Katheterinfektionen

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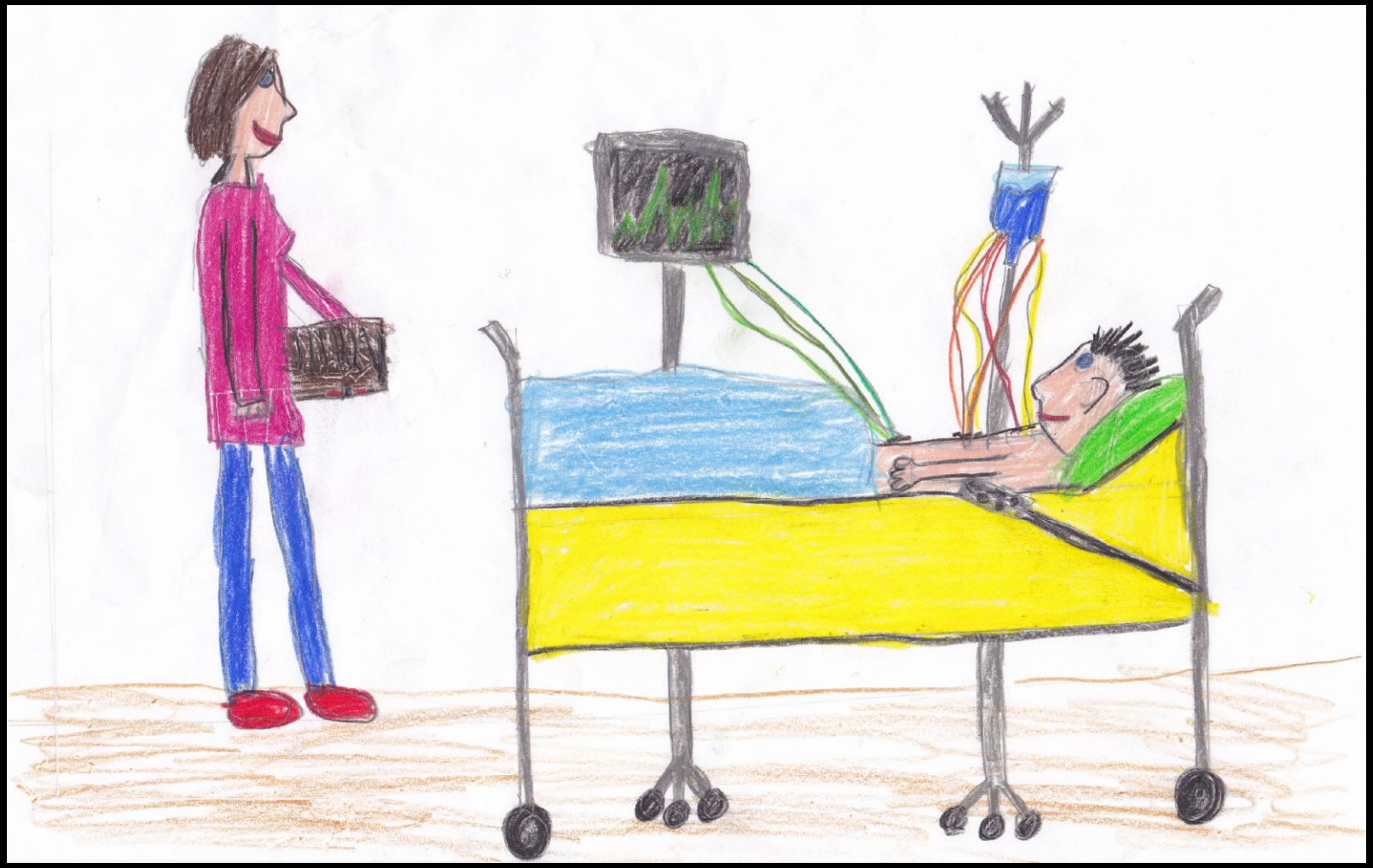
One of the dilemmas of modern medicine that is particularly relevant for intensive care is the risk vs benefit of medical devices and equipment as well as medications…



Epidemiology: CR-BSI

Peripheral intravenous catheters 0.5/1000 IVD-d

Noncuffed central venous catheters
- Nonmedicated and nontunneled 2.7/1000 IVD-d
- Nonmedicateed and tunneled 1.7/1000 IVD-d

Hemodialysis catheters (temporary) 4.8/1000 IVD-d

Arterial catheters (monitoring) 1.7/1000 IVD-d

Pulmonary artery catheters 3.7 /1000 IVD-d

Mayo Clin Proc 2006; 81(9):1159-1171

Epidemiology: CVC-BSI

USA

5.0 per 1000 catheter-days (1992-2004)
2.9 per 1000 catheter-days (2006)

Europe

1-3.1 per 1000 catheter-days

Kantonsspital St. Gallen / Graubünden

2.5 per 1000 catheter-days

Am J Infect Control 2004; 32:420-485 // 2007; 35:290-301
J Hosp Infect 2007; 65:171
Infection 2008; 36:322-327

Epidemiology of CR-BSI

Incidence

10-20% of all nosocomial infections

Attributable mortality

2-15%

Prolongation of the LOS

5-20 days

Attributable costs

3700 - 29000 $

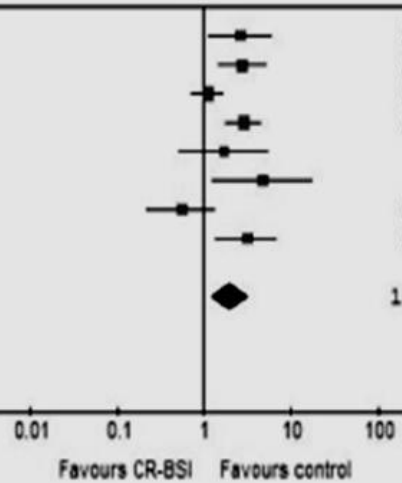
Infection 1997; Int Care Med 2000;
Am J Med 2002; SRLF 2010

Attributable mortality

Review: Impact of catheter-related bloodstream infections on the mortality of critically ill patients: a meta-analysis
Comparison: 01 Mortality
Outcome: 01 In-hospital mortality (all studies)

Study or sub-category	CR-BSI n/N	Control n/N	OR (random) 95% CI	Weight %	OR (random) 95% CI
Higuera	23/55	12/55		12.04	2.58 [1.12, 5.93]
Warren	21/41	301/1091		14.64	2.76 [1.47, 5.16]
Blot	49/176	82/315		17.37	1.10 [0.72, 1.66]
Rosenthal	77/142	42/142		16.44	2.82 [1.73, 4.60]
Renaud	10/26	7/26		8.62	1.70 [0.53, 5.48]
Dimick	5/9	53/251		7.27	4.67 [1.21, 18.00]
Rello	11/49	17/49		11.38	0.54 [0.22, 1.33]
Soufir	20/38	20/75		12.25	3.06 [1.35, 6.92]
Total (95% CI)	536	2004		100.00	1.96 [1.25, 3.09]

Total events: 216 (CR-BSI), 534 (Control)
Test for heterogeneity: $Chi^2 = 21.63$, df = 7 (P = 0.003), $I^2 = 67.6\%$
Test for overall effect: Z = 2.91 (P = 0.004)



All cause in-hospital mortality CR-BSI < no CR-BSI (OR 1.96)
Subgroup (matched for severity of illness) OR 1.70

Crit Care Med 2009; 37:2283-89

Definitions

Catheter colonization

Significant growth ≥1 microorganism in a quantitative or semiquantitative culture of the catheter tip.

Exit site infection

Erythema, induration, and/or tenderness within 2cm of the catheter exit site. May be associated with other signs of infection.

Tunnel infection

Tenderness, erythema and/or induration >2cm from the catheter exit site, along the subcutaneous tract of a tunneled catheter.

Catheter related bloodstream infection

Catheter-related BSI

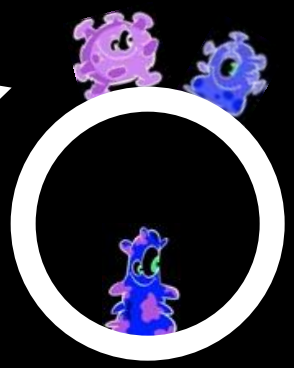
Bacteremia/fungemia in a patient with IVD and >1 pos blood culture (peripheral vein), clinical manifestations of infection, no other source of bloodstream infection

and

- Positive result of catheter culture (same organism)
- Simultaneous quantitative cultures of blood with a ratio of > 3:1 cfu/ml of blood (catheter vs peripheral)
- Differential time to positivity (at least 2h)

IDSA Guidelines for Intravascular Catheter-Related Infection - CID 2009:49

Pathogenesis



Extraluminal route

- Migration of skin organisms from the insertion site

-> Most common route of infection for short-term cvc

Intraluminal route

- Manipulation of the venous line with migration of organisms along the internal lumen of the catheter

Hematogenous

- < 10%

-> From distant infection

Microbiology

Tabelle 1 : Mikrobiologie von Katheterinfekten/-septikamien

Koagulase-negative Staphylokokken (CNS)	30 - 40 %
S. aureus	5 - 10 %
Enterokokkus spp.	4 - 6 %
Pseudomonas aeruginosa	3 - 6 %
Candida spp.	2 - 5 %
Enterobacter spp.	1 - 4 %
Acinetobacter spp.	1 - 2 %
Serratia spp.	< 1 %

Swiss NOSO, 1994

Risk factors I

Host factors

- Male
- Immune deficiency, especially neutropenia
- Chronic illness
- Length of hospital stay before cvc
- Lost of skin integrity (burns)

Catheter handling

- Number of manipulation
- Parenteral nutrition
- Increasing duration of catheterization

Risk factors II

<u>Site and method of insertion</u>

- Insertion site: femoral / intrnal jugular > subclavian
  femoral > internal jugular?
- Submaximal barrier precautions
- Emergent insertion
- Skill of operator
- Nontunneled > tunneled
- Higher risk with multiple lumen catheter

SPÜR DIE ANGST

STOCKHOLM CRIME

Symptoms of CR-BSI

Table 3. Inflammation of the catheter insertion site at central venous catheter (CVC) removal with uninfected and infected CVCs[a]

Parameters	No. (%) of CVCs with Parameter Present	CVC-related BSI, n = 35	Colonized CVCs, n = 333	Noncolonized and Uninfected CVCs, n = 894
Pain (0, 1)	25 (2)	0.0	0.2 ± 0.4	0.2 ± 0.4
Erythema (0–2)	25 (2)	0.0	0.1 ± 0.3	0.1 ± 0.2
Swelling (0, 1)	126 (10)	0.2 ± 0.4	0.1 ± 0.4	0.1 ± 0.4
Purulence (0, 1)	10 (0.8)	0	0.0 ± 0.1	0
Overall (0–5)	126 (10.0)	0.2 ± 0.4	0.1 ± 0.1	0.1 ± 0.1

Sensitivity of local inflammation for diagnosis of CR-BSI 0-3%

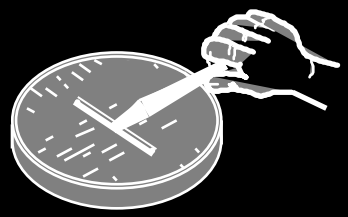
-> In general site appearance cannot be relied on to identify catheter colonization or CR-BSI.

Crit Care Med 2002; 30:2632-35

Diagnosis I

Semi-quantitative Catheter Segment Culture

- Roll-Plate Method, Maki NEJM 1977
- 5cm catheter segment
- $\geq$ 15 cfu
- Samples only the external surface



Quantitative Catheter Segment Culture

- Brun-Buisson AIM 1987; Cleri J Inf Dis 1990;
- Catheter segment, luminal flushing or sonication
- $\geq$ 1000 cfu

Diagnosis II

Paired quantitative blood cultures

- Blood cultures through CVC and from peripheral vein
- Quantitative analysis
- Colony count CVC : peripheral vein $\geq$ 3

Differential time to positivity (DTP)

- Blood cultures throug CVC and from peripheral vein
- Continuously monitoring for microbial growth
- Catheter-drawn blood culture turns positive > 2hours earlier than the peripherally drawn culture

Lancet 1999; 354:107

Meta-Analysis: Methods for Diagnosing Intravascular Device–Related Bloodstream Infection

Nasia Safdar, MD, MS; Jason P. Fine, PhD; and Dennis G. Maki, MD

- Paired quantitative blood cultures is the most accurate test for diagnosis of CR-BSI
- Most of the other methods showed acceptable sensitivity and specifity (both > 0.75) and negative predictive value (> 99%)
- The positive predictive value of all tests increased greatly with high pretest clinical probability
- Catheter should not be cultured routinely but rather only if CR-BSI is suspected

Ann Intern Med 2005; 142:451-466

Diagnosis & management

IDSA GUIDELINES

Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Leonard A. Mermel,[1] Michael Allon,[2] Emilio Bouza,[9] Donald E. Craven,[3] Patricia Flynn,[4] Naomi P. O'Grady,[5] Issam I. Raad,[6] Bart J. A. Rijnders,[10] Robert J. Sherertz,[7] and David K. Warren[8]

[1]Division of Infectious Diseases, Warren Alpert Medical School of Brown University, Providence, Rhode Island; [2]University of Alabama-Birmingham Hospital, Birmingham, Alabama; [3]Tufts University School of Medicine, Lahey Clinic Medical Center, Burlington, Massachusetts; [4]St. Jude Children's Research Hospital, Children's Infection Defense Center, Memphis, Tennessee; [5]National Institutes of Health, Critical Care Medicine Department, Bethesda, Maryland; [6]Section of Infectious Diseases, University of Texas-Cancer Center, Houston; [7]Section of Infectious Diseases, Wake Forest University School of Medicine, Winston-Salem, North Carolina; [8]Division of Infectious Diseases, Washington University School of Medicine, St Louis, Missouri; [9]Servicio de Microbiología Cliínica y E. Infecciosas Hospital General "Gregorio Marañón," Madrid, Spain; and [10]Internal Medicine and Infectious Diseases, Erasmus University Medical Center, Rotterdam, the Netherlands

Clinical Infectious Diseases 2009; 49:1-45

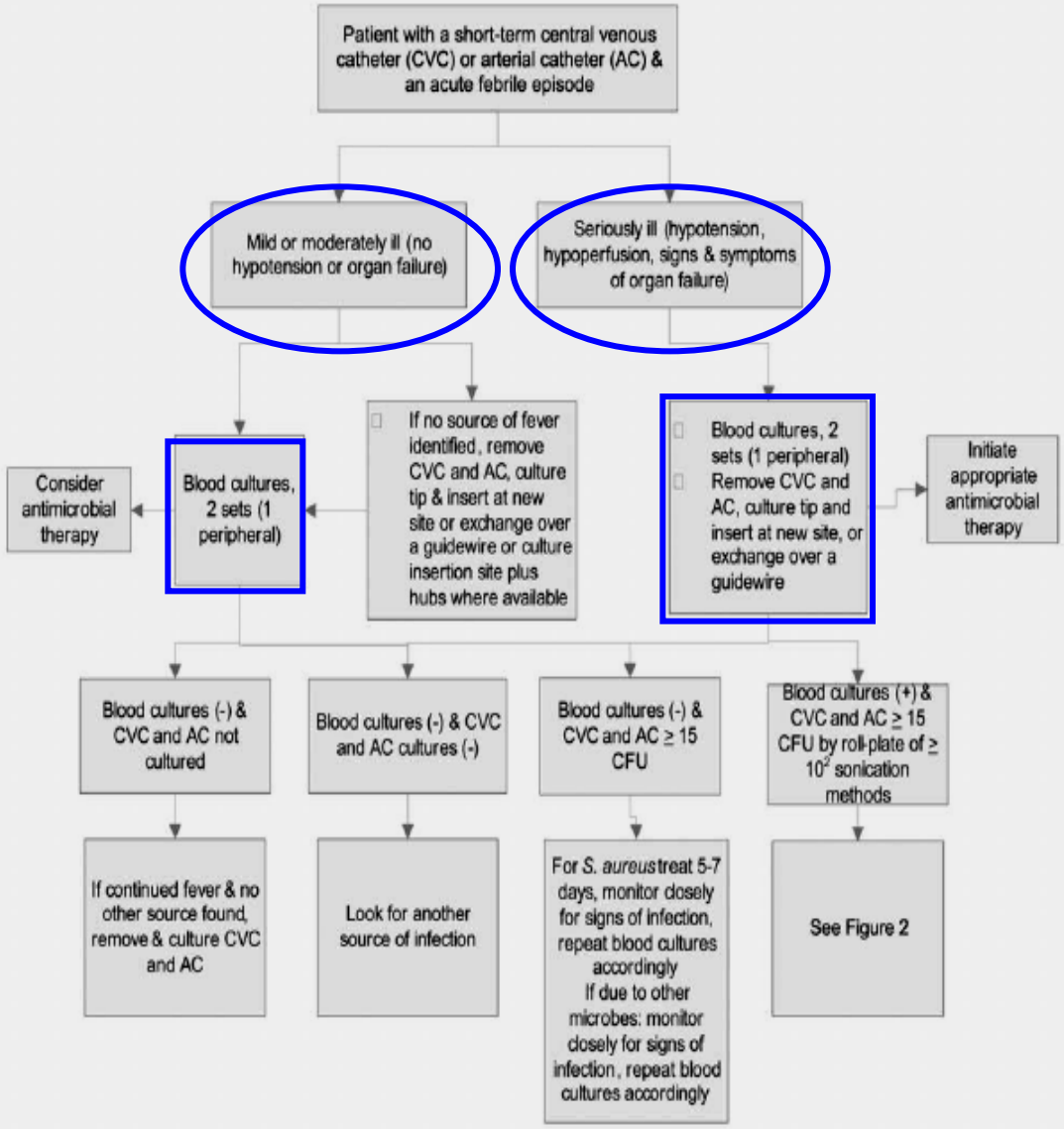


Figure 1. Methods for the diagnosis of acute fever for a patient suspected of having short-term central venous catheter infection or arterial catheter infection. CFU, colony-forming units.

Clinical Infectious Diseases 2009; 49:1-45

How Many Lumens Should Be Cultured in the Conservative Diagnosis of Catheter-Related Bloodstream Infections?

Table 3. Baseline Data for Episodes of Catheter-Related Bloodstream Infection Detected by Culture of Blood Samples Obtained via Double-Lumen and Triple-Lumen Catheters

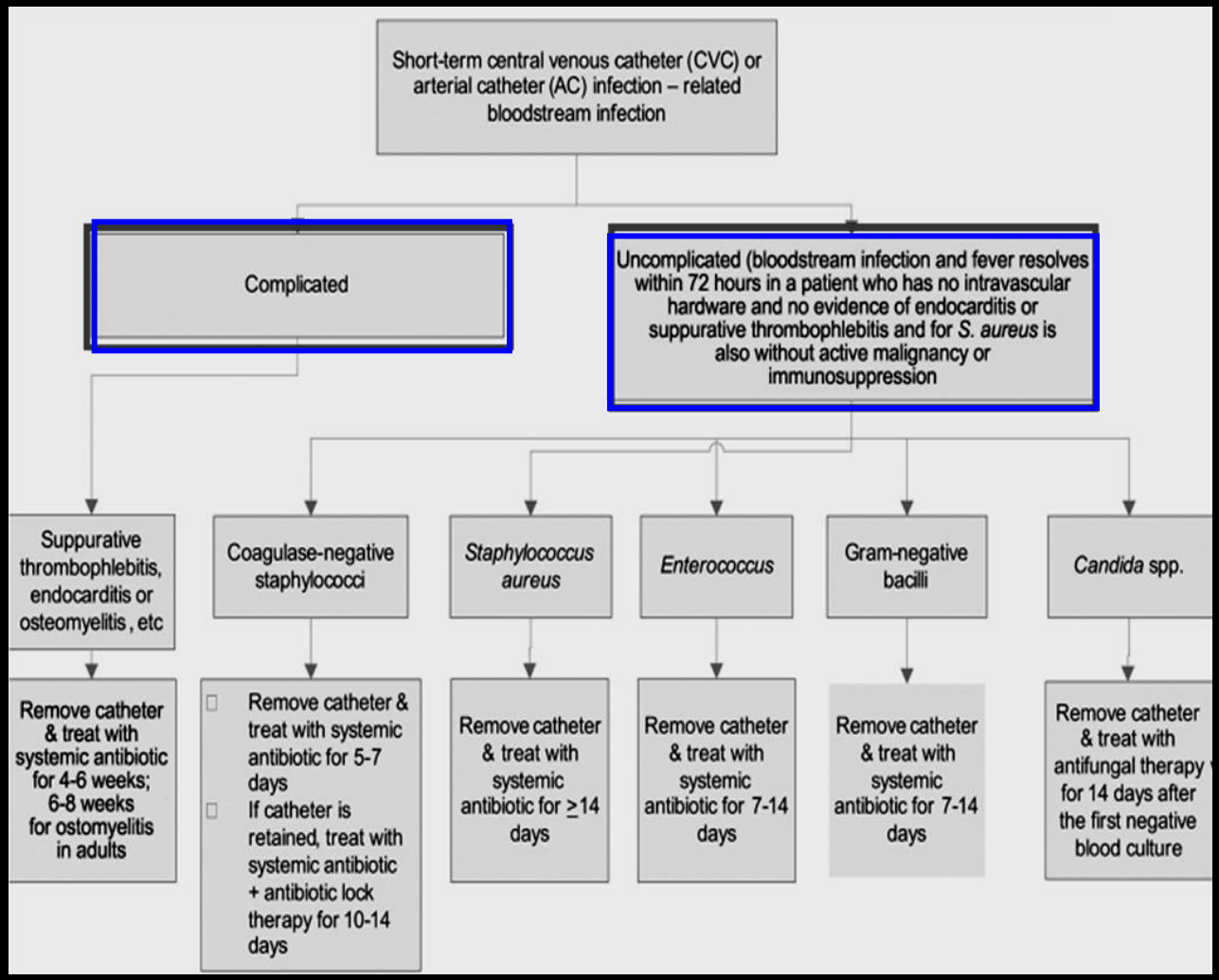
Variable	Double-lumen catheters (n = 112)	Triple-lumen catheters (n = 59)
With 1 lumen causing infection		
No. (%) of episodes	61 (54.5)	28 (47.5)
95% CI, %	44.8–64.1	33.9–61.1
With 2 lumens causing infection		
No. (%) of episodes	51 (45.5)	10 (17.0)
95% CI, %	35.9–55.2	6.5–27.4
With 3 lumens causing infection		
No. (%) of episodes	...	21 (35.6)
95% CI, %	...	22.5–48.7

Table 4. Number and Percentage of Missed Episodes

Variable	Double-lumen catheters (n = 112)	Triple-lumen catheters (n = 59)
When eliminating 1 lumen	27.2%	15.8%
No. (%) of episodes	81.4 (72.8)	49.7 (84.2)
95% CI, %	65.2–81.3	74.6–93.2
P	<.001	.001
When eliminating 2 lumens		37.3%
No. (%) of episodes	...	37 (62.7)
95% CI, %		49.2–74.6
P		<.001

Clinical Infectious Diseases 2010; 50:1575-1579

Therapy



Clinical Infectious Diseases 2009; 49:1-45

Therapy

Remove catheter:

Severe sepsis, complicated, BSI >72h despite antimicrobial therapy

Short-term catheters: S. aureus, gram-neg bacilli, Enterococci, Fungi, Mycobacteria

Long-term catheters: S. aureus, P. aeruginosa, Fungi, Mycobacteria

Antimicrobial therapy:

Gram-pos pathogens: -> MRSA?

Gram-neg pathogens: Severity of disease, local antimicrobial susceptibility

Multidrug resistant pathogens: Neutropenic patients, patients colonized with such pathogens

Prevention

GUIDELINES

Guidelines for the Prevention of Intravascular Catheter–Related Infections

Naomi P. O'Grady,[1] Mary Alexander,[2] E. Patchen Dellinger,[5] Julie L. Gerberding,[6] Stephen O. Heard,[3] Dennis G. Maki,[8] Henry Masur,[1] Rita D. McCormick,[9] Leonard A. Mermel,[10] Michele L. Pearson,[7] Issam I. Raad,[11] Adrienne Randolph,[4] and Robert A. Weinstein[12]

[1]National Institutes of Health, Bethesda, Maryland; [2]Infusion Nurses Society, Cambridge, and [3]University of Massachusetts Medical School, Worcester, and [4]The Children's Hospital, Boston, Massachusetts; [5]University of Washington, Seattle; [6]Office of the Director, Centers for Disease Control and Prevention (CDC), and [7]Division of Healthcare Quality Promotion, National Center for Infectious Diseases, CDC, Atlanta, Georgia; University of Wisconsin [8]Medical School and [9]Hospital and Clinics, Madison; [10]Rhode Island Hospital and Brown University School of Medicine, Providence, Rhode Island; [11]MD Anderson Cancer Center, Houston, Texas; and [12]Cook County Hospital and Rush Medical College, Chicago, Illinois

Clinical Infectious Disease 2002; 35:1281-307

„Central catheter bundle“

A. Hand hygiene

B. Maximal barrier precautions upon insertion

C. Chlorhexidine skin antisepsis

D. Optimal catheter site selection with avoidance of the femoral vein for cvc in adults patients

E. Daily review of catheter necessity with prompt removal of unnecessary catheters

Institute for Healthcare Improvement (www.ihi.org/ihi)

„Central catheter bundle“

Table 1. Published results of use of Institute for Healthcare Improvement central catheter bundle

Study	Site	IHI Bundle?	Mean CRBSI per 1000 Catheter Days	
			Pre	Post
Berriel-Cass et al (13)	Single center	Yes + a,b,c	9.6	3.0
Pronovost et al (14)	Multicentered	Yes + a,b	7.7	2.3
Jain et al (15)	Single ICU	No + c	5.9	3.1
Bonello et al (16)	Multicentered	Yes + a	5.2	2.7
Costello et al (17)	Single CICU	No + a,b,c,d	7.8	2.3
Galpern et al (18)	Single center	Yes + a,b	5.0	0.9
Venkatram et al (19)	Single MICU	Yes + a,b,c,d	10.8	1.7

-> All published results of central catheter bundle studies have shown impressive reductions in the rates of CR-BSI.

-> The bundle acts as a multifocal intervention that can potentially prevent several errors at once.

Crit Care Med 2010; 38:363-372

An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU

Table 3. Rates of Catheter-Related Bloodstream Infection from Baseline (before Implementation of the Study Intervention) to 18 Months of Follow-up.*

Study Period	No. of ICUs	No. of Bloodstream Infections per 1000 Catheter-Days				
		Overall	Teaching Hospital	Nonteaching Hospital	<200 Beds	≥200 Beds
		median (interquartile range)				
Baseline	55	2.7 (0.6–4.8)	2.7 (1.3–4.7)	2.6 (0–4.9)	2.1 (0–3.0)	2.7 (1.3–4.8)
During implementation	96	1.6 (0–4.4)†	1.7 (0–4.5)	0 (0–3.5)	0 (0–5.8)	1.7 (0–4.3)†
After implementation						
0– 3 mo	96	0 (0–3.0)‡	1.3 (0–3.1)†	0 (0–1.6)†	0 (0–2.7)	1.1 (0–3.1)‡
4–6 mo	96	0 (0–2.7)‡	1.1 (0–3.6)†	0 (0–0)‡	0 (0–0)†	0 (0–3.2)‡
7–9 mo	95	0 (0–2.1)‡	0.8 (0–2.4)‡	0 (0–0)‡	0 (0–0)†	0 (0–2.2)‡
10–12 mo	90	0 (0–1.9)‡	0 (0–2.3)‡	0 (0–1.5)‡	0 (0–0)†	0.2 (0–2.3)‡
13–15 mo	85	0 (0–1.6)‡	0 (0–2.2)‡	0 (0–0)‡	0 (0–0)†	0 (0–2.0)‡
16–18 mo	70	0 (0–2.4)‡	0 (0–2.7)‡	0 (0–1.2)†	0 (0–0)†	0 (0–2.6)‡

* Because the ICUs implemented the study intervention at different times, the total number of ICUs contributing data for each period varies. Of the 103 participating ICUs, 48 did not contribute baseline data. P values were calculated by the two-sample Wilcoxon rank-sum test.
† $P \leq 0.05$ for the comparison with the baseline (preimplementation) period.
‡ $P \leq 0.002$ for the comparison with the baseline (preimplementation) period.

An evidence-based intervention resulted in a large and sustained reduction (up to 66%) in rates of CR-BSI that was maintained throughout the 18-month study period.

NEJM 2006; 355:2725-32

CHEST Original Research
CRITICAL CARE

Performance of Medical Residents in Sterile Techniques During Central Vein Catheterization

Randomized Trial of Efficacy of Simulation-Based Training

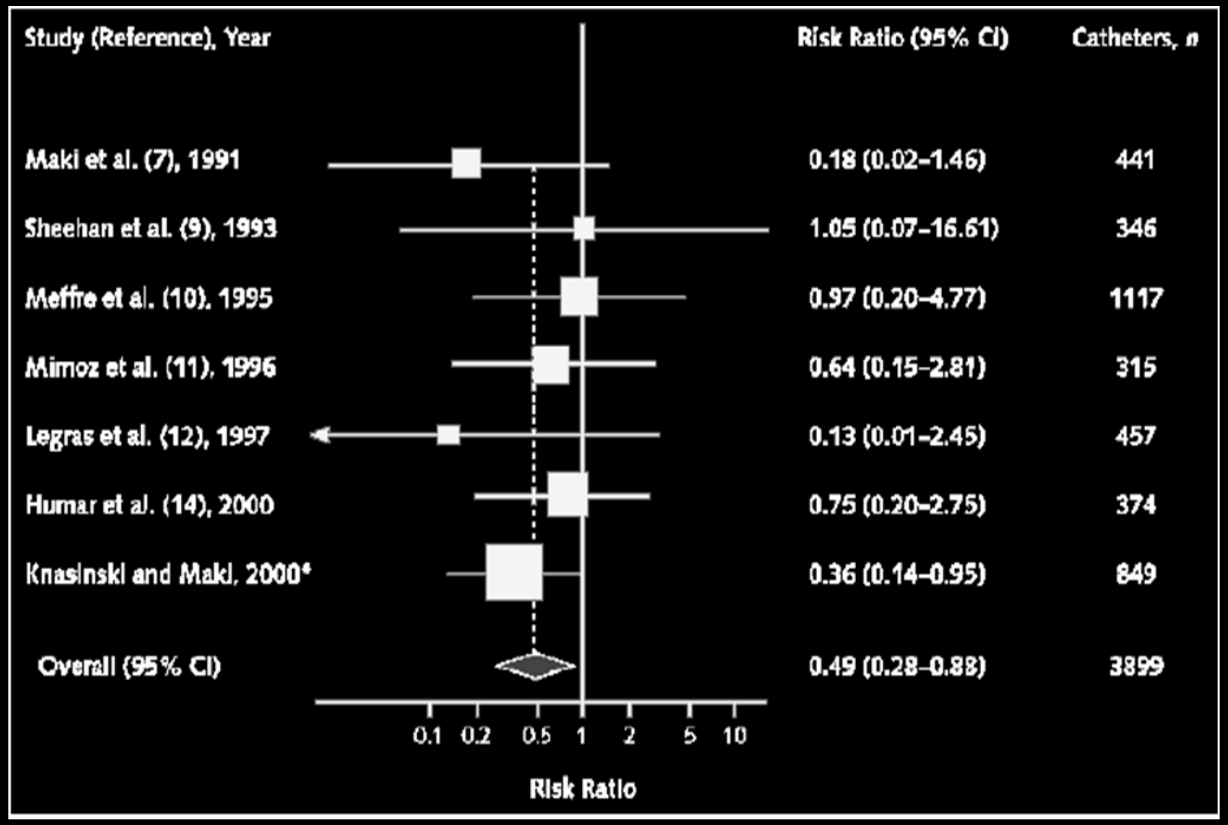
Table 2—*All-or-None Analysis: Comparisons of Number of Residents With Perfect Scores in Each of the Six Sterile Technique Categories Between Video Training Group and Simulation-Based + Video Training Group*

	Phase I			Phase II		
Sterile Technique Category	Video Training Group (n = 23)	Simulation-Based + Video Training Group (n = 24)	*P* Value	Video Training Group (n = 23)	Simulation-Based + Video Training Group (n = 24)	*P* Value
Nonsterile preparation	1	0	.5	7	20	< .001
Hand wash steps	0	0	1.0	8	18	.008
Sterile field/supply preparation	2	2	1.0	10	17	.08
Sterile gowning	0	1	1.0	4	18	< .001
Sterile gloving	8	11	.6	13	19	.12
Sterile draping	5	6	1.0	8	19	.003

~~„See one – do one – teach one“~~

CHEST 2011; 139(1):80-87

Chlorhexidine vs povidone-iodine



Ann Intern Med 2002; 136:792-801

Antisepsis: Chlorhexidine

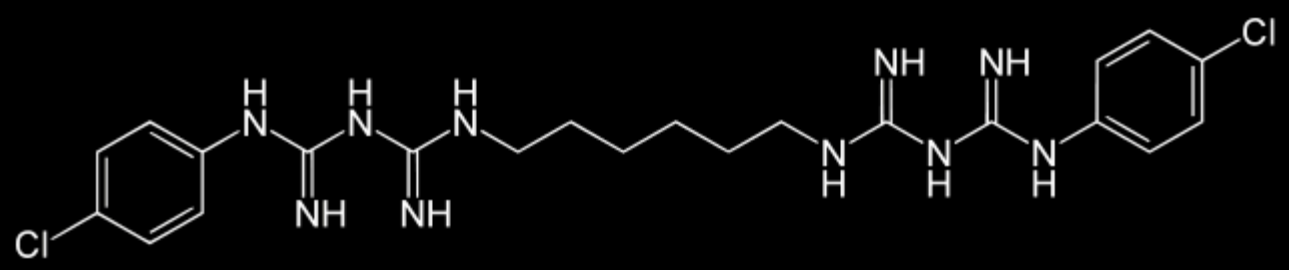
- Prolonged time of antimicrobial effect
- Not inactivated by exposure to protein-rich fluids

- Optimal concentration of chlorhexidine?
- Appropriate solution (aqueous or alcoholic)?

<u>SHEA/IDSA Practice Recommendation:</u>

-> Alcoholic chlorhexidine solution (concentration > 0.5%)

Infect Control Hosp Epidemiol 2008; 29:22-30



Location of insertion

Site	Number of CVCs	Days of CVC	Number of CRLIs	ID of CRLIs	% CVC with CRLI	Number of CRBSIs	ID of CRBSIs	% CVC with CRBSIs
Subclavian	917	8,239	13	1.57	1.42%	8	0.97	0.87%
Jugular	1,390	8,361	64	7.65	4.60%	25	2.99	1.80%
Femoral	288	2,399	38	15.83	13.19%	20	8.34	6.94%
Total	2,595	18,999	115	6.05	4.43%	53	2.79	2.04%

Critical Care 2005;9:R631-635

		n (colonized)	Rate *	HR[b]	95% CI	*P*[c]
Site[a]	Subclavian	102 (6)	8.1	1.00		
	Internal jugular	279 (33)	19.7	3.64	(1.32–10.03)	0.01
	Femoral	208 (24)	26.4	5.15	(1.82–14.51)	0.004
CVC type	Regular	413 (45)	18.3	1.00		
	AM	176 (18)	13.8	0.47	(0.25–0.89)	0.02
Where inserted	ICU	443 (45)	16.0	1.00		
	OR	117 (13)	16.8	1.17	(0.60–2.30)	0.63
	DEM	29 (5)	32.8	2.66	(1.27–5.56)	0.01
Patient gender	Male	349 (41)	20.1	1.00		
	Female	240 (22)	12.9	0.49	(0.26–0.89)	0.02
Sepsis	Absent	415 (51)	21.6	1.00		
	Present	120 (8)	13.4	0.60	(0.31–1.19)	0.14

Int Care Med 2008;34:1038-45

Location of insertion

chanical complications and might have an equivalent infection rate to that of nonfemoral catheters [61–63]. Thus, in adult patients, a subclavian site is preferred for infection control purposes, although other factors (e.g., the potential for mechanical complications, risk for subclavian vein stenosis, and catheter-operator skill) should be considered when deciding where to place the catheter. In a meta-analysis of eight studies, the use of bedside ultrasound for the placement of CVCs substantially reduced mechanical complications compared with the standard landmark placement technique (relative risk [RR], 0.22; 95% confidence interval [CI], 0.10–0.45) [64]. Consideration of comfort, security, and maintenance of asepsis as well as patient-specific factors (e.g., preexisting catheters, anatomic deformity, and bleeding diathesis), relative risk of mechanical complications (e.g., bleeding and pneumothorax), the availability of bedside ultrasound, and the risk for infection should guide site selection.

← **Guidelines CID 2002:35**

IHI-Bundle:

↓

Avoidance of femoral access

Anti-infective Catheters

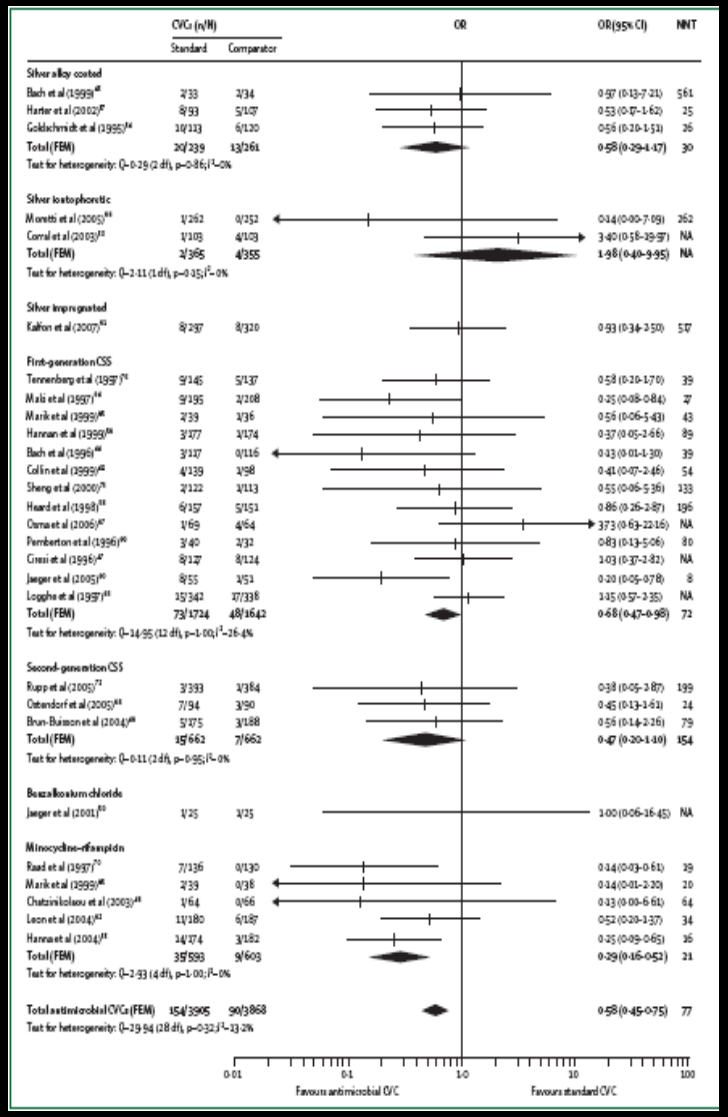
Antimicrobial vs standard CVC

- Reduction in colonialisation
- Reduction in CR-BSI

- Minocycline-rifampicin > Chlorhexidine-silver-sulfadiazine

Potential problems

- Gaps in organism-specific activity
- Hypersensitivity reactions
- Development of antibiotic resistance



Lancet Infect Dis 2008; 8:763-76

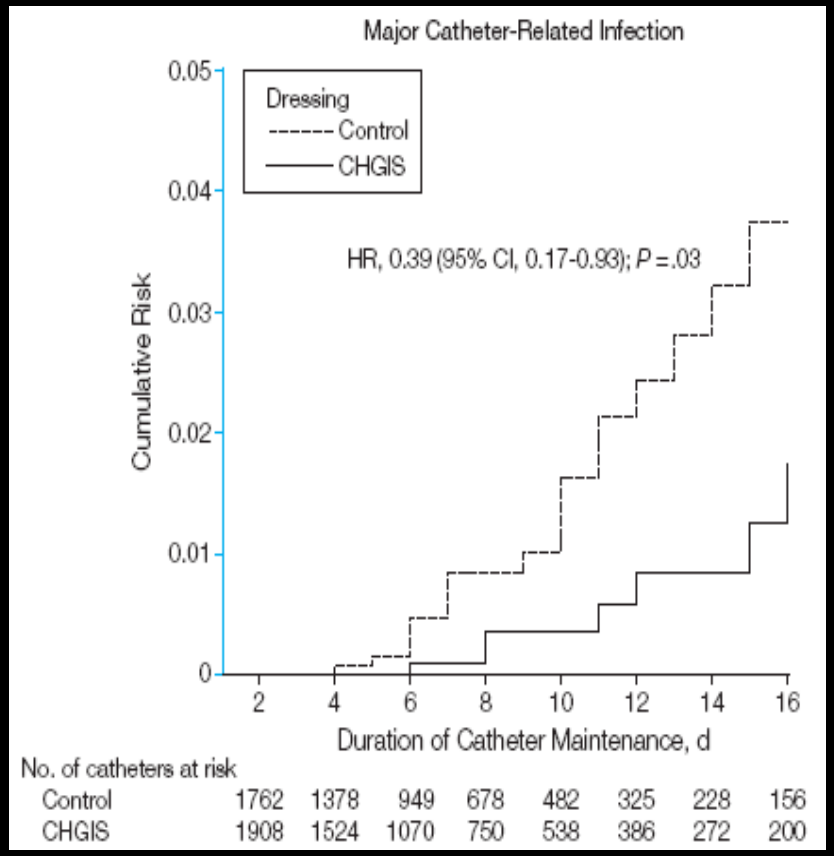
Antimicrobial Catheters

The English epic (evidence-based practice in infection control) guidelines recommend the use of an antimicrobial CVC for adult patients at increased risk of CRBSI who require central venous access for 1–3 weeks.[100] By comparison, the CDC's Hospital Infection Control Practices Advisory Committee recommend the use of antimicrobial CVC in adults whose catheter is expected to remain in situ for greater than 5 days and who are being cared for in a hospital unit in which the CRBSI rate is above the goal set by the individual institution despite implementing a comprehensive strategy to reduce infection rates.[34] The use of CSS and minocycline–rifampicin CVCs might also be cost effective if used for patients in intensive care units in whom the incidence of CRBSI is above the tenth percentile according to published data and only after other interventions have been undertaken to reduce the risk of infection.[34]

Increased risk of CR-BSI
CVC for 1-3 weeks

CVC for > 5days
CR-BSI rate ↑, despite implementing a comprehensive strategy to reduce infection rates

Chlorhexidine-Impregnated Sponges



Significant reduction in the rate of catheter colonization and CR-BSI

JAMA 2009; 301 (12):1231-1241

Impact of chlorhexidine-impregnated sponges on catheter-related infections rate

0162

P. Eggimann[1], C. Joseph[1], MJ Thévenin[2], P Voirol[3], C. Bellini[2], JP Revelly [1], JP Pagani[1].
Critical Care[1] and Infection Control Services[2], Central Pharmacy[3], University Hospital Lausanne, Switzerland.
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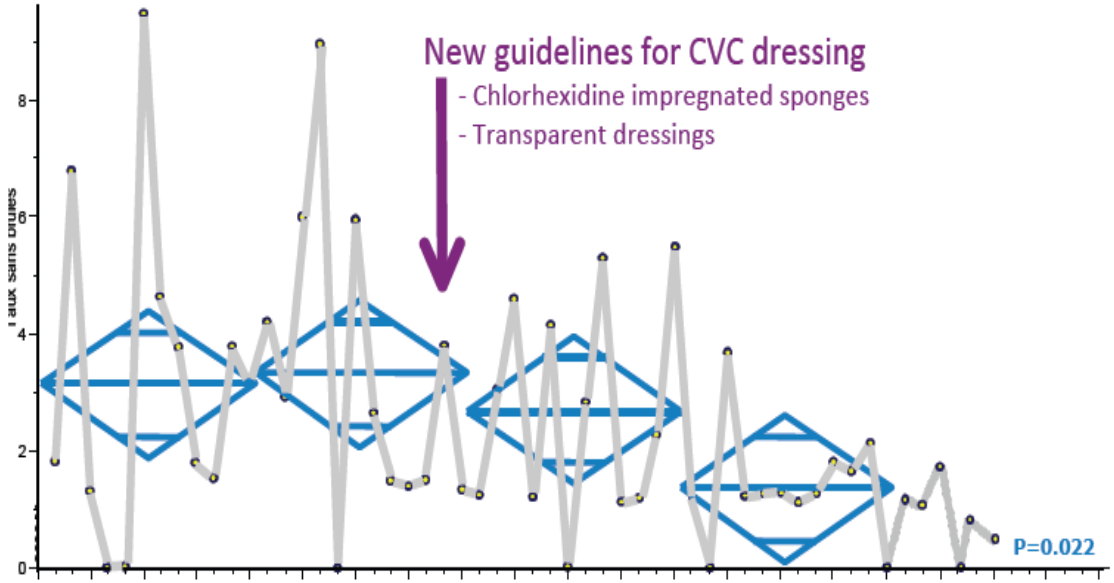
www.soins-intensifs.chuv.ch

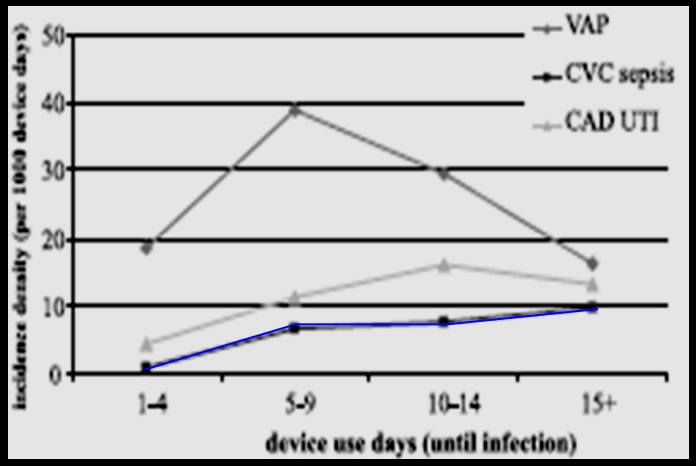
Primary bacteremia and CRBSI median monthly rates/1000 CVC-days at SMIA



	2006 8009 CVC-days	2007 8702 CVC-days	2008 9497 CVC-days	2009 10848 CVC-days	2010 11540 CVC-days*
Annual rate	3.7	3.5	2.7	1.7	1.4*
Number avoided					*extrapoled from 1st semester
Infections	-	2.7	10.9	22.8	28.8*
Hosp.-days	-	33	130	273	346*
Costs ($)	-	54'930	217'214	455'587	576'799*

C. Joseph et al. ICAAC 2010 /ESICM 20.

Catheter changes / removal



Intensive Care Med 2007; 33:271

Duration of catheterization:
Risk factor of infection

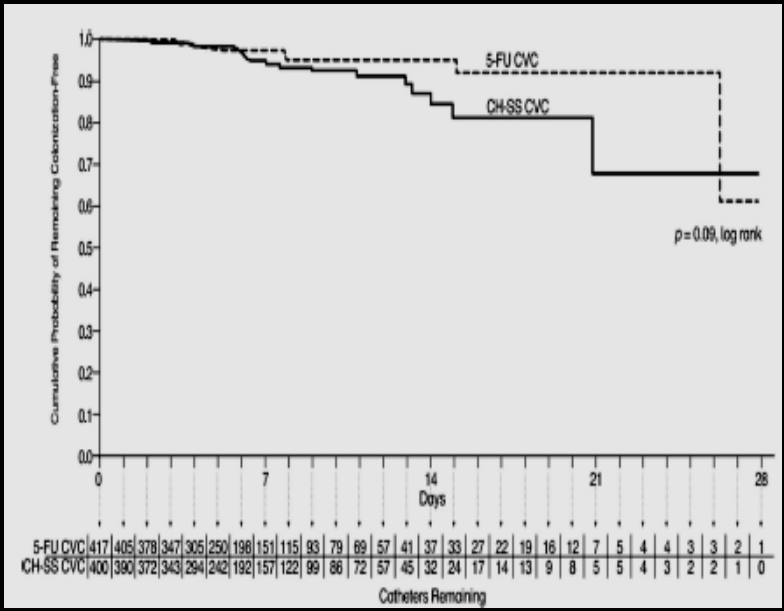
-> Over all, the literature suggest that catheters should be left in place until a change is clinically indicated.

Crit Care Med 1990; 18:1073-1079
NEJM 1992; 327:1062-1068
Crit Care Med 1997; 25:1417-1424
Infection Control and Hospital Epidemiology 2000; 21(6):371-374

Anti-infective external coating of central venous catheters: A randomized, noninferiority trial comparing 5-fluorouracil with chlorhexidine/silver sulfadiazine in preventing catheter colonization*

5-FU

- Antimetabolite
- Inhibit growth of:
  - ~ gram-positive bacteria
  - ~ gram-negative bacteria
  - ~ Candida species



5-FU vs CH-SS

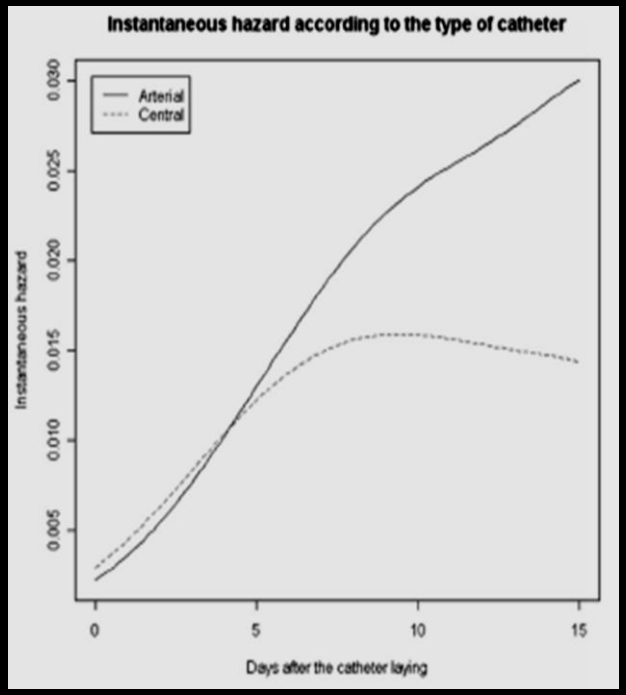
- Colonization 2.9 vs 5.3%

-> Safe and effective alternative

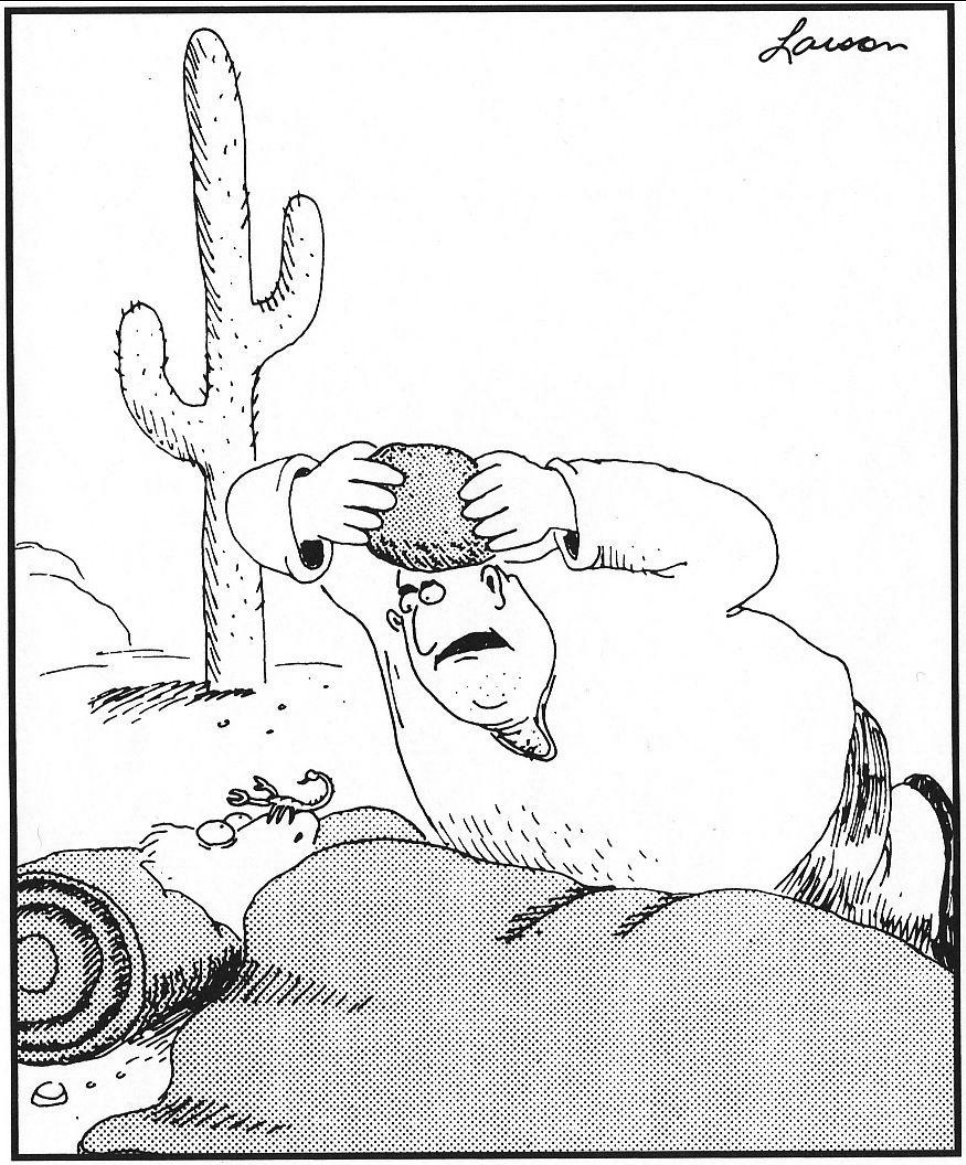
Crit Care Med 2010; 38:2095-2102

Infectious risk associated with arterial catheters compared with central venous catheters*

Variable	Arterial Catheters, n = 1617	Central Venous Catheters, n = 1915
Catheter colonization ≥10^3 colony-forming units,[a] n (%)	127 (7.8)	183 (9.6)
Staphylococcus aureus	6 (4.7)	10 (5.5)
Coagulase-negative staphylococci	63 (49.6)	90 (49.2)
Other Gram-positive cocci	16 (12.6)	18 (9.8)
Pseudomonas spp.	19 (15)	34 (18.6)
Enterobacter spp.	33 (26)	49 (26.8)
Escherichia coli	6 (4.7)	9 (4.9)
Acinetobacter baumannii	11 (8.7)	4 (2.2)
Fungi	3 (2.4)	10 (5.5)
Catheter-related bloodstream infection, n (%)	8 (0.5)	15 (0.8)
Major catheter-related infection,[a] n (%)	11 (0.7)	18 (0.9)
Staphylococcus aureus	1 (9.1)	4 (22.2)
Coagulase-negative staphylococci		4 (22.2)
Other Gram-positive cocci		1 (5.6)
Pseudomonas spp.	5 (45.5)	4 (22.2)
Enterobacter spp.	6 (54.5)	8 (44.4)
Escherichia coli	1 (9.1)	
Acinetobacter baumannii	1 (9.1)	
Fungi		1 (5.6)



Crit Care Med 2010; 38:1030-35



"Hold still, Carl! … Don't … move … an … *inch*!"

Thank you!

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