

Central Venous Catheter Antibiotic Treatment Protocol

Purpose

1. To provide evidence-based practice guidelines for the management of suspected systemic central venous catheter (CVC)-related infection in the **hemodialysis (HD) outpatient population**.

Note: This is a guideline ONLY; there may be times when, based on individual assessments, there is a need to operate outside of this protocol.

2. To provide an accurate and comprehensive record of all vascular access infections via a single point of entry to aid in the development of targeted strategies to reduce vascular related infection rates and optimize patient outcomes.

Personnel Permitted to Perform Procedure

1. Registered nurses (RNs), graduate nurses, and licensed practical nurses (LPNs; in consultation with an RN) who have completed specialized, comprehensive HD training.
2. Patients/designated helpers who have received specialized and comprehensive training by a trained home HD-registered nurse may administer intravenous (IV) antibiotics at home if trained in the procedure and with dosage instructions from the home HD RN (in conjunction with this protocol).

Policy

1. A physician's order is required to initiate the antibiotic protocol
 - ◆ When a patient presents with suspected CVC bacteremia infection, the attending nephrologist must be notified of any significant clinical findings and diagnostic testing prior to the nurse proceeding with antibiotic treatment (ie, Appendix I: "Phase I — Algorithm for SUSPECTED Systemic Catheter Associated Bacteremia")
 - ◆ When blood culture specimen results are confirmed to be positive, the attending nephrologist will be notified of the results and the plan to continue with the antibiotic protocol (ie, Appendix II: "Phase II — Antibiotic Protocol for CONFIRMED Catheter Associated Bacteremia")
 - ◆ Antibiotics should be prescribed in accordance with Appendix III: "Gentamycin, Vancomycin, CeFAZolin, CefTAZidime Dosing Charts"
 - ◆ If the blood culture results are negative, the antibiotic protocol will be discontinued. The attending nephrologist will be notified of the negative results and the clinical status of the patient

Definitions

- **Bacteremia:** Presence of bacteria in the circulating blood
- **Coagulase-negative Staphylococcus (*Staphylococcus epidermidis*):** Normal bacterial skin, gut and upper respiratory tract flora. It is a true opportunistic pathogen. Infection is associated with skin penetration from CVC or peritoneal dialysis (PD) catheter insertion; implanted prosthesis (eg, heart valves); and in immunocompromised patients such as those individuals with end-stage renal disease
- ***Enterococcus fecalis*:** Opportunistic gram-positive bacterium that has become one of the most troublesome pathogens. Lives peacefully in the gut but thrives in wounds. Extremely hardy and can survive for weeks on environmental surfaces
- **Gram-negative microorganisms:** Examples are *Klebsiella*, *Pseudomonas aeruginosa*, *Escherichia coli* (E coli)
- **Metastatic infection:** Transmission of infection from an original site to 1 or more sites elsewhere in the body

Central Venous Catheter Antibiotic Treatment Protocol (cont'd)

2. When a patient becomes an inpatient, the attending physician will assume responsibility for management of the infection (ie, will choose to order the antibiotic protocol or provide individualized prescriptive care).
3. The access nurse and/or designate unit-specific access expert will be notified of all suspected and/or confirmed infections.
4. Strict aseptic technique must be used when performing CVC-related interventions.
5. In the event of suspected catheter-related infection, patient assessment will include the following general clinical manifestations of bacteremia (see Appendix I, "Phase I — Algorithm for SUSPECTED Catheter Associated Bacteremia").

Note: Patients who have artificial heart valves or those who are taking steroids or immunosuppressant medications are more prone to develop systemic infection.

- ◆ Fever $\geq 38^{\circ}\text{C}$ and/or chills and rigors
- ◆ Hypothermia
- ◆ Confusion or altered level of mental state
- ◆ Hyperglycemia
- ◆ Nausea and/or vomiting
- ◆ Complaint of general and unusual feeling of unwellness
- ◆ Signs and symptoms of any of the following:
 - Respiratory infection (eg, cough, colored phlegm or sputum production, hemoptysis, shortness of breath, crackles and/or wheezes on auscultation, oxygen desaturation on room air, increased need for oxygen replacement)
 - Gastrointestinal infection (eg, diarrhea, abdominal cramps, loss of appetite, abdominal distention and/or tenderness)
 - Genitourinary infection (eg, hematuria, pyuria or dysuria in patients with some residual function, pain in lower back, hips or thighs)
 - Integumentary or access site infection (eg, redness, tenderness, serous or purulent exudates, pallor or bruising, cool or warm to touch, edema)
 - Metastatic infection (eg, red, tender, and/or swollen joints; new or worsening cardiac murmur, congestive heart failure)
- ◆ Elevated white blood cell (WBC) count

Definition (cont'd)

- **Sepsis:** Severe and potentially fatal illness caused by overwhelming infection of the bloodstream by toxin producing bacteria
- ***Staphylococcus aureus:*** Gram-positive microorganism that commonly colonizes the human skin and nasal mucosa. Can enter into the blood stream through breakage of the skin or may be ingested in contaminated food particles. Once in the body, it can produce poisons and toxins causing severe illness
- **MSSA:** Methicillin-sensitive *S aureus*
- **MRSA:** Methicillin-resistant *S aureus*
- ***Streptococcus viridans:*** Hemolytic streptococcus that is usually the main culprit for endocardial infection

Central Venous Catheter Antibiotic Treatment Protocol (cont'd)

6. An RN or an LPN (in consultation with a RN), without a physician's order, may obtain the following laboratory specimens:
 - ◆ Blood culture specimens: 2 sets of 2 (4 total) or 1 set of 3 (local laboratory dependent)
 - ◆ Complete blood cell count
 - ◆ Swab(s) for culture and sensitivity from sites where exudate is present
 - ◆ Sputum and/or urine for culture and sensitivity if indicated
 - ◆ Predialysis antibiotic levels if the patient is already being treated for suspected or confirmed infection
 - If the CVC is locked with an antibiotic solution, draw antibiotic levels per PT/INR method (start dialysis, wait 5 minutes, and then draw level). Consult physician if unable to withdraw antibiotic lock solution from the CVC
 - If the predialysis antibiotic levels are not available before the patient completes the dialysis session, the next antibiotic dose can be given during the next session unless the levels are below target. In this case, it is advisable to bring the patient back for dosing. If the patient refuses or there is uncertainty (ie, close to target), check with the nephrologist
7. Unless otherwise ordered, the patient's standard lock solution will continue to be used. Note: There may be some situations where the physician requests use of vancomycin/heparin OR ceftAZidime/heparin lock solution (to replace the patient's standard lock solution).
8. Antibiotics will be adjusted based on the following predialysis antibiotic levels:
 - ◆ Vancomycin greater than 19 mg/L: Hold vancomycin
 - ◆ Gentamicin less than 1.5 mg/L or greater than 3 mg/L: refer to Appendix III. "Gentamicin, Vancomycin, CeFAZolin, CefTAZidime Dosing Charts"

Note for home HD patients: Alternatively, vancomycin 25 mg/kg load followed by 500 mg every HD session to a maximum of 4 sessions/week, may be given without pursuing vancomycin levels.

Procedure for Antibiotic Lock Preparation

(refer to Appendix II — “Phase II Antibiotic Protocol for CONFIRMED CVC Associated Bacteremia According to Bacterial Organism”)

1. Prepare **vancomycin and heparin** lock solution, if ordered, for CVC Locks: Note: Vancomycin lock solution **should be prepared immediately prior to administration** as it is good for 72 hours only (this will ensure potency is maintained within the catheter lumen until the next run). Also note that prevancomycin levels may be influenced by the vancomycin/heparin lock solution and unusual results should be brought to the attention of the physician.

A. Gather equipment/supplies

- ◆ Vancomycin **500-mg** vial
- ◆ Sterile water for reconstitution
- ◆ Heparin **10,000-units/mL** vials
- ◆ Sodium Chloride 0.9% 50 mL minibag
- ◆ Needles, 18 gauge × 5
- ◆ Syringes, 3 mL × 3; 10 mL × 4
- ◆ Medication labels, if required

B. Prepare vancomycin 2.8 mg/mL

- ◆ Add 10 mL sterile water for injection to a 500-mg vial of vancomycin powder to make a 50-mg/mL solution
- ◆ Shake to dissolve
- ◆ Withdraw and discard 4 mL from a 50-mL minibag of sodium chloride 0.9% (this is the standard average overfill in a minibag)
- ◆ Inject 3 mL (150 mg) of vancomycin into the minibag and apply medication label
- ◆ Final concentration: 150 mg in 53 mL = 2.8 mg/mL vancomycin

Points of Emphasis

- Patients must be educated on the signs of CVC access infection and the need to seek immediate medical attention in urgent or emergent situations (eg, septicemia)
- Antibiotic doses may be verified by 2 nurses (1 must be a RN) or 1 nurse and 1 pharmacist at the discretion of the RN

Procedure for Antibiotic Lock Preparation (cont'd)

C. Prepare heparin lock solution

- ◆ Into a 3-mL syringe, draw 0.3 mL (3000 units) from a 10,000-units/mL vial of heparin
- ◆ Using the same syringe, withdraw 2.7 mL (7.5mg) of vancomycin from the above minibag
- ◆ Repeat above 2 steps, using a second 3-mL syringe
- ◆ Flush both lumens with 10-mL sodium chloride 0.9%
- ◆ Instill vancomycin/heparin lock solution equal to the volume of CVC lumens
- ◆ Apply medication labels to the lumens

D. Final products (reflected on medication label)

- ◆ Vancomycin 7.5 mg/3 mL= 2.5 mg/mL
- ◆ Heparin 3000 units/3 mL=1000 units/mL

2. If cefTAZidime/heparin lock is ordered

For inpatients: Order from pharmacy

For outpatients: Mix as follows (prepare immediately prior to administration)

A. Gather equipment/supplies

- ◆ CefTAZidime **1-g** vial
- ◆ Heparin **10,000-units/mL** vials
- ◆ Sterile water for injection 10 mL
- ◆ Sodium chloride 0.9% 50-mL minibag
- ◆ Needles, 18 gauge × 5
- ◆ Syringes, 10 mL × 4; 3 mL × 3; 1 mL × 1
- ◆ Syringe-to-syringe transfer device × 2
- ◆ Medication labels

B. Reconstitute cetTAZidime

- ◆ Inject 4.4 mL sterile water for injection to 1-g vial of cefTAZidime
- ◆ Shake well to reconstitute
- ◆ Yields a 200-mg/mL solution

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Procedure for Antibiotic Lock Preparation (cont'd)

C. Prepare lock solution

- ◆ Draw up 0.25 mL (50 mg) cefTAZidime
- ◆ Draw up 2.5 mL (25,000 units) heparin using the 10,000-units/mL solution
- ◆ Using a syringe-to-syringe transfer device, transfer the contents of both syringes to a 10-mL syringe
 - Fill this final syringe to 10 mL using sodium chloride 0.9%
 - Mix well
 - Using syringe-to-syringe transfer device, fill 2, 3-mL syringes with cefTAZidime/heparin lock solution
 - Flush both lumens with 10 mL sodium chloride 0.9%
 - Instill cefTAZidime/heparin lock solution equal to the volume of CVC lumens
 - Apply medication labels to lumens
- ◆ Final product (reflected on medication label):
 - CefTAZidime 5 mg/mL + heparin 2500 units/mL lock solution

Bibliography (cont'd)

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Appendix

Appendix I. Phase I - Algorithm for Suspected Systemic CVC-Associated Bacteremia

Patient with HD CVC

Presents unwell

(symptomatic or asymptomatic)

For example, fever $\geq 38^{\circ}\text{C}$, chills, rigors, hypothermia, confusion or altered mental state, hyperglycemia, nausea and/or vomiting, complains of general or unusual/vague feeling of unwellness

Perform clinical assessment

(refer to Policy Statement 6)

Signs and symptoms of respiratory, gastrointestinal, genitourinary, integumentary, or metastatic infection, elevated WBC

Obtain lab specimens

(refer to Policy Statement 7)

Blood cultures; CBC; swab(s) for culture and sensitivity from sites where exudates are present; sputum and/or urine for culture and sensitivity, if indicated; pre-dialysis antibiotic levels if patient is already being treated

Check for allergies

To vancomycin, ceFAZolin, gentamicin, and ceTAZidine

If allergies exist to any antibiotics

- Check with pharmacy to determine if applicable to any of the protocol recommended drugs
- Defer to the physician for individualized care
- Do NOT proceed with the Antibiotic Protocol

If no allergies and pending cultures,

obtain physician order to initiate the Antibiotic Protocol

Initiate Antibiotic Protocol

- If patient presents clinically unwell (ie, symptomatic) obtain physician order to administer vancomycin + ceFAZolin + gentamicin*, consider immediate CVC removal (unless another source of infection has been identified), and admit patient to hospital
- If patient appears clinically well (ie, complains of general or unusual/vague feeling of unwellness but otherwise asymptomatic), administer vancomycin + gentamicin*, leave CVC in place, and treat as an outpatient until cultures return
- If patient is gentamicin intolerant, substitute with ceTAZidine*

Predialysis Antibiotic Levels

Vancomycin target = 15 - 19 mg/L

- For home HD patients, refer to Policy Statement 9
- Vancomycin level will be reduced by 30% after dialysis

Gentamicin target = 1.5 - 3.0 mg/L

- Patients should be questioned regularly about hearing problems and/or dizziness (signs of ototoxicity)

- If blood culture results are known to be positive, with no other obvious source of infection, the attending nephrologist will be notified of the results and the plan to continue with the Antibiotic Protocol physician (proceed to Appendix II: Phase II for antibiotic choice and duration of therapy)
- If positive swab but negative blood cultures, check with physician for exit site treatment
- If positive sputum, would and/or urine, check with physician for next steps
- If all diagnostic tests are negative, notify physician and, unless the patient is clinically symptomatic, discontinue antibiotic therapy

*Dosing per Appendix III

Appendix II. Phase II – Antibiotic Protocol for Confirmed CVC-Associated Bacteremia According to Bacterial Organism

Treatment for Organism-Specific CVC-Associated Bacteremia

Note: Significant if ≥ 2 culture bottles positive for organism listed below
Coagulase-Negative *Staphylococcus* (antibiotics x 3 weeks)

- If clinical assessment is negative, leave catheter in place, give IV vancomycin* x 3 weeks total; use standard lock solution unless vancomycin/heparin lock solution ordered
- If clinical assessment positive, obtain physician order to remove the CVC

Note: Significant if ≥ 1 culture bottle positive for organism listed below
***Staphylococcus aureus* (antibiotics x 4 to 6 weeks)**

- Given the high risk of metastatic complications it is ideal practice to remove the CVC and replace at a new site even if clinical assessment is negative (guidewire exchange should not be done)
- If MSSA positive, give ceFAZolin* x 4 weeks
- If MRSA positive, give vancomycin*
- If clinical assessment positive, admit patient to hospital and physician will assume responsibility for prescribing antibiotics (cloxacillin 2 g IV q 4 - 6 h x 4 weeks is recommended)
- If metastatic complications, treatment duration is 6 weeks

Note: Significant if ≥ 1 culture bottle positive for organism listed below
***Enterococcus faecalis* (antibiotics x 3 weeks)**

- Plan for CVC removal and hospital admission; physician will assume responsibility for prescribing antibiotics (ampicillin 2 g IV post HD x 3 weeks is recommended)
- If CVC is left in place, physician will assume responsibility for prescribing antibiotics (vancomycin/ampicillin + gentamicin is recommended)
- Follow sensitivity to ampicillin; if resistant, change to vancomycin

Clinical Assessment

If any of the following are positive, the ideal practice is to remove the catheter and insert a new catheter at a new site:

- Patient is clinically unwell (eg, general malaise, hypotensive, septic, altered mental state, chills, sweating)
- Persistent fever $\geq 38^{\circ}\text{C}$
- Recent CVC bacteremia (with same CVC)
- Signs and symptoms of exit site infection or metastatic infection
- History of prosthetic heart valve

If the catheter is left in place, the physician may order one of the following antibiotic locks (refer to Procedural statements 1 and 2 for mixing):

Vancomycin/heparin lock

- Vancomycin 7.5 mg/3 mL = 2.5 mg/mL
- Heparin 3000 units/3mL = 1000 units/mL

CefTAZidime/heparin lock

- CefTAZidime 5 mg/mL
- Heparin 2500 units/mL

Draw follow-up blood cultures 2 weeks after the last dose of antibiotics

*Dosing per Appendix III

Appendix II. Phase II – Antibiotic Protocol for Confirmed CVC-Associated Bacteremia According to Bacterial Organism (cont'd)

Treatment for Organism-Specific CVC-Associated Bacteremia

***Enterococcus fecium* (antibiotics x 3 weeks)**

- Plan for CVC removal and hospital admission; physician will assume responsibility for prescribing antibiotics (may order Antibiotic Protocol)
- Combination therapy: ampicillin 2 g q24h (post HD on HD days) x 3 weeks and gentamicin recommended
- Follow sensitivity to ampicillin; if resistant, change to vancomycin
- Look for abdominal source or endocarditis

***Streptococcus viridans* (antibiotics x 3 weeks)**

- Guidewire exchange OK if clinical assessment negative
- Give ceFAZolin

Gram-negative organism (antibiotics x 3 weeks)

- Remove CVC (guidewire exchange OK) if clinical assessment positive
- If clinical assessment negative, leave CVC in and give ceftAZidime or gentamicin x 3 weeks (according to sensitivities) and ceftAZidime lock if ordered

***Pseudomonas aeruginosa* (antibiotics x 4 weeks)**

- Irrespective of clinical assessment, removal of catheter is recommended
- If catheter is not removed, use dual antibiotics (ceftAZidime + gentamicin x 4 weeks) pending verification of cultures
- If multidrug resistant, consult the infectious disease team

Draw follow-up blood cultures 2 weeks after the last dose of antibiotics

*Dosing per Appendix III

Appendix III. Gentamycin, Vancomycin, CeFAZolin, CefTAZidime Dosing Charts

Gentamicin LOADING Dose		
Patient Weight, kg	Gentamicin Dose, mg (1.5 mg/kg rounded to the nearest 10 th)	Gentamicin Dilution Amount Required, mL (gentamicin 40 mg/mL vial)
40-43	60	1.5
44-50	70	1.75
51-56	80	2.0
57-63	90	2.25
64-70	100	2.5
71-76	110	2.75
77-83	120	3.0
84-90	130	3.25
91-96	140	3.5
97-103	150	3.75
104-109	160	4.0
110-116	170	4.25
117-123	180	4.5
124-129	190	4.75
> 130	200 (maximum recommendad dose)	5.0

Notes
<ul style="list-style-type: none"> • Draw predialysis gentamicin level on next session after gentamicin loading dose • If level is therapeutic (1.5 - 3.0 mg/L) or greater than 3.0 mg/L, proceed with maintenance dose • If level is < 1.5 mg/L, proceed with a maintenance dose that is increased by 25%

Appendix III. Gentamycin, Vancomycin, CeFAZolin, CefTAZidime Dosing Charts (cont'd)

Gentamicin MAINTENANCE Dose		
Patient Weight, kg	Gentamicin Dose, mg (1.5 mg/kg rounded to the nearest 10 th)	Gentamicin Dilution Amount Required, mL (gentamicin 40 mg/mL vial)
40-44	40	1.0
45-54	50	1.25
55-64	60	1.5
65-74	70	1.75
75-84	80	2.0
85-94	90	2.25
95-104	100	2.5
105-114	110	2.75
115-124	120	3.0
> 134	130 (maximum recommended dose)	3.25

Notes
<ul style="list-style-type: none"> • Draw predialysis gentamicin level at least twice weekly and the next dialysis session after a dose change or nontherapeutic level • If level is < 1.5 mg/L, increase dose by 25% • If level is > 3.0 mg/L, hold next dose, then decrease dose by 25% once level has returned to therapeutic range (1.5 - 3.0 mg/L) • Question patient at each session about hearing problems or dizziness (signs of ototoxicity)

Appendix

Appendix III. Gentamycin, Vancomycin, CeFAZolin, CefTAZidime Dosing Charts (cont'd)

CefTAZidime Dose

2 grams IV every dialysis session up to a maximum of 4 doses per week

Vancomycin Dose

Patient Weight, kg	Vancomycin Dose, mg (20 mg/kg rounded to the nearest 250mg)	Vancomycin Reconstitution Amount Required, mL (vancomycin 1000mg/20mL sterile water)
31-43	750	15
44-56	1000	20
57-68	1250	25
69-81	1500	30
82-93	1750	35
> 94	2000 (maximum recommended dose)	40



Notes

- Draw vancomycin levels before each dialysis session
- If level is > 19 mg/L, hold next vancomycin dose

CeFAZolin Dose

Patient Weight, kg	CeFAZolin Dose, mg (20 mg/kg rounded to the nearest 500mg)	CeFAZolin Dilution Amount Required, vials (ceFAZolin 1000mg/10mL sterile water)
≤ 60	1500	1.5
> 60	2000 (maximum recommended dose)	2