Urolithiasis: Epidemiology and Prevention

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Urinary calculi are common
Prevalence varies with:
- gender
- race
- geography
Associated with:
- medical diseases
- other conditions

Prevalence of Kidney Stone Disease

1 – 15% Estimated
10 – 15% in US*
Probably increasing*
3.8% 1976 – 1990
5.2% 1988 – 1994

*Norlin et al 1976
Swanson et al 1978
Johnson et al 1979
**Gender in Stone Disease**

The difference may be decreasing * 1997 – 2002

A. Hospital discharges for renal or ureteral calculi  
   ↑ 1.6%  
   Hospital discharges for women  
   ↑ 17%  
   Hospital discharges for men  
   ↓ 8.1%

B. Male – Female ratio *  
   1976 – 1980 1.75  
   1988 – 1994 1.54

*Pearle et al J Urol 173:848, 2005  
*Scales et al 2005  
*Stamatelou et al 2003

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**Race/Ethnicity in Stone Disease**

Among males, nonwhite had lower rates of stone prevalence (% of whites)

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td>70</td>
</tr>
<tr>
<td>Asian</td>
<td>63</td>
</tr>
<tr>
<td>African-American</td>
<td>44</td>
</tr>
</tbody>
</table>

*Soucie et al 1987

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**Gender Difference Varies by Race**

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male:Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>2.3 a 1.6 b 2.6 c</td>
</tr>
<tr>
<td>African American</td>
<td>0.065 a 0.5 b 1.8 c</td>
</tr>
<tr>
<td>Asian</td>
<td>1.8 b 3.4 c</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.7 b 2.1 c</td>
</tr>
</tbody>
</table>

a) Sarmina et al 1987  
b) Michaels et al 1994 (ESWL pt)  
c) Soucie et al 1994 (lifetime incidence)
Changes in First Stone Episodes in Japan – Annual Incidence per 100,000*

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Annual</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>64</td>
<td>76</td>
<td>92</td>
<td>118</td>
<td>192</td>
</tr>
<tr>
<td>Women</td>
<td>24</td>
<td>32</td>
<td>41</td>
<td>46</td>
<td>79</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>53</td>
<td>66</td>
<td>81</td>
<td>134</td>
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</table>

Age Standardized

<table>
<thead>
<tr>
<th>Age Standardized</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>81</td>
<td>29</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>42</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>86</td>
<td>52</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>55</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>165</td>
<td>65</td>
<td>114</td>
</tr>
</tbody>
</table>


Age and Sex Distribution of Hospitalized Pediatric Stone Formers (2003)*

<table>
<thead>
<tr>
<th>Age</th>
<th>Male (%)</th>
<th>Female (%)</th>
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<tbody>
<tr>
<td>0-5</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>6-10</td>
<td>57</td>
<td>43</td>
</tr>
<tr>
<td>11-15</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>16-20</td>
<td>23</td>
<td>77</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>Total #</td>
<td>2042</td>
<td>4722</td>
</tr>
</tbody>
</table>

*Novak et al. Urol 74: 104, 2009

Genetic Factors – Twin Study

Vet Study*
7500 male-male twin pairs
11,959 surveyed
8879 (74.2%) responses
Concordance rate
MZ Twins 32.4%
DZ Twins 17.1% (p<0.001)
Heritability risk 56%
Dietary factors in discordant pairs
to ↓ stones
2-5 cups coffee 1/d – (p<0.01)
3-8 x/wk Rice intake (p=0.03)

*Goldfarb DS et al. Kid Intnl 65:1053, 2005
**Nephrolithiasis in Identical Twins**

1. Cystinuria  
   - **↑** (similar levels)

2. Ca ox  
   - **↑** ca
   - **↑** uric acid

3. Ca ox  
   - **↑** -- ca
   - **↓** cit.

*Haleblian et al. BJU Intl 100: 621, 2007

**Genetic Heritability of Urinary Stone Risk in Identical Twins**

<table>
<thead>
<tr>
<th>Heritability</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>calcium</td>
<td>94</td>
</tr>
<tr>
<td>oxalate</td>
<td>94</td>
</tr>
<tr>
<td>citrate</td>
<td>95</td>
</tr>
<tr>
<td>uric acid</td>
<td>96</td>
</tr>
<tr>
<td>brushite (SS)</td>
<td>90</td>
</tr>
<tr>
<td>uric acid (SS)</td>
<td>58</td>
</tr>
<tr>
<td>U. sodium</td>
<td>64</td>
</tr>
</tbody>
</table>


**Geography**

- ↑ In hot, dry and tropical areas
- In US  
  - ↑ Ca ox in Southeast
  - ↑ uric acid in East
- Ambient temperature - ↑ stones
- Ambient sunlight - ↑ stones

*Mandel & Mandel 1989
Soucie et al. 1996*
Urinary tract stone patients/1000 hospital discharges

Stone Prevalence by Location

Asia 1 – 5%
Europe 5 – 10%
No America 13%

Trinchieri Arch Ital Urol Androl 68: 2006

Seasonal Factors

In US, highest incidence – July-September a
In Australia, highest incidence December-March b
In military personnel ↑ colic in summer c
Among military moving to Kuwait or Iraq stone formation – av 93d d

a Prince and Scardino 1960
b Bateson 1973
c Pierce and Bloom 1945
d Evans et al 2005
Occupation – Hot or Cooler
1) Cooks and engineering room personnel have highest rates of stone in Royal Navy.
2) Steel workers in high temperatures 8%.
3) Glass workers in high temperatures had:
   ↓ Urine volume and pH
   ↑ Uric acid
   ↑ Urine specific gravity
   incidence of uric acid stones 38%.
   a Blacklock 1969
   b Aton et al 2005
   c Borghi et al 1993

Obesity
Weight and BMI are directly correlated with prevalence and incident risk of stone disease.
Can be decreased with high fluid intake in men and women and low protein in take in men.
   a) Curkon et al 1998
   b) Taglar et al 2005

Obesity
Obesity and insulin resistance associated with
1) low urine pH and uric acid stones
Obesity and hyperinsulinemia with
2) hypercalciuria
   a) Maalorf et al 2004
   b) Nowicki et al 1998
Urinary Stones in Crohn’s Disease

Incidence (%)  
- Japan: 3.8 – 12  
- Japan with ileostomy: 2.3  
- Lifetime: (of 10 in normal) 25

*Ishii et al. Intl J Urol 2009

Lithogenic Factors in Crohn’s Disease

↓ volume  
↓ urinary pH  
↓ citric acid  
↓ magnesium  
No ▲ calcium  
uric acid  
oxalate  
After bowel resection  
↑ oxalate


Stone Composition in Crohn’s Disease

Ca oxalate: 56  
Ca ox & ca phos: 13  
Ammonium urate: 31

**Effect of Gastric Bypass on Kidney Stone Disease**

Patient 4639 with Roux-en-Y

4639 obese without surgery

Data from private insurance claims – 5 year period

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Roux-en-Y</th>
<th>Obese</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urolithiasis</td>
<td>7.65%</td>
<td>4.63%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SWL</td>
<td>1.75</td>
<td>0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Uretero</td>
<td>2.11</td>
<td>0.58</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>


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**Urolithiasis in Pregnancy**

Incidence

a) 1/200 – 1/2000
   (1/1500 often cited)

b) Same as age-matched controls

c) ↑ in white and Hispanics

d) 80-90% in 2nd – 3rd trimester

e) NO ↑ rate in stone former

f) No laterality


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**Factors Related to Urinary Calculi During Pregnancy**

Hydronephrosis

R – 90%   L – 67%

Cardiac output ↑ 30 – 50%

Total blood volume ↑ 25-40%

Hypercalciuria and ↑ absorption

Hyperuricosuria

Hypercitraturia

*Pais et al. Urol Clin No Am 34: 2007*
Urinary Stone Composition in Pregnancy*

In 27 Patients
20 (74%) ca phos
7 (24%) ca ox
In 7 prior stone formers
3 ca phos 4 ca ox


Calculi in Weightless Spaceflight*

Inflight stones 1
Post flight 14

*Jones et al. p. 293 in Renal Stone Disease2 and Inst. Physics 2008

Bone Loss Observed in Spaceflight Program*

Vostok - ↑ fecal & urinary ca
Gemini - 2-4% loss of heel bone mass after 4-11 d flight
Apollo - 3-5% loss focal bone mass after 10d
Soyuz - 6-10% bone density specific sites
SkyLab - 1-3% no loss in bone minerals
Mir - 19% loss lumbar spine trabecular bone after 1 year 1 cosmonaut
Shuttle Mir - with countermeasure 5.4% ↓ in bone density in tibia
without countermeasure 1.3 - 1.5% /month
(worst case 15-22% total in some bone)

*Jones et al 2008
**Countermeasure to Ca Loss in Spaceflight**

1. ↑ musculoskeletal loading (resistance exercise)
2. Artificial gravity during transit
3. Use of dietary or pharmaceuticals (vit D, bisphosphonates)
4. ↓ Ca ox and uric acid saturation index with inhibitor (potassium citrate)

*Jones et al 2008

**Medication-Related Stones – Direct Effect**

- Indinavir – relatively insoluble in aqueous solution
  - ↑ below pH 5.5
- Triamterene – rare 0.4% of 50,000 calculi can be incorporated into existing stones
- Guaifenesin and ephedrine – stones of metabolites
- Silica – excreted in urine from foods (vegetables, whole grains, water) and silicate containing antacids

*Pearle et al 2007

**Medication Related Stones - Indirect Effect**

- Hypercalciuria – corticosteroids, vitamin D, phosphate binding antacids, furosemide and bumetamide
- Urinary alkalinization - carbonic anhydrase inhibitors
  - acetozolamide, topiramate
- ↑ Ammonia – laxatives
- ↑ Uric acid – cytotoxic agents

*Pearle et al 2007
Melamine Pediatric Nephrolithiasis

Melamine - organic base, 66% nitrogen by mass (1,3, 5 –triazine – 2,4,6 triamine)
- 14% powdered milk formulas in China affected
- Form crystals in urinary tract
- Radiolucent calculi with uric acid
- ↑ fluid
- Alkalization

Ding J. Kidney Int 75: 780, 2009
Guan N et al. NEJ Med 360: 1067, 2009

CONSERVATIVE MANAGEMENT: “STONE CLINIC EFFECT”

• CONSIDER BEFORE MEDICAL MANAGEMENT
• DIET AND LIFESTYLE MODIFICATIONS
  – HYDRATION: URINE OUTPUT > 2500 CC PER DAY
  – LIMIT SODIUM: 2300 – 3300 MG PER DAY
  – LIMIT RED MEAT: NO MORE THAN 6 – 8 oz PER DAY
  – LIMIT OXALATE
  – NORMAL CALCIUM: 800 – 1200 MG PER DAY

Urinary Stone Prevention

↑ fluid
↓ salt
↓ protein
avoid excess oxalate