

ANTIMICROBIAL STEWARDSHIP TREATMENT GUIDELINES FOR COMMON INFECTIONS

Vancouver General Hospital
UBC Hospital
G F Strong Rehabilitation Centre
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1st Edition

“Antimicrobial stewardship is defined as the limitation of inappropriate antimicrobial use while optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection; while limiting unintended consequences, such as the emergence of resistance, adverse drug events, the selection of pathogenic organisms, and cost...”

The Antimicrobial Stewardship “Treatment Guidelines for Common Infections Card” is produced by Pharmaceutical Sciences and the Antibiotic Utilization Subcommittee of the Vancouver General Hospital with representation from Pharmacy, Infectious Diseases, Medical Microbiology, BMT/Leukemia, Critical Care, Family Medicine, General Surgery, Internal Medicine, and Respiriology.

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Intravascular Catheter-related Infection

Catheter Culture	
1.	Obtain catheter culture when removed if catheter-related bloodstream infection suspected.
2.	Do not send catheter tip for culture with routine removal if there is no clinical suspicion of infection.
3.	When catheter infection is suspected and exudate is present on the catheter exit site, swab drainage for Gram stain and culture.
4.	Obtain blood cultures prior to initiation of antibiotics; draw from the catheter and a peripheral vein.
Clinical Highlights	
1.	Vancomycin is recommended for empirical therapy.
2.	Empiric combination antibiotic coverage for Gram-negative bacilli should be used in neutropenic patients, severely ill patients with sepsis, or patients colonized with such pathogens, until susceptibility data is available and de-escalation can be performed.
3.	Empiric therapy for candidemia with fluconazole or micafungin should be considered in septic patients with total parenteral nutrition, prolonged broad-spectrum antibiotics, hematologic malignancy, bone marrow or solid organ transplant, femoral catheterization, or <i>Candida</i> colonization at multiple sites.
4.	Day 3 or when culture and susceptibility results are available, pathogen-directed therapy should be used.
5.	Duration of treatment is dependent on line removal and the pathogen; range is generally from 5-14 days.
6.	For persistent bacteremia or fungemia (i.e. >72 hours after catheter removal), 4-6 weeks of antibiotic therapy should be administered.
7.	Long-term catheters should be removed in severe sepsis, suppurative thrombophlebitis, endocarditis, persistent bacteremia (>72 hours), or infections due to <i>S. aureus</i> , <i>P. aeruginosa</i> , fungi, or mycobacteria.
8.	When salvaging a catheter, additional blood cultures should be obtained, and catheter should be removed if persistent bacteremia occurs 72 hours after initiation of therapy.
9.	If a single positive blood culture grows coagulase-negative <i>Staphylococcus</i> , additional cultures obtained through the suspected catheter and peripheral vein should be performed before initiation of antimicrobial therapy and/or catheter removal to confirm true bloodstream infection.

Reference: Mermel LA et al. CID 2009;49:1-45.

Community-acquired Pneumonia

Indication	Usual Pathogens	Empiric Treatment	Dose	Cost/Day	
Inpatient (non-ICU)	<i>S. pneumoniae</i> <i>M. pneumoniae</i> <i>C. pneumoniae</i> <i>H. influenzae</i> <i>Legionella sp.</i>	a. [Ampicillin or Cefuroxime] + [Doxycycline or Clarithromycin XL or Erythromycin]	1-2 g IV q4h 500 mg PO TID/ 750-1500 mg IV q8h 100 mg PO BID 1000 mg PO daily 500 mg PO/IV q6h	\$ \$ \$\$ \$ \$ \$-\$\$\$	
		b. Moxifloxacin	400 mg PO/IV daily	\$-\$\$\$	
Inpatient (ICU)	<i>S. pneumoniae</i> <i>S. aureus</i> <i>Grp A Streptococci</i> <i>Gram-negative bacilli</i> <i>H. influenzae</i> <i>Legionella sp.</i>	[Ceftriaxone or Piperacillin-tazobactam] + [Clarithromycin or Azithromycin or Erythromycin or Moxifloxacin]	1-2 g IV q24h 3.375 g IV q6h 500 mg PO BID 500 mg IV x 1, then 250 mg q24h 500 mg PO/IV q6h 400 mg PO/IV daily	\$ \$\$ \$ \$\$ \$-\$\$\$ \$-\$\$\$	
		If <i>Pseudomonas</i> suspected*	[Piperacillin-tazobactam or Ceftazidime]* + [Ciprofloxacin or Gentamicin/Tobramycin]	3.375 g IV q6h 2 g IV q8h 750 mg PO BID/ 400 mg IV q12h 4-7 mg/kg IV q24h or 1.5 mg/kg IV q8h	\$\$ \$\$\$ \$ \$ \$-\$\$ \$\$
		If MRSA suspected	Vancomycin	15 mg/kg IV q8-12h	\$\$

*Impipenem-cilastatin 500 mg IV q6h may be an option. Empiric therapy should be guided by previous cultures and tailored according to new susceptibility results.

Clinical Highlights

- Empiric regimen may be broadened based on the following risk factors: Alcoholism, aspiration, COPD, chronic steroids, hospitalization (in past 1 month), HIV, ICU transfer, IV drug use, neutropenia, recent antibiotic use (within 3 months), solid organ transplant, and TB.
 - On Day 3 or when culture and susceptibility results are available, pathogen-directed therapy should be used.
 - Consider conversion from IV to oral therapy, if GI tract is functioning, and patient is hemodynamically stable and improving clinically.
 - Consider discontinuing therapy after Day 5, if patient is afebrile and has no more than 1 sign of CAP-associated sign of instability:
Criteria for Clinical Instability
Temperature >37.8°C
Heart rate >100/min
Respiratory rate >24/min
Systolic blood pressure <90 mmHg
SaO₂ <90% or pO₂ <60 mmHg on room air
Abnormal mental status.
5. Consider outpatient treatment, if CURB-65 score is <2.

Reference: Mandell LA et al. Infectious diseases society of America/American thoracic society consensus guidelines on the management of community-acquired pneumonia in adults. CID 2007;44:S27-72.

CURB-65 Severity Score for Community-acquired Pneumonia

Clinical Factor	Points
Confusion of new onset	1
Urea >7mmol/L	1
Respiratory rate ≥30/minute	1
Blood pressure <90 mmHg systolic or diastolic blood pressure ≥60 mmHg	1
Age ≥65 years	1

CURB-65 Score	Risk of Death	Recommendation
0	0.6%	Low risk; consider home treatment
1	3.2%	
2	13.0%	Short inpatient hospitalization or closely supervised outpatient treatment
3	17.0%	Severe pneumonia; hospitalize and consider admitting to intensive care
4	41.5%	
5	57.0%	

Reference: Lim W et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58(5):377-382.

Legend

Cost (\$/day)			
\$ 0.00-10.00	\$\$ 10.01-25.00	\$\$\$ 25.01-50.00	\$\$\$\$ 50.01-100.00

Hospital-acquired Pneumonia

Indication	Usual Pathogens	Empiric Treatment	Dose	Cost/Day
Mild to moderate (no risk factors)	<i>S. pneumoniae</i> <i>Streptococcus sp.</i> MSSA <i>H. influenzae</i> <i>E. coli</i> <i>Klebsiella sp.</i> <i>Enterobacter sp.</i> <i>Proteus sp.</i> <i>Serratia sp.</i>	a. Moxifloxacin OR b. Ceftriaxone OR c. Piperacillin-tazobactam	400 mg PO/IV daily 1-2 g IV q24h 3.375 g IV q6h	\$-\$\$\$ \$ \$\$
		[Moxifloxacin or Ceftriaxone or Piperacillin-tazobactam] ± Vancomycin (if MRSA suspected)	400 mg PO/IV daily 1-2 g IV q24h 3.375 g IV q6h 15 mg/kg IV q8-12h	\$-\$\$\$ \$ \$\$ \$\$
Mild to moderate (hospitalized ≥5 days and/or received antimicrobials within 3 months)	<i>S. pneumoniae</i> <i>Streptococcus sp.</i> MSSA <i>H. influenzae</i> <i>E. coli</i> <i>Klebsiella sp.</i> <i>Enterobacter sp.</i> <i>Proteus sp.</i> <i>Serratia sp.</i> MRSA <i>Pseudomonas</i>	[Piperacillin-tazobactam or Ceftazidime or Imipenem-cilastatin] + [Ciprofloxacin or Gentamicin/Tobramycin (if <i>Pseudomonas</i> suspected)] ± Vancomycin (if MRSA suspected)	3.375 g IV q6h 2 g IV q8h 500 mg IV q6h 750 mg PO BID/ 400 mg IV q12h 5-7 mg IV q24h or 1.5 mg/kg q8h 15 mg/kg IV q8-12h	\$\$ \$\$\$ \$\$\$\$ \$ \$ \$-\$\$ \$\$
Severe (hypotension, intubation, sepsis, rapid infiltrate progression, end organ dysfunction)	<i>S. pneumoniae</i> <i>Streptococcus sp.</i> MSSA <i>H. influenzae</i> <i>E. coli</i> <i>Klebsiella sp.</i> <i>Enterobacter sp.</i> <i>Proteus sp.</i> <i>Serratia sp.</i> MRSA <i>Pseudomonas</i> <i>Legionella sp.</i>	[Piperacillin-tazobactam or Ceftazidime or Imipenem-cilastatin] + [Ciprofloxacin or Gentamicin/Tobramycin (if <i>Pseudomonas</i> suspected)] ± Vancomycin (if MRSA suspected)	3.375 g IV q6h 2 g IV q8h 500 mg IV q6h 750 mg PO BID/ 400 mg IV q12h 5-7 mg IV q24h or 1.5 mg/kg q8h 15 mg/kg IV q8-12h	\$\$ \$\$\$ \$\$\$\$ \$ \$ \$-\$\$ \$\$

Clinical Highlights

- On Day 3 or when culture and susceptibility results are available, pathogen-directed therapy should be used.
- Consider discontinuing therapy on Day 3, if CPIS score is ≤6 on both Day 0 and Day 3.
- Consider discontinuing therapy after Day 7-8, if patient has improved clinically. (Longer durations of treatment may be required for *Pseudomonas*, *Acinetobacter sp.*, *Stenotrophomonas maltophilia*, and MRSA).

References:

- Rotstein C et al. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. Can J Infect Dis Med Microbiol 2008;19(1):19-53.
- Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388-416.

Modified Clinical Pulmonary Infection Score (CPIS)

Diagnostic Feature	CPIS Points		
	0	1	2
Tracheal secretions	Rare	Present, non-purulent	Present and purulent
Chest x-ray infiltrate	No infiltrate	Diffuse (or patchy) infiltrate	Localized infiltrate
Temperature (°C)	≥36.5 and ≤38.4	≥38.5 and ≤38.9	≥39 or ≤36
White blood cells (x 10 ⁹ /L)	≥4.0 and ≤11.0	<4.0 or >11.0	<4.0 or >11.0 plus band forms ≥ 50%
PaO ₂ /FiO ₂ mmHg	>240 or ARDS		≤240 and no ARDS
Progression of pulmonary infiltrate	No radiographic progression		Radiographic progression (after exclusion of CHF and ARDS)
Microbiology	Negative	Positive	Positive plus positive Gram stain
<ol style="list-style-type: none"> At Day 0, calculate modified CPIS from the first five diagnostic features (maximum score 10). At Day 3 and 7, recalculate the modified CPIS using the seven variables (including the progression of pulmonary infiltrate and microbiology—maximum score 14). 			
Interpretation At Day 0 (baseline): Score of ≤6: Infection is unlikely and decision to treat with antibiotics should be carefully considered. (In ventilated patients with a score between 4 and 6, treatment should be considered if no alternative diagnosis can be obtained). Score of >6: Suggestive of pneumonia; initiate treatment.			
At Day 3 and 7: Score of ≤6: Consider discontinuing therapy if clinically well. Score of >6: Continue therapy.			

Reference: Rotstein C et al. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. Can J Infect Dis Med Microbiol 2008;19(1):19-53.

For more information on the VCH Hospital-acquired Pneumonia and Ventilator-associated Pneumonia guidelines, please visit the hospital intranet at:
http://vhnet/policies_manuals/reg_policy_clinical/page_20117.htm

**Vancouver Coastal Health-Providence Health Care
Clostridium difficile Infection Guideline
November 2010**

(Developed as a collaborative effort between VCH and PHC)

SUSPECTED OR CONFIRMED CDI

- Diarrhea (unformed or watery stools \geq 3 in 24 h)
AND
1. Pending *C. difficile* test with high clinical suspicion
OR
2. Positive *C. difficile* test

INFECTION CONTROL

Notify Infection Control
Isolate on contact precautions
Meticulous hand hygiene (preferably with soap & water)

EVALUATE CDI SEVERITY

Obtain baseline CBC and differential, electrolytes, and serum creatinine

**MILD OR MODERATE
(Does not meet criteria for SEVERE
or FULMINANT)**

SEVERE
Clinical criteria (any of the following):
WBC $>15,000/\text{mm}^3$ † **OR**
Acute kidney injury with rising serum creatinine (SCR)
(e.g. SCR \geq 1.5 times pre-morbid level or SCR \geq 175 $\mu\text{mol/L}$) **OR**
Pseudomembranous colitis **OR**
Clinical judgment
Risk factors for consideration:
Age $>60\text{yr}$, temp $>38.3^\circ\text{C}$, albumin $<25\text{g/L}$

**FULMINANT
(Any of the following):**
Toxic megacolon
Perforation
Signs of peritonitis
Ileus
Severe sepsis/septic shock
Hemodynamically unstable
Severe acute renal failure
(e.g. oliguria or dialysis requirement)

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FIRST EPISODE
Review all antibiotics & discontinue unless clearly indicated
Stop all anti-peristaltic & pro-motility agents
Metronidazole 500 mg PO/NG TID x 10-14 d
If diarrhea not resolving by Day 4-6,
Change to Vancomycin 125 mg PO/NG QID x 10-14 d
If symptoms worsen,
Reevaluate for CDI severity
Consider ID or GI consult

ANY EPISODE
Review all antibiotics & discontinue unless clearly indicated
Stop all anti-peristaltic & pro-motility agents
Vancomycin 125 mg PO/NG QID x 10-14 d
Consider ID, GI, and/or General Surgery consult
Obtain abdominal x-ray (3 views)
Consider CT scan of the abdomen if clinically indicated

ANY EPISODE
Review all antibiotics & discontinue unless clearly indicated
Stop all anti-peristaltic & pro-motility agents
Vancomycin 125 mg PO/NG QID * with OR without Metronidazole 500 mg IV Q8H
If complete ileus **OR**
If unable to take **PO/NG** vancomycin, consider adding **Vancomycin 500 mg** via cecal tube or enema **QID**†
Obtain ID or GI, General Surgery and ICU consult immediately as directed by level of care

FIRST RECURRENCE

Confirm that episode is the 1st recurrence (not 2nd or more recurrences)
Review all antibiotics & discontinue unless clearly indicated
Stop all anti-peristaltic agents & pro-motility agents
Metronidazole 500 mg PO/NG TID x 10-14 d
If diarrhea not resolving by Day 4-6,
Change to vancomycin 125 mg PO/NG QID x 10-14 d
If symptoms worsen,
Reevaluate for CDI severity
Obtain ID or GI consult

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Confirm that episode is the 1st recurrence (not 2nd or more recurrences)
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Stop all anti-peristaltic agents & pro-motility agents
Metronidazole 500 mg PO/NG TID x 10-14 d
If diarrhea not resolving by Day 4-6,
Change to vancomycin 125 mg PO/NG QID x 10-14 d
If symptoms worsen,
Reevaluate for CDI severity
Obtain ID or GI consult

SECOND OR MORE RECURRENCE

Vancomycin 125 mg PO/NG QID x 14 d, then may consider vancomycin tapering over 4 weeks (e.g. vancomycin 125 mg BID x 7 days, then 125 mg once daily x 7 days, then 125 mg every 2 or 3 days for 2 weeks)†
Obtain ID or GI consult
Consider obtaining Special Authority approval for vancomycin PO coverage by Pharmicare for outpatient treatment

SECOND OR MORE RECURRENCE
Vancomycin 125 mg PO/NG QID x 14 d, then may consider vancomycin tapering over 4 weeks (e.g. vancomycin 125 mg BID x 7 days, then 125 mg once daily x 7 days, then 125 mg every 2 or 3 days for 2 weeks)†
Obtain ID or GI consult
Consider obtaining Special Authority approval for vancomycin PO coverage by Pharmicare for outpatient treatment

Clinical Highlights

- Review all antibiotics, anti-peristaltics and pro-motility agents, and discontinue unless clearly indicated.
- Ensure patients are promptly initiated on CDI treatment.
- Assess patients on Day 4-6 for diarrhea resolution and escalate therapy if indicated.
- Refer patients for appropriate consultation, if patient has severe or fulminant disease.

In patients unable to mount a WBC response $>15,000/\text{mm}^3$, an increasing WBC with pronounced left shift may also be considered in these criteria; threshold of $>15,000/\text{mm}^3$ is based on expert opinion.
* May change to vancomycin if patient intolerant to metronidazole.
† Doses of 125 to 500 mg may be considered; appropriate dose has not been established in clinical trials.
‡ Vancomycin IV is not effective for the treatment of CDI.
§ Tapering regimens may vary considerably, as clinical data is limited.

Note: Physician assessment for perforation risk is required prior to rectal tube placement. Prophylactic treatment for patients on antibiotics who have previously had *C. difficile* is not recommended. Consider Infectious Diseases consult.

Intraabdominal Infection

Indication	Usual Pathogens	Empiric Treatment	Dose	Cost/Day
Community-acquired infection (mild to moderate severity: perforated or abscessed appendicitis and other infections)	“Core” pathogens: <i>Streptococcus</i> sp., Enterobacteriaceae (<i>Escherichia coli</i> , <i>Klebsiella</i> sp., <i>Proteus</i> sp., <i>Serratia marcescens</i>), anaerobes (<i>Bacteroides fragilis</i> , <i>Clostridium</i> sp., <i>Fusobacterium</i> sp., <i>Lactobacillus</i> sp., <i>Peptostreptococcus</i> sp., and <i>Veillonella</i> sp.)	a. [Cefazolin or Ciprofloxacin] + Metronidazole OR b. Piperacillin-tazobactam OR c. Clindamycin + Ciprofloxacin	2 g IV q8h 750 mg PO BID/ 400 mg IV q12h 500 mg PO/IV q12h 3.375 g IV q6h 600 mg PO/IV q8h 750 mg PO BID/ 400 mg IV q12h	\$\$ \$ \$ \$\$ \$\$-\$ \$ \$
Community-acquired infection (high risk severity: severe physiologic disturbance, advanced age, or immunocompromised)	As above	a. Piperacillin-tazobactam OR b. [Ciprofloxacin or Ceftriaxone] + Metronidazole	3.375 g IV q6h 750 mg PO BID/ 400 mg IV q12h 1-2 g IV q24h 500 mg PO/IV q12h	\$\$ \$ \$ \$ \$
Healthcare-associated complicated infection	As above <i>Acinetobacter</i> MDR GNB	a. Piperacillin-tazobactam OR b. Ceftazidime + Metronidazole OR c. Imipenem-cilastatin	3.375 g IV q6h 2 g IV q8h 500 mg IV q6h	\$\$ \$\$\$ \$
	If <i>P. aeruginosa</i> suspected	[Piperacillin-tazobactam or Ceftazidime]* + [Ciprofloxacin or Gentamicin/Tobramycin]	3.375 g IV q6h 2 g IV q8h 750 mg PO BID/ 400 mg IV q12h 5-7 mg IV q24h or 1.5 mg/kg IV q8h	\$\$ \$\$\$ \$ \$ \$\$-\$ \$
	If MRSA suspected	Vancomycin	15 mg/kg IV q8-12h	\$\$
	If <i>Candida</i> isolated	a. Fluconazole OR b. Micafungin (if fluconazole-resistant)	400 mg PO/IV daily 100 mg IV daily	\$\$-\$ \$\$\$
If <i>Enterococcus</i> isolated#	a. Add Ampicillin (not required if on Piperacillin-tazobactam or Imipenem-cilastatin) OR b. Vancomycin	2 g IV q4h 15 mg/kg IV q8-12h	\$ \$	

* Imipenem-cilastatin 500 mg IV q6h may be used if known or highly-resistant *Pseudomonas* is suspected.
Cephalosporins, fluoroquinolones, and clindamycin do not cover *Enterococcus*.

- Clinical Highlights**
- On Day 3 or when culture and susceptibility results are available, pathogen-directed therapy should be used.
 - Consider discontinuing treatment at Day 4-7, if source control is adequate and clinical response is good; longer durations of therapy have not been associated with improved outcome.
 - Consider diagnostic investigations, if experiencing inadequate clinical response at Day 4-7. Antibiotics should be discontinued within 24 hours for the following intraabdominal conditions:
 - Acute stomach and proximal jejunum perforations, in the absence of acid-reducing therapy or malignancy and if source control is achieved;
 - Bowel injuries due to penetrating, blunt, or iatrogenic trauma repaired within 12 hours and any intraoperative contamination of the operative field by enteric contents;
 - Acute appendicitis without perforation, abscess, or local peritonitis.

References: Solomkin JS et al. CID 2010;50:133-64, Chow AW et al. Can J Infect Dis Med Microbiol 2010;21:11-37.

Catheter-associated Urinary Tract Infection

Definition
Catheter-associated urinary tract infection (CA-UTI) is defined as **PRESENCE OF SYMPTOMS with $>10^6$ COLONY FORMING UNITS (CFU)/L of ≥ 1 BACTERIAL SPECIES** in a single catheter urine specimen or in a midstream voided urine after catheter removal for 48 hours, with a **POSITIVE URINE ANALYSIS**.

CA-UTI Symptoms
New onset or worsening fever, rigors, altered mental status, malaise, flank pain, costovertebral angle tenderness, acute hematuria, pelvic discomfort; and in those with catheter removed, dysuria, urgent or frequent urination, or suprapubic pain or tenderness.

Urine Culture and Catheter Replacement

- Obtain urine culture and urine analysis prior to antimicrobial therapy to identify the infecting organism.
- If catheter has been in place for >2 weeks and is still indicated, replace catheter.
 - Obtain urine culture and urine analysis from new catheter prior to antimicrobial therapy
 - If catheter is not required, culture voided midstream urine prior to antimicrobial initiation.

Usual Pathogens
Short-term catheterization: *E. coli*, *Klebsiella*, *Serratia*, *Citrobacter*, *Enterobacter*, coagulase (-) *Staph.*, *Enterococcus*.
Long-term catheterization: As above (may be polymicrobial), *Pseudomonas aeruginosa*, *Proteus*, *Morganella*, *P. stuartii*.

Treatment
Mild-moderate symptoms: Nitrofurantoin, cephalexin, co-trimoxazole or amoxicillin. Severe symptoms: Ceftriaxone or gentamicin.

Clinical Highlights

- Do not treat a positive urine culture in the absence of clinical symptoms and a positive urine analysis!
- Discontinue catheter as soon as appropriate.
- On Day 2 or when culture and susceptibility results are available, pathogen-directed therapy should be used.
- Seven days is the recommended duration of treatment if clinically improving and 10-14 days for delayed response, regardless of catheterization or not.
- May consider a 3 day treatment in women aged ≤ 65 years without upper UTI symptoms after removal of the catheter.

Reference: Hooton TM et al. CID 2010;50:625-663.