Intravenous Catheter Related Infection: Microorganisms and Pathogenesis

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In 1865, Louis Pasteur suggested that decay was caused by living organisms in the air, which on entering matter caused it to ferment.

Sir Joseph Lister recognized the relationship between Pasteur's research and his own. He considered that microbes ( "invisible assassins") in the air were likely causing clinical infections and had to be destroyed before they entered the wound.
Impact of CVC Related Infections

- Nosocomial Infections-Hospital acquired, 4th leading cause of death in US (>90,000/yr).
- Over 5 million CVCs are inserted annually in the US. It is estimated that 2-12% of CVCs result in sepsis. National Nosocomial Infections Surveillance (NNIS) data shows that 87% of primary bloodstream infections occurred in patients with a central line. CVCs contribute to more than 250,000 infection cases annually in US.
- Infection is the most common serious complication associated with vascular catheters. Infections are of two types: local and bloodstream.
- Catheter related blood stream infection is probably the most significant and life threatening of all medical device related infections. Mortality is estimated at 12%–25%. Estimated annual deaths 30,000-60,000.
- The cost per infection is on average $25,000 per episode. Estimated annual cost of ~$6.25 billion.

CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections
Morbidity and Mortality Weekly Report Recommendations and Reports August 9, 2002 / Vol. 51 / No. RR-10
IV Catheter Related Infections are Caused by Bacteria & Yeasts: Know the Enemy

- Gram Positive cocci are common to human skin. Coagulase negative Staphylococci (*S. epidermidis*) are the most common cause of IV catheter related infection (37%).
- Staph aureus 13%
- Gram positive enterococci 13%. Enteric bacteria including *E. faecium* and *E. faecalis*.
- Gram negatives bacilli 14%. Source related to water including wastewater. Many gram negatives are found in the human enteric system (*E. coli*).
- Yeasts-8% (*Candida* species). C. albicans is the 4th leading cause of vascular catheter related infections. CVC Infections with *Candida* are associated with the highest mortality rate (26-38%).
- All other pathogens 15%.

Pathogenesis

- Migration of skin organisms from the insertion site into the cutaneous catheter tract with colonization of the catheter tip is the most common route of infection for peripherally inserted, short term catheters.
- Contamination of the catheter hub contributes substantially to intraluminal colonization of long-term catheters.
- Occasionally catheters may become hematogenously seeded from another focus of infection.
- Rarely infusate contamination leads to CRBSI
Types of Vascular Catheter Related Infections: Localized or Systemic

- Colonized Catheter-Significant microbial growth from the device tip, subcutaneous segment, or hub (asymptomatic)
- Phlebitis-Erythema/induration/tenderness/pain near exit site.
- Exit Site infection-Erythema/induration/tenderness/pain with or without pus within 2 cm of exit site. Exudate and positive microbiological culture.
- Tunnel Infection-Erythema/induration/tenderness >2 cm of exit site along the subcutaneous tract.
- Pocket Infection-Infection in the subcutaneous pocket of an implantable port.
- CRBSI-Bloodstream Infection.

Note: Exit site, tunnel and port infections are soft tissue infection along the external surface of the catheter and may or may not involve CRBSI

Site of Catheter Insertion Influences Risk of Infection

- The density of skin flora at the catheter insertion site is a major risk factor for Catheter Related Blood Stream Infection (CRBSI).
- CDC Guideline recommends that CVC be placed in a subclavian site instead of a jugular of femoral site to reduce infection risk.
An Adaptive Enemy-Antibiotic Resistant Clinical Isolates

- Many of the bacteria causing catheter related infections, and infections in general are antibiotic resistant, making treatment difficult.
- Bacteria are very adaptive to adverse environments. Unnecessary and over use of antibiotics has created a significant increase in antibiotic resistant microbes.
- Use of inappropriately low levels of antibiotics selects for the most resistant species.
Resistance to Antimicrobial Agents

- Methicillin resistant *Staphylococcus aureus* (MRSA) and *Staph. epidermidis* (MRSE) are prevalent in clinical settings and responsible for many device related infections.
- Vancomycin resistant enterococci (VRE) which are gram positive cocci, are a growing problem.
- Antibiotics are ineffective against yeasts. *Candida* biofilms are resistant to most antifungal agents. Bacteria in biofilms are markedly resistant to antimicrobial agents.
Understanding the Role of Biofilms in Catheter Related Infections (CRI)

Understanding biofilms is essential to establishing strategies relative to their prevention/treatment.
Biofilm: Definition

- A biofilm is a complex aggregation of microorganisms marked by the excretion of a protective and adhesive matrix.
- Matrix-enclosed microbial populations adherent to each other and/or to surfaces and interfaces.
Microbial Biofilm on a Medical Device
Microorganisms Can colonize both the internal and external surfaces of the IV Catheter
**STEP 1:** Bacteria enter the catheter in a free floating or planktonic form. Characterized by high susceptibility to antimicrobials. Cells are unprotected. This usually occurs between 0-4 hours.

**STEPS 2-4:** Bacteria adhere to the catheter surface and grow/multiply into an organized community known as a biofilm. Characterized by high resistance to antimicrobials. Cells surrounded by glycocalyx matrix. Biofilm begins to form after ~4 hours.
Adherent/biofilm bacteria have the ability to shed cells and move

Examples of biofilm shedding and movement
**Biofilm Behavior**

**Cell-cell communication**: This is called quorum sensing. The ability of a bacterial colony to sense its size and regulate its activity in response. Behave like a tissue. It is an intercellular signaling mechanism that depends on cell density.
Biofilm Resistance to Antimicrobial Treatments

- Slow diffusion of antimicrobial through the glycocalyx matrix
- Cells divide into many different forms with variable antimicrobial susceptibility
- Environment within the biofilm has variable oxygen concentration and pH which affects antimicrobial activity.
- Low metabolically active “persister” cells allow for biofilm regrowth after antimicrobial is used up.
CRBSI-Difficult to Diagnose

- Clinical signs (fever/chills) are sensitive but not specific for diagnosis. Other indicators, such as catheter-site inflammation, are specific but not sensitive.
- Semiquantitative (roll-plate technique) and quantitative (i.e. sonication) used traditionally for past 27 years. Require catheter removal.
- Differential time to positivity-Method to diagnose CRI without removing the catheter.
- Defined as the difference in the time it takes for a blood culture draw through the CVC and a culture drawn from a peripheral vein to become positive.
Treatment of a CRBSI

- Antibiotics, Antifungals, and Device Removal
  - Drug resistance.
  - May need more than one antibiotic.
  - Hypersensitivity.
  - Costly and not always effective.
Best Approach is Prevention

- Providing aseptic barrier and antiseptic agent for skin preparation.
- Providing continuous protection post insertion by treating our CVC with agents which are both safe and efficacious.
$1,000,000 Question

- Can we do better?
- If yes, what?
The Risk of Bloodstream Infection in Adults With Different Intravascular Devices: A Systematic Review of 200 Published Prospective Studies

DENNIS G. MAKI, MD; DANIEL M. KLUGER, MD; AND CHRISTOPHER J. CRNICH, MD

Metanalysis

- Summary of IVD’s bloodstream infections relative risk
- Review of 200 published prospective observational or clinical trials published between January 1, 1966 and July 1, 2005
The most “preventable” classes of nosocomial infections

- IVD’s infections have an associated mortality of approximately 35%
- Increased morbidity and length of hospital stay calculated at 24 days for those who survive any bacteremia.3–4
- Can be reduced by more than 65% by using relatively straightforward infection control procedures6–8

In other words (based on this metaanalysis of some 25,000 CVCs)

- If 4 out of 100 patients will develop blood streem infection

- 1-2 patients will develop into sepsis

- Can we realy prevent 1 patient from developing sepsis?
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<th>Device</th>
<th>No. of studies</th>
<th>No. of catheters</th>
<th>No. of IVD (d)</th>
<th>No. of BSIs</th>
<th>Rates of IVD-related bloodstream infection</th>
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<th>Per 1000 IVD-days</th>
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50% infection reduction filter

- Medicated catheters
  - Chlorhexidin-silver – sulfadiazin
  - Minocyclin-rifampin

- Peripherally inserted central catheters
- Tunneled catheters
NEJM Study


NOTE: Both catheters had similar efficacy for approximately first 10 days. MR catheters were 1/3 as likely as CS to be colonized, and 1/12 (0.3% vs. 3.4%) as likely to result in CRBSI.

Figure 1. Kaplan–Meier Curves for Freedom from Bloodstream Infection with Catheters Impregnated with Either Minocycline and Rifampin or Chlorhexidine and Silver Sulfadiazine.

The numbers of catheters in each group that were at risk for causing infection at various times are shown below the figure. The risk of bloodstream infection was significantly lower for catheters impregnated with minocycline and rifampin than for those impregnated with chlorhexidine and silver sulfadiazine (P = 0.001 by the log-rank test).
Our Focus: Infection Prevention

“When meditating over a disease, I never think of finding a remedy for it but, instead, search for a means to prevent it.”

Louis Pasteur