Infection Control in Dialysis
Dr. Charmaine Lok, University of Toronto
A Webber Training Teleclass

Overview
- Focus on hemodialysis catheter-related infections
  - Background
  - Pathogenesis & Risk Factors
  - Epidemiology - Clinical studies
  - Management
- HICS
- Conclusions

Infection
- Most common cause of morbidity
- 2nd most common cause of death
- 75% of infectious deaths due to bacteremia
- Vascular access = main source of bacteremia
- Central venous catheters (CVC) = highest risk
- ≈ 50% with have CRB by 6 mos
- Sepsis related hospitalizations ↑50% (decade)
- Cost = $22 000 USD /bacteremia
- Multiple organisms involved

Pathogenesis
- Staphylococcus Aureus
  - Binds to nasal mucoproteins
  - Produces glycocalyx
  - Toxins lead to abscess formation
  - Much more toxic than S. epidermidis

Distribution of Culprit Organisms
- Majority are Gram Positive organisms

Staphylococcus Aureus
- Binds to nasal mucoproteins
- Produces glycocalyx
- Toxins lead to abscess formation
- Much more toxic than S. epidermidis

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Staphylococcus Epidermidis

- Common organism that colonizes skin
- Less toxic than S. aureus
- Enveloped by amorphous slimy material
- Host serum proteins aid in production
- Biofilm provides environment for increased bacterial growth

Pathogenesis

Sources of infection:
- Skin contamination (early)
- Hub contamination (later)
- Hematogenous seeding (uncommon)
- Infected infusate (rare)

Extraluminal: Skin contamination

Bacteria from exit site track down the catheter into the catheter tip

Quantitative skin cultures show increased risk of infection with increased cfu/cm²

Bertone S, Inf Cont Hosp Epi 1994
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Intraluminal: Hub contamination

Later Infection

- Caused by touch/hub contamination
- Develops later in course
- Frequent problem with hemodialysis catheters

Biofilm on a Catheter

Biofilms

“SCURF” and “Animalculi”

Anton van Leeuwenhoek

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The Biofilm Micro-cosm

Lessons from Peritoneal Dialysis
- Instructions for PD exchange & catheter access:
  - Remove pets
  - Shut door
  - Put on mask
  - Cut off circulating air – cover or close vents
  - Wash hands for 3 minutes
- What precautions do your nurses, technicians, patients and colleagues follow in the Hemodialysis unit?

Epidemiology

Staphylococcal Infection
- Annual incidence of SA bacteremia ≈ 6.2%
- S. aureus bacteremia in HD ≈ 0.6/1000 days
- 23% hospitalized in ICU
- 21% require re-admission within 3 months
  - 70% of due to recurrent bacteremia
- Death at 12 weeks: 13%, 2%
- 88%: Vascular access is the source of bacteremia
- Avg Cost = $22 000 / uncomplicated bacteremia
- Avg Cost = $32 000 / complicated bacteremia
- Costs and complications increase when MRSA +ve

Staphylococcal Infection
<table>
<thead>
<tr>
<th>Complication</th>
<th>SA</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>Infective endocarditis</td>
<td>17%</td>
<td></td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Septic Arthritis</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Septic Emboli</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Mortality (12 weeks)</td>
<td>19%</td>
<td>35%</td>
</tr>
</tbody>
</table>

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US HD Patient Mortality 2002-2003

- Annual mortality 23.5 /100 pt-years
- Cardiac arrest 5.5
- Septicemia 2.6
- MI 1.9
- Stroke 1.2

Table H.29 Unadjusted Mortality, USRDS 2005 Annual Report

Mortality & Bacteremia

- In the USA in 2004
- 308000 HD patients
- Catheter rate ≈25% (now 1/3)
- 81,000 pts with CVC
- CRB rate average 2/1000 days (0.5-5.5/1000 days)
  - (0.73 infection/pt year)
- Mortality from bacteremia 10% (up to 20%)
- 5913 deaths/year from bacteremia

Mortality and Sepsis

- Mortality and Sepsis: 393,451 patients
- MI → Sepsis → No Sepsis
- Adjusted Mortality Rate (per 100 patient-years)
- N=393,451

Foley et al., JASN 15:1038, 2004

Morbidity, Cost, Mortality

- USRDS retrospective study (1996-2001)
- S. aureus vs. other bacteria
- 11,572 S. aureus admissions

<table>
<thead>
<tr>
<th>S. Aureus</th>
<th>Other</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 ± 13</td>
<td>9 ± 10</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cost (index admission)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$17,307</td>
<td>$15,965</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.5%</td>
<td>3.8%</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Nissenson AR, AJKD 2005

Increase in Staphylococcal Infections

- Any septicemia → Staphylococcal → Unspecified
- Gram negative → Streptococcal
- 393,451 patients

Foley et al., JASN, 2004

Dialysis Surveillance Network (CDC)

- 1999
- Volunteer outpatient dialysis centers
- Internet-based system
- Data from 321,519 patient-months

<table>
<thead>
<tr>
<th>Centres with at least 1 case</th>
<th>1995</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRE</td>
<td>12%</td>
<td>30%</td>
</tr>
<tr>
<td>MRSA</td>
<td>40%</td>
<td>76%</td>
</tr>
</tbody>
</table>

Klevens, RM, NMBI 2005
Finebl, Semin Dial 2005

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Dialysis Surveillance Network (CDC)

- To provide a method for HD centers to record & track rates of vascular access infections, other bacterial infections, & IV antimicrobial starts
- To provide rates for comparisons among various dialysis centers (benchmarking); Rate: 1.5/1000
- To use these data to motivate practice changes & to prevent infections, especially those caused by antimicrobial resistant organisms
- www.cdc.gov/ncidod/dhqp/index.html for protocols

Catheter related bacteremia (CRB)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram Positive</td>
<td>82%</td>
</tr>
<tr>
<td>S. Aureus</td>
<td>32%</td>
</tr>
<tr>
<td>Coag Neg Staph</td>
<td>40%</td>
</tr>
<tr>
<td>Enterococci</td>
<td>8%</td>
</tr>
<tr>
<td>Gram Negative</td>
<td>10%</td>
</tr>
<tr>
<td>Mixed</td>
<td>8%</td>
</tr>
</tbody>
</table>


Extraluminational CRB prophylaxis

- Elimination of Nasal Colonization:
  - Single courses of intranasal mupriocin +/- other
    - Problem: Effective but recurrence after 3 mos
  - Multiple, intermittent courses
    - Problem: Mupirocin resistance

Epidemiology:
Clinical Prevention Trials

CRB Risk factors

- Catheter site: Femoral > IJ > subclavian
- Catheter characteristic: Non-uffed vs. cuffed, Non- tunneled vs. tunneled
- Prolonged duration of catheter use
- Previous bacteremia
- Thrombosis of the catheter
- Patient “stressed state”
  - Recent surgery
  - Diabetes
  - Immunocompromised
- Poor hygiene

Canada

- Canadian Nosocomial Infection Surveillance Program
- Network of Canadian hospital that carries our surveillance examining the frequency & risk factors for hosp acquired infections
- Multiple publications
- HD units
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**Skin Contamination**  
- **Extraluminal**  
  - Touch contamination  
- **Intraluminal**  
  - Bacterial attachment to catheter  

**Biofilm Formation**  
- More Biofilm Formation

**BACTEREMIA**

---

### Extraluminal CRB prophylaxis

<table>
<thead>
<tr>
<th>Placebo (JASN 2003)</th>
<th>PT</th>
<th>RRR</th>
<th>NNT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteremia</td>
<td>2.48</td>
<td>0.63</td>
<td>60%</td>
<td>7</td>
</tr>
<tr>
<td>Death</td>
<td>16%</td>
<td>4%</td>
<td>78%</td>
<td>8</td>
</tr>
</tbody>
</table>

A Reduction in catheter exchanges & hospitalizations seen in PT group (P< 0.05)

* Number of events/1000 catheter days

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### Intraluminal CRB Prophylaxis

- **Antibiotic Lock Prophylactic Therapy (ABL)**
- Developed in late 1980’s for TPN pts  
- Vancomycin and amikacin  
  - [luminal] 40 & 60 20 x systemic peak  
    - [blood] with conventional dosing  
  - Maintained 8-12 hrs, stable & active 12 hrs  
- HD patients: ↓ CRB (interdialytic lock)

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### Prophylaxis with ABL solutions: RCT

<table>
<thead>
<tr>
<th>Author</th>
<th>N/ Endpoint</th>
<th>Study Rx</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogra (JASN 2002)</td>
<td>N=112 PC (20 pts) CRI by CDC definitions</td>
<td>Gentamicin 40mg/ml &amp; Citrate 3.12% vs. heparin 5000 U/ml (+ intranasal mupirocin</td>
<td>0/1000 CRB (Gent-cit) vs. 2.6/1000 (hep)</td>
</tr>
<tr>
<td>McIntyre (KI 2004)</td>
<td>N=50 PC CRI by CDC definitions</td>
<td>Gentamicin 5 mg/ml &amp; heparin 5000 U/ml vs heparin 5000 U/ml</td>
<td>0.31/1000 (gent-hep) vs. 4.0/1000 (hep)</td>
</tr>
<tr>
<td>Bleyer (ICHE 2006)</td>
<td>N=57 TC CRI, thrombosis, both</td>
<td>Minocycline 3 mg/ml &amp; EDTA 30 mg/ml vs. Heparin (concentration?)</td>
<td>0% CRB (minoc-EDTA) 8.3% (hep) NS; 9.1% vs. 64.3% colonizn</td>
</tr>
<tr>
<td>Kim (KI 2006)</td>
<td>N=120 CRB, 2 cultures post same org (tip, CVC or periph)</td>
<td>Cefazolin 10 mg/ml, Gentamicin 5 mg/ml + heparin 1000 U/ml vs. heparin only</td>
<td>0.44/1000 (Gent-Cit) vs. 3.12/1000 (hep)</td>
</tr>
</tbody>
</table>

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Concerns with ABL

- Microbial resistance
  - Systemic leakage of Abx
  - Ototoxicity with AMGs
  - If lumen colonized with intrinsically R strains, overgrowth of resistant strains may occur when Abx susceptible organisms are suppressed
- Physical & chemical compatibility
  - Anticoagulant
  - Catheter material

Are ABL Indicated?

- Artificial Heart Valves
- Pacemaker
- Internal defibrillators
- Femoral cuffed catheters
- Recurrent infections with limited access

Anti-microbial Locks

- Double blind trial: Citrate vs. Heparin
- Newly inserted catheters
- 291 HD patients with CVC randomized

<table>
<thead>
<tr>
<th></th>
<th>Heparin</th>
<th>Citrate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRB</td>
<td>4.1</td>
<td>1.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Patient Deaths</td>
<td>5</td>
<td>0</td>
<td>.028</td>
</tr>
<tr>
<td>Catheter Removal</td>
<td>46%</td>
<td>28%</td>
<td>.005</td>
</tr>
</tbody>
</table>

- Taurollidine & citrate ↓ CRB
  (Betjes NDT 2004; Allon CID, 2003)

Overriding Management Principles

- Avoid CVC as much as possible
- Preserve anatomy for permanent access placement
- Always culture first before administering antibiotics → be clear and specific in orders
- Always follow up with sensitivities
- Catheter specific strategies dependent on clinical situation

What can I do?

- Get rid of those catheters!
- Educate patients
- Measure and monitor bacteremia rate in your unit
- Follow universal infection control precautions
  - Pharmacy
  - Topical antimicrobial usage
- Prescribe anti microbial or ABL solutions (from Pharmacy)
- Appropriate antibiotic use & avoid resistance

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Management Strategies for CVC Related Bacteremias

- Catheter “salvage”
- Salvage + adjunctive antibiotic lock
- Catheter exchange
- Catheter removal + delayed replacement

- Concurrent IV antibiotics for all strategies

HICS

Hemodialysis Infection Control Subcommittee

HICS: What we do

- HD infection surveillance
  - Specifically Vascular Access
  - Expanding
- Identify & confirm suspected infections
  - FU cultures, clinically exam patients prn
  - Health Canada guidelines
- Guidance for management
- Benchmarking
- Develop procedures & protocols
- Educate nurses, physicians, patients

Identifying causative organisms

<table>
<thead>
<tr>
<th>Organism Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive</td>
<td>75%</td>
</tr>
<tr>
<td>Gram-negative</td>
<td>20%</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>5%</td>
</tr>
</tbody>
</table>

Tracking Management Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful treatment</td>
<td>77.2%</td>
</tr>
<tr>
<td>Recurrence at 3 months</td>
<td>4.4%</td>
</tr>
<tr>
<td>Recurrence at 6 months</td>
<td>3.5%</td>
</tr>
<tr>
<td>Infectious complications (septic arthritis)</td>
<td>3.5%</td>
</tr>
<tr>
<td>Catheter removal</td>
<td>43.9%</td>
</tr>
<tr>
<td>Catheter salvage</td>
<td>56.1%</td>
</tr>
<tr>
<td>Hospitalization for infection</td>
<td>36.0%</td>
</tr>
<tr>
<td>Death</td>
<td>1.8%</td>
</tr>
</tbody>
</table>
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Duration of Treatment

Tracking Antibiotic Resistance

<table>
<thead>
<tr>
<th>Organism</th>
<th>Resistance to cefazolin</th>
<th>Resistance to vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coag.-neg. Staph.</td>
<td>(30/44) 68.2%</td>
<td>0%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>(1/11) 9.1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Selected Pathogen Resistance

Tracking Infection Rates

Catheter Related Infection Rates

Follow guideline recommendation to have database to track VA use & outcomes

CQI: Track Outcomes & Rectify

Blood Stream Infection Rates

Non-access related infections

Summary

- Staphylococcal infections are associated with great morbidity, mortality & cost
- Monitoring & benchmarking infections in your own unit is important (DSN)
- The pathogenesis involves an intraluminal and/or extraluminal source
- Organism attachment & biofilm formation = common pathway
- Preventative strategies should targeted to pathophysiology
- Get rid of those catheters!
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The Next Few Teleclasses

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Speaker/Institution</th>
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<tbody>
<tr>
<td>May 17</td>
<td>Ethics of Care During a Pandemic</td>
<td>Dr. Eric Wasylenko, Calgary Health Board</td>
</tr>
<tr>
<td>May 24</td>
<td>Importance of Vaccination Among Dialysis Patients</td>
<td>Dr. Matthew Arduino, CDC</td>
</tr>
<tr>
<td>May 31</td>
<td>Evaluation and Management of Infectious Disease Outbreaks in Nursing Homes</td>
<td>Dr. Chesley Richards, CDC</td>
</tr>
<tr>
<td>June 7</td>
<td>Infection Control in the Living and the Dead: The Angola Marburg Outbreak</td>
<td>Dr. Adriano Duse, University of the Witwatersrand</td>
</tr>
<tr>
<td>June 20</td>
<td>Central Venous Lines and Prevention of Infection</td>
<td>Dr. Steven Chambers, Australia</td>
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</table>

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For registration information [www.webbertraining.com/howtoct.php](http://www.webbertraining.com/howtoct.php)

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