Small feedings of the mind: Nephrology edition
Objectives of this talk

1. To highlight the link between AKI and progression to CKD
2. To discuss the newer agents that have come available for the treatment of hyperkalemia
3. What does the SPRINT trial mean to the internist?
1. Acute kidney injury and Chronic kidney disease: Interconnected syndromes

- AKI and CKD are interconnected
- CKD predisposes to AKI
- AKI is a risk factor for CKD
- Both CKD and AKI are risk factors for cardiovascular disease
AKI and CKD

- Prevalence of AKI is 1-26%
- Incidence of AKI is increasing
- Overlapping risk factors for AKI and CKD
- Most important risk factor for AKI is CKD; risk is increased 10 fold
- AKI is associated with increased risk of mortality
AKI and CKD: Interconnected syndromes

- AKI leads to:
  - new CKD
  - progression of existing CKD
  - an increased long-term risk of end-stage renal disease (ESRD)
  - excess mortality
Pathophysiological Features of Acute Kidney Injury Leading to Chronic Kidney Disease.

Data suggests that few patients with AKI receive follow up care from internists, cardiologists and nephrologists.

Patients with AKI should have periodic assessment of renal function and the urinary albumin-to-creatinine ratio to assess prognosis and outcome after discharge.
Hyperkalemia in CKD: New kids on the block

- Patients with CKD, heart failure or DM treated with RAAS blockers are at increased risk for hyperkalemia
- Patiromer and Sodium zirconium cyclosilicate are two new cation exchange resins that can be used for management of hyperkalemia in CKD.
Study Overview

- In a multicenter placebo-controlled study, patiromer, a nonabsorbable potassium binder, led to a reduction in serum potassium levels in patients with chronic kidney disease and hyperkalemia who were receiving renin–angiotensin–aldosterone system (RAAS) inhibitors.
Serum Potassium Levels over Time during the Initial Treatment Phase


**No. at Risk**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Day 3</th>
<th>Wk 1</th>
<th>Wk 2</th>
<th>Wk 3</th>
<th>Wk 4</th>
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<tr>
<td>Overall</td>
<td>243</td>
<td>217</td>
<td>237</td>
<td>228</td>
<td>221</td>
<td>219</td>
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<tr>
<td>Mild hyperkalemia</td>
<td>92</td>
<td>80</td>
<td>90</td>
<td>87</td>
<td>85</td>
<td>85</td>
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<tr>
<td>Moderate-to-severe hyperkalemia</td>
<td>151</td>
<td>137</td>
<td>147</td>
<td>141</td>
<td>136</td>
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Recurrence of hyperkalemia during the Randomized Withdrawal Phase

A  Time to First Serum Potassium Level ≥5.5 mmol/liter

<table>
<thead>
<tr>
<th>Time to First Serum Potassium Level ≥5.5 mmol/liter</th>
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<tbody>
<tr>
<td>Patients with Recurrent Hyperkalemia (%)</td>
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<td>Time to First Serum Potassium Level ≥5.1 mmol/liter</td>
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<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Placebo</th>
<th>Patiromer</th>
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<tbody>
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<td>Baseline</td>
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<td>8</td>
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<td>32</td>
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</table>

B  Time to First Serum Potassium Level ≥5.1 mmol/liter

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Placebo</th>
<th>Patiromer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
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<td>55</td>
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<tr>
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</table>
This study showed that sodium zirconium cyclosilicate (ZS-9), a highly selective cation exchanger, induces and maintains normokalemia.
Potassium levels during the study

A

B

C

Patients with hyperkalemia who received ZS-9, as compared with those who received placebo, had a significant reduction in potassium levels at 48 hours, with normokalemic maintained during 12 days of maintenance therapy.
SPRINT: The Systolic Blood Pressure Intervention Trial
Randomized control trial of Intensive versus Standard blood pressure control
• Patients at increased cardiovascular risk but without diabetes were assigned to intensive treatment of systolic BP (target, <120 mm Hg) or standard treatment (target, <140 mm Hg).
• Patients with PKD, DM, Stroke and proteinuria > 1gm were excluded.
• After a median of 3.26 years, the rate of cardiovascular events was significantly lower with intensive treatment.
Yet to report....

Progression of CKD in patients with CKD
Incident CKD
Episodes of AKI

Of note: Patients with advanced CKD and proteinuria > 1 gram were excluded from the study
HYVET: Hypertension in the very elderly trial

- 3845 subjects > 80yrs with BP > 160
- Randomized to BP < 150 with diuretic and ACE inh vs placebo
- Average BP in the treated group was 145mm Hg
- Significant reduction in cardiovascular mortality, stroke and heart failure
Hypertension management in CKD

- **ACCORD-BP**
- 4733 patients with DM randomized to BP < 140 vs < 120
- Non significant reduction in primary outcome (cardiovascular death, MI, stroke)
- 2.5 fold increase in serious adverse events
Hypertension management in CKD

- **MDRD and AASK**
- Primary outcome – progression of kidney disease
- 140/90 vs 125/75
- No significant difference
Hypertension management in CKD

- In the meantime......
- Continue hypertension management with RAAS inhibitors with or without diuretics in patients with CKD
- Balance anticipated benefits of therapy with adverse effects
- Careful attention to life style factors including physical activity, sodium restriction, obesity, sleep apnea and alcohol use.
Questions???