Practice Point: Duration of Antibiotic Therapy for Common Infections

Jennifer Grant¹, Nicole Le Saux² and Members of the Antimicrobials Stewardship and Resistance Committee (ASRC) of AMMI Canada *

1 Division of Medical Microbiology and Infectious Diseases, Vancouver General Hospital, Vancouver Costal Health, University of British Columbia

2 Division of Infectious Diseases, Children’s Hospital of Eastern Ontario, University of Ottawa

*Association of Medical Microbiology and Infectious Disease (AMMI) Canada

Edith Blondel-Hill, Paul Bonar, John Conly, Peter Daley, Bruce Dalton, Linda Dresser, Greg German, Yoav Keynan, Tim Lau, Andrew Morris, Caroline Nott, David Patrick, Joanne Salmon, Yvonne Shevchuk, Genevieve Soucy, Daniel Thirion

Correspondence: Jennifer Grant, Department of Pathology and Laboratory Medicine, Vancouver General Hospital, JPPN Room, 1112 899 West 12th Avenue, Vancouver, British Columbia V5Z 1M9.
Telephone: 604-875-4111 x69503. E-mail: jennifer.grant@vch.ca
Historically, durations of antimicrobial therapy for common infections have been largely driven by habits or cultural norms rather than robust scientific data. (1,2) In general, the durations have increased compared to the early days of antimicrobials when patients with pneumococcal pneumonia, for example, were treated for 1 to 4 days. (3) The long-standing belief that antimicrobials had few significant side effects likely contributed to the paucity of trials to critically evaluate minimum effective treatment durations. (4–7) However, in the last decade, increasing infections due to *Clostridioides difficile*, emergence of multidrug-resistant pathogens and the concern for overall safety of antibiotics have led researchers to critically look at this issue. (8–16)

Several reports including a recent study in England used a primary care database between 2013 and 2015 and noted that excess duration compared to recommended guidelines accounted for a staggering 1.3 million days of excess therapy. (17,18) A study among hospitalized patients in the United States reported that one third of unnecessary antibiotics were due to unnecessarily prolonged durations. (19) A recent observational study of patients with pneumonia concluded that two thirds of patients had excess durations with 93.2% of the excess being in the form of discharge antibiotics. Each excess day was associated with a 5% increase in the odds of a patient having an antibiotic-associated adverse event. (20) Many experts have made rational arguments and coined useful slogans such as “shorter is still better” to emphasize the importance of reducing durations of antimicrobials and preserve the efficacy of our antibiotics. (21–23)

The purpose of this practice point is to disseminate contemporary treatment durations for common infectious syndromes for which there are either infectious disease guidelines or substantial evidence to support shorter durations of therapy. Search strategies for appropriate guidelines from North America or Europe where similar health systems exist as well as applicable cohort or randomized controlled studies were carried out between January 2 and June 30, 2020. Subsequently, the draft document was reviewed by the Antimicrobial Stewardship and Resistance Committee (ASRC) of the Association of Medical Microbiology and Infectious Disease (AMMI) Canada, other members at large and approved by the Council of AMMI Canada.

The recommendations do not apply to individuals with genetic immune defects, individuals who are or have received immune-modulating agents, chemotherapy or corticosteroids. Decisions regarding duration of treatment of individual patients should still take into consideration the underlying host, the certainty of the clinical diagnosis and clinical response to treatment. Modifications of duration can also be re-evaluated on a case-by-case basis with ongoing follow-up of patients. Table 1 summarizes current AMMI Canada recommendations for durations of treatment for common infectious syndromes in patients without special host factors such as underlying immunodeficiency.
Adults

UPPER RESPIRATORY TRACT INFECTIONS

Community acquired bacterial sinusitis

Community acquired bacterial sinusitis is usually secondary to a primary viral infection of the upper respiratory tract (viral rhinitis) that results in sinus ostia obstruction and subsequent bacterial proliferation. Patients with bacterial sinusitis either have > 10 days of persistent symptoms, severe symptoms or have initial improvement followed by relapse of symptoms. Symptoms that last greater than 12 weeks suggest chronic sinusitis and are not in the scope of this practice point. In adults, a meta-analysis of 12 randomized controlled trials (RCT) for acute bacterial sinusitis showed that a duration of 3 to 7 days was equally as effective as 6-10 days and a sensitivity analysis of 5 versus 10 days came to a similar conclusion. (24)

Guidelines for adult patients from the American Academy of Otolaryngology in 2015 recommends 5 to 10 days (based on randomized controlled trials (Grade A), but low to moderate certainty)) with a clinical re-evaluation at 7 days to ensure improvement. (25) The Infectious Diseases Society of America (IDSA) recommends 5-7 days (based on weak, low quality evidence) of antibiotics with a re-evaluation at 3-5 days to ensure improvement and no extension of infection.(26)

Children

Recommended durations of therapy for children and youth with acute bacterial sinusitis have varied because of scant evidence and difficulty in assessment of chronicity. A proposed practical alternative to prevent longer durations may be to treat for 7 days after the patient is symptom free. (27) Pneumococcus and H. influenzae isolates may be resistant to trimethoprim-sulphamethoxazole and azithromycin so these antibiotics are not included in the duration recommendations.

AMMI Canada Recommendations

The duration of treatment for acute uncomplicated community acquired sinusitis should be 5-7 days with a planned re-evaluation at 7 days to ensure clinical resolution. Children should also receive about 7-10 days of therapy with a beta-lactam antibiotic with a planned re-evaluation at seven days.

Acute Otitis Media (AOM)

A critical issue in therapy for AOM in children is to ensure that criteria for diagnosis are met (a bulging tympanic membrane is more likely to indicate a bacterial infection) to prevent over treatment of viral otitis media. Trials in children over 2 years of age have favoured a duration of 5-7 days however a trial in children under the age of 2 years noted that 5 days was less effective than 10 days of therapy.(28,29)

The Canadian Pediatric Society recommends durations of amoxicillin therapy for acute otitis media meeting specific diagnostic criteria in children are 10 days in children under 2 years of age and 5 days in
older children. (30) However any child with a tympanic membrane perforation or a recurrent AOM should be given a 10-day course.

AMMI Canada Recommendations

Duration of therapy for bacterial AOM is 10 days in children under 2 years and 5 days in children over 2 years of age.

Streptococcal pharyngitis

Streptococcal pharyngitis if left untreated may lead to acute rheumatic fever or local suppurative complications. A meta-analysis demonstrated that there appears to be better bacteriological eradication with a 10 day course of penicillin versus 5-7 days but no differences in the rate of relapse or recurrence was noted. (31) Another study also non-inferior bacterial eradication with penicillin four times daily for five days versus three times a day for 10 days however the incidence of acute rheumatic fever was not assessed. (32)

Guidelines from the United Kingdom recommend a 5-10-day course of penicillin (10 days if recurrent infection) whereas the Canadian Pediatric Society recommends 10 days of oral penicillin or amoxicillin. (Sauve et al, In Press) (33)

AMMI Canada Recommendations

Penicillin V or amoxicillin for 10 days is the recommended duration of therapy for Streptococcal pharyngitis.

LOWER RESPIRATORY TRACT INFECTIONS

Community acquired pneumonia

Acute community acquired pneumonia is most commonly due to viruses (such as influenza) but common pathogens causing bacterial pneumonia are Streptococcus pneumoniae, Haemophilus influenzae and Mycoplasma pneumoniae with some special populations such as nursing home residents possibly infected with Gram negative pathogens that may be multi-drug resistant.

A systematic review and meta-analysis of randomized controlled trials predominantly of ambulatory or mixed inpatient/outpatients with low severity of illness concluded that ≤ 6 days provided equally effective treatment compared to longer durations and may confer a safety benefit due to fewer side effects. (34) Failure to respond may indicate local complications such as empyema, or other pathogens not commonly seen such as Mycobacterium tuberculosis or endemic fungi such as Blastomyces dermatitidis/gilchristii. One recent observational study reported significantly more antibiotic adverse events in patients who received therapy longer than recommended, predominantly discharge antibiotics, supporting the shorter durations as a safer option. (20) S. pneumoniae bacteremia associated with uncomplicated pneumonia (not meningitis or other serious infections such as septic arthritis which
requires longer courses of therapy) is effectively treated with 5 days of IV therapy, assuming clinical improvement before the discontinuation of therapy. (35)

The 2019 joint American Thoracic Society (ATS) and the IDSA guideline recommend at least 5 days duration for both severe and non-severe pneumonia with the caveat that the total duration depends on the achievement of clinical stability for 48 to 72 hours prior to discontinuing antimicrobial therapy. (36) Clinical stability was defined as normalization of vital signs, ability to eat and normal mentation. While historically there were recommendations for longer therapy (14 d) for Staphylococcus aureus, Pseudomonas aeruginosa and other non-fermenting bacteria, more recent recommendations are for 7 days of therapy in these instances, unless there another reason to extend therapy (e.g. S. aureus bacteremia). In complicated pneumonias (e.g. empyema), the duration is likely longer, but surgical intervention plays a key role in management and decreasing durations of antibiotics.

Children

CAP that is considered to be bacterial in origin in children is commonly due to S pneumoniae. Children who have prolonged cough or are older are more likely to have Mycoplasma pneumonia. One study in preschool children found that pneumonia treated with amoxicillin for 5 days in the outpatient setting was non-inferior to a 10 day course. (37)

The CPS practice point currently recommend a 7-10 day course of antimicrobials for uncomplicated pneumonia with the caveat that shorter courses may be just as effective for children with non-severe uncomplicated pneumonia. (38,39) Pneumonia complicated by empyema could require drainage and a slightly longer duration of therapy of 14-21 days.

AMMI Canada Recommendations

The duration of therapy for acute uncomplicated community acquired pneumonia in adults should be a minimum of 5 days provided there is clinical stability for 48-72 hours. Duration can be extended to 7 days if there is slower resolution or pathogens such as S. aureus or Pseudomonas are identified.

Since viral infections are more common in children, clinicians should use clinical and radiological criteria to distinguish bacterial pneumonia from bronchiolitis in younger infants. Duration of therapy should be 7 days for uncomplicated pneumonia in children.

Lower Respiratory Tract Infections acquired in hospital:

Hospital acquired pneumonia (HAP) is associated with significant morbidity and a high case fatality rate. The entity previously labeled as health care associated pneumonia (HCAP) – which included patients with significant health care contact (e.g. dialysis) and those living in long-term care – has been retired and collapsed back into CAP as the microbiological etiologies are similar. In contrast, HAP and ventilator
associated pneumonia (VAP) are more likely to be associated with antibiotic-resistant organisms, depending on local hospital epidemiology, host factors and duration of hospital stay. Empiric therapy is usually broad. Historically, therapy for VAP (and HAP) was prolonged, up to 21 days, until investigators evaluated the relative efficacy of shorter (8 days) versus longer (15 days) therapy and showed no difference in mortality, intensive care unit (ICU) stay, mechanical ventilation-free days or organ failure free days. (40) Patients who received fewer days of antibiotics had less re-infection with resistant organisms. Subsequent studies are summarized in a meta-analysis confirming that 7-8 days of therapy is as effective as longer courses, except possibly for patients infected with non-fermenting Gram negative bacilli (e.g. *P. aeruginosa*) where there may be more recurrences with a shorter course, however this did not affect clinical outcome. (41)

European (2017) and IDSA guidelines (2016), both recommend durations of 7 days for VAP (moderate quality evidence) and HAP (very low quality evidence). (42–44) However, allowance is made to alter durations both for shorter and longer courses based on clinical response and microbiologic etiology.

**AMMI Canada Recommendations**

The duration of therapy for hospital acquired pneumonias without abscesses (ventilator associated or not) should be limited to less than or equal to 7 days.

**Chronic Obstructive Pulmonary Disease Exacerbation:**

Acute exacerbations (AE) of Chronic Obstructive Pulmonary Disease (COPD) caused by infection are most frequently caused by viruses, with bacteria playing a secondary role. AE-COPD should be managed with bronchodilators, anti-inflammatory therapy and correction of any reversible underlying cause such as environmental or other medical conditions (e.g. heart failure, pulmonary embolism). Antibiotics should only be considered when patients fail to respond to the above measures or when clinical findings such as fever suggest bacteria as a likely cause or when severely ill. (45)

A recent review showed no difference in clinical outcome of durations of <6 days versus 7 or more days but the shorter duration group had a significantly fewer side effects. (46) Durations of therapy of up to 5 days have been compared to longer therapies in a meta-analysis of 21 randomized controlled trials. (47) The meta-analysis supported the effectiveness of short courses of 5 days were equivalent for clinical and bacteriologic cure. Results were the same regardless of antibiotic class.

The Global Initiative for Chronic Obstructive Lung disease initiative (2019) recommend 5-7 days of antimicrobial therapy in patients with severe disease, or signs of bacterial infection. (45) Likewise the United Kingdom National Institute for Health and Care Excellence (NICE) guidelines recommend a 5 day course (if antibiotics are indicated) of any antimicrobial class. (48) The European Respiratory Society and the American Thoracic Society (ATS) guidelines recommend antimicrobial therapy, but do not comment on duration. (49)
AMMI Canada Recommendations

The duration of treatment for AE-COPD believed to be due to bacterial infection should be 5 -7 days.

PREOPERATIVE ANTIMICROBIAL PROPHYLAXIS

**Surgeries with no implantable devices:** Prophylactic antimicrobials should be administered only when recommended, as many types of surgery do not require prophylaxis. (50,51) For effective prevention of surgical site infections, when recommended, antimicrobials should be given 30-60 minutes before surgical incision. There is no evidence to show benefit of antimicrobials continued post-surgically. A study of almost 80,000 patients showed that the risk of *C. difficile* and acute kidney injury increased in a duration dependent fashion in adults who received antimicrobials for prophylaxis for > 24 hours strongly suggesting that prolonging duration adds adverse events without preventing more surgical site infections. (52,53)

World Health Organization is definitive in its recommendations that for surgeries that do not include implants, there is no benefit to prolonging antimicrobials in the post-operative period and antibiotics should be discontinued at the time of skin closure. (54)

Women undergoing caesarean sections should also receive a timely preoperative dose of cefazolin to reduce the likelihood of surgical wound infection and endometritis with no benefit of prolonging after the surgery. (55)(56) In women with preterm labour with ruptured membranes when a gestational age is less than 32 weeks, it is recommended to receive 48 hours of intravenous (IV) ampicillin followed by 5 days of oral amoxicillin and either 1 dose of IV azithromycin or 2 days of IV erythromycin followed by 5 days of oral erythromycin. (56)

AMMI Canada Recommendations

Surgical prophylaxis, including for caesarian sections, should be stopped after skin closure. Pregnant women in pre-term labour with ruptured membranes should receive 7 days of ampicillin and a macrolide as above to decrease the risk of ascending infection to the fetus.

Duration of surgical prophylaxis for surgeries involving implants or valves can be extended 24-48 hours after surgery but this recommendation is mainly due to lack of data. (54,57)

INTRA-ABDOMINAL INFECTIONS

Treatment of intra-abdominal infections involves drainage of infected fluid collections or abscesses (source control) as this removes the source of infection, reduces bacterial load, leads to decreased days of antimicrobials and better overall outcomes.

**Infections With Source Control:** Patients with non-perforated appendicitis need only pre-operative antibiotics. (58) Two large studies of intra-abdominal infections support using shorter courses of therapy emphasizing that source control and drainage of abscesses are key in management. The first study done
compared 4 versus 8 days of therapy after source control and concluded that recurrent surgical-site or intra-abdominal infections were similar. (59) A second large randomised controlled trial done in intensive care units determined that patients treated with shorter courses of 8 days had no difference in length of stay nor mortality or re-operation rates compared to those treated for 15 days. (60) For cholangitis, a systematic review summarizing available literature to 2018 reported 4 studies that met inclusion criteria. The authors concluded that provided there was source control, a shorter course of less than a week did not result in higher mortality, duration of fever or higher rates of recurrence. (61)

Guidelines from the Surgical Infection Society (SIS) and the IDSA advocate <7 days of therapy for patients with source control. (58,62) Tokyo Guidelines for management of acute cholangitis recommend drainage or source control as the mainstay of therapy followed by 4-7 days of appropriate targeted antimicrobial therapy. (63,64)

AMMI Canada Recommendations

Physicians should strongly advocate for source control (drainage of collections) in the setting of intraabdominal infections. Duration of therapy for intraabdominal infections with source control should be less than 7 days.

URINARY TRACT INFECTIONS

Cystitis or lower tract infection:

Acute dysuria, urgency and frequency, without flank pain or fever, accompanied by pyuria, and a positive single uropathogen in urine define cystitis. Since bacteria are limited to the bladder, short courses of antibiotics are sufficient. Cystitis in men is infrequent and likely indicate prostatitis or upper tract infection. Bacteriuria in pregnancy or in post renal transplant situations is beyond the scope of this document. Aside from pregnancy and prior to urologic surgery, asymptomatic bacteriuria should not be treated. (65) AMMI Canada has published a useful toolkit including educational materials for managing asymptomatic bacteriuria “Symptom Free Let it Be” available at https://www.ammi.ca/?ID=127.

Short courses of therapy (3-5 days, depending on antibiotic class) for uncomplicated cystitis in otherwise healthy, young women is well-supported by robust data and recommended in IDSA guidelines. (66) Single dose Fosfomycin (or 3 days if recurrent/complicated cystitis) also holds promise as a treatment for cystitis due to high concentrations and prolonged half-life in the urine. (67,68) Fluoroquinolones are not recommended as empiric therapy as their safely profile and propensity to increase resistance are notable. (69,70)

Children

Non febrile urinary tract infections are uncommon in infants and children but typically occur in adolescents who are sexually active. The same principles of treatment duration in adults apply to adolescents. (71)
AMMI Canada Recommendations

Duration of therapy for uncomplicated cystitis in women is 3-5 days unless using fosfomycin which is one day.

Pyelonephritis

Treatment duration for uncomplicated pyelonephritis in non-pregnant women is well established. For adult men, urinary tract infections are usually considered complicated since this may indicate obstruction, stone or a prostatic focus. Studies of patients with normal male or female anatomy support a 7 day course of antimicrobials. (72–75) A meta-analysis of treatment durations for pyelonephritis comparing ≤ 7 days to >7 days resulted in 8 evaluable trials. The conclusion (irrespective of whether fluoroquinolones had been used) was that there were no differences in clinical or microbiological failure between the short and long-treatment arms. Longer treatment courses may be required for pyelonephritis complicated by abscess or stones as patients with urogenital abnormalities had more microbiological failure at the end of follow-up compared to those with normal anatomy. In this meta-analysis the percentage of bacteremic patients ranged from 3% to 29%. (72) A recent study used a median of 4.5 days of aminoglycoside therapy versus 5 days of non-aminoglycoside based therapy for adults with pyelonephritis with similar outcomes. (76)

In 2011, practice guidelines by IDSA and the European Society for Microbiology and Infectious Diseases recommended a 7 day course of antibiotics for women with uncomplicated pyelonephritis in women (without septic shock or abscesses). (66) NICE Guidelines from the United Kingdom, vary durations according to class of antimicrobial; 7 days for fluoroquinolones (consider safety issues), 7-10 days for β-lactams, however rising rates of resistance emphasize the critical importance of proper cultures and non-response to therapy requires prompt re-evaluation. (77) Some experts have suggested an initial intravenous dose of an aminoglycoside or ceftriaxone or ertapenem especially if oral beta-lactams are planned as definitive therapy.

Children

Pyelonephritis in children refers to the clinical syndrome of fever and symptoms compatible with a urinary tract infection (dysuria, incontinence, urgency) with pyuria and an abnormal urinalysis. No randomised controlled trials specifically examining duration of therapy in children with febrile urinary tract infections (presumed pyelonephritis) have been published. A 2014 Cochrane review determined that 10 to 14 days of therapy was appropriate for clinical success. (78) A more recent 2019 publication a study of almost 800 children with febrile UTI reported similar outcomes with courses of 6-9 days versus ≥ 10 days of therapy. However, children with urologic abnormalities had more treatment failures with short courses. (79) A randomised controlled trial conducted in neonates with Gram-negative bacteremia (of which 69% had a urinary tract source) reported that those treated with 7 days of antibiotics had non-inferior outcomes compared to those treated for 14 days. (80) In children older than one month, treatment durations for bacteremia associated with pyelonephritis have not been the subject of a
randomized controlled trial. A recent retrospective cohort study of pyelonephritis has too few cases of associated bacteremia to determine duration of therapy. (79) Guidelines from the Canadian Paediatric Society and the American Academy of Pediatrics currently recommend 7-14 days of therapy. (81)

AMMI Canada Recommendations

In adults and children with no underlying anatomic abnormalities and rapid response to therapy, duration of therapy for uncomplicated pyelonephritis or urosepsis is 7 days with slightly longer courses if there is a slow response to therapy or development of abscess. Patients with diabetes, underlying immunocompromising conditions or recurrent pyelonephritis may require more individualized plans for slightly longer durations and a slower IV to oral conversion. When considering oral therapy at presentation one dose of IM/IV aminoglycoside or ceftriaxone at diagnosis.

CELLULITIS

Purulent and Non-purulent Cellulitis:

Acute cellulitis is most commonly due to *S. aureus* (usually a purulent cellulitis characterized by abscesses or pus that is visible or can be expressed locally) or *Streptococcus pyogenes* (usually a non-purulent cellulitis characterized primarily by rapid onset of pain, erythema and swelling without abscesses). There may be some overlap in these presentations in persons with underlying dermatitis. Cellulitis associated with bites (animal or human), deeper infections (such as necrotizing fasciitis), fish or water exposure, or in patients who are neutropenic is beyond the scope of this practice point. Cellulitis should also be differentiated from venous stasis, erythema migrans due to Lyme disease and cutaneous herpes infections. One randomized controlled study of patients with uncomplicated cellulitis (both outpatients and inpatients) concluded that despite some residual erythema, 5 days of therapy resulted in similar cure rates compared to 10 days. (82) In a study involving patients admitted to hospital with cellulitis, there appeared to be more readmissions in the shorter (6 days) duration group suggesting that some hospitalized patients may have more extensive disease requiring longer durations of therapy to prevent relapse. (83) In cases of recurrent cellulitis, consideration should be given to penicillin prophylaxis and other supportive measures. (84)

Guidelines from IDSA recommend 5 days of therapy for uncomplicated non-purulent cellulitis however, the duration should be extended to 10 days if the infection has not improved within the 5 day period or if the patient is hospitalized for more severe or extensive disease (85)

AMMI Canada Recommendations

Duration of therapy for uncomplicated cellulitis for adults and children is 5-7 days. Hospitalized patients with more extensive disease may need slightly longer courses of 10 days.
BONE AND JOINT INFECTIONS

A randomized controlled trial of therapy for patients with vertebral osteomyelitis showed similar outcomes for 6 weeks versus 12 weeks of antibiotic therapy. (86) A non-inferiority trial of 154 adult patients with native joint septic arthritis (64% hand and wrist) randomized patients to two versus four weeks of antibiotic therapy post-surgical drainage and reported similar outcomes (not inferior) in the shorter duration group. However, the findings may not be applicable to large joints such as hips and knees since these were underrepresented. (87) Appropriate surgical source control including drainage of joint fluid is paramount to reducing morbidity from joint infections. Management of prosthetic joint infections or septic arthritis due to Neisseria gonorrhoea is outside the scope of this article.

Guidelines currently recommend a 6 week course of antimicrobials for acute native vertebral osteomyelitis commonly due to S. aureus. (88) There are no current guidelines from North American or European organizations for other native joint infections. The British Society for Antimicrobial Chemotherapy (BSAC) made recommendations in 2006 in conjunction with other specialty societies and recommended 2 weeks of IV therapy, followed by a further 4 weeks of oral therapy however, acknowledged that there exists little evidence. (89) Shorter durations of 3-4 weeks could be considered for non-Staphylococcus aureus septic arthritis with a susceptible pathogen and adequate surgical drainage.

Children

In children multiple studies have determined that shortening the duration of antimicrobial therapy for acute hematogenous osteoarticular infection that is uncomplicated from 4-6 weeks to 3-4 weeks has not changed the uniformly good outcomes for in children. (90–92) The common bacteria are S. aureus and Kingella kingae. Treatment duration for osteomyelitis due to methicillin resistant S. aureus (MRSA) may be longer.

CPS practice point on hematogenous osteomyelitis recommends 3-4 weeks of therapy with step-down to oral therapy for uncomplicated osteomyelitis. (93) Similar recommendations are outlined in European guidelines. (94)

AMMI Canada Recommendations

Uncomplicated vertebral osteomyelitis should be treated for 6 weeks. There is less data available for native joint septic arthritis (excludes Neisseria gonorrhoea). Once source control has been achieved septic arthritis of native joints involving the hand and fingers can be treated for two weeks whereas infection of larger joints will require 4 weeks. In children, duration of therapy for acute osteoarticular infections is usually 3-4 weeks with longer courses reserved for complicated infections.
Acute Osteoarticular Infections

AMMI Canada Recommendations

BACTEREMIA

*Staphylococcus aureus* bacteremia

Bacteremia due to *S. aureus* is common, is always considered pathologic and must be treated and managed appropriately. It may be associated with an implantable or intravascular line or a detectable focus of infection such as osteoarticular infection or infective endocarditis. All prosthetic devices or intravascular catheters should be removed, if possible, to effect cure and an echocardiogram is recommended to look for endocarditis.

Current data supports treatment of uncomplicated *S. aureus* bacteremia with 14 days of intravenous antimicrobials from the first negative blood culture. Uncomplicated bacteremia is defined as *S. aureus* bacteremia without evidence of infective endocarditis using echocardiography nor metastatic sites of infection (clinically or other imaging modalities), rapid (3 days) sterilization of blood cultures and rapid (<72 hours) defervescence after appropriate antibiotics, and absence of prosthetic devices. (95)

Newborns with *S. aureus* bacteremia treated with less than 14 days are also more likely to have relapse of infection. (96) Persistent *S. aureus* bacteremia beyond 72 hours despite adequate therapy may be indicative of an endovascular or other deep seated infection requiring prolonged therapy, usually 4-6 weeks. (97) There is also accumulating data indicating improved outcomes and lower mortality in patients with *S. aureus* bacteremia whose management includes infectious diseases consultation. (98,99)

AMMI Canada Recommendations

Fourteen days of IV antimicrobials is required for cases of uncomplicated *S. aureus* bacteremia (see above for important caveats) or associated with a central line provided the catheter has been removed. Most cases of *S. aureus* bacteremia require 4-6 weeks of therapy and should be managed in conjunction with infectious diseases consultation or input.

Non- *S. aureus* bacteremia

Central Line Associated

Bacteremia due to coagulase negative *Staphylococci* associated with an intravascular device that has been removed has generally been treated with for 5-7 days after catheter removal. (100,101) Recently some authors have reported equivalent outcomes in this group of patients who only had catheter removal as definitive therapy. Shorter durations of <5 days should be considered in circumstance where early catheter removal and rapid response is seen. (102)

Catheter associated central line infections due to *Enterobacteriaceae* should include catheter removal followed by 7-14 days of antimicrobial therapy. (100,101) Similar durations of therapy are
recommended for implantable venous access devices provided they are removed, providing source control and not due to *S. aureus*. (103)

**AMMI Canada Recommendations**

Compared to uncomplicated *S. aureus* catheter related bacteremias which require 14 days of therapy, uncomplicated central line associated bacteremias due to Enterobacteraeceae can be treated for 7 days after catheter removal. If the pathogen is a coagulase negative Staphylococcus shorter duration of 5 days after removal of intravascular catheter are recommended especially if there is early catheter removal and good clinical response.

**Non-central line associated bacteremia**

Bacteremia associated with pyelonephritis, generally due to enterobacteriaceae (such as *E. coli* or *Klebsiella*) has been traditionally treated with 7-14 days of antibiotics. A meta-analysis of outcome in 7,695 patients studied outcome in patients treated with shorter (≤ 7 days) versus longer courses of antibiotics. There were no differences in clinical outcome, microbiologic cure nor mortality between patients in the two groups. (104) Subsequent to this meta-analysis several randomised controlled trials of 7-8 versus 14-15 days of antibiotics in patients with Gram-negative bacteremia (of which the majority had a urinary tract source) found that the shorter course was non-inferior to longer courses in clinical outcome. (80,105,106) A more recent meta-analysis comparing ≤ 10 days to > 10 days of therapy in patients with bacteremia showed no differences in clinical or microbiologic cure nor mortality, however there were only 4 studies available to assess specifically this duration. (107) In an observational study, when source control had been achieved, investigators found that patients with *Pseudomonas* bacteremia receiving a median of 9 days of therapy (IQR 8-10) had a similar odds of recurrent infection and death as patients who received a median of 16 days (IQR,14-17). (108) A recent randomised clinical trial of 7 versus 14 days versus a C-reactive protein guided duration study for Gram negative bacteremia found no significant differences in clinical outcome between groups with very few recurrences. (109)

**AMMI Canada Recommendations**

For bacteremia due to enterobacteriaceae, there appears to be a wide variation in duration of antimicrobial therapy however, emerging literature would support a 7-day course for uncomplicated bacteremias due to pyelonephritis, or from a source which has been successfully controlled.

**CONCLUSIONS**

Antibiotics are societal resources and the emerging potential impact of losing these precious resources is enormous as detailed in a recent Canadian report. (12) Notwithstanding the societal benefits of using less antimicrobials, shortening durations of antibiotic therapy for individual patients is increasingly recommended as a better practice choice. Clinicians should be aware of new data, current guidelines and recommendations and adjust their practices accordingly to provide the best patient care while preserving antibiotics for future use.
Table 1: Summary of recommendations for duration of therapy in selected common infections

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<td><strong>Urinary Tract Infections</strong></td>
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<td><strong>Children and Adults</strong></td>
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| Women/adolescents Uncomplicated Cystitis | Nitrofurantoin – 5 days  
TPM-SMX - 3 days  
Fosfomycin – 1 day | Young non- pregnant female adolescents or adults with normal urinary tracts and normal renal function                                       |
| Children Febrile Urinary tract infection | 7 to 14 days                                                                         | Assumes upper tract involvement if febrile                                                                                                 |
| Adults Pyelonephritis and Urosepsis | Consider an initial dose of IV dose  
aminoglycoside or ceftriaxone at outset  
Quinolones or beta-lactams 7 days | Excludes patients with urogenital abnormalities or stents/drips  
Duration depends on rapidity of response to appropriate therapy                                                                         |
| **Respiratory Tract Infections** |                                                                                      |                                                                                                                                           |
| **Children and Adults**          |                                                                                      |                                                                                                                                           |
| Streptococcal pharyngitis         | 10 days (penicillin V or amoxicillin)                                                | Studies limited to pediatrics. Some studies suggest 5 days of QID penicillin for bacterial eradication only                                 |
| Acute Otitis Media               | 6 months to 2 years – 10 days  
Over 2 years – 5 days                     | Should meet diagnostic criteria such as moderately to severely ill with bulging tympanic membrane.                                           |
| Acute sinusitis (uncomplicated)  | 5-7 days                                                                             | Excludes Complicated sinusitis (e.g. epidural, subdural or orbital collection). Revaluation recommended at 7 days.                         |
| Community Acquired Pneumonia     | 5-7 days                                                                             | Patients with underlying lung disease, immunosupression or empyema. Must be improved and have normal vital signs for 2 days when using 5 days of therapy |
| Acute sinusitis                  | 5 to 7 days                                                                           | Clinical re-evaluation at 7 days  
Excludes Complicated sinusitis (e.g. epidural, subdural or orbital collection)                                                          |
<p>| Hospital and Ventilator Acquired Pneumonia (HAP/VAP) | ≤7 days                        | Severely immune suppressed patients with collections or abscesses, associated S. aureus infection                                           |
| Acute bacterial Chronic Obstructive Pulmonary Disease (COPD) exacerbation | 5-7 days | Only for patients meeting criteria for antibiotic treatment                                                                                |
| <strong>Intraabdominal infections</strong>    |                                                                                      |                                                                                                                                           |
| <strong>Children and Adults</strong>          |                                                                                      |                                                                                                                                           |
| Uncomplicated appendicitis       | Pre-operative antibiotics only                                                       | Gangrenous appendicitis or perforated appendicitis should be treated for an additional 24-48 hours after source control                |
| Traumatic bowel perforation      | No more than 24 hours post-operatively                                               | Operated on within 12 hours of trauma                                                                                                    |
| Gastroduodenal perforation       | No more than 24 hours post-operatively                                               | Operated on within 24 hours                                                                                                               |
| Intraabdominal infection/abscess | &lt;7 days                                                                               | Source control required with drainage of infection. No additional days required if adequate drainage is in place                        |
| <strong>Skin Infections</strong>              |                                                                                      |                                                                                                                                           |
| <strong>Children and Adults</strong>          |                                                                                      |                                                                                                                                           |
| Uncomplicated non-purulent or purulent cellulitis | 5-7 days | Usually due to Streptococcus pyogenes (Group A streptococcus) or Staphylococcus aureus                                                  |
| <strong>Osteo-articular infections</strong>   |                                                                                      |                                                                                                                                           |</p>
<table>
<thead>
<tr>
<th>Children Acute osteoarticular infections</th>
<th>3-4 weeks</th>
<th>Should be transitioned to oral therapy once clinically able to use limb and C reactive protein (CRP) decreasing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults Acute Vertebral Osteomyelitis</td>
<td>6 weeks</td>
<td>Not associated with implantable device</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assumes S. aureus but could be longer for Salmonella or Brucella infections</td>
</tr>
<tr>
<td>Adults Acute native joint osteoarticular infections</td>
<td>2 weeks for small joints after drainage 4 weeks for large joints after drainage</td>
<td>Duration recommendation for patients post-surgical drainage, with causal organism and susceptibility profile</td>
</tr>
</tbody>
</table>

### Bacteremia

**Children and Adults**

<table>
<thead>
<tr>
<th>Gram negative enterobacteriaceae such as E. coli</th>
<th>7 days</th>
<th>Assumes source controlled, (i.e. removal of central line, abscess drainage etc) and not associated with a clinical syndrome requiring longer therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus bacteremia</em> (uncomplicated)</td>
<td>14 days intravenously if uncomplicated or following intravenous line removal</td>
<td>Must ensure absence of endocarditis with echocardiogram and or other foci of infection (such as osteomyelitis); infectious diseases consult recommended.</td>
</tr>
<tr>
<td><em>Staphylococcus aureus bacteremia</em> (complicated)</td>
<td>4-6 weeks intravenously</td>
<td>Endocarditis, metastatic foci of infection, prolonged bactereremia &gt; 72 hours while on appropriate therapy. Infectious Diseases consult recommended.</td>
</tr>
<tr>
<td><em>Streptococcus pneumonia</em> associated with pneumonia</td>
<td>5 -7 days</td>
<td>Must show clinical improvement and meet criteria for discontinuation of antibiotics for pneumonia</td>
</tr>
</tbody>
</table>

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