Inaugural infection control webinar series
16 March 2010, 3 pm (CET*)
Epidemiology and prevention of bloodstream infections
Dr. Walter Zingg, Geneva, Switzerland

The slides as well as a recorded version will be available at:
www.webbertraining.com
www.who.int/gpsc/5may/news/webinars

Epidemiology and Prevention of Bloodstream Infections

1. Pathogenesis
2. Definition
3. Epidemiology
4. Risk factors
5. Procedural Interventions
6. Technical Interventions
7. Summary

Sources of intravascular catheter infection

- Intraluminal from tubes and hubs
- Haematogen from distant sites
- Extraluminal from skin

Focus of prevention of infections

- Insertion site
Focus of prevention of infections

Biofilm Formation

Co-factors:
- Fibrinogen¹, Fibronectin²
- Calcium³, Magnesium³, Iron³,⁴
- Production of extracellular matrix⁵,⁶
- DNA⁷
- Stress*¹

Biofilm on a catheter surface

Penetration of antibiotics limited due to viscous matrix
  → Resistance in lower/inner sheets of biofilm due to sub-inhibitory concentrations

The formation of protein layers occurs within seconds of blood contact with a foreign surface.¹

Fibrinogen and S.aureus adherence is reduced on polyurethane catheters with reduced surface roughness and hydrophilic properties.²

Epidemiology and Prevention of bloodstream infections

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BSI-LCBI: laboratory-confirmed bloodstream infection

1. Patient has a recognized pathogen cultured from 1 or more blood cultures
   and
   organism cultured from blood is not related to an infection at another site

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Central line-associated bloodstream infections - CLABSI

BSI-CSEP: Clinical Sepsis

→ CDC: CSEP may be used only to report primary BSI in neonates and infants. It is not used to report BSI in adults and children!

Patient <1 year of age has at least 1 of the following clinical signs or symptoms with no other recognized cause: fever (>38°C rectal), hypothermia (<37°C rectal), apnoea, or bradycardia and blood culture not done or no organisms detected in blood and no apparent infection at another site and physician institutes treatment for sepsis.
National Healthcare Safety Network (NHSN) Report: ICU

| Type of location          | No. of locations | Pooled mean
|---------------------------|------------------|-------------
| Critical care units      |                  |             |
| Burn                      | 35               | 5.3         |
| Medical cardiac           | 228 (221)        | 3.0         |
| Medical major teaching    | 125              | 2.6         |
| Medical all others        | 153 (147)        | 1.9         |
| Medical/surgical teaching| 182 (181)        | 2.1         |
| Medical/other < 15 beds   | 718 (660)        | 1.5         |
| Medical/surgical > 15 beds| 280 (277)       | 1.5         |
| Neurologic                | 24 (23)          | 1.4         |
| Neuroradiology            | 72               | 3.5         |
| Pediatric/cardiothoracic  | 18               | 2.3         |
| Pediatric/medic-surg      | 16 (15)          | 1.3         |
| Pediatric/neurological    | 129 (127)        | 1.0         |
| Respiratory               | 8                | 1.7         |
| Surgical                  | 308 (307)        | 2.3         |
| Surgical cardiothoracic   | 203 (202)        | 1.4         |
| Trauma                    | 62               | 2.6         |

Per 1'000 catheter-days


| Type of ICU                | No. of ICUs | No. of Pooled mean
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary</td>
<td>9</td>
<td>8845</td>
</tr>
<tr>
<td>Surgical-cardiothoracic</td>
<td>4</td>
<td>1669</td>
</tr>
<tr>
<td>Medical</td>
<td>12</td>
<td>11,410</td>
</tr>
<tr>
<td>Medical-surgical</td>
<td>83</td>
<td>85,989</td>
</tr>
<tr>
<td>Neurosurgical</td>
<td>5</td>
<td>2996</td>
</tr>
<tr>
<td>Pediatric</td>
<td>22</td>
<td>23,047</td>
</tr>
<tr>
<td>Surgical</td>
<td>13</td>
<td>7925</td>
</tr>
<tr>
<td>Trauma</td>
<td>3</td>
<td>2237</td>
</tr>
<tr>
<td>Burn</td>
<td>1</td>
<td>191</td>
</tr>
<tr>
<td>Overall</td>
<td>152</td>
<td>144,323</td>
</tr>
</tbody>
</table>

175 ICUs from: Latin America, Asia, Africa, and Europe

Epidemiology and Prevention of Bloodstream Infections

<table>
<thead>
<tr>
<th>NHSN</th>
<th>INICC¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary ICU</td>
<td>2.8</td>
</tr>
<tr>
<td>Surgical cardiothoracic ICU</td>
<td>1.6</td>
</tr>
<tr>
<td>Medical ICU</td>
<td>2.9</td>
</tr>
<tr>
<td>Medical/surgical ICU</td>
<td>2.4</td>
</tr>
<tr>
<td>Neurosurgical ICU</td>
<td>3.5</td>
</tr>
<tr>
<td>Surgical ICU</td>
<td>2.7</td>
</tr>
<tr>
<td>Trauma ICU</td>
<td>4.6</td>
</tr>
</tbody>
</table>

79 ICUs from: Argentina, Brazil, Colombia, Costa Rica, Cuba, India, Korea, Lebanon, Macedonia, Mexico, Morocco, Nigeria, Peru, Philippines, Turkey, Uruguay

Epidemiology and Prevention of Bloodstream Infections

Europe

United Kingdom 2.8-5.4 per 1000 patients at risk (84 hospitals; hospital-wide)

Germany 2.1 per 1000 catheter-days (309 ICUs)

Non - Intensive Care Units

Epidemiology and Prevention of Bloodstream Infections

University of Geneva Hospitals

Table III: Catheter-related bloodstream infections, days at risk, utilisation rate, transfer details and reasons for placement stratified by medical department

<table>
<thead>
<tr>
<th>CRBSI, ID (%)</th>
<th>CRIC Days</th>
<th>UTIC</th>
<th>IMM</th>
<th>NON</th>
<th>NUR</th>
<th>OUT</th>
<th>OTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVC-utilisation rate</td>
<td>4.9% (0.0-10.0)</td>
<td>1.8% (0.0-6.0)</td>
<td>3.8% (0.0-10.5)</td>
<td>2.6% (0.0-12.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfer at any time</td>
<td>31/100 (31%)</td>
<td>76 (76%)</td>
<td>55 (55%)</td>
<td>44 (44%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location at insertion</td>
<td>304 (71%)</td>
<td>88 (88%)</td>
<td>34 (34%)</td>
<td>29 (29%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfer to other departments</td>
<td>267 (73.0%)</td>
<td>58 (58%)</td>
<td>27 (27%)</td>
<td>22 (22%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRBSI, ID (%)</td>
<td>CRIC Days</td>
<td>UTIC</td>
<td>IMM</td>
<td>NON</td>
<td>NUR</td>
<td>OUT</td>
<td>OTH</td>
</tr>
<tr>
<td>Anticoagulant treatment</td>
<td>53/116 (45%)</td>
<td>31/99 (31%)</td>
<td>19/75 (25%)</td>
<td>9/42 (21%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>24/318 (8%)</td>
<td>10/91 (11%)</td>
<td>3/75 (5%)</td>
<td>28/45 (63%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline condition</td>
<td>44/150 (29%)</td>
<td>31/99 (31%)</td>
<td>12/55 (22%)</td>
<td>3/42 (12%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume monitoring</td>
<td>273/146 (88%)</td>
<td>59/91 (65%)</td>
<td>36/75 (48%)</td>
<td>20/45 (44%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Retransplantation
² CRBSI: catheter-related bloodstream infection; CRIC: central venous catheter; ID: incidence density; OTH: other CRBSIs at days at risk; CI: confidence interval; UTIC: ultrasound imaging; IMM: infection; NON: non-infected; NUR: nurses; OUT: other departments.
Central Venous Catheter (CVC) Utilization and Catheter-Associated Bloodstream Infection (CA-BSI) Rates for 4 General Medicine Wards at a Teaching Hospital in St. Louis, Missouri

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ward A</th>
<th>Ward B</th>
<th>Ward C</th>
<th>Ward D</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of CVC-days</td>
<td>1,704</td>
<td>1,989</td>
<td>1,610</td>
<td>2,014</td>
<td>7,337</td>
</tr>
<tr>
<td>No. of patient-days</td>
<td>7,978</td>
<td>8,112</td>
<td>8,618</td>
<td>8,466</td>
<td>33,174</td>
</tr>
<tr>
<td>Catheter utilization ratio</td>
<td>0.23</td>
<td>0.92</td>
<td>0.51</td>
<td>0.24</td>
<td>0.22</td>
</tr>
<tr>
<td>CA-BSI ratio</td>
<td>5.2</td>
<td>8.0</td>
<td>4.3</td>
<td>4.9</td>
<td>5.7</td>
</tr>
</tbody>
</table>

* Defined as the number of CVC-days divided by the number of patient-days.
* Defined as the number of CA-BSIs per 1,000 catheter-days.

Epidemiology and Prevention of Bloodstream Infections

Incidence density

- **CVC (2.7‰) >> Port system (0.1‰)**
- However, in proportions:
  - **CVC (4.4%) ≈ Port system (3.6%)**


<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of locations</th>
<th>No. of CLABSI</th>
<th>Central line-days</th>
<th>Pooled mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical/surgical</td>
<td>617 (575)</td>
<td>733</td>
<td>618,196</td>
<td>1.2</td>
</tr>
<tr>
<td>Neurosurgical</td>
<td>12 (10)</td>
<td>8</td>
<td>10,723</td>
<td>0.7</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>56 (47)</td>
<td>32</td>
<td>40,425</td>
<td>0.8</td>
</tr>
<tr>
<td>Pediatric medical</td>
<td>12 (11)</td>
<td>18</td>
<td>10,232</td>
<td>1.8</td>
</tr>
<tr>
<td>Pediatric medical/surgical</td>
<td>61 (53)</td>
<td>102</td>
<td>32,581</td>
<td>3.1</td>
</tr>
<tr>
<td>Postpartum</td>
<td>36 (3)</td>
<td>0</td>
<td>943</td>
<td>0.0</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>121 (106)</td>
<td>39</td>
<td>47,052</td>
<td>0.8</td>
</tr>
<tr>
<td>Surgical</td>
<td>93 (87)</td>
<td>189</td>
<td>132,336</td>
<td>1.4</td>
</tr>
</tbody>
</table>

Risk for CLABSI

- **CVC (2.7‰) >> Port system (0.1‰)**
- However, in absolute numbers:
  - **CVC ≈ Peripheral lines**
**Epidemiology and Prevention of Bloodstream Infections**

**1. Pathogenesis**

**2. Definition**

**3. Epidemiology**

**4. Risk factors**

**5. Procedural Interventions**

**6. Technical Interventions**

**7. Summary**

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**Time to infection: CVC**

ICU


Non-ICU


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**Time to infection: port systems**

- Adults: median of 80 days
- Children: mean of 100 days

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**Dwell-time**

Dwell-time > 7 days → RR: 1.0-8.7

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**Insertion Site**

<table>
<thead>
<tr>
<th>Access</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal jugular access</td>
<td>1.0-3.3</td>
</tr>
<tr>
<td><strong>Subclavian access</strong></td>
<td>0.4-1.0</td>
</tr>
<tr>
<td>Femoral access</td>
<td>3.3-4.8</td>
</tr>
</tbody>
</table>

**However:** no difference of catheter colonization (40.8 vs. 35.7 per 1000 catheter-days) and CLABSI (2.3 vs. 1.5 per 1000 catheter-days) hemodialysis catheters
Epidemiology and Prevention of Bloodstream Infections

**Contaminated intravenous products**

There is evidence in the literature about smaller and larger epidemics with contaminated intravenous products.

Matsaniotis. Infect Control 1984:5:471

**Insertion without using appropriate (maximal) sterile barrier precautions (MSB)**

Sterile gloves, sterile body gown, face mask, head cap, full-size sterile drape around the insertion site

- Insertion without MSB:\( \rightarrow \) Risk CRBSI ↑ (RR 2.1)
- Insertion with MSB:\( \rightarrow \) Risk CRBSI ↓ (RR 0.2)

Raad II. Infect Control Hosp Epidemiol 1994;15:231

**Guidewire exchange**

The use of a guidewire for CVC replacement may be a risk factor

RR: 1.0-3.3

Safdar. Medicine 2002;81:466
Cook. Crit Care Med 1997;25:1417

**Parenteral nutrition**

Parenteral nutrition and especially the lipids are associated with the risk for catheter-associated bloodstream infection: RR 1.04–4.79

Safdar. Medicine 2002;81:466
Opilla. JPEN J Parenter Enteral Nutr 2007;31:302

**Catheter-related thrombosis**

Catheter-related central vein thrombosis is a “frequent” complication of central venous catheterization in ICU patients and is closely associated with catheter-related sepsis: RR 2.62

Timsit. Chest 1998;114:207
Composition of nursing staff and workload

Lower regular-nurse-to-patient and higher pool nurse-to-patient ratios (OR 3.4) are risk factors for CRBSI.

Hugonnet. Crit Care Med 2007;35:76

Povidone iodine vs. Chlorhexidine

The use of chlorhexidine (2% aqueous or 0.25-0.5 alcohol-based), rather than 10% povidone-iodine for cutaneous disinfection before insertion of an intravascular device and for post-insertion site care can substantially reduce the incidence of device related infection.

Mimoz. Crit Care Med 1996;24:1818

Hand hygiene

Hand hygiene promotion, guided by health care workers’ perceptions, identification of the dynamics of bacterial contamination of health care workers’ hands, and performance feedback, is effective in sustaining compliance improvement and is independently associated with infection risk reduction.

Pessoa-Silva. Pediatrics 2007;120:e382

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Multimodal Intervention:
- Education
- Standardized Processes
- MSB
- Chlorhexidine
- Hand hygiene
- CVC care

Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care

Eggimann. Lancet 2000;355:1864
**Epidemiology and Prevention of Bloodstream Infections**

- 2 Intensive care units
- 2'104 patients at baseline
- 1'050 patients at intervention
- 13'200 patient days

---

**Bundle:**
- Hand hygiene
- MSB
- Skin antisepsis with chlorhexidine
- Avoiding femoral access
- Remove of needless CVC

---

**Epidemiology and Prevention of Bloodstream Infections**

- 103 Intensive care units in Michigan
- 18 Months follow-up
- 1’981 Months cumulated
- 375’757 CVC days
Epidemiology and Prevention of Bloodstream Infections

- 5 Intensive care units
- Cohort study
- Baseline and intervention
- 7279 CVC days

Impact of a prevention strategy targeting hand hygiene and catheter care on the incidence of catheter-related bloodstream infections

Rother Doris, MD; Alexander Imhof, MD; Marco Maggiore, MD; Robi Stocker, MD; Emmanuela Kübler, MD; Héctor Furtado, MD

Interventions:
- Hand hygiene
- Catheter care

Project adoption
Education of head nurses and teaching nurses
Ex-cathedra teaching
Bedside teaching
Compliance with hand hygiene

→ improvement not impressive...

BUT...

<table>
<thead>
<tr>
<th>%</th>
<th>Baseline</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>61</td>
<td>68</td>
</tr>
</tbody>
</table>

Time-to-infection

- CVC care
- Hand hygiene

Epidemiology and Prevention of Bloodstream Infections

The effect of process control on the incidence of central venous catheter–associated bloodstream infections and mortality in intensive care units in Mexico®

Interventions:
- CVC care
- Hand hygiene

Decrease of CRBSI in a high prevalence setting by improving hand hygiene and catheter care.

Epidemiology and Prevention of Bloodstream Infections

- 2 Intensive care units
- 12 Baseline and intervention
- 3,429 CVC days
Epidemiology and Prevention of Bloodstream Infections

CVC-bundle

1. Hand hygiene
2. Use of maximal sterile barrier precaution measures at catheter insertion
3. Skin antisepsis with chlorhexidine-containing products*
4. Subclavian access as the preferred insertion site for non-tunnelled catheters
5. Daily review of line necessity with prompt removal of unnecessary catheters

* e.g., 70% alcohol & 0.5% chlorhexidine-gluconate.

Meta-analysis: 4 identical interrupted time-series cohort trials

Open fluid containers (glass or semi-rigid plastic) vs closed system (plastic fluid bags)

Methods: open system for 6-9 months followed by exclusive use of a closed system

Pooled results:

<table>
<thead>
<tr>
<th>Meta-analysis: 4 identical interrupted time-series cohort trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open fluid containers (glass or semi-rigid plastic) vs closed system (plastic fluid bags)</td>
</tr>
<tr>
<td>Methods: open system for 6-9 months followed by exclusive use of a closed system</td>
</tr>
<tr>
<td>Pooled results:</td>
</tr>
<tr>
<td>Patients</td>
</tr>
<tr>
<td>CLABSI:</td>
</tr>
<tr>
<td>*All-cause mortality</td>
</tr>
<tr>
<td>Hypothesis:</td>
</tr>
</tbody>
</table>
Chlorhexidine-impregnated sponge

Control
n/1'000 CVC-days
7.2

Sponge
n/1'000 CVC-days
3.8

p=0.02
Dwell-times: 15.8 (control), 16.6 (sponge)


Chlorhexidine-impregnated sponge
Multicenter randomized controlled trial – ICUs in France

Control
n/1'000 CVC-days
1.3

Sponge
n/1'000 CVC-days
0.4

p=0.004

Timsit. JAMA 2009;301:1231

Lock solutions

- Taurolidine-citrate
- Ethanol
- Chelators
- Methylene blue

In vitro studies: 6
In vivo studies: 11 (2 case reports; 7-70 included patients in cohort or randomized studies)
7/11 used taurolidine-citrate 4%


Controls       TauroLock™
Patients         90      89
Age (median)    10.4     7.2
Port-days       3672    3989
Tunneled CVC-days  2414    2716

Bacteraemia   30  25 ns
Bacteraemia with CoNS*  14  3  0.004
ID all bacteraemia  4.9  3.8 ns
ID CoNS*         2.3  0.5  0.004

More infections with Gram-positives et Gram-negatives!

Results encouraging but not conclusive!

Simon. BMC Infect Dis 2008;8:102

*CoNS: coagulase negative Staphylococcus
**Lock solutions**

**Ethanol**

Ethanol 40-80% efficient in vitro…

…but results were disappointing in a large randomized controlled trial (359 catheters*; 4 vs. 5 CLABSI)

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**Lock solutions: Chelators**

- **Sodium-citrate:** 7%
- **Methylene blue:** 0.05% + paraben

408 patients with 49,565 catheter-days (207 controls [heparin]; 201 in C-MB-P group)

<table>
<thead>
<tr>
<th>Lock solution</th>
<th>Catheter lock solution group</th>
<th>Control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>M-EDTA</td>
<td>1/11</td>
<td>9/14</td>
<td>0.01</td>
</tr>
<tr>
<td>M-EDTA</td>
<td>0/14</td>
<td>10/48</td>
<td>0.05</td>
</tr>
<tr>
<td>M-EDTA</td>
<td>1/7</td>
<td>47/77</td>
<td>0.0001</td>
</tr>
<tr>
<td>M-EDTA</td>
<td>0/3</td>
<td>40/99</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tauridine-citrate</td>
<td>0/37</td>
<td>4/39</td>
<td>0.047</td>
</tr>
<tr>
<td>Gentamicin-citrate</td>
<td>1/20</td>
<td>16/30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TSC</td>
<td>0/53</td>
<td>7/55</td>
<td>0.002</td>
</tr>
<tr>
<td>C-MB-P</td>
<td>9/148</td>
<td>33/143</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Small numbers!

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**Luer Activated Device (V-Link®)**

The proprietary coating process results in a surface deposition consisting of tightly bound silver nano-particles that serve as reservoirs of silver ions.

The V-Link device’s VitalShield coating contains a nano-structure with a surface layer of Ag₂O that controls the release of Ag⁺ when in contact with solution.
1. Pathogenesis
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Zero Central Line Associated Bloodstream Infections: …how to get there…
- Multimodal intervention
- Bundle approach
- The "last mile" may require the use of some technical device (chlorhexidine patch, coated catheters, impregnated luer activated device, lock solutions…)

The most important measures:
Standardized Processes of insertion, catheter care and catheter removal – Written Protocols

The most important measures:
Insertion
- Maximal sterile precautions
- Hand hygiene
- Avoid femoral insertion site
- Checklist (stop CVC insertion procedures if guidelines are not followed)

The most important measures:
Good catheter care
- Accurate dressings
- Daily evaluation of CVC and insertion site
- Accurate changing of tubes and hubs
- Remove CVC, as soon as possible

Thank you
19 January 2010, 3 pm (CET)
The global burden of health care-associated infections
(B. Allegranzi, Geneva, Switzerland)

16 February 2009, 3 pm (CET)
The modern approach to infection control
(D. Pittet, Geneva, Switzerland)

16 March 2010, 3 pm (CET)
Epidemiology and prevention of bloodstream infection
(W. Zingg, Geneva, Switzerland)

13 April 2010, 3 pm (CET)
Proven strategies to control influenza virus transmission, with special focus on H1N1 (HW Seto, Hong Kong SAR, China)