



Preventing Hemodialysis Catheter-Related Infections: Where do Antimicrobial Locks Stand?

Speakers



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*Financial Disclosures: Consulting for
11TEN innovations*



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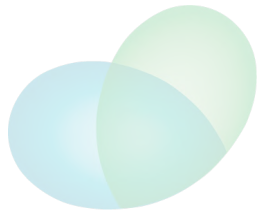


Definitions before we get started.....

- Bloodstream Infection (BSI)
 - Bacteremia or fungemia confirmed with a positive blood culture, typically accompanied with clinical symptoms or signs
- Catheter-related BSI (CRBSI)
 - A clinical definition, in which a central venous catheter is identified as the source of the BSI
- Central-line associated BSI (CLABSI)
 - A surveillance definition, BSI in a patient with catheter, and not related to an alternate source
- Dialysis Access-Related BSI
 - A surveillance definition, BSI secondary to dialysis vascular access

<https://academic.oup.com/cid/article/49/1/1/369414>

<https://www.cdc.gov/infectioncontrol/guidelines/bsi/background/terminology.html>



Learning Objectives

- Highlight the burden of CRBSI in hemodialysis
- Discuss CDC's core interventions for preventing BSI in outpatient dialysis facilities
- Explore Antimicrobial Locks for preventing CRBSI
- Highlight some catheter devices for preventing BSI



Clinical Scenario

You are the medical director of Dialysis Facility O. The nurse manager is concerned about an increased rate of CLABSI over the past 6 months. She reviewed results of infection control audits including hand hygiene, catheter connection and disconnection, and catheter exit site dressing care. Based on the audits, she identified areas for education and training. She asks you if antibiotic locks should be implemented for all catheters.

Catheter care procedures for Facility O:

- Catheter hub disinfection: scrub the hub with sterile alcohol pad every time catheter is accessed, disconnected, cap removed, cap replaced
- Catheter exit site care: disinfect exit-site with alcohol swab, apply chlorhexidine-impregnated transparent dressing, change dressing once a week and when visibly wet/soiled
- Catheter lumen: heparin lock

In addition to performing staff education/trainings, **consider what you would recommend?**



Catheter-Related Infections and Hemodialysis

- Central venous catheters (catheters) have the highest risk of bloodstream infection (BSI) compared to grafts (AVG) and fistulas (AVF)
 - From 2014-2018, **50,000 BSIs** (or **70%** of dialysis access related BSIs) occurred in patients with catheters¹

Attributable **Mortality** from CLABSI: **12-25%**²

Estimated **Costs** per CLABSI episode: **3,700-45,000 dollars**^{2,3}

1. National Healthcare Safety Network (NHSN) Unpublished Data

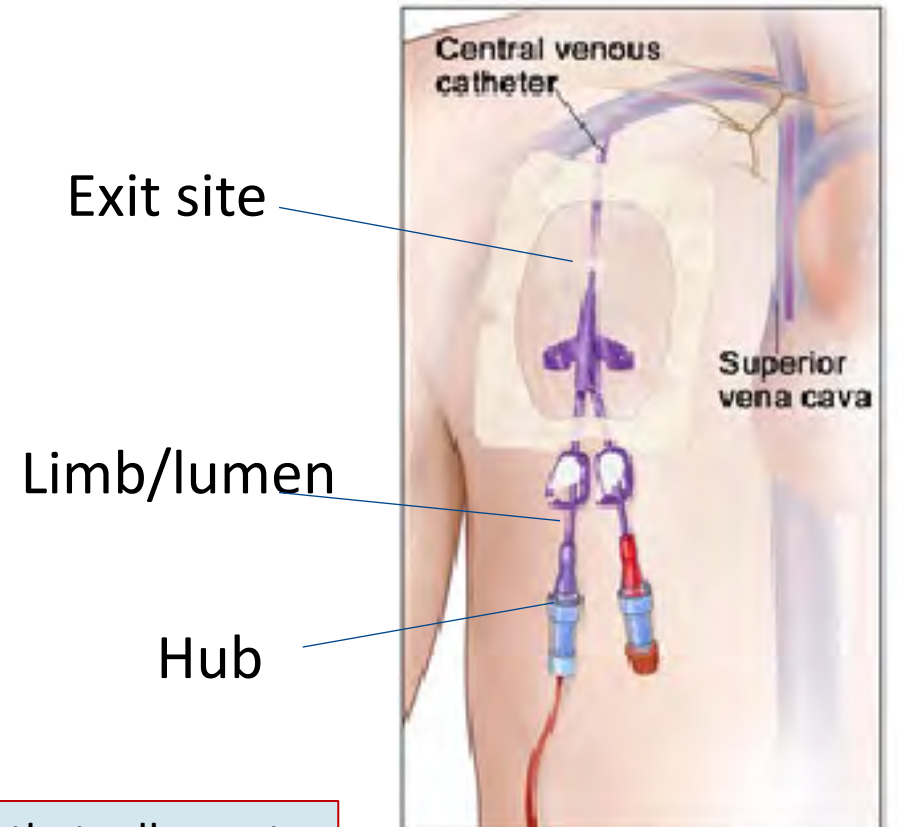
2. CDC. MMWR 2011; 60(08);243-248

3. Zimlichman E. et al. JAMA Intern Med. 2013;173(22):2039-2046

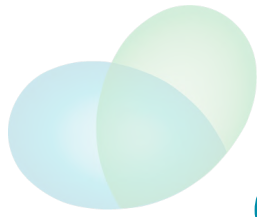
How do Catheter-Related BSIs Occur?

- Bacteria migration from skin/exit site to catheter
- Direct contact of catheter, or catheter hub with contaminated hands, fluids or devices
- Hematogenous seeding from other focus of infection
- Infusate contamination

Bacterial contamination leads to formation of extracellular matrix that adheres to catheter surface, called **biofilm**



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Core Interventions for Dialysis BSI Prevention


CDC Approach to BSI Prevention in Dialysis Facilities
(i.e., the Core Interventions for Dialysis Bloodstream Infection (BSI) Prevention)

- 1. Surveillance and feedback using NHSN**
Conduct monthly surveillance for BSIs and other dialysis events using CDC's National Healthcare Safety Network (NHSN). Calculate facility rates and compare to rates in other NHSN facilities. Actively share results with front-line clinical staff.
- 2. Hand hygiene observations**
Perform observations of hand hygiene opportunities monthly and share results with clinical staff.
- 3. Catheter/vascular access care observations**
Perform observations of vascular access care and catheter accessing quarterly. Assess staff adherence to aseptic technique when connecting and disconnecting catheters and during dressing changes. Share results with clinical staff.
- 4. Staff education and competency**
Train staff on infection control topics, including access care and aseptic technique. Perform competency evaluation for skills such as catheter care and accessing every 6-12 months and upon hire.
- 5. Patient education/engagement**
Provide standardized education to all patients on infection prevention topics including vascular access care, hand hygiene, risks related to catheter use, recognizing signs of infection, and instructions for access management when away from the dialysis unit.
- 6. Catheter reduction**
Incorporate efforts (e.g., through patient education, vascular access coordinator) to reduce catheters by identifying and addressing barriers to permanent vascular access placement and catheter removal.
- 7. Chlorhexidine for skin antiseptics**
Use an alcohol-based chlorhexidine (>0.5%) solution as the first line skin antiseptic agent for central line insertion and during dressing changes.*
- 8. Catheter hub disinfection**
Scrub catheter hubs with an appropriate antiseptic after cap is removed and before accessing. Perform every time catheter is accessed or disconnected.**
- 9. Antimicrobial ointment**
Apply antibiotic ointment or povidone-iodine ointment to catheter exit sites during dressing change.***

* Povidone-iodine (preferably with alcohol) or 70% alcohol alternatives for patients with chlorhexidine intolerance.
** If closed needleless connector device is used, disinfect device per manufacturer's instructions.
*** See information on selecting an antimicrobial ointment for hemodialysis catheter exit sites on CDC's Dialysis Safety website (<http://www.cdc.gov/dialysis/prevention-tools/core-interventions.html#sites>). Use of chlorhexidine-impregnated sponge dressing might be an alternative.

For more information about the Core Interventions for Dialysis Bloodstream Infection (BSI) Prevention, please visit <http://www.cdc.gov/dialysis>

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion




- Introduced in 2011
- Studies have shown the effectiveness of Core Interventions in decreasing BSIs^{1,2,3}
 - 54% reduction in dialysis access-related BSIs¹
 - Decrease in IV antibiotic starts³
 - Decrease in sepsis-related hospitalizations³

More can be done!
You can play a role in decreasing BSIs

1. Patel PR et al. Am J Kidney Dis 2013.62(2):322-330
2. Yi SH, et al. Infect Control Hosp Epidemiol 2016. 37:863–866
3. Rosenblum A. et al. Am J Kidney Dis 2014. 63(2):259-267



**Surveillance
and feedback** →

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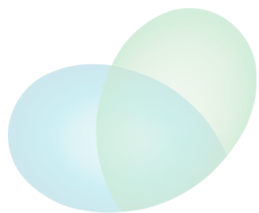
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Infection control observations



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Infection
control
education



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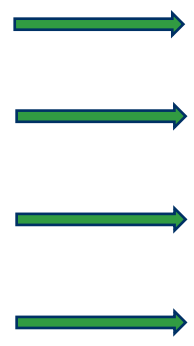
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Catheter care





Clinical Scenario

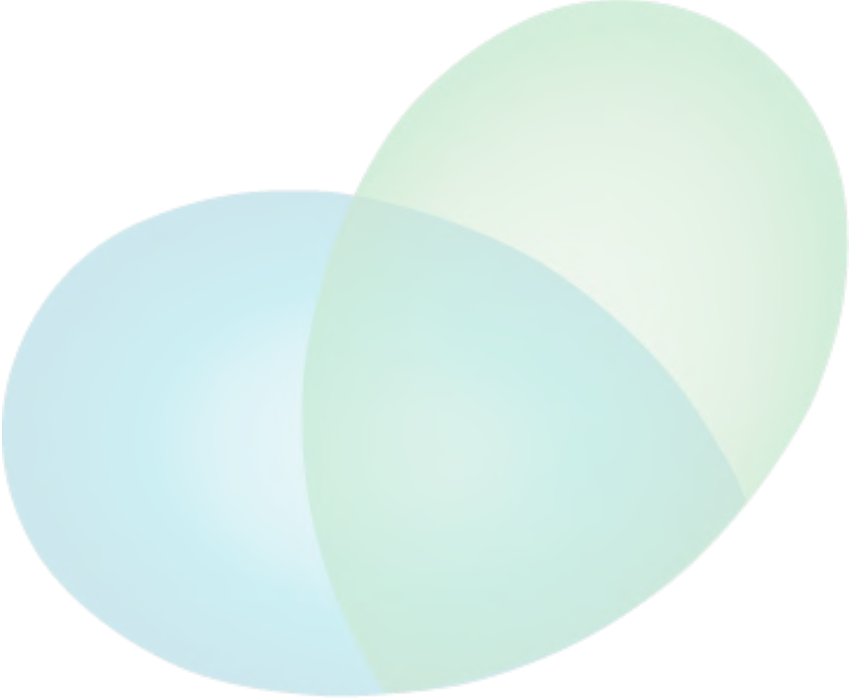
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Catheter care procedures for Facility O:

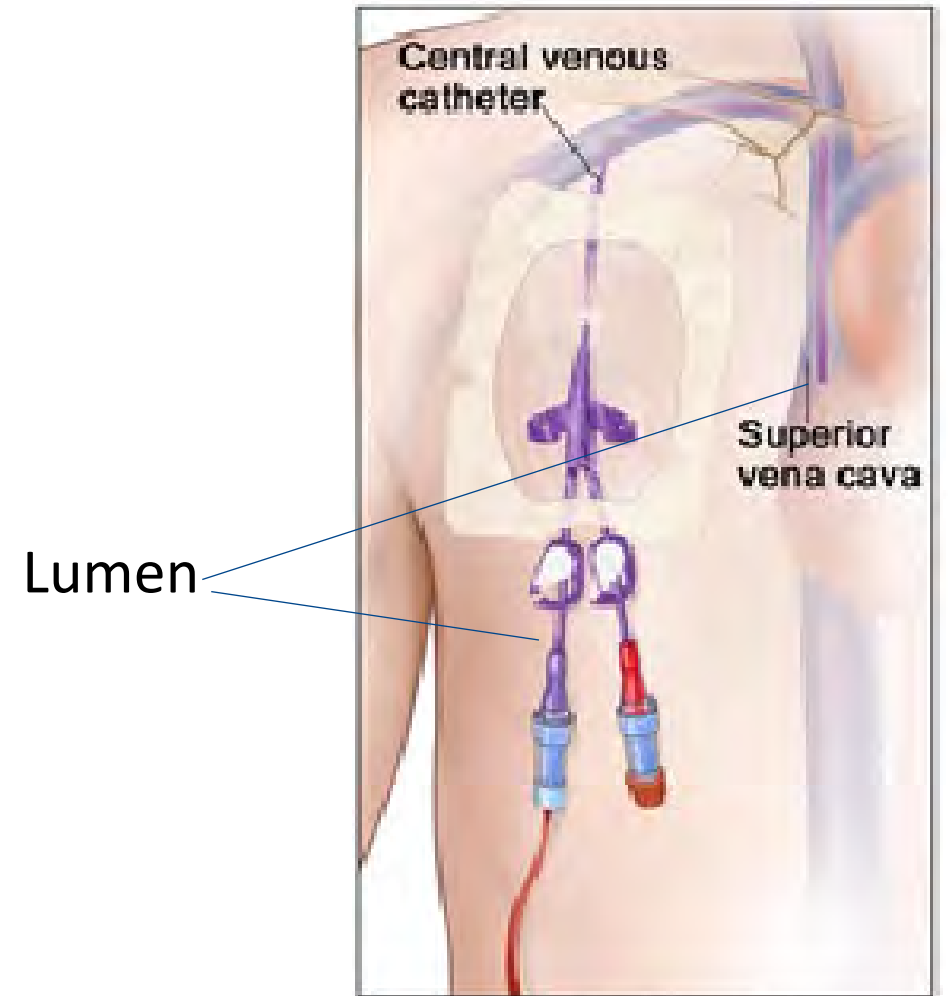
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- Catheter lumen: heparin lock

In addition to performing staff education/trainings, **what do you recommend?**

- A) Institute gentamicin locks for all catheters
- B) Replace alcohol swab with >0.5% alcohol-based chlorhexidine solution for catheter exit site disinfection
- C) Add antimicrobial mupirocin ointment to exit site during dressing change
- D) Continue current procedures without change



Catheter Lumen- Antimicrobial Locks



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Antimicrobial Locks for Preventing CRBSI

Antimicrobial lock is a technique by which an antimicrobial solution is used to fill a catheter lumen and then allowed to dwell for a period of time while the catheter is idle.

The antimicrobial agent is usually combined with a compound acting as an anticoagulant (heparin/citrate).

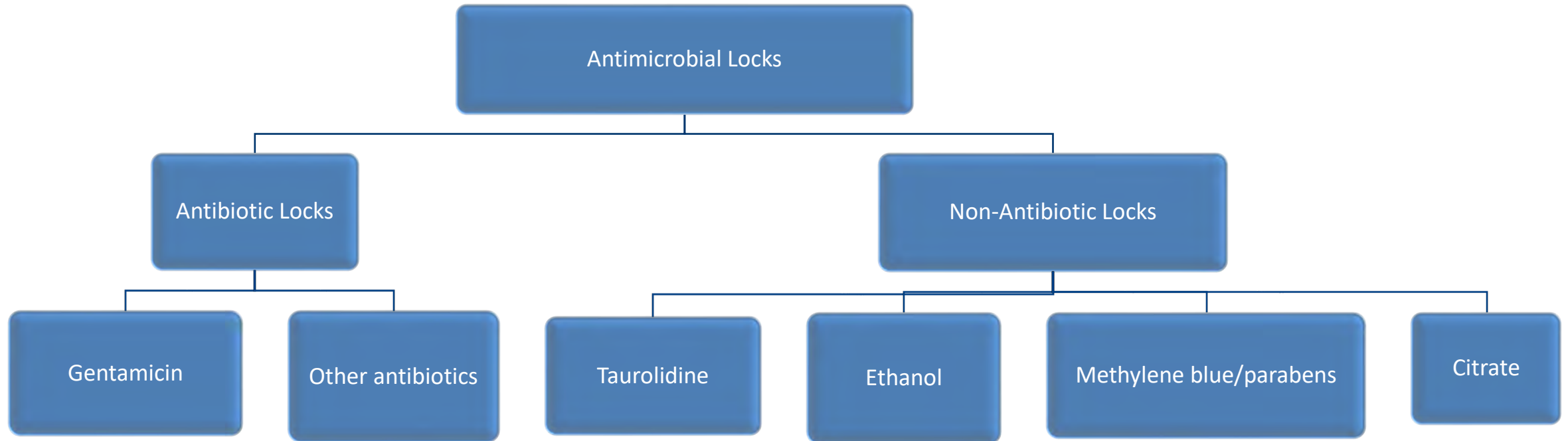
Discussing antimicrobial locks for **preventing CRBSI**
(Not locks for treatment of CRBSI or catheter salvage)



Ideal Antimicrobial Lock Solution Properties

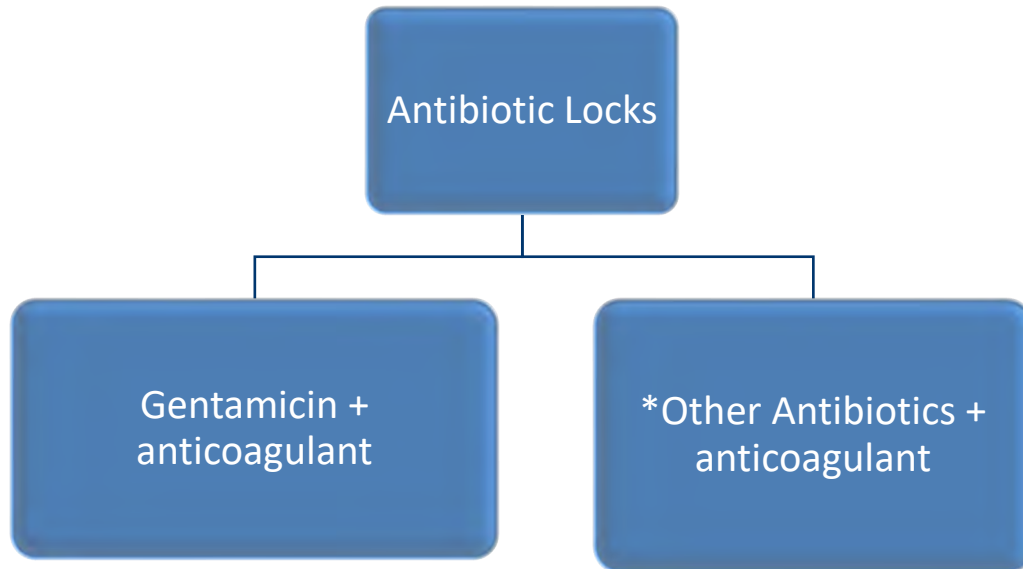
- Spectrum of activity should include common or targeted pathogens
- Ability to penetrate or disrupt a biofilm
- Compatibility with anticoagulants
- Prolonged stability
- Low risk of toxicity and adverse events
- Low potential for resistance
- Cost-effective

Justo et al. Infect Drug Resist. 2014 Dec 12;7:343-63





Antibiotic Locks



*Other antibiotics: minocycline, linezolid, cefotaxime, vancomycin, cefazolin, ciprofloxacin, etc.

Gentamicin Locks

- Most studied antibiotic lock
- Has been combined with vancomycin, cefazolin
- Associated with decreased CRBSI rates
- Concern for systemic absorption, ototoxicity, and gentamicin resistance

Most studied- and combined with vanc/cefazolin Yahav et al. *Clinical Infectious Diseases* 47: 83-93, 2008
Ototoxicity- Dogra GK et al. *J Am Soc Nephrol* 13: 2133-2139, 2002



Gentamicin Lock Studies

Gentamicin (4mg/mL) + Heparin Lock

Landry et al. CJASN 2010.

- Retrospective chart review
- 1,410 patients over a 4-year study period
- Catheter care:
 - Hubs soaked in Povidone Iodine (PI)
 - Exit site cleansed with PI
 - Exit site dressing- Mupirocin ointment/dry gauze

CRBSI rates: 17.0 → 0.83/1,000 catheter days, in 1 year

Gentamicin resistance – 26%, discontinued use



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Gentamicin (0.32mg/mL in 4% Citrate) vs. Heparin

Moore et al, CJASN 2014

- Prospective, observational cohort study
- 555 patients over 3 years (crossover from heparin to Gent lock)
- Catheter Care:
 - Hubs soaked in Chlorine (Alcavis)
 - Exit site cleansed with chlorhexidine (3.15%).
 - Exit site dressing- Triple antibiotic ointment (bacitracin, neomycin, and polymyxin B)/dry gauze

CRBSI rate: 0.45 (gent) vs 1.68 (heparin) episodes/1,000 catheter days (p =0.001)

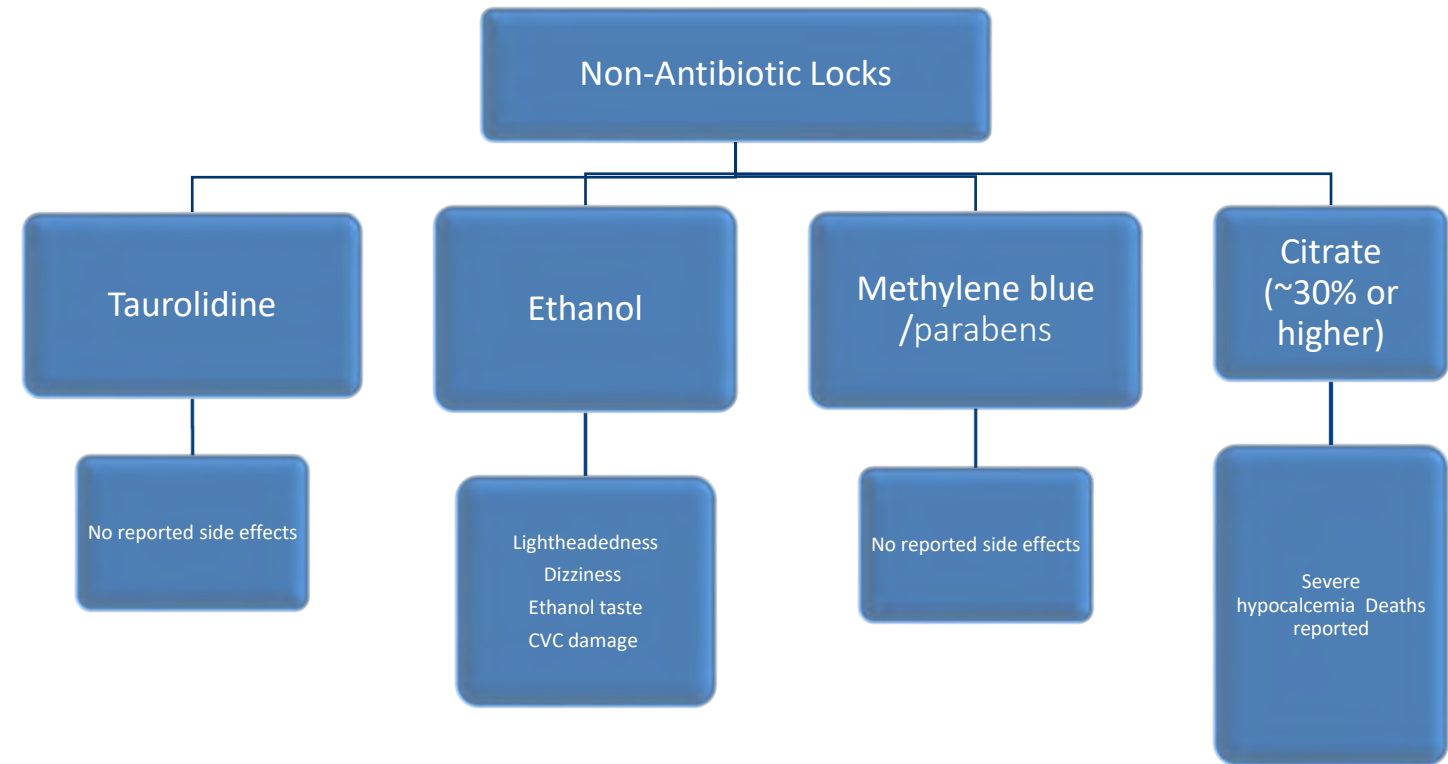
- No emergence of gentamicin resistance
- Antibiotic lock was associated with a mortality reduction (hazard ratio 0.36; 95% CI, 0.22 to 0.58 in unadjusted analyses)



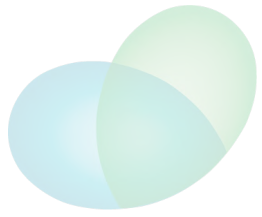
Non-Antibiotic Locks

Taurolidine Locks

- Considered promising non-antibiotic lock
 - May mitigate issue of antibiotic resistance
- Broad spectrum activity
- No resistance reported
- Multiple studies showing associated with decreased CRBSI
- No reported side effects



Mermel, L.A. et al J Antimicrob ,Chemother, 2014



A Meta-Analysis of Antimicrobial Lock Solutions for Hemodialysis Catheters

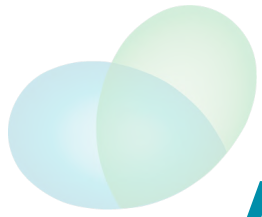
Methods: Included 26 randomized control studies comparing antimicrobial locks (i.e., antibiotic and non-antibiotic locks) to heparin (control group)

Results: Compared to heparin, antimicrobial locks associated with **30%** lower incidence of CRBSI.

- **Antibiotic lock** led to decreased risk of CRBSI episodes by 28% compared to heparin
- **Non-antibiotic lock** led to decreased risk of CRBSI episode by 32%

Limitations: few studies, low sample size of individual studies

Salim SA et al. ASAO Journal. 2021



Antimicrobial Locks Considerations

- Ideal antimicrobial lock for preventing CRBSI among is yet to be decided
- No FDA approved formulations approved for marketing
 - No pre-mixed antimicrobial locks in the market, in the USA
 - How and where will the lock be prepared
 - If mixed dialysis staff, mixing locks, will require training and quality checks
- Cost- Center for Medicare and Medicaid Services does not provide reimbursement for antimicrobial locks



So...Where Do Antimicrobial Locks Stand?

- Evidence supports antimicrobial locks effectiveness in reducing CRBSIs
 - Gentamicin well-studied, lower dose did not appear to lead to antibiotic resistance
 - Taurolidine may be promising solution to antibiotic resistance
- In most studies, CDC Core Interventions for preventing BSI were not used
 - Opportunities for decreasing CRBSI without locks, given high rates of CRBSI in some studies
 - Studies are needed to determine if there is additional benefit of antimicrobial locks when the Core Interventions are followed
- No antimicrobial lock has been approved by FDA
 - Several considerations to ensure patient safety and preventing dosage errors or contamination if locks are prepared by dialysis staff



CDC's Recommendations on Antimicrobial Locks, 2011

CDC recommends **against** routine use of antimicrobial locks for prevention of CRBSIs

“Use prophylactic antimicrobial lock solution in patients with long term catheters who have a **history of multiple CRBSI despite optimal maximal adherence to aseptic technique.**”

<https://www.cdc.gov/infectioncontrol/guidelines/bsi/recommendations.html#rec9>



Clinical Scenario

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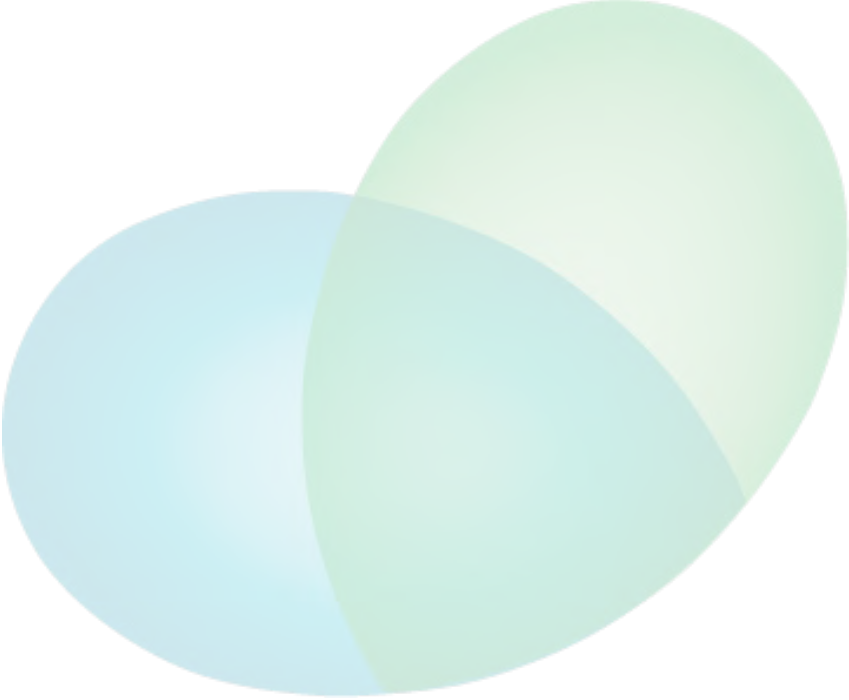
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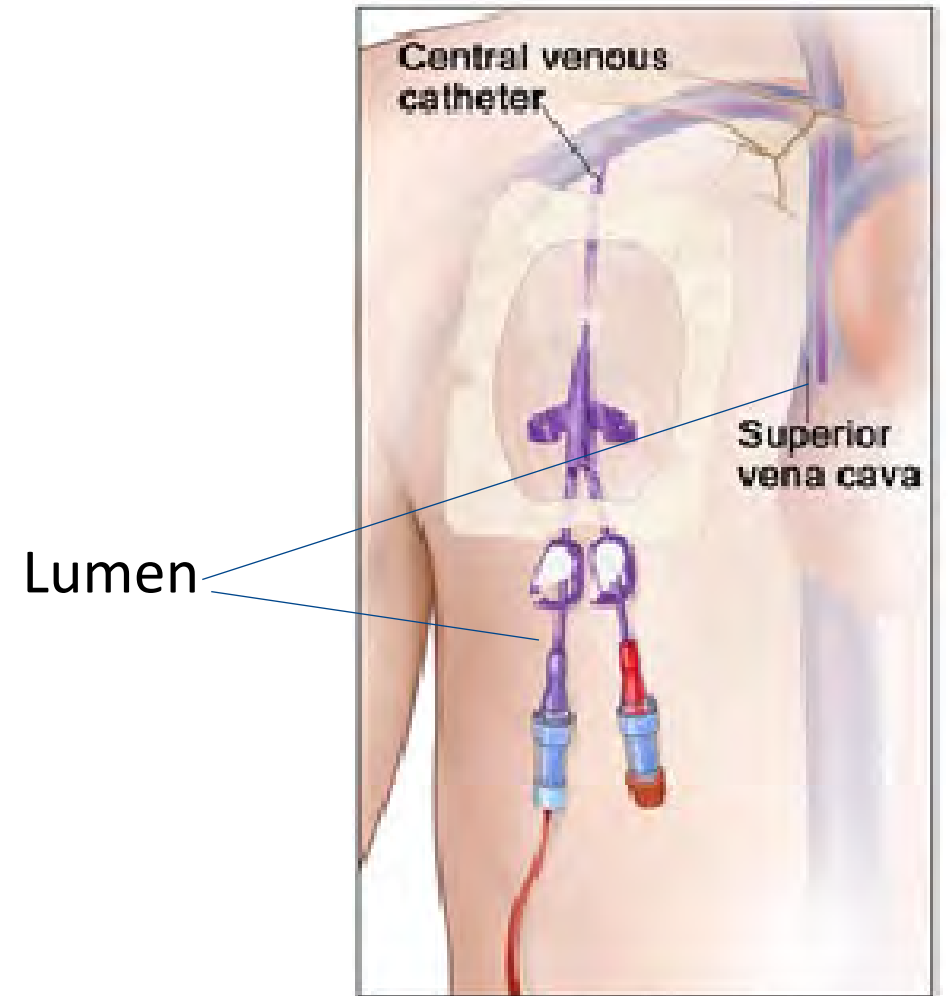
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Catheter Lumen- ClearGuard

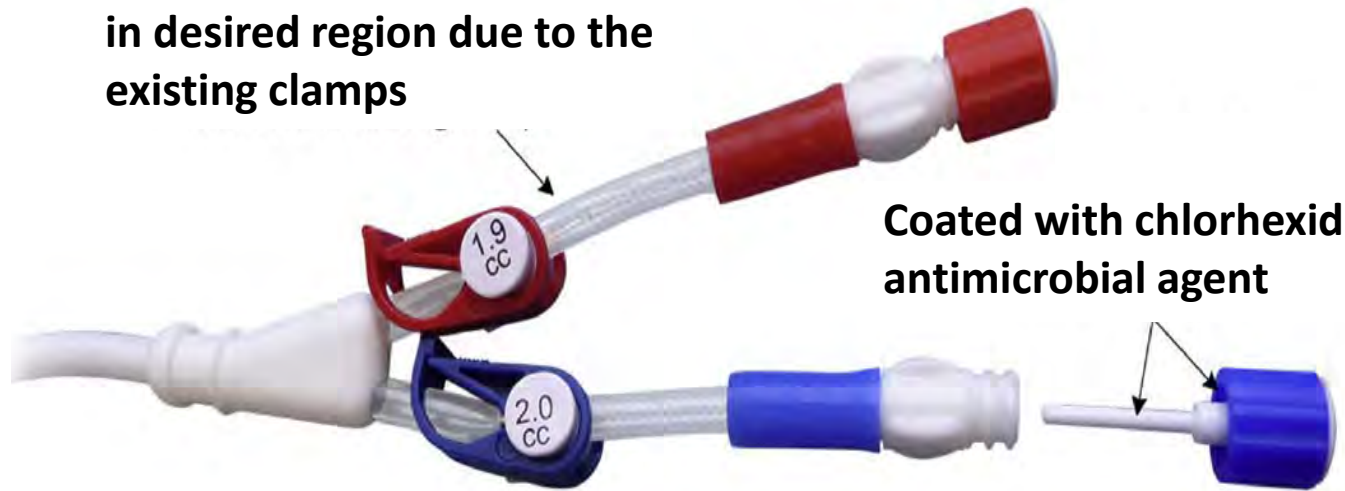


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ClearGuard™ HD

Antimicrobial agent remains in desired region due to the existing clamps



Coated with chlorhexidine a broad-spectrum antimicrobial agent



ClearGuard versus Tego + Curo



ClearGuard



Tego + Curo

Curo- Contains 70% isopropyl alcohol –kills bacteria on outer surface of needleless connector

Tego- Closed-system with a silicone barrier to prevent bacteria from entering lumen

ClearGuard HD vs. Tego + Curo

Favored ClearGuard:

- Decreased positive blood culture
- Decreased IV antibiotic starts

Brunelli SM et al. JASN 2018



Wrapping Up...

- The best way to prevent CRBSI, is to avoid catheter use
- Remember CDC Core Interventions to prevent BSI
- Your patient, with multiple CRBSI episodes in spite of adhering to optimal maximal aseptic techniques, may benefit from an **antimicrobial lock**
- Stay tuned for innovations (e.g., FDA approved locks, devices) to prevent CRBSI

You have an important role to play in promoting patient safety by decreasing BSI

Important Resources

-CDC Dialysis Webpage- <https://www.cdc.gov/dialysis/index.html>

-Nephrologists Transforming Dialysis Safety Infection Control Training Curriculum-https://epc.asn-online.org/learning_course/ntds-a-curriculum-to-achieve-zero-preventable-infections/



Thank you



A Meta-analysis of Antimicrobial Lock Solutions for Hemodialysis Catheters

Methods: Included 7 prospective randomized control studies comparing antimicrobial lock solution (i.e., antibiotic and non-antibiotic locks) with heparin

Results: Catheter-related infections were **7.72 times** less likely when using antimicrobial lock solutions compared to heparin

Limitations: relatively short duration of follow-up of the included studies

Jaffer Y et al Am J Kidney Dis. 2008;51(2):233