An ounce of prevention is worth a pound of cure!

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Residency Program Director
Interim Chief of Nephrology
Department of Medicine
Upstate Medical University
Disclosures
SET GOALS

1. Describe who is at risk
2. Explain the chemistry
3. Review management/prevention
Who gets stones?
Epidemiology: USA

Incidence: ~2/1000
Prevalence: ~100/1000

~180K
# Epidemiology: Gender and Age

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>History of kidney stones, % (95% CI)</th>
<th>History of passing at least one kidney stone, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age group, yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>3.4 (2.1–4.7)</td>
<td>3.4 (2.2–4.7)</td>
</tr>
<tr>
<td>30–39</td>
<td>6.9 (5.0–8.8)</td>
<td>5.9 (4.5–7.2)</td>
</tr>
<tr>
<td>40–49</td>
<td>9.8 (7.3–12.3)</td>
<td>7.6 (5.6–9.5)</td>
</tr>
<tr>
<td>50–59</td>
<td>13.1 (10.3–15.9)</td>
<td>8.1 (5.9–10.3)</td>
</tr>
<tr>
<td>60–69</td>
<td>19.1 (15.9–22.4)</td>
<td>9.4 (6.6–12.2)</td>
</tr>
<tr>
<td>70+</td>
<td>18.8 (16.5–21.0)</td>
<td>9.4 (7.5–11.3)</td>
</tr>
<tr>
<td>All ages</td>
<td>10.6 (9.4–11.9)</td>
<td>7.1 (6.4–7.8)</td>
</tr>
</tbody>
</table>

CI = confidence interval.

Scales, CD et al. EUROPEAN UROLOGY 62 (2012) 160-165
## Epidemiology: Race

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>History of kidney stones, males</th>
<th>History of kidney stones, females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted, % (95% CI)</td>
<td>Adjusted, % (95% CI)</td>
</tr>
<tr>
<td>All groups</td>
<td>10.6 (9.4–11.9)</td>
<td>10.3 (9.2–11.3)</td>
</tr>
<tr>
<td>Non-Hispanic, white</td>
<td>12.8 (11.3–14.3)</td>
<td>11.8 (10.4–13.2)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>7.1 (5.7–8.4)</td>
<td>8.8 (7.4–10.2)</td>
</tr>
<tr>
<td>Non-Hispanic, black</td>
<td>4.5 (3.4–5.6)</td>
<td>4.8 (3.7–5.9)</td>
</tr>
<tr>
<td>Other race/multiracial</td>
<td>5.6 (2.5–8.8)</td>
<td>5.3 (2.2–8.5)</td>
</tr>
</tbody>
</table>

Cl = confidence interval.  

*Scales, CD et. al. EUROPEAN UROLOGY 62 (2012) 160-165*
Epidemiology: Diseases and Drugs
**Epidemiology: Weight**

Family History is Important

Increases your risk 3-fold!
Recurrence is Likely!

- The chance of becoming a repeat stone-former:
  - 10% at 1 year
  - 35% at 5 years
  - 50% at 10 years
Epidemiology: USA

Incidence ≈ 2/1000
Prevalence ≈ 100/1000

Epidemiology: Gender and Age

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>History of family history, % (95% CI)</th>
<th>History of prior history of testicular cancer, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12 (4-20)</td>
<td>15 (5-30)</td>
</tr>
<tr>
<td>Female</td>
<td>18 (7-26)</td>
<td>20 (5-35)</td>
</tr>
</tbody>
</table>

Epidemiology: Race

Epidemiology: Weight

Family History is Important

Recurrence is Likely!

- The chance of becoming a repeat stone-former:
  - 10% at 1 year
  - 35% at 5 years
  - 50% at 10 years

Infects your risk 3-fold!
How are stones formed?
The Chemistry of Stone Formation

Crystallization *will occur*

Metastable Range (this means crystallization is a maybe/maybe not)

Crystallization *will not/can not occur*

Formation Product

Solubility Product /Supersaturation Point

Salt “X”
The Chemistry of Stone Formation

Crystallization will occur

Metastable Range (this means crystallization is a maybe/maybe not)

Crystallization will not/can not occur

Salt “X”

Formation Product

Promoters favor maybe

Inhibitors favor maybe not

Solubility Product /Supersaturation Point
Adding a Promoter

Salt “CaOx”

Formation Product

Ion Activity Product

Solubility Product / Supersaturation Point
Adding an Inhibitor

Salt “CaOx”

Formation Product

Ion Activity Product

Solubility Product / Supersaturation Point
Heterogeneous Nucleation

• Promoters favor maybe

• Inhibitors favor maybe not
Classification of Kidney Stones

Calcareaous (calcium-containing) ~75%

Non-Calcareaous

Radioopaque (by KUB)

Radiolucent (by KUB)

Struvite 8%

Sulfur-containing

Uric Acid 10%

Indinavir

Hypoxanthine

Cystine ~1%

Drugs (Triamterene, Bactrim, etc.)
The Chemistry of Stone Formation

Crystallization will occur: this is termed homogeneous nucleation

Metastable Range (this means crystallization is a maybe/maybe not)

Crystallization will not/can not occur

Formation Product

Solubility Product / Supersaturation Point

Salt “X”

Heterogeneous Nucleation

- Promoters favor maybe

- Inhibitors favor maybe not

Classification of Kidney Stones

- Calcereous (calcium-containing) ~75%
- Non-Calcereous

- Radiopaque (by KUB)
- Radiolucent (by KUB)

- Sulfur-containing
- Uric Acid 10%
- Indinavir
- Hypoxanthine

- Drugs (Thiazides, Oxybutynin, etc.)
How are stones managed?
What We do when it Hurts!
The “3Ps”

**Pain**
- IV isotonic saline – pressure natriuresis
- NSAIDs – analgesic and smooth muscle relaxant
- +/- Alpha Blockers – ureteral dilatation
- Urologic Procedure – intractable pain

**Plugging**
- Infection \(\rightarrow\) Abx + Decompression (stent, nephrostomy)
- AKI \(\rightarrow\) Decompression (stent, nephrostomy)
- Admit and refer to Urology for stone removal

**Passage**
- If unobstructed or obstructed, but not “plugged”:
  - Distal ureteral stone up to 10mm \(\rightarrow\) Alpha Blocker
  - For unpassed stone after 1-2 weeks \(\rightarrow\) Urologic procedure
  - For >10mm stone anywhere \(\rightarrow\) Urologic evaluation
Stone-Former Age<18

Stone-Former with Family History

Recurrent Stone-Former
## Metabolic Evaluation

### Patient Results Report

Values larger, bolder and more towards red indicate increasing risk for kidney stone formation. Be sure to review for further details.

**Stone Risk Factors / Oxyntic Screening**  Negative (11/09/2005)

<table>
<thead>
<tr>
<th>Date</th>
<th>Sample ID</th>
<th>Vol 24</th>
<th>SS CaOx</th>
<th>Ca 24</th>
<th>ox 24</th>
<th>C1r 24</th>
<th>SS CaP</th>
<th>pH</th>
<th>SS UA</th>
<th>UA 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/27/06</td>
<td>44778988</td>
<td>4.65</td>
<td>3.03</td>
<td>329</td>
<td>35</td>
<td>70</td>
<td>1.51</td>
<td>7.068</td>
<td>6.04</td>
<td>1.016</td>
</tr>
<tr>
<td>09/27/06</td>
<td>53711952</td>
<td>3.60</td>
<td>1.07</td>
<td>71</td>
<td>37</td>
<td>56</td>
<td>0.42</td>
<td>7.615</td>
<td>0.06</td>
<td>0.087</td>
</tr>
<tr>
<td>09/27/06</td>
<td>55796960</td>
<td>3.37</td>
<td>1.43</td>
<td>99</td>
<td>41</td>
<td>47</td>
<td>0.99</td>
<td>7.278</td>
<td>0.09</td>
<td>0.026</td>
</tr>
<tr>
<td>09/28/06</td>
<td>55051500</td>
<td>4.60</td>
<td>2.26</td>
<td>269</td>
<td>47</td>
<td>72</td>
<td>1.19</td>
<td>7.358</td>
<td>0.04</td>
<td>1.057</td>
</tr>
<tr>
<td>10/05/06</td>
<td>53957100</td>
<td>4.66</td>
<td>3.10</td>
<td>342</td>
<td>46</td>
<td>73</td>
<td>1.56</td>
<td>7.037</td>
<td>0.04</td>
<td>0.919</td>
</tr>
<tr>
<td>10/05/06</td>
<td>55545158</td>
<td>4.44</td>
<td>3.25</td>
<td>399</td>
<td>46</td>
<td>67</td>
<td>1.57</td>
<td>7.116</td>
<td>0.04</td>
<td>0.878</td>
</tr>
<tr>
<td>11/27/06</td>
<td>53975046</td>
<td>4.73</td>
<td>3.13</td>
<td>371</td>
<td>43</td>
<td>73</td>
<td>1.76</td>
<td>7.227</td>
<td>0.05</td>
<td>0.857</td>
</tr>
</tbody>
</table>

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**Dietary Factors**

<table>
<thead>
<tr>
<th>Date</th>
<th>Sample ID</th>
<th>Na 24</th>
<th>K 24</th>
<th>Mg 24</th>
<th>P 24</th>
<th>Nb 24</th>
<th>CI 24</th>
<th>Sud 24</th>
<th>UN 24</th>
<th>PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/20/06</td>
<td>54710030</td>
<td>351</td>
<td>146</td>
<td>191</td>
<td>1.972</td>
<td>22</td>
<td>236</td>
<td>44</td>
<td>14.65</td>
<td>1.1</td>
</tr>
<tr>
<td>03/20/06</td>
<td>53710381</td>
<td>195</td>
<td>130</td>
<td>161</td>
<td>1.020</td>
<td>34</td>
<td>189</td>
<td>47</td>
<td>14.17</td>
<td>1.0</td>
</tr>
<tr>
<td>03/20/06</td>
<td>53797098</td>
<td>182</td>
<td>111</td>
<td>135</td>
<td>0.978</td>
<td>99</td>
<td>210</td>
<td>40</td>
<td>10.47</td>
<td>0.8</td>
</tr>
<tr>
<td>03/20/06</td>
<td>52059009</td>
<td>233</td>
<td>96</td>
<td>110</td>
<td>1.171</td>
<td>32</td>
<td>189</td>
<td>52</td>
<td>13.60</td>
<td>1.0</td>
</tr>
<tr>
<td>03/20/06</td>
<td>52819129</td>
<td>221</td>
<td>107</td>
<td>150</td>
<td>1.305</td>
<td>37</td>
<td>199</td>
<td>68</td>
<td>13.88</td>
<td>1.0</td>
</tr>
<tr>
<td>10/05/06</td>
<td>51075410</td>
<td>214</td>
<td>128</td>
<td>115</td>
<td>1.363</td>
<td>28</td>
<td>193</td>
<td>50</td>
<td>13.99</td>
<td>1.0</td>
</tr>
<tr>
<td>10/05/06</td>
<td>55574568</td>
<td>236</td>
<td>111</td>
<td>164</td>
<td>1.221</td>
<td>26</td>
<td>222</td>
<td>59</td>
<td>12.06</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**NORMAL RANGE**

- Na 24: 10-250
- K 24: 3.0-11.0
- Mg 24: 5.0-12.5
- P 24: 0.5-1.2
- Nb 24: 15-50
- CI 24: 70-150
- Sud 24: 30-80
- UN 24: 4-14,

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**KIDNEY STONE**
DRINK!!!

Prevention of Calcium Oxalate Stones
Prevention of Calcium Oxalate Stones

**Diet**
- Sodium < 2000mg/day
- Calcium ~1200-1500mg/day
- Reduce Oxalate Intake (?)

**Drugs**
- Thiazide Diuretics
- Potassium Citrate
- Xanthine Oxidase Inhibitors

Blood stream
Diet
Calcium

Sodium < 2000mg/day
Calcium ~1200-1500mg/day

Calcium_i \propto \frac{1}{Oxalate_a}

Borghi, L et al. NEJM. 2002;346:77-84

Von Unruh, GE et al., JASN, 15: 1567–1573, 2004
**Prevention of Calcium Oxalate Stones**

**Diet**
- Sodium < 2000mg/day
- Calcium ~1200–1500mg/day
- Reduce Oxalate Intake (?)

**Blood stream**

**Drugs**
- Thiazide Diuretics
- Potassium Citrate
- Xanthine Oxidase Inhibitors
**Diet**

**Reduce Oxalate Intake (?)**


<table>
<thead>
<tr>
<th>24-h Urine Lithogenic Risk Profile</th>
<th>DASH (n = 21)</th>
<th>Low Oxalate (n = 20)</th>
<th>Point Estimate of Difference (95% CI)</th>
<th>P for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxalate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (mg/d)</td>
<td>49.1 ± 8.5</td>
<td>51.1 ± 12.5</td>
<td>9.0 (-1.1 to 19.1)</td>
<td>0.08</td>
</tr>
<tr>
<td>End of trial (mg/d)</td>
<td>53.9 ± 14.0</td>
<td>47.0 ± 13.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change (mg/d)</td>
<td>4.8 (-1.8 to 11.4)</td>
<td>-4.2 (-12.4 to 4.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate supersaturation</td>
<td></td>
<td></td>
<td>-1.24 (-2.80 to 0.32)</td>
<td>0.08</td>
</tr>
<tr>
<td>Baseline</td>
<td>7.16 ± 3.76</td>
<td>6.28 ± 5.38</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End of trial</td>
<td>4.62 ± 3.11</td>
<td>5.38 ± 2.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change</td>
<td>-2.14 (-3.3 to -0.9)</td>
<td>-0.90 (-1.9 to 0.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Weight-loss surgeries

The surgical technique known as banding promotes weight loss by restricting the amount of food a person can eat. The Roux-en-Y gastric bypass procedure works by restricting absorption of food in the intestines.

Banding
Rubber band is placed around the upper portion of the stomach to limit food consumption

Roux-en-Y gastric bypass
Surgeons staple off a large section of the stomach and reroute the intestine

© 2011 MCT
Source: www.postgradmed.com,
Allergan, stronghealth.com
Graphic: Los Angeles Times

Prevention of Calcium Oxalate Stones

**Diet**
- Sodium < 2000mg/day
- Calcium ~1200-1500mg/day
- Reduce Oxalate Intake (?)

**Blood stream**

**Drugs**
- Thiazide Diuretics
- Potassium Citrate
- Xanthine Oxidase Inhibitors

**Intestinal tract**

**Urinary tract**

**Hydrochlorothiazide Tablets USP**
- 25 mg
Hydrochlorothiazide Tablets, USP

25 mg

Prevention of Calcium Oxalate Stones

Blood stream

Intestinal tract

Drugs
- Thiazide Diuretics
- Potassium Citrate
- Xanthine Oxidase Inhibitors

Urinary tract
Prevention of Calcium Oxalate Stones

**Diet**
- Sodium < 2000mg/day
- Reduce Purine Intake (?)

**Drugs**
- Thiazide Diuretics
- Potassium Citrate
- Xanthine Oxidase Inhibitors
Ettinger, B et.al. NEJM. 1986. 315:1386-1389
A Quick Word About...
# Calcium Kidney Stones and Osteoporosis

Table 2. Twenty-four-hour and fasting urine parameters comparing 3 groups with the ANOVA test

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine clearance (mL/min)</td>
<td>99.86 ± 32.28</td>
<td>114.18 ± 45.27</td>
<td>102.94 ± 33.80</td>
<td>.06</td>
</tr>
<tr>
<td>Calciuria (mg/24 h)</td>
<td>187.34 ± 106.90</td>
<td>269.98 ± 119.49</td>
<td>207.06 ± 98.12</td>
<td>.0001†</td>
</tr>
<tr>
<td>Oxaluria (mg/24 h)</td>
<td>28.21 ± 17.65</td>
<td>29.83 ± 24.41</td>
<td>22.11 ± 16.49</td>
<td>.06</td>
</tr>
<tr>
<td>Citraturia (mg/24 h)</td>
<td>1010.75 ± 647.83</td>
<td>537.72 ± 292.64</td>
<td>617.64 ± 315.86</td>
<td>.0001‡</td>
</tr>
<tr>
<td>Uricosuria (mg/24 h)</td>
<td>540.76 ± 186.20</td>
<td>587.24 ± 222.20</td>
<td>511.91 ± 167.06</td>
<td>.06</td>
</tr>
<tr>
<td>Calcium/creatinine 24 h</td>
<td>0.14 ± 0.06</td>
<td>0.18 ± 0.07</td>
<td>0.17 ± 0.07</td>
<td>.0001‡</td>
</tr>
<tr>
<td>Calcium/citrate 24 h</td>
<td>0.22 ± 0.14</td>
<td>0.63 ± 0.46</td>
<td>0.56 ± 1.08</td>
<td>.001†</td>
</tr>
<tr>
<td>Phosphate tubular resorption 24 h</td>
<td>82.72 ± 6.96</td>
<td>81.24 ± 8.53</td>
<td>83.63 ± 4.82</td>
<td>.13</td>
</tr>
<tr>
<td>Fasting calcium (mg/dL)</td>
<td>9.58 ± 5.07</td>
<td>16.52 ± 8.76</td>
<td>15.14 ± 7.27</td>
<td>.0001‡</td>
</tr>
<tr>
<td>Fasting oxalate (mg/dL)</td>
<td>1.22 ± 0.69</td>
<td>1.48 ± 1.30</td>
<td>1.11 ± 0.68</td>
<td>.07</td>
</tr>
<tr>
<td>Fasting citrate (mg/dL)</td>
<td>50.82 ± 20.43</td>
<td>30.09 ± 15.04</td>
<td>42.32 ± 26.39</td>
<td>.0001*‡</td>
</tr>
<tr>
<td>Fasting uric (mg/dL)</td>
<td>36.65 ± 21.81</td>
<td>31.34 ± 12.70</td>
<td>34.57 ± 18.48</td>
<td>.22</td>
</tr>
<tr>
<td>Fasting calcium/creatinine</td>
<td>0.09 ± 0.03</td>
<td>0.16 ± 0.06</td>
<td>0.16 ± 0.05</td>
<td>.0001‡</td>
</tr>
</tbody>
</table>

* Abbreviation as in Table 1.
† There are significant differences between group 1 vs groups 1 and 3 but not between groups 1 and 3.
‡ There are significant differences between group 1 vs groups 2 and 3 but not between groups 2 and 3.
Kidney Stones and Bone Fracture

Fig. 3. Observed (solid line) and expected (dashed line) cumulative incidence of vertebral fractures among Rochester, Minnesota, residents following the initial episode of symptomatic urolithiasis, 1950 to 1974.

Thiazides + Potassium Citrate on BMD of hypercalciuric kidney stone formers

Prevention of Uric Acid Stones
Prevention of Uric Acid Stones

**Diet**

- Sodium < 2000mg/day
- Reduce Purine Intake (?)

**Blood stream**

**Drugs**

- Urine Alkaliniizers
- Xanthine Oxidase Inhibitors
Diet
Reduce Purine Intake (?)

- Seafood such as shrimp, lobster, shellfish, anchovies, tuna and sardine
- Beer and other alcoholic products
- Animal organ such as liver, kidney
- Carbonated drink
- Red meat such as pork, beef and mutton
Prevention of Uric Acid Stones

**Diet**
- Sodium < 2000mg/day
- Reduce Purine Intake (?)

**Drugs**
- Urine Alkalinizers
- Xanthine Oxidase Inhibitors
Prevention of Uric Acid Stones

Blood stream

Intestinal tract

Urine Alkalinizers

Xanthine Oxidase Inhibitors

Drugs

Urinary tract

Allopurinol Tablets, USP

300 mg

Rx Only
Allopurinol Tablets, USP
300 mg
Rx Only
Who Should Have a Metabolic Evaluation?

Stone-Former Age<18
Stone-Former with Family History
Recurrent Stone-Former

Metabolic Evaluation

Prevention of Calcium Oxalate Stones

Prevention of Uric Acid Stones

DRINK!!!
D R I N K ! ! !

FRUITS And VEGGIES

1st Stone
<18y/o - evaluation a must
Adult - evaluation a maybe
More than One Stone
Any Age - evaluation a must