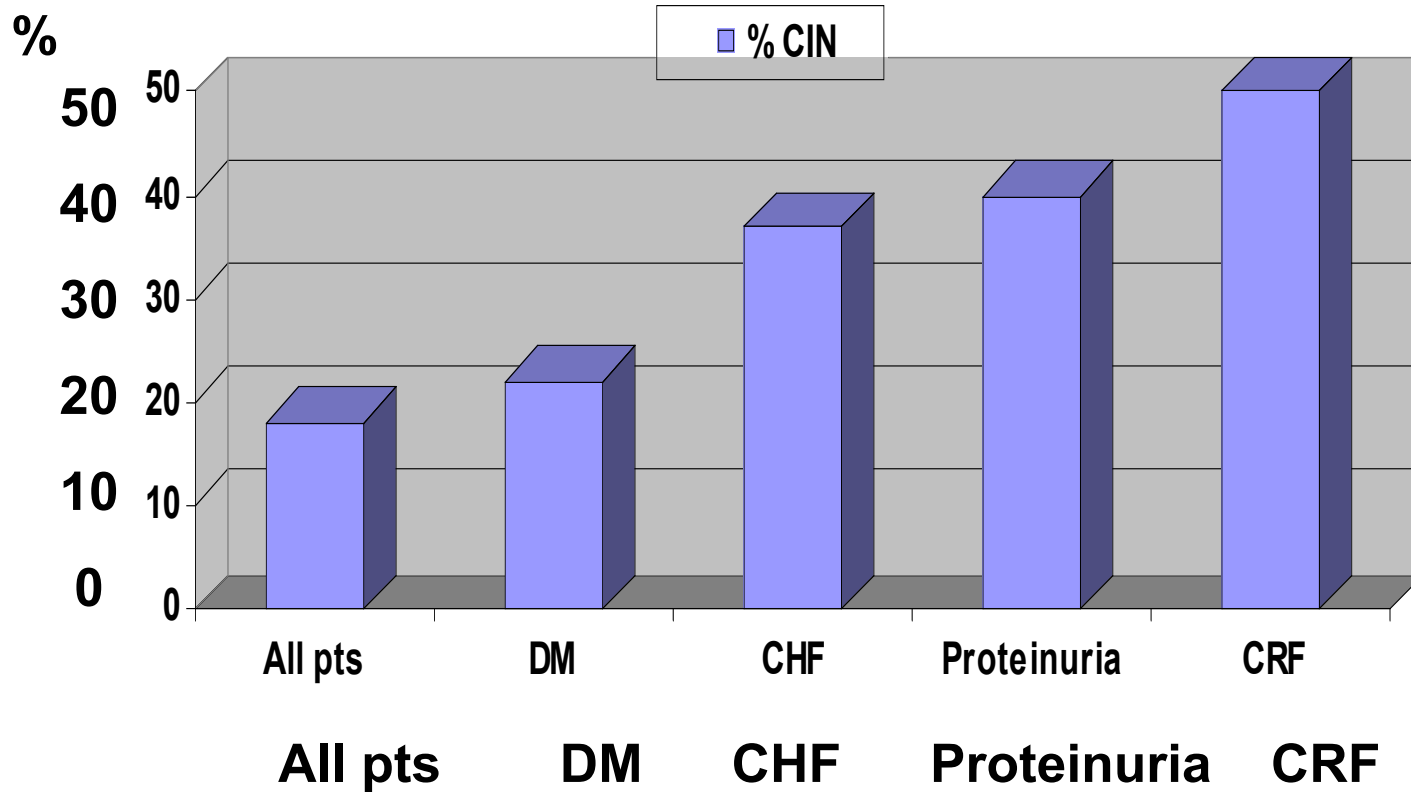
The Kaufhold Nomogram, 2003



Incidence of CN

- Nationally 4%
- GVH 2005 18%
- GVH 2006 5
- DHH 4%

Contrast Nephropathy at GVH 2005

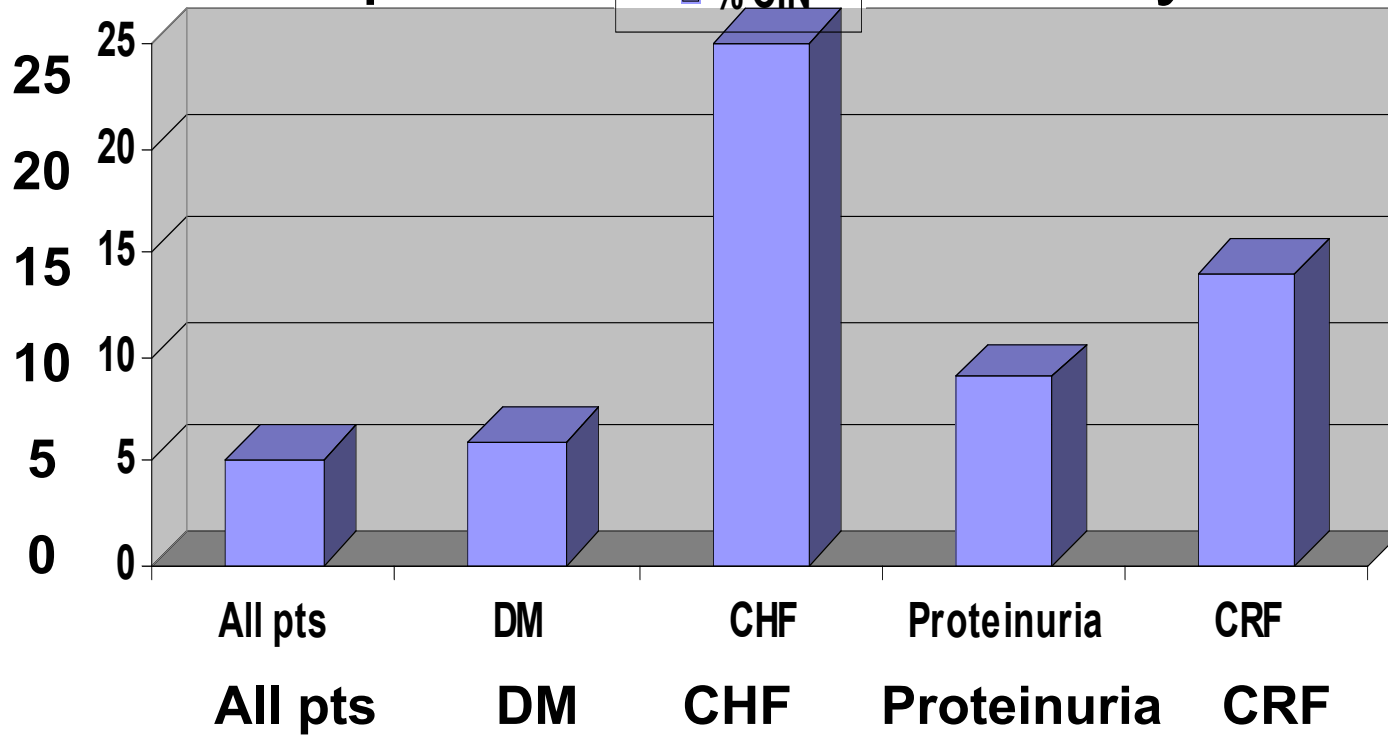


Policy / Recommendations

- Stop ACE/ ARB, NSAIDs, Diuretics day before procedure
- IVF for everyone
 - NS for low risk pts
 - Bicarb for high risk pts?
- Urinalysis for all pts/ calculate Creat Clear for all pts.
 - Proteinuria or creat clear < 40 considered High risk.
- Mucomyst for High risk pts
- Limit volume of contrast in High Risk Pts.
- Consider Nephrology consult if considering Mannitol, Corlebam, or identified as high risk.

Contrast Nephropathy GVH 2006

% • After Implementation of Policy



Staging for Acute renal Failure

- RIFLE criteria
- ADQI stages 1,2 ,3 correspond to RIF of the RIFLE criteria.

Acute Dialysis Quality Initiative

- RIFLE Criteria Helps risk stratify patients with acute renal failure.
- Increased mortality seen with increases in creatinine of 0.3 to 0.5 mg/dl (70 % increase for all pts, 300 % increase in cardiac surgery pts)

RIFLE criteria

- **Risk** low uop for 6 hours, creat up 1.5 to 2 times baseline
- **Injury** creat up 2 to 3 times baseline, low uop for 12 hours
- **Failure** Creat up > 3 times baseline or over 4, anuria
- **Loss of Function** Dialysis requiring for > 4 weeks
- **ESRD** Dialysis requiring for > 3 months

RIFLE estimate of Mortality

• Two studies	Uchino	Hoste
• No renal failure	4.4 %	5.5
• Risk	15%	8.8
• Injury	29%	11.4
• Failure	53.9%	26%
• Loss of Function		
• ESRD		

Crit Care Med 2006; 34:1913-7, Hoste CCM 2006; 10:R73

RIFLE criteria

- When markers of severity of illness are looked at *excluding* renal data, no difference in groups is seen.

New markers for ARF

- Creatinine is not very sensitive
- Cystatin C identifies ARF 1.5 days earlier than creatinine
 - KI 2004; 60:1115-1122
- KIM-1 – an adhesion molecule
- NGAL – another adhesion molecule
 - Shows up in urine and blood after tubular injury

New markers for ARF

- Insulin like growth Factor 7 in urine
- Tissue inhibitor of metalloproteinases also in urine
- Can rapidly identify patients at risk for ARF in 76-92% of cases
- False positive in half of patients in the ICU who do not develop ARF
- Offered by NephroCheck
 - ACP Hospitalist, Nov 2014, pg 45

Agents to Treat ARF

- Lasix still improves urine output, but may worsen mortality
 - Intensive care Med. 2005; 31: 79-85, JAMA 2002;288:2547-2553
- Fenoldapam may be helpful, especially in cardiac surgery pts
 - AmJKid Dis 2005;46:26-34
- Atrial Natriuretic Peptide may reduce need for dialysis and mortality
 - Crit Care Med 2004;32:1310-5.
- Dopamine still doesn't work
 - Ann Int Med 2005;142:510-24.

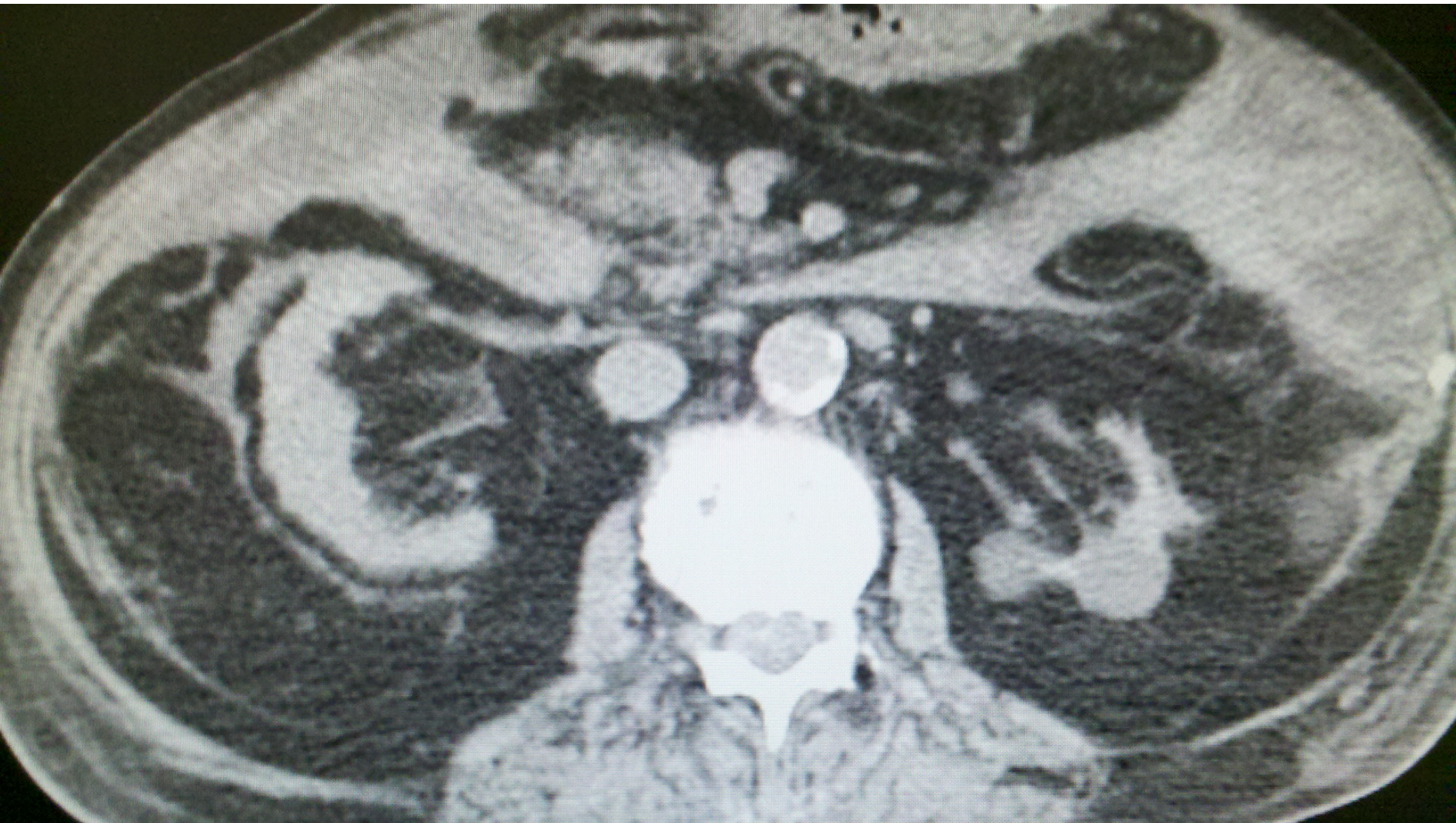
How do you differentiate ARF from CRF.

- What physical exam finding tells you the pt has Chronic Kidney Disease?
- What Would you see on renal Imaging for a pt with CKD?

Lindsey's Nails



Atrophic Kidneys on CT



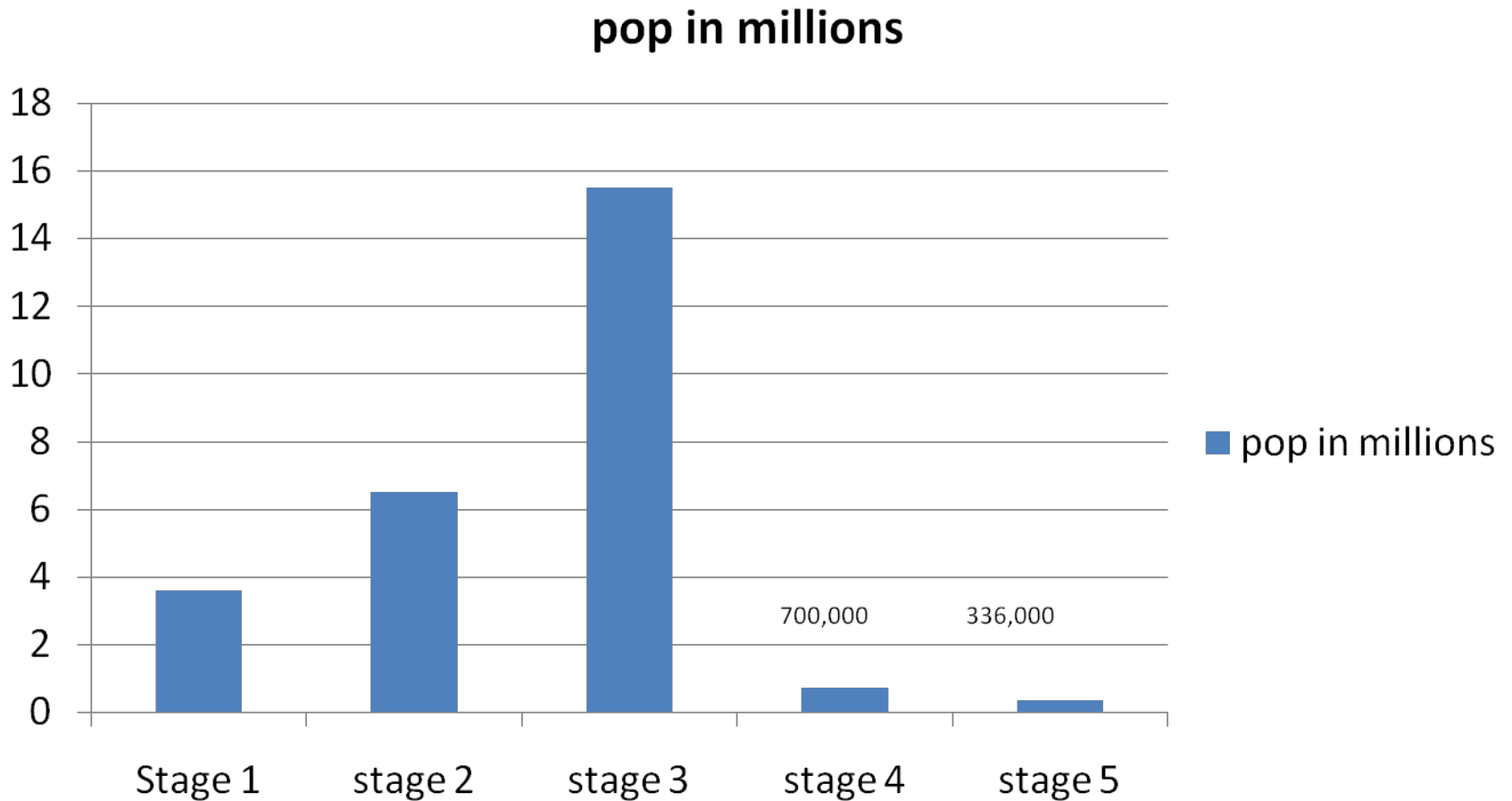
CKD prevalence in world Populations

• Country	Population	CKD est.
– China	1.298.847.624	35.336.295
– India	1.065.070.607	28.976.185
– Indonesia	238.452.952	6.487.322
– Pakistan	159.196.336	4.331.076
– Phillipines	86.241.697	2.346.281
– Vietnam	82.662.800	2.248.914
• Assumes 2.72 % incidence		

CKD Stages

- Stage 1. Normal function with known dz
- Stage 2. GFR 60-80
- Stage 3. GFR 30-60
- Stage 4. GFR 15-30.
- Stage 5. GFR less than 15.
- Stage 6. ESRD on dialysis.

US Population with CKD

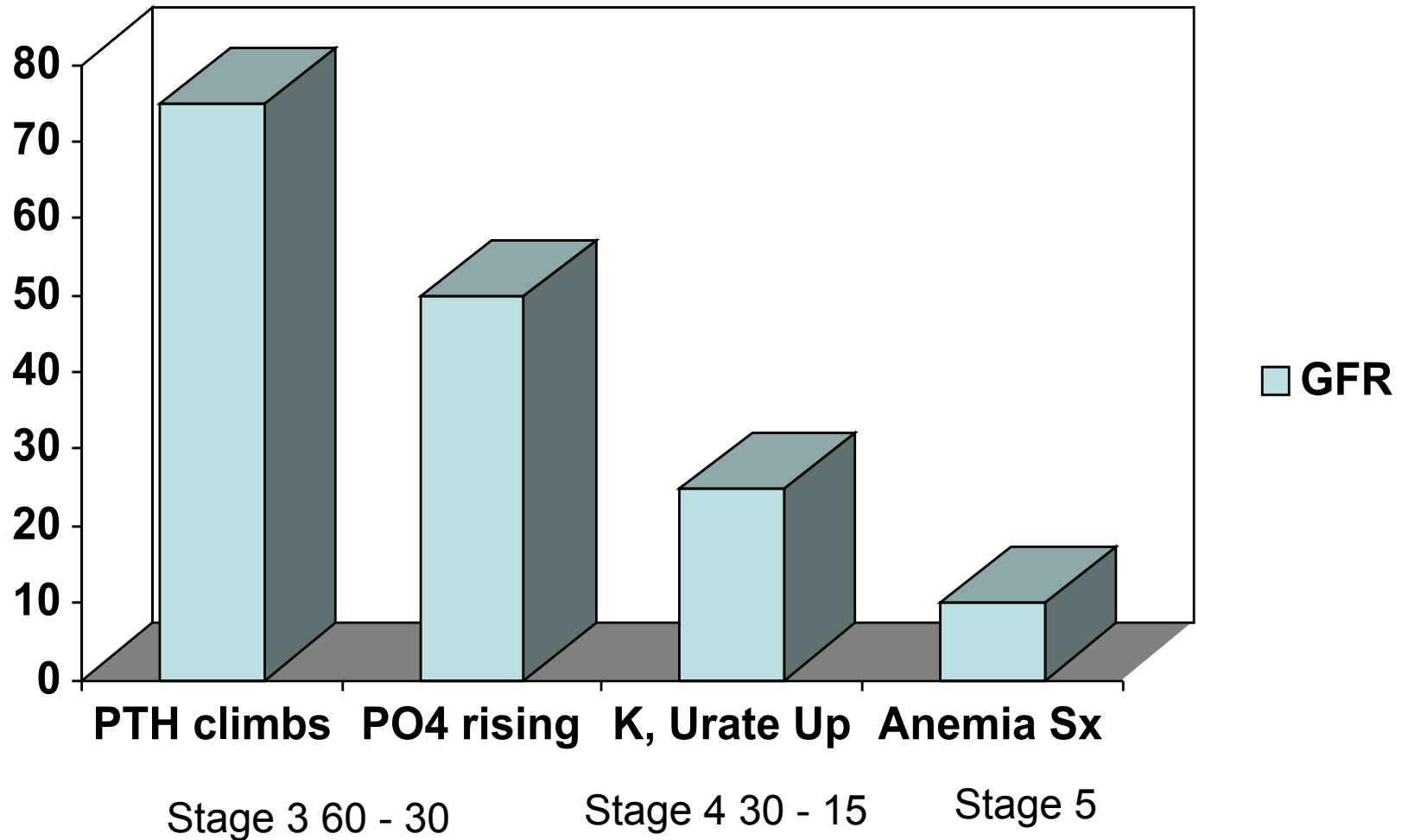


Coresh, Selvin, Stevens. Prevalence of CKD in the US. JAMA.2007;298(17)2038.

US Population with CKD

- Most people will age into Stage 3, and do not have progressive renal disease.
- A subgroup of people do have a progressive kidney disease, and these should be seeing a Nephrologist.
- Some authors assign a Stage 3a and 3b with 3b being those with evidence of renal disease (proteinuria etc)

Progression of CRF



Preparation of the Patient

- Manage CRF
 - Control BP
 - Control glucose
 - Careful with oral agents!
 - Prevent Hyper PTH
 - Vit D
 - Calcium acetate
 - Phosphate binder
 - Diet Education

Preparation of the Patient

Most of this will be in Stage 4

- Manage Fluids
- Dialysis education
- Access Placement
- Prevent anemia
- Prevent Malnutrition
- Start ACE?
- metolazone
- NKF program
- AV fistula, PD cath
- Epogen, Iron
- This can get tricky
- Stop ACE?

Diuretic use in CKD

- Lasix dosing:
 - House of God : $\text{BUN} + \text{Age} = \text{lasix dose}$
 - Creatinine $\times 40 \text{ mg} = \text{lasix dose}$
 - Creatinine = Bumex dose in mg
 - Maximum dose of lasix is about 400 mg/day
 - For refractory patients
 - we use drip rates of 20-40 mg Lasix /hour (= close to 1000 mg/day)
 - Bumex drip rate 0.5 to 1 mg bumex/hour

Diuretic use in CKD

- If lasix /loop diuretic is not enough:
 - Add a long acting diuretic based on pts potassium:
 - Potassium normal or high: Metolazone
 - Potassium low or needs a lot of potassium supplement: spironolactone
 - Do you Need to give metolazone 30 min prior to the loop diuretic?

Diuretic use in CKD

- Need to give metolazone 30 min prior to the loop diuretic? --- MYTH



lasix Lasix Lasix

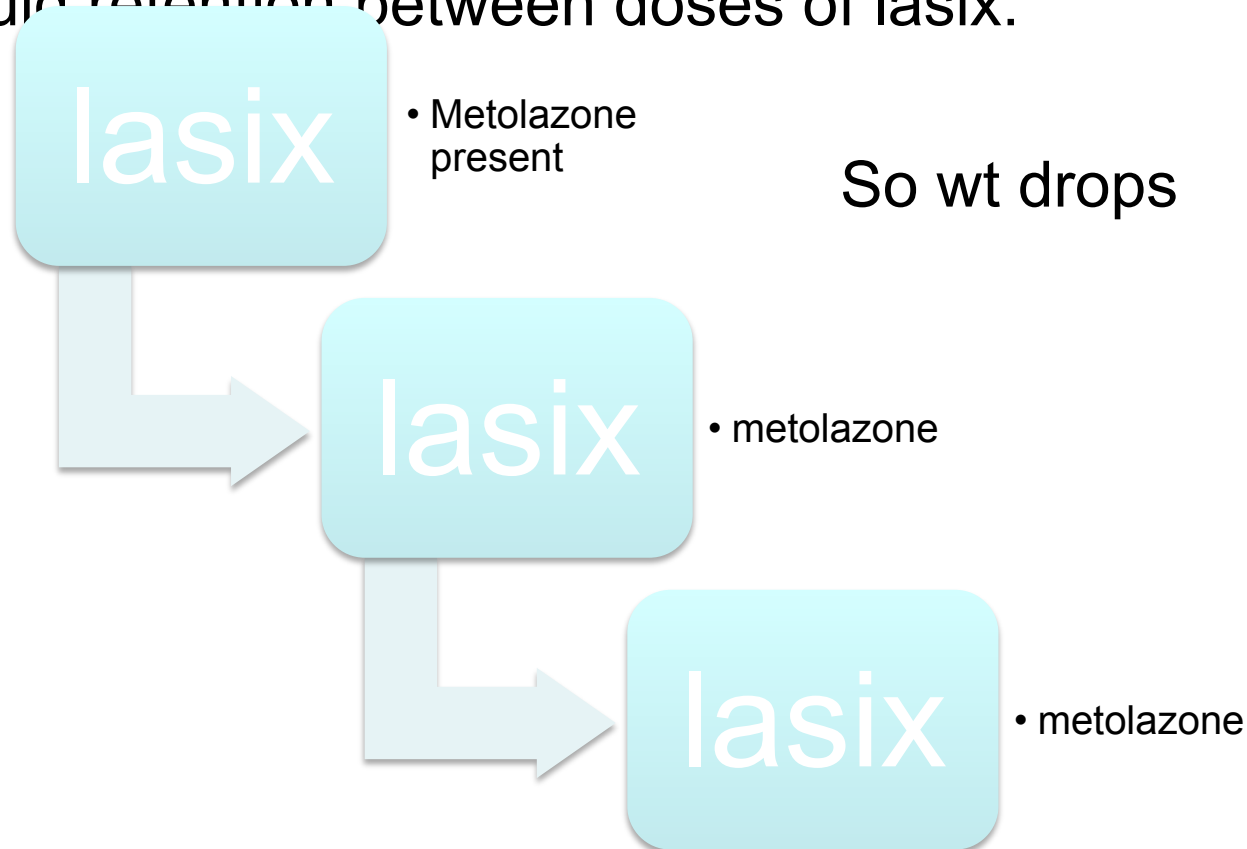
Metolazone $T_{1/2}$ = 72 hours

Spironolactone half-life: 16 hrs*

Weight will vary around a mean

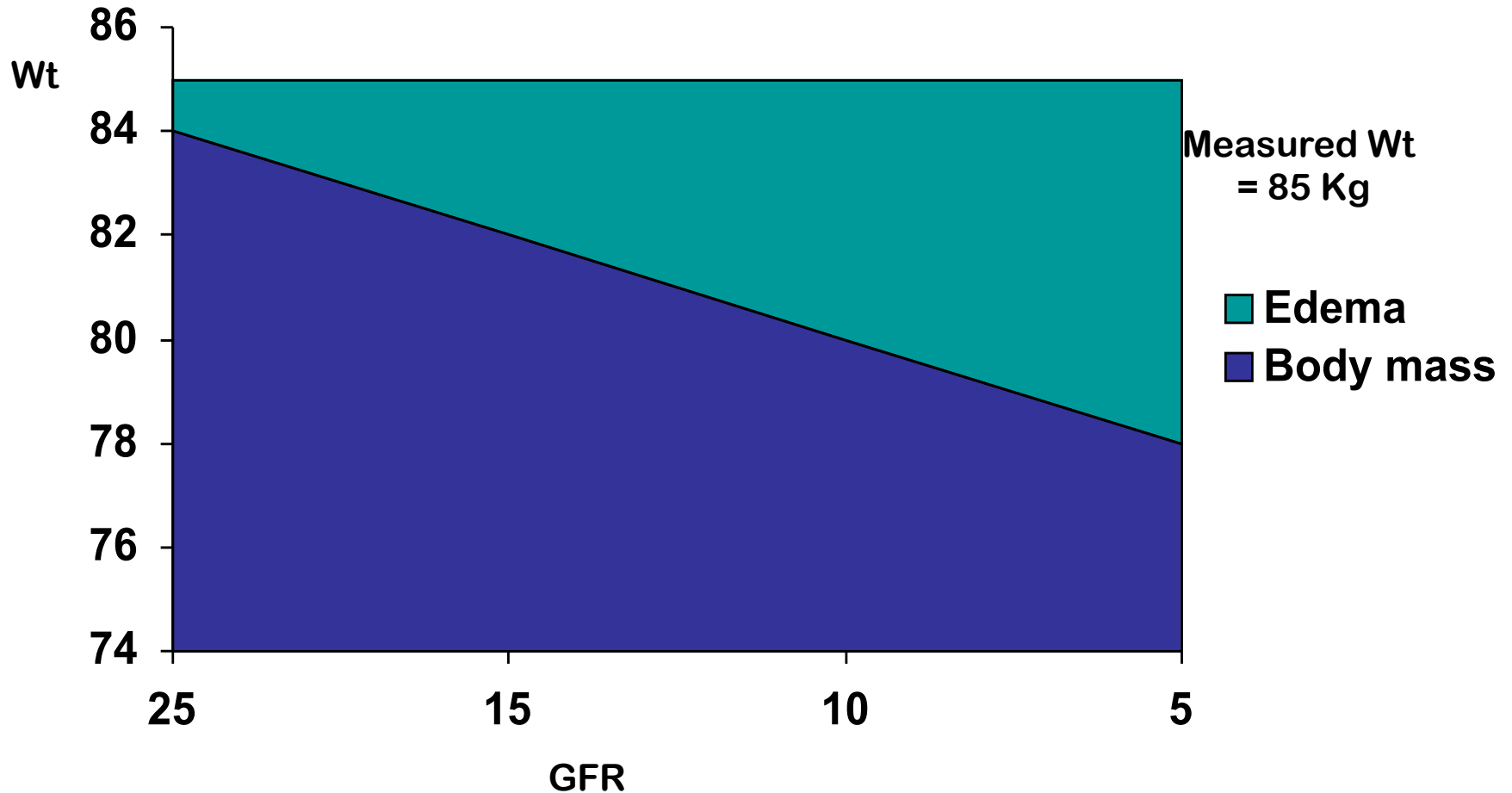
Actual mechanism for Metolazone – loop combo

- The long acting agents prevent aldosterone mediated fluid retention between doses of lasix:



Transition to End Stage

Effect of Malnutrition

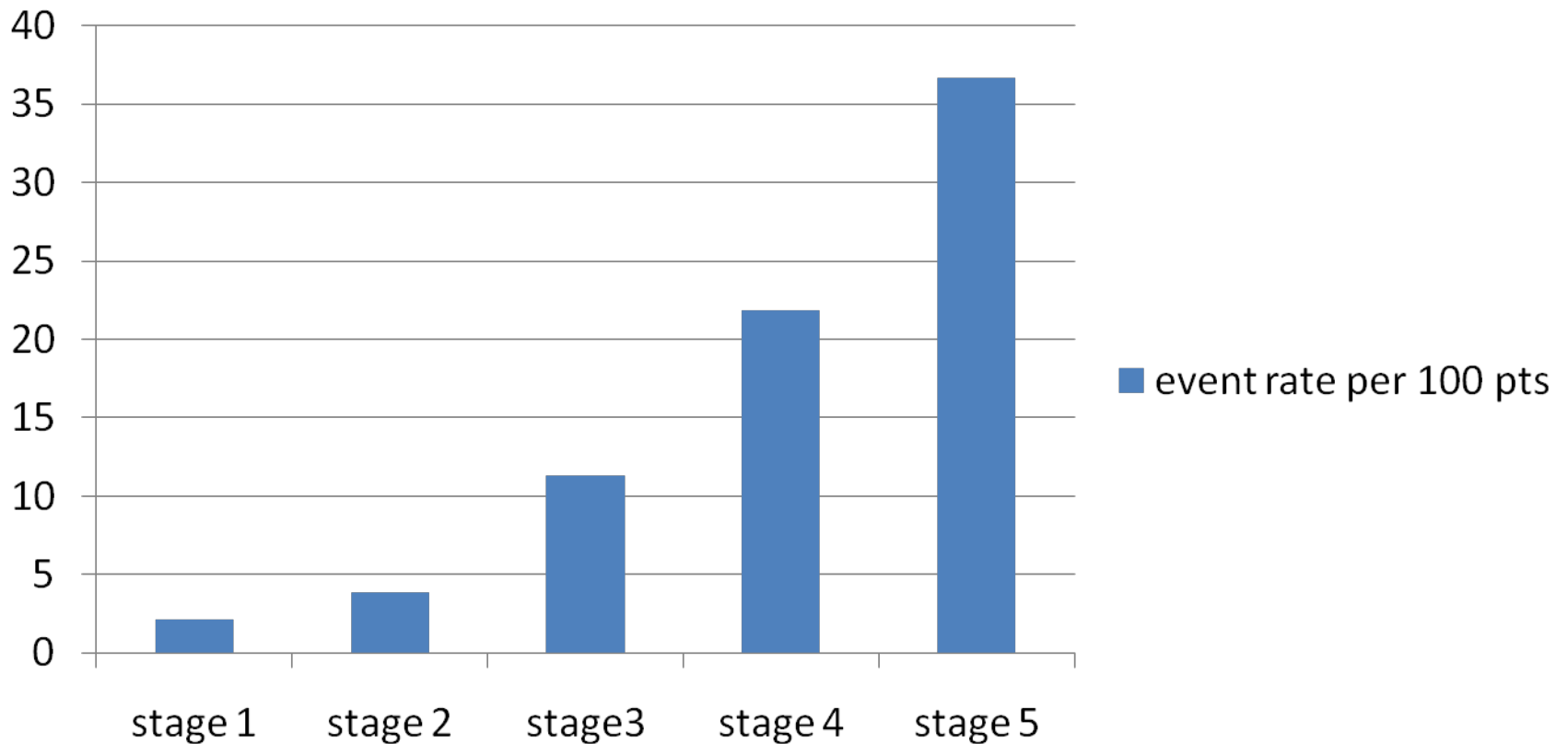


Relative Contraindications to starting dialysis

- Alzheimer' s disease
- Multi-infarct Dementia
- Hepatorenal syndrome
- Advanced cirrhosis with encephalopathy
- Advanced malignancy
- HIV with dementia

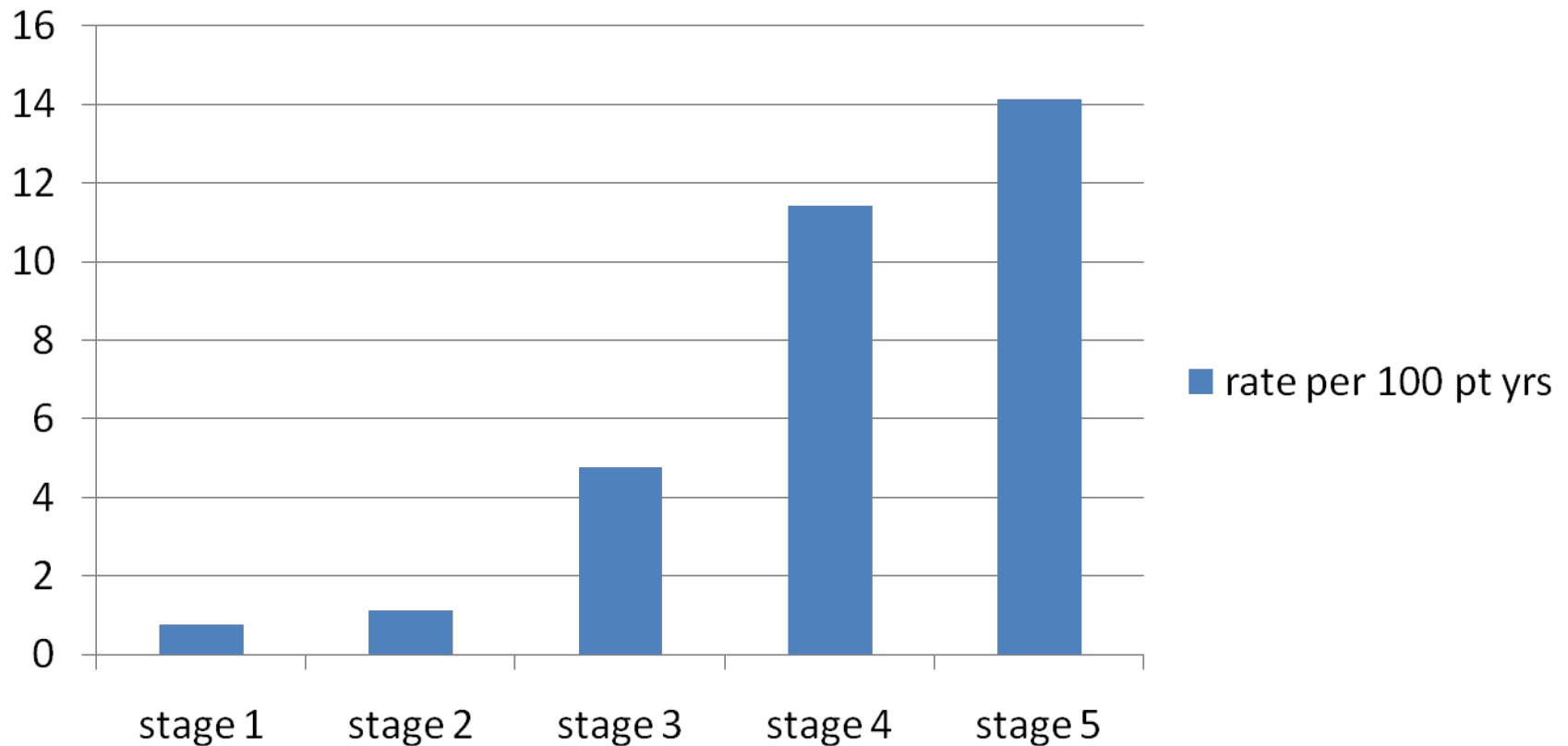
Cardiovascular events by Stage of CKD

event rate per 100 pts



All Cause Mortality By Stage of CKD

rate per 100 pt yrs



Causes of Outpatient Mortality

- Cardiovascular events
- GI bleed
- Infection

Inpatient Mortality

- Sepsis/Infection
- Cardiovascular events
- GI bleed

Cardiovascular Risk of Patients with CKD

- Treat them as if they have already had their first MI.
- Should be on B-Blocker, ASA, Statin, and ACE or ARB.
- May need to stop the ACE/ARB as renal function declines
- Think about restarting it once they are on dialysis.
- Be careful about writing “no ACE/ARB or Contrast” in these pts.

Reminders

- When you evaluate a patient keep in mind that CKD and HD patients are different
- These patients need the same workup for the same complaints
- Your differential will be the same
- Your treatment may be modified

Meds to Think about/ adjust or avoid

- Demerol – avoid below GFR of 30
- Morphine – Dose adjust
- NSAID' s – avoid below GFR of 30 and try to limit in patients with progressive disease
- ACEI / ARBS – stop when potassium or creatinine start rising too much
- Glucophage – stop below GFR of 40.
- Antibiotics – dose adjust

Meds to Avoid/Think About

- Contrast- IV contrast can be given in dialysis patients
- Keep in mind that the osmotic effects of contrast can shift fluid into the intravascular space and cause pulmonary edema
- MRI contrast (Gadolinium etc) should be avoided over creat of 2.0 or GFR less than 40 ml/min

Advances in Artificial Kidneys

- Membraneless artificial kidney
 - Uses fluid layer in microtubule for solute exchange
 - Worn on arm, connected to avf continuously
 - The fluid layer collects wastes and is exchanged periodically
 - Infoscitex Inc and Columbia University
 - Reach market in 2015?

Wearable Artificial Kidney

- Miniaturized dialysis machine worn around waist. Wt 5 lbs.
- Utilizes a unique battery powered pump for blood and dialysate
- Sorbent cartridge based dialysate
- Already proven for SCUF in CHF pts.
- UCLA Victor Gura, MD

Wearable artificial Kidney



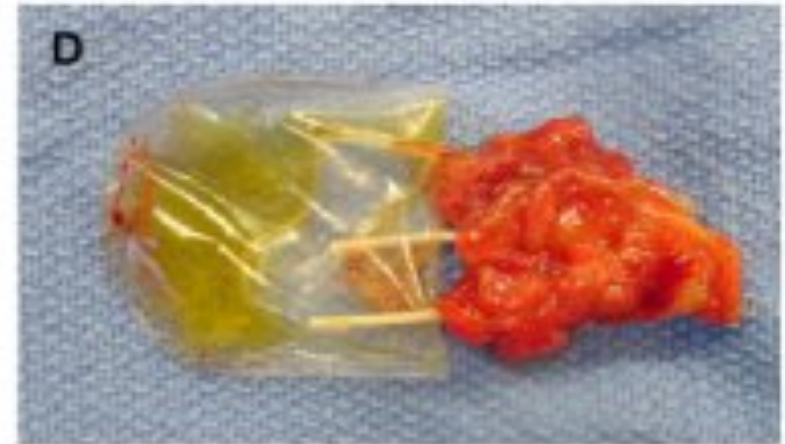
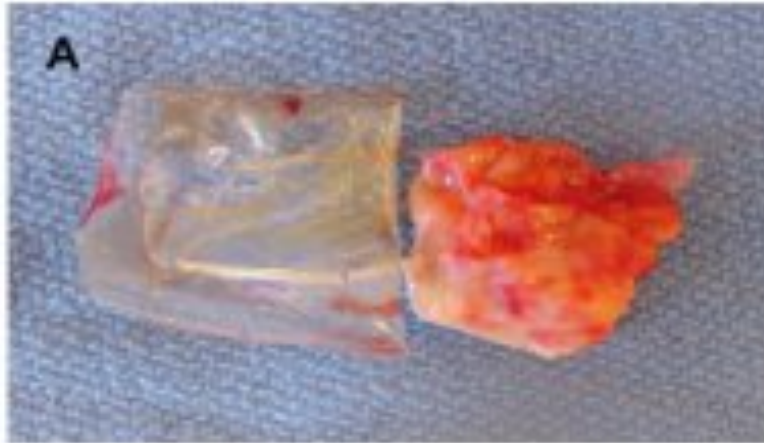
Human Nephron Filter

- Nanomembrane technology
- May be able to tailor dialysis
- Would lend itself to wearable, continuous modalities
- Philtre, Alan Nissenson, MD

Bioartificial Kidney

- Uses cloned renal tubular cells from unusable donor kidneys
- Cells line capillary tubules in a kidney similar to conventional dialysis kidney
- Renal Assist Device can assume endocrine and metabolic functions
- In phase II study reduced mortality in ICU ARF pts from 61 to 34 %.
- University of Michigan David Humes, MD

Cloning Kidney Tissue



Resources

- This lecture and other materials at
 - www.Jeffkaufhold.com/Family

Post Test Question:

Regarding CKD:

Which of the following is FALSE:

1. Pt with advanced CKD has same risk as if they have already had their first MI.
2. Should be on B-Blocker, ASA, Statin, and ACE or ARB if tolerated.
3. May need to stop the ACE/ARB as renal function declines
4. MRI contrast is safe in patients with CKD even if GFR is less than 40.