Let us build a strong team

Patient
Primary Care Provider
Nephrologist

Nithin Karakala MD
Associate Professor
Department of Medicine

UAMS
University of Arkansas for Medical Sciences
Scope of the problem

More than 1 in 7

15% of US adults are estimated to have chronic kidney disease—that is about 37 million people.
Exhibit 4. Geographical Distribution of Nephrology Fellowship Programs and ESRD Patients per Nephrologist by HRR, 2011

ESRD Patients per Nephrologist

- 28.0 - 61.7
- 61.8 - 74.2
- 74.3 - 86.6
- 86.7 - 105.2
- 105.3 - 446.9

Number of Programs

- 1
- 2
- 3 - 4
- 5 - 6
- 7 - 13
Who is in the best position for managing patients with chronic kidney disease?

You (primary care providers) are the first and the best line of defense in the management of patients with chronic kidney disease.
Impact of primary care CKD detection with a patient safety approach

Objectives

1. Who do I refer to nephrology?
2. Do I call my nephrology or urology friend?
3. Management of hypertension in patients with chronic kidney disease
4. Principals of diuretic dosing
5. How to overcome diuretic response
Other than CKD are there other reasons to refer a patient to a nephrologist?
Who is at a risk of worsening renal function and mortality?

**Miss Scarlet**
- eGFR: 80 ml/min
- Albumin creatinine ratio: 680 mg/g

**Mr. Green**
- eGFR: 32 ml/min
- Albumin creatinine ratio: 15 mg/g
<table>
<thead>
<tr>
<th>eGFR</th>
<th>ACR &lt;10</th>
<th>ACR 10-29</th>
<th>ACR 30-299</th>
<th>ACR &gt;300</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;105</td>
<td>Ref</td>
<td>Ref</td>
<td>0.4</td>
<td>3.0</td>
</tr>
<tr>
<td>90-105</td>
<td>Ref</td>
<td>Ref</td>
<td>0.9</td>
<td>3.3</td>
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<tr>
<td>75-90</td>
<td>Ref</td>
<td>Ref</td>
<td>1.9</td>
<td>5.0</td>
</tr>
<tr>
<td>60-75</td>
<td>Ref</td>
<td>Ref</td>
<td>3.2</td>
<td>5.1</td>
</tr>
<tr>
<td>45-60</td>
<td>3.1</td>
<td>4.0</td>
<td>9.4</td>
<td>57</td>
</tr>
<tr>
<td>30-45</td>
<td><strong>3.0</strong></td>
<td>19</td>
<td>15</td>
<td>22</td>
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<tr>
<td>15-30</td>
<td>4.0</td>
<td>12</td>
<td>21</td>
<td>7.7</td>
</tr>
</tbody>
</table>

Risk OF PROGRESSIVE CKD

KDIGO
### Risk of CARDIOVASCULAR, and ALL CAUSE MORTALITY

**KDIGO**

<table>
<thead>
<tr>
<th>Cardiovascular mortality</th>
<th>ACR &lt;10</th>
<th>ACR 10-29</th>
<th>ACR 30-299</th>
<th>ACR&gt;300</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR&gt;105</td>
<td>0.9</td>
<td>1.3</td>
<td>2.3</td>
<td>2.1</td>
</tr>
<tr>
<td>eGFR 90-105</td>
<td>Ref</td>
<td>1.5</td>
<td>1.7</td>
<td>3.7</td>
</tr>
<tr>
<td>eGFR 75-90</td>
<td>1</td>
<td>1.3</td>
<td>1.6</td>
<td>3.7</td>
</tr>
<tr>
<td>eGFR 60-75</td>
<td>1.1</td>
<td>1.4</td>
<td>2.0</td>
<td>3.1</td>
</tr>
<tr>
<td>eGFR 45-60</td>
<td>1.3</td>
<td>2.2</td>
<td>2.8</td>
<td>4.3</td>
</tr>
<tr>
<td>eGFR 30-45</td>
<td>2.2</td>
<td>2.7</td>
<td>3.4</td>
<td>5.2</td>
</tr>
<tr>
<td>eGFR 15-30</td>
<td>4.4</td>
<td>7.9</td>
<td>4.8</td>
<td>8.1</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>All Cause Mortality</th>
<th>ACR &lt;10</th>
<th>ACR 10-29</th>
<th>ACR 30-299</th>
<th>ACR&gt;300</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR&gt;105</td>
<td>1.1</td>
<td>1.5</td>
<td>2.2</td>
<td>5</td>
</tr>
<tr>
<td>eGFR 90-105</td>
<td>Ref</td>
<td>1.4</td>
<td>1.5</td>
<td>5.1</td>
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<tr>
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<td>1</td>
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<td>1.8</td>
<td>2.7</td>
</tr>
<tr>
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<td>1.7</td>
<td>2.2</td>
<td>3.6</td>
</tr>
<tr>
<td>eGFR 30-45</td>
<td>1.9</td>
<td>2.3</td>
<td>3.3</td>
<td>4.9</td>
</tr>
<tr>
<td>eGFR 15-30</td>
<td>3.5</td>
<td>3.6</td>
<td>4.7</td>
<td>6.6</td>
</tr>
</tbody>
</table>
Referral to Nephrology for proteinuria

### Persistent albuminuria categories

<table>
<thead>
<tr>
<th>Description and range</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal to mildly increased</td>
<td>Normal or high</td>
<td>≥90</td>
<td>Monitor</td>
</tr>
<tr>
<td>Moderately increased</td>
<td>60–89</td>
<td>Monitor</td>
<td>Refer*</td>
</tr>
<tr>
<td>Severe increased</td>
<td>30–300 mg/g</td>
<td>3–30 mg/mmol</td>
<td>Monitor</td>
</tr>
<tr>
<td>&gt;300 mg/g</td>
<td>&gt;30 mg/mmol</td>
<td>&gt;30 mg/mmol</td>
<td>Monitor</td>
</tr>
</tbody>
</table>

#### GFR categories (ml/min/1.73 m²)

<table>
<thead>
<tr>
<th>GFR categories</th>
<th>Description and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
</tr>
<tr>
<td>G3a</td>
<td>Moderately to moderately decreased</td>
</tr>
<tr>
<td>G3b</td>
<td>Severe decreased</td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
</tr>
</tbody>
</table>

Do I need to consult a nephrologist after discharge if the patient was diagnosed with AKI while in the hospital following?
Natural history of renal function in patients who develop AKI in the hospital
AKI and Nephrology Consultation

- AKI Survivors Following Discharge within 30 days
  - 11.9% Nephrology follow up
  - 29.5% Cardiology follow up
  - 74.5% Primary care visit

- AKI Requiring Dialysis Survivors Following Discharge
  - 33% Nephrology visit within 30 days
  - 48.6% Nephrology visit within 1 year

- Acute Myocardial Infarction Survivors After Discharge
  - 76% Cardiology Consultation within 30 days
Hypertension

- Any patient on 3 or more medications one of them a diuretic, but still with poorly controlled hypertension.

- Suspicion of hyperaldosteronism or like states; difficult to controlled hypertension, persistent hypokalemia, and or metabolic alkalosis.

- Evidence of unprovoked pulmonary edema in patients with difficult to control hypertension.
Risk stratification for contrast nephropathy

- Incidence in general population is <2%
Pre-procedural Clinical Risk Factors for Contrast Induced Nephropathy

• **Modifiable Risk Factors**
  - Contrast volume
  - Hydration status
  - Concomitant nephrotoxic agents
  - Recent contrast administrations

• **Non-modifiable Risk Factors**
  - Diabetes/Chronic kidney disease
  - Shock/hypotension
  - Advanced age (> 75 yrs)
  - Advanced congestive heart failure

Klein LW, Cathet Cardiovasc Int 2009; 74: 728-46
Risk scoring of AKI

A Risk Score for Prediction of CIN

Table 1. Mehran Risk Scores

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Integer Score</th>
<th>Class of Risk</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>5</td>
<td>Low</td>
<td>5 ≤</td>
</tr>
<tr>
<td>IABP</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt; 75 y</td>
<td>4</td>
<td>Medium</td>
<td>6 to 10</td>
</tr>
<tr>
<td>Anemia</td>
<td>3</td>
<td>SUM</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contrast media volume</td>
<td>1 for each 100 cc³</td>
<td>High</td>
<td>11 to 16</td>
</tr>
<tr>
<td>eGFR &lt; 20 mL/min/1.73 m²</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR 20–40 mL/min/1.73 m²</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR 40–60 mL/min/1.73 m²</td>
<td>2</td>
<td>Very high</td>
<td>≥16</td>
</tr>
</tbody>
</table>

Risk group: Low ≤5, Moderate 6 to 10, High 11 to 15, Very High ≥16

Development dataset N=5571
Prediction dataset N=2786
Nephrology or Urology
Urology or Nephrology

- Hematuria
- Nephrolithiasis
- Recurrent UTI
- Structural lesions in the kidney
<table>
<thead>
<tr>
<th>Hematuria: who do I refer to?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nephrology</strong></td>
</tr>
<tr>
<td>• &lt; 50 years</td>
</tr>
<tr>
<td>• Persistent hematuria</td>
</tr>
<tr>
<td>• Rapid decline in renal function</td>
</tr>
<tr>
<td>• History of autoimmune disease</td>
</tr>
<tr>
<td>• Proteinuria</td>
</tr>
<tr>
<td>• Family history of glomerular diseases</td>
</tr>
<tr>
<td><strong>Urology</strong></td>
</tr>
<tr>
<td>• &gt; 50 years</td>
</tr>
<tr>
<td>• History of kidney stones</td>
</tr>
<tr>
<td>• Exposure to benzenes</td>
</tr>
<tr>
<td>• History of smoking</td>
</tr>
<tr>
<td>• Blood clots</td>
</tr>
</tbody>
</table>
Hematuria: what workup do I order?

- Renal ultrasound
- Urine protein creatinine ratio
- CBC
- Urinalysis and microscopy
- Pregnancy
Kidney stones: who do I refer to?

- **Nephrology**
  - Evaluation and prevention
  - Recurrent kidney stones

- **Urology**
  - Treatment
  - Management of acute episode of kidney stone
Abnormal radiology findings
Understanding age related changes in the kidney
What do I do if I find a renal cyst?
Cysts: who do I refer to?

- **Nephrology**
  - Multiple renal cysts in both kidneys
  - Cysts with decline in kidney function

- **Urology**
  - Complex cysts
  - Mass in the kidney
  - Cyst with blood
  - Painful cysts.
Guidelines for managing Hypertension

• **2003:** The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
• **2012:** The National Kidney Foundation
• **2012:** Kidney Disease Improving Global Outcome
• **2013:** American Society of Hypertension and International Society of Hypertension
• **2013:** JNC 8
• **2017:** The American College of Cardiology/American Heart Association
<table>
<thead>
<tr>
<th>Population</th>
<th>JNC 8</th>
<th>ACC/AHA</th>
<th>NKF</th>
<th>KDIGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 60 years</td>
<td>&lt;150/90</td>
<td>&lt;130/80</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 60 years</td>
<td>&lt;140/90</td>
<td>&lt;130/80</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Diabetics</td>
<td>&lt;140/90</td>
<td>&lt;130/80</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>With CKD</td>
<td>&lt;140/90</td>
<td>&lt;130/80</td>
<td>&lt;130/80</td>
<td>&lt;140/90</td>
</tr>
<tr>
<td>With CVD</td>
<td>&lt;140/90</td>
<td>&lt;130/80</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Urine Albumin &gt; 300 mg/24 hrs</td>
<td></td>
<td></td>
<td>&lt;130/80</td>
<td></td>
</tr>
</tbody>
</table>
Sprint Trial
SPRINT: Population

- Aged 50 years and older
- Systolic blood pressure $\geq 130$ mm Hg and at least one other cardiovascular risk factor:
  - Presence of clinical or subclinical cardiovascular disease other than stroke
  - Estimated glomerular filtration rate between 20-59 mL/min/1.73 m$^2$
  - A Framingham 10-year cardiovascular risk score $\geq 15$
  - Age $\geq 75$ years
SPRINT: Interventions

• In the intensive BP (< 120 mm Hg) arm, additional pills were “required” if SBP ≥ 120 mm Hg.

• In the standard BP (< 140 mm Hg) arm, doses were to be down-titrated if SBP < 130 mm Hg at 1 visit, or < 135 mm Hg at 2 consecutive visits!
Systolic BP During Follow-up

Year 1
Mean SBP
136.2 mm Hg
Standard
Mean SBP
121.4 mm Hg
Intensive

Average SBP
(During Follow-up)
Standard: 134.6 mm Hg
Intensive: 121.5 mm Hg

Average number of antihypertensive medications

Number of participants

Mean SBP 136.2 mm Hg
Mean SBP 121.4 mm Hg
SPRINT Primary Outcome
Cumulative Hazard

Hazard Ratio = 0.75 (95% CI: 0.64 to 0.89)

During Trial (median follow-up = 3.26 years)
Number Needed to Treat (NNT) to prevent a primary outcome = 61
## SPRINT Primary Outcome and its Components

**Event Rates and Hazard Ratios**

<table>
<thead>
<tr>
<th></th>
<th>Intensive</th>
<th>Standard</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>243</td>
<td>319</td>
<td>0.75 (0.64, 0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>All MI</strong></td>
<td>97</td>
<td>116</td>
<td>0.83 (0.64, 1.09)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Non-MI ACS</strong></td>
<td>40</td>
<td>40</td>
<td>1.00 (0.64, 1.55)</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>All Stroke</strong></td>
<td>62</td>
<td>70</td>
<td>0.89 (0.63, 1.25)</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>All HF</strong></td>
<td>62</td>
<td>100</td>
<td>0.62 (0.45, 0.84)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>CVD Death</strong></td>
<td>37</td>
<td>65</td>
<td>0.57 (0.38, 0.85)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

- **No. of Events**
- **Rate, %/year**

**Notes:**
- HR represents hazard ratios.
- P values indicate statistical significance.
<table>
<thead>
<tr>
<th>Population</th>
<th>JNC 8</th>
<th>ACC/AHA</th>
<th>NKF</th>
<th>KDIGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 60 years</td>
<td></td>
<td></td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Age &lt; 60 years</td>
<td>Initial Thiazide diuretic or ACE I or ARB or CCB</td>
<td>Initial Thiazide diuretics</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Diabetics</td>
<td></td>
<td>ACE I or ARB</td>
<td>NA</td>
<td>ACE I or ARB</td>
</tr>
<tr>
<td>With CKD</td>
<td>ACE I or ARB</td>
<td>ACE I or ARB</td>
<td>Thiazide</td>
<td>ACE I or ARB</td>
</tr>
<tr>
<td>With CVD</td>
<td></td>
<td></td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Urine Albumin &gt; 30 mg/24 hrs</td>
<td></td>
<td></td>
<td></td>
<td>ACE I or ARB</td>
</tr>
</tbody>
</table>
Diuretic Handling “Art and science”
Case

• 55 yr old male with history of HTN, CHF, DM and CKD stage 3 (GFR 45 ml/min). BP 156/82 mm Hg, 1+ lower ext edema. He is currently on lisinopril 40 mg

• How do you manage his HTN and edema?
• JNC 8 recommends Thiazide diuretics as the initial choice of drug for patients with diabetes and chronic kidney disease.

• HCTZ:
  – Hypertension: 12.5 to 25 mg once daily.
  – Edema: 25 to 100 mg in 1 or 2 divided doses.

• Chlorthalidone:
  – Hypertension: 25 to 50 mg once daily.
  – Edema: 50 to 100 mg once daily.
Case

• You start HCTZ 25 mg once daily. You see him after 3 weeks. His BP is 132/74 mm Hg, edema has improved. You follow this patient yearly for the next 3 yrs.

• The patient comes back to seen 2 yrs after his last visit. He is complaining of worsening lower extremity edema for the last few months. He is on HCTZ 50 mg once daily. On exam his BP is 140/82 mm Hg, has 2 + pitting edema. Cr is 3.2 mg/dl, GFR 20 ml/min.
Selecting diuretics in patients with CKD

- **Stage 1**: Thiazide
- **Stage 2**: Thiazide
- **Stage 3**: Thiazide → Loop
- **Stage 4**: Loop → Combination
- **Stage 5**: Loop → Combination
Salt restriction

• Salt restriction should be continued, and is a critical step in patients on diuretic therapy.

• Salt restriction: 1.5 to 2 gram sodium restriction is the most important step in managing edema.
How to determine compliance?

• Check 24 urine for sodium excretion.

Important considerations during 24 urine test.
• Make sure it is an accurate 24 hr urine collection.
• Total 24 urine creatinine
  – Males: 20-25 mg/kg
  – Females: 15-20 mg/kg.
• Wait for 5-7 days after starting diuretics or after changing the dose of diuretic.
Interpreting results.

• Total sodium in 24 hour urine collection
  – Greater than 100 meq: The patient is consuming more than 2 grams of sodium per day.
  – Less than 100 meq: Patient is compliant with sodium intake.
Case

• You stop HCTZ and start the patient on lasix 40 mg once daily. He calls you back in 3 days and tells that the swelling is starting to improve. You see him in clinic after a month and the patient tells you that his LE swelling has been worsening for the last 2 weeks.
Frequency of dosing

- Half life of diuretics is relatively short.
- Diuretic concentration is below the therapeutic range for a significant period of the day.
- During this period there is increased Na reabsorption.
Effect of once daily diuretic dosing

U Sodium, mmols/6 hours

U Na, mmol/6h

Daily Na intake 140 meq
Diuretics

<table>
<thead>
<tr>
<th></th>
<th>Onset of action</th>
<th>Peak effect</th>
<th>Duration</th>
<th>Half life</th>
<th>Oral Bioavailability %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>30 to 60 min</td>
<td>1-2 hr</td>
<td>6 hr</td>
<td>0.5 to 2 hr</td>
<td>20-90</td>
</tr>
<tr>
<td>Torsemide</td>
<td>1 hr</td>
<td>1-2 hr</td>
<td>~10 hr</td>
<td>3-4 hr</td>
<td>80-100</td>
</tr>
<tr>
<td>Bumetanide</td>
<td>30 to 60 min</td>
<td>1-2 hr</td>
<td>6 hr</td>
<td>0.5 to 2 hr</td>
<td>80-100</td>
</tr>
<tr>
<td>Metolazone</td>
<td>1 hr</td>
<td>6-8 hr</td>
<td>24 hr</td>
<td></td>
<td>70</td>
</tr>
<tr>
<td>HCTZ</td>
<td>2 hr</td>
<td>4-6 hr</td>
<td>8-12 hr</td>
<td>3 hr</td>
<td>75</td>
</tr>
</tbody>
</table>
How to manage post diuretic Na retention?

• Strict salt restriction
• Increase frequency of diuretic dosing to every 8 hrs to 12 hrs.
• Switch to longer acting loop diuretic like torsemide.

• Acute decompensated heart failure: Consider continuous lasix infusion in patient admitted to the hospital with acute decompensated heart failure.

Case

• You increase frequency of lasix to 40 mg twice daily. Patient call you in 4 days and tells you that that his swelling is not improving, you increase lasix to 3 times a day. When you see the patient in clinic in 3 weeks you notice that the swelling has not improved.
Diuretic dosing in CKD

- In patients with CKD there is significant increase in total body volume increasing the volume of distribution ($V_d$), causing decreased serum concentration of the drug.
- Decreased secretion of the diuretic into the proximal tubule causing decreased drug availability at the site of action.
Diuretic Dose Responsive Curve

- **Normal/Mild CKD**
  - Sodium excretion rate
  - Efficiency
  - Maximal response

- **Advanced CKD**
  - Decreased efficiency
  - Altered dose-response relationship

**Diuretic dose**

- **a**
  - Dose
  - Bioavailability
  - Tubular secretory capacity
  - Rate of absorption
  - Time course of delivery

- **b**
  - Altered dose-response relationship
  - Braking phenomenon
Managing diuretic dosing in CKD

• The diuretic dose that was effective in patient with mild CKD may not be effective in advanced CKD.
• Increasing the frequency of diuretics below the threshold dose is of little or no benefit.
• Double the dose of diuretic till diuresis is achieved or till ceiling dose reached.

Switch to loop diuretics with high bioavailability: Torasemide and Bumetanide.
## Daily ceiling doses for commonly used loop diuretics

<table>
<thead>
<tr>
<th></th>
<th>Furosemide/day</th>
<th>Bumetanide/day</th>
<th>Torsemide/day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV (mg)</td>
<td>PO (mg)</td>
<td>IV (mg)</td>
</tr>
<tr>
<td>GFR 60 to 30ml/min</td>
<td>80</td>
<td>80-160</td>
<td>2-4</td>
</tr>
<tr>
<td>GFR &lt;30ml/min</td>
<td>160</td>
<td>240</td>
<td>8-10</td>
</tr>
<tr>
<td>CHF with normal GFR</td>
<td>80-120</td>
<td>160-240</td>
<td>2-3</td>
</tr>
</tbody>
</table>
Braking Phenomenon
Combination therapy

- Combination therapy with loop diuretic and thiazide like drug are synergistic in patients with CHF and advanced CKD.
- Metolazone 2.5 to 10 mg once daily enhances diuresis in furosemide resistance patients.
- Combination therapy should be started under close observation to avoid hypokalemia.
Conclusion

• Please refer any patient you think could benefit from a nephrology consult

• Or call us with any questions.

• Phone: 732-829-6182
QUESTIONS?