Stanford Health (SHC) Intra-Abdominal Infections:

Guidance on Empiric Antibiotic Regimens

Pancreatitis	Diverticulitis	
Secondary Peritonitis	Acute Cholecystitis/Cholangitis	PD Peritonitis
SBP Treatment and Prophylaxis	Appendicitis	

Uncomplicated	Complicated
Definition: Infection contained to walls of the organ. No evidence of abscess, perforation, or sepsis/shock	**Definition**: Infection extends beyond the walls of the organ. Evidence of abscess, perforation, or sepsis/shock

Common causative pathogens:	What about MRSA?	What about *Candida?*	What about *Enterococcus*?	What about ESBL-producing bacteria?
• Gram negative Enterobacterales • Gram positive streptococci • Obligate anaerobes SHC antibiogram shows good susceptibility of these pathogens to piperacillin/tazobactam, thus it is chosen as first-line regimen for high-risk patients.	Empiric MRSA coverage is generally not recommended[1]. Empiric MRSA coverage with the addition of Vancomycin IV may be considered for hospital-acquired infection with known MRSA colonization or invasive infection within the past year[1] and should be discontinued at 48 hours if MRSA is not recovered from cultures.	Empiric *Candida* coverage is not recommended[1].	Empiric coverage for *E faecalis* is only recommended for high-risk patients with at least one risk factor. At SHC, 100% of *E faecalis* isolates are susceptible to piperacillin/tazobactam. If a regimen other than pip/tazo is used, addition of Vancomycin IV may be considered in the presence of risk factors. Risk factors include hospital-acquired infection, post-operative infection, recent cephalosporin use, and immunocompromised state[1]. Consider empiric VRE coverage in septic or severely ill patients with prior known colonization or invasive infection.	In cases where a patient has a history of colonization with ESBL Enterobacterales within the past year, recommend use of ertapenem in lieu of piperacillin/tazobactam.

[1]Solomkin, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and Infectious Diseases Society of America. Clinical Infectious Diseases 2010; 50:133-164.

Diverticulitis

Uncomplicated diverticulitis: **Absence of abscess, perforation, fistula, colonic obstruction as per CT imaging**			
	Empiric Therapy	**Duration**	**Notes**
	Non-pregnant immunocompetent* patient without sepsis or inflammatory bowel disease (IBD) • Monitor without antibiotic therapy with supportive IVF and anti-inflammatory regimen Note: There is increasing data based on RCTs that antibiotic therapy does not hasten time to recovery or reduce rates of complications.[1,2,3,6]		*Absence of oncologic or hematologic malignancy, HIV with low CD4 (<200), concomitant immunosuppressant therapy, transplant, splenectomy, and genetic immunodeficiency
	If patient does not meet criteria above: • **Primary regimens***:* ▪ Ceftriaxone 2g IV q24h + metronidazole 500mg PO/IV q8h ▪ If stable for outpatient management: Amoxicillin-clavulanate 875/125mg PO TID • **Alternative regimen***:* ▪ Ciprofloxacin 500mg PO BID or 400mg IV q12h + metronidazole 500mg PO/IV q8h	5 - 7 days[4]	*Antibiotic dosing is to be adjusted for impaired renal function*

Complicated diverticulitis:
Presence of abscess, perforation, fistula, or colonic obstruction

	Empiric Therapy	Duration

Community-acquired without sepsis/shock	• **Primary regimen**:
	  ○ Ceftriaxone 2g IV q24h + metronidazole 500mg PO/IV q8h
	• **Alternate regimen**:
	  ○ Ciprofloxacin 500mg PO BID or 400mg IV q12h + metronidazole 500mg PO/IV q8h
		5 – 7 days

Community-acquired with sepsis/shock
OR MDR-GNR Risk Factor
1. Hospitalization within past 90 days
2. Broad-spectrum antibiotic use within past 90 days
3. History of resistant organisms within past year
4. Hospital-acquired infection (>48 hours into hospitalization)
	• **Primary regimen**:
	  ○ Piperacillin-tazobactam 4.5g IV q8h extended infusion
	• **Alternative regimens***:*
	  ○ Cefepime 2g IV q8h extended infusion + metronidazole 500mg PO/IV q8h
	  Regimen does not provide Enterococcal coverage, [&]see Notes
	  ○ If high-risk allergy to beta-lactams: Vancomycin IV + aztreonam 2g IV q8h + metronidazole 500mg PO/IV q8h
	Oral Step-Down therapy:
	• First line: Ciprofloxacin 500mg PO BID + metronidazole 500mg PO q8h **OR**
	• Second line: Amoxicillin-clavulanate 875/125mg PO TID*
		Adequate source control obtained (successful percutaneous drainage of abscess or surgery): 4 days post-procedure[5]
		
		Associated gram-negative bacteremia: 7 days after source control
		
		Inadequate source control or persistent signs of infection: consider ID and surgical consultation

Notes

- Antibiotic dosing to be adjusted for impaired renal function
- [&] Consider addition of Vancomycin IV for empiric Enterococcal coverage in the presence of at least one of the following: hospital-acquired infection, post-operative infection, prior cephalosporin use, or immunocompromised state
- * Amox/clav includes coverage for *E faecalis,* however does not include coverage for *Enterobacter spp, Klebsiella aerogenes*, or *Citrobacter freundii,* use with caution in high-risk patients with MDR-GNR risk factors and those with bacteremia
- Empiric MRSA coverage with Vancomycin IV may be considered for hospital-acquired infection with known MRSA colonization or invasive infection within the past year. Vancomycin IV should then be discontinued at 48 hours if MRSA is not recovered from cultures. If Vancomycin IV is combined with piperacillin-tazobactam IV for greater than 72 hours, would consider alternative regimen to avoid risk of nephrotoxicity.
- High-risk allergies include angioedema, anaphylaxis, wheezing, laryngeal edema, hypotension, SJS/TEN, DRESS, etc please see link for details

References:

[1]Chabok A, Pahlman L, Hjern F, Haapaniemi, and Smedh K. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis.

[2]Unlü C et al. A multicenter randomized clinical trial investigating the cost-effectiveness of treatment strategies with or without antibiotics for uncomplicated acute diverticulitis (DIABOLO trial). BMC Surg. 2010 Jul 20;10:23. doi: 10.1186/1471-2482-10-23. PMID: 20646266; PMCID: PMC2919453.

[3]van Dijk ST et al. Long-term effects of omitting antibiotics in uncomplicated acute diverticulitis. *Am J Gastroenterol* 2018 Jul; 113:1045. (https://doi.org/10.1038/s41395-018-0030-y)

[4]Schug-Pass C, Geers P, Hügel O, Lippert H, Köckerling F. Prospective randomized trial comparing short-term antibiotic therapy versus standard therapy for acute uncomplicated sigmoid diverticulitis. Int J Colorectal Dis. 2010 Jun;25(6):751-9. doi: 10.1007/s00384-010-0899-4. Epub 2010 Feb 6. Erratum in: Int J Colorectal Dis. 2010 Jun;25(6):785. PMID: 20140619.

[5]Sawyer RG, Claridge JA, Nathens AB, Rotstein OD, Duane TM, Evans HL, Cook CH, O'Neill PJ, Mazuski JE, Askari R, Wilson MA, Napolitano LM, Namias N, Miller PR, Dellinger EP, Watson CM, Coimbra R, Dent DL, Lowry SF, Cocanour CS, West MA, Banton KL, Cheadle WG, Lipsett PA, Guidry CA, Popovsky K; STOP-IT Trial Investigators. Trial of short-course antimicrobial therapy for intraabdominal infection. N Engl J Med. 2015 May 21;372(21):1996-2005. doi: 10.1056/NEJMoa1411162. Erratum in: N Engl J Med. 2018 Jan 25;:null. PMID: 25992746; PMCID: PMC4469182.

[6]Stollman N, et al. American Gastroenterological Association Institute guidelines on the management of acute diverticulitis 2015; 149:1944-1949.

Acute Cholecystitis and Acute Cholangitis

Acute Cholangitis/Acute Cholangitis		
	Empiric Therapy	**Duration**
Community-acquired infection <u>without</u> sepsis/shock	• **Primary regimen***:* ▪ Ceftriaxone 2g IV q24h[#] • **Alternate regimen**: ▪ Ciprofloxacin 500mg PO BID or 400mg IV q12h[#]	<u>Cholecystectomy is performed</u> If no infection outside of the wall of gallbladder: Stop antibiotics within 24h of surgery[2] If infection outside wall of gallbladder: 4 days after surgery
Community-acquired infection <u>with</u> sepsis/shock **<u>OR</u> MDR-GNR Risk Factor** 1. Hospitalization within past 90 days 2. Broad-spectrum antibiotic use within past 90 days 3. History of resistant organisms within past year 4. Hospital-acquired infection (>48 hours into hospitalization)	• **Primary regimen**: ▪ Piperacillin-tazobactam 4.5g IV q8h extended infusion • **Alternative regimens***:* ▪ Cefepime 2g IV q8h extended infusion[#] Regimen does not provide Enterococcal coverage, [&]see Notes ▪ <u>If high-risk allergy to beta-lactams</u>: Vancomycin IV + aztreonam 2g IV q8h[#] **Oral Step-Down therapy:** • First line: Ciprofloxacin 500mg PO BID[#] **<u>OR</u>** • Second line: Amoxicillin-clavulanate 875/125mg PO TID*	<u>Successful ERCP</u> 3-4 days post-procedure[1] <u>Associated gram-negative bacteremia</u>: 7 days from source control <u>Source control not adequate or patient without clinical improvement:</u> Recommend ID consult

Notes

- Antibiotic dosing to be adjusted for impaired renal function
- [#]Add metronidazole 500mg PO/IV q8h if entero-biliary anastomosis[3,5]
- [&] Consider addition of Vancomycin IV for empiric Enterococcal coverage in the presence of at least one of the following: hospital-acquired infection, post-operative infection, prior cephalosporin use, or immunocompromised state.
- * Amox/clav includes coverage for *E faecalis,* however does not include coverage for *Enterobacter spp, Klebsiella aerogenes*, or *Citrobacter freundii,* use with caution in high-risk patients with MDR-GNR risk factors and those with bacteremia
- Empiric MRSA coverage with Vancomycin IV may be considered for hospital-acquired infection with known MRSA colonization or invasive infection within the past year. Vancomycin IV should then be discontinued at 48 hours if MRSA is not recovered from cultures. If Vancomycin IV is combined with piperacillin-tazobactam IV for greater than 72 hours, would consider alternative regimen to avoid risk of nephrotoxicity.
- High-risk allergies include angioedema, anaphylaxis, wheezing, laryngeal edema, hypotension, SJS/TEN, DRESS, etc please see link for details

References:

[1]Uno S, Hase R, Kobayashi M, Shiratori T, Nakaji S, Hirata N, Hosokawa N. Short-course antimicrobial treatment for acute cholangitis with Gram-negative bacillary bacteremia. Int J Infect Dis. 2017 Feb;55:81-85. doi: 10.1016/j.ijid.2016.12.018. Epub 2016 Dec 24. PMID: 28027992.

[2]Doi A, Morimoto T, Iwata K. Shorter duration of antibiotic treatment for acute bacteraemic cholangitis with successful biliary drainage: a retrospective cohort study. Clin Micro and Infection. 2018 Nov;24(11):1184-89.

[3]Regimbeau JM, Fuks D, Pautrat K, et al. Effect of postoperative antibiotic administration on postoperative infection following cholecystectomy for acute calculous cholecystitis: a randomized clinical trial. JAMA. 2014 Jul; 312(2):145-54. PMID: 25005651.

[4]Solomkin, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and Infectious Diseases Society of America. Clinical Infectious Diseases 2010; 50:133-164.

[5]Mazuski JE, et al. The Surgical Infection Society revised guidelines on the management of intra-abdominal infection. Surgical Infections 2017; 18:1-76.

[6]Kiriyama S, Kozaka K, Takada T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci 2018; 25:17.

Acute Appendicitis

Acute Appendicitis		
	Empiric Therapy	**Duration**
Community-acquired infection without sepsis/shock	• **Primary regimen***:* ▪ Ceftriaxone 2g IV q24h + metronidazole 500mg PO/IV q8h • **Alternate regimen:** ▪ Ciprofloxacin 500mg PO BID or 400mg IV q12h + metronidazole 500mg PO/IV q8h	Non-perforated appendicitis Appendectomy performed: discontinue antibiotics within 24h of surgery Appendectomy not performed: 10-day course[1]
Community-acquired infection with sepsis/shock OR MDR-GNR Risk Factor 1. Hospitalization within past 90 days 2. Broad-spectrum antibiotic use within past 90 days 3. History of resistant organisms within past year 4. Hospital-acquired infection (>48 hours into hospitalization)	• **Primary regimen:** ▪ Piperacillin-tazobactam 4.5g IV q8h extended infusion • **Alternative regimens***:* ▪ Cefepime 2g IV q8h extended infusion + metronidazole 500mg PO/IV q8h Regimen does not provide Enterococcal coverage, [&]see Notes ▪ If high-risk allergy to beta-lactams: Vancomycin IV + aztreonam 2g IV q8h + metronidazole 500mg PO/IV q8h **Oral Step-Down therapy:** • First line: Ciprofloxacin 500mg PO BID + metronidazole 500mg PO q8h **OR** • Second line: Amoxicillin-clavulanate 875/125mg PO TID*	Perforated appendicitis Surgical source control is adequate: stop antibiotics after 4 days Associated gram-negative bacteremia: 7 days from source control Source control not adequate or patient without clinical improvement: recommend ID consult
Notes		

- Antibiotic dosing to be adjusted for impaired renal function
- [&] Consider addition of Vancomycin IV for empiric Enterococcal coverage in the presence of at least one of the following: hospital-acquired infection, post-operative infection, prior cephalosporin use, or immunocompromised state
- * Amox/clav includes coverage for *E faecalis,* however does not include coverage for *Enterobacter spp, Klebsiella aerogenes*, or *Citrobacter freundii,* use with caution in high-risk patients with MDR-GNR risk factors and those with bacteremia
- Consider addition of Vancomycin IV for empiric MRSA coverage for hospital-acquired infection with known MRSA colonization or invasive infection within the past year. Vancomycin IV should then be discontinued at 48 hours if MRSA is not recovered from cultures. If Vancomycin IV is combined with piperacillin-tazobactam IV for greater than 72 hours, would consider alternative regimen to avoid risk of nephrotoxicity.
- High-risk allergies include angioedema, anaphylaxis, wheezing, laryngeal edema, hypotension, SJS/TEN, DRESS, etc please see link for details

References:

[1]Salminen P, Paajanen H, Rautio T, Nordström P, Aarnio M, Rantanen T, Tuominen R, Hurme S, Virtanen J, Mecklin JP, Sand J, Jartti A, Rinta-Kiikka I, Grönroos JM. Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. JAMA. 2015 Jun 16;313(23):2340-8. doi: 10.1001/jama.2015.6154. PMID: 26080338.

[2]Solomkin, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and Infectious Diseases Society of America. Clinical Infectious Diseases 2010; 50:133-164.

[3]Mazuski JE, et al. The Surgical Infection Society revised guidelines on the management of intra-abdominal infection. Surgical Infections 2017; 18:1-76.

Pancreatitis

Syndrome	Empiric Therapy	Duration	Notes
Interstitial edematous acute pancreatitis	No antibiotics		
Necrotizing pancreatitis	No antibiotics		Prophylaxis for sterile necrosis is not recommended[1]
Suspected infected pancreatic necrosis	• **Primary regimen**: ▪ Piperacillin-tazobactam 4.5g IV q8h extended infusion • **Alternative regimens***:* ▪ Cefepime 2g IV q8h extended infusion + metronidazole 500mg PO/IV q8h Regimen does not provide Enterococcal coverage [&]See Notes ▪ <u>If high-risk allergy to beta-lactams</u>: Vancomycin IV + aztreonam 2g IV q8h + metronidazole 500mg PO/IV q8h	Short course of antibiotics until surgically obtained cultures are negative	Infected necrosis should be suspected in patients with worsening clinical trajectory and/or signs of infection (increasing leukocytosis, fevers) or CT imaging demonstrating presence of gas within necrosis. Highest risk if above occurs after 7-10 days of conservative therapy
Confirmed infected pancreatic necrosis	• **Primary regimen:** ▪ Piperacillin-tazobactam 4.5g IV q8h extended infusion • **Alternative regimens***:* ▪ Cefepime 2g IV q8h extended infusion + metronidazole 500mg PO/IV q8h Regimen does not provide Enterococcal coverage [&]See Notes ▪ <u>If high-risk allergy to beta-lactams:</u> Vancomycin IV + aztreonam 2g IV q8h + metronidazole 500mg PO/IV q8h Antibiotic dosing should be adjusted for renal function High-risk allergies include angioedema, anaphylaxis, wheezing, laryngeal edema, hypotension, SJS/TEN, DRESS, etc please see link for details	Duration dependent on adequate source control via drainage and/or necrosectomy: <u>Consider ID consult</u>	Infection of necrotic tissue is confirmed via direct needle-aspiration or drainage [&] Consider addition of IV Vancomycin for empiric Enterococcal coverage in the presence of at least one of the following: hospital-acquired infection, post-operative infection, prior cephalosporin use, or immunocompromised state

References:

[1]Crockett SD, Wani S, Gardner TB, et al. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. Gastroenterology 2018; 154:1096.

Secondary Peritonitis

	Empiric Therapy	Duration
Community-acquired infection without sepsis/shock	• **Primary regimen***:* ▪ Ceftriaxone 2g IV q24h + metronidazole 500mg PO/IV q8h • **Alternate regimen**: ▪ Ciprofloxacin 500mg PO BID or 400mg IV q12h + metronidazole 500mg PO/IV q8h	Adequate source control obtained (successful percutaneous drainage of abscess or surgery): **4 days** post-procedure[5] Gastroduodenal perforation operated within 24h: Discontinue antibiotics **within 24h of surgery** Traumatic bowel perforations repaired within 12h: discontinue antibiotics **within 24h of surgery** Ischemic, non-perforated bowel: discontinue antibiotics **within 24h of surgery** Associated gram-negative bacteremia: 7 days If inadequate source control or persistent signs of infection, consider ID and surgical consultation
Community-acquired infection with sepsis/shock OR MDR-GNR Risk Factor 1. Hospitalization within past 90 days 2. Broad-spectrum antibiotic use within past 90 days 3. History of resistant organisms within past year 4. Hospital-acquired infection (>48 hours into hospitalization)	• **Primary regimen:** ▪ Piperacillin-tazobactam 4.5g IV q8h extended infusion • **Alternative regimens***:* ▪ Cefepime 2g IV q8h extended infusion + metronidazole 500mg PO/IV q8h Regimen does not provide Enterococcal coverage [&]See Notes ▪ If high-risk allergy to beta-lactams: Vancomycin IV + aztreonam 2g IV q8h + metronidazole 500mg PO/IV q8h **Oral Step-Down therapy:** • First line: Ciprofloxacin 500mg PO BID + metronidazole 500mg PO q8h **OR** • Second line: Amoxicillin-clavulanate 875/125mg PO TID*	

Notes

- Antibiotic dosing should be adjusted for impaired renal function
- [&] Consider addition of Vancomycin IV for empiric Enterococcal coverage in the presence of at least one of the following: hospital-acquired infection, post-operative infection, prior cephalosporin use, or immunocompromised state
- * Amox/clav includes coverage for *E faecalis,* however does not include coverage for *Enterobacter spp, Klebsiella aerogenes*, or *Citrobacter freundii,* use with caution in high-risk patients with MDR-GNR risk factors and those with bacteremia
- Empiric MRSA coverage with Vancomycin IV may be considered for hospital-acquired infection with known MRSA colonization or invasive infection within the past year. Vancomycin IV should then be discontinued at 48 hours if MRSA is not recovered from cultures. If Vancomycin IV is combined with piperacillin-tazobactam IV for greater than 72 hours, would consider alternative regimen to avoid risk of nephrotoxicity.
- High-risk allergies include angioedema, anaphylaxis, wheezing, laryngeal edema, hypotension, SJS/TEN, DRESS, etc please see link for details

SBP Treatment and Prophylaxis

Clinical syndrome	Empiric Therapy	Duration	Notes
Spontaneous Bacterial Peritonitis	• **Primary regimen** ▪ Ceftriaxone 2g IV q24h • **Alternative regimens** ▪ If high-risk allergy to beta-lactams and **NOT** receiving fluoroquinolone prophylaxis: Ciprofloxacin 400mg IV q12h ▪ If high-risk allergy to beta-lactams and **receiving** fluoroquinolone prophylaxis: Vancomycin IV + aztreonam 2g IV q8h **Oral Step-Down therapy** (if susceptible isolate): Ciprofloxacin 500mg PO BID	5-7 days	SBP as defined by presence of ≥ 250 neutrophils in peritoneal fluid Treatment to be tailored based on culture results from peritoneal fluid
Prophylaxis for patients with liver cirrhosis and GI bleed	• **Primary regimen** ▪ Ceftriaxone 2g IV q24h • **Alternative regimens** ▪ If high-risk allergy to beta-lactams and **NOT** receiving fluoroquinolone prophylaxis: Ciprofloxacin 400mg IV q12h ▪ If high-risk allergy to beta-lactams and **receiving** fluoroquinolone prophylaxis: Vancomycin IV + aztreonam 2 g IV q8h **Oral Step-Down therapy:** Ciprofloxacin 500mg PO BID	5-7 days	SBP prophylaxis for patients with cirrhosis and ascites if: (1) Prior episode of SBP OR (2) Ascitic protein level <1.5g/dL AND either impaired renal function (Cr ≥1.2, BUN ≥25, or Na^+ ≤130) or liver failure (Child score ≥ 9 and bilirubin ≥3)[1]
Long-term SBP prophylaxis for patients with prior episode of SBP or high-risk for SBP	• **Primary regimen** ▪ Ciprofloxacin 500mg PO q24h • **Alternate regimen** ▪ Bactrim DS 1 tab q24h Antibiotic dosing should be adjusted for renal function High-risk allergies include angioedema, anaphylaxis, wheezing, laryngeal edema, hypotension, SJS/TEN, DRESS, etc please see link for details	Indefinite	

References:

[1]Biggins SW, Angeli P, Garcia-Tsao G, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 2021; 74(2):1014-48.

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