Prevention of CRBSI: state of the art

A/Prof Agnes van den Hoogen
ahoogen@umcutrecht.nl

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State of the ART

Definitions
What is known ?
Facts
Risks
Prevention bundles
What is (relatively) new ?

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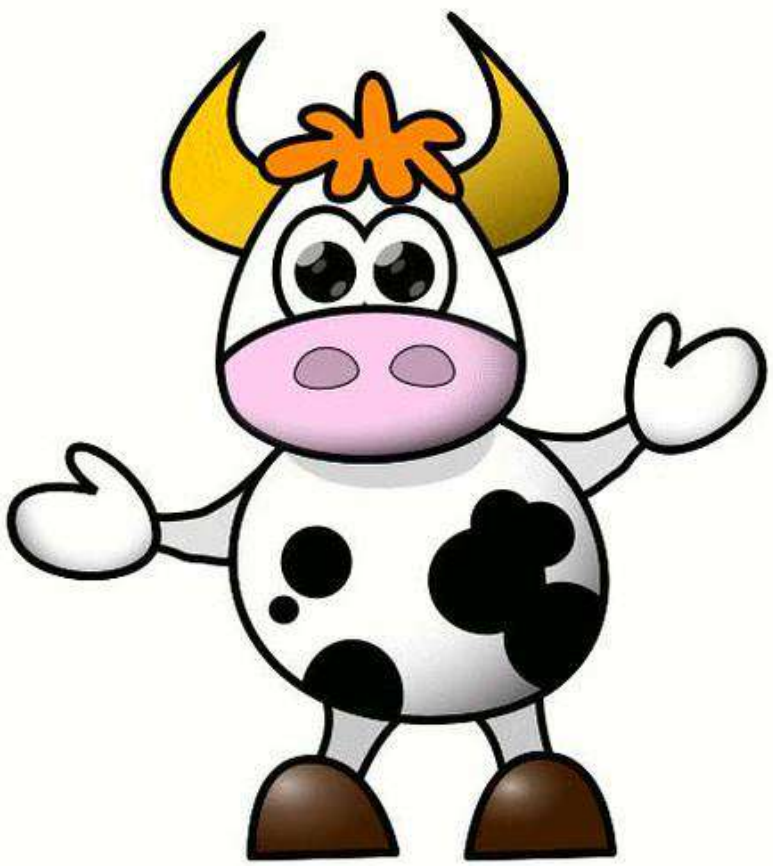
WHY



Important to know

2 major definitions to describe bloodstream infections related to CVCs

- **CRBSI** → catheter-related bloodstream infection &
- **CLABSI** → central line-associated bloodstream infection

CRBSI is a clinical definition based on clinical criteria related to a specific patient in which the diagnosis is being considered (more often used for research)

Diagnosis of **CLABSI** is a simplified definition based on surveillance criteria that identify bloodstream infections in patients with CVCs in which there is no other obvious secondary source for bacteremia.

Bell T, O'Grady NP. Prevention of Central Line-Associated Bloodstream Infections. Infect Dis Clin North Am. 2017 Sep;31(3):551-559. doi: 10.1016/j.idc.2017.05.007. Epub 2017 Jul 5. PMID: 28687213; PMCID: PMC5666696.

Numbers

- Central venous catheters (CVCs) are life-saving
- Many patients in ICUs have them
- Placed in order to receive medicine and fluids

Use of these CVCs can result in serious **bloodstream infections**

- ❑ In **adult** Intensive Care Units (ICUs) 2.0/1000 per catheter days
- ❑ In **children** 4.87 per 1,000 catheters days
- ❑ In **neonates** 1.2-21.8/1,000 catheters days

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Bassetti M, Righi E, Carnelutti A. Bloodstream infections in the Intensive Care Unit. Virulence. 2016 Apr 2;7(3):267-79. doi: 10.1080/21505594.2015.1134072. Epub 2016 Jan 13. PMID: 26760527; PMCID: PMC4871677.

Catheter related bloodstream infections (CRBSI)

- Incidence of CRBSI reported varies from country to country and even from hospital to hospitals
- 60% of CRBSIs caused by micro-organisms from the patient's skin

- A diagnosis of CRBSI can often be made without catheter removal by application of the differential time to positivity blood culture assay
- Increasing experience is being gained with successful catheter salvage and treatment without catheter removal using antimicrobial lock therapy

Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc. 2006;81:1159–71
Intravascular Catheter-Related Bloodstream Infections. Mark E Rupp, Rajendra Karnatak. Review Infect Dis Clin North Am. 2018 Dec;32(4):765-787. doi: 10.1016/j.idc.2018.06.002. Epub 2018 Sep 18.

FACTS CRBSI

- Approximately 30,000 to 40,000 episodes of catheter-related bloodstream infection(CRBSI) occur in the United States each year
- Resulting in a significantly increased odds of death and an estimated cost of $45,000 per event*
- **Related to the use of an intravascular device** also in children and in critically-ill neonates

- **Incidence of CRBSI as high as 18 cases per 1000 catheter-days**

Intravascular Catheter-Related Bloodstream Infections. Mark E Rupp, Rajendra Karnatak. Review Infect Dis Clin North Am. 2018 Dec;32(4):765-787. doi: 10.1016/j.idc.2018.06.002. Epub 2018 Sep 18.

External risk factors CRBSI

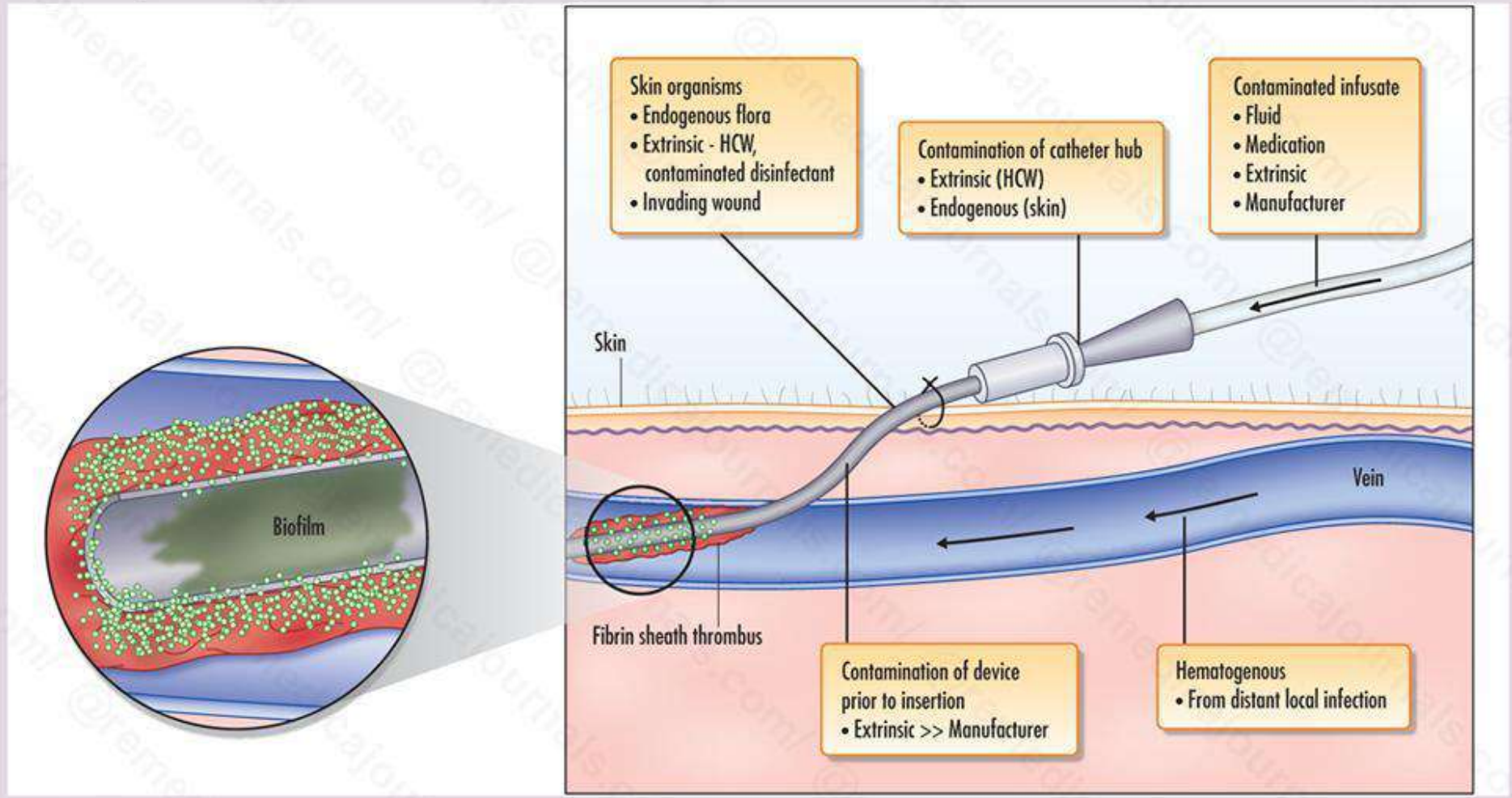
- Long term venous access for TPN, medication, transfusion and repeated blood sampling
- TPN predictor of CVC related infections[1]
- Bad adherence to hand hygiene
- Hands important vectors of pathogens[2]

- Each person carrying average of 7 bacterial cultures[3]

1 NNIS 2004, 2 Perlman et al 2007, 3 Saiman 2006, 4 Cook et al 2007

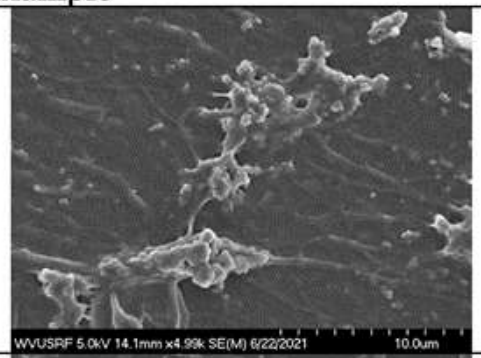
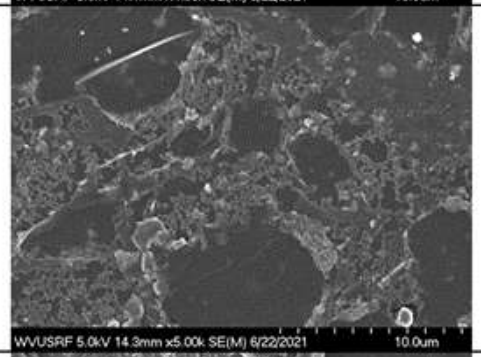
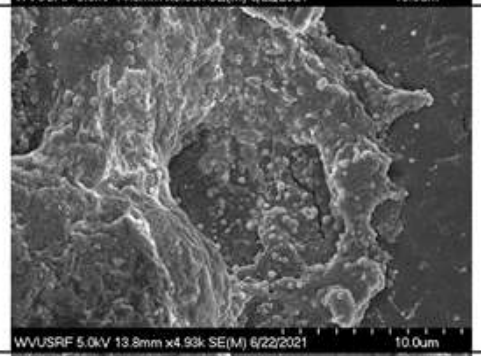
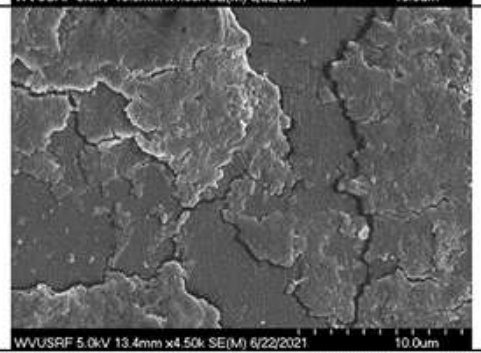
Biofilm

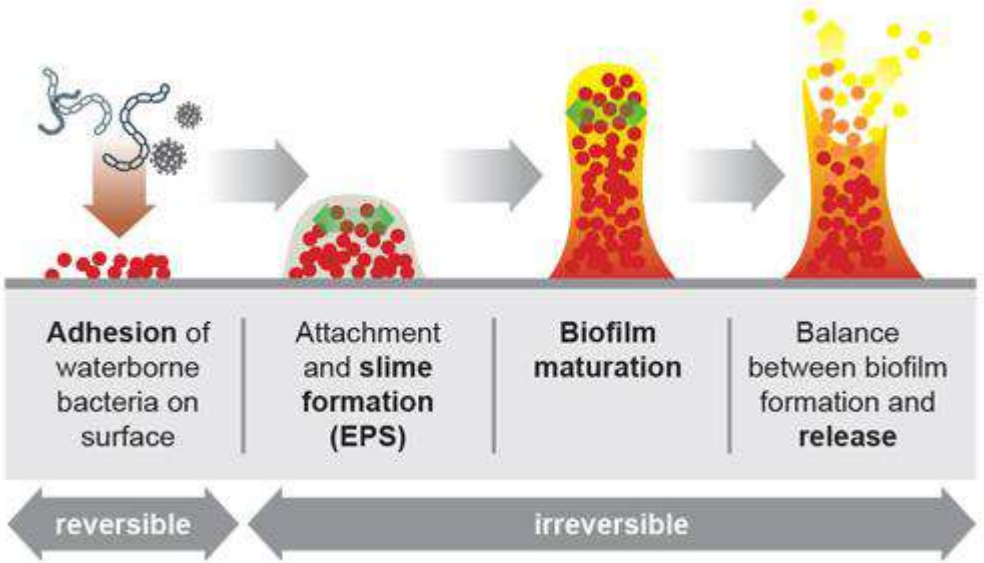
Figure 2. Diagram of an intravenous catheter with biofilm growth.



HCW: healthcare worker.

Image courtesy of Remedica Journals
http://www.remedicajournals.com/The-Journal-of-Invasive-Fungal-Infections/BrowseIssues/Volume-5-Issue-2/Article-The-Story-of-Biofilms

Stage	Definition	Example
I (Attachment)	Background substrate is visible and single to small groups of loosely adherent bacteria are seen. Glycocalyx is sometimes present.	
II (Sessile Growth)	Biomass is increased, as is variety of bacteria. Both biofilm and planktonic bacteria are present.	
III (Colonization)	Highly structured and complex. Well-hydrated and large biomass with covering of glycocalyx. This is a mature biofilm.	
IV (Dispersal)	Dehydrated biomass with cracking visible. Individual bacteria or clusters are sometimes seen, but no substrate seen.	



https://www.aqua-free.com/en/magazine/what-is-a-biofilm

Biofilm Formation on Central Venous Catheters: A Pilot Study

Britney Niemann, MD, Lauren Dudas, MD, FACS, Dana Gray, MS, Andrea Pettit, MS, Alison Wilson, MD, FACS, James M. Bardes, MD, FACS

Journal of Surgical Research
Volume 280 Pages 123-128 (December 2022)
DOI: 10.1016/j.jss.2022.06.072

Known for the prevention of CRBSI's

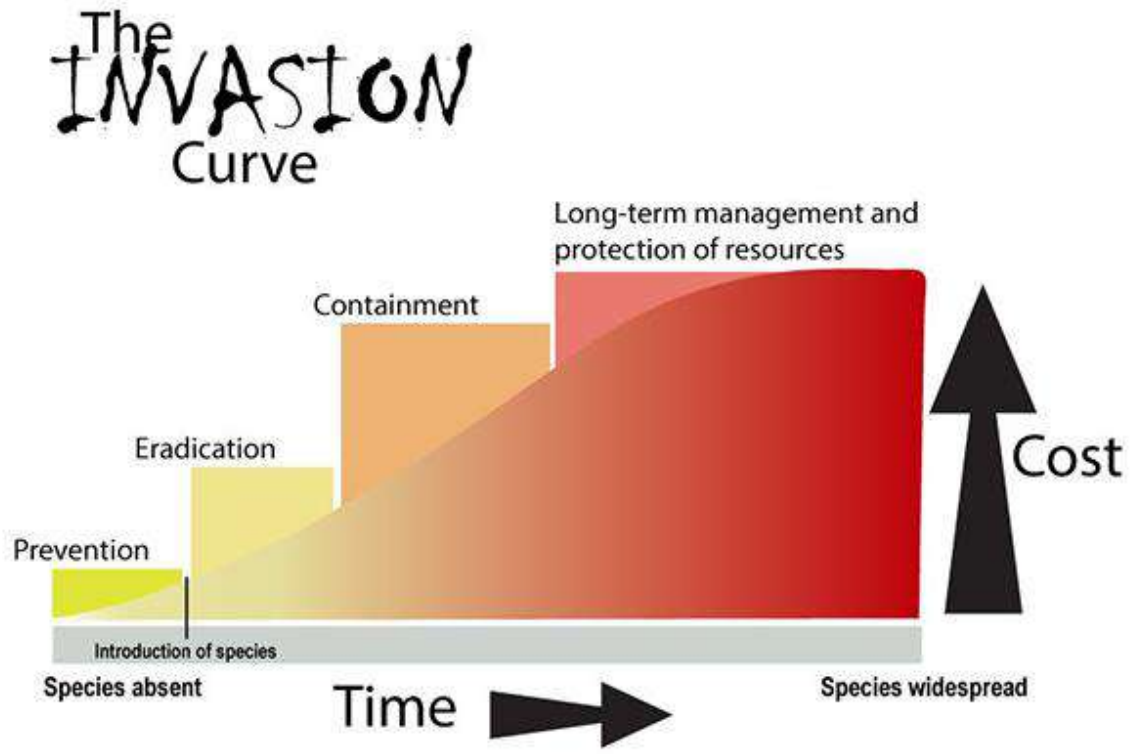
Interesting findings have been published in the field after the latest guidelines (2011) of the Centers for Disease Control and Prevention (CDC) for the prevention CRBSI

1. Skin disinfection with chlorhexidine alcohol reduced the risk of CRBSI compared to skin disinfection with povidone iodine alcohol
2. Implementation of quality improvement interventions reduced the incidence of CRBSI
3. Use of chlorhexidine impregnated dressing compared to standard dressings reduced the risk of CRBSI and catheter related cost in an health economic model
4. The use of antimicrobial/antiseptic impregnated catheters reduced the incidence of CRBSI and catheter related cost in clinical studies.

Ann Transl Med. 2016 Mar;4(6):119. doi: 10.21037/atm.2016.03.10. PMID: 27127772; PMCID: PMC4828748.

PREVENTION

- Education, quality improvement program
- IV TEAM
- Bundles of care for insertion &
- Maintenance
- Evidence
- Compliance



Strategies for prevention CRBSI

Rates of CR-BSI higher than 1 per 1,000 catheter days are **no longer acceptable**

Continuous quality improvement program effective

Studies in **adults**, **PICU and NICU** → significant decrease in CRBSI after implementation of **bundles** and or **changing practice**

Key elements & Implementation of prevention bundles

- Hand hygiene
- Sterile barrier precautions for line insertion
- Chlorhexidine gluconate for skin disinfection
- Selection of optimal catheter site
- Early removal of catheter

Effectiveness of insertion and maintenance bundles to prevent central-line-associated bloodstream infections in critically ill patients of all ages: a systematic review and meta-analysis. Ista E, van der Hoven B, Kornelisse RF, van der Starre C, Vos MC, Boersma E, Helder OK. Lancet Infect Dis. 2016 Jun;16(6):724-34.

Central-line bundles need a multimodal implementation strategy. Walter Zingg, Didier Pittet. The Lancet Infectious Diseases, Volume 16, Issue 6, June 2016, 631-632

Buetti N, Timsit JF. Semin Respir Crit Care Med. 2019 Aug;40(4):508-523. doi: 10.1055/s-0039-1693705. Epub 2019 Oct 4. PMID: 31585477.

Estrada-Orozco K, Cantor-Cruz F, Larrotta-Castillo D, Díaz-Ríos S, Ruiz-Cardozo MA. [Central venous catheter insertion and maintenance: Evidence-based clinical recommendations]. Rev Colomb Obstet Ginecol. 2020 Jun;71(2):115-162. Spanish. doi: 10.18597/rcog.3413. PMID: 32770871.

Bundles of Care

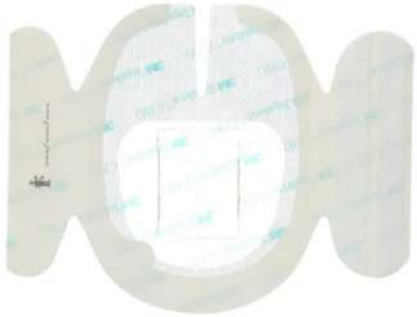
Insertion Bundle	Maintenance Bundle
a) Establish a central line kit or cart to consolidate all items necessary for the procedure	a) Perform hand hygiene with hospital approved alcohol-based product or antiseptic-containing soap before and after accessing a catheter or before and after changing the dressing
b) Perform hand hygiene with hospital-approved alcohol-based product or antiseptic-containing soap before and after palpating insertion sites and before and after inserting the central line	b) Evaluate the catheter insertion site daily for signs of infection and to assess dressing integrity
c) Use maximal barrier precautions (including: sterile gown, sterile gloves, surgical mask, hat, and large sterile drape)	c) At a minimum, if the dressing is damp, soiled, or loose change dressing aseptically and disinfect the skin around the insertion site with an appropriate antiseptic (eg, 2% chlorhexidine, 70% alcohol)
d) Disinfect skin with appropriate antiseptic (eg, 2% chlorhexidine, 70% alcohol) before catheter insertion	d) Develop and use standardized intravenous tubing setup and changes
e) Use either a sterile transparent semipermeable dressing or sterile gauze to cover the insertion site	e) Maintain aseptic technique when changing intravenous tubing and when entering the catheter including “scrub the hub”
	f) Daily review of catheter necessity with prompt removal when no longer essential

Management and Prevention of CRBI's in the ICU

- **Audit and feedback** of the process, infection rates, & **periodic re-education** of health care providers is key
- **Catheter removal**, especially in the case of sepsis or shock
- While awaiting culture results, an **empiric antimicrobial treatment** should target gram-positive microorganism (i.e., Staphylococcus aureus). Gram-negative coverage should be based on clinical variables, patients' risk factors, and previous colonization status
- **Short course of antimicrobials** (7 days) is sufficient for non-complicated CRBSI
- Longer course of 14 days should be preferred for uncomplicated S. aureus and Candida CR-BSI
- Persisting fever or positive blood culture after 3 days despite adequate antimicrobial therapy and catheter removal, catheter-related complications (e.g., endocarditis, thrombophlebitis, septic metastasis) **should be ruled out!!!!**

Buetti N, Timsit JF. Semin Respir Crit Care Med. 2019 Aug;40(4):508-523. doi: 10.1055/s-0039-1693705. Epub 2019 Oct 4. PMID: 31585477.

Biopatch and Tegaderm CHG



Both have

- Chlorhexidine as active agent,
- Same action of skin around catheter insertion site
- Local chlorhexidine directly to the catheter insertion site and surrounding skin, and similar time span of delivery (e.g. while dressing is present)

Both have been shown to reduce catheter colonization and catheter related infections

Moderate-quality evidence showing that chlorhexidine impregnated dressings reduce the frequency of CRBSI per 1000 patient days compared with standard polyurethane dressings (RR 0.51, 95% CI 0.33 to 0.78) and reduce catheter tip colonization compared to standard dressings (RR 0.58, 95% CI 0.47 to 0.73)

*Department of Health and Human Services Centers for Disease Control and Prevention HIPAC Meeting. 2015 Nov; http://www.cdc.gov/HICPAC/presentations.html. *Arvaniti K, et al. Comparison of Oligon catheters and chlorhexidine-impregnated sponges with standard multilumen central venous catheters for prevention of associated colonization and infections in intensive care unit patients: a multicenter, randomized, controlled study. Crit Care Med. 2012;40(2):420–9. *Ruschulte H, et al. Prevention of central venous catheter related infections with chlorhexidine gluconate impregnated wound dressings: a randomized controlled trial. Ann Hematol. 2009;88(3):267–72. *Timsit JF, et al. Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. Am J Respir Crit Care Med. 2012;186(12):1272–8. *Timsit JF, et al. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. Jama. 2009;301(12):1231–41. *Ullman AJ, et al. Dressings and securement devices for central venous catheters (CVC) Cochrane Database Syst Rev. 2015;(9):Cd010367.

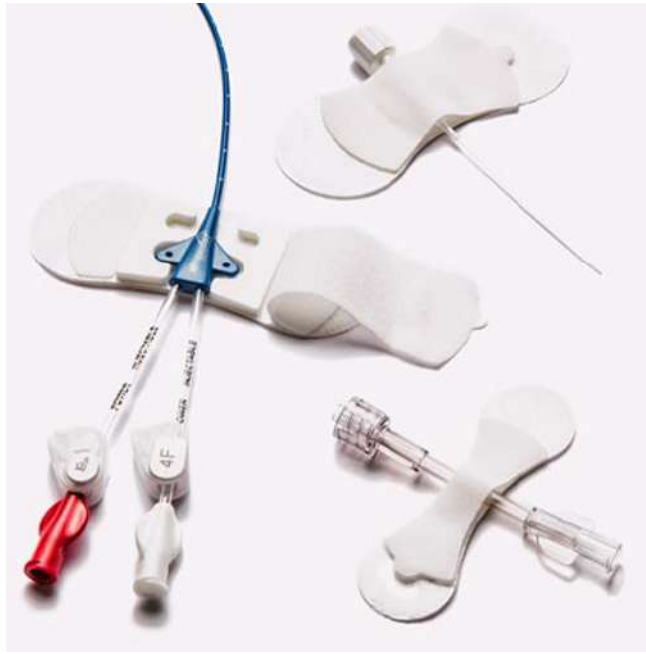
Needleless Securement Devices

- CVCs sutured to the surrounding skin to prevent accidental dislodging

- SSDs (sutureless securement devices) dislodging without violating the skin
- SSDs secure catheters to the skin and often use the catheter hub suture wings as a key contact area
  - Bard StatLock CV Plus Stabilization Device
  - 3M PICC/CVC Needleless Securement Device

Given the benefits of using SSDs in reducing CRBSI,

they are recommended by guidelines for the securement of CVCs



O'Grady NP, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162–93

https://deltamed.pro/en/news/sutureless-stabilization-devices

Relative new and under study

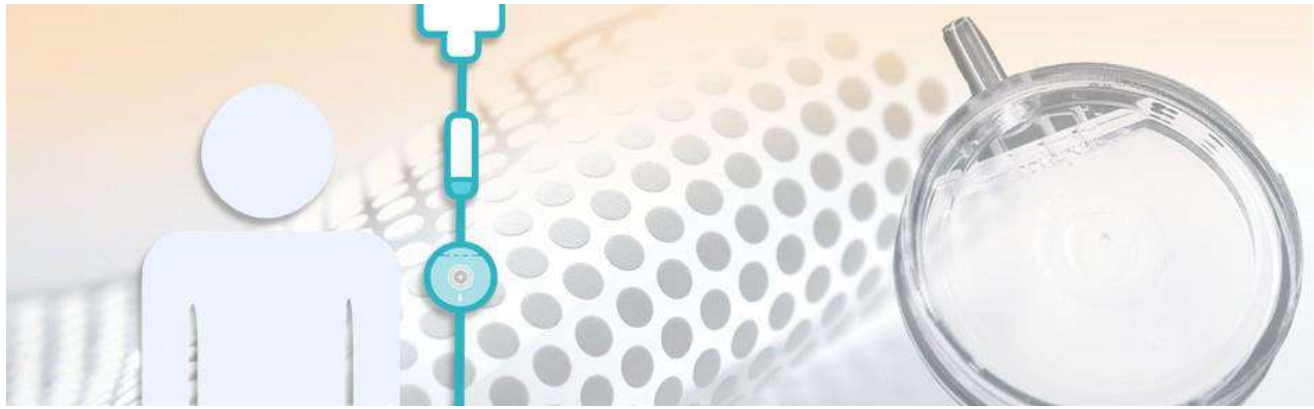
- Evidence
- Increasing knowledge
- However

- **Work to be done**

WoCoVA consensus on the clinical use of in-line filtration during intravenous infusions: Current evidence and recommendations for future research

The rationale for the use of in-line filters relies in the **possibility of reducing the potential systemic effect of undesired micro-particles entering the circulation** via the infusion line

Many studies on this topic are quite old and it is obviously difficult to draw conclusions from evidence accumulated in a span of almost four decades, considering the inevitable changes in product characteristics (both filters and infusate), techniques and knowledge about intravenous management



Van Boxtel T, Pittiruti M, Arkema A, Ball P, Barone G, Bertoglio S, Biffi R, Dupont C, Fonzo-Christe C, Foster J, Jones M, Keck C, Ray-Barruel G, Sasse M, Scoppettuolo G, Van Den Hoogen A, Villa G, Hadaway L, Ryder M, Schears G, Stone J. WoCoVA consensus on the clinical use of in-line filtration during intravenous infusions: Current evidence and recommendations for future research. J Vasc Access. 2022 Mar;23(2):179-191. doi: 10.1177/1129729821989165. Epub 2021 Jan 28. PMID: 33506747.

WoCoVA consensus on the clinical use of in-line filtration during intravenous infusions

Table 2. Summary of the conclusions of the panel

(1) Evidence about possible harmful effects of inert particles in intravenous infusions

The types and dimensions of the potentially harmful particles are extremely variable.

Particles **10–12 micron can occlude the microcirculation** and may potentially be associated with local tissue damage, particularly in the lung.

A great variety of pathological conditions has been potentially ascribed to the effect of particles, most of it anecdotical.

Filters with 0.2 micron are expected to stop the vast majority of particles, including bacteria and air bubbles; 1.2-micron filters are used for removing lipid aggregates during administration of PN.

Larger filters are unlikely to remove most of the potentially harmful particles.

WoCoVA consensus on the clinical use of in-line filtration during intravenous infusions

Table 2. Summary of the conclusions of the panel

(2) Potential benefits of in-line filters in reducing peripheral phlebitis

Inert particles, drug precipitates, endotoxin, bacteria, etc. might be successfully removed by in-line filters.

The results of clinical studies dealing with the potential beneficial effect of in-line filters is overall uncertain and controversial.

WoCoVA consensus on the clinical use of in-line filtration during intravenous infusions

Table 2. Summary of the conclusions of the panel

(3) **Potential benefits of in-line filters in reducing systemic inflammation/infection**

The accurate pathogenesis of systemic infection is still largely unclear.

At present, there is no clear and direct evidence that particles may be involved in this pathogenesis.

The available clinical evidence suggests that in-line filters may play a role in reducing systemic complications in the pediatric and neonatal populations, particularly in the critically ill or in children receiving PN. Though, data suggest some effects on the reduction of the incidence of SIRS and of organ failure, but not on mortality or on the incidence of sepsis.

Disinfection Caps

- Prevent the potential transmission of pathogenic organisms when administering drugs or fluids
- Several disinfection cap products are available and have been shown to be effective in reducing hub colonization and CRBSI
- Observational study, a total of 3,005 catheter-days and 1 CLABSI (0.3 infections/1,000 catheter-days) were documented during an intervention period where alcohol-impregnated port-protectors were introduced, compared with 6,851 catheter-days and 16 CLABSIs (2.3 infections/1,000 catheter-days) during the control period (RR, 0.14; 95% CI, 0.02–1.07; p = .03)
- As an effective antiseptic method, not relying on active human intervention, disinfection caps are away to complement a comprehensive CRBSI reduction strategy

Sweet MA, et al. Impact of alcohol-impregnated port protectors and needleless neutral pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. Am J Infect Control. 2012;40(10):931–4.

Taurolidine lock solutions for the prevention of catheter-related bloodstream infections: a systematic review and meta-analysis of randomized controlled trials 2013

- Benefits of taurolidine lock solutions (TLS) for prevention of CRBSIs controversial
- Six randomized controlled trials (RCTs) (2004 through 2013) involving 431 patients and 86,078 catheter-days included.
- **TLS were significantly associated with a lower incidence of CRBSIs when compared to heparin lock solutions** (Risk Ratio [RR], 0.34; 95% Confidence Interval [CI], 0.21-0.55)
- TLS significantly **decreased the incidence of CRBSIs from gram-negative (G-) bacteria** (P = 0.004; RR, 0.27; CI, 0.11-0.65), and associated with a non-significant decrease in gram-positive (G+) bacterial infections (P = 0.07; RR, 0.41; CI, 0.15-1.09). No association was observed with TLS and catheter-associated thrombosis (RR, 1.99; CI, 0.75-5.28)
- TLS reduced the incidence of CRBSIs without obvious adverse effects or bacterial resistance
- Limited sample sizes and methodological deficiencies of included studies.

TauroLock™

Liu Y, Zhang AQ, Cao L, Xia HT, Ma JJ. Taurolidine lock solutions for the prevention of catheter-related bloodstream infections: a systematic review and meta-analysis of randomized controlled trials. PLoS One. 2013 Nov 21;8(11):e79417. doi: 10.1371/journal.pone.0079417. PMID: 24278133; PMCID: PMC3836857.

The efficacy of taurolidine containing lock solutions for the prevention of central-venous-catheter-related bloodstream infections: a systematic review and meta-analysis 2021

8 years later

- RCTs comparing the efficacy of taurolidine containing lock solutions (TL) to other lock solutions in all patient populations
- Random effects model to pool individual study incidence rate ratios (IRRs).
- 14 articles included in the qualitative synthesis describing 1219 haemodialysis, total parenteral nutrition and oncology patients
- Pooled IRR estimated for all patient groups together (nine studies; 918 patients) was 0.30 (95% confidence interval 0.19-0.46), favouring the TLs
- Adverse events (10 studies; 867 patients) were mild and scarce
- Quality of the evidence was limited due to a high risk of bias and indirectness of evidence
- TLs might be promising for the prevention of CRBSI's
- **Again: Large-scale RCTs are needed to draw firm conclusions on the efficacy of TLs.**

van den Bosch CH, Jeremiasse B, van der Bruggen JT, Frakking FNJ, Loeffen YGT, van de Ven CP, van der Steeg AFW, Fiocco MF, van de Wetering MD, Wijnen MHWA. The efficacy of taurolidine containing lock solutions for the prevention of central-venous-catheter-related bloodstream infections: a systematic review and meta-analysis. J Hosp Infect. 2022 May;123:143-155. doi: 10.1016/j.jhin.2021.10.022. Epub 2021 Nov 9. PMID: 34767871..

A longitudinal analysis of nosocomial bloodstream infections among preterm neonates 2022

- Further research aimed at reducing NBSI, in particular CLABSI, is warranted, particularly with regard to limiting central-line dwell-time and fine-tuning insertion and maintenance practices.

- Jansen SJ, van der Hoeven A, van den Akker T, Veenhof M, von Asmuth EGJ, Veldkamp KE, Rijken M, van der Beek M, Bekker V, Lopriore E.. Eur J Clin Microbiol Infect Dis. 2022 Sep 30. doi: 10.1007/s10096-022-04502-8. Epub ahead of print.

  PMID: 36178568.

Patient participation in prevention strategies?

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https://www.hra.nhs.uk/planning-and-improving-research/best-practice/public-involvement/putting-people-first-embedding-public-involvement-health-and-social-care-research/

Evelina London

NHS
Guy's and St Thomas'
NHS Foundation Trust

Infection prevention and control for families

Information about how you can help us minimise risk of infections while your child is in hospital. If you have any questions, please speak to the nurse caring for your child.

This information explains the key principles that will help to prevent infections.

Hand hygiene

What we do

- All our staff have been trained in hand hygiene.
- We expect all staff to wash or use the alcohol hand rub on their hands before and after having contact with your child.
- Every month, we audit compliance with our hand hygiene protocol.

What you can do (and ask your visitors to do the same)

- If you are not sure if a staff member has cleaned their hands, it is OK for you to ask.
- Make sure that your child washes their hands before meals and after using the toilet.
- Make sure that you wash your hands before and after visiting your child, before meals or feeding your child, after visiting the toilet, and after changing your child's nappy or helping them use the toilet or bed pan.

Conclusion

Work in process and ongoing research

- Recommendations in almost all papers
- Future studies for filters, should be designed to identify the occurrence of potentially particle-related complications in different groups of patients
- More clinical studies are needed
- Critical points in the design of future studies are:
  - the proper identification of the patient population (e.g neonates vs children)
  - type of treatment (PN solutions vs non-nutritional IV therapies)
  - definition of the primary endpoint (organ failure; SIRS; systemic infection; mortality; etc.)
- Etc.

References

- Arvaniti K, et al. Comparison of Oligon catheters and chlorhexidine-impregnated sponges with standard multilumen central venous catheters for prevention of associated colonization and infections in intensive care unit patients: a multicenter, randomized, controlled study. Crit Care Med. 2012;40(2):420–9.
- Bell T, O'Grady NP. Prevention of Central Line-Associated Bloodstream Infections. Infect Dis Clin North Am. 2017 Sep;31(3):551-559. doi: 10.1016/j.idc.2017.05.007. Epub 2017 Jul 5. PMID: 28687213; PMCID: PMC5666696.
- Department of Health and Human Services Centers for Disease Control and Prevention HIPAC Meeting. 2015 Nov; http://www.cdc.gov/HICPAC/presentations.html.
- O'Grady NP, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011;52(9):e162–93
- Ruschulte H, et al. Prevention of central venous catheter related infections with chlorhexidine gluconate impregnated wound dressings: a randomized controlled trial. Ann Hematol. 2009;88(3):267–72.
- Timsit JF, et al. Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. Am J Respir Crit Care Med. 2012;186(12):1272–8.
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- Sweet MA, et al. Impact of alcohol-impregnated port protectors and needleless neutral pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. Am J Infect Control. 2012;40(10):931–4.
- Ullman AJ, et al. Dressings and securement devices for central venous catheters (CVC) Cochrane Database Syst Rev. 2015;(9):Cd010367.

Catheter Dressing and Maintenance

- Chlorhexidine-Impregnated Dressings Two types of chlorhexidine gluconate–impregnated dressings are widely available: Biopatch (http://www.ethicon.com/healthcare-professionals/infection-prevention/biopatch-protective-disk-chg)
- Tegaderm™ CHG Chlorhexidine Gluconate IV Securement Dressing (http://www.3m.com/3M/en_US/company-us/all-3m-products/~/3M-Tegaderm-CHG-Chlorhexidine-Gluconate-I-V-Securement-Dressing?N=5002385+3293321978&rt=rud)