PRACTICE POINT

Duration of antibiotic therapy for common infections

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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, durations have increased compared with 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 adverse 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 concern for overall safety of antibiotics have led researchers to look critically at this issue (8–16).

Several reports highlight the problem of longer-than-recommended treatment durations, including a recent study from England that used a primary care database to show that antibiotic treatment durations that exceeded guideline recommendations accounted for 1.3 million days of excess therapy between 2013 and 2015 (9,17). A recent observational study of patients with pneumonia concluded that two-thirds of patients had excess durations, with 93.2% of the excess attributed to antibiotics prescribed at discharge. Each excess day was associated with a 5% increase in the odds of a patient having an antibiotic-associated adverse event (18). Many experts have made rational arguments and coined useful slogans such as "shorter is still better" to emphasize the importance of reducing durations not only to preserve the efficacy of our antibiotics but also to reduce the risk of unnecessarily prolonging durations that have no added benefit (19–21).

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 and other members at large and approved by the Council of AMMI Canada.

The recommendations do not apply to individuals younger than 2 months of age, individuals who have underlying immune deficiencies, or those who have received immune-modulating agents, chemotherapy, or corticosteroids, where there is lack of data on shorter durations of therapy. Durations of therapy for fungal infection is also beyond the scope of this document. Decisions regarding duration of treatment of individual patients should still take into consideration patient characteristics, the certainty of the clinical diagnosis, clinical response to treatment, and medication side effects. 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. The sections that follow describe these recommendations in detail.

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 longer than 12 weeks suggest chronic sinusitis and are outside the scope of this practice point. In adults, a meta-analysis of 12 randomized controlled trials (RCTs) for acute bacterial sinusitis showed that 3 to 7 days of antibiotic treatment was as effective as 6 to 10 days, and a sensitivity analysis of 5 versus 10 days came to a similar conclusion (22).

Adults

The American Academy of Otolaryngology's 2015 guidelines for adult patients recommends 5 to 10 days (based on RCTs [grade A evidence, but low to moderate certainty]), with clinical re-evaluation at 7 days to ensure improvement (23). The Infectious Diseases Society of America (IDSA) recommends 5 to 7 days of antibiotics (based on weak, low quality evidence) with a re-evaluation at 3 to 5 days to ensure improvement and no extension of infection (24).

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 (25). *Pneumococcus* and *Haemophilus influenzae* isolates may be resistant to trimethoprim-sulfamethoxazole 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 to 7 days with a planned re-evaluation at 7 days to ensure clinical resolution. Children should also receive about 7 days of therapy with a β-lactam antibiotic, with follow-up if not improving.

Acute otitis media

A critical issue in therapy for acute otitis media in children is to ensure that criteria for diagnosis are met (typically including a bulging tympanic membrane). Children who have a mild or moderately bulging tympanic membrane, who are mildly ill, alert, responding to antipyretics, have a low-grade fever (<39°C), and mild otalgia, can be safely managed with a 'watchful waiting' period of 24 to 48 hours if timely reassessment is possible. Children with a high fever (≥39°C) and who are moderately to severely systemically ill, or children who have severe otalgia or have been significantly ill for 48 hours should be treated with antimicrobials (26). Trials in children over 2 years of age have favoured a duration of 5 to 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 (27,28).

The Canadian Paediatric Society (CPS) recommends that children with acute otitis media meeting specific diagnostic criteria be treated with amoxicillin for 10 days if under 2 years of age and 5 days if older (26). However, any child with a tympanic membrane perforation or recurrent acute otitis media should receive a 10-day course of amoxicillin.

AMMI Canada recommendations

Duration of therapy for bacterial acute otitis media is 10 days in children under 2 years of age 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 than with 5 to 7 days, but no differences in rates of relapse or recurrence were noted (29). Another study showed equivalent clinical cure but slightly less bacterial eradication (80% versus 90%) with 5 versus 10 days of penicillin (30).

Guidelines from the United Kingdom recommend a 5- to 10-day course of penicillin (10 d for recurrent infection) whereas the CPS recommends 10 days of oral penicillin or amoxicillin (31,32).

AMMI Canada recommendations

Ten days is the recommended duration of penicillin V or amoxicillin treatment for Streptococcal pharyngitis.

LOWER RESPIRATORY TRACT INFECTIONS

Community-acquired pneumonia

Adults

Acute community-acquired pneumonia is most commonly caused by viruses (such as influenza), but common pathogens associated with bacterial pneumonia are *Streptococcus pneumoniae*, *H. influenza,* and *Mycoplasma pneumonia,* with some populations, such as nursing home residents, more likely to be infected with gram-negative pathogens that may be multidrug resistant.

A systematic review and meta-analysis of RCTs predominantly of ambulatory or mixed inpatient/outpatient populations with low severity illness concluded that ≤6 days provided equally effective treatment compared with longer durations and may confer a safety benefit owing to fewer adverse effects (33). 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 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 intravenous therapy, assuming clinical improvement before the discontinuation of therapy (34).

The 2019 joint American Thoracic Society (ATS)/ IDSA guideline recommends at least 5 days of treatment 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 (34). Clinical stability was defined as normalization of vital signs, ability to eat, and normal mentation. While historically recommended treatment was longer (14 d) for *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and other non-fermenting bacteria, more recent guidance recommends 7 days of therapy for these infections, unless there is reason to extend therapy (eg, *S. aureus* bacteremia). In complicated pneumonias (eg, empyema, lung abscess), the duration is likely longer, but surgical intervention plays a key role in managing infection and decreasing the duration of antibiotic therapy.

Children

Community-acquired pneumonia that is considered to be bacterial in origin in children is commonly due to *S. pneumoniae*. Children who are older than 5 years of age and have prolonged cough are more likely to have *M. pneumoniae*. One study in preschool children with pneumonia found that treatment with amoxicillin for 5 days in the outpatient setting was non-inferior to a 10-day course (35).

The CPS practice point currently recommends a 7- to 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 (36,37). The U.K. guidelines from the National Institute for Health and Care Excellence also recommend 5 days for childhood pneumonia (38). Pneumonia complicated by empyema could require drainage and a longer duration of therapy of 14 to 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 to 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 children and infants. Duration of therapy should be 5–7 days for uncomplicated pneumonia in children who have clinically improved and have normal vital signs.

Lower respiratory tract infections acquired in hospital

Hospital-acquired pneumonia is associated with significant morbidity and a high case fatality rate. The entity previously labeled as health care–associated pneumonia, which included patients with significant health care contact (eg, dialysis) and those living in long-term care, has been retired and collapsed back into community-acquired pneumonia, as the microbiological etiologies are similar (39). In contrast, hospital-acquired pneumonia and ventilator-associated pneumonia are more likely to be associated with antibiotic-resistant organisms, depending on local hospital epidemiology, patient characteristics, and duration of hospital stay. Empiric therapy is usually broad. Historically, therapy for

ventilator-associated pneumonia (and hospital-acquired pneumonia) was prolonged, up to 21 days, until investigators evaluated the relative efficacy of shorter (8 d) versus longer (15 d) 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 to 8 days of therapy is as effective as longer courses, except possibly for patients infected with non-fermenting gram-negative bacilli (eg, *P. aeruginosa*), where there may be more recurrences with a shorter course; however, clinical outcomes were not affected (41).

European (2017) and IDSA guidelines (2016) both recommend durations of 7 days for ventilator-associated pneumonia (moderate quality evidence) and hospital-acquired pneumonia (very low quality evidence) (39,42,43). 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 7 days, provided there is clinical stability for 48 to 72 hours.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION

Acute exacerbations of chronic obstructive pulmonary disease (COPD) caused by infection are most frequently caused by viruses, with bacteria playing a secondary role. Acute exacerbations of COPD should be managed with bronchodilators, anti-inflammatory therapy, and correction of any reversible underlying cause such as environmental or other medical conditions (eg, heart failure, pulmonary embolism). Antibiotics should only be considered when patients fail to respond to these measures or when clinical findings such as fever suggest bacteria as a likely cause or when the patient is severely ill (44).

A recent review showed no differences in clinical outcomes with a duration of <6 days versus ≥7 days, but the shorter duration group had significantly fewer adverse effects (45). Durations of up to 5 days have been compared with longer therapies in a meta-analysis of 21 RCTs. The meta-analysis found that short courses of 5 days were equivalent to longer ones for clinical and bacteriologic cure. Results were the same regardless of antibiotic class (46).

The 2019 Global Initiative for Chronic Obstructive Lung Disease guide recommends 5 to 7 days of antimicrobial therapy in patients with severe disease, or signs of bacterial infection (44). Likewise, NICE guidelines recommend a 5-day course (if antibiotics are indicated) of any antimicrobial class (47). The European Respiratory Society and the ATS guidelines recommend antimicrobial therapy, but do not comment on duration (48).

AMMI Canada recommendations

The duration of treatment for acute exacerbations of COPD that are believed to be caused by bacterial infection should be 5 to 7 days.

PRE-OPERATIVE ANTIMICROBIAL PROPHYLAXIS

For surgeries that do not involve implantable devices, prophylactic antimicrobials should be administered only when recommended, as many types of surgery do not require prophylaxis (49,50). When recommended, antimicrobials should be given 30 to 60 minutes before surgical incision. There is no evidence of benefit when antimicrobials are continued post-operatively. 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 decreasing surgical site infections (51,52).

The World Health Organization is definitive 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 (53).

Women undergoing cesarean delivery should also receive a timely pre-operative dose of cefazolin to reduce the likelihood of surgical wound infection and endometritis; there is no benefit with prolonging cefazolin after the surgery (54,55). Women with preterm rupture of membranes (<32 weeks gestation), should receive 48 hours of intravenous ampicillin followed by 5 days of oral amoxicillin and either 1 dose of intravenous azithromycin or 2 days of intravenous erythromycin followed by 5 days of oral erythromycin (55).

AMMI Canada recommendations

Surgical prophylaxis, including for cesarean delivery, should be stopped after skin closure. Pregnant women with preterm rupture of membranes should receive 7 days of ampicillin and a macrolide, as previously described, to decrease the risk of infection to the fetus.

Duration of surgical prophylaxis for surgeries involving implants or valves can be extended 24 to 48 hours after surgery, but this recommendation is not based on evidence of benefit, but rather absence of evidence. This recommendation should apply regardless of the presence of drains or chest tubes (53,56).

INTRA-ABDOMINAL INFECTIONS

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

Patients who undergo appendectomy for acute appendicitis and have a non-perforated appendix need only pre-operative antibiotics (57). For infected intra-abdominal/peritoneal collections, data support using shorter courses of therapy, emphasizing that source control and drainage of abscesses are critical in management. One study compared 4 versus 8 days of therapy after source control and concluded that recurrent surgical site or intra-abdominal infections were similar (58). A second large RCT conducted in ICUs determined that patients treated with shorter courses of 8 days had no differences in length of stay, mortality, or re-operation rates when compared with those treated for 15 days (59). For cholangitis, a systematic review summarizing available literature to 2018 found 4 studies that met inclusion criteria. The authors concluded that, provided there was source control, a shorter course of antibiotics of less than 1 week did not result in higher mortality, longer duration of fever, or higher rates of recurrence (60).

Guidelines from the Surgical Infection Society (2017) and the IDSA (2010) advocate <7 days of therapy for patients with source control (57,61). Tokyo Guidelines for management of acute cholangitis recommend drainage or source control as the mainstay of therapy followed by 4 to 7 days of appropriate, targeted antimicrobial therapy (62,63).

AMMI Canada recommendations

Physicians should strongly advocate for source control (drainage of collections) in the setting of intra-abdominal infections. Duration of therapy for intra-abdominal 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 non-catheterized men is infrequent and likely indicates prostatitis, obstruction, or upper tract infection. Bacteriuria in pregnancy or post–renal transplant is beyond the scope of this document. Except during pregnancy and prior to urologic surgery, asymptomatic bacteriuria should not be treated (64). AMMI Canada has published a useful toolkit including educational materials for managing asymptomatic bacteriuria called "Symptom Free Pee: LET IT BE" (65).

Short courses of therapy (3–5 d, depending on antibiotic class) for uncomplicated cystitis in otherwise healthy young women is well-supported by robust data and is recommended in IDSA guidelines (66). Single-dose fosfomycin (or 3 d if recurrent/complicated cystitis) also holds promise as a treatment for cystitis owing to the drug's high concentration. Men should receive 7 days of therapy, as cystitis may be more complicated in this population.

Pyelonephritis

Adults

Uncomplicated pyelonephritis is defined as a UTI with systemic symptoms (usually fever, malaise, chills, or flank or pelvic pain) that occurs in a non-pregnant, premenopausal woman without underlying comorbid conditions or anatomic urologic abnormalities. For adult men, pyelonephritis should be considered complicated, since the presence of a UTI may indicate urinary tract obstruction or a prostatic focus. Recent studies of patients with normal male or female anatomy support a 7-day course of antimicrobials with some caveats (73–76). A meta-analysis found 8 evaluable trials that compared ≤7 with >7 days of treatment for pyelonephritis. The conclusion of the meta-analysis (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 were recommended for pyelonephritis complicated by abscess or stones, as patients with urogenital abnormalities experienced more microbiological failure (but equivalent clinical failure) at the end of follow-up than those with normal anatomy. In this meta-analysis, the percentage of bacteremic patients ranged from 3% to 29% (73). A recent study (65% females) compared a median of 4.5 days of aminoglycoside therapy with 5 days of non-aminoglycoside-based therapy for adults with pyelonephritis and found similar outcomes (77).

The 2011 practice guidelines from the IDSA and the European Society for Microbiology and Infectious Diseases recommended a minimum 7-day course of antibiotics (if using fluoroquinolones) in the setting of uncomplicated pyelonephritis (without septic shock or abscesses) in women who rapidly respond to therapy. However, other than fluoroquinolones, for which 7 days of treatment was shown to be sufficient, there

were limited data on shorter durations with other classes of antibiotics; therefore, a 10- to 14-day course was recommended if other antibiotic classes are used (66). The NICE guidelines, also vary treatment duration according to class of antimicrobial, with 7 days for fluoroquinolones (consider safety issues), and 7 to 10 days for ß-lactams (78). Rising rates of resistance and safety issues (especially with fluoroquinolones) emphasize the critical importance of proper diagnosis and cultures as well as prompt re-evaluation in the event of a slow response to therapy. Some experts have suggested an initial intravenous dose of an aminoglycoside, ceftriaxone, or ertapenem, especially if oral β-lactams are planned as definitive therapy.

Children

Pyelonephritis in children refers to the clinical syndrome of fever and symptoms compatible with UTI (eg, dysuria, incontinence, urgency) with pyuria and an abnormal urinalysis. No RCTs specifically examining duration of therapy in children with febrile UTIs (presumed pyelonephritis) have been published. A 2014 Cochrane review determined that 10 to 14 days of therapy was appropriate for clinical success (79). A more recent 2019 study of almost 800 children with febrile UTI reported similar outcomes with courses of 6 to 9 days versus ≥10 days of therapy. However, children with urologic abnormalities had more treatment failures with short courses (80). An RCT 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 to those treated for 14 days (81). In children older than 1 month, treatment durations for bacteremia associated with pyelonephritis have not been the subject of an RCT. A recent retrospective cohort study of pyelonephritis has too few cases of associated bacteremia to determine duration of therapy (80). Guidelines from the CPS and the American Academy of Pediatrics currently recommend 7 to 14 days of therapy (72).

AMMI Canada recommendations

A 7-day course of a fluoroquinolone (ciprofloxacin or levofloxacin) is likely adequate for the treatment of uncomplicated pyelonephritis in men and non-pregnant women with no underlying anatomic abnormalities and rapid response to an antibiotic to which the pathogen is susceptible, as these antibiotics attain high renal concentrations. If β-lactam agents (ie, cephalosporins, aminopenicillins, or trimethoprim-sulfamethoxazole) are given based on susceptibilities, longer courses of 10 to 14 days should be considered.

In persons with underlying comorbidities (eg, diabetes, anatomic abnormalities of the urinary tract, urinary tract outflow obstruction or renal calculi, recurrent pyelonephritis, immunocompromising conditions) or slow response to therapy, durations of 10 to 14 days or longer are recommended.

If outpatient therapy is being contemplated at presentation, empiric therapy with 1 dose of intramuscular or intravenous aminoglycoside, ceftriaxone, or ertapenem can be considered. Adequate follow-up of the patient and the ability to modify treatment based on pathogen susceptibility should be assured.

The same principles for duration apply to children older than 2 months of age who have an uncomplicated febrile UTI (not associated with a bacteremia or meningitis), where recommended durations range from 7 to 14 days. Children with no underlying renal abnormalities and non-bacteremic UTI who have a rapid response to therapy should receive a minimum of 7 days of effective therapy. Longer durations will likely be required in the event of a slow response to therapy or underlying renal structural abnormalities, and treatment should be individualized. Aminoglycosides attain high renal concentrations and may be given as an initial empiric therapeutic dose if consideration is being given to outpatient therapy. In children, fluoroquinolones should be reserved for pathogens resistant to other agents.

SKIN AND SOFT TISSUE INFECTIONS

Purulent and non-purulent cellulitis

Cellulitis in patients who are neutropenic, cellulitis associated with bites (animal or human), periorbital swelling caused by complicated sinusitis, and cellulitis associated with chronic ulcers, deeper infections (such as necrotizing fasciitis), or fish or water exposure are beyond the scope of this practice point. Additionally, cellulitis should be differentiated from venous stasis, erythema migrans caused by Lyme disease, cutaneous herpes infections, and subperiosteal abscesses associated with childhood acute osteomyelitis.

Acute cellulitis is most commonly caused by *S. pyogenes* (usually a non-purulent cellulitis characterized primarily by rapid onset pain, erythema, and swelling without abscesses) or *S. aureus* (usually a purulent cellulitis characterized by abscesses or pus that is visible or can be expressed from the site). There may be some overlap in these presentations in persons with underlying dermatitis.

One RCT of patients with uncomplicated cellulitis (outpatients and inpatients) concluded that, despite some residual erythema, 5 days of therapy resulted in similar cure rates compared with 10 days (82). In a study involving patients admitted to hospital with cellulitis, there appeared to be more readmissions in the shorter (6 d) 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). IDSA guidelines 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).

Purulent cellulitis can be accompanied by folliculitis or tender, erythematous, often fluctuant nodules or boils and is caused by *S. aureus* in the majority of cases. IDSA guidelines recommend incision and drainage of cutaneous abscesses (85). Two subsequent RCTs, with a majority of cases caused by methicillin-resistant *S. aureus* (MRSA), concluded that antimicrobial therapy for 7 to 10 days along with incision and drainage was superior to incision and drainage alone (86,87). These conclusions, however, may not apply to small (<2-cm) abscesses caused by methicillin-susceptible *S. aureus* (MSSA), which may only need incision and drainage.

AMMI Canada recommendations

Duration of therapy for uncomplicated, non-purulent cellulitis for adults and children is 5 to 7 days. Skin abscesses should undergo incision and drainage with culture of pus. Antimicrobial therapy should be considered if the abscess is large (>2 cm) or if MRSA is suspected. If antibiotics are prescribed, the recommended duration is 7 days. Hospitalized patients with more extensive disease may need longer courses of 10 days.

BONE AND JOINT INFECTIONS

Adults

An RCT of patients with vertebral osteomyelitis showed similar outcomes for 6 versus 12 weeks of antibiotic therapy (88). A non-inferiority trial of 154 adult patients with native joint septic arthritis (64% hand and wrist) randomly assigned patients to 2 or 4 weeks of antibiotic therapy post-surgical drainage and reported similar outcomes for both groups (ie, the shorter duration was non-inferior). However, the findings may not be applicable to large joints such as hips and knees, since these joints were underrepresented in the study (89). 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 gonorrhoeae* is outside the scope of this practice point.

Guidelines currently recommend a 6-week course of antimicrobials for acute native vertebral osteomyelitis, commonly due to *S. aureus* (90). There are no current guidelines from North American or European organizations for other native joint infections or for osteomyelitis at other sites. In 2006, the British Society for Antimicrobial Chemotherapy, in conjunction with other specialty societies, recommended 2 weeks of intravenous therapy, followed by a further 4 weeks of oral therapy; however, they acknowledged that there exists little evidence for this recommendation (91). Shorter durations of 3 to 4 weeks could be considered for non–*S. 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 to 3 to 4 weeks is likely sufficient to treat acute (symptom duration <4 wk), uncomplicated (rapid clinical response to therapy and rapid decline in C-reactive protein) hematogenous osteoarticular infections, which are likely due to MSSA or *Kingella kingae* (92–94). Treatment duration for osteomyelitis caused by MRSA or other pathogens has not been systematically studied, but it is very likely to be longer (4–6 wk), as these patients often have complicated infections.

The CPS practice point on acute hematogenous osteomyelitis recommends a total of 3 to 4 weeks of therapy with step-down to oral therapy for uncomplicated osteomyelitis. Acute osteoarticular infections caused by MRSA or other pathogens will need a more individualized approach (95). Similar recommendations are outlined in European guidelines (96).

AMMI Canada recommendations

Uncomplicated vertebral osteomyelitis should be treated for 6 weeks. There are less data available for native joint septic arthritis (excludes *N. gonorrhoeae*). Once source control has been achieved, septic arthritis of native joints involving the hand and fingers can be treated for 2 weeks, whereas infection of larger joints will require 4 weeks of treatment. In children, duration of therapy for acute hematogenous osteoarticular infections is usually 3 to 4 weeks, with longer courses reserved for complicated infections.

BACTEREMIA

Staphylococcus aureus bacteremia

Bacteremia caused by *S. aureus* is common, is always considered pathologic, and must be treated and managed appropriately. The source of infection 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 as part of the assessment for endocarditis.

Current data support 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, or metastatic sites of infection (clinically or other imaging modalities), rapid (3 d) sterilization of blood cultures and rapid (<72 h) defervescence after appropriate antibiotics, and absence of prosthetic devices (97).

Newborns with *S. aureus* bacteremia treated less than 14 days are also more likely to have relapse of infection (81). Persistent *S. aureus* bacteremia beyond 72 hours despite adequate therapy may indicate endovascular or other deep-seated infection requiring prolonged therapy (usually 4–6 wk) (98). Accumulating data indicate improved outcomes and lower mortality in patients with *S. aureus* bacteremia whose management includes infectious diseases consultation (99,100).

AMMI Canada recommendations

Fourteen days of intravenous antimicrobials is required for cases of uncomplicated *S. aureus* bacteremia (see the previous section for important caveats) or for those associated with a central line, provided the catheter has been removed. However, many cases are either associated with a source (eg, musculoskeletal infection, abscesses) or complications (eg, endocarditis) and require 4 to 6 weeks of therapy. Therefore, most cases of *S. aureus* bacteremia should be managed in conjunction with infectious diseases consultation or input.

In healthy children, MSSA bacteremia associated with uncomplicated acute hematogenous osteomyelitis should be treated with 3 to 4 weeks of antibiotics, with intravenous to oral conversion as per recommendations (see section on osteoarticular infections).

Enterobacterales bacteremia

Adults

Bacteremia associated with pyelonephritis, generally caused by Enterobacteriaceae (such as *E. coli* or *Klebsiella*), has been traditionally treated with 7 to 14 days of antibiotics. In a meta-analysis of outcomes in 7,695 patients treated with shorter (≤7 d) versus longer courses of antibiotics, there were no differences in clinical outcomes, microbiologic cure, or mortality between the two groups (101). Subsequent to this meta-analysis, several RCTs of 7 to 8 versus 14 to 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 the longer course with respect to clinical outcomes (102–104). A more recent meta-analysis that compared ≤10 to >10 days of therapy in patients with bacteremia showed no differences in clinical or microbiologic cure or in mortality; however, there were only 4 studies available to assess this specific duration (105). In an observational study, when source control had been achieved, investigators found that patients with *Pseudomonas* bacteremia treated with a median of 9 days of therapy (interquartile range 8–10) had similar odds of recurrent infection and death as patients who received a median of 16 days (interquartile range 14–17) (106). A recent RCT in adults that evaluated 7 versus 14 days versus a C-reactive protein–guided duration study for gram-negative bacteremia found no significant differences in clinical outcomes between groups with very few recurrences (107).

Children

Definitive studies of duration of treatment for *Enterobacterales* bacteremia in children are not available. Although this practice point does not apply to infants younger than 2 months of age, the possibility of secondary meningitis should be considered in infants in the setting of *Enterobacterales* bacteremia, and, if clinically warranted, a lumbar puncture should be performed to exclude meningitis. Treatment duration and management for secondary meningitis or primary sources of infection (eg, abdominal abscesses) are beyond the scope of this practice point.

AMMI Canada recommendations

For bacteremia caused by *Enterobacterales* in adults, there appears to be wide variation in duration of antimicrobial therapy; however, emerging literature would support a 7-day course for uncomplicated bacteremias from pyelonephritis or from a source that has been successfully controlled. Duration of therapy for *Enterobacterales* bacteremia in children should follow guidelines for the specific pathogen and clinical diagnosis, being careful to exclude meningitis, especially in infants.

Central line–associated bacteremia

Bacteremia caused by coagulase-negative staphylococci associated with an intravascular device that has been removed has generally been treated with antibiotics for 5 to 7 days after catheter removal (108,109). Shorter durations of <5 days can be considered in circumstances with early catheter removal and where rapid response is seen (110).

Catheter-associated central line infections caused by *Enterobacterales* should include catheter removal followed by 7 to 14 days of antimicrobial therapy (109,110). Similar durations of therapy are recommended for implantable venous access devices, provided they are removed, source

Table 1: Summary of recommendations for duration of therapy in selected common infections (excludes infants ≤ 2 months of age)

Infection	Population	Recommended duration	Comments
Urinary tract			
Uncomplicated cystitis	Women/adolescents	• Nitrofurantoin – 5 d • TMP-SMX – 3 d • Fosfomycin – 1 d	Young non-pregnant female adolescents or adults with normal urinary tracts and normal renal function
Complicated cystitis	Men	7 d	• Afebrile • Urine analysis abnormal and consistent with UTI
Febrile UTI	Children	7–14 d	Assumes upper tract involvement if febrile
Pyelonephritis and urosepsis	Adults	• Consider an initial dose of IV dose aminoglycoside or ceftriaxone at outset • Quinolones or β-lactams 7 d	Minimum 7 d, consider longer for other antibiotics, patients who are slow to respond to therapy or underlying urinary tract pathology. Excludes patients with stents/ drains as this will require an individualized approach.
Respiratory tract			
Streptococcal pharyngitis	Children and adults	10 d (penicillin V or amoxicillin)	Studies limited to pediatrics. Some studies suggest 5 d of 4 x daily penicillin for bacterial eradication only
Acute otitis media	Children and adults	• 6 mo to 2 y – 10 d • >2 y – 5 d	• Should meet diagnostic criteria including fever • >39°C, moderately ill with bulging tympanic membrane
Acute sinusitis (uncomplicated)	Children and adults	5–7 d	• Excludes complicated sinusitis (eg, epidural, subdural or orbital collection) • Revaluation if not clinically improving
CAP	Children and adults	5–7 d	• Patients with underlying lung disease, immunosuppression or empyema • Must be improved and have normal vital signs for 2 d when using 5 d of therapy • Similar recommendation for uncomplicated CAP associated with *S. pneumoniae* bacteremia
HAP/VAP	Children and adults	≤7 d	Severely immune suppressed patients with collections or abscesses, *S. aureus* and *Pseudomonas* infection
Acute bacterial COPD exacerbation	Children and adults	5–7 d	Only for patients meeting criteria for antibiotic treatment
Intra-abdominal			
Uncomplicated appendicitis	Children and adults	Pre-operative antibiotics only	Gangrenous appendicitis or perforated appendicitis without evidence of abscess should be treated for an additional 24–48 h after appendectomy
Traumatic bowel perforation	Children and adults	No more than 24 h post-operatively	Operated on within 12 h of trauma
Gastroduodenal perforation	Children and adults	No more than 24 h post-operatively	Operated on within 24 h of perforation

(continued)

Table 1: (*continued*)

Infection	Population	Recommended duration	Comments
Intra-abdominal infection/ abscess	Children and adults	<7 d after source control	Source control required with drainage of infection. No additional days required if adequate drainage is in place
Cellulitis			
Uncomplicated non-purulent or purulent cellulitis	Children and adults	5–7 d unless hospitalized with extensive or severe disease	Usually due to *S. pyogenes* (group A *Streptococcus*) if non purulent or *Staphylococcus* aureus if purulent cellulitis. incision and drainage with culture recommended for skin abscesses.
Osteoarticular			
Acute osteoarticular infections	Children	3–4 wk	Should be transitioned to oral therapy once clinically able to use limb and CRP decreasing. Complicated infection, MRSA or other pathogens may require longer therapy.
Acute vertebral osteomyelitis	Adults	6 wk	• Not associated with implantable device • Assumes *S. aureus* but could be longer for *Salmonella* or *Brucella* infections
Acute native joint osteoarticular infections	Adults	• 2 wk for small joints after drainage • 4 wk for large joints after drainage	Duration recommendation for patients post-surgical drainage, with causal organism and susceptibility profile
Bacteremia			
Gram-negative *Enterobacterales* such as *E. coli*, usually from a urinary source	Children and adults	7 d	• Assumes source controlled, (eg, removal of central line, abscess drainage) and not associated with a clinical syndrome requiring longer therapy. • Assumes meningitis ruled out in infants.
S. aureus bacteremia (uncomplicated)	Children and adults	• 14 d IV if uncomplicated or following IV line removal • If musculoskeletal infection, IV to oral can be used in children.	Must ensure absence of endocarditis with echocardiogram and or other foci of infection (such as osteomyelitis); infectious diseases consult recommended.
S. aureus bacteremia (complicated)	Children and adults	4–6 wk IV	Endocarditis, metastatic foci of infection, prolonged bacteremia >72 h while on appropriate therapy. Infectious Diseases consult recommended.

UTI = Urinary tract infection; CAP = Community-acquired pneumonia; S. pneumoniae = Streptococcus pneumoniae*; HAP/VAP = Hospital- and ventilator-acquired pneumonia;* S. aureus = Staphylococcus aureus*; COPD = Chronic obstructive pulmonary disease; IV = Intravenous;* S. pyogenes = Streptococcus pyogenes*; CRP = C-reactive protein; MRSA = Methicillin-resistant* Staphylococcus aureus*;* E. coli = Escherichia coli

control is in place, and the infection is not caused by *S. aureus* (111).

AMMI Canada recommendations

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

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 fewer antimicrobials, shortening durations of antibiotic therapy for individual patients is increasingly recommended as a better practice choice. Clinicians should be aware of new data and current guidelines and recommendations and adjust their practices accordingly to provide the best patient care while preserving antibiotics for future use.

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