LO1/O2 AKI

a single isolated elevated sCr does NOT mean AKI

★ KDIGO definition of AKI:

TQ
- sCr ↑1.5x over 7days
- or sCr ↑0.3 mg/dL over 48 hours
- or UOP <0.5 mg/kg/hr over 6hours

Biggest risk factor = CKD

★ AKI presentation:

★ Sepsis is most common cause of AKI → know px: fever, tachy, hypotensive, lactic acidosis

★ AKI Patterns:

TQ

★ PRERENAL [BUN/sCr ≥20:1, FENa <1%] Reversible, NO parenchymal injury

TQ ?

↓EABV, renal hypoperfusion, ACE-I + NSAID ★

TX w/ fluids

★ expand intravascular space THEN replete ECF (NS or LR initially)

effarent arteriole goes to peritubular capillaries

★ INTRINSIC [BUN:sCr <20:1, usually <10:1] FENa >2%

= structural damage to parenchyma !!

- Glomeruli - glomerulonephritis ...etc
- Tubules – ATN, contrast ...etc
- Blood vessels - Atheroemboli ...etc
- Interstitium – "allergic" nephritis due to NSAIDs, abx, etc

TQ ★ Post strep GN → RBC casts (Nephritic syndrome)

★ Cholesterol emboli

★ TTP, HUS, APS, Pre-eclampsia

ATN

★ Acute Tubular Necrosis = MC AKI in hospitalized pts → ① Ischemia ② Sepsis ③ Nephrotoxins

TQ ATN → muddy brown casts

Example: Rhabdomyolysis "Heme pigment nephropathy"

★ Nephrotoxin - dipstick shows blood but ØRBCs = MYOGLOBIN

- Meth user, marathon runner, pt found down

TQ ATN ★ Tumor Lysis Syndrome - release of intracellular contents after chemo

★ uric acid crystals lead to tubular injury + Hyperkalemia → Necrosis

ATN ★ Contrast induced Nephropathy

★ via direct toxicity & vasoconstriction

★ Acute Interstitial Nephritis - inflammatory infiltrate in interstitium

★ DRUGS - NSAIDs, PPI, sulfonamides, aminoglycosides ★

TQ ★ TRIAD: ① FEVER ② RASH ③ Eosinophilia + eosinophiluria & hematuria & RBC casts

TQ @ bladder neck, Both kidneys

★ POST RENAL [BUN:sCr variable] → MC bc BPH & Kidney stones + Hydronephrosis

★ REVIEW:

CONDITION	FINDINGS
PRERENAL	TRANSPARENT HYALINE CAST ★
POSTRENAL	HYALINE CAST/PUS CELLS/HEMATURIA
ATN - sepsis, tumor lysis(?) → uric acid crystals	MUDDY BROWN GRANULAR/EPITHELIAL CAST
INTERSTITIAL NEPHRITIS rash, eosinophilia, fever	WBCs, RBC CASTS, NON-PIGMENTED GRANULAR CAST, EOSINOPHILS,
AGN post strep!	RBC CASTS

INTRINSIC

★L03/04 CKD

TQ

★ CKD: GFR <60 for more than 3 mos OR normal GFR w/ structural abnormality
- horseshoe kidney
- one kidney
- PKD
- scars
- tumors

★ small ΔSCr = big ΔGFR
during AKI, sCr is rapidly changing ∴ GFR = less accurate
★ use albuminuria & GFR to assess for CKD

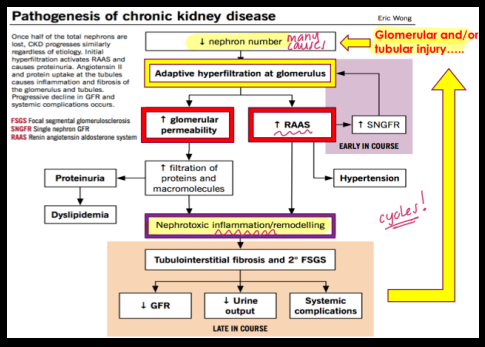
- Mr Smith has stage **G2A2 CKD** attributed to HTN/DM presents today.....
- Ms Smith has stage **G4A3 CKD** from biopsy proven glomerular dz from SLE
- Mr Jones has stage **G1A1 CKD** based on being a kidney donor for transplant
- Ms Jones has stage **G2A1 CKD** from bilateral ADPKD
- Mr Doe has stage **G1A2 CKD** based on history of PSGN
- Ms Doe has stage **G5A3 CKD** based on HTN/DM and medication renal injury from vancomycin(aminoglycoside...) she is not on dialysis yet and has no symptoms of uremia(and has complications of anemia and metabolic acidosis and hyperkalemia), she is not a transplant candidate and has had a AV shunt placed in her LUE, she presents today.....

TQ
any of these w/ normal GFR & <30 mg albuminuria = G1A1
pt w/
- one kidney
- tumor
- horseshoe kidney
- stones
- scars / PKD

CKD with G1A1?
Fig 52.2 pg 480

GFR Stages				Albuminuria categories: A1 Normal to mildly increased <30 mg/g <3 mg/mmol	A2 Moderately increased 30-299 mg/g 3-29 mg/mmol	A3 Severely increased ≥300 mg/g ≥30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

TQ
★ CKD Etiology: HTN & DMII → causes Hyperfiltration → damages endothelium = ↓GFR
★ glomerulosclerosis / rapidly progressive glomerulonephritis
★ worsened w/ NSAIDs



TQ
CYCLE!
★ AKI predisposes you to CKD, which ↓ nephron #, which ↑ chance of AKI, worsening CKD

→ control underlying dz - HTN & DM to limit progression

★ #1 cause of death in CKD pts = Cardiovascular complications (10-200 fold)
→ HTN
→ ECV expansion = fluid overload
→ Anemia
→ LV Hypertrophy ★
→ vascular calcifications → PAD/CAD, cholesterol emboli → MI

TQ
★ intimal = atherosclerosis = occlusion
★ medial = arteriolosclerosis = stiffening

★ CKD Mineral Bone Dz

↓GFR → ★ phosphate retention begins in G3 → ↑PO_4^-, ↑FGF23
Kidney Damage → ↓Vit. D
↓Ca^{2+}
↑PTH → Osteitis fibrosis cystica (↑PTH & ↑AlkPhos) from high bone T/D
SECONDARY
Pt in G4/G5 = get PTH levels

TQ

HYPERPARATHYROIDISM (TQ)

★ Anemia of CKD: starts ~G3 bc ① kidneys make 90% EPO ② CKD ↓ lifespan of RBCs
EPO is made in peritubular interstitial cells ★★ (TQ)

★ Metabolic Acidosis & Hyperkalemia
★ ↓ nephron # = ↓ acid handing & ↓ K^+ excretion
★ Hyporenin / Hypoaldosterone state
(TQ) → ESRF (G5) = HAGMA
→ CKD (RTA or early renal dz) = NAGMA
GIVE THEM $NaHCO_3$ ★★
PEAKED T-WAVES

★ LO6 Renal Dz in special populations
★ Mother's prenatal hx = super important ★
★ nephron # determined by birth weight ★
★ Neonates/infants unable to concentrate urine → easily volume depleted = PRErenal AKI risk
★ Peds CKD
Px: failure to thrive / not meeting milestones
- GFR < 60 3 months
or
- structural abnormality (CAKUT)
→ Calculate GFR using
★★ Modified Schwartz Formula ★★ (TQ)
→ uses sCr & height
ø albuminuria
→ staging only in pts >2 yrs

★ Pregnancy: ↑GFR ↓sCr + some proteinuria = normal (<300)
→ so the only way to measure kidney f(x) / detect AKI (TQ) = 24HR Cr Clearance
→ pre-eclampsia = most common etiology of AKI in pregnancy
→ High Risk Factors:
Hx of HTN dz in pregnancy
CKD
Autoimmune dz
DM
Chronic HTN
★ HTN after 20WK w/ significant proteinuria (TQ)
★ glomerular endotheliosis
★ subsides postpartum

APOL1 in AA → FSGS
★ Sickle Cell Nephropathy: glomerular hyperfiltration → FSGS w/ vasa recta occlusion ★★
★ manifests as impaired ability to concentrate urine → prone to hypovolemia
★ risk for papillary necrosis & renal medullary carcinoma

★ LO7 cystic Kidney Disease

ADPKD - in adults, cysts over kidneys & liver, maybe intracranial aneurysms
2 genotypes:
PKD1 chromosome 16 PC1
PKD2 chromosome 4 PC2
] ciliopathies ★
get a good family history

ARPKD - in children, maybe detected in utero (oligohydramnios)
→ dilation of CD
genotype: PKHD1 gene on chromosome 6 encodes for fibrocystin - ciliopathy ★

(TQ) Medullary Sponge Kidney - prone to STONES ★, MCKD1 or 2 genes (A.D.)

Medullary Cystic Dz – prone to hyperuricemia & gout – rare auto. dom. more likely

★ L08/09 Renal Manifestations of Systemic Dz

★ Hepatorenal syndrome:

★ cirrhotic pt w/ portal HTN release NO ★★
→ Hypoperfusion of kidneys

★ Diabetic Nephropathy: DM 1 > 2

★ persistent albuminuria >300mg/day
★ pathogenesis: ① ↑GFR @ first ★ Hyperfiltration
② ↓GFR w/ microalb.
③ ↓↓GFR w/ proteinuria
④ ESRD
TQ
★ Extreme mesangial expansion → Kimmelstein Wilson nodules ★
★ tx: control sugar + ACE-I/ARB

★ HIV Associated Nephropathy

★ FSGS + acute tubular necrosis
★ linked to APOL1 gene in African Americans TQ
★ px: PROTEINURIA + ↓GFR ★★
BUT Ø Edema & Ø HTN
★ tx: HAART + ACE/ARB
★ acute renal failure caused by:
★ Hypovolemia
★ ATN
★ Med toxicity!

Table 1. Classification of CRS Based on the Consensus Conference of the Acute Dialysis Quality Initiative

Phenotype	Nomenclature	Description	Clinical Examples
Type 1 CRS	Acute CRS	HF resulting in AKI	ACS resulting in cardiogenic shock and AKI, AHF resulting in AKI
Type 2 CRS	Chronic CRS	Chronic HF resulting in CKD	Chronic HF
Type 3 CRS	Acute renocardiac syndrome	AKI resulting in AHF	HF in the setting of AKI from volume overload, inflammatory surge, and metabolic disturbances in uremia
Type 4 CRS	Chronic renocardiac syndrome	CKD resulting in chronic HF	LVH and HF from CKD-associated cardiomyopathy
Type 5 CRS	Secondary CRS	Systemic process resulting in HF and kidney failure	Amyloidosis, sepsis, cirrhosis

ACS indicates acute coronary syndrome; AHF, acute heart failure; AKI, acute kidney injury; CKD, chronic kidney disease; CRS, cardiorenal syndrome; HF, heart failure; and LVH, left ventricular hypertrophy.

Table 28.1 Important Clinical Features of Viral Nephropathies

	HIV	HCV	HBV
Major Risk Groups	Blacks, individuals of African ancestry	Adults with risk factors for chronic HCV infection	Children of HBV endemic areas
Presentation	Proteinuria, nephrotic syndrome CKD with rapid progression Large, echogenic kidneys CD4 count <200 cells/μL	↓ Hematuria ↓ Proteinuria Hypocomplementemia Palpable purpura Systemic vasculitis	Proteinuria Spontaneous remission in childre
Primary Renal Pathology	Collapsing FSGS Microcystic dilation of tubules Interstitial inflammation	Membranoproliferative glomerulonephritis MPGN	Membranous nephropathy
Pathogenesis	Direct HIV infection of the kidney Host genetic factors	Direct HCV toxicity Cryoglobulinemia	Antigen-antibody complex deposition Vasculitis PAN
Therapy	cART ACE-inhibitors and ARBs tx underlying cause	Antiviral therapy Rituximab Cyclophosphamide Plasmapheresis in severe cases	Antiviral therapy

ACE, Angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; cART, combination antiretroviral therapy; CKD, chronic kidney disease; FSGS, focal segmental glomerulosclerosis; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus

★ Hep C (RNA virus) → Membranoproliferative GN ★ w/ cryoglobulinemia & palpable purpura
ESRD → dialysis/renal transplant
px ★ HTN & oliguric AKI, ↑ALT/AST
★ @ risk populations = NEEDLES
tx ★ antivirals PLUS immunosuppressives

★ Hep B → membranous nephropathy
★ insidious onset, Nephrotic syndrome, ★ HTN or normal BP, EDEMA ★, Ø RBC casts TQ?
★ proteinuria & ↑ALT/AST
★ PAN → vasculitis = fever weight loss, ↑CRP (also happens in Hep C.)
tx ★ immunosuppressives NOT helpful, give them antivirals
sex workers?

★ Sickle cell Dz → Nutcracker in late childhood from LEFT KIDNEY, SMA presses on vein
★ avoid nephrotoxic agents, give hydroxyurea, refer to Nephrology @ G3

★ Sickle Cell Trait → Renal Medullary Carcinoma ★ Dx w/ CT + contrast TQ
★★ = young black male w/ back pain & fatigue & hematuria

★ Lupus

Amyloidosis

Acute Uncomplicated Cystitis

- Nitrofurantoin (low risk of collateral damage)
- Trimethoprim/Sulfamethoxazole (if local resistance rates do not exceed 20%)
- Fosfomycin (low risk of collateral damage) cell wall
- Pivmecillinam (NOT IN THE US)(extended spectrum penicillin)
- Fluoroquinolones (collateral damage)
- Beta-lactams generally have inferior efficacy and more adverse effects than others and should be used with caution for uncomplicated cystitis
  - Amoxicillin or ampicillin should not be used for empiric treatment

TMP/SMX = G6PD deficiency

Infections in Men

- Uncomplicated Cystitis: data is extrapolated from women (male studies limited)
  - TMP/SMX or Fluoroquinolones ! 2 options !
  - DO NOT USE beta-lactams or nitrofurantoin (fosfomycin has limited data) they do not achieve reliable tissue concentrations and less effective for occult prostatitis
- Uncomplicated Pyelonephritis: (same as women)

Complicated Cystitis

- Treatment:
  - Fluoroquinolones (not moxifloxacin... why?) — No urine concentration Ø pseudomonas
    - Achieve high levels in the urine, broad spectrum and cover most organisms
  - AVOID: nitrofurantoin and fosfomycin (high prevalence of resistance)
  - SMX/TMP: depends on local data used in diagnostic uncertainty regarding cystitis vs early pyelonephritis
  - Ceftriaxone
  - Carbapenem (Especially if ESBL producing)
  - Aminoglycoside
- Mild cystitis due to ESBL-producing E. coli and low suspicion for pyelonephritis: nitrofurantoin and fosfomycin are ok but data is limited
- Gram + cocci (suggests enterococcal UTI): ampicillin or amoxicillin

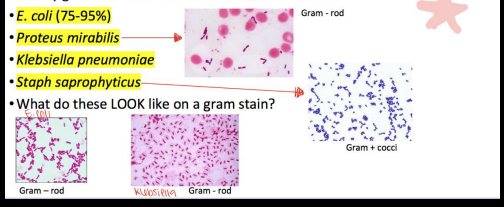
→ complicated = MEN & WOMEN

- Flouroquinolones
- Aminoglycosides
- Carbapenems
- Ceftriaxone
- Trimethoprim
- Sulfamethoxazole

Ø nitrofurantoin
Ø fosfomycin

Acute **Uncomplicated** Cystitis Organisms

- Same in men and women
- Mostly gram – from normal flora of intestinal tract
- *E. coli* (75-95%)
- *Proteus mirabilis*
- *Klebsiella pneumoniae*
- *Staph saprophyticus*
- What do these LOOK like on a gram stain?



Acute Pyelonephritis Treatment

- Fluroquinolones
- Trimethoprim/Sulfamethoxazole (if pathogen is known to be susceptible)
  - If susceptibility is unknown, consider 1 does of long acting antimicrobial (like ceftriaxone) or 24 hr dose of aminoglycoside
- Women requiring hospitalization should be initially treated with IV regimen (choice based on local resistance data)
  - Fluoroquinolone OR
  - Aminoglycoside (with or without ampicillin) OR — gram+ → s. saprophyticus
  - Cephalosporin (with or without an aminoglycoside) OR — pseudomonas
  - Extended spectrum penicillin (with or without aminoglycoside) OR
  - Carbapenem — atonic

Pyelonephritis:
TMP/SMX or FQ

IV: FQ
Aminoglycoside ± amp
Cephalosporin ± aminoglycoside
Carbapenem
Extended BL ± aminoglycoside

In pregnant women

- Acute Cystitis
  - Beta-lactams (cefpodoxime, amoxicillin/clavulanate), nitrofurantoin (during 2nd or 3rd trimester), fosfomycin
- Recurrent Cystitis
  - Prophylaxis (can be postcoitally if suspected cause)
  - Nitrofurantoin or cephalexin
- Acute Pyelonephritis
  - Broad spectrum beta-lactams for empiric therapy of pyelonephritis
  - Cefazolin or ceftriaxone was shown to be equivalent to ampicillin + gentamicin
  - Meropenem, ertapenem, doripenem
  - Possibly TMP/SMX if in 2nd trimester (remember its effects on folic acid!!! (antagonist)

NUTSHELL

Risk factors

- Diabetes mellitus
- Hypertension
- Acute kidney injury
- Microalbuminuria or proteinuria
- Overweight or obesity
- Smoking, alcohol, and drug abuse

Complications

- Anemia
- Mineral and bone disease
- Hypertension
- Edema
- Cardiovascular disease

Pharmacologic Drugs

- **ACE inhibitors or ARBs:** considered first-line for strict blood pressure control
- **Vitamin D supplementation:** for prevention and treatment of secondary hyperparathyroidism
- **Erythropoietin:** can be considered to manage anemia in patients with CKD
- **Statins:** used as cholesterol lowering therapy in patients with CKD
- **Dialysis:** in patients with severe metabolic acidosis, hyperkalemia, pericarditis, intractable volume overload.