

Intravascular Catheter-Related Infections

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Epidemiology

- >150.000.000 intravascular devices each year
- >5,000,000 CVCs (USA)
- >200,000 CVC-related infections
- >120,000 Catheter-related Blood Stream Infections (USA)
- ~80,000 CVC-related BSIs occur in ICUs each year
- **71% of BSIs in Europe are CR-BSIs (ESGNI)**

Ann Intern Med 2000; 132:391

CID 2001; 32:1249

Clin Microbiol Infect 2002; 8:265

Central line associated BSI

2003 NNIS

TYPE OF ICU	MEAN BSI/1000 DEVICE-DAYS (RANGE)	DEVICE-DAYS/ TOTAL ICU DAYS
BURN	8.5 (0-18)	51%
CORONARY	4.2 (0-8.4)	32%
CARDIOTHORACIC	2.9 (0.4-4.9)	80%
MEDICAL	5.7 (2.1-7.6)	51%
SURGICAL	5.2 (2.6-9.3)	65%
PEDIATRIC	7.3 (0.7-11.5)	46%
TRAUMA	7.8 (2.5-12.3)	47%
RESPIRATORY	3.4	-

Biofilms may form within 3 days after catheter insertion

Anaissie E, Samonis G, Kontoyiannis D, et al. EJCMI 1995;14:135–7.



Catheter and biofilm formation

- Biofilm formation is more predominant on the external surface of catheters in place for <10 d
- However, with increasing catheter duration (≥ 30 days), biofilm formation in the catheter lumen tends to predominate.
- After organisms become established in a biofilm, the individual cells exhibit tolerance to antimicrobial agents.

Pathogenesis

these microbes are made for walking...

Focus of preventive strategies

Catheter hubs

Catheter insertion site

Microbes migrate intraluminally from colonized hubs, less often from contaminated infusate

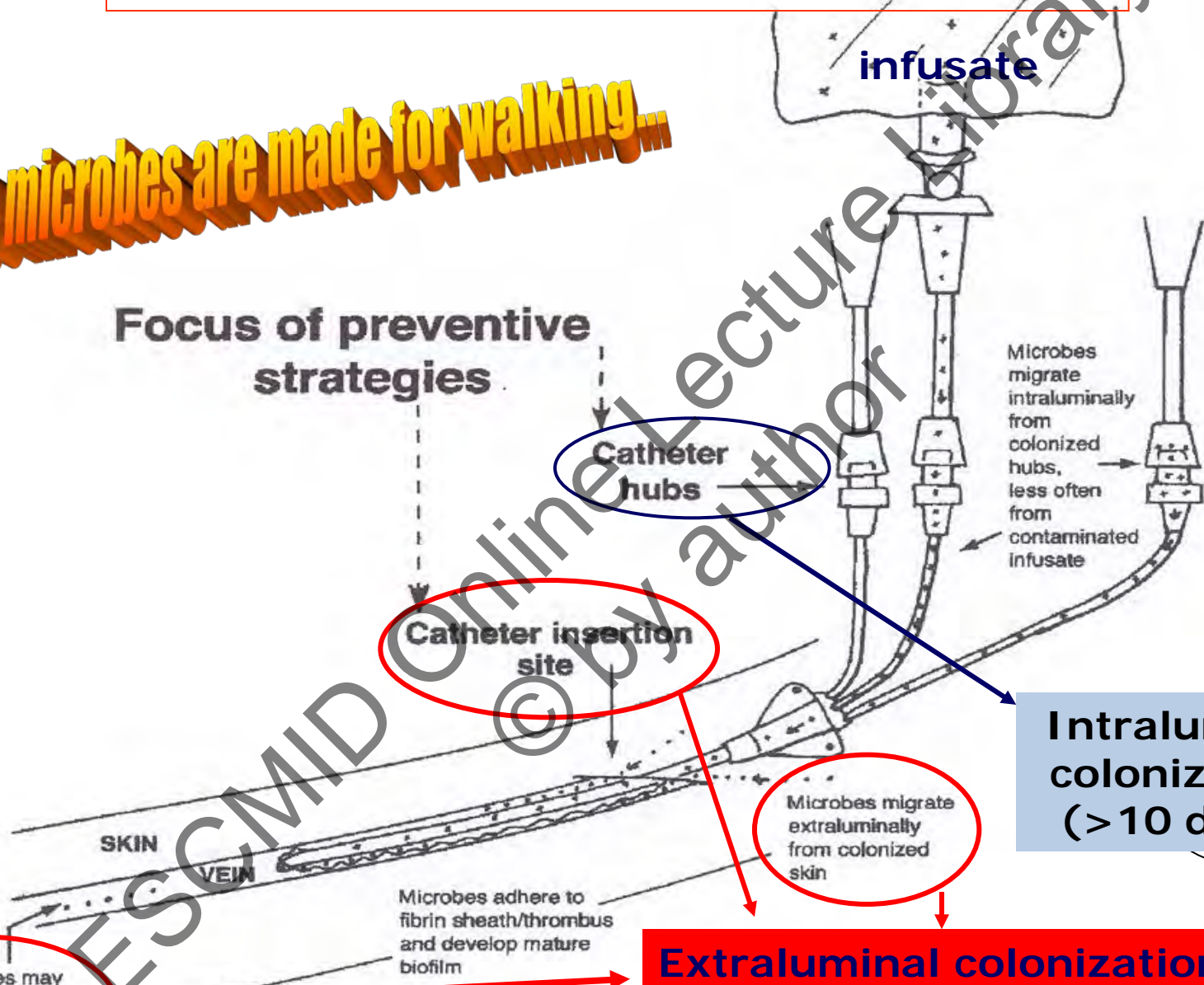
Intraluminal colonization (> 10 days)

Microbes migrate extraluminally from colonized skin

Extraluminal colonization (< 10 days)

Microbes may hematogenously seed catheter from distant infection sites

Microbes adhere to fibrin sheath/thrombus and develop mature biofilm



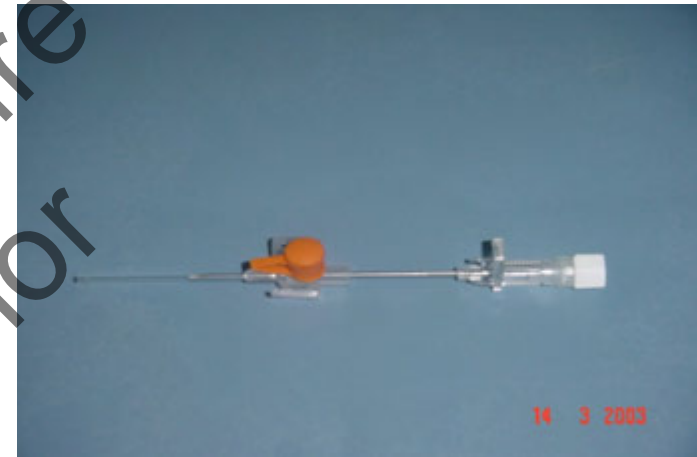
Different types of catheters

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Peripheral catheters (<3 inches)

- **Peripheral venous catheters**

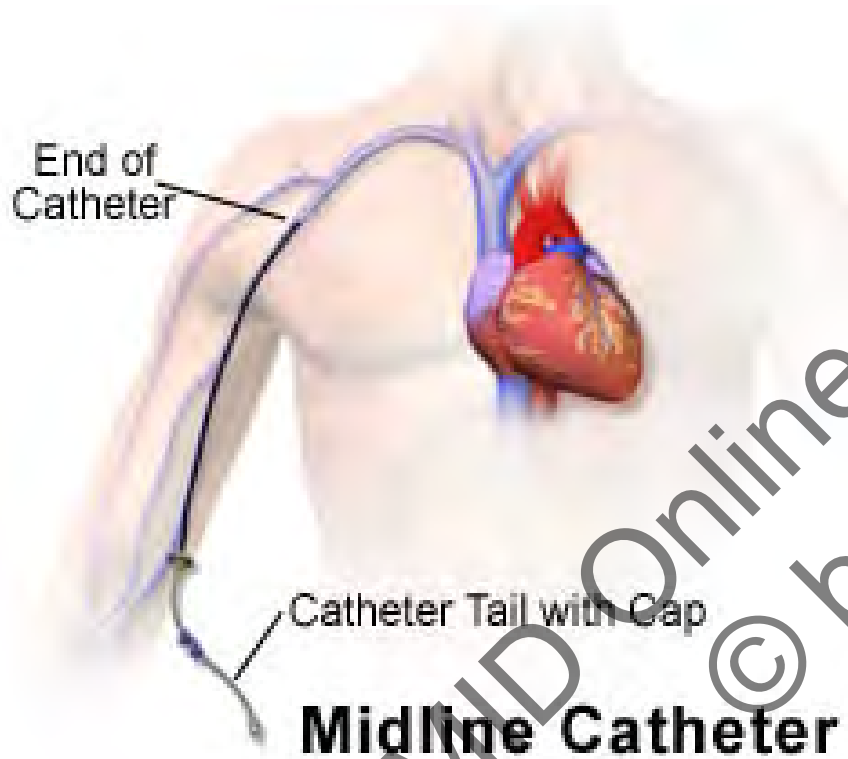
- Usually inserted in veins of forearm or hand
- Phlebitis with prolonged use
- **Rarely cause BSI**



- **Peripheral arterial catheters**

- Usually inserted in radial artery; can be placed in femoral, axillary, brachial, posterior tibial arteries.
- **Low infection risk; rarely associated with BSI**

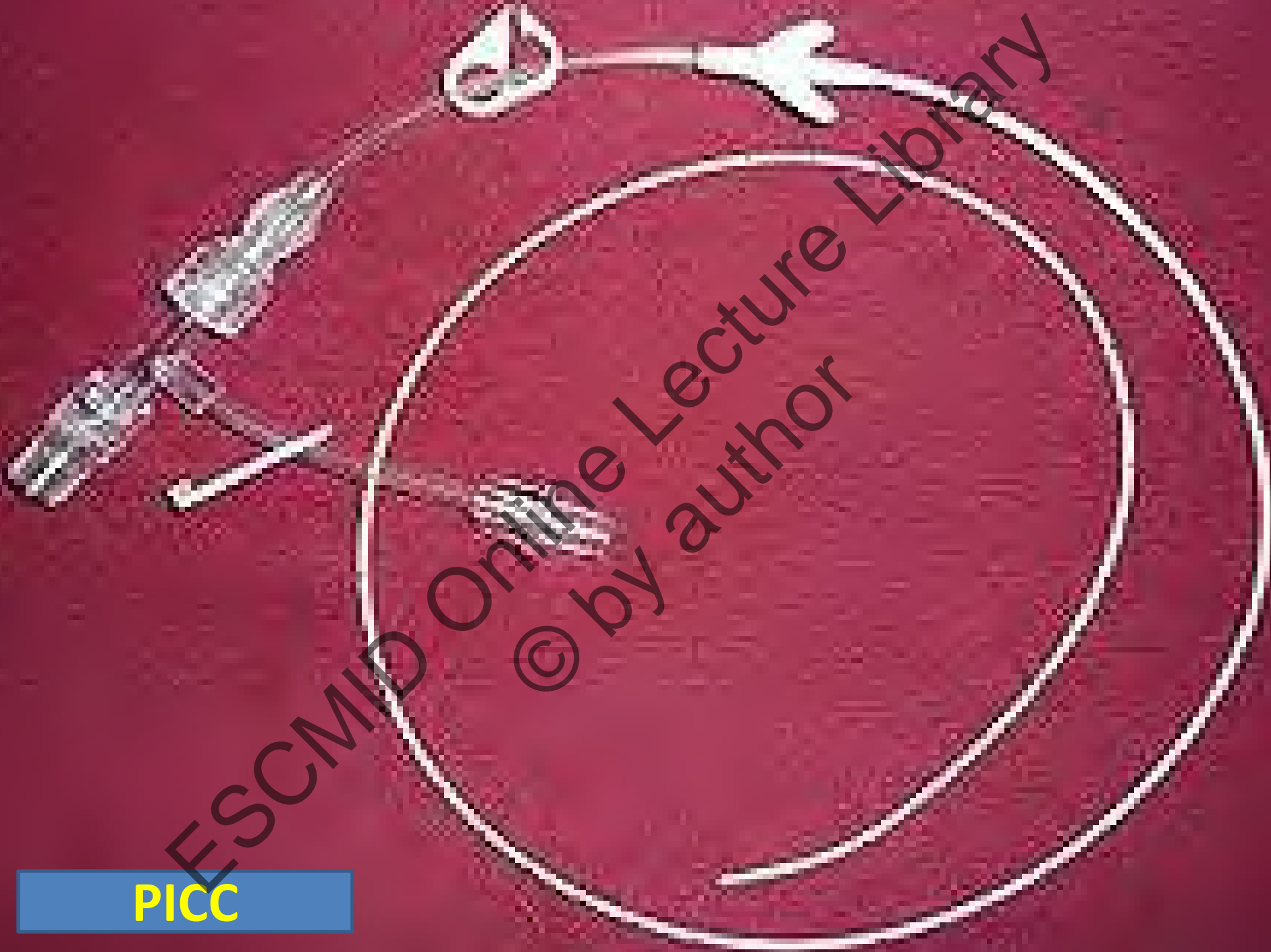
Midline Catheters



- Inserted into the proximal basilic or cephalic veins.
- Lower rates of phlebitis than short peripheral catheters

Peripherally inserted central venous catheters (PICCs)

- Inserted into basilic, cephalic, or brachial veins and enter the superior vena cava.
- >20 cm depending on patient size.
- Lower rate of infection than non-tunneled CVCs.



PICC

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Non-tunneled central venous catheters*

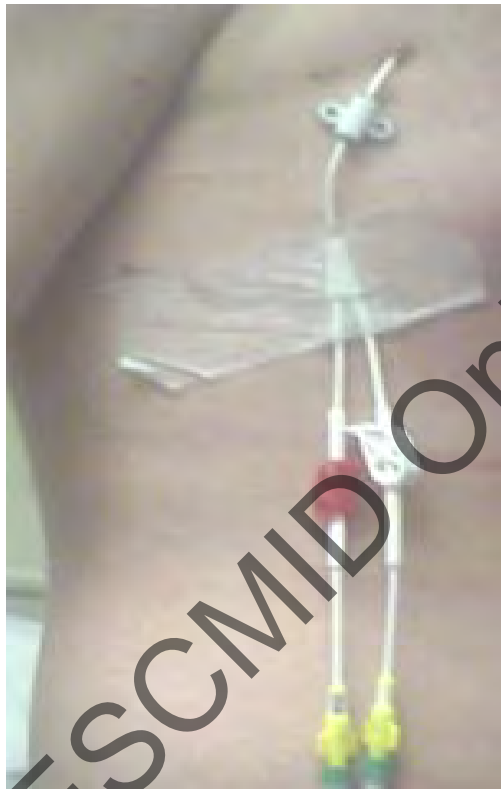
- Percutaneously inserted into central veins
 - subclavian
 - internal jugular
 - femoral
- >8 cm depending on patient size
- **Account for majority of CR-BSI**

* Pulmonary artery catheters



Tunneled and Totally Implantable Central Venous Catheters

Tunneled CVCs



Implanted into subclavian, internal jugular, or femoral veins

Totally implantable



Tunneled beneath skin and have sub-cutaneous port accessed with a needle.
Implanted in subclavian or internal jugular vein

Tunneled and Totally implantable central venous catheters

- **Tunneled central venous catheters**
 - Cuff inhibits migration of organisms into catheter tract
 - **Lower rate of infection than non-tunneled CVCs**
- **Totally implantable**
 - **Lowest risk for CR-BSI**
 - Improved patient self-image
 - No need for local catheter-site care
 - Surgery required for catheter removal

**Clinical Practice Guidelines for the
Diagnosis and Management of
Intravascular Catheter-Related Infection**

2009 Update by the IDSA

Mermel LA, et al. Clin Infect Dis 2009; 49:1–45

**Patient with a short-term CVC (<14 days)
or arterial catheter (AC)**

and

a febrile episode



**Blood cultures
(2 sets, 1 peripheral)**

Mild or moderately ill
(No hypotension or organ failure)

**Consider empiric
antimicrobial
therapy**

If no source of fever identified

- Remove CVC and AC, culture tip and insert at new site
or
- Culture insertion site plus hubs where available

Seriously ill
(hypotension, hypoperfusion, signs
and symptoms of organ failure)

**Initiate
appropriate
antimicrobial
therapy**

- **Remove CVC or AC,**
- **Culture tip *and***
- **Insert at new site**

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Guidelines for the Prevention of Intravascular Catheter-related Infections

Clin Infect Dis 2011;52DOI: 10.1093/cid/cir257

**Do not use guidewire exchanges
to replace a non-tunneled catheter
suspected of infection.**

**Blood cultures (-)
and
CVC and AC cultures (-)**



**Look for another source of
infection**

**Blood cultures (-)
and
CVC and AC not cultured**



**If continued fever
and
no other source found**



Remove and culture CVC and AC

**Blood cultures (-)
and
CVC and AC \geq 15 CFU**

For *S. aureus*

- treat for 5-7 days,
- monitor closely for signs of infection
- repeat blood cultures accordingly

If due to other microbes

- monitor closely for signs of infection
- repeat blood cultures accordingly

**Blood cultures (+)
and
CVC and AC ≥ 15 CFU by roll plate
or $\geq 10^2$ CFU by sonication**

**Short-term CVC or AC infection-
related bloodstream infection**

Uncomplicated ?

Complicated ?

**Short-term CVC or AC
Uncomplicated**

Bloodstream infection and fever resolves within 72h in a pt who:

- has no intravascular hardware
- has no evidence of endocarditis or suppurative thrombophlebitis
and
- for *S. aureus*, has no active malignancy or immunosuppression

- Remove the catheter *and*
- Treat with systemic antibiotics
(Rx duration depends on pathogen)

**Short-term CVC or AC
Complicated**

**Suppurative thrombophlebitis
Endocarditis
Osteomyelitis**

- **Remove the catheter *and***
- **Treat with systemic antibiotics for 4-6 weeks
(6-8 weeks for osteomyelitis in adults)**

**Long-term CVC or Port (P)
related bacteremia or fungemia**

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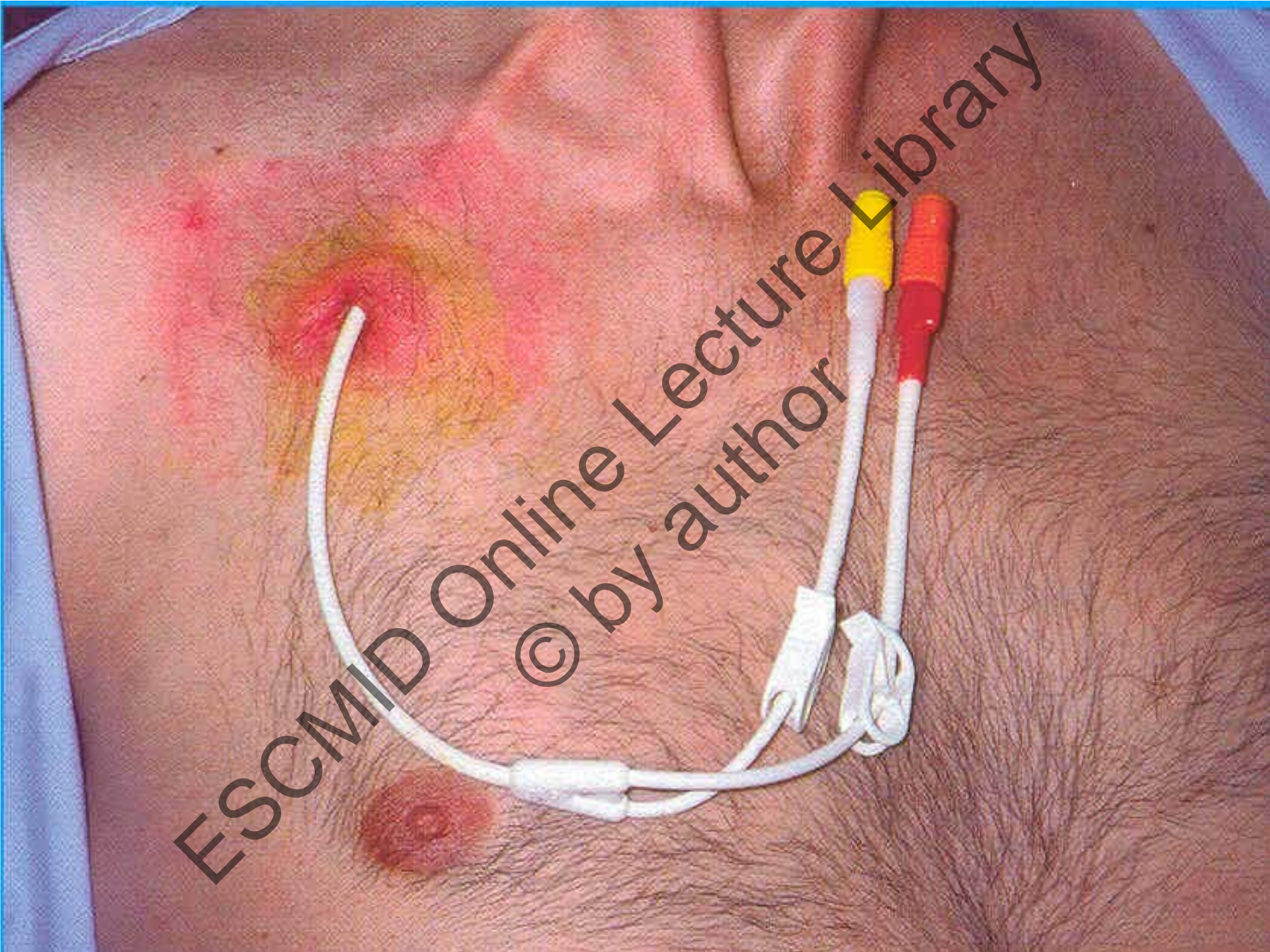
Long-term CVC or Port: Complicated

- Tunnel infection
- Port abscess

Remove the catheter
and
Treat with antibiotics
for **7-10 days**

- Septic thrombosis
- Endocarditis
- Osteomyelitis

Remove the catheter
and
Treat with antibiotics
for **4-6 weeks**
(6-8w for Osteo in adults)



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Long-term CVC or Port: Uncomplicated

- CNS
- Enterococcus

May retain the catheter
and
Treat with antibiotics

- *Staphylococcus aureus*
- Gram (-) bacilli
- *Candida spp.*

Remove the catheter
and
Treat with antibiotics

How should catheter-related infections generally be managed?

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Empirical therapy

Vancomycin is recommended for empirical therapy in health care settings with an elevated prevalence of MRSA.

Empirical therapy

For institutions in which the preponderance of MRSA isolates have **MIC_{vanco} >2 mg/mL (!)**, alternative agents, such as **daptomycin**, should be used.

Daptomycin vs vancomycin in CRBSIs in cancer patients

Outcomes	Daptomycin (n=38) n/n (%)	Vancomycin (n=40) n/n (%)	P-value
Symptoms at 48 h	28/37 (76)	20/38 (53)	0.04
Blood culture negative at 48h	29/37 (78)	11/32 (34)	<0.001
Blood culture negative at 7days	34/37 (92)	27/32 (84)	0.46
Overall response*	25/37 (68)	11/34 (32)	0.003

*Defined as clinical and microbiological cure at 72 hours, no relapse, no late complication correlated mortality at 30 days

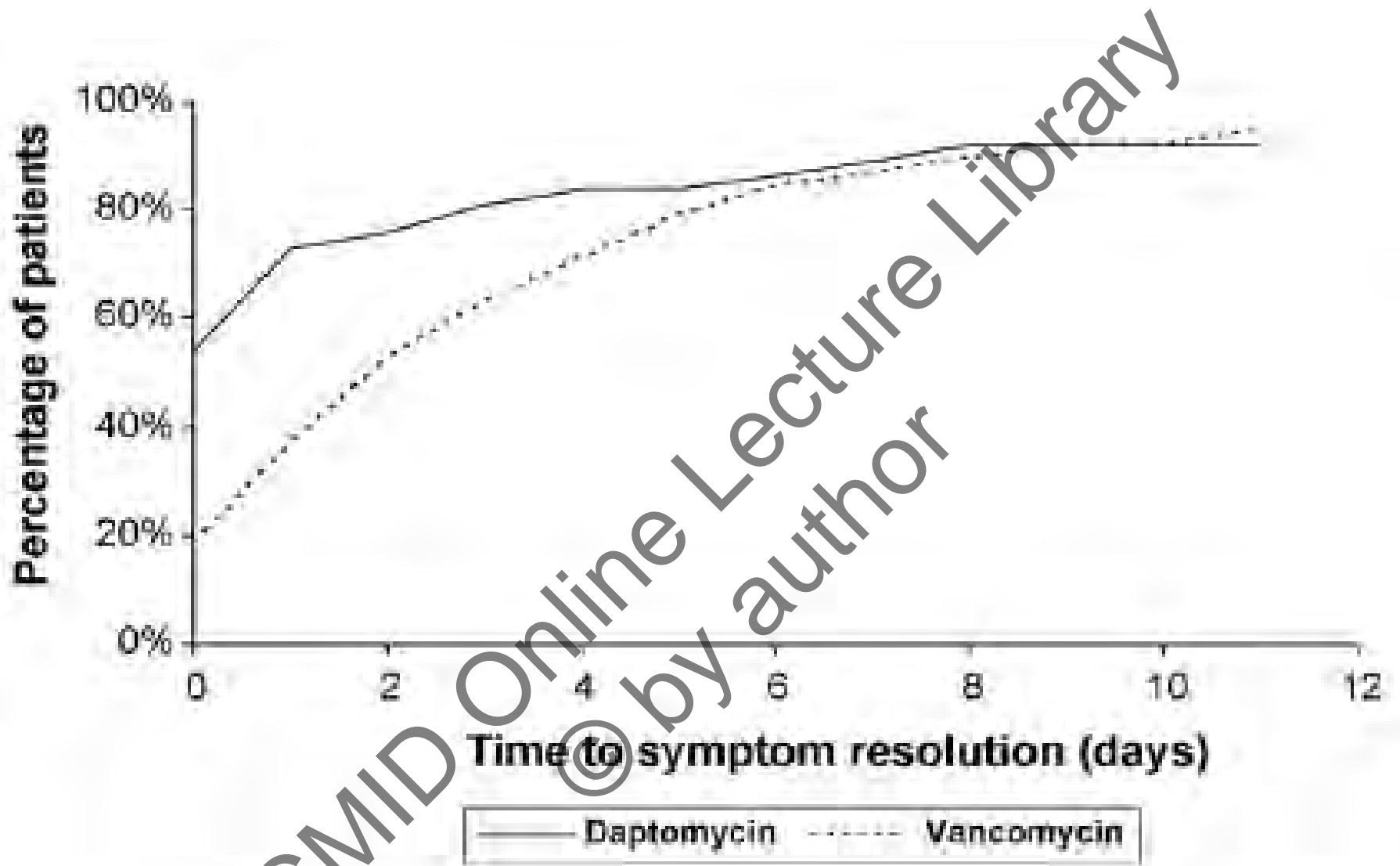


Fig 1. Time to symptom resolution for each study drug.

Empirical therapy

Linezolid should not be used
for empirical therapy of
suspected but not proven CRBSI.

Empirical coverage for **Gram (-) bacilli**

It should be based on local antimicrobial susceptibility data and the severity of disease:

- **4th-generation cephalosporin, *or***
- **carbapenem, *or***
- **b-lactam/b-lactamase combination**
± an aminoglycoside

Empirical therapy for MDR Gram (-) bacilli

It should be used when CR-BSI is suspected in:

- **neutropenic patients,**
- **severely ill patients with sepsis**
- **pts known to be colonized with such pathogens**

until the culture and susceptibility data are available and de-escalation of the antibiotic regimen can be done.

Empirical therapy for suspected CR-BSI involving femoral catheters in critically ill pts

Should include coverage for:

- Gram (+) pathogens
- Gram (-) bacilli *and*
- *Candida* species

Empirical therapy for suspected catheter-related candidemia

Should be used for septic patients with any of the following risk factors:

- Total parenteral nutrition
- Prolonged use of broad-spectrum antibiotics
- Hematologic malignancy
- Receipt of bone marrow or solid-organ transplant
- Femoral catheterization, or
- Colonization due to *Candida sp.* at multiple sites

Empirical therapy for suspected catheter-related candidemia

- Use an **Echinocandin**.
- **Fluconazole** can be used for:
 - patients without azole exposure in the previous 3 months
 - and**
 - in health care settings where the risk of *C. krusei* or *C. glabrata* infection is very low.

For how long?

- **Persistent fungemia or bacteremia**
 - after catheter removal (>72 h)
- and*
- in patients found to have infective endocarditis or suppurative thrombophlebitis and pediatric patients with osteomyelitis:
 - 4-6 weeks**
- **Osteomyelitis in adults: 6-8 weeks**

Antibiotic lock therapy

- **Antibiotic lock therapy should be used for catheter salvage.**
- However, if antibiotic lock therapy cannot be used in this situation, systemic antibiotics should be administered through the colonized catheter.

When the catheter should be removed ?

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Short-term catheters

should be removed from patients with CR-BSI due to:

- **Gram (-) bacilli**
- ***S. aureus***
- **Enterococci**
- **Fungi**
- **Mycobacteria**

Long-term catheters

should be removed from patients with CR-BSI associated with any of the following:

- **Severe sepsis**
- **Suppurative thrombophlebitis**
- **Endocarditis**
- **Bloodstream infection that continues >72 h despite of antimicrobial therapy to which the infecting microbes are susceptible**
- **Infections due to *S. aureus*, *P. aeruginosa*, fungi, or mycobacteria**

Pathogen-specific treatment recommendations

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Coagulase-negative *Staphylococcus*

For uncomplicated CR-BSI treat with antibiotics

- for **5–7 days** if the catheter is removed and
- for **10–14 days**, in combination with antibiotic lock therapy, if the catheter is retained.

S. aureus and *S. lugdunensis*

Patients with CR-BSI should have the infected catheter removed, and they should receive 4–6 weeks of antimicrobial therapy, unless they have some exceptions.

Candidates for shorter duration of antimicrobial therapy (minimum of 14 days)

- **Not diabetic**
- **Not immunosuppressed** if the infected catheter is removed
- **No prosthetic intravascular device** (e.g., pacemaker or recently placed vascular graft)
- **No evidence of endocarditis or suppurative thrombophlebitis** on TEE and US, respectively.
- **Fever and bacteremia resolve within 72 h** after initiation of appropriate antimicrobial therapy.
- **No evidence of metastatic infection** on physical examination and sign or symptom-directed diagnostic tests.

S. aureus and *S. lugdunensis*

Patients who are being considered for a shorter duration of therapy should have a **TEE obtained at least 5–7 days after** onset of bacteremia to minimize the possibility of false-negative results.

Patients with *S. aureus* CR-BSI

- **Short-term catheters** should be removed immediately.
- **Long-term catheters** should be removed unless there are major contraindications.
- In the rare circumstance that the catheter is **retained** for a patient with *S. aureus* CR-BSI involving a long-term catheter, the patient should receive **systemic and antibiotic lock therapy for 4 weeks.**

The catheter tip grows *S. aureus* but peripheral blood cultures are negative

They should receive:

- a **5–7**-day course of antibiotics
and
- close monitoring for signs and symptoms of ongoing infection, including additional blood cultures, as indicated.

Catheter exchange or replacement

After a catheter has been removed
as a result of *S. aureus* CR-BSI,
placement of a new catheter can proceed when
additional blood cultures show no growth.

Enterococcus species

- **Removal of infected short-term IVC is recommended**
- Removal of infected **long-term** catheters should be done in cases of:
 - **insertion site or pocket infection,**
 - **suppurative thrombophlebitis,**
 - **sepsis,**
 - **endocarditis,**
 - **persistent bacteremia, or**
 - **metastatic infection**

Enterococcus species - Rx

- **Ampicillin** is the drug of choice for ampicillin-susceptible enterococci.
- **Vancomycin** should be used if the pathogen is resistant to ampicillin.

Enterococcus species - Rx

- Antibiotic lock therapy should be used in addition to systemic therapy if the catheter is retained.
- In cases of CR-BSI due to ampicillin-resistant strains and VRE
 - **linezolid** or
 - **daptomycin**may be used, based on susceptibility results.

Gram-negative bacilli

- Patients who are critically ill with suspected CR-BSI and who have recent colonization or infection with an **MDR Gram(-) pathogen** should receive **2 antimicrobial agents** of different classes with Gram(-) activity as initial therapy.
- De-escalation of the initial regimen to a single appropriate antibiotic is recommended once culture and susceptibility results are available.

Candida species

- Catheters should be removed in cases of CR-BSI due to *Candida species*.
- For patients with candidemia and a short-term CVC for whom no source of candidemia is obvious, the catheter should be removed and the catheter tip sent for culture.

Candida species - Rx

Antifungal therapy is recommended
for all cases of CR-BSI due to *Candida species*,
including cases in which clinical manifestations
of infection and/or candidemia resolve
after catheter withdrawal and
before initiation of antifungal therapy.

How should you manage suppurative thrombophlebitis?

Suppurative thrombophlebitis should be suspected in patients with

persistent bacteremia or fungemia

(i.e., patients whose blood culture results remain positive after 3 days of adequate antimicrobial therapy) without another source of intravascular infection (e.g., endocarditis)

Suppurative thrombophlebitis - Dx

A diagnosis of suppurative thrombophlebitis requires:

- **the presence of positive blood culture results.**
- ***plus***
- **the demonstration of a thrombus**
by radiographic testing (CT, US, other)

Suppurative thrombophlebitis - Rx

Indications for Surgical resection of the involved vein:

- **purulent superficial veins**
- **infection extending beyond the vessel wall,**
- **failure of conservative Rx** with an appropriate antimicrobial regimen

The role of heparin use in this setting is unresolved

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Mermel LA, et al. Clin Infect Dis 2009; 49:1–45

**Guidelines for the Prevention of
Intravascular Catheter-related Infections**

Naomi P. O'Grady, et al.

Clin Infect Dis 2011;52DOI: 10.1093/cid/cir257

Thank you for your attention

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