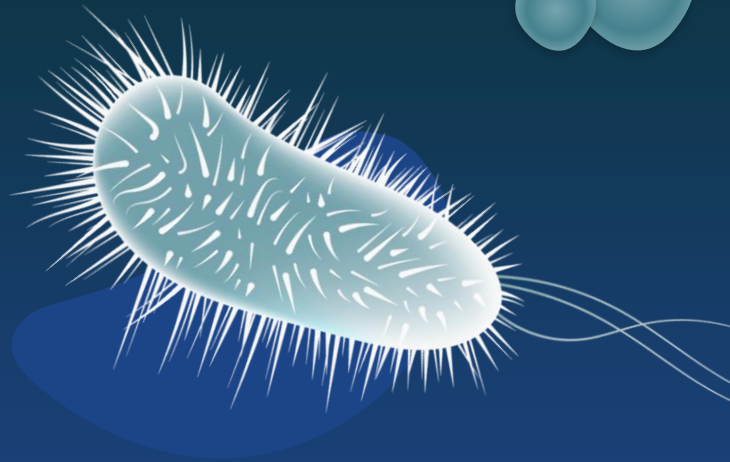
Intravascular catheter-related infection : Treatment



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Treatment protocols:

- Antibiotic therapy
- Removal of catheter
- Salvage therapy
- AB lock therapy

Common organisms

- Coagulase-negative staphylococci (most common)
- Gram –positive organisms : S. aureus
- Gram-negative bacilli
- Candida

Gram –positive organisms

- For empiric therapy： Because of high rates of infection due to methicillin-resistant S. aureus (MRSA) Vancomycin is choice
- Alternative agent : Daptomycin in units with high rates of infection due to VRE.
- Linezolid is not appropriate for empiric therapy of CRBSI

Gram-negative bacilli

- Empirical AB based on : the drug susceptibility history of child, local antimicrobial susceptibility data and the severity of disease

- In chronically hospitalized patients & not severely ill (repeated exposure to third-generation cephalosporins or broad-spectrum antibiotic therapy is not desirable) initial treatment with an Aminoglycoside is reasonable.

- Severe ill or immune compromise patients , severe burns : A third or fourth-generation cephalosporin or a beta-lactam/beta-lactamase combination (piperacillin-tazobactam) , meropenem.

- For patients with hemodynamic instability and local resistance :

- Additional antipseudomonal agent (aminoglycoside or ciprofloxacin) is appropriate while awaiting culture results

Candida

- Empirical therapy for suspected catheter-related candidemia should be used for patients with neutropenia and fever lasting > 5 days.
- Risk factors for candidemia include:
- Total parental nutrition
- Prolonged use of broad-spectrum antibiotics
- Hematologic malignancy
- Receipt of bone marrow or solid organ transplant
- femoral catheterization
- colonization due to Candida species at multiple sites

Directed systemic antibiotic therapy and duration

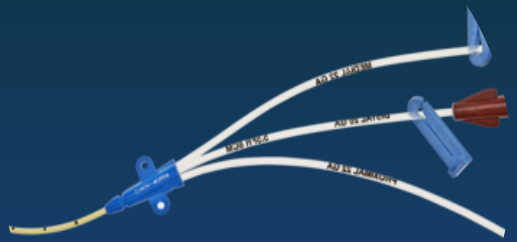
Pathogen	Preferred antimicrobial agents and dosing (adult)	Alternative antimicrobial agents and dosing (adult)
Staphylococci		
Methicillin susceptible	Nafcillin 2 g IV every 4 hours Oxacillin 2 g IV every 4 hours Cefazolin 2 g IV every 8 hours Flucloxacillin* 2 g IV every 6 hours	Vancomycin (dosing as summarized below)
Methicillin resistant	Vancomycin:¶ ▪ Loading dose: 20 to 35 mg/kg IV once ▪ Initial maintenance dose and interval: determined by nomogram; typically 15 to 20 mg/kg IV every 8 to 12 hours for most patients with normal kidney function ▪ Subsequent dose and interval adjustments based on AUC-guided (preferred) or trough-guided serum concentration monitoring	Daptomycin$^{\Delta}$ 6 to 10 mg/kg IV every 24 hours
Enterococci◇		
Ampicillin susceptible	Ampicillin 2 g IV every 4 hours	Vancomycin (dosing as summarized above)
Ampicillin resistant, vancomycin susceptible	Vancomycin (dosing as summarized above)	Daptomycin$^{\Delta}$ 6 to 10 mg/kg IV every 24 hours Linezolid 600 mg IV (or orally) every 12 hours
Ampicillin resistant, vancomycin resistant	Daptomycin$^{\Delta}$ 6 to 10 mg/kg IV every 24 hours	Linezolid 600 mg IV (or orally) every 12 hours

Enterobacteriaceae (examples include *E. coli*, *Klebsiella* spp, *Enterobacter* spp)		
ESBL negative	Ceftriaxone 2 g IV every 24 hours	Ciprofloxacin 400 mg IV every 12 hours
ESBL positive	Imipenem 500 mg IV every 6 hours Meropenem 1 g IV every 8 hours Ertapenem 1 g IV every 24 hours	Ciprofloxacin 400 mg IV every 12 hours
***Pseudomonas* spp**[§]		
	Ceftazidime 2 g IV every 8 hours Cefepime 2 g IV every 8 hours Piperacillin-tazobactam 4.5 g IV every 6 hours[¥]	Imipenem 500 mg IV every 6 hours Meropenem 1 g IV every 8 hours Ciprofloxacin 400 mg IV every 8 hours

sing recommendations are for adult patients with normal organ function. For more detail, including duration of treatment and dosage adjustments (eg, for organ impairment)

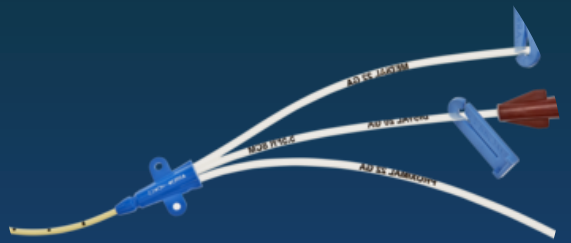
Removal

- **Remove infected catheters by:**
- S.ureus
- P. aeruginosa
- Drug-resistant gram-negative bacilli
- Candida



Removal

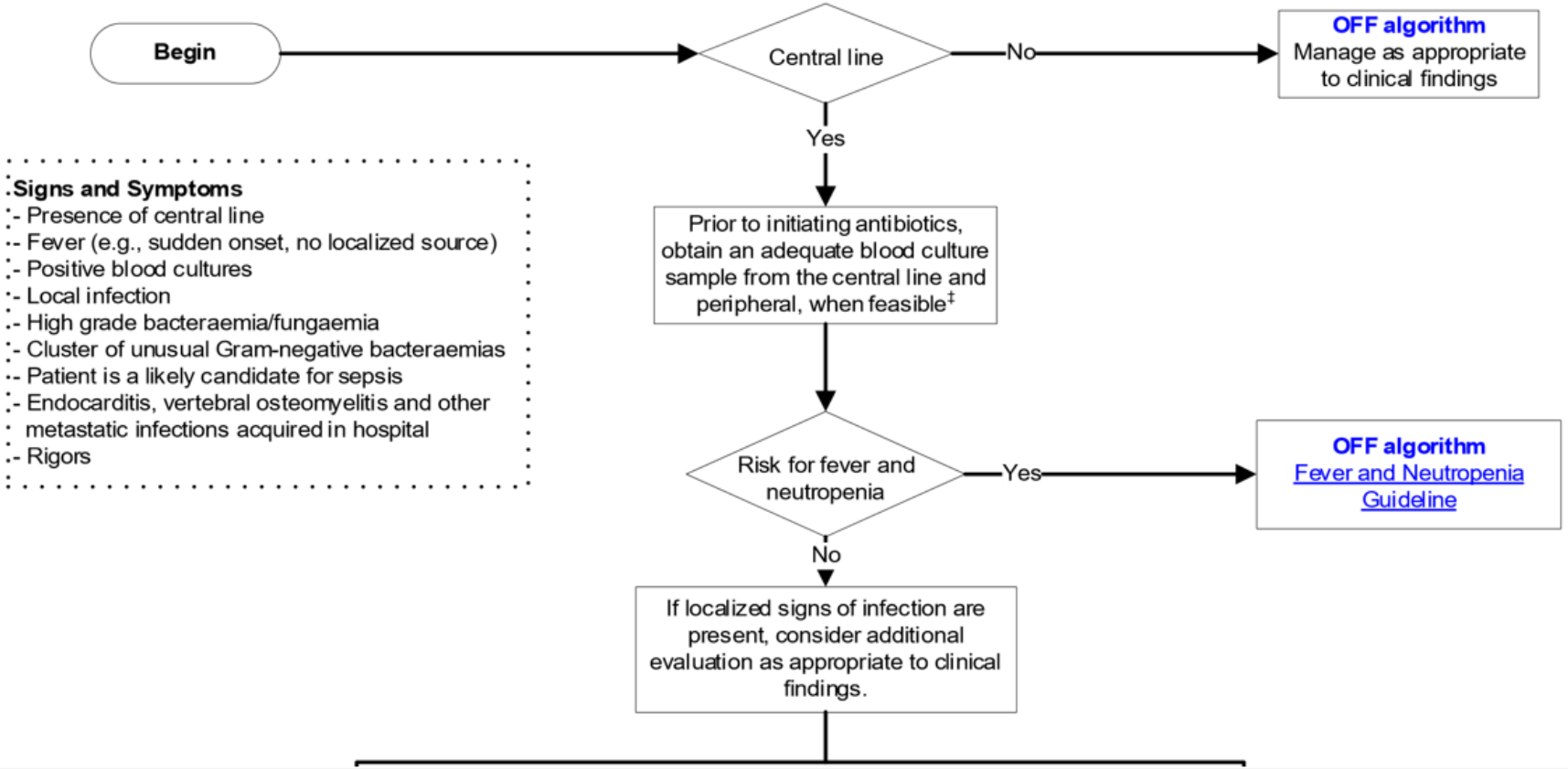
- Sepsis
- Hemodynamic instability
- Presence of endocarditis or evidence of metastatic infection
- Presence of suppurative thrombophlebitis
- Presence of a propagating clot
- Persistent bacteremia after 72 hours of appropriate antimicrobial therapy



Studies about Removal

- Early catheter removal (within three days of bacteremia onset) :lower relapse rates and lower rates of hematogenous complications
- In CRBSI due to drug-resistant gram-negative bacteria, delayed catheter removal has been associated with increased mortality
- Catheter removal based on the above pathogen-related considerations must be weighed against the clinical indication for the catheter and the risks associated with removal and replacement of a catheter at another site.
- Catheter removal is not necessary for patients with unexplained fever & hemodynamically stable in the absence of documented bloodstream infection

TCH Evidence-Based Outcomes Center
Clinical Algorithm for Diagnosis and Initial Management of Suspected Central Line Associated Bloodstream Infections (CLABSI)



Empiric Therapy

- Vancomycin
- Empirical coverage for gram-negative bacilli should be based on the drug susceptibility history of child, local antimicrobial susceptibility data and the severity of disease
- Empirical therapy for suspected catheter-related candidemia should be used for patients with neutropenia and fever lasting > 5 days.˜(Fever and Neutropenia Guideline)

Upon availability of culture and susceptibility data, de-escalation of antibiotic therapy can be performed, if feasible

Removal of the Central Line

Prompt removal of the central line ***should be considered*** when any of the following conditions and/or organisms exists:

- Severe sepsis
- Endocarditis
- Bloodstream infection that continues despite > 72 h of antimicrobial therapy to which the infecting microbes are susceptible
- Infections due to *S. aureus*, , gram-negative bacilli including *P. aeruginosa*, *Bacillus* species, and/or enterococci

Prompt removal of the catheter ***is necessary*** in cases of:

- Infections due to mycobacteria and/or fungi
- Tunnel site infection (e.g., redness, inflammation along catheter line, purulent drainage)
- Suppurative thrombophlebitis

Weight in kg	Optimal total blood volume (ml)[#]	Volume of blood per bottle (ml)	Number and type of bottles NOTE: Priority should be given to the aerobic blood culture.
≤ 3	2	1	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
> 3-5	3	1.5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
> 5-7	5	2.5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
> 7-12	10	5	1 pediatric aerobic blood culture order (central) 1 pediatric aerobic blood culture order (peripheral)
> 12-20	15	5	1 adult blood culture order^ (central) 1 pediatric aerobic blood culture order (peripheral)
> 20-30	30	10	1 adult blood culture order^ (central) 1 pediatric aerobic blood culture order (peripheral)
> 30-45	40	10	1 adult blood culture order^ (central) 1 adult blood culture order^ (peripheral)
> 45	60	10	2 adult blood culture orders^ (central) 1 adult blood culture order^ (peripheral)

[#] per a 24 h time period

*max blood volume/DAY is 3-4 ml/kg of body weight (or 3.8% of total blood volume) [10]

Manage as appropriate to clinical findings

˜ **Risk factors for candidemia include:**

- total parental nutrition
- prolonged use of broad-spectrum antibiotics
- hematologic malignancy
- receipt of bone marrow or solid organ transplant
- femoral cathertization
- colonization due to *Candida* species at multiple sites

Catheter Salvage

- Retention of the catheter with systemic antimicrobial therapy in addition to AB lock therapy.
- Catheter salvage should not be attempted in condition warranting catheter removal

- CRBSI due to CoNS and drug-susceptible Enterobacteriaceae (E. coli, Klebsiella species, Enterobacter species)

- Some pediatricians favor attempting catheter salvage: difficulty in vascular access among children and several studies have reported successful catheter salvage among children

Antibiotic lock therapy (ALT)

- Indications :
- ALT is used as adjunctive therapy together with systemic antibiotics for treatment of CRBSI in the setting of catheter salvage.
- Patients with a long-term intravascular device (>14 days)
- Hemodynamic stable with CRBSI due to low virulence pathogen
- No complications

- Antibiotic solution into the catheter lumen with the intention of achieving a drug level high enough to kill bacteria within the biofilm of the catheter.

- Antibiotic concentrations must be 100- to 1000-fold higher to kill sessile bacteria

Antibiotic lock therapy (ALT)

- For patients on total parenteral nutrition or other continuous infusions, ALT may not be feasible .
- For multilumen catheters, ALT may be rotated between lumens
- Heparin in ALT : help maintain catheter patency and facilitate antibiotic penetration into microbial biofilm

- Antibiotics that are compatible with heparin and active and stable for prolonged periods : Vancomycin, cefazolin, ceftazidime, and gentamicin.

- Determine the fill volume: flush the line with normal saline, attach a new 5 mL syringe to the catheter, and aspirate slowly until blood appears at the syringe tip; the amount of saline in the syringe is the "fill volume" of lock solution

- Ideally ALT : at least once daily.

Studies about ALT

- Some studies support a minimum dwell time of 8 to 12 hours
  In one prospective study with once daily ALT instillation with a dwell time as short as 2 hours

- In a retrospective study including 21 episodes of CRBSI due to Co-Ns managed with systemic and ALT (three days of daptomycin), the rate of successful catheter salvage was 76 percent .

- Some studies support as ALT in prevention CRBSI

Adverse effects

- Systemic toxicity
- Antibiotic resistance
- Secondary candidemia
- Bleeding from inadvertent systemic anticoagulation
- Risk of heparin–induced thrombocytopenia.

Antibiotic lock solution concentrations for CRBSI

	Antibiotic agent	Antibiotic concentration	Heparin concentration	Maximum dwell time (duration of stability)*	References
Antibiotic agents with activity against gram-positive organisms	Vancomycin	2.5 mg/mL¶	2500 units/mL	72 hours	Krishnasami[1]
		5 mg/mLΔ	5000 units/mL	72 hours	Luther[2]
		5 mg/mL	none	72 hours	Luther[2]
	Cefazolin	5 mg/mL◇	2500 units/mL	72 hours	Krishnasami[1]
		5 mg/mL§	none	48 hours	Vercaigne[3]
		10 mg/mL	5000 units/mL	72 hours	Vercaigne[3]
	Daptomycin	5 mg/mL¥	5000 units/mL	72 hours	LaPlante[4]
		5 mg/mL	none	72 hours	LaPlante[4]
	Nafcillin	100 mg/mL	none	12 hours	Nafcillin[5]
	Ampicillin	10 mg/mL‡	none	8 hours	Ampicillin[6]
Antibiotic agents with activity against gram-negative organisms	Gentamicin	1 mg/mL†	2500 units/mL	72 hours	Krishnasami[1]
		5 mg/mL**	5000 units/mL	72 hours	Vercaigne[3]
		5 mg/mL	none	72 hours	Vercaigne[3]
	Ceftazidime	10 mg/mL¶¶	5000 units/mL	48 hours	Vercaigne[3]
		1 to 10 mg/mL	none	48 hours	Lee[7]
	Cefepime	1 to 10 mg/mL	none	48 hours	Lee[7]
	Ciprofloxacin	1 to 5 mg/mL	none	48 hours	Lee[7], Lee[8]
	Ceftriaxone	100 mg/mL	none	48 hours	Ceftriaxone[9]

Guidewire exchange

- Guidewire exchange of the catheter is a management approach of last resort（ impossible change catheter ）
- For situations in which catheter removal is not readily feasible, catheter salvage is preferable to guidewire exchange.
- Patients should receive systemic antimicrobial therapy and ALT

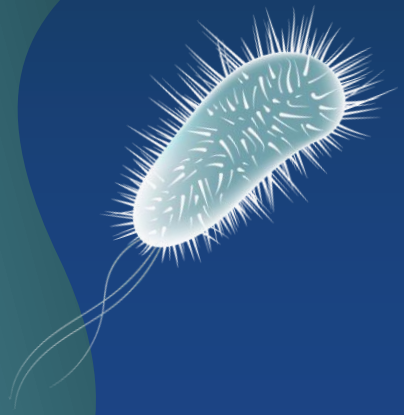
MANAGEMENT OF CATHETER COLONIZATION

- Single positive catheter blood culture positive for coagulase-negative staphylococci or other potential skin contaminant

- Increased risk for subsequent development (CRBSI)
- Following the patient for clinical manifestations of CRBSI
- Obtaining additional peripheral blood cultures.

- Alternative approaches : catheter removal or administration of antibiotic lock therapy

Thanks



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