Ureteroscopy and Ureteral Stents: Is ESWL on the Decline?

Ben H. Chew MD, MSc, FRCSC

Outline

• Ureteral stones
  – Expulsive therapy
  – Shockwave lithotripsy
  – Ureteroscopy
  – Proximal vs distal ureteral stones
• Ureteral stent use
  – Stent vs no stent
• Antimicrobial stent
• Stone prevention: Hyperoxaluria treatment
Spontaneous Passage Rates according to Stone Size

Spontaneous Passage Rates according to Stone Location
Management of Ureteral Calculi
AUA Guidelines Panel (1997)

• Goal:
  – To make practice policy recommendations for the treatment of ureteral calculi based on treatment outcomes data.

• Review of literature (1966 to Jan. 1996)
• Data meta-analyzed to produce outcome estimates for alternative treatments of ureteral stones.

AUA Ureteral Stones Guidelines Panel

Proximal Ureter:
SWL- recommended as first line treatment for proximal stones (≤ 1 cm).
Ureteroscopy- acceptable alternative when SWL not appropriate or as salvage procedure.

Distal Ureter:
SWL or Ureteroscopy Acceptable
AUA Ureteral Stones Guidelines Panel

- ~ 98% of stones < 0.5 cm spontaneously pass (especially in distal ureter)
- Open surgery should be last resort
  - Very large ureteral stones
  - Nonstandard situations
- Blind basketting is not acceptable
- Proximal stones > 1 cm
  - SWL
  - PNL
  - Ureteroscopy (dec. success if large stone)

Medical Therapy to Aid Spontaneous Stone Passage

<table>
<thead>
<tr>
<th></th>
<th>Corticosteroid + Tamsulosin</th>
<th>Corticosteroid + Nifedipine</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to Stone Passage</td>
<td>7.9 days*</td>
<td>9.3 days*</td>
<td>12 days</td>
</tr>
</tbody>
</table>

- Steroid to reduce edema
- Ca^{2+} channel / α₁ blocker inhibit ureteral spasm

Porpiglia J Urol 172:568, 2004
Results of Expulsive Therapy

<table>
<thead>
<tr>
<th>Author</th>
<th>Agent(s)</th>
<th>Agent(s)</th>
<th>Agent(s)</th>
<th>Recommend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borghi, J Urol 1994 N=86</td>
<td>Prednisolone + nifedipine</td>
<td>Prednisolone + placebo</td>
<td></td>
<td>Steroid + Ca++ blocker</td>
</tr>
<tr>
<td></td>
<td>87% / 11.2d</td>
<td>65% / 16.4d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dellabella J Urol 2003 N=60</td>
<td>Tamsulosin</td>
<td>floroglucine-trimetossibenzene (anti-spasmodic)</td>
<td></td>
<td>Tamsulosin</td>
</tr>
<tr>
<td></td>
<td>100% 2.75d</td>
<td>70%: 4.6 d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dellabella J Urol 2005 N=210</td>
<td>Phloroglucinol</td>
<td>Tamsulosin</td>
<td>Nifedipine</td>
<td>Tamsulosin</td>
</tr>
<tr>
<td></td>
<td>64% 5 d</td>
<td>97% 3 d</td>
<td>77% 5 d</td>
<td></td>
</tr>
<tr>
<td>Dellabella Urology 2005 N=60</td>
<td>Tamsulosin</td>
<td>Corticosteroid</td>
<td>Tamsulosin + Steroid ↓ time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>90% 5 d</td>
<td>97% 3 d</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Proximal Ureteral Stones: Shockwave Lithotripsy

Pros and Cons of Shockwave Lithotripsy

**SWL Pros**
- Least invasive
- Avoid general anesthetic
- Outpatient procedure
- Low complication rate

**SWL Cons**
- Stone-free rates ~ 80% but not as high as ureteroscopy
- Higher re-treatment / ancillary procedure rates - higher cost
- Not available in every centre
Shockwave Lithotripsy
Upper Ureteral Stones - Results

• Stone-free rates:
  – 50 to 90%
  – Re-treatment rates
  – Ancillary treatment rates
    • 10-30%

Proximal Ureteral Stones - SWL
How Many Re-Treatments are Reasonable?

• Pace et al (Toronto)
  – Determined # of SWL treatments that should be given for a single ureteral stone before other modalities are used.
  – Compared SFR of initial SWL with SFR of re-treatments (Dornier MFL 5000).

Pace J UROL 164(6):1905, 2000
### Shockwave Lithotripsy
#### Upper Ureteral Stones - Results

**Stone-Free Rate after SWL for Ureteral Stones**

<table>
<thead>
<tr>
<th>Machine Type</th>
<th>Initial Tx</th>
<th>Re-tx #1</th>
<th>Re-tx #2</th>
<th>Re-tx #3 or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dornier U30</td>
<td>1086/1593</td>
<td>126/273</td>
<td>19/61</td>
<td>13/39</td>
</tr>
<tr>
<td>Schmidt J Endo 1995</td>
<td>(68%)</td>
<td>(46%)</td>
<td>(31%)</td>
<td>(33%)</td>
</tr>
<tr>
<td>Lithostar 54 Ahlawat J Urol 1991</td>
<td>1086 (68%)</td>
<td>1212 (76%)</td>
<td>1231 (77%)</td>
<td>1245 (78%)</td>
</tr>
</tbody>
</table>

**Results of Re-Treatment of Upper Ureteral Stones with SWL**

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts.</th>
<th>Machine Type</th>
<th>SFR Initial</th>
<th>SFR-ReTx#1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim J Endo 1996</td>
<td>220</td>
<td>Lithostar</td>
<td>65%</td>
<td>48%</td>
</tr>
<tr>
<td>Mishriki BJU 1992</td>
<td>123</td>
<td>Lithostar</td>
<td>72%</td>
<td>58%</td>
</tr>
<tr>
<td>Voce Scand JUN 1993</td>
<td>247</td>
<td>Dornier MFL 9000</td>
<td>77%</td>
<td>80%</td>
</tr>
<tr>
<td>Ahlawat J Urol 1991</td>
<td>54</td>
<td>Lithostar</td>
<td>59%</td>
<td>49%</td>
</tr>
<tr>
<td>Schmidt J Endo 1995</td>
<td>130</td>
<td>Dornier U30</td>
<td>77%</td>
<td>67%</td>
</tr>
</tbody>
</table>

Pace J UROL 164(6):1905, 2000
**Shockwave Lithotripsy**  
*Upper Ureteral Stones - Results*

- Stone-free rate after one treatment not as good as ureteroscopy, BUT
  - Treatment is non-invasive
  - Does not require general anesthesia
  - Will make 70-80% of patients stone-free after 1-2 treatments.
- Recommendation: If first SWL fails, perform ancillary procedure

**Proximal Ureteral Stones:**  
Ureteroscopy
Pros and Cons of Ureteroscopy

**Ureteroscopy Pros**
- Close to 100% stone-free rates
- Negligible re-treatment rates
- Less costly
- Available to most urologists

**Ureteroscopy Cons**
- More invasive
- Higher complication rate i.e. strictures, sepsis
- Need for a general anesthetic

### Early Ureteroscopy Stone Free Rates by Stone Location (%)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Ureter</td>
<td></td>
<td>50</td>
<td>33</td>
<td>50</td>
<td>22</td>
<td>60</td>
<td>_</td>
<td>58</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td></td>
<td>83</td>
<td>66</td>
<td>80</td>
<td>75</td>
<td>67</td>
<td>71</td>
<td>36</td>
</tr>
<tr>
<td>Lower Ureter</td>
<td></td>
<td>96</td>
<td>90</td>
<td>95</td>
<td>94</td>
<td>97</td>
<td>99</td>
<td>84</td>
</tr>
</tbody>
</table>

**Terrible Stone Free Rates in the Upper Ureter!**
## Ureteroscopy: Effect of Instrumentation

<table>
<thead>
<tr>
<th>Year</th>
<th>Endoscopes</th>
<th>Lithotriptors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>Rigid</td>
<td>U/S, 5F EHL</td>
</tr>
<tr>
<td>1990</td>
<td>10F Flexible</td>
<td>3F EHL, 60mJ Pulsed Dye Laser</td>
</tr>
<tr>
<td>1996</td>
<td>7F Rigid, 7.5F Flexible</td>
<td>1.6 - 1.9F EHL</td>
</tr>
<tr>
<td>1999</td>
<td>6.9F Rigid, 7.5F Flexible</td>
<td>Holmium Laser</td>
</tr>
</tbody>
</table>

Bagley, 2002
CIRCON-ACMI DUR8-E Ureteroscope

Deflection Range

Intracorporeal Lithotriptors

Pneumatic

Electrohydraulic

Ultrasonic

Laser: Holmium, Pulsed Dye
Holmium Laser
Advantages

• Fragments stones of all composition

• Can be used with rigid or flexible instruments

• Short learning curve

• Absorption of radiation in water decreases surrounding tissue damage

Ureteral Access Sheaths

• Provide a continuous working channel

• Ureteral access sheaths (UAS):
  – Easy scope insertion (less buckling)
  – Repeated removal/insertion (basketting)
  – Ureteral dilation (Kourambas)
  – Improved irrigation/visualization
  – Decreased renal pelvis pressure (Auge)
  – Less scope damage (Preminger)
Ureteral Access Sheaths & Ureteroscopy: Does it Affect the Stone Free Rate?

A Prospective Randomized Controlled Clinical Trial

Ben H. Chew - UWO
Kenneth T. Pace – U of T
Jim Watterson – U of Ottawa
Darren T. Beiko – Queen’s
Ryan F. Paterson - UBC
Joel Teichman - UBC
Timothy Wollin – U of Alberta
John D.A. Honey - U of Toronto
Stephen E. Pautler - UWO
John D. Denstedt - UWO
Hassan Razvi - UWO

N=82

<table>
<thead>
<tr>
<th></th>
<th>SWL</th>
<th>URS+ laser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Stone size</td>
<td>1.28 cm</td>
<td>1.5 cm</td>
</tr>
<tr>
<td>Stone Free Rate</td>
<td>61%</td>
<td>92%</td>
</tr>
</tbody>
</table>

Recommendation: Ureteroscopy first line therapy for proximal ureteral stones > 1 cm

Wu J Urol 172:1899, 2004
Holmium:YAG vs ESWL for Proximal Ureteral Calculi

Lam and associates

- 81 pts with proximal stones treated as outpatients
- Calculi > 1cm
  - 93% stone-free with Holmium:YAG
  - 50% stone-free with ESWL
- Calculi < 1cm
  - 100% stone-free with Holmium:YAG
  - 80% stone-free with ESWL
- No major complications in either cohort


- February 1993 – December 1999
- 598 patients (1042 stones)
- Age range 4 - 93 yr
  - mean: 53 yr

UPJ
11%

Proximal
22%

Mid
11%

Distal
56%
Results

<table>
<thead>
<tr>
<th>Location</th>
<th>Ave size (mm)</th>
<th>Stone free (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal Ureter</td>
<td><strong>10.3 ± 4 (3-29)</strong></td>
<td>232 / 237 (98)</td>
</tr>
<tr>
<td>Mid Ureter</td>
<td><strong>10.6 ± 3.2 (5-20)</strong></td>
<td>111 / 111 (100)</td>
</tr>
<tr>
<td><strong>Upper Ureter</strong></td>
<td><strong>12.1 ± 5.2 (4-35)</strong></td>
<td>188 / 194 (97)</td>
</tr>
<tr>
<td>Intrarenal</td>
<td><strong>13.3 ± 6.8 (5-30)</strong></td>
<td>47 / 56 (84)</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>11.3 ± 4.6 (3-35)</strong></td>
<td>580 / 598 (97)</td>
</tr>
</tbody>
</table>

Sofer J Urol 167:31, 2002

Role of Flexible URS and Laser Lithotripsy of Upper Ureteral Stones at University of Western Ontario

- Salvage of failed ESWL
- Primary therapy if:
  - Cystine
  - Obese (>300 lbs)
  - Multiple proximal ureteral stones
  - >1 cm
  - Radiolucent stone
  - Patient preference
Distal Ureteral Stones: Shockwave Lithotripsy versus Ureteroscopy

Ureteroscopy Results
University of Western Ontario

<table>
<thead>
<tr>
<th>Location</th>
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<td>11.3 ± 4.6 (3-35)</td>
<td>580 / 598 (97)</td>
</tr>
</tbody>
</table>

Sofer J Urol 167:31, 2002
### Distal Ureteral Stones - Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts.</th>
<th>Machine</th>
<th>SFR SWL</th>
<th>SFR URS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearle, J Urol 2001</td>
<td>64</td>
<td>HM-3</td>
<td>97%</td>
<td>97%</td>
</tr>
<tr>
<td>Peschel, J Urol 1999</td>
<td>80</td>
<td>MFL-5000</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>Turk, J Urol 1999</td>
<td>187</td>
<td>HM-3 or MFL-5000</td>
<td>73%</td>
<td>95%</td>
</tr>
<tr>
<td>Paralidis, J Endo 1999</td>
<td>1,028</td>
<td>Lithostar</td>
<td>93%</td>
<td>92%</td>
</tr>
<tr>
<td>Eden, J Endo 1998</td>
<td>404</td>
<td>SL-20</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>Park, J Endo 1998</td>
<td>442/115</td>
<td>MPL 9000</td>
<td>80%</td>
<td>88%</td>
</tr>
<tr>
<td>Chang, J Endo 2001</td>
<td>524/430</td>
<td>Lithostar</td>
<td>87%</td>
<td>96%</td>
</tr>
<tr>
<td>Strohmaier, Eur Urol 1999</td>
<td>146</td>
<td>70%</td>
<td>95%</td>
<td></td>
</tr>
</tbody>
</table>

### Distal Ureteral Calculi SFR by Size

![Bar chart showing stone free rate (%) for different sizes of calculi using URS and SWL methods](chart)

**Chang, J Endourol, 2001**
**Distal Ureteral Stones**

**SWL vs Ureteroscopy (URS)**

- **Recommendations:**
  - Dependent on stone size
  - Either SWL or URS acceptable if < 1 cm
  - Recommend ureteroscopy if size > 1 cm
    - Known hard composition
    - Failed SWL x 1
  - URS is more cost effective
To Stent or Not to Stent: That is the Question

• Routine stents = standard of care
  – renal colic
    • balloon dilatation or
    • ureteral manipulation
  – aid in stone passage
  – facilitates outpatient care

Hosking et al, 1999

• No stent placed in 93 pts after ureteroscopy for distal stones (82/93 pts had balloon dilation)
• All followed prospectively for post-op pain:

_Routine placement of a ureteric stent following ureteroscopy for of distal ureteric calculi is not necessary_
• 58 Patients enrolled prospectively
• Surgery:
  – 6.9F rigid or 7.5F flexible ureteroscope
  – holmium laser or electrohydraulic lithotripsy
  – patient randomized if procedure uncomplicated

• All patients followed at one, six and twelve weeks post-operatively:
  – Stented patients have stents removed at first visit with flexible cystoscopy

**Post-operative Symptoms (one week)**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Stent</th>
<th>No Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flank Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abd Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* * p = 0.001

* Student’s t-test
Post-operative Symptoms (six weeks)

<table>
<thead>
<tr>
<th>Flank Pain</th>
<th>Abd Pain</th>
<th>Dysuria</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*p = NS

* Student t test

Conclusion

Ureteral stenting following ureteroscopy and intracorporeal lithotripsy is not necessary if:
- no ureteral dilatation performed
- no ureteral injury / edema
- atraumatic lithotripsy device (Holmium:YAG laser)
- small stone burden
### Stone-Free Rate

<table>
<thead>
<tr>
<th>Authors</th>
<th># of Pts Stent / No Stent</th>
<th>Stent</th>
<th>No Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denstedt et al, 2001</td>
<td>29 / 29</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Netto et al, 2001</td>
<td>133 / 162</td>
<td>98.5%</td>
<td>97.5%</td>
</tr>
<tr>
<td>Borboroglu et al, 2001</td>
<td>53 / 54</td>
<td>99.1% (Overall)</td>
<td></td>
</tr>
<tr>
<td>Chen et al, 2002</td>
<td>30 / 30</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Cheung et al, 2003</td>
<td>29 / 29</td>
<td>97% (IVP)</td>
<td>97% (IVP)</td>
</tr>
</tbody>
</table>

### Pain / LUTS

<table>
<thead>
<tr>
<th>Authors</th>
<th># of Pts Stent / No Stent</th>
<th>Flank Pain</th>
<th>LUTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denstedt et al, 2001</td>
<td>29 / 29</td>
<td>↑ in stented</td>
<td>↑ in stented</td>
</tr>
<tr>
<td>Borboroglu et al, 2001</td>
<td>53 / 54</td>
<td>↑ in stented</td>
<td>↑ in stented</td>
</tr>
<tr>
<td>Byrne et al, 2002</td>
<td>38 / 22 (renal units)</td>
<td>↑ in stented</td>
<td>↑ in stented (day 6 only)</td>
</tr>
<tr>
<td>Chen et al, 2002</td>
<td>30 / 30</td>
<td>No difference</td>
<td>↑ in stented</td>
</tr>
<tr>
<td>Cheung et al, 2003</td>
<td>29 / 29</td>
<td>↑ in stented (overall pain)</td>
<td>↑ in stented</td>
</tr>
</tbody>
</table>

*p ≤ 0.05 for all groups*
### OR Time / Cost

<table>
<thead>
<tr>
<th>Authors</th>
<th># of Pts Stent/No Stent</th>
<th>OR Time</th>
<th>Additional Cost of Stenting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denstedt et al, 2001</td>
<td>29 / 29</td>
<td>No difference</td>
<td>NA</td>
</tr>
<tr>
<td>Netto et al, 2001</td>
<td>133 / 162</td>
<td>Stenting = ↑ 19 min</td>
<td>$1607.64</td>
</tr>
<tr>
<td>Byrne et al, 2002</td>
<td>38 / 22 (renal units)</td>
<td>Stenting = ↑ 12 min</td>
<td>$750.00</td>
</tr>
<tr>
<td>Cheung et al, 2003</td>
<td>29 / 29</td>
<td>No difference</td>
<td>NA</td>
</tr>
</tbody>
</table>

### Admissions/Secondary Stent Insertion

<table>
<thead>
<tr>
<th>Authors</th>
<th># of Pts Stent / No Stent</th>
<th>Readmission (%) Stent / No Stent</th>
<th>Secondary Stent Insertion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denstedt et al, 2001</td>
<td>29 / 29</td>
<td>3.4 / 0</td>
<td>0</td>
</tr>
<tr>
<td>Borboroglu et al, 2001</td>
<td>53 / 54</td>
<td>0 / 7.4</td>
<td>3.7</td>
</tr>
<tr>
<td>Byrne et al, 2002</td>
<td>38 / 22 (renal units)</td>
<td>2.6 / 9.1</td>
<td>4.5</td>
</tr>
<tr>
<td>Chen et al, 2002</td>
<td>30 / 30</td>
<td>0 / 0</td>
<td>0</td>
</tr>
</tbody>
</table>
Ureteroscopy and Stenting: Considerations

- Stone-free rates
- Patient pain and voiding symptoms
- Re-admissions
- Delayed stenting
- Stricture formation
- Cost

% of Ureteroscopies with Stent Insertion at the University of Western Ontario
Stent Related Problems

- LUTS
- Pain
- Hematuria
- Reflux
- Migration
- Infection
- Stent Fracture
- Stent Occlusion
- Encrustation
- Ureteral erosion
- Ineffective drainage
- Forgotten stent….renal damage

Triclosan

- Inhibits bacterial fatty acid synthesis (membrane destabilizer)
  - Acyl-Carrier Protein reductase highly conserved
- Gram +/- organisms
- Bacterio-static/-cidal

- Used in:
  - Mouthwashes
  - Toothpastes
  - Soaps
  - Surgical scrubs
  - Cutting boards
  - Children’s toys
  - Vicryl suture
Antimicrobials diffuse out of stent and elute into urine

Dead Bacteria

Triclosan Eluting Stent

Urine diffuses into polymer

Bacteria

Antimicrobials diffuse out of stent and elute into urine

Triclosan Eluting Stent

Dead Bacteria
Objectives

- To test triclosan loaded-ureteral stents against 6 common bacterial uropathogens \textit{in vitro}
  - Assess bacterial growth in artificial urine
  - Assess bacterial adherence to ureteral stents
    - Biofilm
    - Viable bacteria
- **HYPOTHESIS**: that triclosan ureteral stents would be effective against bacterial uropathogens*
Methods

• **Growth Inhibition Assay**
  – Triclosan stents tested *in vitro* against 6 common uropathogens:
    • *Escherichia coli*
    • *Proteus mirabilis*
    • *Staphylococcus aureus*
    • *Klebsiella pneumoniae*
    • *Enterococcus faecalis* *
    • *Pseudomonas aeruginosa* *
  – Triclosan eluted from stents for 24 h, diluted, and combined with bacteria
  – Spectrophotometry to measure optical density (ie bacterial growth)
  – Agar plating to confirm growth

Methods: Bacterial Growth

- Artificial urine + Triclosan stent → 37°C X 24 hours
- Eluate diluted
- Control
- Bacteria
- Spectrophotometer (600 nm) 37°C Measure growth q1h x 24 h
- 96 well plate triplicate
**Results**

**Staphylococcus aureus**

**Klebsiella pneumoniae**

**Proteus mirabilis**

**E. coli**

*Natural resistance due to triclosan efflux pump*
Methods: Bacterial Adherence and Biofilm Assay

- Assess bacterial growth and viability in stent biofilm

37°C X 24 hours

\[ \text{Stent} + \text{bacteria} \rightarrow \text{Stent washed w/ saline to remove loose bacteria} \rightarrow \text{Scanning Electron Microscopy} \rightarrow \text{Agar plating: Bacterial viability} \rightarrow \text{Fluorescence Microscopy} \]

*GFP expressing E.Coli (fluoresces green)

- Triclosan had decreased adherent bacteria AND these were NOT viable on culture.
- Triclosan stents may avoid providing a nidus for infection.

SEM of Stent Biofilms

Control stent

Triclosan stent

\[ \text{S. aureus embedded in biofilm: Viable} \quad \text{Less embedded S. aureus in biofilm: Dead} \]

- Triclosan had decreased adherent bacteria AND these were NOT viable on culture.
- Triclosan stents may avoid providing a nidus for infection.
**E. coli Stent Adherence**

*green fluorescence = E. coli binding*

**Control stent**

**Prior to Incubation**

**After Incubation**

**Triclosan stent**

**ompX Promoter Activity**

**ompA Promoter Activity**

**papA Promoter Activity**
Summary

- Triclosan prevents growth and stent adherence in susceptible common uropathogenic bacteria
- Less bacterial adherence and viability of bacteria on triclosan stents
- Triclosan may prevent stents from being a nidus for infection
- Triclosan reduce virulence factors in *E. coli*
- Current research:
  - Clinical trial underway:
    - Will triclosan stents reduce stent-related UTI?
    - Reduce stent biofilm formation and encrustation?

*Best Scientific Paper: World Congress Endourology, Amsterdam, 2005

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**Oxalate Degradation By Recombinant Lactic Acid Bacteria: The Basis For a New Probiotic Treatment of Hyperoxaluria**

Ben H. Chew, Peter A. Cadieux, Gregor Reid, John D. Denstedt, John K. McCormick

*Best Abstract Prize: AUA, 2005*  
San Antonio (Stone Disease)
Oxalate

- Organic compound
- Toxic byproduct of metabolism (difficult to catabolize)
- Strong chelator of cations (esp \( \text{Ca}^{2+} \))
- High concentrations = death (corrosive effects)
  - Various pathology:
    - Hyperoxaluria
    - Pyridoxine deficiency
    - Cardiomyopathy
    - Calcium oxalate stones (85% stones: calcium oxalate)
    - Renal failure
- In most foods in various concentrations

Food High in Oxalate

- Tea
- Peanuts
- Spinach
- Chocolate
- Cocoa
- Rhubarb
- Beetroots
**Oxalobacter formigenes**

- **Oxalobacter formigenes**
  - Total dependence on oxalate as an energy source
  - Regulates intestinal oxalate absorption
- Colonizes GI tract of vertebrates
- Degrades oxalate via 3 genes:
  1. Ox1T
  2. frc
  3. oxc
Introduction

- Hyperoxaluria = ↑ risk of CaOx stones

Endogenous metabolism of Glycine, Glyoxylate, Ascorbic acid

Oxalate absorbed in bloodstream

Excreted in feces

50-80% oxalate

Breakdown in colon by *Oxalobacter formigenes*

Excreted in feces

Hyperoxaluria

Oxalate absorbed in bloodstream

Excreted in feces
Oxalobacter formigenes

- O. formigenes present in:
  - 65% non-stone formers (controls)
  - 30% CaOx stone formers
    - > 3 stones, 6% colonized with O. formigenes
- Reduced colonic O. formigenes = hyperoxaluria
  - (Sidhu et al, Lancet 352:1026, 1998)
- Hyperoxaluric rats fed O. formigenes = ↓ urinary oxalate
- Less O. formigenes = More stones

Why not oral Oxalobacter formigenes?

Oxalobacter formigenes
- Not found in commercial products
- Strict anaerobe (difficult to culture)
- Good GI colonizer
- Not approved for human consumption

Lactobacillus
- Consumed daily worldwide
- found in yogurts, sauerkraut, fermented milk (GRAS)
- Easy to grow
- Good GI colonizer
- Genome sequenced

BUT..... lactobacilli do NOT degrade oxalate
**Purpose:** Construct a *Lactobacillus* That Degrades Oxalate

- *O. formigenes* oxalate degradation complex (3 genes)
- *Bacillus subtilis* = 1 gene (*yvrK*) for oxalate degradation
- Goal: clone *yvrK* gene into *L. plantarum* to express oxalate decarboxylase
  - To test oxalate degradation *in vitro*

**Cloning Method**

- *Bacillus subtilis*
  - PCR
  - *YvrK* gene amplified
- *Lactococcus lactis* – 1st
- *Lactobacillus plantarum*
  - Control
  - Clone expressing oxalate decarboxylase
  - *YvrK* gene cloned
**In vitro Oxalate Degradation**

L. Lactis w/ yvrK + nisin promoter

Stimulate promoter (0 – 10 ng/ml nisin) = oxalate decarboxylase production (YvrK)

Lyse cells to release oxalate decarboxylase

Incubate w/ oxalate 0 - 60 minutes

Measure remaining oxalate

**Results**

![Graph showing oxalate remaining over time with different nisin concentrations](image)
Discussion

• Genetic clone of oxalate decarboxylase to degrade oxalate \textit{in vitro}
• \textit{In vivo} effects?
• Currently:
  – Transformed into \textit{Lactobacillus plantarum}
  – Constitutive promoter (constantly ‘on’)
  – Testing in hyperoxaluric rats
  – Clinical testing in future

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