ESSENTIALS OF NEPHROLOGY:

ACUTE AND CHRONIC KIDNEY DISEASE

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Well, Mr. Osborne, it may not be kidney stones, after all.
OVERVIEW

Part 1:
ACUTE RENAL FAILURE - ACUTE KIDNEY INJURY:

- History
- Physical Exam
- Evaluation: Lab/Studies
- Treatment

45 minutes

Acute Kidney Injury (AKI)
Chronic Kidney Disease (CKD)
Complications of CKD

TODAY: The Left Kidney

The Right Kidney (come back next year!)
Part 2: CHRONIC KIDNEY DISEASE

Screening for CKD:
– Whom do you screen?
– Why do you screen?
– How do you screen?

Diagnosing CKD:
– How do you diagnose the cause of CKD?
– How do you slow the progression of CKD?
– How do you treat the effects of CKD?

AKI - IN A NUTSHELL:
3 QUESTIONS TO EVALUATE:

- Pre-renal ? are they DRY?
- Post-renal ? are they OBSTRUCTED?
- Renal ? is it the KIDNEYS?
Intrinsic renal

PRE-Renal: 60-70%

POST-Renal: 5-10%

PRE-Renal: 5-10%

POST-Renal: 30%
ACUTE KIDNEY INJURY

Case - Mr. M.

• 55 yo man, hx DM, HTN, DJD:

• 3 day h/o N/V/poor po intake/Diarrhea

• 1 day hx oliguria → anuria, confusion, pruritis

Meds: Benazepril, Hctz, Glipizide, Ibuprofen

PHYSICAL EXAMINATION:

• Vital Signs: BP 95/50, HR 125, RR 28, O2: 91% RA
• Gen: confused, tired
• HEENT: mucus membranes DRY
• Heart: tachycardic
• Lungs: tachypneic, diffuse rales
• Abdomen: no mass, NT
• Skin: excoriations, no rash/petechiae/purpura
• Prostate: normal size

Labs:

Na= 129
K= 6.0
CO2= 20
BUN= 64
Creat= 3.6 (baseline =1.2 one month ago)
Glucose= 425
INITIAL TREATMENT

- **IV STARTED** – GIVEN NS BOLUSES FOR HYPOTENSION
- **FOLEY CATHETER** INSERTED: NO URINE→ not obstructed at bladder level
- **HYPERKALEMIA**: EKG= WITHOUT ACUTE CHANGES, TREATED WITH INSULIN/GLUCOSE, CALCIUM, KAYEXALATE
- **HCTZ, ACEI, AND NSAIDS HELD**

HOSPITAL COURSE

- **OVER NEXT HOURS**: BP INCREASED, UOP IMPROVED, MENTAL STATUS CLEARED
- **BUN, CREAT DECREASED** OVER NEXT DAYS IN HOSPITAL, WITH IV FLUIDS
- **Dx**: **AKI**: PRE-RENAL AZOTEMIA, SECONDARY TO ACUTE VIRAL GASTROENTERITIS
  - (also had demand ischemia concurrently)
- **UA SENT FOR MICROSCOPY AND CX**: S.G.1.025, NO RBC, NO WBC, NO CELLULAR CASTS (HYALINE ONLY)
- **RENAL U/S** NEGATIVE FOR HYDRONEPHROSIS (obstruction)
- **KUB** NEGATIVE FOR CALCULI
**ACUTE KIDNEY INJURY (AKI)**

- **Definition**: no universal definition—generally noted by a rapid rise in Creat, BUN, +/- dec’d UOP:

  -- if the baseline Creat is < 2.5 mg/dl: AKI can be defined by an increase in serum Creatinine of at least 0.5 mg/dl, for <2 weeks

  -- Or, if the baseline Creat is > 2.5 mg/dl: AKI can be defined by an increase in serum Creatinine by >20%

**note if today’s creat is 1.0, but BASELINE is 0.38, this IS AKI!**

**Mortality is due to Complications:**

- pulmonary edema 30-50%
- cardiac (MI, arrhythmias) 30-40%
- GI (GI bleed, pancreatitis) 30%
- Infections 50-70%
- Neurologic abnormalities 30-50%
- Electrolyte disorders (hyperkalemia, metabolic acidosis, hyperuricemia, hyperphosphatemia) 50-75%

**AKI**

- can be **nonoliguric** or can be **oliguric** (oliguria=less than 400 ml urine output/day in adults or less than ½ cc/kg/hr)

- **Anuria** usually has worse prognosis (except in dehydration) and is defined as less than 100 ml/day of urine output in adults.
Evaluating for Causes of AKI:

- History
- Physical Exam
- Lab/Studies

IN A NUTSHELL:

Hx, PE, Labs are to determine:

- Pre-renal? are they DRY?
- Post-renal? are they OBSTRUCTED?
- Renal? is it the KIDNEYS?

History:

- Ask for clues to help determine CAUSE: (dry vs. obstructed vs. kidneys?)

1. “Are You Dry?”:
   - Decreased PO intake?
   - Increased fluid Losses? (N/V/D/diuretic use)
   - Other reasons for volume depletion?
   - anaphylaxis, sepsis, MI/CHF, cirrhosis
History:

2. “Is There An Obstruction?”:
   - Abdominal pain / signs of bladder obstruction?
   - *Sudden* anuria?
   - Hematuria? Flank pain? Renal/bladder stones?
   - Weight loss / cancer symptoms?
   - *(also may have no urinary symptoms at all)*

3. “Is it the Kidneys?”:
   - MEDS: Nephrotoxic medicines? IV contrast? aminoglycosides, amphotericin, cisplatin, PCNs, cephalosporins, sulfas, NSAIDs, rifampin? *(suspect any new med)*
   - Family History Kidney Disease?
   - Previous urologic / renal history?
   - Autoimmune/ vasculitis history?
   - Viral diseases which can affect kidneys?
Also, ASK for SYMPTOMS which can be the effects of AKI:

- **Encephalopathy**? (confusion/somnolence)
- Chest pain? (*pericarditis*)
- CHF/Fluid *overload* symptoms?
  - Pulmonary or Peripheral Edema?
  - Significant Hypertension?
- **Bleeding**? (platelet dysfunction)
PHYSICAL EXAMINATION

Physical Exam:

- **Volume status** (orthostatic vital signs, tachycardia, dry mucous membranes)
- Neuro: mental status, asterixis (encephalopathy)
- Heart: tachycardia, pericardial rub
- Lungs: signs of pulmonary edema (increased RR, decreased O2 sat, rales)
- Abdomen: bladder distention, mass?
- Skin: petechiae (HUS, TTP), palpable purpura (vasculitis), edema
- Pelvic/Prostate exam (R/O obstruction)

LABS / STUDIES
LABS/STUDIES:

- CBC, CHEM 7: Na, K, Cl, CO2, BUN, Cr, Glucose (STAT EKG if Hyperkalemic)
- UA with microscopy (casts, RBC, WBC, protein)
- +/- Urine Culture
- Renal ultrasound (R/O Obstruction)
  - Serum Na& Creat, Urine Na & Creat (to calculate FENa)
  - Optional: KUB (for stones), CT Abdomen (for masses) (note: many stones are radiolucent and not seen on KUB)

Hyperkalemia: EKG changes:

- Often a sequential progression
- Peaked T waves, Prolonged PR interval
- Absent P wave, widened QRS
- Ventricular tachycardia / VFib

**Note:** EKG can progress to VT/VF at ANY level of hyper-K!
**Evaluation**

Calculate the FENa: (Fractional Excretion of Sodium)

\[
\frac{U_{Na}}{P_{Na}} \times \frac{100}{U_{Cr} / P_{Cr}}
\]

(make sure the U and P values are in the same units)

FENa < 1 % usually suggests Pre-renal
FENa > 1 % usually suggests ATN (renal)

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**Fractional Excretion of Urea**

FE-Urea

- If pt has recently received diuretic, can use FE-Urea instead of FE-Na: (less influenced by diuretic therapy)

\[
\frac{U_{Urea}}{P_{Urea}} \times \frac{100}{U_{Cr} / P_{Cr}}
\]

- FE-Urea:
  - < 35 % favors pre-renal
  - >35 % favors ATN

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**Can make Laboratory DIAGNOSIS of AKI by:**

1. UA with MICROSCOPY (looking at urine sediment: cells / casts)
2. URINE Na
3. FE-Na
**SUMMARY**

Urinalysis with microscopy:

- Hyaline and fine granular casts often seen in pre-renal failure

- Tubular epithelial cells or casts → ATN, (AIN)

- WBC CASTS, Urine eosinophils → AIN (Hansel’s stain)

- RBC, RBC CASTS → suggests Glomerulonephritis

- + blood on Dipstick but no RBCs on microscopic → consider Rhabdomyolysis, check serum CK level
**SUMMARY**

**Urinalysis with *microscopy***:

- WBC cast: **AIN, chronic GN**
- RBC casts: **GN**
- Oval fat bodies: *nephrotic syndrome*
- Hyaline and fine granular casts often seen in *pre-renal failure*
- Tubular epithelial cells or casts → **ATN, AIN**
- WBC casts, Urine eosinophils → **AIN** (Hansel’s stain)
- RBC, RBC casts → suggests *Glomerulonephritis*
- + blood on Dipstick but no RBCs on microscopic → consider *Rhabdomyolysis*, check serum CK level
Treatment

TREATMENT

Generally:
- 1st manage **CONSEQUENCES** of AKI and look for **Pre-Renal and Post-Renal** causes and treat accordingly

THEN

- 2nd consider **Intrinsic Renal** causes
  it is generally more difficult to assess for Intrinsic Renal Causes of ARF, & not as immediate

INTERVENTIONS/TREATMENT

- Give IV Fluids as trial, since pre-renal is most common cause (60-70%)… (unless volume overloaded)

- **Foley catheter**—to relieve obstruction/urine retention. (5-10%)

- If **Foley is already in place**→**flush with NS** (to clear any sediment/clot obstructing)
MOST LIFE-THREATENING CONSEQUENCES:

- hyperkalemia
- acidosis
- fluid overload (CHF)
- bleeding

REASONS FOR INITIATING EMERGENT HEMODIALYSIS

- **1 ~ HYPERKALEMIA**
- **2 ~ CHF**
- **3 ~ METABOLIC ACIDOSIS**
- **4 ~ UREMIC ENCEPHALOPATHY**
- **5 ~ UREMIC PERICARDITIS**

(BUN, Creat values are not independent indications for dialysis)

REASONS FOR INITIATING EMERGENT HEMODIALYSIS

aka :“A-E-I-O-U”

- **A = ACIDOSIS**
- **E = ELECTROLYTES** (high K)
- **I = INGESTIONS**
- **O = OVERLOAD**
- **U = UREMIA**

(uremic ENCEPHALOPATHY/PERICARDITIS)
Some ingestions which may require dialysis:

- Lithium
- Ethylene glycol
- Methanol
- Salicylates
- Valproic acid
- Metformin
- Theophylline
- INH
- Tricyclics

**Pericarditis**

- Diffuse ST elevations

**Pericarditis**

- Diffuse ST elevations, PR depressions
Until you can get the pt to dialysis, treat accordingly:

- **1 HYPERKALEMIA**: treat with glucose/insulin, IV calcium, Kayexalate, Furosemide, check EKG STAT and monitor...
- **2 CHF**: Oxygen, diuresis...
- **3 METABOLIC ACIDOSIS**: bicarbonate if severe pH<7.2...
- **4 UREMIC ENCEPHALOPATHY**: treat seizures, agitation...
- **5 UREMIC PERICARDITIS**: treat pain (NO NSAIDS!! And NO ANTICOAGULANTS—can cause hemorrhagic conversion of pericarditis)

**AVOID**: KCL, K-SPARING DIURETICS, ACE INHIBITORS, NSAIDS, NEPHROTOXIC DRUGS, IV CONTRAST.....

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**TREATMENT**

Generally:

- **1st** manage **CONSEQUENCES** of ARF and look for **Pre-Renal and Post-Renal** causes and treat accordingly

Then

- **2nd** consider **Intrinsic Renal** causes it is generally more difficult to assess for Intrinsic Renal Causes of ARF, & not as immediate
**CAUSES**

- **Intrinsic Renal (30-40%)**:
  - **90% = Acute Tubular Necrosis (ATN)** induced by hypotension, nephrotoxins / drugs (aminoglycosides, amphotericin, IV contrast, chemotherapy, rhabdomyolysis)
  - **Acute Interstitial Nephritis (AIN)**: can be as late as 10-14 days after last dose of antibiotic, only 1/3 have eosinophils in urine: eg, due to PCN, Sulfon, Quinolones, Cephalosporins, NSAIDS, diuretics...
  - **Vascular** causes such as Emboli (from SBE, MI, Afib, left heart thrombi), aortic aneurysms, post aortic surgery, Renal Artery Thrombosis, or worsening of Renal Artery Stenosis / renal artery atherosclerosis
  - **Nephritis** such as acute glomerulonephritis, SLE, vasculitides
  - renal infection, renal infiltration (lymphoma, sarcoid)

**Causes**

***MOST COMMON : Pre-renal***

- **Pre-renal (60-70%)**: Volume depletion, hypotension, anaphylaxis, sepsis, decreased cardiac output (MI, CHF), hepatorenal syndrome, Aortic Dissection

- **Post-renal (5-10%)**: OBSTRUCTION caused by urethral strictures/tumors, bladder stones/tumors, enlarged prostate, cervical/ovarian mass, neurogenic bladder, anti-cholinergic drugs, or ureteral stones/tumors/clots, lymphadenopathy, blocked Foley catheter
**INTRINSIC RENAL:**

1. Interstitial nephritis

- Clinical clues: Medications, fever, rash, eosinophilia (hypersensitivity)
- Urine Sediment: WBCs, WBC casts, eosinophils (eos only seen by Hansel's staining of WBC)
- Protein:Creatinine Ratio: 30 to 3,000 mg of protein per g of creatinine
- Other Tests: less common= CMV, HIV, HBV, ACE level; SS-A, SS-B (Ab to ribonuclear proteins : antiSS-A = anti-Ro antibody; antiSS-B = anti-La antibody) (Sjogrens, SLE) (Tx= withdraw offending agent; +/- steroids possibly needed)

2. Glomerulonephritis

- Clinical clues: History and physical examination: infections; rash, arthritis; patient older than 40 years
- Urine Sediment: Dysmorphic RBCs or RBC casts
- Protein:Creatinine Ratio: > 30 to > 3,500 mg of protein per g of creatinine
- Other Tests: C3 and C4 for all patients
  --Tests for infections: anti-ASO, HIV, HBsAg, HCV, RPR, blood cultures
  --Tests if there is rash or arthritis: ANA, ANCA, cryoglobulin, anti-GBM
  --Tests if patient is > 40 years:SPEP, UPEP

3. Vasculitis

- Clinical clues: Constitutional symptoms, peripheral neuropathy, rash, respiratory symptoms
- Urine Sediment: RBCs; granular casts
- Protein:Creatinine Ratio: > 30 to > 3,500 mg of protein per g of creatinine
- Other Tests: C3, C4, ANA, ANCA; HBsAg, HCV, cryoglobulins, ESR, RF, SS-A, SS-B, HIV
  (SS-A = anti-Ro antibody; SS-B = anti-La antibody)
- Treatment = tx complications +/- immunosuppressants
A Few Caveats:

- In GN, acute post-renal obstruction, and some vascular diseases, FENa may often be < 1%

- Protein deficient states can produce a lower BUN/creat ratio in pre-renal states.

- GI bleeding, high protein diet, corticosteroids can cause a higher BUN level.

- Creatinine can be increased with certain meds: trimethoprim, cimetidine

A Few Final Notes:

- Remember to adjust doses of all drugs for new GFR/Creat clearance (assume the lowest eGFR if status is still dynamic)

- For ATN from rhabdomyolysis, treat with IV bicarbonate: D5W w/ 3 amps NaHCO3/L at 100-150ml/hr, titrate to high volume UOP, and use furosemide to force diuresis.
Prevention of contrast nephropathy
in patients with risk factors for ARF
(elderly, CKD, hepatic disease)

- **Hold Metformin** x 48 hrs prior to IV contrast
- **Hold diuretics and NSAIDS** and any potentially nephrotoxic meds if possible
- **Start IV fluids**: normal saline x 24 hrs prior to contrast
- **Sodium Bicarbonate**: RCT showed 12% absolute risk reduction w/ administration of NaHCO3 prior to contrast load—though f/u study in JAMA was negative
  -- dosage: 154 mEq/L Sodium Bicarbonate as a bolus of 3cc/kg/hr for 1 hour prior to contrast, followed by infusion of 1 cc/kg/hr for 6 hours after procedure.

Prevention of contrast nephropathy

- Use oral **acetylcysteine** (Mucomyst) before administering iodinated contrast loads in patients with risk factors
- **Dose** = 600 mg po bid the day before and the day of the study, along with adequate hydration. (4 doses total)

- controversial, with meta-analyses reaching different conclusions about efficacy in prevention

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THE END

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of Part 1!!
A deep, restoring b-r-e-a-t-h . . . . .

BEFORE   PART 2!
Part 2: CHRONIC KIDNEY DISEASE

Screening for CKD:
- **Whom** do you screen?
- **Why** do you screen?
- **How** do you screen?

Diagnosing CKD:
- How do you diagnose the **cause** of CKD?
- How do you **slow the progression** of CKD?
- How do you **treat the effects** of CKD?

**WHOM to screen for CKD:**

Screen all w/ risk factors for kidney disease:
- **DM** (*DM is most common cause of CKD*),
- **HTN,**
- **age over 60 yo,**
- Family Hx of renal dz,
- h/o recurrent UTI,
- h/o urinary obstruction,
- or systemic illness that affects the kidneys
Of note, regarding ESRD:

- 40-60% of pts w/ ESRD have DM
- 15-30% of pts w/ ESRD have HTN
- <10% have glomerulonephritis
- 2-3% have cystic kidneys

WHY screen for CKD:

- It’s inexpensive & easy
- To slow disease progression to kidney failure, and reduce complications from decreased kidney function,
- And to prevent development of cardiovascular disease and other effects
  - CKD is a risk factor for cardiovascular disease
  - Cardiovascular disease is the most common cause of death in patients with chronic kidney disease.
  - The risk of cardiovascular disease and associated mortality increases in proportion to the decrease in the GFR.

How to screen for CKD:

- Blood pressure
- Creat → eGFR (w/ serum electrolytes = Chem7)
- Random urine sample for Proteinuria
  (Instead of a timed urine collection, a random urine sample for the albumin-creatinine ratio or protein-creatinine ratio)
- UA with microscopy
  (to examine urine sediment/casts/cells etc)

History of detecting Kidney Disease

- Smell the urine, if sweet → then DM
  If foul → then infection
  If smell of asparagus → you ate asparagus

- Advent of Laboratory medicine: Serum Creatinine measured

  ↓ Proteinuria:

  24hr urine protein can detect earlier than Creat
  Spot Urine Prot: creat, Albumin: creat ratio (easy/accurate)

  ↓ eGFR calculation

  → can detect disease earlier than Proteinuria
A bit about

1. eGFR

and

2. proteinuria

About Creatinine and GFR...

- Glomerular Filtration Rate (GFR) is a more accurate estimate of the filtering capacity of the kidneys.
  - It is expressed as mL per minute, & adjusted to a “standard” body size with a surface area of 1.73 meters². (mL/min/1.73m²)
  - Normal GFR ranges between 95 - 120 mL/min/1.73m² but it varies depending on age, gender and body size.
  - GFR is usually estimated (eGFR) from a mathematical equation based principally on the serum creatinine, age, gender, and race.

Average GFR by Age

- According to National Kidney Foundation (NKF), the average estimated GFR for a given age group is: (DECREASE BY ~ 10 / DECADE)
  - Age 20-30: 116 mL/min/1.73m²
  - Age 30-40: 107 mL/min/1.73m²
  - Age 40-50: 99 mL/min/1.73m²
  - Age 50-60: 93 mL/min/1.73m²
  - Age 60-70: 85 mL/min/1.73m²
  - Age 70+: 75 mL/min/1.73m²

Kidneys remove creatinine
“OK, but a creatinine of 1 reflects normal kidney function, no matter what, right?”

OR

“I don’t have to worry if the creatinine is around 1, right?”

“An estimation of the GFR based on the serum creatinine level correlates better with direct measures of the GFR and detects more cases of chronic kidney disease than does the serum creatinine level alone.”

There can be considerable renal dysfunction despite a normal serum creatinine level:

Abbreviated MDRD equation:

\[
eGFR = 186 \times \left(\frac{\text{Creat}}{88.4}\right)^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})
\]

Go to: http://mdrd.com/

Not accurate in extremes of age, kidney function, muscle mass
CKD-EPI equation (2009)

CKD-EPI equation uses the same variables as MDRD equation (age, sex, race, and creatinine level) but it applies different coefficients to those variables.

When the CKD-EPI equation was used instead of the MDRD Study equation, significant percentages of patients were reclassified to a higher eGFR category:

- 24.4% of participants from the general population cohorts,
- 15.4% from high-risk cohorts,
- and 6.6% from CKD cohorts.

The CKD-EPI equation found a lower prevalence of CKD in all cohorts except the elderly.

(*about 1 in 4 pts will no longer be starred as abnormal eGFR)*
A bit about

1. eGFR

and

2. proteinuria

random urine for **proteinuria**:

- Screening for proteinuria can detect chronic kidney disease even before changes in GFR occur.
- Significant kidney disease can present with decreased GFR or proteinuria, or both.
- Proteinuria is associated with more rapid progression of CKD disease and a greater chances of developing ESRD

random urine for **proteinuria**:

- Reducing proteinuria slows the progression of chronic kidney disease in patients with or without diabetes.
- ACE inhibitor or ARB dosage should be adjusted as tolerated, with the goal of eliminating albuminuria.

Urine Dipstick: good for detecting a large amount of protein the urine (> 300 mg) but not as good for smaller amounts (microalbuminuria)
The most common methods of screening for protein in the urine are:

- **Urine Dipstick:** Uses a chemical that binds to albumin and changes different shades of green. It is a good screening test for detecting a large amount of protein in the urine (> 300 mg) but not as good for smaller amounts (microalbuminuria).
- Its results can be affected by how concentrated the urine is and that it checks only for albumin and **not other proteins.**

- **Urine Albumin:** Since the dipstick is not very sensitive to low levels of albumin in the urine, it is helpful to **measure the urine albumin directly** (microalbuminuria).
- Microalbumin is the term ascribed to the measurement of albumin in urine at concentrations below the sensitivity of dipstick tests for total protein (<300 mg).

Collecting urine for a 24-hour period has been considered **the gold standard.**

However, because it is very inconvenient and prone to error if the urine isn’t collected properly, we use urine protein : creatinine ratio instead. (or albumin: creat ratio)

- It is requires only a small sample of urine and it is relatively accurate and convenient.

**Interpretation of Urine Protein to Urine Creatinine Ratio**

- **Child under age 2 years**
  - Normal Ratio <0.5 (500 mg/g)

- **Adults and children over age 2 years**
  - Normal ratio <0.2 grams protein per gm **Creatinine (normal is < 200mg per gram of Creatinine)**
    - Correlates with 0.2 g protein/day
  - Nephrotic Ratio >3.5 (correlates with 3.5 g protein)
Interpretation of Urine Albumin to Creatinine Ratio

- Normal Ratio (in general <30 mg/g is normal)
  - Men: < 0.017 (or 17 mg albumin to 1 gram Creatinine)
  - Women: <0.025 (or 25 mg albumin to 1 gm Creatinine)

- Microalbuminuria: 30-300 mg albumin/g Creatinine
- Macroalbuminuria: >300 mg albumin/g Creatinine

SCREENING FOR PROTEINURIA

HOW to screen (special pts): 24 hour urine collection for creatinine clearance is needed in certain patients (since Creat & eGFR are less accurate)

- Pregnant women
- Patients with extremes of age and weight
- Patients with malnutrition
- Patients with skeletal muscle diseases
- Patients with paraplegia or quadriplegia
- Patients with a vegetarian diet and rapidly changing kidney function

How to screen for CKD:

- BP check
- Creat→eGFR (w/ serum electrolytes = Chem7)
- random urine sample for Proteinuria
  (Instead of a timed urine collection, a random urine sample for the microalbumin-creatinine ratio or protein-creatinine ratio)
- UA with microscopy (for RBC, WBC, casts)
Overview

Screening for CKD:
- **Whom** do you screen? DM, HTN, age >60
- **Why** do you screen? to reduce progression of dz
- **How** do you screen? eGFR, proteinuria

Diagnosing CKD:
- How do you diagnose the cause of CKD?
- How do you slow the progression of CKD?
- How do you treat the effects of CKD?

Definitions from the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative

**Definition of Chronic kidney disease (CKD):**
- Kidney damage for 3 or more months based on findings of abnormal structure (imaging studies) or abnormal function (blood tests, urinalysis).
- Or GFR below 60 mL per minute per 1.73 m2 for 3 or more months with or without evidence of kidney damage.

**Definition of End-stage renal disease (kidney failure):**
- GFR below 15 mL per minute per 1.73 m2
- OR Need for kidney replacement therapy (dialysis or transplant)

**TABLE 2**

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (mL per minute per 1.73 m2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;= 90</td>
</tr>
<tr>
<td>2</td>
<td>60 to 89</td>
</tr>
<tr>
<td>3</td>
<td>30 to 59 &lt;60</td>
</tr>
<tr>
<td>4</td>
<td>15 to 29 &lt;30</td>
</tr>
<tr>
<td>5</td>
<td>&lt; 15 or dialysis &lt;15</td>
</tr>
</tbody>
</table>
Note: eGFR is less accurate for normal creatinine (eGFR underestimates function at normal Creatinine, so labs will only report “eGFR >60”)

eg for a 50 year old white woman:

- Creatinine 0.6 → eGFR =112 stage 1 ?
- Creatinine 0.7 → eGFR =94 stage 1 ?
- Creatinine 0.9 → eGFR =70 stage 2 ?
- Creatinine 1.1 → eGFR =56 stage 3
- Creatinine 1.5 → eGFR =39 stage 3
- Creatinine 2.0 → eGFR =28 stage 4

Evaluation for Causes of Chronic Kidney Disease:

- CBC, CHEM 7: Na, K, Cl, CO2, BUN, Cr, Glucose (STAT EKG if Hyperkalemic)
- UA with microscopy (casts, RBC, WBC, protein)
- +/- Urine Culture
- Urine protein-creat or albumin-creat ratio
- Renal ultrasound
  - Optional: KUB (for stones), CT Abdomen (for masses if suspicion exists by Hx/PE)
  - If needed: other “special labs”
Best to have done these tests at least prior to referring to Nephrologist

Review:
Urinalysis with *microscopy*:

- Hyaline and fine granular casts often seen in *pre-renal failure*
- Tubular epithelial cells or casts: *ATN, AIN*
- WBC CASTS, Urine eosinophils → *AIN*
- RBC, RBC CASTS proteinuria suggests *Glomerulonephritis*
- + protein +/- *Oval fat bodies* → *nephrotic syndrome* (check albumin and 24 hr urine protein)
- + blood on Dipstick but no RBCs on microscopic → consider *Rhabdomyolysis*, check serum CK level

LABS/STUDIES:

- **CBC, CHEM 7**: Na, K, Cl, CO2, BUN, Cr, Glucose (STAT EKG if Hyperkalemic)
- **UA with microscopy** (casts, RBC, WBC, protein)
- +/- Urine Culture
- Urine protein-creat or albumin-creat ratio
- Renal ultrasound
  - Optional: KUB (for stones), CT Abdomen (for masses if suspicion exists by Hx/PE)
  - If needed: other “special labs”
SPECIFIC CLUES FOR SEEKING CAUSES OF CKD:

- Commonly ordered labs to R/O GN or Vasculitis:
  - **Glomerulonephritis**: C3,C4, anti-ASO, ASK, HIV, HBsAg, HCV, RPR, blood cultures; if there is rash or arthritis: ANA, ANCA, cryoglobulin, SPEP, UPEP
  - **Vasculitis**: C3, C4, ANA, ANCA; HBsAg, HCV, cryoglobulins, ESR, RF, SS-A, SS-B, HIV
    (SS-A = anti-Ro antibody; SS-B = anti-La antibody)

Slow the progression

- **Interventions proven to slow the progression** of chronic kidney disease include:
  1. **blood pressure control**
  2. **glycemic control** (goal HbA1c <7)
  3. **reduction of proteinuria** with an angiotensin-converting enzyme inhibitor or angiotensin-II receptor blocker.
Complications in Chronic Kidney Disease

Patients with a GFR below 60 mL should have monitoring for these complications:

- Hyperkalemia
- Hyperphosphatemia, Hypocalcemia (secondary hyperparathyroidism)
- Hyponatremia, Acidosis
- Hypoalbuminemia
- Decreased immunoglobulins

More Complications in Chronic Kidney Disease

- Dyslipidemia, CAD
- HTN
- Anemia
- Renal Osteodystrophy (2‘high PTH)
- Uremia (→ needing dialysis or transplant)
WHEN TO REFER to NEPHROLOGIST:

- Underlying cause unclear after basic work-up
- Renal biopsy indicated
- Management of underlying cause beyond the scope of primary care
- Stage 3 chronic kidney disease (GFR < 60 mL per minute per 1.73 m²): consider co-management
- Stage 4 chronic kidney disease (GFR < 30 mL per minute per 1.73 m²): nephrologist involvement essential
- Rapid progression of chronic kidney disease
- Superimposed acute kidney failure

NATIONAL KIDNEY FOUNDATION

www.kidney.org
Get to know the web site as a reference for Guidelines and Patient Education
And use: applications for eGFR calculators

the end
Dyslipidemia

Very common—increases risk for CAD
(CAD/cardiovascular mortality is 10 to 20 times higher in dialysis patients than in the normal population even after adjustments are made for age, sex, and diabetes mellitus)

- animal models suggest that dyslipidemia worsens kidney function.
- A recent meta-analysis of 13 small studies showed that lipid reduction preserves GFR and reduces proteinuria. (controversial)

Dyslipidemia

Pts w/ CKD have:
- elevated TG level possibly because of defective clearance.
- elevated ratio of LDL to HDL
- low HDL

Guidelines from the NKF K/DOQI:
- treat dyslipidemia aggressively in CKD pts:
  with goals of \( \text{LDL} < 100 \text{ mg/dL} \)
  and \( \text{TG} < 200 \text{ mg/dL} \)

"Your pulse is very, very weak!"
**HTN**

HTN leads to direct damage to small blood vessels in the nephron, loss of regulation of GFR, & proteinuria.

Several trials prove the benefit of BP control in slowing the progression of kidney disease.

**ACEs and ARBs** preferentially lower intraglomerular pressure and reduce proteinuria, and are more effective than other antihypertensive drugs in preventing the progression of kidney disease.

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**ACE / ARB treatment**

- When starting ACE-inhibitor, CKD pts often have initial decrease in GFR (usually less than 10 mL per minute per 1.73 m2) → EXPECT a mild increase in creatinine (less than 20-30% of baseline), and mild increase in K+

- Creatinine and potassium levels should be monitored 1 to 2 weeks after the initiation of therapy with ACE inhibitor—COMMON MISTAKE IS TO STOP THE ACE/ARB WHEN Cr increases by <= 30% !
  - DO NOT STOP → RECHECK AGAIN IN 1-2 WKS

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**Guidelines**: blood pressure goal of 130/80 mm Hg is recommended in patients with normal urinary albumin concentrations, and a blood pressure goal of 125/75 mm Hg is recommended in patients with proteinuria equal to or greater than 1 g per 24 hours.

**Angiotensin II has more effect on efferent than afferent arteriole**

- ACEI (blocking conversion A I → A II) means less A II, so less constriction/more dilation of efferent than afferent arteriole, so expect decrease in GFR:

  ![Diagram showing GFR/pressure and efferent arteriole dilation](attachment://diagram.png)
Anemia

- normocytic, normochromic, hypoproliferative
- due to lower erythropoietin production by the decreased # of functioning renal tubular cells.
- Sxs are of decreased quality of life: fatigue, less exercise tolerance, lower immunity & cognition, increased work on heart can lead to LVH & cardiomyopathy.

Anemia

- correction of anemia may slow progression of chronic kidney disease, possibly decrease mortality.
- NKF K/DOQI guidelines recommend:
  - target hemoglobin concentration of 10 - 12
  - give Iron supplement if low ferritin(<100 ng/mL)
  - give Erythropoietin to predialysis pts w/ anemia-dependent angina or severe anemia w/ Hb <10
Renal Osteodystrophy

- In early CKD, hyperphosphatemia leads to increased PTH (secondary hyperparathyroidism), which causes increased bone turnover, decreased cortical bone and decreased bone strength→ causing fractures
- Can reduce hyperparathyroidism by treating & preventing hyperphosphatemia:
  - restrict dietary phosphate intake (e.g., colas, nuts, peas, beans, dairy products)
  - use phosphate binders
  - vitamin D to suppress parathyroid hormone secretion.
  (some patients can have refractory hyperparathyroidism due to parathyroid gland hyperplasia, and may require surgical treatment)

Nutrition

- CKD pts are at risk for malnutrition and hypoalbuminemia, both of which may be associated with poor outcomes
- Question/Subject of debate:

  What amount of protein intake may reduce the risk of CKD progression and also minimize risk of malnutrition?

Nutrition

- NKF K/DOQI recommendation for pre-dialysis CKD: protein intake of 0.8 to 1.0 g per kg per day
  (controversial --based on evidence from animal studies and is NOT first line treatment plan)

- CKD pts, especially those requiring dialysis, should have albumin and weight monitored, to prevent malnutrition.

- CKD pts should be referred to a nutritionist for recommendations on optimal protein and caloric intake
Smoking cessation

- CKD pts are at high risk for CV mortality
- Smoking is a strong ADDED CV disease risk factor
- Smoking is also strongly associated with the progression of CKD

- Guideline: (obvious!)
  Recommend and help with smoking cessation!

Emotional and spiritual well-being

- Positive moods
- Feeling understood & validated
- Conflict management
- Social support
- Intimacy
- Affection
- Nurture
- Forgiveness
- Satisfaction
- Self-disclosure
- Secure attachment
- Accommodation
- Happiness
- Fewer feelings of hostility
- Less of depression
- Self-advancement
- Constructive responses
- Lesser feelings of loneliness
- Psychological adjustment
- Self-esteem
- Trust
NATIONAL KIDNEY FOUNDATION

www.kidney.org

Get to know the web site as a reference for Guidelines and Patient Education
And use:

References:
6. Comparison of Risk Prediction Using the CKD-EPI Equation and the MDRD Study Equation for Estimated Glomerular Filtration Rate, JAMA, May 9, 2012