Intravenous Antimicrobial Renal Dose Adjustments

Antimicrobial	Usual Dose	CrCl 50-30mL/min	CrCl 30-10mL/min	CrCl < 10mL/min	HD*
Ampicillin	1-2g q4-6h	1-2g q6-8h		1-2g q8-12h	HD: 1-2g q8-12h
Ampicillin/Sulbactam	1.5-3g q6h	1.5-3g q6-8h	1.5-3g q12h	(<15 mL/min) 1.5-3g q24h	HD: 1.5-3g q24h (post HD)
Aztreonam	1-2g q8h	1-2g q8h	1-2g q12h	1-2g q24h	HD: 1-2g q24h (post HD)
Cefazolin	1-2g q8h		(<35 mL/min) 0.5-1g q12h	1 g q24h	HD: 1g q24h (post HD)
Cefepime	1g q6h	(60-30mL/min) 1g q8h	1g q12h	1g q24h (post HD)	
Cefepime (Neutropenic fever)	2g q8h	(60-30mL/min) 2g q12h	1g q12h	1g q24h (post HD)	
Ciprofloxacin	400mg q12h		400 mg q24h		HD: 400mg q24h (post HD)
Ciprofloxacin (*Pseudomonas*, critically ill)	400mg q8h		400 mg q12h	400 mg q24h	HD: 400mg q24h (post HD)
Ertapenem	1g q24h		500mg q24h		HD: 500mg q24h (post HD)
Fluconazole	100-400mg q24h	50% of dose q24h			HD: 50% of dose q24h (post HD)
Levofloxacin	500mg q24h	(50-20mL/min) 500mg x1, then 250mg q24h	(20-10ml/min) 500mg x1, then 250mg q48h	500mg x1, then 250mg q48h	
Levofloxacin (Nosocomial PNA, skin, intraabdominal, pyelo)	750mg q24h	(50-20mL/min) 750mg q48h	(20-10ml/min) 750mg x1, then 500mg q48h	750mg x1, then 500mg q48h	
Meropenem	500mg q6h	(50-26 mL/min) 500mg q8h	(25-10 mL/min) 500mg q12h	500mg q24h	HD: 500mg q24h (post HD)
Penicillin G	2-4 mU q4	1-3 mU q4h		1-2 mU q6h	HD: 1-2 mU q6h
Piperacillin/Tazobactam (Extended-infusion)	3.375g q8h	3.375g q8h	(<20mL/min) 3.375g q12h	3.375g q12h	
TMP/SMX (Dose based on TMP)	5mg/kg q12h		5mg/kg q24h (post HD)		
TMP/SMX (Dose based on TMP, PCP treatment)	5 mg/kg q6-8h		2.5 mg/kg q6-8h	2.5 mg/kg q8h	HD: 2.5 mg/kg q8h
Amikacin, Gentamicin Tobramycin, Vancomycin	Dosing per pharmacy				

•*For antimicrobials dosed every 24 hours in patients on hemodialysis, doses should be administered after dialysis on dialysis days. Alternatively, all doses may be administered once daily in the evening to ensure administration after dialysis on dialysis days.

# ISOLATES	ASPIRUS REFERENCE LAB ANTIBIOGRAM REPORTED AS % SUSCEPTIBLE JAN.2017-DEC.2017 GRAM-NEGATIVE BACILLI	Ampicillin	Amp/Sul	Pip/Tazo	Aztreonam	Cefazolin	Ceftriaxone	Ceftazadime	Cefepime	TMP/SMX	Levofloxacin	Gentamicin	Tobramycin	Nitrofurantoin	Ertapenem	Meropenem
32	*Acinetobacter baumannii*		97							97	97	97	97			100
91	*Serratia marcescens*				99		99	99	99	99	99	98	88		99	99
575	*Pseudomonas aeruginosa*			98				95	96		81	97	100			97
604	*Proteus mirabilis*	78	84	100	98	91	98	98	98	69	65	77	78		100	100
1334	*Klebsiella pneumoniae*		88	97	98	96	98	98	98	93	98	98	99	40	100	100
303	*Klebsiella oxytoca*		62	94	95	62	97	98	98	96	98	97	97	89	100	100
8232	*Escherichia coli*	65	69	97	96	90	95	95	96	85	85	94	95	97	100	100
345	*Enterobacter cloacae* complex			87	90		89	89	98	89	97	99	100	41	97	98
163	*Enterobacter aerogenes*			94	94		96	93	99	98	96	98	98	29	99	100
242	*Citrobacter freundii*			88	88		88	86	99	84	91	90	94	90	99	99

# ISOLATES	ASPIRUS REFERENCE LAB ANTI-BIOGRAM REPORTED AS % SUSCEPTIBLE JAN.2017-DEC.2017 GRAM-POSITIVE COCCI	Ampicillin	Oxacillin	Penicillin	Ceftriaxone	Clindamycin	Erythromycin	Levofloxacin	Gentamicin*	Nitrofurantoin	Rifampin*	Tetracycline	TMP/SMX	Vancomycin
69	*Enterococcus faecium*	29		26					SYN 88	35		36		57
1129	*Enterococcus faecalis*	100		99					SYN 69	98		21		100
2432	*Staphylococcus aureus*		67			74	52	69	99	99	100	92	97	100
1628	MSSA (67% of *Staph aureus*)		100			81	70	89	100	99	100	95	98	100
804	MRSA (33% of *Staph aureus*)		0			58	16	29	98	98	99	87	94	100
208	*Staphylococcus coag negative*		71	25		67	49	78	96	99	99	79	89	100
493	*Staphylococcus epidermidis*		49	10		70	41	59	90	99	99	88	59	100
255	*Staphylococcus lugdunensis*		91	53		83	84	99	100	100	100	96	99	100
261	*Staphylococcus saprophyticus*		56			71	39	100	100	100	100	91	95	100
114	*Streptococcus agalactiae* (Grp B)			100		41						13		100
72	*Streptococcus pneumoniae*					77	44	100				80		100
	71 Non-meningitis			98	94									
	1 Meningitis^			100	100									

CY 2017 ***Haemophilus influenzae*** n=122, **41% Beta-lactamase positive**
**should not be used alone to treat staphylococcal infections*
SYN: Synergy with Ampicillin or Vancomycin
^Strep pneumoniae Meningitis breakpoints are lower than pneumonia/bacteremia

IC-002 draft (3/10/2018)

Suggested Empiric Antimicrobial Agents of Choice In Hospitalized Adults

(11th Edition)

Aspirus Wausau Hospital 2018 - 2020

Antimicrobial Stewardship Subcommittee

&

Pharmacy and Therapeutics Committee

ASPIRUS™

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Compassion for people.

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I. ANTIMICROBIAL STEWARDSHIP

1) Before initiating empiric therapy or changing antibiotics (abx) due to lack of response to a current regimen, make certain that all relevant cultures have been obtained or repeated.

2) Switch & De-escalate: "switch" IV to PO, and change to narrower-spectrum agent(s) ("de-escalate") based on microbiology results.
   - Consider discontinuing Vancomycin if: cultures are negative for MRSA, MRSE, or penicillin-resistant *Enterococcus*; and, no Hx of MRSA colonization; and, no Type I allergy to penicillins (PCNs).
   - Combination therapy with [Ciprofloxacin OR Levofloxacin] PLUS [Pip-tazo, Cefepime, OR Aztreonam] is not beneficial beyond 48h - [Cipro or Levo] should be discontinued.

3) ESBL - Ertapenem is the drug of choice for infections due to ESBL-producing Gram-negative rods, except for *Pseudomonas*, which would require Meropenem.

4) Bioavailability: Levofloxacin, TMP/SMX, Clindamycin, Azithromycin, Fluconazole, and Metronidazole are highly bioavailable (90-100% GI absorption). They should be given PO if the GI tract is functional.

5) Use of Cephalosporins in Patients with Penicillin (PCN) Allergy: After taking a careful history, cephalosporins may be given safely to any patient without a history of a Type I rxn to PCN (immediate hypersensitivity = anaphylaxis, hives, angioedema).

6) Empiric antimicrobial choices in EPIC order set: =**AWH Blue Card – Empiric Antibiotics**

II. SEPSIS OF UNKNOWN ETIOLOGY

1) Community-Acquired/Normal Host:
   Ceftriaxone 2g q 24h PLUS Vancomycin

   ± Tobramycin x1 (if septic shock)

2) Health Care-Associated/Compromised Host:
   [Pip-Tazo 3.375g q8h (x4h) PLUS Vancomycin]
   OR [Cefepime 1g q6h PLUS Vancomycin]± Tobramycin x1 with above options (if septic shock)

3) Type I PCN Allergy:
   Aztreonam 2g q8h PLUS Vancomycin
   PLUS Tobramycin 7mg/kg q24h

III. SKIN AND SOFT TISSUE INFECTIONS

- Nonpurulent/Moderate Severity (Cellulitis):
  Preferred: Penicillin-G 4 million units q6h
  (Alternative: Cefazolin 1-2g q8h)
  - Type I PCN Allergy: Vancomycin
- Purulent (Abscess): I&D + C&S.
  TMP/SMX 1-2DS q12h OR Doxycycline 100mg q12h (if severe: Vancomycin). Switch to Nafcillin or Cefazolin if MSSA in C&S.
- Nonpurulent/Severe (Necrotizing): Surgical intervention (C&S).
  Pip-Tazo 3.375g q8h (x4h) PLUS Clindamycin 600mg q8h PLUS Vancomycin
  - Type I PCN Allergy: Aztreonam 2g q8h
    PLUS Metronidazole 500mg q8h PLUS Linezolid 600mg q12h
- Diabetic or Ischemic Foot Infection (AFTER deep tissue, or bone biopsy culture):

  [Pip-tazo 3.375g q8h (x4h) PLUS Vancomycin]
  OR [Cefepime 1g q6h PLUS Vancomycin PLUS Metronidazole 500mg q8h]
  - D/C Vanco if no MRSA/MRSE/Enterococcus
  - Type I PCN Allergy: Aztreonam 2g q8h
    PLUS Metronidazole 500mg q8h
    PLUS Vancomycin

IV. COMMUNITY-ACQUIRED PNEUMONIA (CAP)

- Ceftriaxone 1g q 24h
  PLUS [Azithromycin 500mg q 24h OR Doxycycline 100mg q12h]
  - Type I PCN Allergy: Levofloxacin 750mg q 24h
- If aspiration, add Metronidazole to above regimens

V. HOSPITAL-ACQUIRED/VENTILATOR-ASSOCIATED PNEUMONIA (HAP/VAP)

- [Cefepime 1g q6h OR Pip-Tazo 3.375g q8h (x4h)] PLUS Vancomycin (D/C Vancomycin at 48h if no MRSA in a quality respiratory culture)
  - Type I PCN Allergy: Aztreonam 2g q8h PLUS Tobramycin 7mg/kg q24h PLUS Vancomycin
- Consider addition of inhaled Tobramycin
- If aspiration, add Metronidazole to [Cefepime OR Aztreonam] above
- Duration = 7 days (including *Pseudomonas*)

VI. COMPLICATED INTRA-ABDOMINAL (cIAI) or BILIARY TRACT INFECTIONS, and PANCREATITIS

Note: At Aspirus, only ~85% of E. coli, and ~65% of *P. mirabilis* are susceptible to Levofloxacin/Ciprofloxacin, or TMP/SMX; *E. coli* sensitivity to Amp-sul is only 69%.

- Community-Acquired/Normal Host and Mild-Moderate Severity:
  Ceftriaxone 2g q24h PLUS Metronidazole 500mg q8h
- Community-Acquired/Compromised Host or High Severity:
  [Pip-Tazo 3.375g q8h (x4h)]
  OR [Cefepime 1g q6h PLUS Metronidazole 500mg q8h]
  - Type I PCN Allergy: Aztreonam 2g q8h PLUS Metronidazole 500mg q8h PLUS Vancomycin
- Health Care-Associated (HCA):
  [Pip-Tazo 3.375g q8h (x4h) PLUS Vancomycin PLUS Fluconazole 400mg q24h]

  OR

  [Cefepime 1g q6h PLUS Metronidazole 500mg q8h PLUS Vancomycin PLUS Fluconazole 400mg q24h]
  - Type I PCN Allergy: Aztreonam 2g q8h PLUS Metronidazole 500mg q8h PLUS Vancomycin PLUS Fluconazole 400mg q24h
- Duration: 4-7 days after adequate source control.
- Pancreatitis: Routine "prophylactic" antibiotics on admission are NOT routinely recommended. Abx indicated if admission CT, or repeat CT w/contrast 48h after admit has ≥ 30% pancreatic necrosis. Then CT-directed FNA for cx to guide abx.

VII. MANAGEMENT of *Staph aureus* BACTEREMIA

- MSSA = Nafcillin OR Cefazolin (Vancomycin NOT recommended due to worse outcomes)
- MRSA = Vancomycin (unless MIC > 1)

1) Repeat BCx daily until negative x48hrs.
2) Remove indwelling IV catheters.
3) Obtain TTE. If prosthetic valve, or TTE negative and fever/ bacteremia not resolved in 48hr, obtain TEE.
4) Duration = 4-6 wks IV abx from most recent negative BCx. 2wks IV abx may be considered in select cases (ID consult).
5) In general, obtain ID consult to guide management.

VIII. URINARY TRACT INFECTIONS (UTI)

1) Asymptomatic Bacteriuria (ASB) in Noncatheterized Adults:
   - Except in pregnancy or prior to urologic procedures, urine studies (UA and/or C&S) in noncatheterized adults should NOT be obtained in the absence of UTI Signs and Symptoms, defined as any 2 of the following: fever (> 38˚C); worsened urgency or frequency; new dysuria; suprapubic tenderness; CVA pain or tenderness; and, in the frail elderly a change (unresponsive to hydration) in mental status or character of urine (odor, color).
   - Frail, disabled older adults have a prevalence of pyuria and/or bacteriuria as high as 45% in the absence of UTI symptoms.
   - ASB should NOT be treated.
2) Catheter-Associated UTI (CA-UTI) and Catheter-Associated Asymptomatic Bacteriuria (CA-ASB).
   - CA-UTI - Signs and Symptoms: new onset or worsening fever, altered mental status, malaise, or lethargy with no other identified cause; flank pain; CVAT; acute hematuria; pelvic discomfort; AND > 10,000 cfu/mL AND pyuria (> 10WBC/ hpf). The absence of pyuria in a symptomatic patient (i.e. fever) suggests a diagnosis other than CA-UTI.
   - CA-ASB: ≥ 100,000 cfu/mL, with or without pyuria, in the absence of sx of UTI. Pyuria in the absence of sx is NOT an indication for antibiotics.
3) Uncomplicated UTI (uUTI)/Cystitis:
   - Nitrofurantoin 100mg PO BID x5d;
     OR TMP/SMX 1DS PO BID x3d;
     OR Cefpodoxime 100mg PO BID x7d
4) Complicated UTI (cUTI) and Pyelonephritis:
   - Symptomatic UTI = signs and symptoms of UTI (above), AND bacteriuria (>100,000 CFU/mL) AND pyuria (>10 WBC/hfp).
   - Community-Acquired/Normal Host:
     Ceftriaxone 1g q 24h
     - Type I PCN Allergy: Aztreonam 1g q8h
   - Health Care-Associated:
     Cefepime 1g q 6h PLUS Ampicillin 2g q6h
     - Type I PCN Allergy: Aztreonam 1g q8h
       PLUS Vancomycin

Beta-Lactam Cross-Reactivity Table

Agent	FDA-Approved	Beta-Lactam Antibiotics with Similar/Identical Side Chains			
Amoxicillin	Ampicillin	Cefactor	Cefadroxil	Cefprozil	Cephalexin
Ampicillin	Amoxicillin	Cefactor	Cefadroxil	Cefprozil	Cephalexin
Cefactor	Amoxicillin	Cefadroxil	Cefprozil	Cephalexin	
Aztreonam	Ceftazidime	Ceftolozane			
Ceftazidime	Aztreonam	Ceftolozane			
Cefadroxil	Amoxicillin	Ampicillin	Cefprozil	Cephalexin	
Amoxicillin	Ampicillin	Cefactor	Cefprozil	Cephalexin	
Cefdinir	Cefixime				
Cefixime	Cefdinir				
Cefotaxime	Cefpime	Cefpodoxime	Ceftriaxone		
Cefpime	Cefotaxime	Cefpodoxime	Ceftriaxone		
Cefpodoxime	Cefotaxime	Ceftriaxone			
Ceftriaxone	Cefotaxime	Cefpodoxime	Ceftaroline		
Cefotaxime	Ceftriaxone	Cefpodoxime	Ceftaroline		
Cefpodoxime	Cefpime	Ceftriaxone	Ceftaroline		
Cefuroxime	Penicillin G				
Cefoxitin	Cefpime	Ceftriaxone	Ceftaroline		
Cefpime	Cefotaxime	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefotaxime	Cefpodoxime	Ceftriaxone			
Cefpodoxime	Cefotaxime	Ceftriaxone	Ceftaroline		
Ceftriaxone	Cefpodoxime	Ceftaroline			
Ceftolozane	Ceftazidime				
Ceftazidime	Ceftolozane				
Cefepime	Cefotaxime	Ceftriaxone	Ceftaroline		
Cefotaxime	Cefepime	Ceftriaxone	Ceftaroline		
Ceftriaxone	Cefpodoxime	Ceftaroline			
Cefoxitin	Amoxicillin	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefuroxime	Cefoxitin	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefdinir	Cefpodoxime	Ceftriaxone	Ceftaroline		
Cefpodoxime	Cefoxitin	Cefpime	Ceftriaxone	Ceftaroline	
Cefpime	Cefoxitin	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefoxitin	Cefpodoxime	Ceftriaxone	Ceftaroline		
Cefpodoxime	Cefoxitin	Cefpime	Ceftriaxone	Ceftaroline	
Ceftriaxone	Cefpodoxime	Ceftriaxone	Ceftaroline		
Ceftaroline	Ceftriaxone	Ceftaroline			
Ceftazidime	Ceftolozane				
Ceftolozane	Ceftazidime				
Cefepime	Cefotaxime	Ceftriaxone	Ceftaroline		
Cefotaxime	Cefepime	Ceftriaxone	Ceftaroline		
Ceftriaxone	Cefpodoxime	Ceftaroline			
Cefoxitin	Amoxicillin	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefuroxime	Cefoxitin	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefdinir	Cefpodoxime	Ceftriaxone	Ceftaroline		
Cefpodoxime	Cefoxitin	Cefpime	Ceftriaxone	Ceftaroline	
Cefpime	Cefoxitin	Cefpodoxime	Ceftriaxone	Ceftaroline	
Cefoxitin	Cefpodoxime	Ceftriaxone	Ceftaroline		
Cefpodoxime	Cefoxitin	Cefpime	Ceftriaxone	Ceftaroline	
Ceftriaxone	Cefpodoxime	Ceftaroline			
Ceftaroline	Ceftriaxone	Ceftaroline			
Ceftazidime	Ceftolozane				
Ceftolozane	Ceftazidime				
Cefepime	Cefotaxime	Ceftriaxone	Ceftaroline		
Cefotaxime	Cefepime	Ceftriaxone	Ceftaroline		
Ceftriaxone	Cefpodoxime	Ceftaroline			
Penicillin G	Cefoxitin				

- 10% of patients report a PCN allergy, but only 1% are found to be real.
- Over time patients lose their Type I allergy to PCNs. After 10 years, 80% of patients won't have the allergy anymore.
- Cross-reactivity between beta-lactams is associated with similar or identical side chains. The cross-reactivity table above can be used to identify beta-lactam antibiotics to AVOID administering to patients with reported allergies due to similar/identical side chains. Find the agent the patient is allergic to in the first column. Avoid administering any of the agents with similar/identical side chains in the row following it. If an agent is not listed as being similar/identical to the patient's allergen then it can be safely administered as cross-reactivity between PCNs and cephalosporins or PCNs and carbapenems is <1%.
  - For example, a patient with a Type I allergy of rapid-onset hives to amoxicillin should NOT receive cephalexin as they have similar R1 side chains. Ceftriaxone, with a dissimilar side chain, would be a good choice.